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DEPT: ANATOMY

COURSE: ANA 206

**ASSIGNMENT:**

Write notes on the following;

1. Development of the lungs
2. Rotation of the stomach and the formation of the omental bursa
3. Development of the esophagus

**ANSWER:**

1. **DEVELOPMENT OF THE LUNGS:**

**Development of the lung can be divided into two phases, lung growth (structural development) and lung maturation (functional development). Lung growth can be influenced by a host of physical factors. Lung maturation and the achievement of functionality is primarily a biochemical process and is under the control of a number of different hormones. Lung growth proceeds through gestation. There is progressive branching of the airways and finally development of alveolar spaces capable of gas exchange in the last trimester. The surfactant system, composed of phospholipids that decrease surface tension within the alveoli and prevent alveolar collapse during exhalation, develops in the last trimester, and reaches maturity by approximately 36 weeks. Lung growth continues after birth as alveolar number continues to increase. The end result of the development of the lung is an organ with a tremendously large surface area that is approximately 50-100 m2, capable of exchanging oxygen and carbon dioxide across a very thin membrane.**

**Successful development and function of the lung requires the completion of both physical development, required for the structure of the lung, and biochemical development of the surfactant system, required for the stability of this very large surface area. The two processes clearly are related. Incomplete development of lung structure and premature birth prior to the development of the surfactant system will lead to respiratory compromise or insufficiency in the newborn.**

**There are five phases of structural lung development that occur at progressive times during gestation. The timing of the phases is approximate, with variation between fetuses, and in fact, there is no absolute agreement about the weeks that comprise each phase among various authors and texts. The embryonic stage is apparent in the 3 week old embryo. The lung bud develops from the foregut and in communication with it. Separation of the two lung buds comes about with fusion of the esophagotracheal ridges to form the esophagotracheal septumI** **When the embryo is 5 weeks old, two primary lung buds are identifiable. The lung buds go on to form their first subdivisions, with 3 lobar buds developing in the right lung bud and 2 lobar buds** **developing in the left. These are the forerunners of the right upper, middle and lower lobes and the left upper and lower lobes (Figure 12-2 Development progresses in the 8 week old embryo as the lobar buds subdivide and form the bronchopulmonary segments (Figure 12-3).** **Lung buds are lined by endodermal derived epithelium which differentiates into respiratory epithelium that lines the airways and specialized epithelium that lines the alveoli. The innervation of the lungs is derived from ectoderm, while the mesoderm is the origin of pulmonary blood vessels, smooth muscle, cartilage and other connective tissue.** **There are a number of physical influences on lung growth. Proper development of the lung is dependent on the presence of both lung liquid and amniotic fluid. The lung liquid is secreted by pulmonary epithelium. The volume of lung fluid is maintained by the activity of the upper airway which acts as a gatekeeper by controlling the resistance to efflux of fluid out of the lung and trachea during non-breathing periods, and by diaphragmatic movement associated with fetal breathing movements. The larynx is the major site of regulation of efflux and therefore of lung liquid volume. During fetal breathing movements, when the upper airway resistance is decreased, diaphragmatic movements help to maintain lung liquid volume (Figure 12-10). The experimental drainage of lung liquid leads to pulmonary hypoplasia.**

**Amniotic fluid is also required for normal lung development. Amniotic fluid originates in the lung and fetal kidney.**

**Clinical importance**

**Lung hypoplasia may be caused by a number of other factors that restrict or better, compress the fetal lung.**

**Tracheoesophageal fistula results from the failure of the normal formation of tracheoesophageal septum.**

**Diaphragmatic hernia results from failure of one of the pleuroperitoneal membranes to close** **This occurs predominantly on the left side**

**II.) FORMATION OF THE STOMACH**:

The GIT is best imagined as a simple tube, the upper part being the foregut diverticulum, which is further divided into esophagus and stomach. During week 4 at the level where the stomach will form the tube begins to dilate, forming an enlarged lumen. The dorsal border grows more rapidly than ventral, which establishes the **greater curvature** of the stomach.[[1]](https://embryology.med.unsw.edu.au/embryology/index.php/Gastrointestinal_Tract_-_Stomach_Development#cite_note-PMID28242610-1) A second rotation (of 90 degrees) occurs on the longitudinal axis establishing the adult orientation of the stomach. **Stomach curvature is generated by left-right asymmetric gut morphogenesis.**

The **primitive gut tube** is derived from the dorsal part of the **yolk sac**, which is incorporated into the body of the embryo during folding of the embryo during the fourth week. The primitive gut tube is divided into three sections.

|  |  |  |
| --- | --- | --- |
| Section | Blood supply | Adult derivatives |
| Foregut | Celiac artery | Pharynx, lower respiratory system, esophagus, stomach, proximal half of duodenum, liver and pancreas, biliary apparatus |
| Midgut | Superior mesenteric artery | Small intestine, distal half of duodenum, cecum and vermiform appendix, ascending colon, most of the transverse colon |
| Hindgut | Inferior mesenteric artery | Left part of transverse colon, descending colon, sigmoid colon, rectum, superior part of anal canal, epithelium of urinary bladder, most of the urethra |

* The **epithelium** of and the **parenchyma of glands** associated with the digestive tract (e.g., liver and pancreas) are derived from **endoderm**. The **muscular walls** of the digestive tract (lamina propria, muscularis mucosae, submucosa, muscularis externa, adventitia and/or serosa) are derived from **splanchnic mesoderm**.
* During the **solid stage** of development the endoderm of the gut tube proliferates until the gut is a solid tube. A process of **recanalization** restores the lumen.

## Proctodeum and Stomodeum

* The proctodeum (anal pit) is the **primordial anus**, and the stomodeum is the **primordial mouth**. In both of these areas ectoderm is in direct contact with endoderm without intervening mesoderm, eventually leading to degeneration of both tissue layers.

## Foregut

### Esophagus

* The **tracheoesophageal septum** divides the foregut into the esophagus and trachea. See the chapter on Respiratory system for more information.

### Stomach

* The primordium of the **primitive stomach** is visible about the end of the fourth week. It is initially oriented in the median plane and suspended from the dorsal wall of the abdominal cavity by the **dorsal mesentery** or **mesogastrium**. During development the stomach rotates 90 in a clockwise direction along its longitudinal axis, placing the **left vagus nerve** along its anterior side and the **right vagus nerve** along its posterior side. Rotation of the stomach creates the **omental bursa** or **lesser peritoneal sac**.

### Duodenum

* The duodenum acquires its C-shaped loop as the stomach rotates. Because of its location at the junction of the foregut and the midgut, branches of both the **celiac trunk** and the **superior mesenteric artery** supply the duodenum.

### Pancreas

* The pancreas develops from two outgrowths of the endodermal epithelium, the **dorsal pancreatic bud** and the **ventral pancreatic bud**. During rotation of the gut these primordial come together to form a single pancreas. The ventral pancreatic bud forms the uncinate process and part of the head, while the dorsal pancreatic bud forms the remainder of the head, body, and tail of the pancreas. The ducts of the pancreatic buds join together to form the **main pancreatic duct**, but the proximal part of the duct of the dorsal pancreatic bud may persist as an **accessory pancreatic duct**.

### Liver and Biliary Apparatus

* The liver develops from endodermal cells that form the **hepatic diverticulum**. The liver grows in close association with the **septum transversum**, which later forms part of the diaphragm. As it grows the hepatic diverticulum divides into a **cranial part**, which forms the **parenchyma** of the liver, and the **caudal part**, which gives rise to the **gallbladder** and **cystic duct**. The **hemopoietic** **cells**, **Kupffer cells**, and **connective tissue** of the liver are derived from **mesenchyme** in the septum transversum. The embryonic liver is large and fills much of the abdominal cavity during the seventh through ninth weeks of development.
* Blood formation (hemopoiesis**)** begins in the liver during the sixth week of development, and bile formation begins in the twelfth week.

### Spleen

* The spleen develops from mesenchymal cells located between layers of the dorsal mesogastrium.

## Midgut

* The midgut communicates with the yolk sac via the **yolk stalk**. As the midgut forms, it elongates into a U-shaped loop (**midgut loop**) that temporarily projects into the umbilical cord (**physiological umbilical herniation**). The cranial limb of the midgut elongates rapidly during development and forms the **jejunum** and **cranial portion of the ileum**. The caudal limb forms the **cecum**, **appendix**, **caudal portion of the ileum**, **ascending colon**, and **proximal two-thirds of the** **transverse colon**. The caudal limb is easily recognized during development because of the presence of the **cecal diverticulum**.
* The midgut loop rotates **270 counterclockwise** around the **superior mesenteric artery** as it retracts into the abdominal cavity during the **tenth week** of development.

## Hindgut

* The hindgut is defined to begin where the blood supply changes from the superior mesenteric artery to the **inferior mesenteric artery**, i.e. at the distal third of the transverse colon.

### Partitioning of the Cloaca

* The cloaca is the endodermally lined cavity at the end of the gut tube. It has a diverticulum into the body stalk called the **allantois**. The **cloacal membrane** separates the cloaca from the proctodeum (**anal pit**). During development a sheet of mesenchyme (**urorectal septum**) develops to divide the cloaca into a ventral (**urogenital sinus**) and a dorsal portion (**anorectal canal**). By week seven the urorectal septum reaches the cloacal membrane, dividing it into ventral (**urogenital membrane**) and dorsal (**anal membrane**) portions.

### Anal Canal

* The epithelium of the superior two-thirds of the anal canal is derived from the endodermal hindgut; the inferior one-third develops from the ectodermal proctodeum. The junction of these two epithelia is indicated by the **pectinate line**, which also indicates the approximate former site of the **anal membrane** that normally ruptures during the **eighth week** of development.

## Clinical Correlations

### Esophageal Atresia

* **Esophageal atresia** usually results from abnormal division of the tracheoesophageal septum. The fetus is unable to swallow and this results in **polyhydramnios** (excessive amount of amniotic fluid) because amniotic fluid cannot pass into the intestines for return to the maternal circulation.

### Annular Pancreas

Imperforate Anus:The anal membrane fails to break down before birth. The anus must be reconstructed surgically, with severity depending on the thickness of the intervening tissue

OMENTAL BURSA:

The omental bursa or lesser sac is a hollow space that is formed by the [greater and lesser omentum](https://www.kenhub.com/en/library/anatomy/greater-and-lesser-omentum) and its adjacent organs. It communicates with the greater sac via the epiploic foramen of winslow, which is known as the general cavity of the [abdomen](https://www.kenhub.com/en/library/anatomy/abdomen-and-pelvis) that sits within the [peritoneum](https://www.kenhub.com/en/library/anatomy/the-peritoneum), but outside the lesser sac.This space has well-defined borders which are represented by certain organs or their parts, so they are quite easy to spot and form a mental image of the omental bursa. In addition, like anything in anatomy, the omental bursa doesn't just exist as a standalone and isolated entity, but rather it communicates with several other spaces and recesses found throughout the body.

**The borders of the omental bursa are demarcated as follows:**

* anteriorly by the [quadrate lobe of the liver](https://www.kenhub.com/en/library/anatomy/functional-division-of-the-liver), the gastrocolic ligament and the lesser omentum
* to the left it is limited by the left [kidney](https://www.kenhub.com/en/library/anatomy/kidneys) and the left [adrenal gland](https://www.kenhub.com/en/library/anatomy/adrenal-glands)
* posteriorly it is walled off by the [pancreas](https://www.kenhub.com/en/library/anatomy/the-pancreas)
* to the right, the epiploic foramen and lesser omentum can be found and the greater sac beyond that.

The cavity itself is almost completely closed, save its communication with the greater sac and the entrance through the omental foramen and is filled with a capillary film. The greater part of the omental bursa consists of its **superior recess** which extends cranially between the [esophagus](https://www.kenhub.com/en/library/anatomy/esophagus) and the [inferior vena cava](https://www.kenhub.com/en/library/anatomy/inferior-vena-cava)

## Embryology

During embryonic development, the peritoneum is anchored to the gut in the midline of the abdomen anteriorly, with the dorsal mesentery securing it posteriorly. The mesenteric layers develop in an **anterior** **direction** around the upper alimentary canal, carrying the blood supply and creating the **ventral** **mesentery**.

Due to the growth of the organs, they gradually become larger and have to shift in order to fit into the abdominal cavity. The stomach rotates 90 degrees, the [spleen](https://www.kenhub.com/en/library/anatomy/the-spleen) is displaced to the left and the liver moves to the right. The peritoneum twists with these movements which lead to the formation of the falciform ligament, the lesser omentum and the [coronary ligaments of the liver](https://www.kenhub.com/en/library/anatomy/ligaments-of-the-gastrointestinal-tract) . Throughout this entire process, the cavity of the lesser sac is created.

OSOPHAGUS DEVELOPMENT

Gut and more specifically esophageal development are most easily understood starting at week four. At this stage, the early embryo consists of three distinct layers, in what is known as a trilaminar disc, connected to the yolk sac. The trilaminar disc is composed of outer ectoderm, middle mesoderm, and an inner layer known as the endoderm.[[1]](https://www.ncbi.nlm.nih.gov/books/NBK542304/) The layers orient in such a way that the endoderm layer is in contact with the outer ectoderm layer at the poles of the embryo. At the start of the fourth week, folding occurs such that corresponding cranial, caudal, and lateral edges of the disc come together. This folding occurs through the ventral midline, and the layers fuse allowing for internalization of the endoderm layer, such that the embryo takes on a tube within a tube configuration, an inner tube composed of endoderm and an outer tube consisting of ectoderm, and between the two layers, mesoderm.

* Initially, this inner tube is blind-ended at both poles and is the precursor to the final digestive tract.[[1]](https://www.ncbi.nlm.nih.gov/books/NBK542304/) The inner tube itself divides into three anatomical parts, the foregut, midgut, and hindgut. The foregut being the most cranial portion and hindgut the most caudal. The foregut and hindgut delineation is the center component, the midgut, which is continuous with the yolk sac through the vitelline duct. The mechanisms of early folding and tube position have their basis in concentration-dependent signaling which sets up a ventral-dorsal, rostral-caudal, and left-right axis.[[1][2]](https://www.ncbi.nlm.nih.gov/books/NBK542304/) These axes are influenced by and contribute, in a reciprocal manner to local endodermal and mesodermal interactions. The component of the foregut that will give rise to the esophagus also will give rise to the trachea and lungs. From the foregut endoderm will arise the esophageal epithelium as well as mucosal glands. The mesodermal layer surrounding the foregut will give rise to the striated muscular and smooth muscle layers of the esophagus.  These processes are associated with numerous signaling molecules.[[3]](https://www.ncbi.nlm.nih.gov/books/NBK542304/) However, the first step of esophageal organogenesis from the foregut is the differentiation of the foregut cells into the trachea, lung, and esophagus. This process begins with the cellular expression of many genes.[[2][4]](https://www.ncbi.nlm.nih.gov/books/NBK542304/)
* After esophageal specification occurs, several notable changes are visible in the developing embryo. At approximately week 6 of development, the circular and longitudinal muscular layers begin to form, and ganglion cells of the myenteric plexus first present. Moving into week 7, cells of mesodermal origin proliferate into the submucosal layer forming the eventual blood supply to the esophagus. The muscular layers which began in week 6, are completed by the 9th week.[[5]](https://www.ncbi.nlm.nih.gov/books/NBK542304/) Rostral-caudally, a distinction occurs in the muscular subtypes found within the esophagus. The cranial third of the esophagus contains mostly striated muscle, the caudal third transitions into mostly smooth muscle, and the middle third being a combination of both muscular subtypes.[[6][7]](https://www.ncbi.nlm.nih.gov/books/NBK542304/) Along with this change in musculature, cranially to caudally, there is hypothesized to be a dual set of innervation of these layers from the enteric nervous system and the vagal nerve, which is a product of branchial arch 6.
* Co-innervation of muscle cells is hypothesized to allow for early peristalsis after birth while the nervous system is not fully mature. The process of esophageal innervation occurs throughout the development of the embryo and requires proliferation and migration of neural crest cells which migrate rostrally-caudally through the gut tube starting during the 4th week and ending their migration around the 9th week of development.[[8]](https://www.ncbi.nlm.nih.gov/books/NBK542304/) Setting the precursor cells for innervation along the entire gut. During the 6th week, when the muscular layers have begun to form, cells of neuronal crest origin migrate inward between the muscular layers eventually giving rise to the submucosal plexus.[[9]](https://www.ncbi.nlm.nih.gov/books/NBK542304/) This process which began the neuronal development early in the 4th week continues through a slow maturation process which continues after birth.[[8]](https://www.ncbi.nlm.nih.gov/books/NBK542304/) At around the 4th month of development, the columnar epithelium of the foregut begins to undergo a transition into a squamous epithelium a process which will continue well into the third trimester.[[2][10]](https://www.ncbi.nlm.nih.gov/books/NBK542304/)
* Esophageal embryogenesis involves complex signaling pathways. The first step of organogenesis of the esophagus from the foregut is the specification of the foregut cells into respiratory lineages or esophageal lineage.[[2][4]](https://www.ncbi.nlm.nih.gov/books/NBK542304/). The process begins with the cellular expression of the Nkx2-1 gene in the anterior foregut ventral wall, Nkx2-1 being a specific marker of respiratory tract cells. Concurrently, endodermal cells in the posterior aspect of the foregut begin to express Sox2 which seems to guide the dorsal foregut towards esophageal differentiation.[[1][2]](https://www.ncbi.nlm.nih.gov/books/NBK542304/) This sequence indicates that the specification of foregut cells occurs before lung bud outpouching and morphogenic changes. The specification occurs across the ventral-dorsal axis of the foregut. The notochord plays a key role in setting up this ventral-dorsal axis, which allows for the differential expression of Nkx2-1 and Sox2 by releasing Noggin.[[1][2][3][11]](https://www.ncbi.nlm.nih.gov/books/NBK542304/)
* Dose-dependent signaling of Noggin from the notochord as well as specific timed signaling from the surrounding mesoderm via Wingless-related Integration site proteins (Wnt) and fibroblast growth factor (FGF) allows for the progression of the dorsal aspect of the foregut to begin differentiation into the esophagus while the ventral aspect of the foregut. Also, expressing NKx2-1 in conjunction with a lower dose of Noggin begins the specification into the future trachea and lungs.[[3]](https://www.ncbi.nlm.nih.gov/books/NBK542304/) Additional key mesenchymal signaling molecules include the BMP family, which play critical roles in tissue patterning and trachea formation.[[12]](https://www.ncbi.nlm.nih.gov/books/NBK542304/) The activity of one member of the BMP family, BMP4, has been shown by research to be antagonized by Noggin, and thus preferentially acts on the ventral sections of the foregut, which get subjected to decreased Noggin because of the dorsally located notochord.[[1][4][12][11]](https://www.ncbi.nlm.nih.gov/books/NBK542304/)
* Another crucial event in the development of the foregut into the esophagus is the separation of the trachea from the esophagus. While the precise mechanisms of separation have not yet been elucidated, signaling from lateral mesoderm to the ventral foregut allows for differentiation into the two final structures which, once separated, both experience a rapid elongation. Wnt signaling, specifically, Wnt5a and Ror2 (a receptor tyrosine kinase) signaling appears to play an important role in this elongation.[[2][3]](https://www.ncbi.nlm.nih.gov/books/NBK542304/) Knockout of Wnt5a in mice results in an altered short tube esophagus, and Wnt5a-Ror2 signaling promotes straight tube morphogenesis for both esophagus elongation as well as the trachea.[[1][2][12]](https://www.ncbi.nlm.nih.gov/books/NBK542304/)
* Another important development is the differentiation of esophagus from the structures that are continuous with the esophagus, namely the pharynx and the stomach. Many cell signaling molecules regulate esophageal differentiation and transition from the pharynx and into the stomach.  Several mediators that have identifiable roles in esophageal and respiratory differentiation also play a part in the differentiation of the pharynx and the stomach from the esophagus, serving to highlight the numerous roles these factors play.[[13]](https://www.ncbi.nlm.nih.gov/books/NBK542304/) The upper esophageal sphincter derives from mesenchymal tissue from brachial arches 4 to 6. And the lower esophageal sphincter is derived from mesenchymal cells of somites located in the region of the foregut.[[11][13]](https://www.ncbi.nlm.nih.gov/books/NBK542304/) The gastroesophageal junction's origin is thought to be a combination of cell signaling as well as cell-cell interactions which occur as a consequence of rotational changes of the stomach.[[5]](https://www.ncbi.nlm.nih.gov/books/NBK542304/) Studies with mice have demonstrated the role of Sonic hedgehog (Shh), BMP, Foxp1, and Foxp2 in the differentiation of the esophagus into the stomach during organogenesis.[[14]](https://www.ncbi.nlm.nih.gov/books/NBK542304/) Shh role seems to play important roles throughout the esophagus and at the level of the lower esophageal sphincter, as defects in Shh result in the decreased formation and the maturation of smooth muscle cells in both the esophagus and the stomach.[[15][16]](https://www.ncbi.nlm.nih.gov/books/NBK542304/) Foxp1 and Foxp2 appear to play similar roles in muscularization, and BMP signaling appears to be important in initiating the change from squamous epithelium into glandular columnar epithelium although the exact roles are not fully understood.