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ANA 206: SYSTEMIC EMBRYOLOGY

1. DEVELOPMENT OF THE LUNGS

**Phases of lung development**

* Introduction
* Embryonic phase
* Pseudoglandular phase
* Canalicular phase
* Saccular phase
* Alveolar phase

**Embryonic phase**

The embryonic phase of lung development begins with the formation of a groove in the ventral lower pharynx, the sulcus laryngotrachealis (stage 10, ca. 28 days, 10). After a couple of days - from the lower part - a bud forms, the true lung primordium (stage 12, ca. 30 days,12). In the further subdivision into the two main bronchi (stage 14, ca. 33 days,14) the smaller bud on the left is directed more laterally than the somewhat larger one on the right that - parallel to the esophagus - is directed more caudally. Thus the asymmetry of the main bronchi, as they present in adults, is already established. The subsequent divisions of the endodermal branches also take place unequally in that on the right three further buds form and, on the left, only two, corresponding to the later pulmonary lobes. In the next division step, which occurs at the end of the embryonic period, the segments of the individual pulmonary lobes arise.

At the end of the embryonic period the first segments appear in the five (three right and two left) lobes of the lungs. With their distended ends the lungs resemble an exocrine gland.
At this time the **pulmonary vessels** have formed themselves

The pulmonary circulation system (smaller circulation system) is formed out of the 6th pharyngeal arch artery. These develop somewhat differently than the other 4 aortic arches in that first a vessel plexus forms around the lung anlage, originating from the aortic sac. The true 6th aortic arch is only then formed after vessels - also from the dorsal aorta - grow into this plexus and thus a connection between the truncus pulmonalis and dorsal aorta has arisen.

**Pseudoglandular phase**

At this stage the lungs resemble the development of a tubulo-acinous gland. According to the classical view, the entire air-conducting bronchial tree up to the terminal bronchioli are set down in this phase (16 generations). Recent morphometric studies (3) have shown that with the end of the pseudoglandular phase 20 generations are partially present in the lungs, which means that at this point in time the respiratory ducts have already been formed.

The primordial system of passages, the air-conducting bronchial tree, is initially coated by cubic epithelium. These are the precursor cells of the ciliated epithelium and of the secretory cells. In humans, the first ciliated epithelial cells can be found in the 13th week of pregnancy

The differentiation of the lungs takes place in a **centrifugal direction**. In the **central, air-conducting portions** of the lungs the epithelium begins to differentiate into **cilia-carrying cells** and **goblet cells**. After the 10th week cartilage and smooth muscle cells as well as bronchial glands can be found in the wall of the bronchi. The peripheral sections partially retain - until far beyond the pseudoglandular phase - cubic epithelium that is still little differentiated. This is important for a further proliferation of the bronchial tree into the surrounding mesenchymal tissue.

CANALICULAR PHASE

In the classical description of lung development, in this phase the **canaliculi branch out of the terminal bronchioli**. The canaliculi compose the proper **respiratory part** of the lungs, the **pulmonary parenchyma**. All of the air spaces that derive from a **terminal bronchiolus** form an **acinus**. Each one comprises **respiratory bronchioli** and the **alveolar ducts** and later the **alveolar sacculi**. The chief characteristic of this canalicular phase is the **alteration of the epithelium and the surrounding mesenchyma**. Along the acinus, which develops from the terminal bronchiolus, an **invasion of capillaries** into the mesenchyma occurs. The capillaries surround the acini and thus form the foundation for the later exchange of gases. The **lumen of the tubules** becomes wider and a part of the epithelial cells get to be flatter. From the **cubic type II pneumocytes** develop the **flattened type I pneumocytes**.

At the end of this canalicular phase which is the beginning of the saccular phase (25 weeks) - a large part of the amniotic fluid is produced by the lung epithelium. From this time on, the maturity of the lungs can be measured clinically based on the activity of the type II pneumocytes, which begin to produce the surfactant. The ratio of lecithin to sphingomyelin in the amniotic fluid, which increases with fetal age is determined.

**SACCULAR PHASE**

From the last trimester whole clusters of sacs form on the terminal bronchioli, which represent the last subdivision of the passages that supply air. In the saccular phase the last generation of air spaces in the respiratory part of the bronchial tree is born. At the end of each respiratory tract passage smooth-walled sacculi form, coated with type I and type II pneumocytes. The septa (primary septa) between the sacculi are still thick and contain two networks of capillaries that come from the neighboring sacculi. The interstitial space is rich with cells and the proportion of collagen and elastic fibers is still small. This matrix, though, plays an important role for the growth and differentiation of the epithelium that lies above it (9).

At the end of this phase the interstitial fibroblasts begin with the production of extracellular material in the interductal and intersaccular space.

In this stage developmental damage already affects the gas-exchange components and result in structural alterations of the later pulmonary parenchyma.

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| **Alveolar phase** |  |  |

Depending on the author, the alveolar phase begins at varying times. Probably in the last few weeks of pregnancy, new sacculi and from them, the first alveoli form. Thus, at birth, 1/3 of the roughly 300 million alveoli should be fully developed. The alveoli, though are only present in their beginning forms. Between them lies the parenchyma, composed of a double layer of capillaries, that forms the primary septa between the alveolar sacculi.

Already before birth these alveolar sacculi get to be increasingly complex structurally. Thereby, a large number of small protrusions form along the primary septa. Soon, these become larger and subdivide the sacculi into smaller subunits, the **alveoli**, which are delimited by **secondary septa**.
Ultrastructural investigations show that overall where such alveoli appear, they are surrounded by **elastic fibers** that form the interstitial septa between two capillary nets.
In the first 6 months, their number increases massively. This "**alveolarization**" and therewith the formation of **secondary septa** should - to a limited extent still - continue up to the **first year and a half of life**.

1. ROTATION OF THE STOMACH AND FORMATION OF THE OMENTAL BURSA

The GIT is best imagined as a simple tube, the upper part being the foregut diverticulum, which is further divided into oesophagus 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. A second rotation (of 90 degrees) occurs on the longitudinal axis establishing the adult orientation of the stomach.

**Stomach Mesentery**

In the second trimester, the ventral and dorsal mesenteries associated with the stomach are still anatomically different from the newborn. The figure shows a lateral view of this process comparing the early second trimester arrangement with the newborn structure.

**Ventral Mesogastrium**

Attached to the superior end of the stomach will form the [lesser omentum](https://embryology.med.unsw.edu.au/embryology/index.php/L#lesser_omentum). This structure will connect the lesser curvature of the stomach to the liver as a ligamentous structure.

**Dorsal Mesogastrium**

Attached to the inferior end of the stomach initially as an extended fold, this later fuses as a single "apron-like" structure, the [greater omentum](https://embryology.med.unsw.edu.au/embryology/index.php/G#greater_omentum). Fusion will also incorporate the transverse colon part of the large intestine. This will also contribute the gastrosplenic ligament (gastrolienal ligament).

The greater omentum hangs like an apron over the small intestine and transverse colon. It begins attacted to the inferior end of the stomach as a fold of the dorsal mesogastrium which later fuses to form the structure we recognise anatomically. The figure below shows a lateral view of this process comparing the early second trimester arrangement with the newborn structure.

 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.

**Borders**

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.

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.

**Clinical aspects**

The lesser sac has seven distinctly categorized pathological groups under which its potential disorders may be listed:

* **Congenital anomalies** include duplication cysts and cystic lymphangiomas.
* A **hematoma** or a **biloma** are classed as traumatic injuries.
* **Inflammatory states** could be due to an abscess, a pseudocyst or even acute pancreatitis.
* **Neoplastic changes** may lead to the growth of a stromal tumor, a leiomyoblastoma, a leiomyosarcoma, a liposarcoma, a schwannoma, both benign and malignant pancreatic neoplasms that may have endocrine involvement or not, hepatic tumors and desmoid tumors.
* A **hydatid cyst** indicates a parasitic infestation.
* The only infective cause of a lesser sac disorder as yet known of is **tuberculosis**.
* **Mechanical irritation** could potentially be caused by hernias of the cecum, transverse colon, [small intestine](https://www.kenhub.com/en/library/anatomy/the-small-intestine) and [gallbladder](https://www.kenhub.com/en/library/anatomy/gallbladder)
1. Development of the esophagus

The **esophagus** informally known as the **food pipe** or **gullet**, is an [organ](https://en.wikipedia.org/wiki/Organ_%28anatomy%29) in [vertebrates](https://en.wikipedia.org/wiki/Vertebrate) through which [food](https://en.wikipedia.org/wiki/Food) passes, aided by [peristaltic contractions](https://en.wikipedia.org/wiki/Peristalsis), from the [pharynx](https://en.wikipedia.org/wiki/Human_pharynx) to the [stomach](https://en.wikipedia.org/wiki/Stomach). The esophagus is a [fibromuscular](https://en.wiktionary.org/wiki/fibromuscular) tube, about 25 centimeters long in adults, which travels behind the [trachea](https://en.wikipedia.org/wiki/Trachea) and [heart](https://en.wikipedia.org/wiki/Human_heart), passes through the [diaphragm](https://en.wikipedia.org/wiki/Thoracic_diaphragm) and empties into the uppermost region of the [stomach](https://en.wikipedia.org/wiki/Stomach). During swallowing, the [epiglottis](https://en.wikipedia.org/wiki/Epiglottis) tilts backwards to prevent food from going down the [larynx](https://en.wikipedia.org/wiki/Larynx) and lungs. Runs posteriorly after leaving pharynx. The wall of the esophagus from the [lumen](https://en.wikipedia.org/wiki/Lumen_%28anatomy%29) outwards consists of [mucosa](https://en.wikipedia.org/wiki/Mucosa), [submucosa](https://en.wikipedia.org/wiki/Submucosa) (connective tissue), [layers of muscle fibers](https://en.wikipedia.org/wiki/Muscular_layer) between layers of [fibrous tissue](https://en.wikipedia.org/wiki/Fibrous_tissue), and an outer layer of connective tissue. The mucosa is a [stratified squamous epithelium](https://en.wikipedia.org/wiki/Stratified_squamous_epithelium) of around three layers of squamous cells, which contrasts to the [single layer of columnar cells](https://en.wikipedia.org/wiki/Simple_columnar_epithelia) of the stomach. The transition between these two types of epithelium is visible as a zig-zag line. Most of the muscle is [smooth muscle](https://en.wikipedia.org/wiki/Smooth_muscle) although [striated muscle](https://en.wikipedia.org/wiki/Striated_muscle) predominates in its upper third. It has two muscular rings or [sphincters](https://en.wikipedia.org/wiki/Sphincter) in its wall, one at the top and one at the bottom. The lower sphincter helps to prevent reflux of acidic stomach content. The esophagus has a rich blood supply and venous drainage. Its smooth muscle is innervated by involuntary nerves ([sympathetic nerves](https://en.wikipedia.org/wiki/Sympathetic_nerve) via the [sympathetic trunk](https://en.wikipedia.org/wiki/Sympathetic_trunk) and [parasympathetic nerves](https://en.wikipedia.org/wiki/Parasympathetic_nerve) via the [vagus nerve](https://en.wikipedia.org/wiki/Vagus_nerve)) and in addition voluntary nerves ([lower motor neurons](https://en.wikipedia.org/wiki/Lower_motor_neurons)) which are carried in the vagus nerve to innervate its striated muscle.

 In early [embryogenesis](https://en.wikipedia.org/wiki/Human_embryogenesis), the esophagus develops from the [endodermal](https://en.wikipedia.org/wiki/Endoderm) [primitive gut tube](https://en.wikipedia.org/wiki/Gastrointestinal_tract). The ventral part of the embryo abuts the [yolk sac](https://en.wikipedia.org/wiki/Yolk_sac). During the second week of embryological development, as the embryo grows, it begins to surround parts of the sac. The enveloped portions form the basis for the adult gastrointestinal tract.[[21]](https://en.wikipedia.org/wiki/Esophagus#cite_note-LARSEN2009-21) The sac is surrounded by a network of [vitelline arteries](https://en.wikipedia.org/wiki/Vitelline_arteries). Over time, these arteries consolidate into the three main arteries that supply the developing gastrointestinal tract: the [celiac artery](https://en.wikipedia.org/wiki/Celiac_artery), [superior mesenteric artery](https://en.wikipedia.org/wiki/Superior_mesenteric_artery), and [inferior mesenteric artery](https://en.wikipedia.org/wiki/Inferior_mesenteric_artery). The areas supplied by these arteries are used to define the [midgut](https://en.wikipedia.org/wiki/Midgut), [hindgut](https://en.wikipedia.org/wiki/Hindgut) and [foregut](https://en.wikipedia.org/wiki/Foregut).[[21]](https://en.wikipedia.org/wiki/Esophagus#cite_note-LARSEN2009-21)

The surrounded sac becomes the primitive gut. Sections of this gut begin to differentiate into the organs of the gastrointestinal tract, such as the esophagus, [stomach](https://en.wikipedia.org/wiki/Stomach), and [intestines](https://en.wikipedia.org/wiki/Intestine).[[21]](https://en.wikipedia.org/wiki/Esophagus#cite_note-LARSEN2009-21) The esophagus develops as part of the foregut tube.[[21]](https://en.wikipedia.org/wiki/Esophagus#cite_note-LARSEN2009-21) The innervation of the esophagus develops from the [pharyngeal arches](https://en.wikipedia.org/wiki/Pharyngeal_arch).