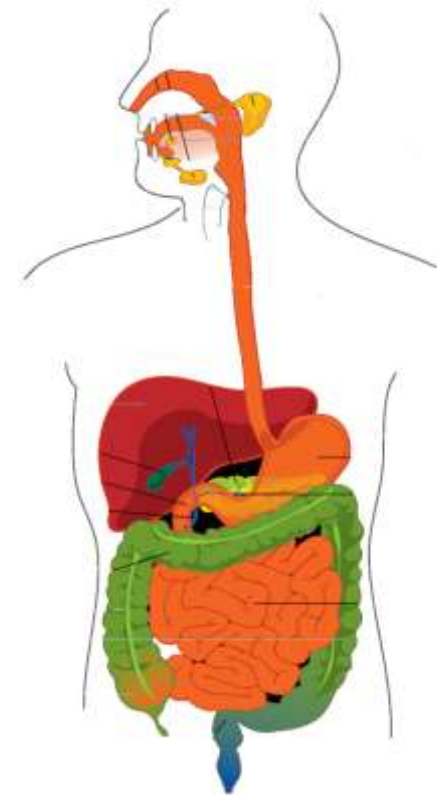


Digestive system

1. **Microscopic anatomy of esophagus, stomach, small and large intestine**
2. Microscopic anatomy of liver, pancreas



Petr Vaňhara, PhD

Department of Histology and Embryology LF MU
PVanhara@med.muni.cz

1. Development and general structure of hollow organs/gut tube

- Tunica mucosa
- Tela submucosa
- Tunica muscularis externa
- Serosa/adventitia

2. Esophagus (*Oesophagus*)

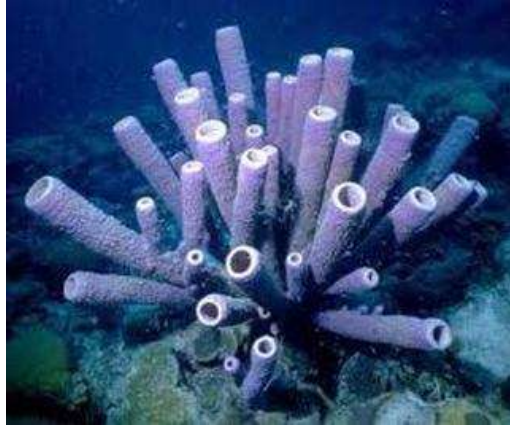
- Microscopic anatomy
- Gl. oesophageae propriae

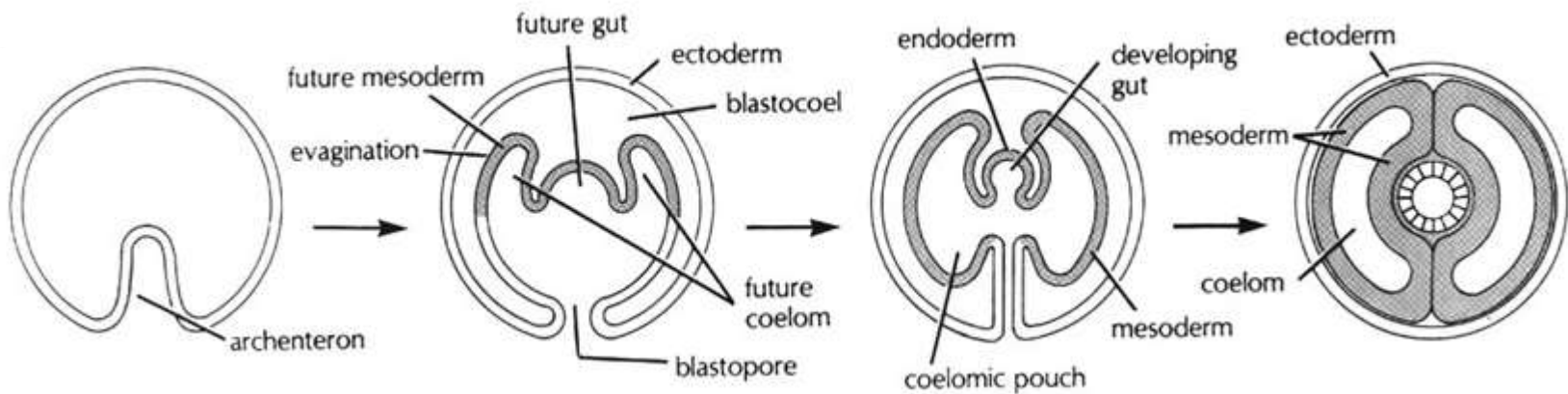
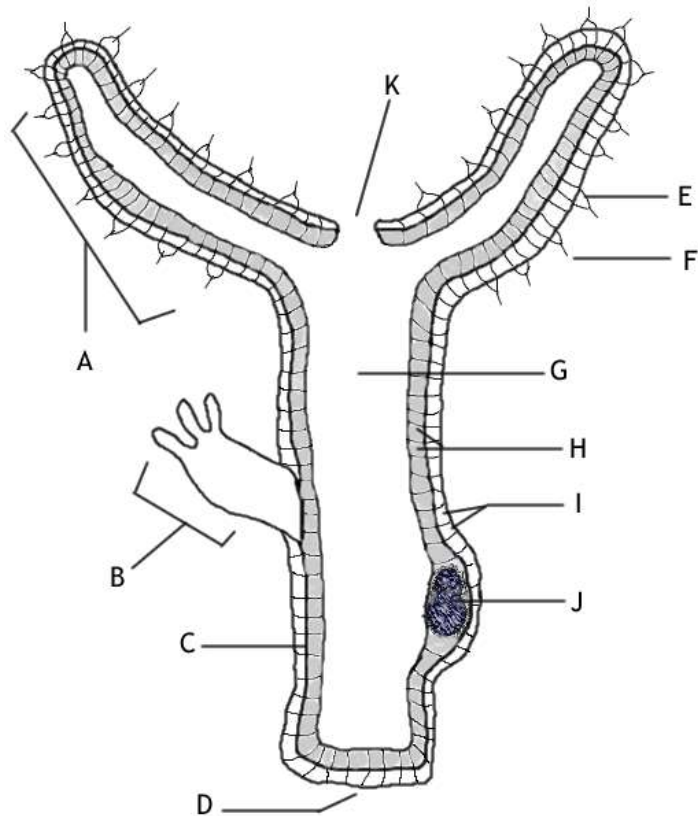
3. Stomach (*Ventriculus, Gaster*)

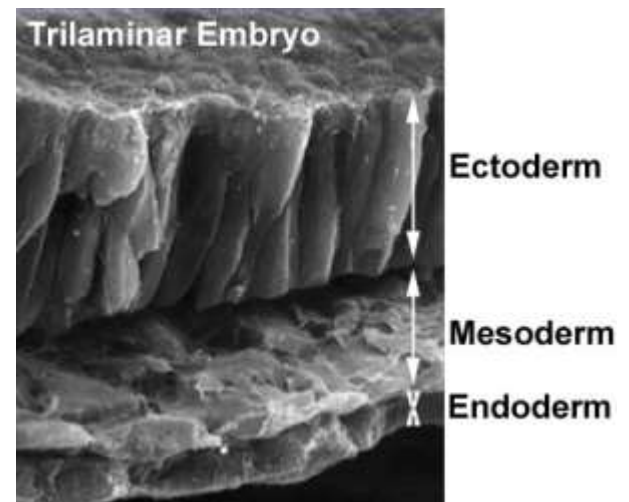
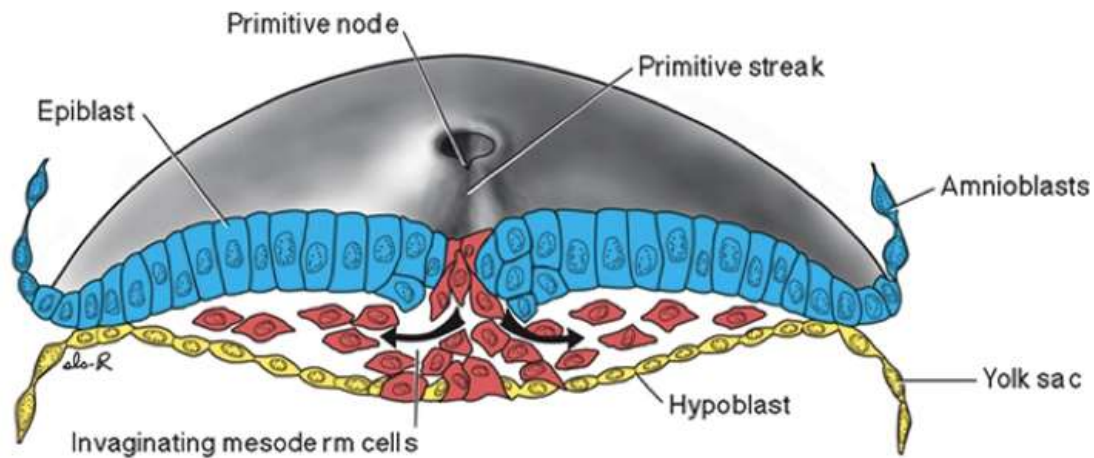
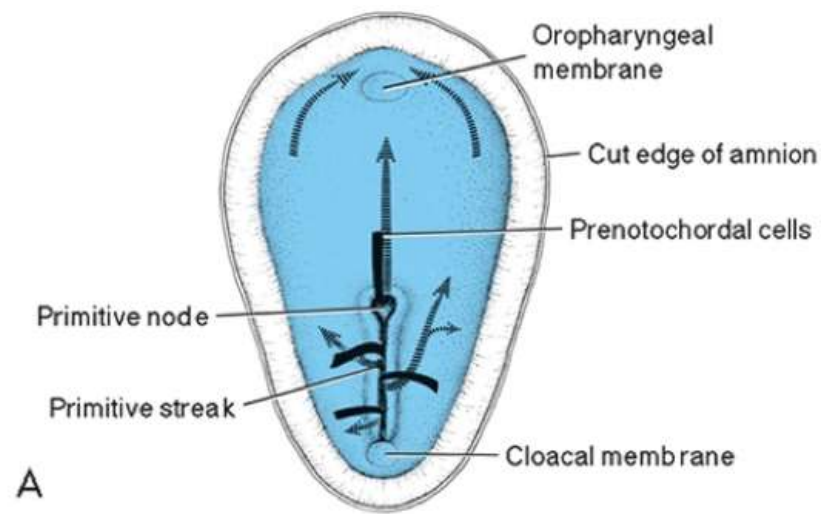
- Microscopic anatomy
- Functional modification of gastric mucosa and gastric glands
- Enteroendocrine system

4. Small and large intestine (*Duodenum, Ileum, Jejunum, Colon*)

- Microscopic anatomy
- Functional modification of intestinal mucosa and Lieberkühn crypts
- Enteroendocrine system

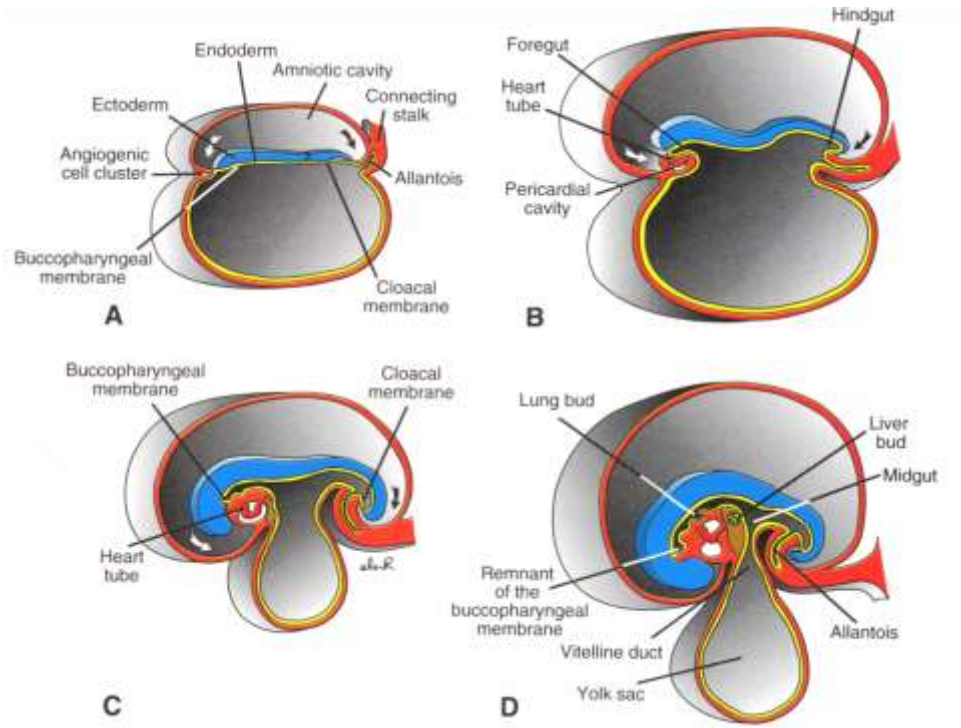






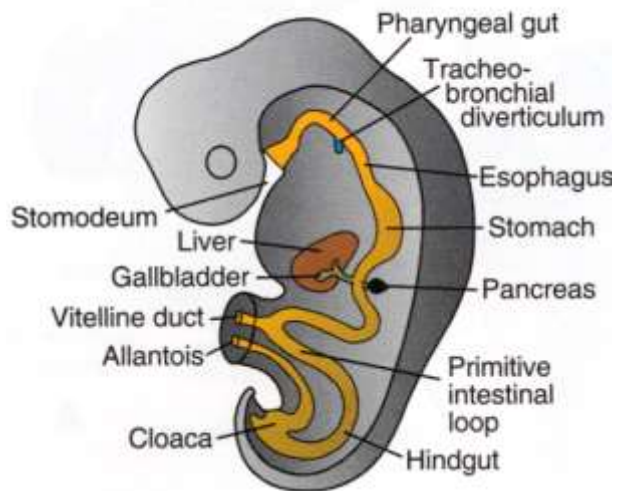
Development of gut tube

- cephalocaudal and lateral folding
- **primitive gut** (endoderm)
- oral cavity and rectum – ektoderm
- glandular parenchyma (pancreas, liver)
 - endoderm of gut tube



Four regions:

- pharynx – from buccopharyngeal membrane to tracheobronchial diverticulum
- foregut – caudal to pharyngeal tube to liver diverticulum
- midgut – caudal to liver to junction of the 2/3 of adult transverse colon
- hindgut – left 1/3 of trasverse colon to cloacal membrane



Development of gut tube

- Esophagus

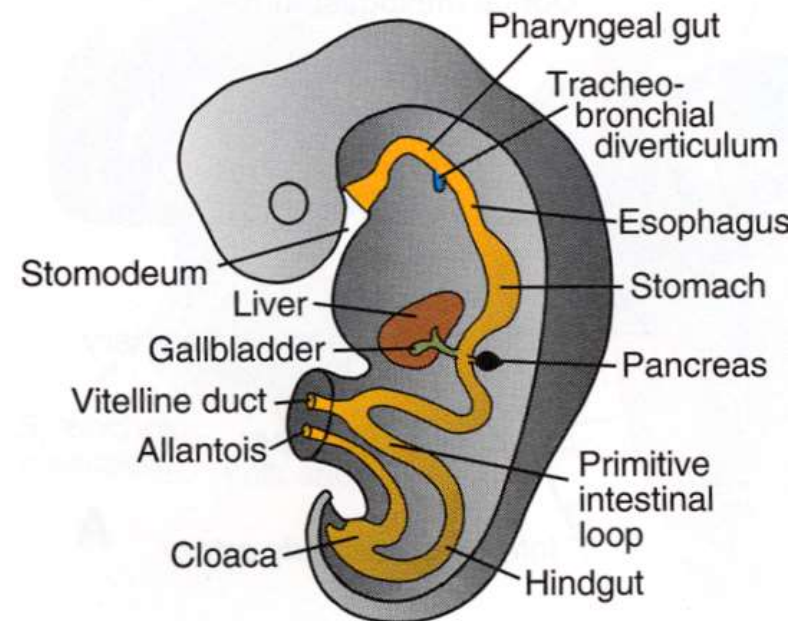
- region of foregut caudal of respiratory diverticulum
- endoderm (epithelium and glands), connective tissue - mesoderm

- Stomach

- fusiform dilatation of the foregut
- different growth rates in various regions → greater and lesser curvature)
- rotation 90° clockwise around longitudinal and anteroposterior axis
- definitive location and shape - 2nd month i.u.

- Intestine

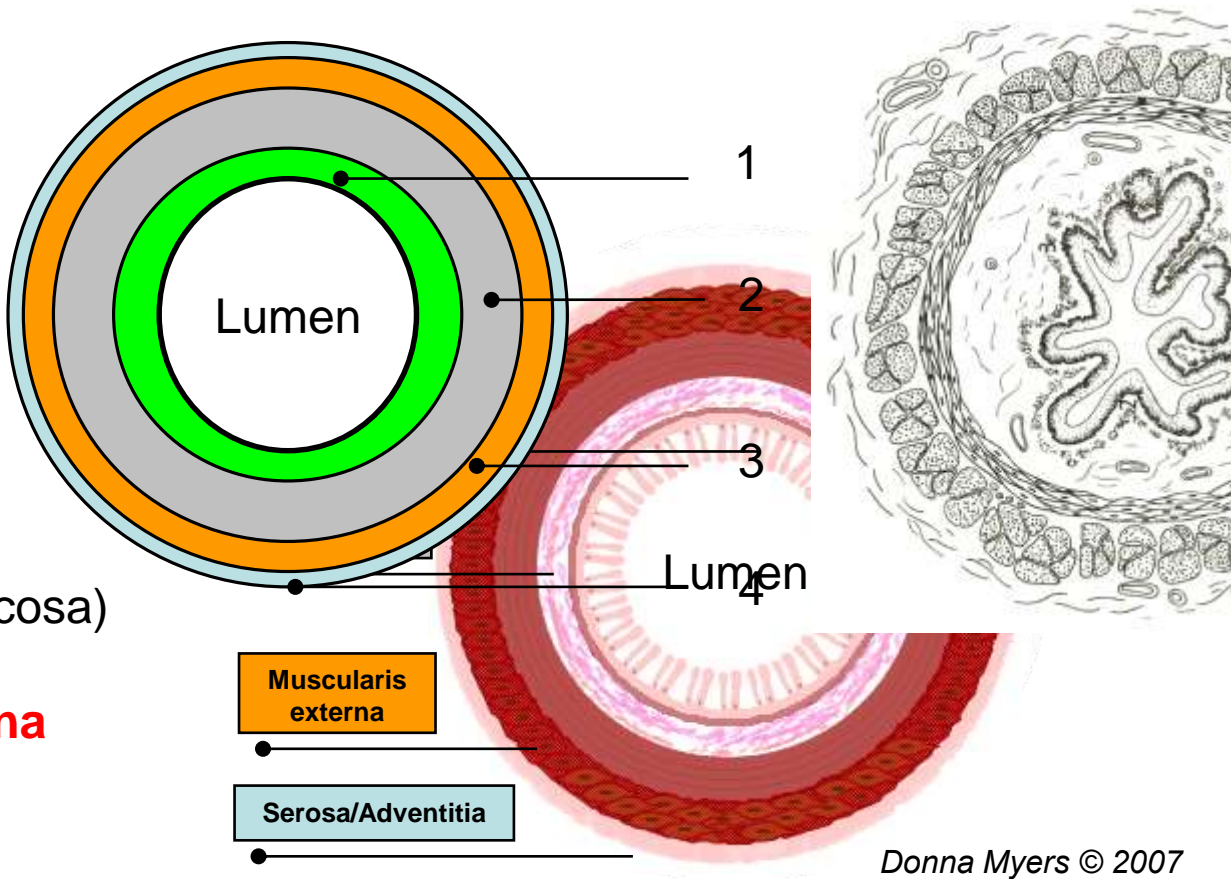
- midgut – primary intestinal loop
- rotation during development
- physiological umbilical herniation



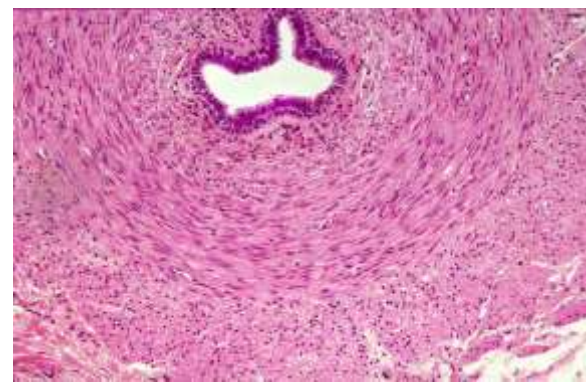
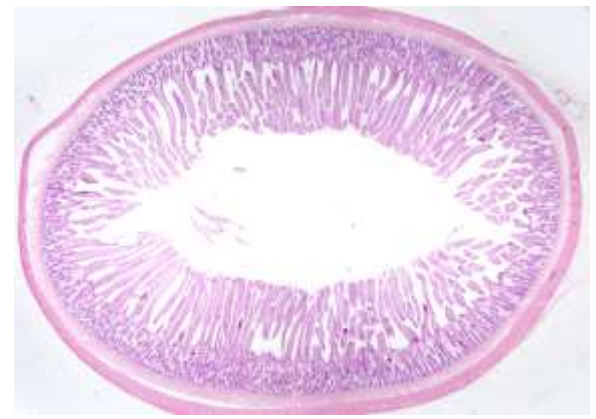
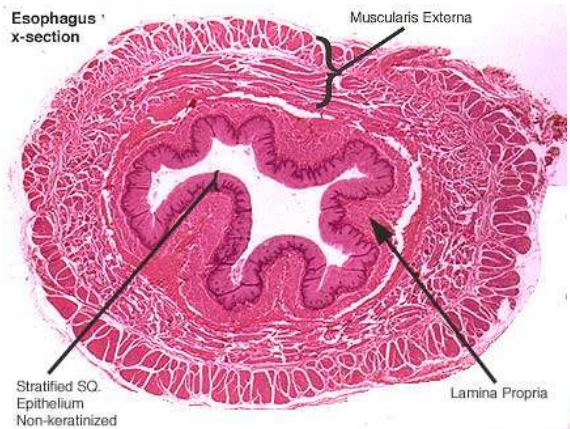
General architecture of hollow organs incl. gut tube

Four layers

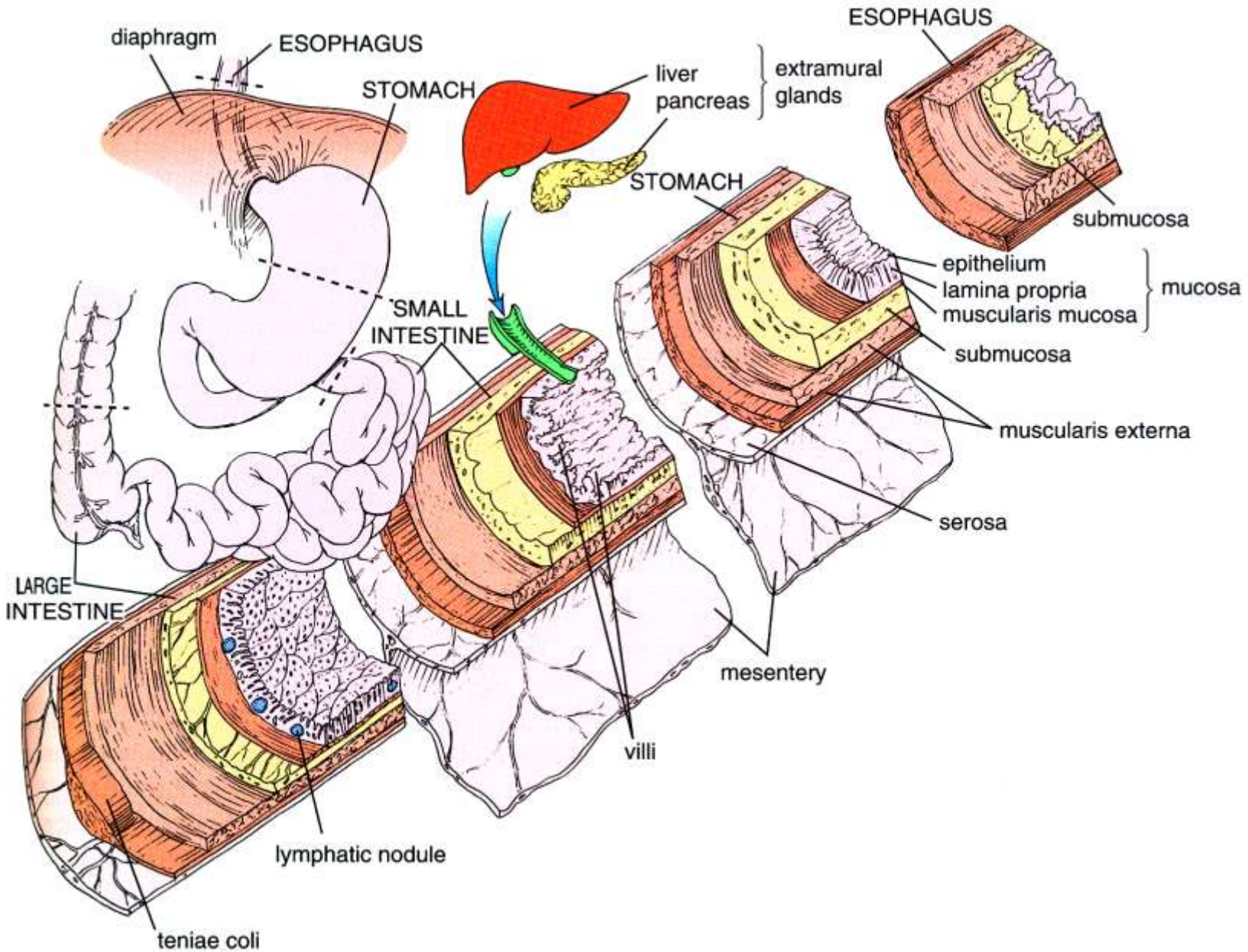
- 1. **Mucosa** (Tunica mucosa)
- 2. **Submucosa** (Tela submucosa)
- 3. **Tunica muscularis externa**
- 4. **Serosa/adventitia**



Esophagus
x-section



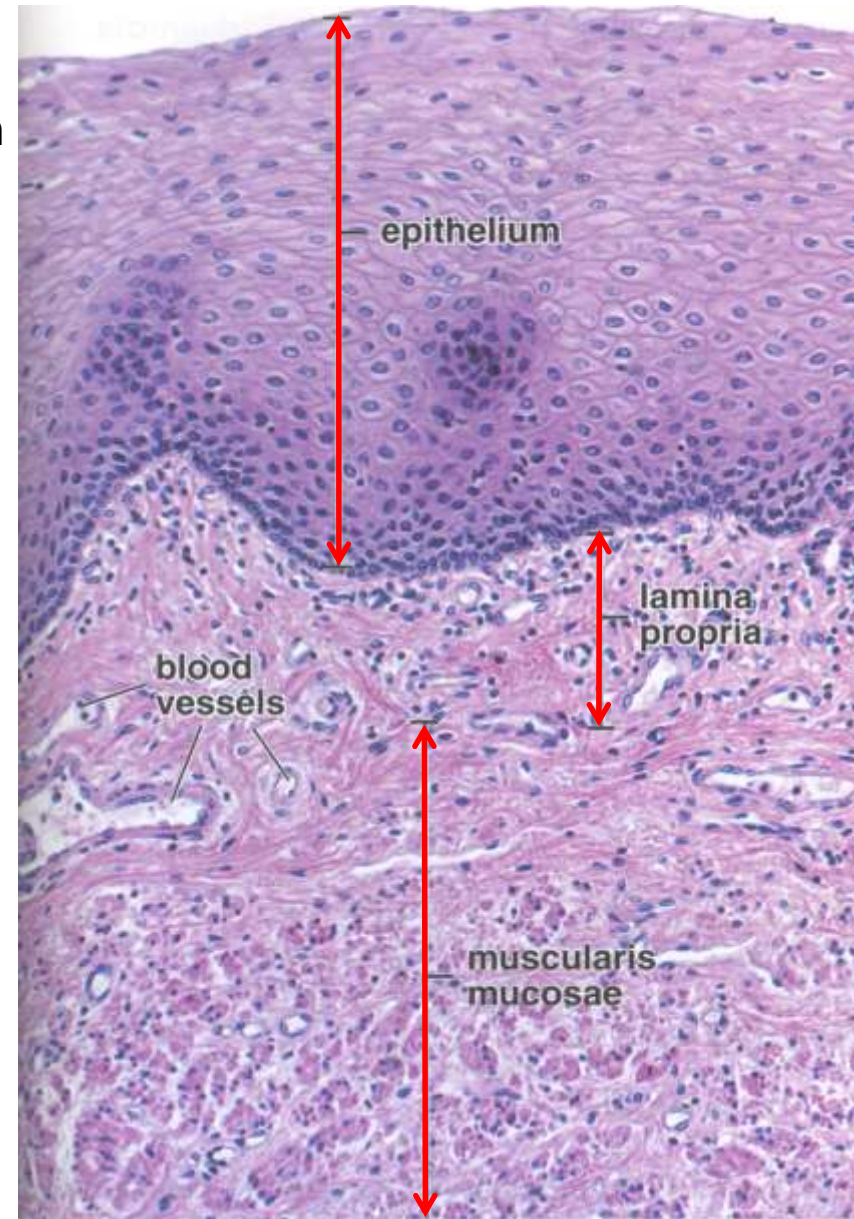
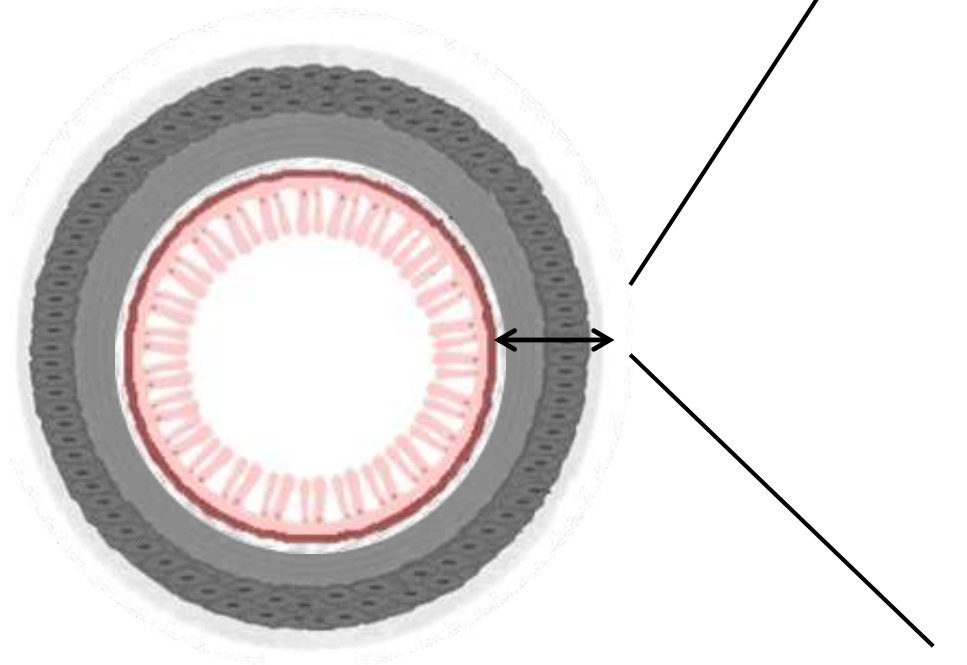
General architecture of hollow organs incl. gut tube



Mucosa (Tunica mucosa)

- inner layer of gut tube
- protective, absorption and resorption
- microscopic structure depending on localization

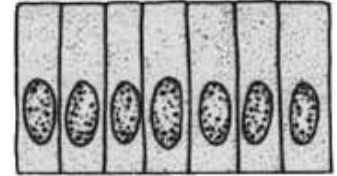
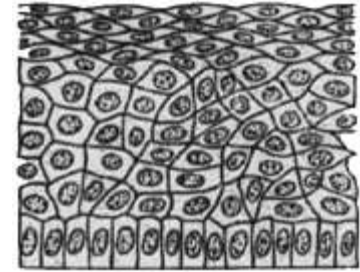
- **Lamina epithelialis** mucosae
- **Lamina propria** mucosae
- **Lamina muscularis** mucosae



Mucosa (Tunica mucosa)

- Lamina epithelialis mucosae

- epithelium type corresponding to function of gut tube
- oral cavity, pharynx, esophagus, anus – **stratified squamous ep.**
- stomach, intestine – **simple columnar**
- **mucus** - secreted by mucosal or submucosal glands (oral cavity, esophagus), secretory epithelium (stomach) or goblet cells (intestine)



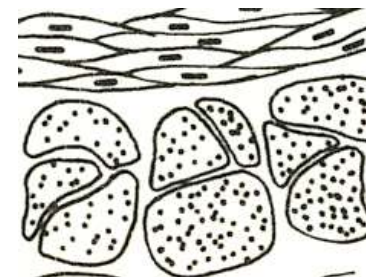
- Lamina propria mucosae

- Layer of mucosal connective tissue – loose collagen
- Fenestrated blood capillaries – transport of metabolite (intestine)
- mucosal glands in some regions /esophagus)
- innervations, immune system



- Lamina muscularis mucosae

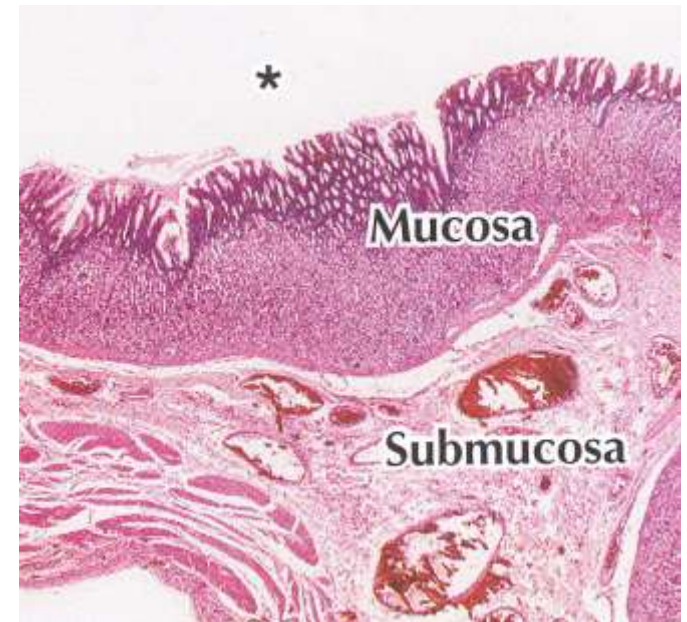
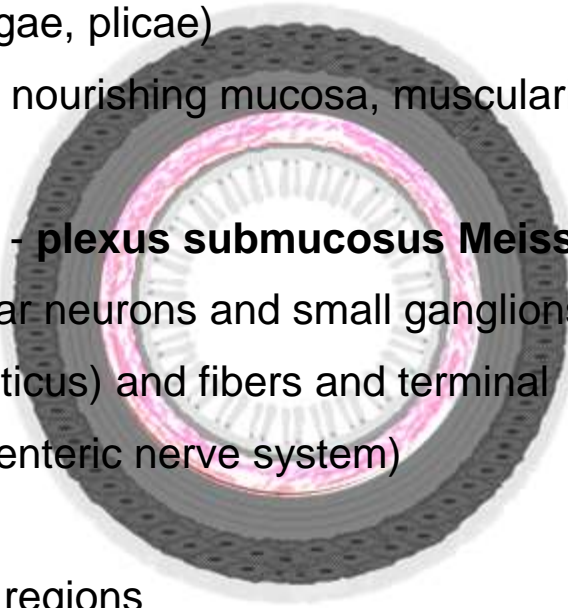
- smooth muscles in two layers (inner circular, outer longitudinal)
- small mechanical movements of mucosa facilitating secretion and absorption independently on peristaltic movements.



Submucosa (Tela submucosa)

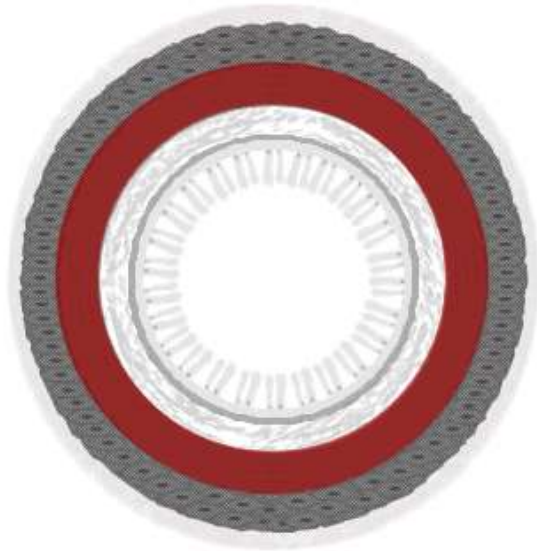
Submucosal connective tissue

- distinct layer of loose connective tissue
- defines shape of mucosa (rugae, plicae)
- larger blood and lymph veins nourishing mucosa, muscularis externa and serosa
- **innervations** – nerve plexus - **plexus submucosus Meissneri**
 - = groups of multipolar neurons and small ganglions, visceral sensory fibers (sympaticus) and fibers and terminal ganglions of parasympaticus (enteric nerve system)
- glands – different in different regions
 - protective function

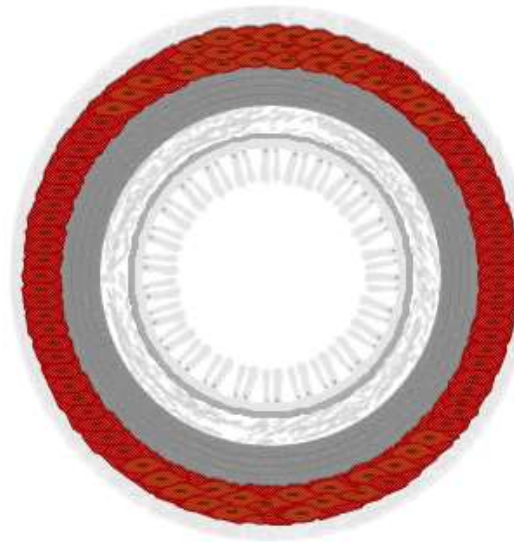


Outer muscular layers (Tunica muscularis externa)

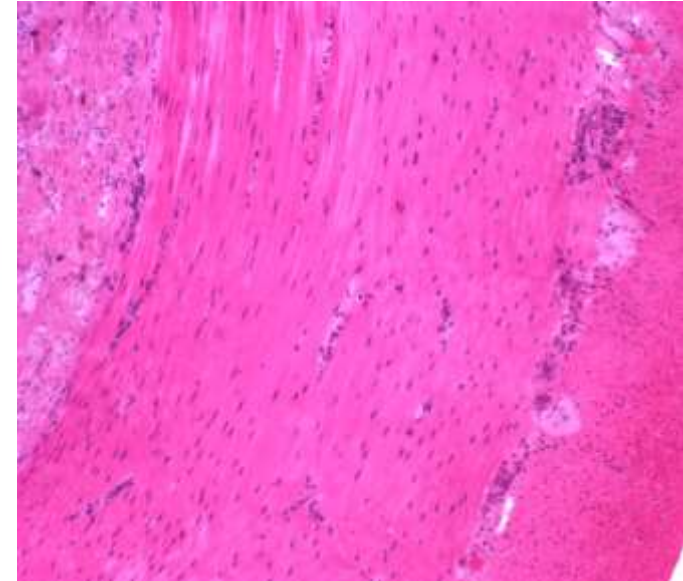
- Two concentric, thick layers of smooth muscle, separated by thin layer of connective tissue
- Inner – **circular**, outer – **longitudinal** (spiral)
- Myenteric (Auerbach) plexus
- Peristaltic – passage through the gut tube
- **Local modifications of m.e.**
 - pharyngoesophageal sphincter + external anal sphincter – skeletal muscles
 - stomach – third - oblique - layer
 - taenie coli – thickened part of longitudinal layer in colon



Circular



Longitudinal



Serosa/Adventitia (Tunica serosa/adventitia)

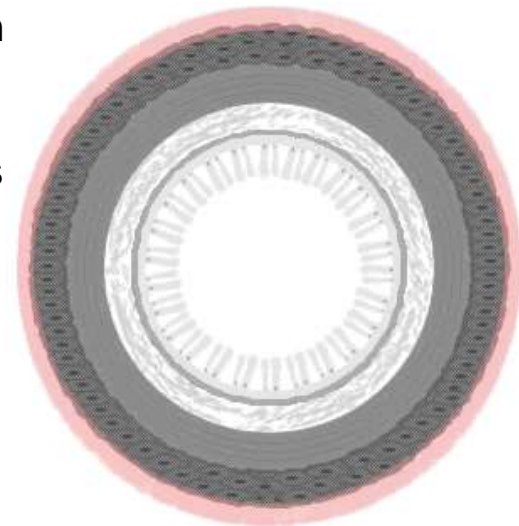
- outermost layer of gut tube

- Serosa

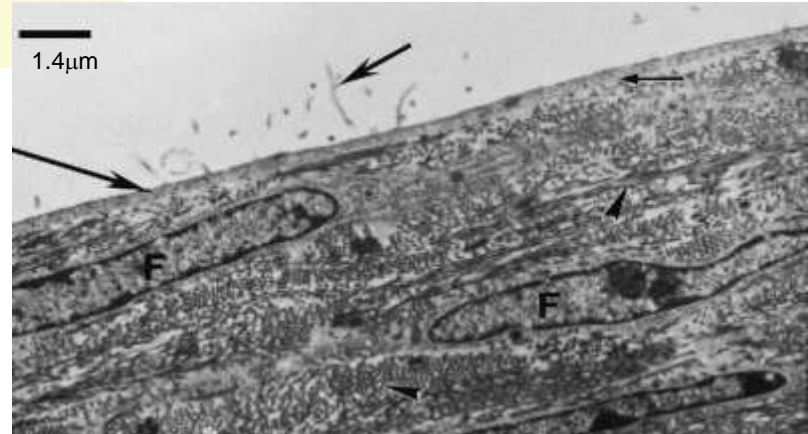
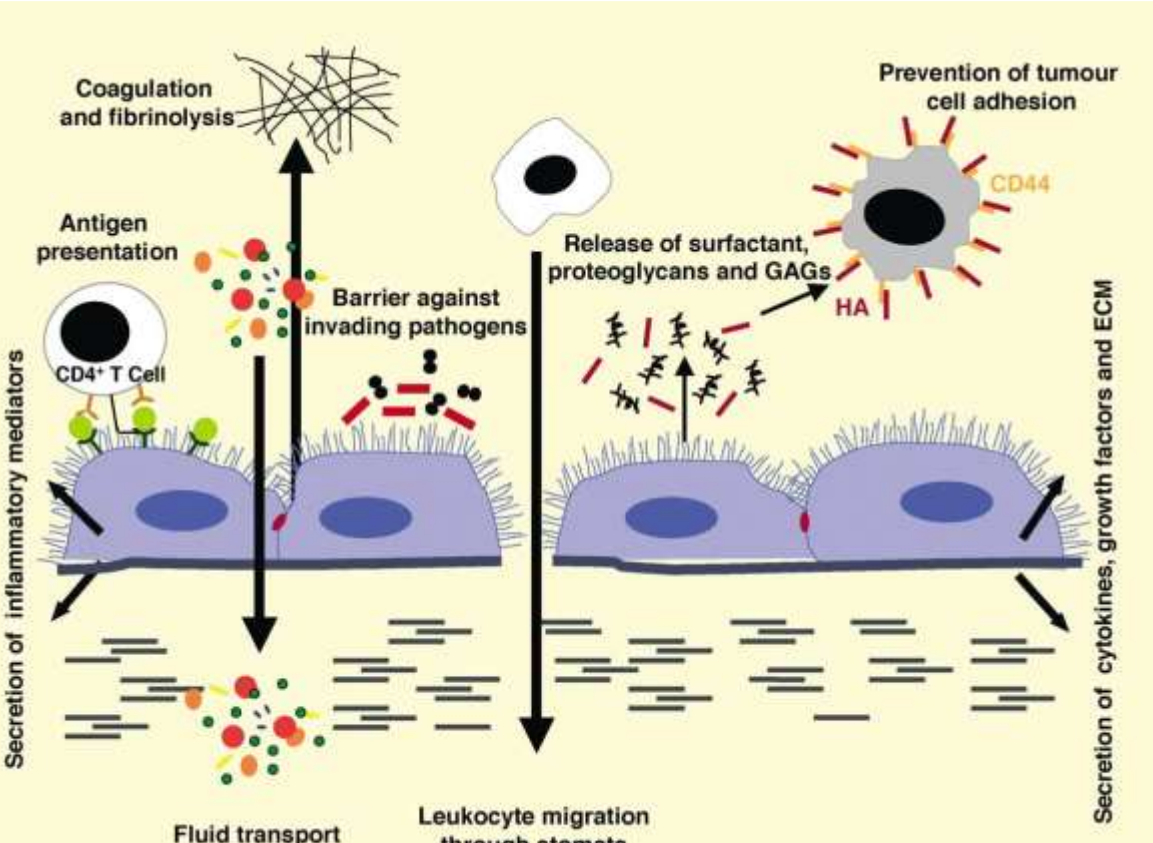
- serous membrane of loose connective tissue (Lamina propria serosae) and single layer squamous epithelium (L. epithelialis serosae)
- syn. mesothelium, visceral peritoneum
- continuous with mesenterium
- barrier against various pathogens , antiadhesive properties – intracoelomic movements, immune functions (Ag presentation), ECM production, etc.

- Adventitia

- some parts of the tube are not covered with epithelium
- esophagus in thorax, parts of digestive system in peritoneal cavity in walls (duodenum, part of colon, rectum, anal canal)
- connective tissue only continuous with connective tissue of the walls



Serosa/Adventitia (Tunica serosa/adventitia)



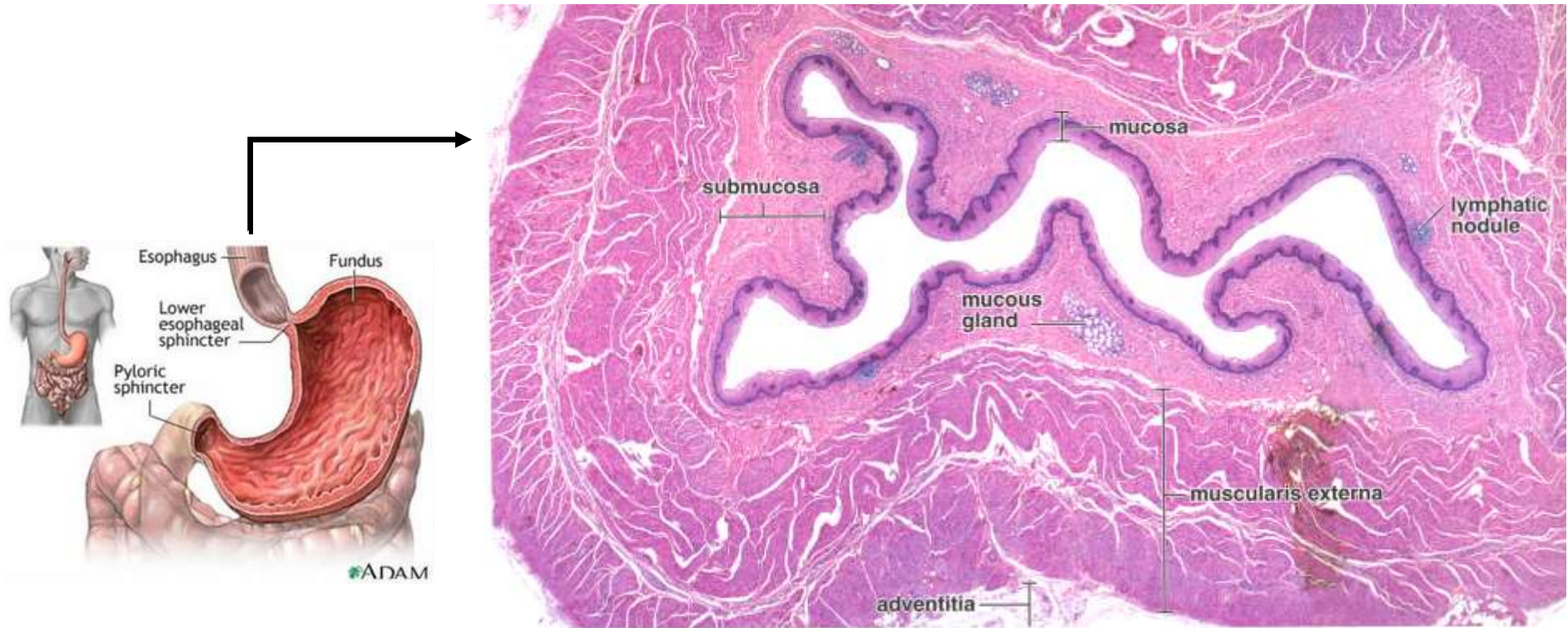
Esophagus (Oesophagus)

- Mucosa

- nonkeratinized stratified squamous epithelium → mechanically protects esophageal tissue
- L. propria contains cardiac glands (tubular mucinous) and diffuse lymphatic tissue

- Submucosa

- loose collagen connective tissue, defines shape of mucosa
- blood and lymph veins, plexus submucosus Meissneri
- submucosal glands (tubular mucinous)
- diffuse lymphatic tissue



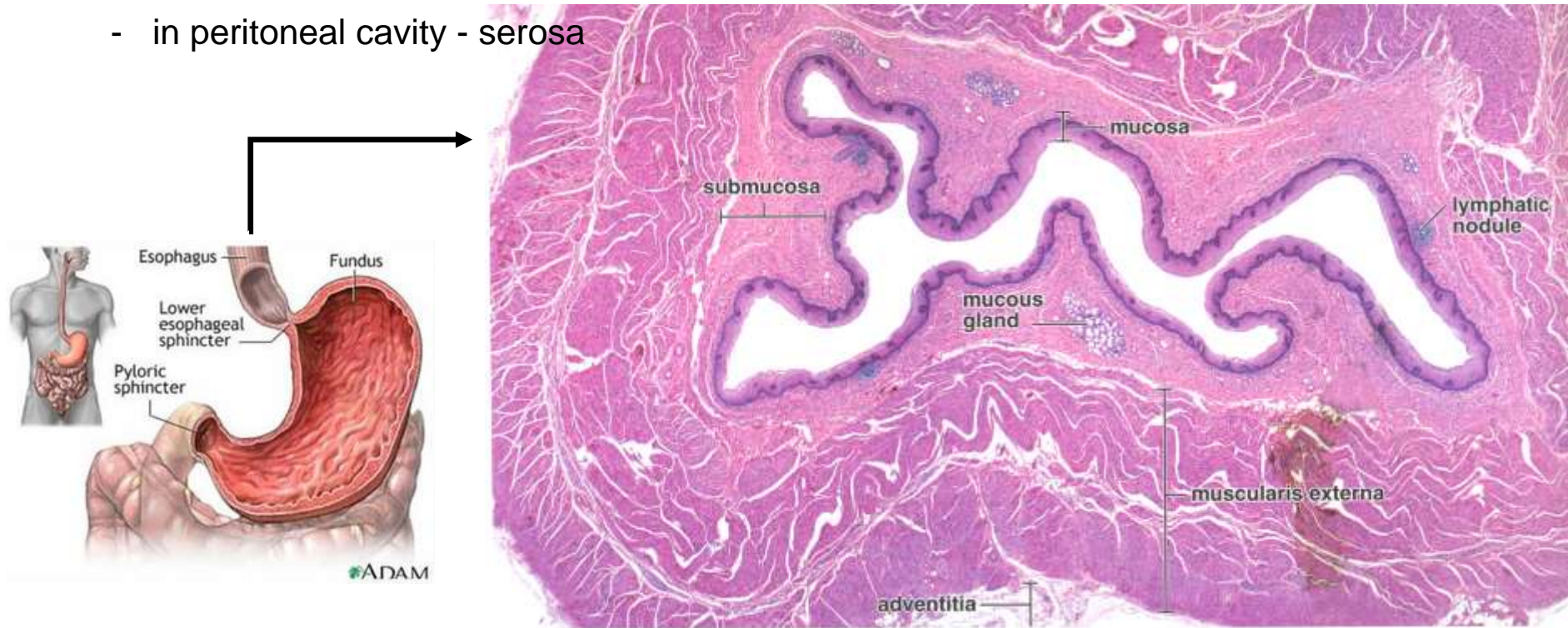
Esophagus (Oesophagus)

- Muscularis externa

- inner circular and outer longitudinal layer
- plexus myentericus Auerbachi
- upper third – skeletal muscle, mid third – mixed smooth and skeletal, lower third – smooth muscles only

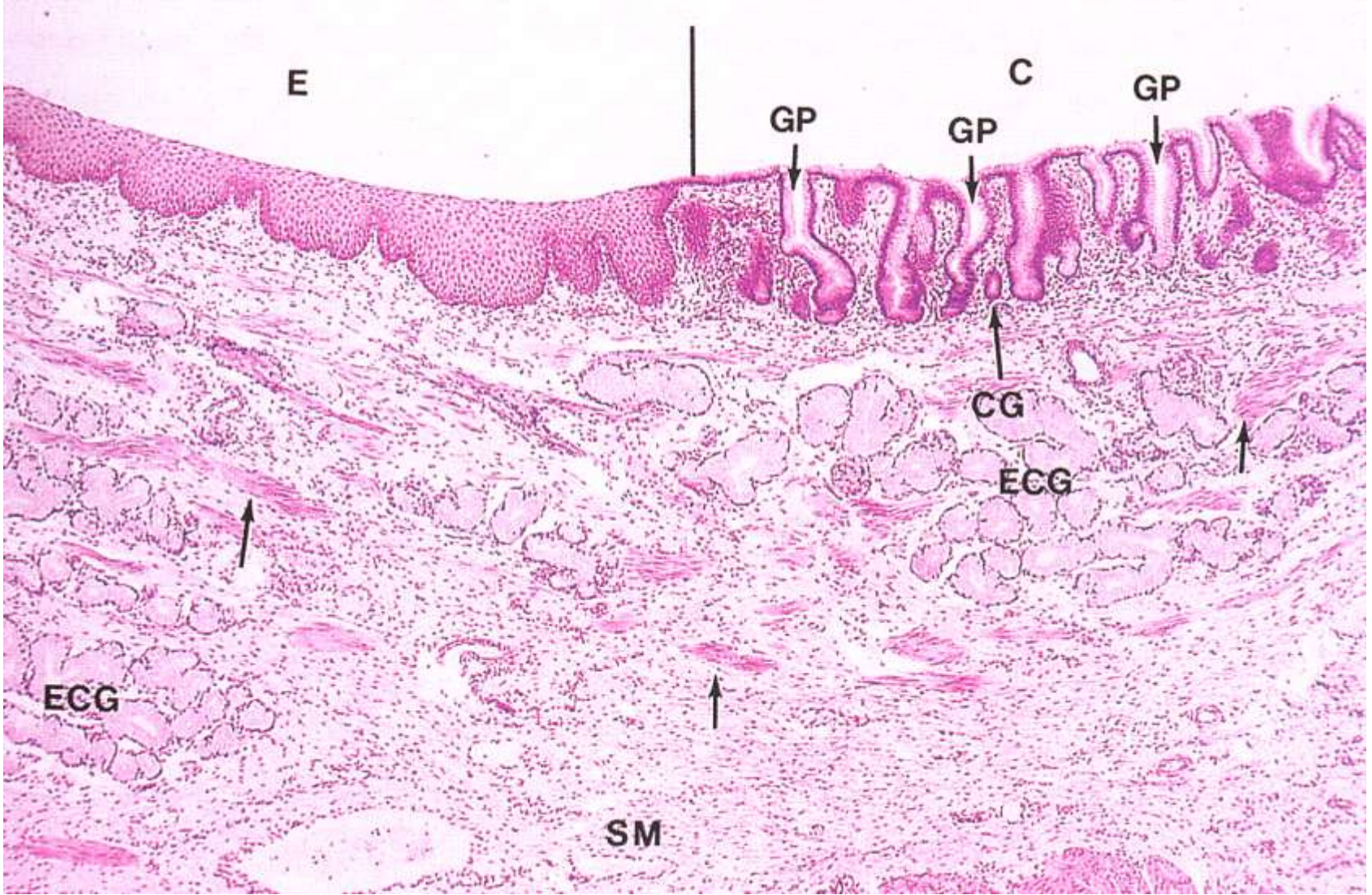
- Adventitia

- neck and chest – connects esophagus with surrounding tissue
- loose connective tissue
- in peritoneal cavity - serosa



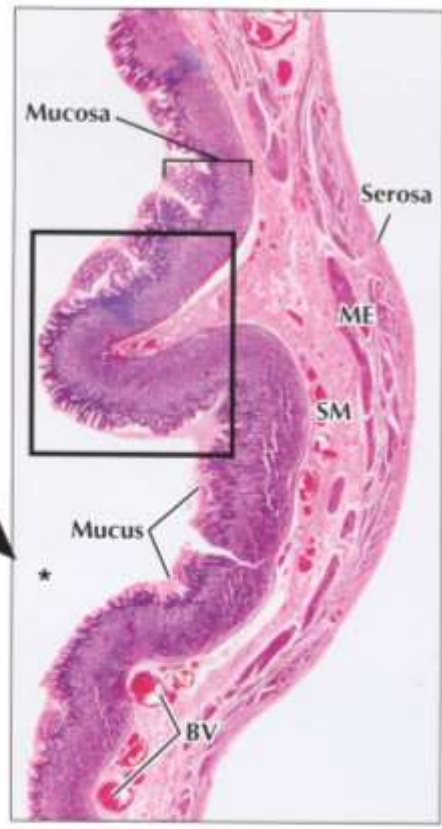
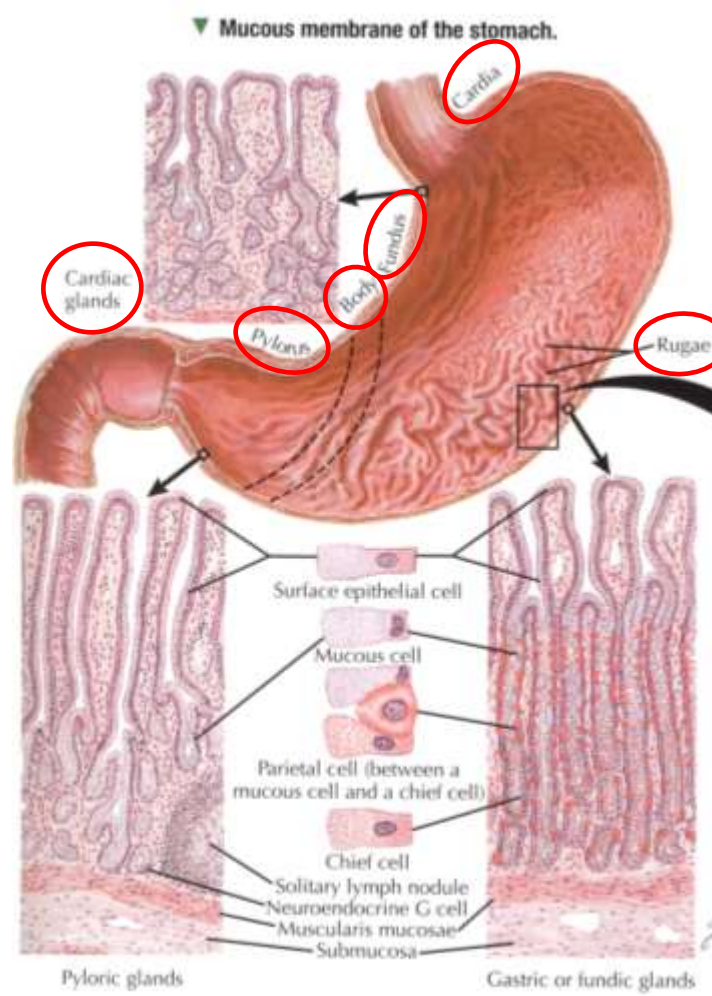
Cardia of stomach – connection with esophagus

Nonkeratinized stratified squamous epithelium → simple columnar epithelium



Stomach (Ventriculus, Gaster)

- general anatomy of hollow tube
- anatomical regions differ also in histologic structure
- rugae gastricae (submucosa)



▲ Light micrograph (LM) of the stomach wall showing four concentric layers at low magnification. A thick mucosa (formed mostly of tightly packed gastric glands) lines the lumen (*). The rectangle indicates a ruga consisting of a submucosal connective tissue core covered by mucosa. A thick layer of mucus secreted by surface cells forms a barrier over the mucosa for protection of tissues from acid and proteolytic enzymes in the lumen. The submucosa (**SM**) has prominent blood vessels (**BV**). Serosa covers the muscularis externa (**ME**) externally. 10x. H&E.

F. Netter

Stomach (Ventriculus, Gaster)

- Gastric mucosa

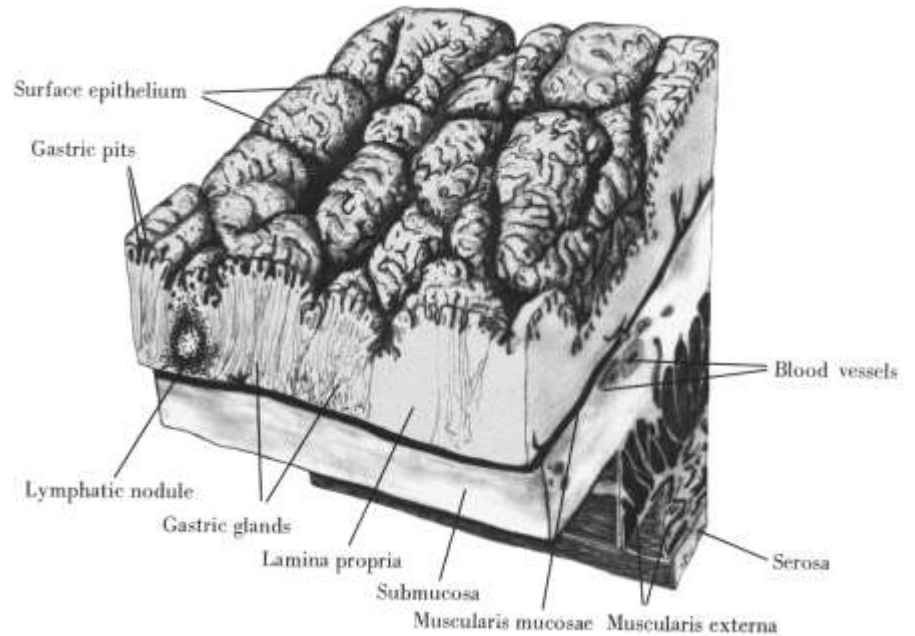
- simple columnar epithelium

- surface epithelium produces mucus

(mucinogenic granules, high content of HCO_3^- , K^+)

= protective function

- *areae gastricae*, *foveolae gastricae*

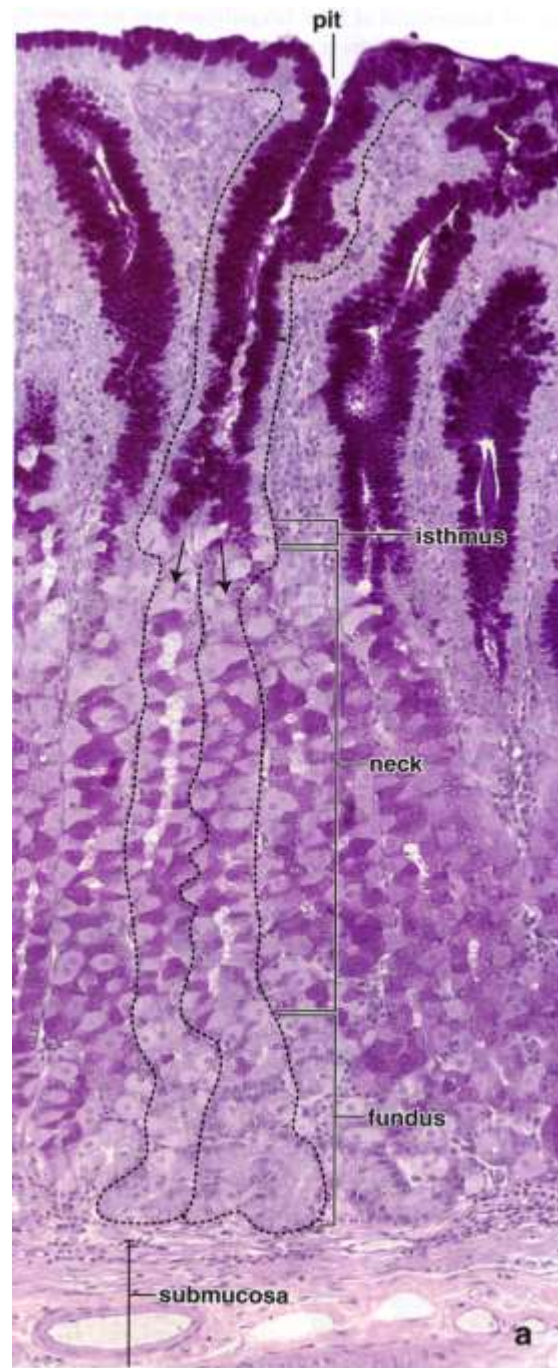
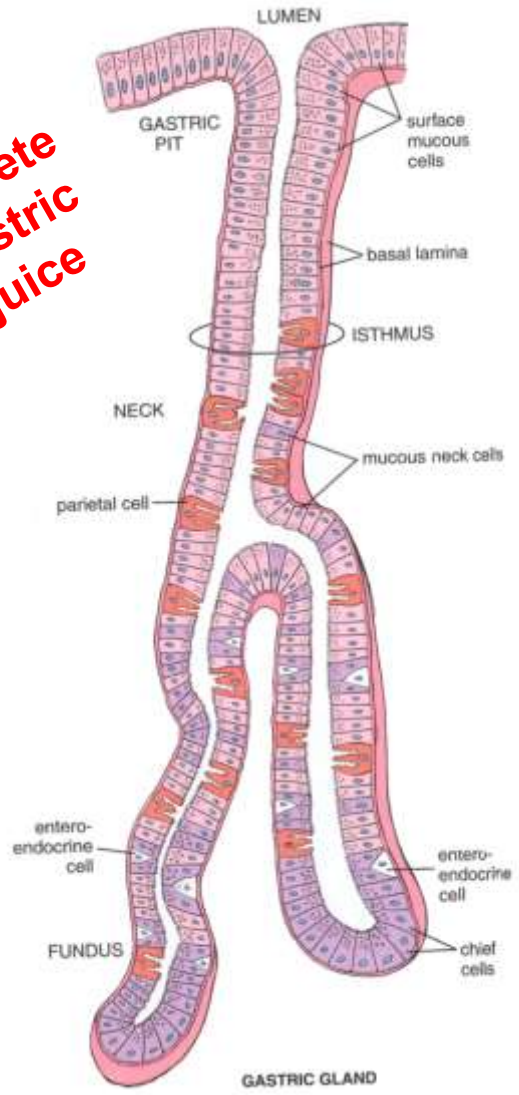
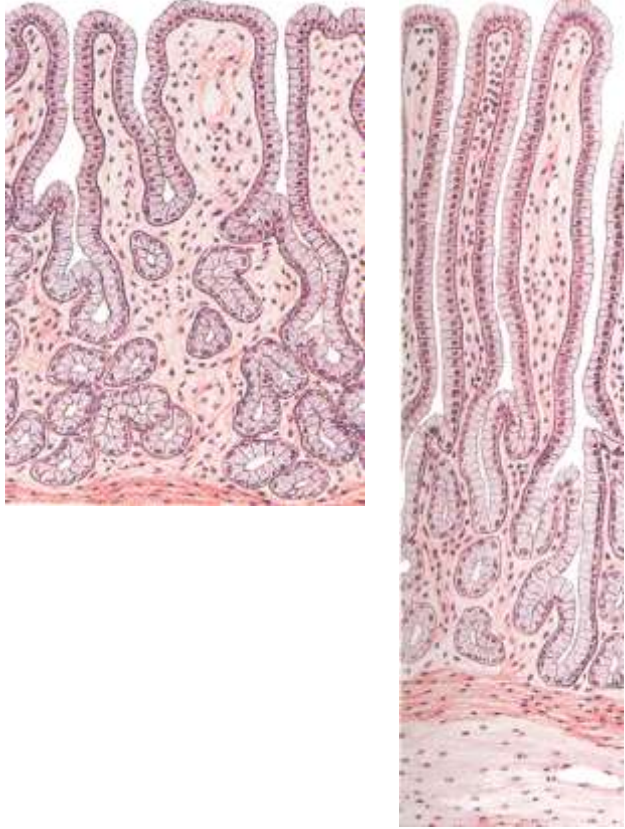


Stomach (Ventriculus, Gaster)

- Gastric mucosa
- L. propria contains large amount of glands

- Gl. cardiacae
- Gl. pyloricae
- Gl. gastricae propriae

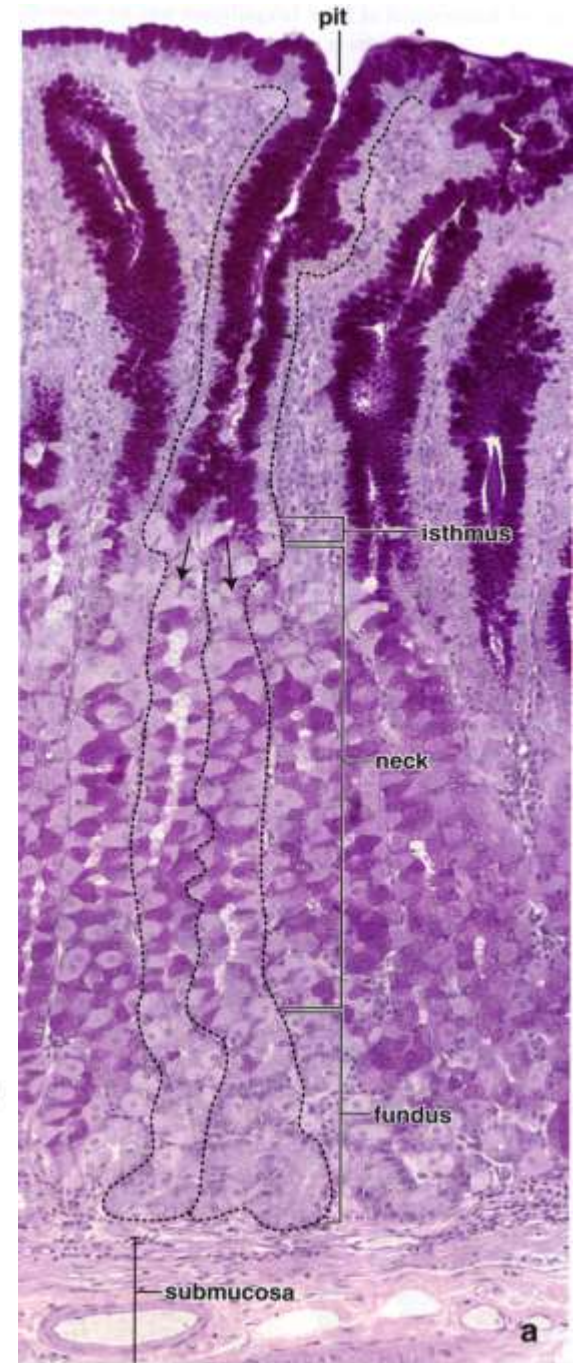
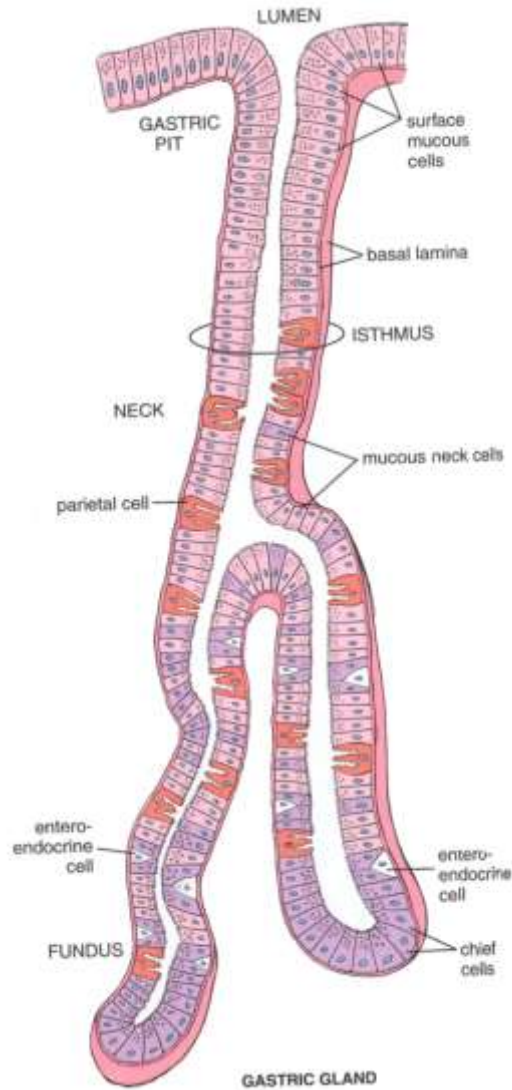
Mucous
Secrete gastric juice



Stomach (Ventriculus, Gaster)

- **Gl. gastricae propriae**
- glands of fundus and body
- simple tubular or branched
- 2-4 opens to the gastric pits

- **four cell types of gl. gastricae propriae**



Stomach(Ventriculus, Gaster)

Gl. gastricae propriae

chief

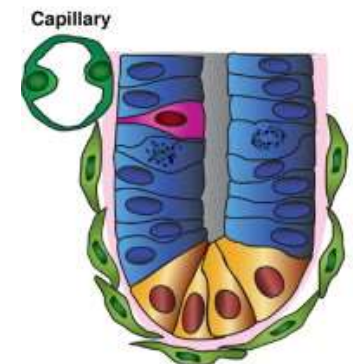
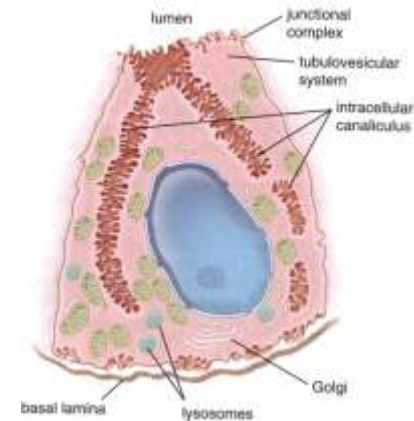
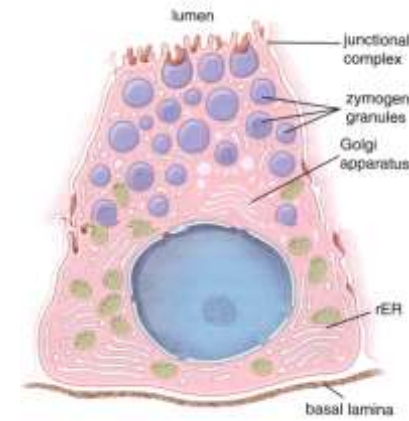
- most abundant, lower part of body and fundus of the gland
- pyramidal shape, basophilic cytoplasm, RER, pepsinogenic granules

parietal

- neck-body junction
- eosinophilic cytoplasm, high numbers of mtch., SER
- complex and dynamic ultrastructure
- intracellular canals in apical part with microvilli – membrane bound enzyme complexes producing H^+ a Cl^- (HCl originates extracelullarly)

neck cells

- cubic, mucinous
- capable of regeneration of all cell types in gastric epithelium

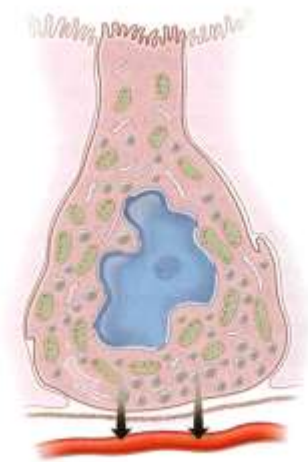
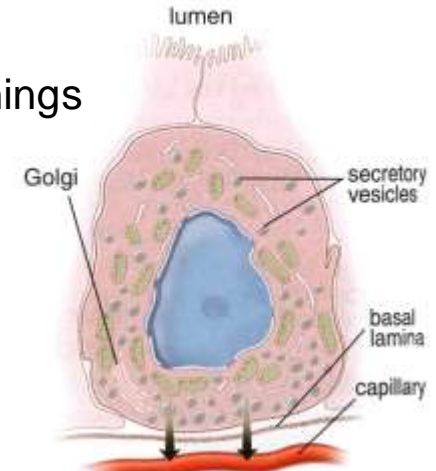
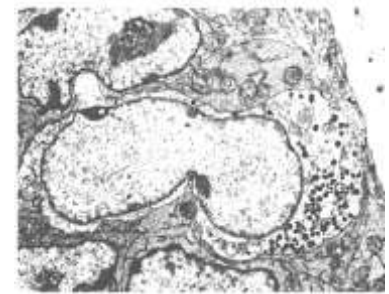


Stomach (Ventriculus, Gaster)

Gl. gastricae propriae

(entero)endocrine

- minor, secretion
- granules
- different cell types with different sensitivity to various histological stainings
- secretion of various biologically active compounds
- DNES/APUD
- GIT chemosensing
- see lesson spring semester 2012 - Epithelial tissue

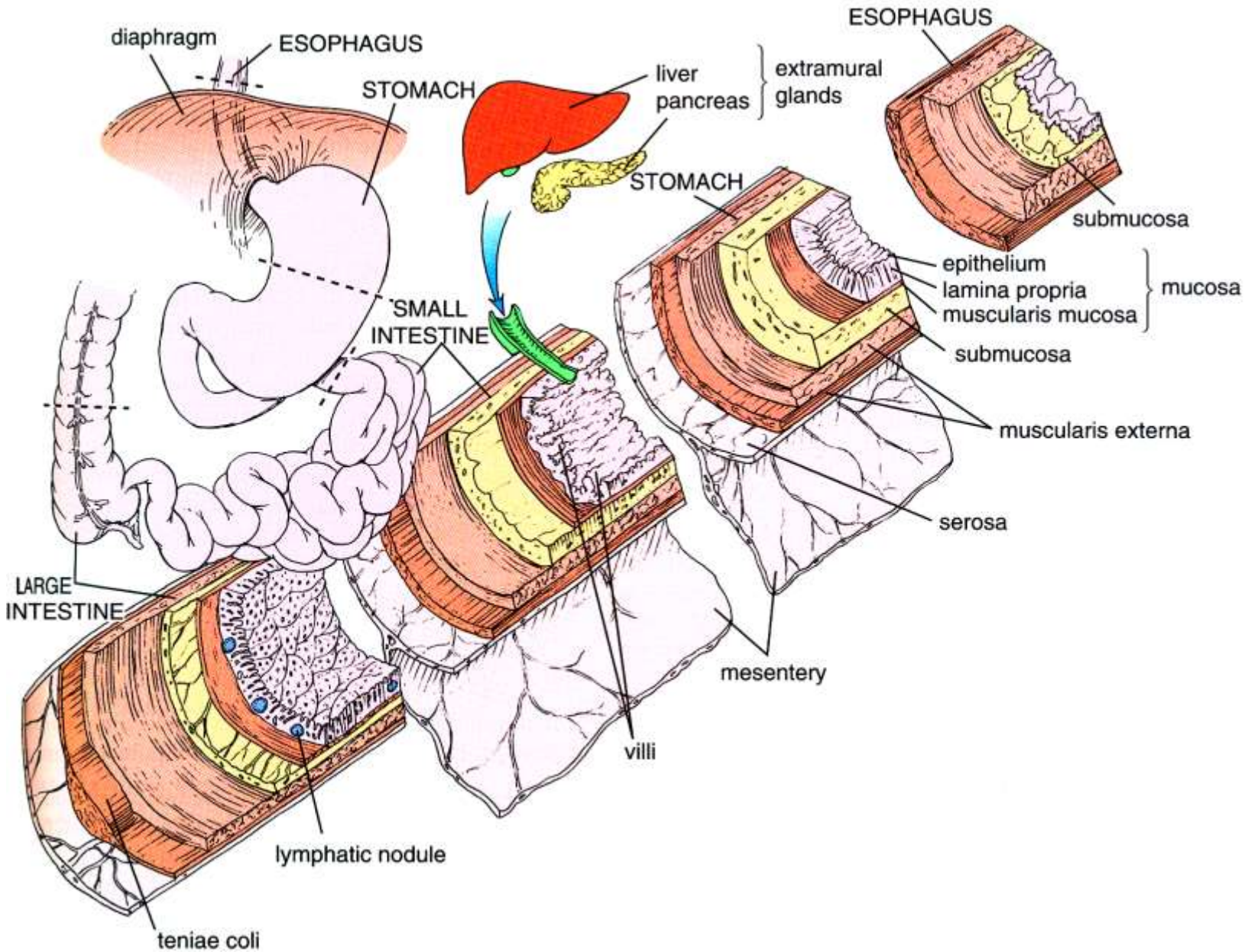


Type	Hormone	Localization/Function
D cells	Somatostatin	- Stomach, intestine, hepatic and pancreatic ducts
EC cells	Serotonin	- Stomach, gallbladder, intestine - Peristaltics
ECL cells	Histamin	- Stomach - HCl secretion
G cells	Gastrin	- Pars pylorica, duodenum - HCl, pepsin secretion
L (EG) cells	Enteroglucagon	- Stomach, intestine - attenuates secretion of pancreatic enzymes and peristaltics

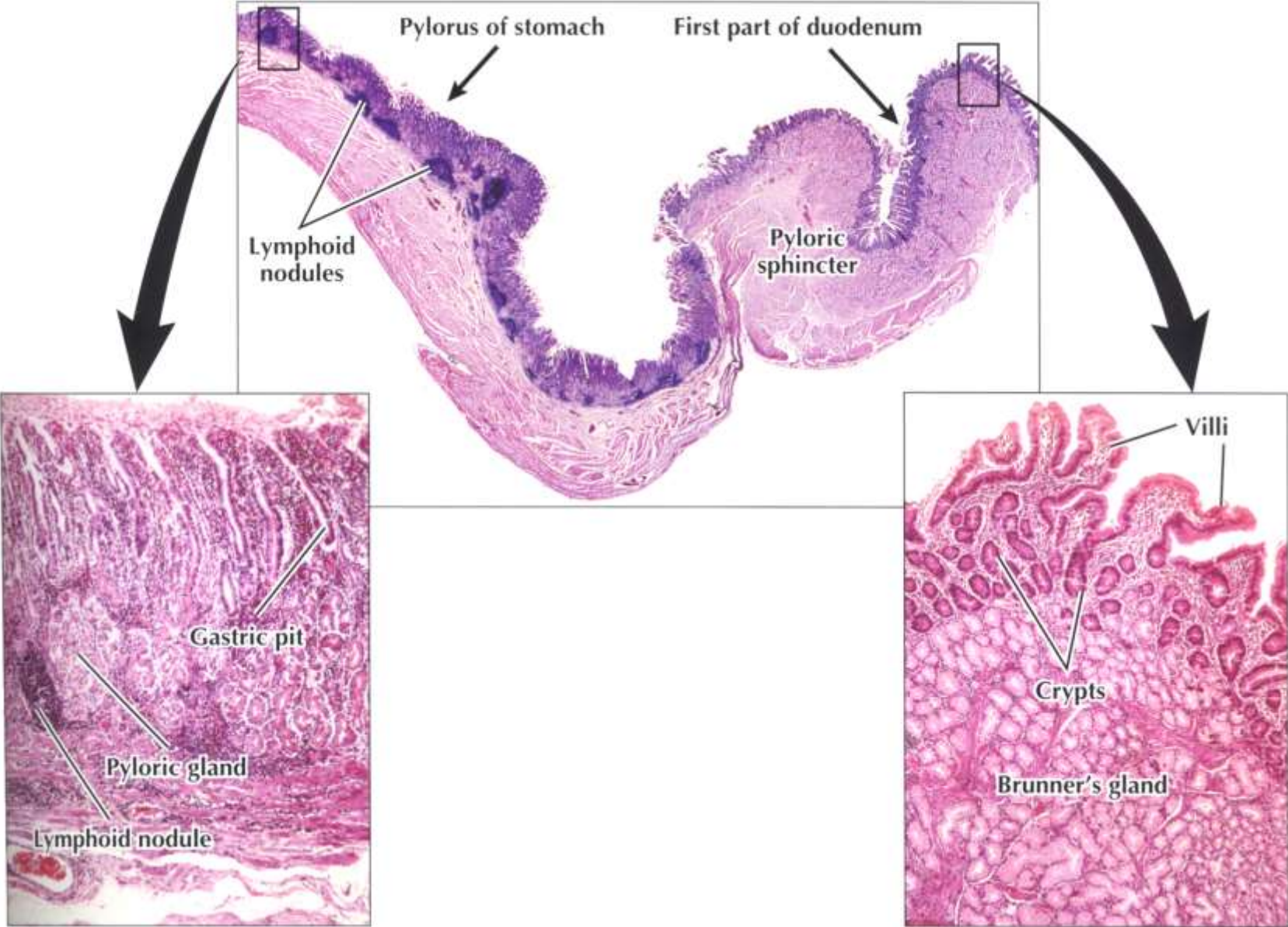
Break



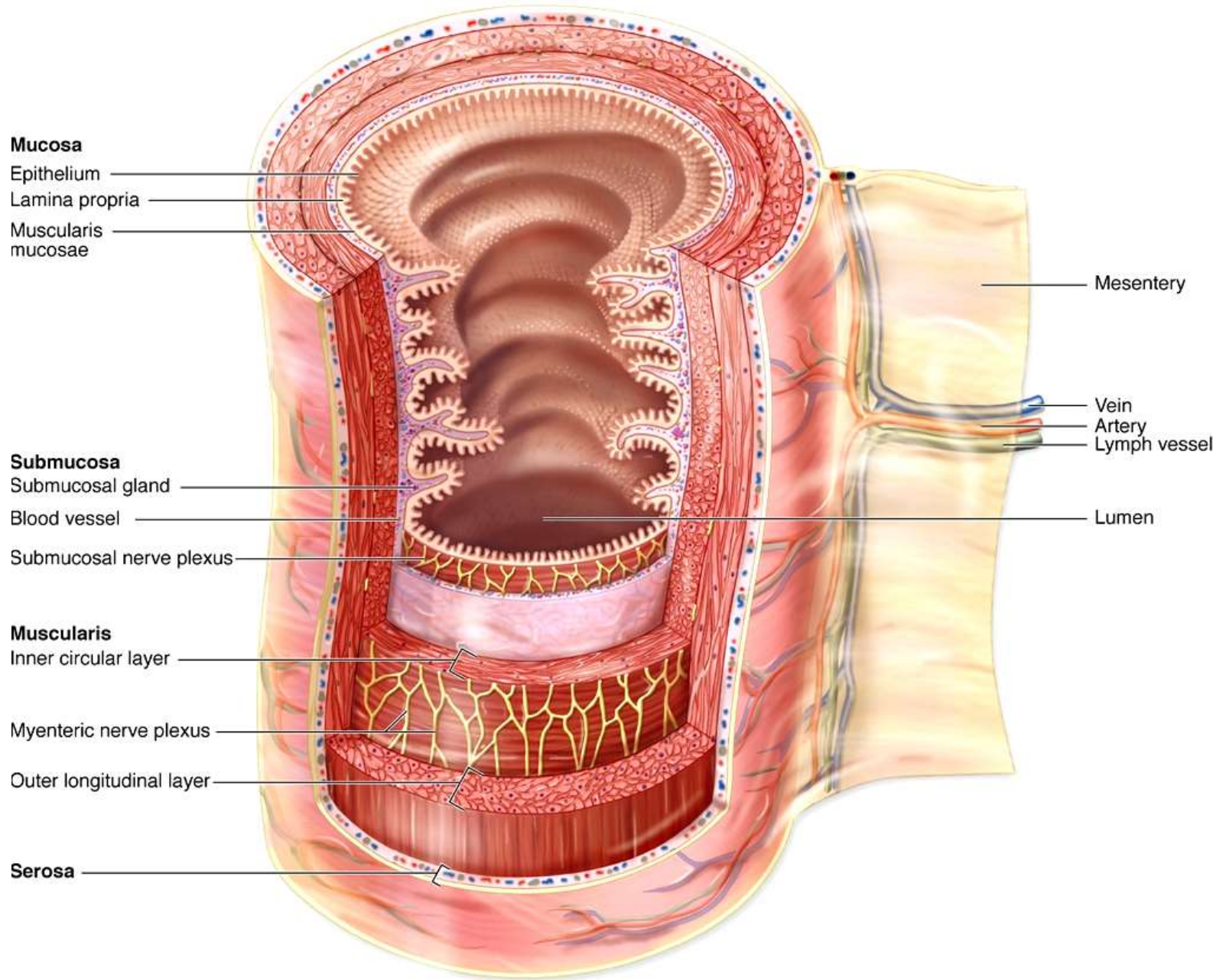
General architecture of hollow organs incl. gut tube



Gastroduodenal junction



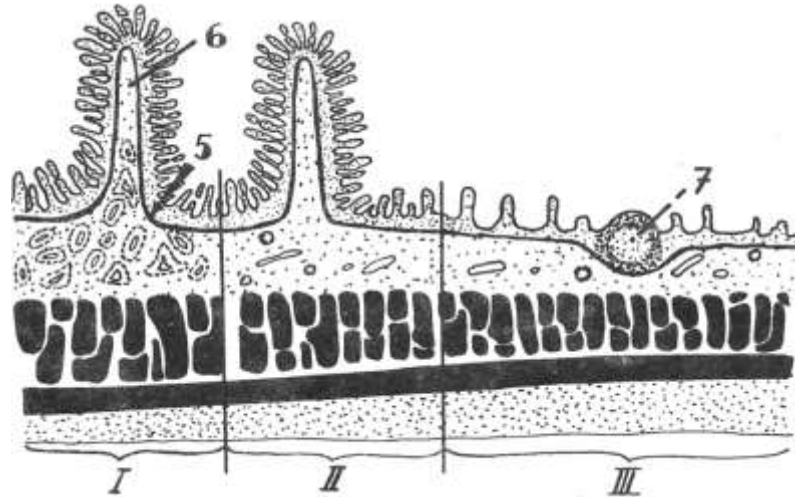
General architecture of the intestine



Small intestine – adaptation to efficient resorption

Four basic layers: **mucosa, submucosa, muscularis externa, serosa**
mucosa and submucosa maximise the resorptive area

- **plicae circulares** (Kerckringi) – **mucosa + submucosa**, ca 800, increase **2-3x**, distal region of duodenum



- **villae** (villi intestinales) – **mucosa** (l. propria + epithelium) 0,5-1,5 mm long, 10-40/mm², 4 000 000, increase **5-10x**
- **microvillae** – **apical part of enterocytes** – 1- 2 μm long, 0,1 μm wide, 100 mil./mm², increase **20x**

Small intestine adaptation to effective resorption

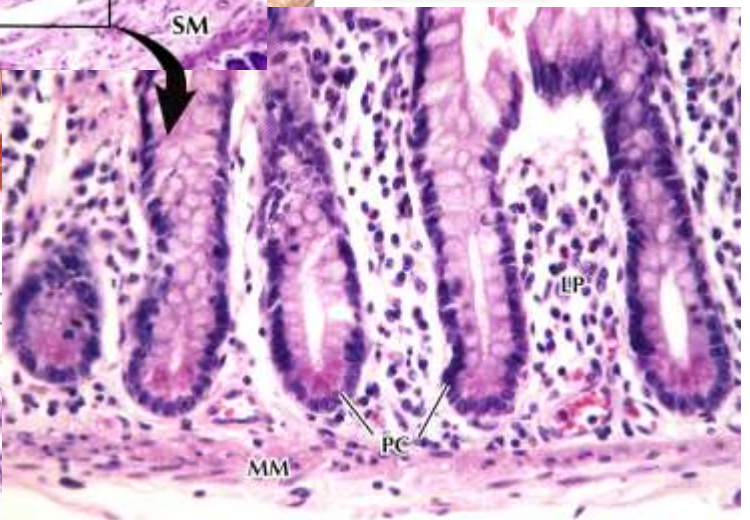
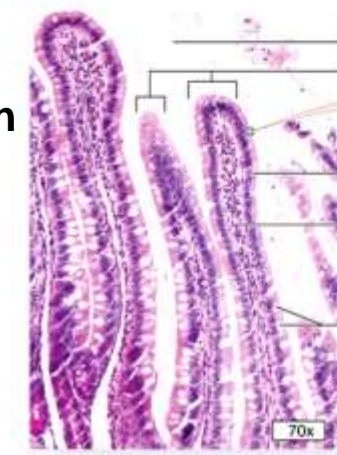
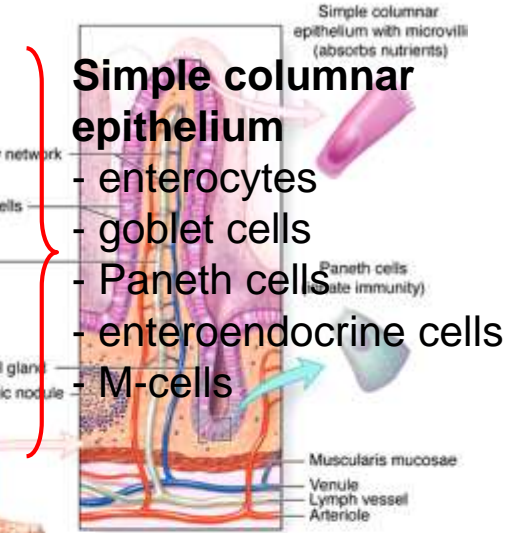
plicae circulares (Kerckring's folds)
 - 2-3x

villi (villi intestinales)
 - 5-10x

microvilli (striated border)
 - 20x

Crypts of Lieberkühn

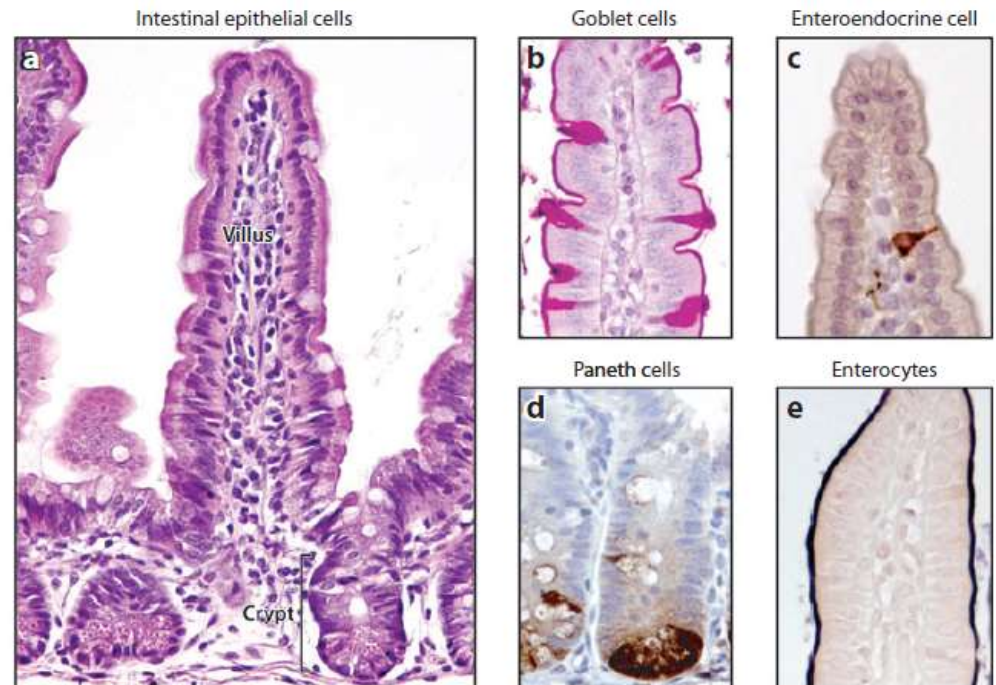
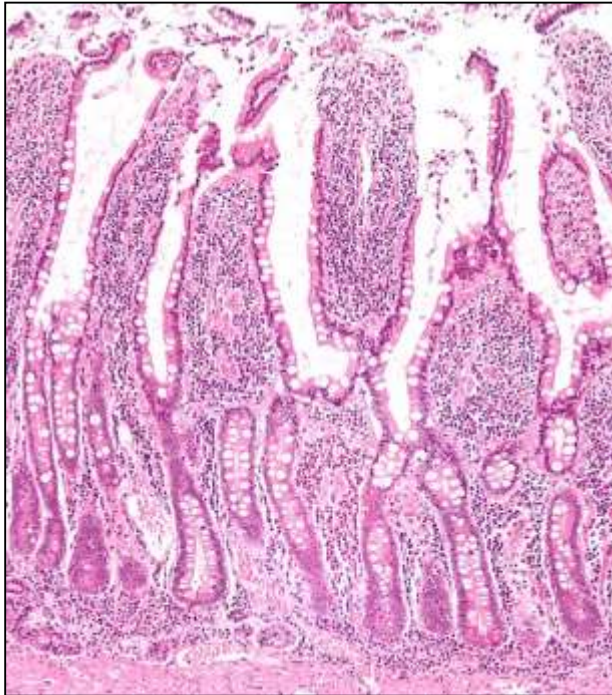
200-600x



e Microvilli

Crypts of Lieberkühn (gl. intestinales)

- simple tubular structures of intestinal mucosa, depth 0,3-0,5 mm
- pass through l. propria and open to lumen
- different cell types
 - secretion of digestive enzymes
 - epithelial renewal
 - enteroendocrine cells
 - immune response



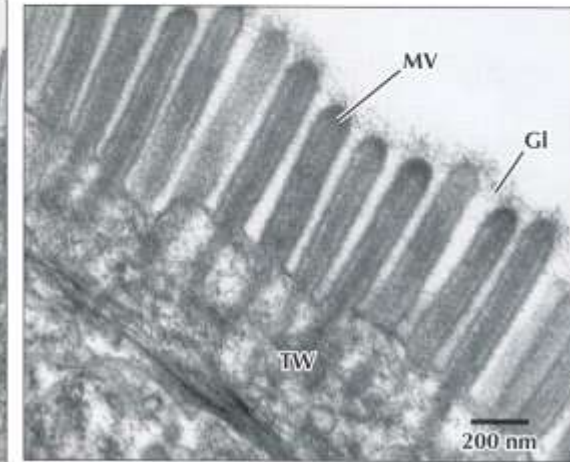
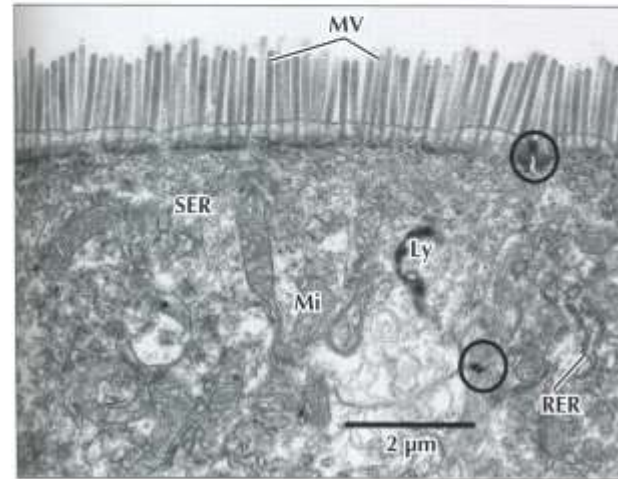
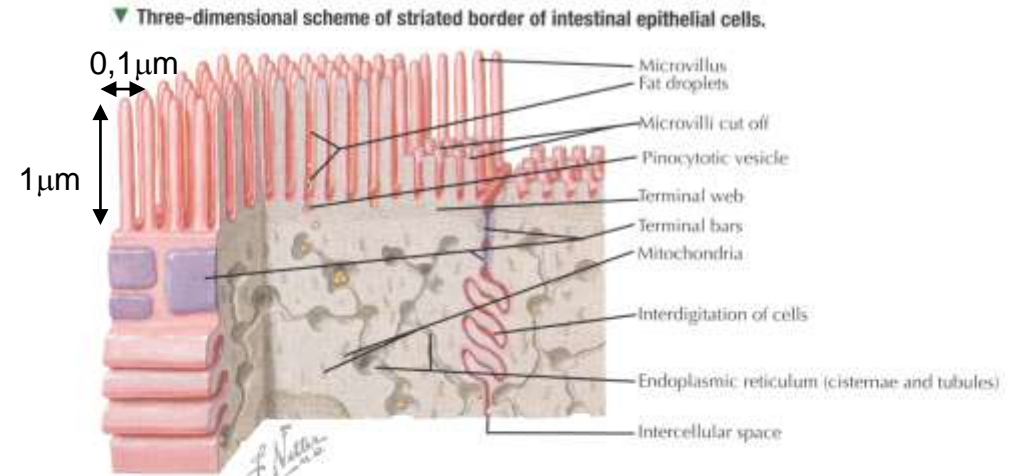
Intestinal mucosa

Enterocytes

- tall, columnar cells
- nucleus located in basis of the cell
- apical surface modified- microvilli (3000) + glycocalyx (0,5 μ m) = *striated border (cuticle)*
- tight intercellular connections, interdigitations

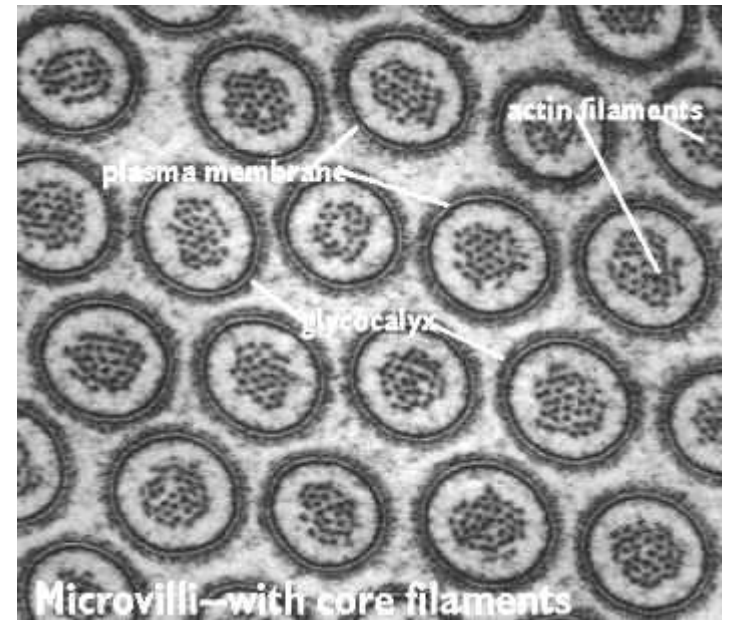
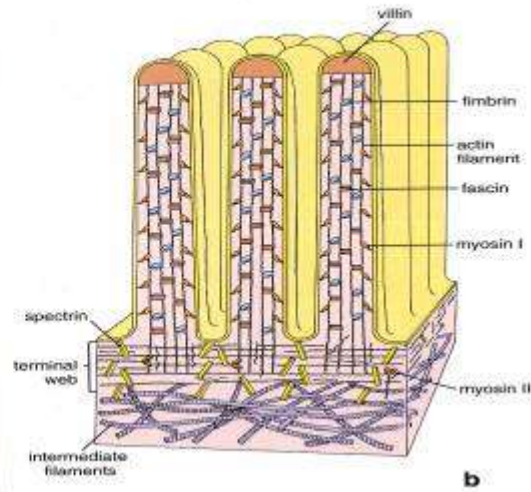
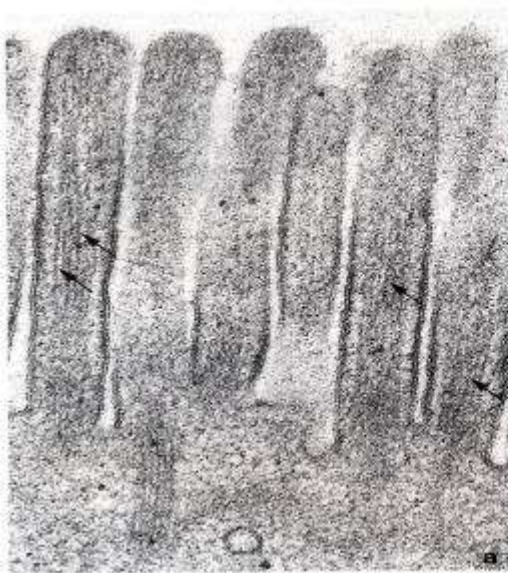
Function:

- digestion – enzymatic complexes on microvilli membrane
- absorption and transport – passive, facilitated i active
- lipid uptake - chylomicrons

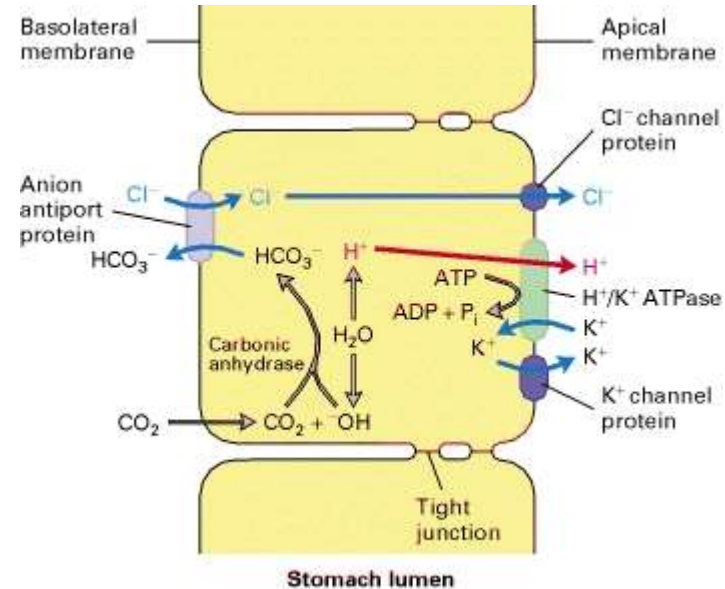
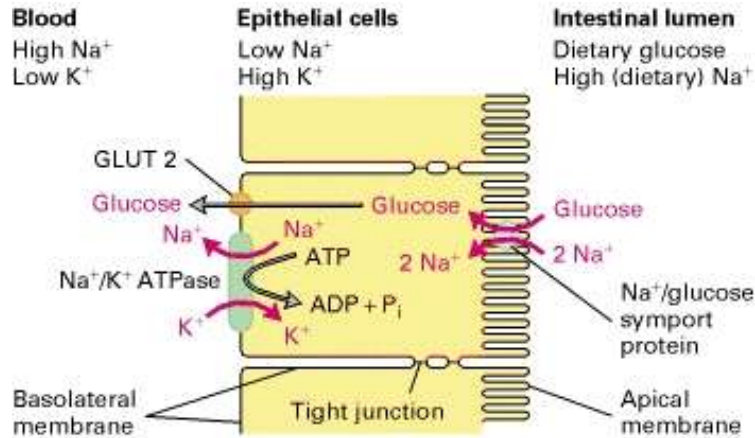


▲ EMs of enterocytes at low (Left) and high (Right) magnification. Apical microvilli (MV) make up a striated border and extend from free surfaces of the cells. A fuzzy glycocalyx (GI) covers them. A terminal web (TW) of actin filaments in the apical cytoplasm reaches into microvilli. Intercellular junctions (circles) are between adjacent cells. The cytoplasm contains mitochondria (Mi), lysosomes (Ly), and smooth (SER) and rough (RER) endoplasmic reticulum. **Left:** 10,000 \times ; **Right:** 50,000 \times .

Microvilli



Transport and resorption



Transport of glucose from intestinal lumen to blood stream

Na⁺/K⁺ ATPase - basolateral surface - concentration gradient Na⁺ and K⁺

K⁺ gradient generates negative membrane potential

Na⁺/glucose symport on apical surface

Facilitated diffusion by glucose uniporter (GLUT2) in basolateral membrane

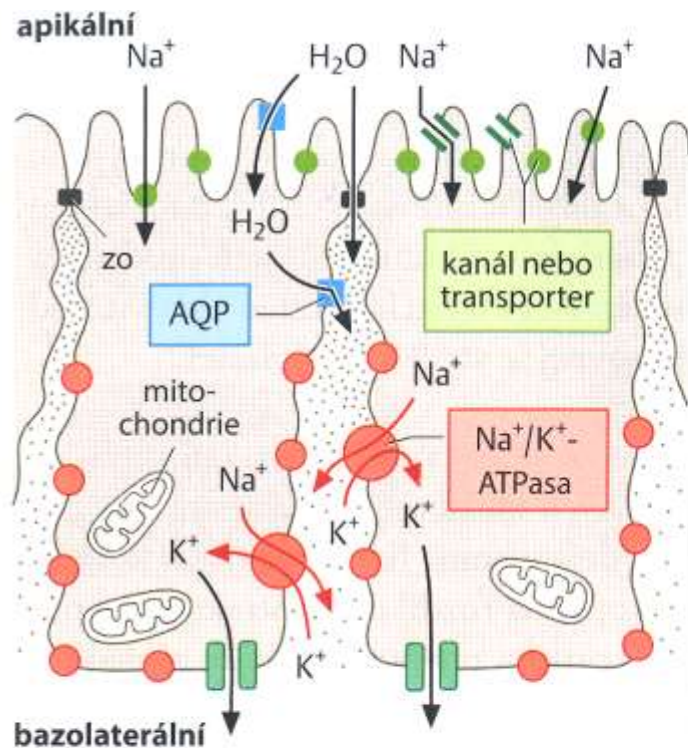
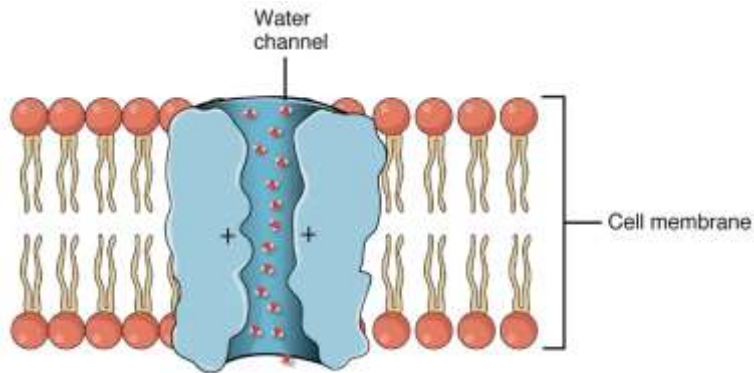
Acidification of stomach fluid by parietal cells

Apical membrane - H⁺/K⁺ ATPase + Cl⁻ a K⁺ canals

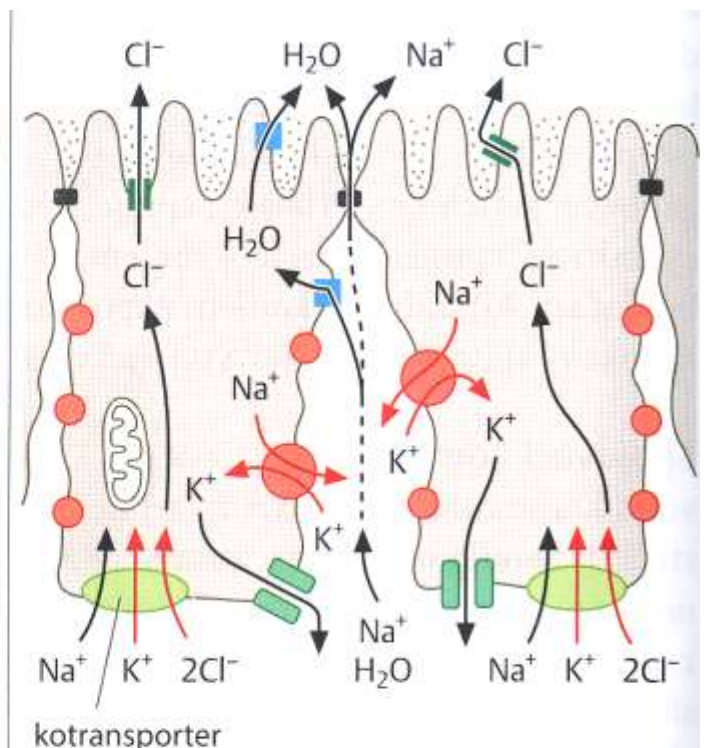
Basolateral membrane – anion antiporter HCO₃⁻ and Cl⁻ ions

Combined activity of ion channels a cells keeps the electroneutrality and neutral cytoplasmic pH while reaching high extracellular concentration of H⁺ and Cl⁻ in lumen of stomach

Transportation and resorption



a vodu resorbující epitel



b vodu vylučující epitel

Secretory epithelium

Unicellular glands

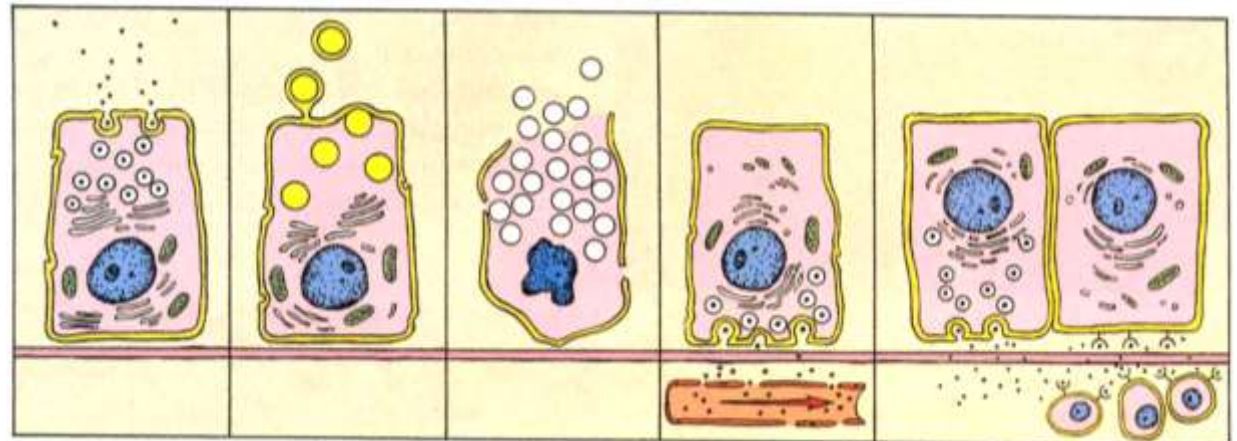
Multicellular glands

Mechanism of secretion

Exocrine ×

Endocrine × Paracrine

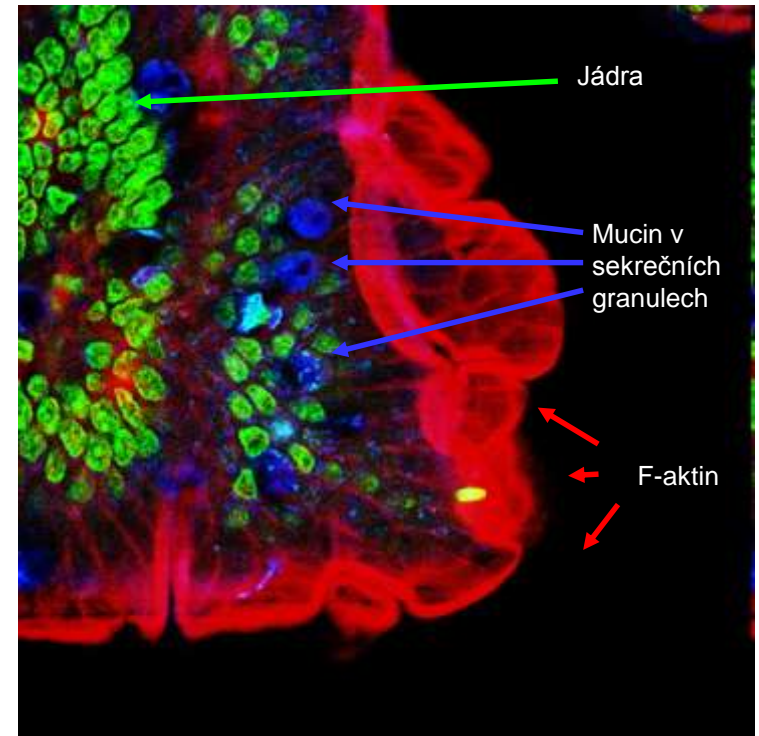
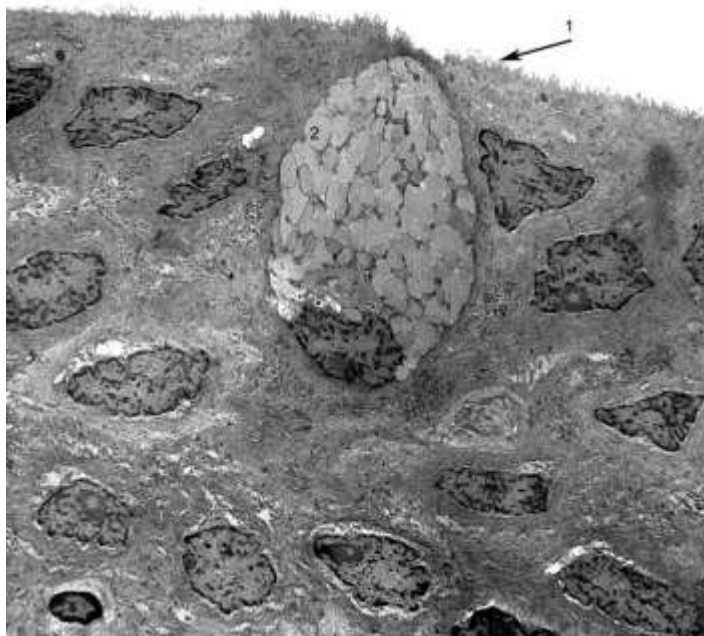
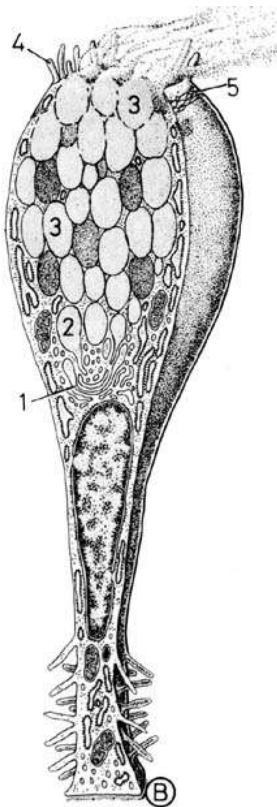
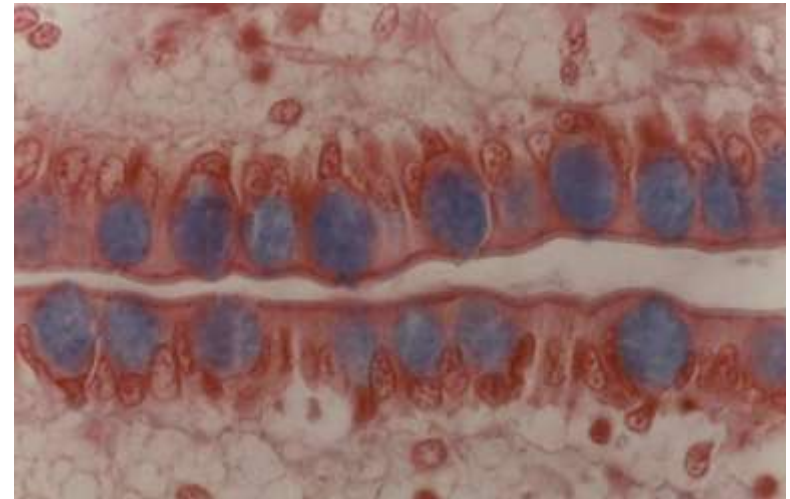
Merocrine × Apocrine × Holocrine



Intestinal mucosa

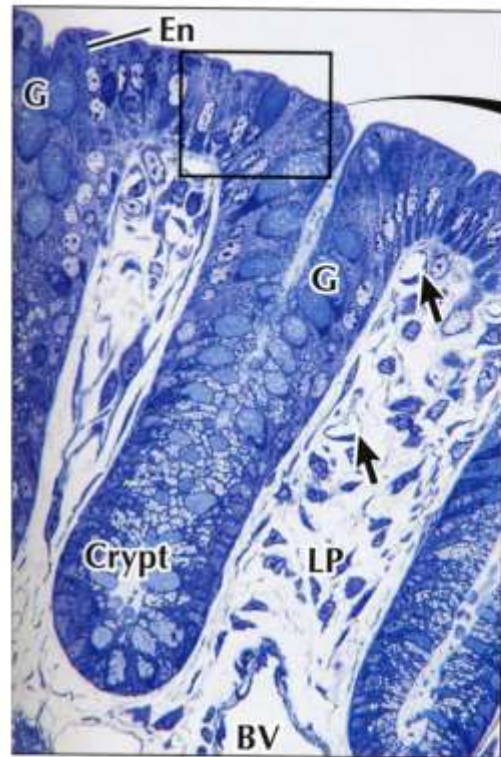
Goblet cells

- Cylindrical glandular epithelial cells
- Apical surface – apocrine/merocrine secretion of mucin
- Basal part – RER, GA, nucleus, mitochondria
- Mucinogenic granules
- see lesson spring semester 2015 - Epithelial tissue

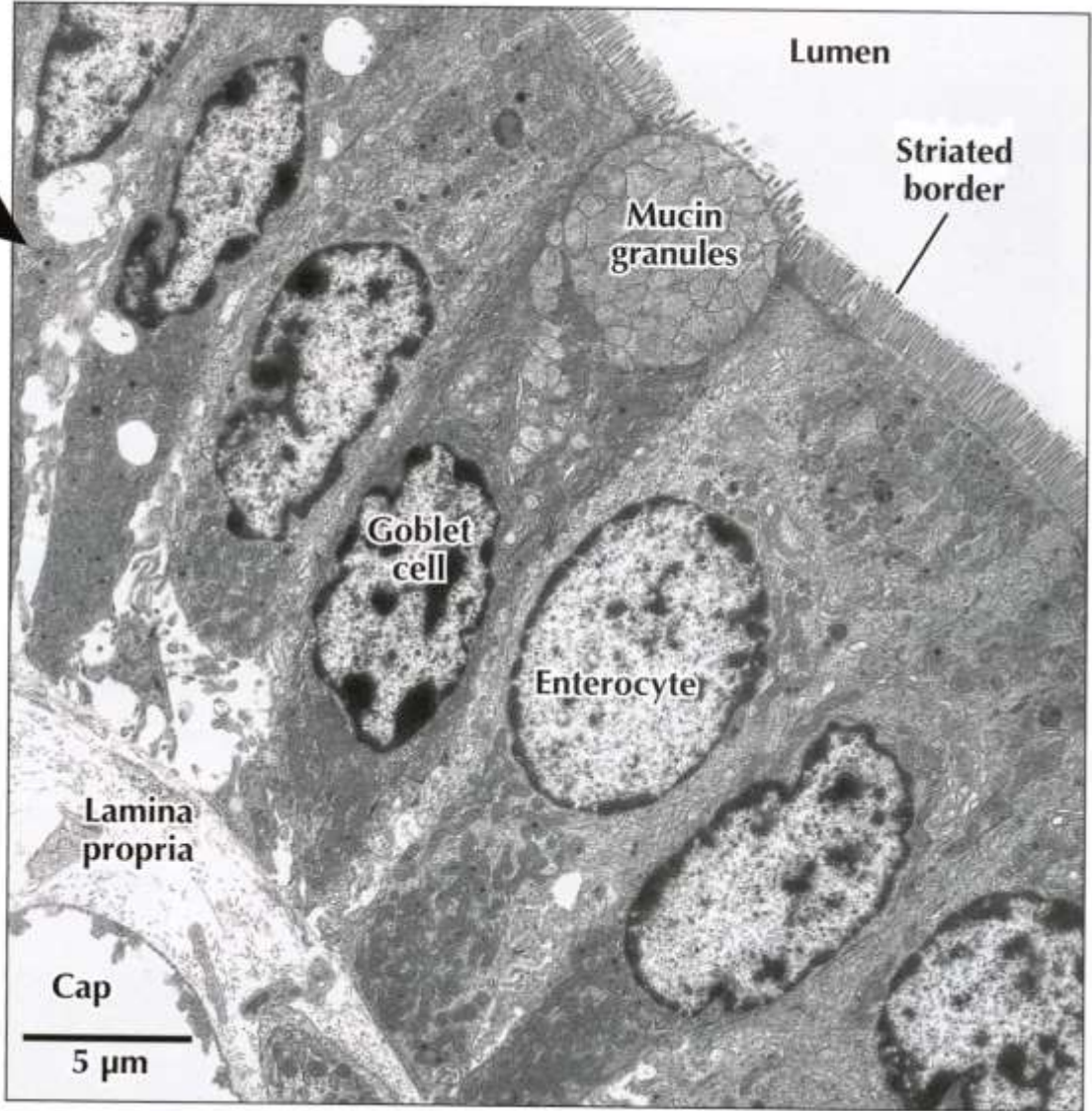


Intestinal mucosa

Goblet cells



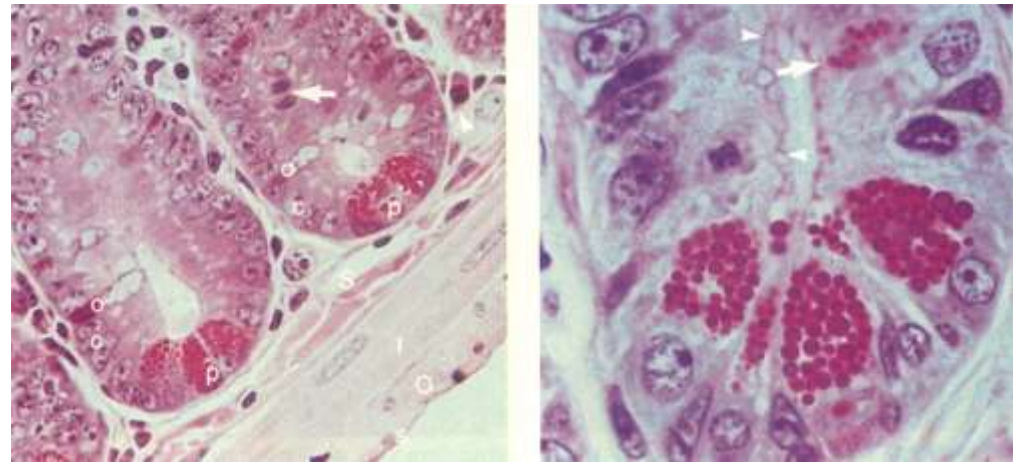
▲ LM of the colonic mucosa. Surface epithelium containing goblet cells (G) and enterocytes (En) invaginates to form an intestinal crypt. The lamina propria (LP), with capillaries (arrows) and larger blood vessels (BV), is richly cellular. 600x. Toluidine blue.



Intestinal mucosa

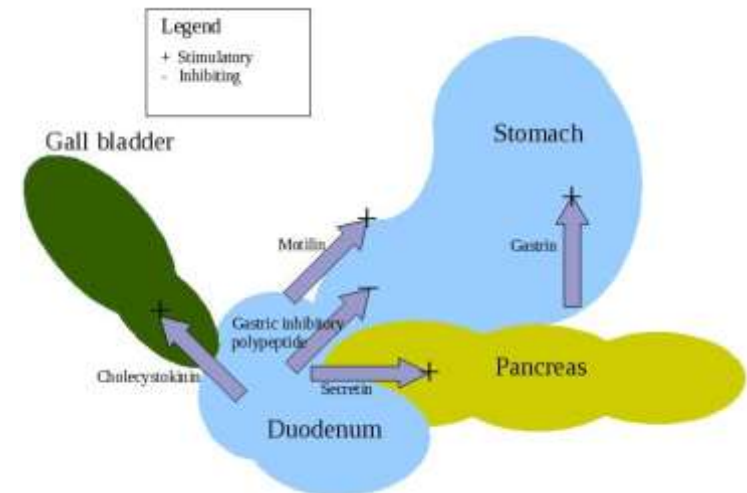
Paneth cells

- basal part of crypts of Lieberkühn
- basophilic cytoplasm
- GA located above nucleus
- acidophilic (red) granules
- immune system
- secretion granules contain biologically active substances e.g. lysozym)
- influence intestinal microflora



Enteroendocrine cells

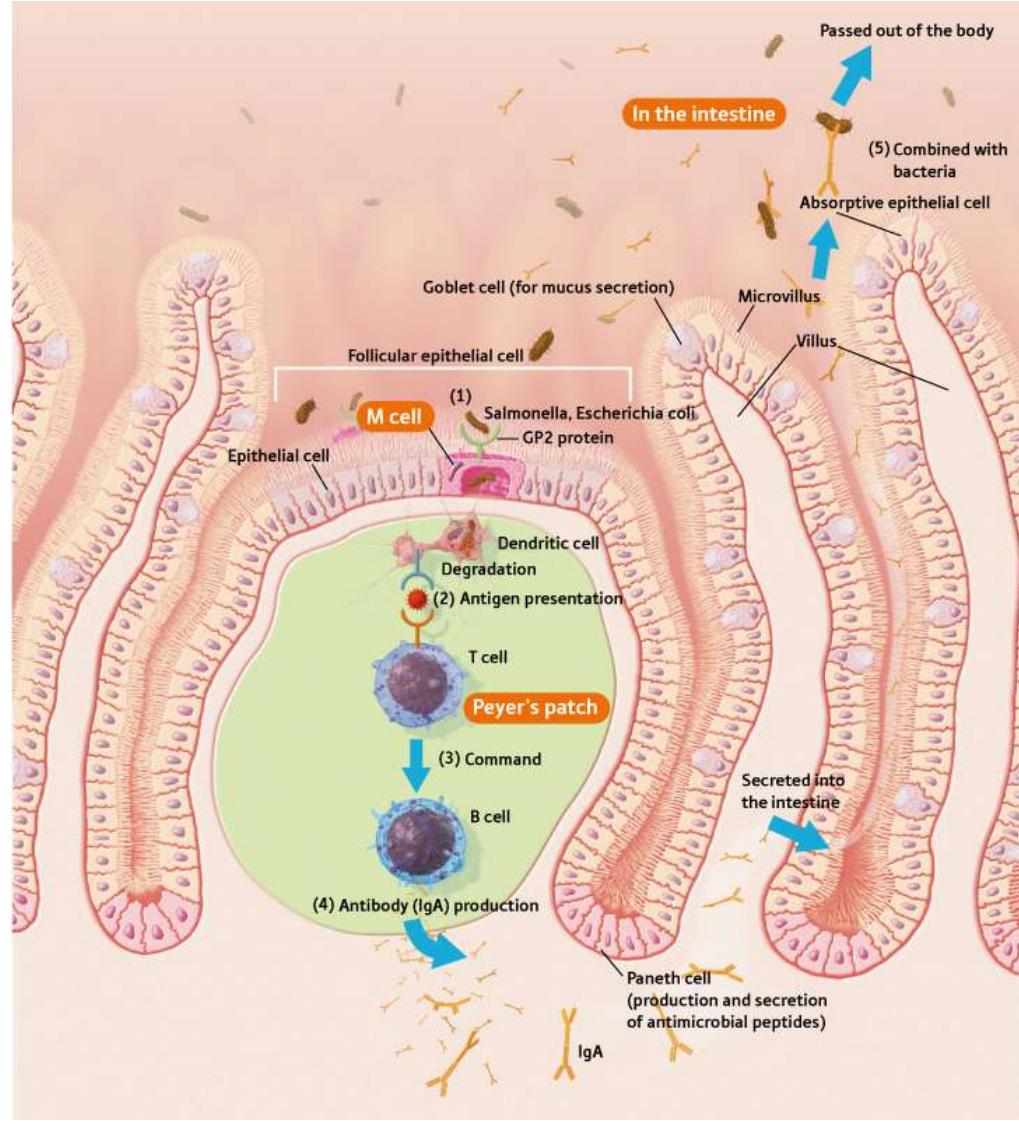
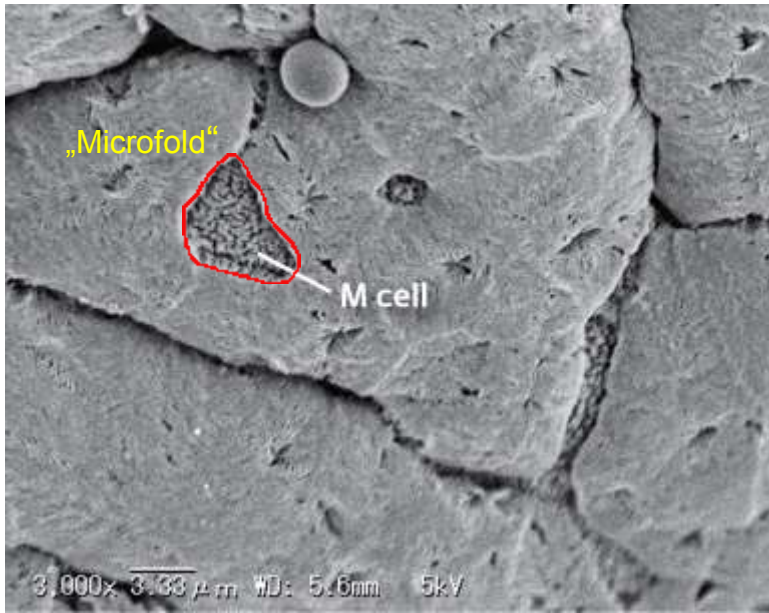
- similar to gastric enteroendocrine cells
- regulate pancreatic secretions
- homeostatic axis (brain-intestine-adipose tissue)
- cholecystokinin, secretin, GIP, motilin, neurocrine peptides etc.



Intestinal mucosa

M cells (microfold)

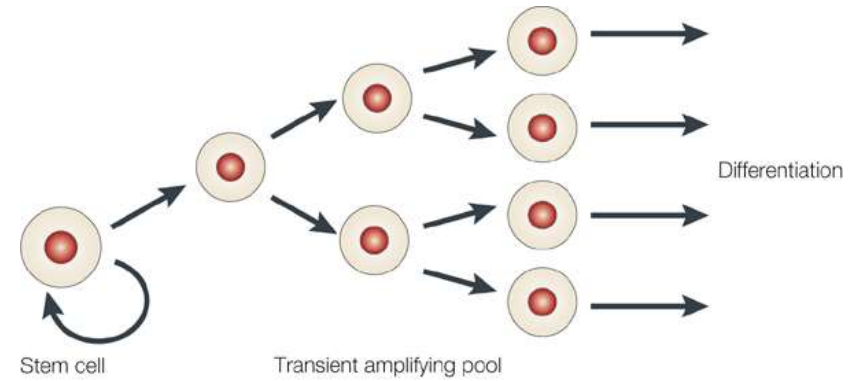
- epithelial cells above Peyer's patches and lymphatic nodules
- no microvilli
- induces immune response
- MHCII
- antigen presentation to dendritic cells and lymphocytes



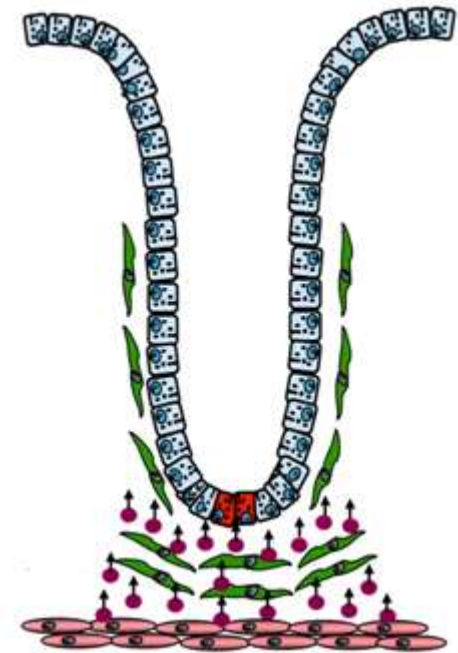
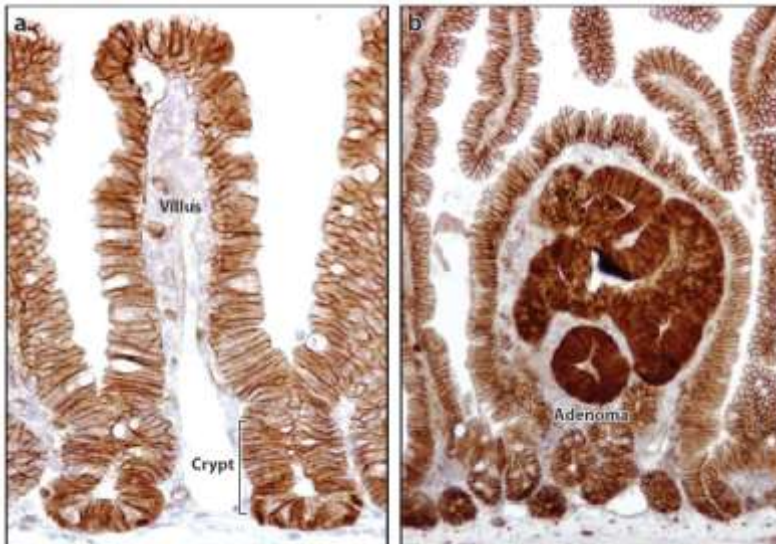
Intestinal mucosa

Intestinal stem cells

- bottom of crypts of Lieberkühn
- epithelial renewal (4-5 days)
- stem cell niche
- tumour transformation



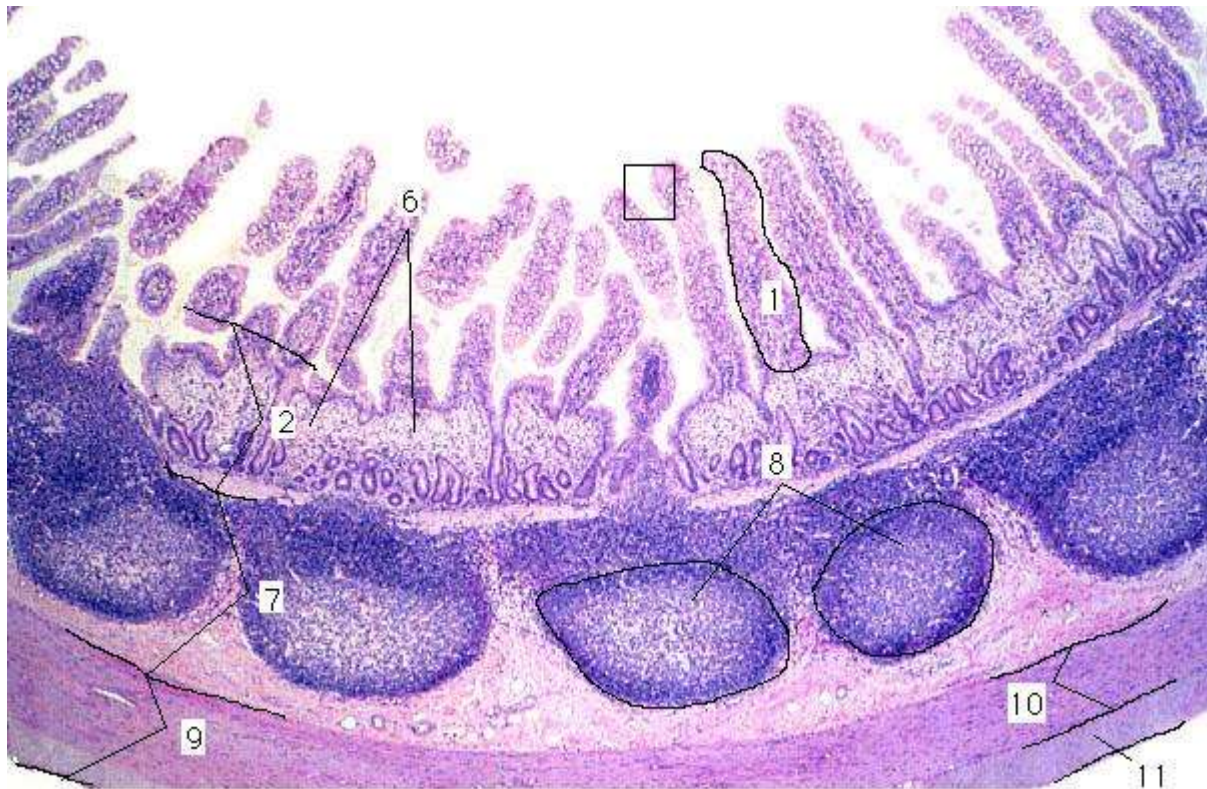
Nature Reviews | Molecular Cell Biology



Intestinal mucosa

L. propria

- immune system – GALT
- immunologic barrier
- Peyer's patches



Submucosa

Brunner's glands

- gl. duodenale Brunneri
- branched tuboalveolar glands, columnar mucinous cells
- connective tissue reduced to thin septa between glandular lobules
- open to crypts of Lieberkühn

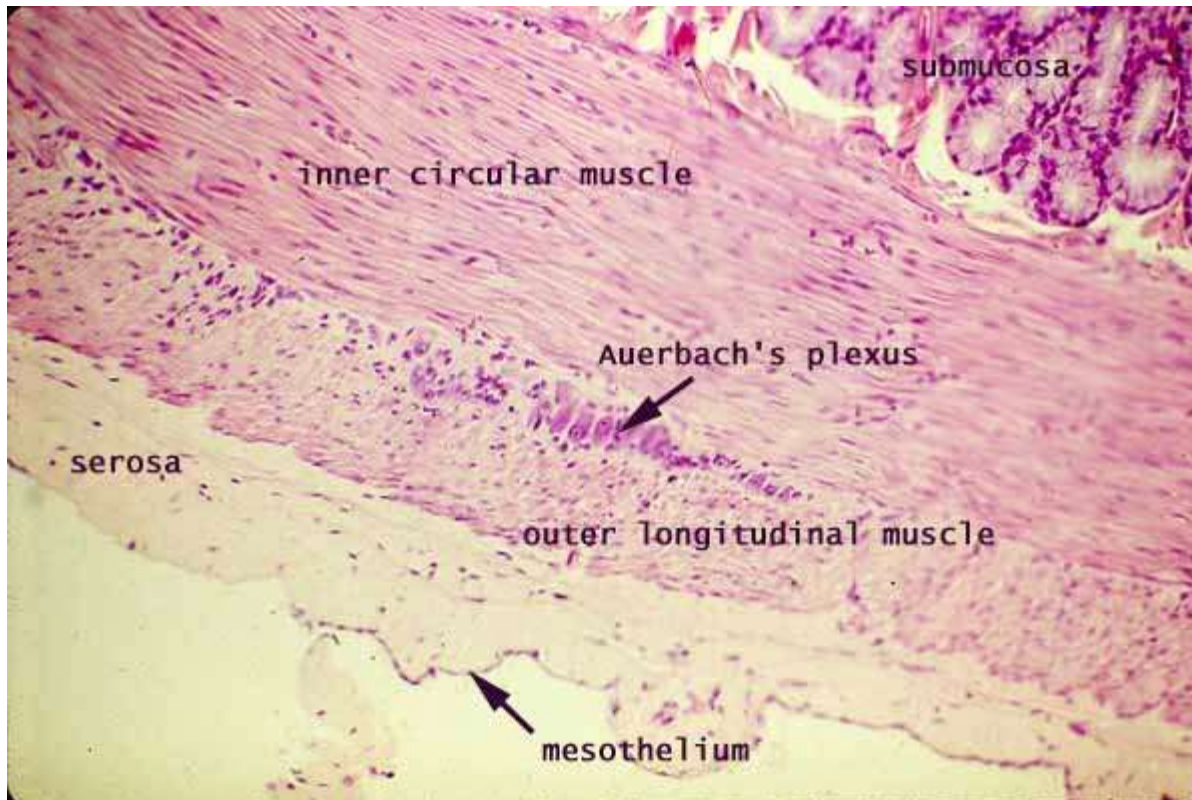


Muscularis externa

- two layers of smooth muscle (inner circular, outer longitudinal)
- plexus myentericus Auerbachi

Serosa

- loose collagen connective tissue + simple squamous epithelium (mesothelium)

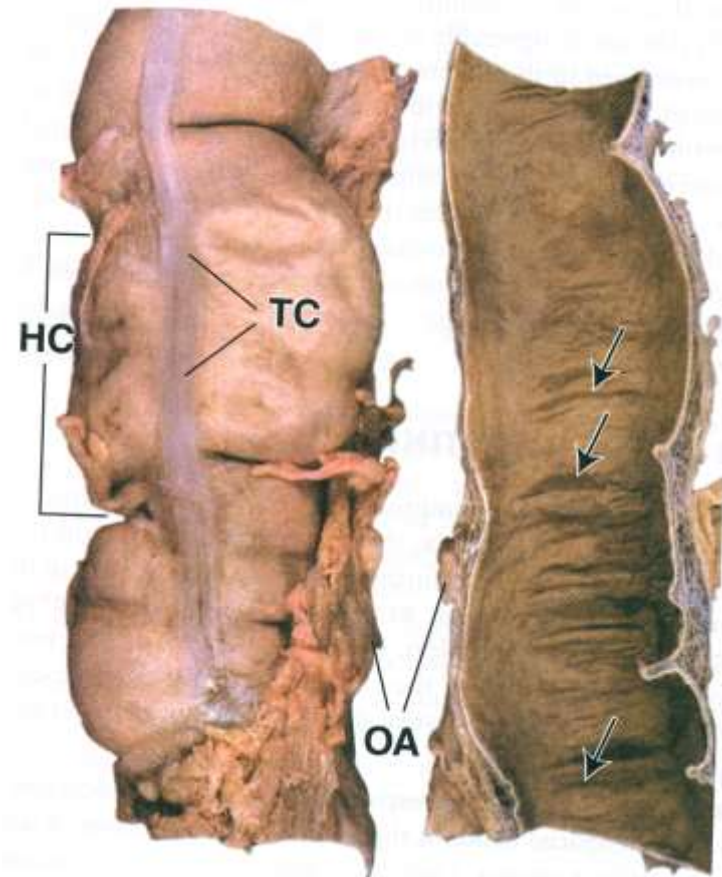


Colon

- no plicae of Kerckring, villi
- muscularis externa – longitudinal layer forms taenie coli
- surface serosa forms appendices epiploicae (adipose)



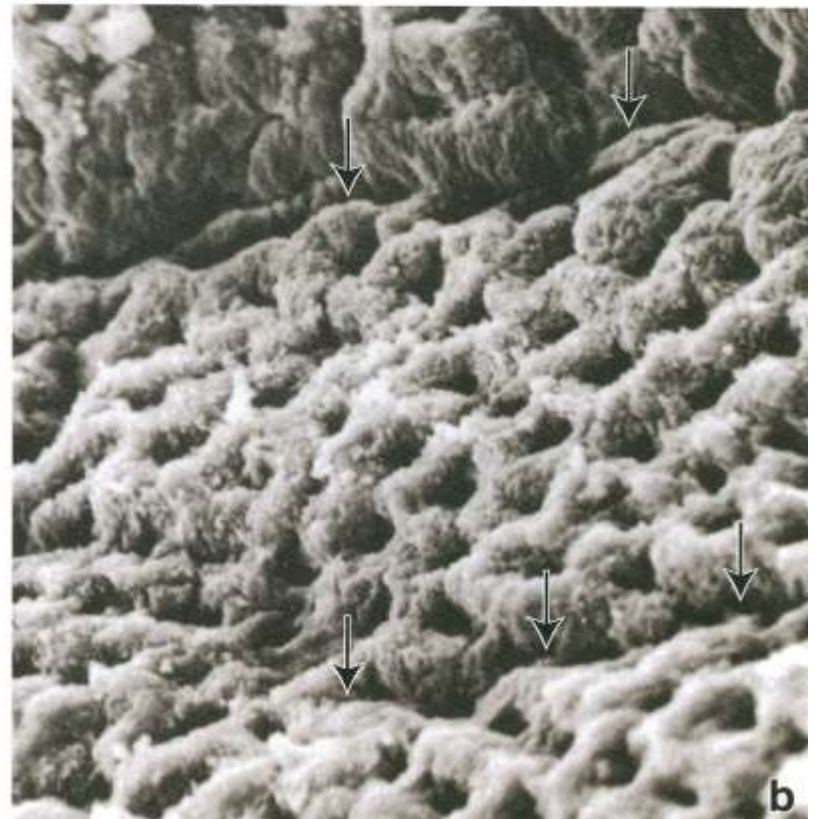
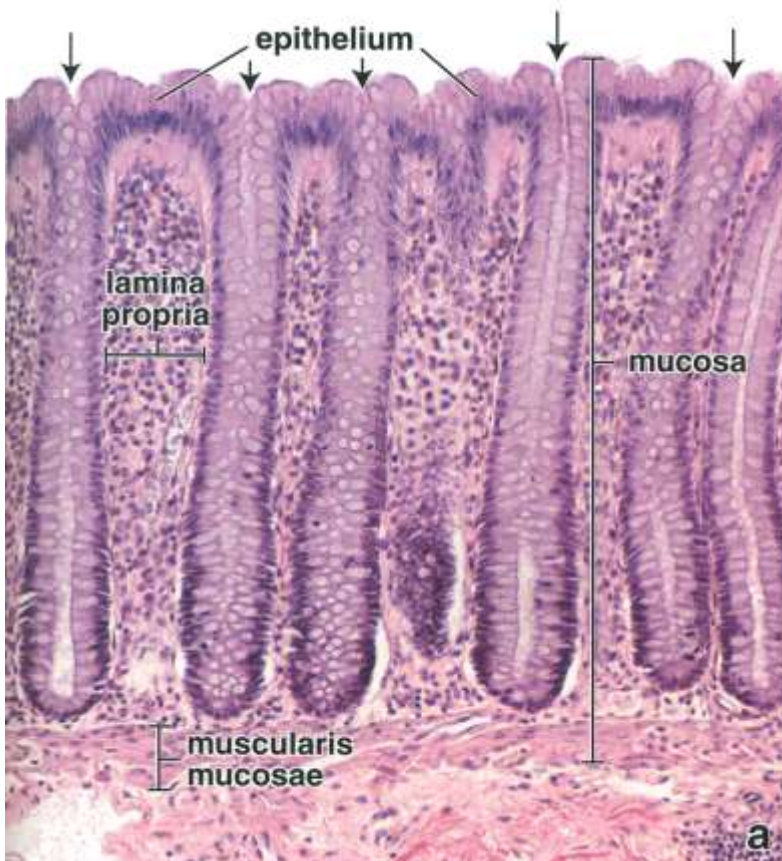
Small intestine



Colon

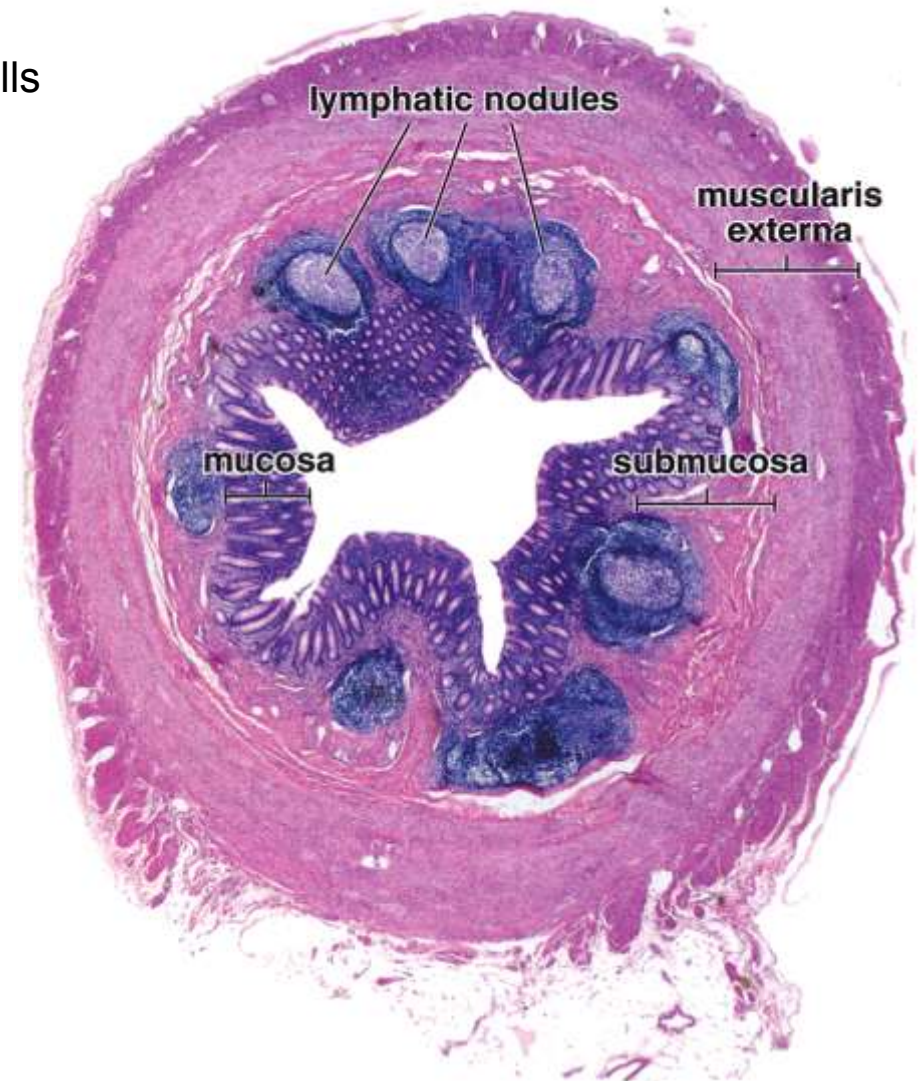
Colon

- absorption of water, electrolytes
- deeper crypts of Lieberkühn, no Paneth cells
- abundant goblet cells
- abundant lymphatic follicles in l. propria (GALT)



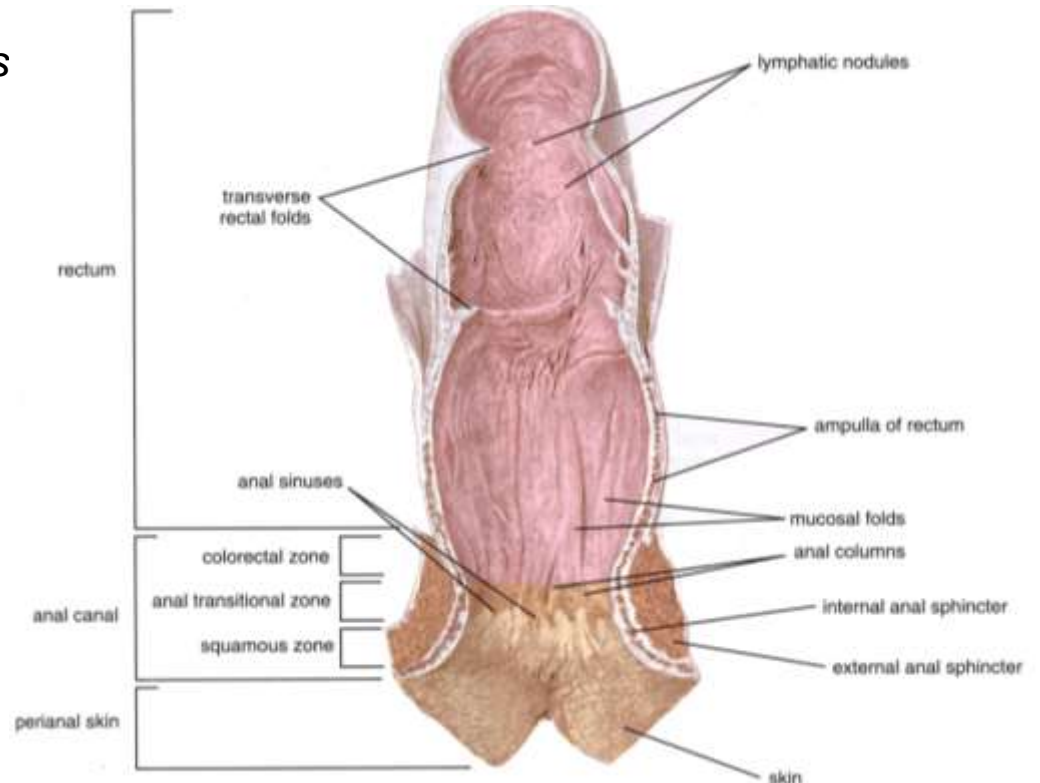
Apendix

- develops from and is connected to caecum 8-10 cm (0,5-1cm)
- continuous longitudinal layer of m. externa
- lymphatic follicles reaching submucosa
- irregular crypts of Lieberkühn with Paneth cells

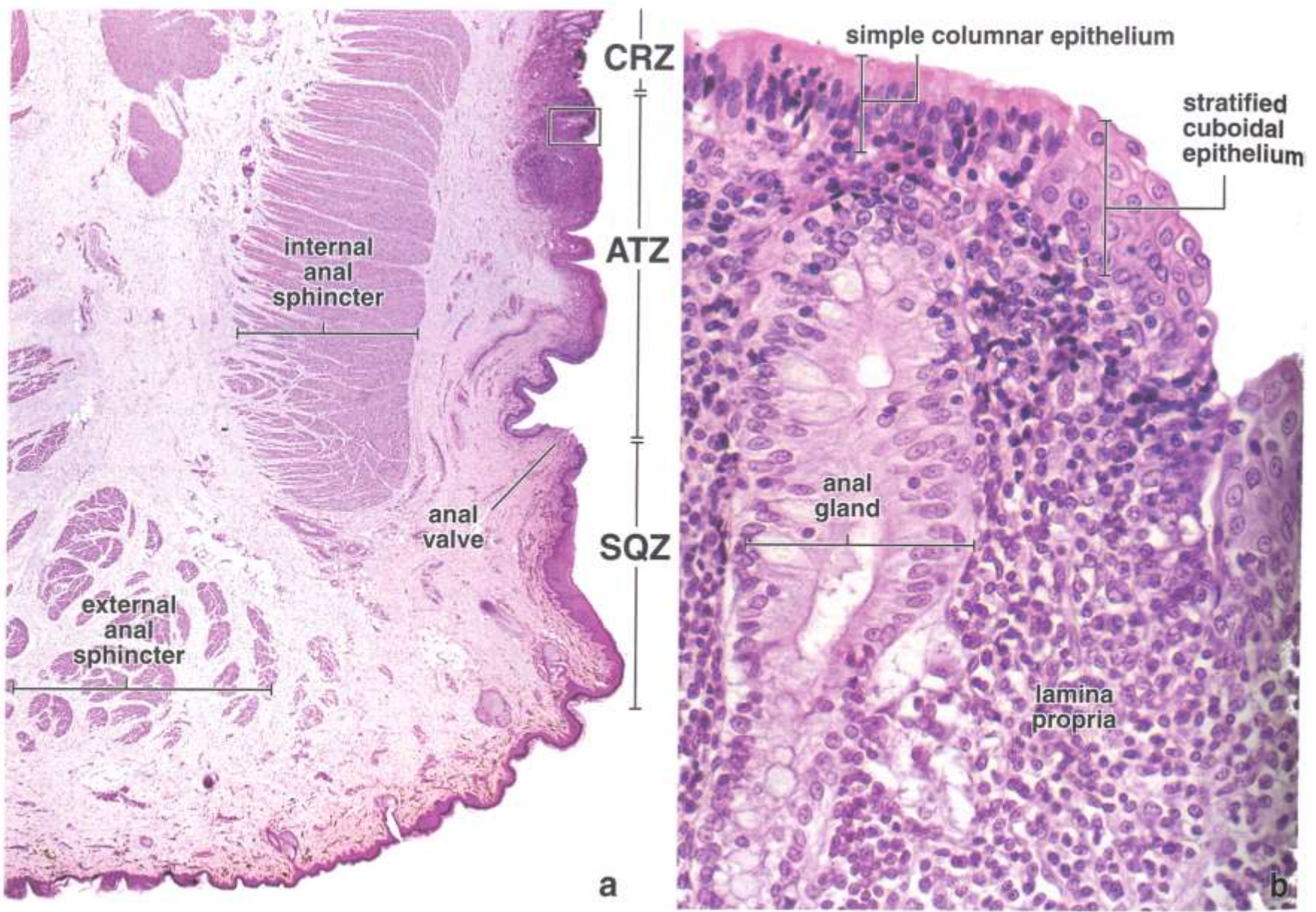


Rectum and anal canal

- Pars pelvina
 - *plicae transversae recti*
 - histological architecture identical to colon
- Canalis analis
 - anulus hemorrhoidalis – **no L. crypts, simple columnar epithelium replaced by stratified squamous epithelium**
 - rich venous plexus
 - *columnae rectales*
 - *sinus rectales* and *valvulae rectales*
 - *zona cutanea* – typical skin



Rectum and anal canal



- **General architecture of hollow organs and gut tube:** mucosa (l. epithelialis m., l. propria, l. muscularis m.), submucosa, t. muscularis externa, serosa (l. propria s., l. epith. s.), adventitia
- **Esophagus** - structure, epithelium, mucosal and submucosal glands, differences in t. muscularis ext.
- **Stomach** – anatomical and histological structure, mucosa - areae gastricae, foveolae gastricae, gastric glands (pyloricae vs. propriae), localization, ultrastructure and function of gl. gastricae propriae and its cells (chief, parietal, neck, enteroendocrine)
- **Small and large intestine, appendix** - anatomical and histological structure, mucosa, glands (crypts of Lieberkühn, Brunner's glands), cell types of intestinal mucosa, lymphatic system, modifications of intestinal wall
- **Rectum and anal canal** - anatomical and histological structure, mucosa, epithelium, description of associated structures

Embryonal development

- Development of primitive gut and its derivatives, embryonic flexion, differentiation and characteristics of individual regions and associated organs

Study materials



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- **Ovalle&Nahirney: Netter's Essential Histology, 2008**
- **Klika&Vacek: Histologie, 1974**
- **Ross&Pawlina: Histology (a text and atlas), 2011**
- **Ross&Romrell: Histology (a text and atlas), 1989**
- **Berman: Color Atlas of Basic Histology**
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- **Čech S., Horký D., Sedláčková M.: Přehled embryologie člověka, Brno, LF MU, 2011**
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