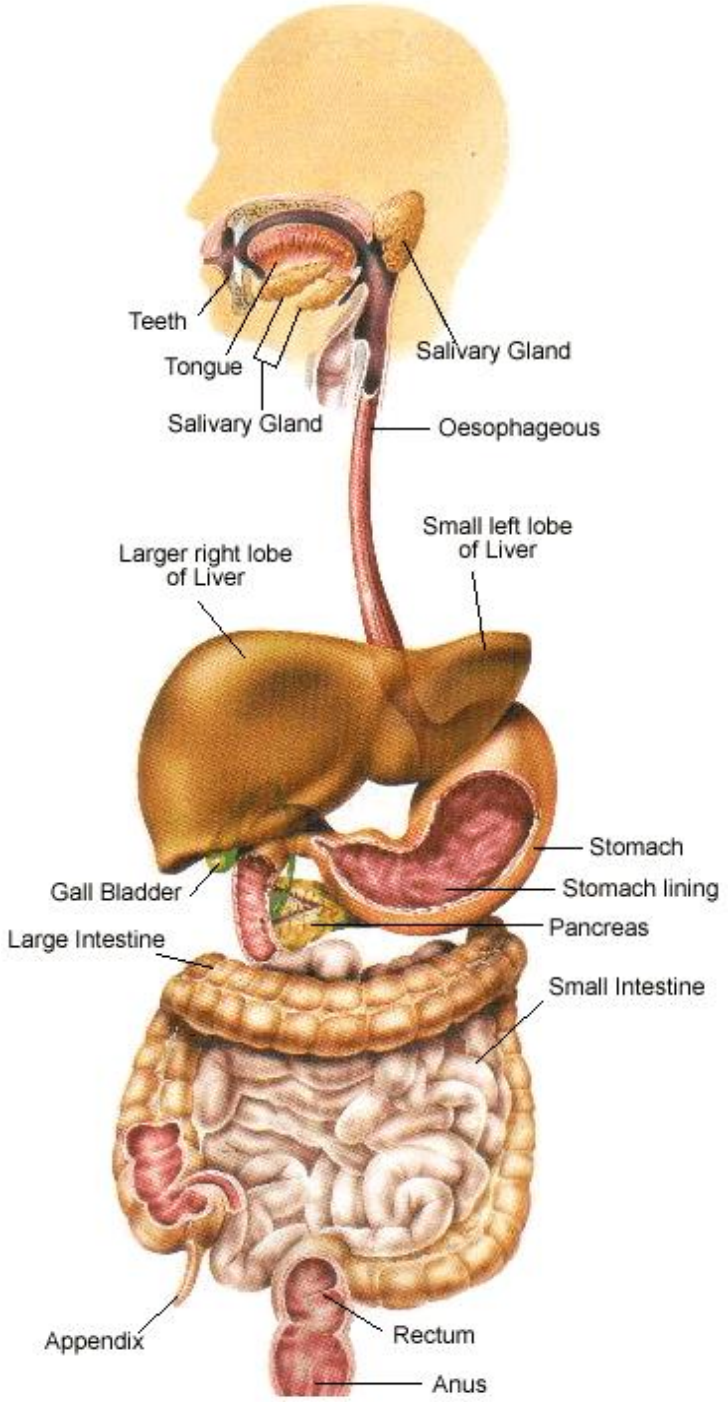
Digestive system – part 2 & 3

Topics

- Part 1:
  - General microscopic structure of the esophagus, stomach, as well as small and large intestine
  - Glands in stomach and intestines, their structure and function
- Part 2:
  - Relationship between structure and function of the liver
  - General microscopic structure of the gallbladder and pancreas

Digestive system

- consists of:
  1. **gastrointestinal tract (alimentary canal):**
     - oral cavity with tongue and teeth
     - pharynx – a common section of the respiratory tract and gastrointestinal tract
     - esophagus
     - stomach
     - small intestine
     - large intestine
  2. **large glands:**
     - salivary glands
     - liver
     - pancreas



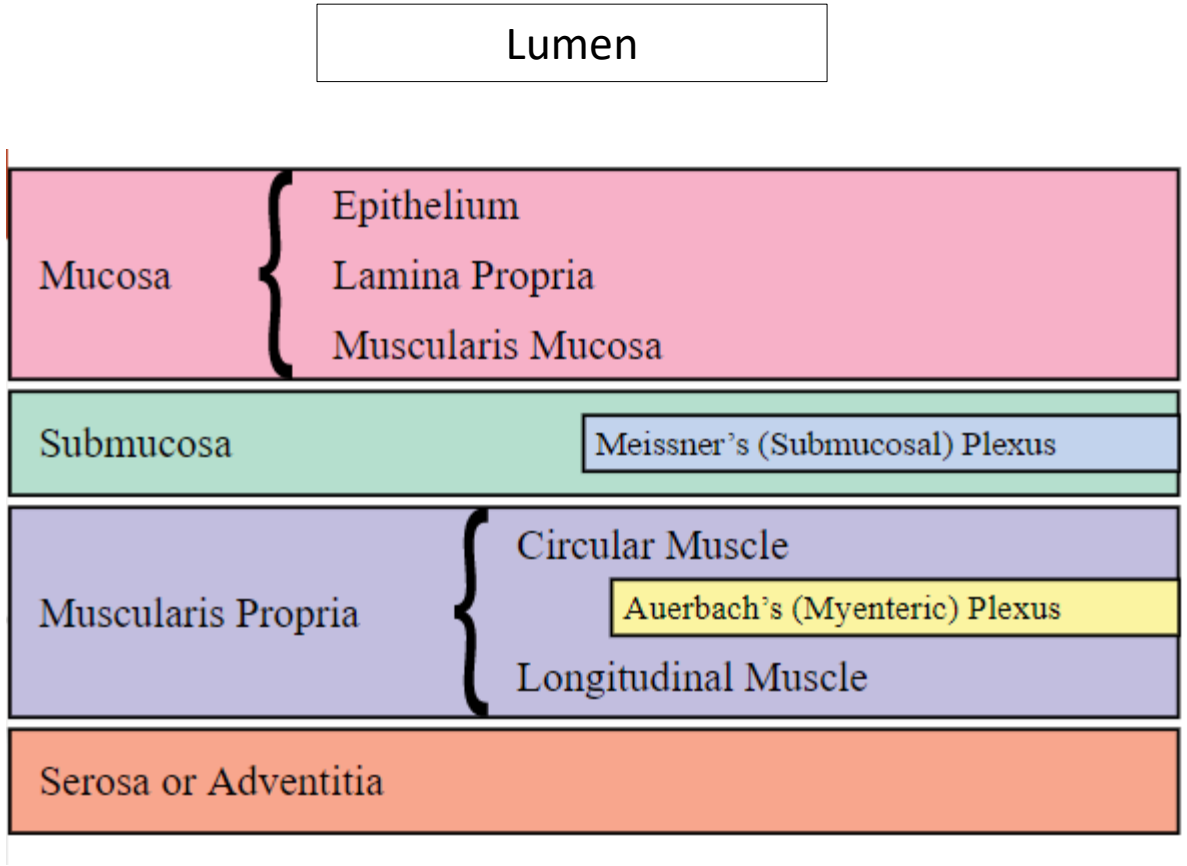
Gastrointestinal tract (alimentary canal):

- **muscular tube lined with epithelium**

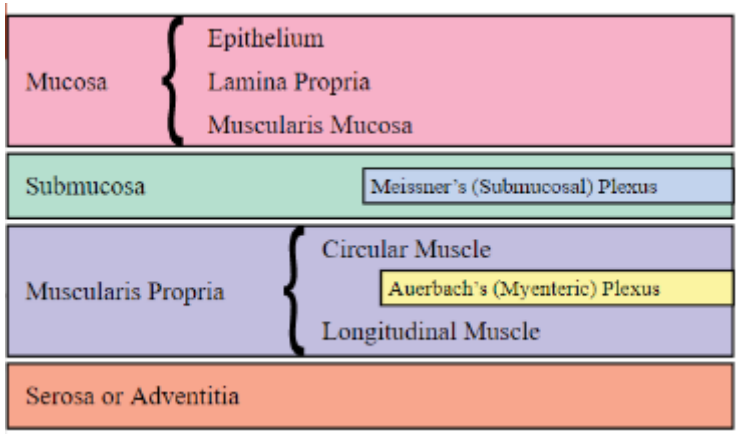
- **the lumen G.I. t. is an extension of the outside world (!)**
  - the presence of immune system cells
    - mainly in 2 layers next to the lumen → in the mucosa and submucosa
    - GALT – gut associated lymphoid tissue
      - GALT is a part of MALT – mucosa associated lymphoid tissue

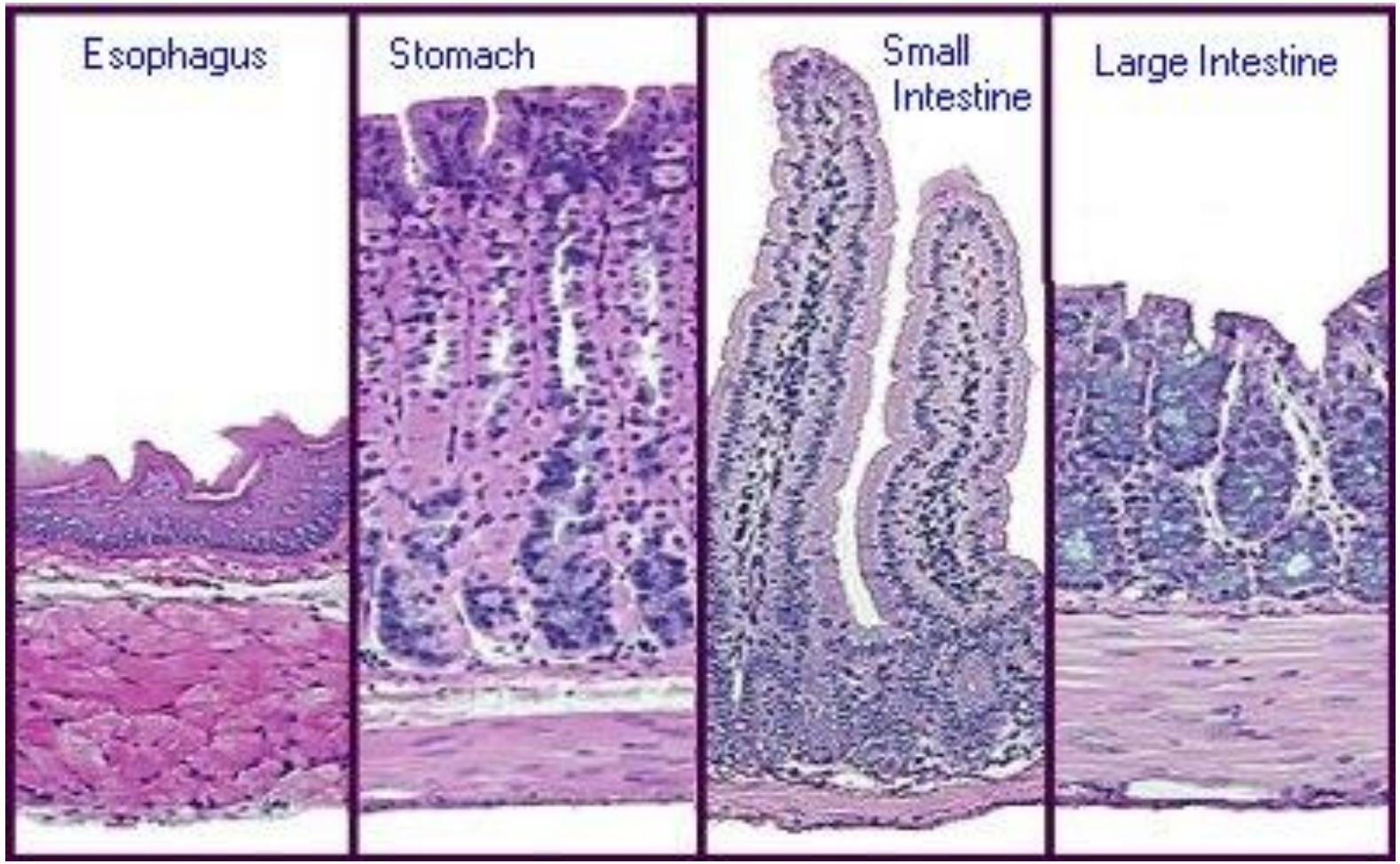
Gastrointestinal tract (alimentary canal):

- starting from the esophagus, the wall of the G.I. tract
  - has a similar structure
  - consists of 4 layers (membranes):
    1. mucosa
       i. epithelium
       ii. lamina propria
       iii. muscularis mucosae
    2. submucosa
    3. muscularis externa (propria)
    4. serosa / adventitia



Gastrointestinal tract (alimentary canal):



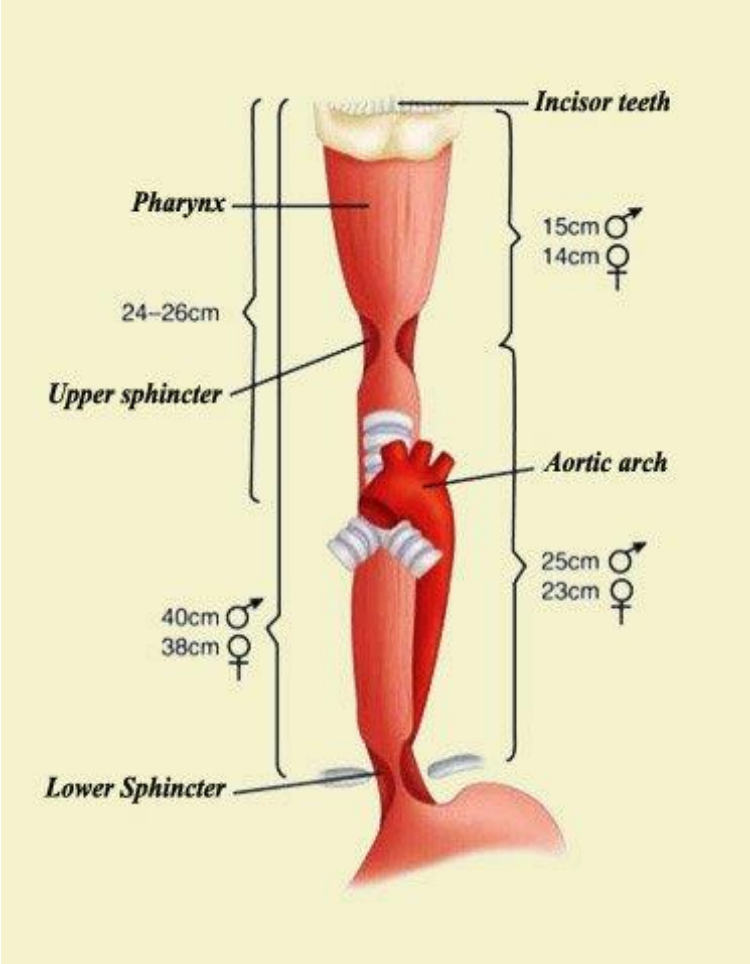


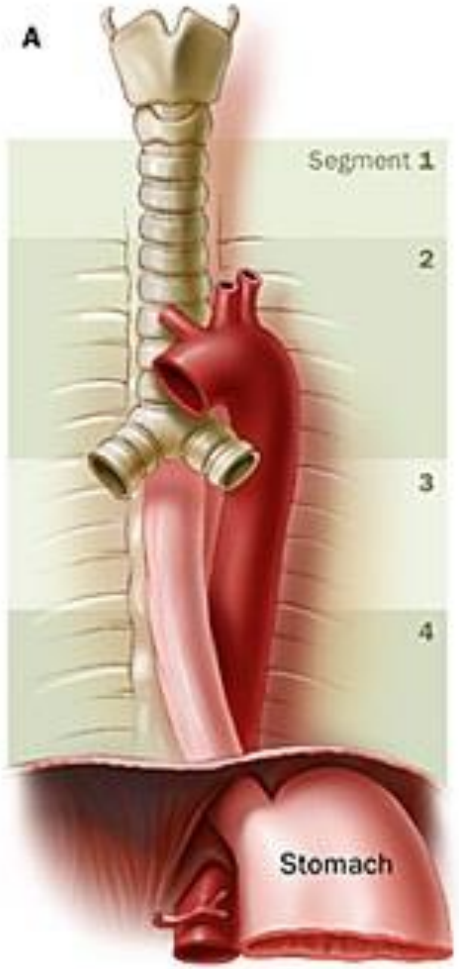
Similar basic construction end to end, however, with local modifications !!!

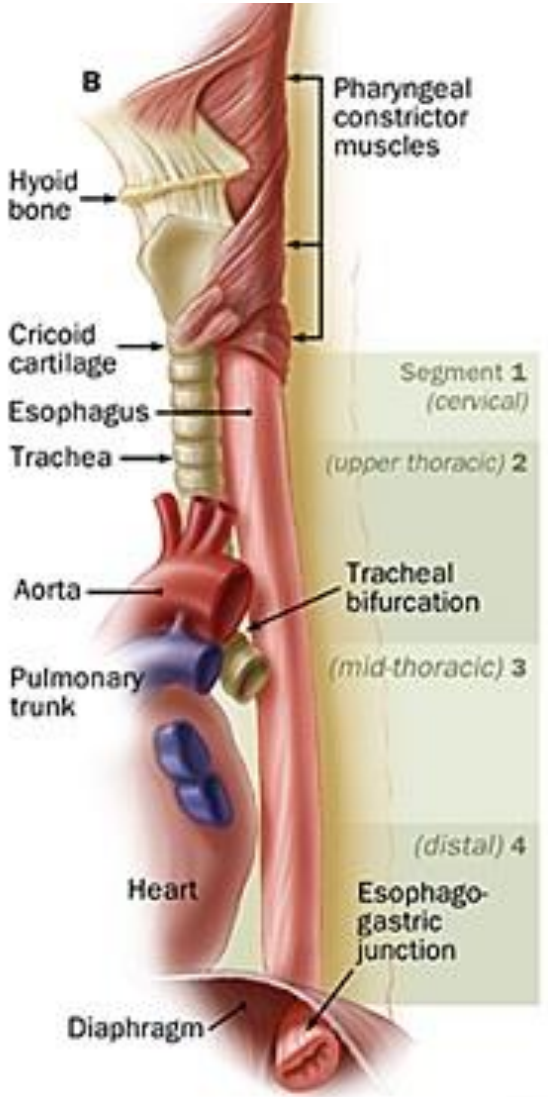
Esophagus

Esophagus (#47)

- ~25 cm in length



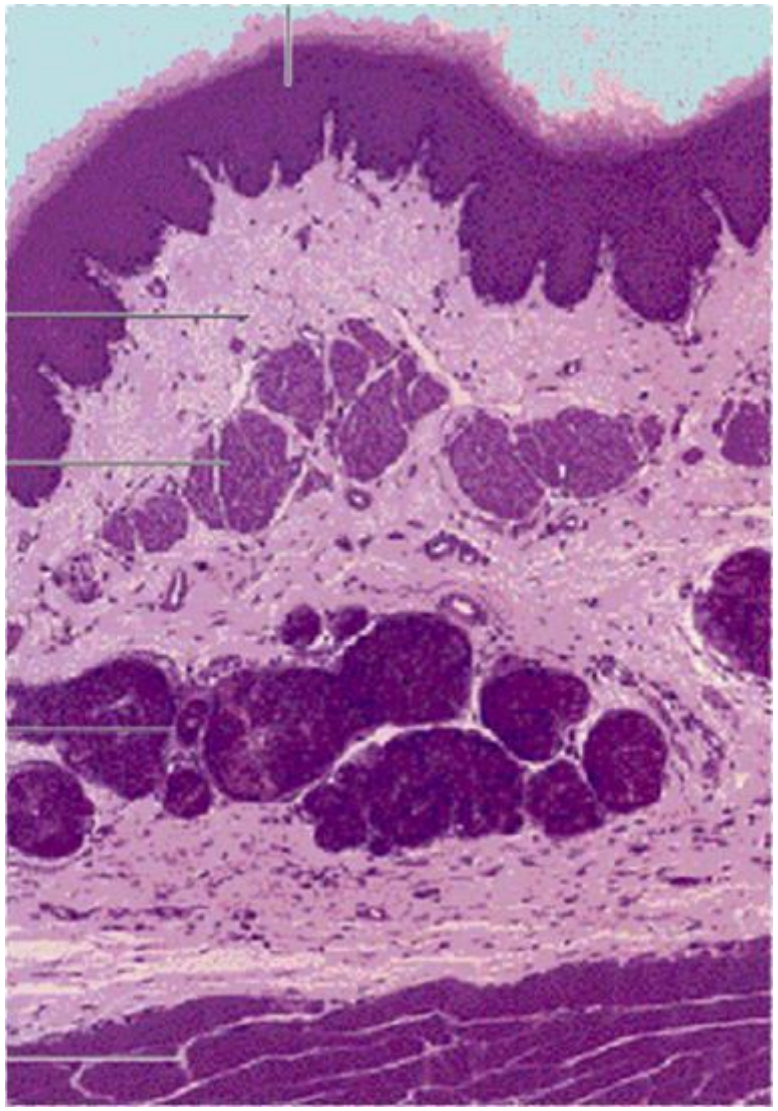




Esophagus (#47)

- in the wall of esophagus
  - **4 typical layers**:
    1. mucosa
    2. submucosa
    3. muscularis externa
    4. serosa

  ➢ there are <u>differences</u> in individual parts of the organ



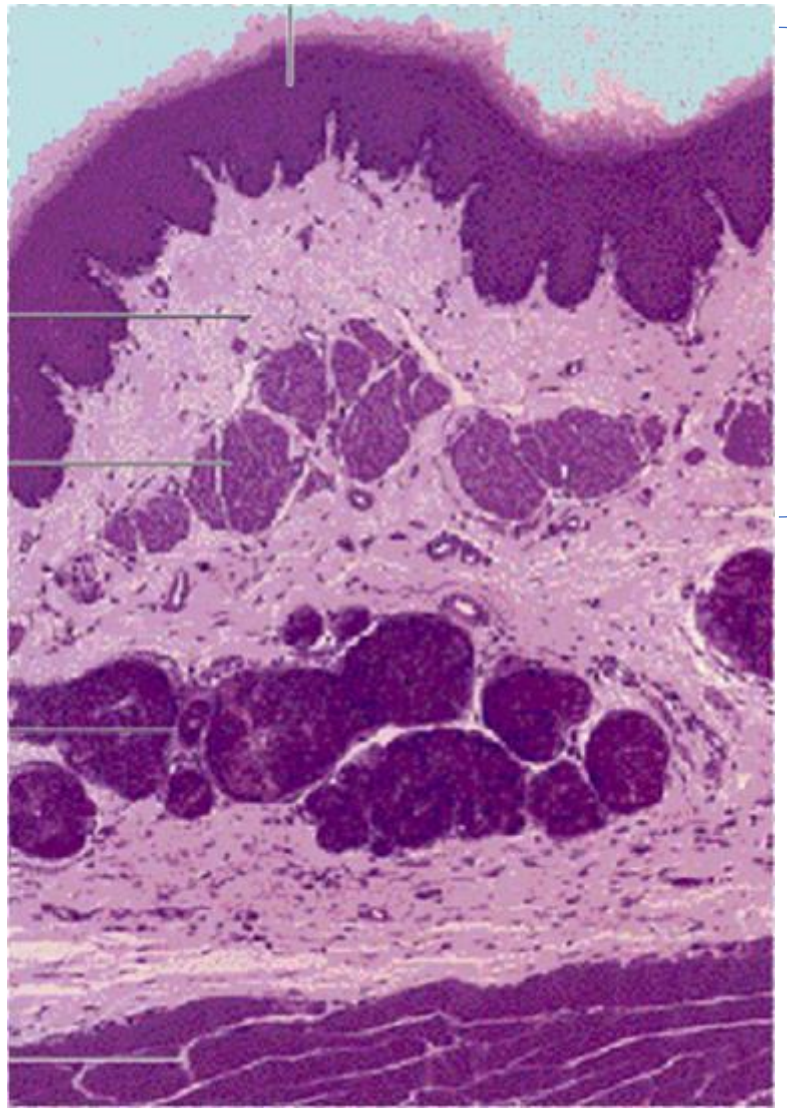
Esophagus (#47)

Mucosa

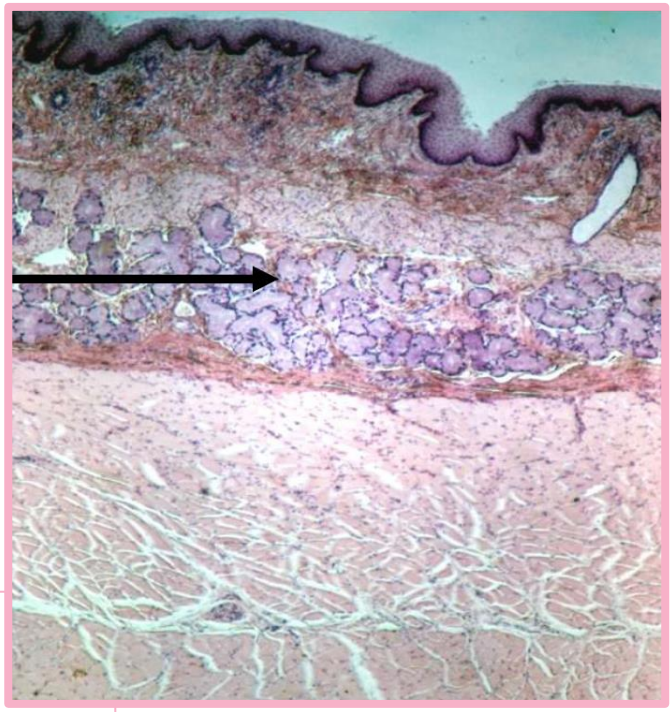
- **Epithelium**
  - **stratified squamous nonkeratinized** - along the entire length
  - presence of Langerhans cells (APC)
  - relative slow regeneration potential (~3 weeks)

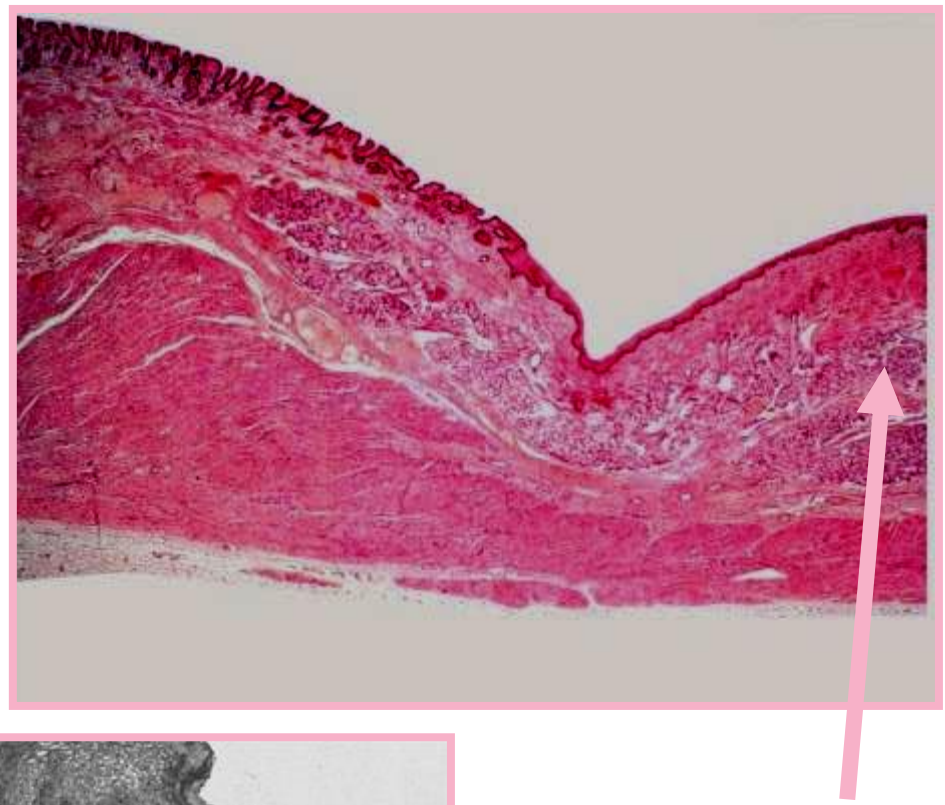
- **Lamina propria**
  - fibroelastic connective tissue proper
  - presence of **mucous glands in 2 regions** - at the beginning (near the pharynx) and at the end (near the stomach)
    ⇒ **esophageal cardiac glands**
  - presence of diffuse lymphatic tissue and lymphoid nodules

- **Muscularis mucosae**
  - **only one longitudinal layer** of smooth myocytes

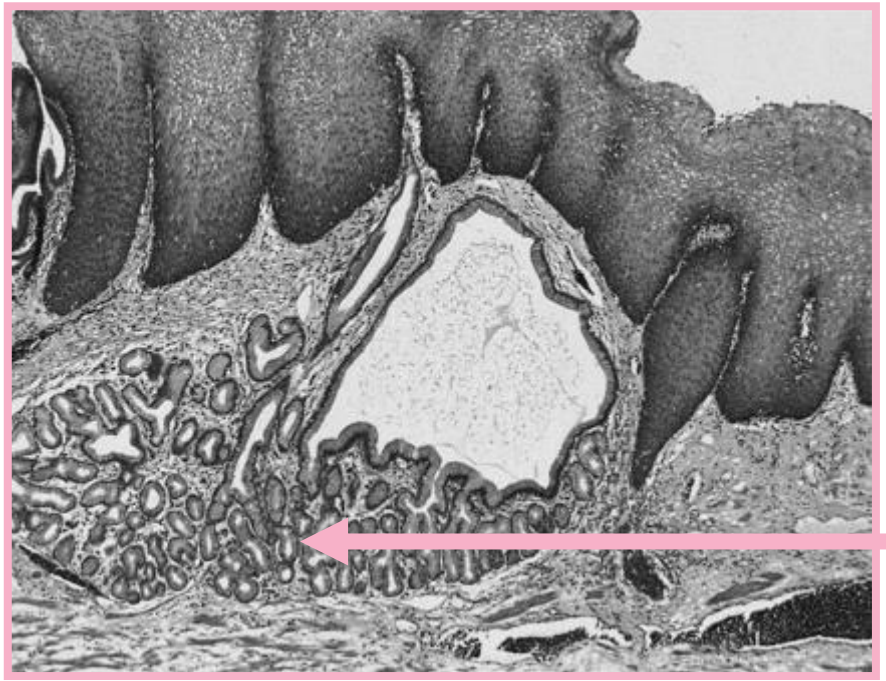


Esophageal **Cardiac** Glands





- occur in lamina propria of mucosa
- similar to cardiac glands of stomach
- present in terminal part of esophagus
- produce **neutral mucin** → protect against regurgitated acidic chyme from the stomach



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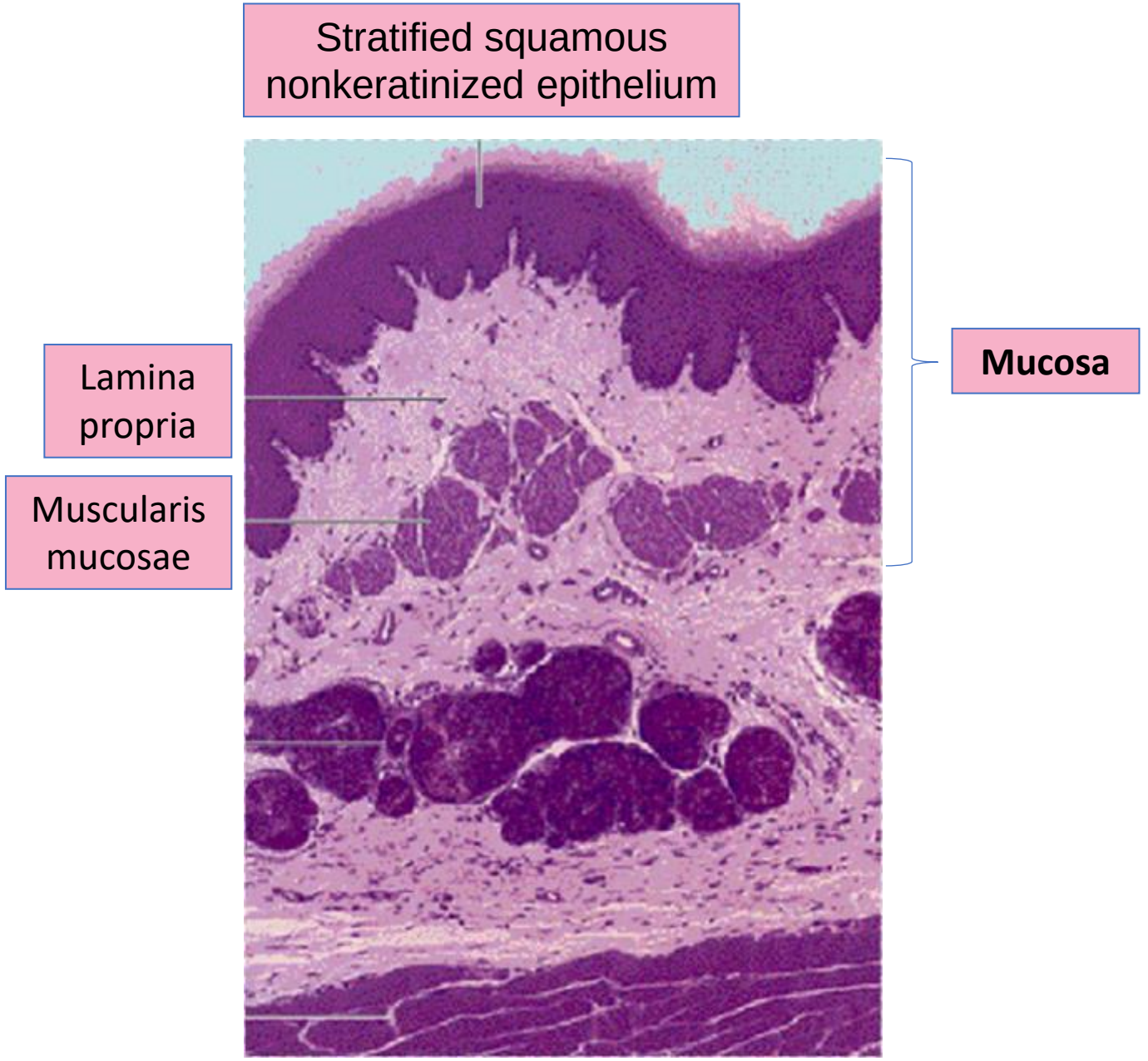
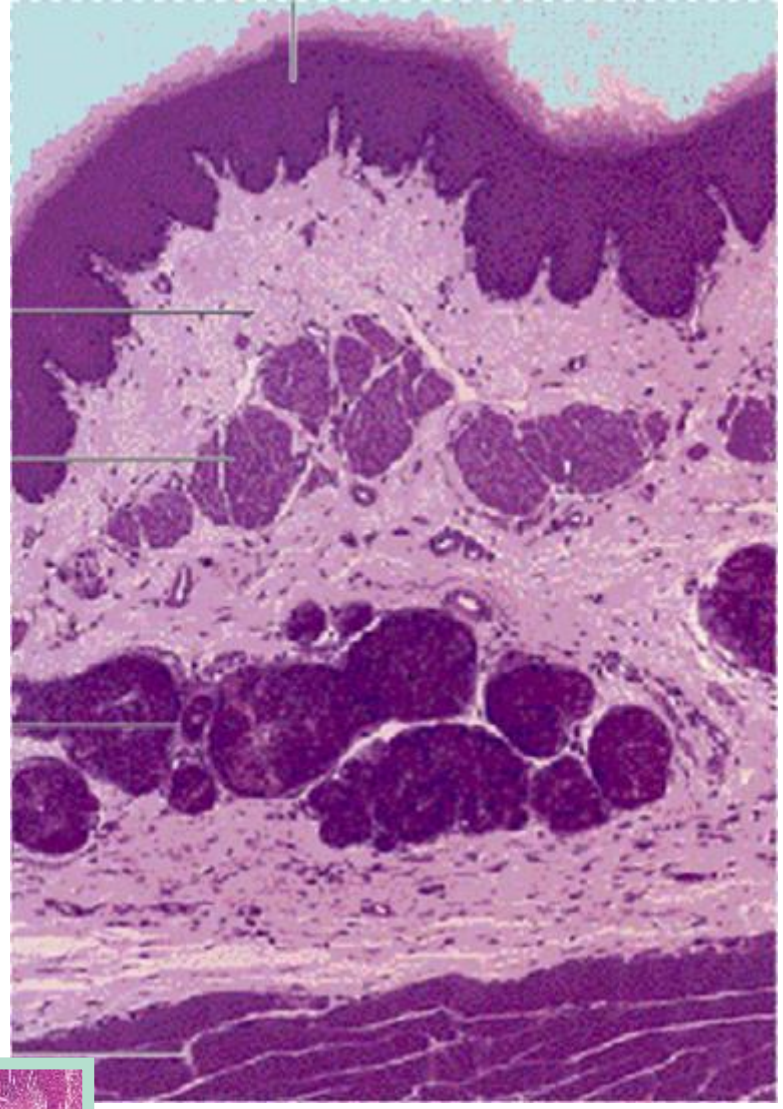


Esophagus (#47)

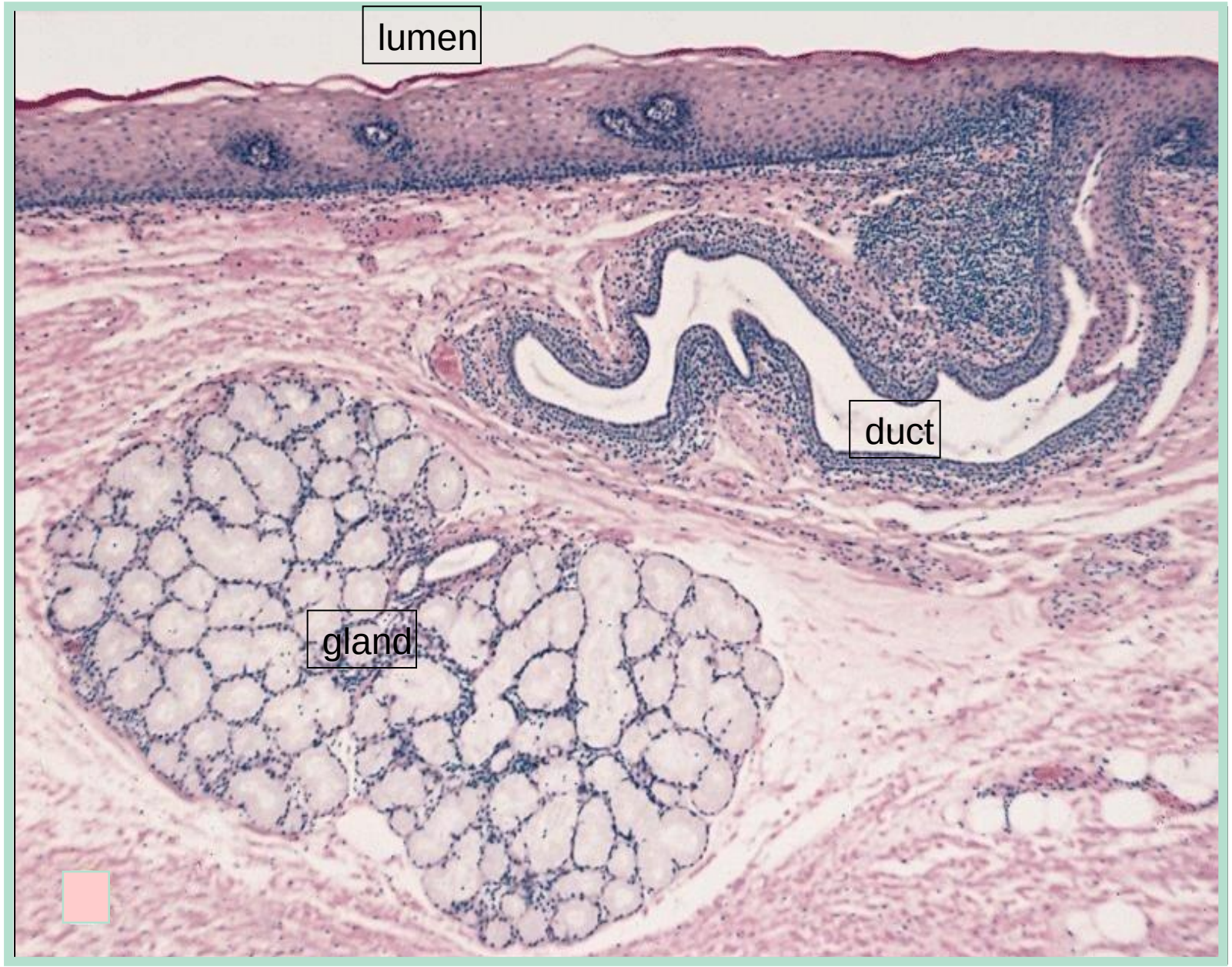
Submucosa

- dense, fibroelastic connective tissue proper
- presence of the **esophageal glands proper**
  - **tubuloacinar secretory units** – 2 cell types
    - mucous cells
      - basally located, flattened nuclei
      - secretory granules with mucinogen
    - serous cells
      - round, centrally placed nuclei
      - secretory granules with pepsinogen and lysozyme
  - **ducts** - deliver secretions into the lumen
- presence of the **submucosal plexus**
- forms longitudinal folds
  - create very irregular luminal profile when seen in small magnification

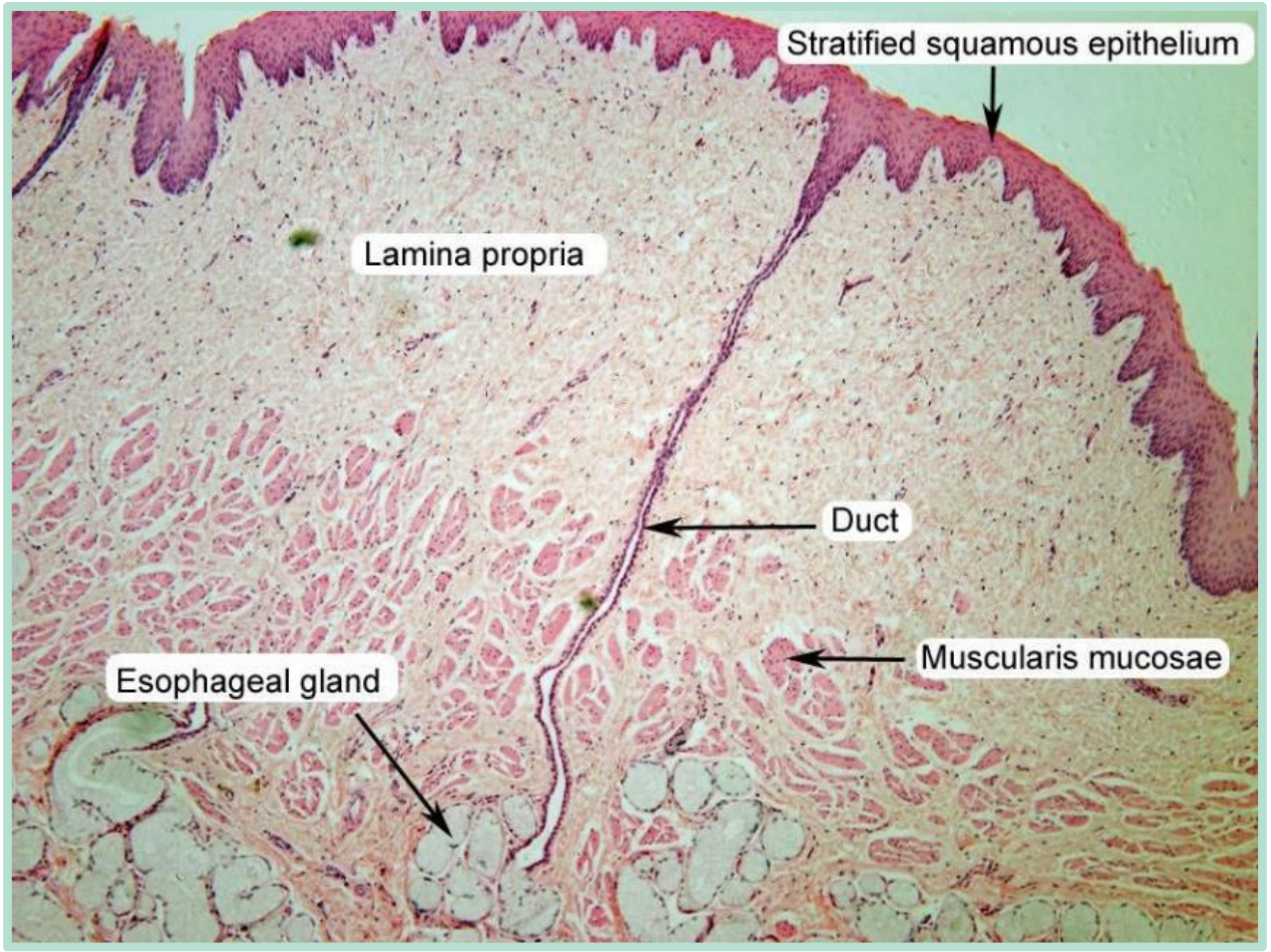


Esophageal Glands Proper

- occur in submucosa
- scattered throughout the length of esophagus;
  - ➢ most in upper one half
- small compound tubuloalveolar glands
- produce **acid mucin**
- some serous cells are also present



Esophageal Glands Proper*



* the presence of these glands helps distinguish the esophagus from the vagina

Esophagus (#47)

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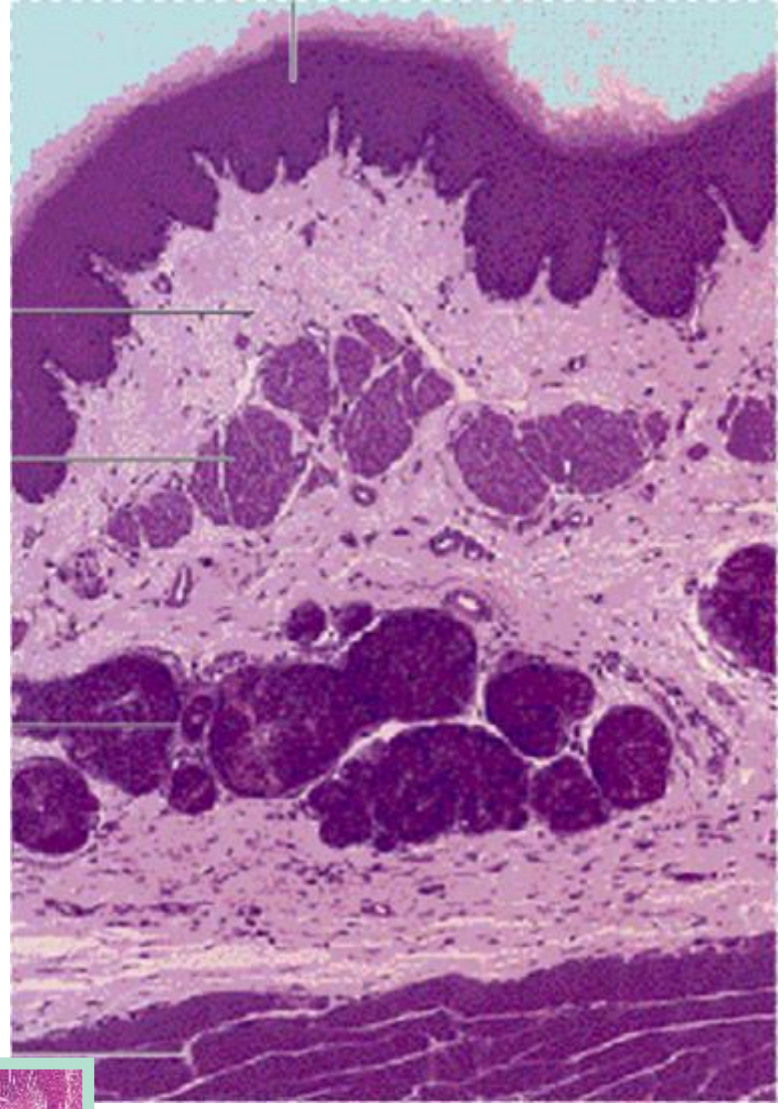


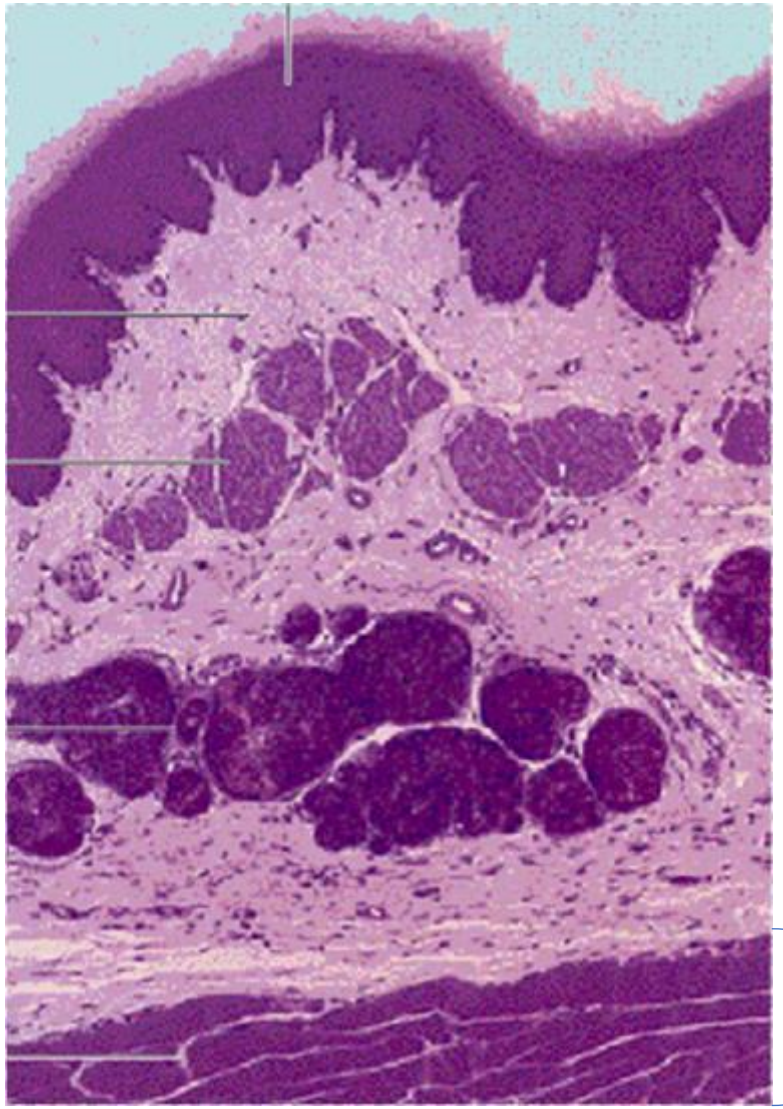
Esophagus (#47)

Muscularis externa

- **2 muscle layers**:
  1. inner circular
  2. outer longitudinal
- composed of **both skeletal and smooth muscle fibers**
  1. upper third - mostly skeletal muscle;
  2. the middle third - both skeletal and smooth muscle;
  3. the lowest third - only smooth muscle fibers
- **Auerbach plexus** - between the inner circular and outer longitudinal smooth muscle layers

Adventitia / Serosa

- **Adventitia** - above the diaphragm
- **Serosa** - below the diaphragm



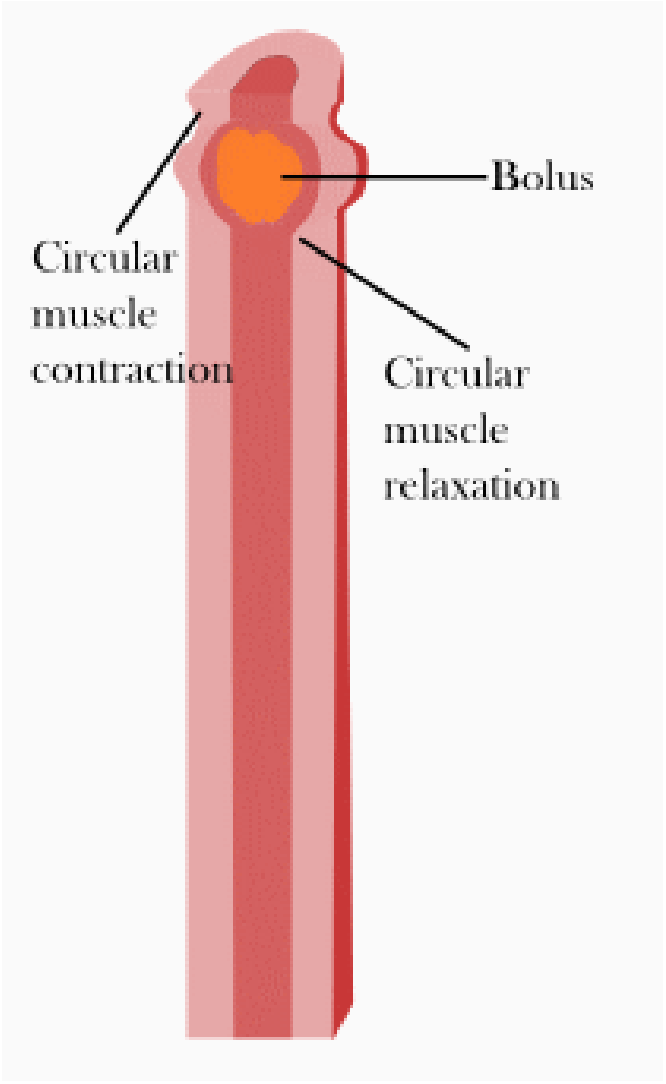
Muscularis externa

Adventitia / in peritoneal cavity - **Serosa**

Esophagus (#47)

- **food conduit (→ food pipe)**
- **conveys the masticated food (bolus) from pharynx to the stomach** at a rate of about 50 mm/sec. ⇒ a bolus spends here ~12,5 seconds **thanks to peristaltic movements of muscularis externa**

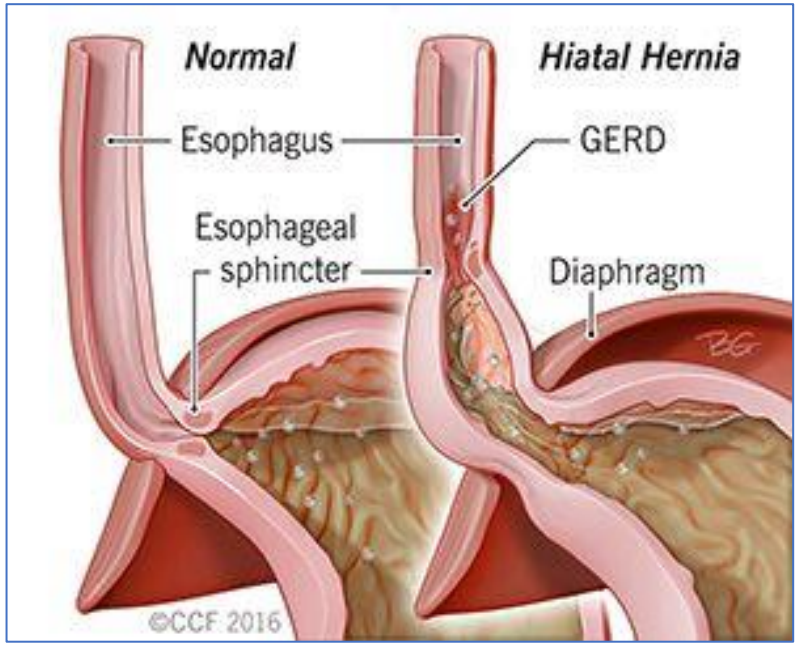
peristaltic action of the muscularis externa



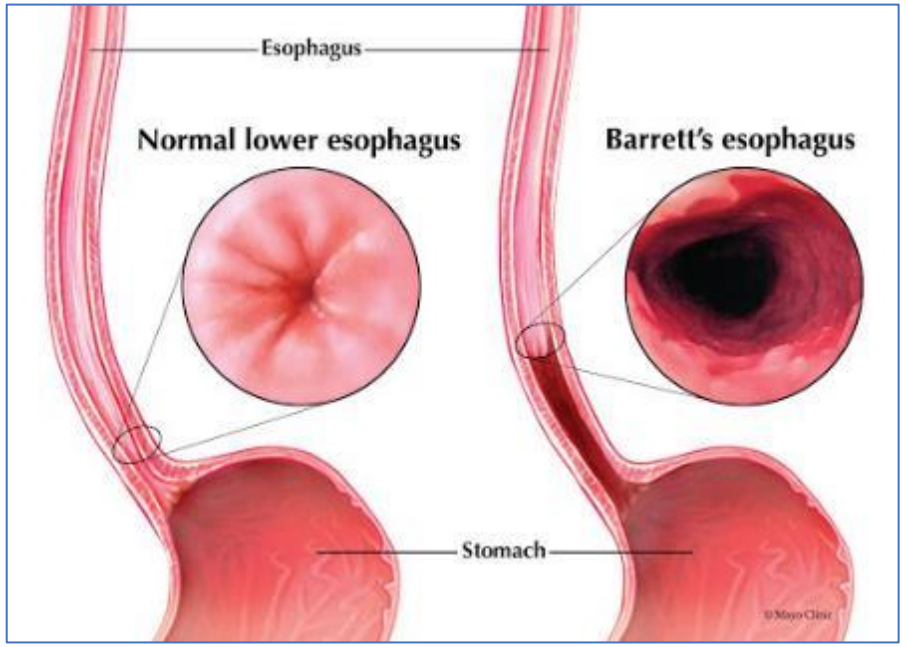
Esophagus (#47)

- **no anatomical** sphincter but **physiological sphincters at 2 levels:**
  - the pharyngoesophageal sphincter (<u>upper</u> esophageal sphincter)
  - the internal and external gastroesophageal sphincters (<u>lower</u> esophageal sphincters)
- <u>Clinical correlations</u>
  - **hiatal hernia**
  - **gastroesophageal reflux disease (GERD)** ⇒ heartburn
  - **Barrett syndrome**

Hiatal hernia

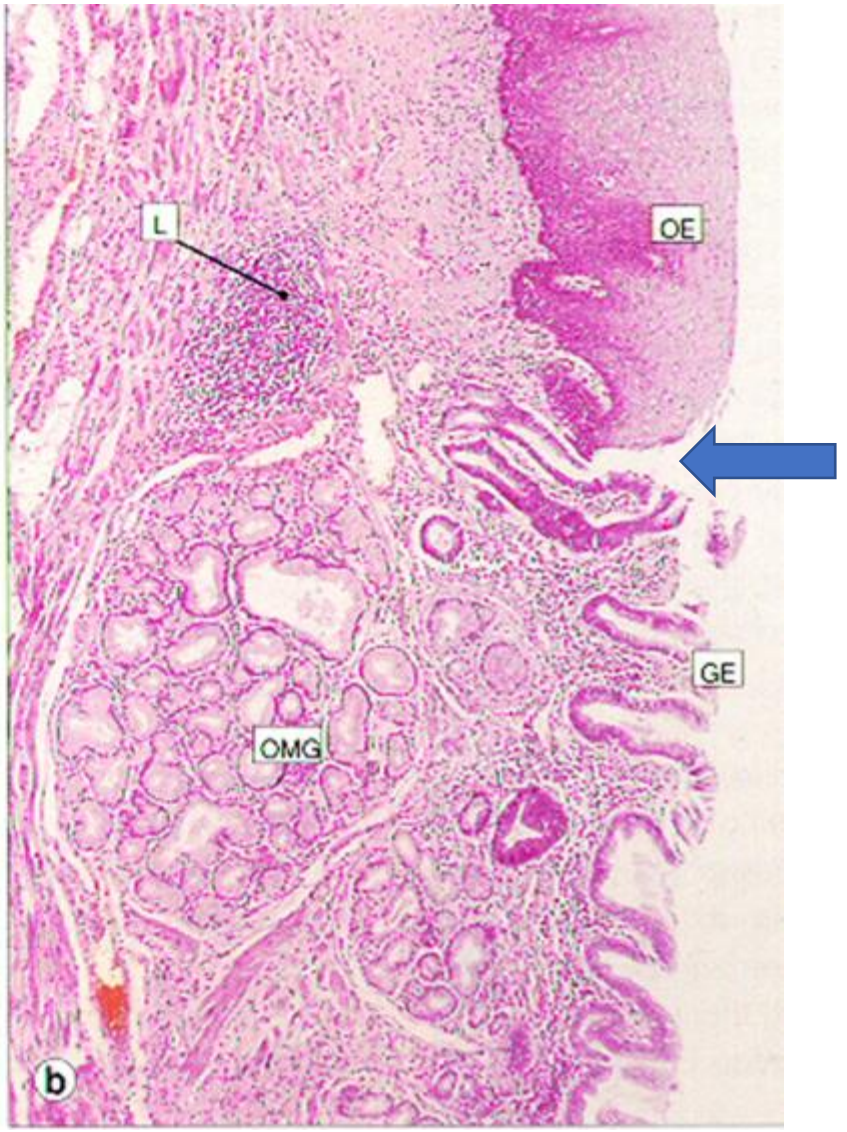


Barret syndrome



Gastroesophageal Junction

Esophagogastric junction



Abrupt transition between esophageal and columnar gastric epithelium. L – lymphoid follicle; OMG - oesophageal mucous glands

Stomach

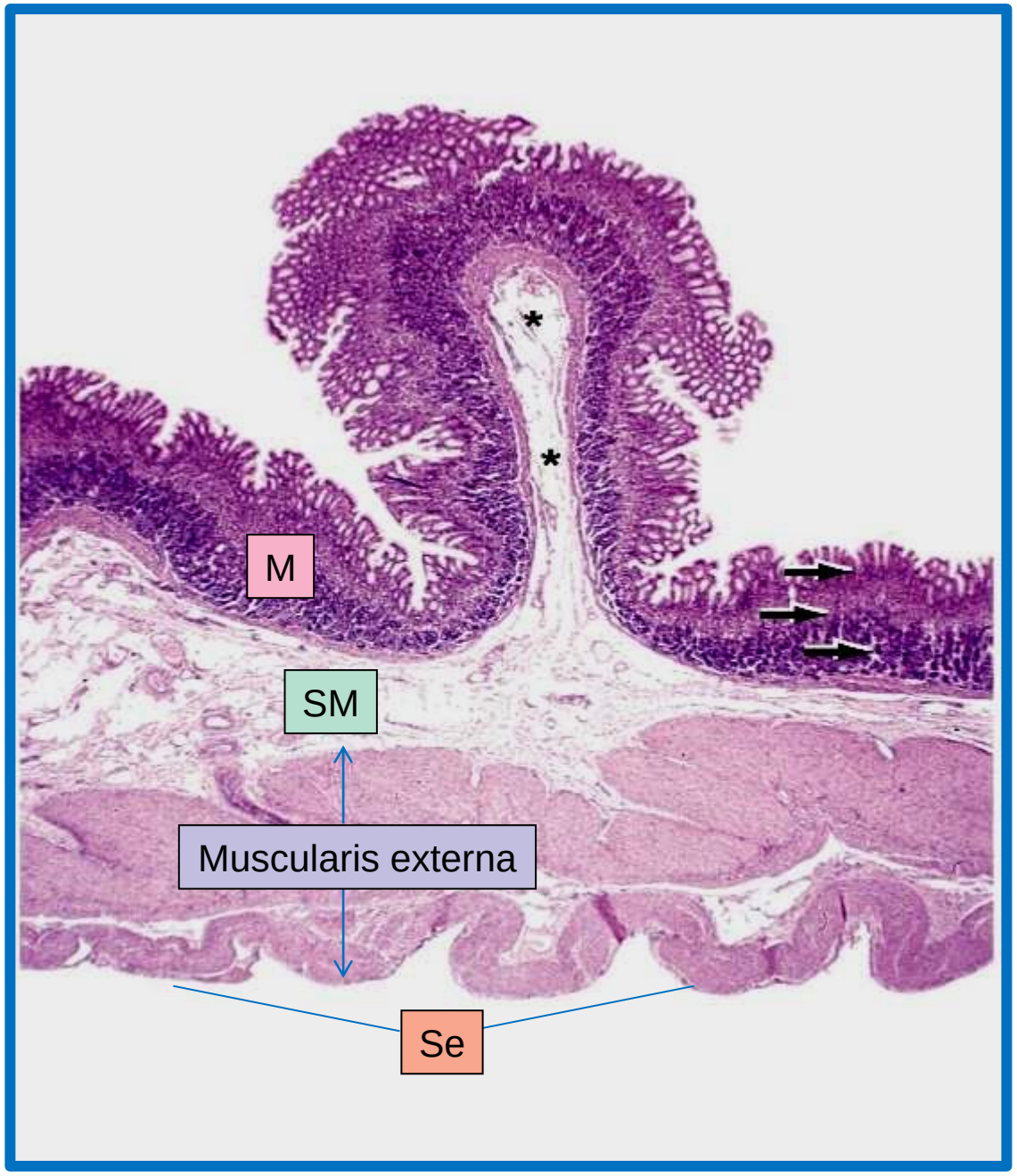
Stomach (#48)

- the most dilated region of the alimentary canal
- s. has several functions:
  - <u>secretory</u> f. (HCl, (pro)enzymes, mucus, bicarbonates, intrinsinc factor, water),
  - <u>motor</u> f. (mixing with gastric secretions, reduction in particle size)
  - <u>humoral</u> f. (gastrin, somatostatin)

(s. is not required for survival)

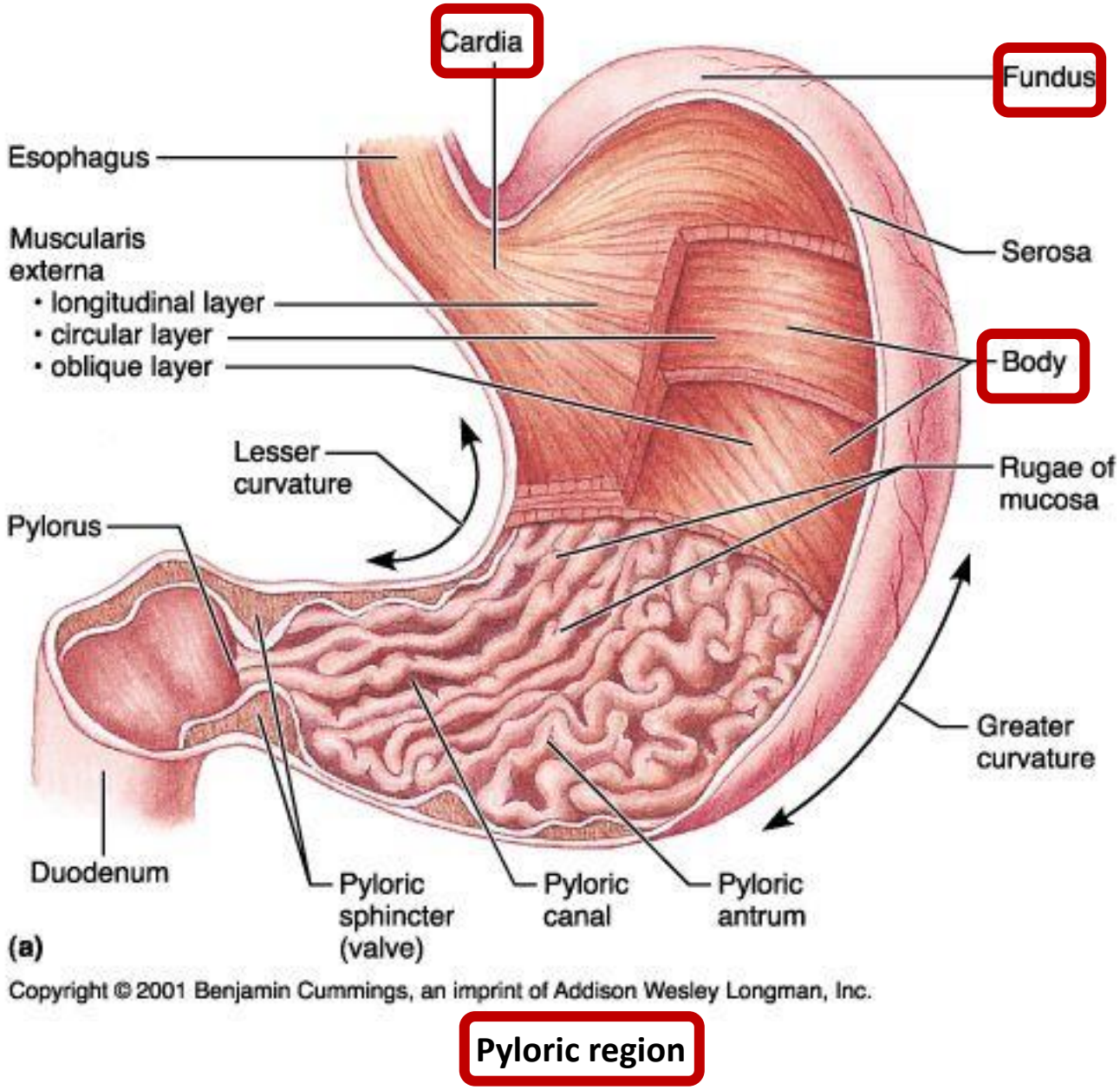
- in the stomach wall
  - **4 typical layers**:
    1. mucosa
    2. submucosa
    3. muscularis externa
    4. serosa

➢ there are <u>differences</u> in individual parts of the organ



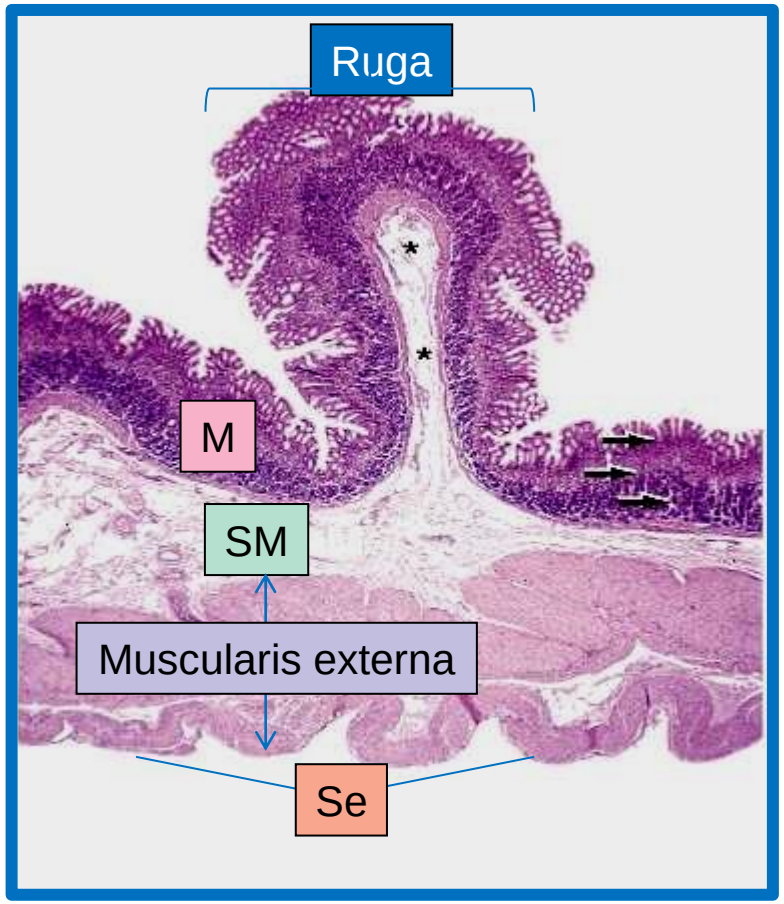
Stomach (#48)

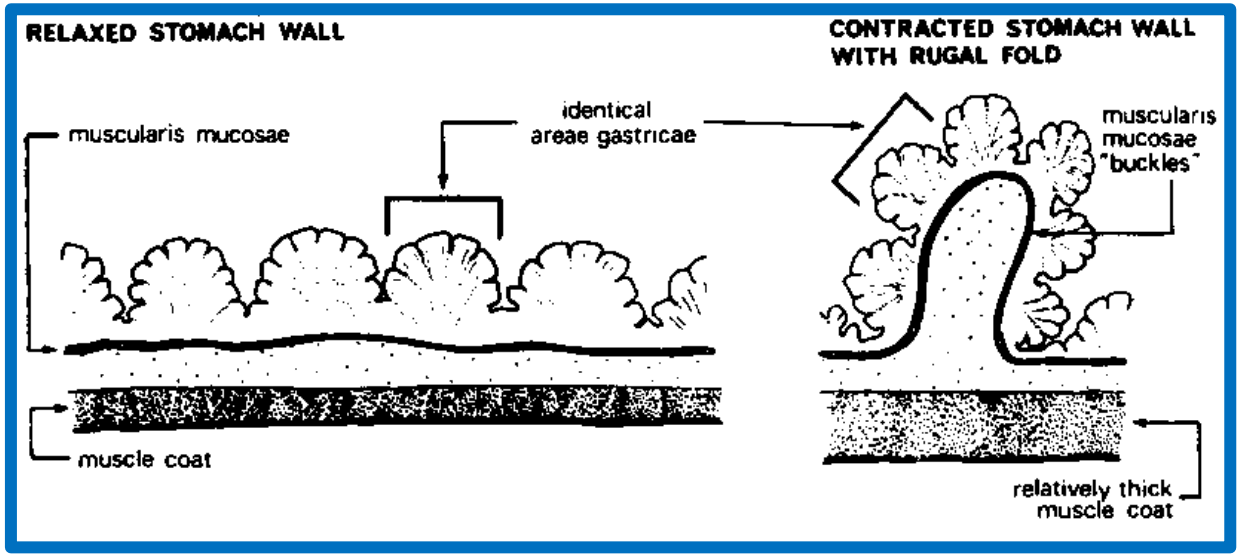
- **in gross observation**
  – 4 regions:
  1. cardia
  2. fundus
  3. body (corpus)
  4. pyloric region
     i. pyloric antrum
     ii. pyloric canal
     iii. pyloric sphincter
     iv. pylorus



Stomach (#48)

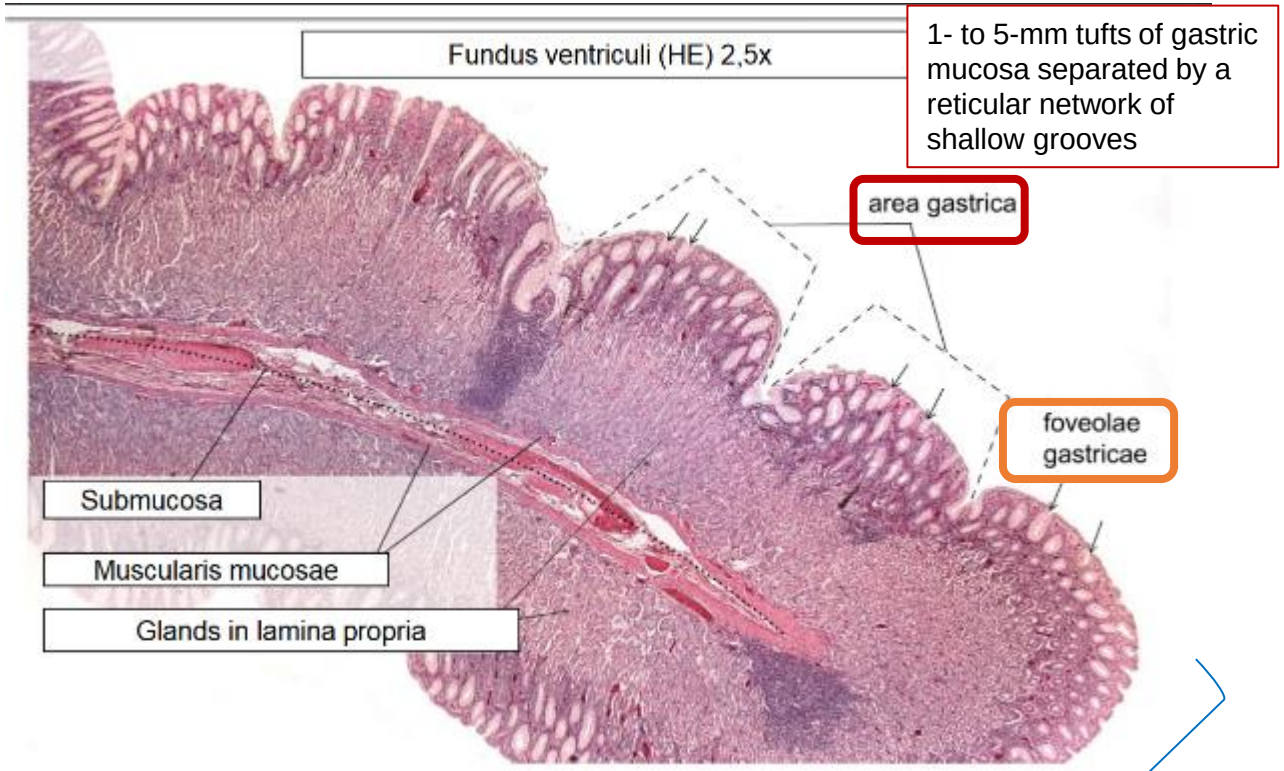
- **in gross observation - inner surface - <u>uneven</u>**
  - **longitudinal folds** of mucosa & submucosa called **rugal folds** or **rugea** (sing. ruga)
    - ➢ poorly developed in upper stomach, more elaborate in lower part
    - ➢ disappear when stomach is distended

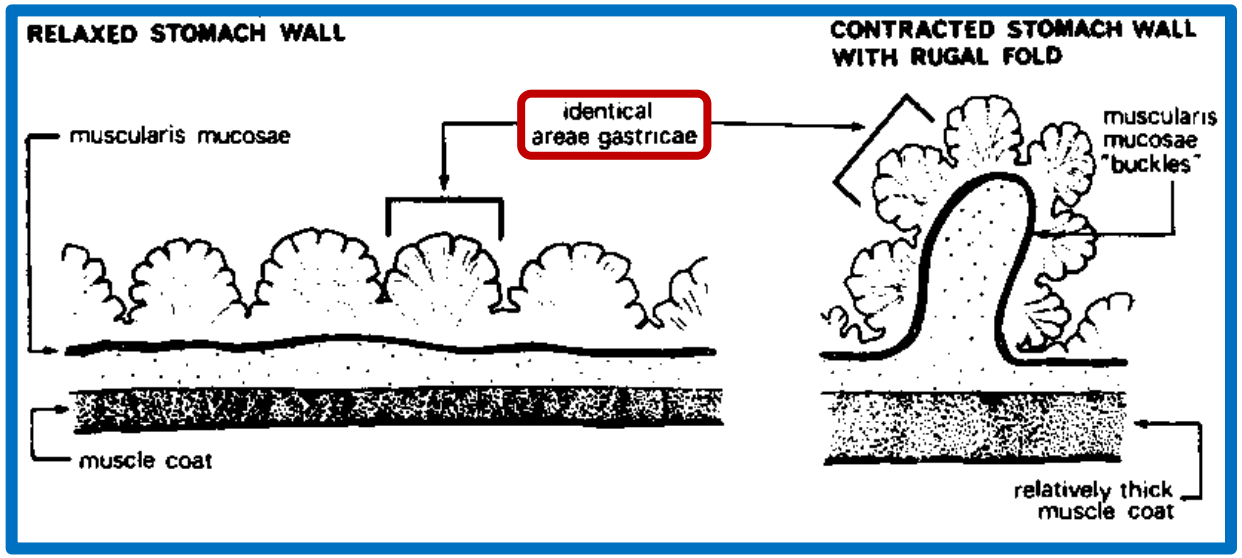


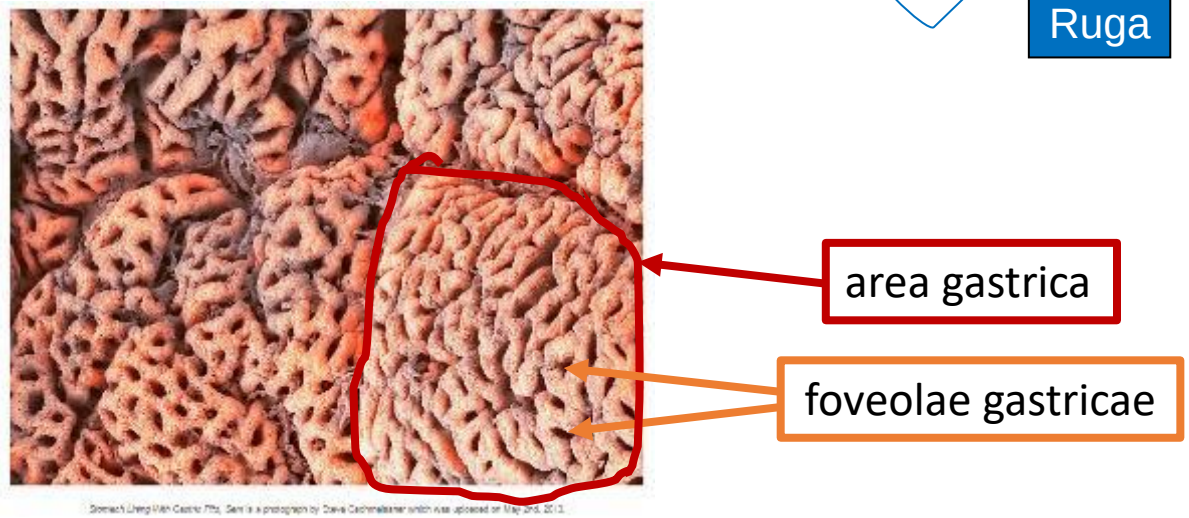


Stomach (#48)

- **inner surface - <u>uneven</u>**
  - **irregularities at the <u>macroscopic</u> level**
    - ➢ distensible **rugal folds** (**rugea**)
  - **irregularities at the <u>microscopic</u> level** (at small magnification)
    - ➢ permanent ***area gastricea***
    - ➢ permanent ***foveolea gastricea***
      → **gastric pits**







Stomach (#48)

Mucosa

Lining Epithelium (LE)

- a **simple columnar epithelium**
  - composed of: mucus-bicarbonate barrier
    1. **surface-lining cells → visible mucus → M-B barrier**
    2. regenerative (stem) cells
    3. taste cells (sweet, bitter, and umami taste sensations)
  - e. invaginates into the lamina propria of mucosa, forming **gastric pits*** (**foveolae gastricea**)

Lamina propria (LP)

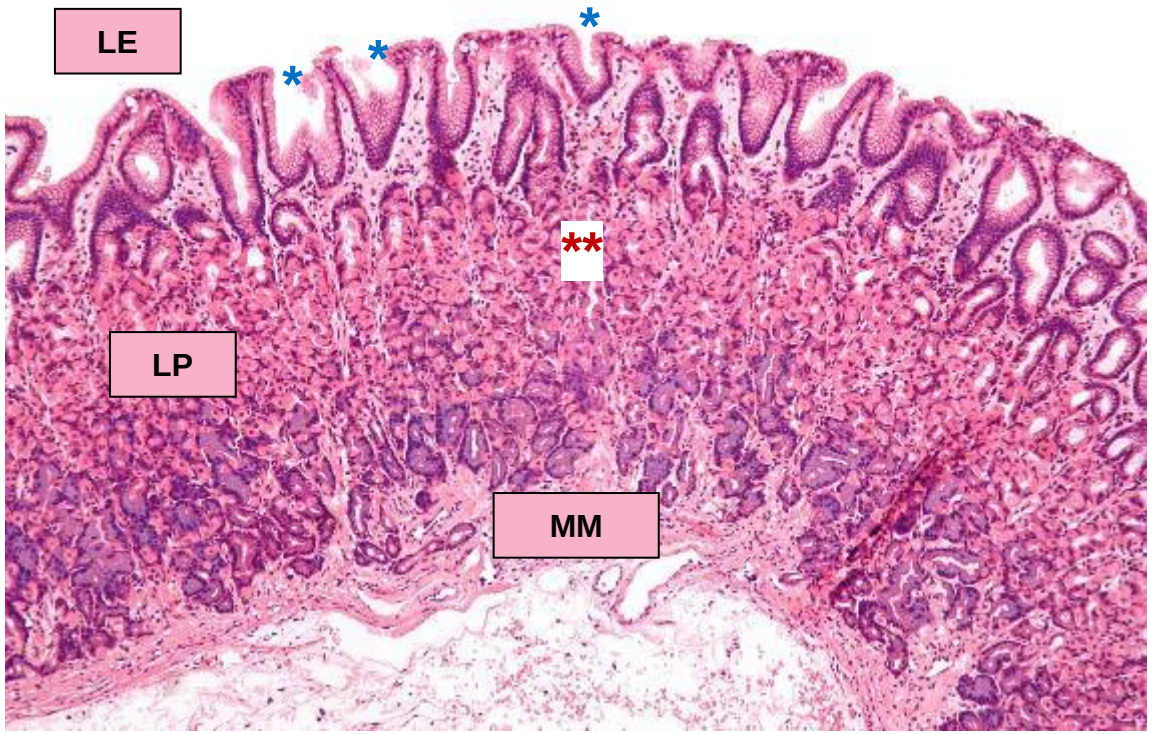
- **loose, highly vascularized connective tissue proper** (a rich population of plasma cells, lymphocytes, mast cells, fibroblasts, and occasional smooth muscle cells)
- **presence of glands**** – 3 types of glands in 3 different regions; → 5-7 glands open into the bottom of each gastric pit
- presence of GALT

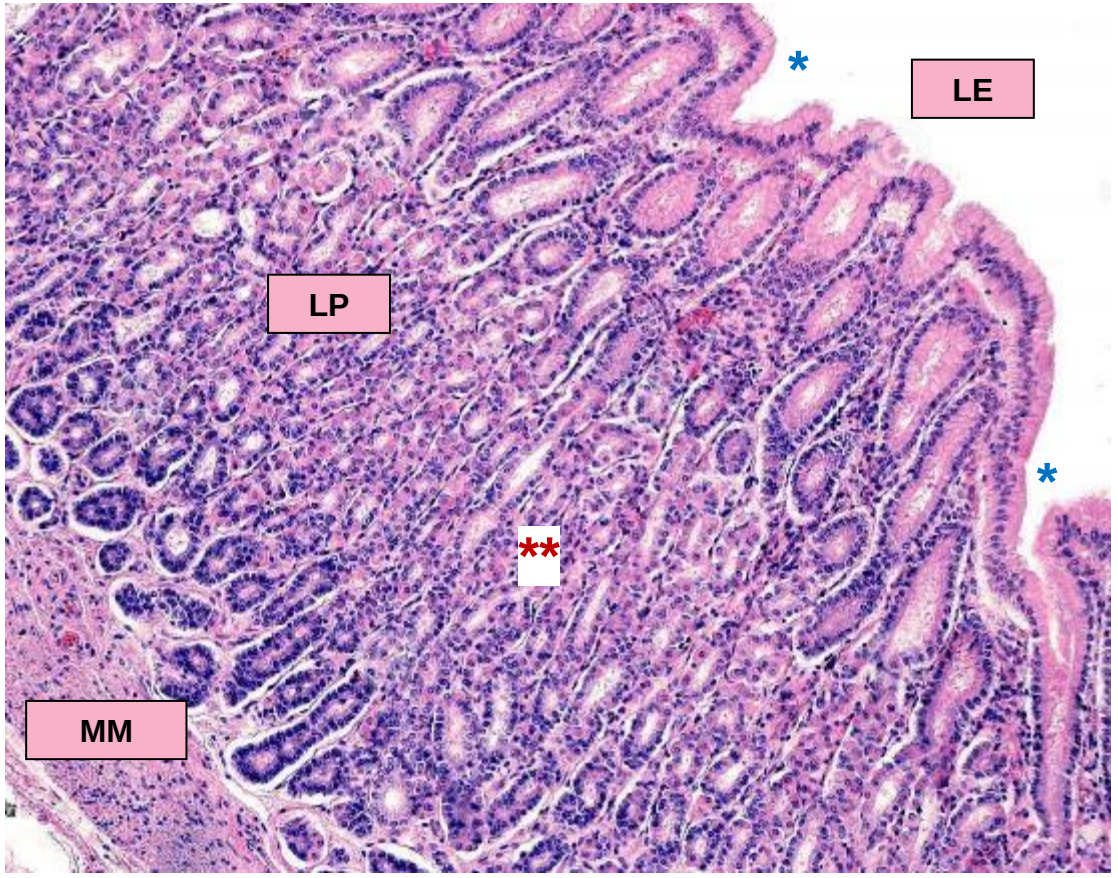
Muscularis mucosae (MM) don't mix it up with muscularis externa (ME)

- is arranged in **3 layers of smooth myocytes**
  1. inner circular (well defined)
  2. outer longitudinal (well defined)
  3. outermost circular (not always evident)

Stomach (#48)

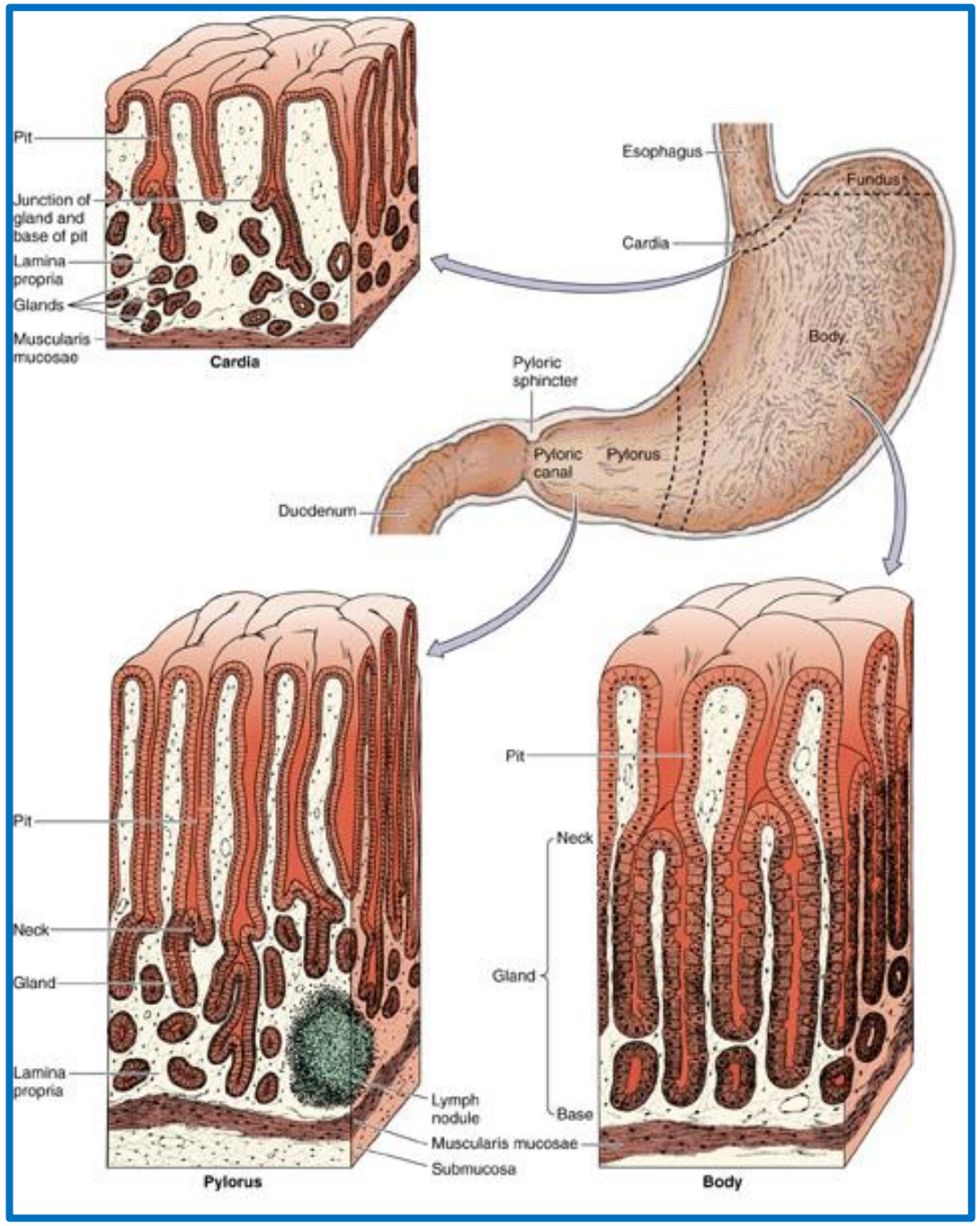
Mucosa





Stomach (#48)

- in gross observation – **4 regions**
- **histologically - 3 regions**:
  1. cardiac
     - part near esophagus
     - contains **cardiac glands**
  2. fundic
     - part between cardiac and pyloric region (fundus+body/corpus)
     - contains **fundic glands**
       - *aka* gastric glands
  3. pyloric
     - part proximal to pyloric sphincter
     - contains **pyloric glands**



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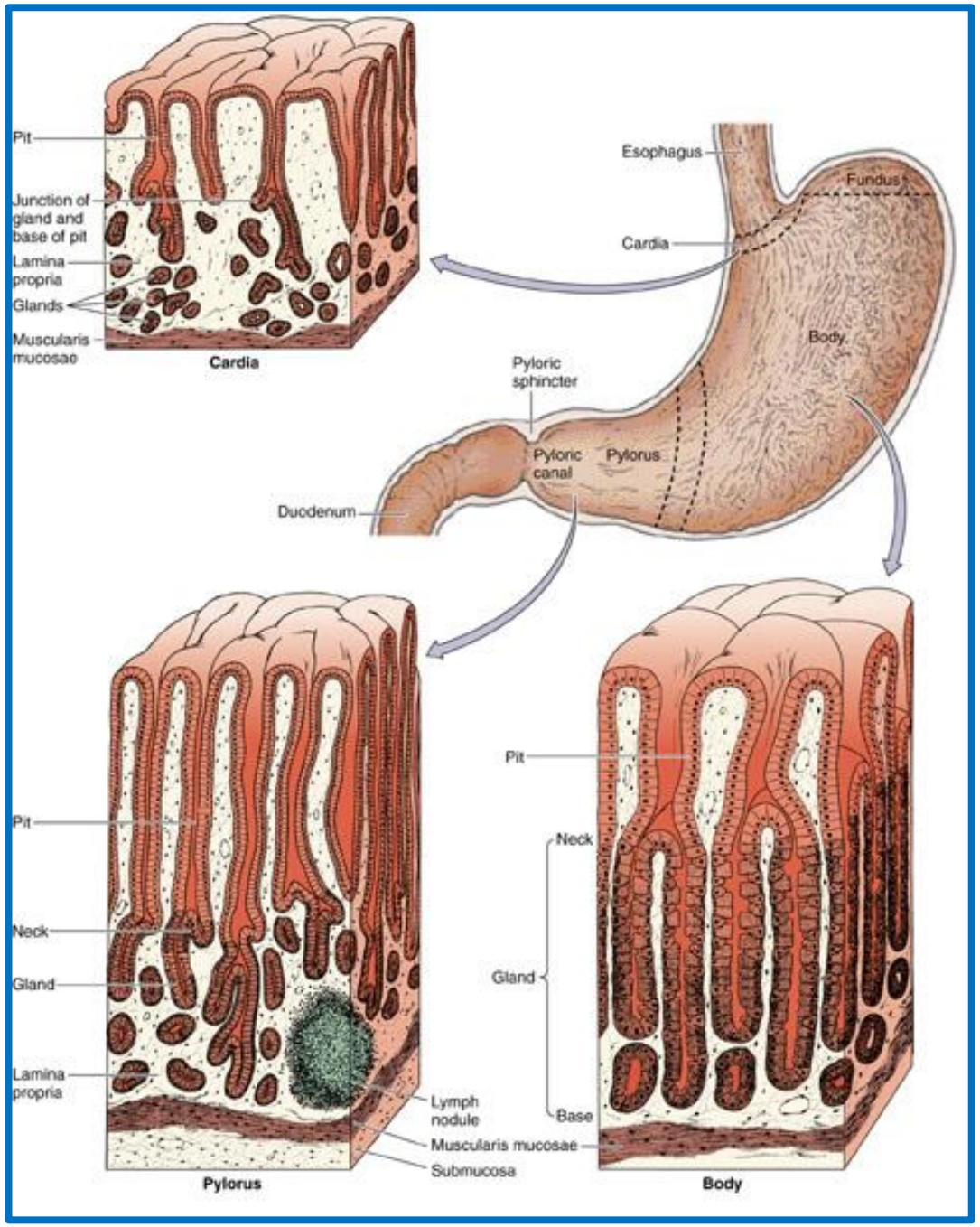
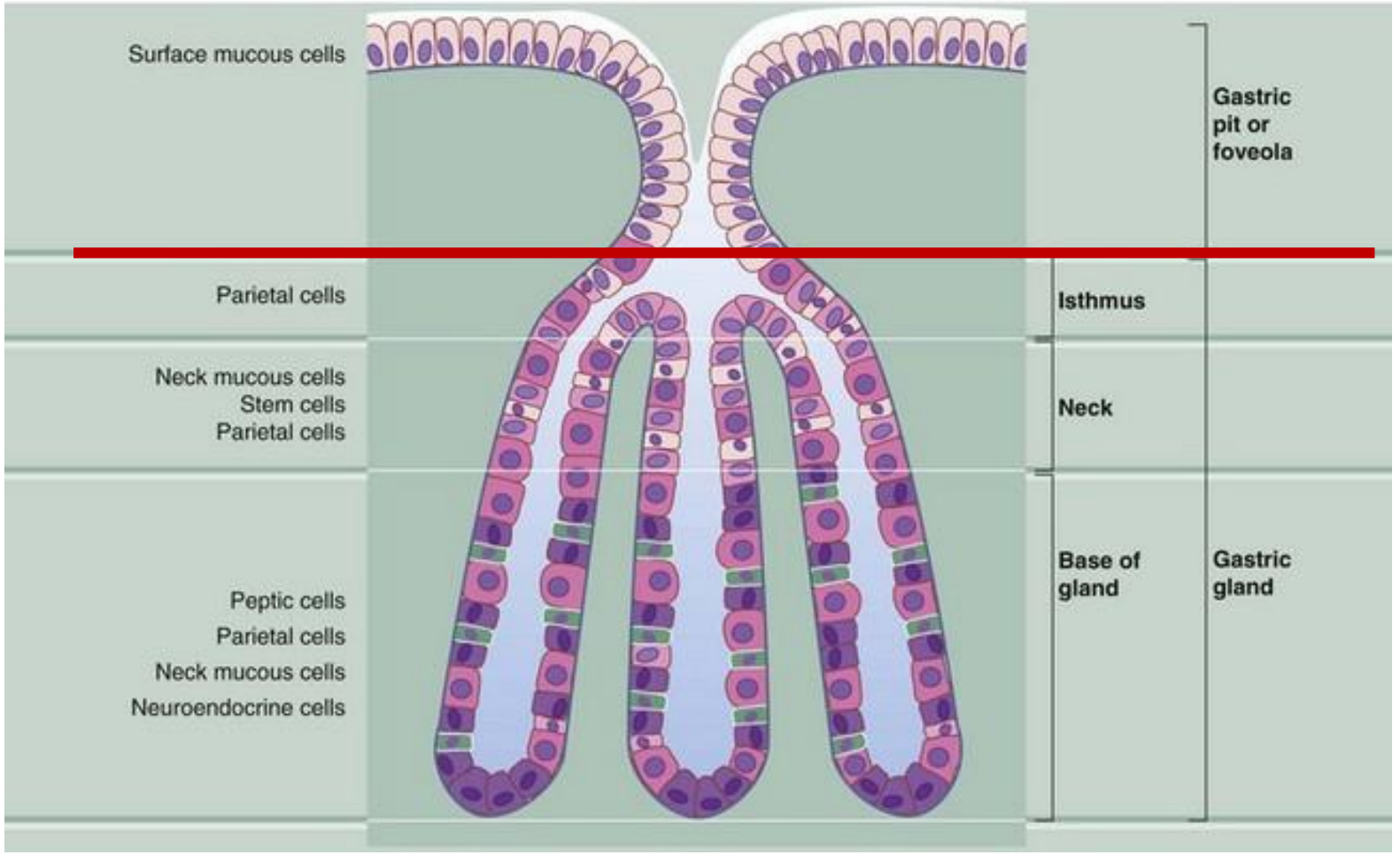


Stomach (#48)

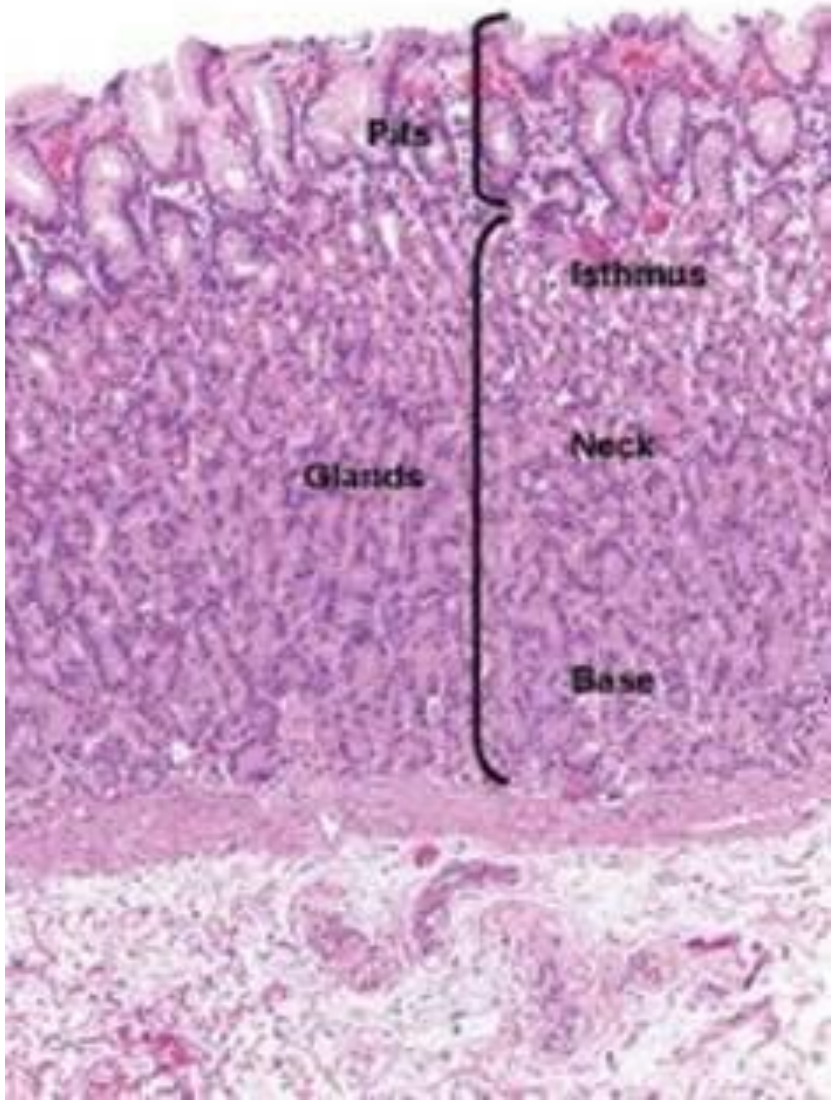
Fundic (oxyntic) gland

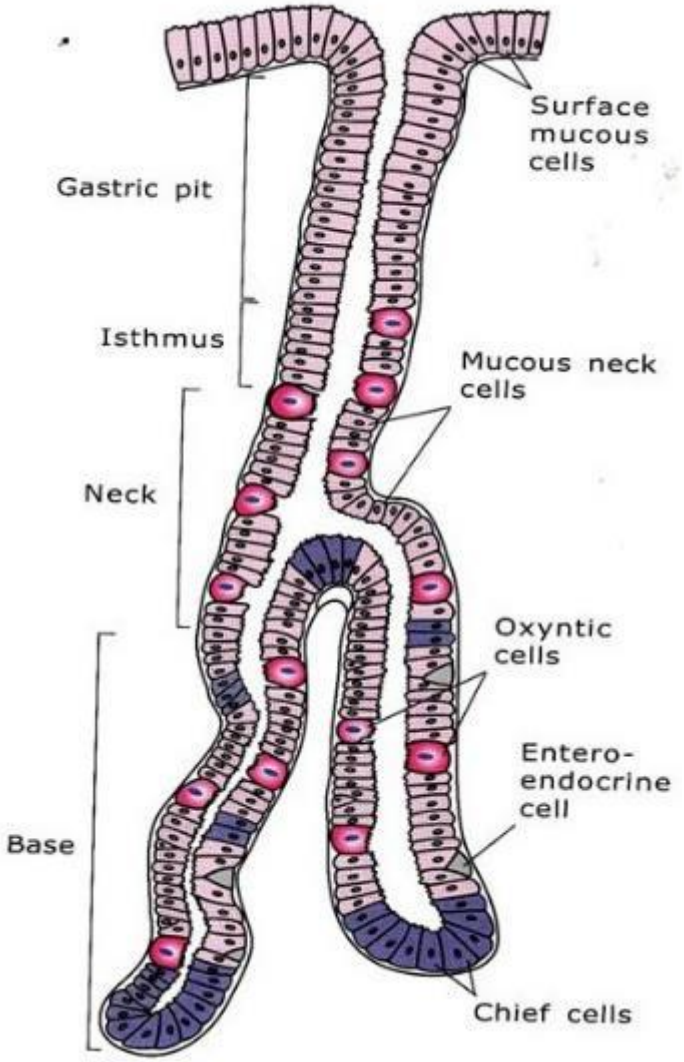
- in the fundus & the body/corpus
- extends from the base of the gastric pit to the muscularis mucosae
- is subdivided into 3 regions:
  1. the **isthmus**
  2. the **neck**
  3. the **base**
- formed by **simple columnar epithelium**
  → 6 cell types:
  1. **surface-lining** cells
  2. **parietal** (**oxyntic**) cells
  3. **regenerative** (**stem**) cells
  4. **mucous neck** cells
  5. **chief** (**zymogenic**) cells
  6. **DNES** cells

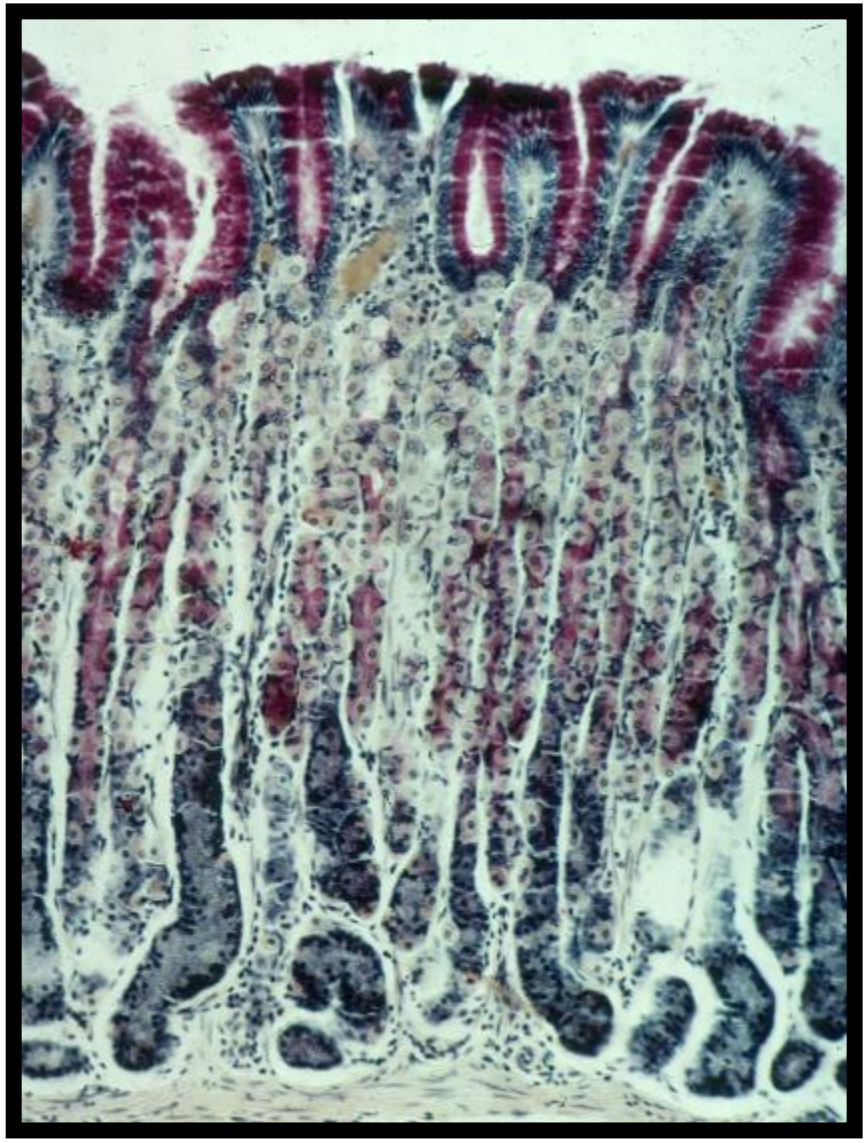


Region	Cell Types
Isthmus	Surface-lining cells and few DNES cells (few parietal cells)
Neck	Mucous neck cells, regenerative cells, parietal cells, and few DNES cells
Base	Chief cells, occasional parietal cells, and few DNES cells

Stomach (#48)

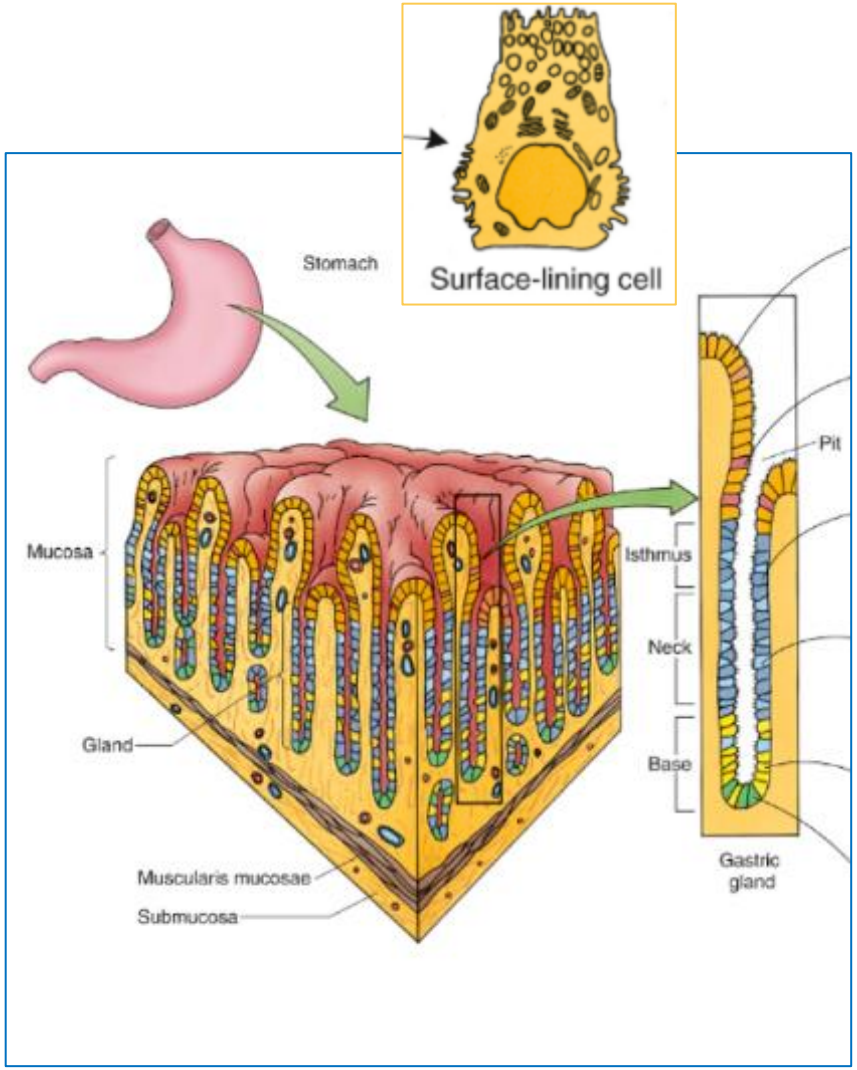






Fundic (oxyntic) glands – they are rather straight

Stomach (#48)



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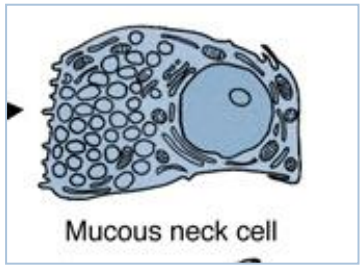
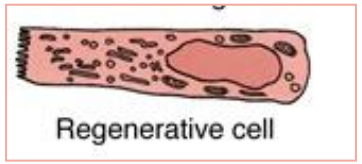
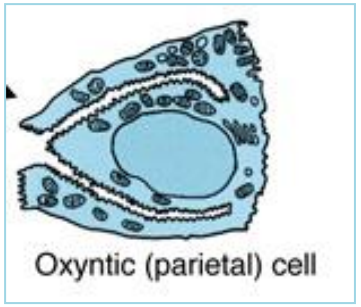


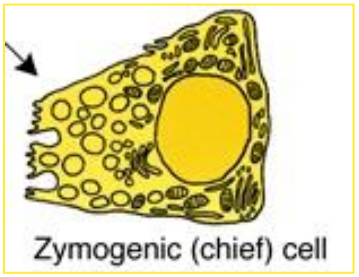
Produce **soluble mucus** mixed with and lubricates the chyme, reducing friction as it moves along the digestive tract.



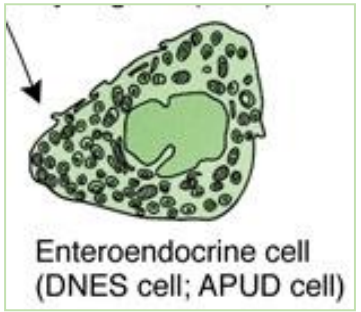
Proliferate to **replace** all of the cells of stomach epithelium every 5-7 days → migration of the new cells is bidirectional in the stomach



Manufacture **hydrochloric acid** (H^+, Cl^-) and **gastric intrinsic factor** (Castle's factor)

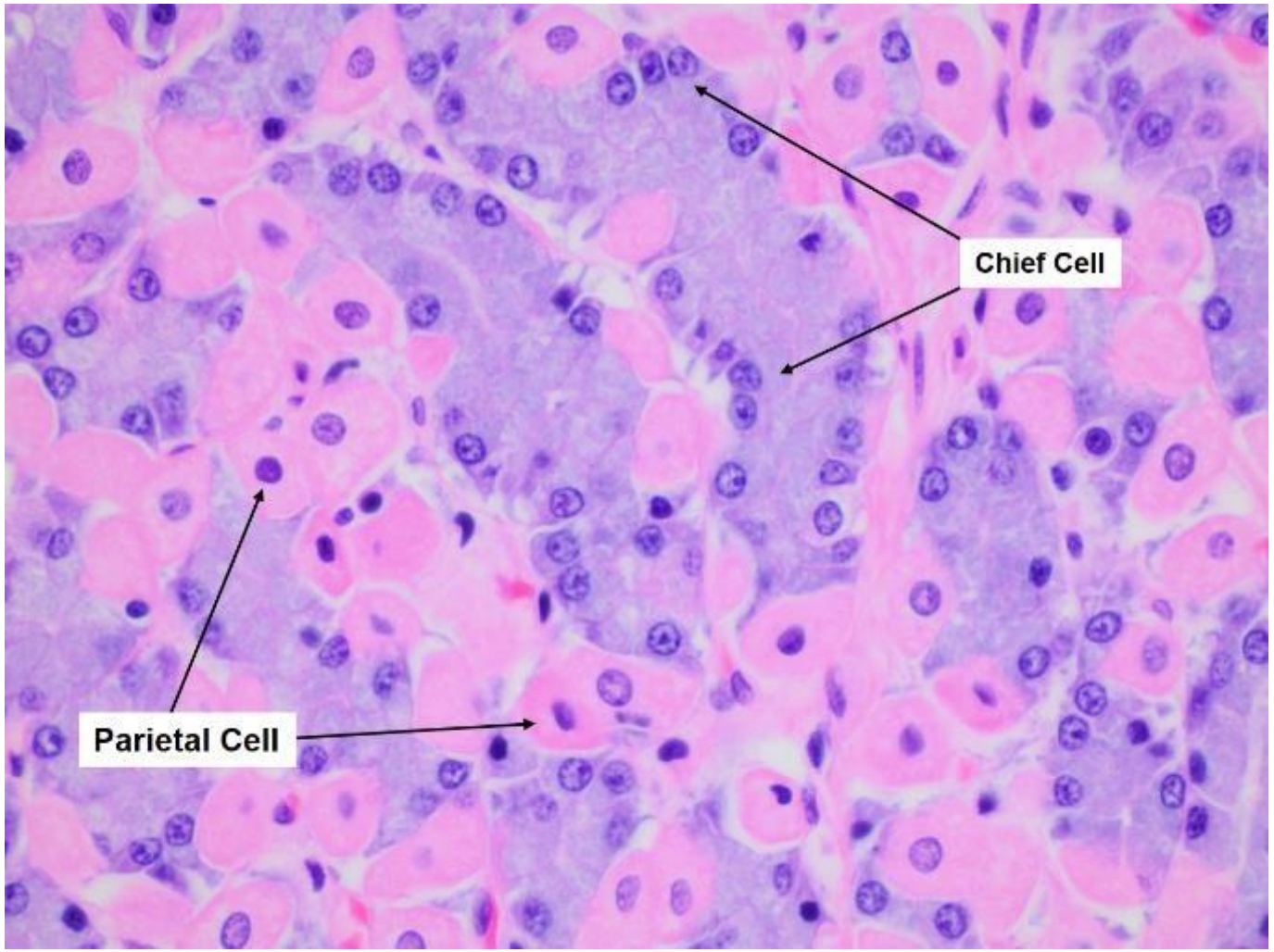


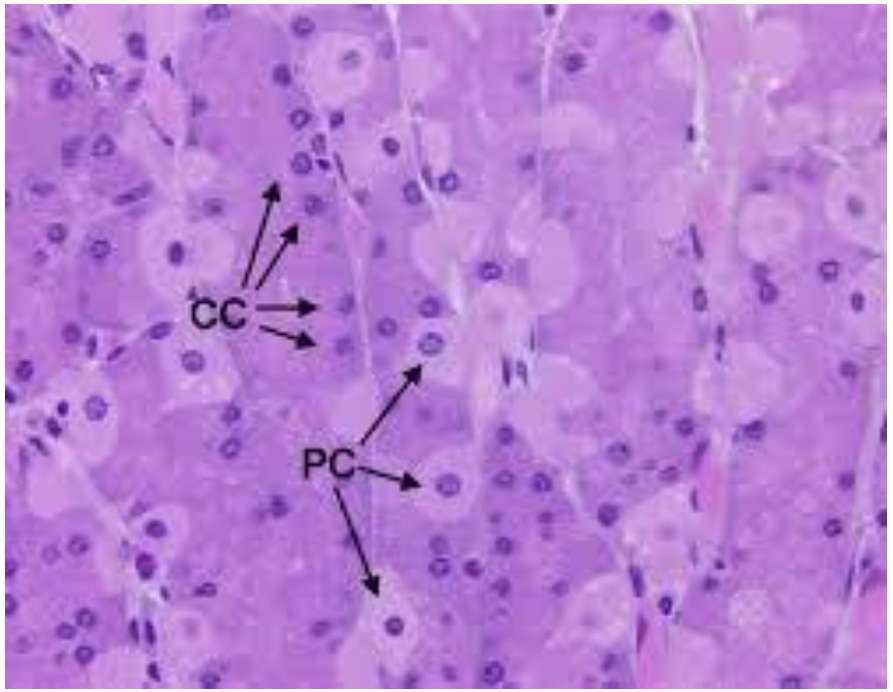
Manufacture the **(pro)enzymes**: pepsinogen, rennin and gastric lipase.

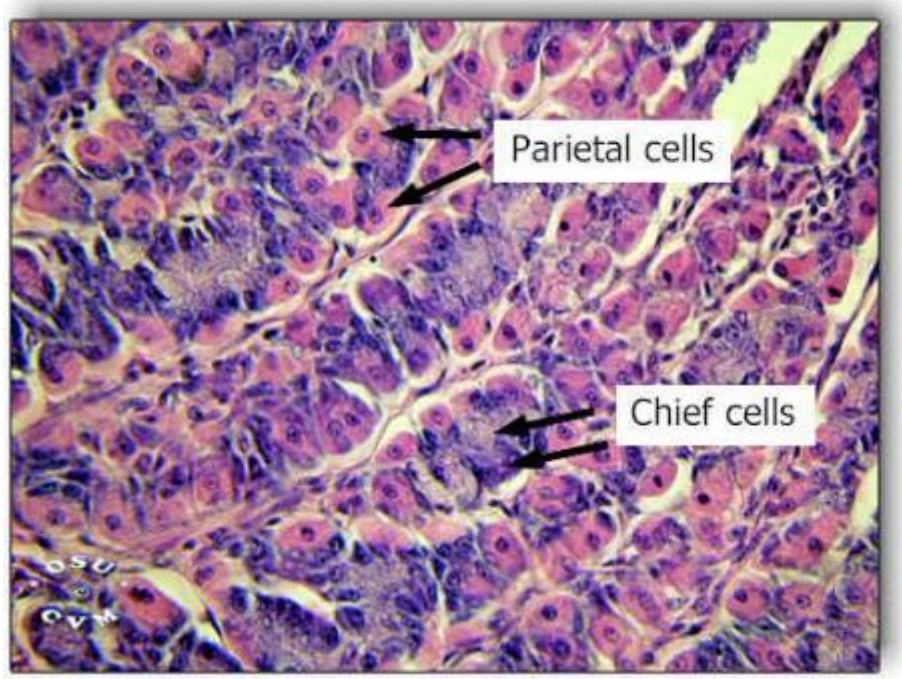


Manufacture endocrine, paracrine and neurocrine **hormones** (e. g. gastrin - G, histamine –ECL cells).

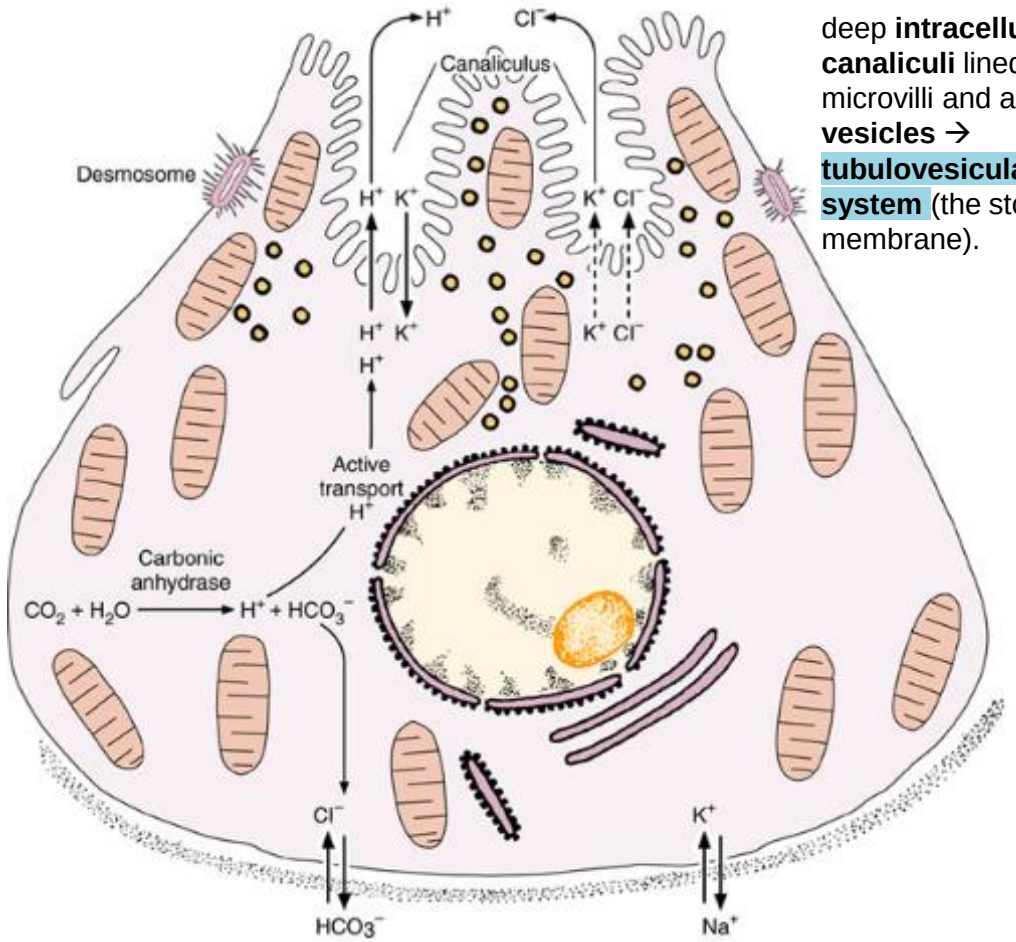
Stomach (#48)







Parietal (oxyntic) cell



deep **intracellular canaliculi** lined by microvilli and a lot of **vesicles** → **tubulovesicular system** (the storage of membrane).

Gastric intrinsic factor is necessary for vitamin B_{12} absorption in the ileum → deficiency of vitamin B12 the development of **pernicious anemia**

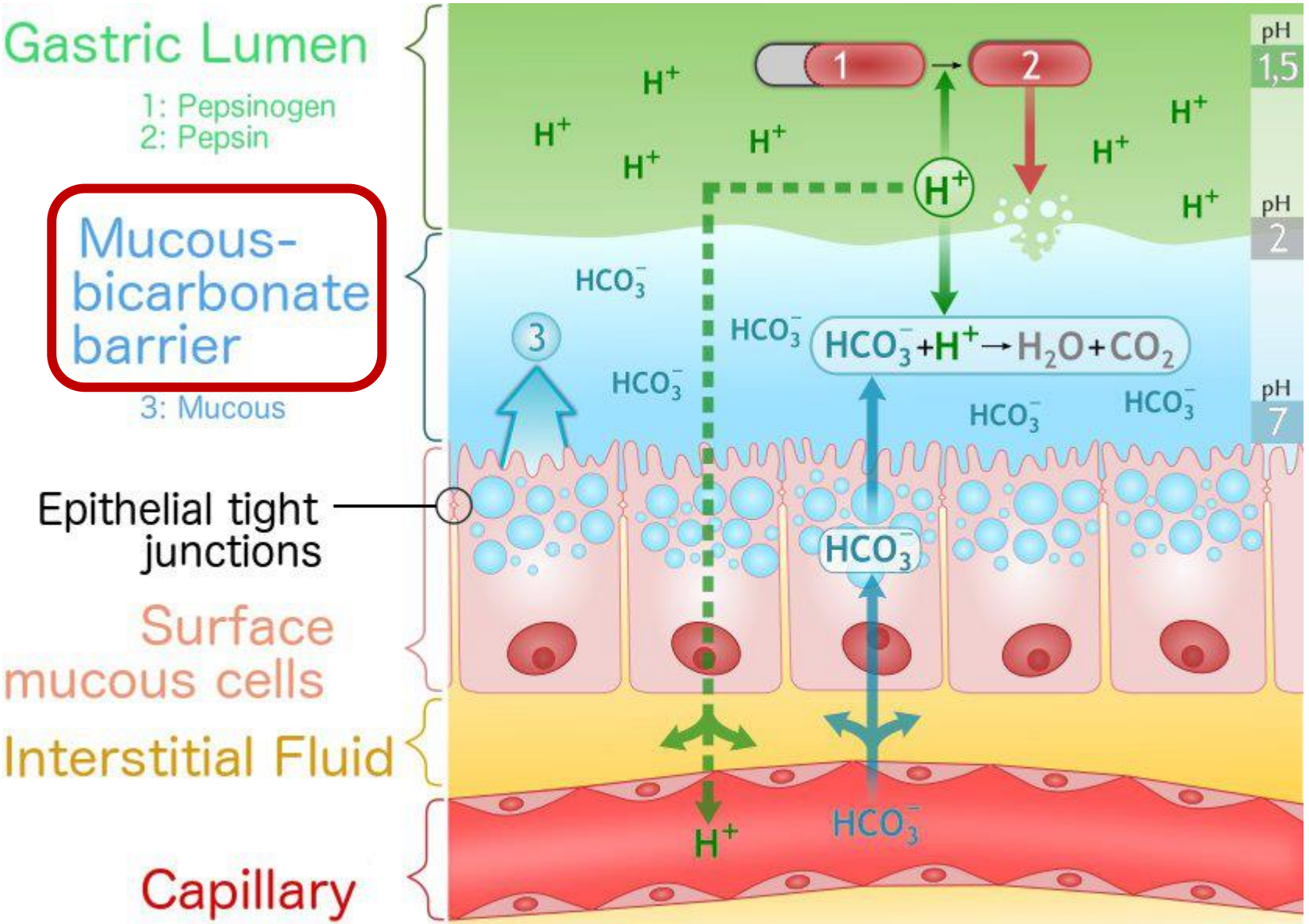
- Mechanism of Gastric Hydrochloric Acid Production
  1. Carbonic anhydrase catalyzes formation of H_2CO_3 (carbonic acid) from CO_2 and H_2O
  2. H_2CO_3 dissociates into H^+ ions and HCO_3^- (bicarbonate) ions
  3. H^+,K^+- ATPase – H^+ out, K^+ in.
  4. HCO_3^- ions are exchanged for a Cl^- ions and HCO_3^- ions diffuse into the venous blood.
  5. Cl^- ions are transported out of the cell by ion channels and the formation of HCl occurs.

- HCl breaks down food material and activates pepsinogen to become active enzyme – pepsin.

- Production of HCl is regulated by:
  - **gastrin** (G cells), **histamine** (ECL cells), **acetylcholine** – stimulation (⇑ HCl)
  - **gastric inhibitory peptide** (K cells), **somatostatin** (D cells), **prostaglandins**, **urogastrone** (EGF; cells of Brunner glands in duodenum) – inhibition (⇓ HCl)

Mucous-Bicarbonate barrier (M-B barrier)

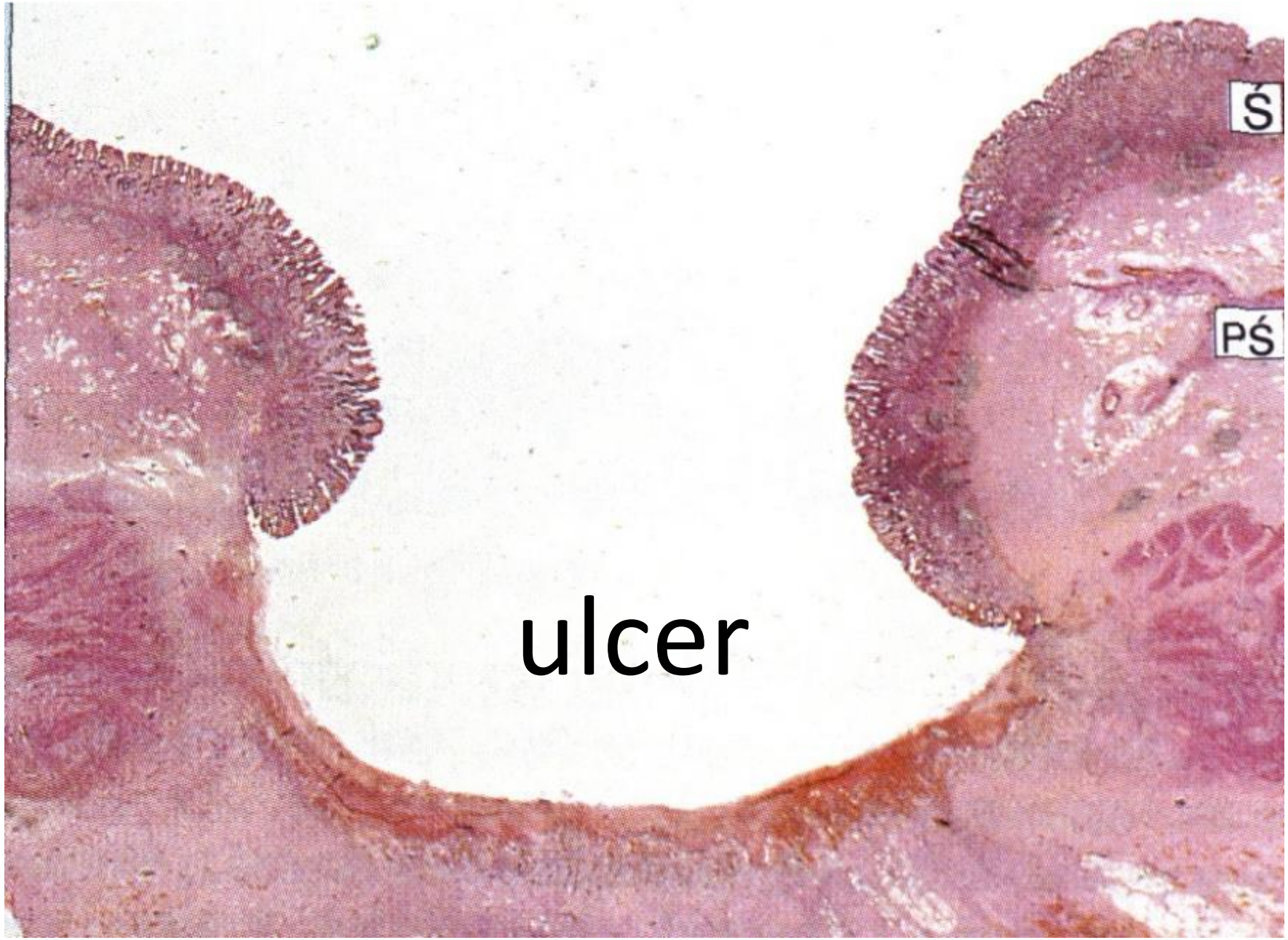
Stomach (#48)



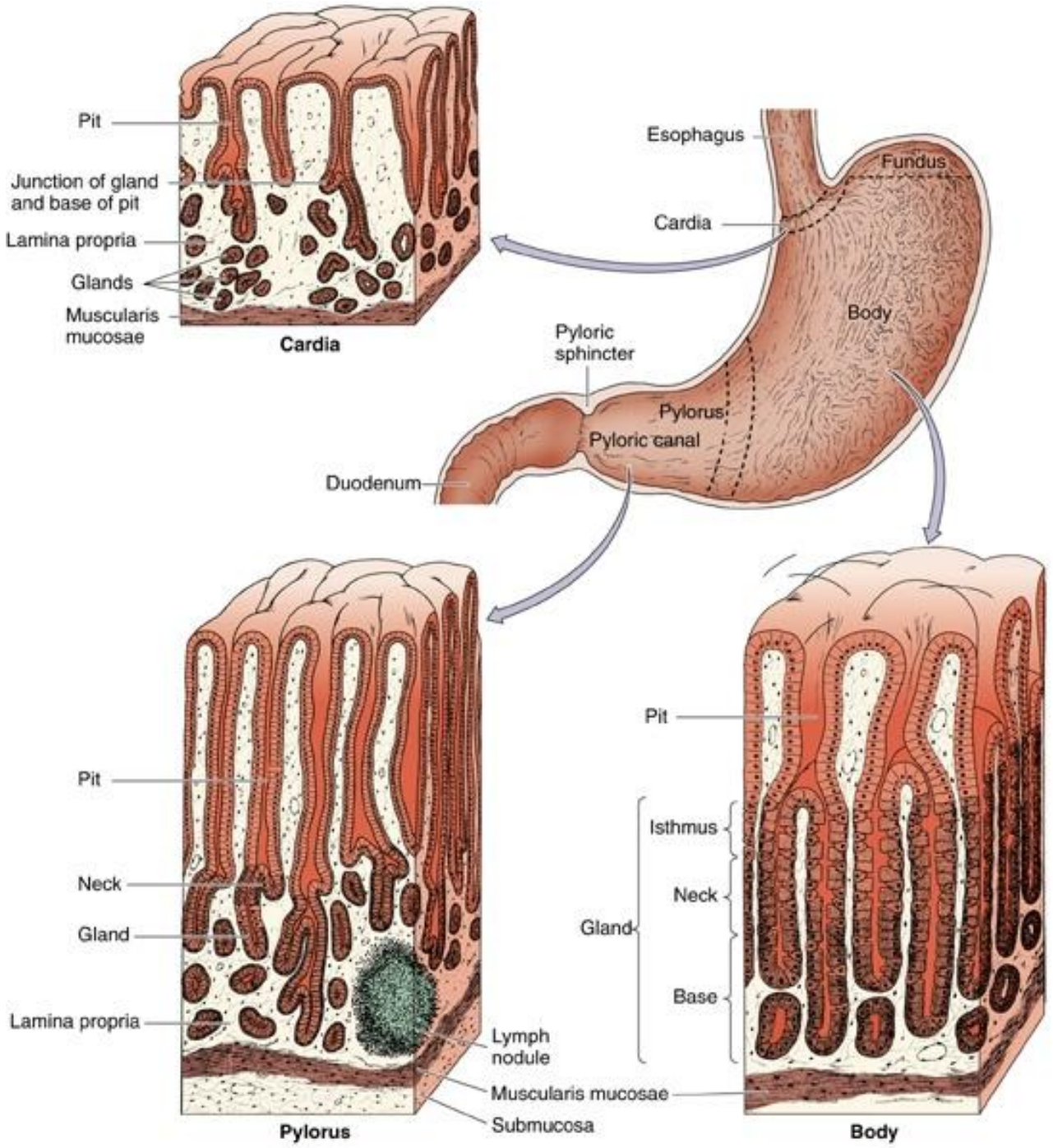
visible mucus, containing trapped bicarbonate ions adheres to the epithelium - protects it from autodigestion and maintains neutral pH.

- components of the M-B barrier:
  1. **tight junctions** between surface-lining cells
  2. substances secreted by surface-lining cells:
     i. **insoluble visible mucus** - a protective gel-like coating over the entire surface of the gastric mucosa;
     ii. **bicarbonate ions**
- factors that can damage the barrier
  1. bacterial infection by *Helicobacter pylori*
  2. alcohol
  3. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) like aspirin

Stomach (#48)



Stomach (#48)



- **<u>The mucosa of the cardiac region</u>**
  - **gastric pits** are <u>shallower</u> than in the fundic region
  - **cardiac glands**
    - the base of glands is <u>highly coiled</u>
    - contain mostly <u>surface-lining cells</u> (thick, insoluble, visible mucus), some <u>mucous neck cells</u> (soluble mucus), <u>regenerative cells</u>, <u>DNES</u> cells and a few <u>parietal cells</u> (**no chief cells**).

- **<u>The mucosa of the pyloric region</u>**
  - **gastric pits** are deeper than in the fundic region
  - **pyloric glands**
    - are <u>highly coiled</u> and <u>tend to branch</u>
    - contain the same cell types as in the cardiac region but predominant are the <u>mucous neck cells</u>, which beside mucus, produce – lysozyme – bactericidal enzyme.

Stomach (#48)

Submucosa

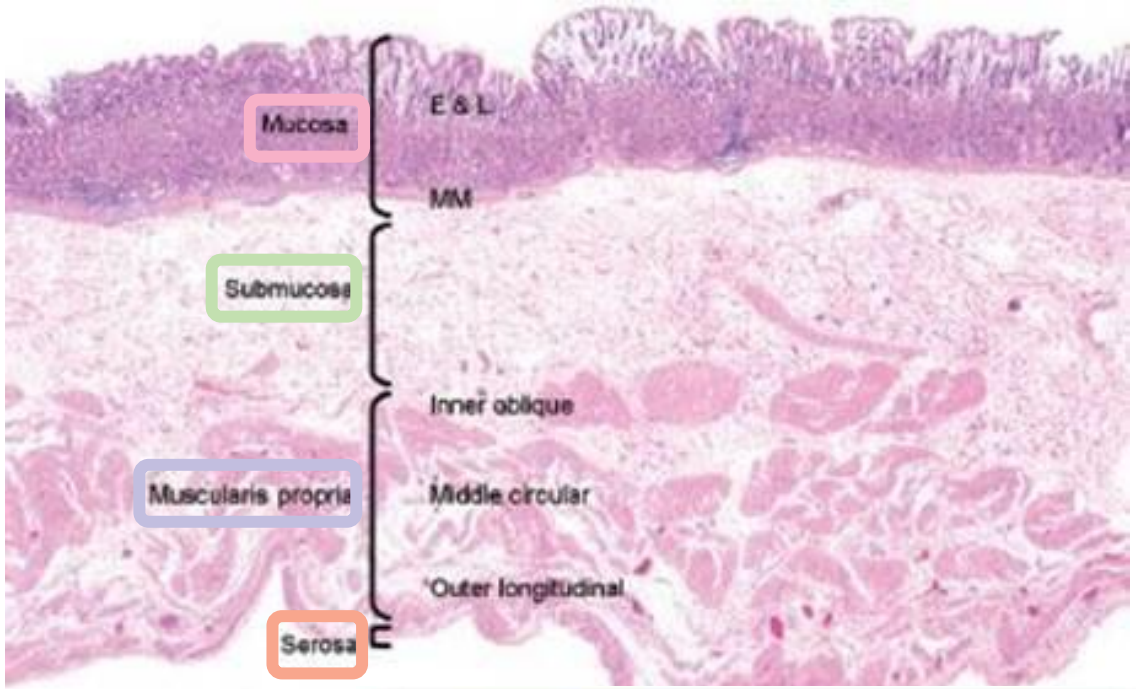
- **dense, irregular collagenous** connective tissue proper
- presence of
  - ➢ a rich vascular and lymphatic network
  - ➢ **Meissner submucosal** plexus

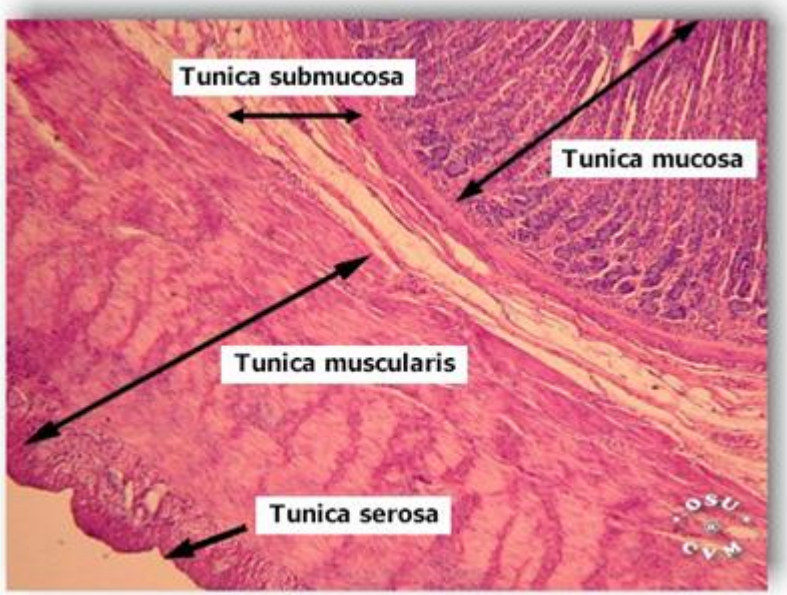
Muscularis externa

- **3 layers of smooth muscle**:
  1. **innermost oblique** layer - not well defined, except in the cardiac region
  2. **middle circular** layer - especially pronounced in the pyloric region (pyloric sphincter)
  3. **outer longitudinal** layer - poorly developed in the pylorus
- presence of **Auerbach myenteric** plexus
  - ➢ between the middle circular and outer longitudinal layers of smooth muscle

Serosa

- **thin, loose connective tissue proper** covered by a smooth, wet, **simple squamous** epithelium`(**mesothelium**)



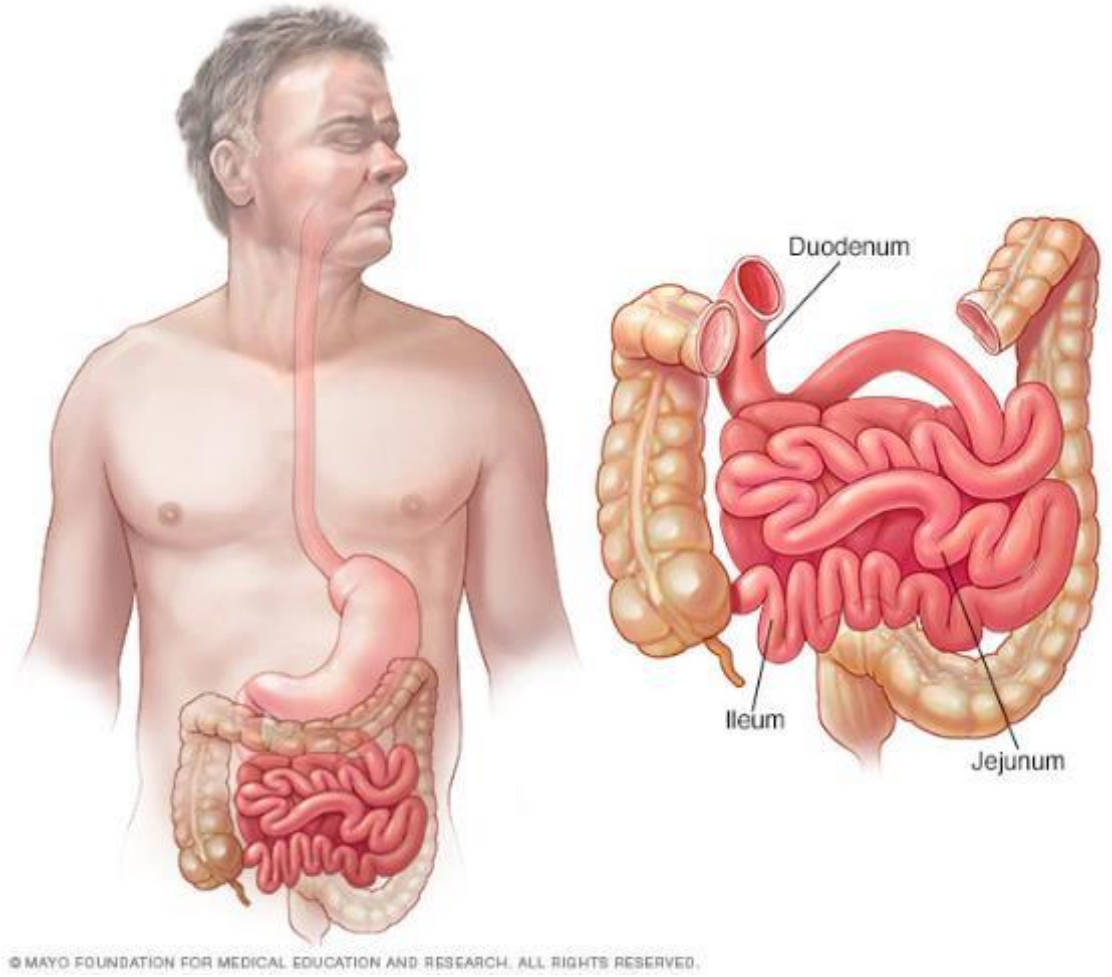


Small intestine

Small intestine

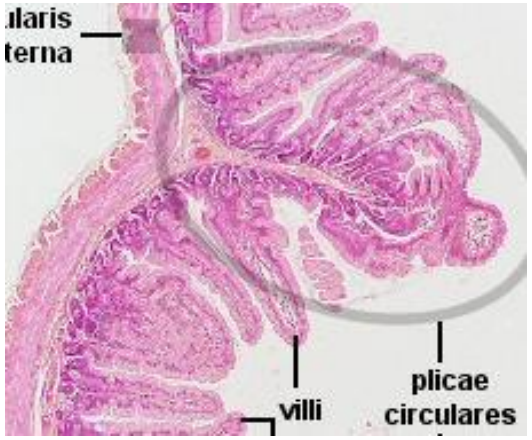
- longest part of the digestive tract
  - ➢ runs from pyloric sphincter to ileocecal valve (ICV) or Bauhin's valve
- consists of **three segments**
  1. **duodenum** – 5% of length
  2. **jejunum** – almost 60% of length
  3. **ileum** – almost 40% of length
- main functions – site of the
  1. **enzymatic digestion** of gastric contents (chyme)
     - enzymes are secreted by pancreas
     - brush border enzymes - enzymes are located on microvilli of enterocytes (absorptive cells)
  2. **absorption of nutrients** into blood capillaries & lymphatic lacteals

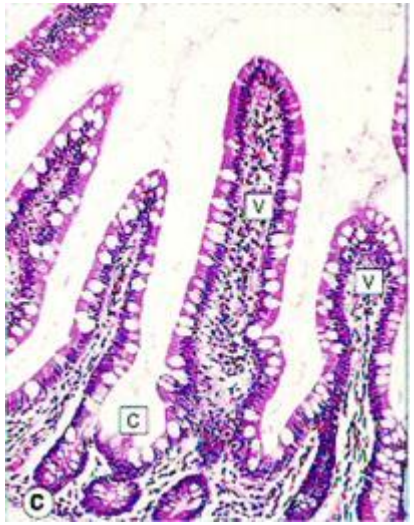
3-6-hour process



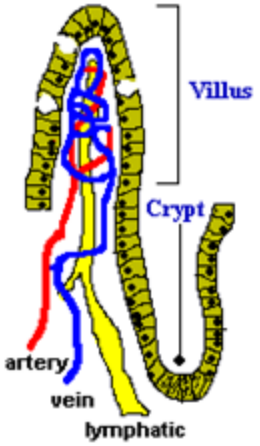
Small intestine

- **surface modifications of small intestine for absorption** include
  1. **plicae circulares** (valves of Kerckring)
     - **permanent spiral folds of the mucosa with a submucosal core** that extend into the intestinal lumen
     - increase the surface area by up to 3 times
  2. **villi**
     - **permanent finger-like projections of lamina propria** of the mucosa that extend into the intestinal lumen
     - covered by **simple columnar epithelium**
     - the connective tissue **core of each villus** contains a lymphatic capillary called a **lacteal**, **blood capillaries**, and individual strands of **smooth muscles**
     - increase the surface area 10 times
  3. **microvilli**
     - **cytoplasmic extensions** that cover the apices of the intestinal absorptive cells
     - visible under a light microscope as a **brush border**
     - coated by glycocalyx, which contains **brush border enzymes**
     - increase the surface area 20 times

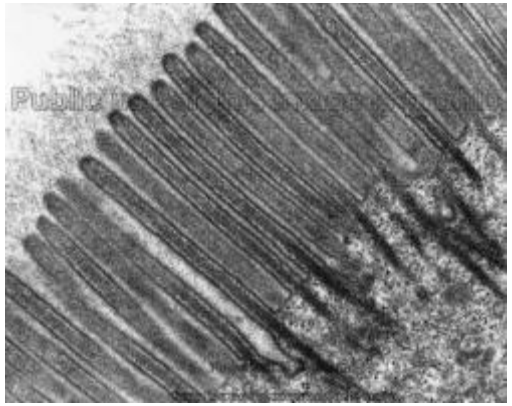




villi



microvili



Small intestine

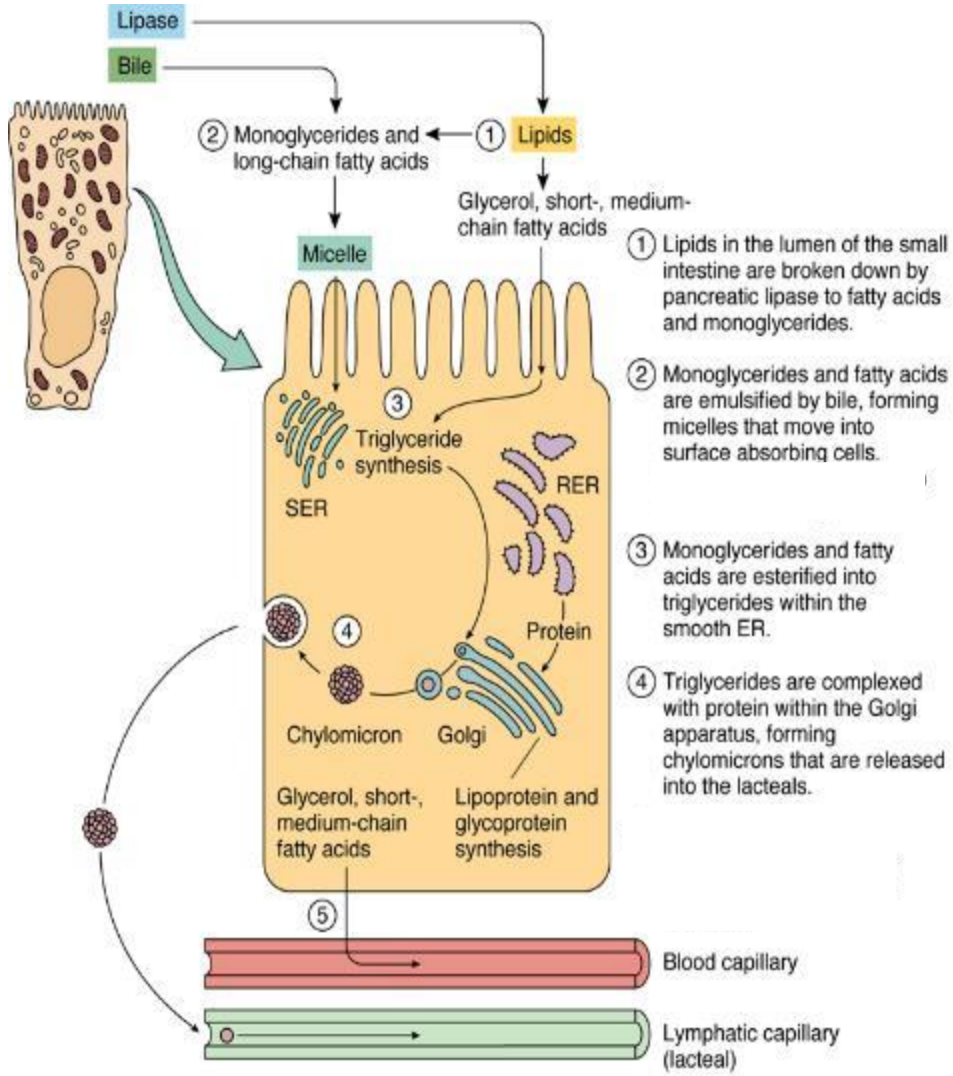
Absorption

- The final breakdown of proteins and carbohydrates occurs at the microvilli, where dipeptidases and disaccharidases, adherent to the glycocalyx, liberate individual amino acids and monosaccharides (glucose, fructose)

- Absorption of nutrients in the small intestine occurs via diffusion, facilitated diffusion, osmosis, and active transport

- Water, amino acids, ions, monosaccharides, glycerol and short-chain fatty acids enter into absorptive cells and are released into lamina propria and enter the capillary bed of the villi to be transported to the liver via portal vein

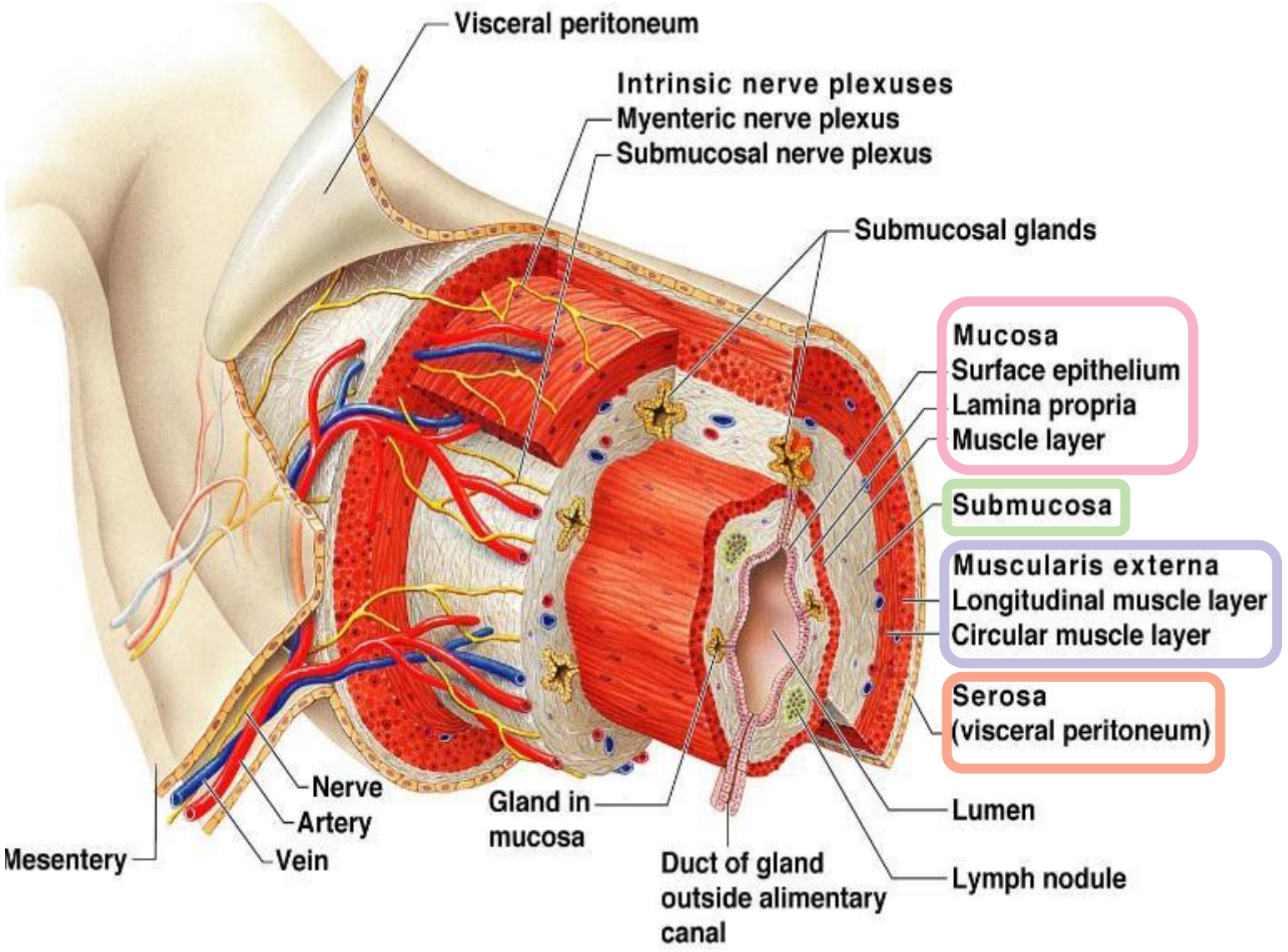
- Most of the long-chain fatty acids and monoglycerides do not enter the blood capillaries but instead enter the lacteals.
  - Smooth muscle fibers in the villi move and contract the villi. This action forces the contents from the lacteals into larger lymph vessels in the submucosa.



Small intestine

- in the small intestine wall
  - **4 typical layers**:
    1. mucosa
    2. submucosa
    3. muscularis externa
    4. serosa

  ➢ there are <u>differences</u> in individual parts of the organ

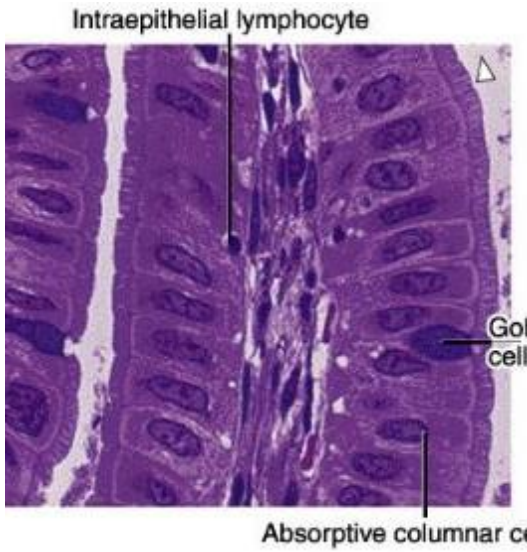


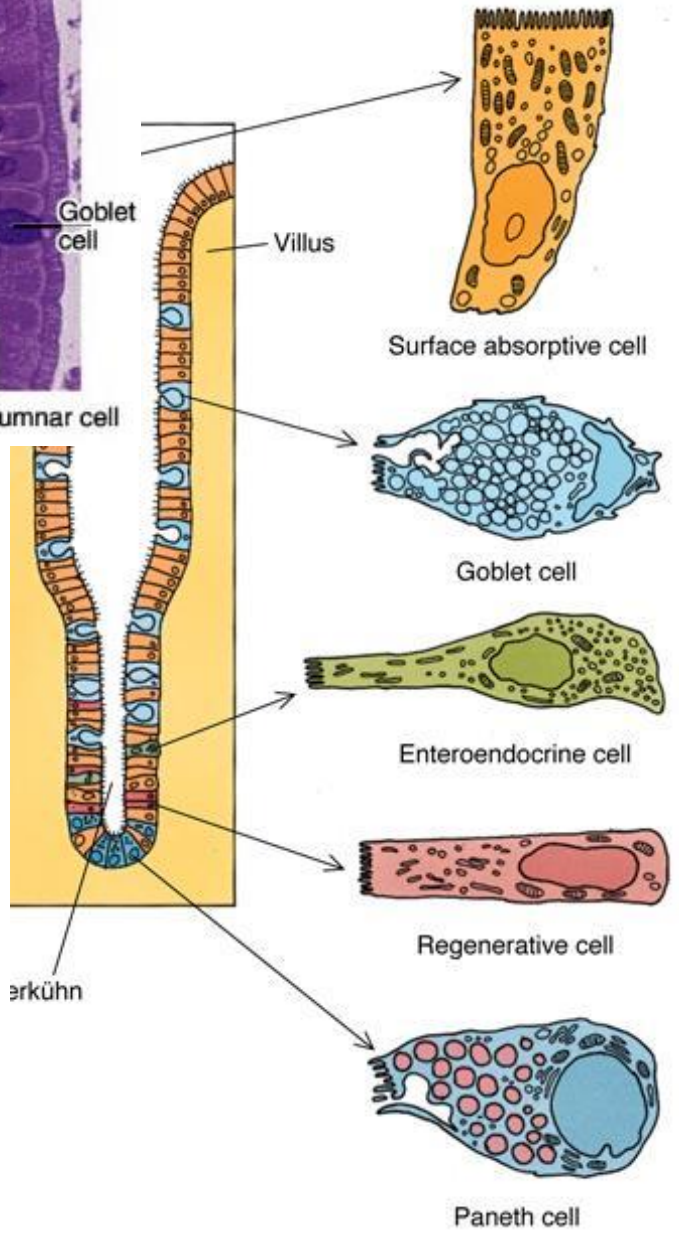
Small intestine

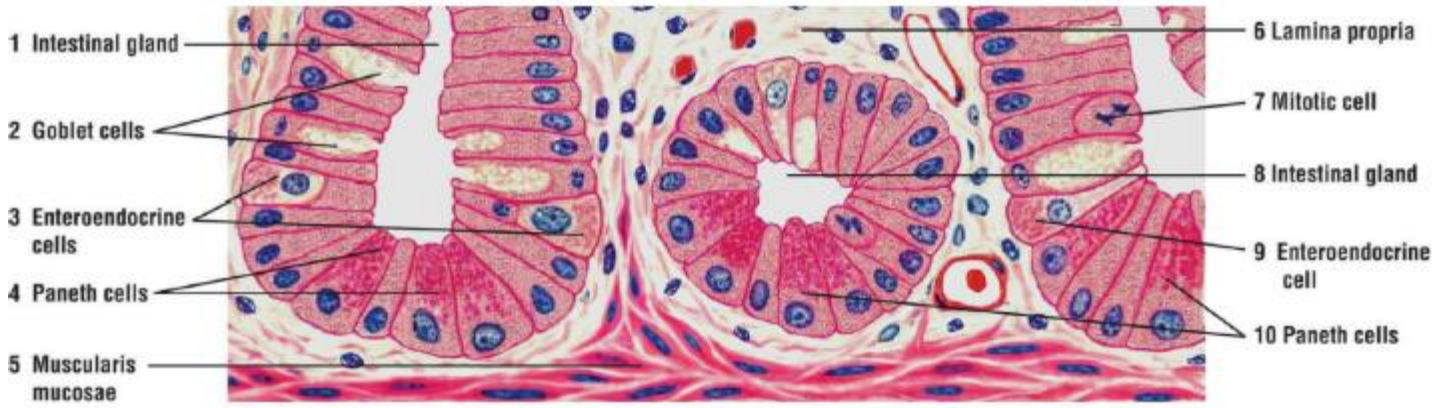
Mucosa

Epithelium

- a **simple columnar epithelium**
  - **on villi** composed of:
    1. surface absorptive cells with microvilli responsible for terminal digestion and absorption of water and nutrients
    2. goblet cells - produce mucinogen, whose hydrated form – mucin is a component of mucus (lubricating and protective layer)
  - e. invaginates into the lamina propria of mucosa, forming **tubular intestinal glads** (**crypts of Lieberkühn**). The epithelium **in glands (crypts)** contain **also**:
    3. DNES cells - enteroendocrine cells, produce paracrine and endocrine hormones
    4. regenerative cells
    5. Paneth cells - produce lysozyme, defensin and TNF
- Microfold Cells (M cells) - belong to the mononuclear phagocyte system of cells, sample, phagocytose, and transport antigens present in the intestinal lumen







Small intestine

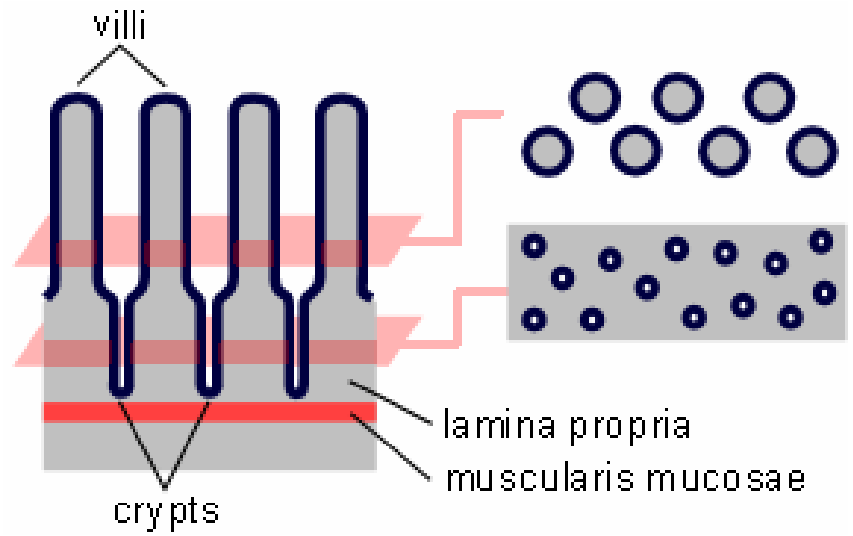
Mucosa

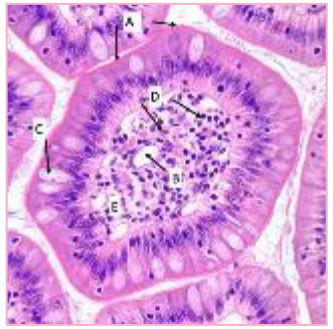
Lamina propria (LP)

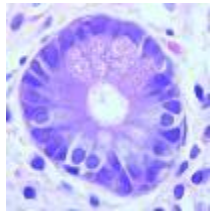
- **loose irregular connective tissue proper** with plasma cells, tissue eosinophils, macrophages, and mast cells
- form **villi** (a lacteal, blood capillaries, and individual strands of smooth muscles from the muscularis mucosae to induce shortening)
- presence of **crypts of Lieberkühn**
- presence of **GALT** - lymphoid cells and occasional lymphoid nodules

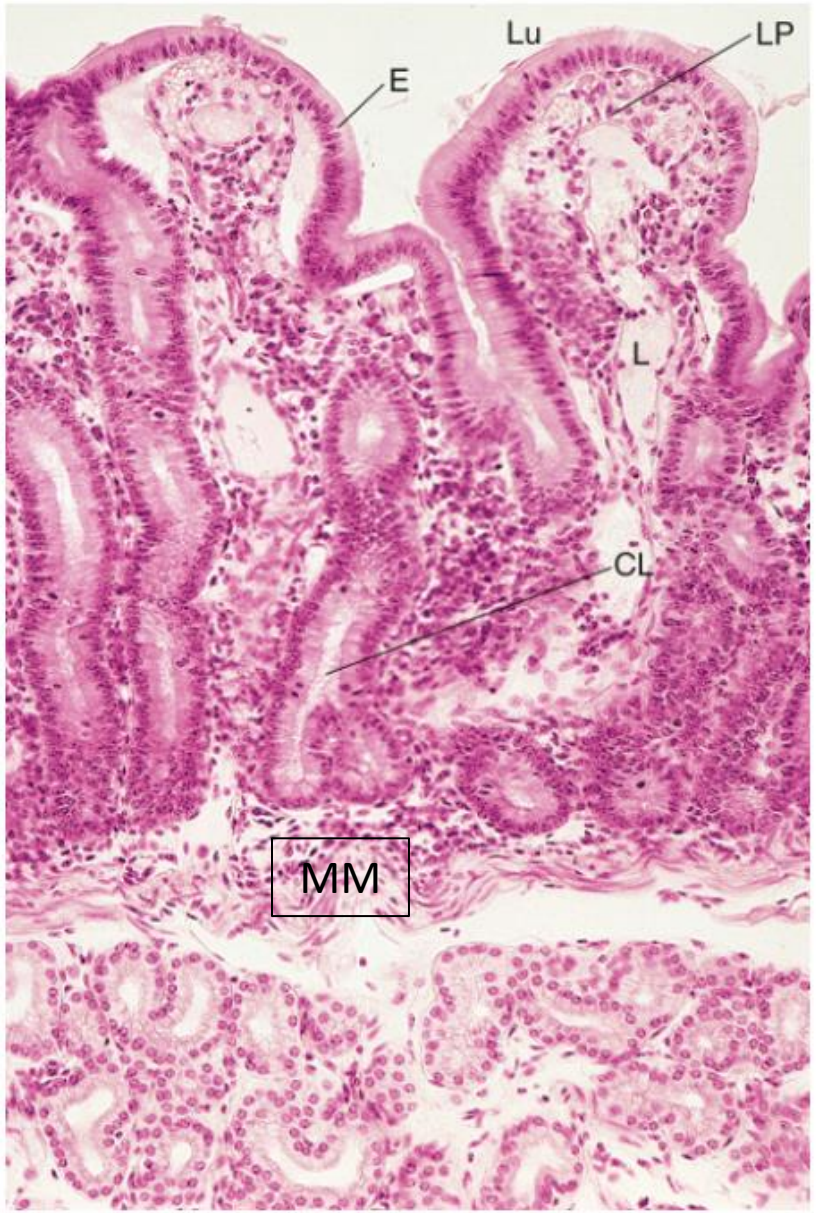
Muscularis mucosae (MM)

- are arranged in **2 layers of smooth myocytes**
  1. inner circular – muscle fibers enter the villus and extend through its core to the tip of the connective tissue → shortening the villus during digestion
  2. outer longitudinal









Small intestine

Submucosa

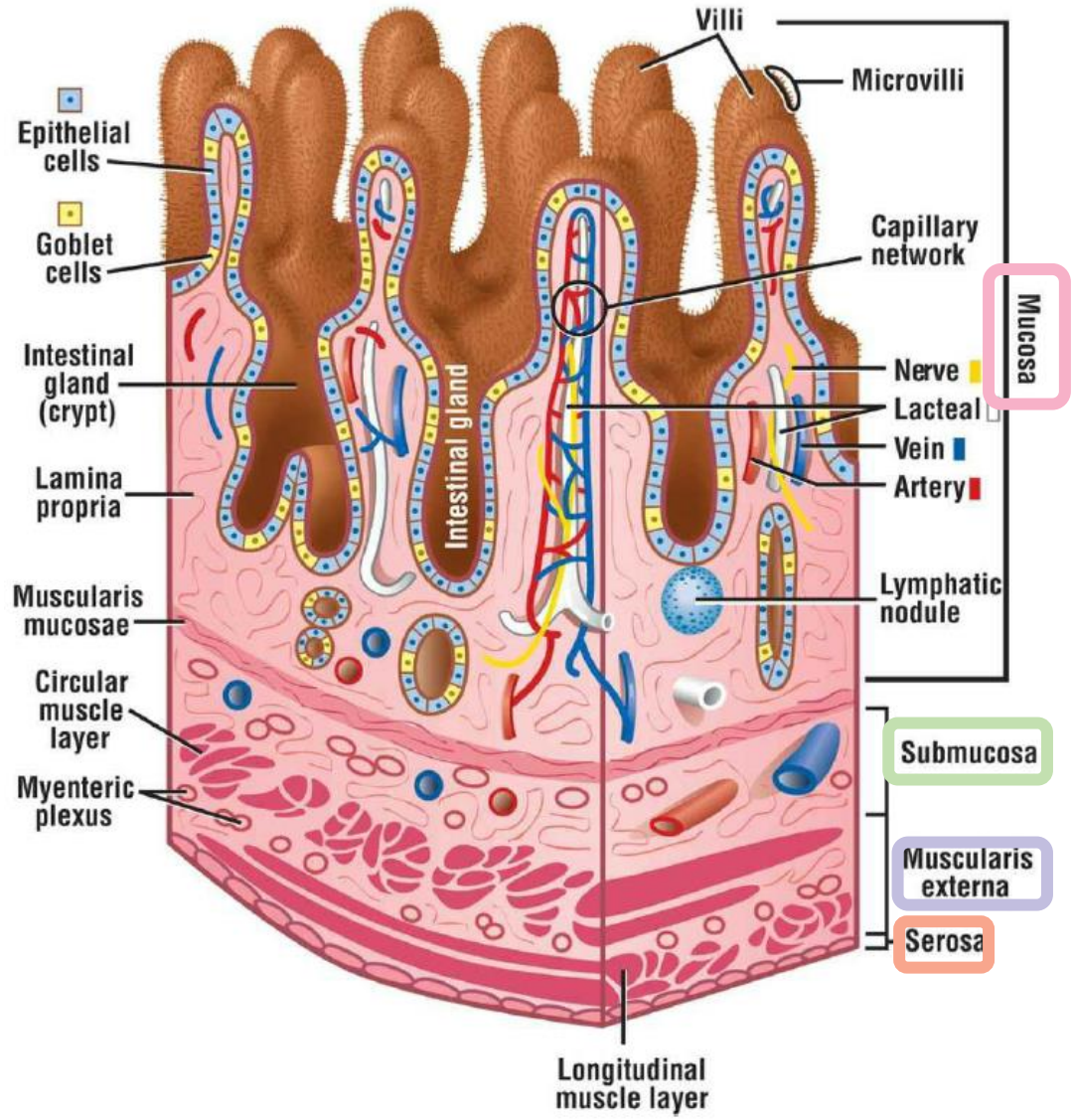
- **dense, irregular fibroelastic** connective tissue proper
- presence of
  - **submucosal lymphatic and vascular plexus**
  - **Meissner submucosal plexus**
  - **Brunner glands** in duodenum

Muscularis externa

- **2 layers of smooth muscle**:
  1. **inner circular** layer
  2. **outer longitudinal** layer
- presence of **Auerbach myenteric plexus**
  - between the two muscle layers

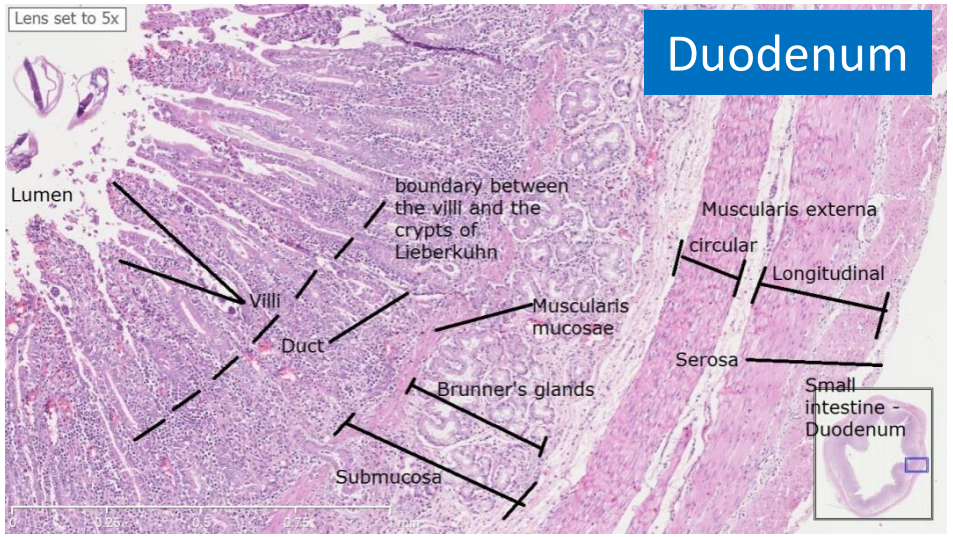
Serosa

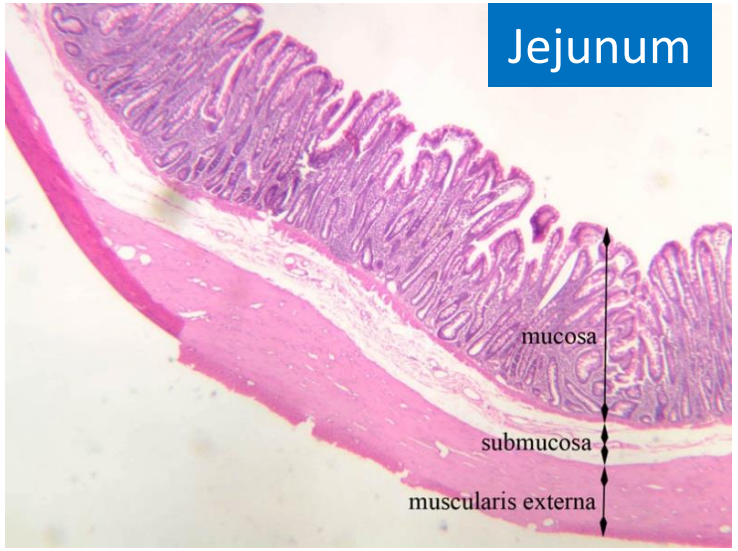
- **thin, loose connective tissue proper** covered by a smooth, wet, **simple squamous** epithelium`(**mesothelium**) - except for the second and third parts of the duodenum

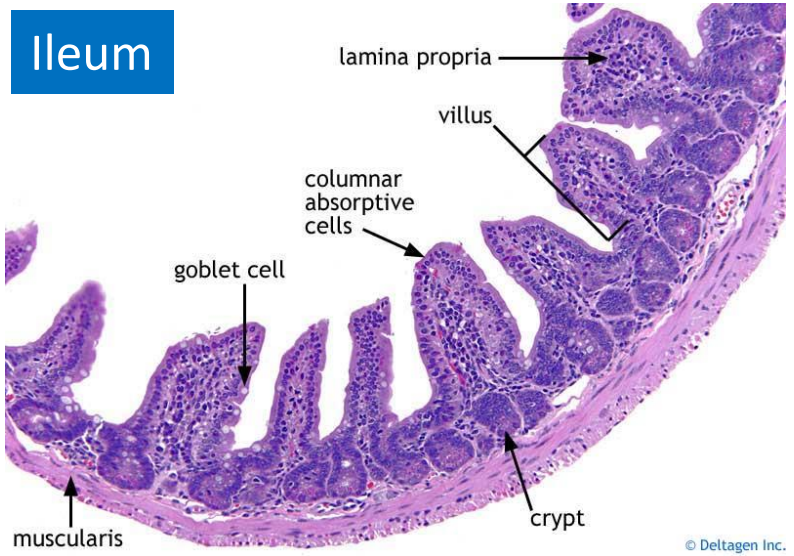


Small intestine

Histological differences

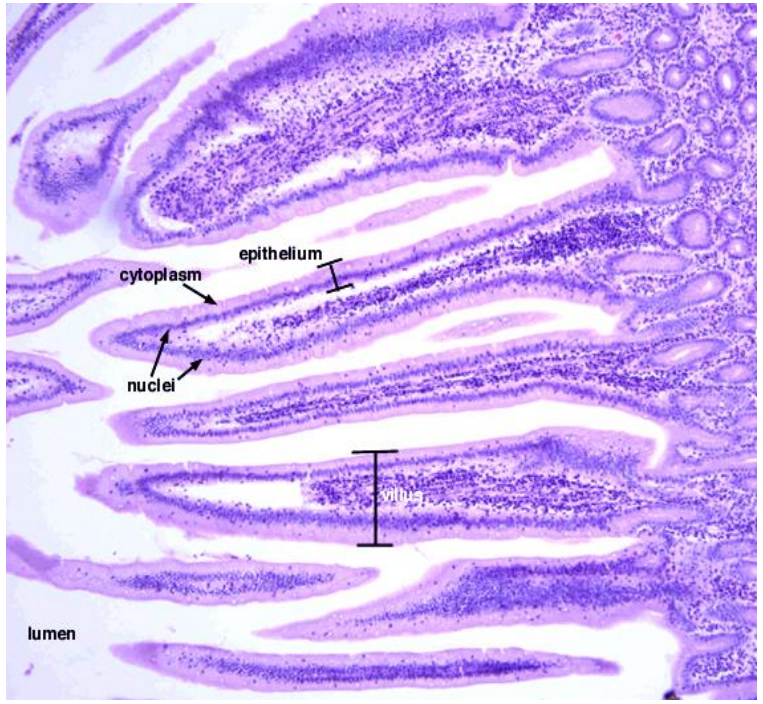




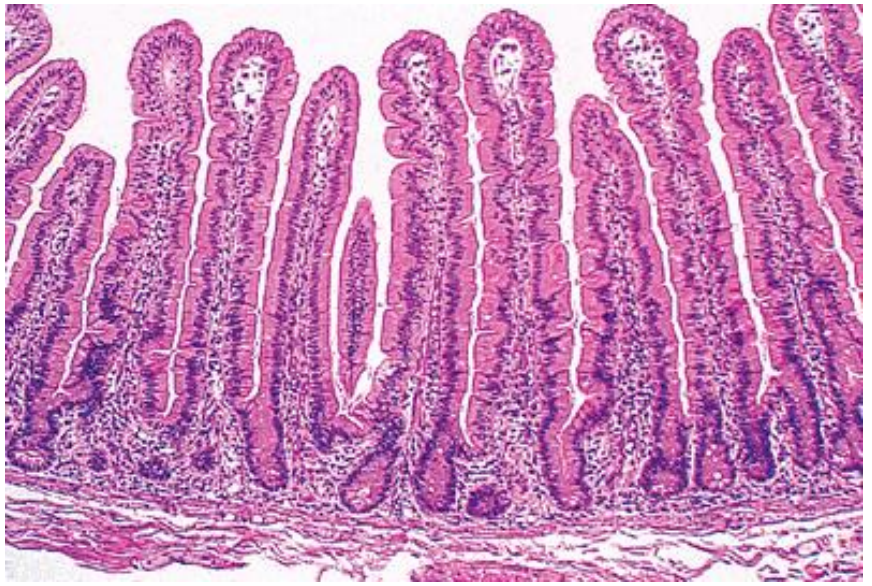


Small intestine

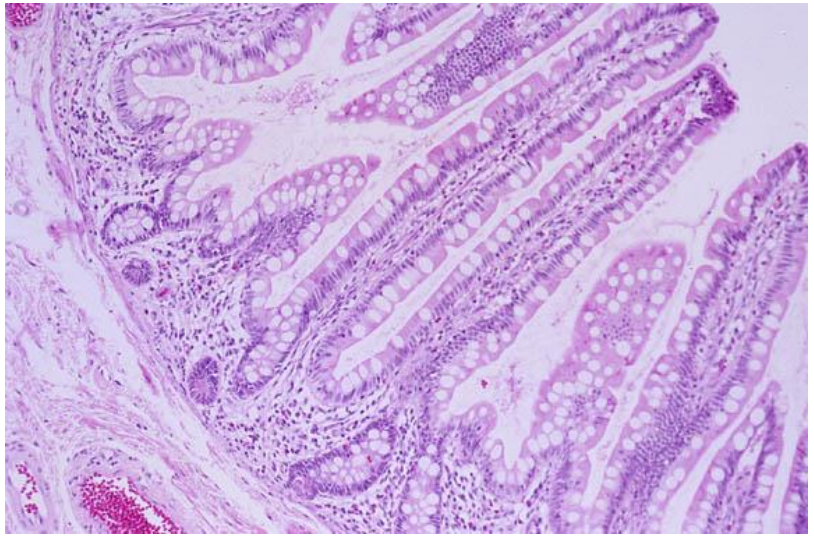
Histological differences



Duodenum



Jejunum



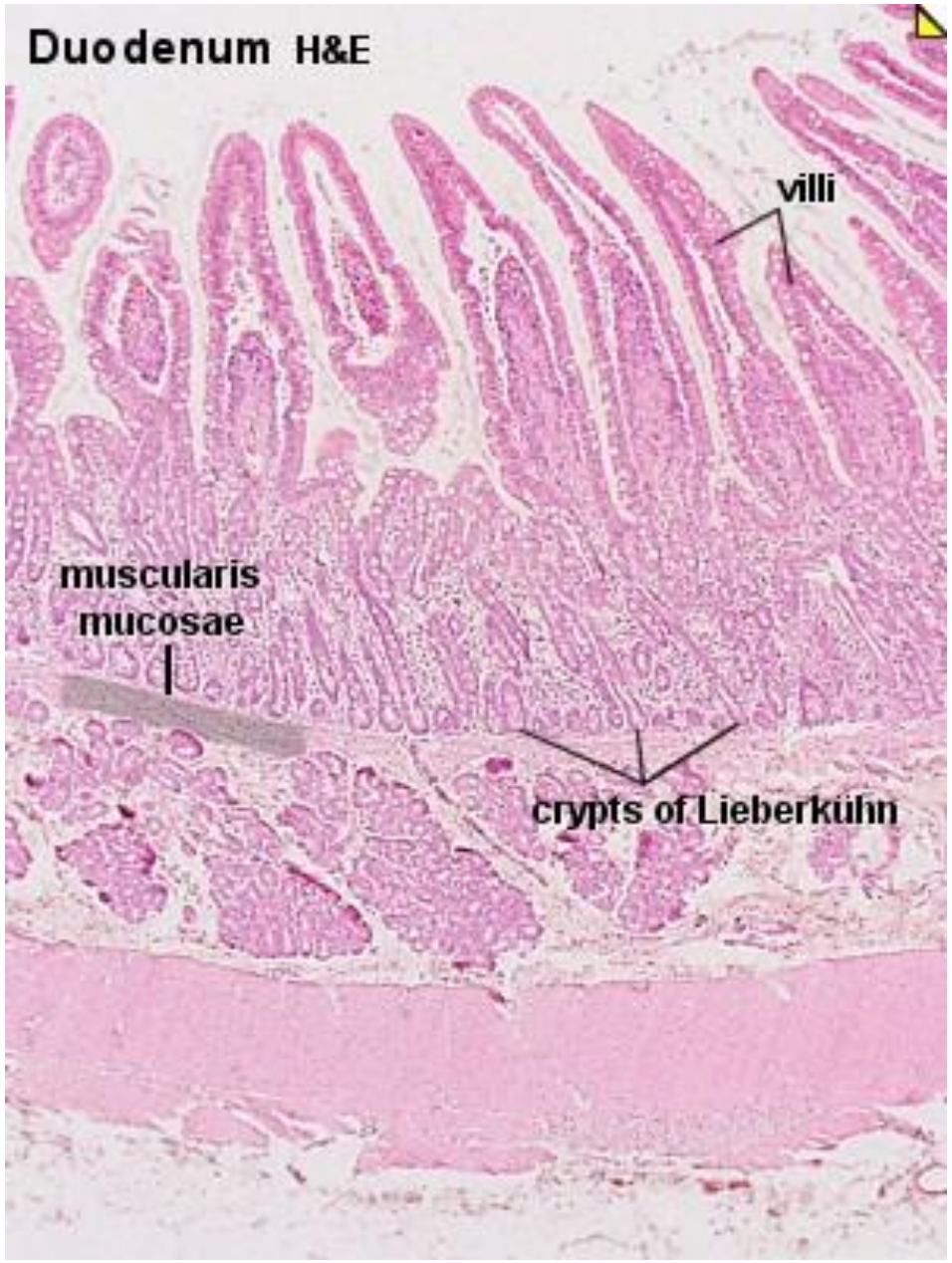
Ileum

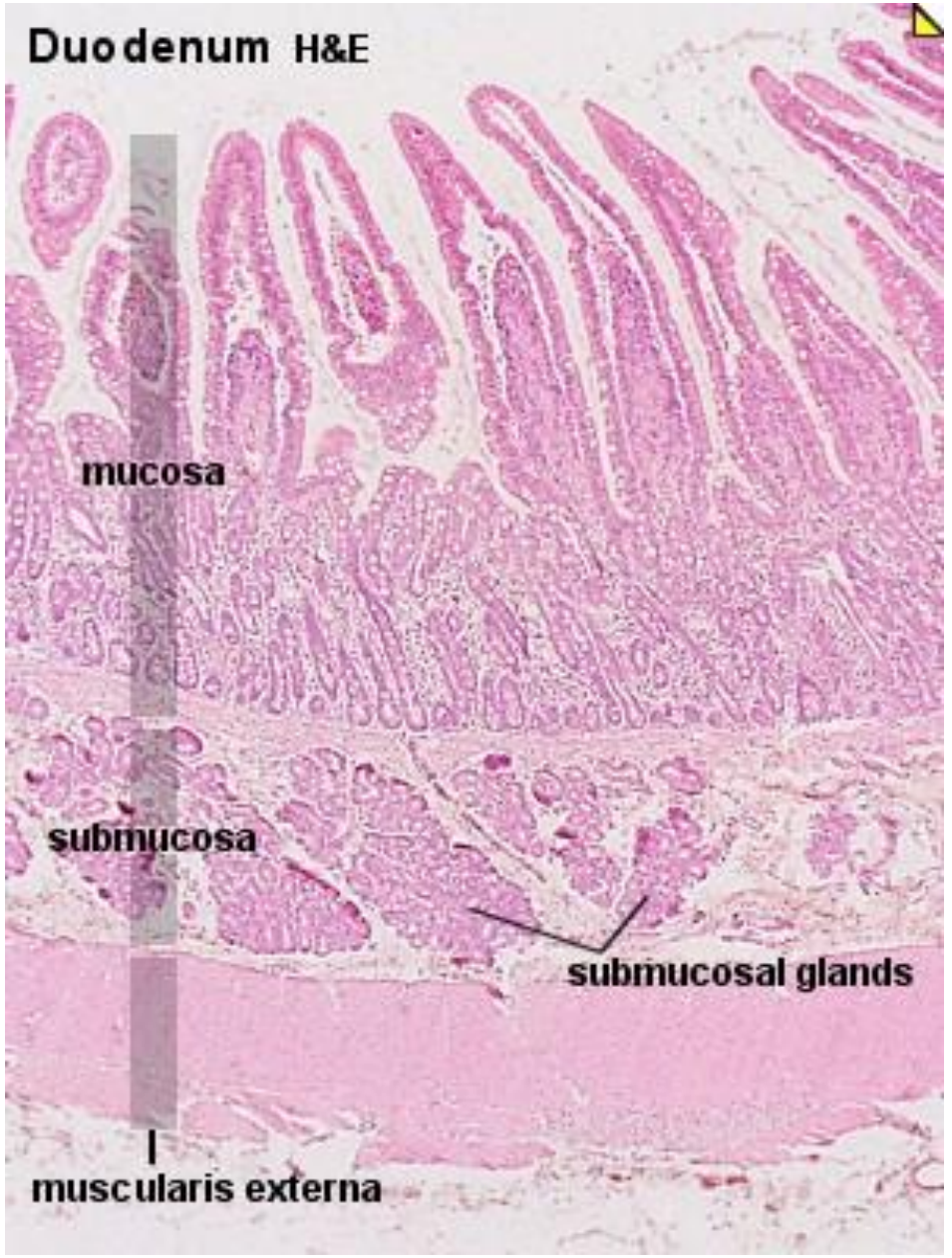
The villi of **DUODENUM** are the broadest, the tallest and the most numerous

The number of goblet cells increases down the gastrointestinal tract.

The villi of **ILEUM** are the most spars, most narrow and most short

Duodenum #50

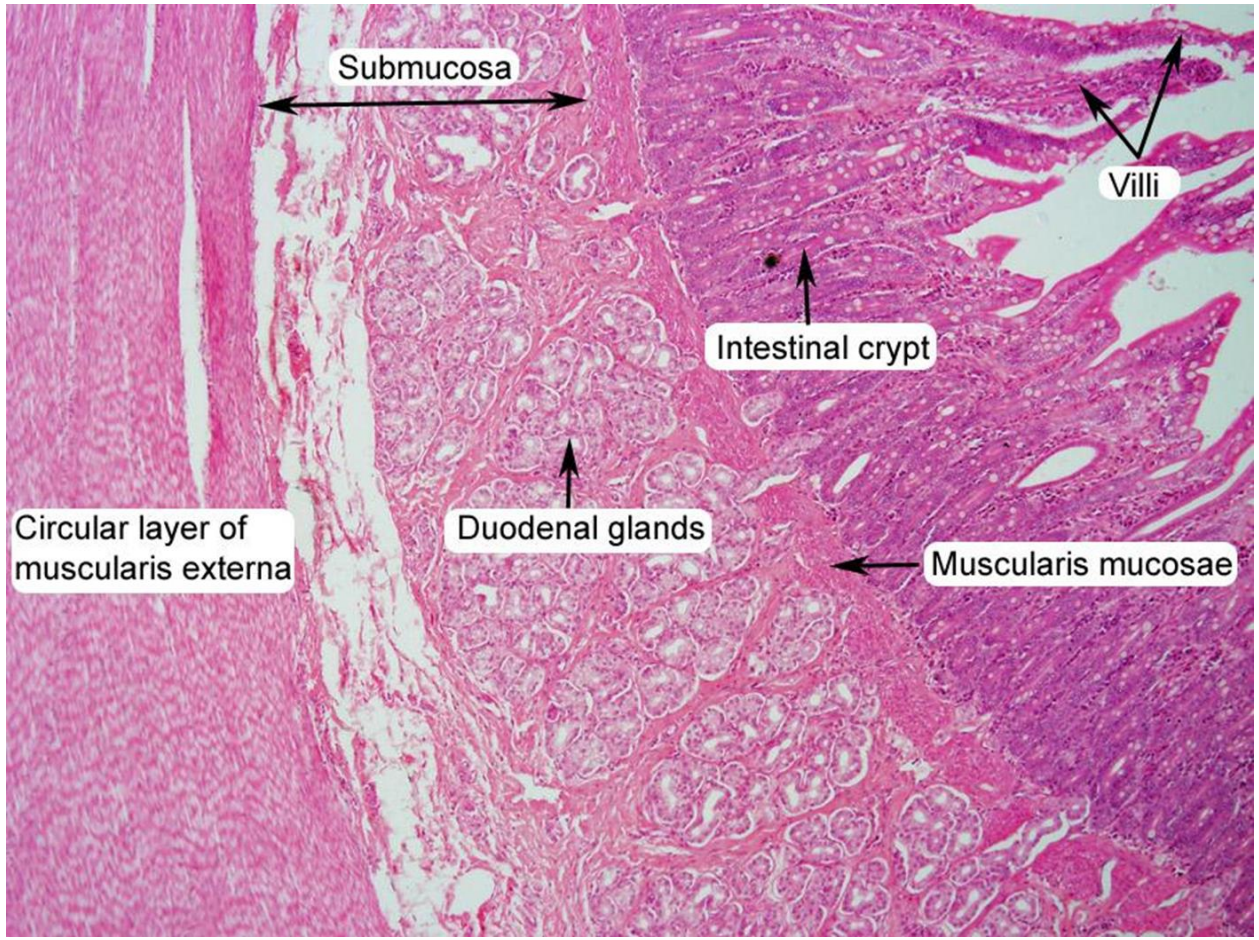

Duodenum H&E
villi
muscularis
mucosae
crypts of Lieberkühn


Duodenum H&E
mucosa
submucosa
submucosal glands
muscularis externa

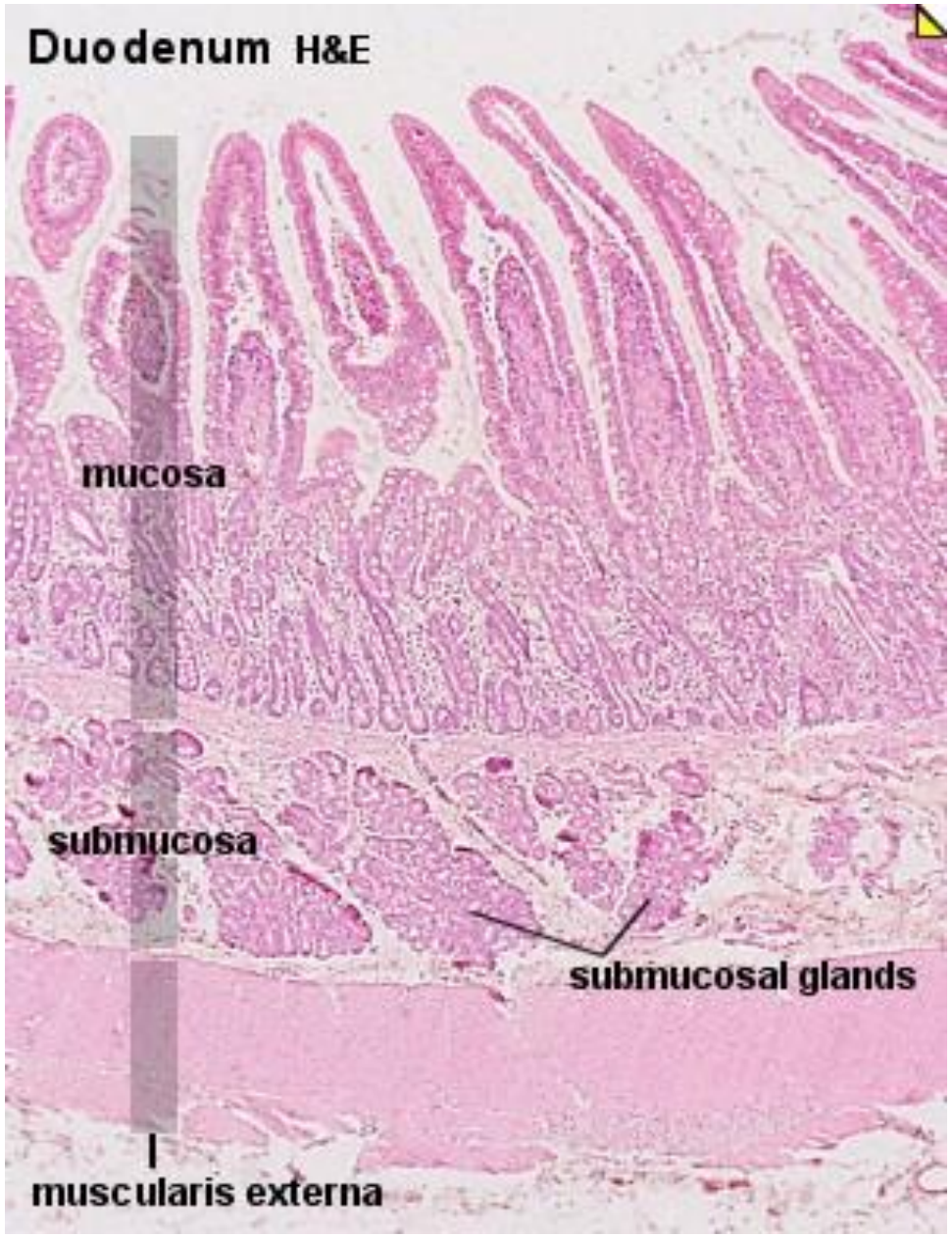
Duodenum #50

Brunner's duodenal glands

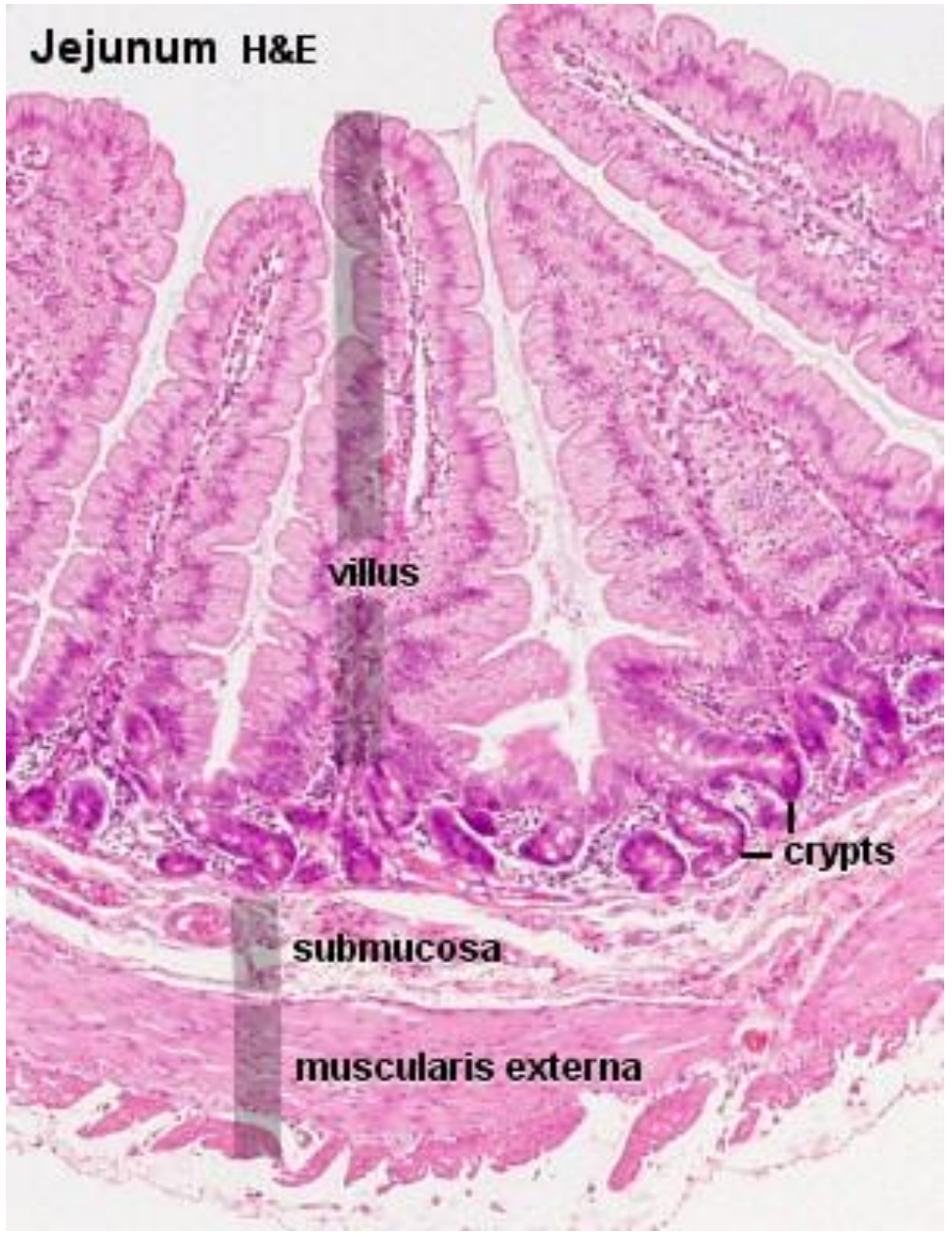
- branched, tubuloalveolar glands, in lobules
- mainly in submucosa, may extend above the muscularis mucosae (MM) into the mucosa
- small excretory ducts
  - ➢ extend through the MM and lamina propria
  - ➢ opened at the base of crypts of Lieberkühn
- secrete:
  1. a mucous, alkaline fluid
     - ➢ **alkaline mucus** participate in neutralization of the acidic chyme from stomach
     - ➢ supplements the mucus from goblet cells in lubricating and protecting the lining of the small intestine
  2. polypeptide hormone – **urogastrone**
     - ➢ u. inhibits production of HCl
     - ➢ amplifies the rate of mitotic activity of the regenerative cells in crypts of L.



Duodenum (#50)

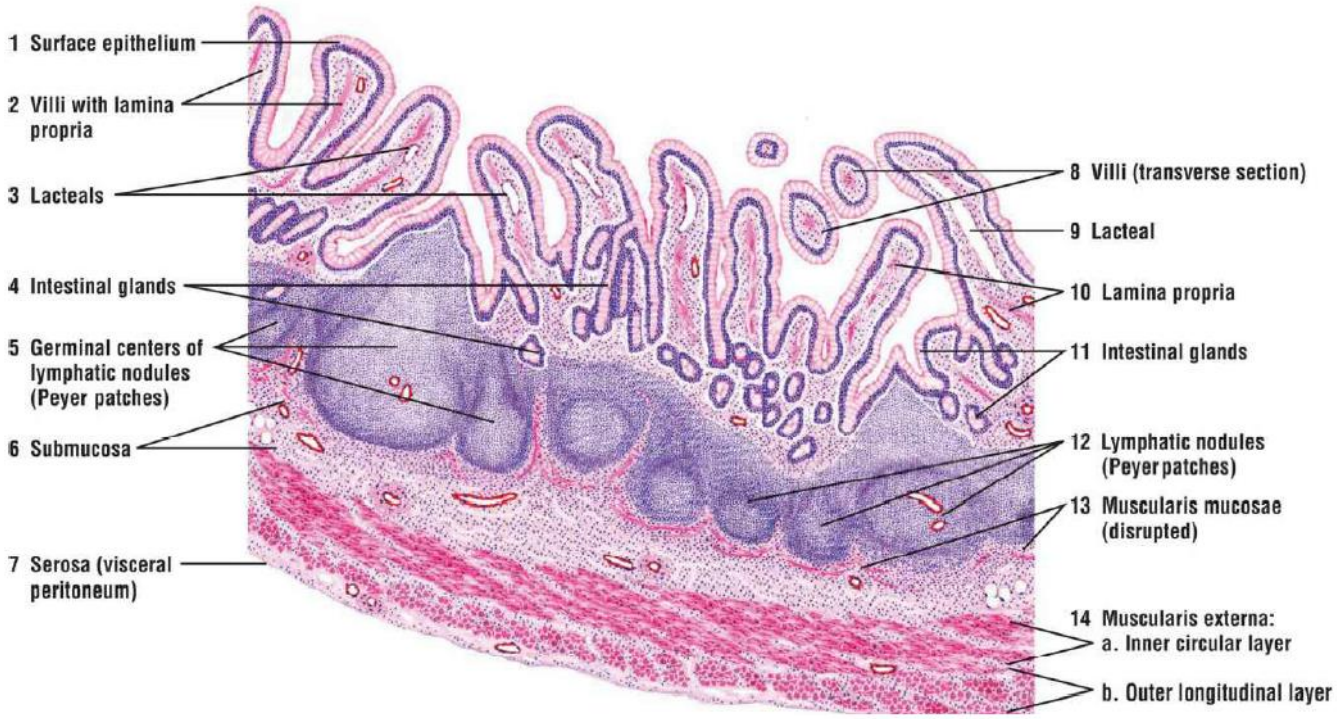


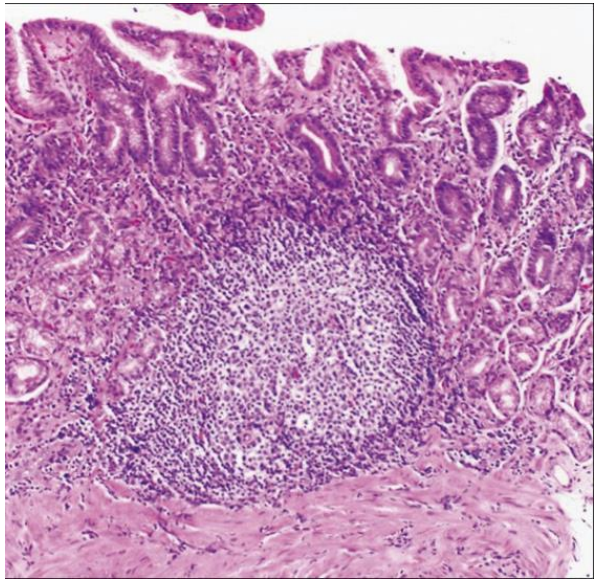
Jejunum (#51)



Ileum #55

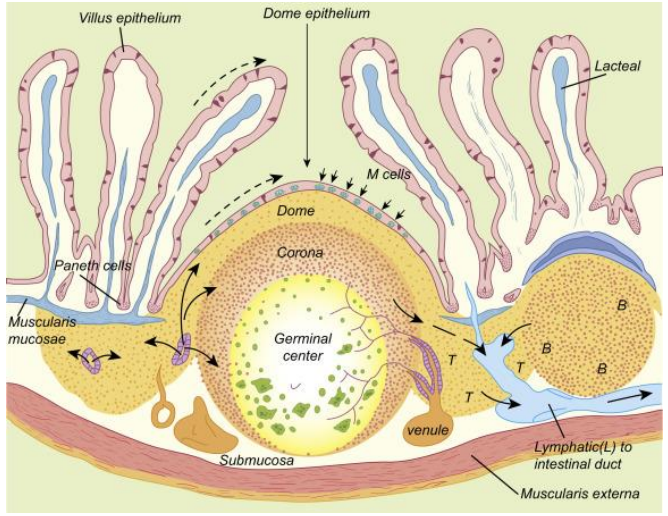
- the final section of the small intestine
- the function of the ileum is mainly **absorption** of vitamin B12, bile salts, and products of digestion that were not absorbed by the jejunum
- has abundant **Peyer's patches**,
  - the part of **Gut Associated Lymphoid Tissue** (**GALT**) which is a part of the Mucosa Associated Lymphoid Tissue (MALT)
  - **aggregated lymphoid (lymphatic) nodules,** most of which exhibit germinal centers
  - **originate in** the diffuse lymphatic tissue of the **lamina propria of the mucosa and extending into the submucosa**

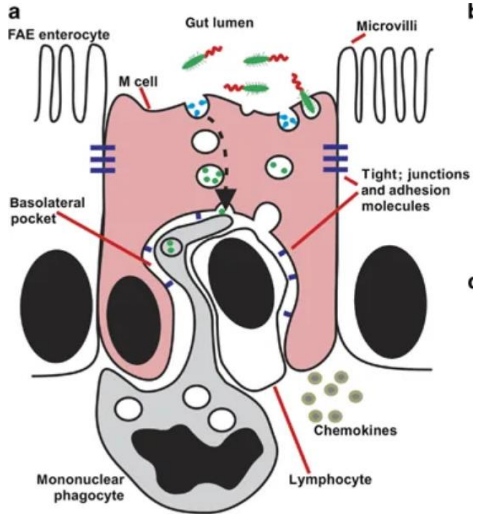


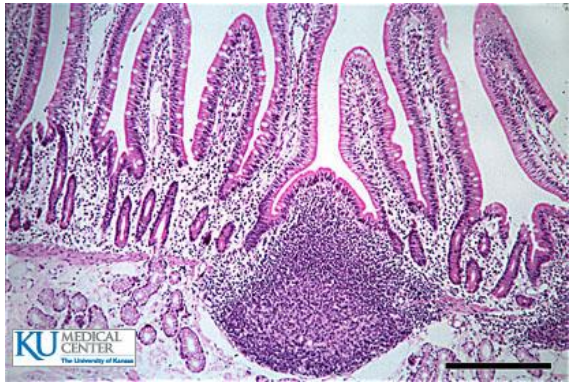


Ileum #55

- has abundant **Peyer's patches cont.**
  - ➢ in the area of the intestinal lumen <u>where the nodules</u> expand to reach <u>the surface</u> of the mucosa and spread out in the submucosa
    - **<u>villi are absent</u>**
    - the covering epithelium contains **<u>M cells (Microfold Cells)</u>**
      - ➢ belong to the mononuclear phagocyte system of cells,
      - ➢ **sample, phagocytose, and transport antigens** present in the intestinal lumen to lamina propria **to antigen presenting cells** (APCs)







<u>Warning #2</u>: single lymphoid (lymphatic) nodules are present also in other parts of the small intestine (e.g. in duodenum)

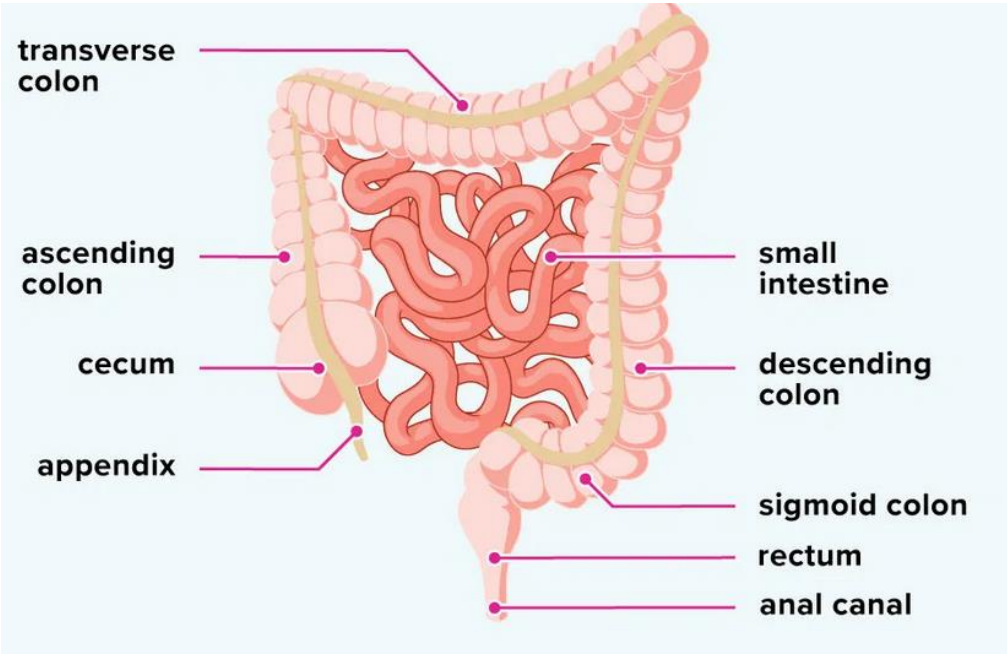
<u>Warning #1</u>: Not all the regions of the ileum have this many Peyers patches

Large intestine

Large intestine

- part of the digestive tube between the terminal ileum and anus
- consists of **major three segments**
  1. **cecum** – with worm-like extension called vermiform **appendix**
  2. **colon** – subclassified into (a) ascending, (b) transverse, (c) descending, and (d) sigmoid
  3. **rectum** continuous with the **anal canal**

  cecum and colon are identical histologically,
  rectum is similar, but crypts are deeper and fewer in number
- main functions:
  1. **recovery of water and electrolytes from ingesta**
  2. **formation and storage of feces**
  3. **microbial fermentation**

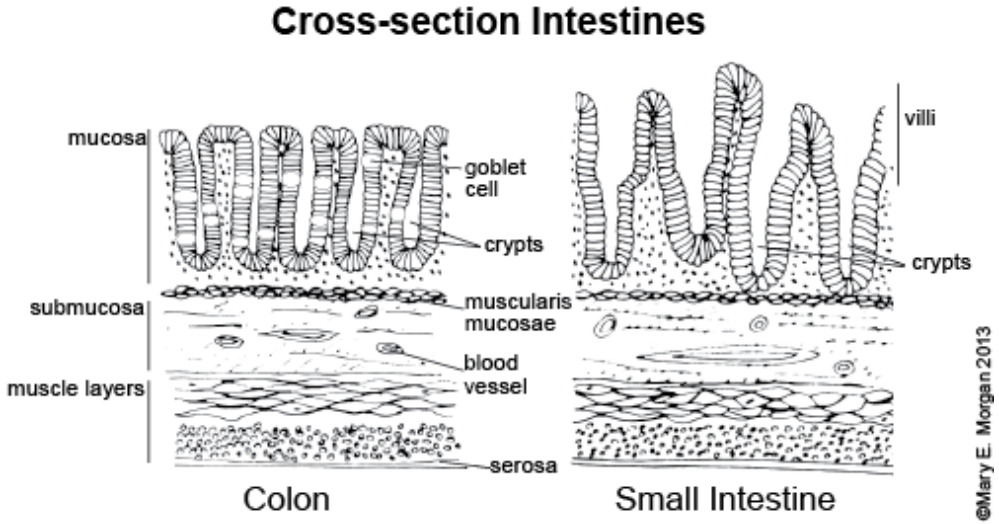


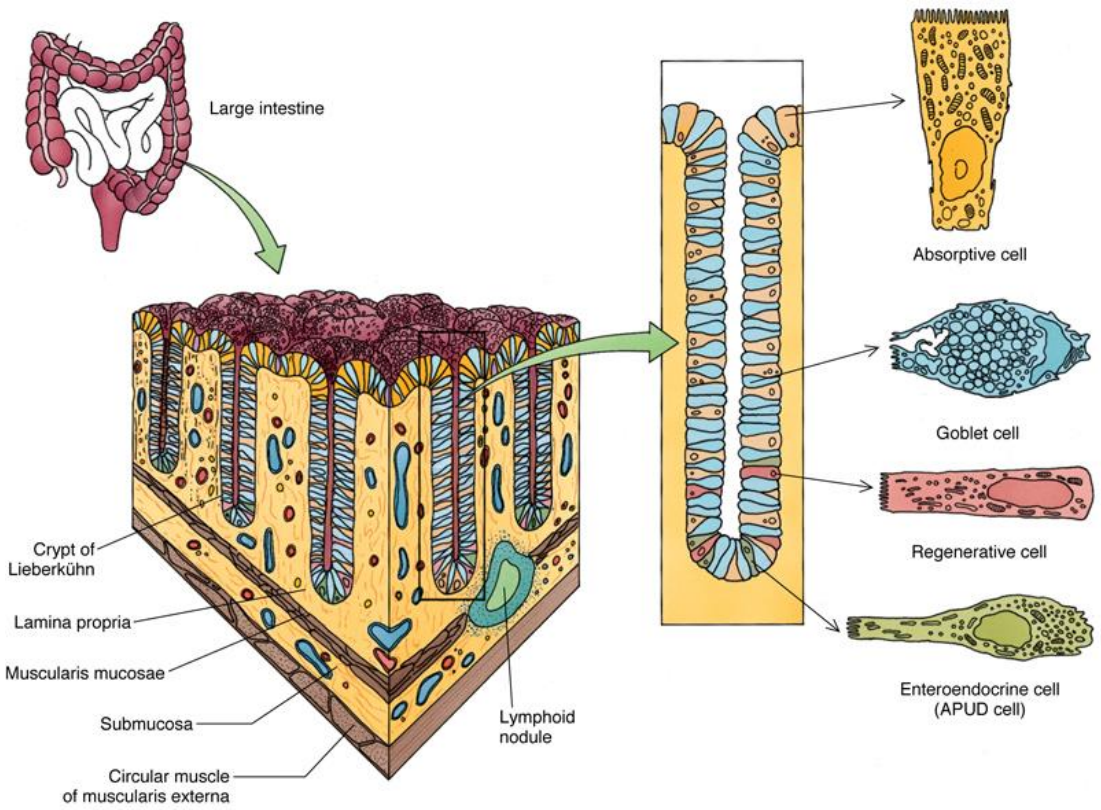
Large intestine

- a wall - **4 typical layers**
  (mucosa, submucosa, muscularis externa, serosa)

Mucosa

- **3 typical layers:**
  1. **epithelium (simple columnar),**
  2. **lamina propria,**
  3. **muscularis mucosae**
- **no villi** but **a lot of crypts of Lieberkühn** that are similar to those of the small intestine, except for **the absence of Paneth cells**
- in the e. there are a lot of **goblet cells**
  - for mucus which lubricates stool
  - the number of goblet cells increases from the cecum to the sigmoid colon
- DNES (enteroendocrine, APUD) cells are also present, but they are few in number
- presence of **lymphoid tissue** (a lot of bacteria in stool)





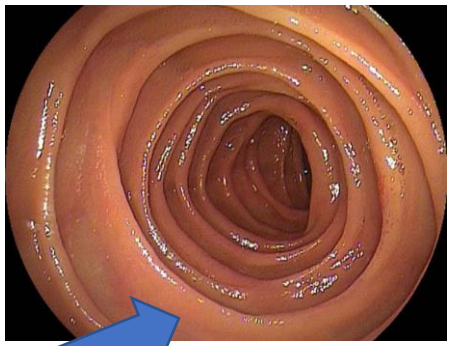
Large intestine

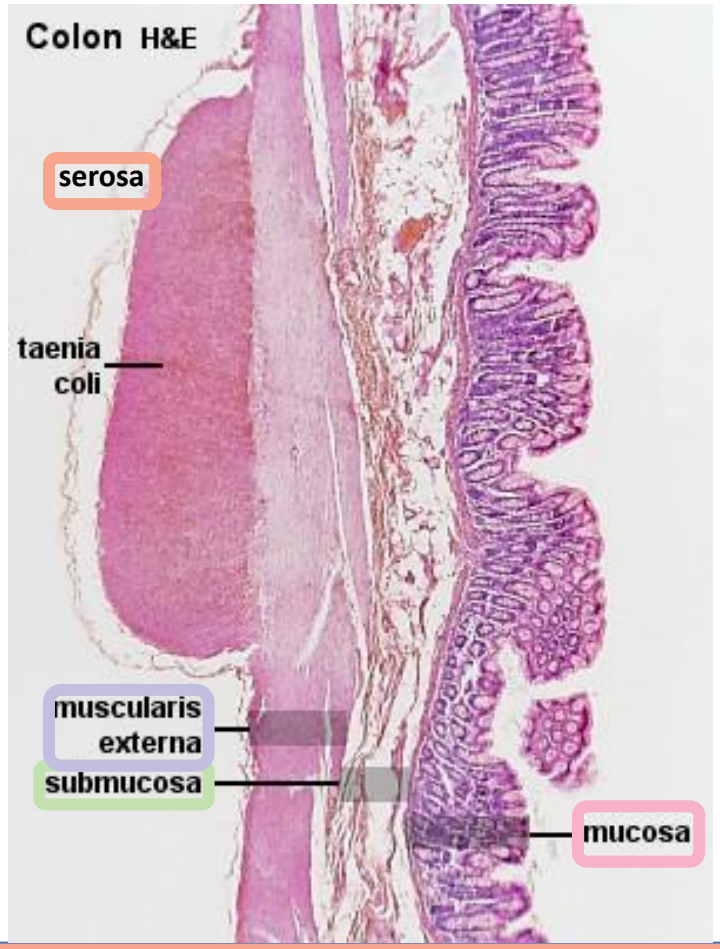
Submucosa

- resemble that in the small intestine
- **dense, irregular fibroelastic** connective tissue proper
- presence of
  - ➢ a rich lymphatic and vascular network
  - ➢ **Meissner submucosal plexus**

Muscularis externa

- **2 layers of smooth muscle**:
  1. **inner circular** layer
  2. **outer longitudinal** layer
     - ➢ is not of continuous thickness along the surface, but most of it is gathered into **three** narrow **ribbons** of muscle fascicles, known as **taeniae coli**.
     - ➢ the constant tonus maintained by the taeniae coli puckers the large intestine into sacculations, called **haustra coli**
- presence of **Auerbach myenteric plexus**
  - ➢ between two muscle layers

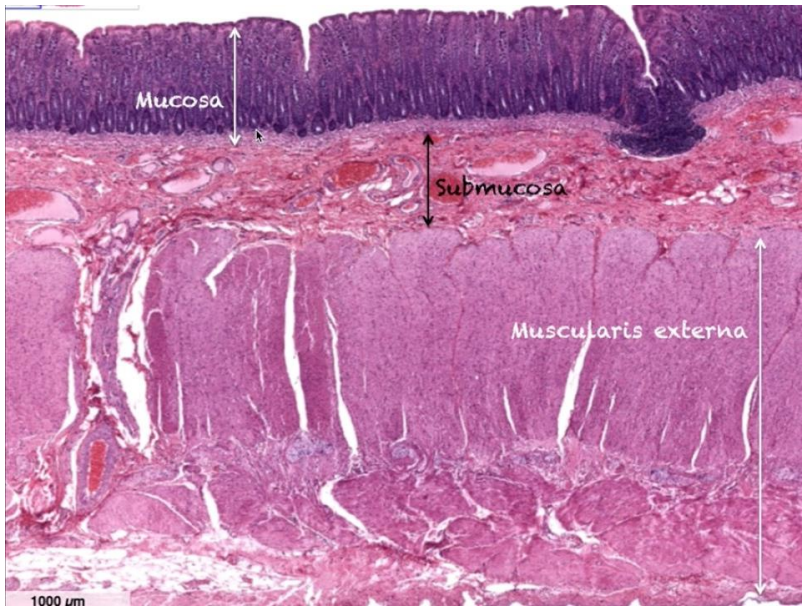


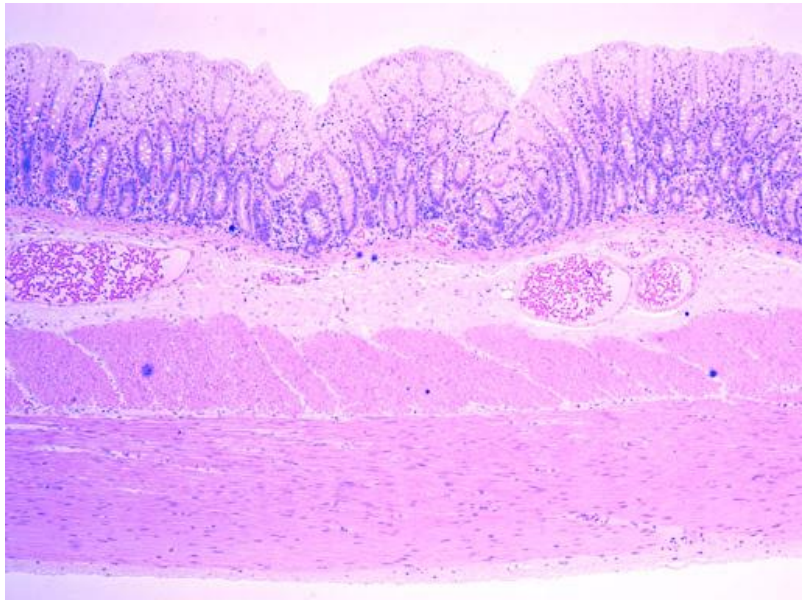


Serosa

- **thin, loose connective tissue proper** covered by a smooth, wet, **simple squamous mesothelium**
- s. displays numerous fat-filled pouches - **appendices epiploicae**.

Large intestine (colon) #52





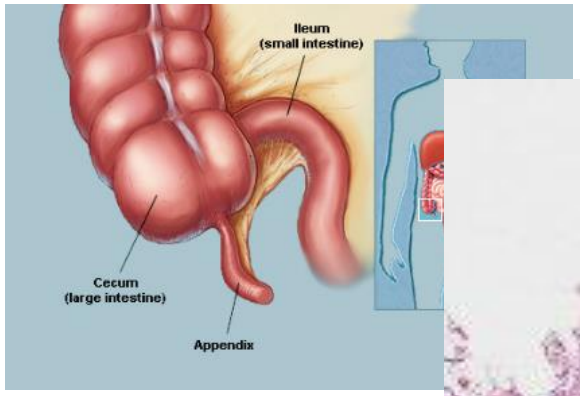
Appendix #53

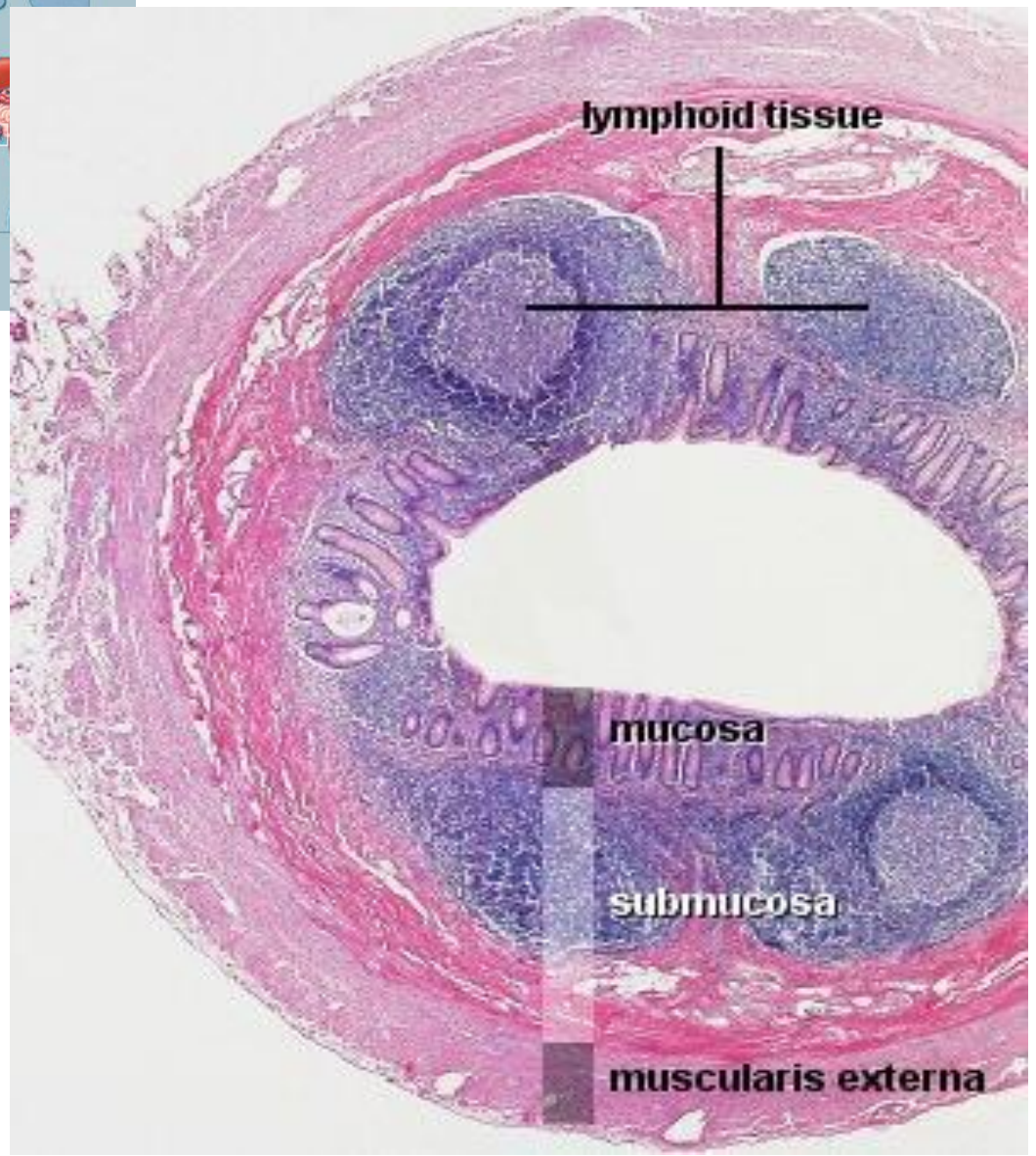
- a blind-ended tube connected to the cecum.

- a wall - **4 typical layers**:
  1. mucosa – no villi, crypts of Lieberkühn, goblet cells
  2. submucosa,
  3. muscularis externa
  4. serosa

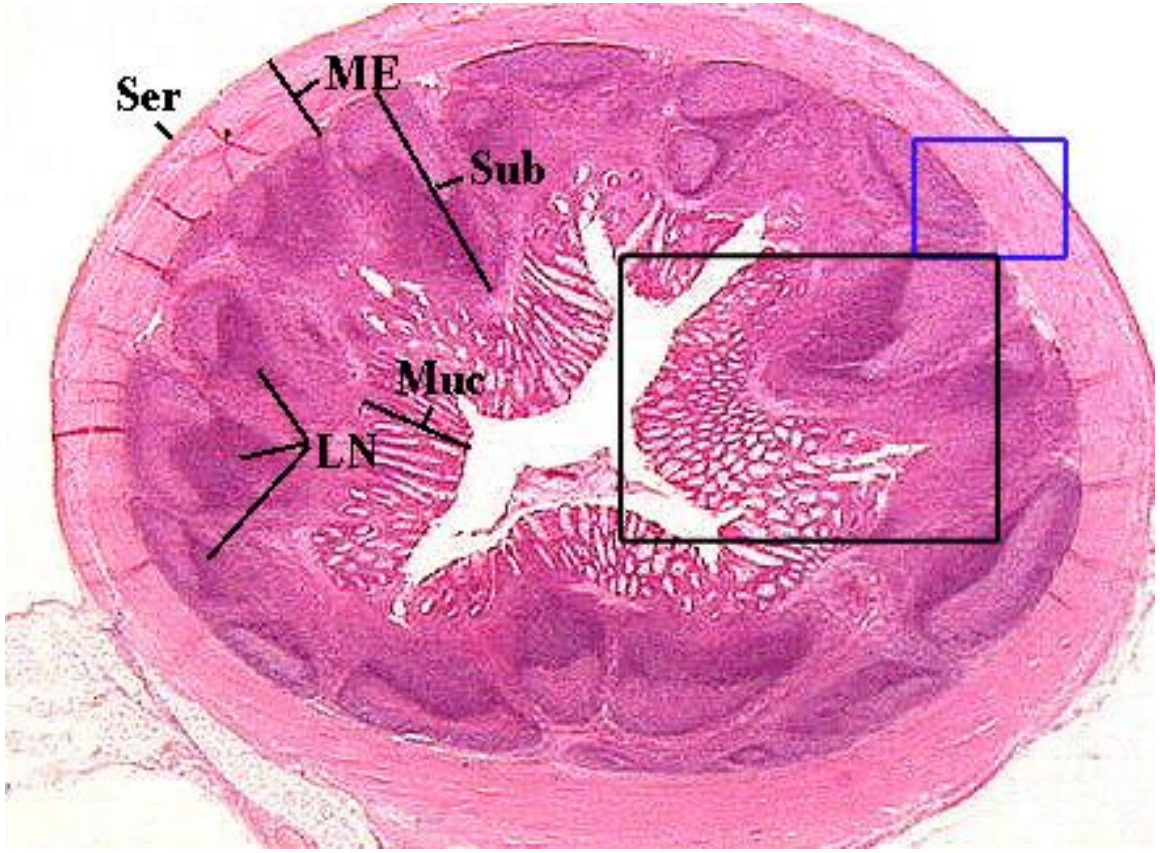
- contains **numerous lymphoid nodules** in lamina propria extending to submucosa ← **GALT**

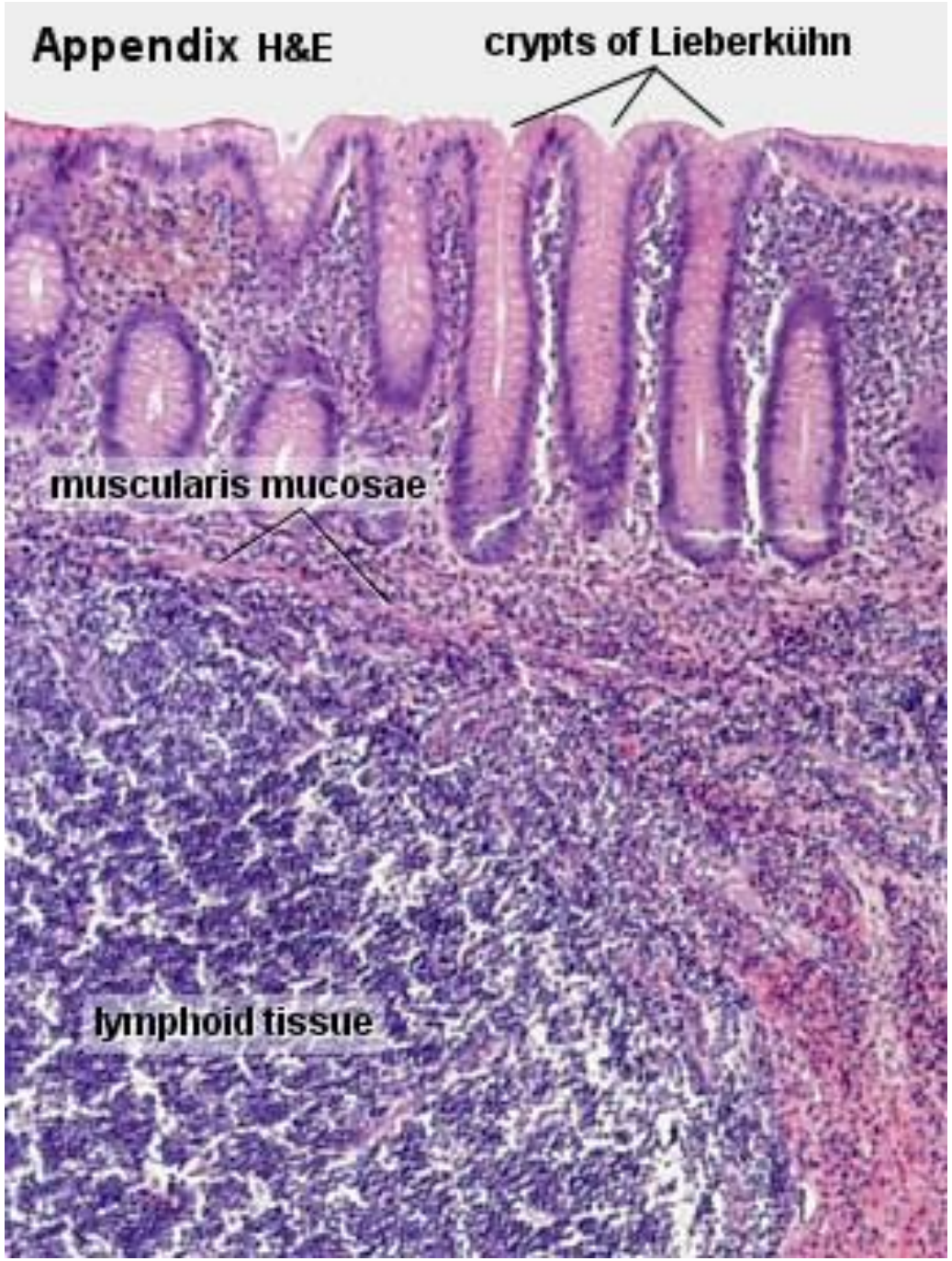
- acts as **a safe house for good bacteria**, which can be used to effectively reboot the gut following attack of pathogens





Appendix #53

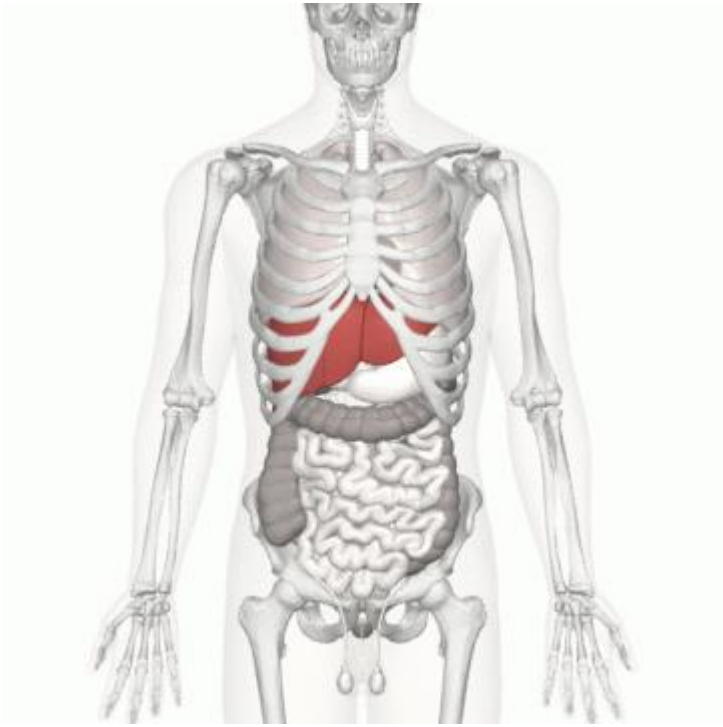

Ser
ME
Sub
Muc
LN

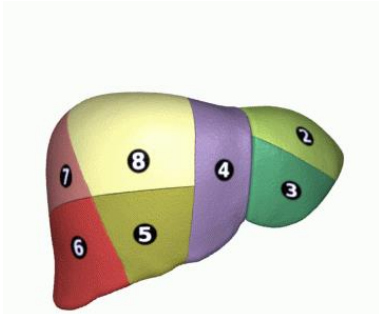

Appendix H&E
crypts of Lieberkühn
muscularis mucosae
lymphoid tissue

Liver

Liver (in Greek - *hepar*)

- located in the **right upper quadrant** of the abdomen, below the diaphragm
- the **second largest organ** in our body (skin is in the first place)
- the **largest internal organ**
- weighs approximately **1,5 kg**
- **4 lobes** (right, left, quadrate, and caudate), **8 segments**
- **a vital organ** ← liver transplantation is the only option for complete liver failure
- **~500(!) functions**





Liver (#54)

Cells:

1. **hepatocytes** (60-70% of liver mass)
2. **Kupffer cells** = macrophages
3. **Ito cells** = perisinusoidal fat cells = lipocytes = hepatic stellate cells (HSC)
4. Other:
   i. **endothelial cells of sinusoids**
   ii. **cholangiocytes** – cells of bile ductules and ducts (3-5% of liver mass)
   iii. **pit cells** = granular cells = NK cells

Kupffer cells + endothelial cells + NK lymphocytes → 30-35% of liver mass

Liver (#54)

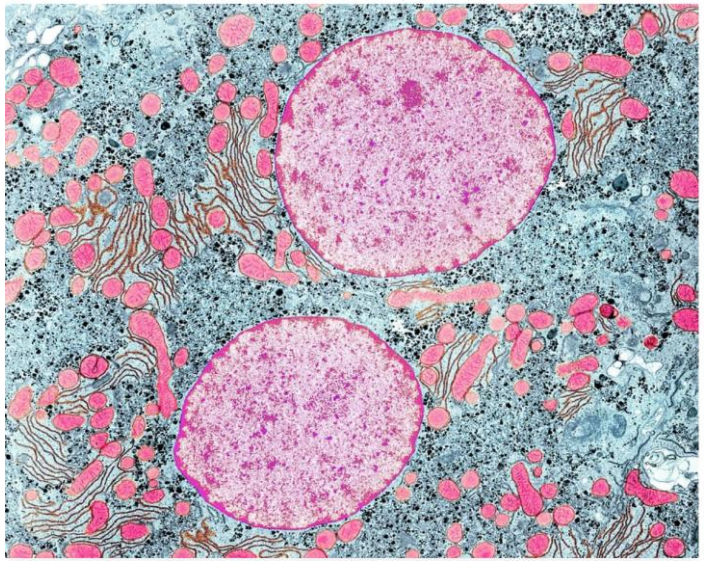
Cells

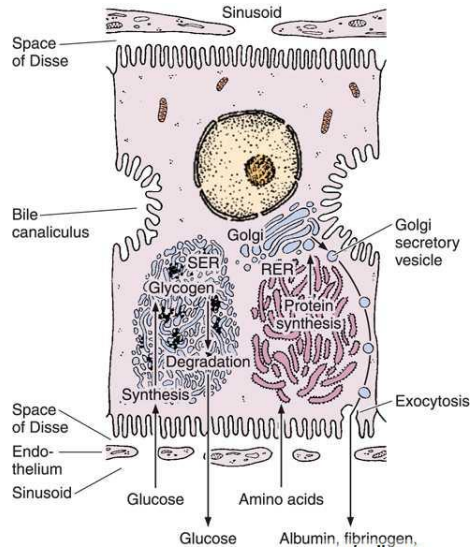
- **hepatocytes**
  - glandular epithelial cells of endodermal origin
  - form cords surrounded by sinusoids
  - have an approximate life span of 150 days (~5 mo)
  - are responsible for the most function of liver
- Browicz-Kupffer cells = hepatic macrophages
  - inside the sinusoids
  - are responsible for the purification of blood by phagocytosis m.in. pathogens, particulate matter, damaged erythrocytes
- Ito cells = perisinusoidal fat cells = lipocytes = hepatic stellate cells (HSC)
  - in perisinusoidal spaces (of Disse)
  - when not activated they store wit. A, secrete erythropoietin (EPO)
  - in chronic inflammation → activation → collagen synthesis → liver fibrosis → liver cirrhosis

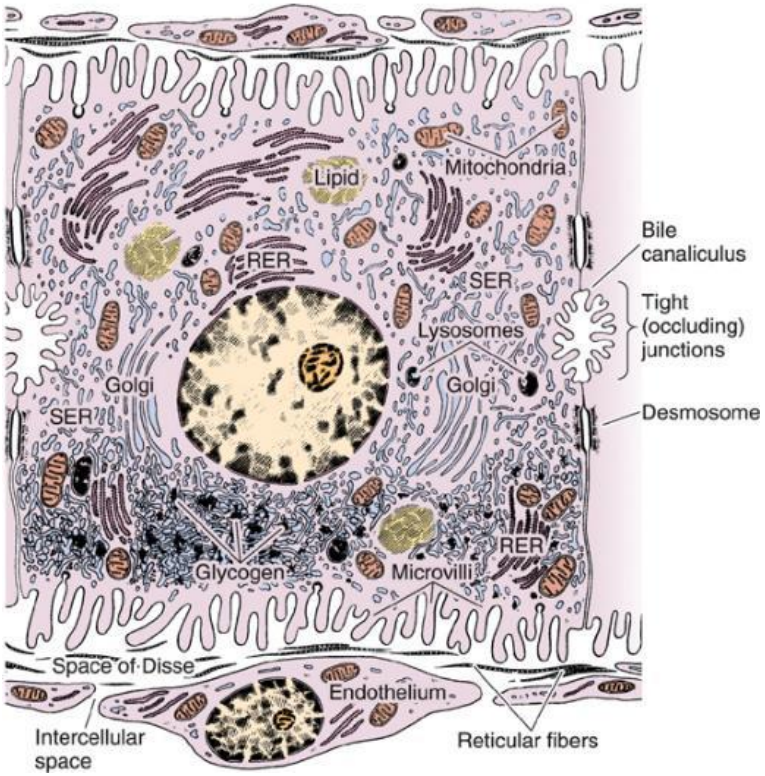
Liver (#54)

Hepatocytes

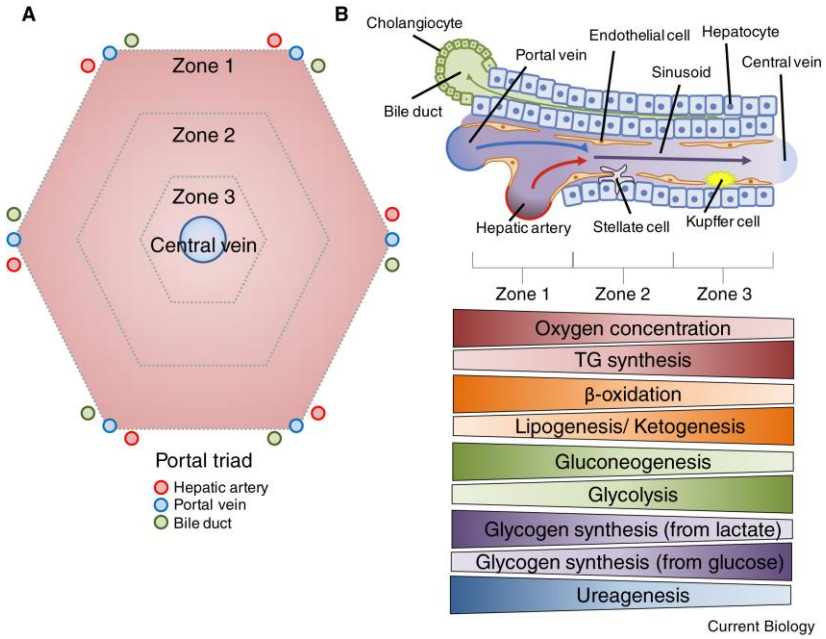
- are **large** cells with
  - **1-2 nuclei**
  - hard-working **Golgi apparatus**
  - extensive **SER** and **RER**
  - numerous **mitochondria**
  - **lysosomes**
  - **peroxisomes**
  - **glycogen, lipid droplets**







- **exhibit variations** in their structural, histochemical, and biochemical properties, <u>depending on their location within liver lobules</u>

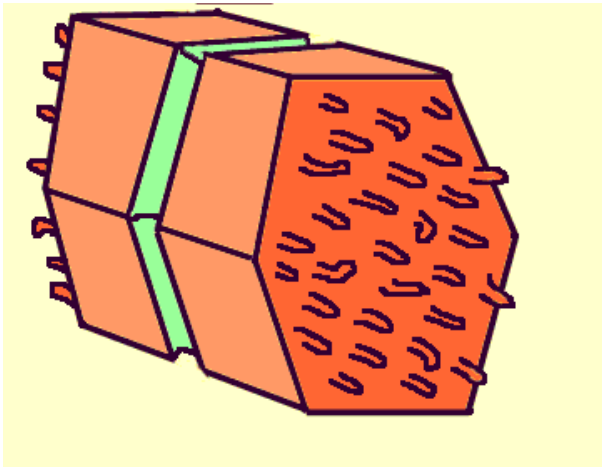


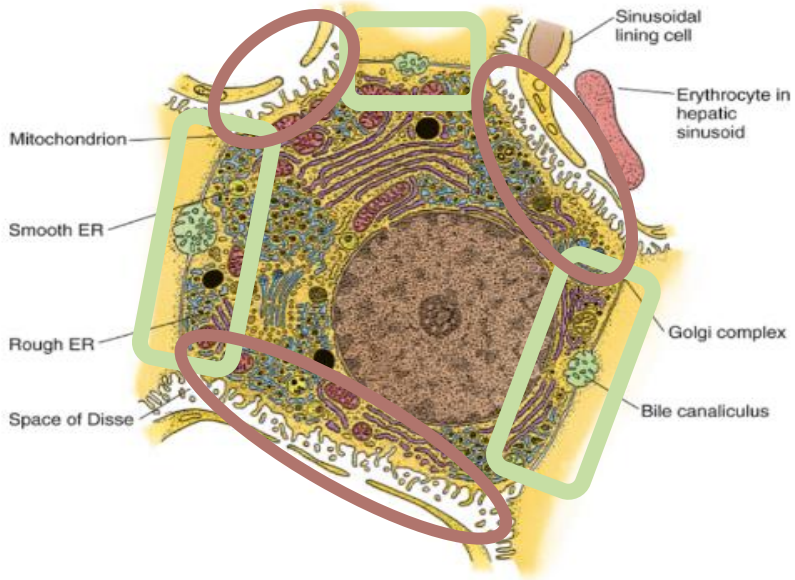
Liver (#54)

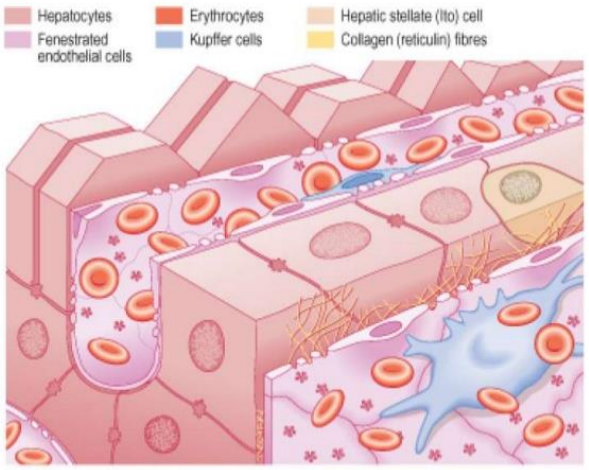
Hepatocytes cont.

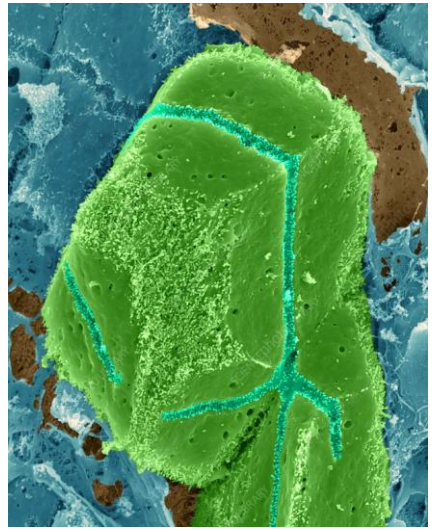
- are **polarized** → the plasmalemma of hepatocytes have **2 types of domains**
  1. **lateral domains** that contact other hepatocytes ← ½ of **bile canaliculus**
  2. **sinusoidal domains** that face the space of Disse

- are 5- to 12-sided **polygonal** cells

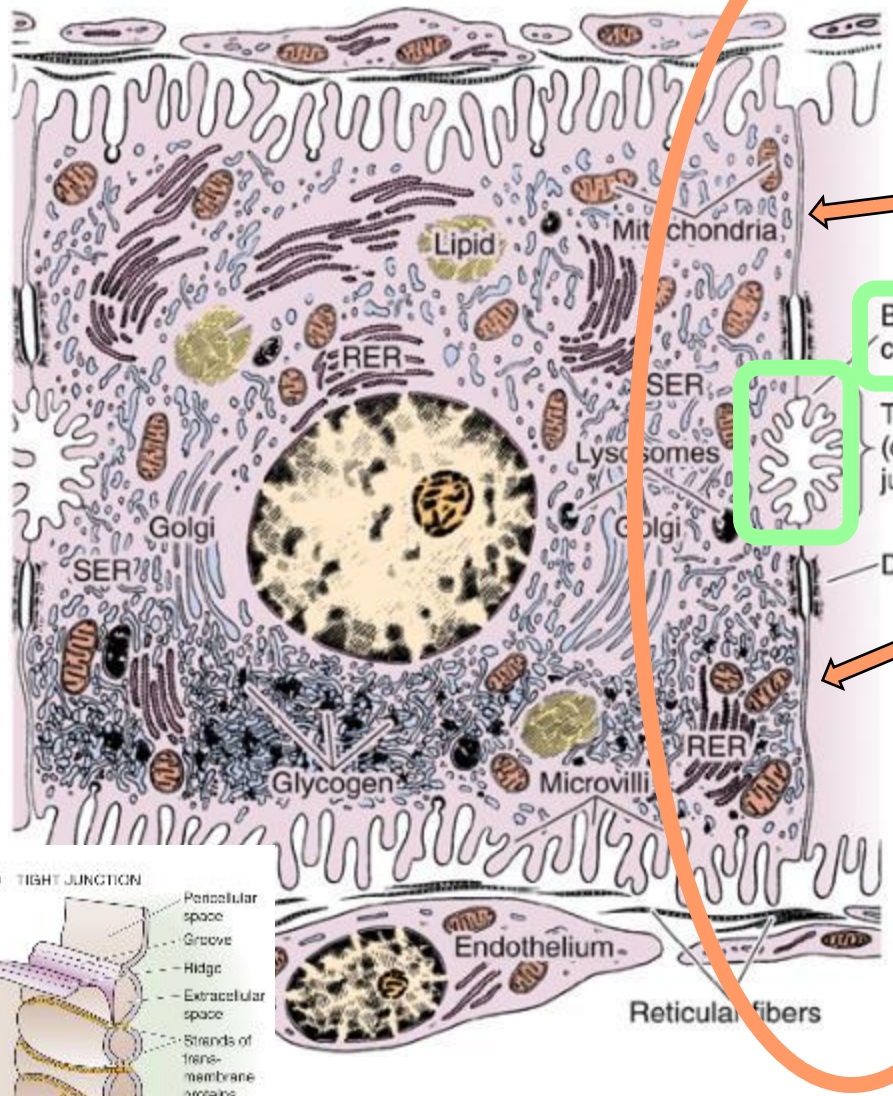


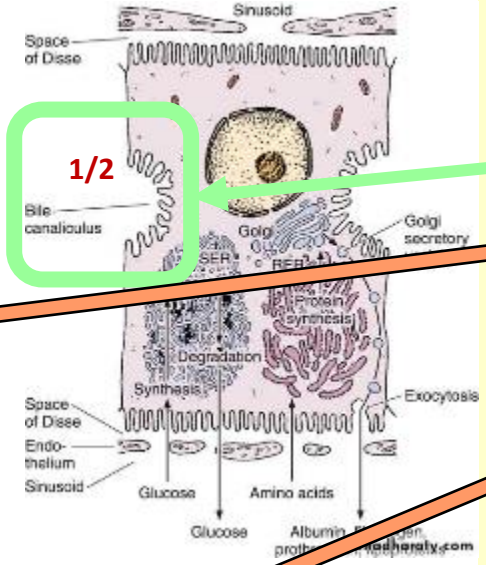


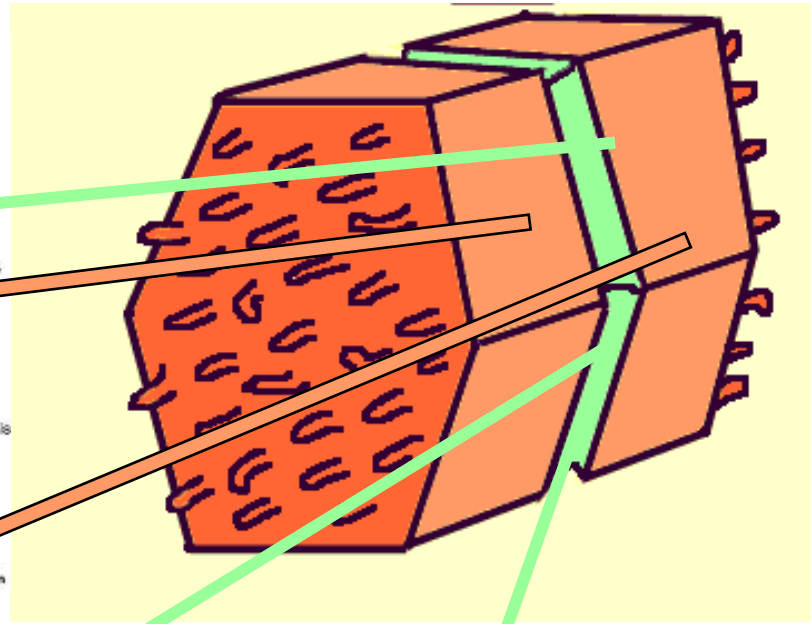


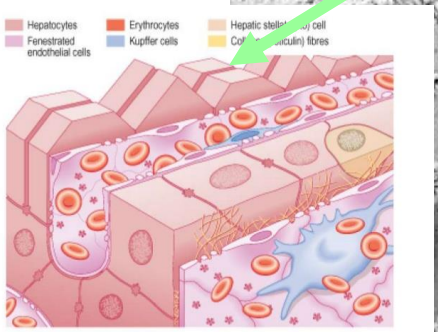


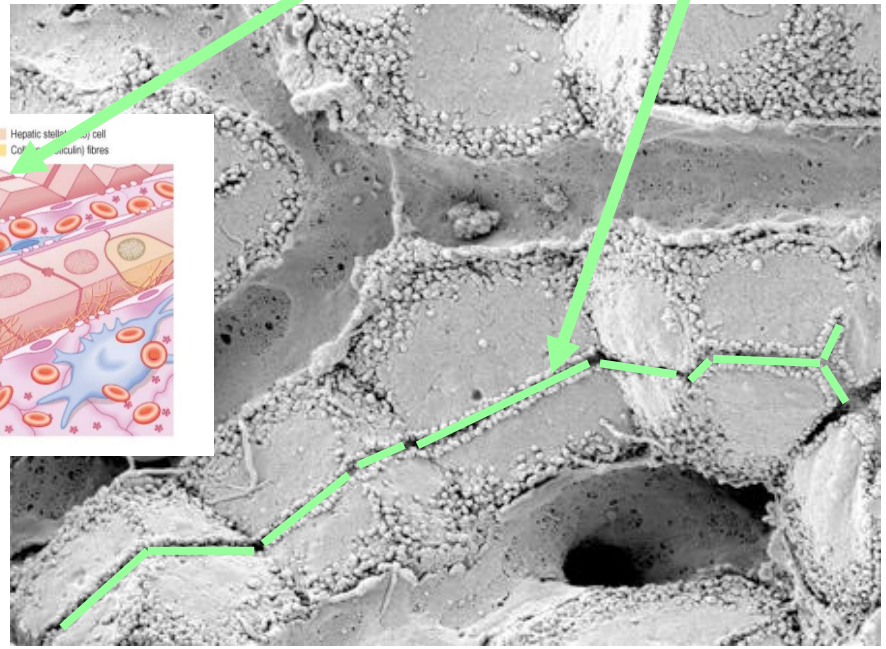
Liver (#54)


Lipid
Mitochondria
RER
SER
Golgi
SER
Glycogen
Microvilli
RER
Endothelium
Reticular fibers
Bile canaliculus
Tight (occluding) junctions
Desmosome


Sinusoid
Space of Disse
1/2
Bile canaliculus
Golgi
Golgi secretory
SER
RER
Protein synthesis
Degradation
Synthesis
Exocytosis
Space of Disse
Endothelium
Sinusoid
Glucose
Amino acids
Glucose




Hepatocytes
Erythrocytes
Fenestrated endothelial cells
Kupffer cells



D TIGHT JUNCTION
Pericellular space
Groove
Ridge
Extracellular space
Strands of trans-membrane proteins
Lumen of bile canaliculus
Cytosol of the hepatocyte

Liver (#54)

Cells

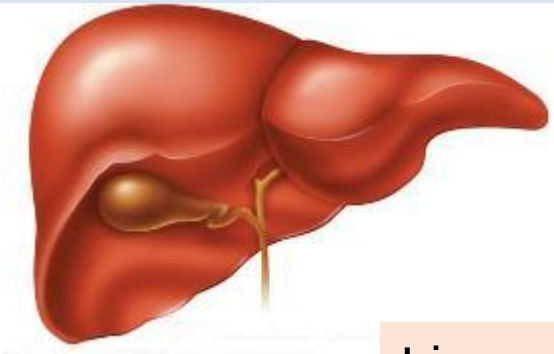
- hepatocytes
  - glandular epithelial cells of endodermal origin
  - forms cords surrounded by sinusoids
  - have an approximate life span of 150 days (~5 mo)
  - are responsible for the most function of liver
- **Kupffer cells** = hepatic (liver) macrophages
  - inside the sinusoids
  - are responsible for the cleansing of blood by phagocytosis i.a. pathogens, solid particles, damaged erythrocytes
- **Ito cells** = perisinusoidal fat cells = lipocytes = hepatic stellate cells (HSC)
  - in perisinusoidal spaces (of Disse)
  - when not agitated they store vit. A, secrete erythropoietin (EPO) & ECM
  - in chronic inflammation → activation → collagen synthesis → liver fibrosis → liver cirrhosis

The **liver** have a lot of different functions, most of which are performed by the **hepatocytes**

Hepatocytes take part in **metabolism of (1) carbohydrates** (maintaining normal blood glucose level via /a/ storage of glucose as glycogen, /b/ glycogen breakdown and glucose release, /c/ glucose synthesis)**, (2) lipids** (/a/ degradation of chylomicrons to fatty acids and glycerol, /b/ production of VLDLs, cholesterol, phospholipids), **(3) and proteins**

Enzymes in hepatocytes **metabolize** (modify) (1) many **xenobiotics** such as alcohol and drugs. Drugs can be activated or deactivated; (2) e.g., **toxic ammonia** into urea and **toxic free bilirubin** into bilirubin glucuronide for excretion; (3) steroid hormones (e.g., **estrogens**); (4) **Vitamin D to 25 hydroxyvitamin D** (25OHD)

Liver **storages** of many essential nutrients (**glucose as glycogen, fatty acids**), vitamins (**A, D, E, K, B12**), and minerals (**iron-Fe, copper-Cu**)



Liver participate **in digestion** through the production of the bile (the primary **bile salts** & **phospholipids**) → **fats emulsification**

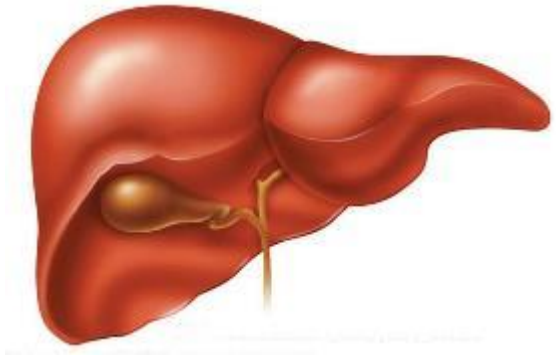
Liver participates **in immune processes**. Kupffer cells destroy bacteria, fungi, parasites and worn-out RBC.
Hepatocytes produce complement proteins & combine IgA to dimers (into the bile)

Some **metabolites are secreted by hepatocytes into the bile**, then transported together with it into the lumen of the duodenum **and** finally **excreted with the feces**. Some **metabolites** are secreted by hepatocytes **into the blood** and excreted **by the kidneys with the urine** (e.g. urea)

The **liver** have a lot of different functions, most of which are performed by the **hepatocytes**

Hepatocytes continually **synthesize** in large amounts vital **protein** components of blood plasma, which play different roles

- inactive **clotting factors** i.a. prothrombin, fibrinogen which are necessary for blood coagulation
- **albumins** (they maintain the oncotic pressure of the blood, which tends to pull fluid back into the capillaries)
- inactive proteins of **complement system** (a part of the immune system that (1) enhances (complements) the ability of antibodies and phagocytic cells to remove microbes and damaged cells from an organism, (2) promote inflammation, and (3) attack the pathogen's cell membrane)



Hepatocytes **synthesize thrombopoietin (TPO)**

TPO, glycoprotein, stimulates megakaryocyte precursors to become mature megakaryocytes, which form platelets responsible for blood clotting

Perisinusoidal Ito cells **synthesize erythropoietin (EPO)**

EPO, glycoprotein, is an essential hormone for red blood cell production. These cells are an additional source of EPO in adults. The primary source of EPO in adults is fibroblasts in the kidney

Hepatocytes **synthesize angiotensinogen**

Angiotensinogen, α2-globulin, is cleaved by renin (enzyme produced by kidneys) into the angiotensin I, which is cleaved in lungs by another enzyme ACE into angiotensin II. Angiotensin II is engaged in regulation of blood pressure (increase).

Hepatocytes **synthesize Insulin-like Growth factor 1 (IGF-1)**

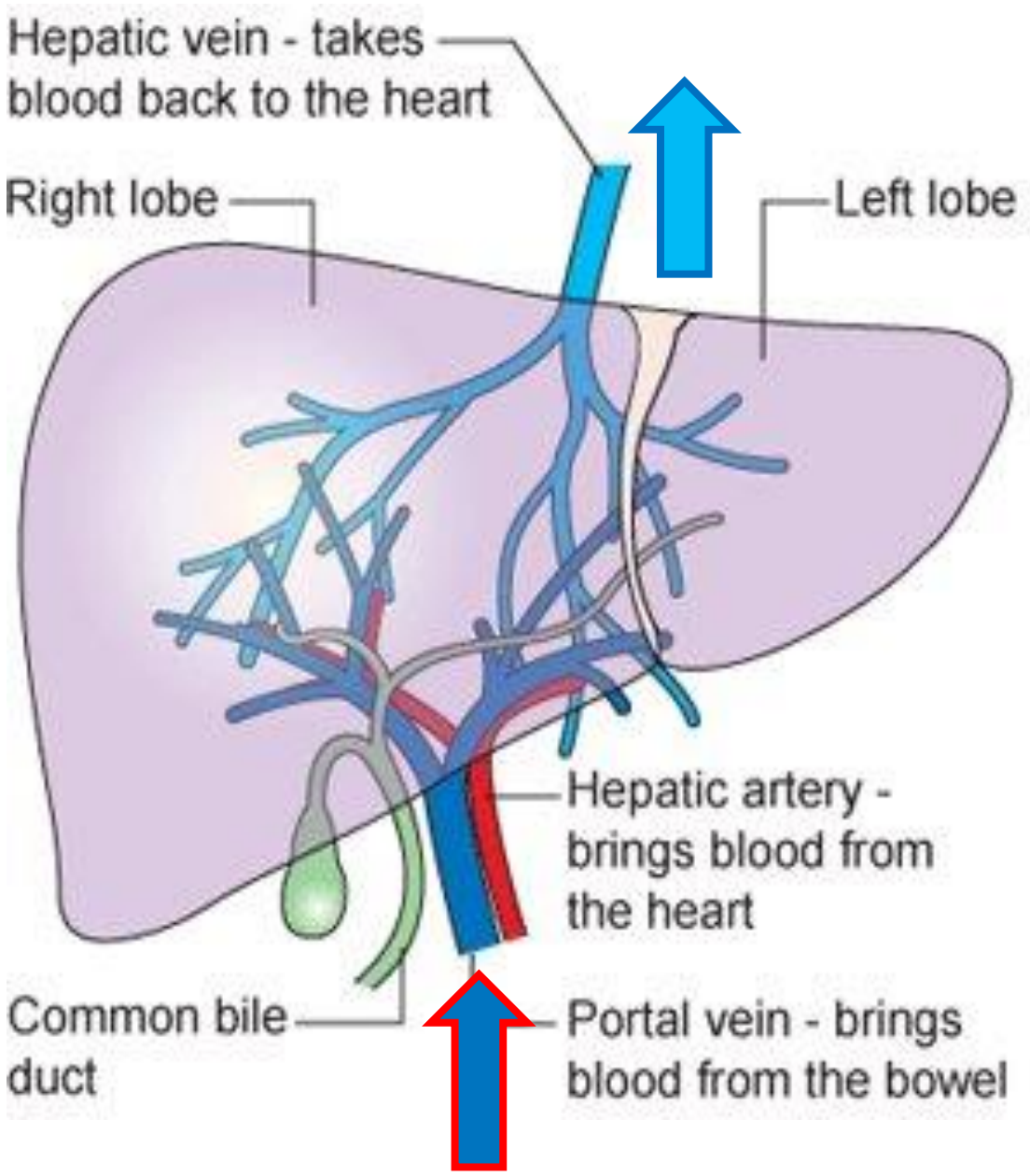
IGF-1 (aka **somatomedin C**), polypeptide, plays an important role in the regulation of cell growth and development (proliferation of chondrocytes of growth plate) and also has some insulin-like effects. A deficiency of this hormone in the childhood results in dwarfism. **Production of IGF-1 in the liver is stimulated by growth hormone (GH).**

Liver (#54)

blood flow through the liver

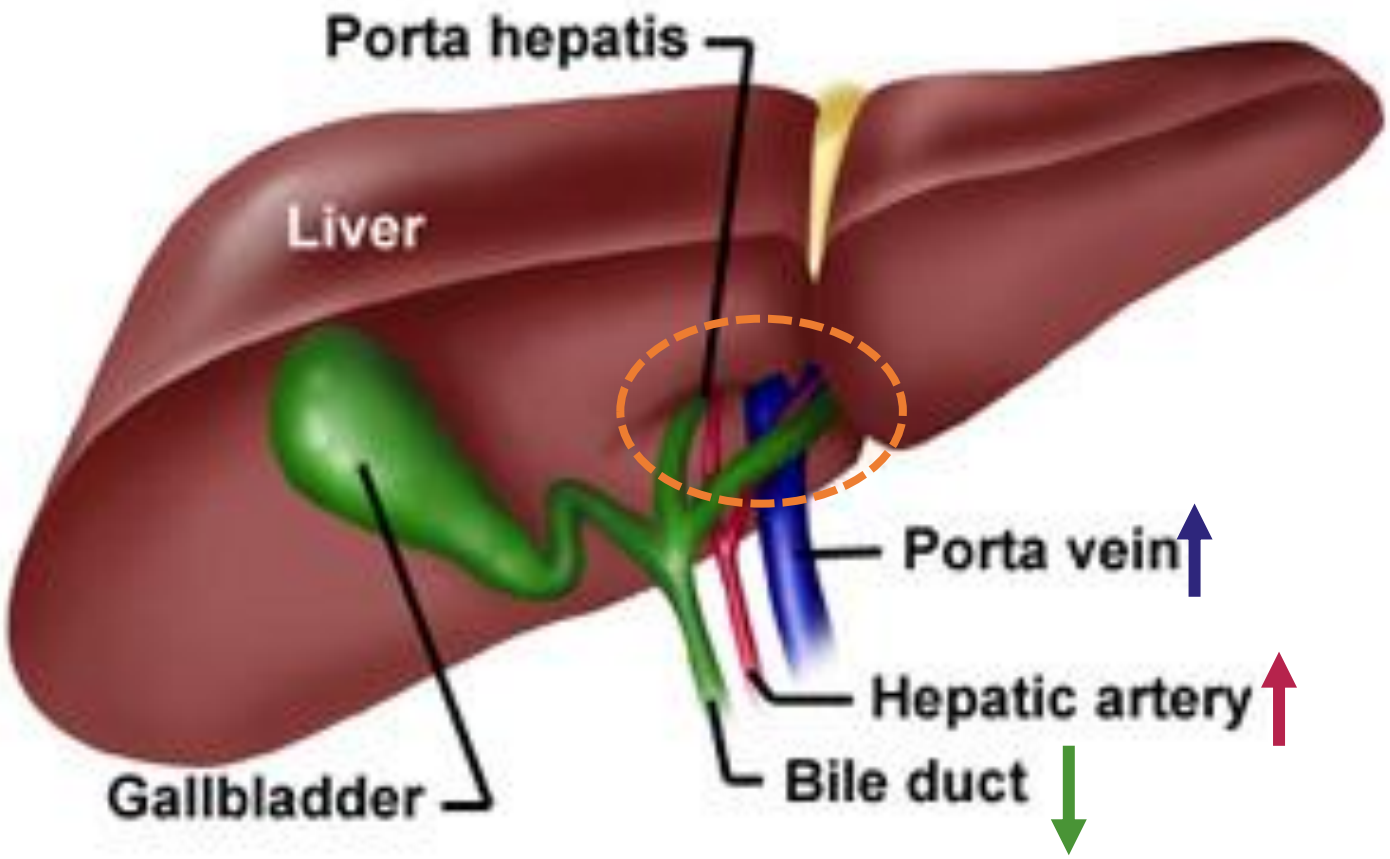
- **blood supply to the liver**
  120 ml blood/ 100 g parenchyme / minute
  - The liver has a **dual blood supply**
    → it receives:
    - oxygenated blood from the **hepatic arteries** (25%),
    - nutrient-rich blood from intestines and iron & bilirubin-rich blood from spleen via the **portal vein** (75%)
    - these vessels enter the liver at the **porta hepatis**

- **outflow of blood from the liver**
  - The liver has a **single venous drainage system**
    - Blood leaves the liver at the posterior aspect of the organ through three **hepatic veins**

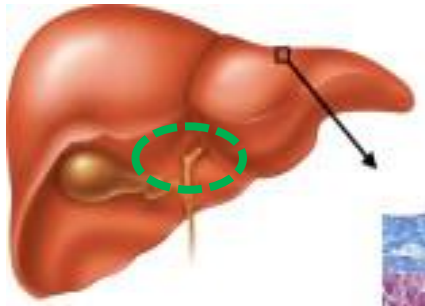


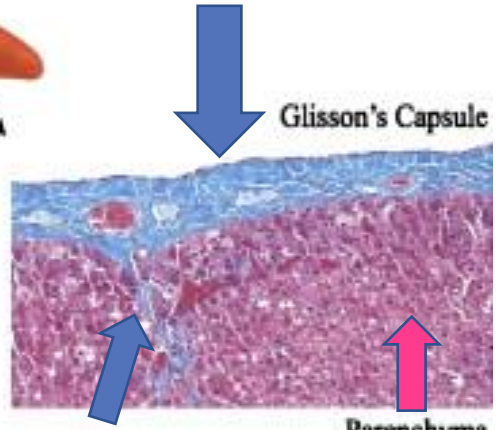
- **porta hepatis** contains:
  - portal vein (entering)
  - hepatic arteries (entering)
  - bile duct (leaving)
  - lymphatic vessels (leaving)
  - nerves (entering)
  - Glisson's capsule (entering)

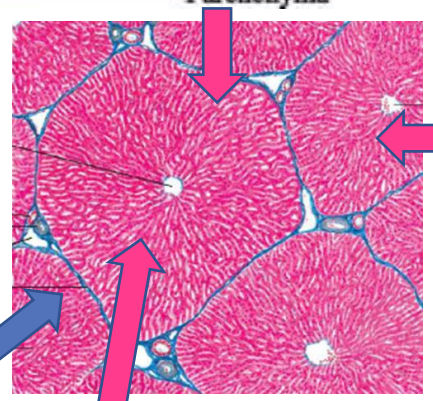
not shown

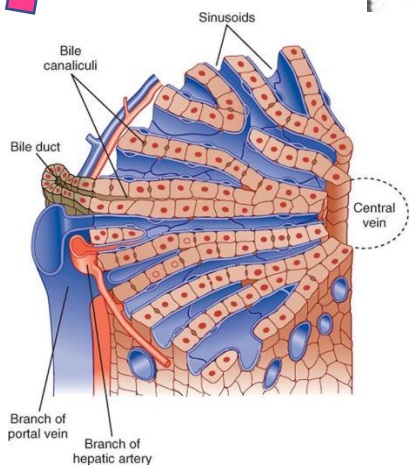


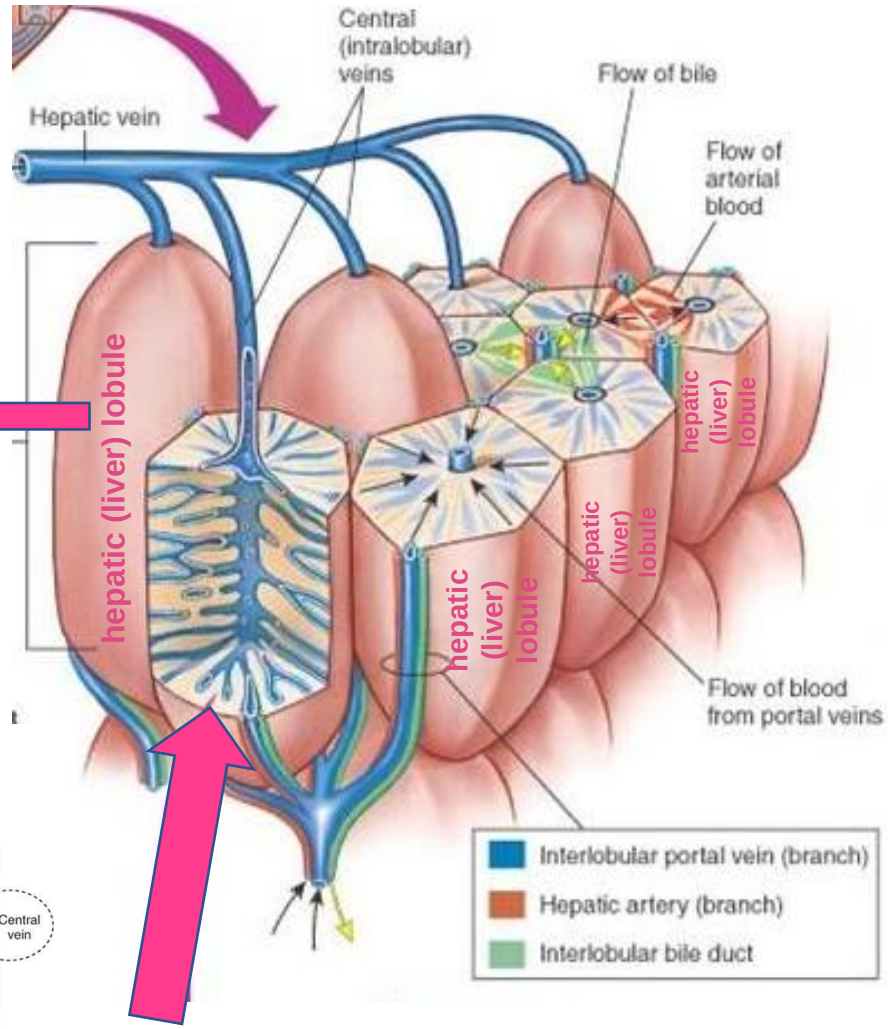
Liver (#54)











- the liver is covered by connective tissue capsule, **Glisson's capsule**
  - G.c. is loosely attached except at the **porta hepatis**, where it enters the liver,
  - G.c. branches and extends throughout the substance of the liver as **septae** - conduits for the blood and lymph vessels and bile ducts

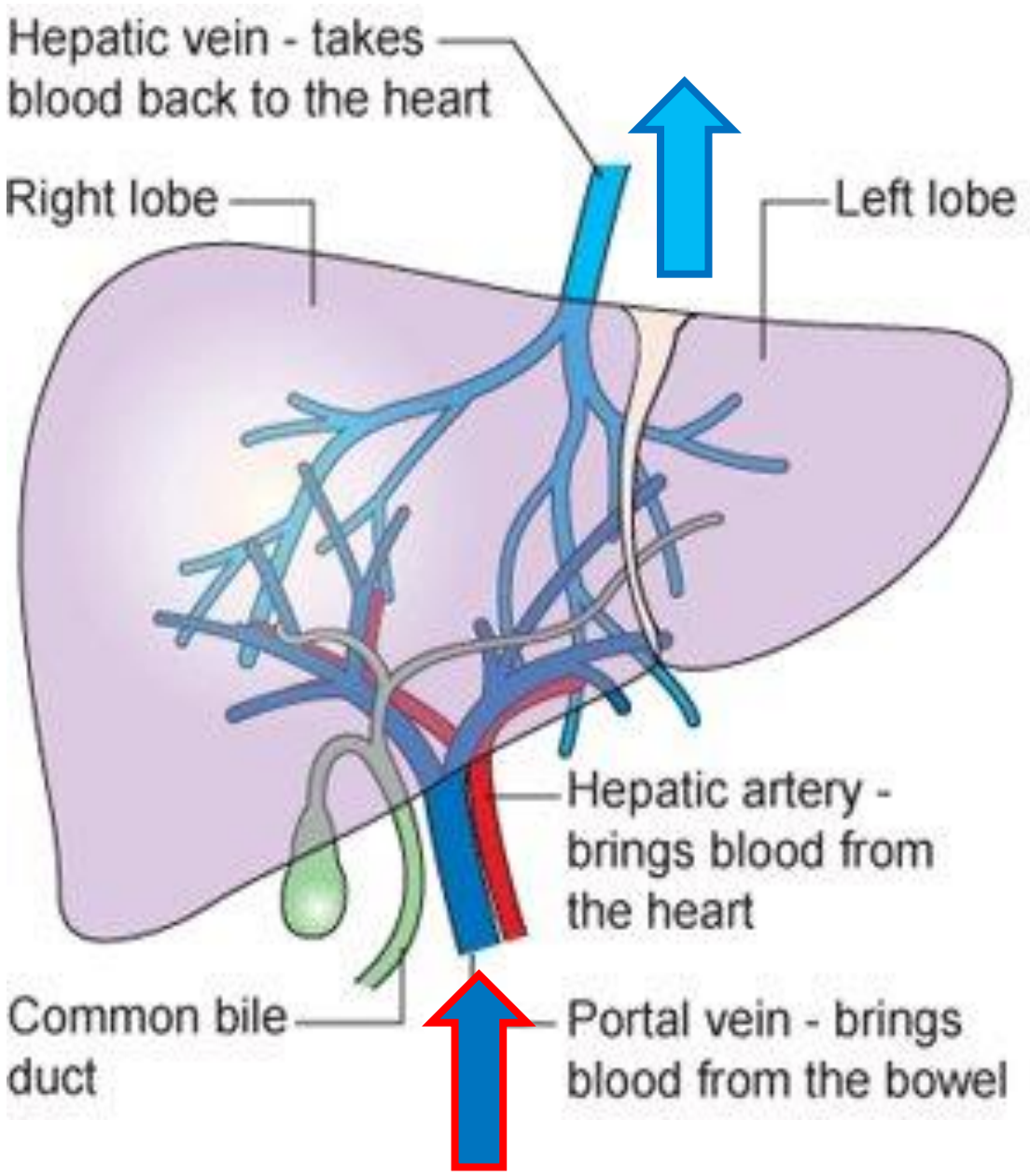
- **the sheets of connective tissue from septae** divide **the parenchyma of the liver** into thousands of small units called **hepatic (liver) lobules**

- in each **hepatic (liver) lobule**
  - anastomosing **cords** (aka plates or trabeculae) **of hepatocytes**
  - between cords - **hepatic (liver) sinusoids**

Liver (#54)

blood flow through the liver

- **blood supply to the liver**
  120 ml blood/ 100 g parenchyma / minute
  - The liver has a **dual blood supply**
    → it receives:
    - oxygenated blood from the **hepatic arteries** (25%),
    - nutrient-rich blood from intestines and iron & bilirubin-rich blood from spleen via the **portal vein** (75%)
    - these vessels enter the liver at the **porta hepatis**
- **outflow of blood from the liver**
  - The liver has a **single venous drainage system**
    - Blood leaves the liver at the posterior aspect of the organ through three **hepatic veins**



Liver (#54)

hepatic artery
& portal vein

blood flow through the liver cont.

portal area

distributing vessels

interlobular vessels

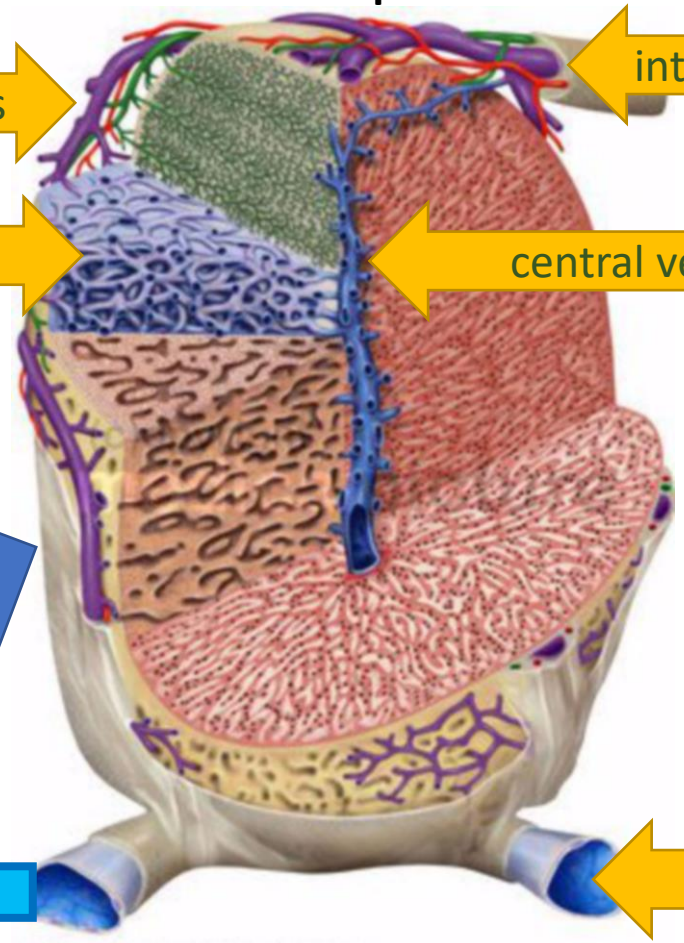
sinusoids

central vein

hepatic (liver) lobule

to hepatic vein

sublobular vein



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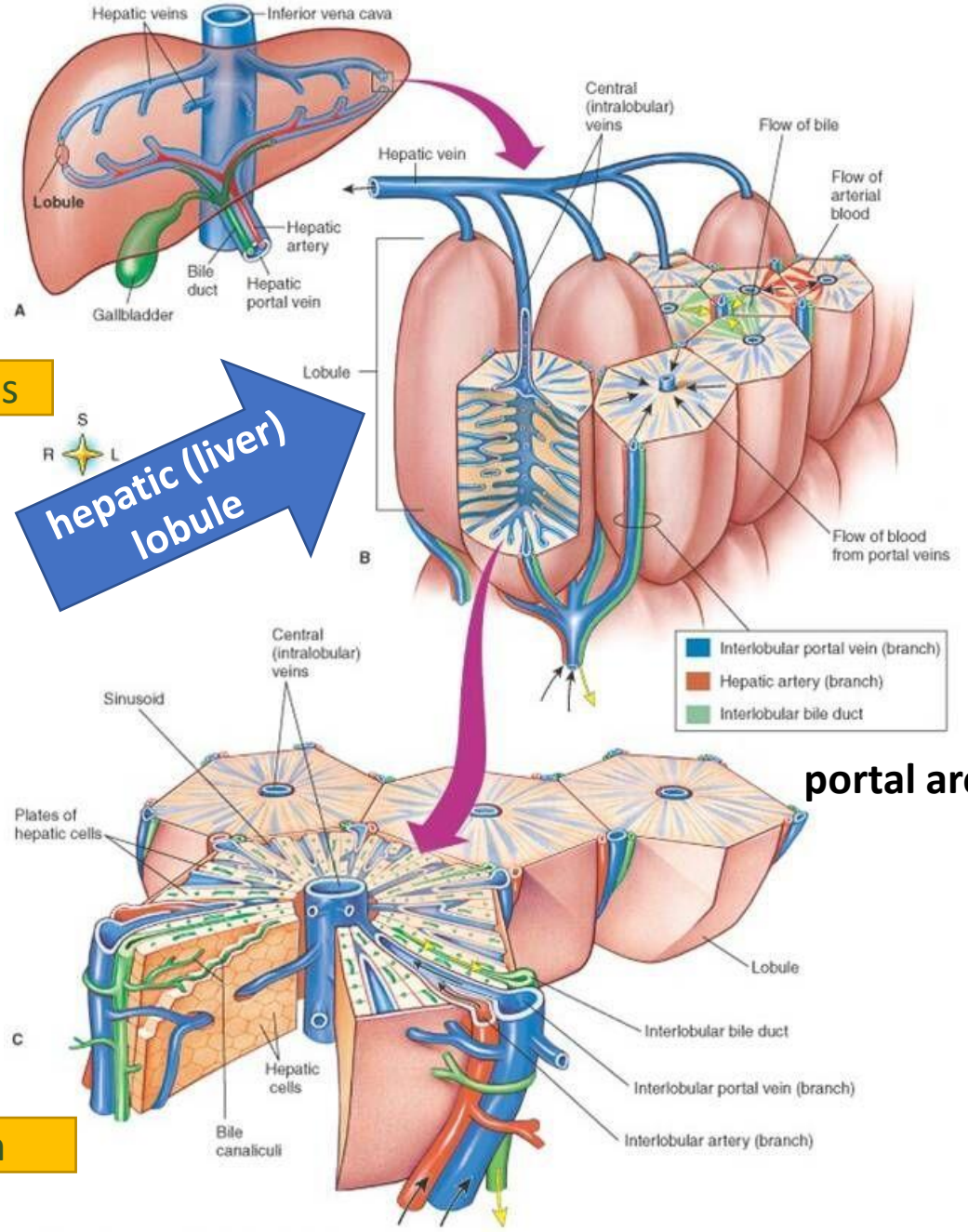


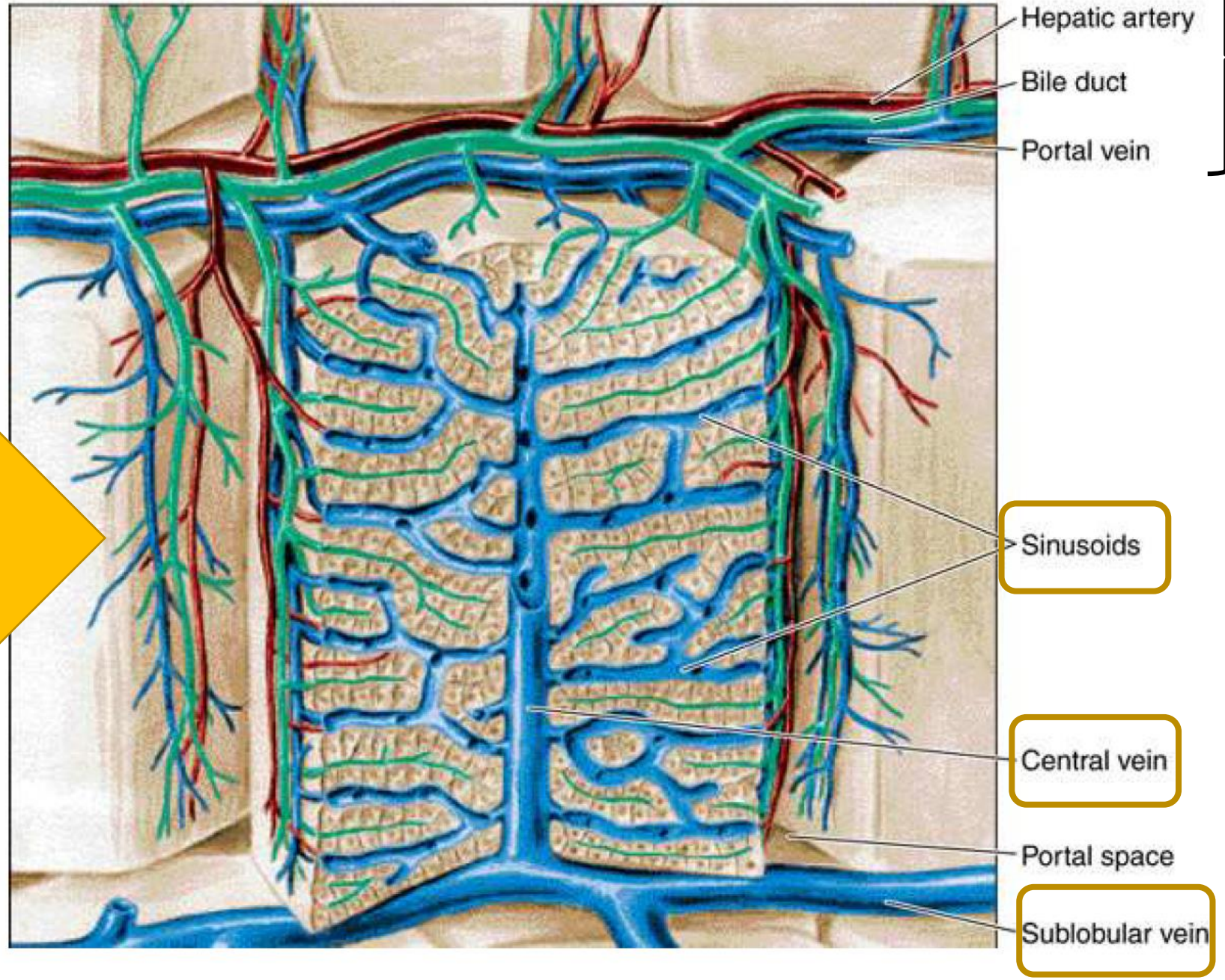
hepatic (liver) lobule

portal area

Liver (#54

blood flow through the liver cont.

distributing vessels – terminal branches of p.v. & h.a.

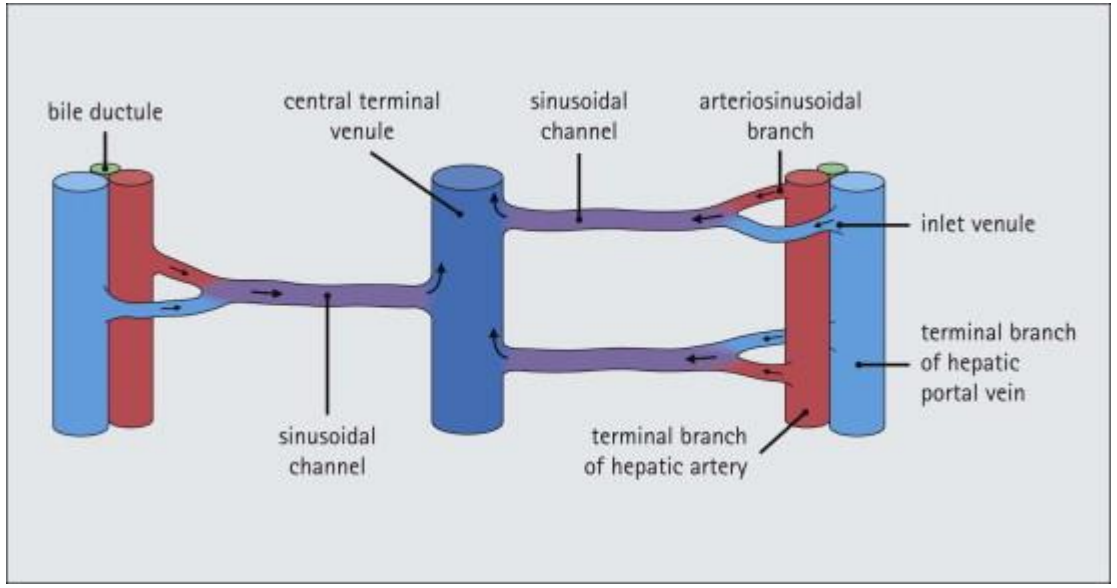


Liver (#54)

blood flow through the liver cont.

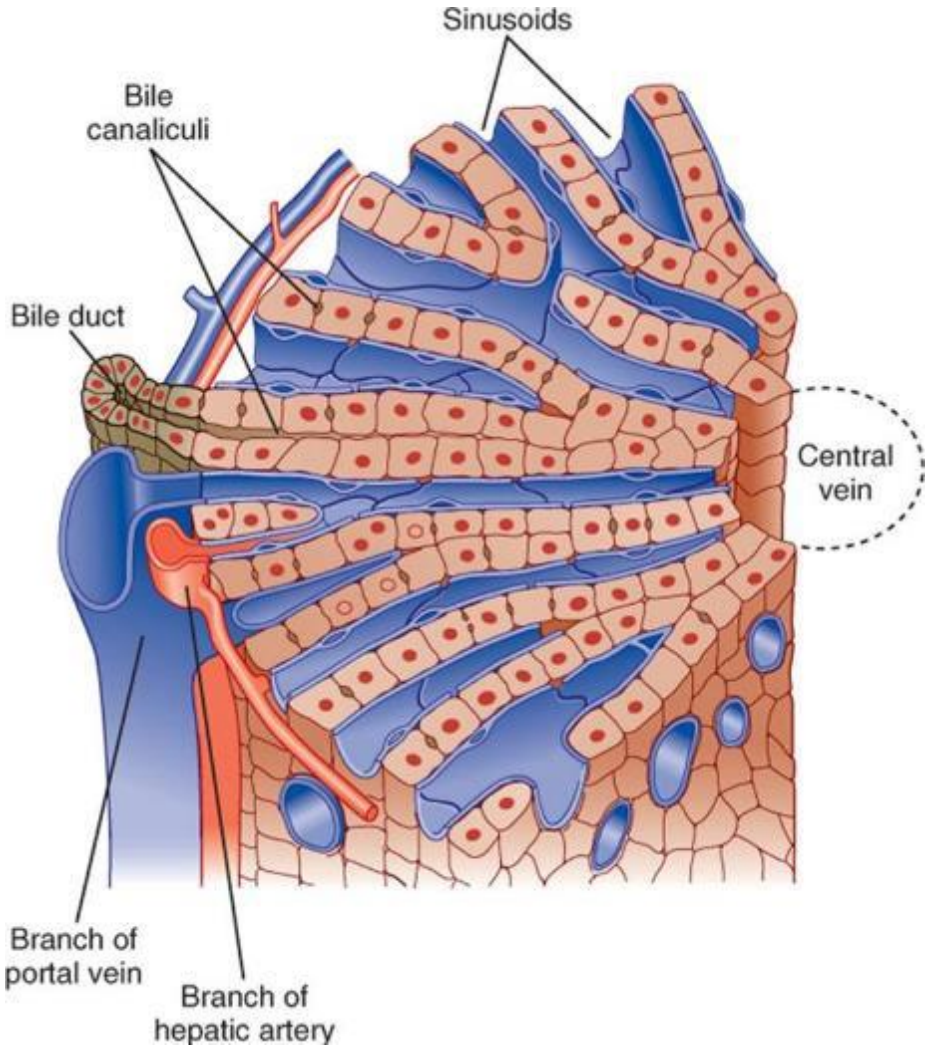
Hepatic (liver) sinusoids

- Branches of the distributing vessels, so-called inlet vessels merge into sinusoids lined with endothelium

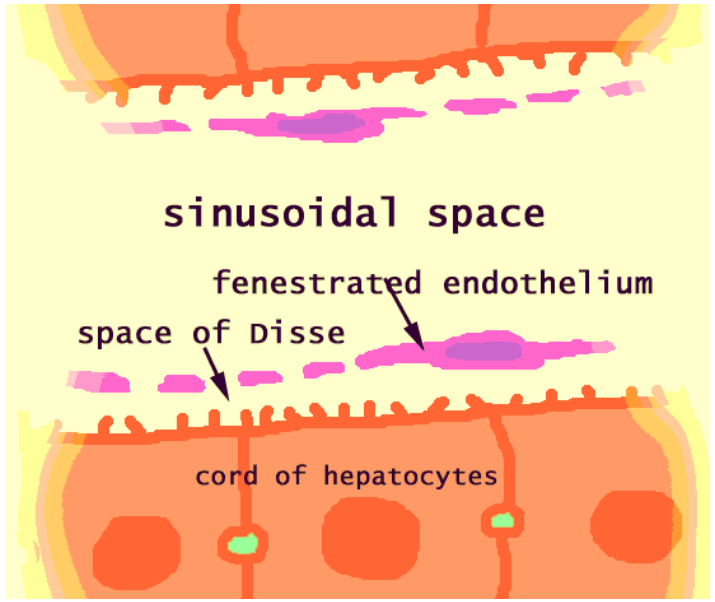


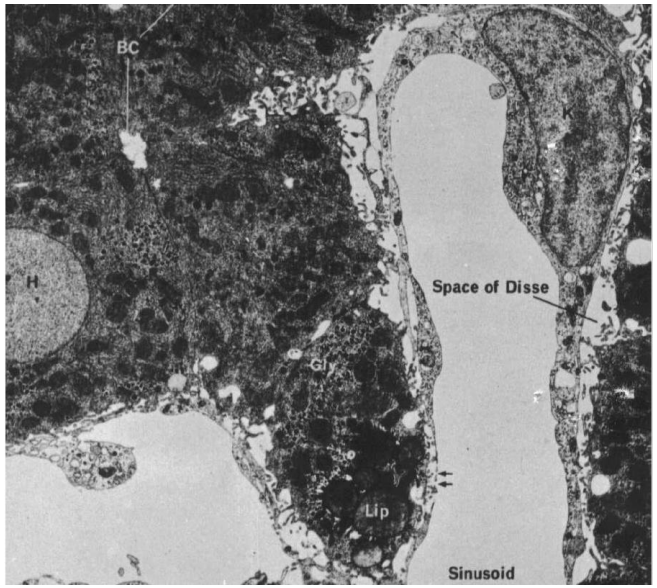
- in sinusoids **blood from both portal vein and hepatic artery mixes together**

- hepatocytes form anastomosing cords (aka plates or trabeculae) which lie between **hepatic (liver) sinusoids**

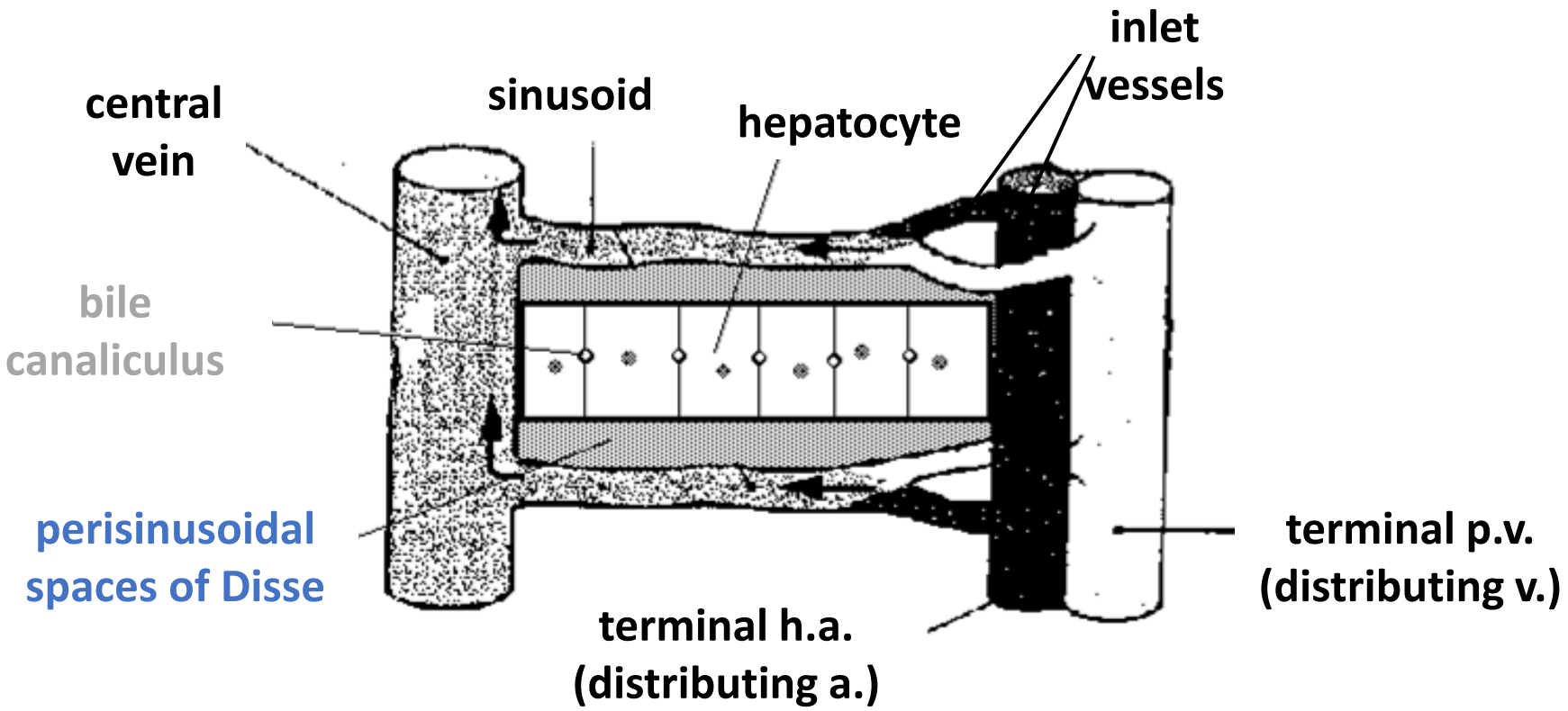


Liver (#54)





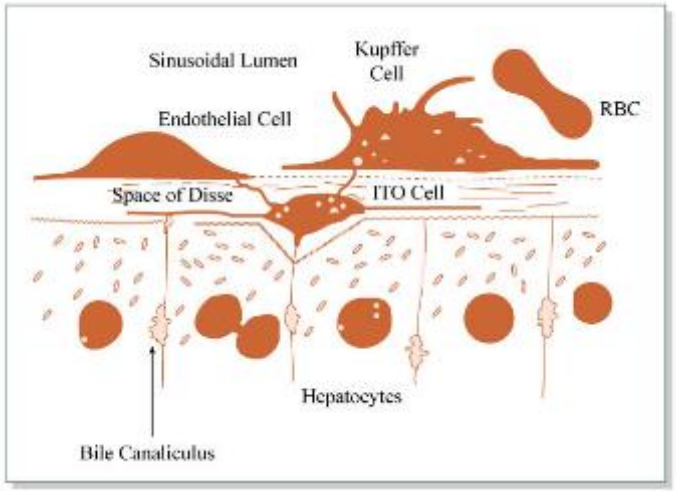
Hepatic (liver) sinusoids cont.

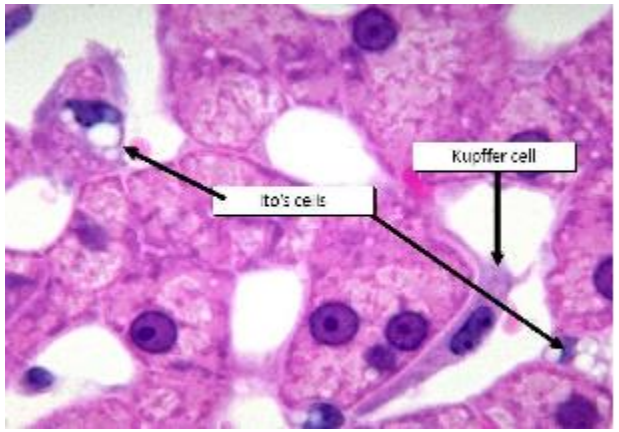


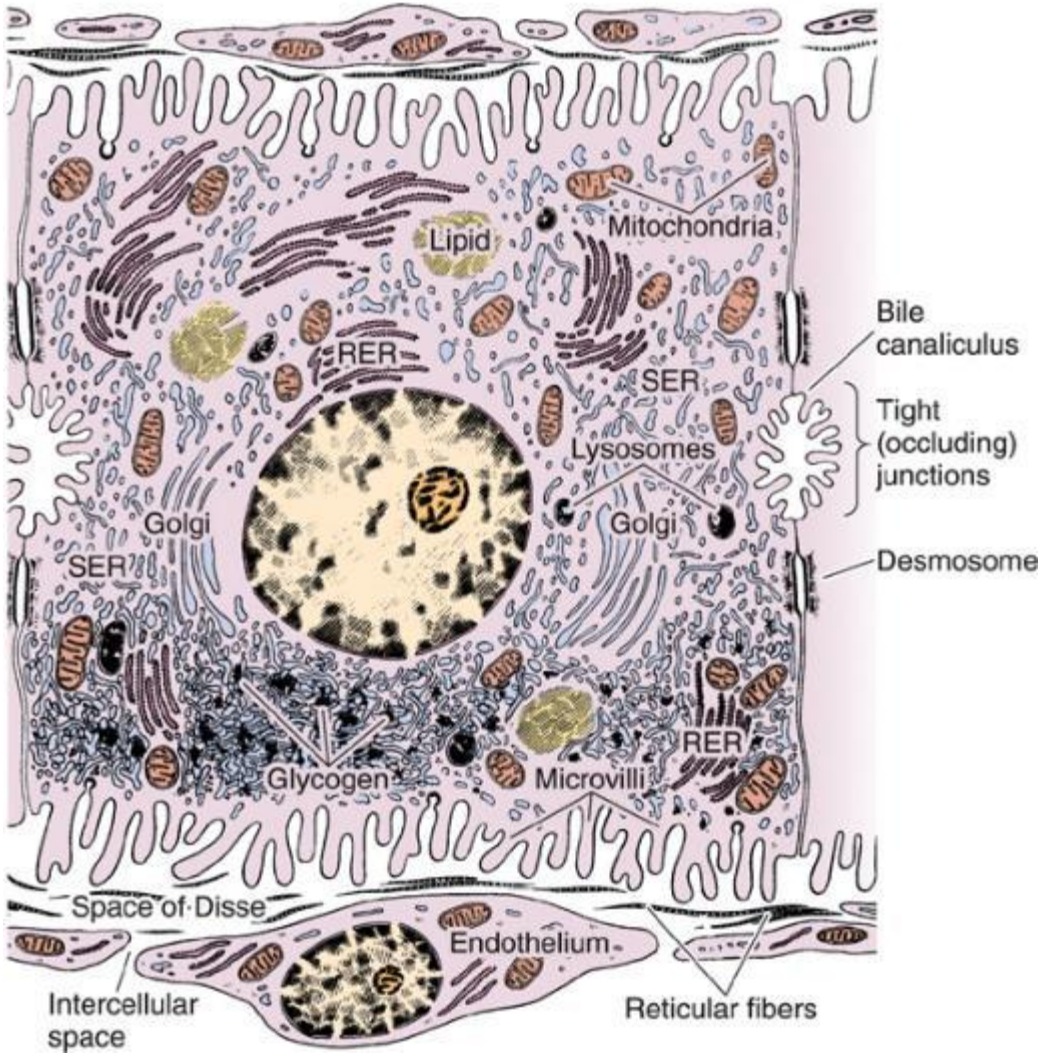
Liver (#54)

Perisinusoidal space of Disse

- **between** sinusoidal domain of hepatocyte and a fenestrated epithelium
- contains:
  - **Ito cells** (aka **hepatic stellate cells** (HSC)),
    - ✓ store fat incl. fat soluble vitamins (like **vitamin A**, D, K),
    - ✓ produce ECM incl. reticular fibers (collagen III)
    - ✓ erythropoietin (EPO)
  - reticular fibers
  - microvilli of hepatocytes
  - plasma







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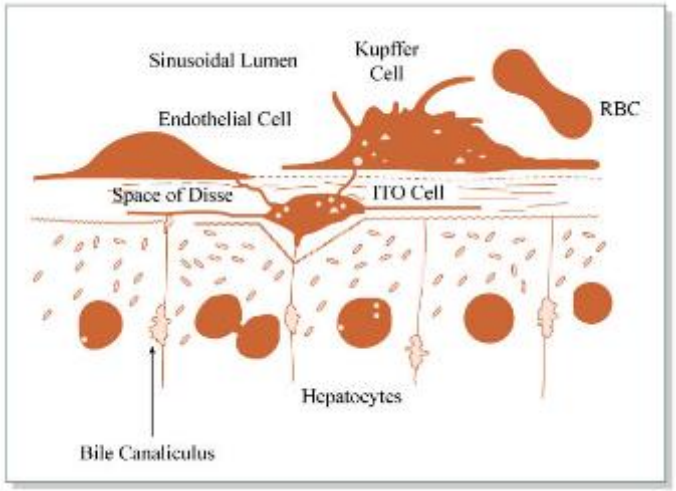
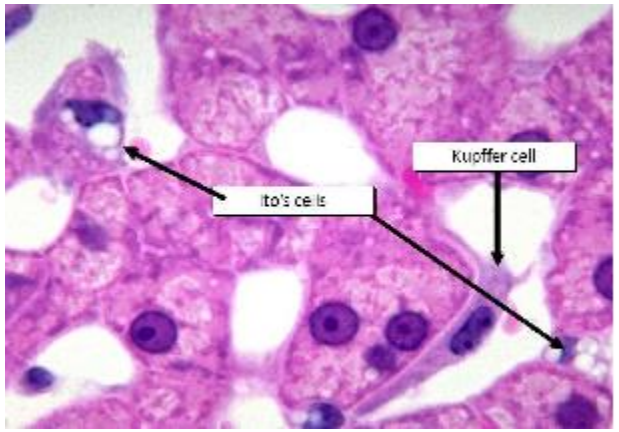
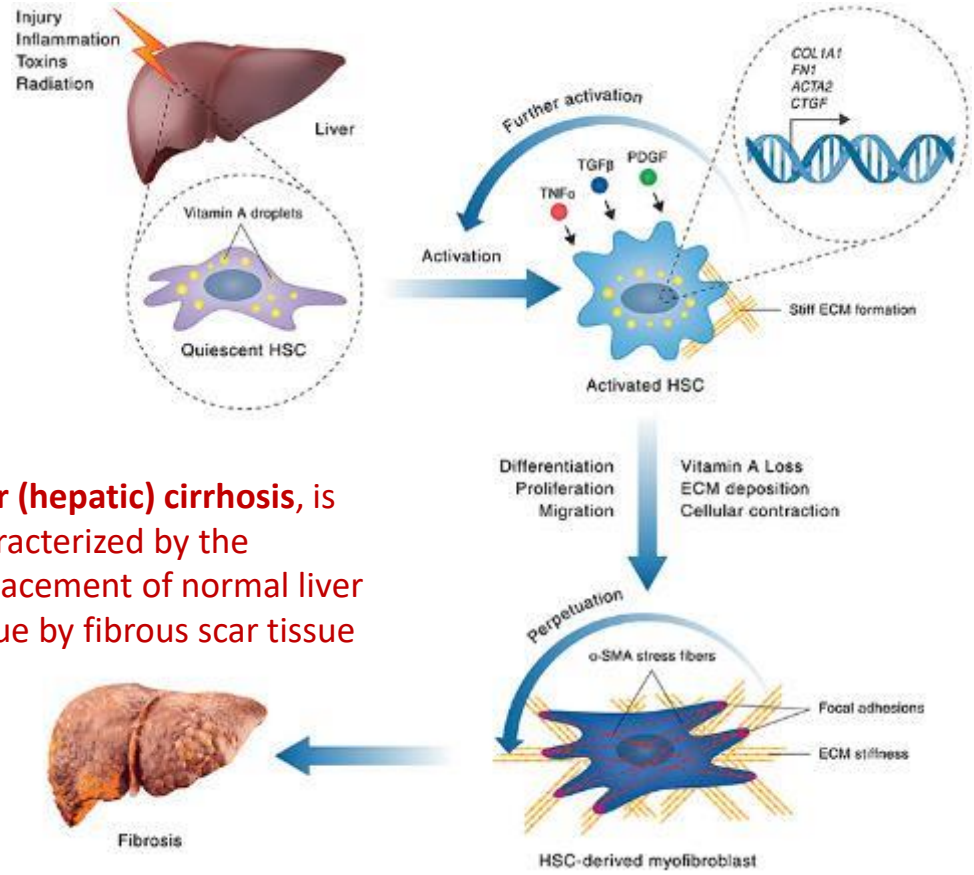




- In the case of liver injury Ito cells are activated → **Ito cells transdifferentiate** from quiescent, vitamin-A-storing cells **into proliferative, fibrogenic myofibroblasts**



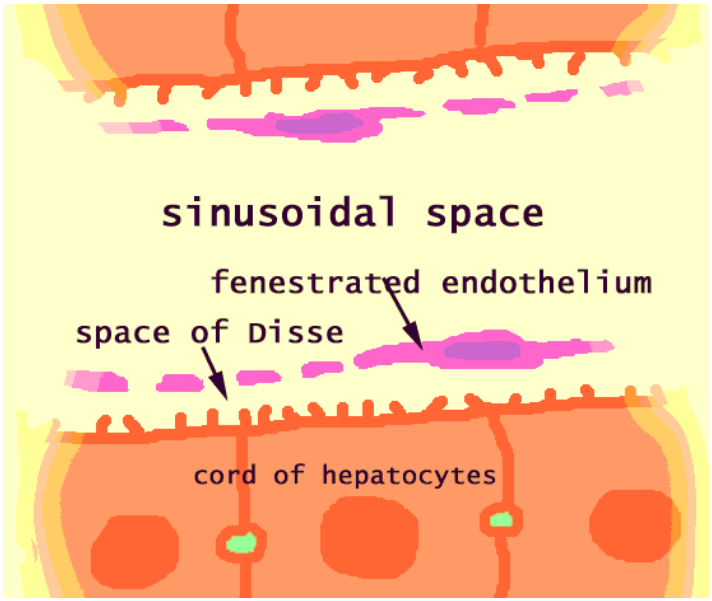
liver (hepatic) cirrhosis, is characterized by the replacement of normal liver tissue by fibrous scar tissue

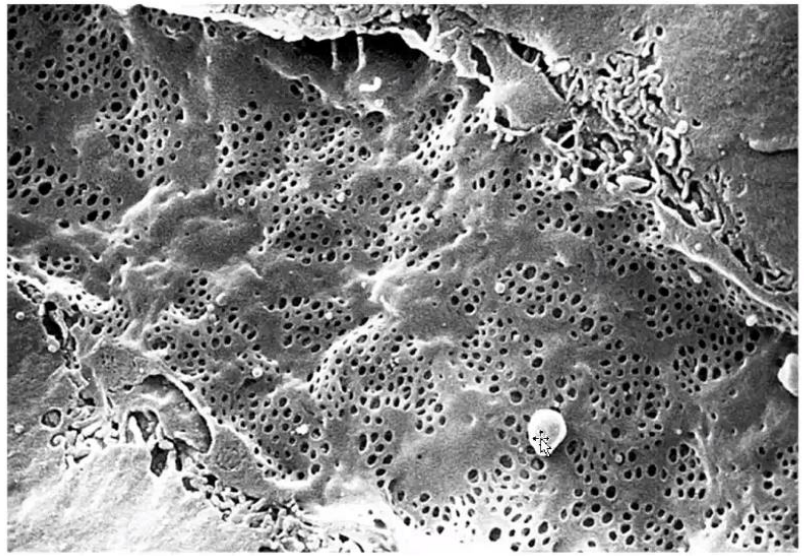
Liver (#54)

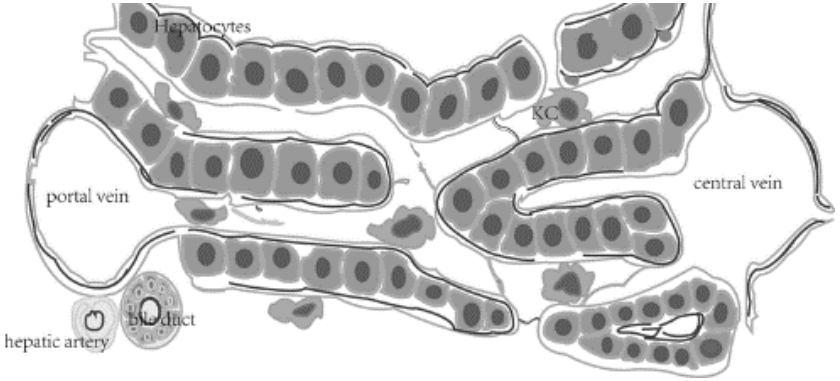
Hepatic (liver) sinusoids cont.

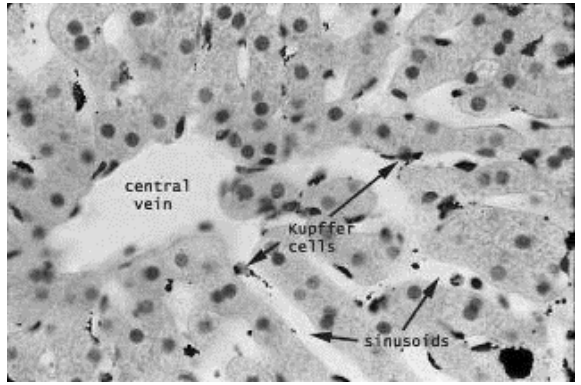
- the endothelium which lines liver sinusoids
  - is discontinuous and fenestrated
  - lacks a basement membrane
- fenestrations permit plasma to wash freely over the exposed surfaces of the hepatocytes through the space of Disse ← **hepatocytes do not come in direct contact with blood**

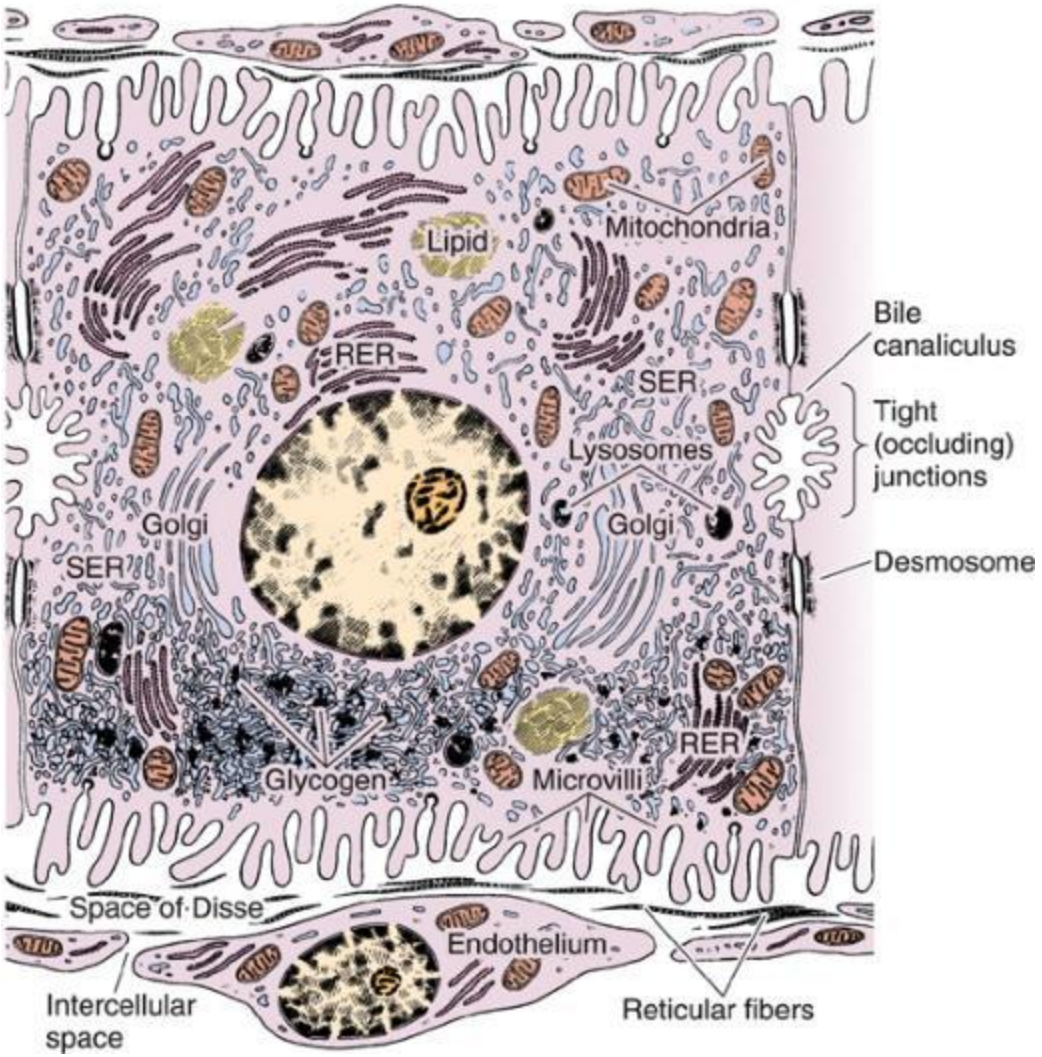
- associated with the sinusoids are Kupffer cells -- liver macrophages which effectively catch and destroy pathogens and other particles which entered the blood in the intestine.

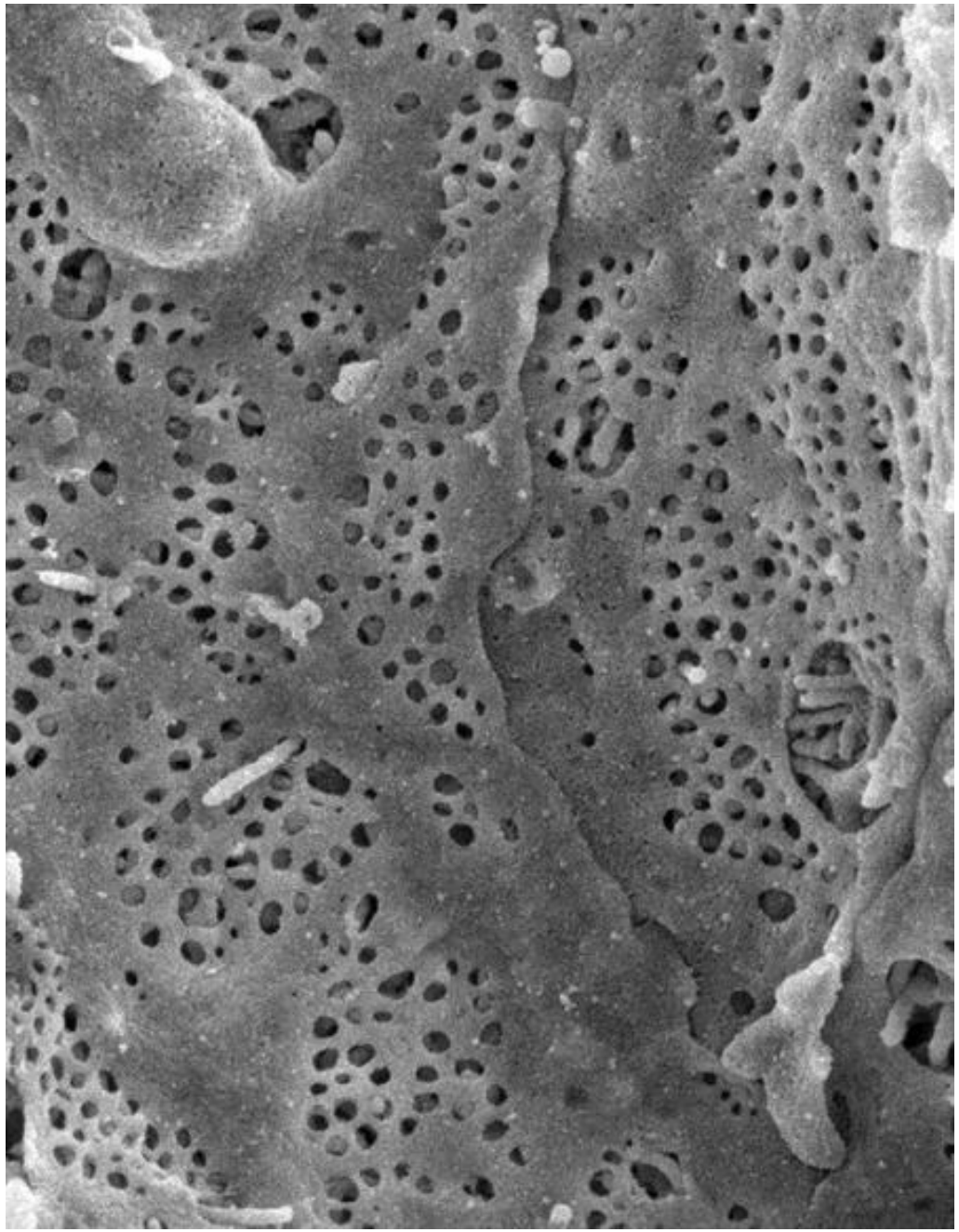












Scanning electron micrograph of hepatocyte microvilli protruding through the sinusoidal endothelial cell fenestrations.

Liver (#54)

Hepatic (liver) sinusoids cont.

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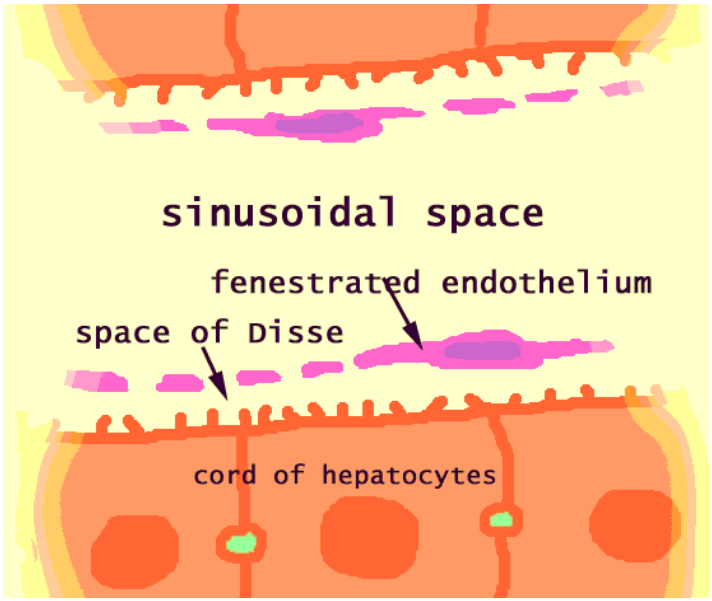
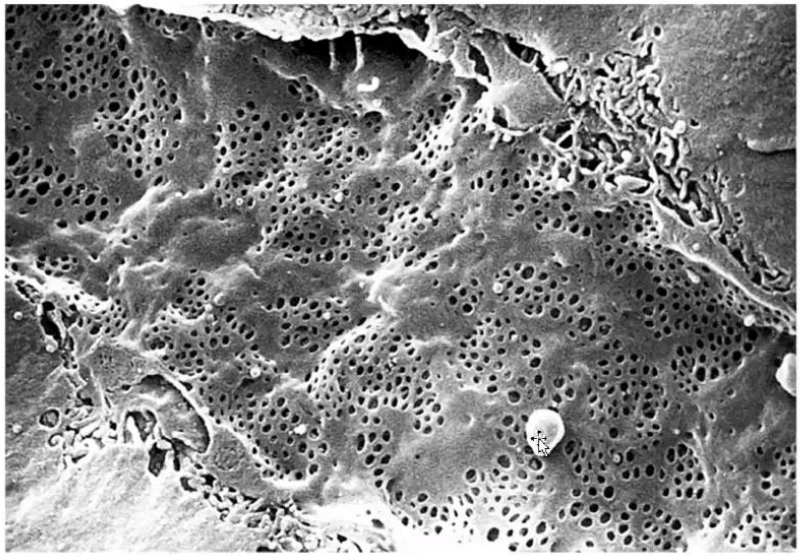
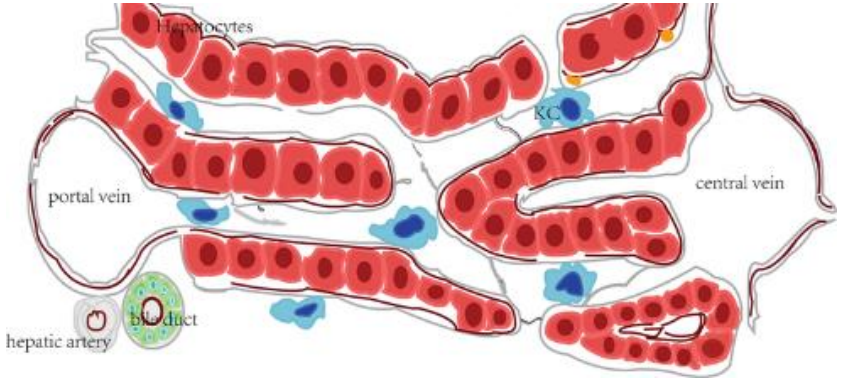
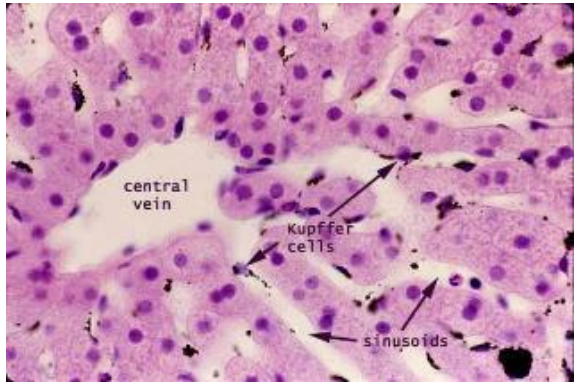


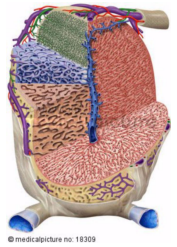






Liver (#54)

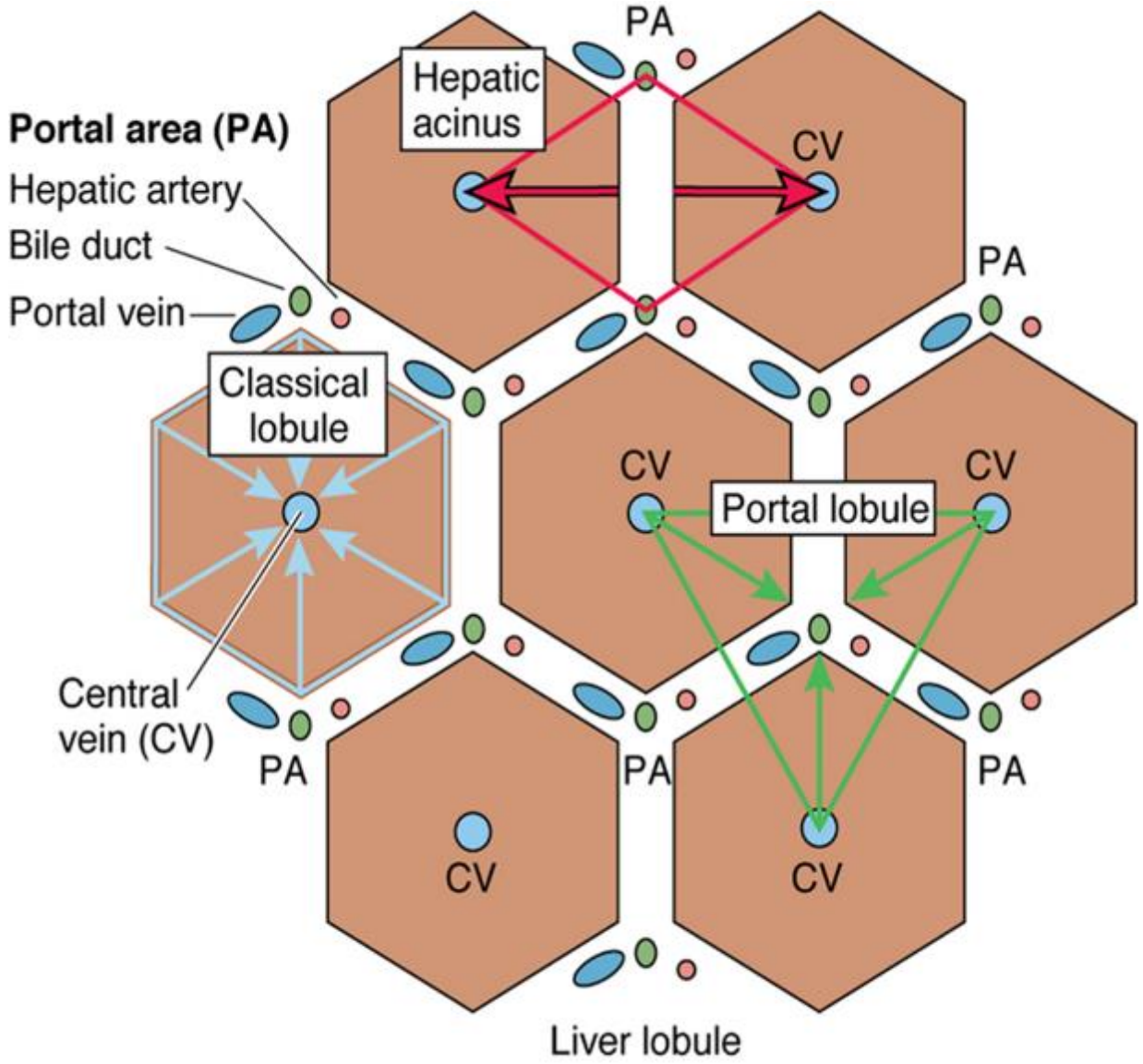
hepatic (liver) lobule *aka* **anatomical lobule** or **classical lobule**

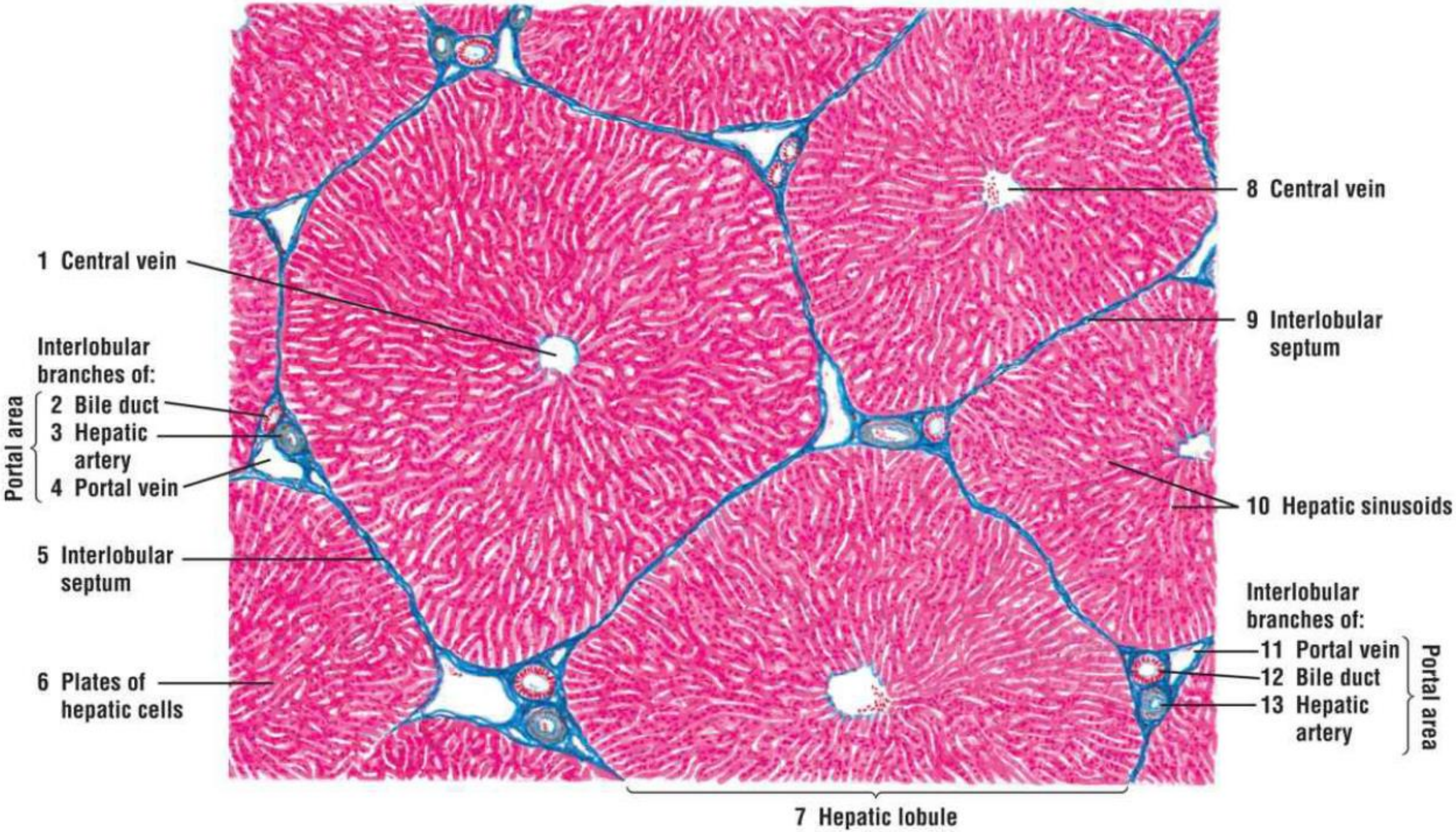


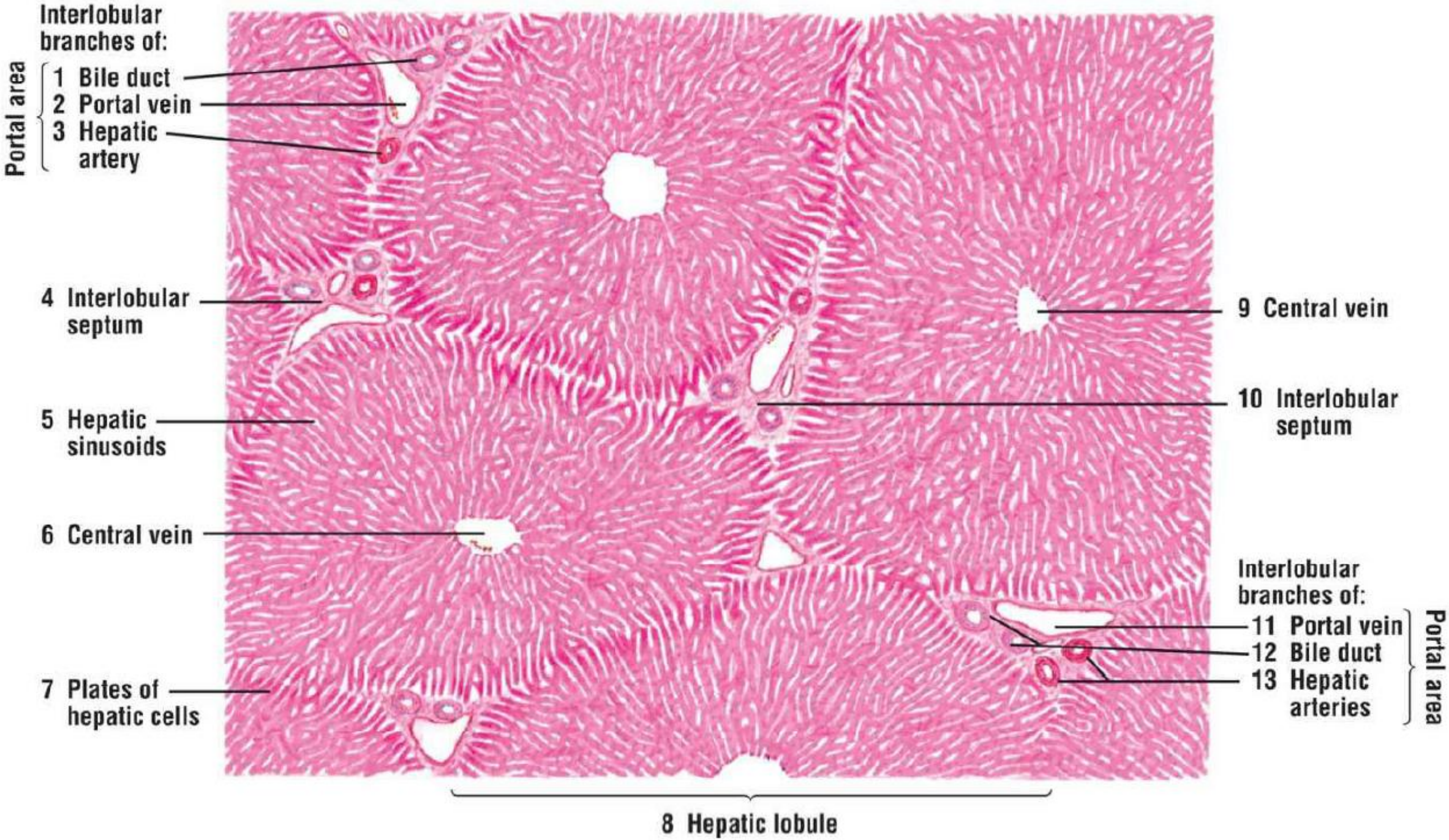
- the structural units of the liver
- the shape of a hexagon
- based on blood flow
  - h.l. shows from which region the blood is collected by one central vein ← the unit drained by a central vein.
  - **blood flows** from the periphery to the center of the lobule into the central vein.

portal lobule

- the shape of a triangle
  - its center is the interlobular bile duct in the portal area
  - its periphery is bounded by imaginary straight lines connecting the three surrounding central veins
- based on bile secretion
  - bile, manufactured by hepatocytes, enters into small intercellular spaces, **bile canaliculi,** located between hepatocytes and **flows** to the periphery of the lobule to the interlobular bile ducts of the portal areas




1 Central vein
Interlobular branches of:
Portal area
2 Bile duct
3 Hepatic artery
4 Portal vein
5 Interlobular septum
6 Plates of hepatic cells
8 Central vein
9 Interlobular septum
10 Hepatic sinusoids
Interlobular branches of:
11 Portal vein
12 Bile duct
13 Hepatic artery
Portal area
7 Hepatic lobule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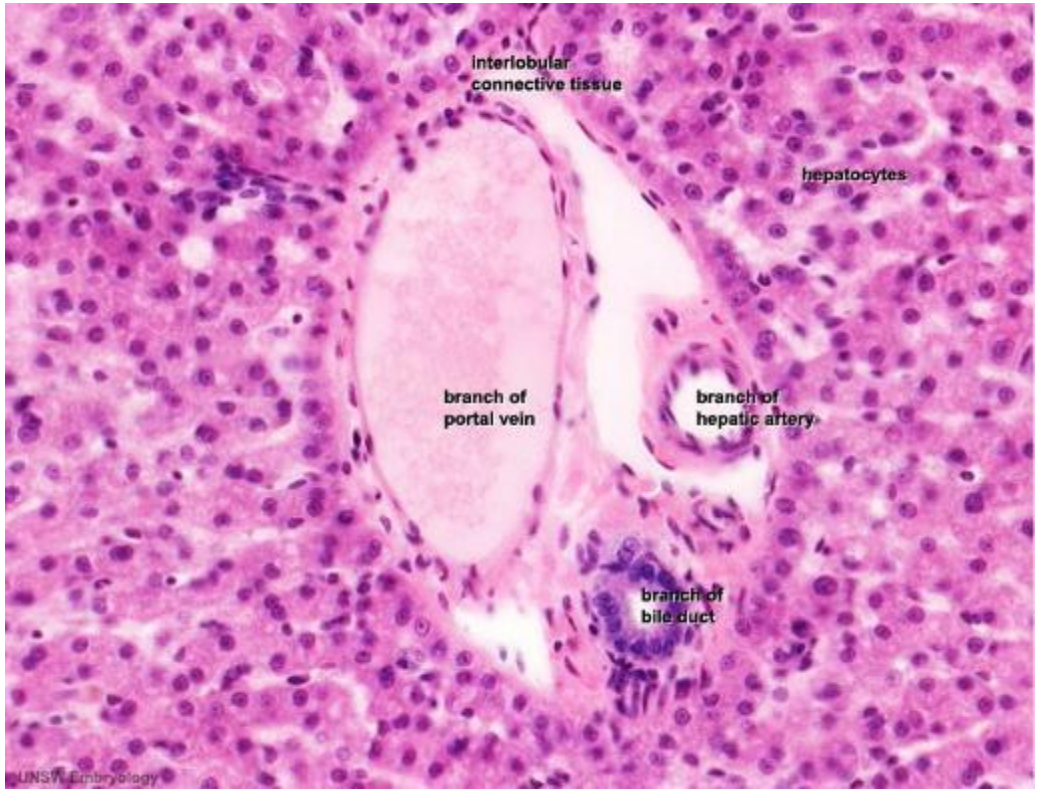
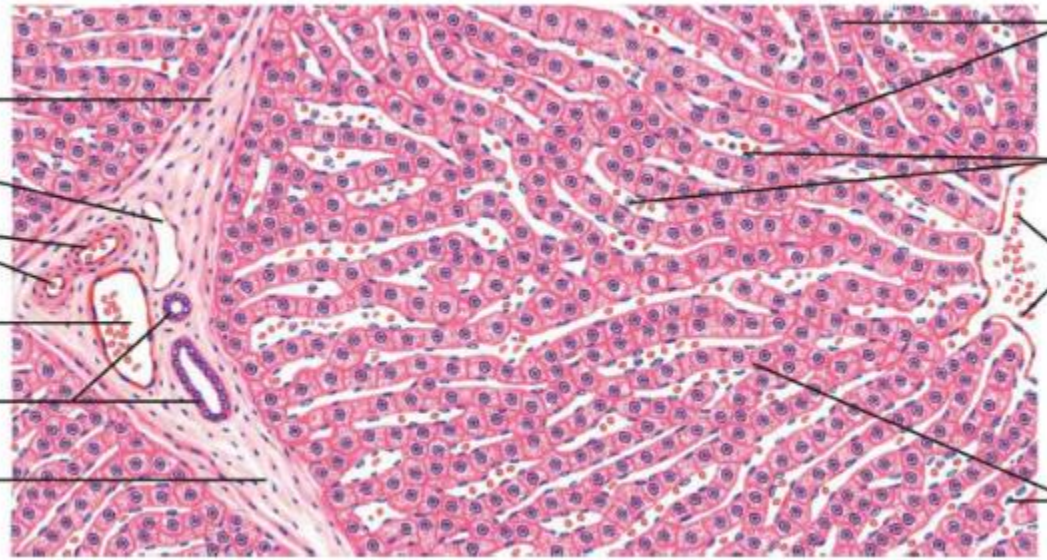
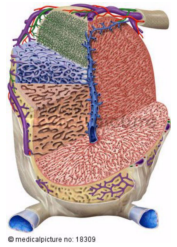




1 Interlobular septum
2 Lymphatic vessel
3 Hepatic arteries
4 Portal vein
5 Bile ducts
6 Interlobular septum
7 Plates of hepatic cells
8 Blood cells in sinusoids
9 Central vein
10 Endothelial cells in sinusoids

Liver (#54)

hepatic (liver) lobule *aka* **anatomical lobule** or **classical lobule**



- the structural units of the liver
- the shape of a hexagon
- based on blood flow
  - h.l. shows from which region the blood is collected by one central vein ← the unit drained by a central vein.
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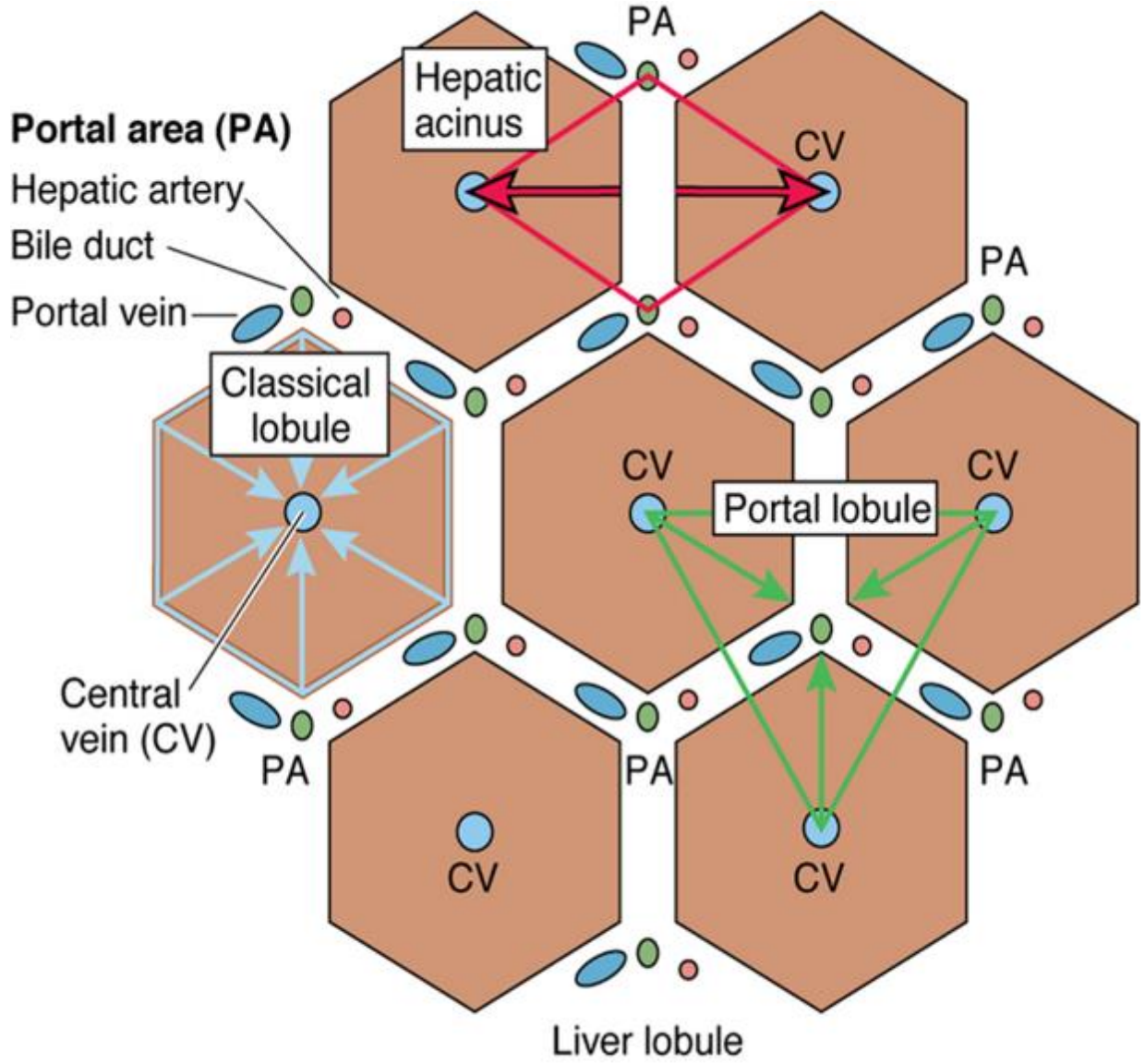
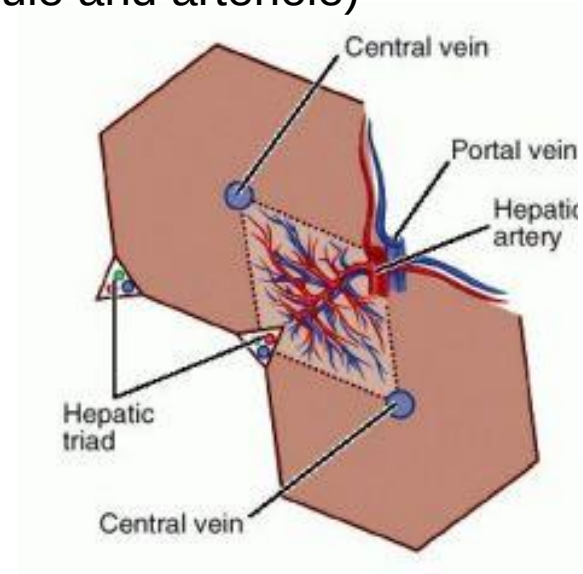
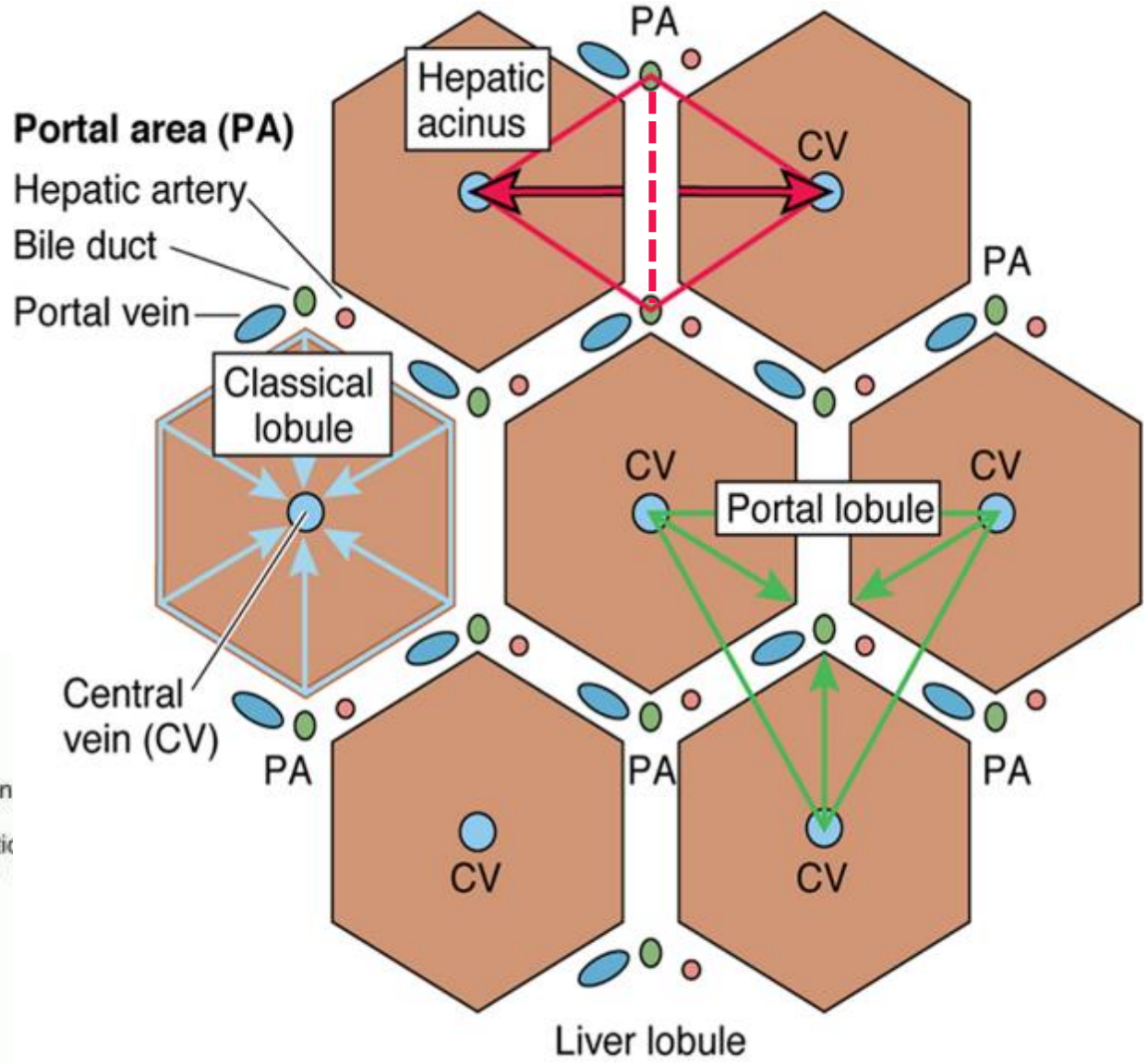


Liver (#54)

hepatic acinus (acinus of Rappaport)

- the functional units of the liver
- the shape of a diamond
  - h.a. is centered on the line connecting two portal areas
  - h.a. extends outwards to the two adjacent central veins
- also based on blood flow
  - h.a. shows region which is supplied by a terminal branch of the portal vein and hepatic artery (distributing venule and arteriole)

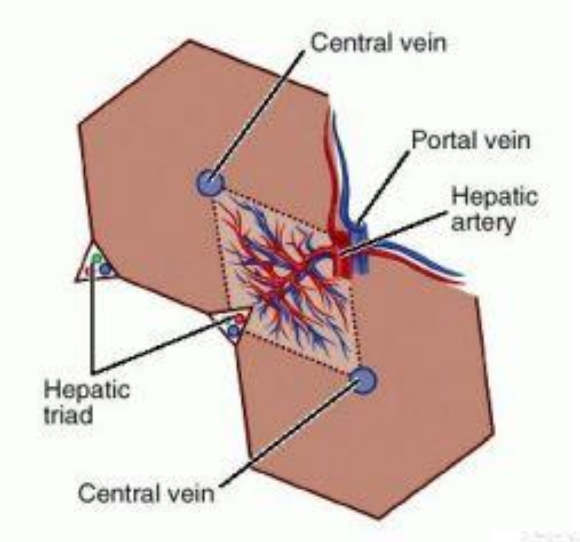


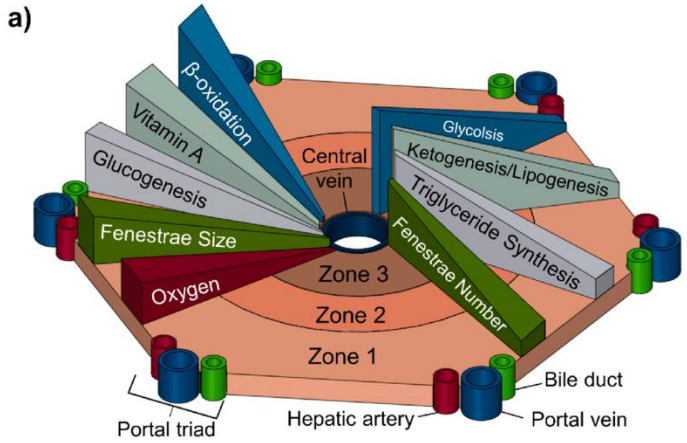


Liver (#54)

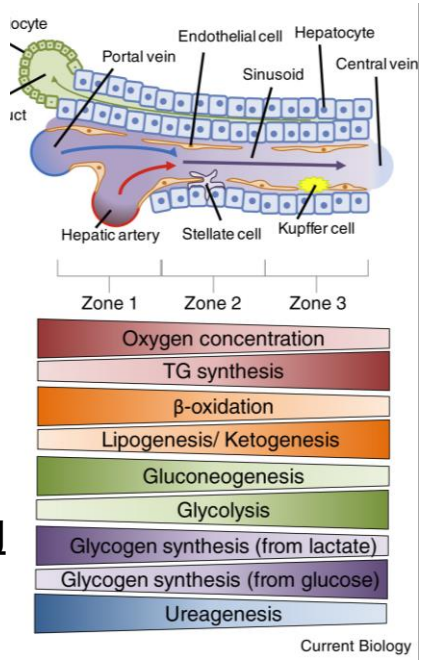
hepatic acinus (acinus of Rappaport) cont.

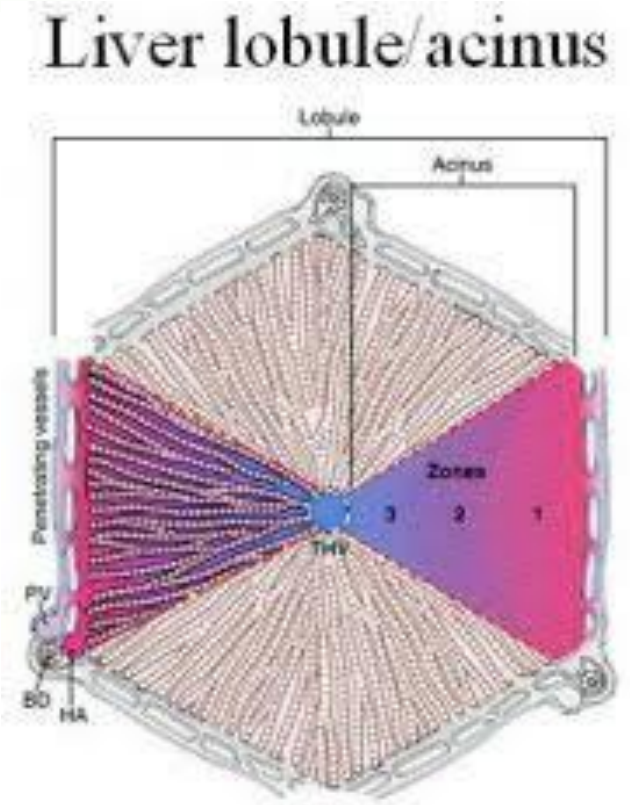
- h.a. contains three concentric regions (zones) of hepati parenchyma surrounding distributing vessels in the center
- based on oxygen level
  - the outermost layer, zone 3, extends as far as the central vein and is the most oxygen-poor of the three zones.
  - the remaining region is equally divided into two zones (1 and 2) → zone 1 is the richest in oxygen.





- **hepatocytes exhibit variations** in their structural, histochemical, and biochemical properties, depending on their location within liver lobules and hepatic acinus





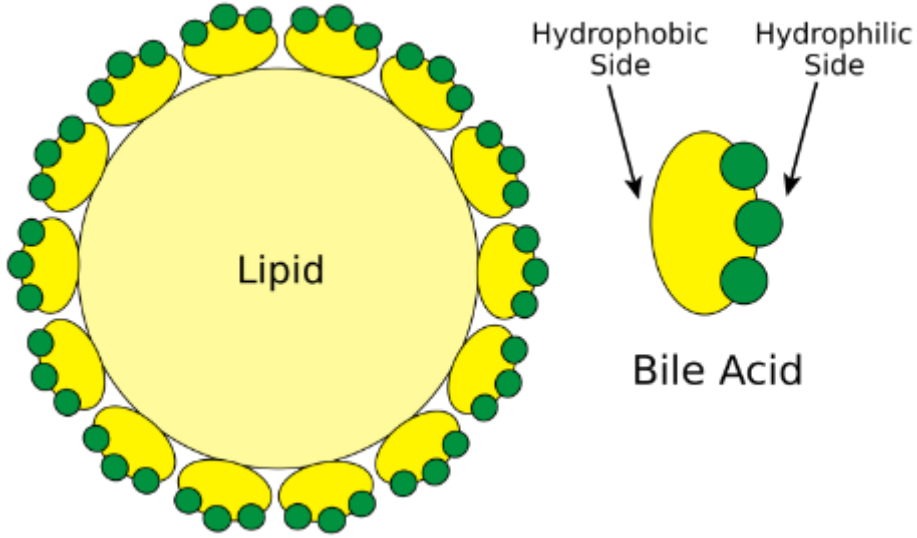
Liver (#54)

Bile

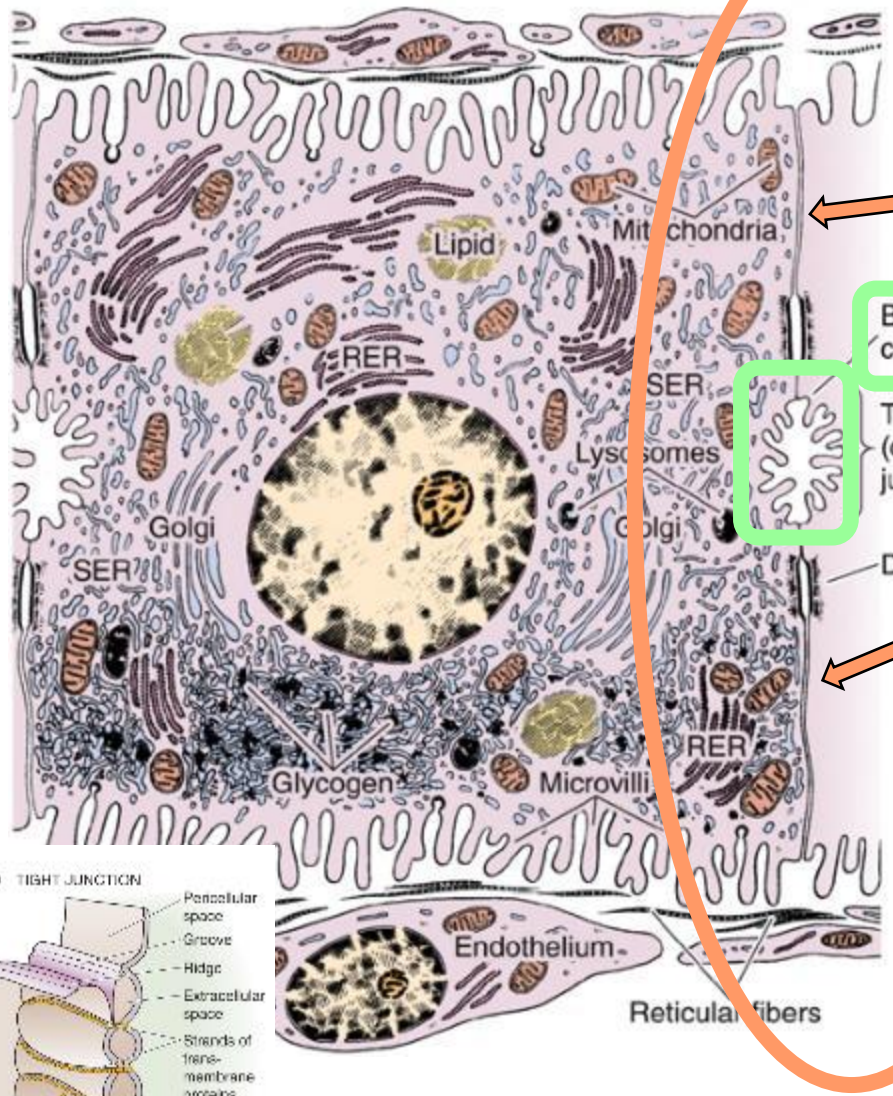
- bile function
  - emulsification of lipids
  - elimination of:
    - excess cholesterol
    - bilirubin – a toxic product of degradation of hemoglobin – in the form bilirubin glucuronide
  - delivery of sIgA, water & electrolytes

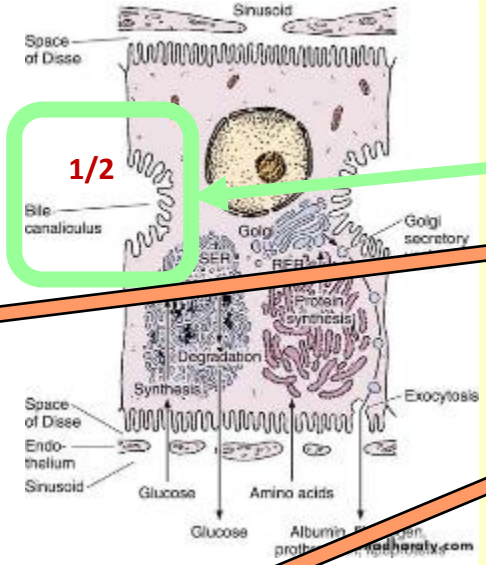
- bile composition
  - water
  - bile salts (sodium and potassium salts of primary and secondary bile acids conjugated with taurine or glycine residues)
  - phospholipids, such as lecithin incl. phosphatidylcholines
  - bilirubin glucuronide (bile pigment)
  - cholesterol
  - electrolytes
  - sIgA

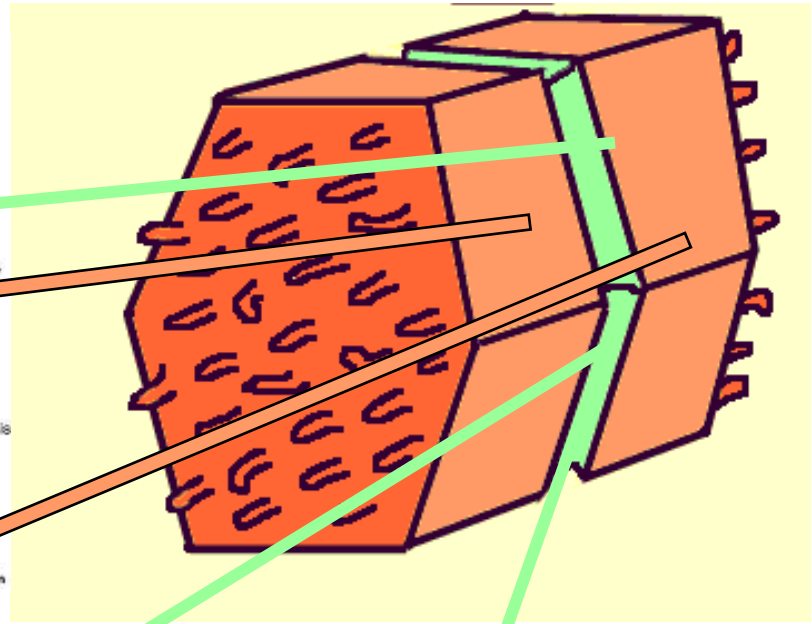
- Most of the bile salts are resorbed from the lumen of small intestine and are transported by hepatocytes to the bile canaliculi (**enterohepatic recirculation of bile salts**) → only 10% is produced de novo in SER of hepatocytes.

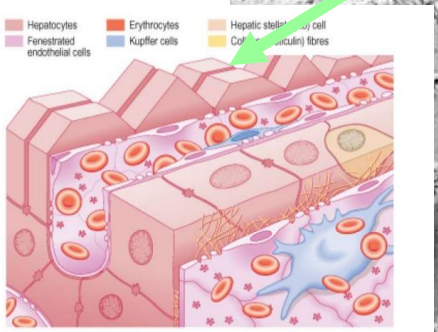


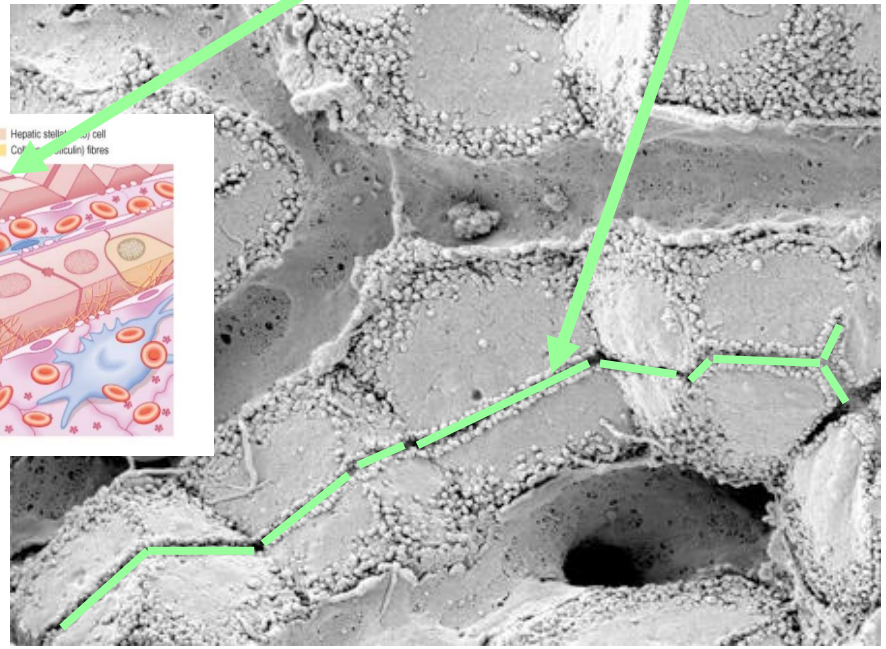
Liver (#54)


Lipid
Mitochondria
RER
SER
Golgi
SER
Glycogen
Microvilli
RER
Endothelium
Reticular fibers
Bile canaliculus
Tight (occluding) junctions
Desmosome


Sinusoid
Space of Disse
1/2
Bile canaliculus
Golgi
Golgi secretory
SER
RER
Protein synthesis
Degradation
Synthesis
Exocytosis
Space of Disse
Endothelium
Sinusoid
Glucose
Amino acids
Glucose



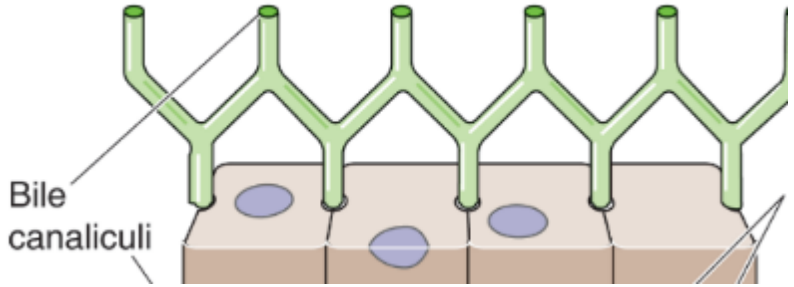

Hepatocytes
Erythrocytes
Fenestrated endothelial cells
Kupffer cells



D TIGHT JUNCTION
Pericellular space
Groove
Ridge
Extracellular space
Strands of trans-membrane proteins
Lumen of bile canaliculus
Cytosol of the hepatocyte

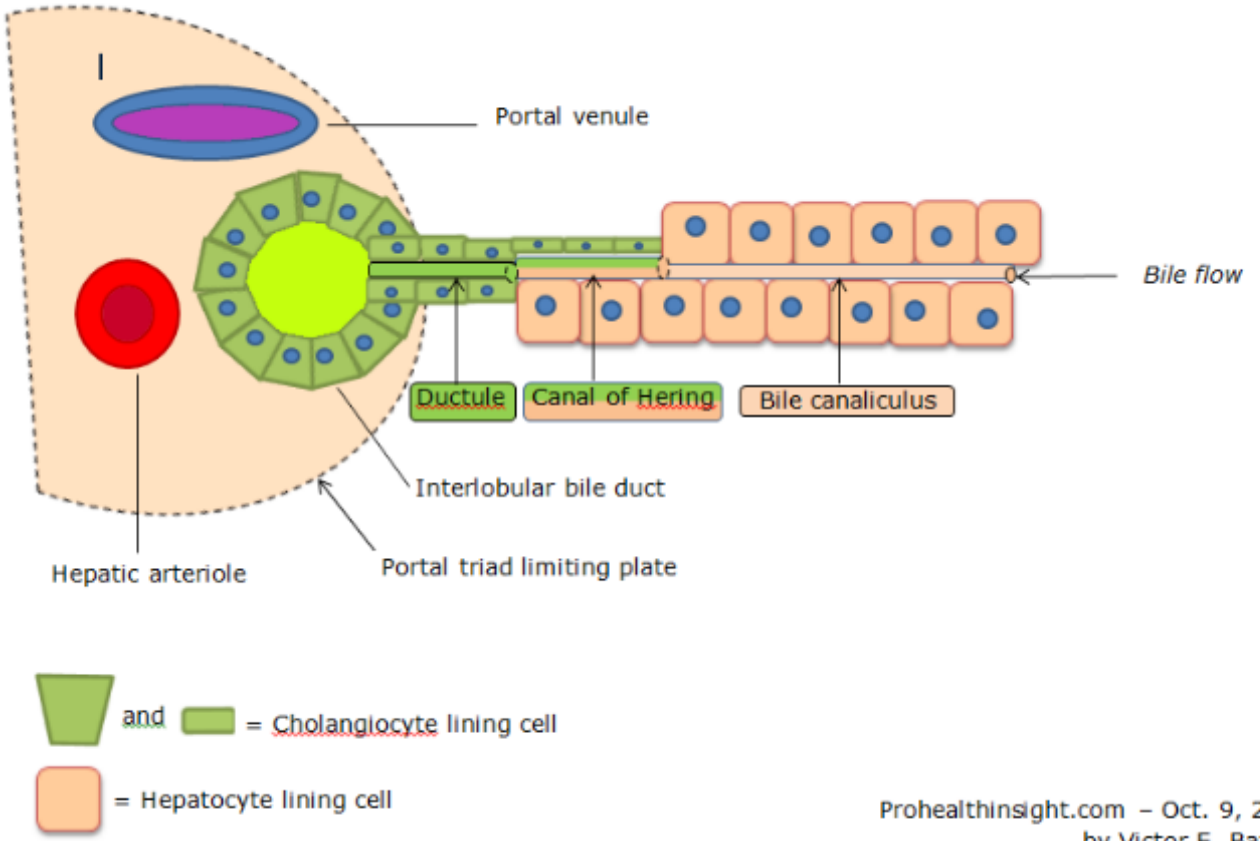
Liver (#54)

Bile duct system



- **Bile canaliculi** anastomose with one another, forming **labyrinthine tunnels** among the hepatocytes.
- As these **bile canaliculi** reach the periphery of the classic lobules, they merge with canals of Hering
- **Canals of Hering**
  - slender conduits
  - formed by hepatocytes in combination with low cuboidal (or ovoid) cells known as cholangiocytes.

- Bile from the canals of Hering flow via **bile ductules** (composed only of cholangiocytes) into **interlobular bile ducts** (cuboidal cholangiocytes) located in the portal areas of the classical lobules



Liver (#54)

Bile duct system

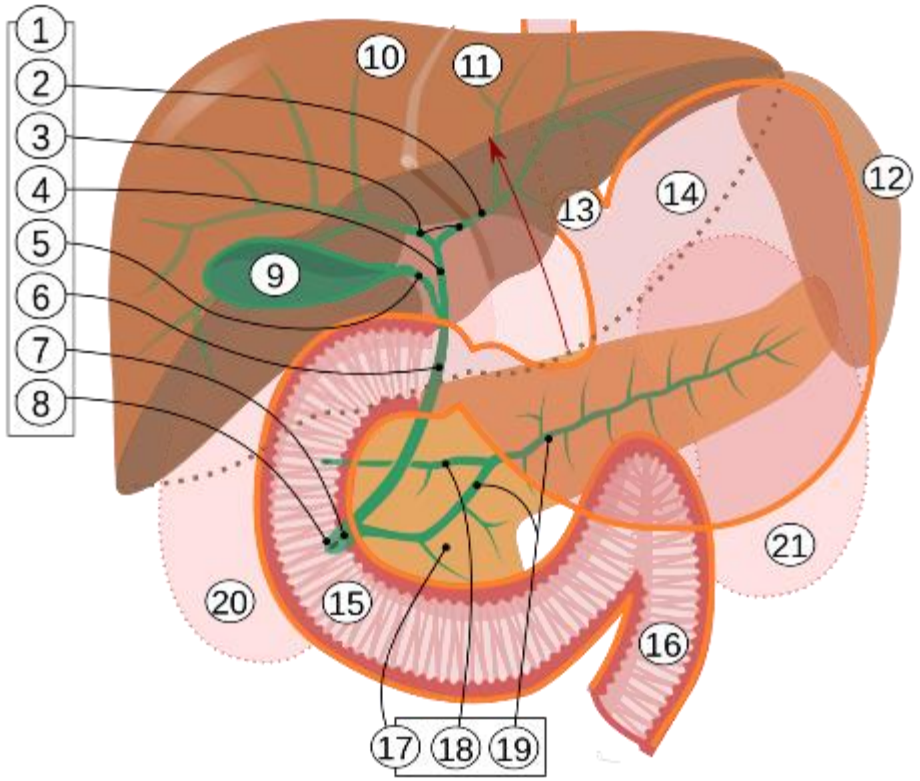
Bile flow

intralobular b.f.

- from bile canaliculi (no wall of its own!) to the canals of Hering (hepatocytes+cholangiocytes)
- from canals of Hering to the **bile ductules** (flat/ovoid cholangiocytes)

- **from** bile ductules via → the **interlobular** bile ducts (simple cuboidal epithelium) → **interlobar** ducts (↑∅) → → **right and left hepatic** ducts, → **common hepatic** duct
  - → **common bile** duct to the duodenum

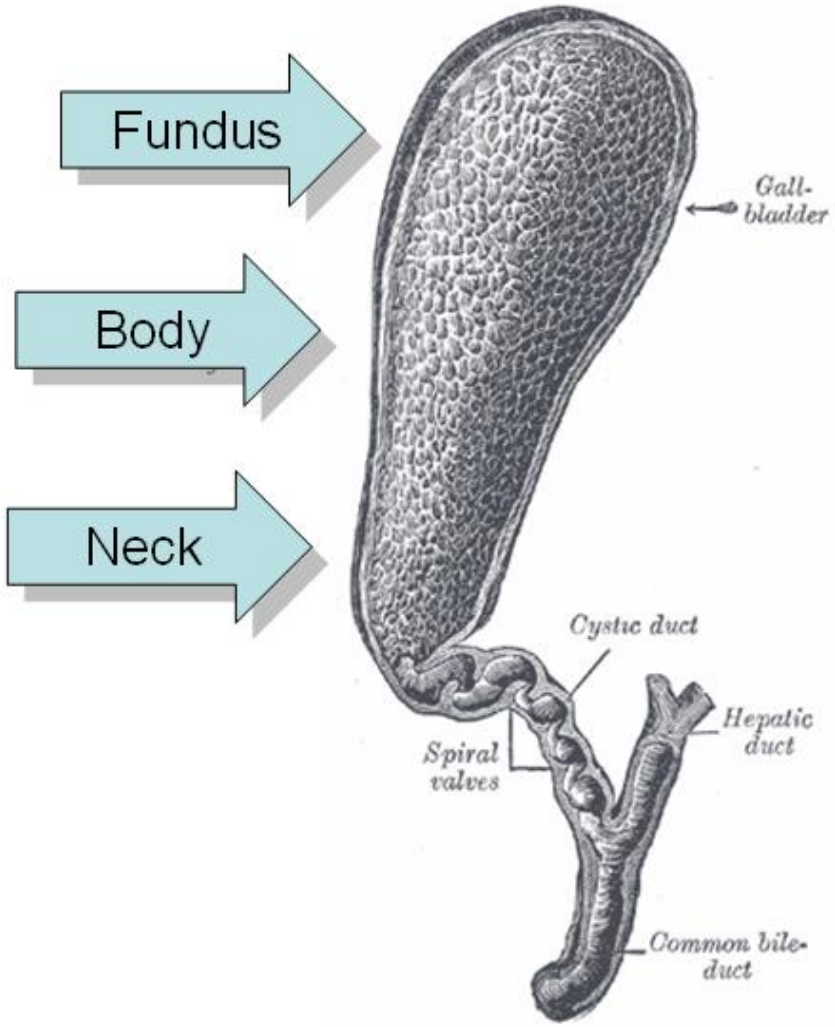
  or
  - → **cystic** duct to gallbladder for storage.



2. Intrahepatic bile ducts, 3. Left and right hepatic ducts, 4. Common hepatic duct, 5. Cystic duct, 6. Common bile duct, 7. Ampulla of Vater, 8. Major duodenal papilla 9. Gallbladder, 10–11. Right and left lobes of liver. Pancreas: 18: Accessory pancreatic duct, 19: Pancreatic duct.

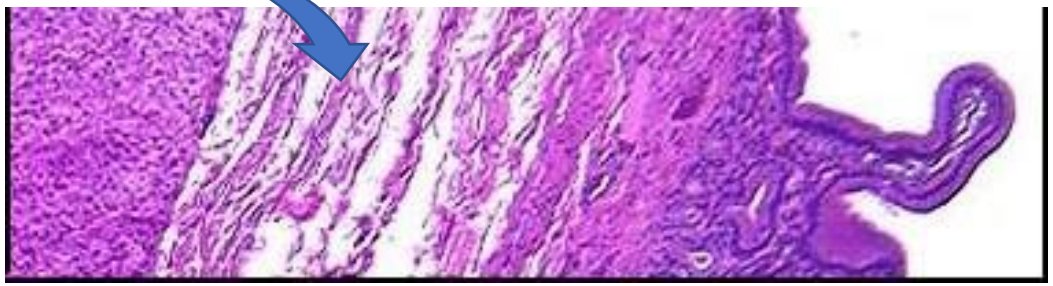
Gall blader (#57)

- a small, pear-shaped organ situated on the inferior aspect of the liver
- it **concentrates, stores** and **releases the bile into duodenum** as required.
  - contraction of gallbladder is stimulated by **cholecystokinin** (produced by **I cells** of small intestine)
- it is divided into **three sections**:
  - the fundus,
  - the body
  - the neck which is continuous with the **cystic duct**
    - at the junction of the neck of the gallbladder and the cystic duct, there is an out-pouching of the gallbladder wall forming a mucosal fold known as **Hartmann's pouch**, where gallstones commonly get stuck



Gallblader (#57)

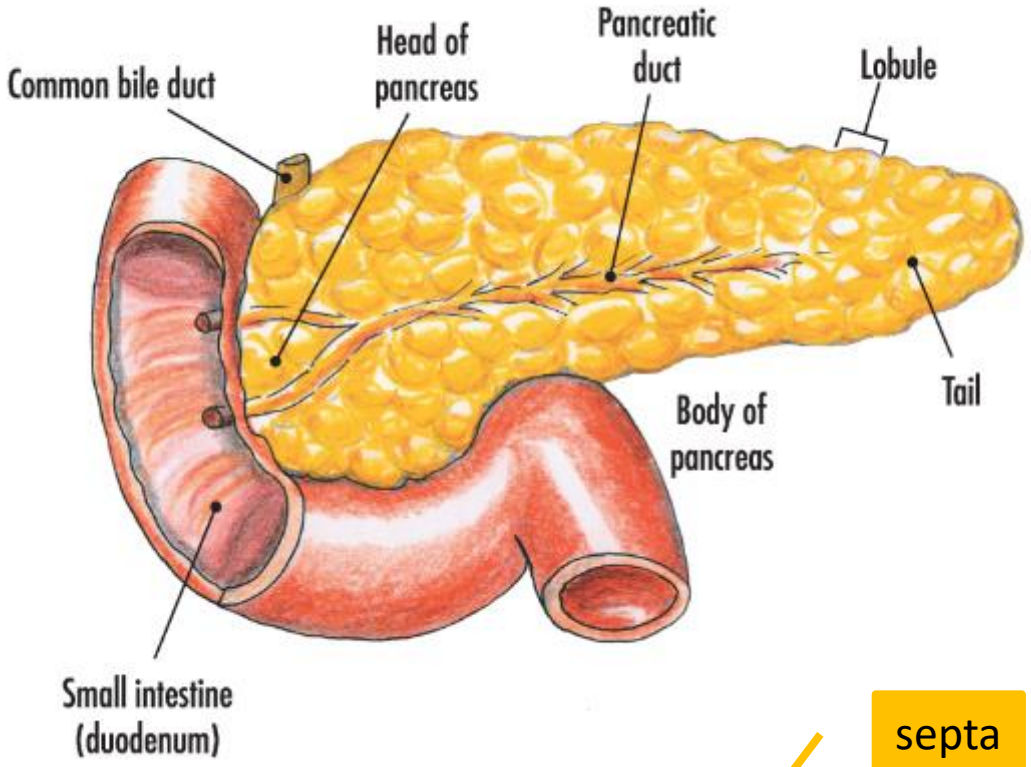
- is composed of
  1. mucosa
  2. smooth muscle layer
  3. serosa or adventitia
- **<u>mucosa</u>** of the gallbladder (form **mucosal folds**)
  - epithelium
    - **simple columnar epithelium** composed of **clear cells** and the infrequent **brush cells** with microvilli
  - lamina propria
    - richly vascularized loose connective tissue,
- **<u>thin smooth muscle layer</u>**
  - obliquely and longitudilally oriented fibers,
- connective tissue
  - **<u>adventitia</u>** which is attached to the Glisson capsule of the liver
  - **<u>serosa</u>** on the surface which is not attached tho the liver

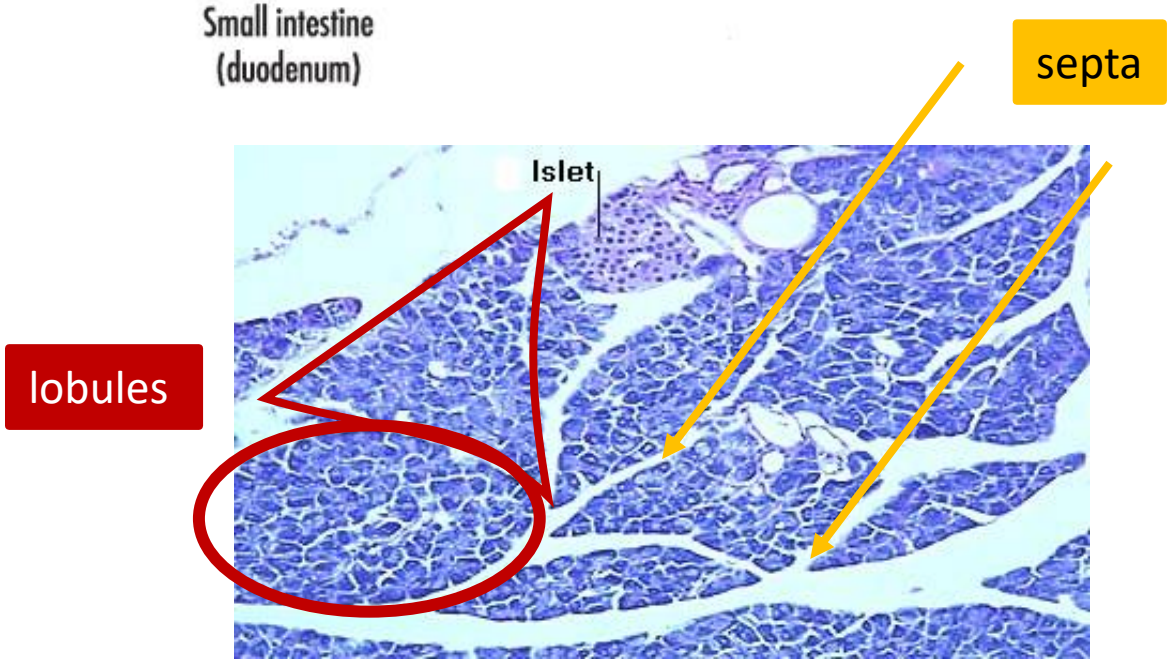


Pancreas

Pancreas (#58)

- a soft, elongated organ located **posterior to the stomach**
- composed of **head, body and tail**
  - the head lies in the duodenal loop
  - the tail extends across the abdominal cavity to the spleen
- surrounded by very thin **connective tissue capsule** that invaginates into the gland to form **septa**
  - septa divide the pancreas into distinctive **lobules**.
  - nerves, vessels and ducts are in connective tissue
- a **mixed organ**;
  - both **endocrine and exocrine** components.

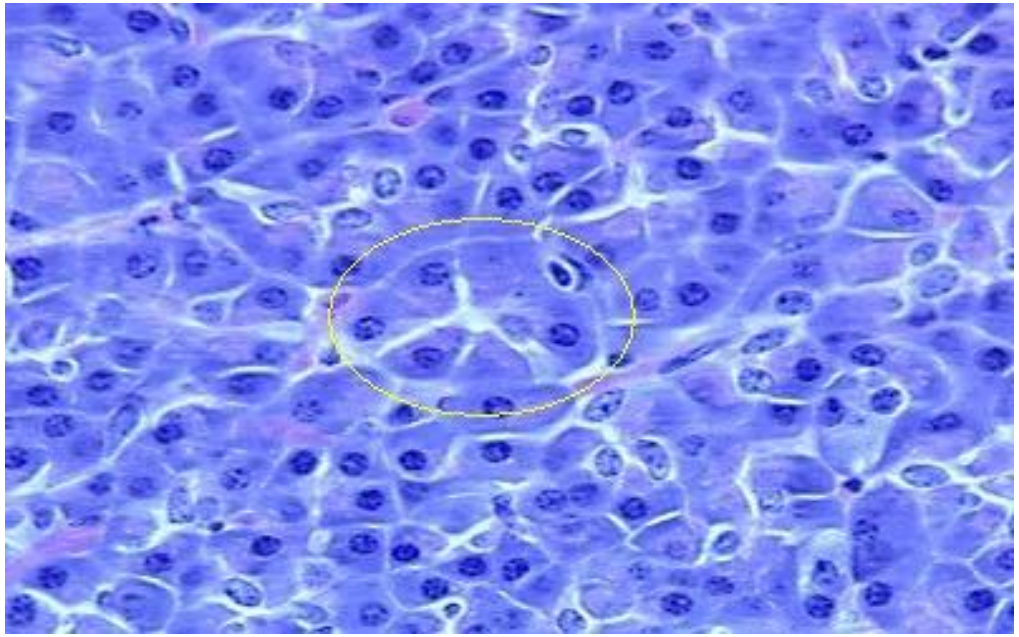


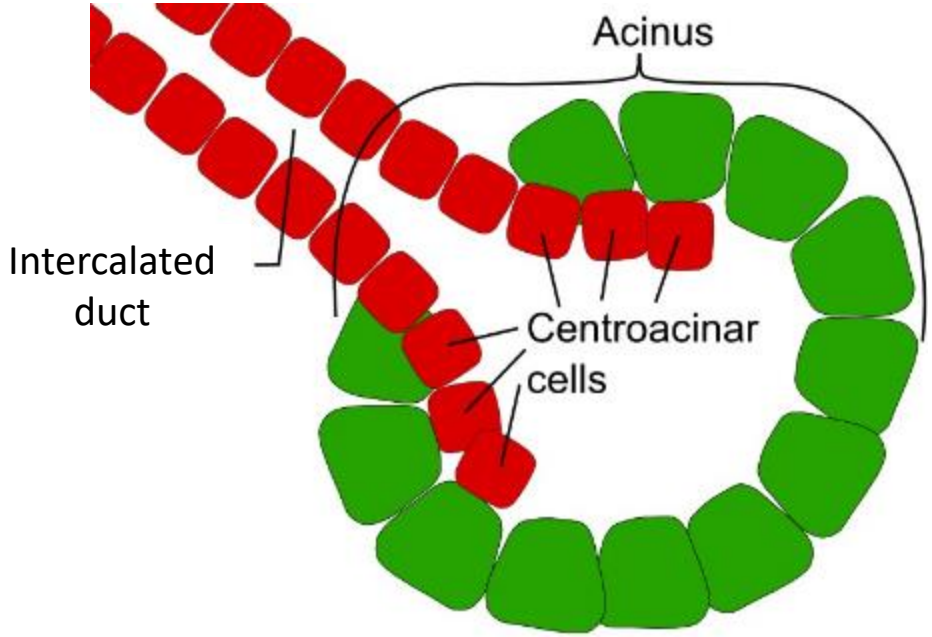


Pancreas (#58)

Exocrine pancreas

- produces **bicarbonate-rich fluid with digestive proenzymes & enzymes**
- **compound tubuloacinar gland**
- is composed of **grape-like clusters** called **acini**
  - ➢ very similar to what is seen in salivary glands (especially in the parotid gland)
  - ➢ **the** pyramid-shaped **serous acinar cells**
    - have basophilic cytoplasm
    - are surrounded by basal lamina
    - contain **zymogen granules** filled with proenzymes.
  - ➢ a lumen of the acinus is occupied by **centroacinar cells**, the beginning of the duct system of the pancreas.

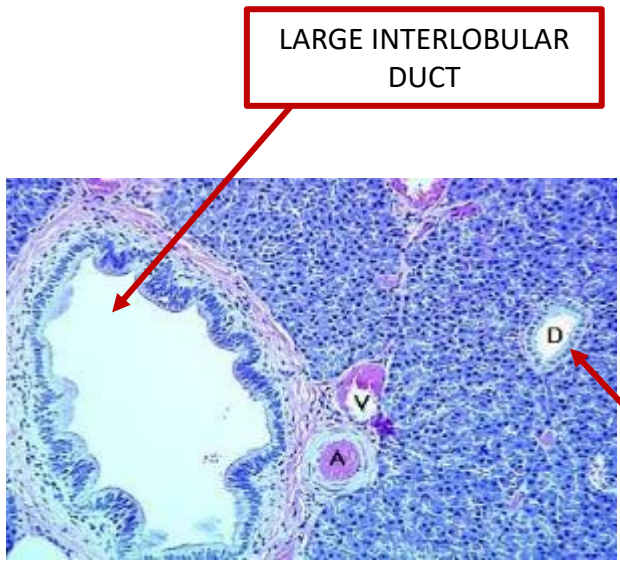


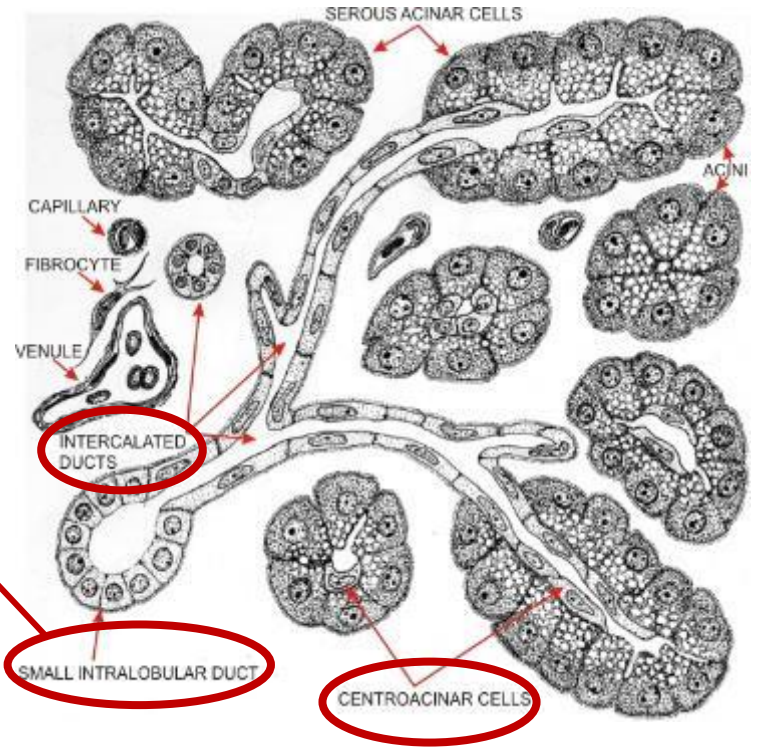


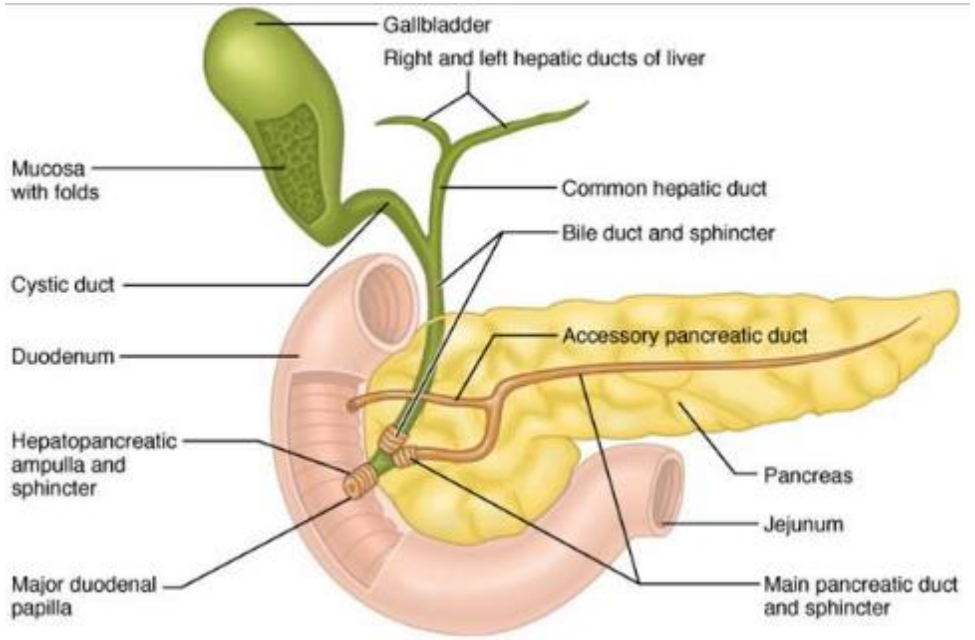
Pancreas (#58)

The duct system of the exocrine pancreas

- begins in the center of each individual acinus
- → **centroacinar cells**
- → **intercalated ducts**
  - flattened cuboidal epithelium
- intercalated ducts join each other to form → **intralobular ducts**
  - a classical cuboidal epithelium
- intralobular ducts converge to form → **interlobular ducts**
  - they vary considerably in size
  - the smaller forms have a cuboidal epithelium, while a **columnar epithelium** lines the larger ducts.
- interlobular ducts deliver their content into → **the main pancreatic duct**
  - in humans the pancreatic duct joins the bile duct prior to entering the intestine







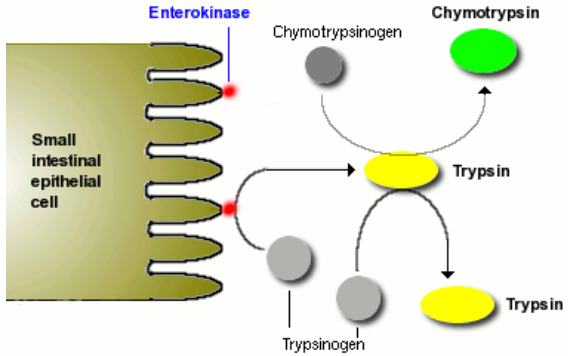
Pancreas (#58)

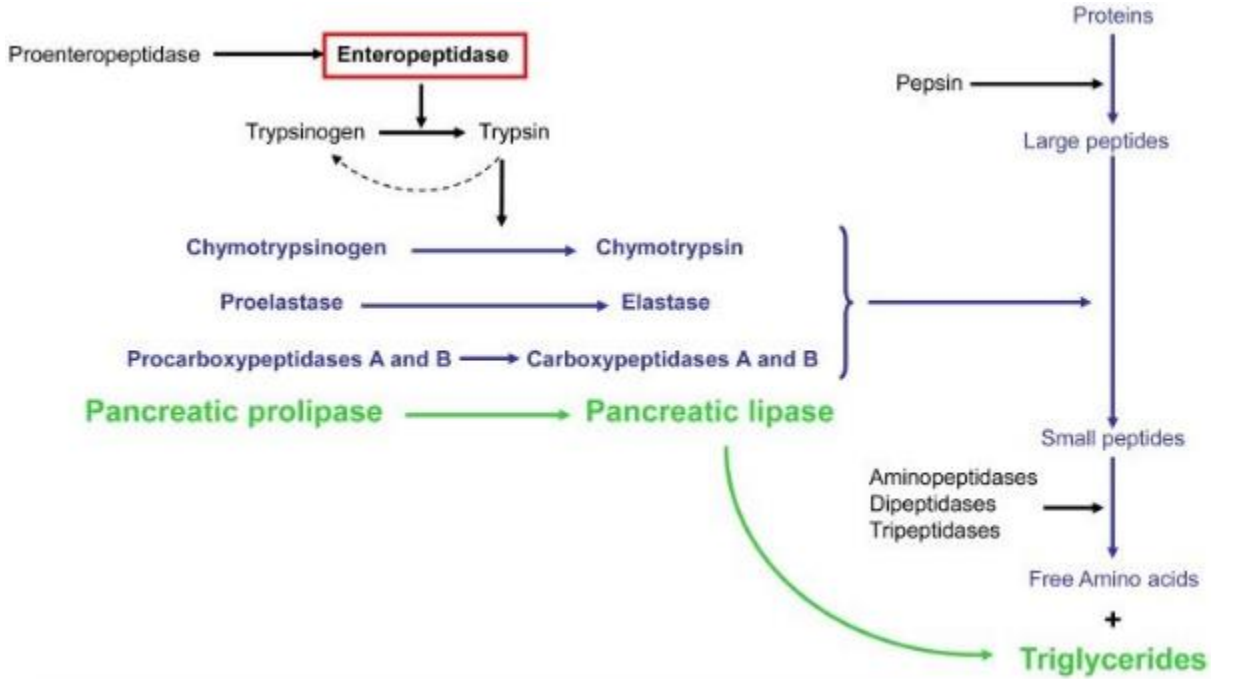
Exocrine pancreas function

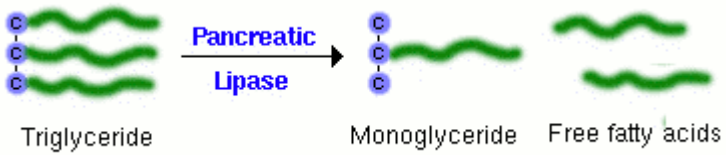
- **Three major groups of enzymes** - the acinar cells release:
  1. **proteases** ← in form of proenzymes
     - trypsinogen (+ trypsin inhibitor)
     - chymotrypsinogen
     - procarboxypeptidase
     - proelastase
  2. **pancreatic prolipase**
  3. **pancreatic amylase**
  4. other pancreatic enzymes
     - ribonuclease & deoxyribonuclease

- the **centroacinar cells &** cells in the **intercalated ducts** manufacture
  - ➢ a watery **fluid** rich in sodium **bicarbonate ions** (carbonic anhydrase).

Enterokinase (**Enterpeptidase**) converts trypsinogen to trypsin, and trypsin then converts all inactive pancreatic enzymes into active digestive enzymes.







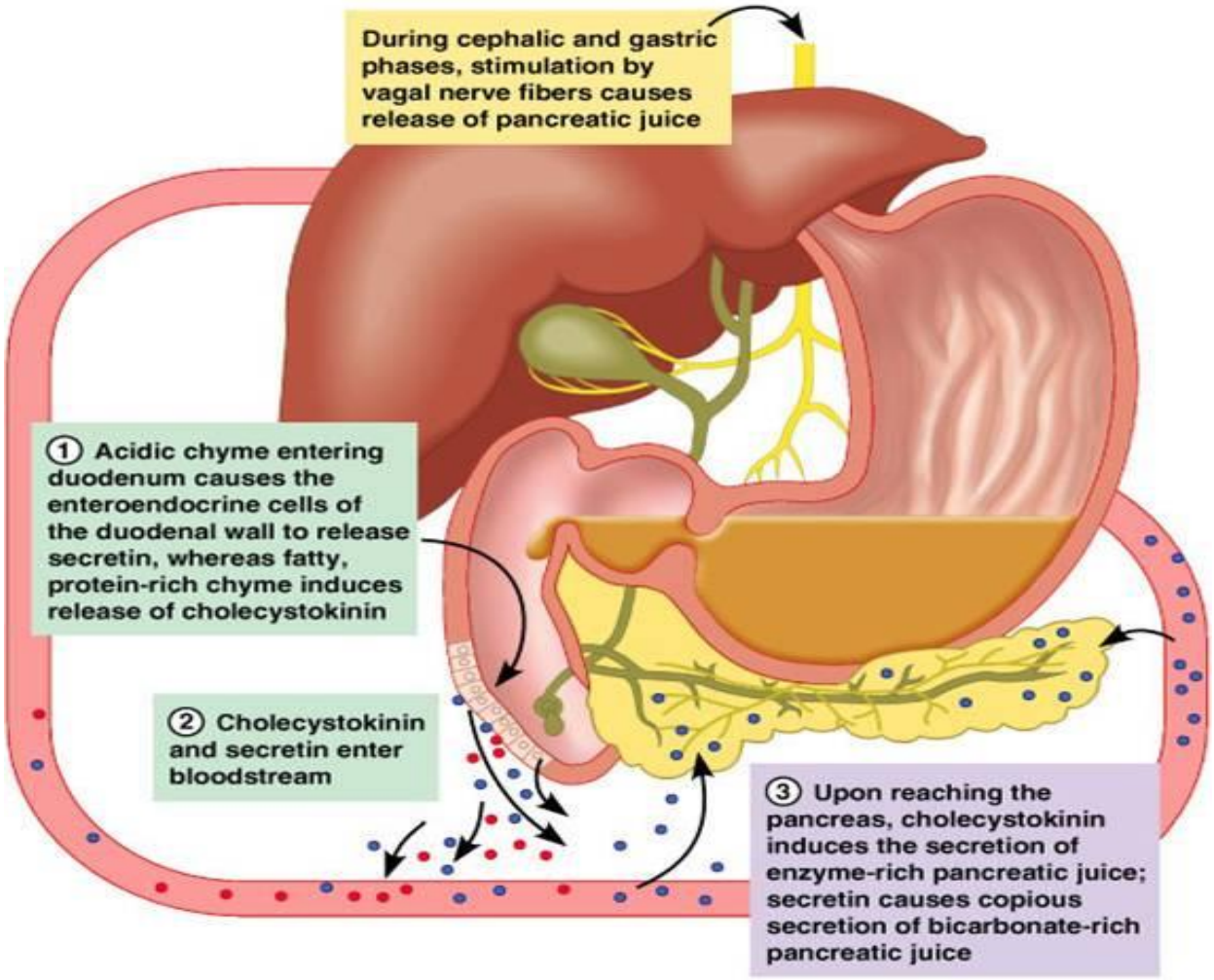
Pancreas (#58)

Control of Pancreatic Exocrine Secretion

- **(2 components - (pro)enzymes + fluid)**

- stimulation by **vagal nerve (ACh)**

- chyme from stomach entering duodenum → DNES cells release to bloodstream:
  1. **cholecystokinin / pancreozymin**
  2. **secretin**
  3. **gastrin**



Pancreas (#58)

Control of Pancreatic Exocrine Secretion

- **cholecystokinin / pancreozymin**
  - a **peptide** secreted as preprohormone by **I cells** in duodenum in response to the **fatty, protein-rich chyme**
  - very similar in structure to **gastrin**
  - the principal stimulus for :
    1. **release of digestive enzymes** (*pancreozymin*)
    2. **contraction of the gallbladder to deliver bile** into the duodenum (cholecystokinin - to "move the gallbladder“)

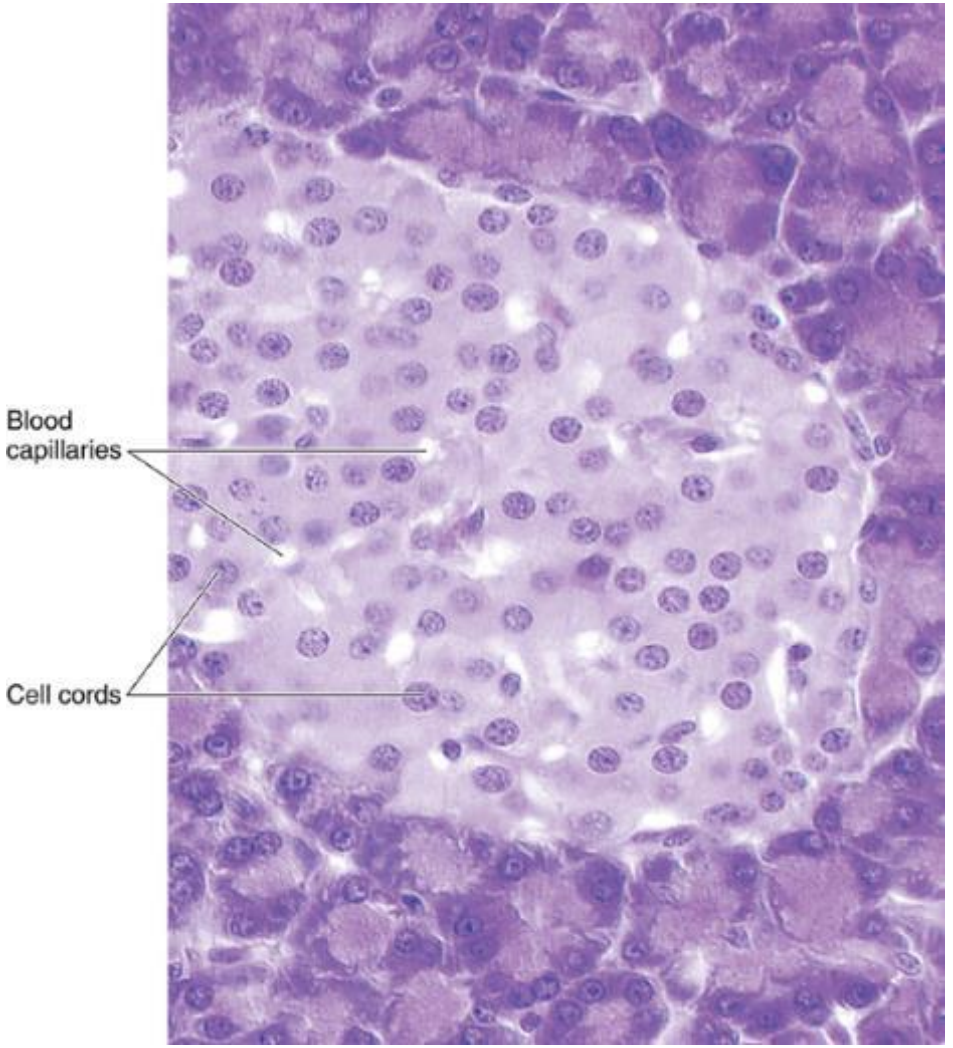
- **secretin**
  - a **peptide** secreted as preprohormone by **S cells** in duodenum in response to the **acidic chyme**
  - structure related to that of glucagon, vasoactive intestinal peptide and gastric inhibitory peptide
  - the principal stimulus for :
    1. **release of a bicarbonate-rich fluid**

- **gastrin**
  - a **peptide** secreted as preprohormone by **G cells** in stomach in response to the **bolus**
  - very similar in structure to secretin
  - the principle stimulus for :
    1. **stimulation of gastric acid secretion**
    2. **promotion of gastric mucosal growth**
    3. release of digestive enzymes from the pancreas into the duodenum

Pancreas (#58)

Endocrine pancreas
- islets of Langerhans

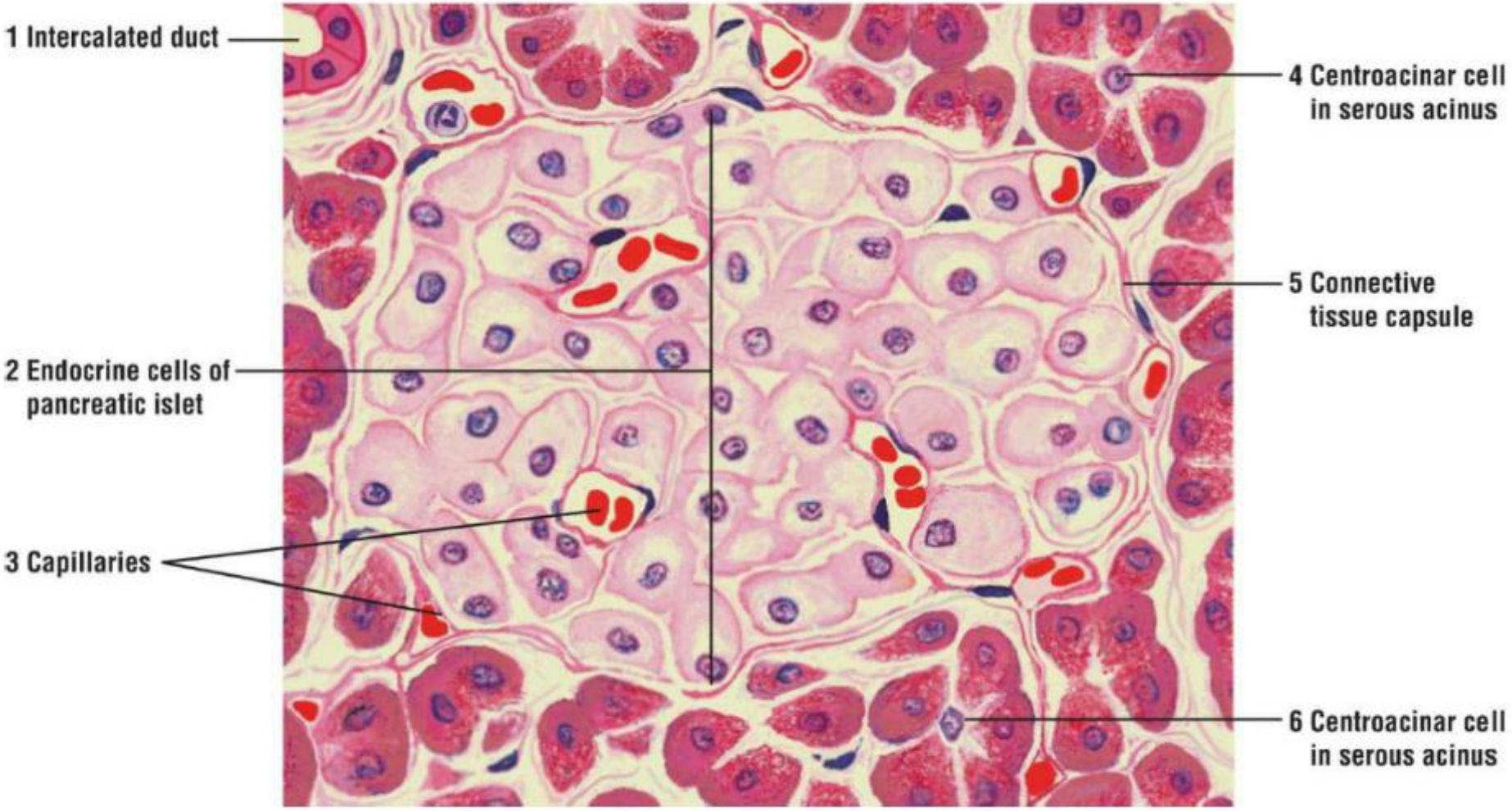
- scattered among the acini
- humans have roughly **10^6 islets**
- a **thin connective tissue capsule** separates the endocrine pancreatic islet from the surrounding exocrine serous acini
- the islet cells form **cords or clumps** between which are found **fine connective tissue fibers** and an **extensive capillary network**

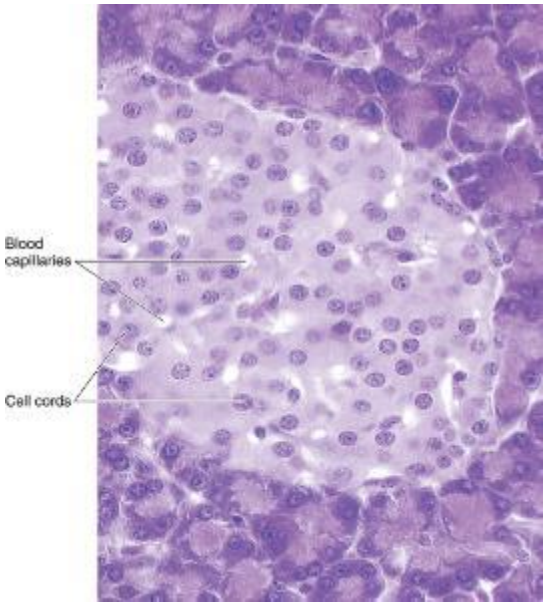


In standard histological sections of the pancreas, islets are seen as **relatively pale-staining groups of cells** embedded **in a sea of darker-staining exocrine tissue**.

Pancreas (#58)

Endocrine pancreas
- islets of Langerhans





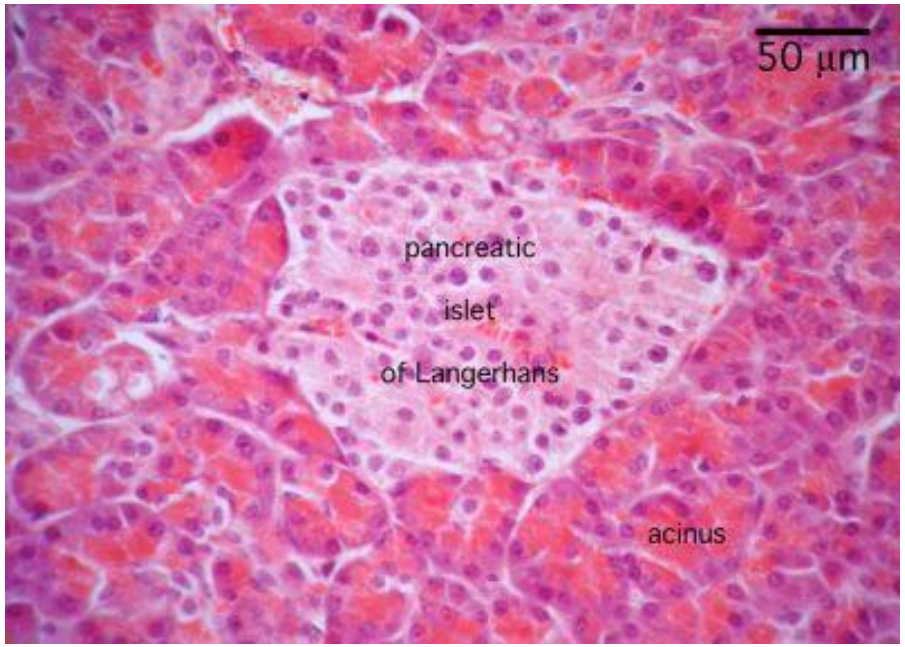
Pancreas (#58)

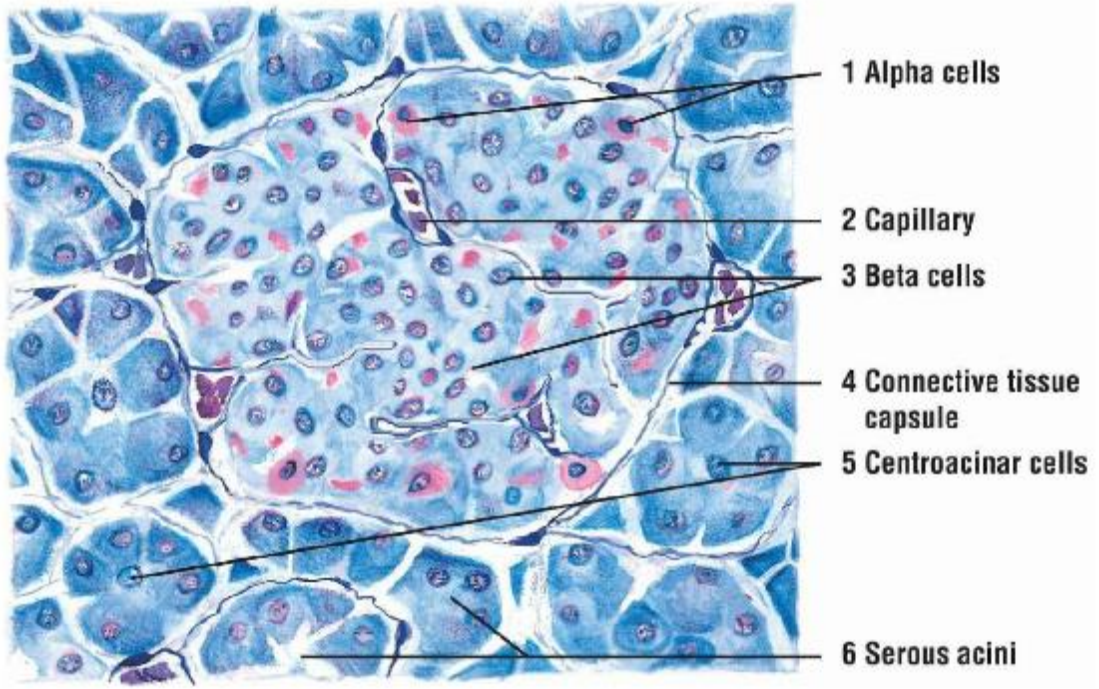
Endocrine pancreas - islets of Langerhans

Cells of islets of Langerhans secrete i.a. :

- A (α) cells – **glucagon**
  (increases of glucose level in blood)
- B (β) cells – **insulin**
  (decreases of glucose level in blood)
  → clinical correlation - lack of insulin: diabetes mellitus
- D (δ) cells – **somatostatin**
  (regulates/stops A(α) and B(β) cells)
- PP cells – **pancreatic polypeptide** (**PP**)
  (inhibits the exocrine secretions of the pancreas and stimulates the release of enzymes by the gastric chief cells)

HE staining:
In routine histologic preparations, the cells that secrete different hormones from the pancreatic islet cannot be identified.

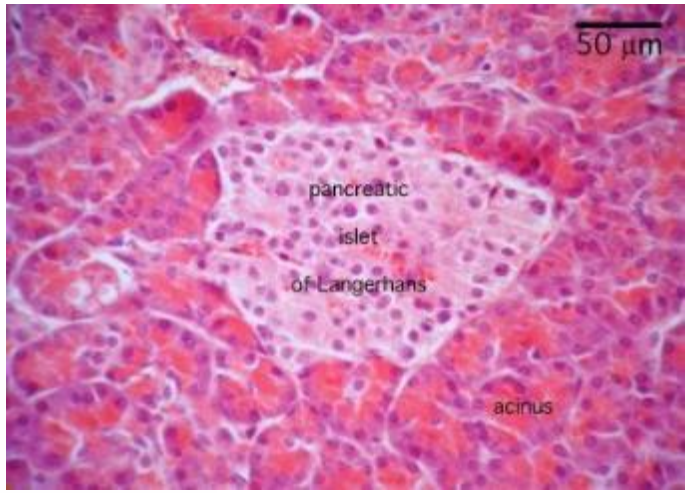


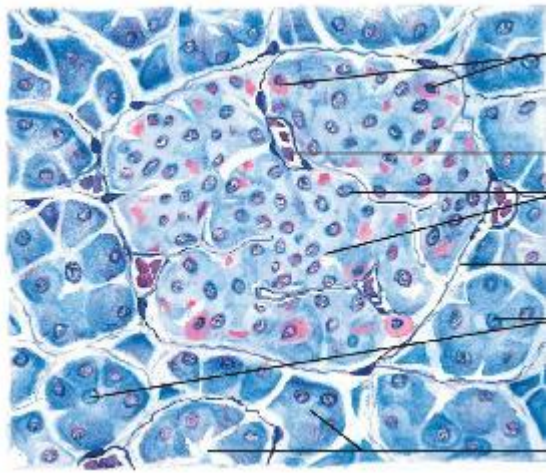


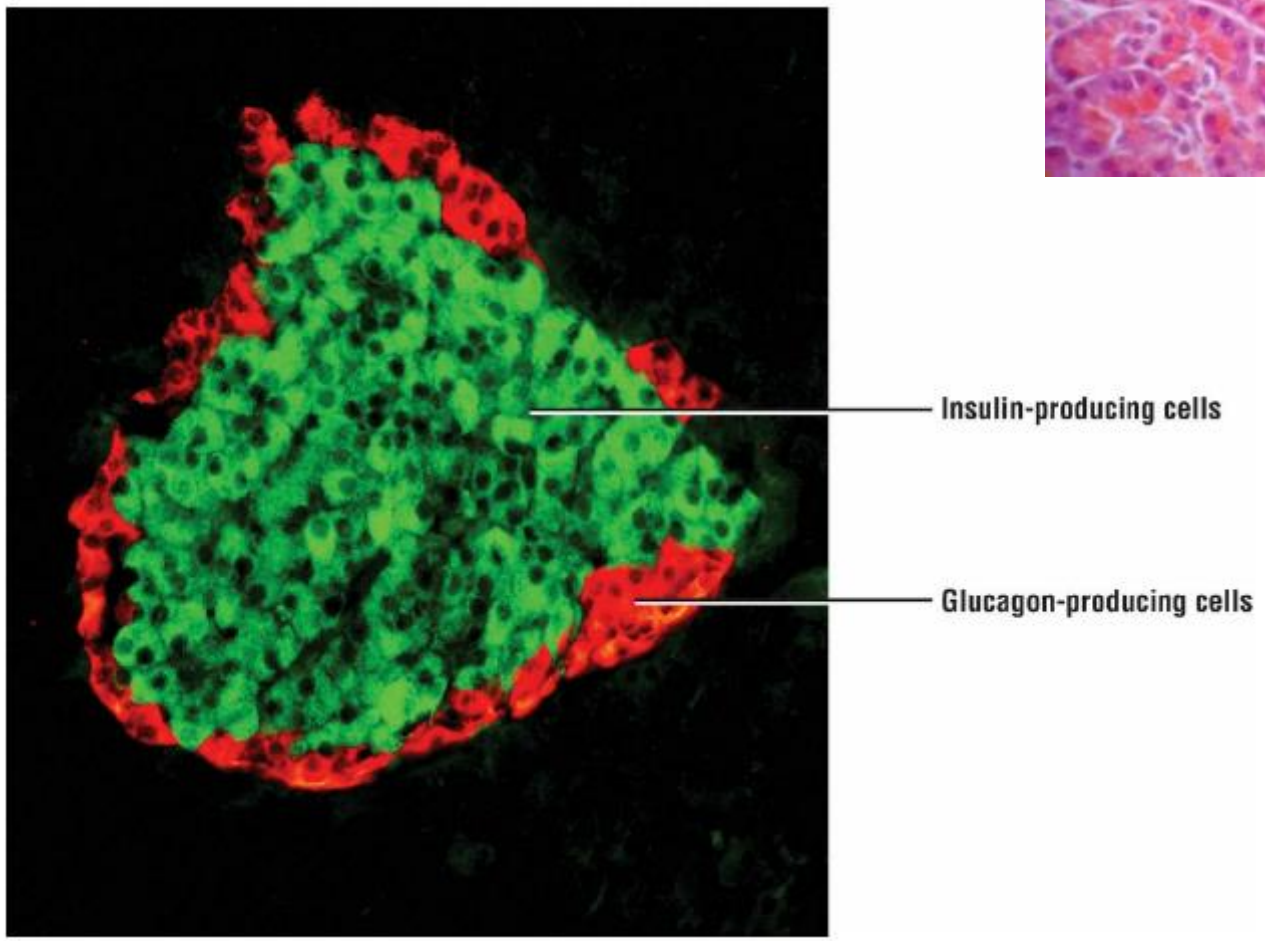
Special staining *Gomori chrome alum hematoxylin and phloxine staining*

Pancreas (#58)

Endocrine pancreas
- islets of Langerhans







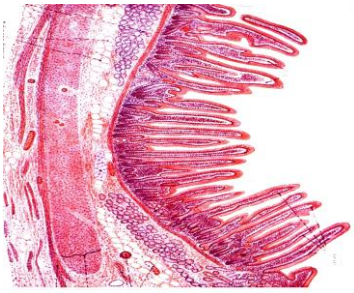
Immunohistochemical preparation of a mammalian pancreatic islet.

Precise **distribution of the two major cell types in the pancreatic islet**.

- The glucagon-producing cells (A cells) are stained bright red and are located peripherally in the islet.
- The insulin producing cells (B cells) are stained bright green and are located on the inside of the islet surrounded by the peripheral A cells.

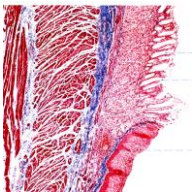
Seminar: Glands in stomach and intestines, structure and function.
Practical class: Gastro-intestinal system, part 2.

- **oesophagus (no. 47),**
- **stomach (no. 48),**
- **duodenum (no. 50),**
- **small intestine – jejunum (no. 51),**
- **large intestine – colon (no. 52),**

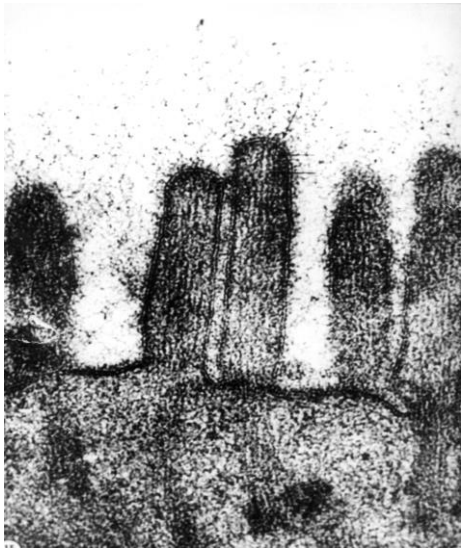


duodenum

- **microvilli of jejunal resorptive cell (EM 83),**
- **parietal cells (text & fig. 91),**



stomach

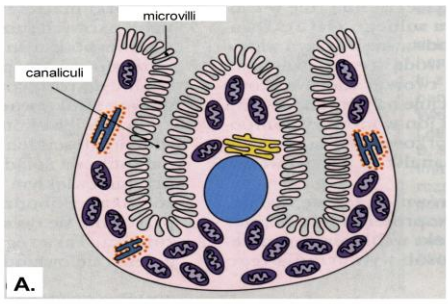


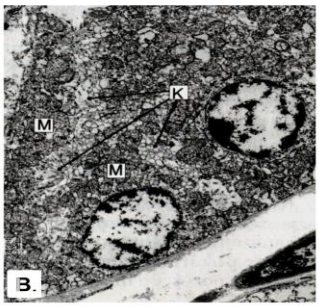
EM - 83

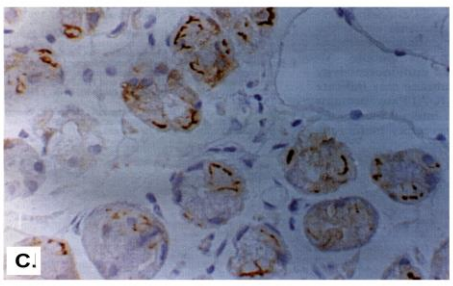
Microvilli on the surface of the micrograph shows: cell membrane, glycocalix, and bundles of microfilaments, which run inside the microvilli, reach the apical part of cytoplasm and form so called terminal web.

Text & fig. # 91

Parietal cells







A. Parietal cells has a well developed system of invaginations (canaliculi) containing microvilli. These invaginations can be observed in light microscope as vacuolised cytoplasm around nucleus.
B. Canaliculi of parietal cell observed in electron microscope. Numerous mitochondria are also present.
C. H, -K, -ATPase (an enzyme transporting H^+ to the lumen of the gland and activated by K+) demonstrated in the wall of parietal cells canaliculi by monoclonal antibody against its catalytic subunit (subunit α). Parietal cells have histamine receptors H_2.

HOW POPULAR DRUGS INHIBIT SECRETION OF HYDROCHLORIC ACID?

Parietal cells produce HCL after stimulation by histamine reacting with H_2 receptor. Histamine in gastric mucosa occurs in mast cells and in some enterochromaffin cells. Release of histamine occurs after stimulation of histamine-containing cells by gastrin which is produced by G cells present in antrum (part of the stomach close to the duodenum). Gastrin from these cells is secreted in to blood and gets into contact with mucosa of the stomach's body throughout circulation. Gastrin stimulates release of histamine from enterochromaffin cells and probably also from mast cells.

Omeprasol inhibits activity of H, -K, -ATPase. It causes degeneration of parietal cells.

Ranitidine is reversible inhibitor of H_2 receptor. It inhibits both basic and gastrin-stimulated secretion of HCL.