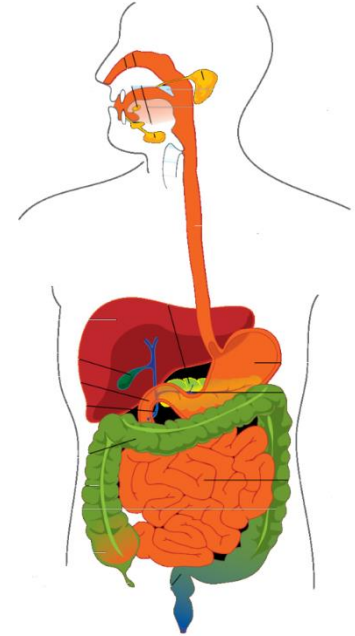


DIGESTIVE SYSTEM II

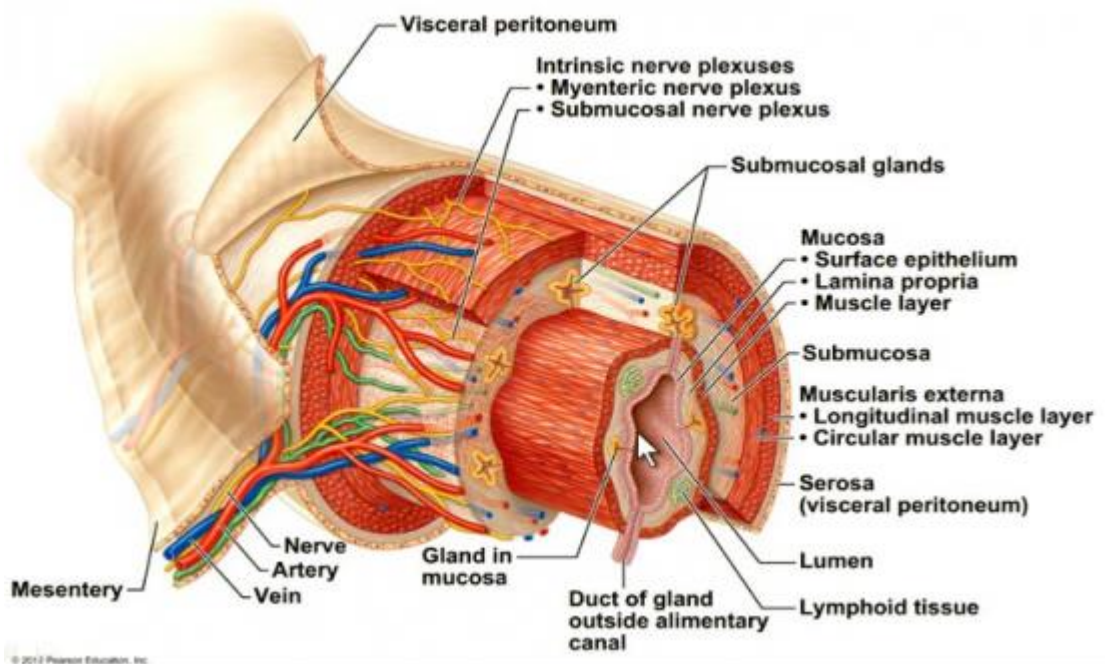


- Microscopic anatomy of pharynx, esophagus, stomach, small and large intestine, rectum
- Early embryonic development of GIT

Petr Vaňhara

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ALIMENTARY CANAL

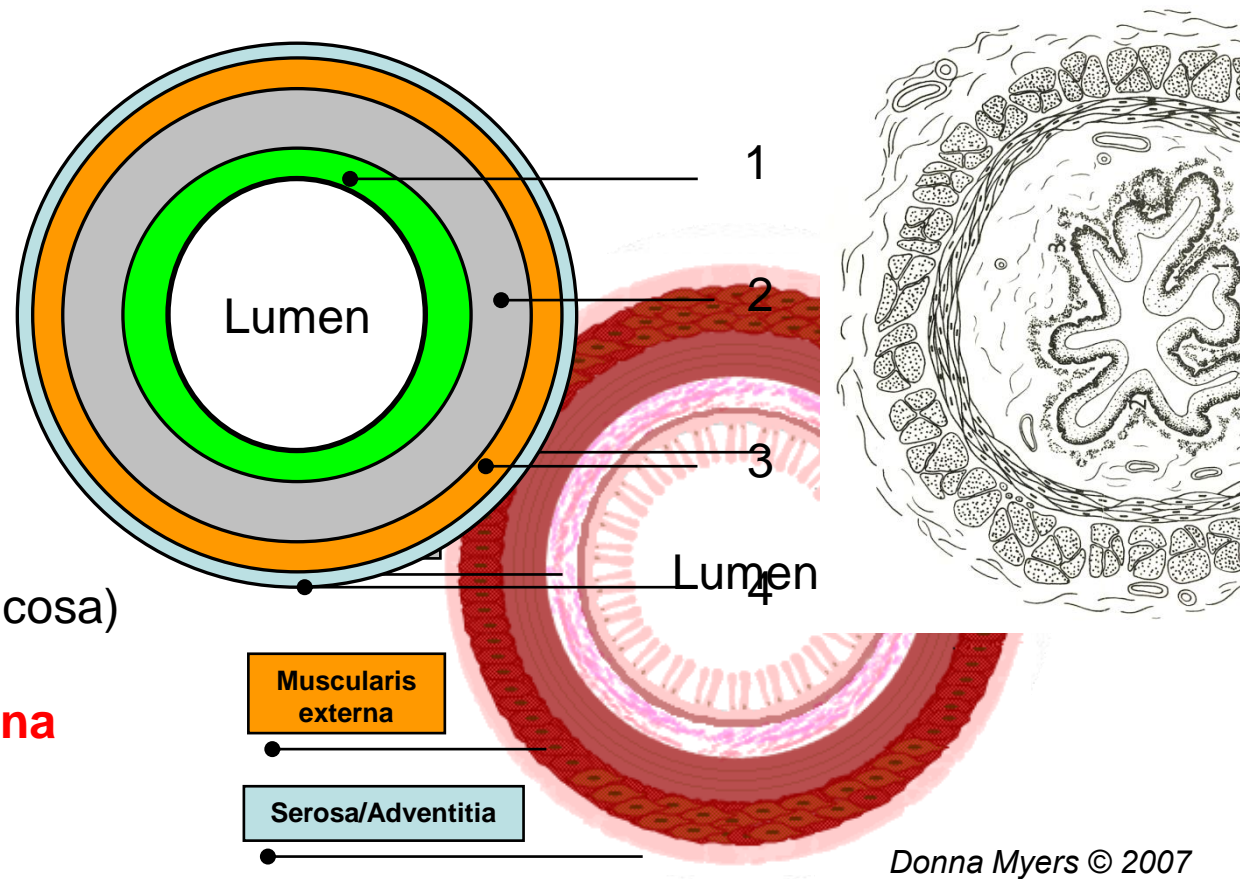


General architecture of hollow organs

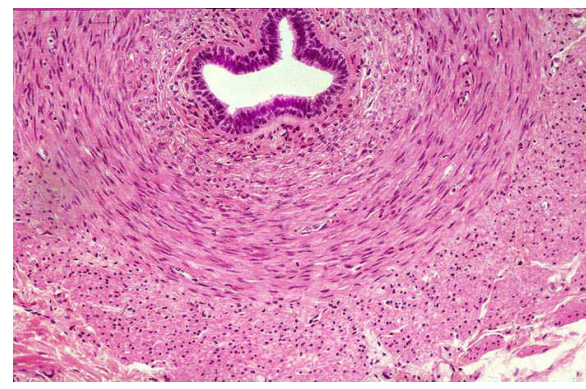
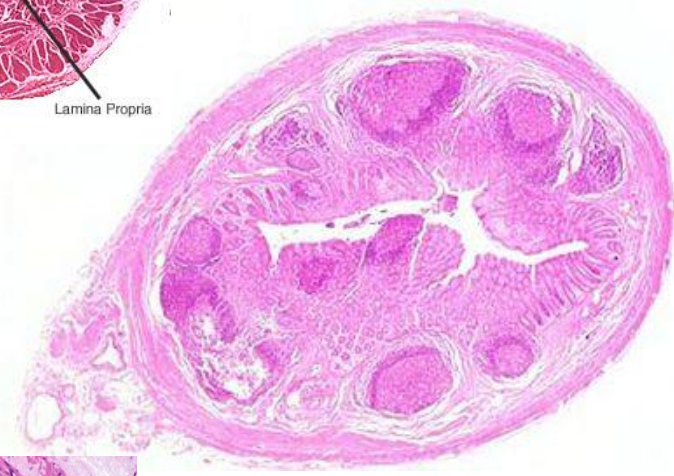
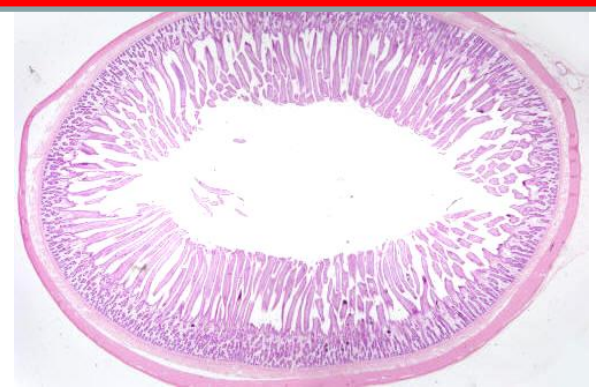
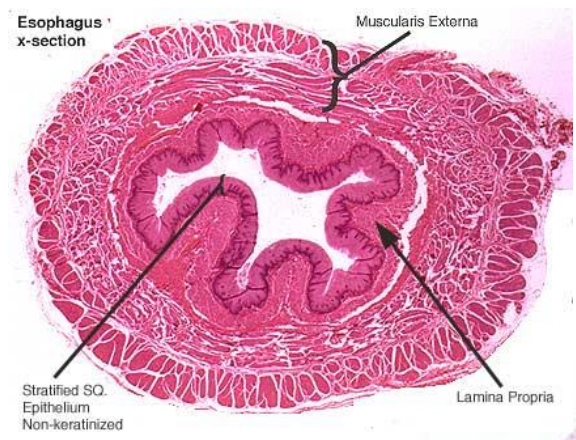
General architecture of hollow organs incl. gut tube

Four layers

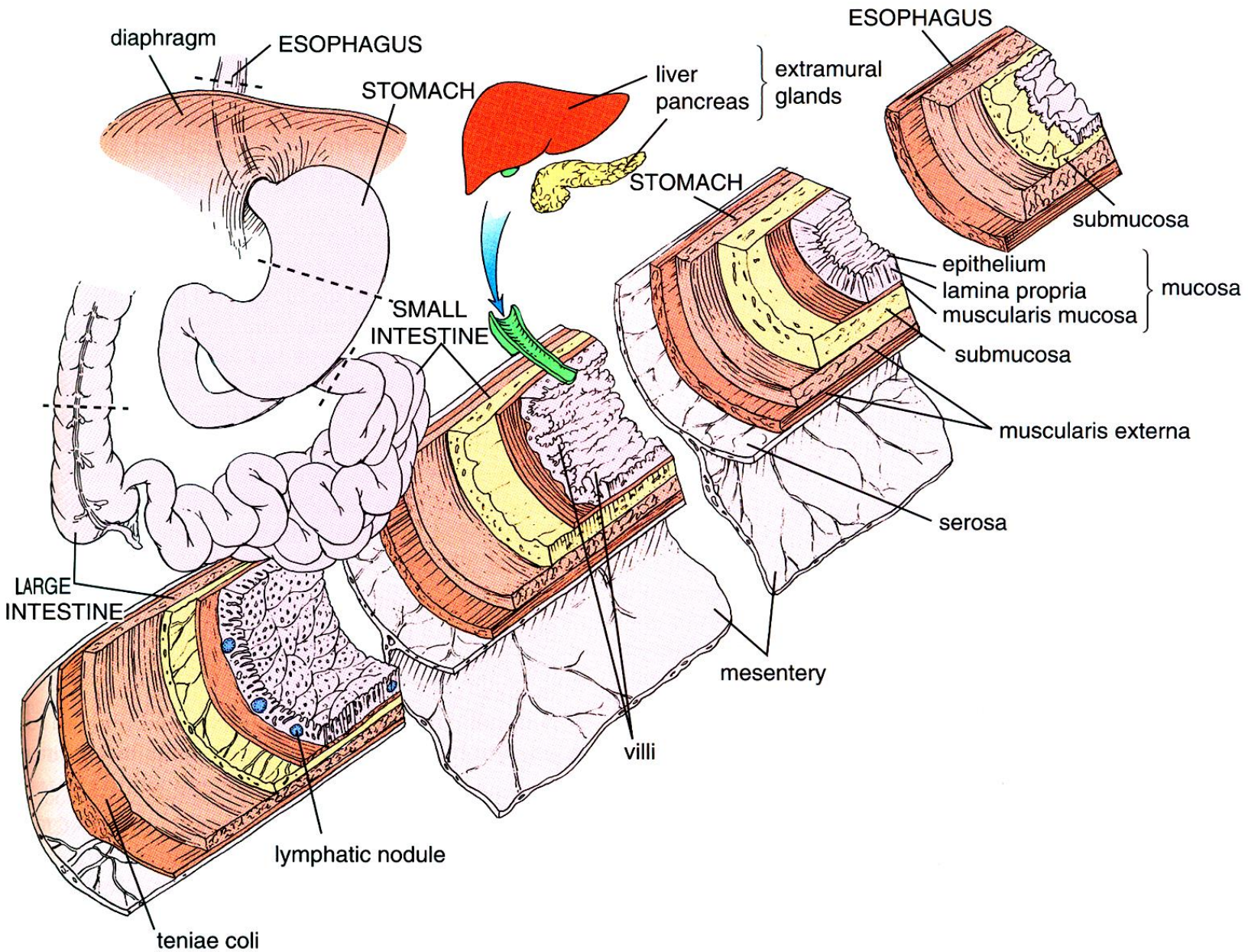
- 1. **Mucosa** (Tunica mucosa)
- 2. **Submucosa** (Tela submucosa)
- 3. **Tunica muscularis externa**
- 4. **Serosa/adventitia**



GENERAL ARCHITECTURE OF HOLLOW ORGANS



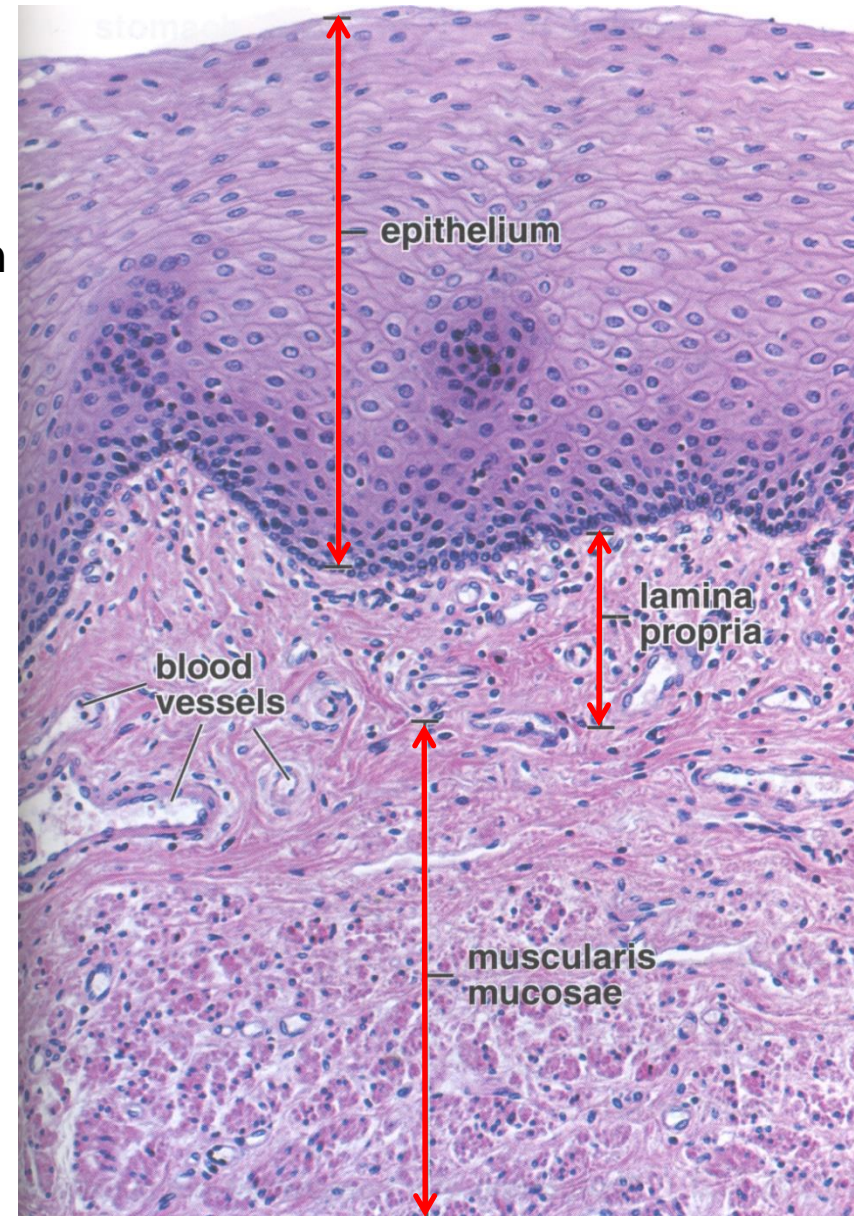
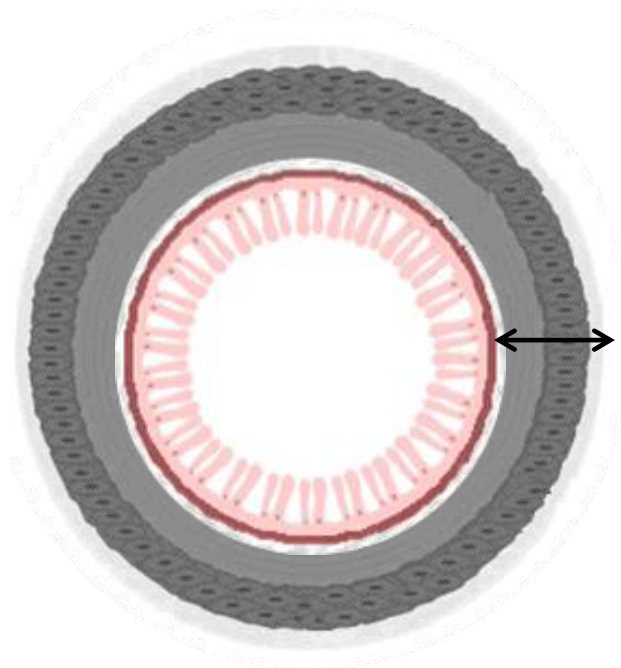
GENERAL ARCHITECTURE OF HOLLOW ORGANS



GENERAL ARCHITECTURE OF HOLLOW ORGANS

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

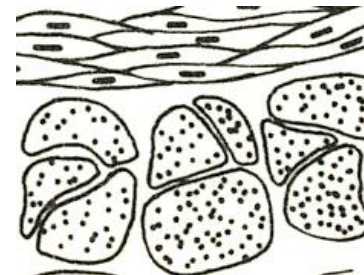
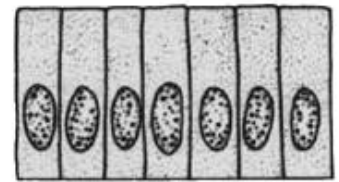
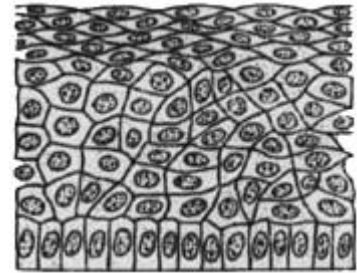
- epithelium type corresponding to function of gut tube
- oral cavity, pharynx, esophagus, anus – **stratified squamous ep.**
- stomach, intestine – **simple columnar**
- **mucus** - secreted by mucosal or submucosal glands (oral cavity, esophagus), secretory epithelium (stomach) or goblet cells (intestine)

- 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

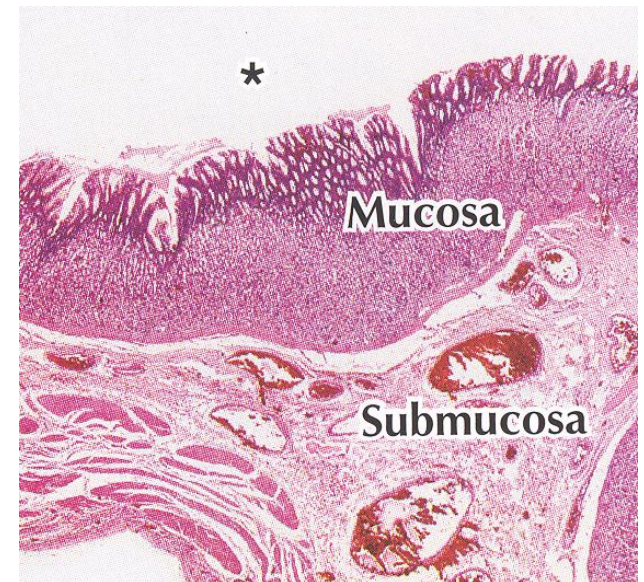
- smooth muscles in two layers (inner circular, outer longitudinal)
- small mechanical movements of mucosa facilitating secretion and absorption independently on peristaltic movements.



Submucosa (Tela submucosa)

Submucosal connective tissue

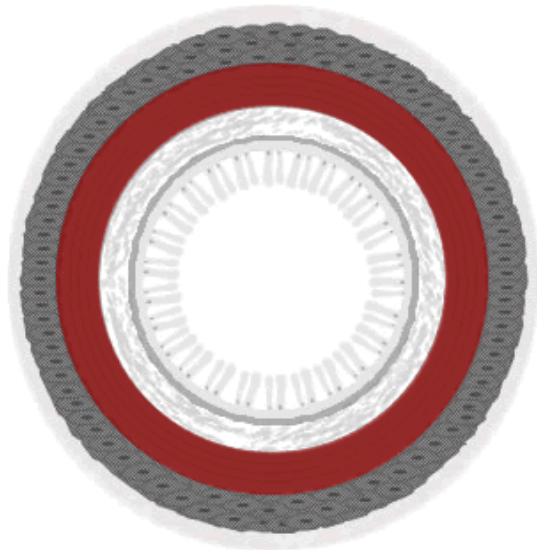
- distinct layer of loose connective tissue
- defines shape of mucosa (rugae, plicae)
- larger blood and lymph veins nourishing mucosa, t. muscularis externa and t. serosa
- **innervation** – nerve plexus - **plexus submucosus Meissneri**
= groups of multipolar neurons and small ganglions, visceral sensory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



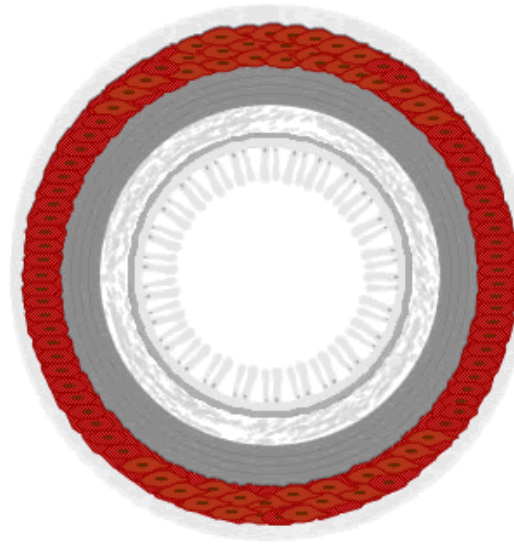
GENERAL ARCHITECTURE OF HOLLOW ORGANS

Outer muscular layers (Tunica muscularis externa)

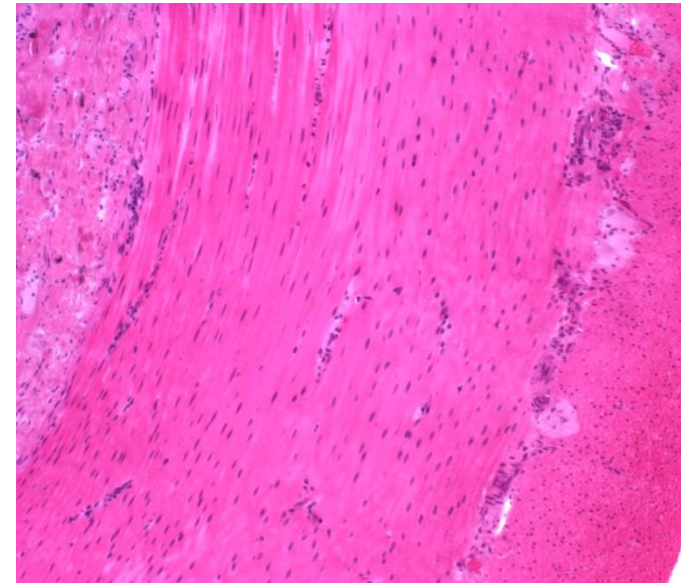
- Two concentric, thick layers of smooth muscle, separated by thin layer of connective tissue
- Inner – **circular**, outer – **longitudinal** (spiral)
- Myenteric (Auerbach) plexus
- Peristaltic – passage through the gut tube
- **Local modifications of m.e.**
 - pharyngoesophageal sphincter + external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



Circular



Longitudinal



Serosa/Adventitia (Tunica serosa/adventitia)

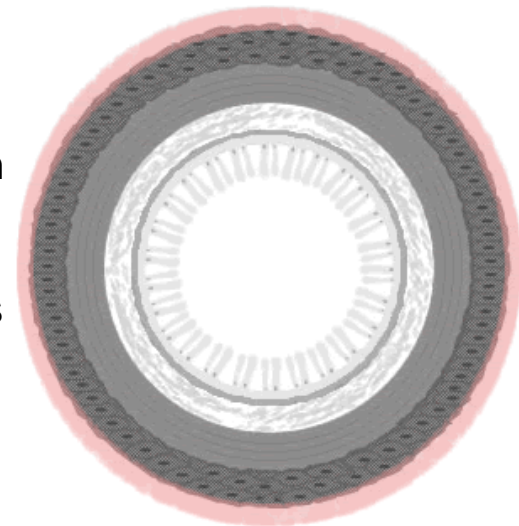
- outermost layer of gut tube

- **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.

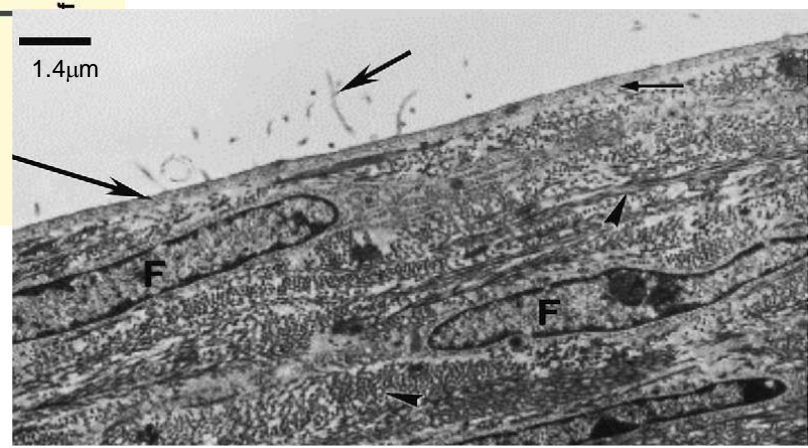
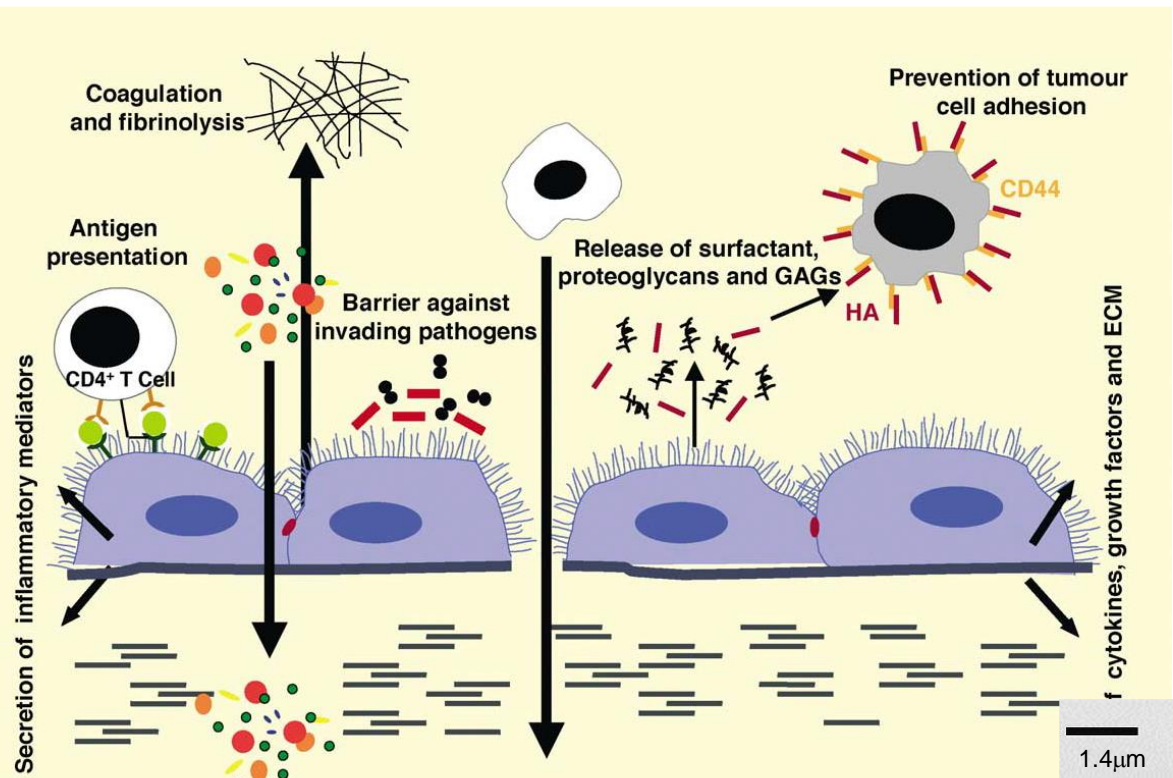
- **Adventitia**

- 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



GENERAL ARCHITECTURE OF HOLLOW ORGANS

Serosa/Adventitia (Tunica serosa/adventitia)



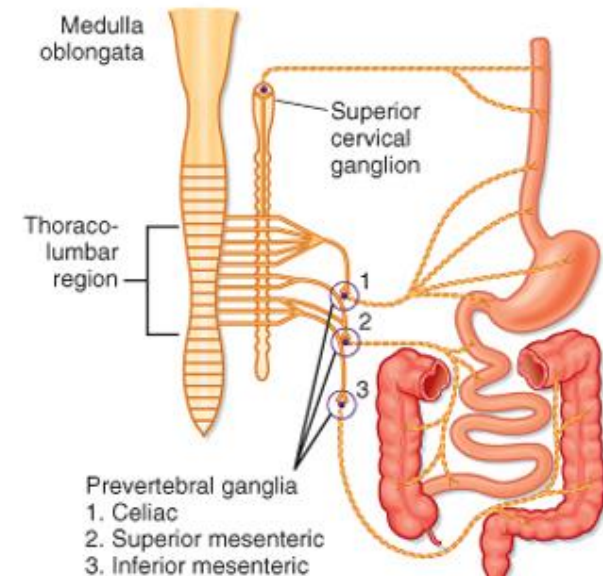
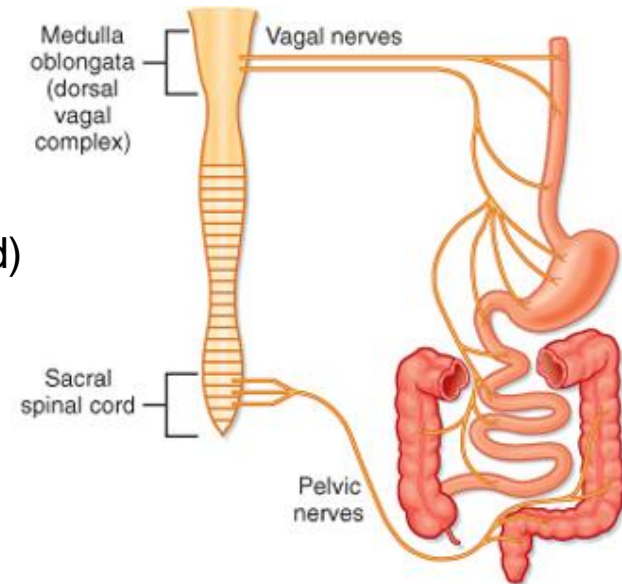
Innervation of the digestive tube

Enteric nervous system

- self-contained nervous system
- numerous ganglia, 100×10^6 neurons (more than in spinal cord)
- Meissner submucosal plexus and Auerbach myenteric plexus
- peristaltic motility, secretory function, mucosal movements, regulation of blood flow
- sensory components

Parasympathetic and sympathetic supply

- **parasympathetic supply** mostly by vagus nerve (cranial X), colon and rectum by sacral spinal nerves
- vagus nerve – mostly sensory fibers (from mucosa)
- secretion from glands, smooth muscle contractions
- *inhibits sphincters, stimulates peristaltics and secretion*
- **sympathetic supply** by splanchnic nerves
- vasomotor fibers – control of blood flow
- *activates sphincters, inhibits peristaltics and secretion*



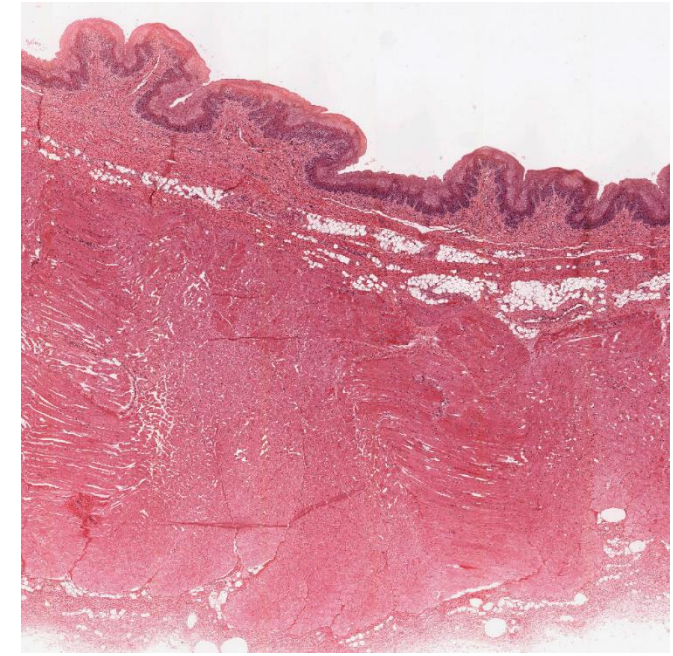
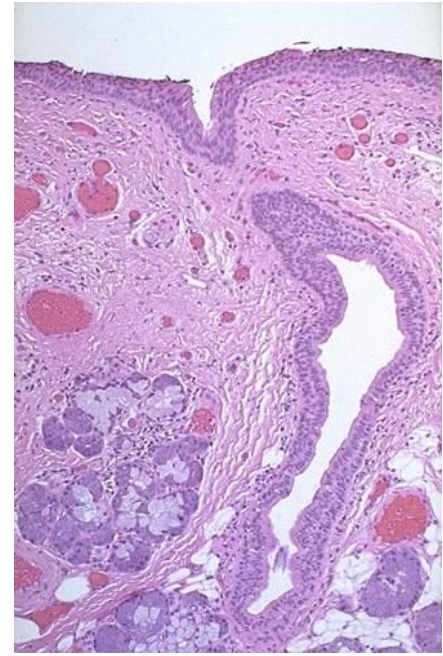
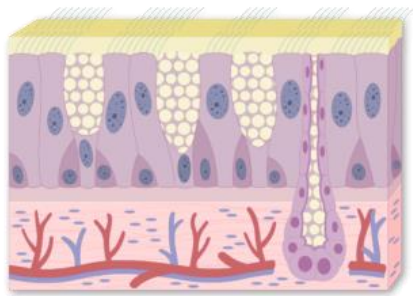
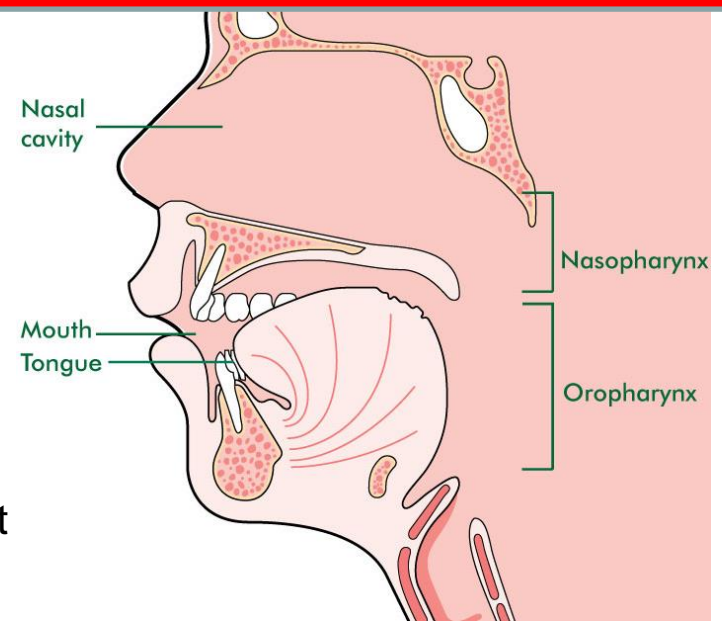
PHARYNX

- pars nasalis

- pseudostratified columnar ciliated epithelium
- seromucous glands

- pars oralis et laryngea

- nonkeratinized stratified squamous epithelium
- mucous glands
- collagen c.t. (lamina propria), typical tela submucosa absent
- skeletal muscles



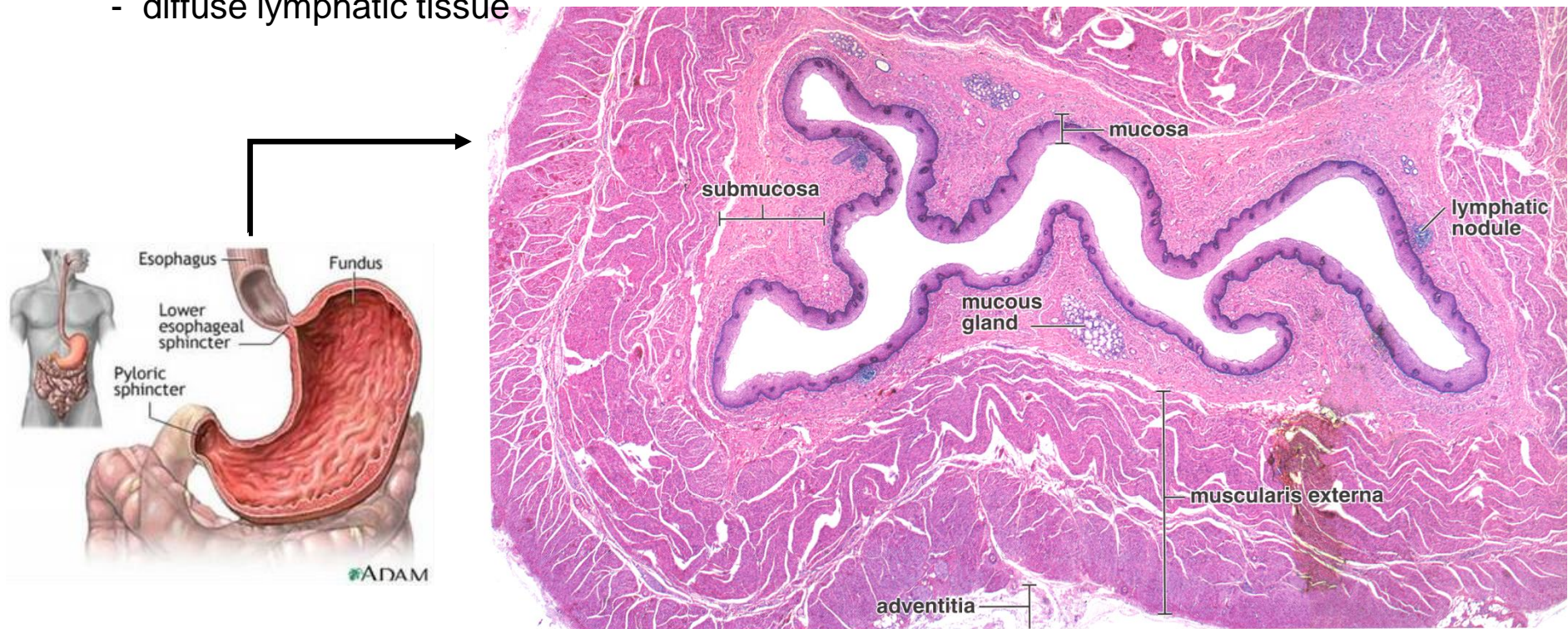
ESOPHAGUS (OESOPHAGUS)

- 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



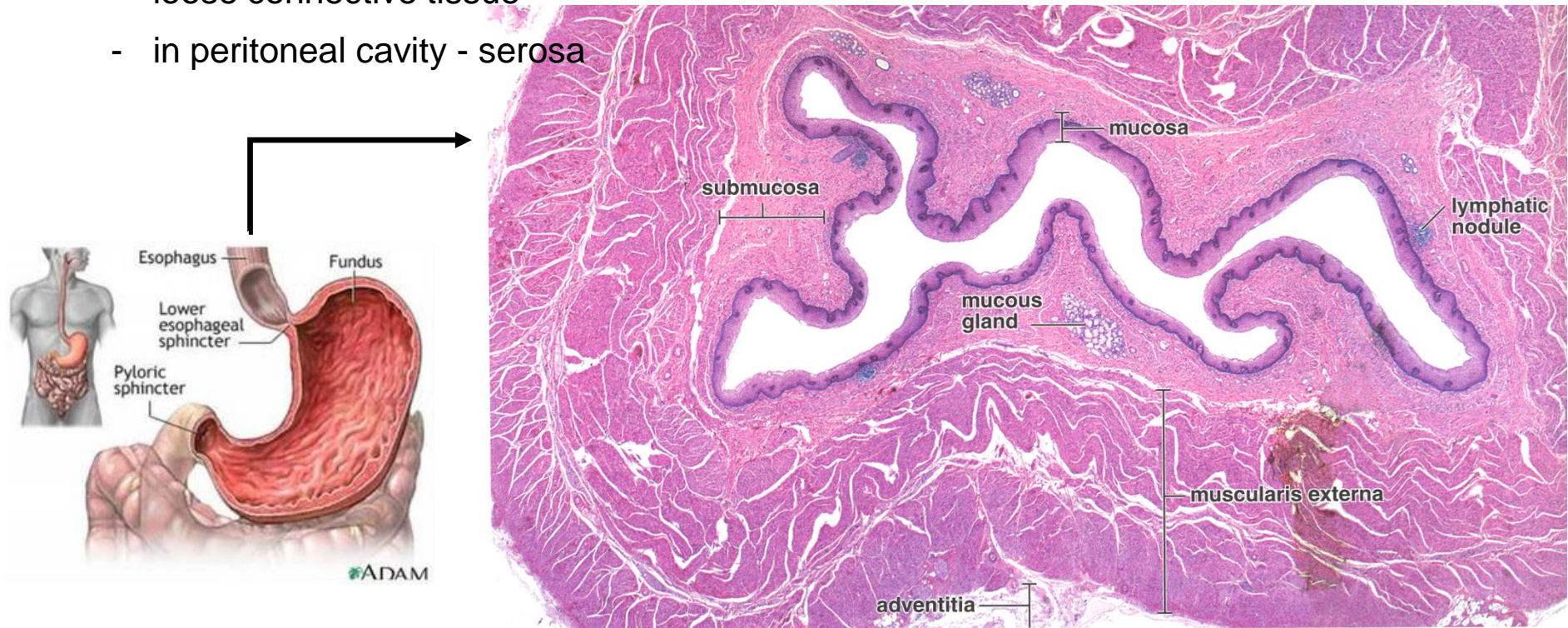
ESOPHAGUS (OESOPHAGUS)

- 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

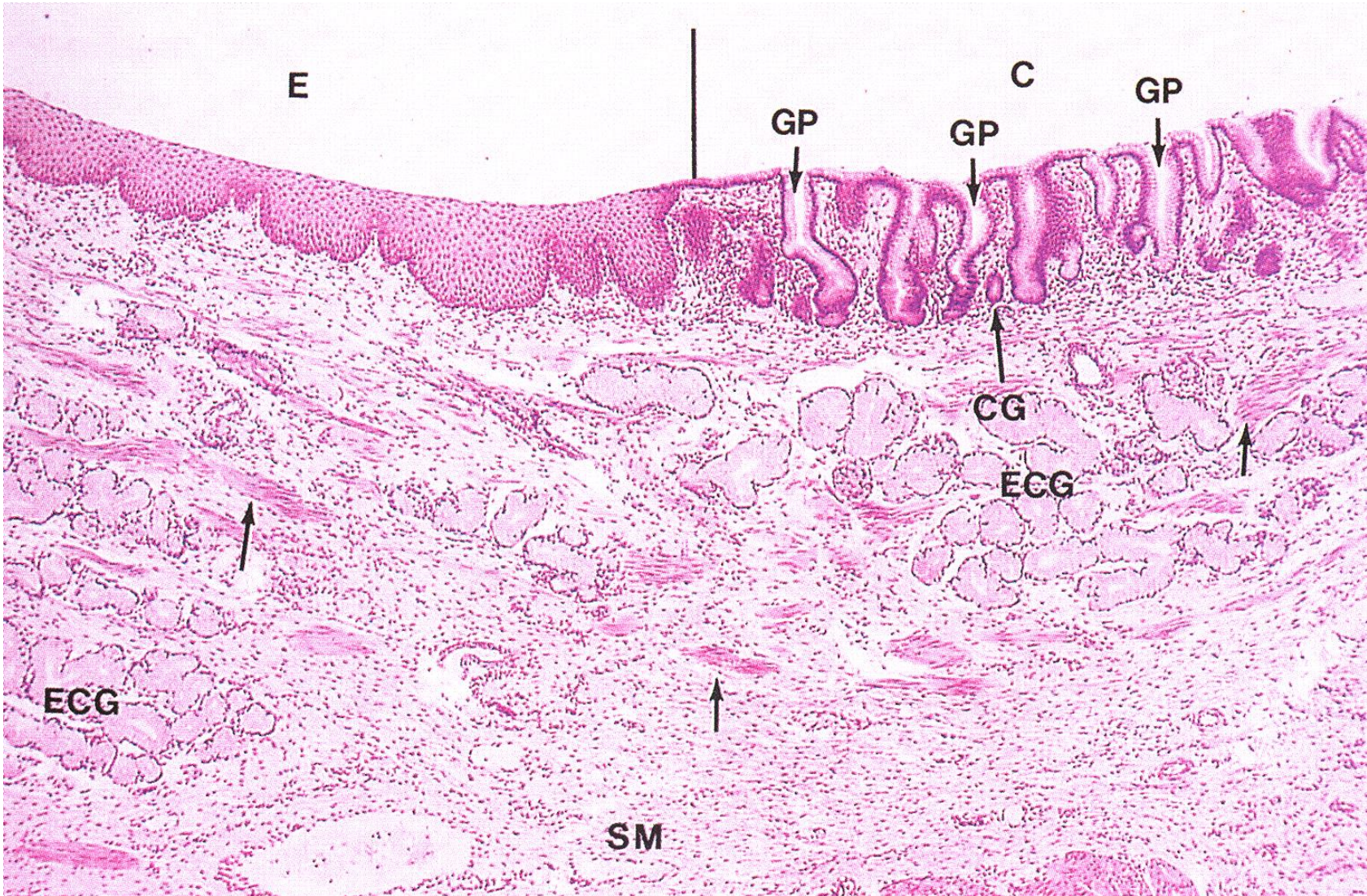
- neck and chest – connects esophagus with surrounding tissue
- loose connective tissue
- in peritoneal cavity - serosa



CARDIO-ESOPHAGEAL JUNCTION

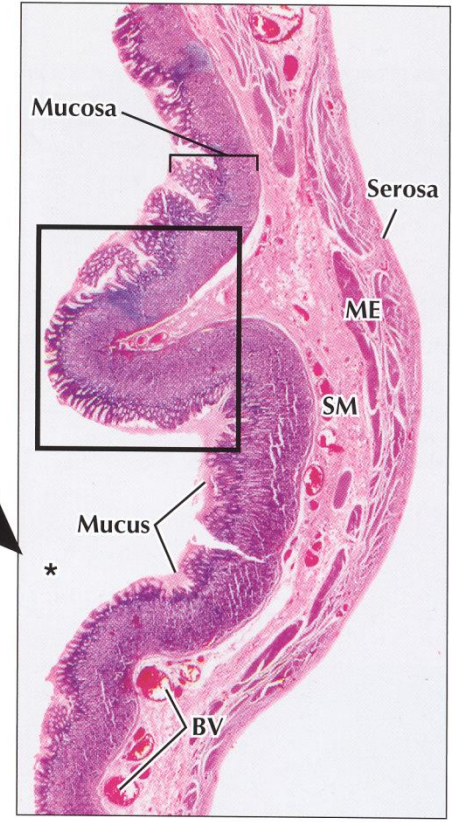
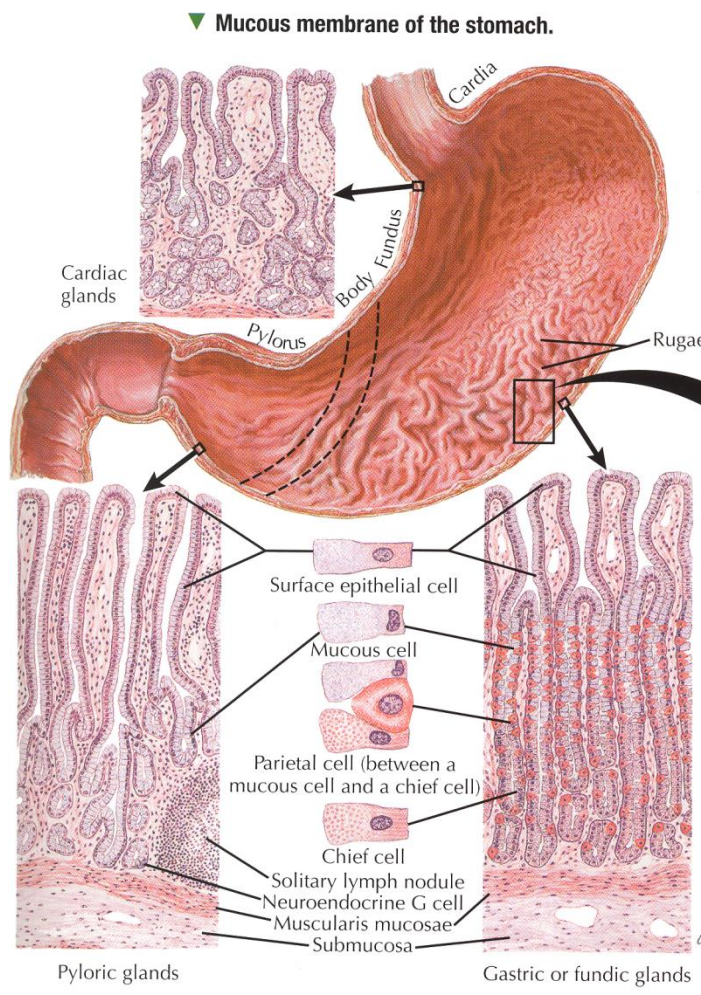
Cardia of stomach – connection with esophagus

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)

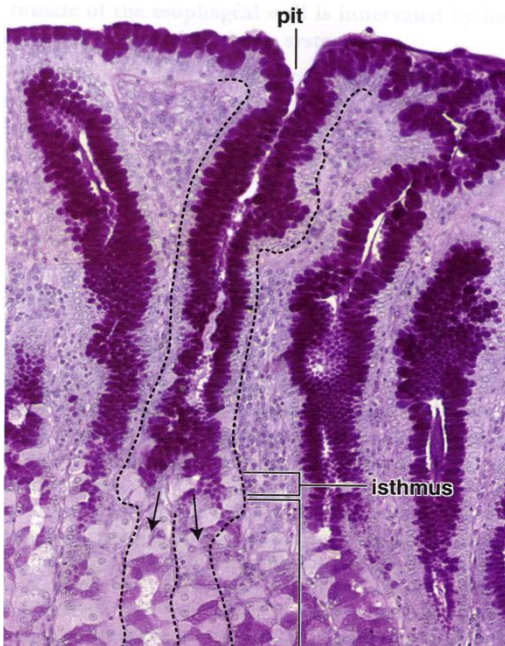
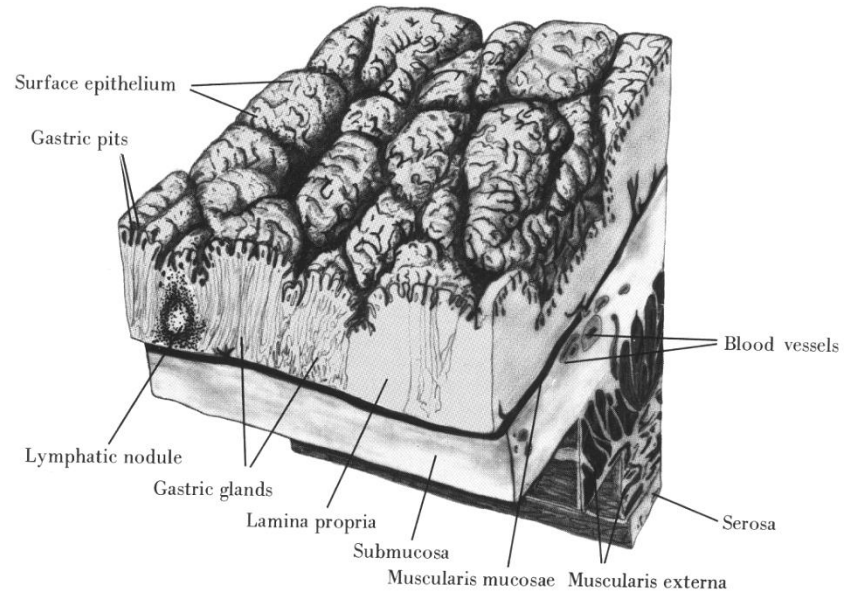


▲ Light micrograph (LM) of the stomach wall showing four concentric layers at low magnification. A thick mucosa (formed mostly of tightly packed gastric glands) lines the lumen (*). The rectangle indicates a ruga consisting of a submucosal connective tissue core covered by mucosa. A thick layer of mucus 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. 10×. H&E.

F. Netter M.D.

STOMACH (VENTRICULUS, GASTER)

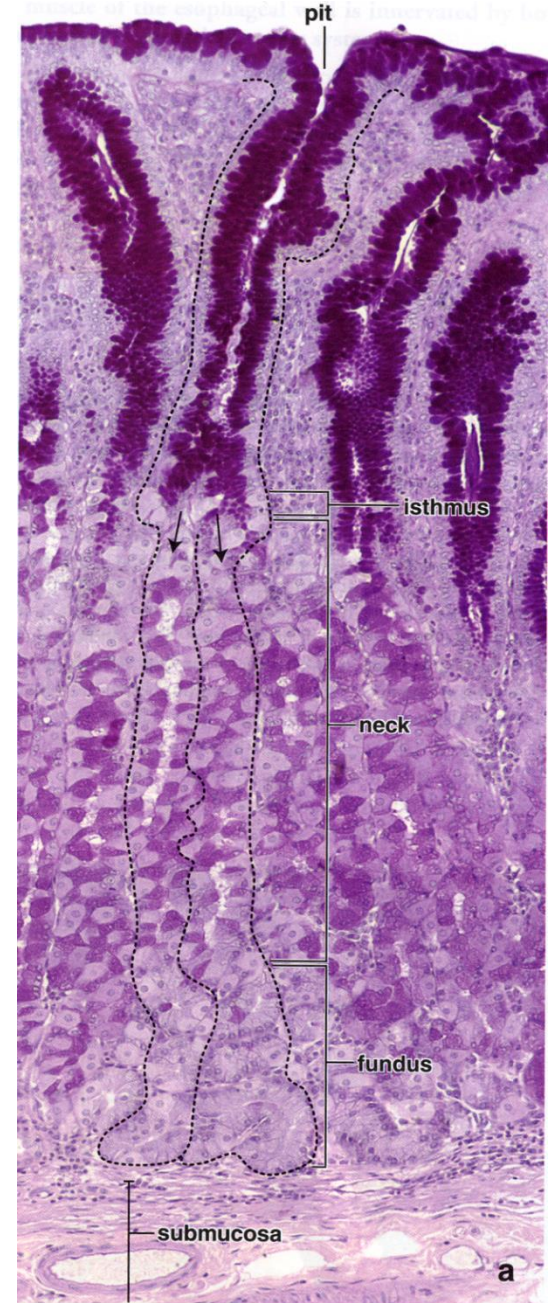
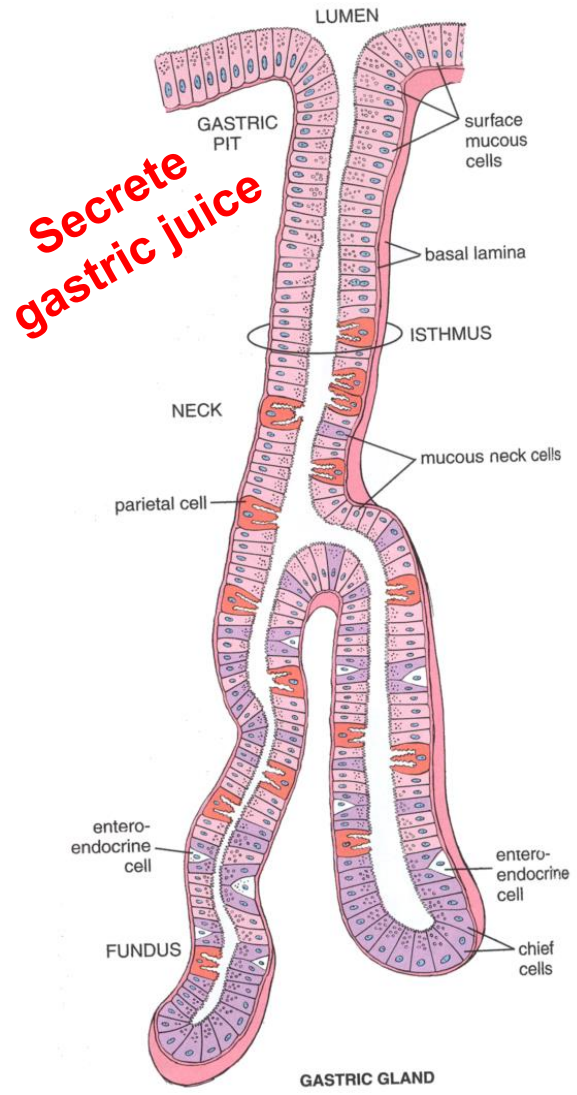
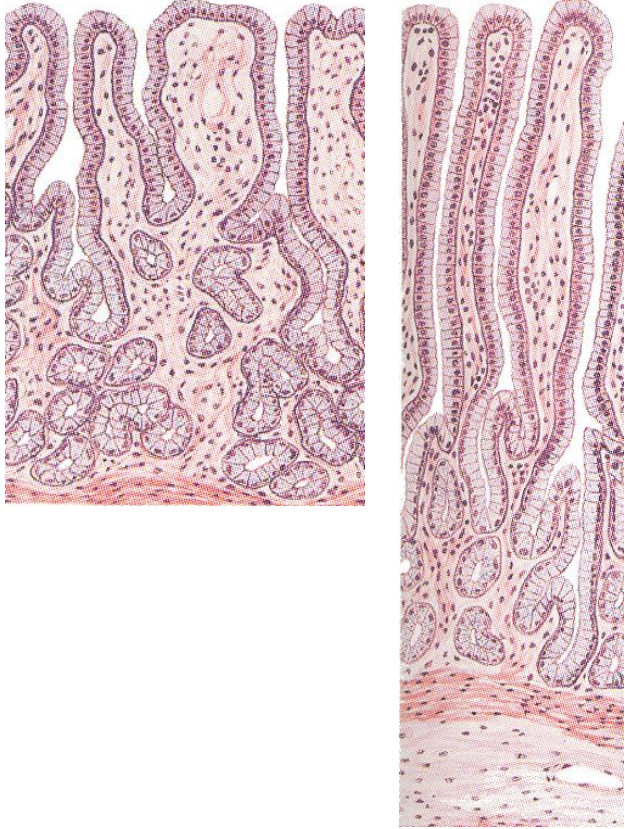
- **Gastric mucosa**
- simple columnar epithelium
- surface epithelium produces mucus
(mucinogenic granules, high content of HCO_3^- , K^+)
= protective function
- *areae gastricae*, *foveolae gastricae*



STOMACH (VENTRICULUS, GASTER)

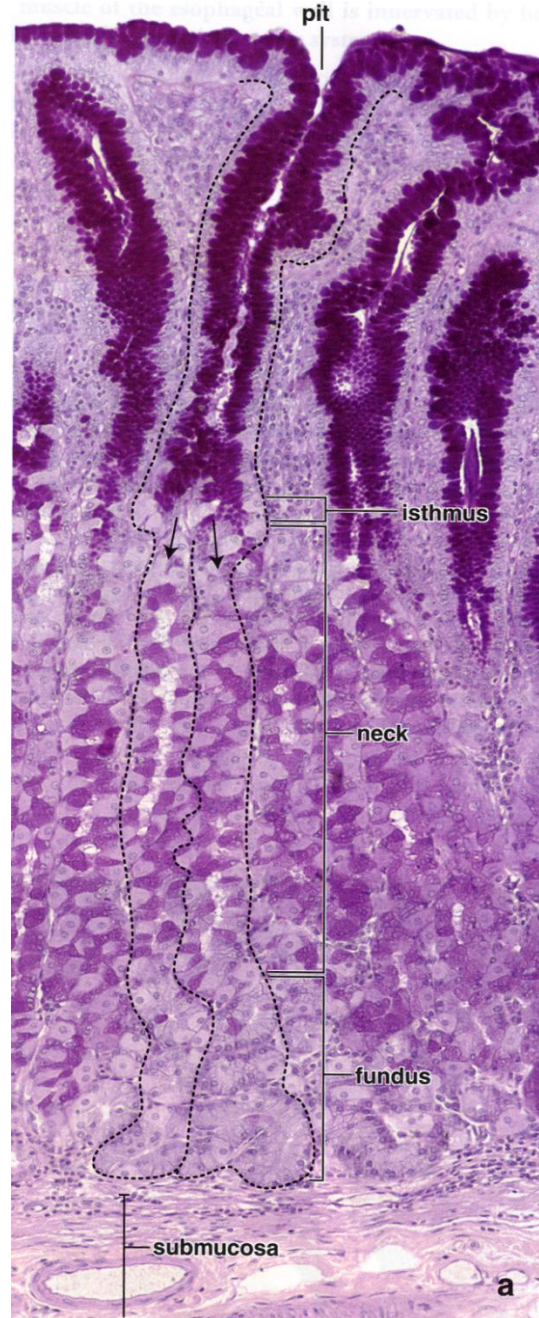
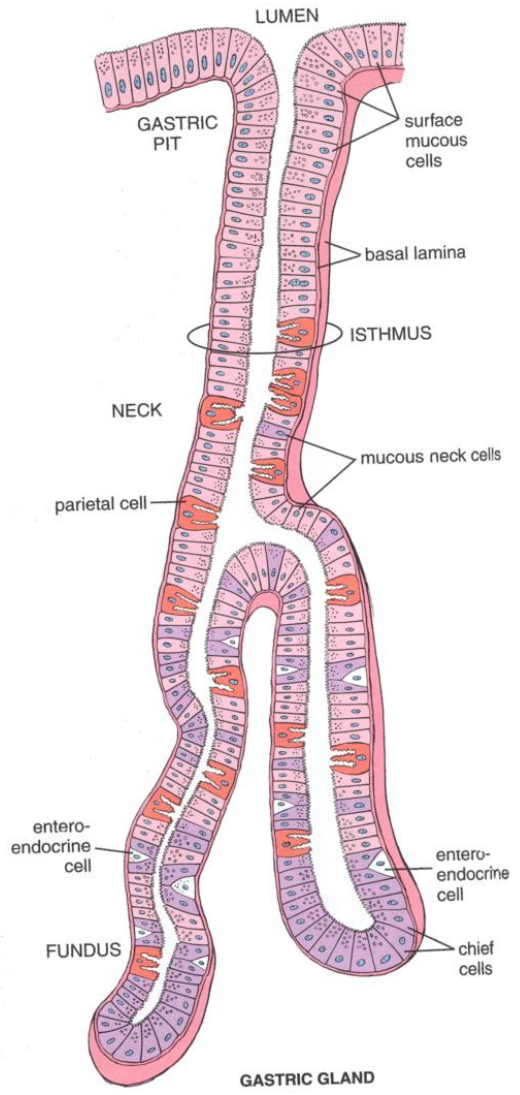
- Gastric mucosa
- L. propria contains large amount of glands

- Gl. cardiacae
 - Gl. pyloricae
 - Gl. gastricae propriae
- Secrete mucus**



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

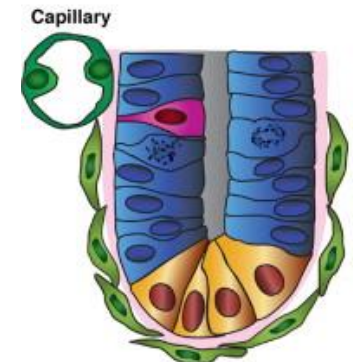
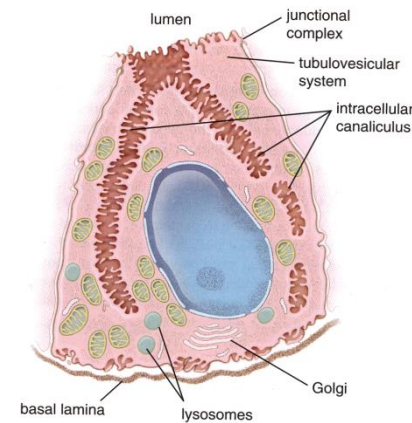
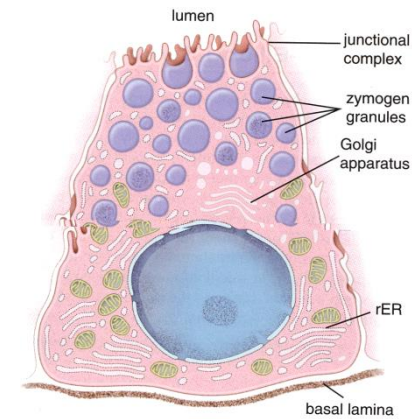
- most abundant, lower part of body and fundus of the gland
- pyramidal shape, basophilic cytoplasm, RER, pepsinogenic granules

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 extracellularly)

neck cells

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

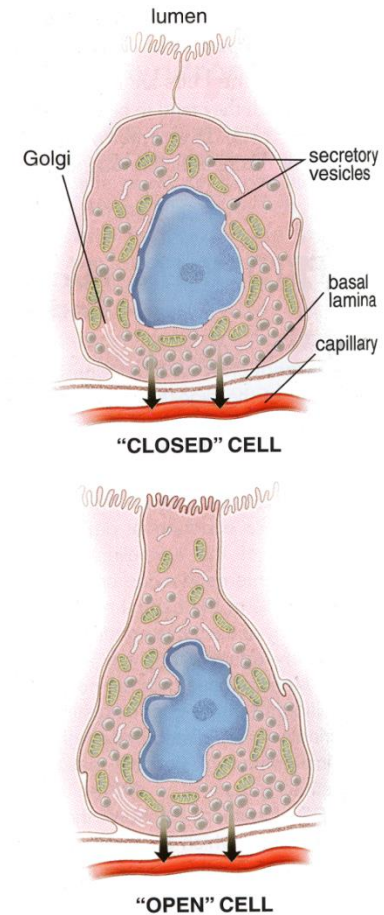
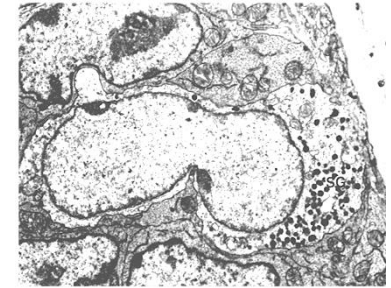


STOMACH (VENTRICULUS, GASTER)

Gl. gastricae propriae

(entero)endocrine

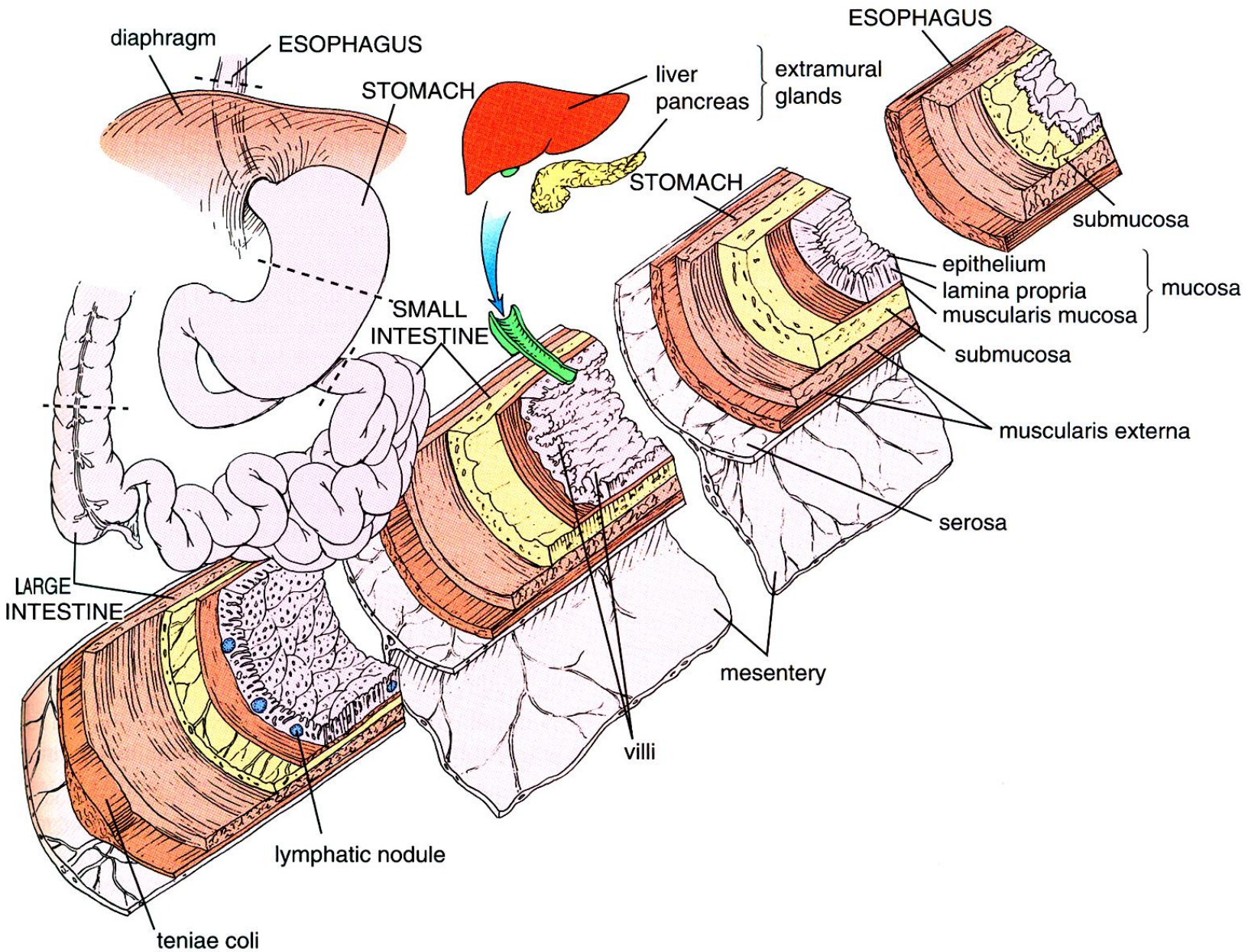
- minor, secretion
- granules
- different cell types with different sensitivity to various histological stainings
- secretion of various biologically active compounds
- DNES/APUD
- GIT chemosensing
- see spring semester lesson- Epithelial tissue



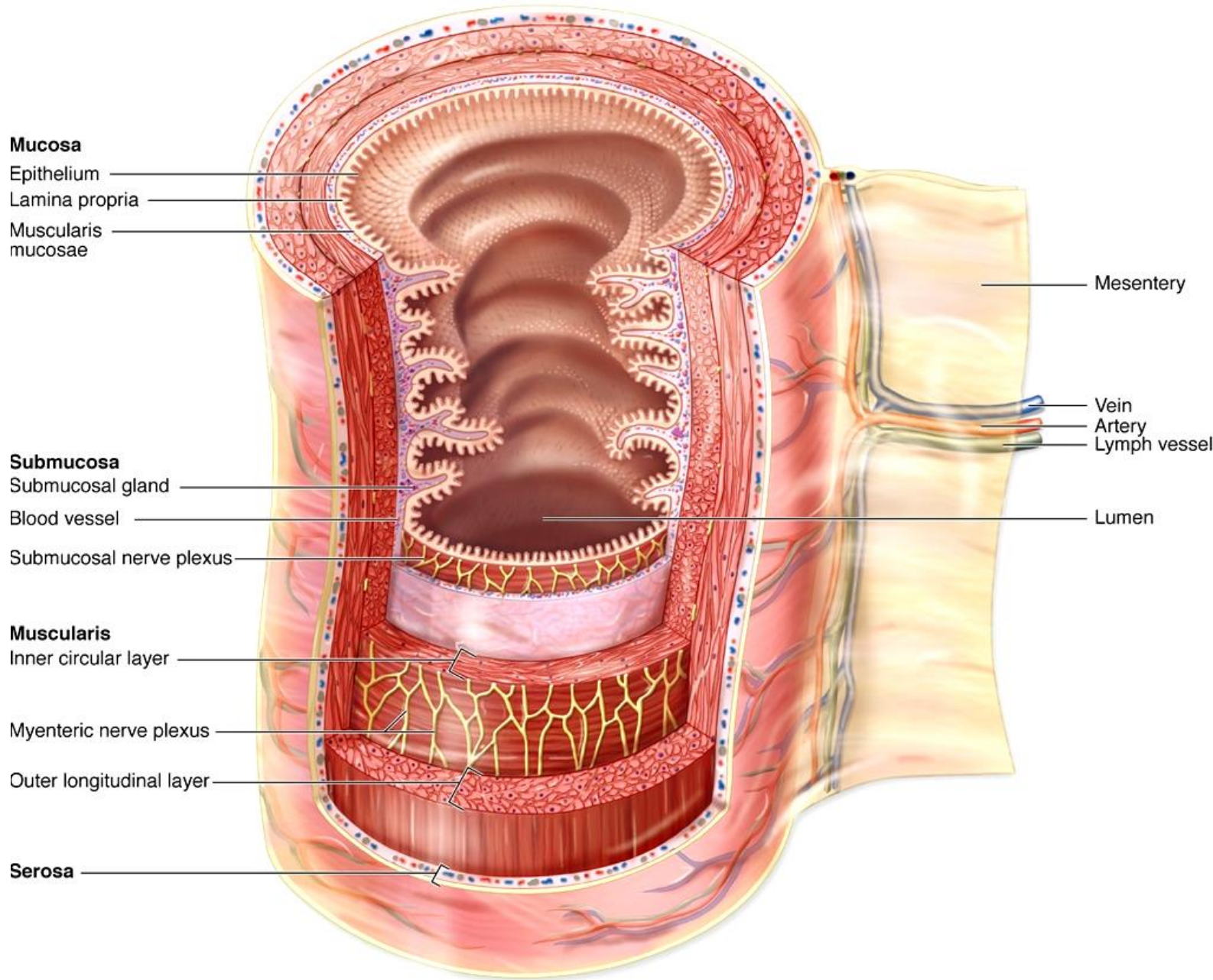
Type	Hormone	Localization/Function
D cells	Somatostatin	- Stomach, intestine, hepatic and pancreatic ducts
EC cells	Serotonin	- Stomach, gallbladder, intestine - Peristaltics
ECL cells	Histamin	- Stomach - HCl secretion
G cells	Gastrin	- Pars pylorica, duodenum - HCl, pepsin secretion
L (EG) cells	Enteroglucagon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

GASTRIC ACID PRODUCTION AND REGULATION

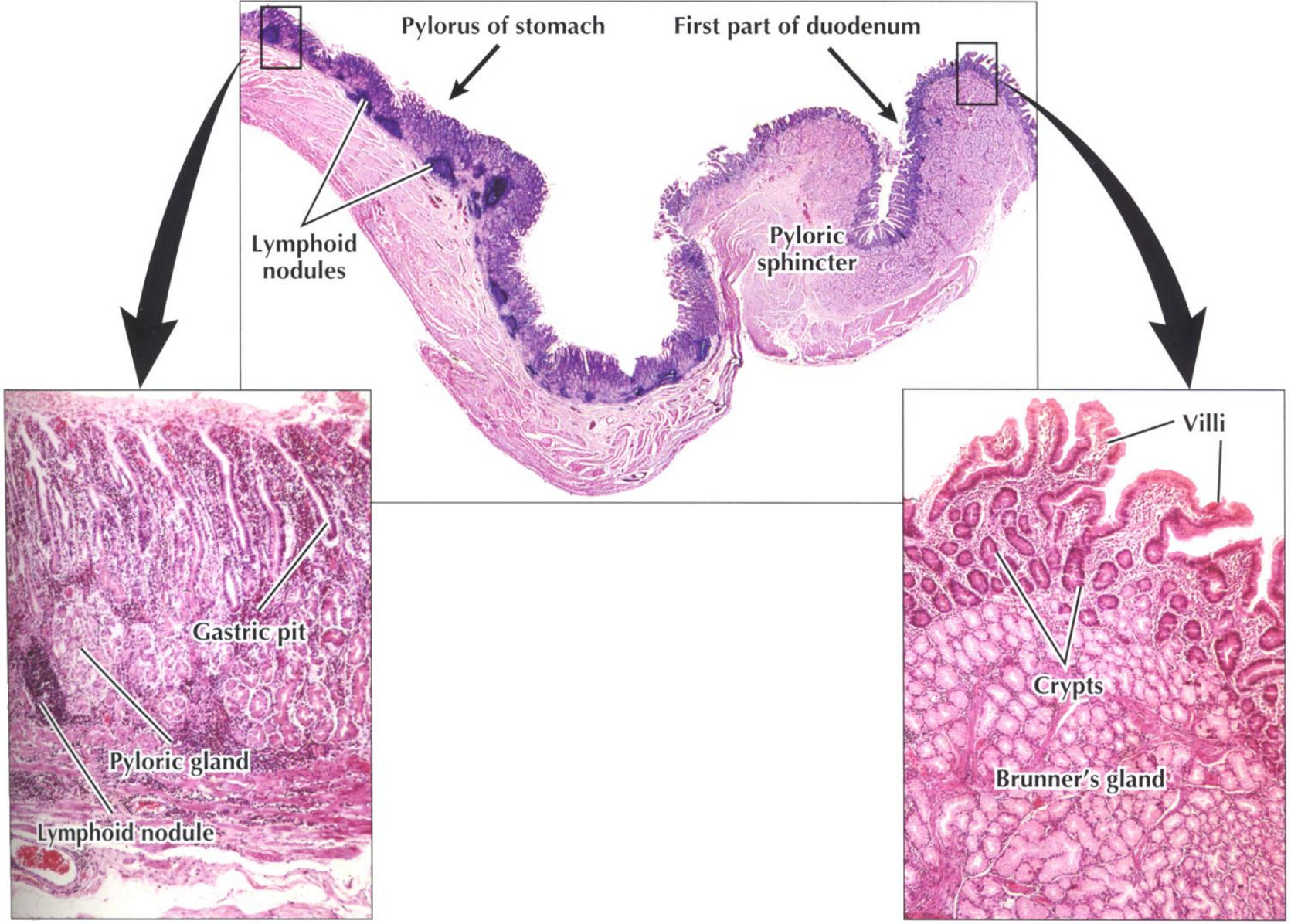
GENERAL ARCHITECTURE OF HOLLOW ORGANS



SMALL INTESTINE - DUODENUM



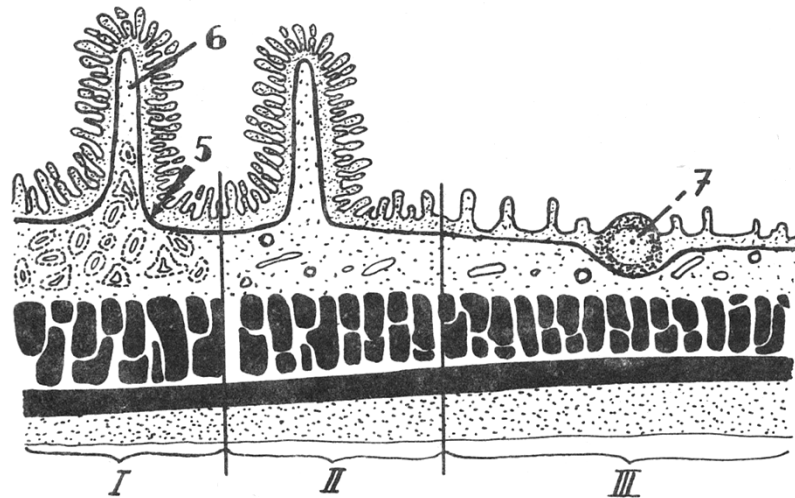
GASTRO-DUODENAL JUNCTION



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 EFFICIENT RESORPTION

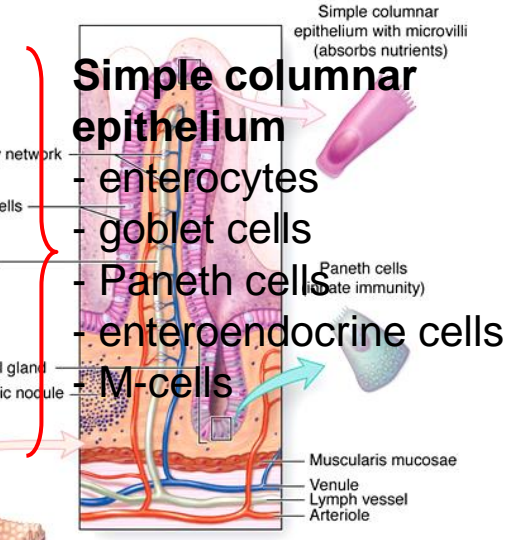
Intestinal mucosa

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

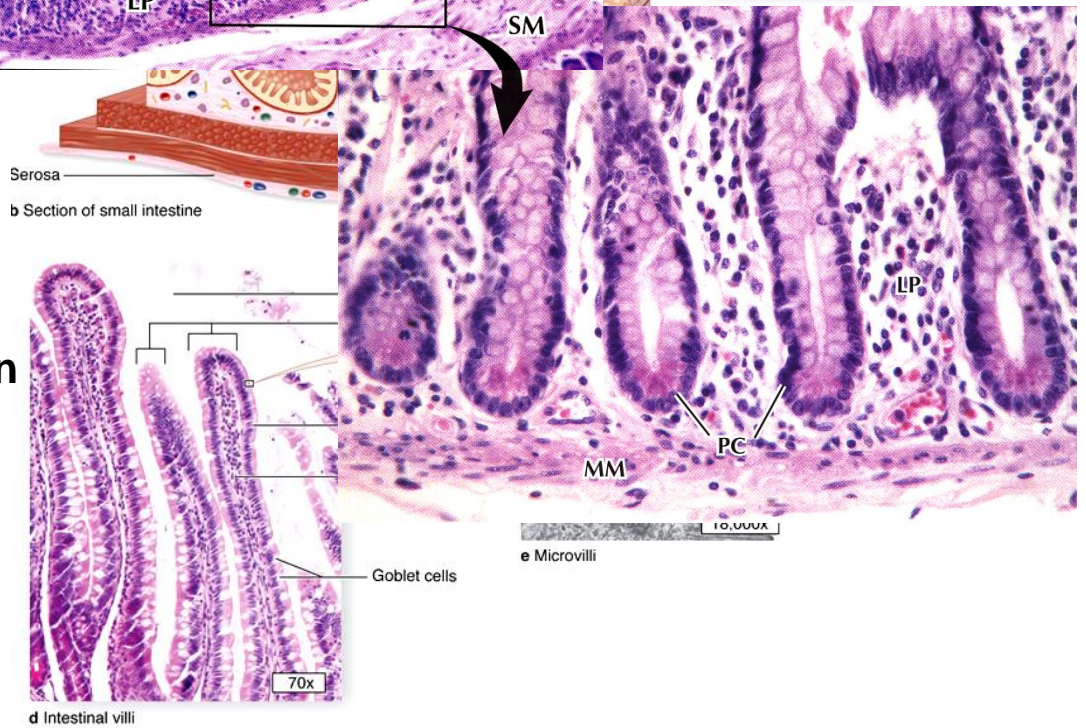
villi (villi intestinales)
– 5-10x

microvilli (striated border)
– 20x

200-600x

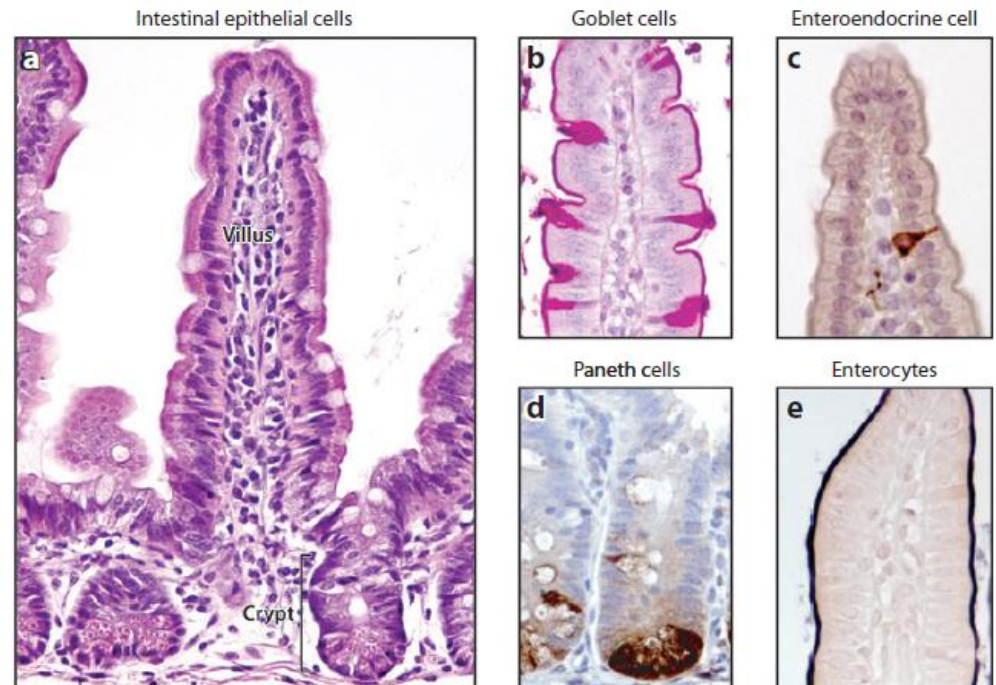
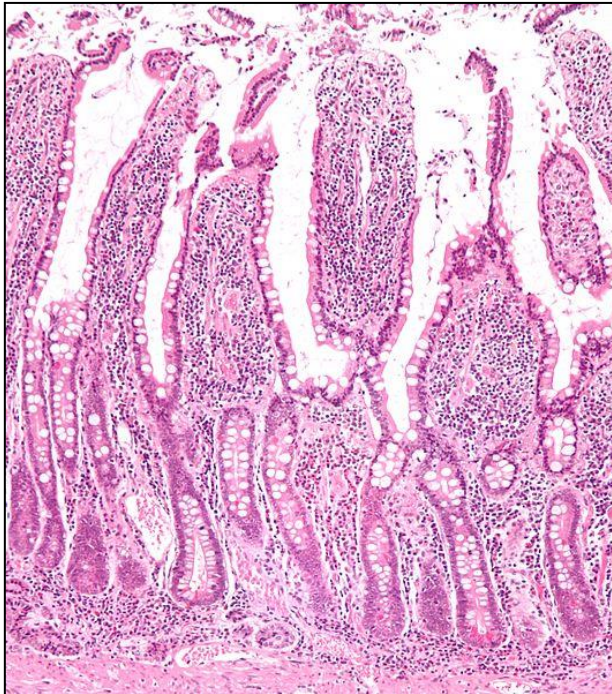


Crypts of Lieberkühn



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



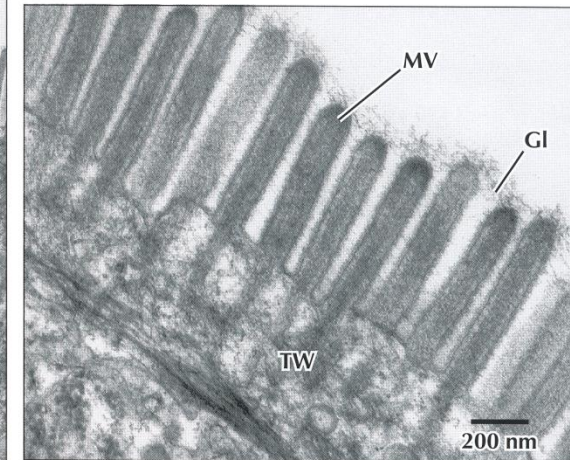
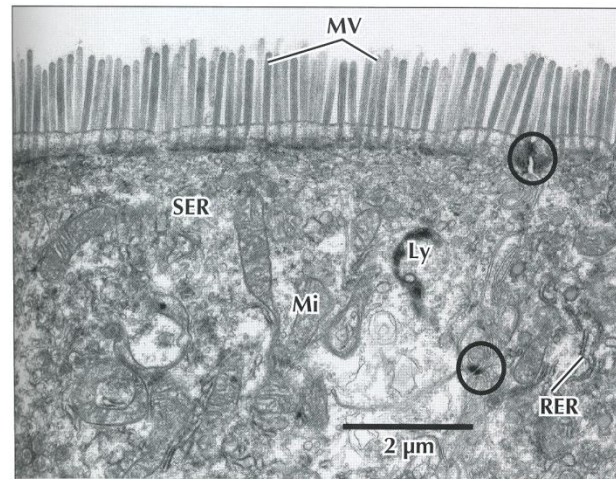
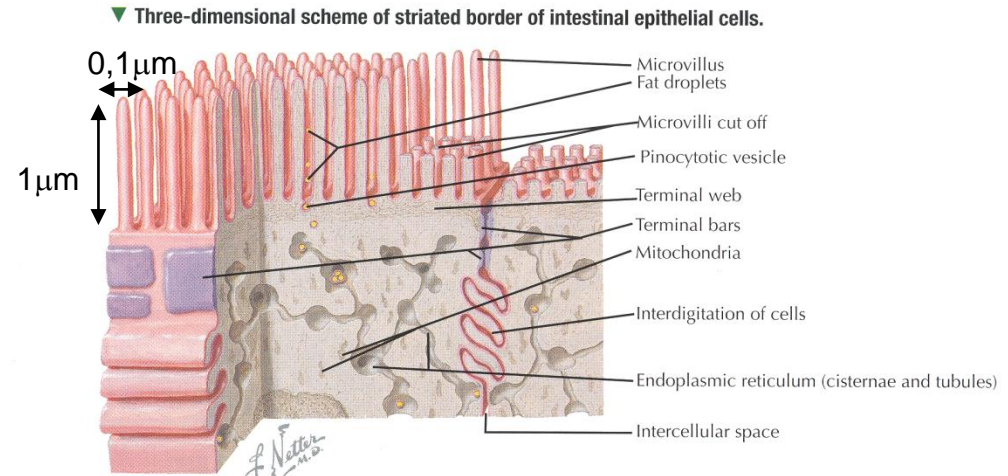
CELLS OF INTESTINAL MUCOSA

Enterocytes

- tall, columnar cells
- nucleus located in basis of the cell
- apical surface modified- microvilli (3000) + glycocalyx (0.5 μm) = *striated border (cuticle)*
- tight intercellular connections, interdigitations

Function:

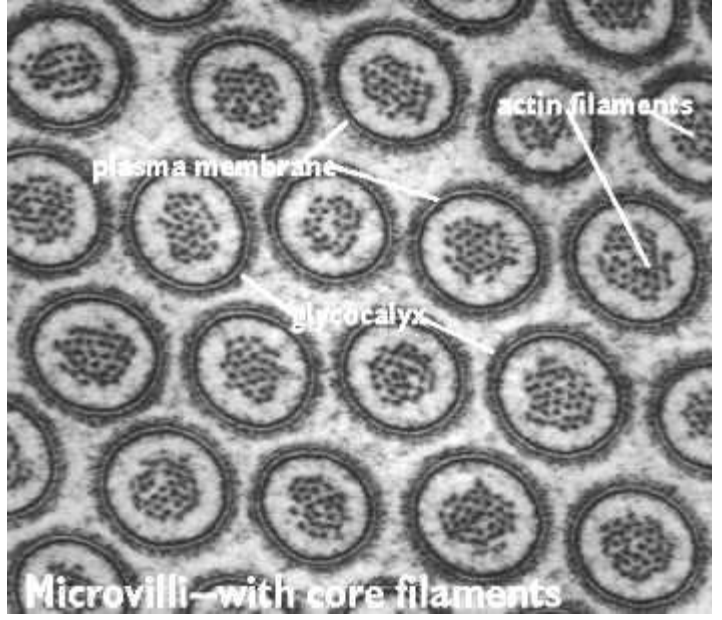
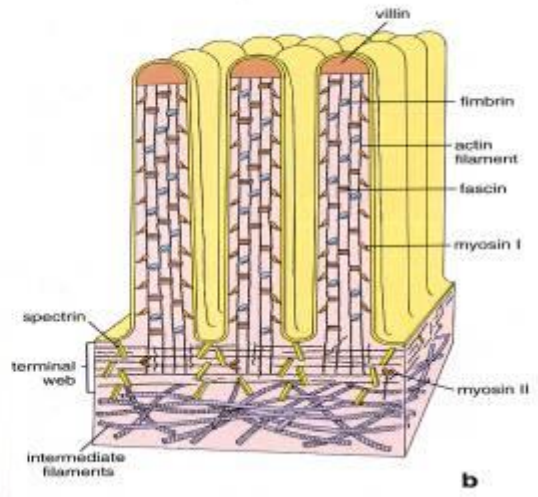
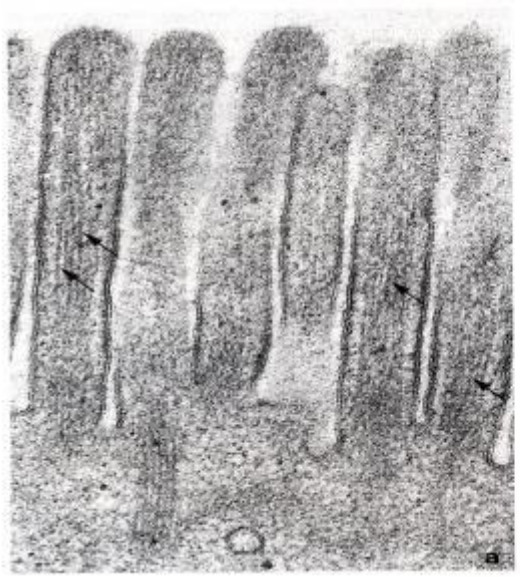
- digestion – enzymatic complexes on microvilli membrane
- absorption and transport – passive, facilitated i active
- lipid uptake - chylomicrons



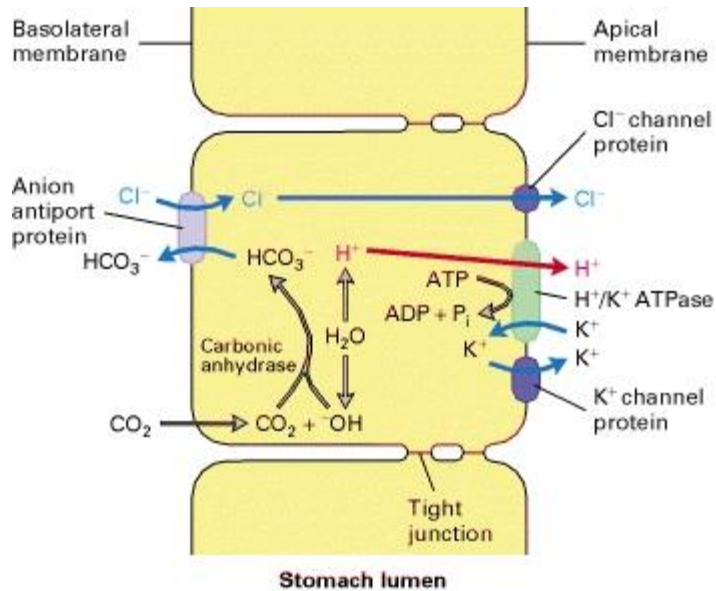
▲ EMs of enterocytes at low (Left) and high (Right) magnification. Apical microvilli (MV) make up a striated border and extend from free surfaces of the cells. A fuzzy glycocalyx (GI) covers them. A terminal web (TW) of actin filaments in the apical cytoplasm reaches into microvilli. Intercellular junctions (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 .

CELLS OF INTESTINAL MUCOSA

Microvilli



Principles of transport and resorption

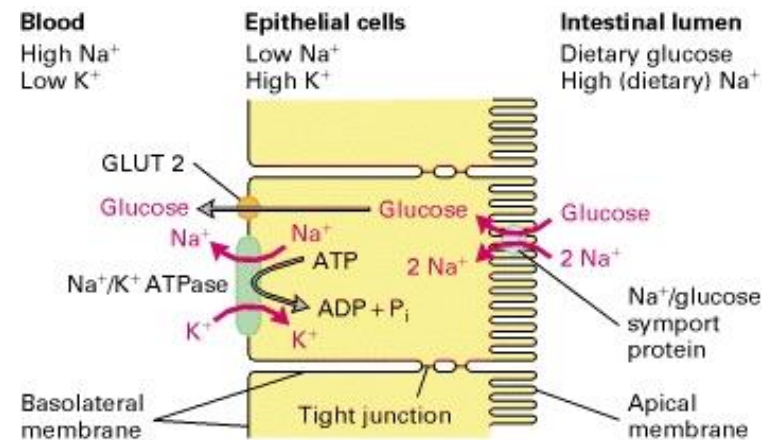


Acidification of stomach fluid by parietal cells

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



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

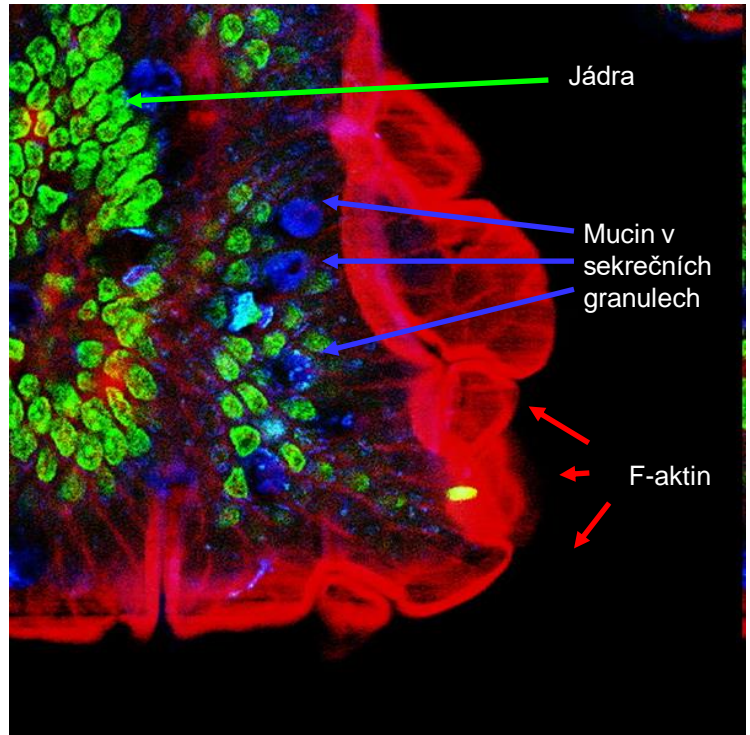
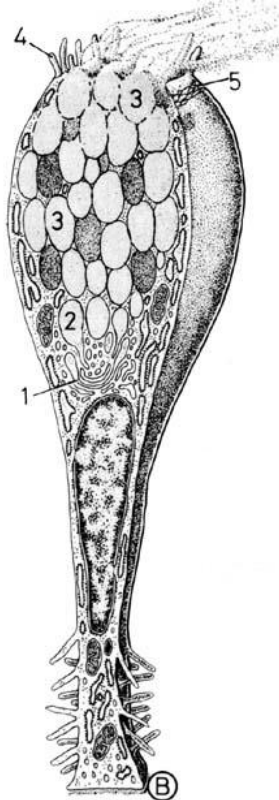
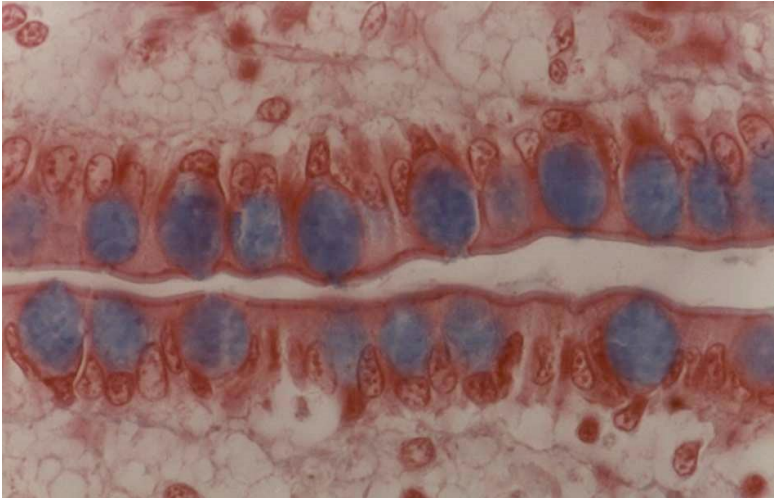
Na⁺/glucose symport on apical surface

Facilitated diffusion by glucose uniporter (GLUT2) in basolateral membrane

CELLS OF INTESTINAL MUCOSA

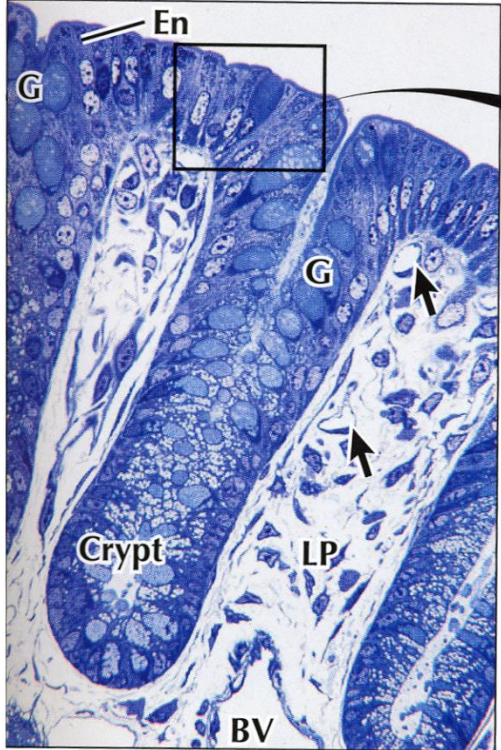
Goblet cells

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

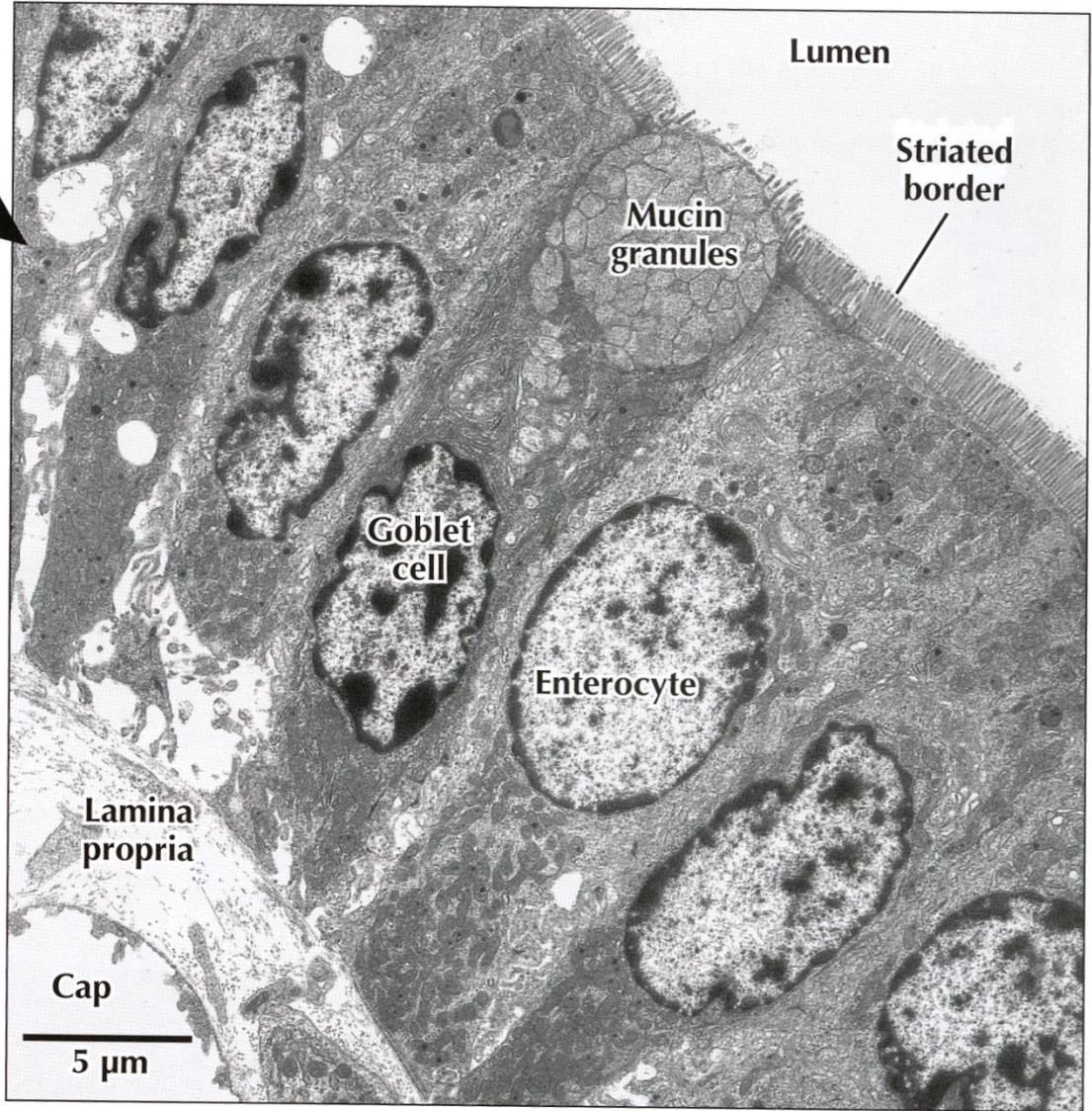


CELLS OF INTESTINAL MUCOSA

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. 600×. Toluidine blue.

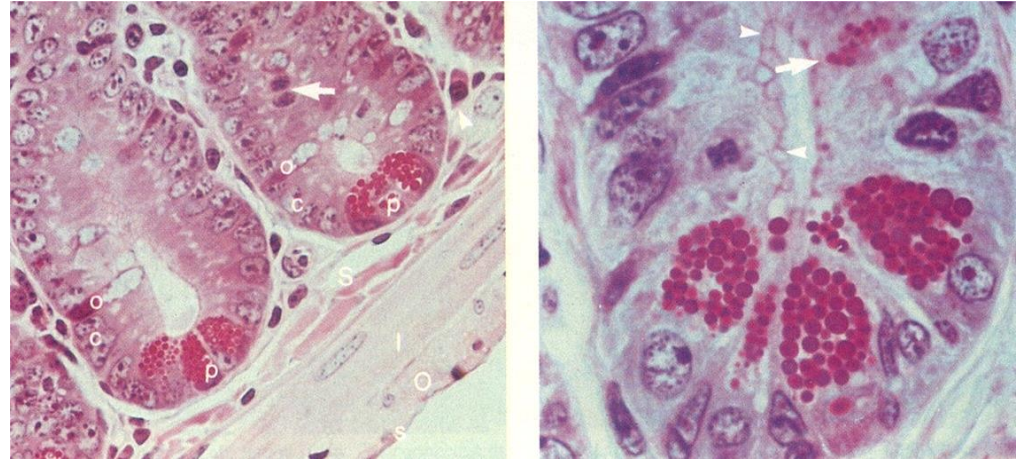


Cap
5 μm

CELLS OF INTESTINAL MUCOSA

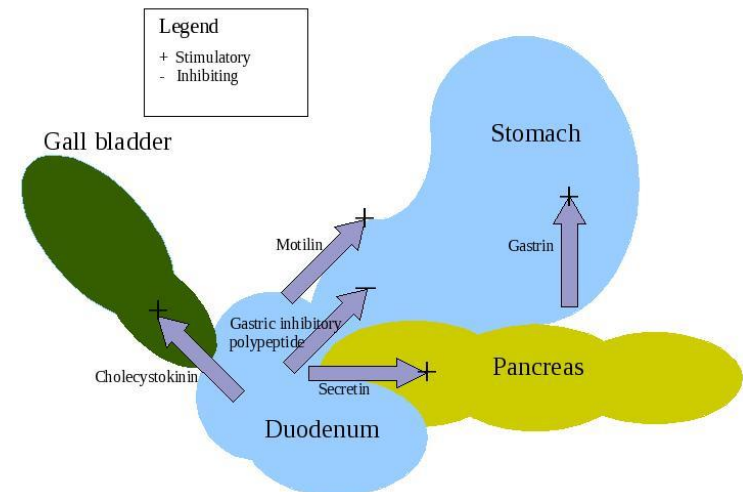
Paneth cells

- 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

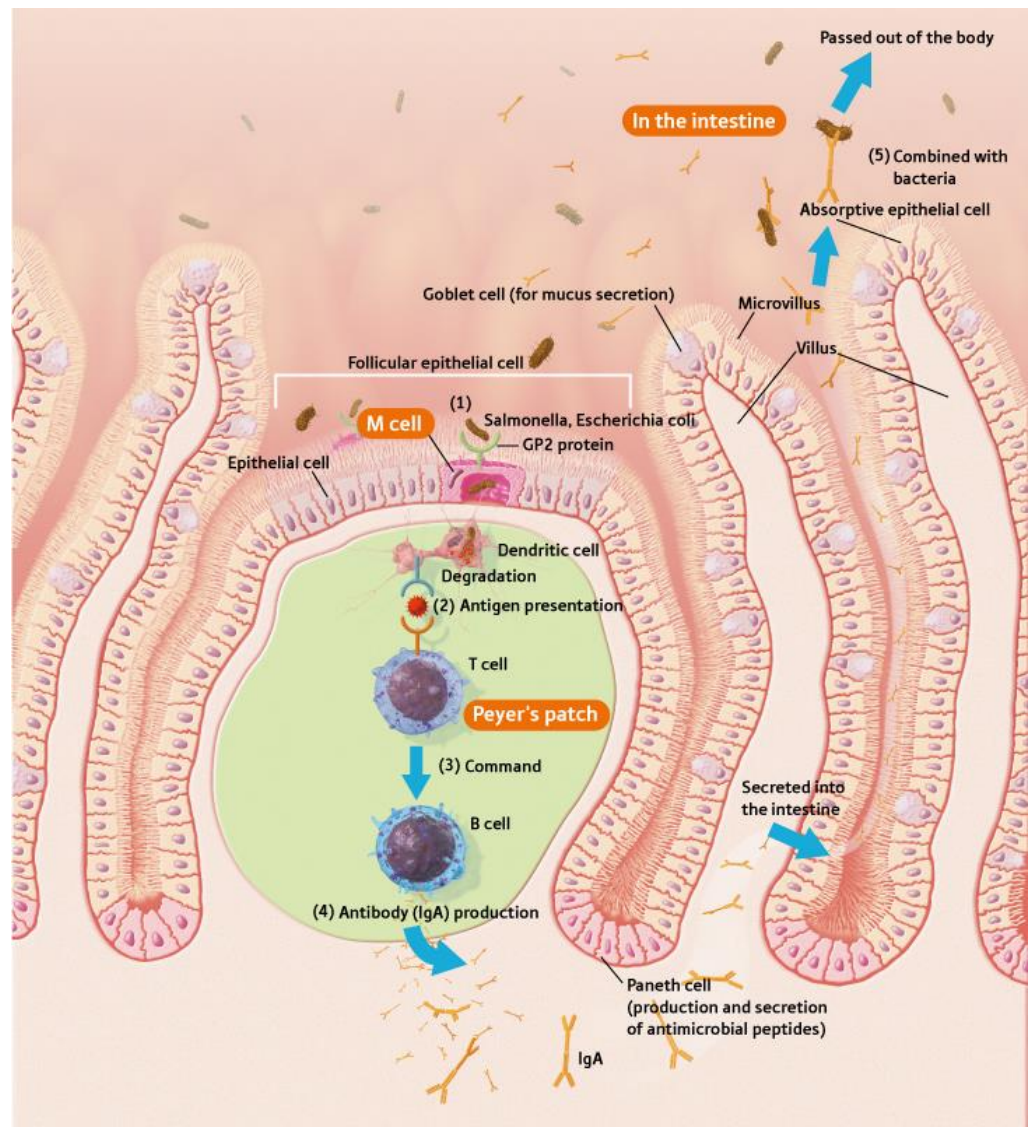
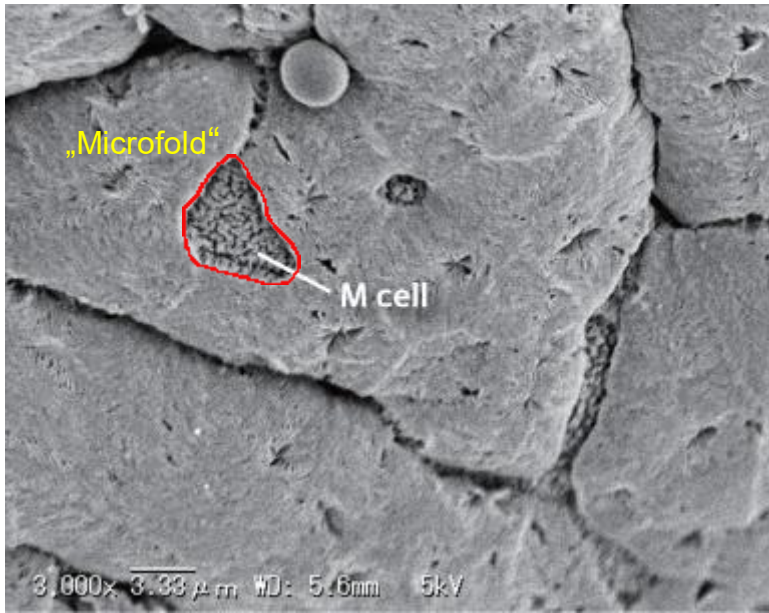
- similar to gastric enteroendocrine cells
- regulate pancreatic secretions
- homeostatic axis (brain-intestine-adipose tissue)
- cholecystokinin, secretin, GIP, motilin, neurocrine peptides etc.



CELLS OF INTESTINAL MUCOSA

M cells (microfold)

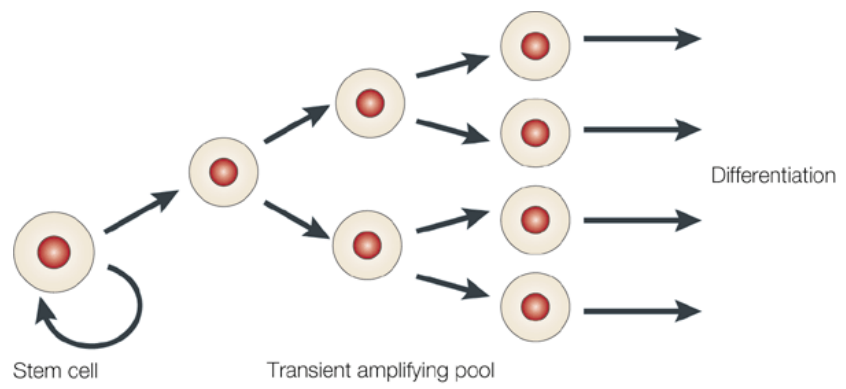
- epithelial cells above Peyer's patches and lymphatic nodules
- no microvilli
- induces immune response
- MHCII
- antigen presentation to dendritic cells and lymphocytes



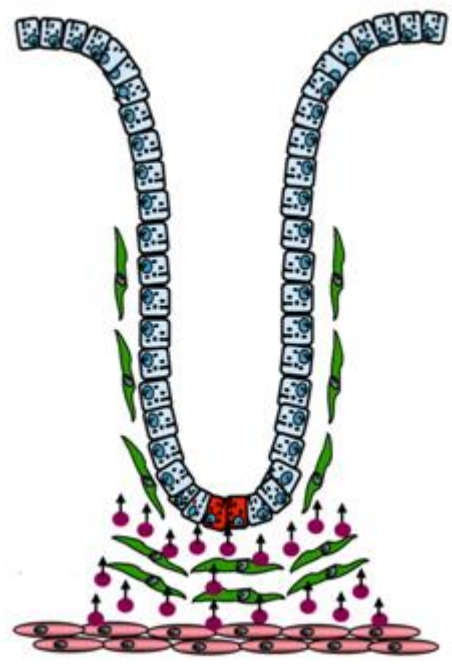
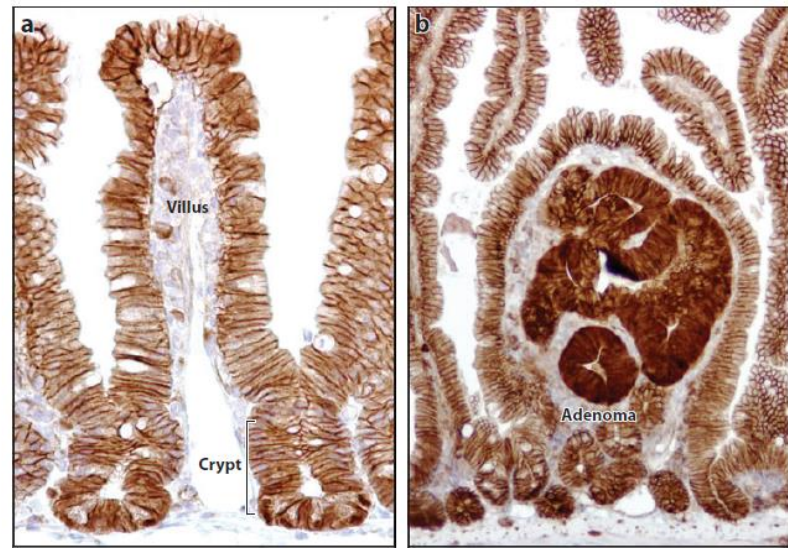
CELLS OF INTESTINAL MUCOSA

Intestinal stem cells

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



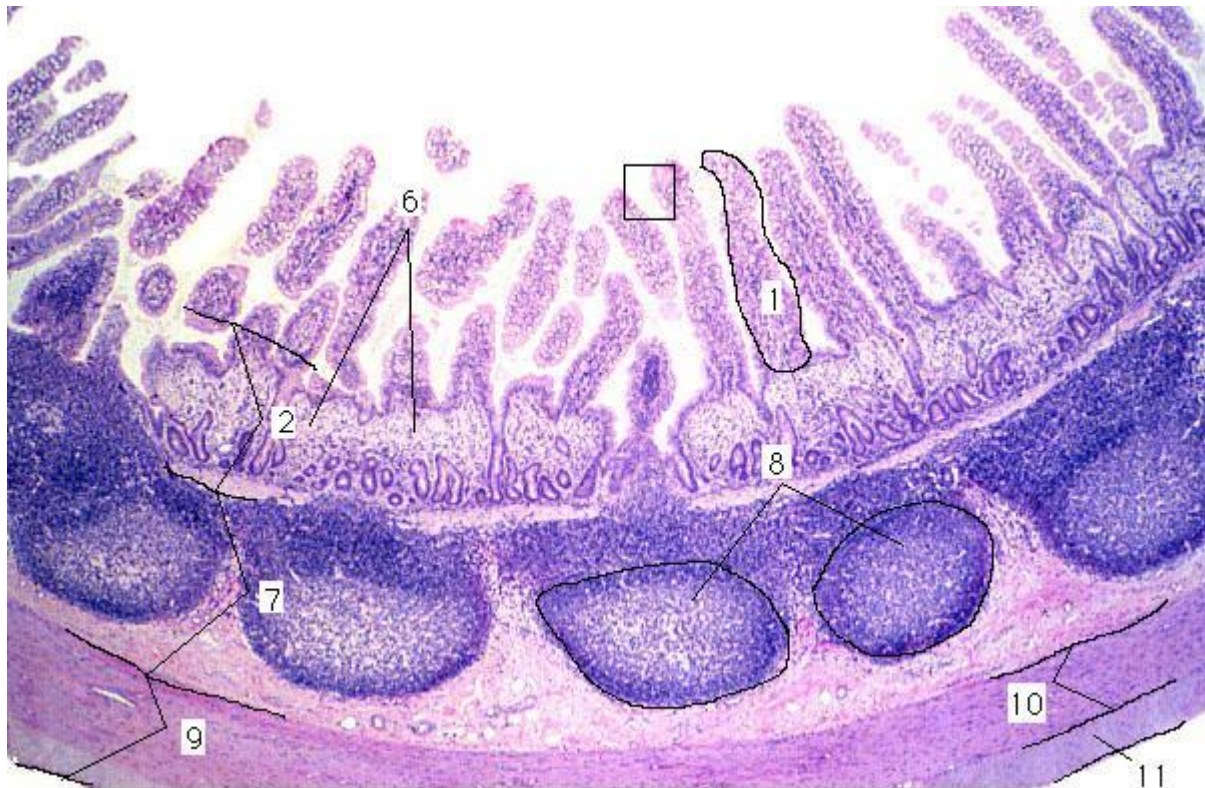
Nature Reviews | Molecular Cell Biology



CONNECTIVE TISSUE OF INTESTINAL MUCOSA

L. propria

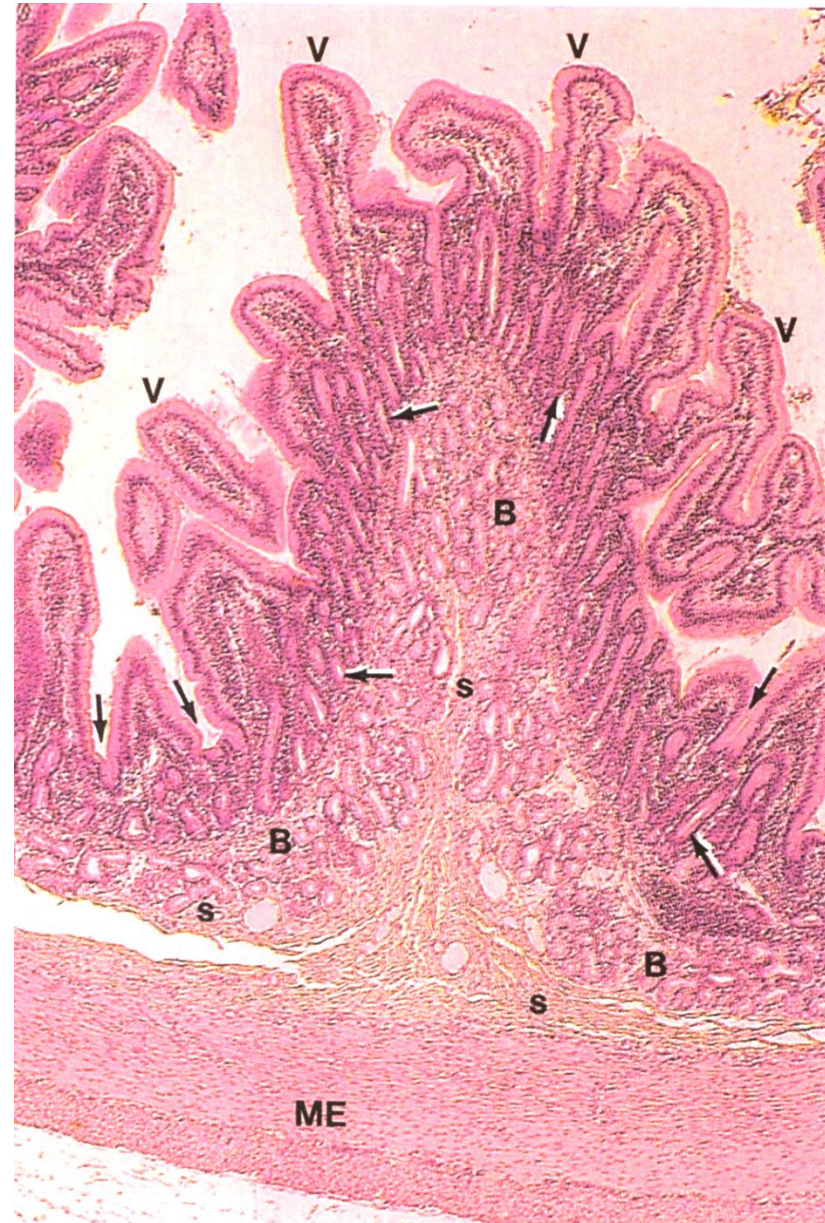
- immune system – GALT
- abundance of reticular fibers
- immunologic barrier
- Peyer's patches



CONNECTIVE TISSUE OF INTESTINAL MUCOSA

Brunner's glands

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



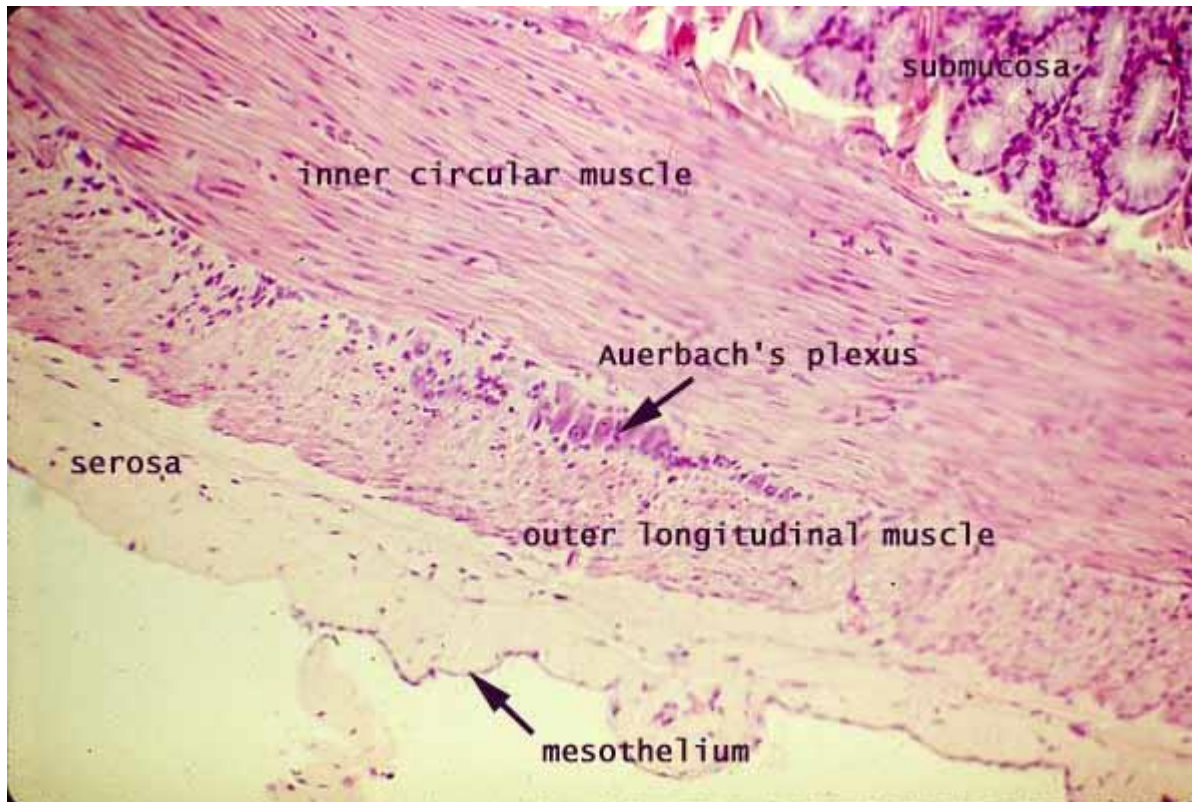
OUTER LAYERS OF INTESTINAL WALLS

Muscularis externa

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

Serosa

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

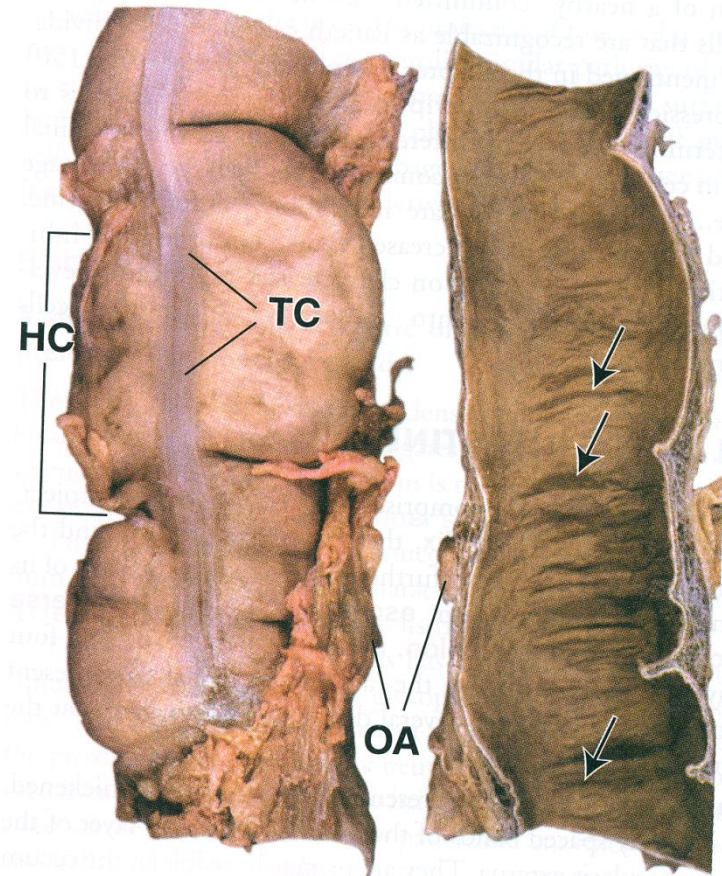


COLON

- general architecture of hollow organs
- plicae of Kerckring, villi absent
- muscularis externa – longitudinal layer - **taenie coli**
- surface serosa - **appendices epiploicae** (adipose)

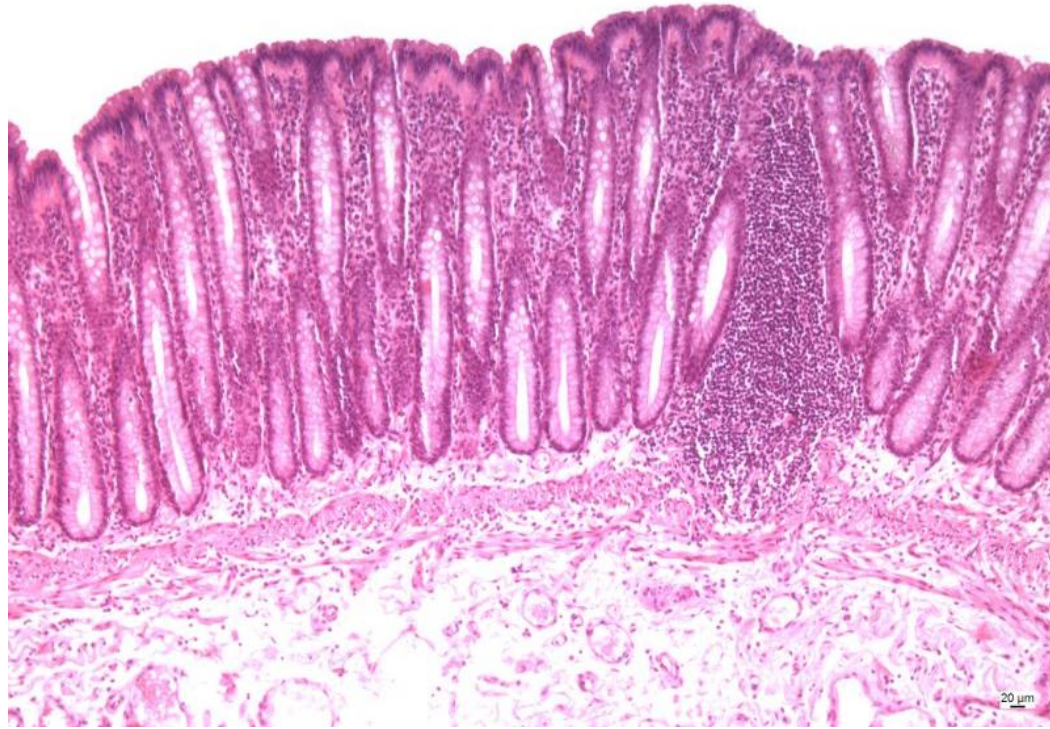


Small intestine



Colon

COLON

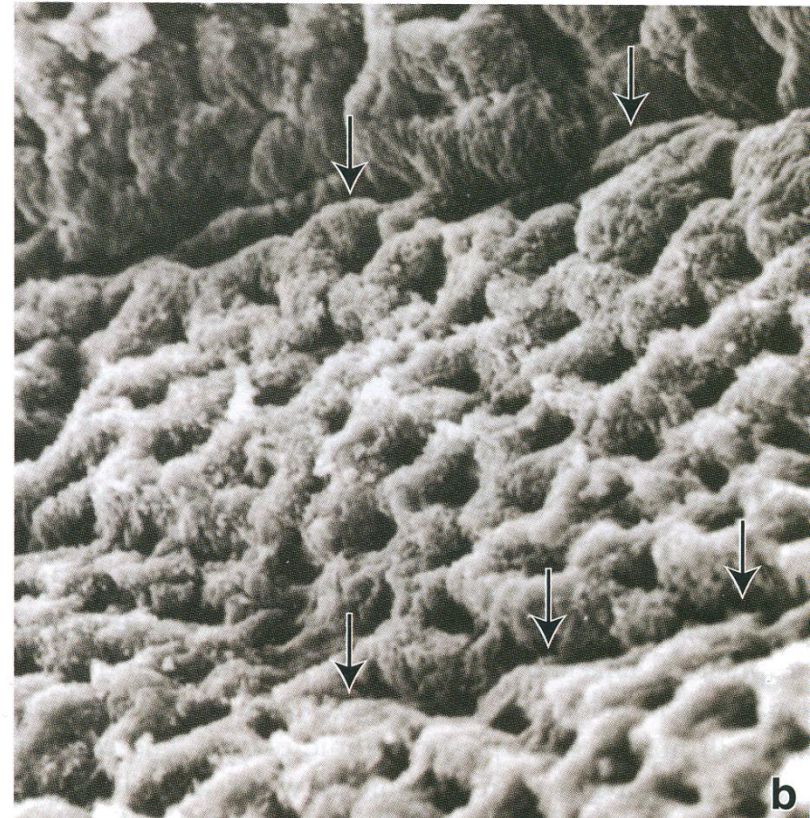
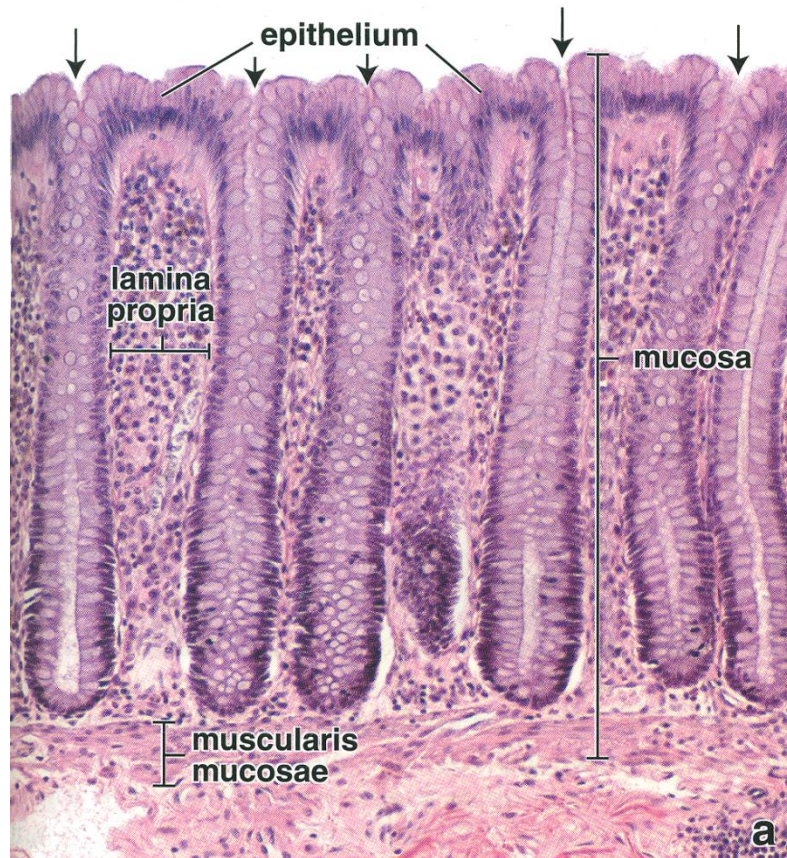


- absorption of water, electrolytes
- deeper crypts of Lieberkühn, no Paneth cells
- abundant goblet cells
- abundant lymphatic tissue in l. propria (GALT)



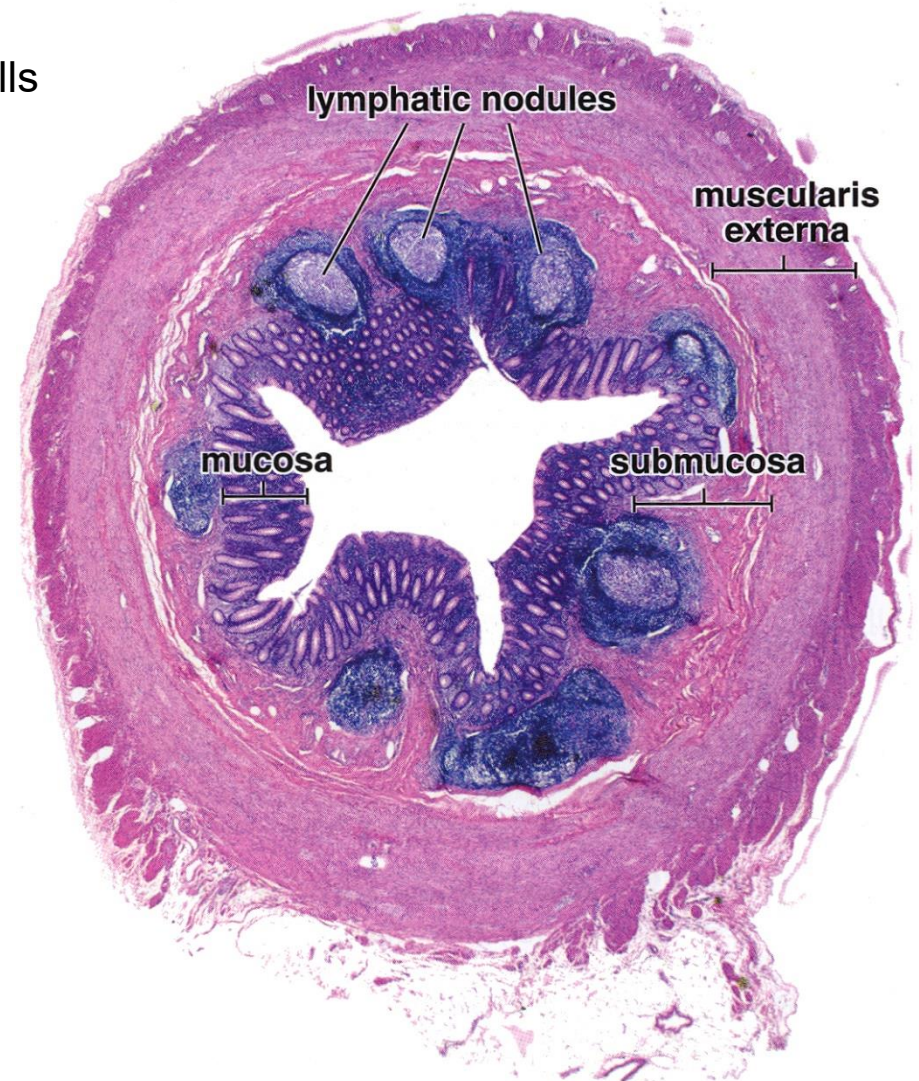
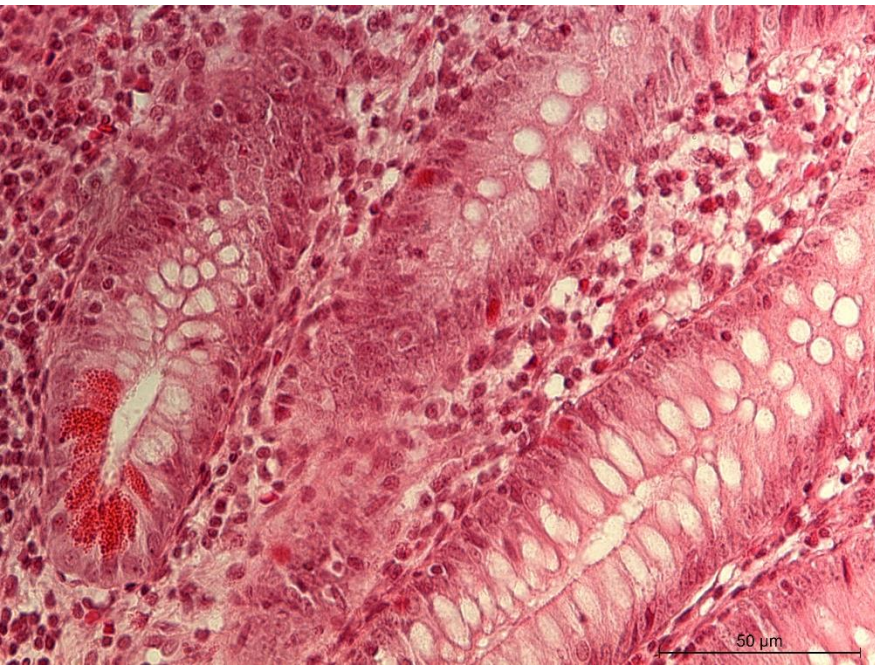
COLON

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



APPENDIX

- 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

- Ampula recti

- 10-12cm
- *plicae transversales recti* (3)
- histological architecture identical to colon
- anorectal junction (*linea anorectalis*)

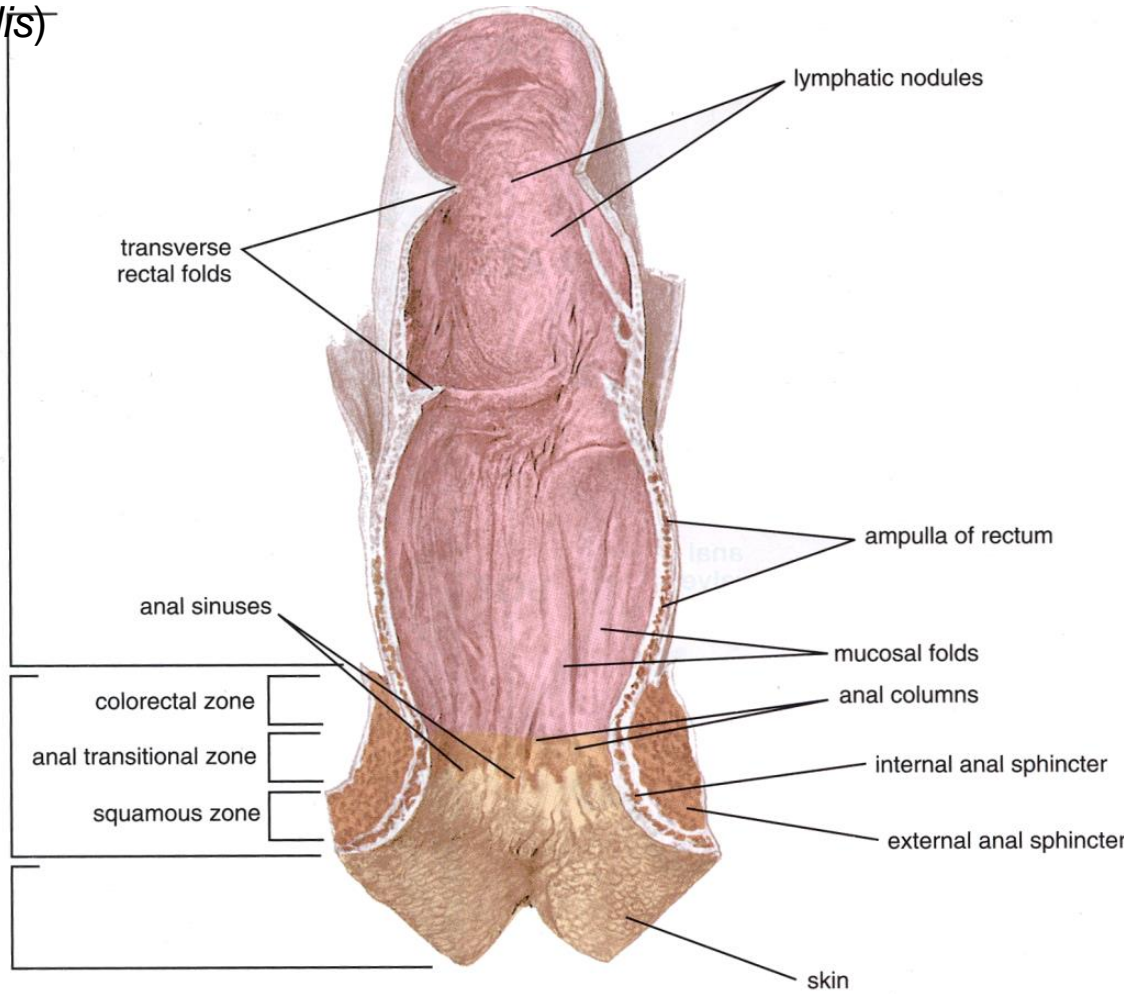
- Canalis analis

- 3 cm
- simple columnar e. gradually replaced by stratified squamous e. (*pecten analis*)
- lymphatic tissue
- *columnae anales*
- *sinus anales – gl. anales*
- *valvulae rectales*

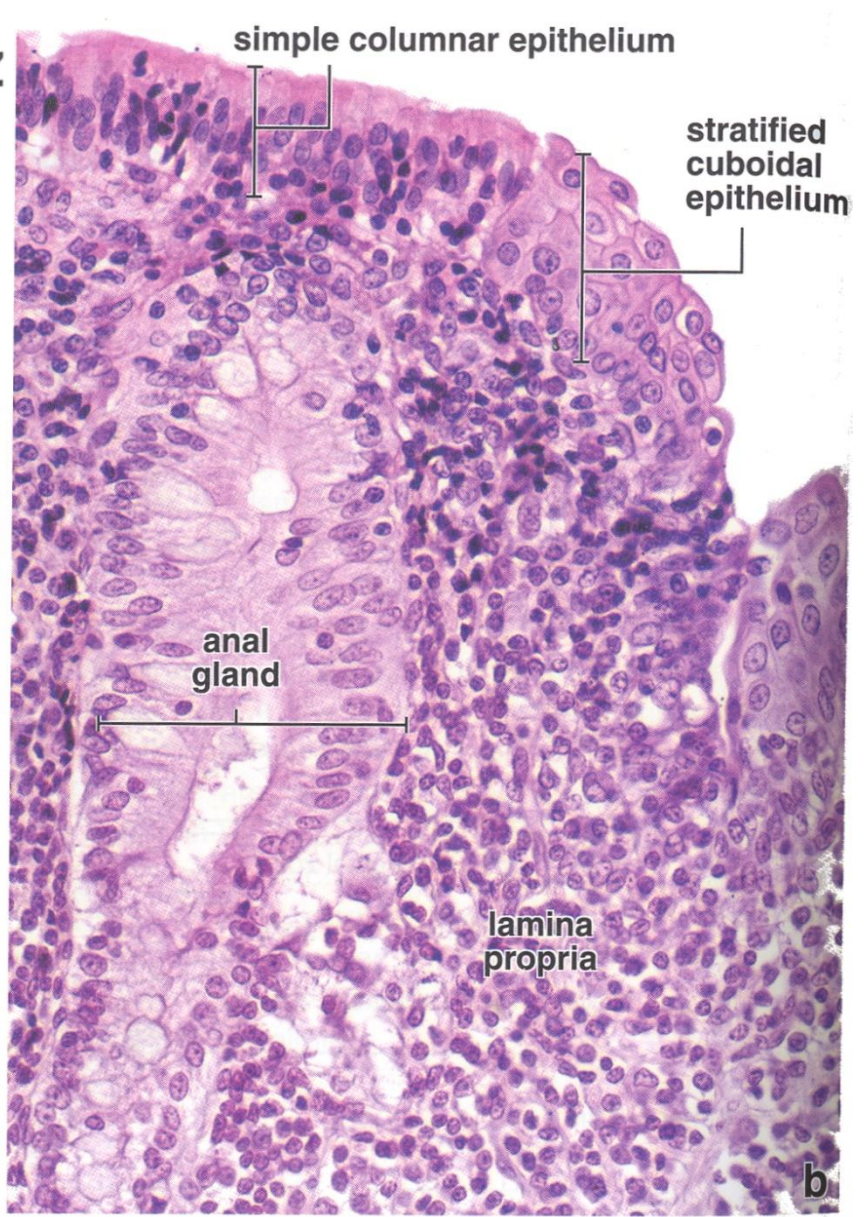
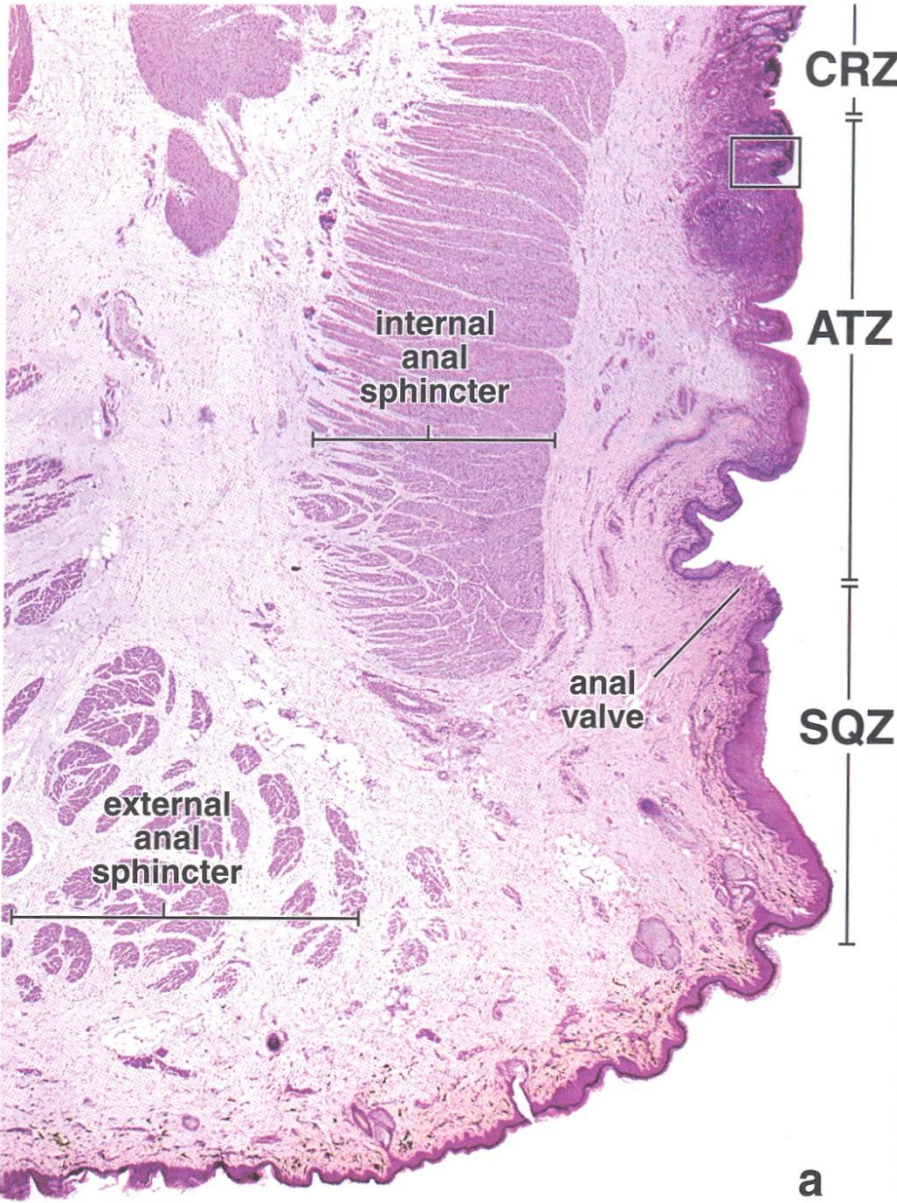
zona hemorrhoidalis

- at anal sinuses and columns
- rich venous plexus

- *zona cutanea* – typical skin



RECTUM AND ANAL CANAL



Organ	Region	Mucosa			Submucosa	Muscularis externa	Serosa/ Adventitia
		LEM	LPM	LMM			
Esophagus	1/3	stratified squamous e.	glandulae oesophageae cardiaca	full	gll. oesophageales	skeletal	A
	2/3					both	
	3/3					smooth	S
Stomach	cardia	simple columnar e.	gll. cardiaca	full		three layers oblique, circular, longitudinal	S
	fundus/ corpus		gll. gast. prop.				
	pylorus		gll. pyloricae				
Small intestine	duodenum	simple columnar e. brush border goblet cells	L. crypts villi	úplná	gll. duodenales Brunneri		A+S
	jejunum		Peyer's plaque		plicae circulares		S
	ileum						
Colon and rectum	apendix	simple columnar e. brush border goblet cells	lymph. follicles	partial	lymph. nodes	full	S
	caecum		villi absent	full			taeniae coli
	colon					A+S	
	rectum	columnae rectales				A	
Canalis analis	anorectal/ anocutaneous	stratified squamous e. non-keratinized	venous plexus	partial-absent	mucosal folds venous plexus	inner anal sphincter	A
	zona cutanea	stratified squamous e. keratinized	hair follicles, sweat glands				

Embryonic development

EARLY EVENTS IN GIT DEVELOPMENT

- cephalocaudal flexion
- **primitive gut** (endoderm)
- oral cavity and rectum – ectoderm
- glandular parenchyma (pancreas, liver) - entoderm of primitive gut

- epithelial-mesenchymal interactions
- Shh a Hox morphogenetic code

Four regions according to structural and molecular patterns

pharynx

- from buccopharyngeal membrane to tracheobronchial diverticle

foregut

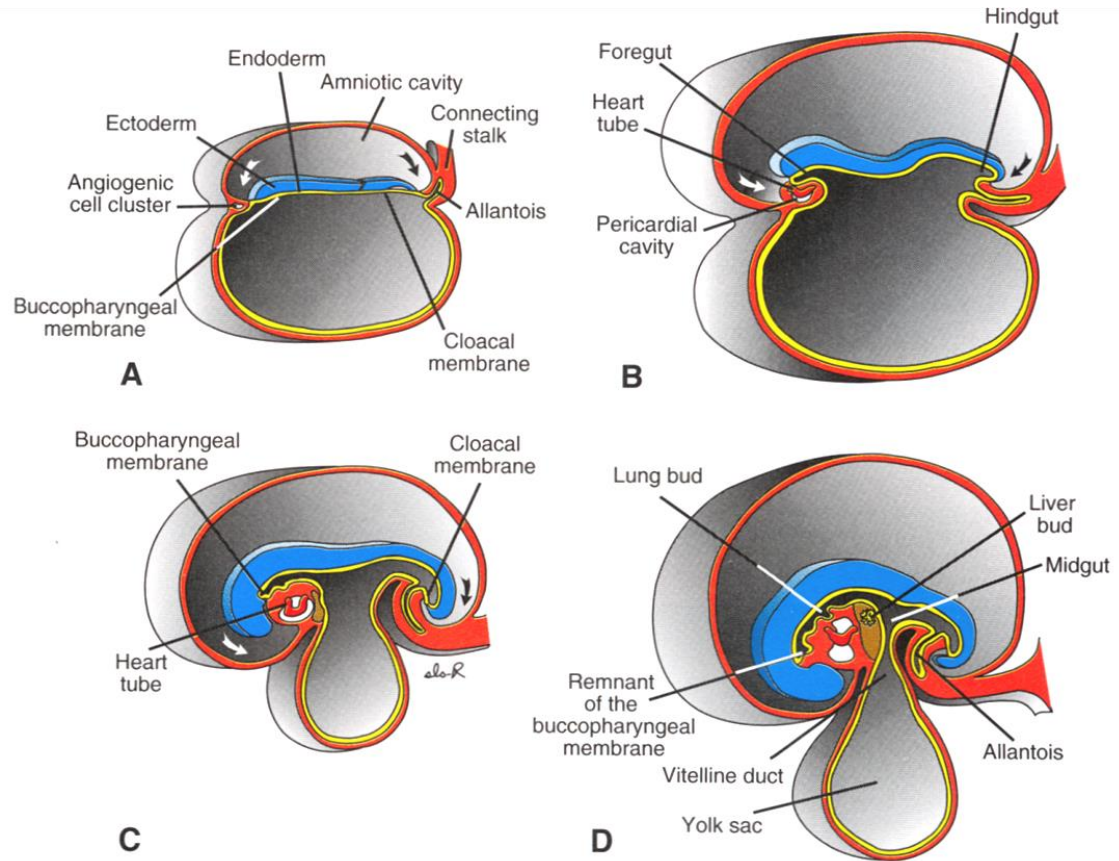
- caudally to liver diverticle

midgut

- duodenum to proximal 1/3-half of colon transversum

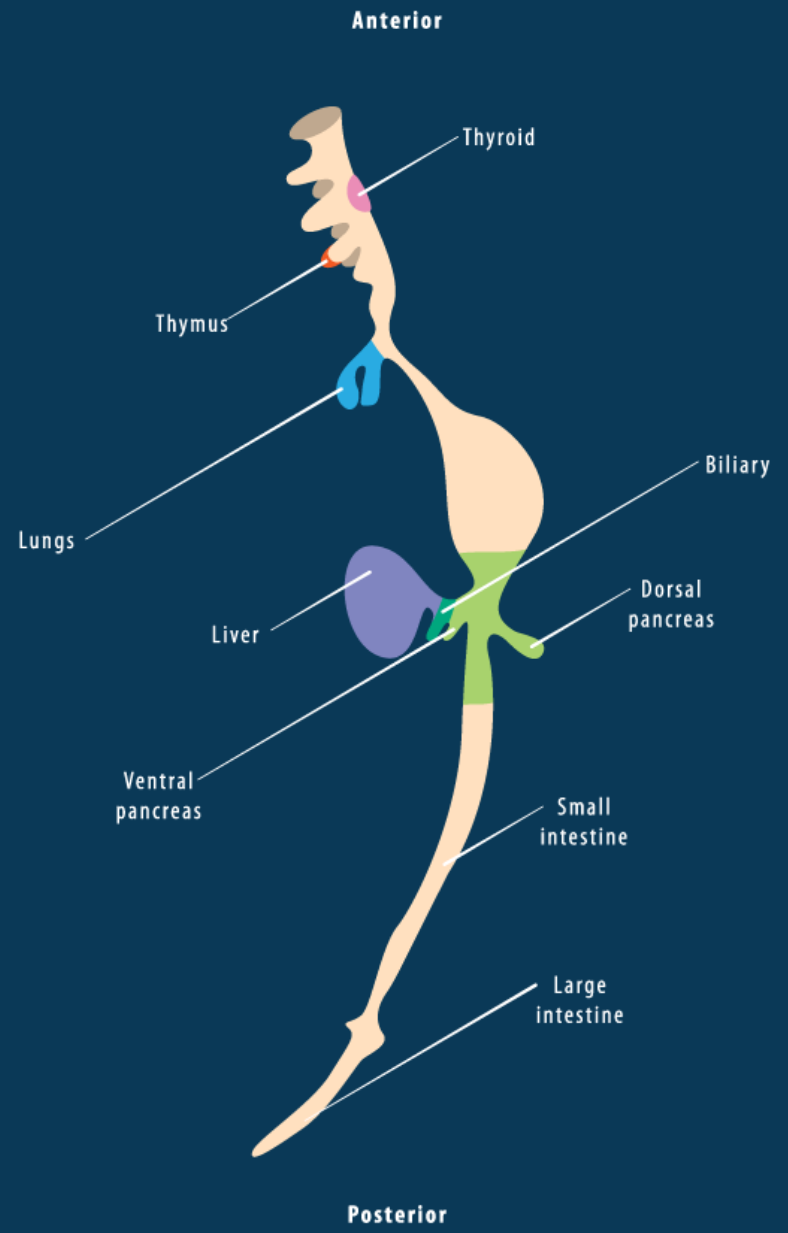
hindgut

- Distal half-2/3 of colon transversum to cloacal membrane



PRIMITIVE GUT

Derivatives of primitive gut



PRIMITIVE GUT VASCULARISATION

Four regions according to structural and molecular patterns

pharynx

- buccopharyngeal membrane – tracheobronchial diverticle

foregut

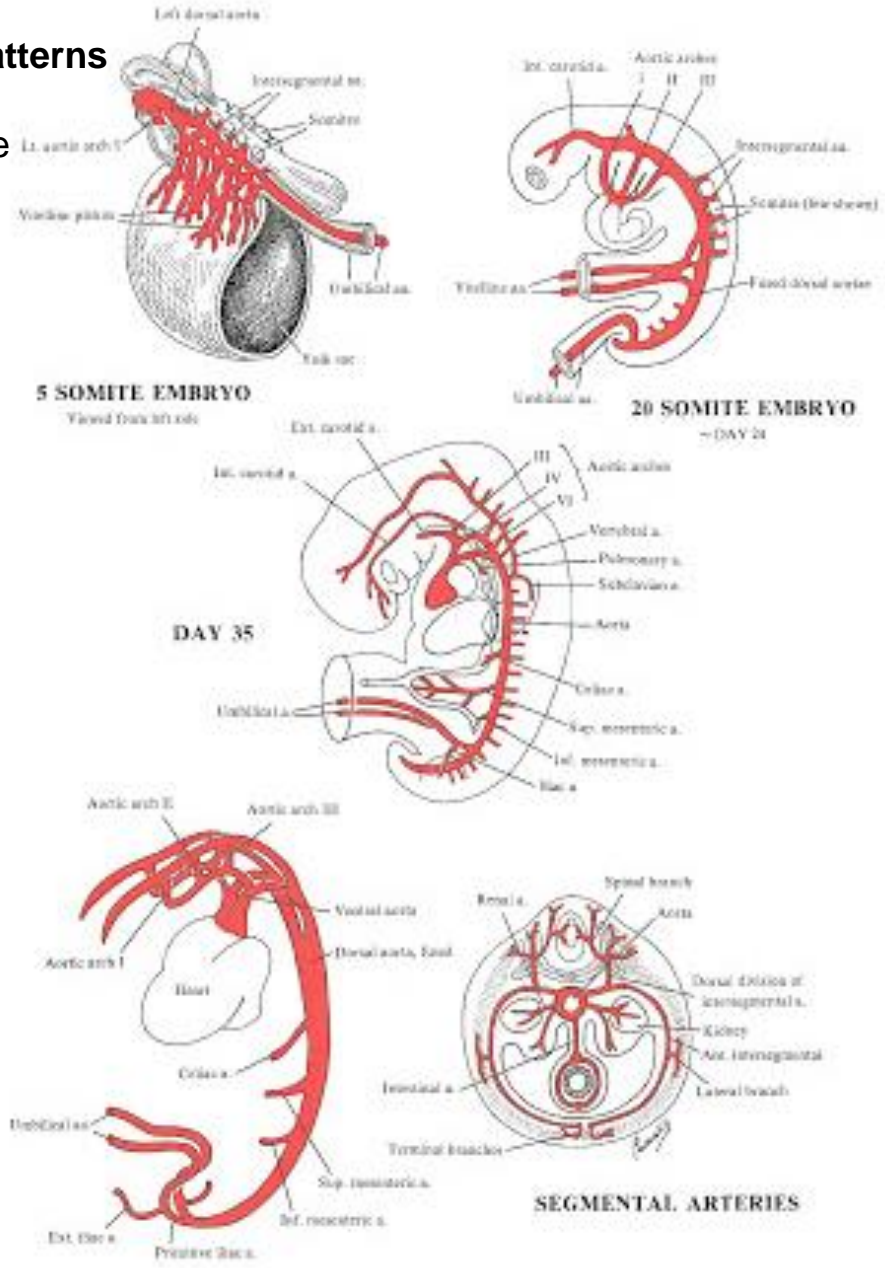
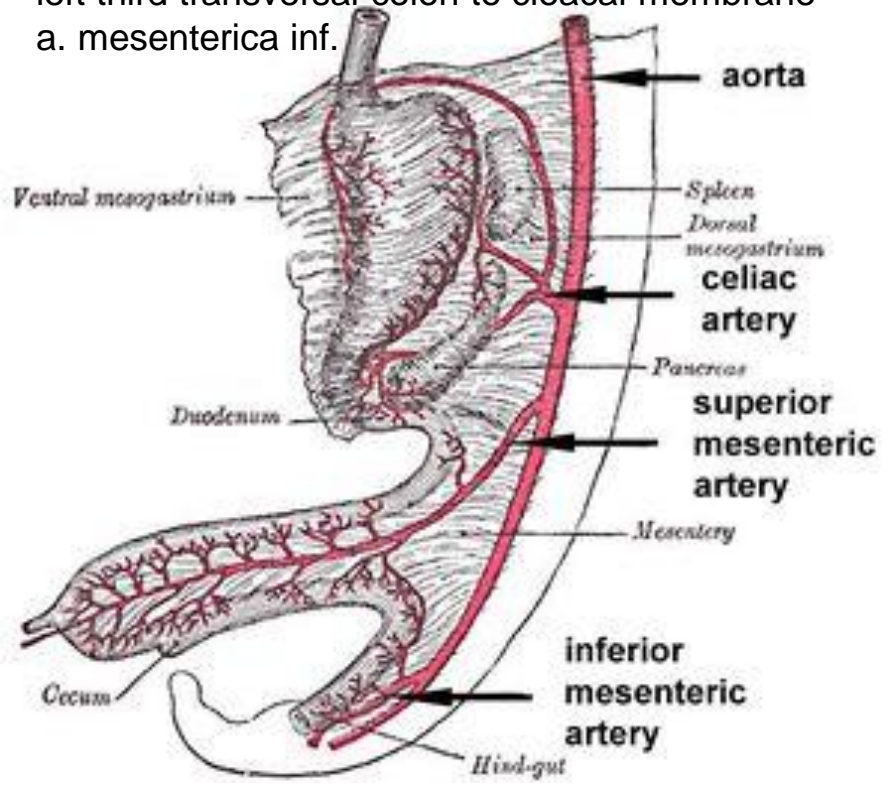
- caudally to liver diverticle
- t. coeliacus

midgut

- a. mesenterica sup.

hindgut

- left third transversal colon to cloacal membrane
- a. mesenterica inf.



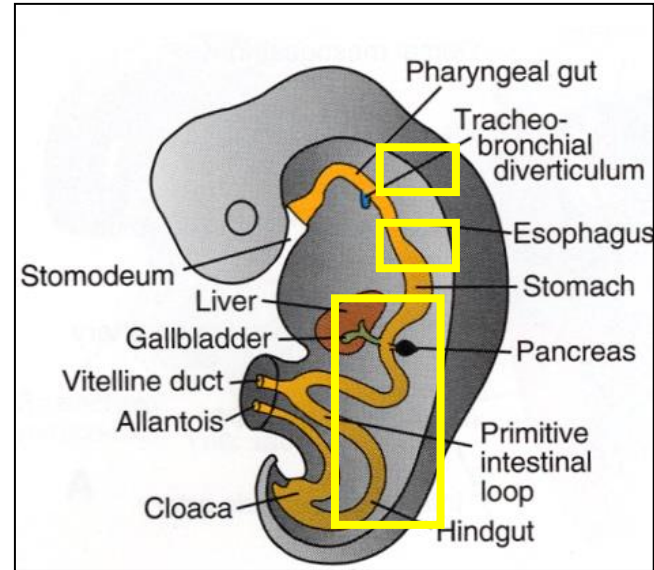
EARLY EVENTS IN GIT DEVELOPMENT

- Esophagus

- caudal part of foregut from laryngotracheal diverticle
- endoderm (epithelium and glands), c.t. - mesoderm

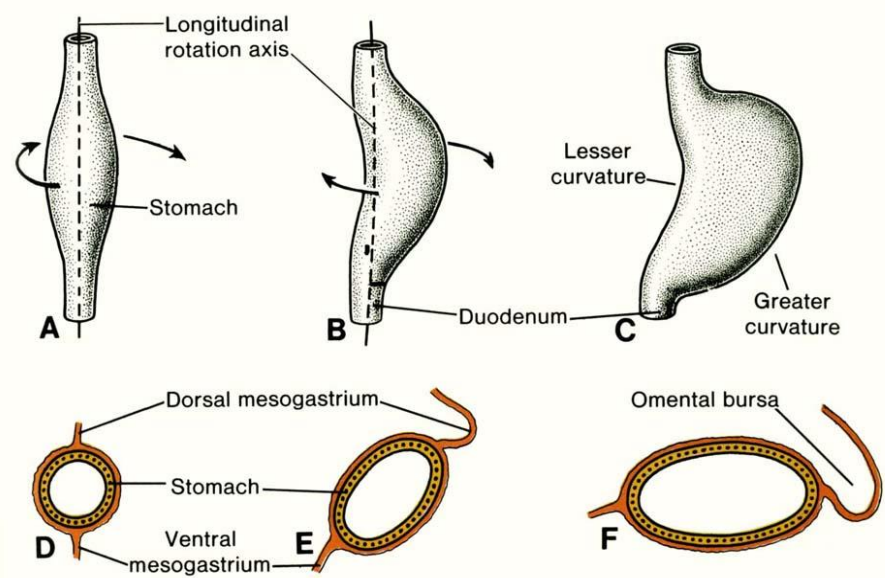
- Stomach

- 4th week – fusiform dilatation of foregut
- symmetric - asymmetric
- major and minor curvature
- rotation - longitudinal and sagittal axis
- definitive localization and morphology about week 8 i.u.



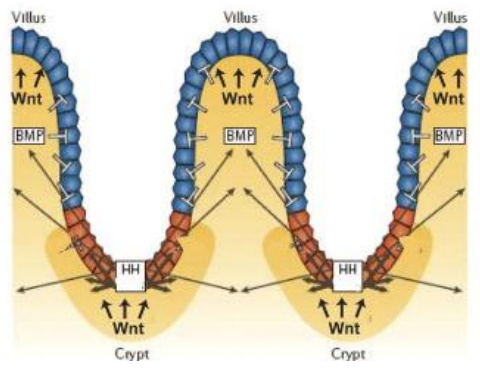
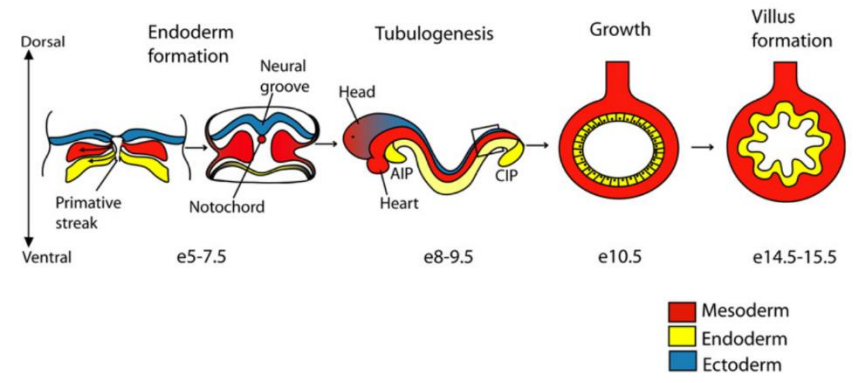
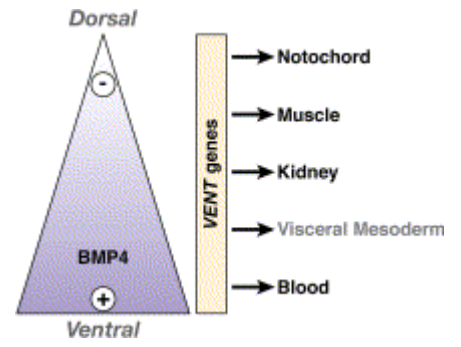
- Gut

- midgut – duodenal and umbilical loop
- rotation
- physiological umbilical hernia

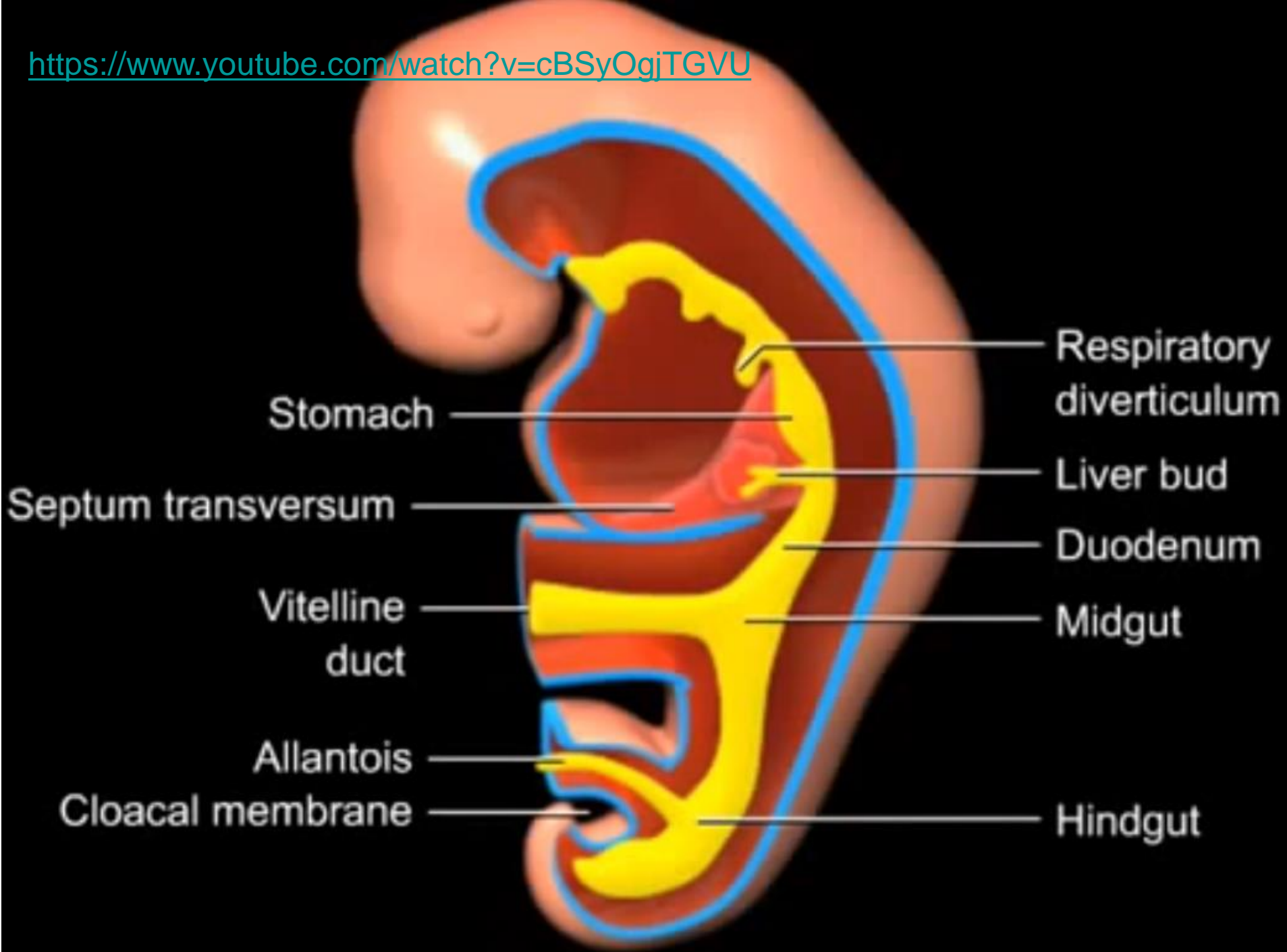


EARLY EVENTS IN GIT DEVELOPMENT

1. Differentiation of entoderm, tube formation, A-P patterning
 - growth and differentiation factors during development
 - Simple nondifferentiated epithelium
2. Morphogenesis of villi
 - expansion and condensation of mesenchyme into lumen
 - proliferation and parallel differentiation of temporary epithelium to simple columnar epithelium
3. Lieberkühn crypts - intestinal stem cells
4. Mesoderm-endoderm interactions



<https://www.youtube.com/watch?v=cBSyOgjTGvU>



Microscopic anatomy and development of the gut tube

see also the requirements for exam

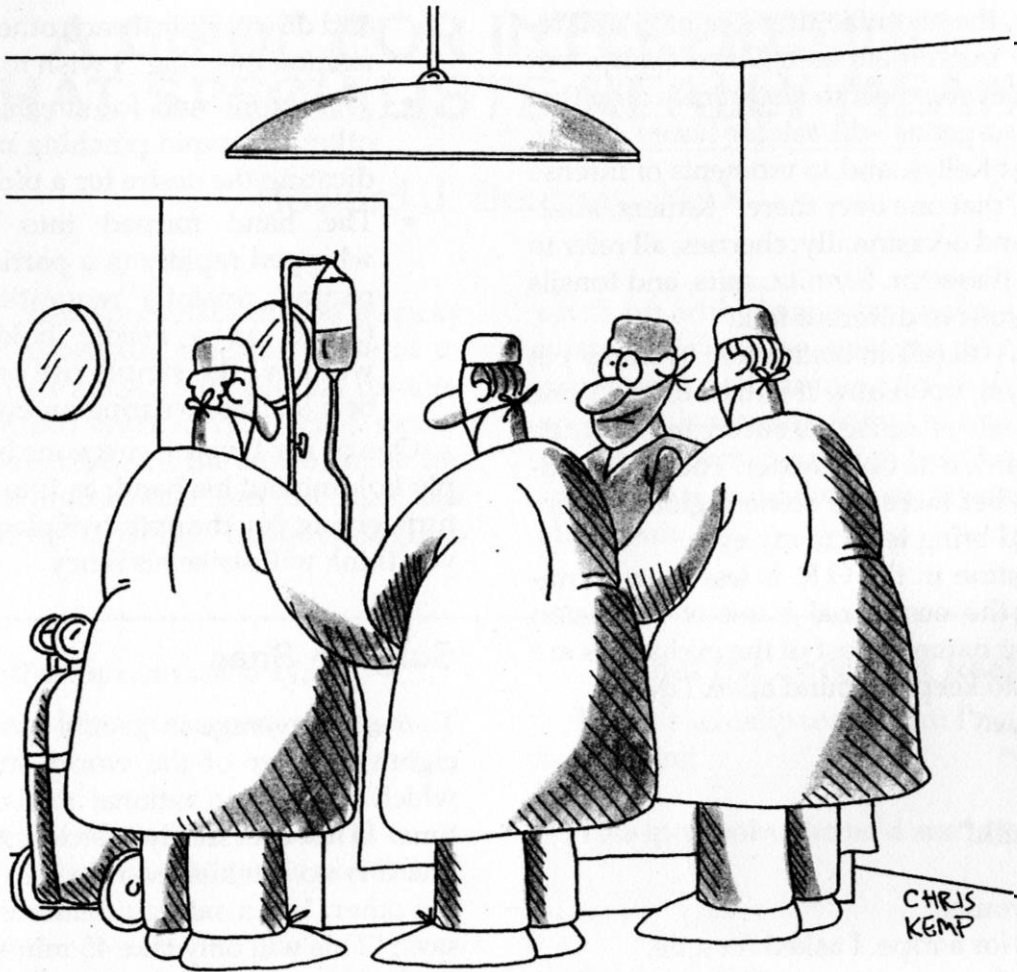
- **General architecture of hollow organs and gut tube:** mucosa (l. epithelialis m., l. propria, l. muscularis m.), submucosa, t. muscularis externa, serosa (l. propria s., l. epith. s.), adventitia
- **Pharynx** – structure and microscopic anatomy
- **Esophagus** - structure, epithelium, mucosal and 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
- **Early events of GIT development**
 - primitive gut development
 - specification of morphological structures



EMBRYONIC DEVELOPMENT & STEM CELL COMPENDIUM

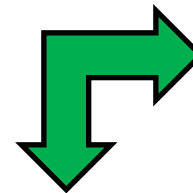
<https://discovery.lifemapsc.com>

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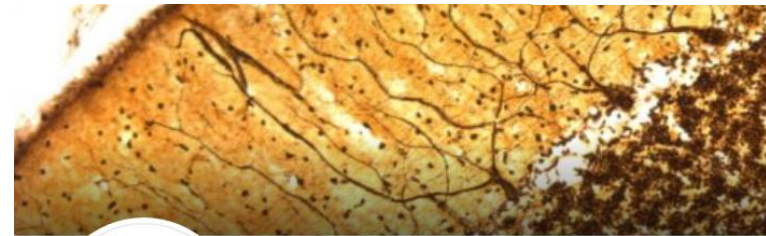


*With the chest cavity open and the heart fully exposed,
Dr. Robbyn suddenly regretted cutting class to go pub crawling
that crisp fall day four years ago.*

Questions? Comments?



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Department
Histology and
Embryology

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