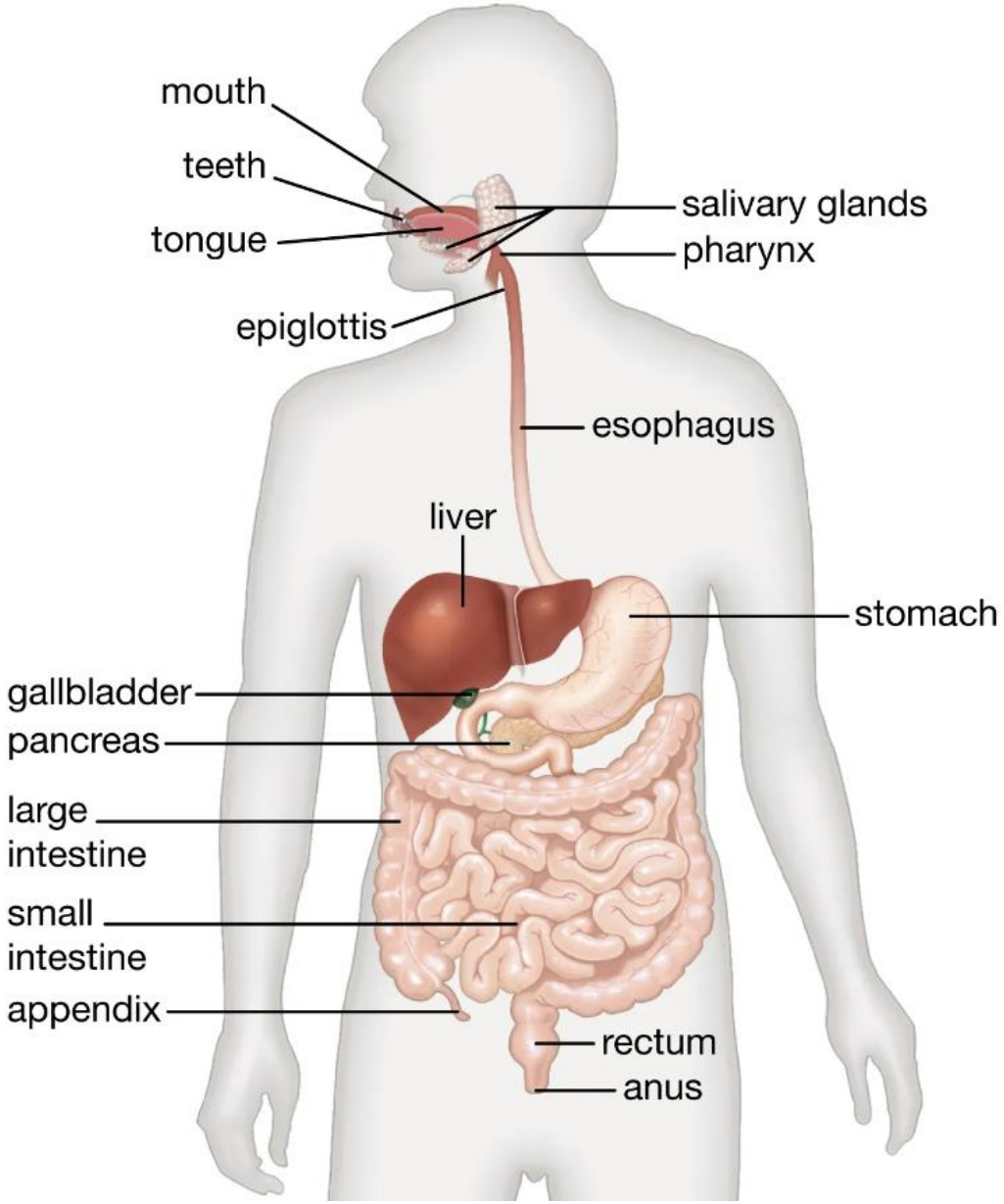
The Digestive System

Dr. Aron Emmi



The Human Digestive System

Formed by:

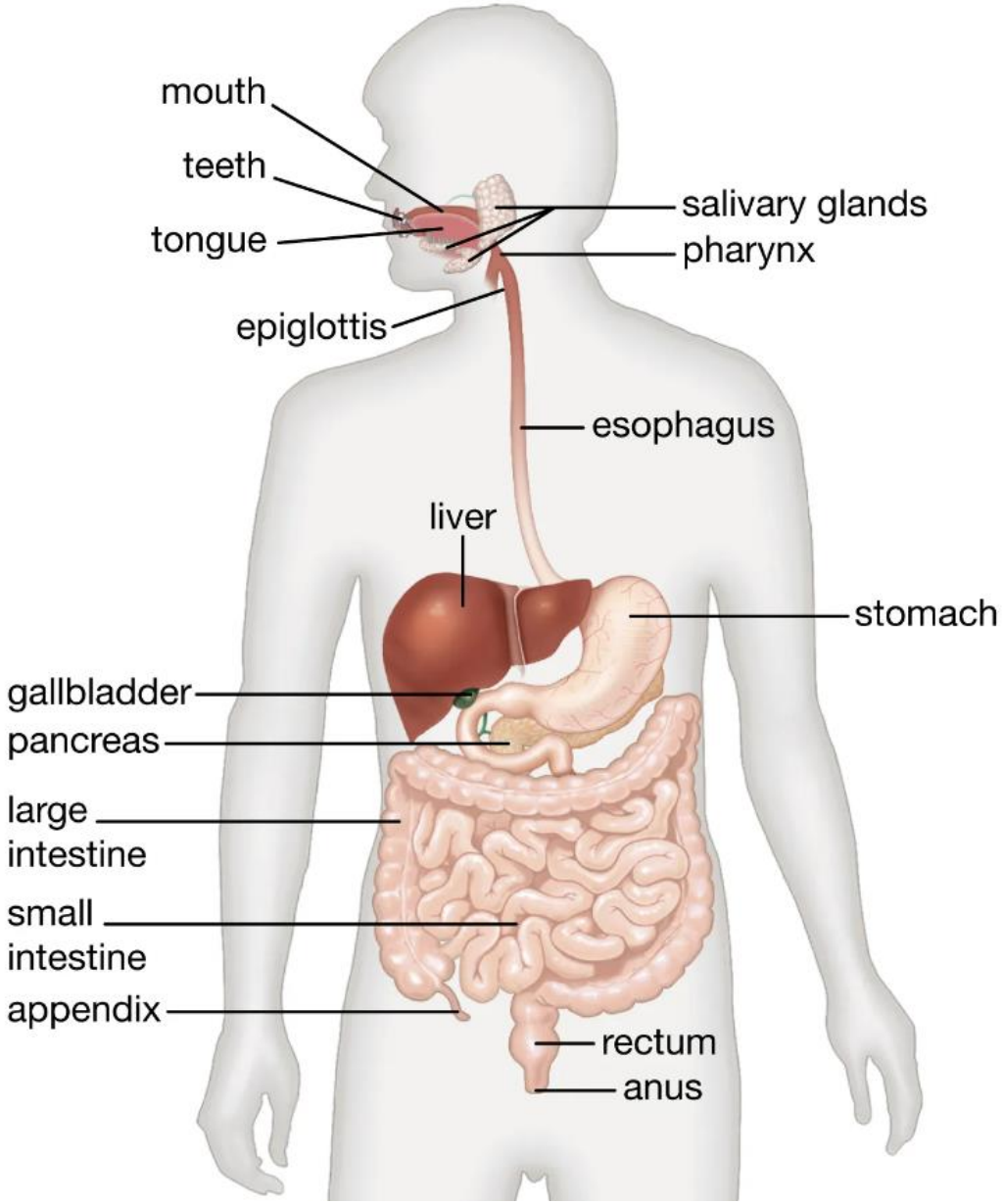
1. The gastro-intestinal tract (Alimentary Canal)

- Oral cavity
- Esophagus
- Stomach
- Small intestine
- Large Intestine

2. The annexed glands:

- Intramural glands (within the walls of the GI tract)
- Extramural glands (Salivary Glands, Liver, Gallbladder, Pancreas)

The Human Digestive System



Responsible for different processes related to food intake:

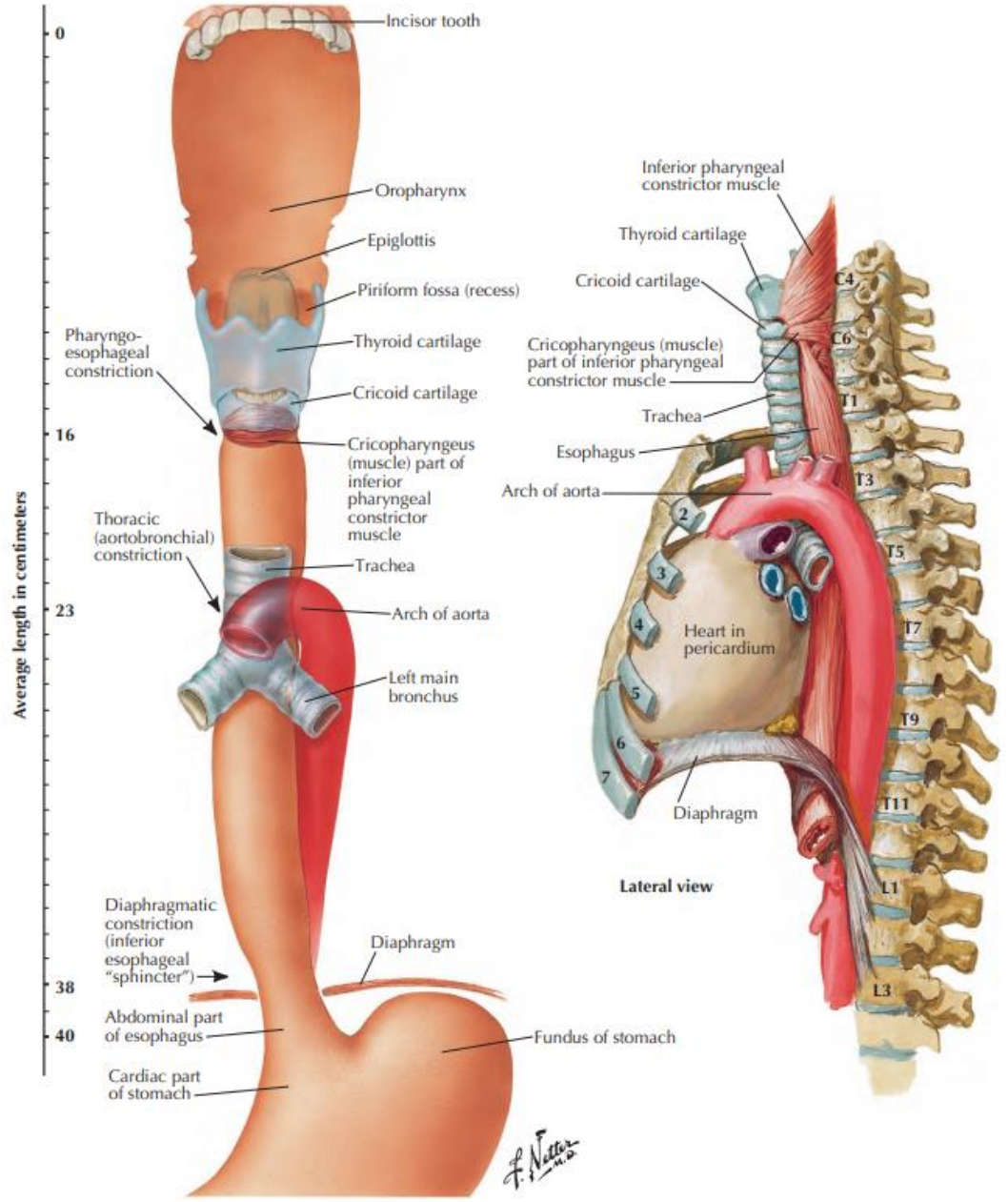
- **Ingestion** (oral cavity) → formation of the **Bolus**
- **Digestion** (oral cavity, esophagus, stomach, duodenum) → Formation of the **Chimum**
- **Absorption** (small intestine, colon) → Formation of the **Chilum**
- **Elimination** (rectum, anus) → formation and elimination of **faeces**

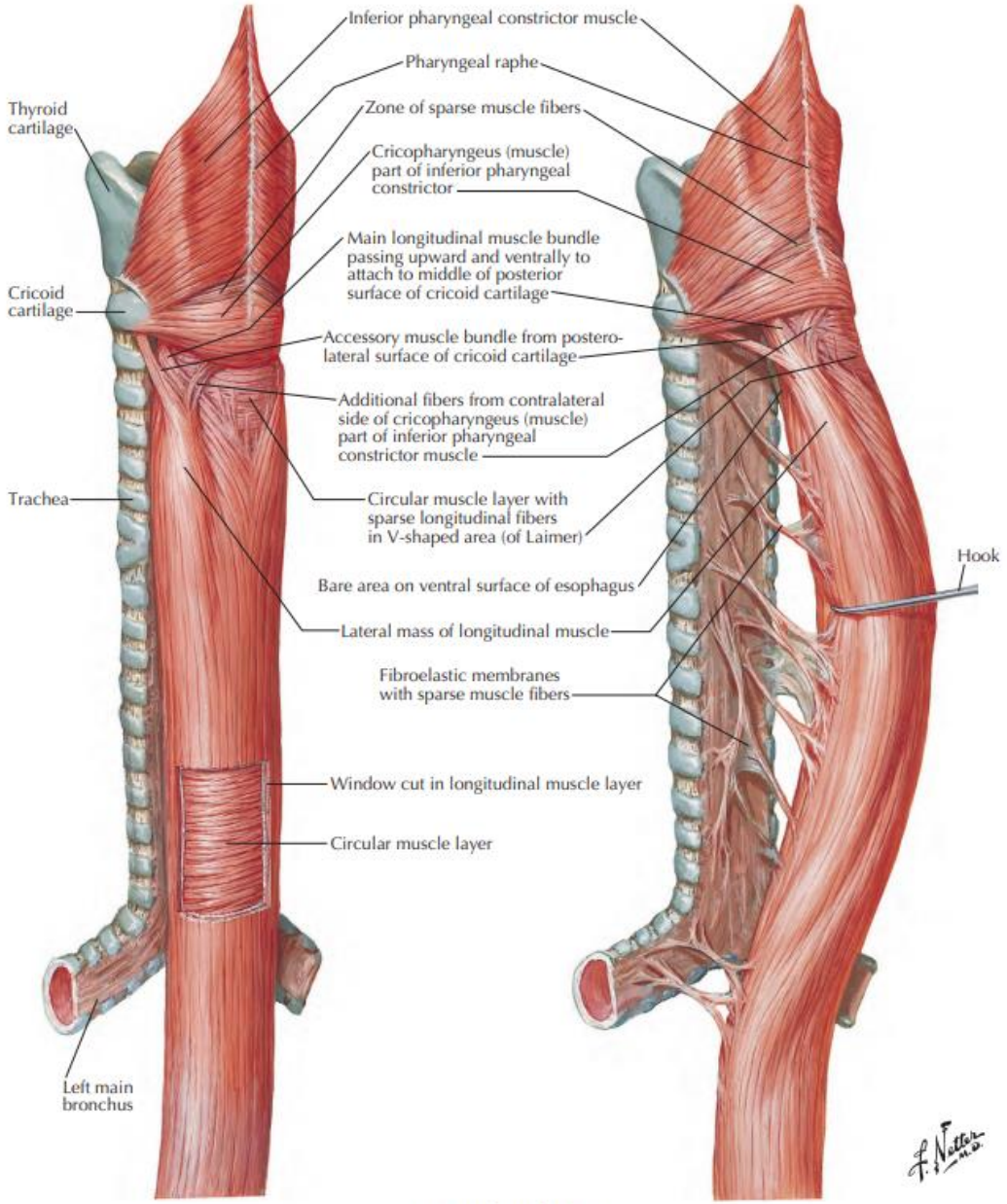
The Esophagus

The esophagus is a hollow organ through which the **bolus** passes. The bolus is formed within the oral cavity by the combined action of mastication and the enzymatic activity of the saliva. The function of the esophagus is to mediate the passage of the bolus from the oral cavity and the pharynx to the stomach.

It presents an average lenght of **25-30cm** and can be subdivided into four segments:

- **Cervical**
- **Thoracic**
- **Diaphragmatic**
- **Abdominal**



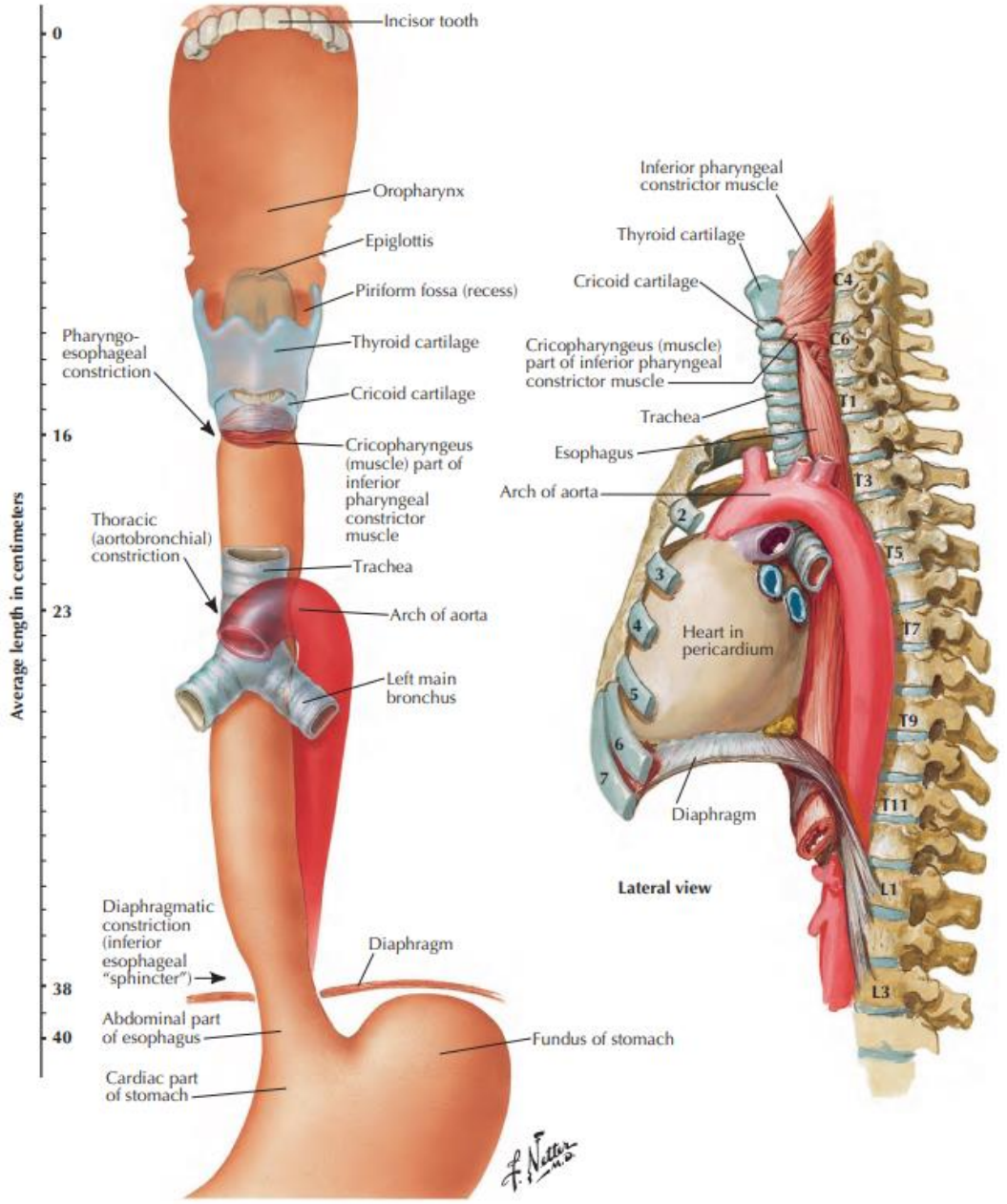


Posterolateral view

Cervical segment (where it passes between the trachea and the vertebral column)

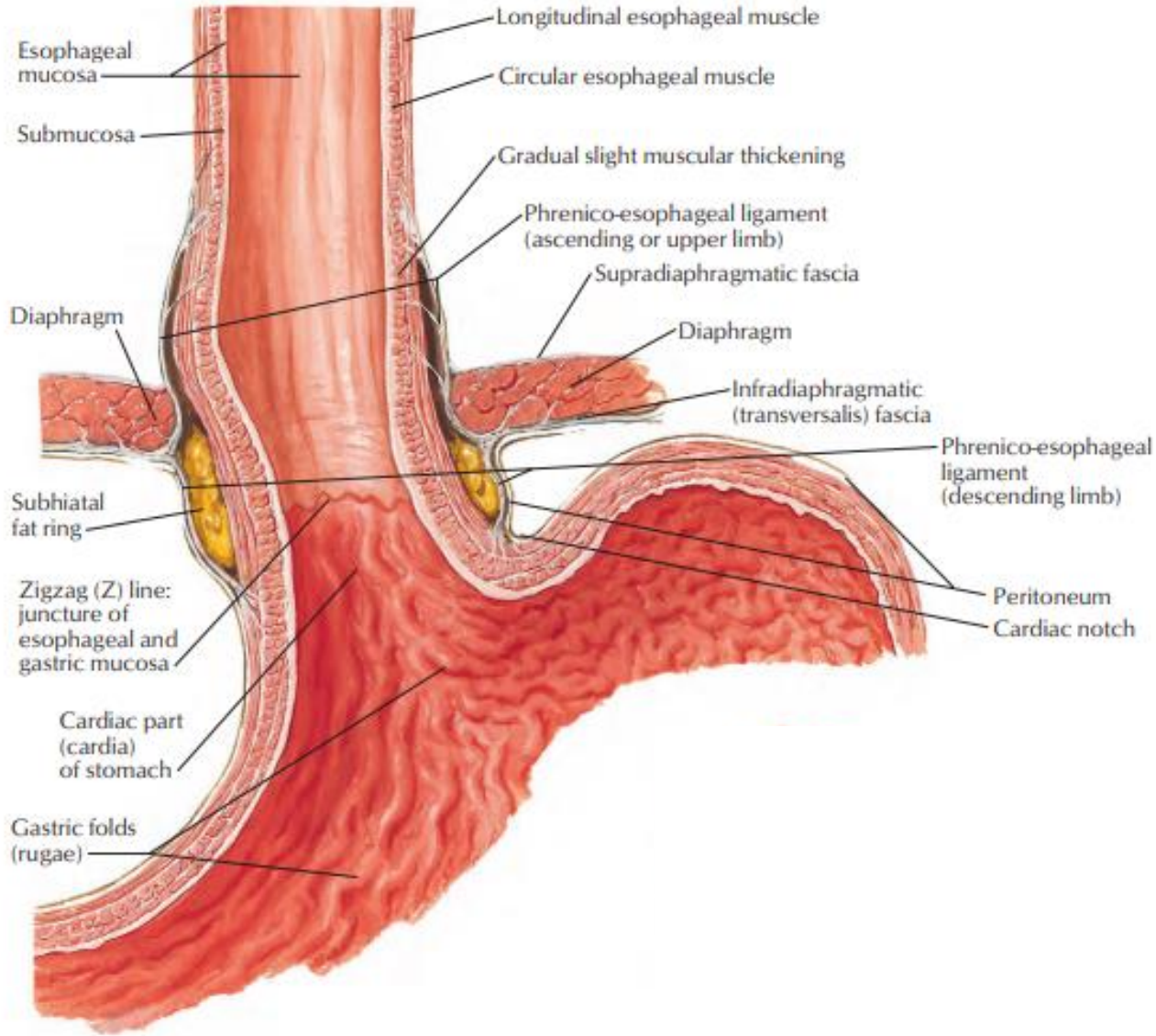
→ Relationship with the trachea anteriorly (tracheal muscle → incompleteness of the rings of the tracheal cartilage).

Thoracic (where it passes between the right lung and the aorta, moving anteriorly to it)



Diaphragmatic (where it crosses the diaphragm)

Abdominal (below the diaphragm where it ends with the **cardias**, the «valve» connecting it to the stomach).



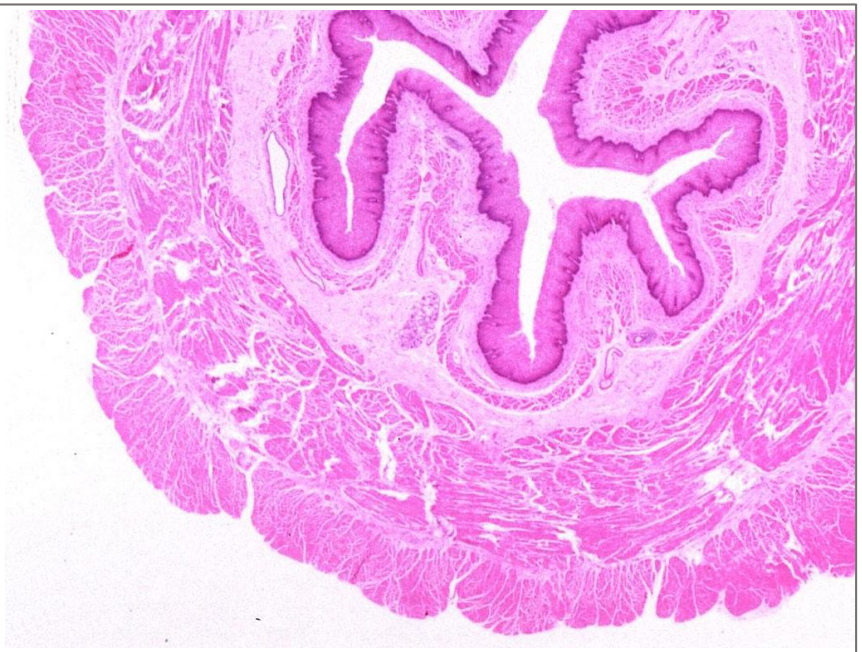
Formed by four layers:

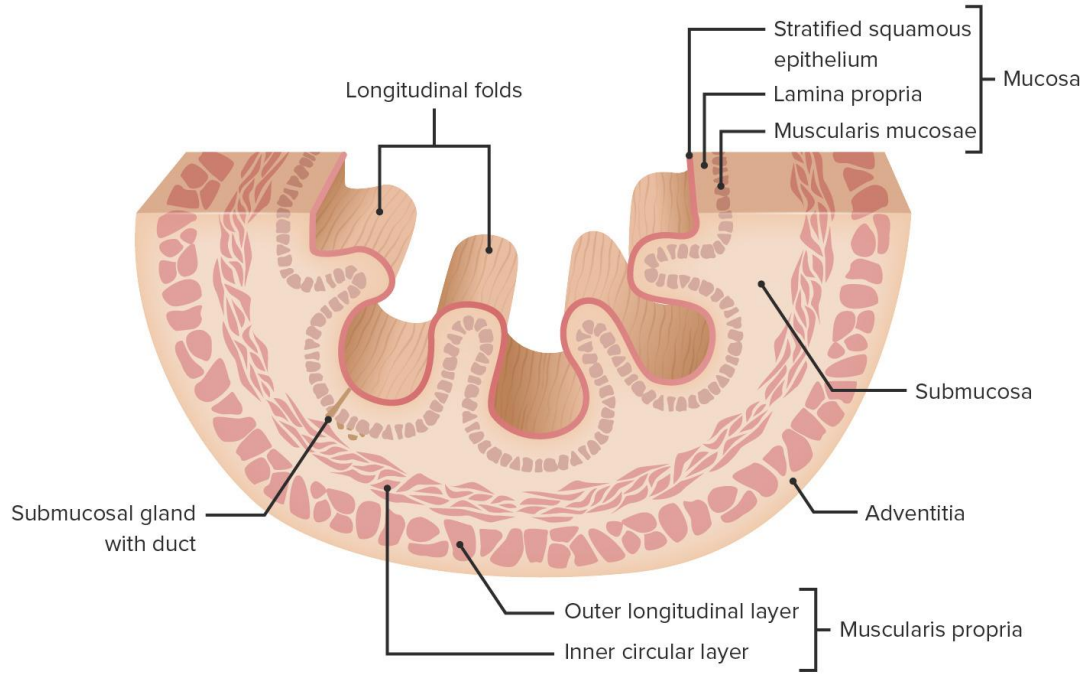
- **Mucosa** (stratified squamous epithelium, lamina propria, muscolaris mucosa)

- **Submucosa** → esophageal glands (produce mucus)

- **Muscularis propria** (inner circular, outer longitudinal muscle fibers)
  - → Upper part of the esophagus: under voluntary control (swallowing)
  - → Lower part of the esophagus: under autonomous NS control (peristalsis)

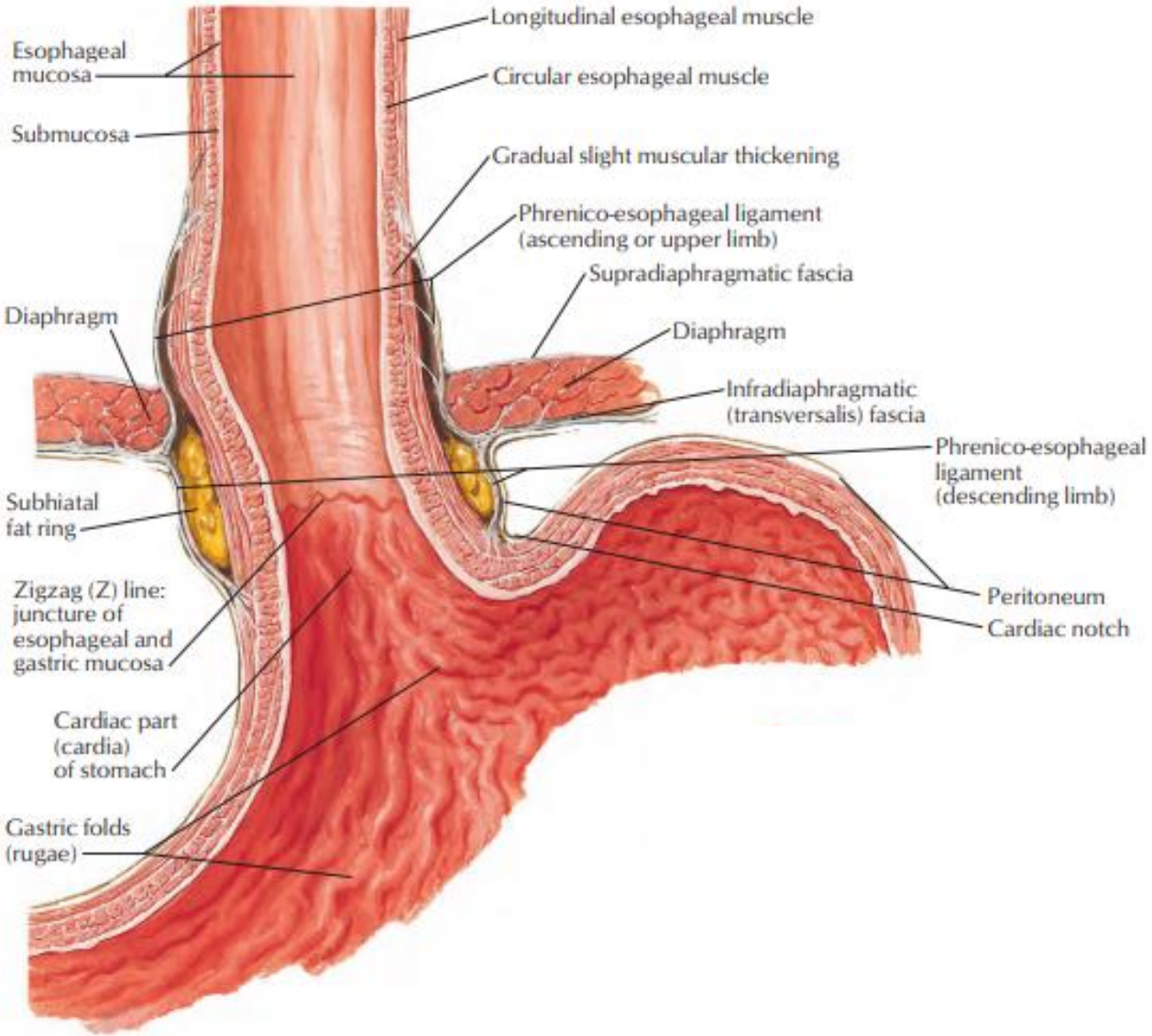
- **Adventitia** (in the thorax, sierosa in the abdomen).





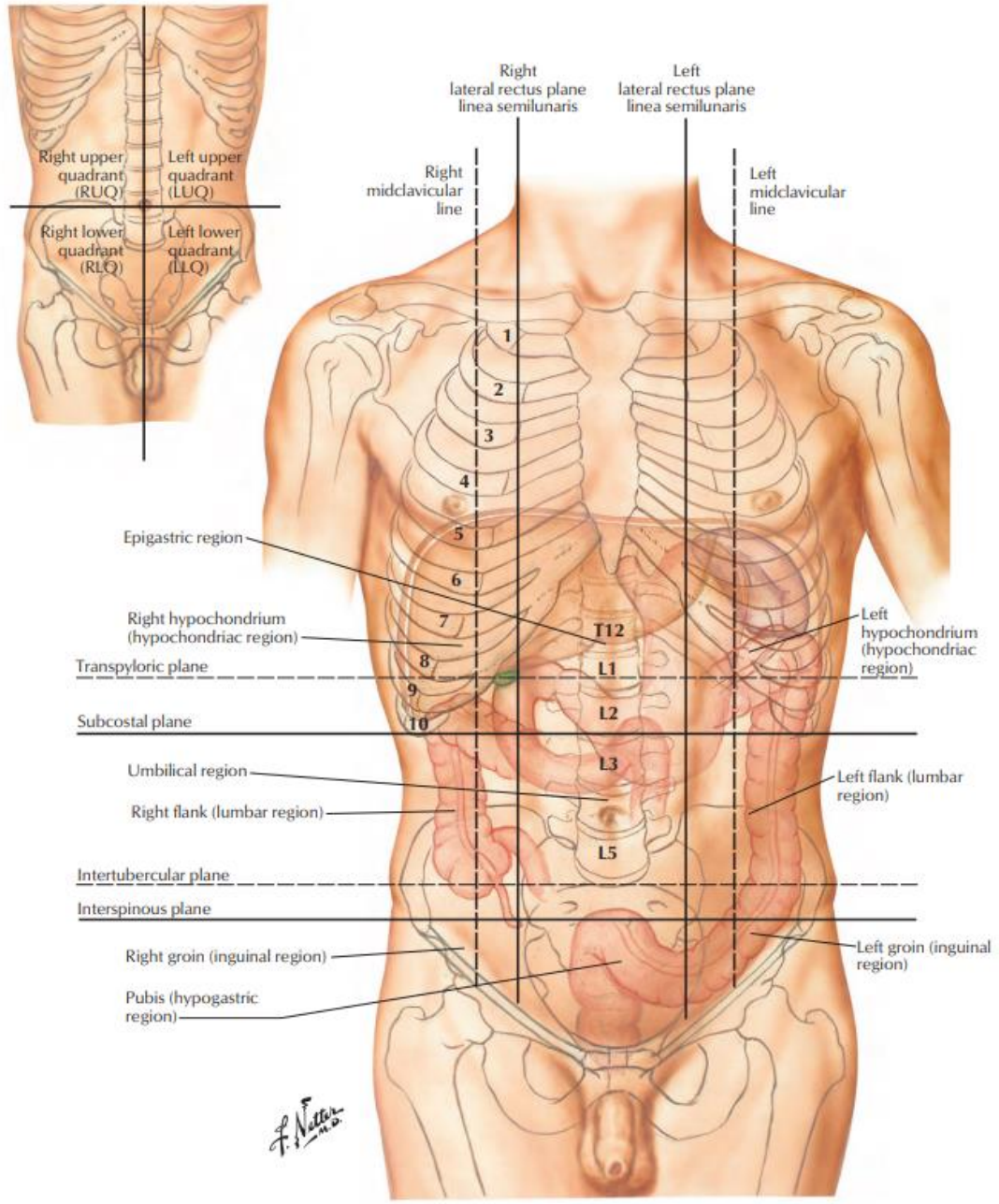
Cardias: Gastro-esophageal junction (valve)

→ Abrupt change in the epithelium (from stratified squamous to simple columnar).



The Stomach

The stomach is a hollow organ found in the upper-middle and upper-left quadrant of the abdomen.



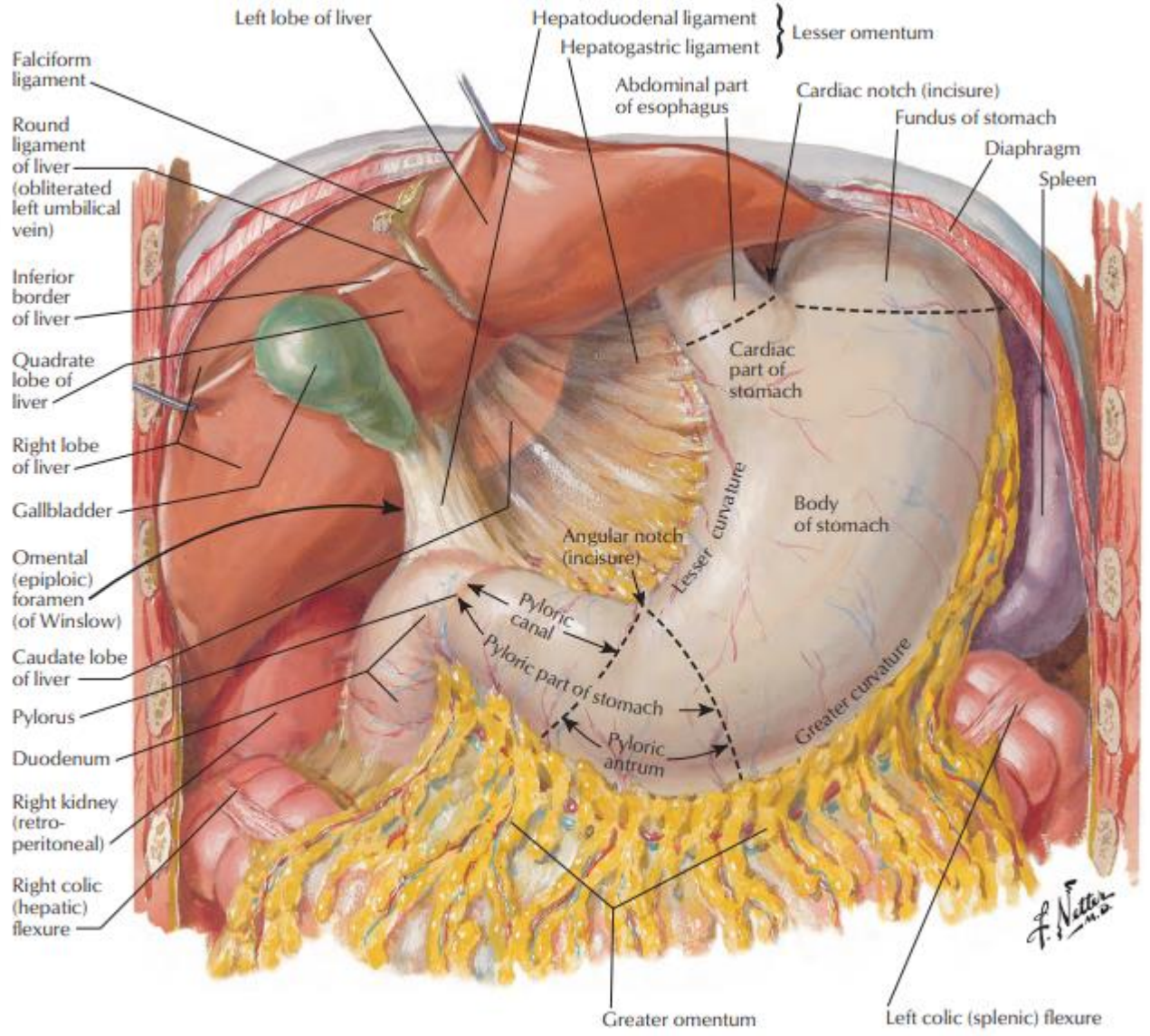
The Stomach

Topography:

The stomach is found below the diaphragm and is in relationship with the liver and gallbladder (right) and with the slpeen (left).

Inferiorly to it, the large intestine (transverse part) is found.

The stomach continues with the small intestine, and in particular the duodenum.



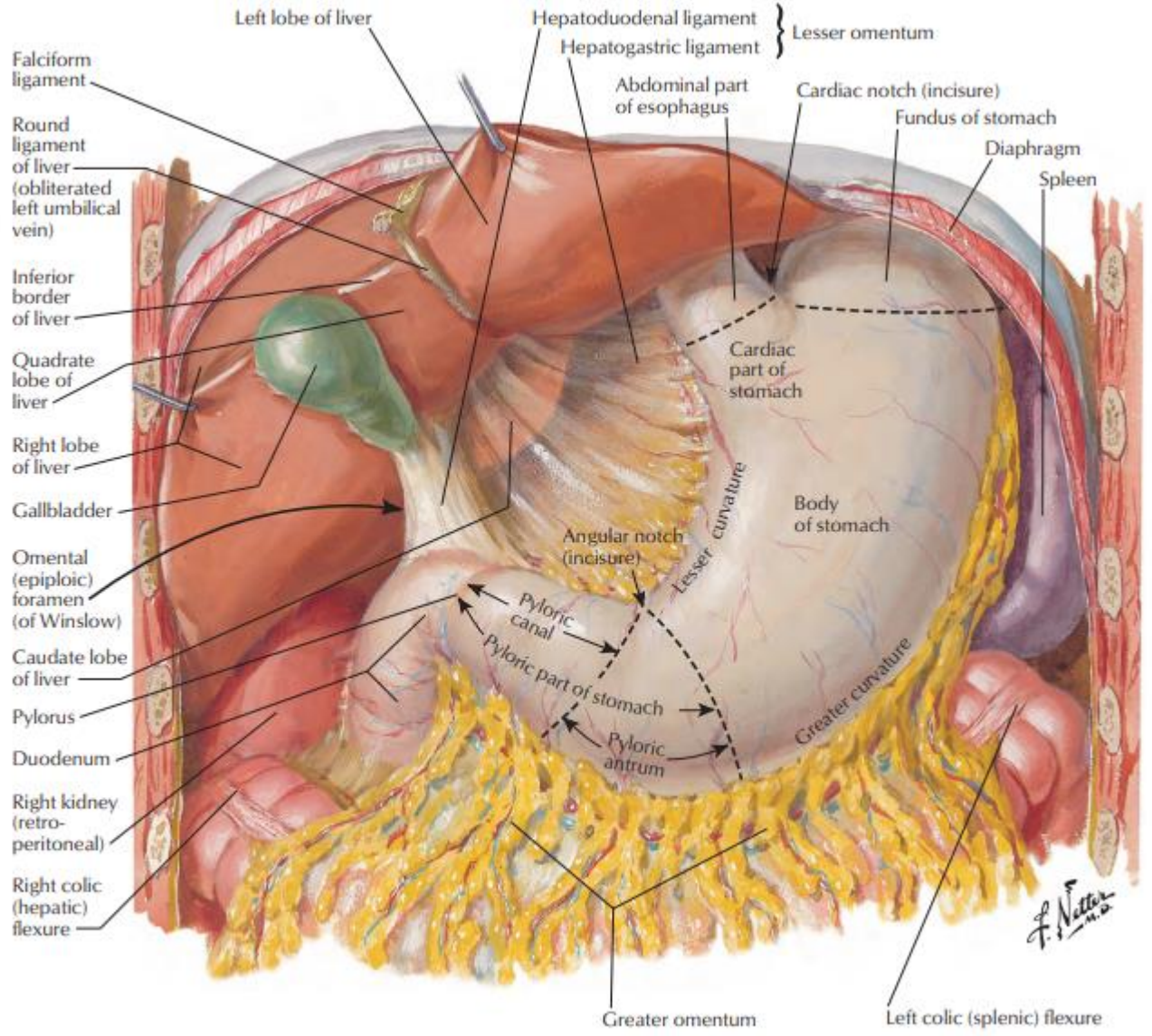
The Stomach

It presents a recurve shape, often compared to a **waterskin**.

The two lateral margins of the stomach are known as:

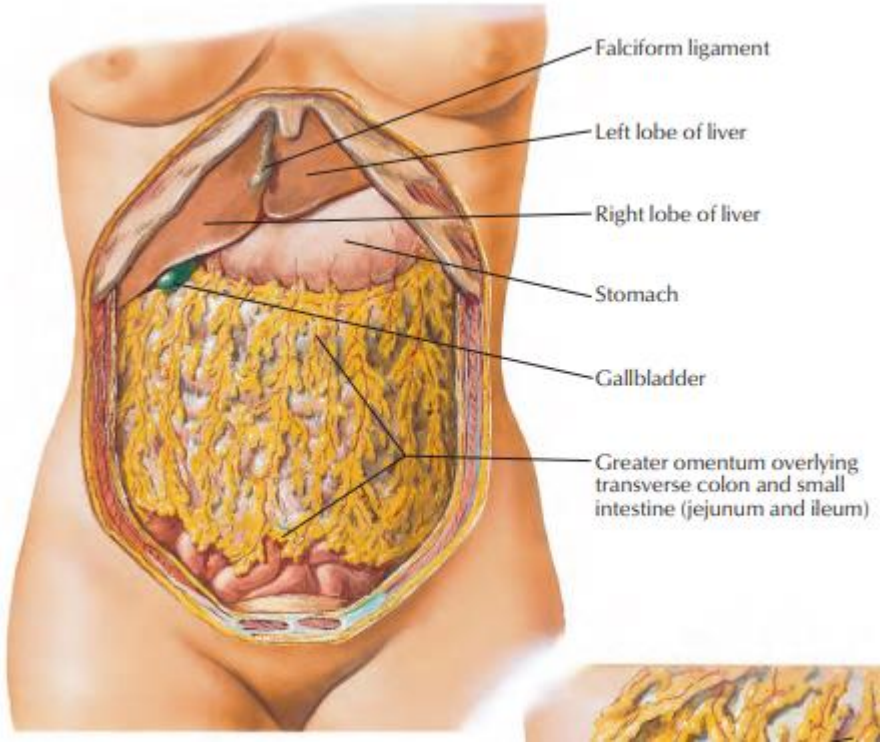
- **Lesser curvature**, facing to the right, and in relationship with the liver and gallbladder. It attaches to them via the hepatogastric ligament. This, together with the hepatoduodenal ligament forms the lesser omentum.

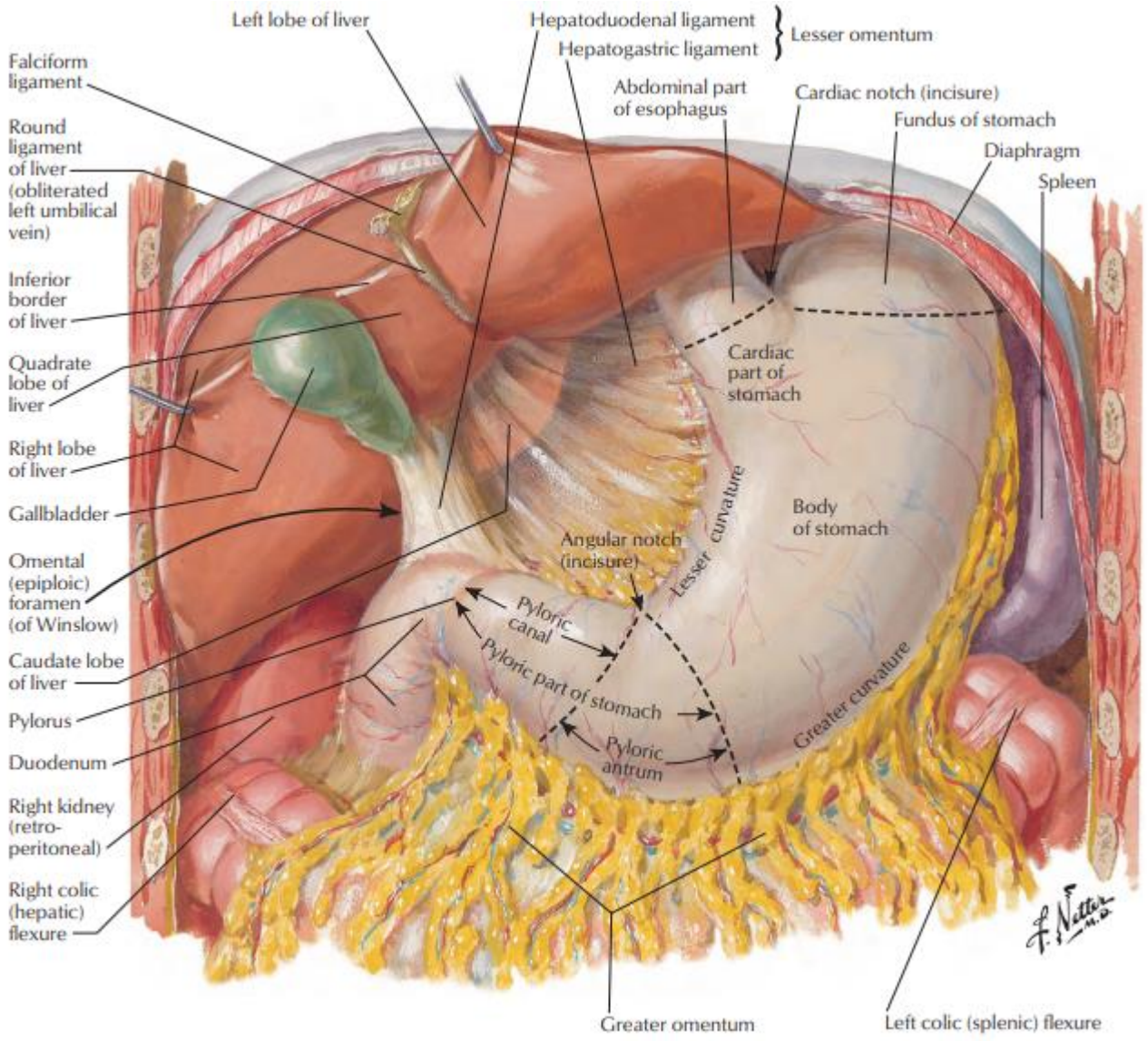
- **Greater curvature**, facing to the left and downwards, which gives rise to the attachmen of the greater omentum. This covers the intestines below.



The Epiploons

Lesser omentum (epiploon): from the liver to the stomach and duodenum
Greater omentum (epiploon): from the great curvature of the stomach covering the intestines





The Stomach

It presents a recurve shape, often compared to a **waterskin**. The two lateral margins of the stomach are known as:

- **Lesser curvature**, facing to the right, and in relationship with the liver and gallbladder
- **Greater curvature**, facing to the left and downwards, which gives rise to the attachmen of the greater omentum.

Anatomically, the stomach can be divided into three regions.

- **The fundus**, superiorly, facing upwards towards the diaphragm.
- **The body of the stomach**, which represents the main and largest part.
- **The pyloric antrum**, where the stomach continues into the duodenum at the level of the pyloric sphincter

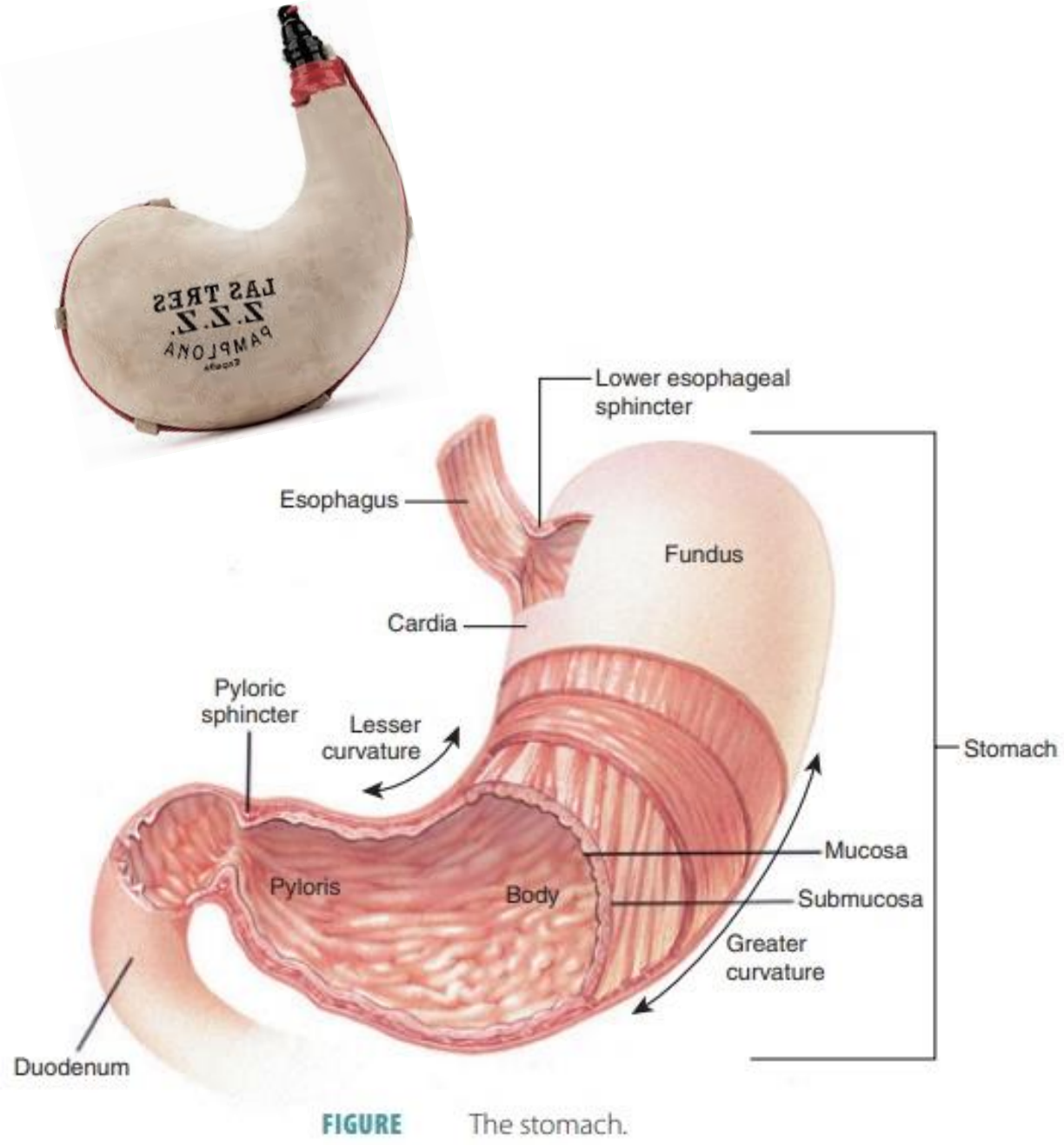


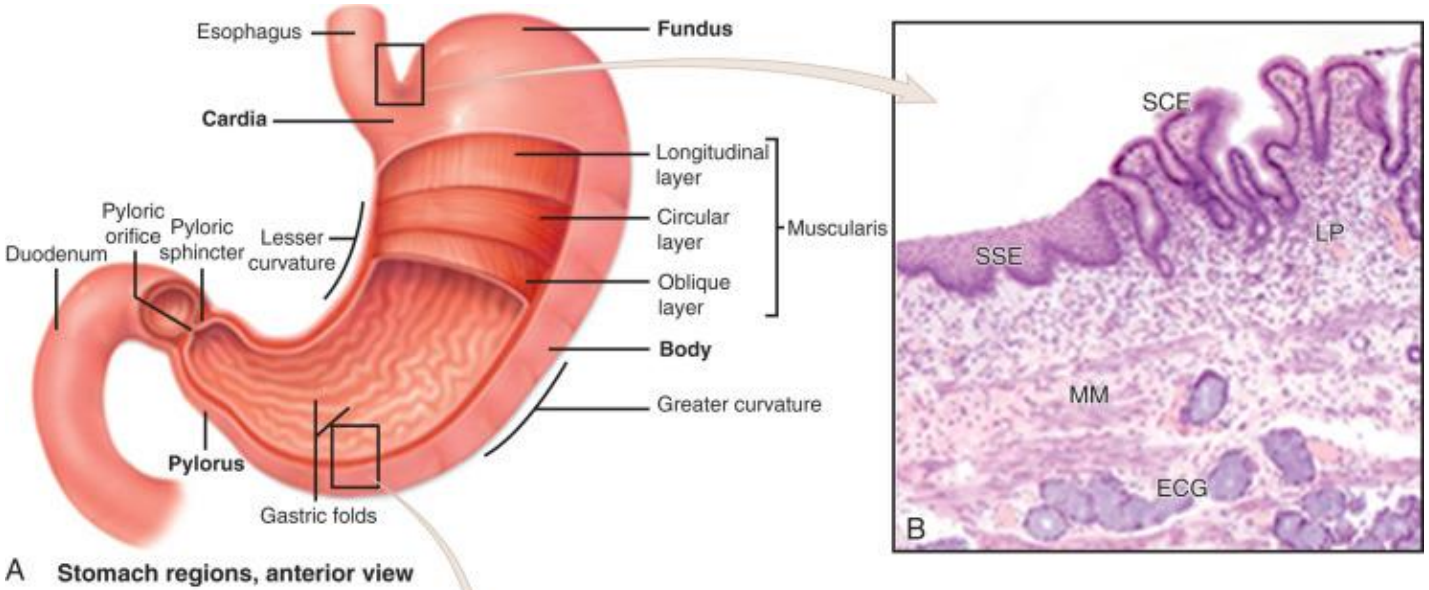
FIGURE The stomach.

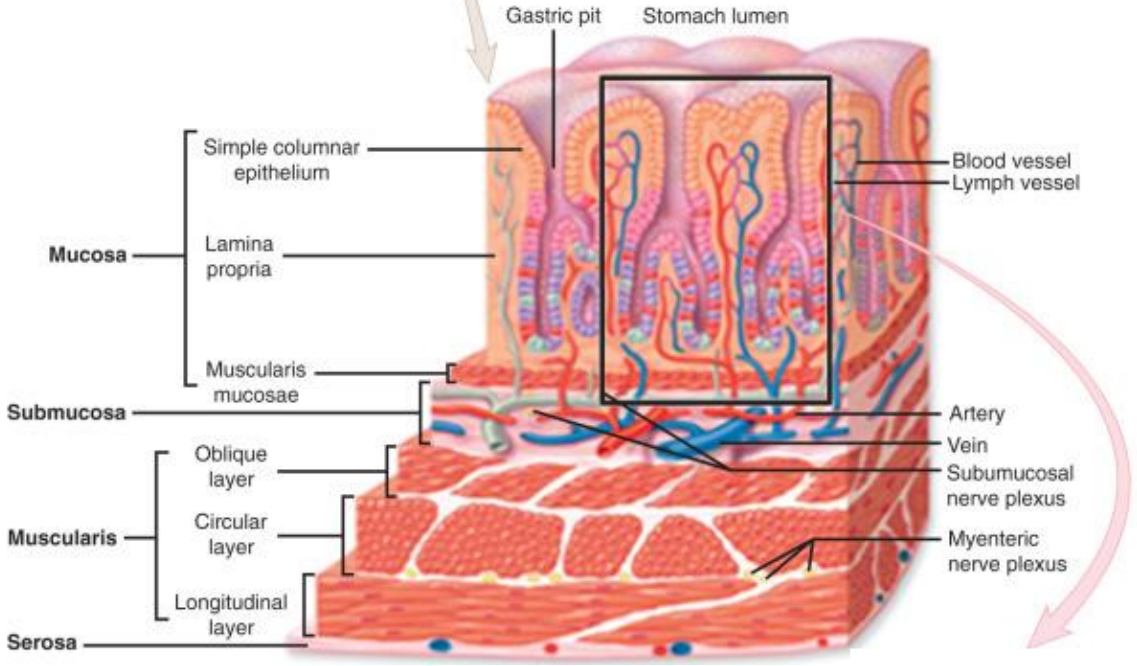
The Stomach

The stomach presents a similar structure to the rest of the GI tract:

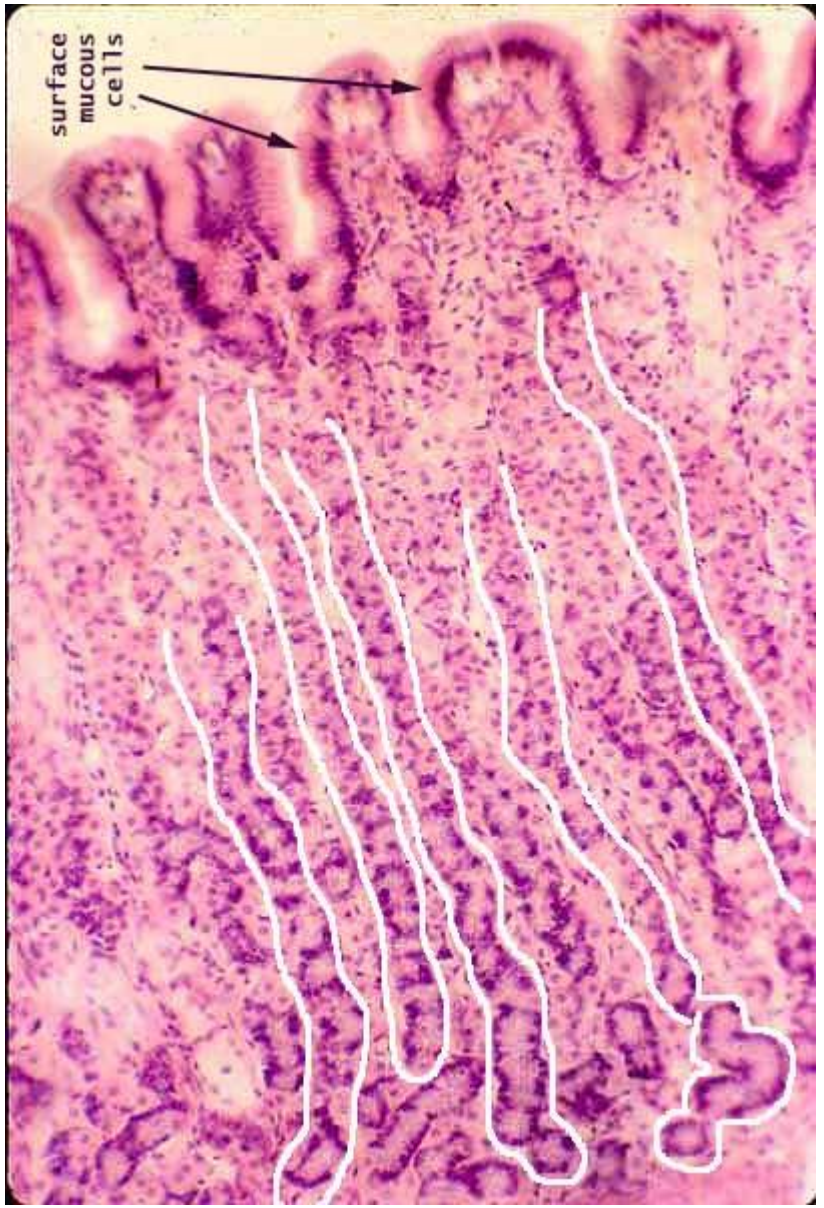
- **The mucosa**, formed by a simple columnar epithelium which is rich in mucosal glands (gastric glands, of various types), the lamina propria and the muscolaris mucosae.
- **The submucosa** (contains the submucosal plexus)
- **The muscularis propria** (three layers: oblique, circular, longitudinal)
- **The serosa** (peritoneum)

When empty, the inner walls of the stomach form gastric folds (indicating that the stomach can enlarge significantly when filled).





The stomach, through the gastric glands, secretes the **gastric acids**, which are crucial for **digestion** (particularly of **proteins**). This is achieved by the synthesis of pepsinogen, the precursor of pepsin. Pepsinogen is activated and transformed in pepsin by the acid envirnoment. Cells within the gastric glands produce both HCL (for the acid pH) and pepsinogen, toghether with hormones (gastrin) and mucus (to protect the cells of the mucosa from the acids secreted by the glands).



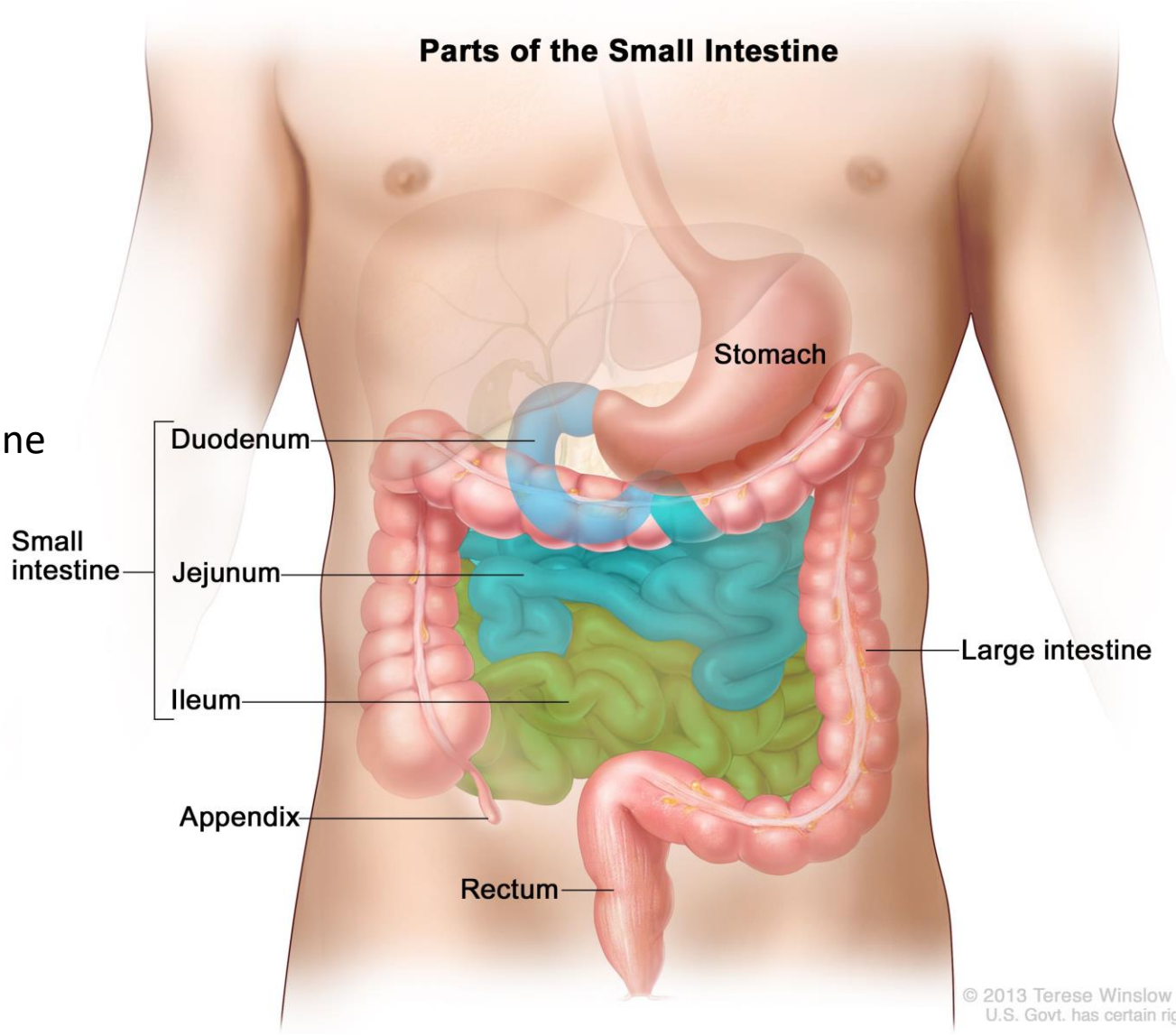
The Small Intestine

Formed by:

- **The duodenum**

- **The jejunum (digiunum)**
- **The Ileum**

} Mesenteric intestine

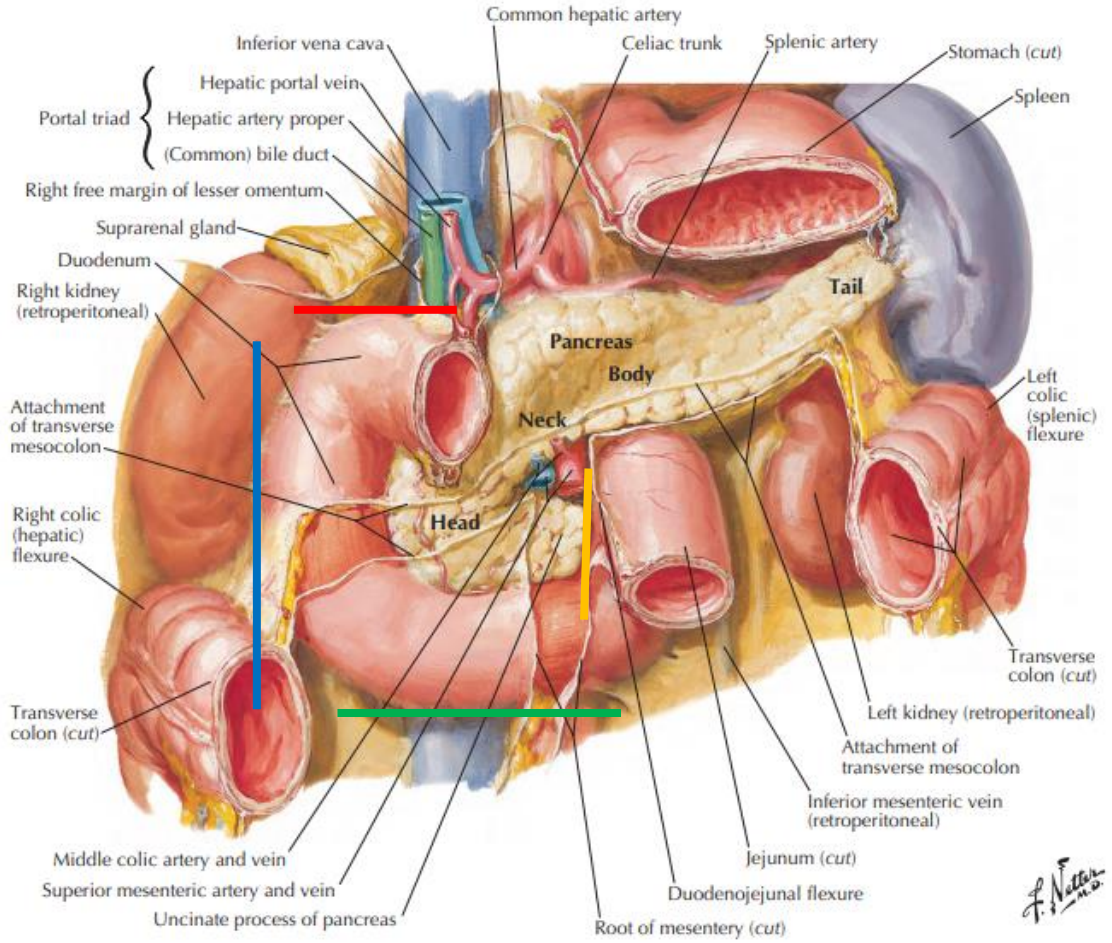


The Duodenum

It is the proximal part of the small intestine, which immediately follows the stomach and the pyloris. It presents a **<<C>>** shaped course that contours the head of the pancreas, bends forwards and forms the duodenal-jejunal flexure, where it continues with the jejunum.

It can be subdivided into four parts:

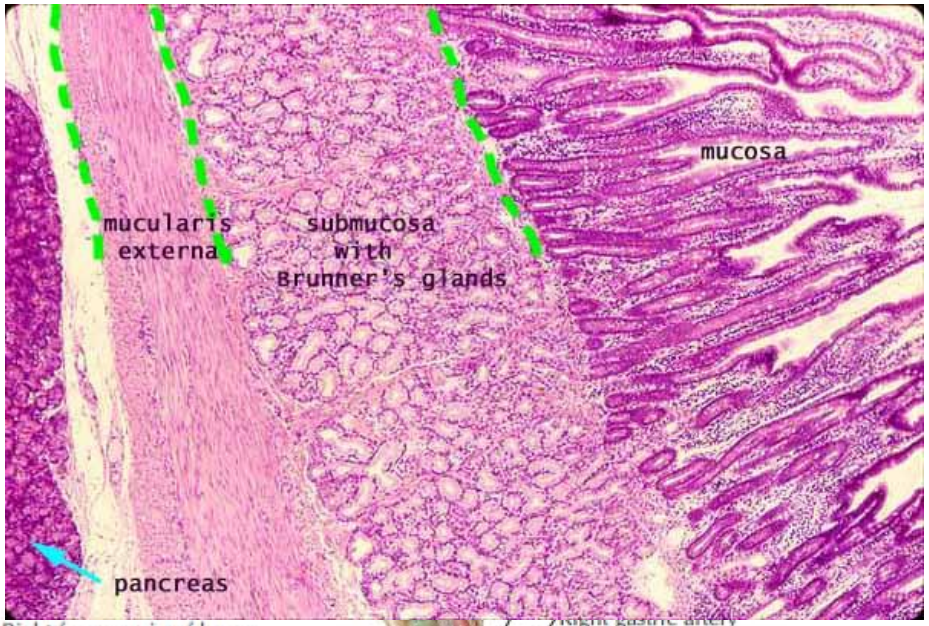
- **1° part:** follows the pyloris and is found inferiorly and posteriorly to the gallbladder. Is directed horizontally towards the right.
- **2° part:** descends downwards and is found anteriorly to the right kidney. Medially it is in relationship and borders the head of the poancreas (→ duodenocephalopancreasectomy)
- **3° part:** directed horizontally towards the left, anteriorly to the aorta and inferior vena cava.
- **4° part:** ascending, bends to form the duodeno-jejunal flexure.

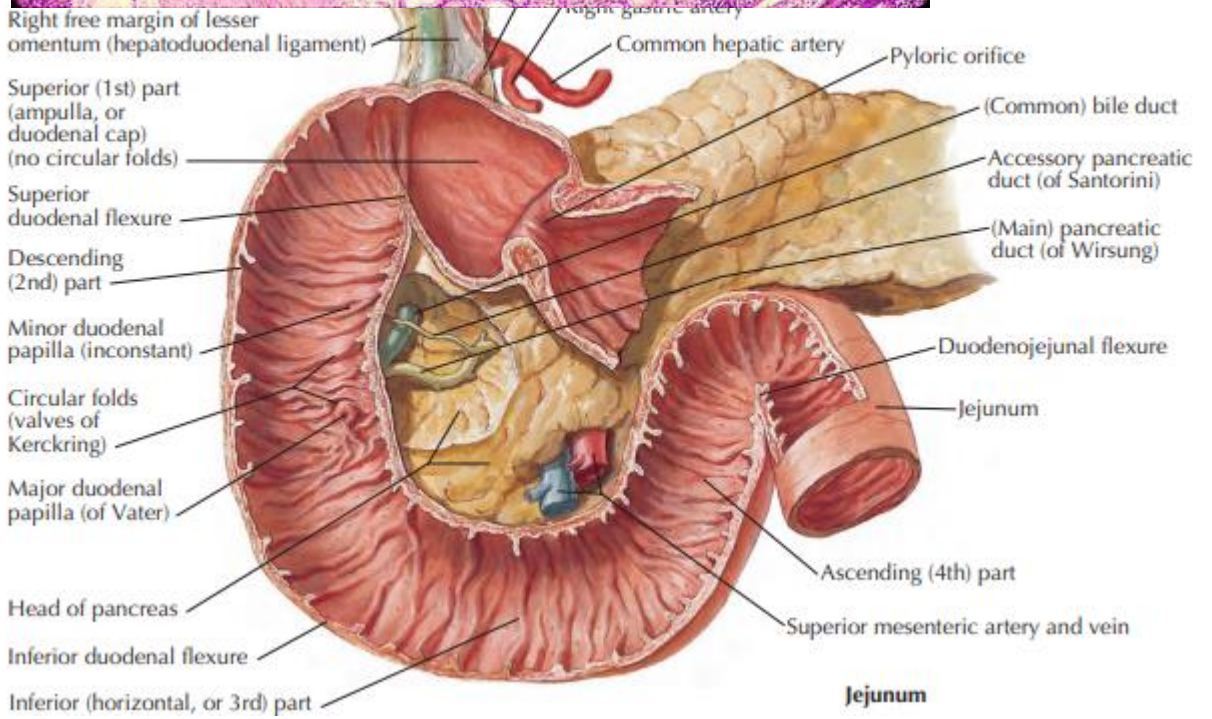


Similarly to the rest of the GI, the duodenum presents:

- **The mucosa**, whose main function here is to absorb nutrients. It presents a simple columnar epithelum (enterocites) and forms intestinal villi, which increase the absorption surface.
- **The submucosa**, with duodenal glands (Brunner's glands) producing mucus to lower the pH of the gastric acids coming from the stomach.
- **The muscolaris propria**: two layers: circular and longitudinal
- **The serosa** and (only in specific parts) the peritoneum.

The walls of the duodenum present, except of the first portion, **circular folds** (valves of Kerckring) which is given by the elasticity of the submucosa. This allows elasticity to the structure and flexibility of movement of the overlaying mucosa.



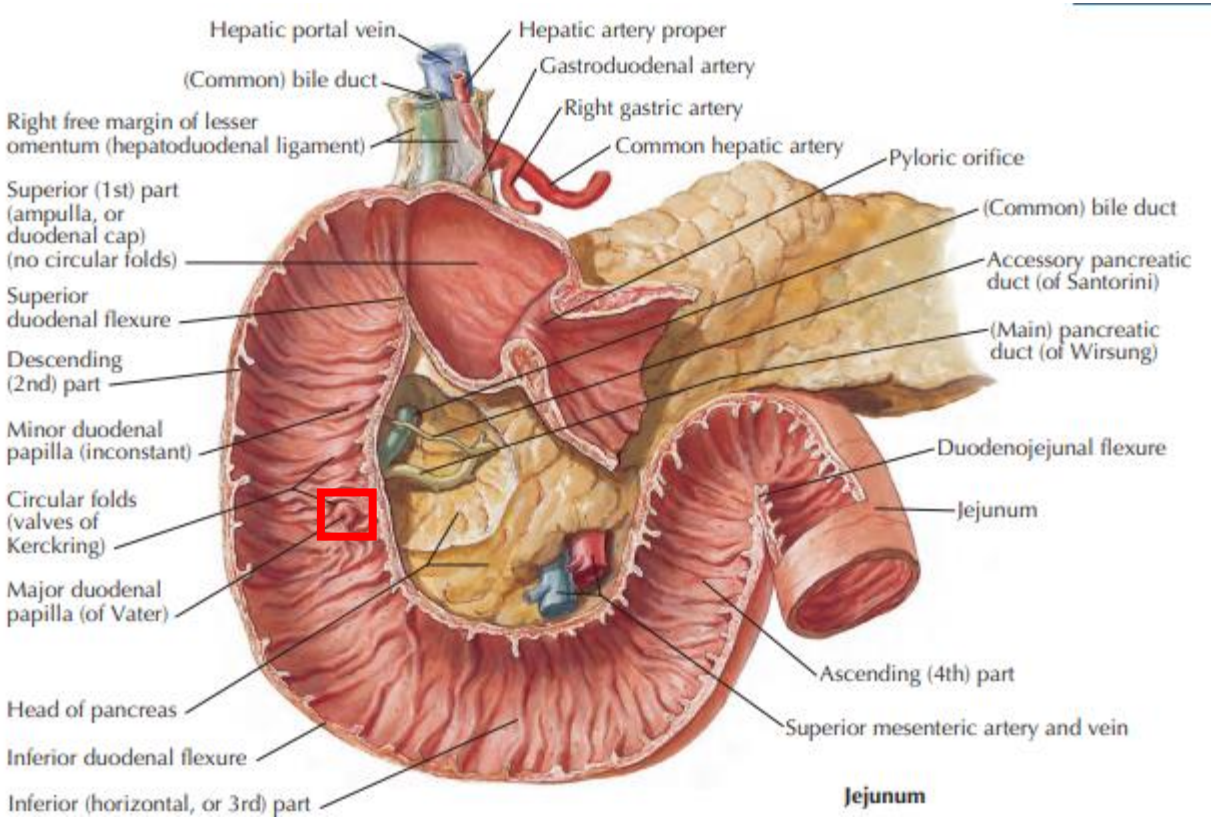


In the second portion of the duodenum, we find the duodenal papillae:

- The **main duodenal papilla** represents the point in which the 1) the bile duct and 2) the main pancreatic duct enter the duodenum and release the **Bile** (produced by hepatocites in the liver and accumulated in the gallbladder) and the **Pancreatic Juice** (secreted by the pancreas). The bile serves to emulsionate fat and fatty acids, while the pancreatic juice serves to further break down pepties into amminoacids.

- The secondary duodenal papilla (inconstant) that receives the accessory pancreatic duct.

Thus in the duodenum, **digestion is completed** while **absorption begins**.



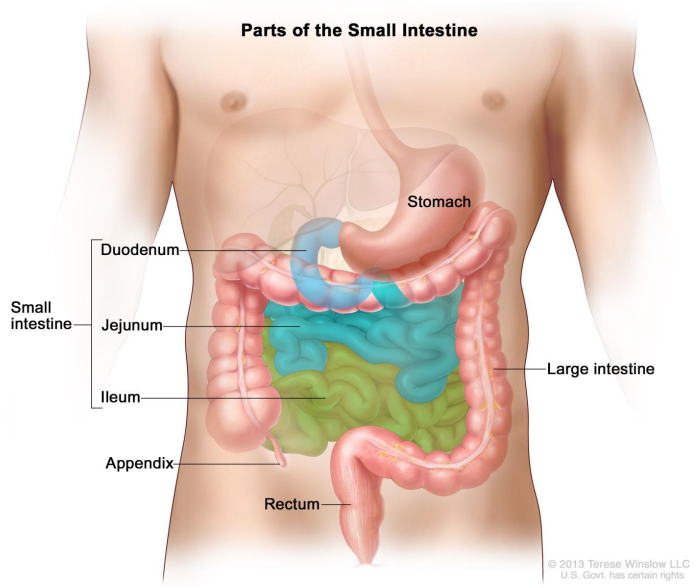
The Mesenteric Intestine

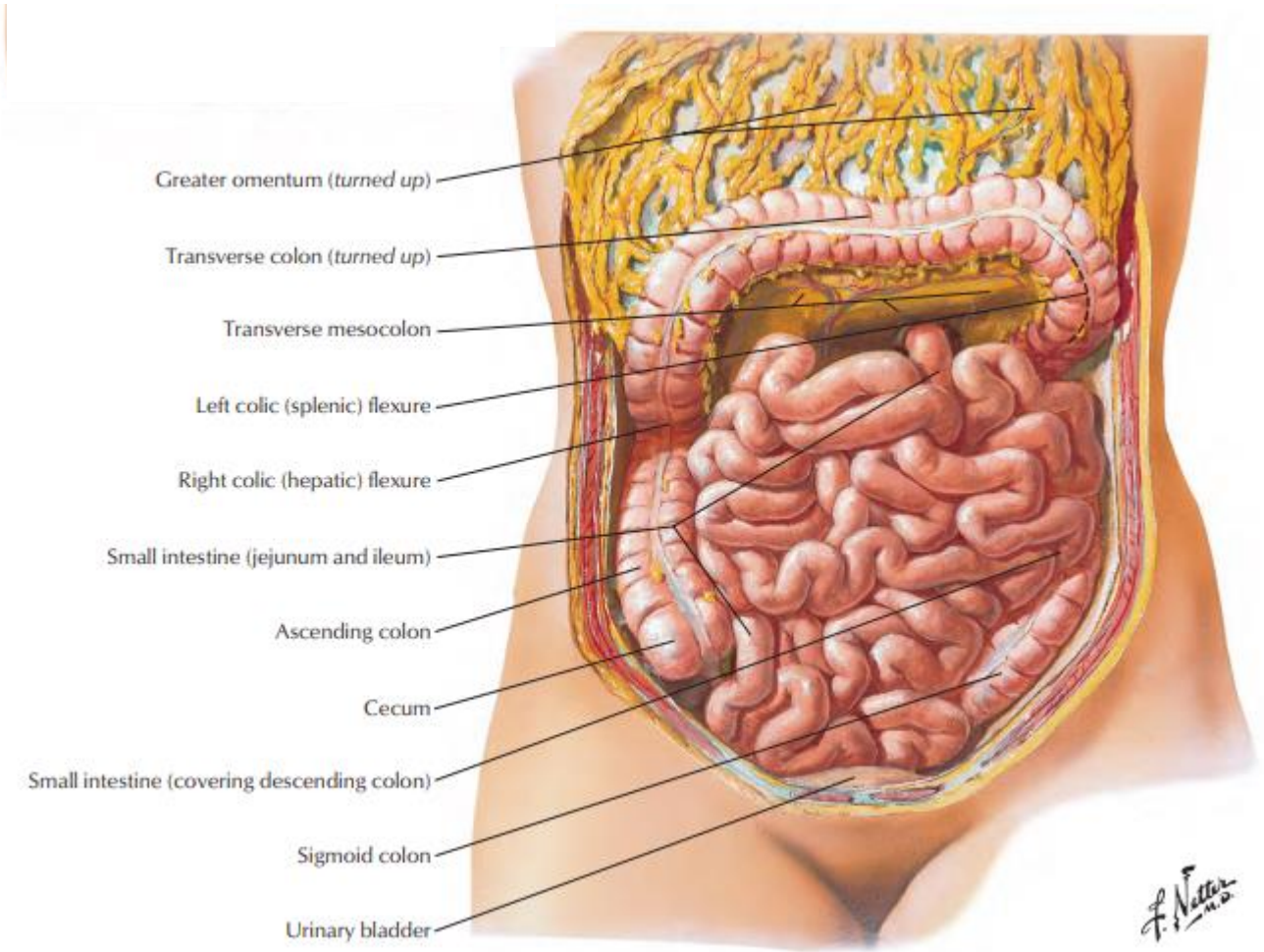
Jejunim and Ilum

Composed of two consecutive parts of 3-5 meters in lenght:

- **The jejunum** (latin: digiunum; means empty) that directly follows the duodo-jejunal flexure.

- **The Ileum**, that continues indistinctly from the jejunum and ends in the ileocecal joint at the level of the large intestine.



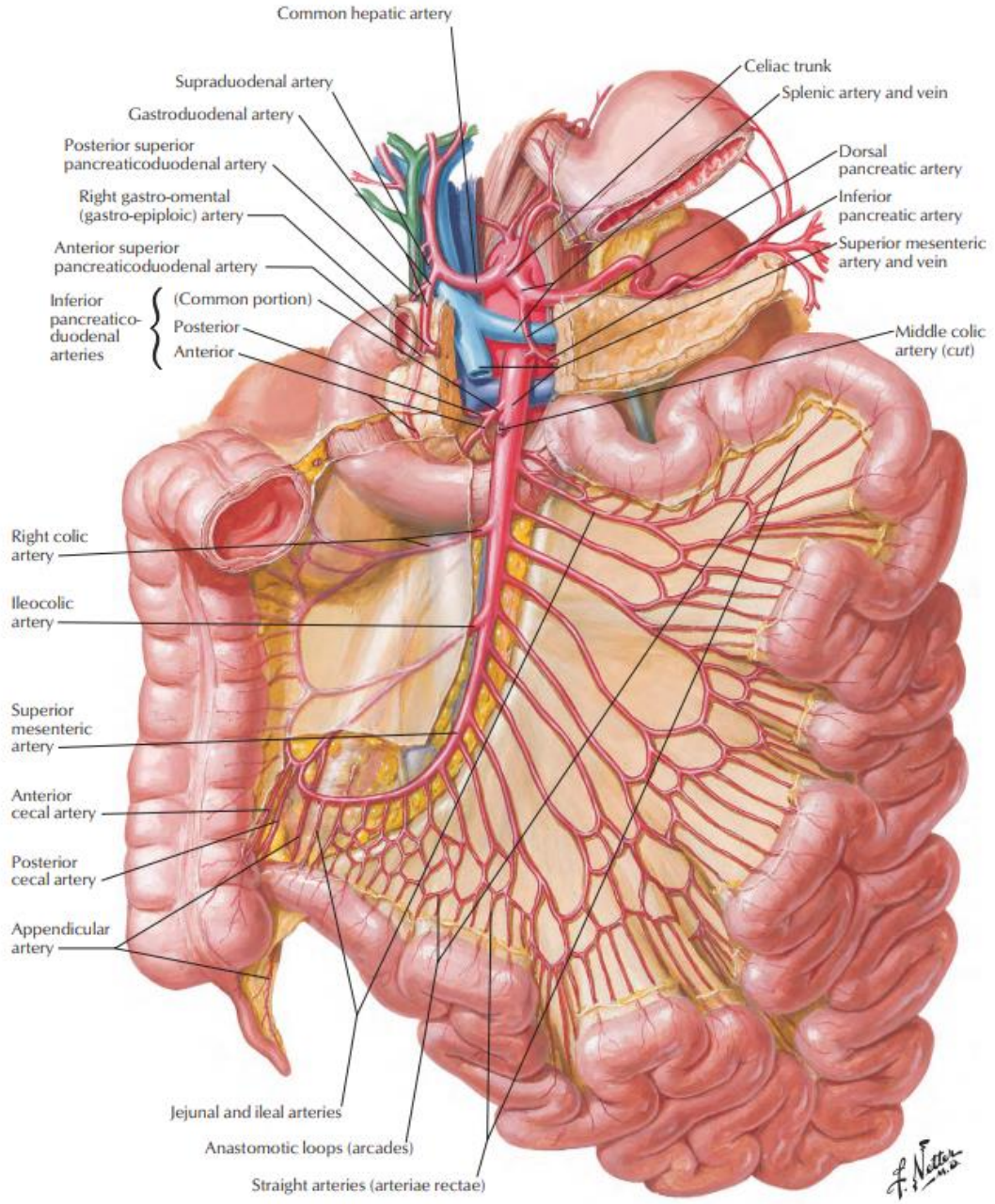


The Mesenteric Intestine

Jejunim and Ilum

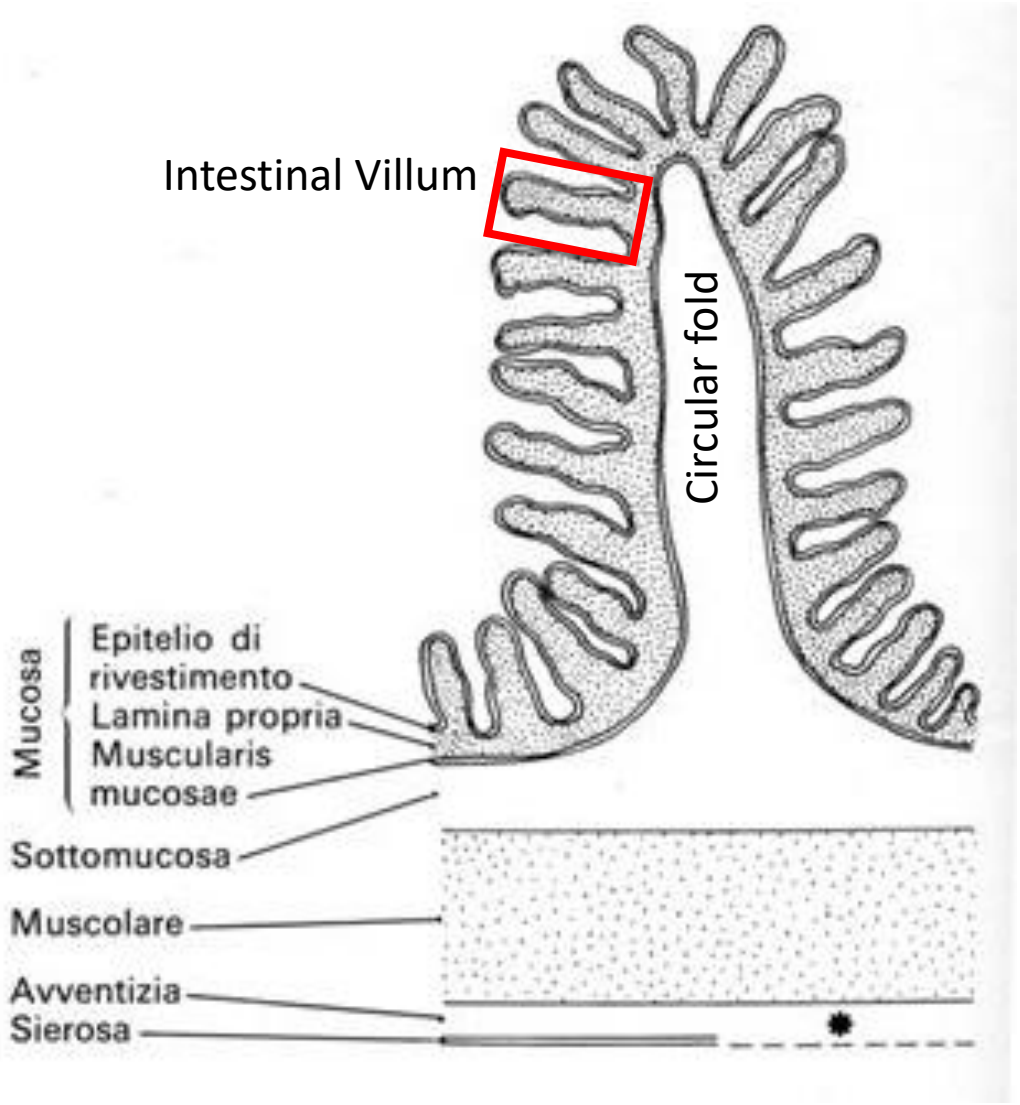
These two parts are known as mesenteric intestine because they are attached to the posterior abdominal wall through a lamina of connective tissue, known as **mesentery**.

The mesentery allows for a degree of mobility of the intestines, without risking twisting and turning (→ leading to ischemia and necrosis) and by keeping the intestinal turns in place. Furthermore, within the mesentery, the blood vessels that supply the small intestine are found (branches of the superior mesenteric artery).



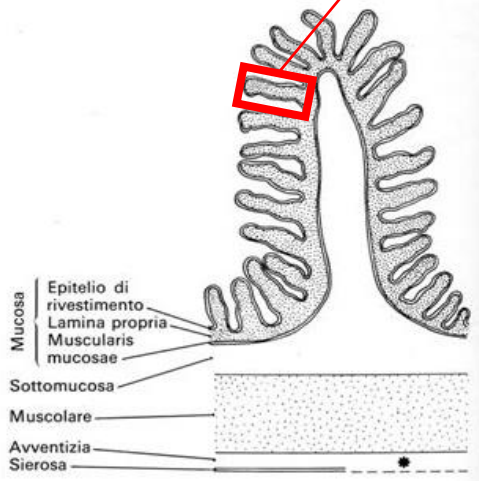
The microscopic anatomy of the small intestine is quite similar to the duodenum:

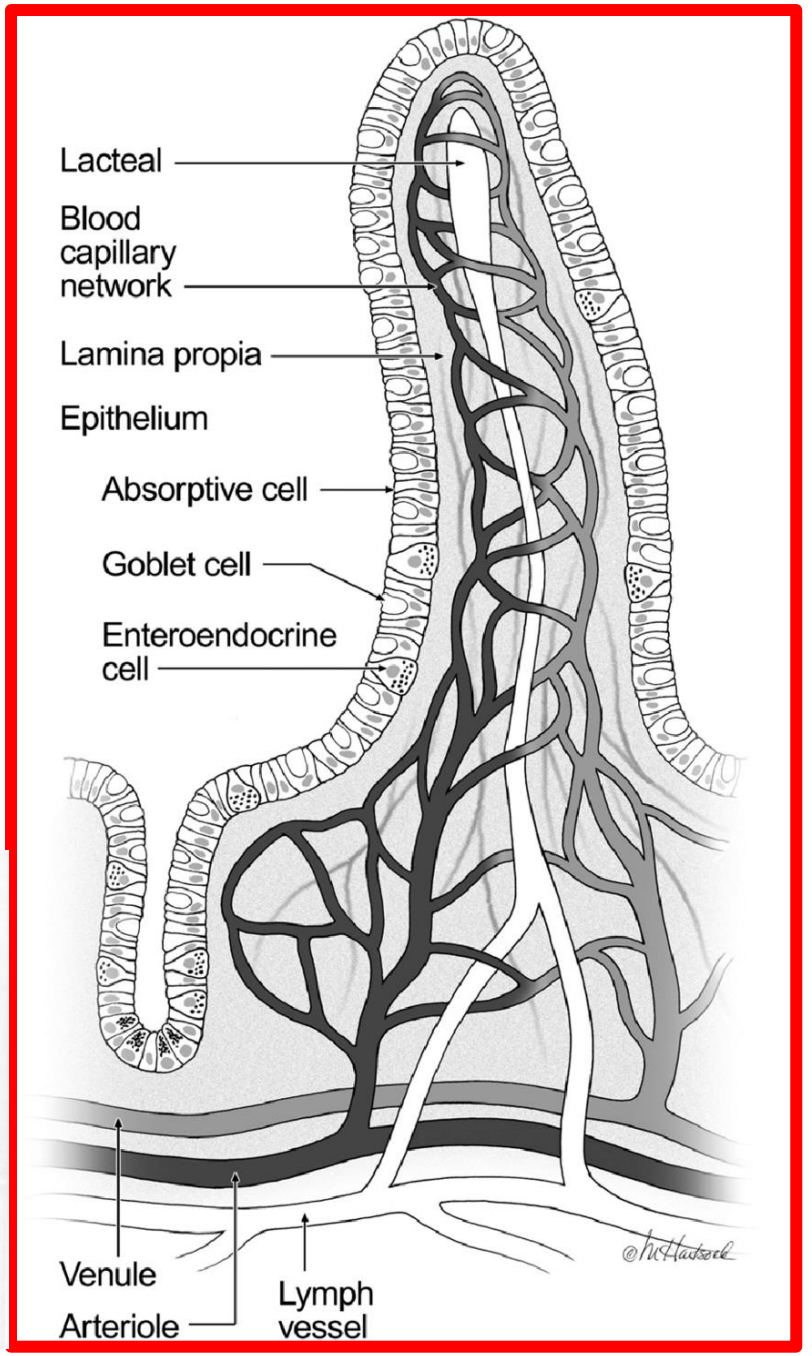
- **The mucosa** → absorb nutrients. It presents a simple columnar epithelum (enterocites and goblet cells) and forms intestinal villi, which increase the absorption surface.
- **The submucosa** containing the submucosa plexus (ENS) and often numerous lymphoid aggregates.
- **The muscolaris propria**: two layers: circular and longitudinal and the myenteric plexus (ENS)
- **The adventitia and serosa** of the peritoneum.



Intestinal villi are extroflexions of the mucosa (lamina propria) covered with epithelial cells (enterocytes and goblet cells). The presence of villi exponentially increases the absorption surface of the small intestine.

Within the thickness of the villi, we find arterious and venous blood vessels, as well as **lacteal ducts.** These are lymphatic vessels which collect fatty acids which are then distributed (as chilomicrons) to tissues through the lymphatic system.





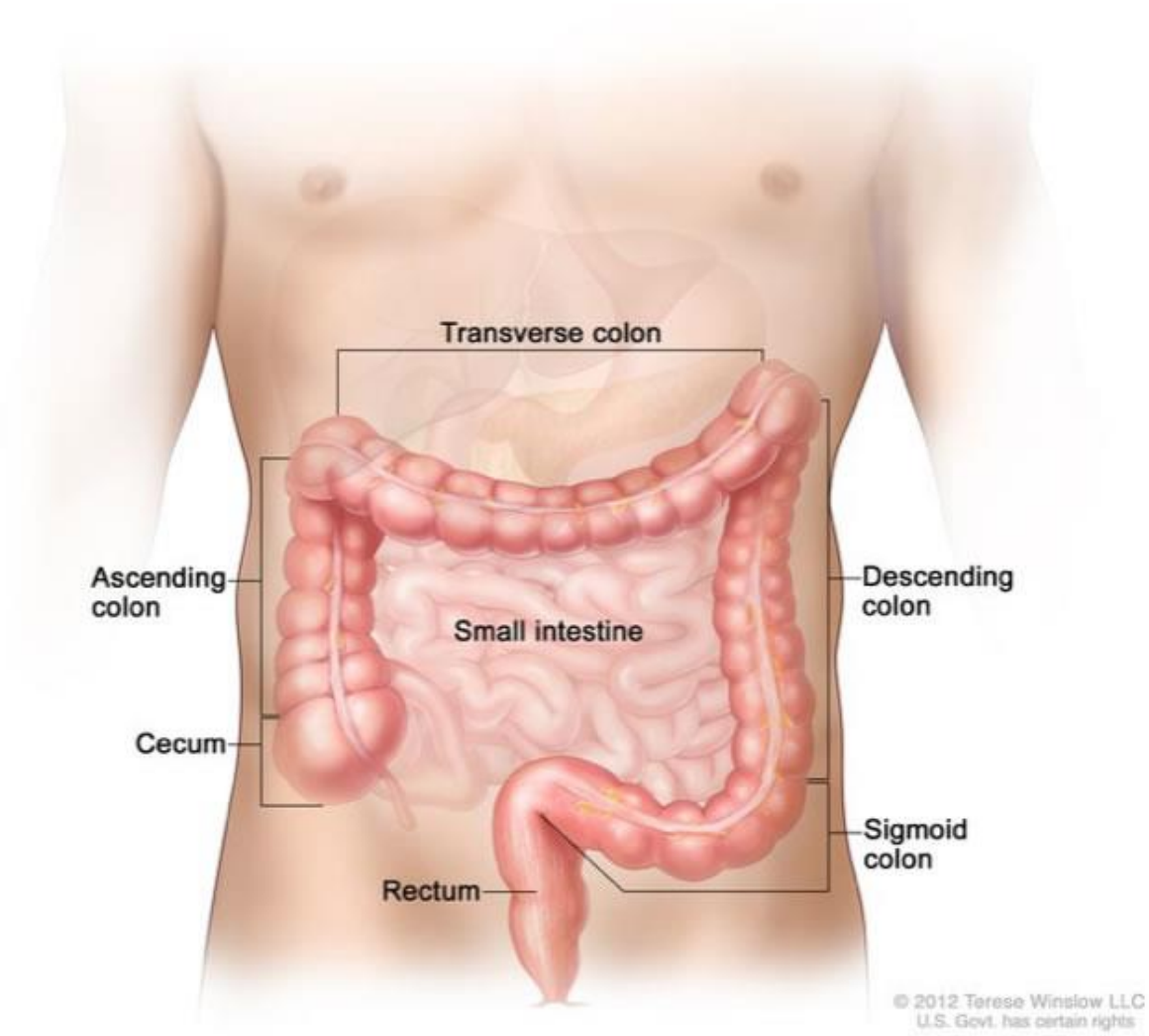
The Large Intestine

The large intestine is formed by the cecum, the colon and

Colon

The colon is the second part of the large intestine and is formed by three parts:

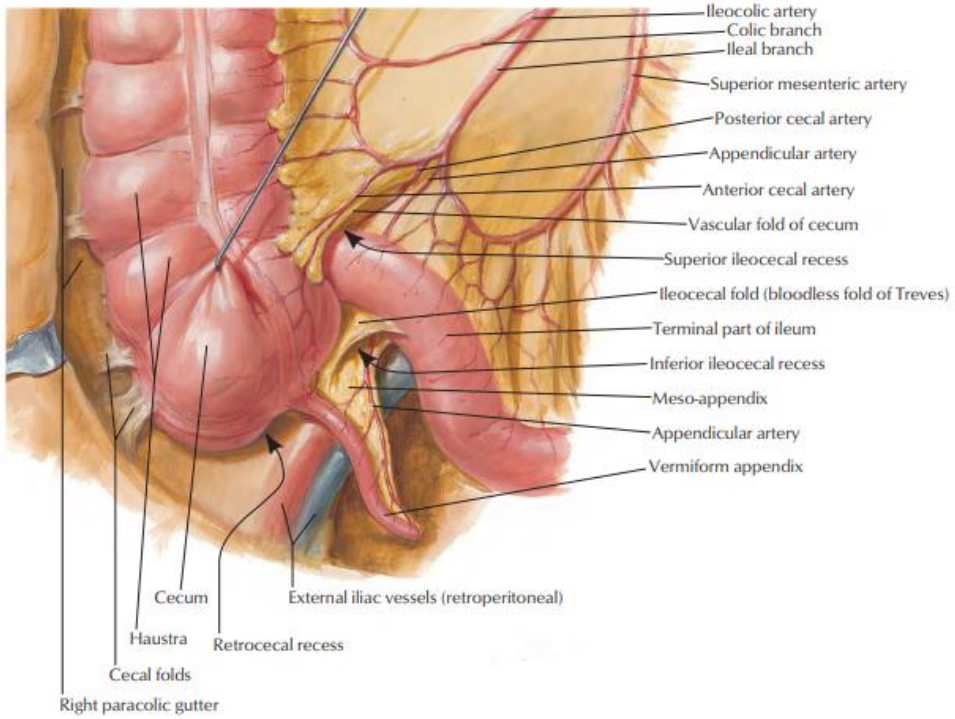
- **Ascending colon (right)**
- **Transverse colon**
- **Descending colon (left)**
- **Sigmoid colon (bending towards the pelvis).**

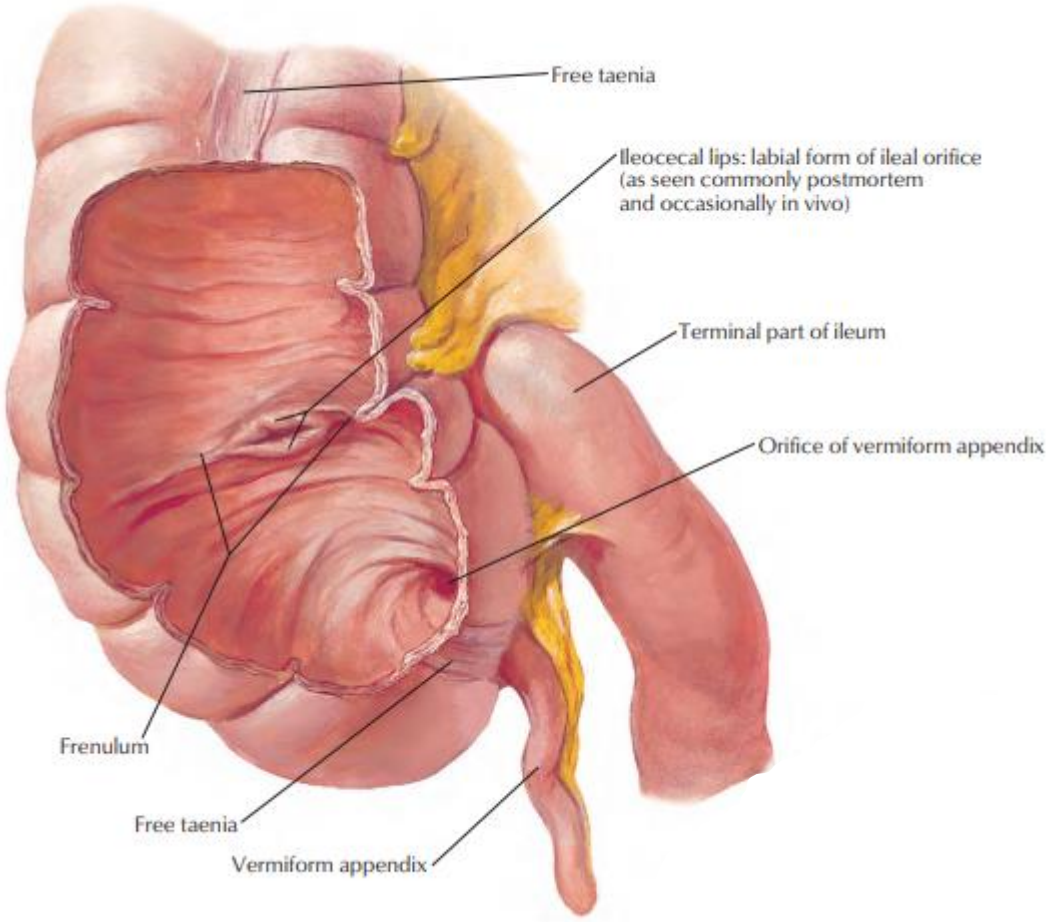


Cecum

The cecum is the first part of the large intestine, and is found in the right iliac fossa. It is separated from the ileum by the ileocecal valve.

It presents, at its posterior extermity, a 7cm long diverticulum known as the **appenidx**. This is a structure with prominent immune cell clusters in its wall and likely related to gut immune health.

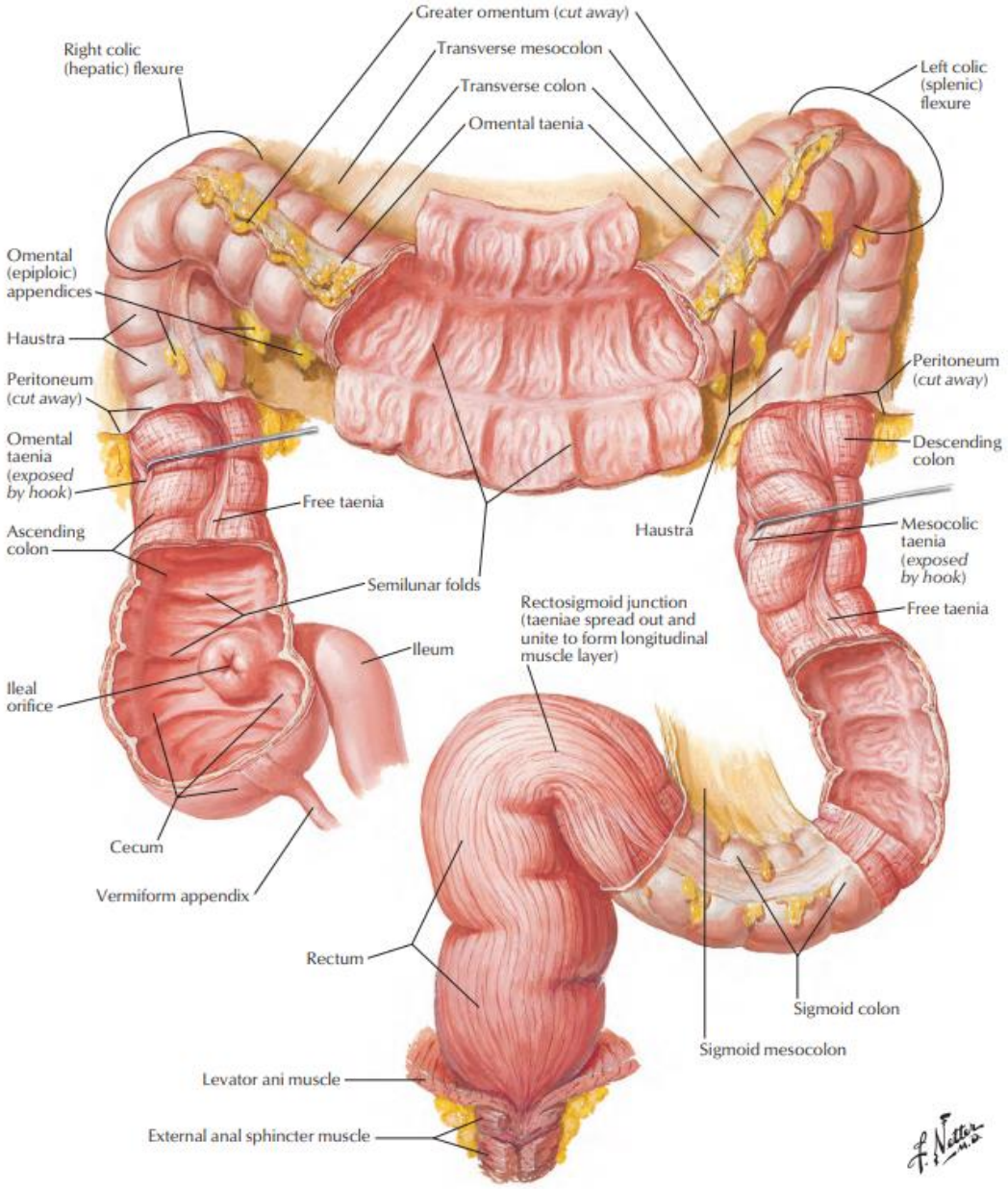




Colon

- It is characterized by a larger diameter than the small intestine.
- It presents three bundles of longitudinally oriented muscle fibers called **Taenia Coli** (because they are SIMILAR in appearance to the tapeworm → Taenia solium).
- It presents a bumpy appearance due to the presence, on the inside, of semilunar folds which divide the colon into segments called **Haustra Coli**.
- Unlike the small intestine, it does not present intestinal villi.

The main function of the colon is the absorption of fluids (mainly water) and the consolidation of faeces.



Colon

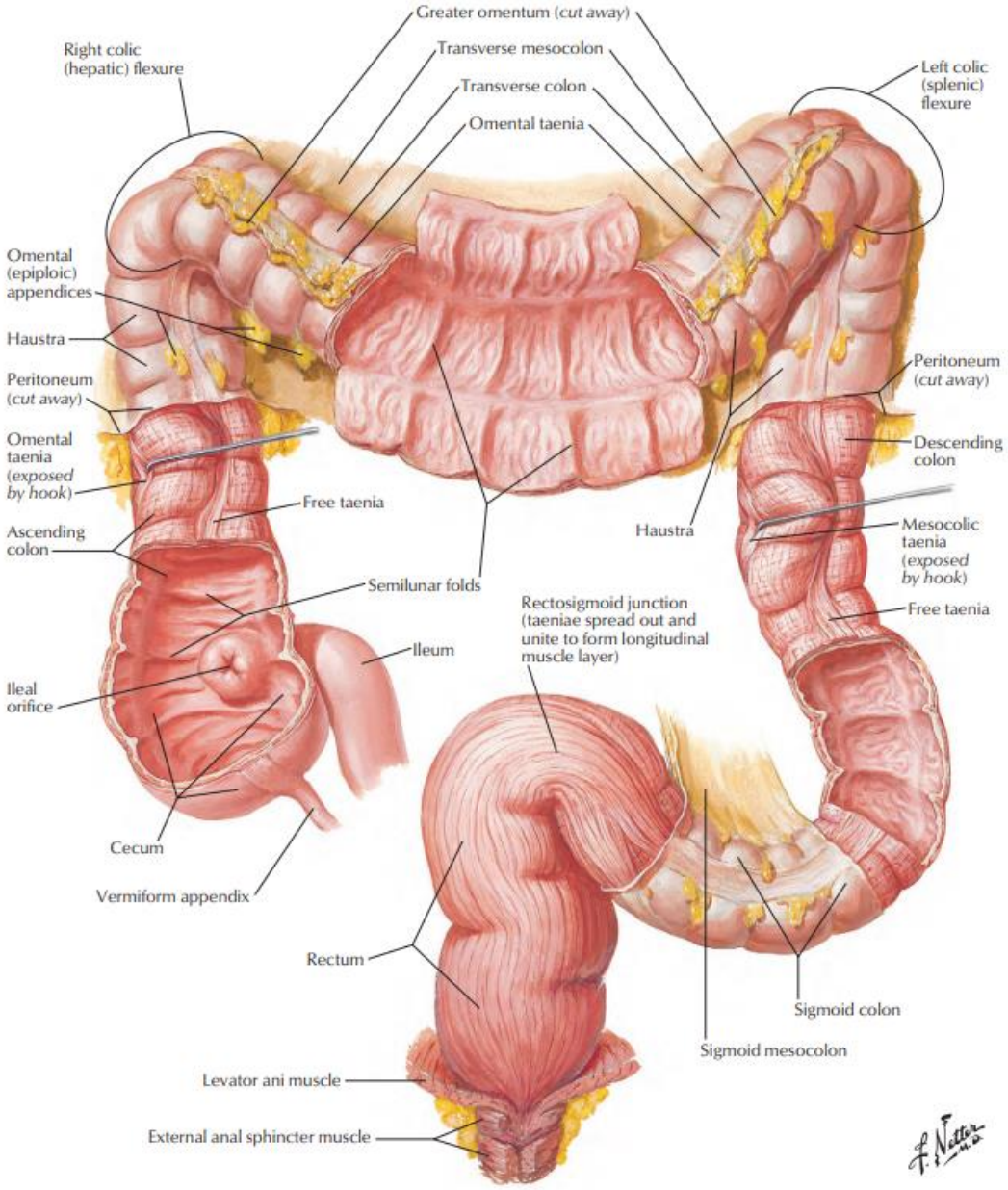
- **Ascending colon (right):** continues upwards from the cecum. Bends to the left (right colic flexure) at the level of the liver.

- **Transverse colon:** passes transversally below the stomach from the right colic flexure towards the left colic flexure (at the level of the spleen), where it bends downwards.

- **Descending colon (left):** descends from the left colic flexure towards the pelvis, where it enters the large pelvis to form the Sigmoid Colon.

- **Sigmoid colon (bending towards the pelvis):** presents an S shaped course from the large pelvis towards the small pelvis, then continues to from the rectum.

Each segment is attached to the posterior abdominal wall through a **mesocolon** which stabilizes the large bowel's position within the abdomen.

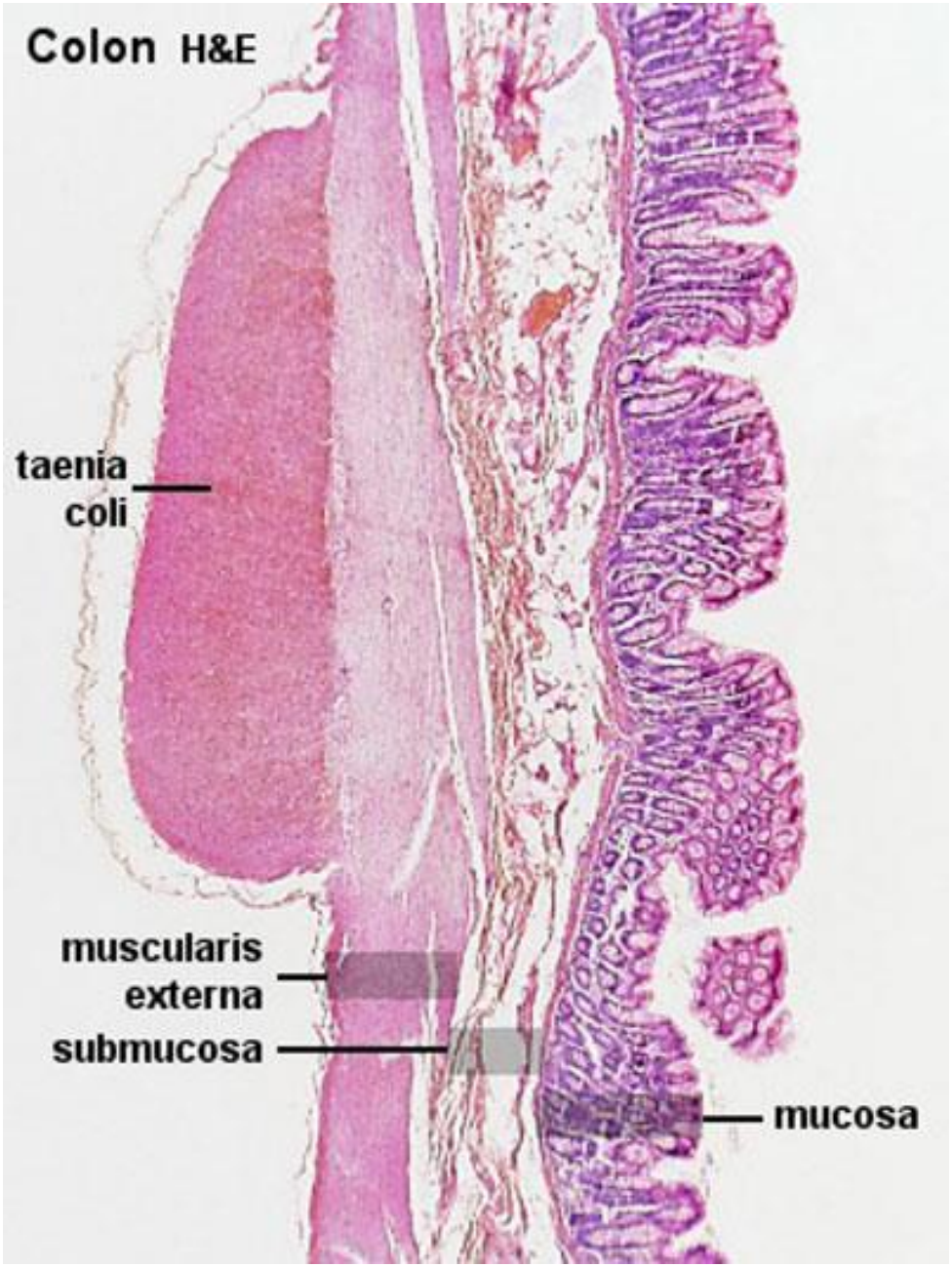


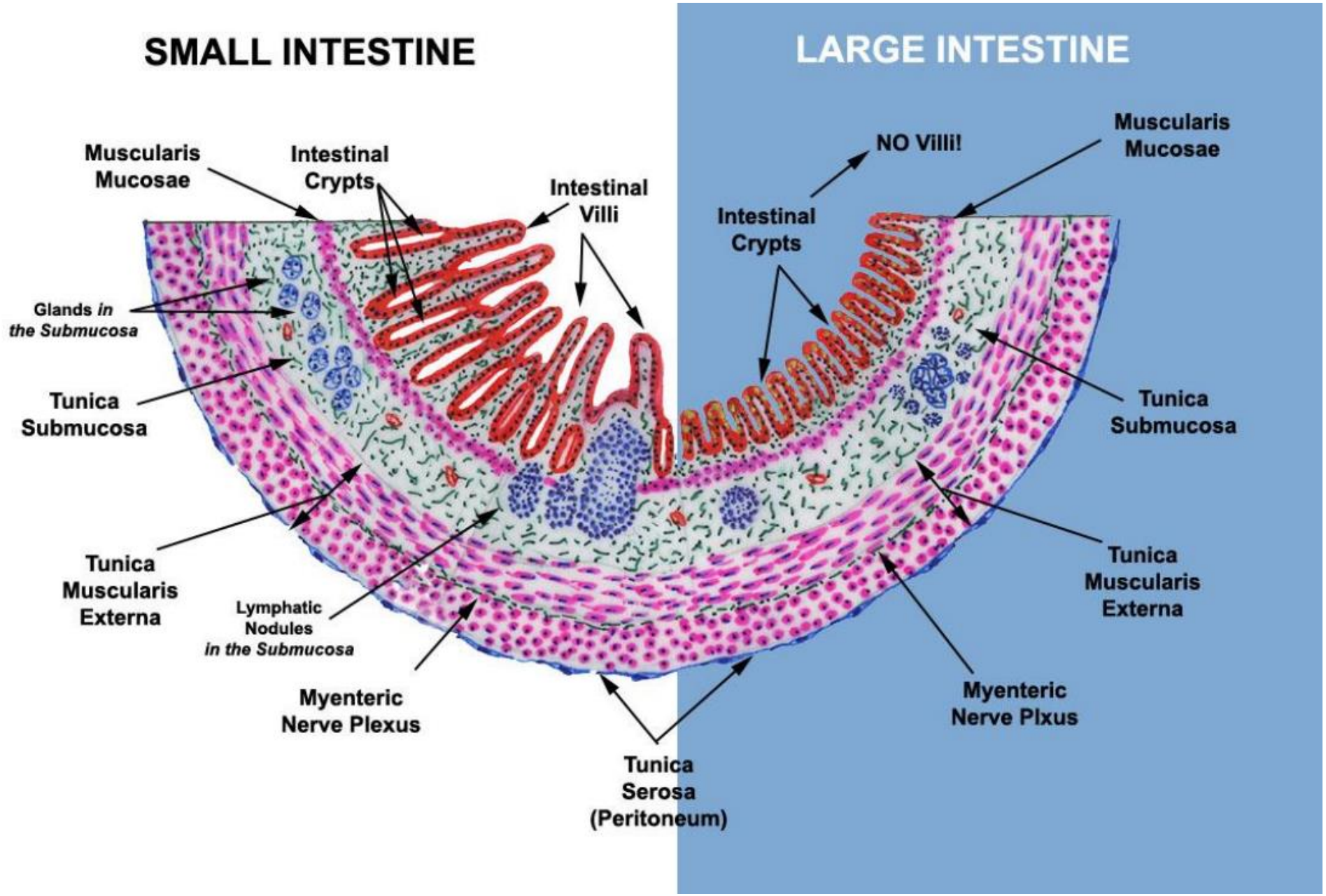
Colon

Similarly to the rest of the GI system, the colon presents:

- **The mucosa** without any intestinal villi. The epithelium is formed mostly by goblet cells which produce mucus, and by colonocytes (for fluid absorption). The epithelium presents numerous invaginations, known as **colonic crypts**.
- **The submucosa** contains often lymphoid aggregates (Peyer's Plaques) and the submucosal plexus (ENS).
- **The muscolaris propriae** has a well developed circular layer, while the longitudinal layer is present under the appearance of taenia coli. It contains the myeneteric plexus (ENS).
- **The adventitia and sierosa.**

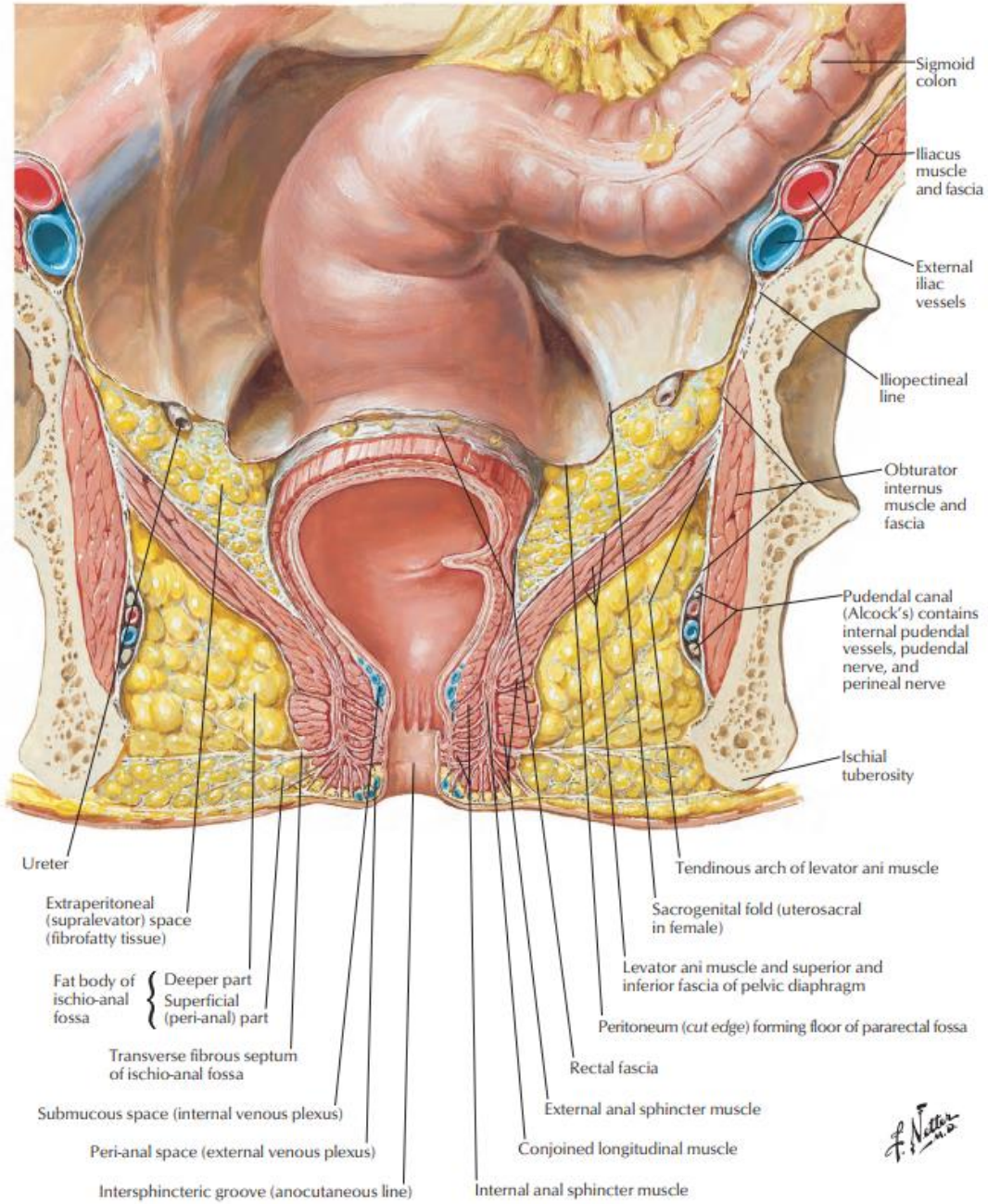
→ Gut flora and microbiota are relevant for gut health and function!




SMALL INTESTINE
LARGE INTESTINE
Muscularis Mucosae
Intestinal Crypts
Intestinal Villi
Glands in the Submucosa
Tunica Submucosa
Tunica Muscularis Externa
Lymphatic Nodules in the Submucosa
Myenteric Nerve Plexus
Tunica Serosa (Peritoneum)
NO Villi!
Intestinal Crypts
Muscularis Mucosae
Tunica Submucosa
Tunica Muscularis Externa
Myenteric Nerve Plxus

The rectum

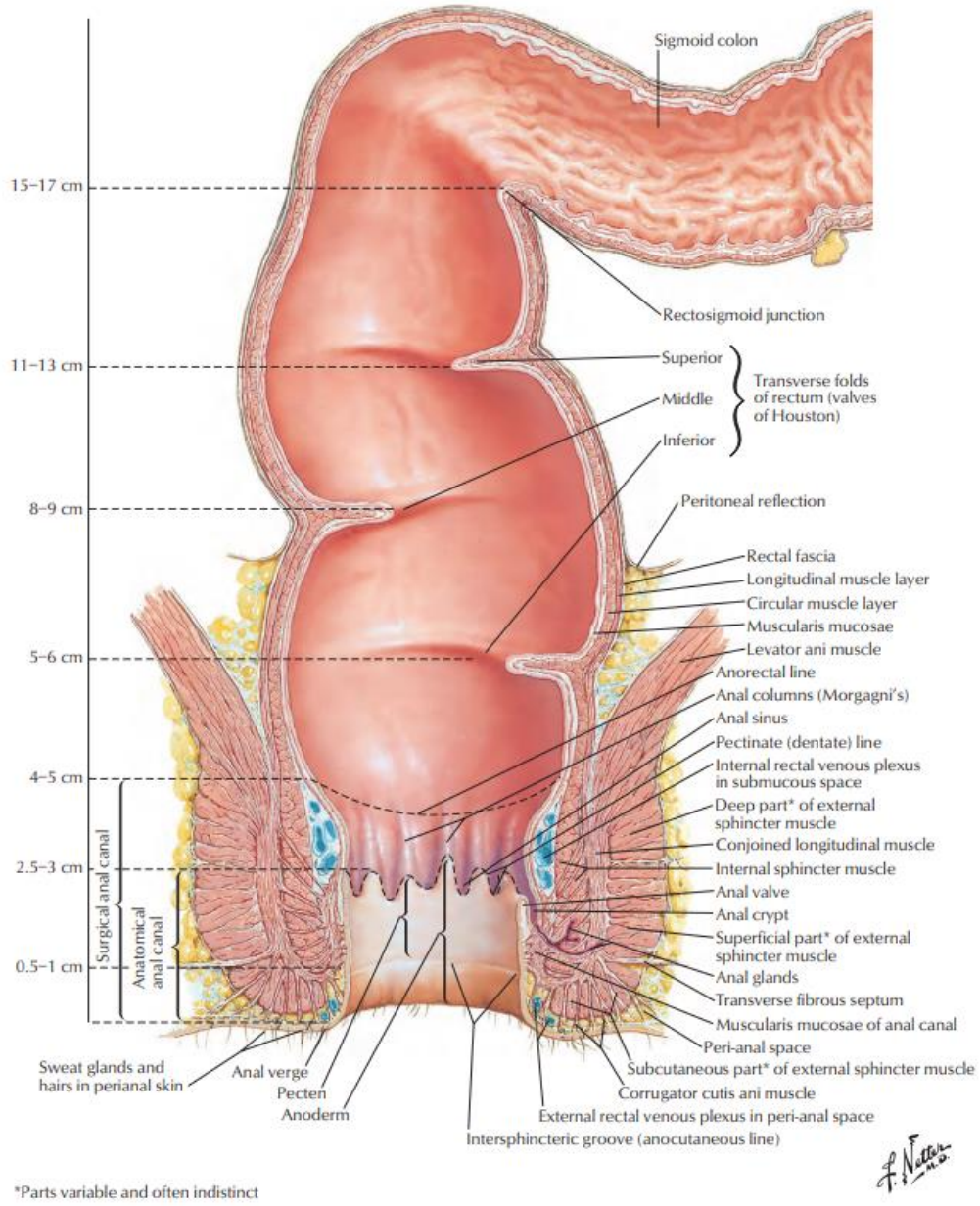
It is a straight structure (rectum → staight) that develops from the sigmoid colon within the small pelvis at the level of sacral promontory. It descends within the small pelvis and, at the level of the pelvic floor, continues with the **anal canal.** The latter is the lower portion of GI that taverses the pelvic floor and gives rise to the external orifice of the GI system, known as **anus.**



The rectum and the anal canal

The rectal ampulla : An elarged part within the small pelvis whose function is to store the faeces. Here we find three transverse folds (valves of Houston) which help to split the faeces into smaller parts.

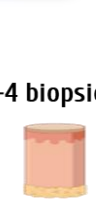
The anal canal: which acts as a conduit for the faeces towards the outside, culminating in the anus, passes within the muscles of the pelvic floor.
The internal and external anal sphincter, togheter with the muscles of the pelvic floor, serve to hold the faeces and control defecation.



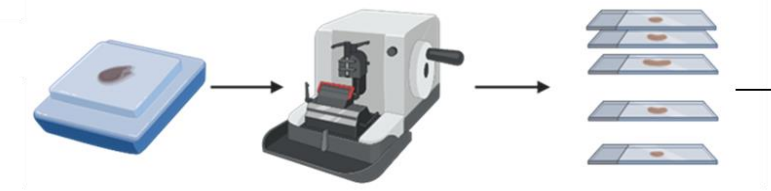
The Enteric Nervous System

In collaboration with Prof. Farinati and Prof. Russo (DISCOG - UNIPD)

3-4 biopsies



5-10 mg
2mm^3



Immunohistochemistry with antibody:
- 5G4 (specific for aggregated forms of α-synuclein)

Movement Disorders — Official Journal of the International Parkinson and Movement Disorder Society

Letters: New Observations | Full Access

α-Synuclein antibody 5G4 identifies manifest and prodromal Parkinson's disease in colonic mucosa

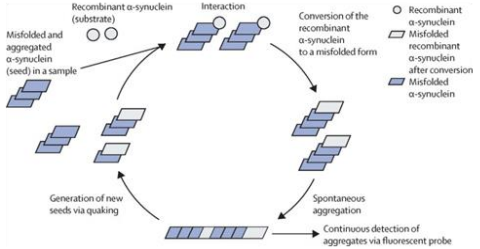
Matej Skorvanek MD, PhD, Ellen Gelpi MD, PhD, Eva Mechirova MD, PhD, Zuzana Ladomirjakova MD, Vladimir Han MD, Norbert Lesko MD, Eva Feketeova MD, PhD, Barbora Repkova MD, Zuzana Urbancikova MD, Adriana Vargova MD, Peter Spisak MD, Joaquim Ribeiro Ventosa, Filip Kudela, Kristina Kulcsarova, Simona Babinska, Stefan Toth MD, PhD, Laura Gombosova MD, PhD, Maria Zakuciova MD, Eduard Veseliny MD, PhD, Frantisek Trebuna MD, PhD, Mirjam I. Lutz PhD, Zuzana Gdovinova MD, PhD, Gabor G. Kovacs MD, PhD, the PARCAS studygroup

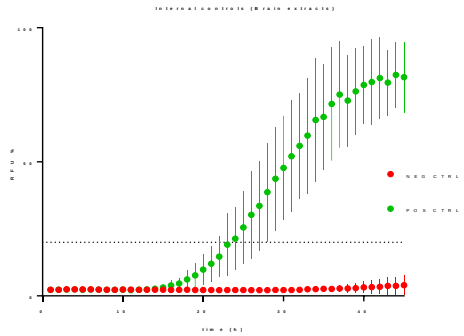
First published: 19 September 2018 | https://doi.org/10.1002/mds.27380 | Citations: 3

N2 Frozen and
stored at -80°C

Mechanical homogenization in PBS and proteinase inhibitor, sonication

RT-QuIC assay





REAL-TIME QUAKING-INDUCED CONVERTION (RT-QuIC) ASSAY TO PROPAGATE POLYMERIZATION FROM α-SYN PATIENT SEEDS
(in collaboration with Prof. Parchi – ISNB/UNIBO)

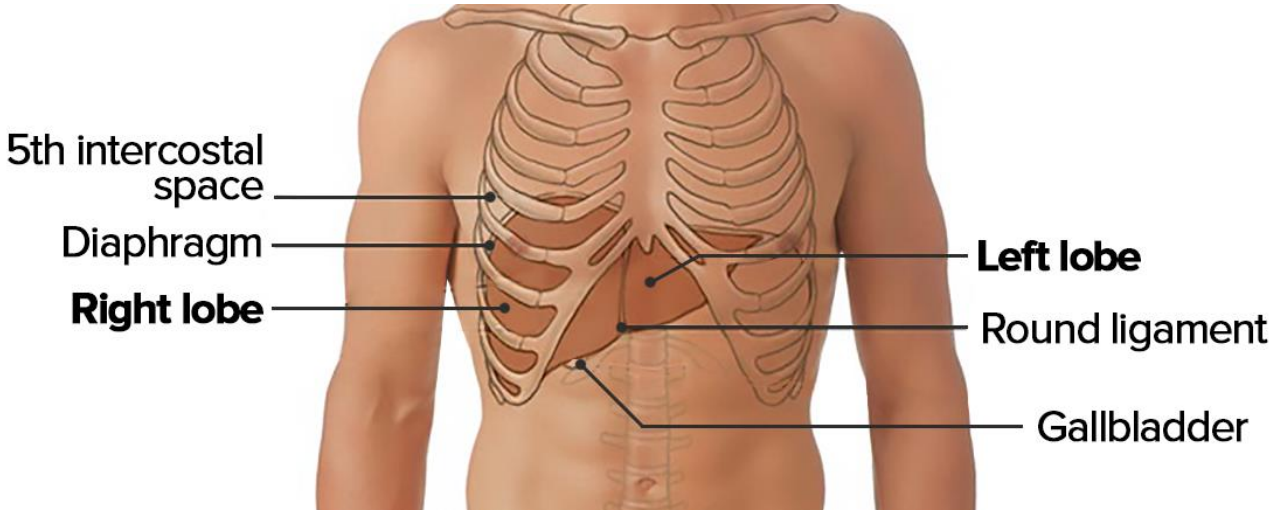
Emmi et al., 2023

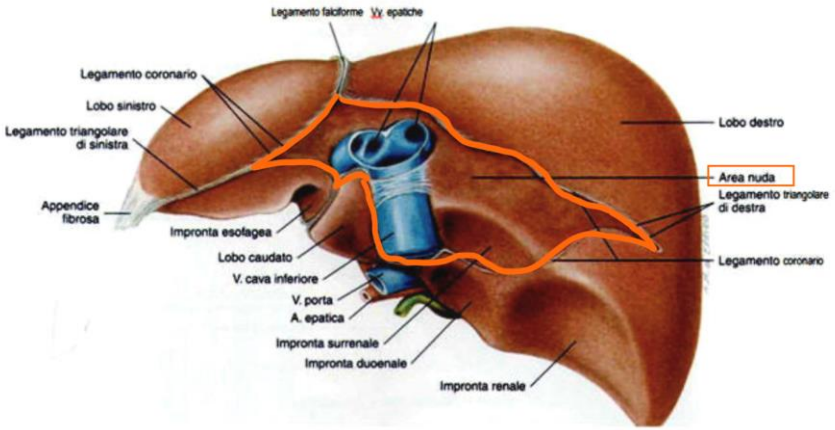
Movement Disorders
Official Journal of the International Parkinson and Movement Disorder Society

Liver and Pancreas

The extramural glands

The Liver





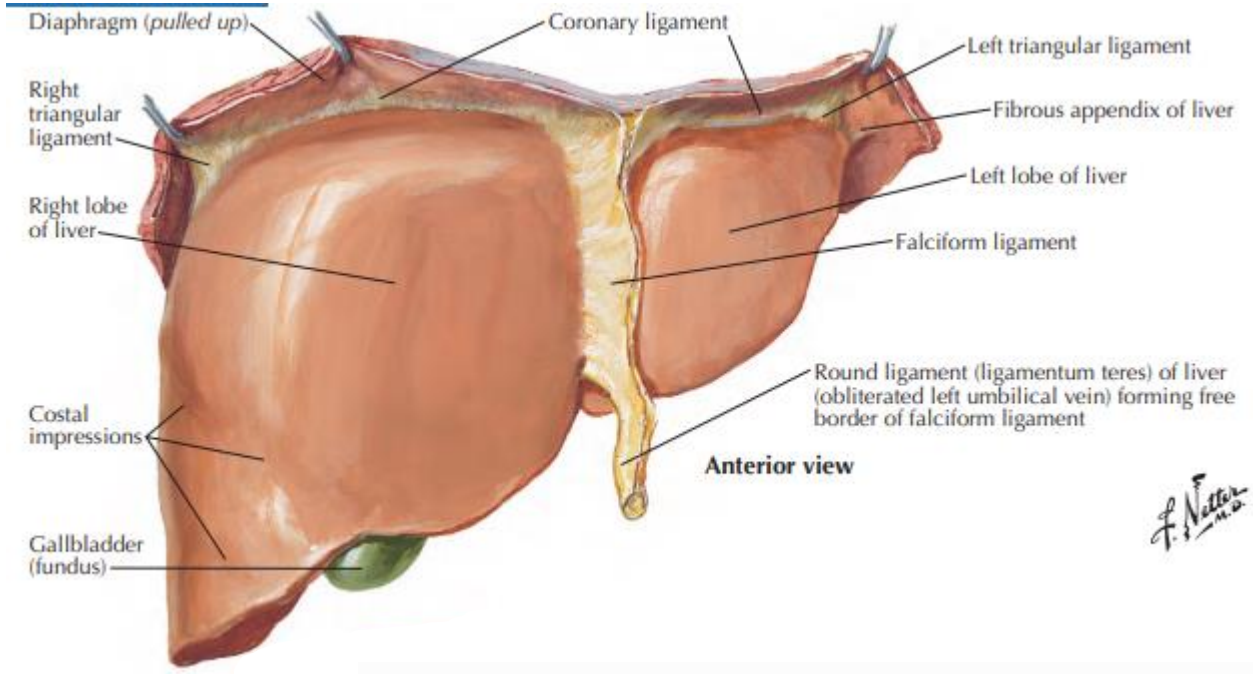
The liver is the biggest **gland** of the human body (average weight 1.5kg). It is found in the superior right quadrant of the abdomen; superiorly it broders with the diaphragm, which covers most of it superior surface. On the right and below it borders with the stomach and, partially, with the colon (right colic flexure). Posteriorly it borders with the thoracic vertebral column.

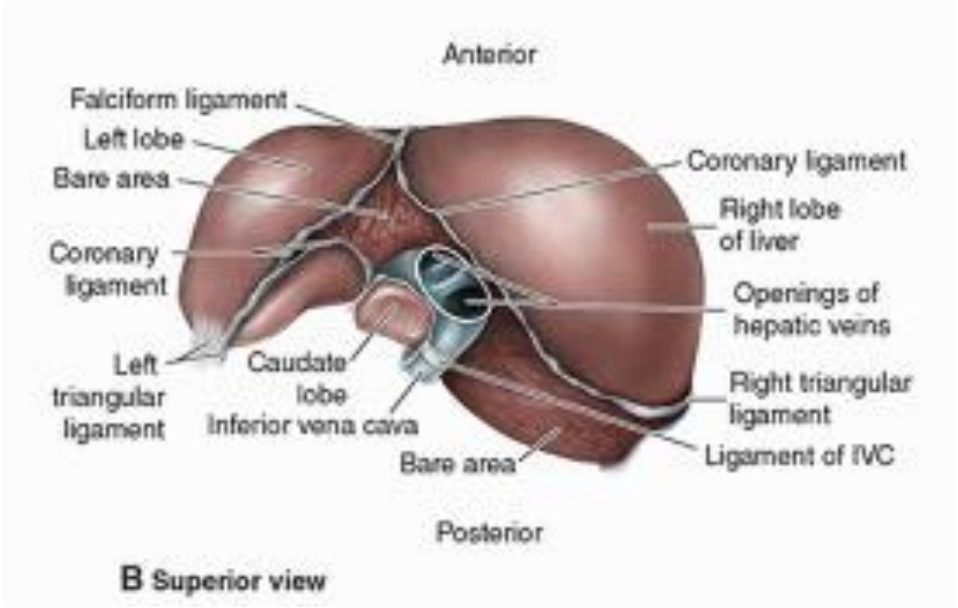
For most of its extention, it is covered by the **ribcage.**

It is covered by the peritoneum and by a capsule of connective tissue, known as **Glisson's capsule**. The only exception is a region below the diaphragm, known as bare area of the liver.

The liver is a **parenchymatous organ** (full organ) with a brown-reddish color and an approximately triangular shape.

Anteriorly, the falciform ligament, which connects the liver to the anterior abdominal wall, separates the liver into the **right and left lobe**. The falciform ligament continues upwards into the **coronaric ligament**, which attaches the liver to the diaphragm. Below, the falciform ligament is strenghtened by the passage of the **round ligament of the liver** (a residue of the fetal ombilical vein).





Posteriorly, the liver's surface is in relationship with the stomach, small intestine, right kidney and right part of the colon. At this level, the **Hilum of the liver** is found, which represents the entry/emergence point for:

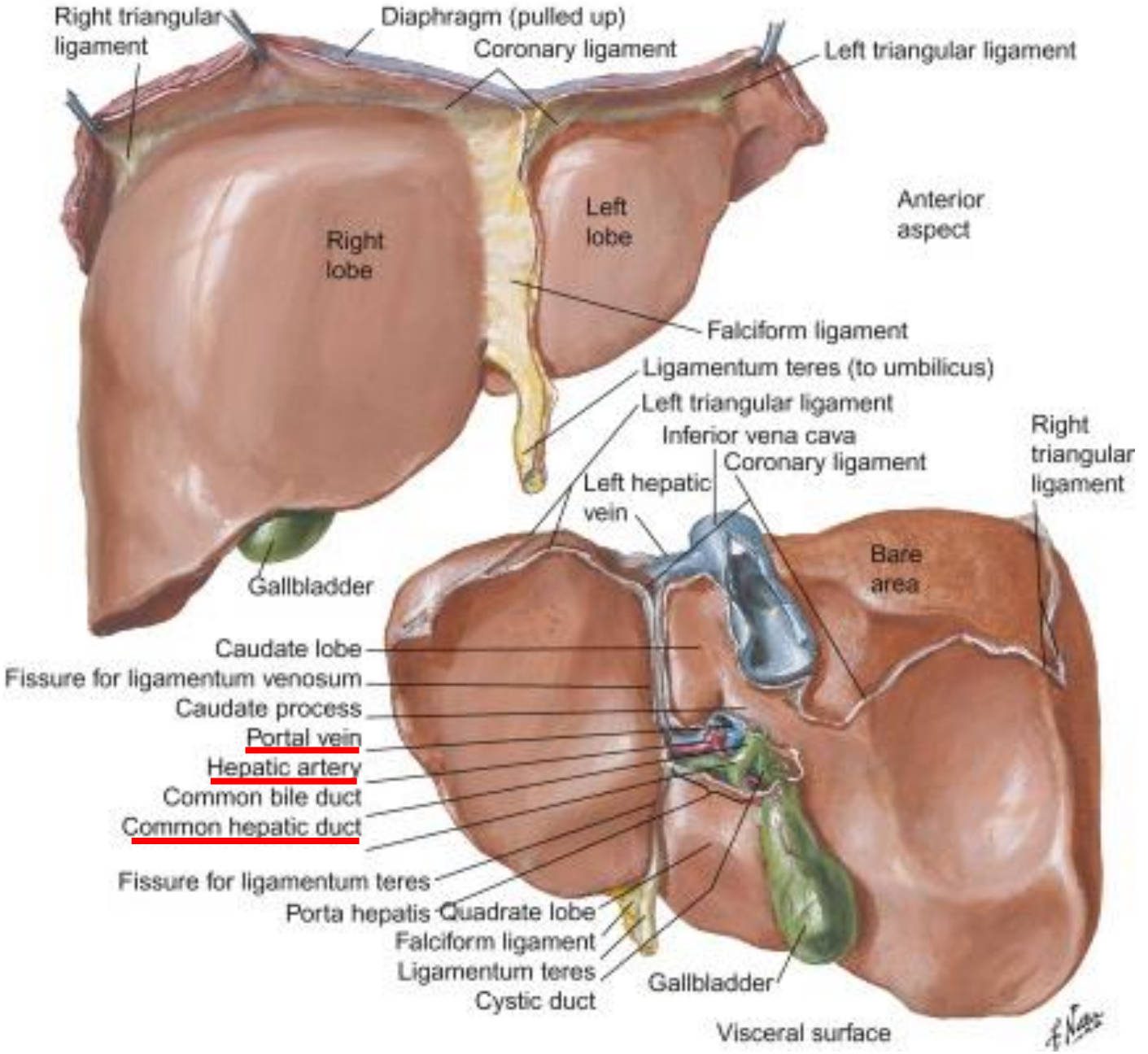
- **The hepatic artery**
- **The portal vein**
- **The hepatic duct**

Which are togheter known as **Portal Triad.**

Aside of these structures, the posterior and inferior surface of the liver allows to identify **two more lobes:**

- **The Caudate lobe** (to the left of the inferior vena cava)
- **The Quadrate lobe** (left to the gallbladder).

As well as the **Gallbladder**, which is annexed to the hilum and rests upon the inferior surface.



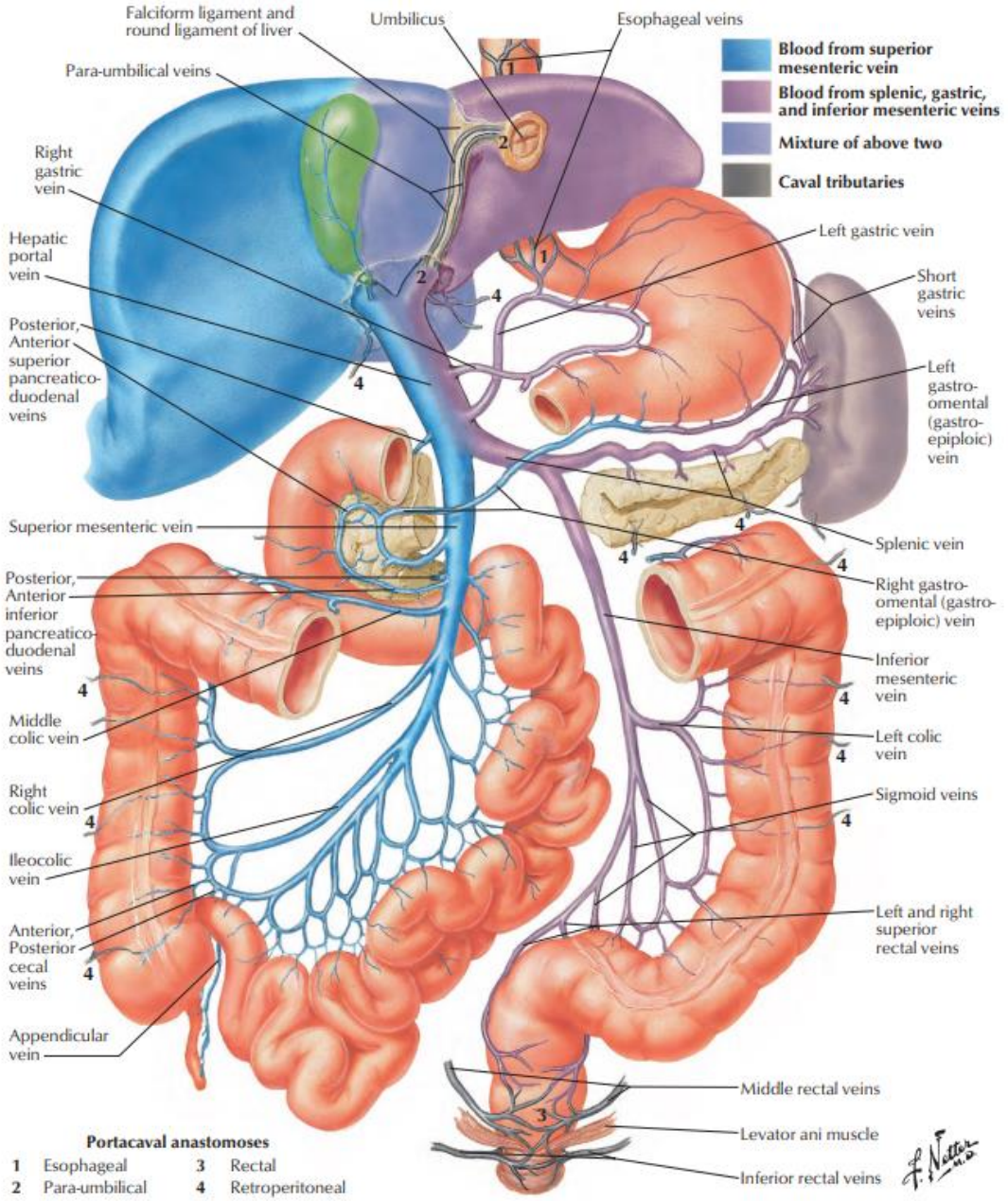
PORTAL CIRCULATION

The liver receives blood from the hepatic artery (1/3) and from the portal vein (2/3). The latter collects the blood from:

- Superior mesenteric vein
- Inferior Mesenteric vein
- Splenic vein

Therefore, it **transports the blood coming from the gastrointestinal system**. → the portal vein DOES not drain blood away from the liver, but brings blood to it! This allows the liver to convert, store and excrete the substances absorbed by the intestine (e.g. toxins).

The true drainage system of the liver are the **hepatic veins**, which convey the venous blood from the liver to the inferior vena cava.

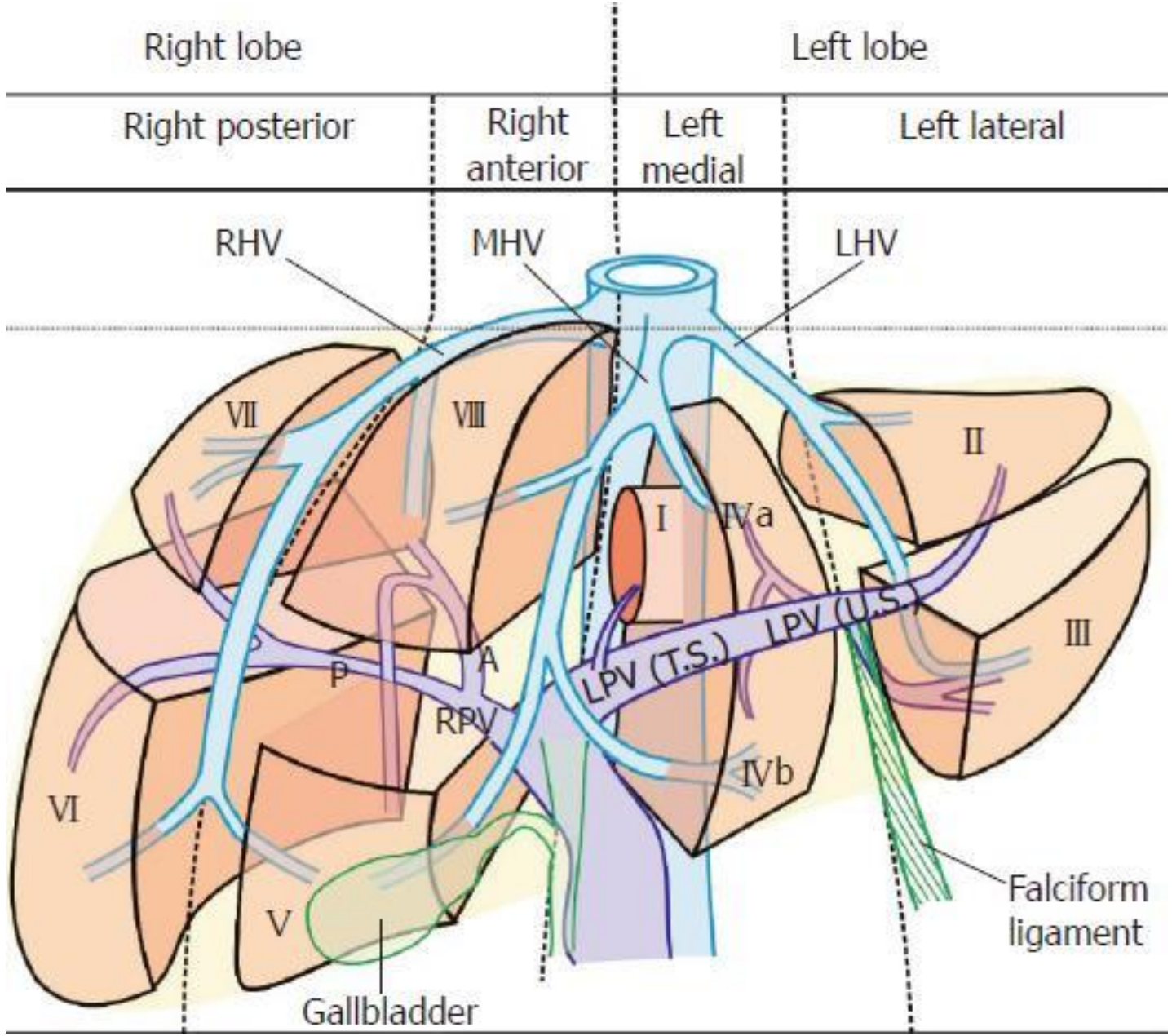


The liver is macroscopically subdivided into:

- **Lobes** (right, left, caudate, quadrate) (this is an anatomical subdivision by the ligaments, but has no functional significance!)
- **Sectors** (divided by the hepatic veins)
- **Segments** (divided by branches of the portal vein).

This is important for surgery as it allows excision of parts of the liver without compromising the rest.

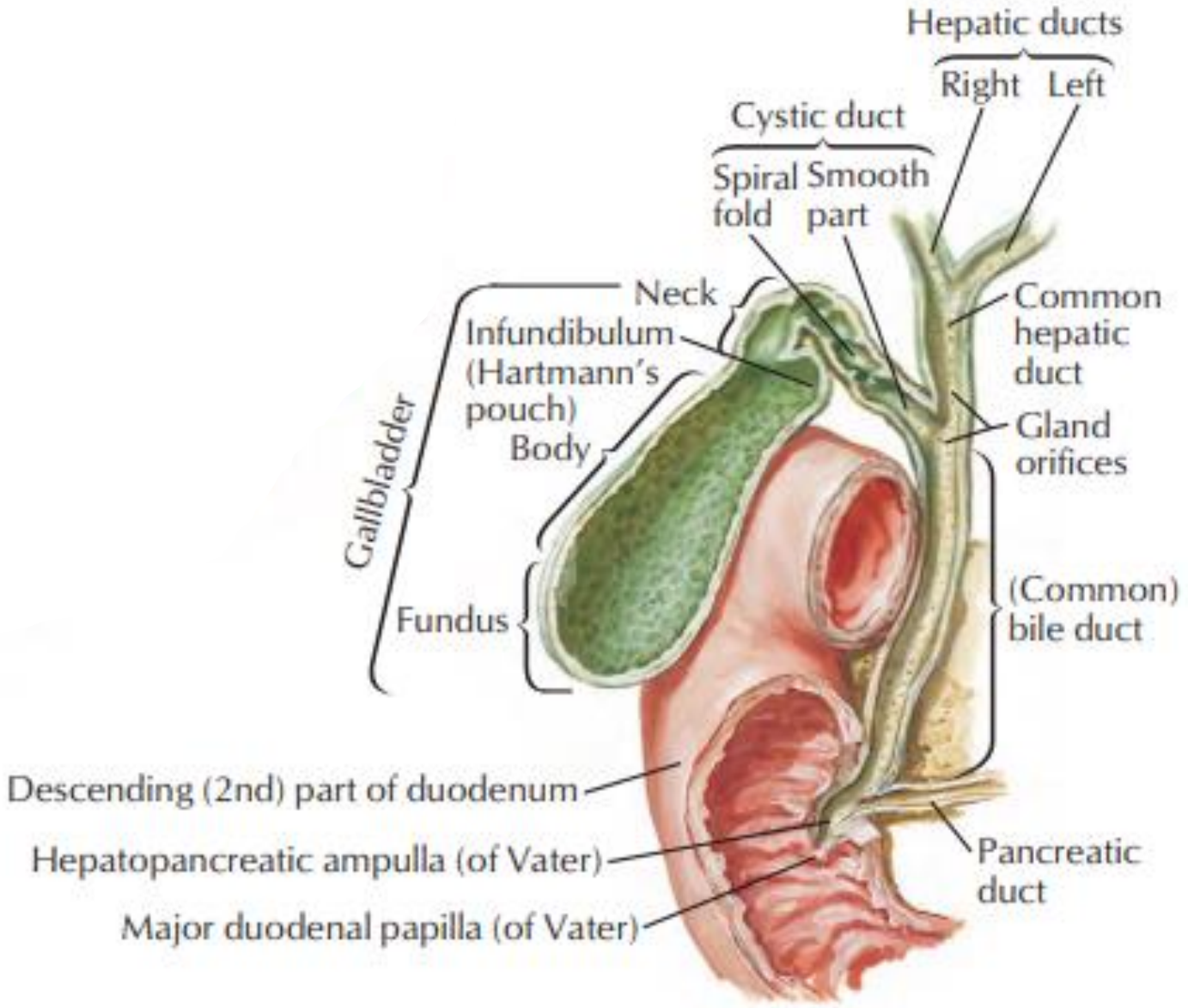
Microscopically: → **classic hepatic lobules** (→ histology classes)



Bile ducts

The bile ducts represent the system through which the bile (or gall) is collected. The bile ducts of the portal spaces (periphery of the hepatic lobules) converge to form the **right and left hepatic ducts,** and then form the **common hepatic duct**.

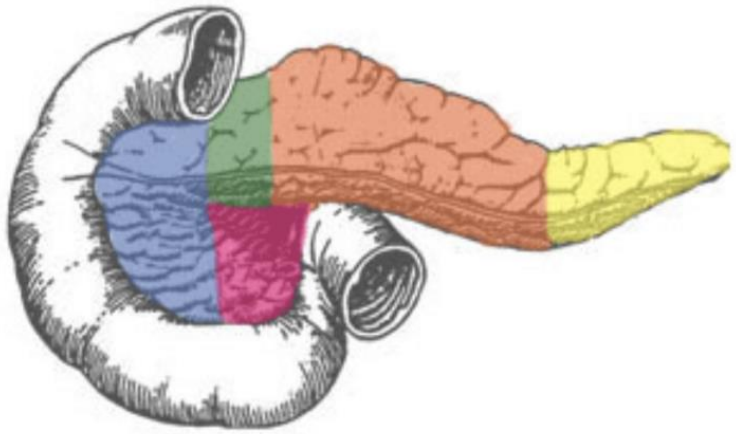
The **gallbladder** stores and concentrates the bile produced by the liver and joins the common hepatic duct via the cystic duct. The union of these is called **common bile duct,** which then enters the duodenum togheter with the pancreatic duct (greater duodenal papilla).



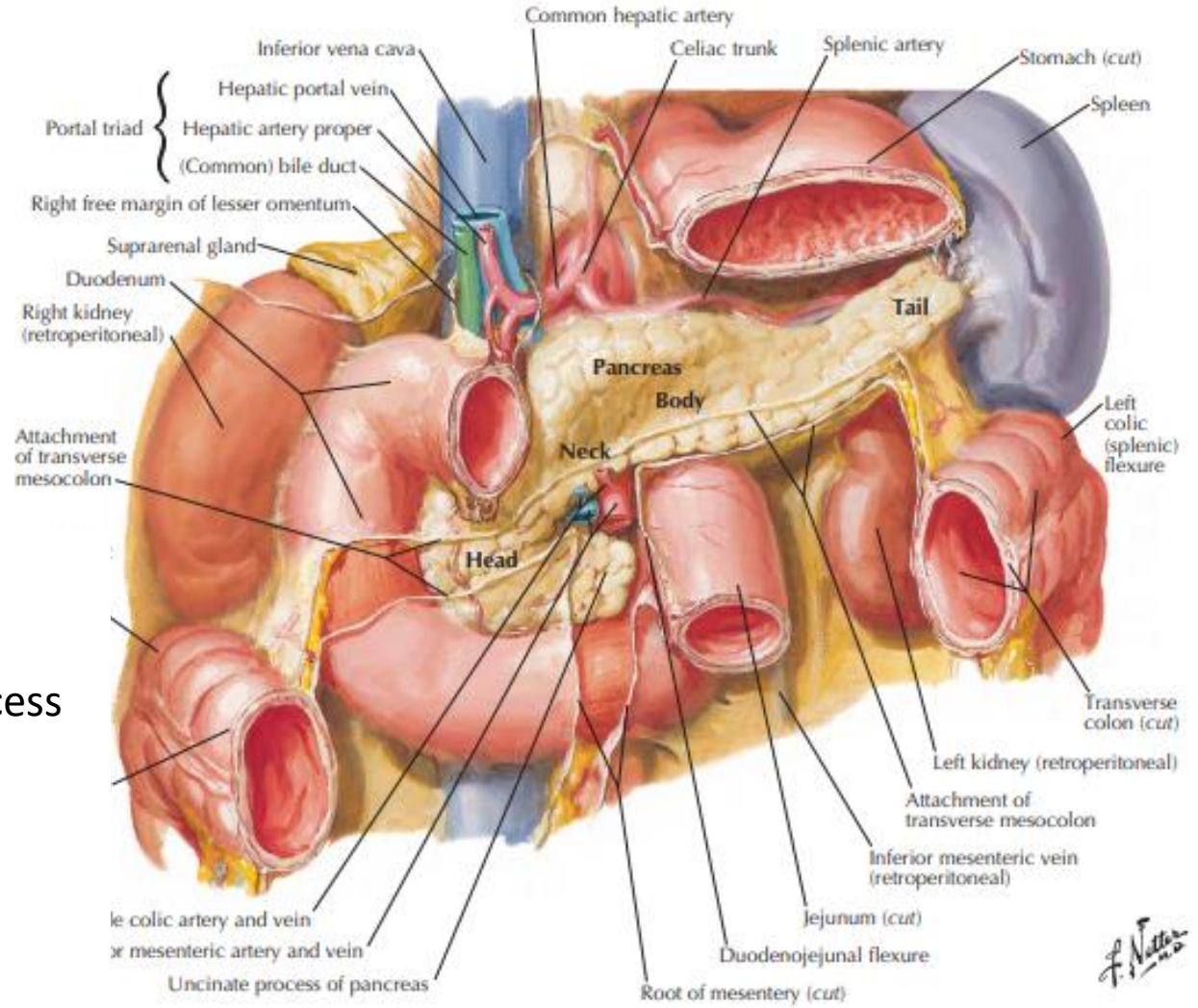
PANCREAS

The pancreas is a **gland** found in the superior part of the abdominal cavity. It is found posteriorly to the stomach and it is interposed between the spleen (left) and the duodenum (right), with the duodenal <<C>> encircling the head of the pancreas.

It presents a hammer-like shape and a lobulated surface.



- Uncinate process
- Head
- Neck
- Body
- Tail

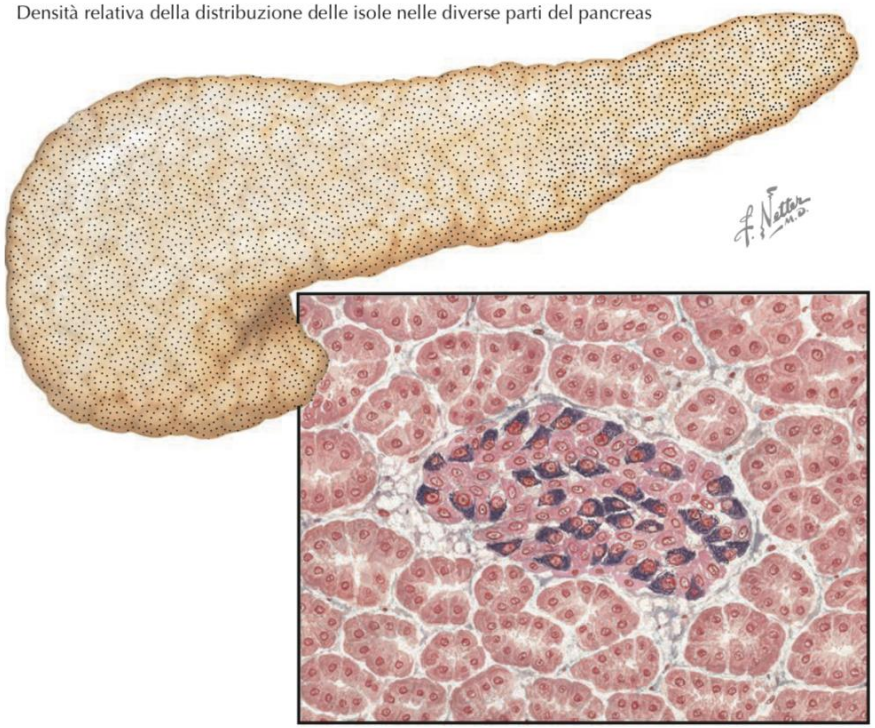


The pancreas is an **amphicrine gland:** it possesses both endocrine and exocrine functions.

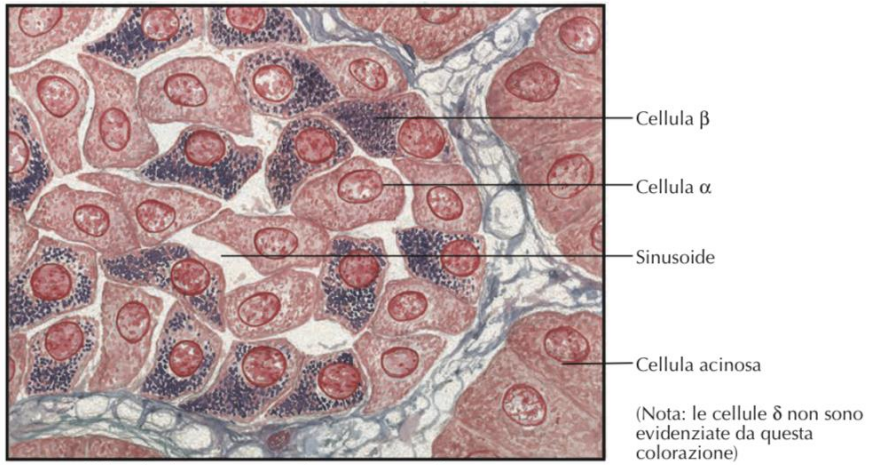
The majority of the pancreas's parenchyme is formed by pancreatic cell clusters (acini) with **exocrine – digestive functions**. These cells secrete the pancreatic juice, composed of amilases, lipases and proteases. The pancreatic juice reaches the duodenum via the main and accessory pancreatic ducts.

The endocrine pancreas is formed by sparse cell clusters, known as **Islets of Langherhans** which produce:

- Glucagone – *alpha cells*
- Insuline – *beta cells*
- Somatostatine – *delta cells*



Sezione di un'isola circondata da acini (×220); colorazione con aldeide fucsina di Gomori e di Ponceau: granuli delle cellule β in blu-porpora intenso; cellule α in rosa o in rosso



Porzione dell'isola altamente ingrandita (×1.200); colorazione con aldeide fucsina di Gomori e di Ponceau

The pancreas is an **amphicrine gland:** it possesses both endocrine and exocrine functions.

The majority of the pancreas's parenchyme is formed by pancreatic cell clusters (acini) with **exocrine – digestive functions**. These cells secrete the pancreatic juice, composed of amilases, lipases and proteases. The pancreatic juice reaches the duodenum via the main and accessory pancreatic ducts.

The endocrine pancreas is formed by sparse cell clusters, known as **Islets of Langherhans** which produce:

- Glucagone – *alpha cells*
- Insuline – *beta cells*
- Somatostatine – *delta cells*