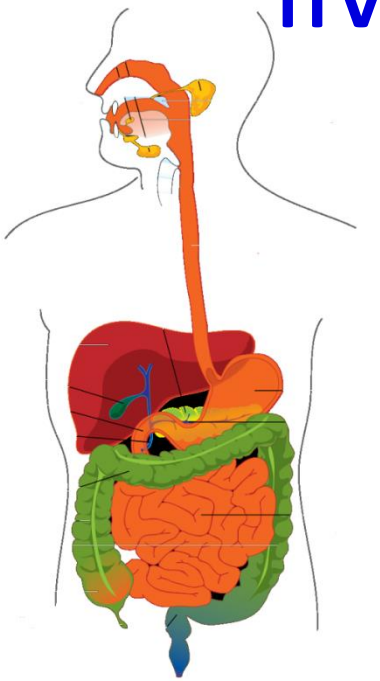
MUNI MED Ústav histologie a embryologie

MICROSCOPIC ANATOMY + DEVELOPMENT OF GIT

liver, pancreas, salivary glands development of GIT



Petr Vaňhara, PhD

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

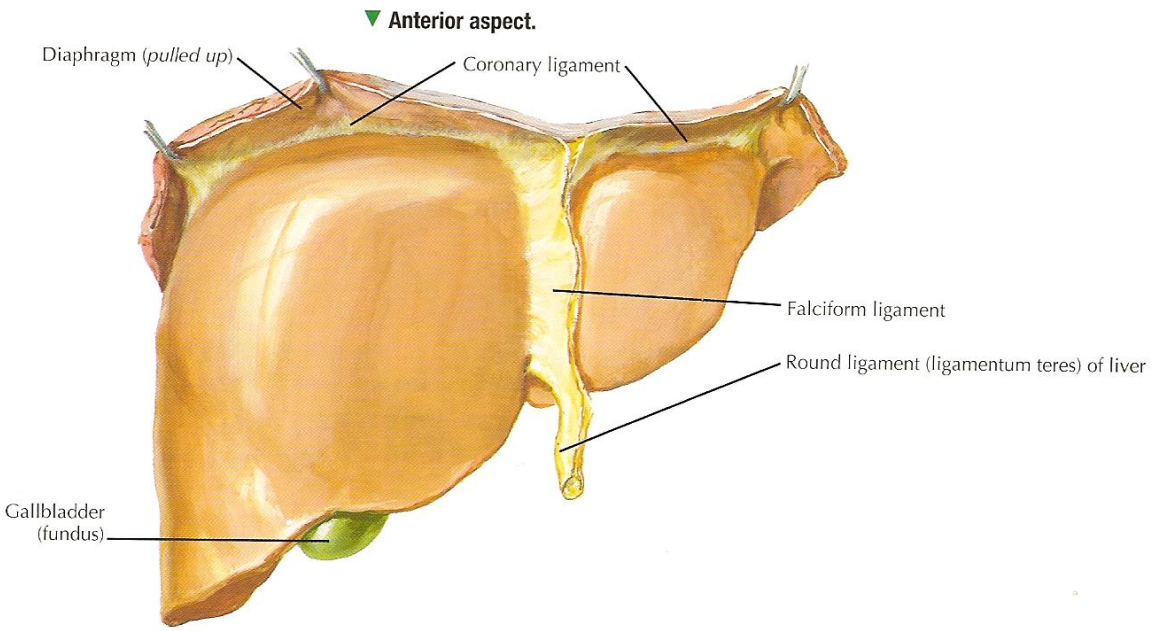
LIVER AND BILE DUCTS

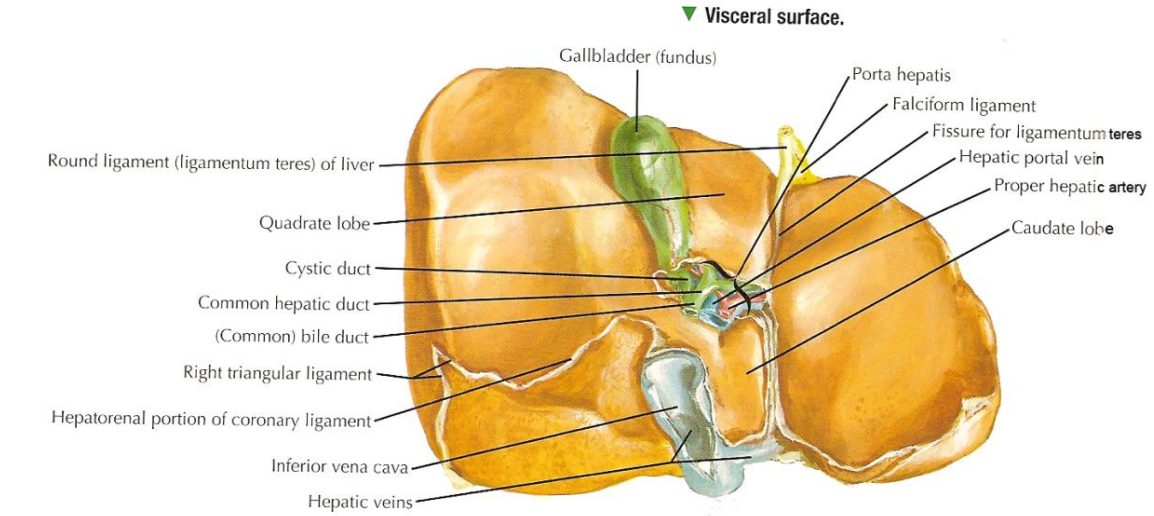
LIVER (HEPAR)

- Liver parenchyma – biggest gland in human body
- C.t. capsule
- Nutritive and functional blood supply
- Endocrine and exocrine function
- Uniform histology of all four major anatomic lobules and segments:

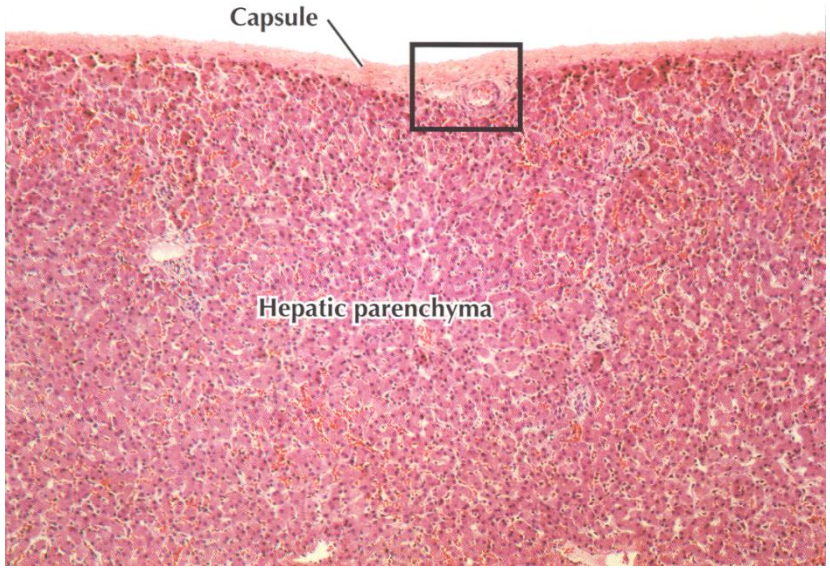
  - Hepatocytes and other cell types
  - C.t. stroma
  - Blood and lymphatic vessels
  - Sinusoids
  - Innervation

  - C.t. capsule
  - Serosa

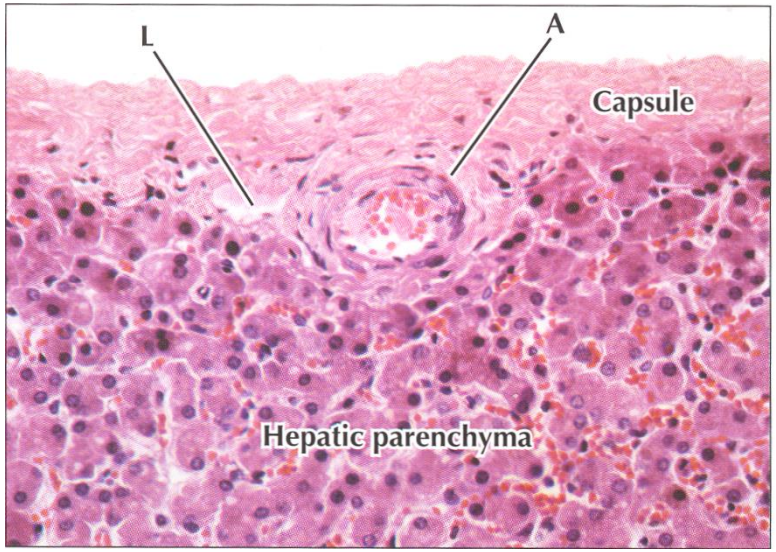


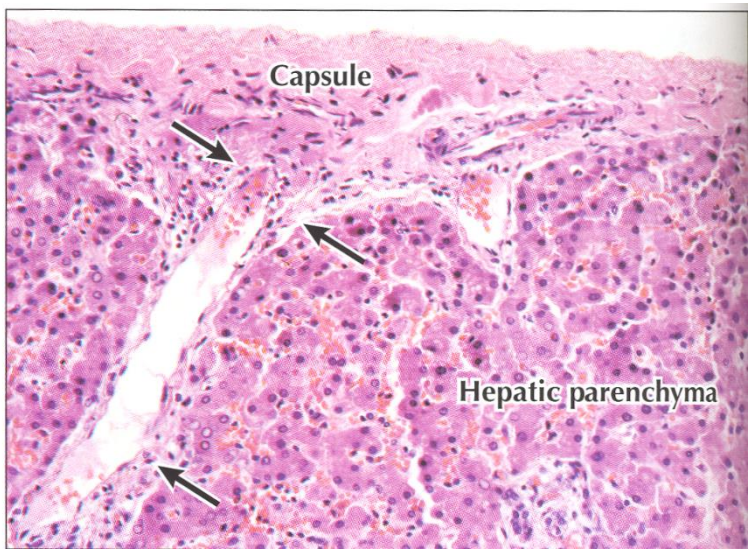


CAPSULA FIBROSA HEPATIS



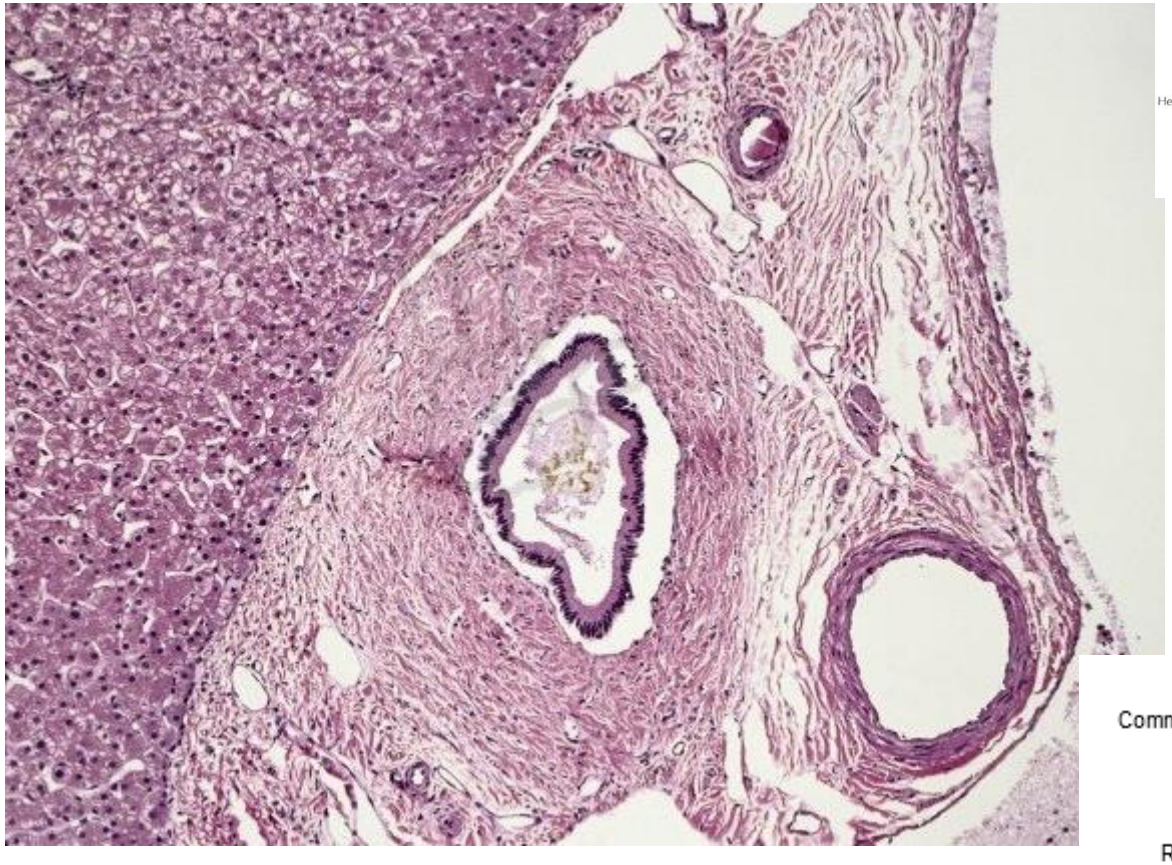
- Serous mesothelium
- Dense collagen c.t. – collagen and elastic fibers
- 70-100μm
- Porta hepatis

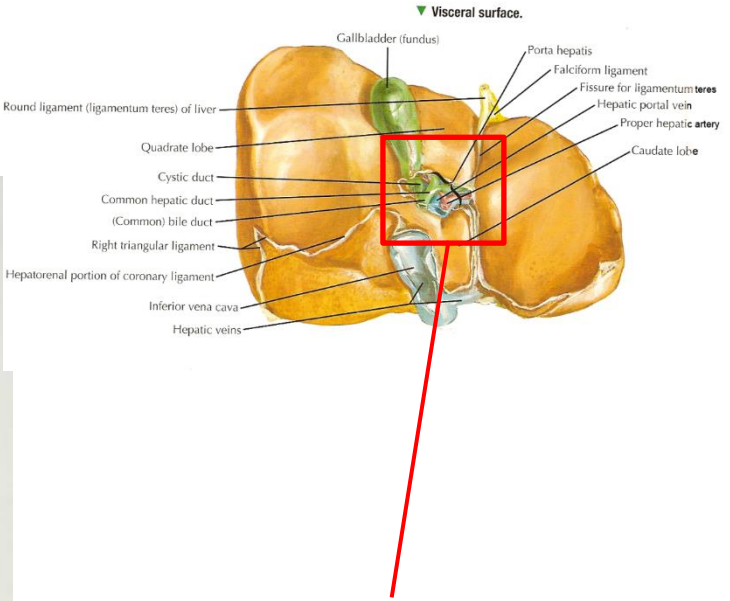




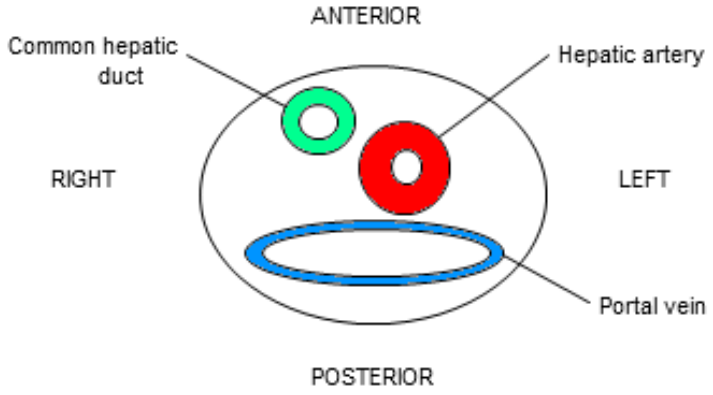
LIVER (HEPAR)

CAPSULA FIBROSA HEPATIS





Porta hepatis



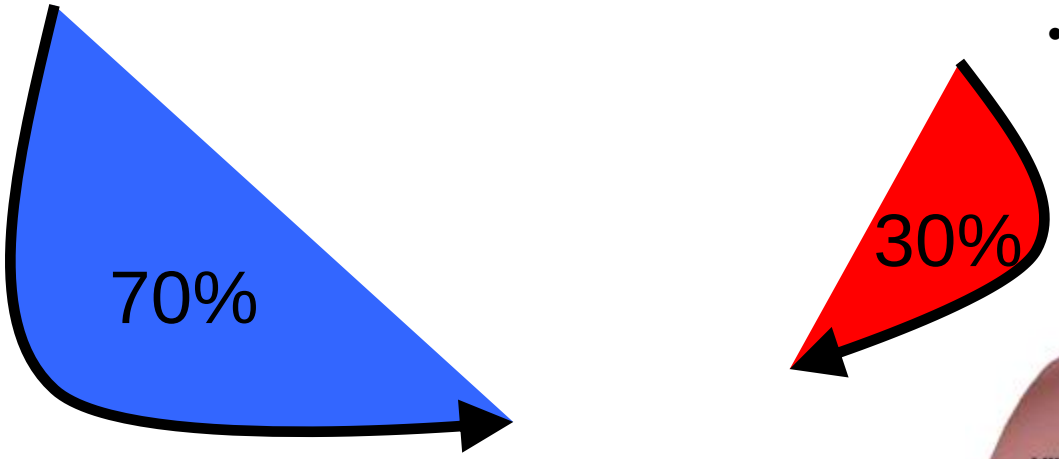
LIVER VASCULARISATION

FUNCTION

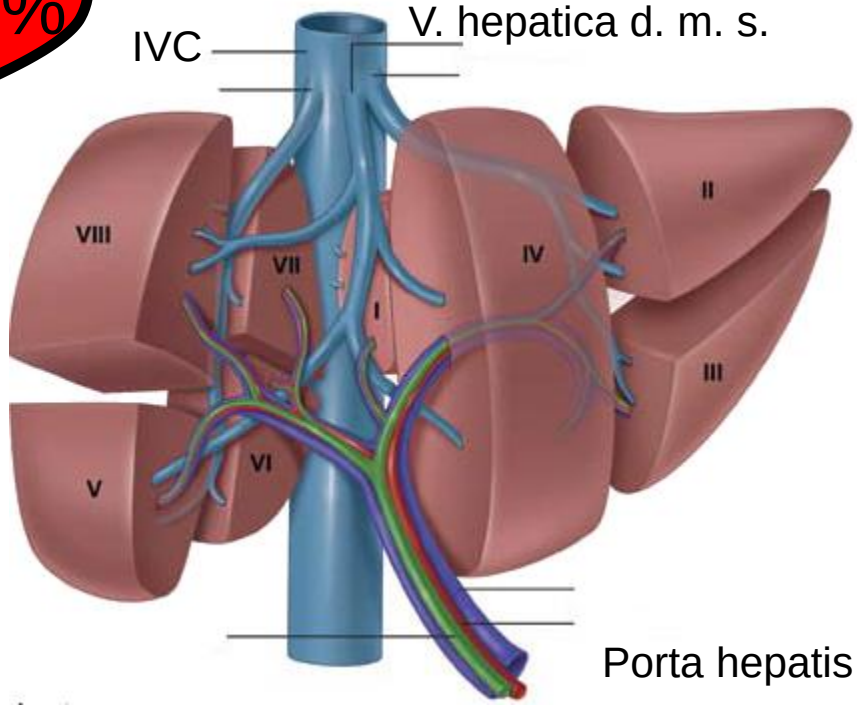
- capillary stream of stomach and intestine
- vena portae
- interlobular veins
- circumlobular venules

NUTRITITION

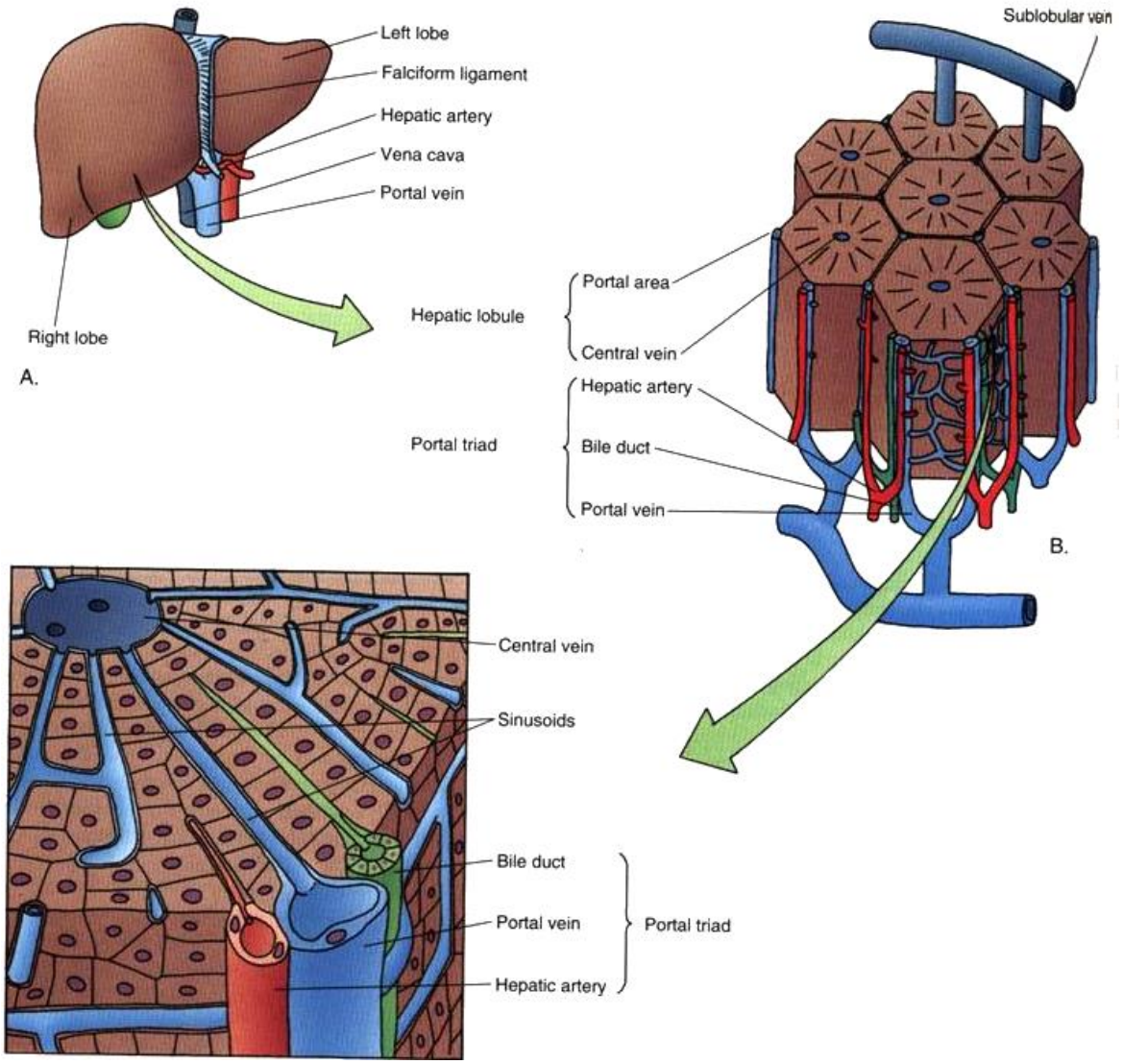
- aorta
- arteria hepatica
- segmental arteries
- interlobular arteries
- circumlobular arteriols



- **hepatic sinusoids**
- venae centrales hepatis
- venae sublobulares
- venae hepaticae
- vena cava inferior

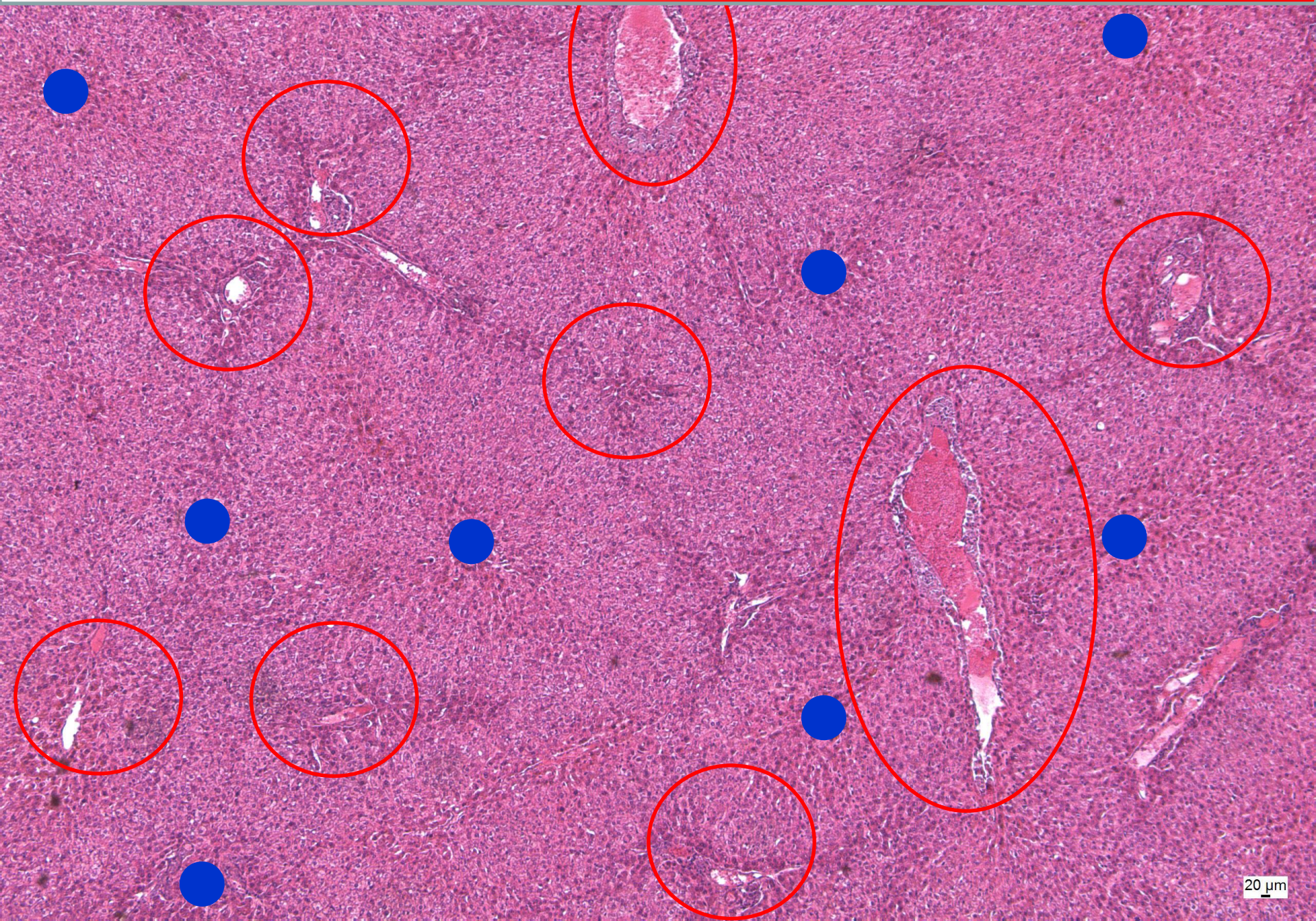


LIVER VASCULARISATION



Gartner, Hiatt: Color Textbook of Histology (2001)

MICROSCOPIC SEGMENTATION OF LIVER



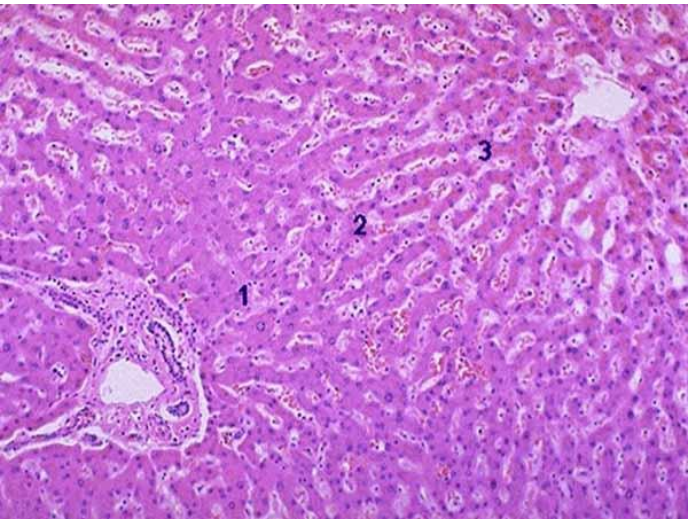
MICROSCOPIC SEGMENTATION OF LIVER

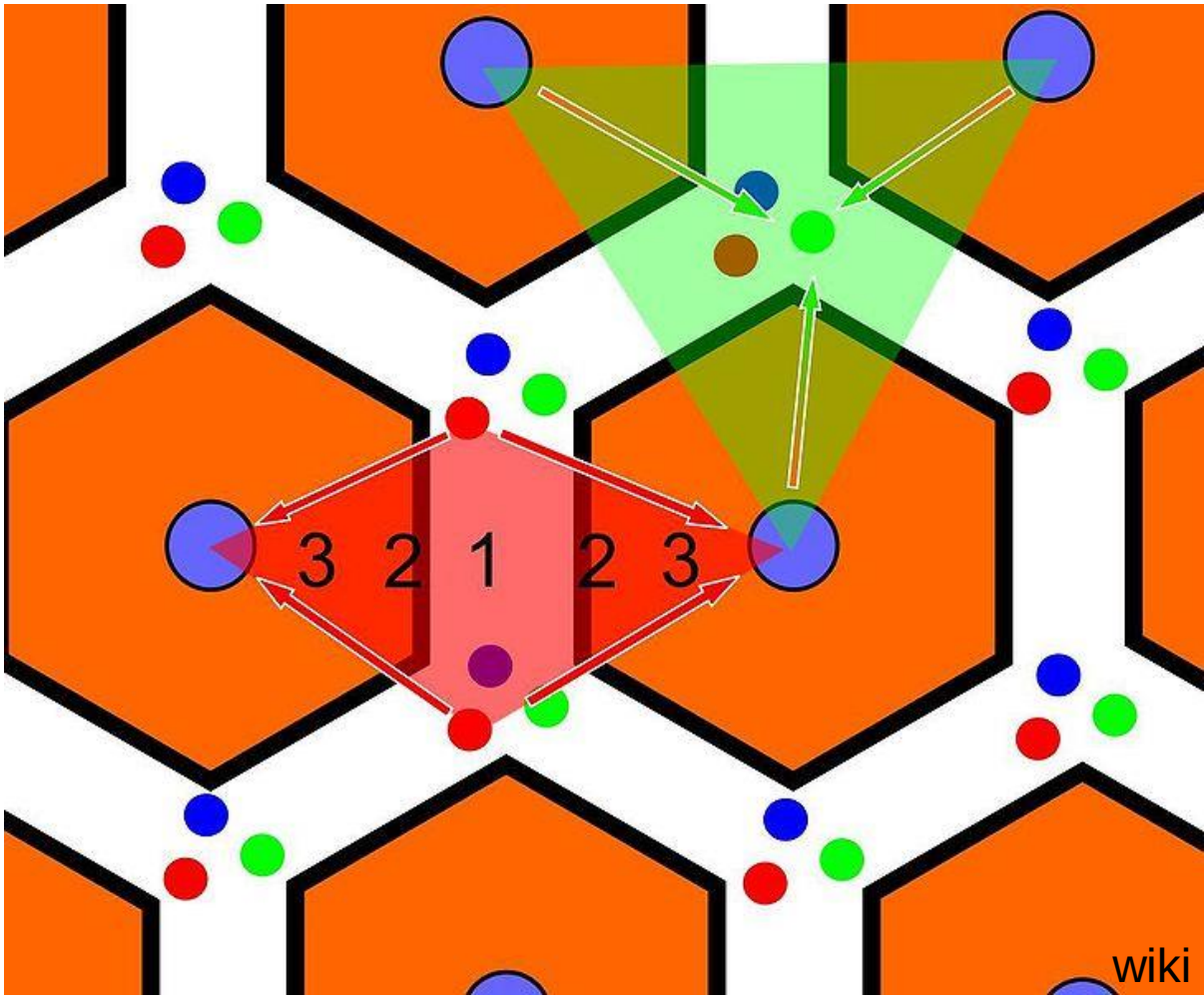
Definitions:

- **Histological – liver lobulus (lobulus venae centralis)**

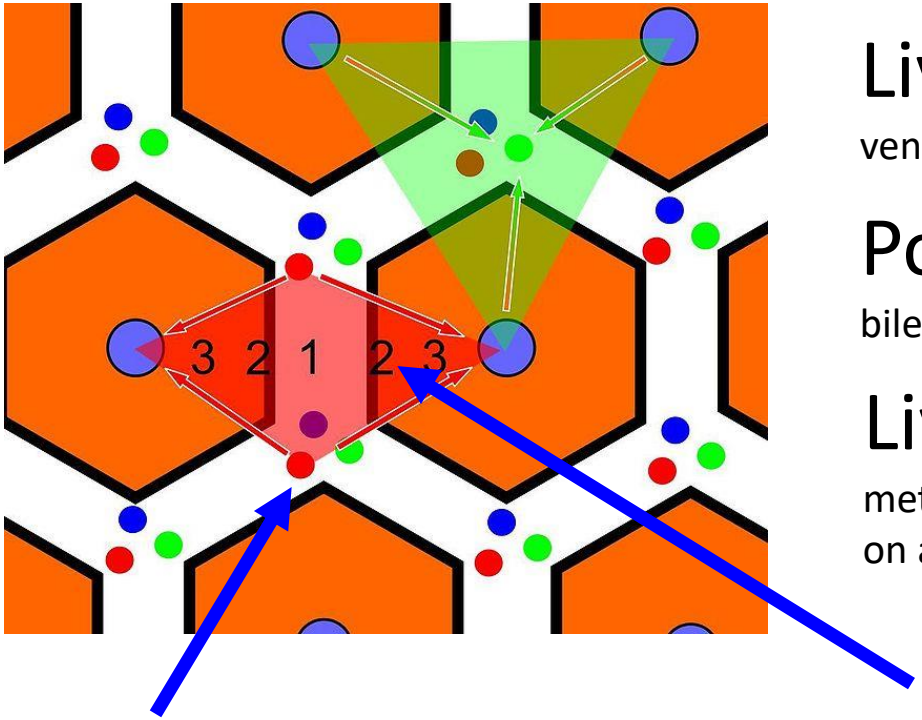
- **Metabolic** – liver acinus
  - metabolic zone 1 – 3
  - oxygenation of hepatocytes

- **Functional unit**
  – lobulus venae interlobularis
  (portal acinus)





MICROSCOPIC SEGMENTATION OF LIVER



Liver lobulus

venous drainage

Portal acinus

bile drainage

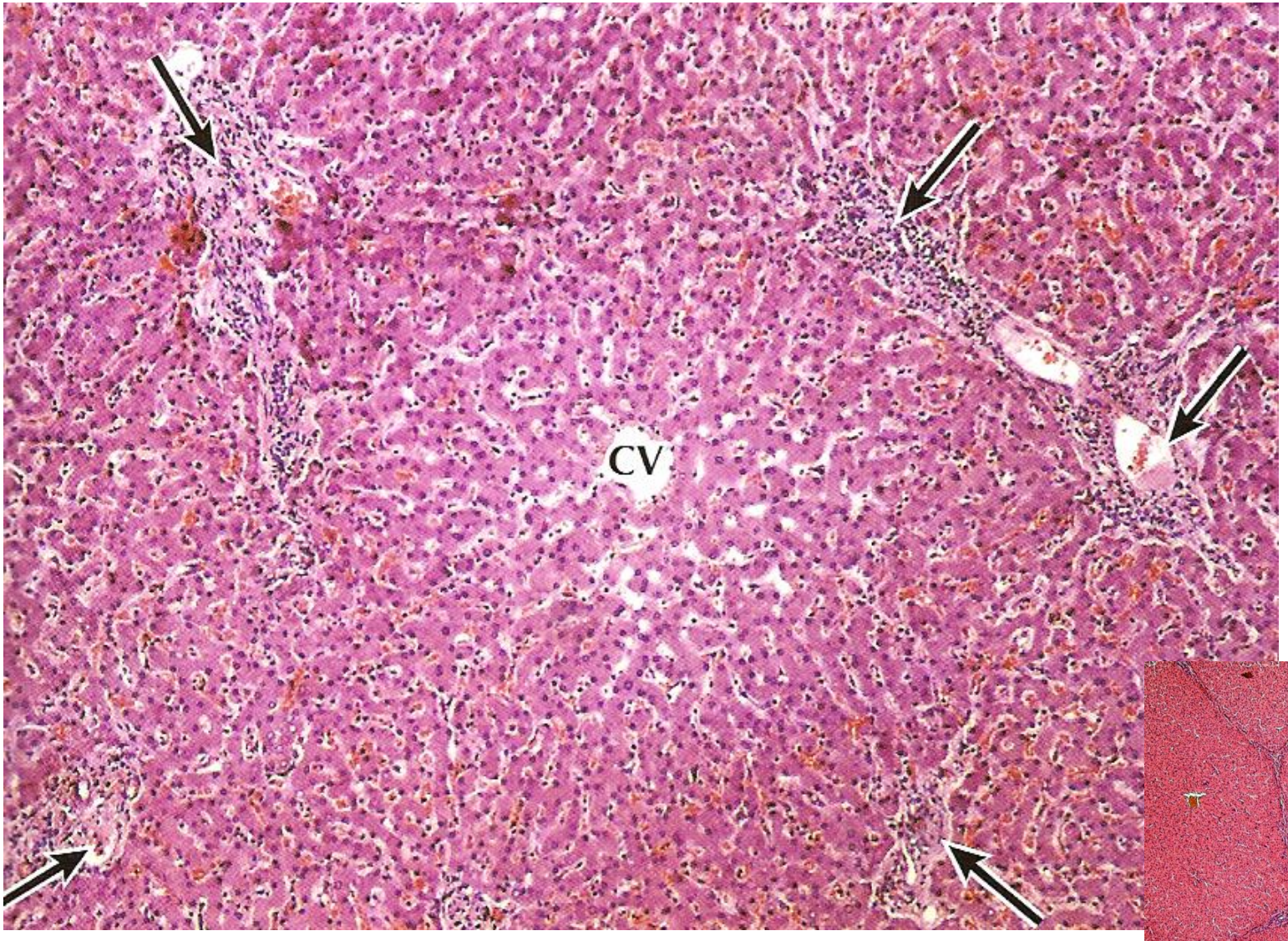
Liver acinus

metabolic divergence dependent on arterio-venous gradients

Zone I (periportal)	Zone III (perivenous)
oxidative processes	glycogen synthesis
beta-oxidation of fatty acids	glycolysis
catabolism of aminoacids	lipogenesis
gluconeogenesis	ketogenesis
production of urea	production of glutamine
synthesis of cholesterol	synthesis of bile acids
glycogenolysis	biotransformation
production of bile	

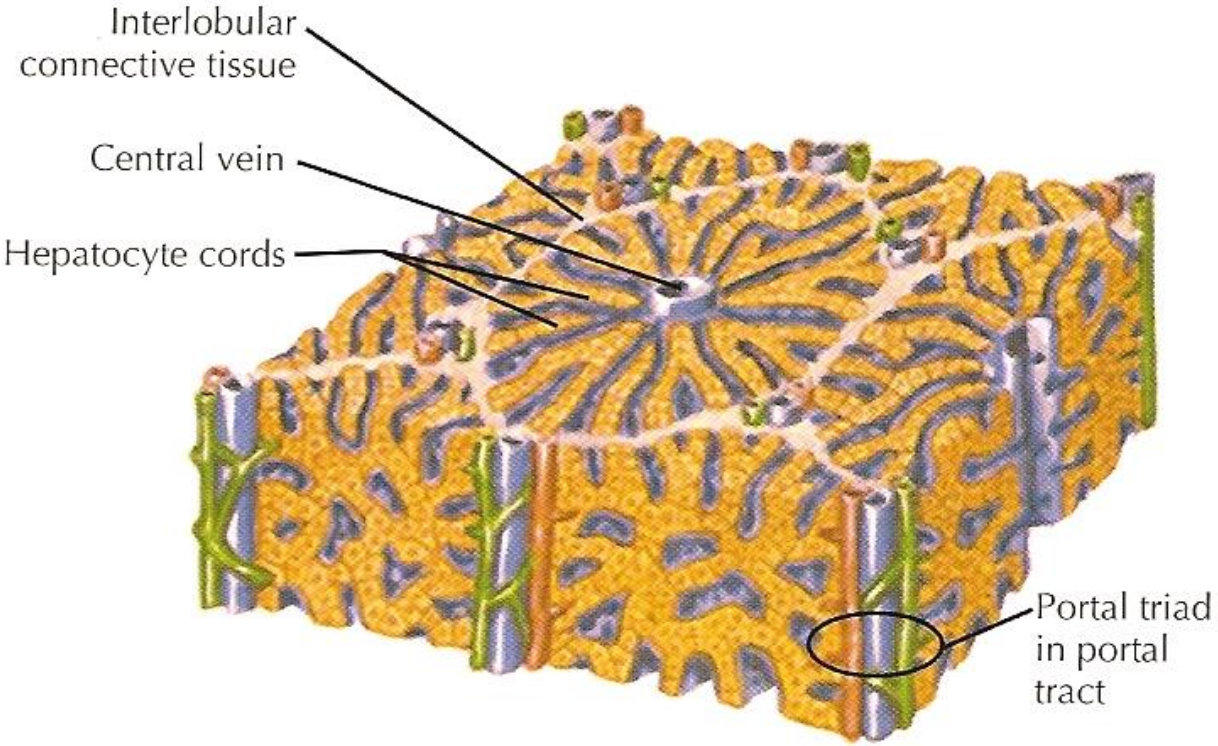
LIVER LOBULUS

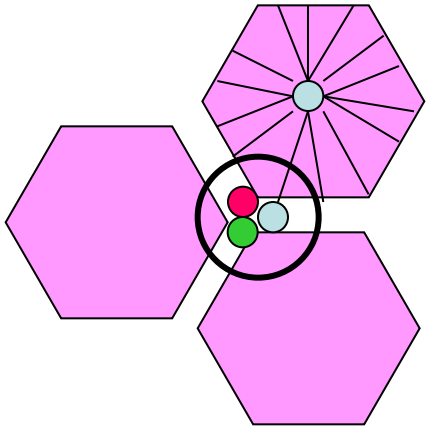
Lobulus venae centralis



LIVER LOBULUS

- Classical morphological unit
- Polygonal cells (hexagonal), 0.7 x 2mm
- Central vein
- Radial cords of hepatocytes
- Liver sinusoids
- Portal triad, portobilliary region



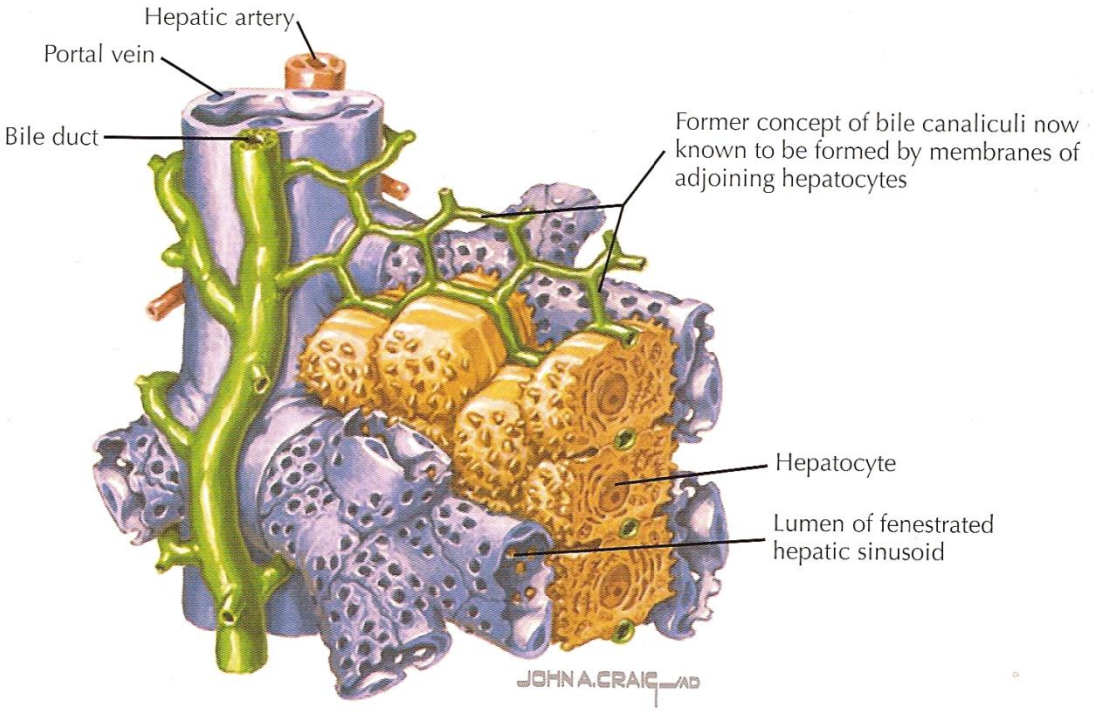


LIVER LOBULUS – PORTAL TRIAD

Contact of 3-4 neighboring lobuli

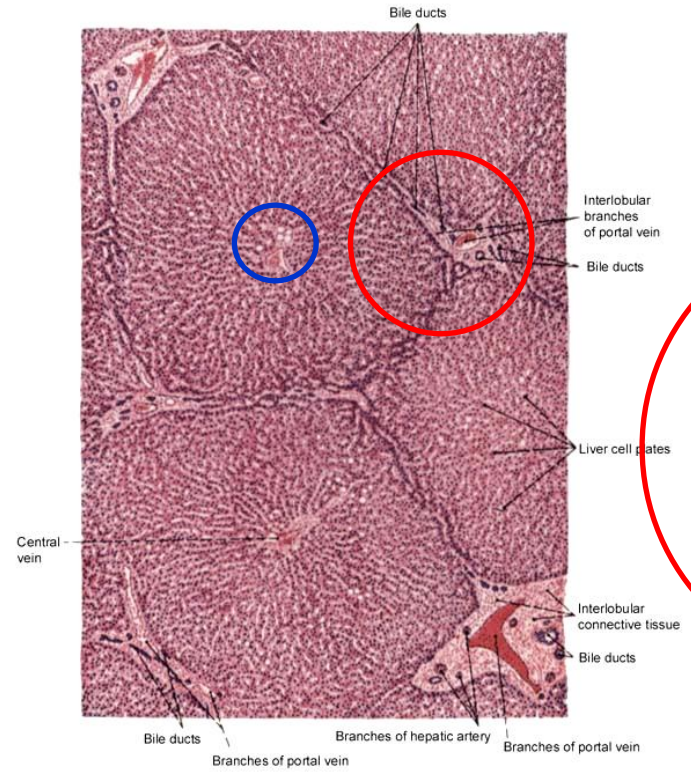
- Interlobular artery (*a. interlobularis*)
- Interlobular vein (*v. interlobularis*)
- Interlobular bile duct (*d. bilifer interlobularis*)
- Lymphatic vessels
- Innervation – *nervus vagus*

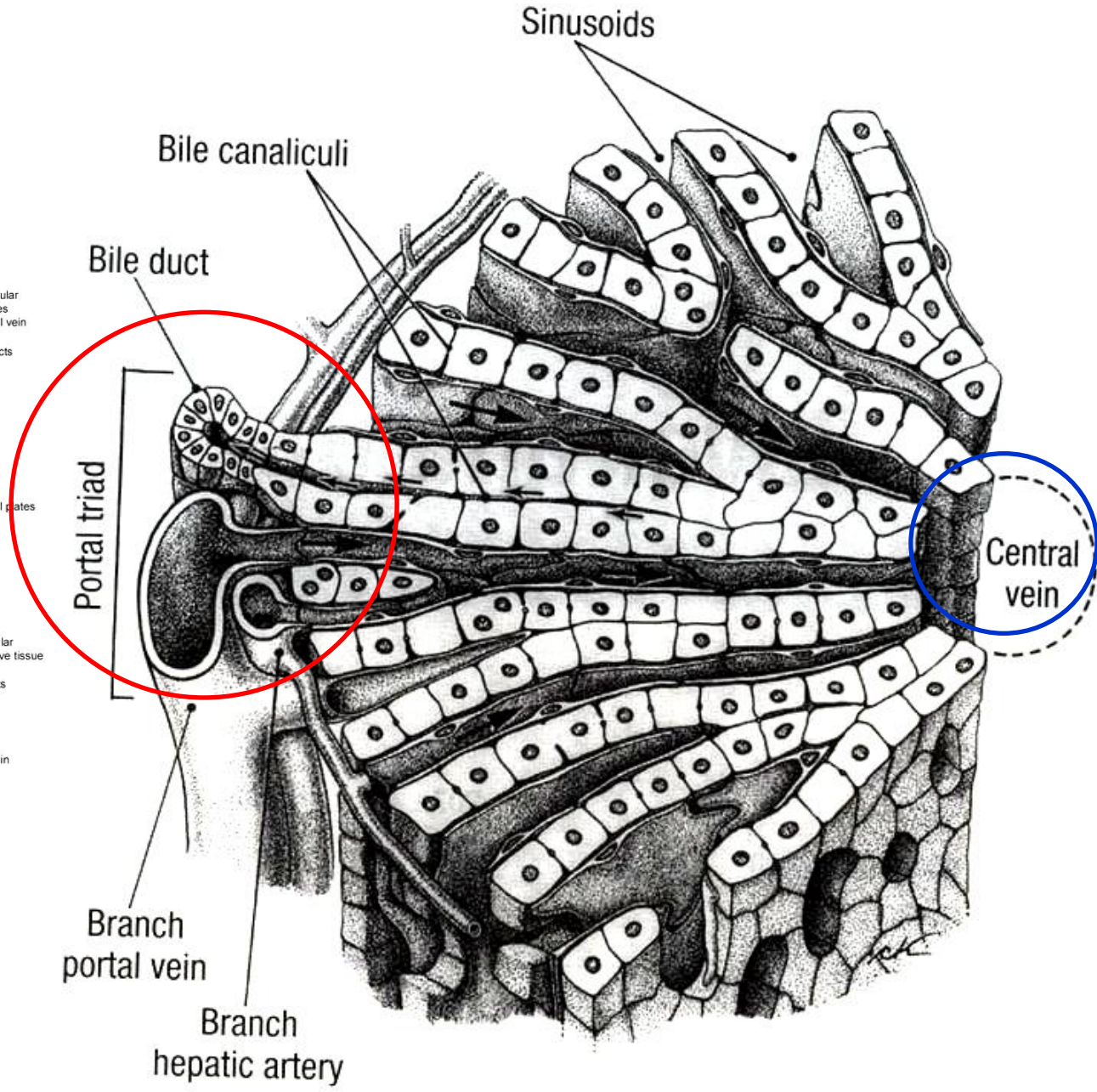
Loose interstitial c.t.



▲ **Parts of hepatic lobule at portal triad (high magnification).**

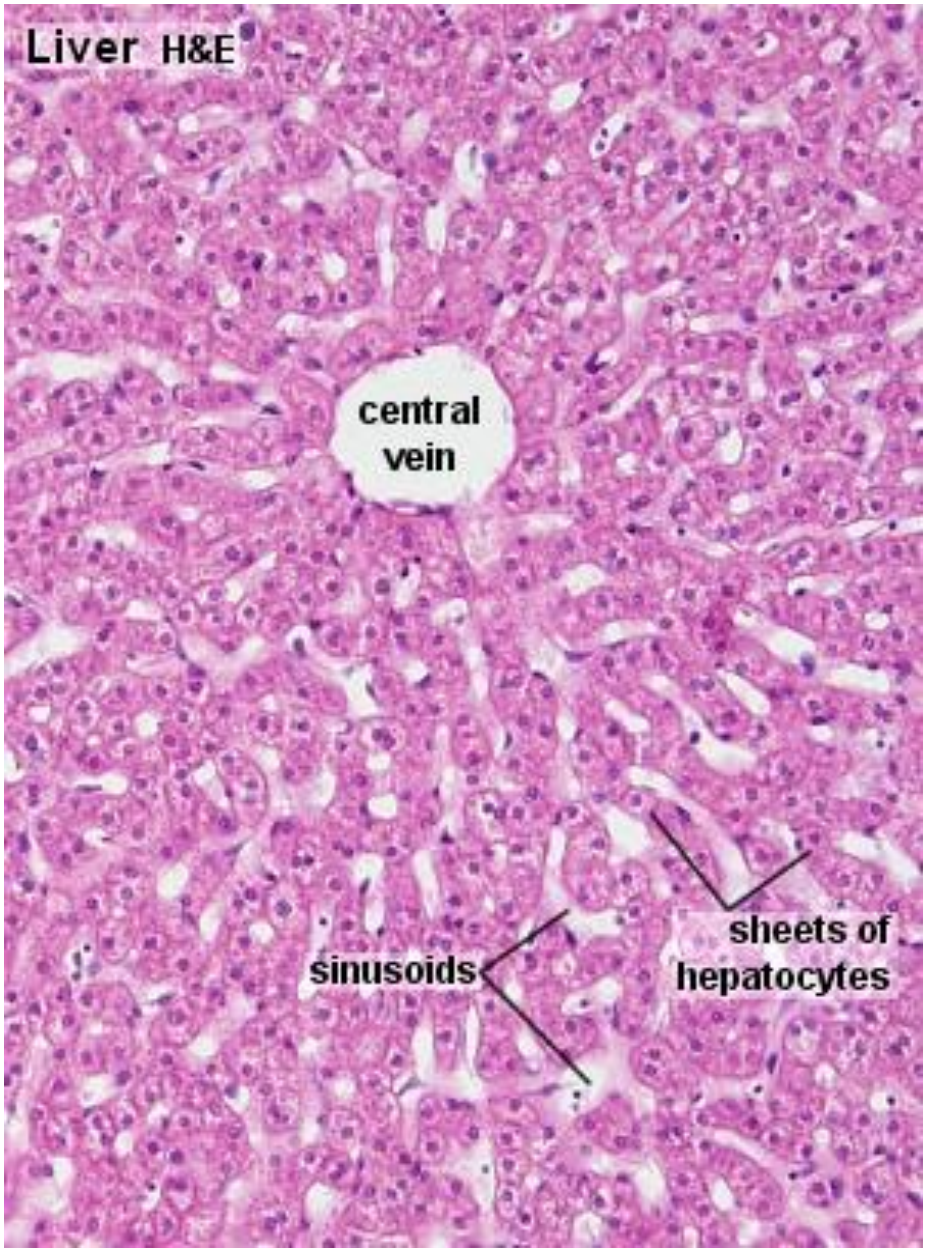
LIVER LOBULUS – CENTRAL VEIN AND PORTAL TRIAD

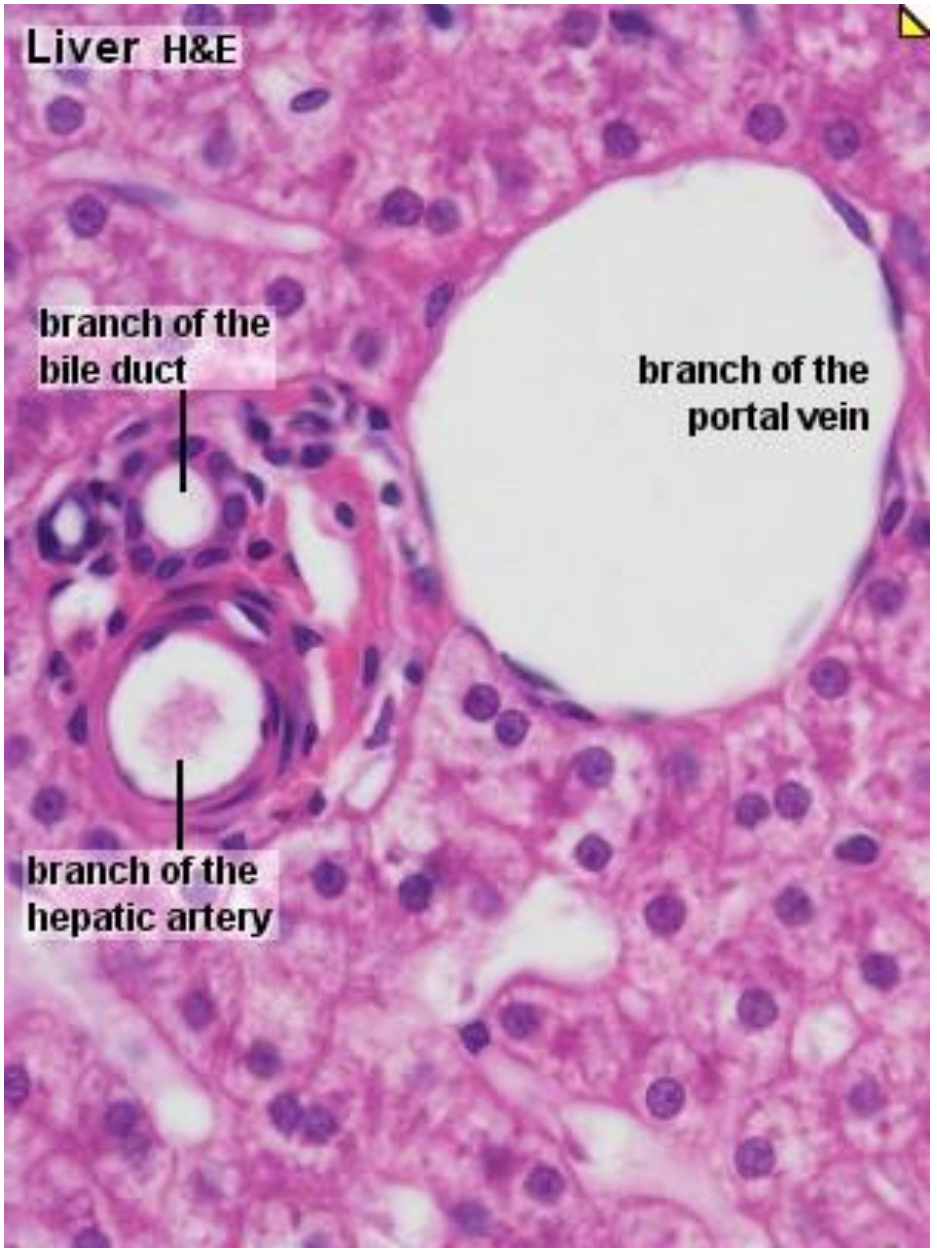




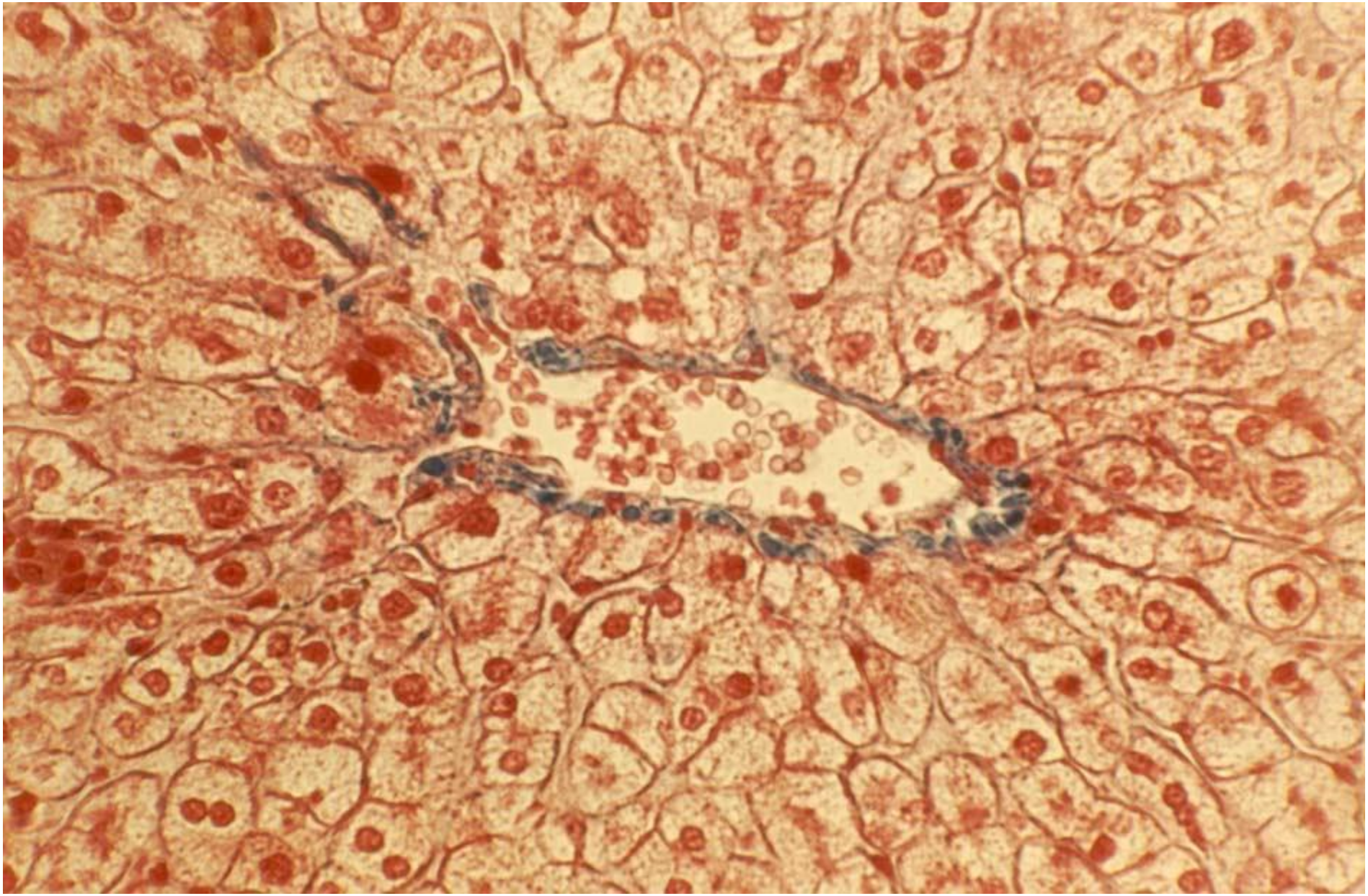
Ham: Textbook of Histology

LIVER LOBULUS – CENTRAL VEIN AND PORTAL TRIAD





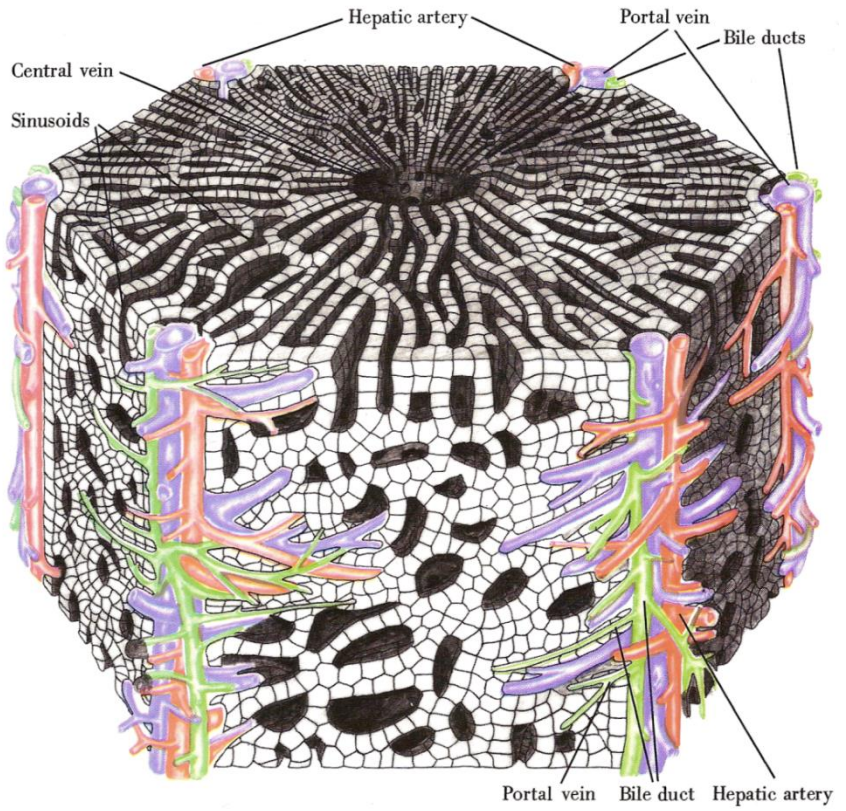
LIVER LOBULUS – CENTRAL VEIN



LIVER PARENCHYMA – HEPATOCYTES AND LIVER SINUSOIDS

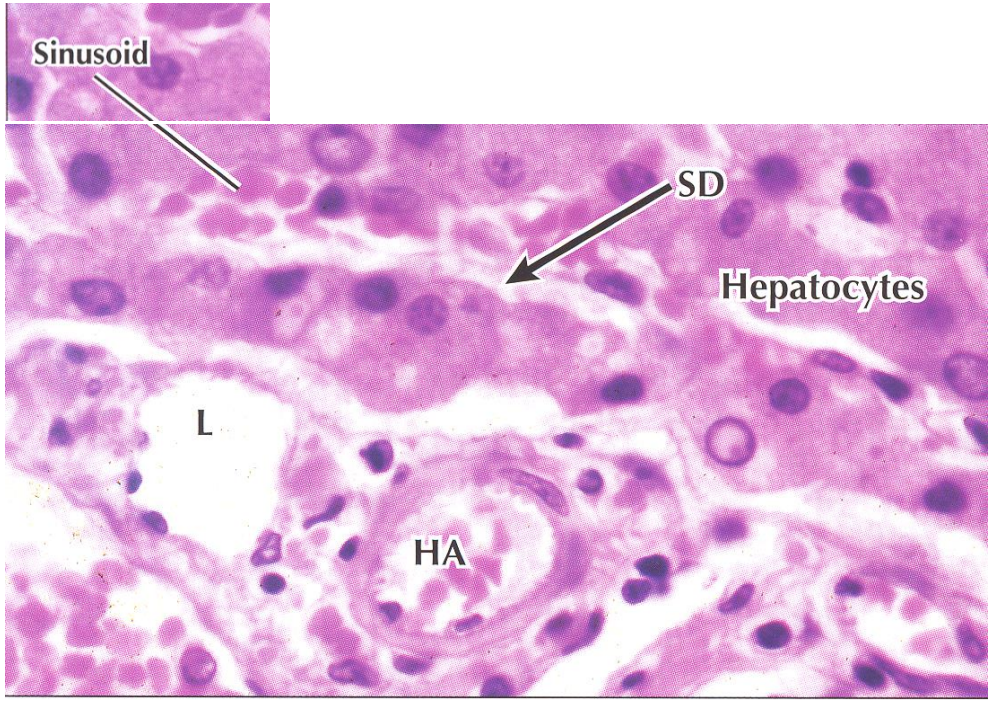
- **Hepatocytes** arranged to cords, width 1-2 cells, often anastomoses
- **Sinusoids**
  - 9-15μm
  - Anastomosing network of flat endothelial cells
  - Basal membrane absent - no diffusion barrier
  - **Fenestrations** - 100nm, diaphragm absent
  - Intercellular space
  - **Perisinusoidal space (of Disse)**
  - Reticular fibers
  - Dispersed **Kuppfer cells** (monocyte-macrophage system)
  - **Perisinusoidal cells** of Ito

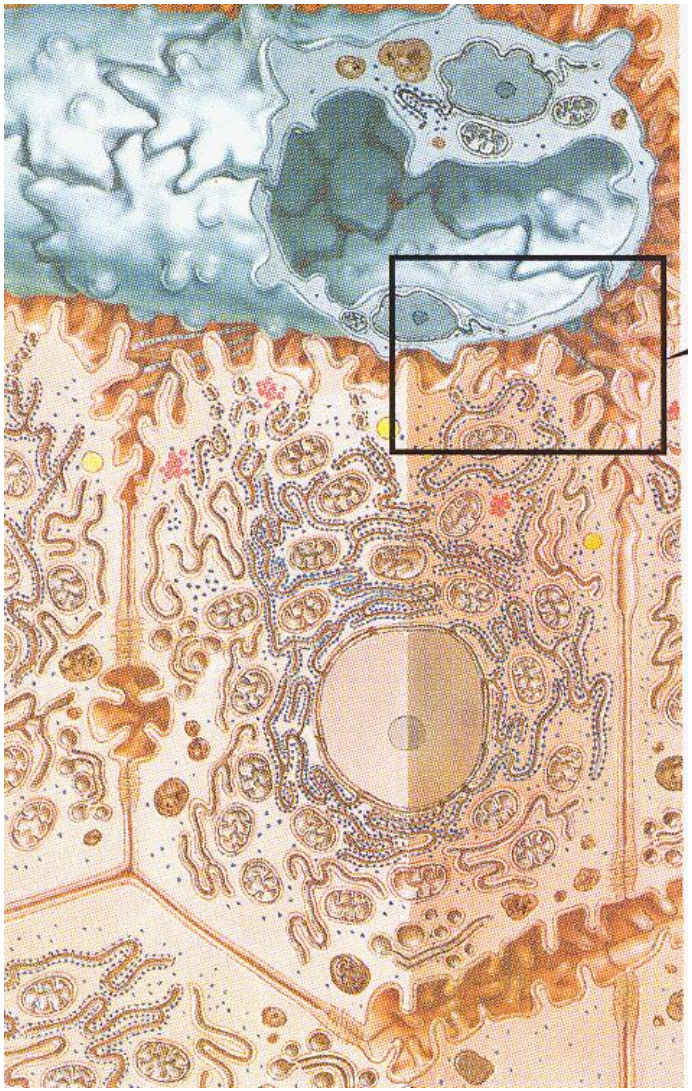
- Vena centralis – thin-walled vessel, draining blood from sinusoids



LIVER PARENCHYMA – HEPATOCYTES AND LIVER SINUSOIDS

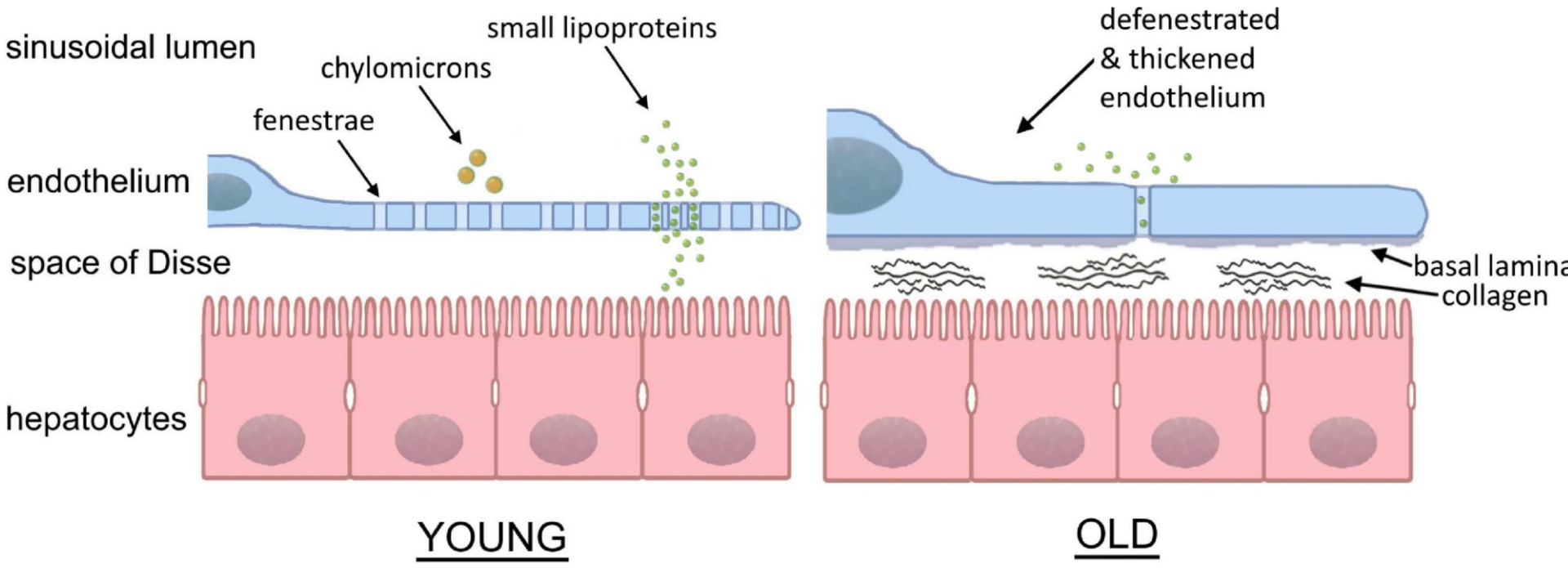
- Space of Disse
  - Connection of space of Disse and sinusoidal lumen by fenestrated endothelium
  - Hepatocytes in direct contact with plasma (microvilli)
  - Cells of Ito





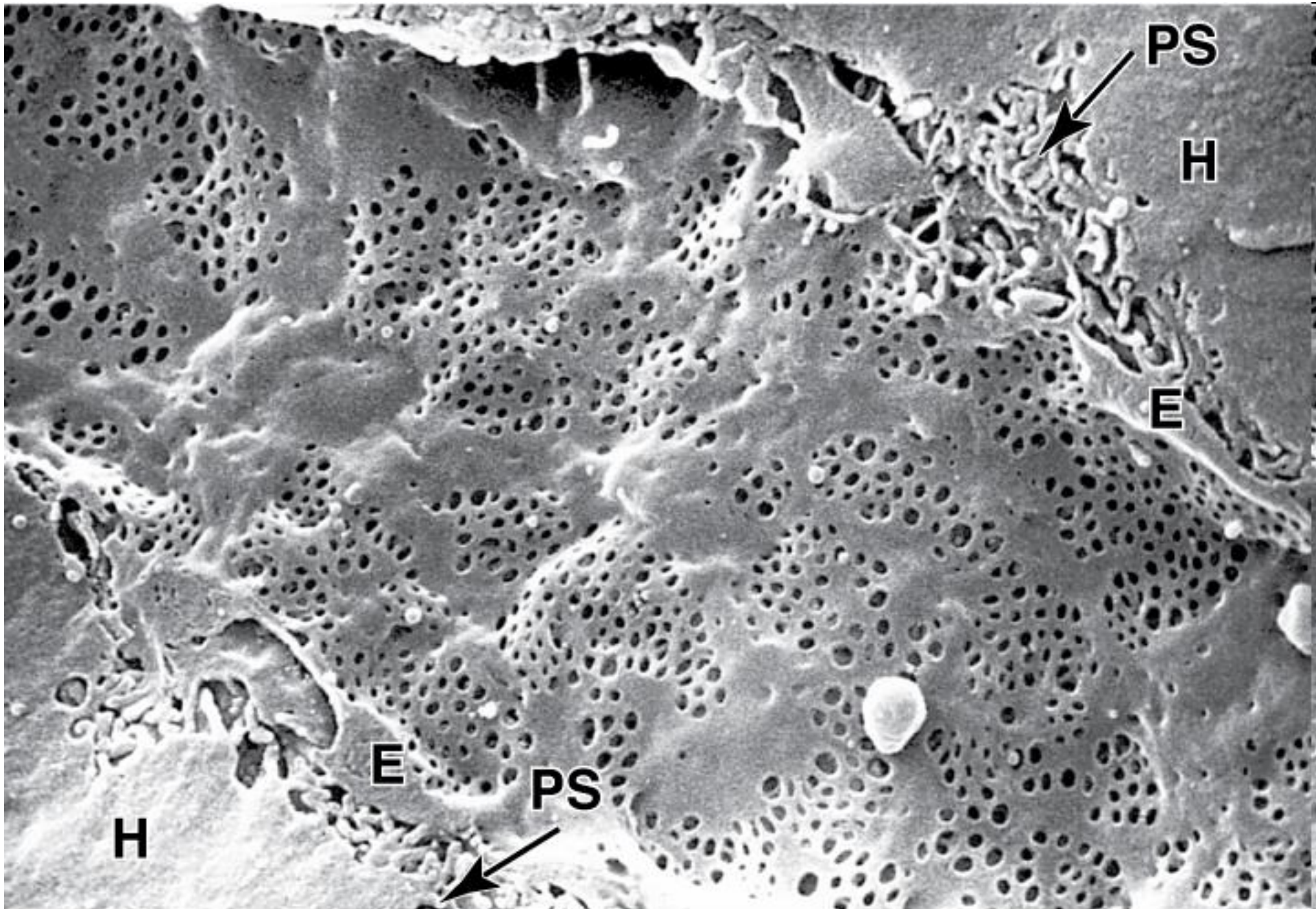
LIVER SINUSOIDS

- Fenestrations are complex structures involved in selective transport
- They deteriorate with age compromising sinusoid functions

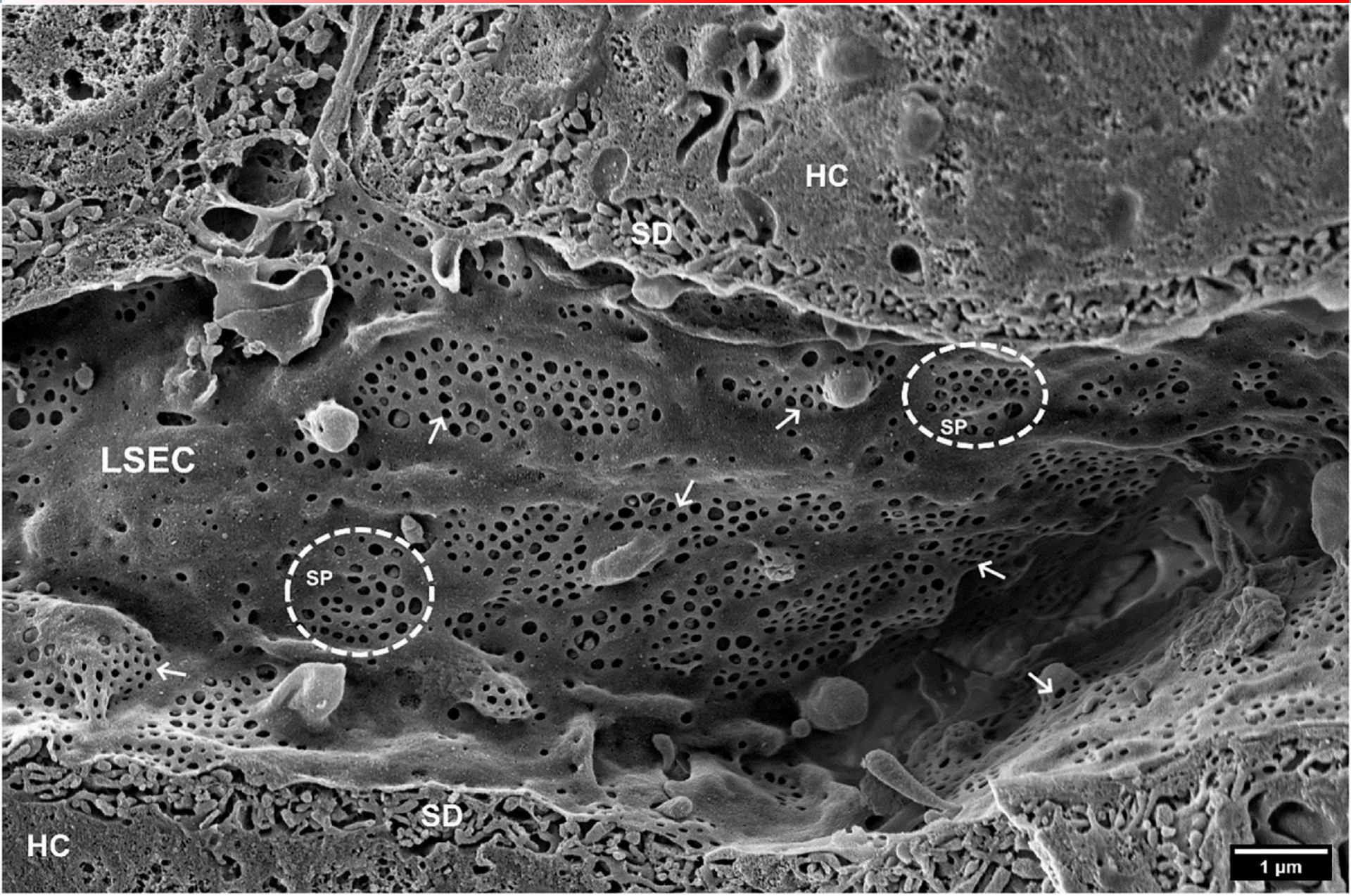


https://doi.org/10.3389/fphys.2021.735573

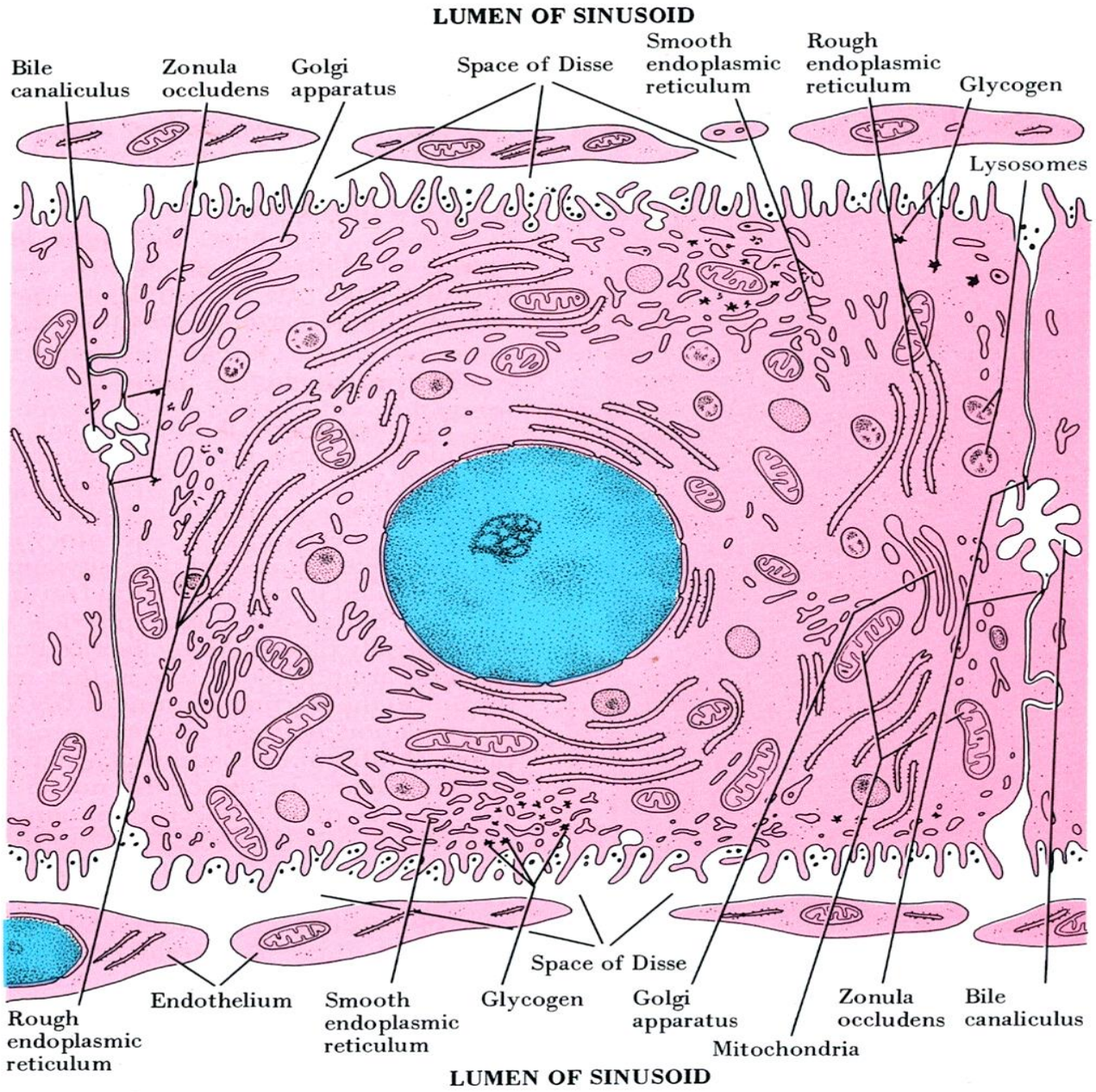
LIVER PARENCHYMA – LIVER SINUSOIDS



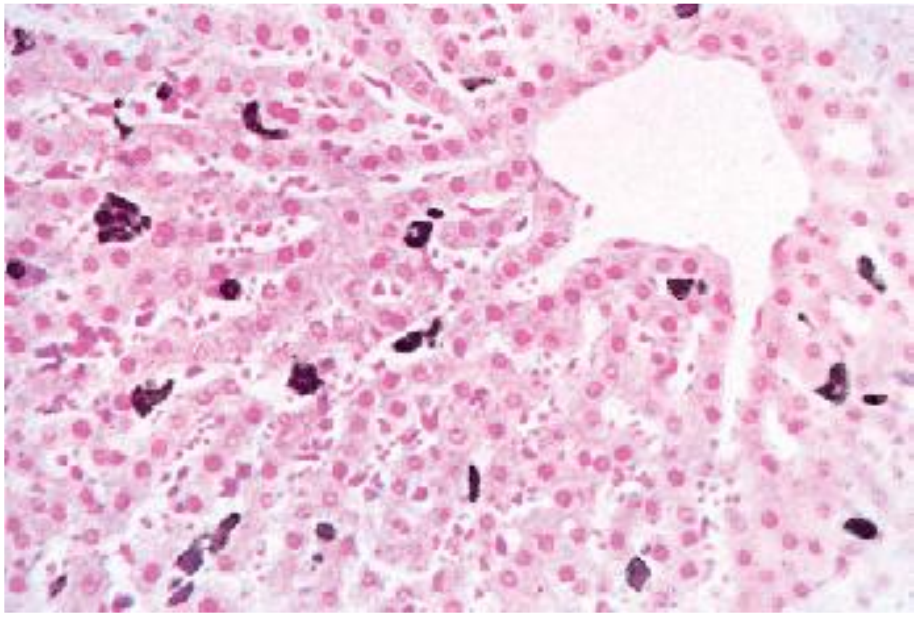
LIVER SINUSOIDS

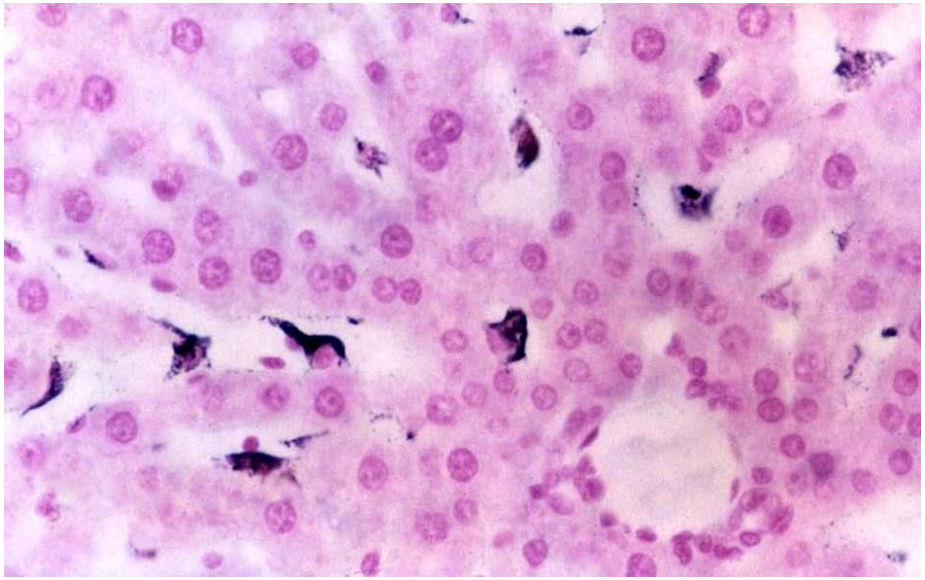


LIVER PARENCHYMA – HEPATOCYTES AND LIVER SINUSOIDS



LIVER PARENCHYMA – OTHER CELL TYPES

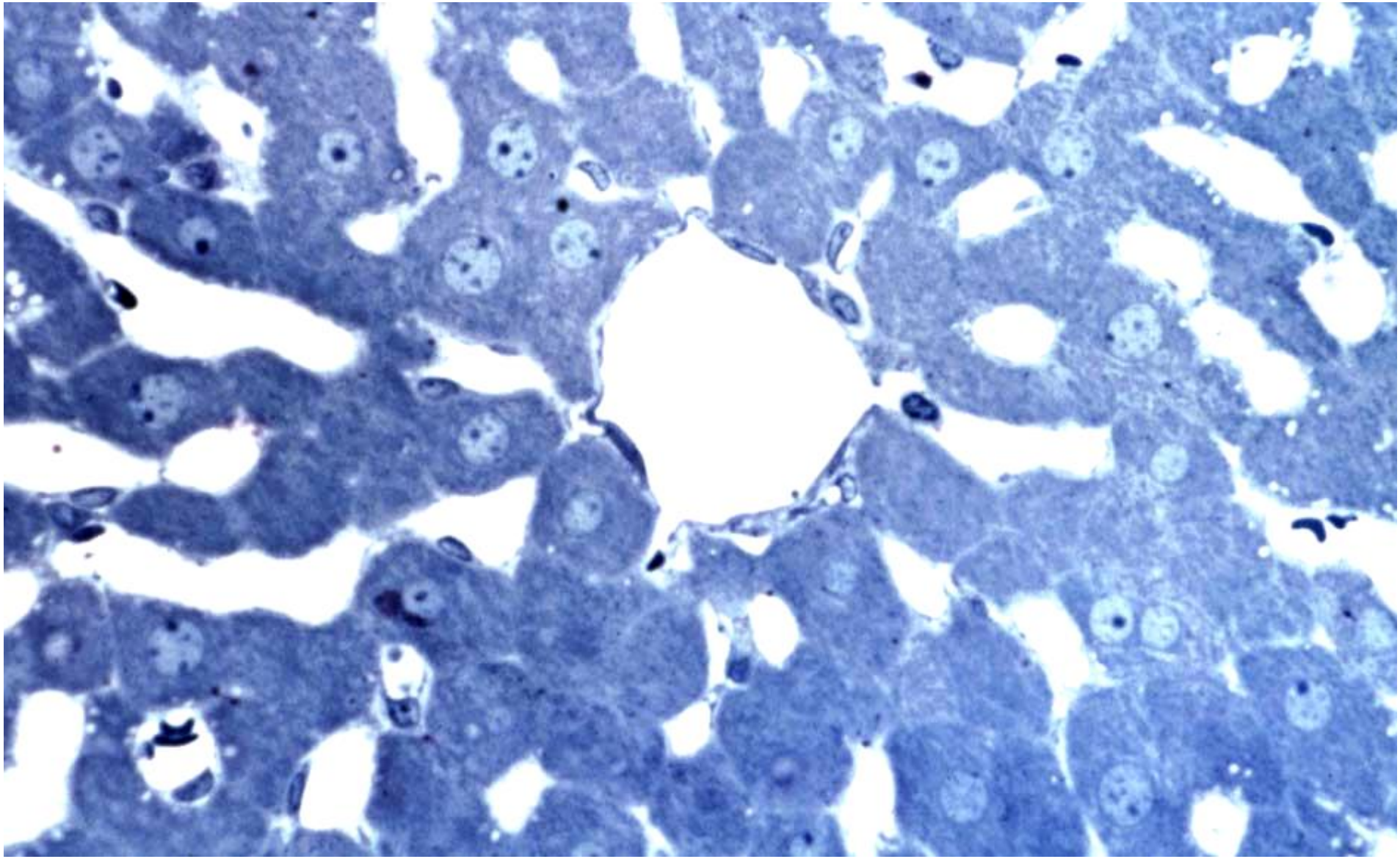




KUPFFER CELLS

- Liver macrophages
- Mononuclear phagocyte system
- Phagocytosis of particles, damaged erythrocytes and pathogens

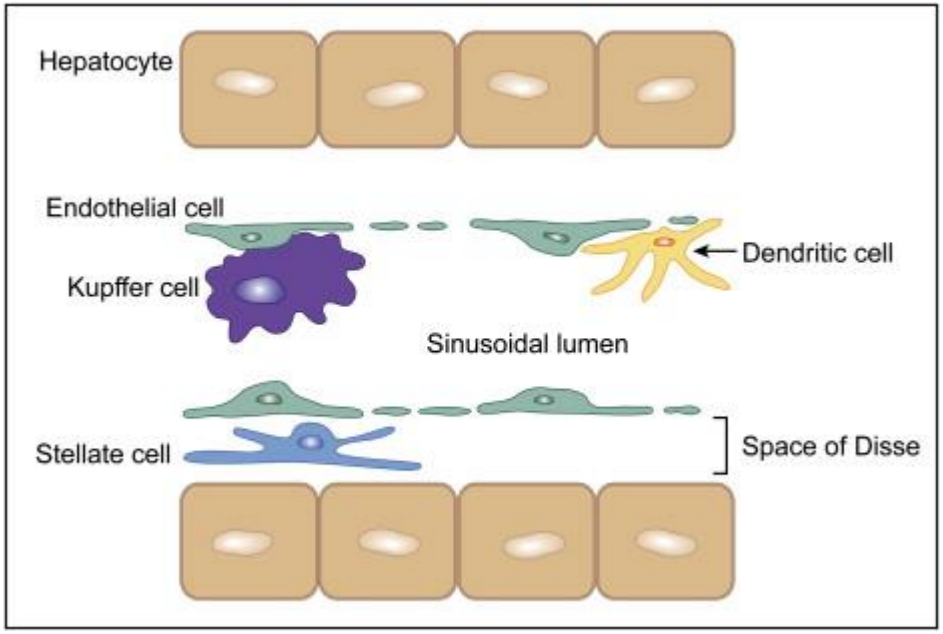
LIVER PARENCHYMA – HEPATOCYTES AND LIVER SINUSOIDS

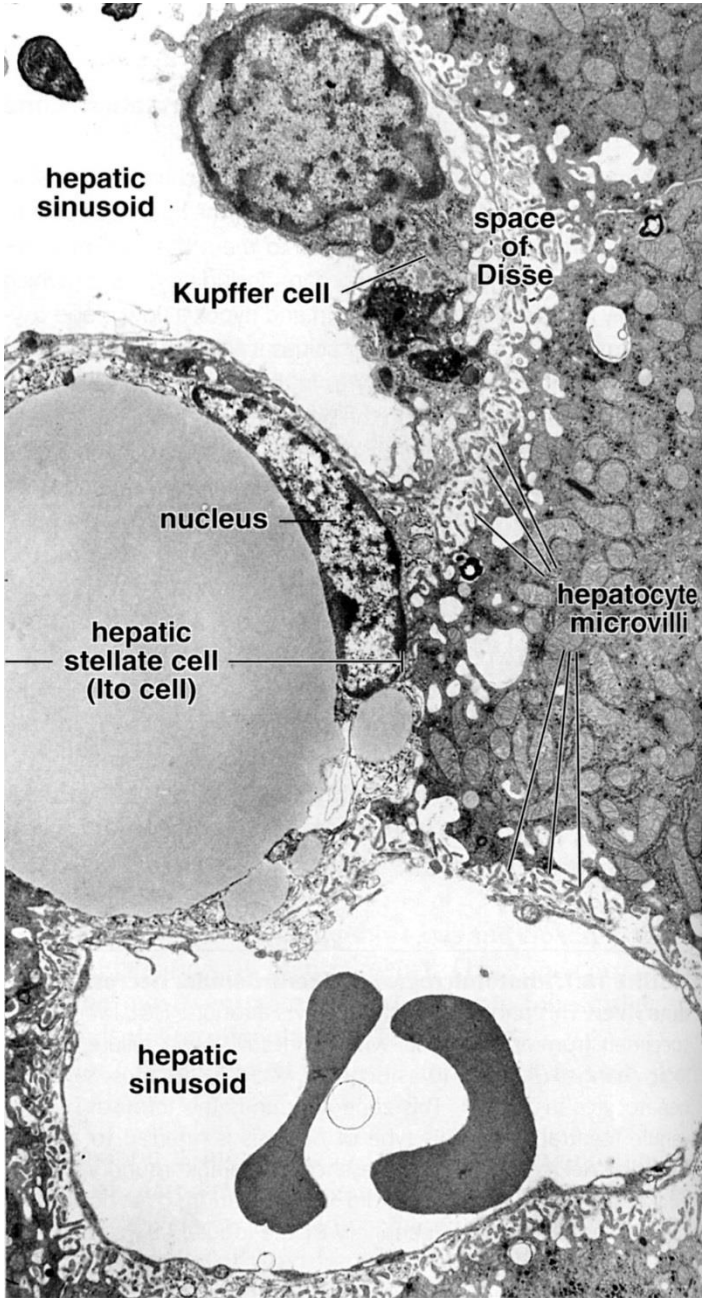


LIVER PARENCHYMA – OTHER CELL TYPES

CELLS OF ITO

- Star-shape (stellate, perisinusoidal) cells
- Lipid droplets
- Deposition of vitamin A
- Fine reticular c.t.
- Antigen presenting cells (lipid antigens)

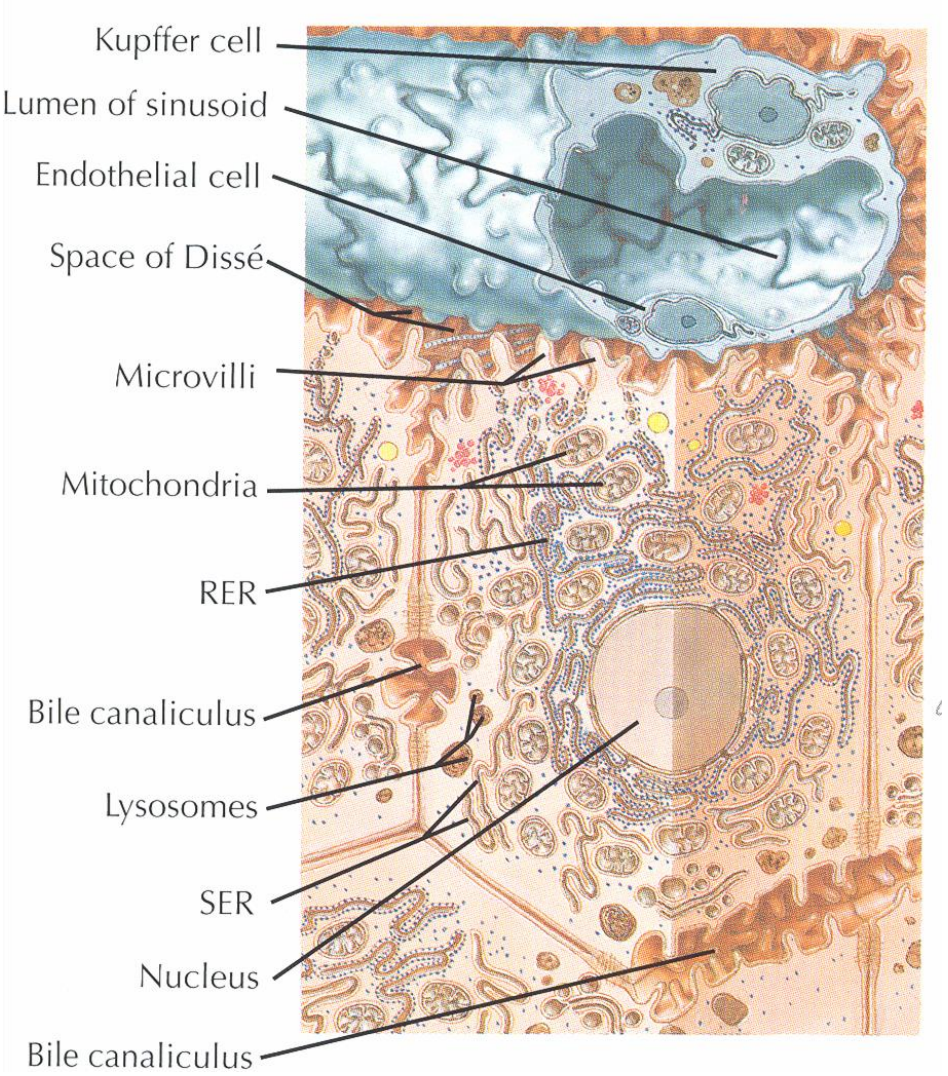




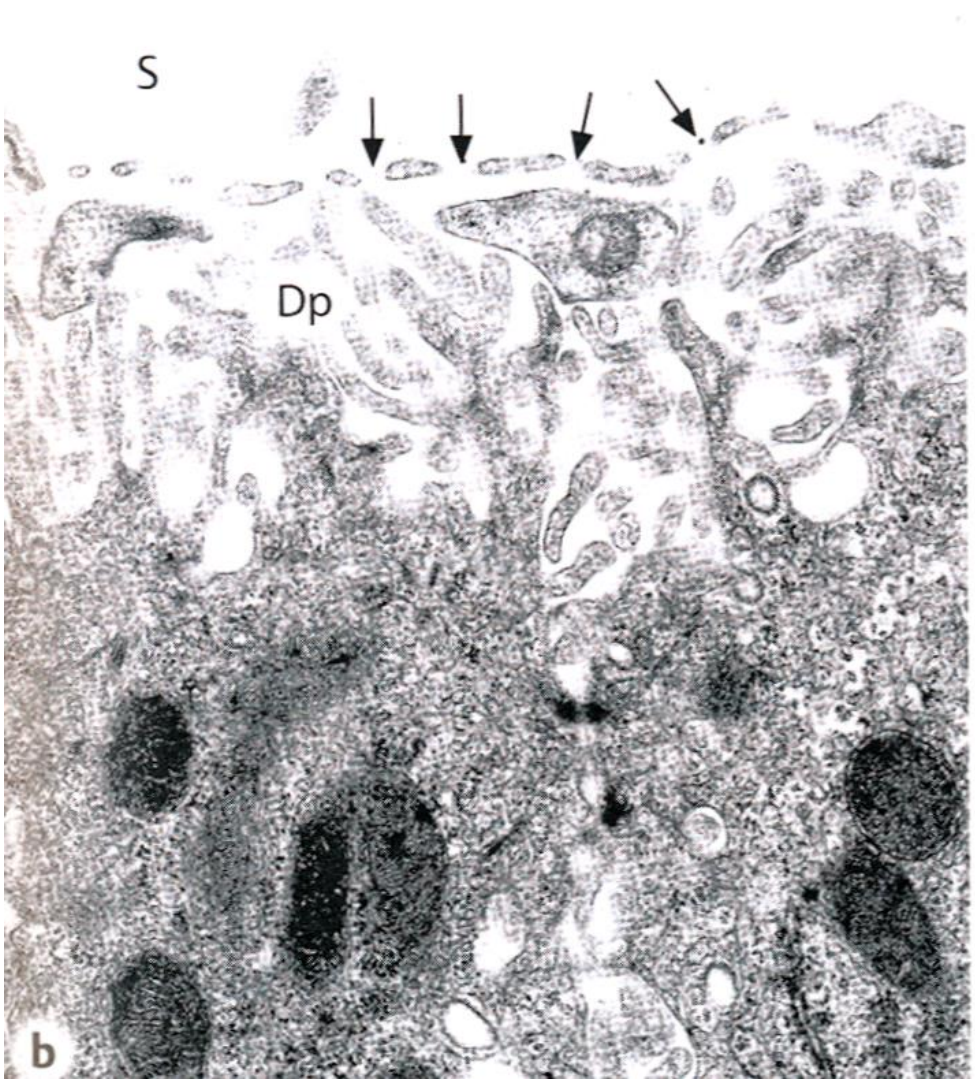
HEPATOCYTES

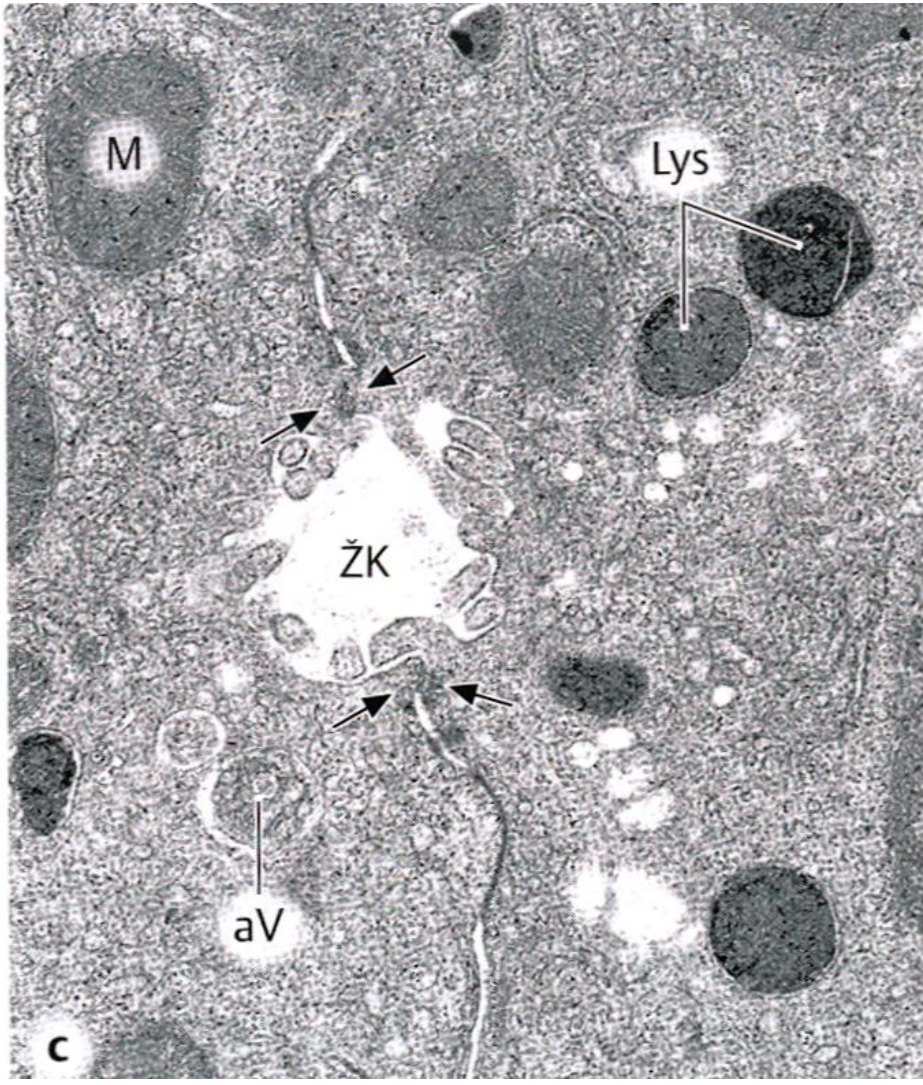
- Polygonal cells of liver parenchyma
- 20x30μm
- Irregular trabecules between sinusoids
- Usually one central nucleus. Bi- and multi-nuclear cells common (20%)
- Nucleoli
- Lysosomes
- Glycogen

- Functional surfaces:
  - Bile pole – secretory – membranes of neighboring hepatocytes form bile canaliculli
  - Blood pole - absorptive - sinusoidal – microvilli oriented to space of Disse
  - Membranes with intercellular junctions

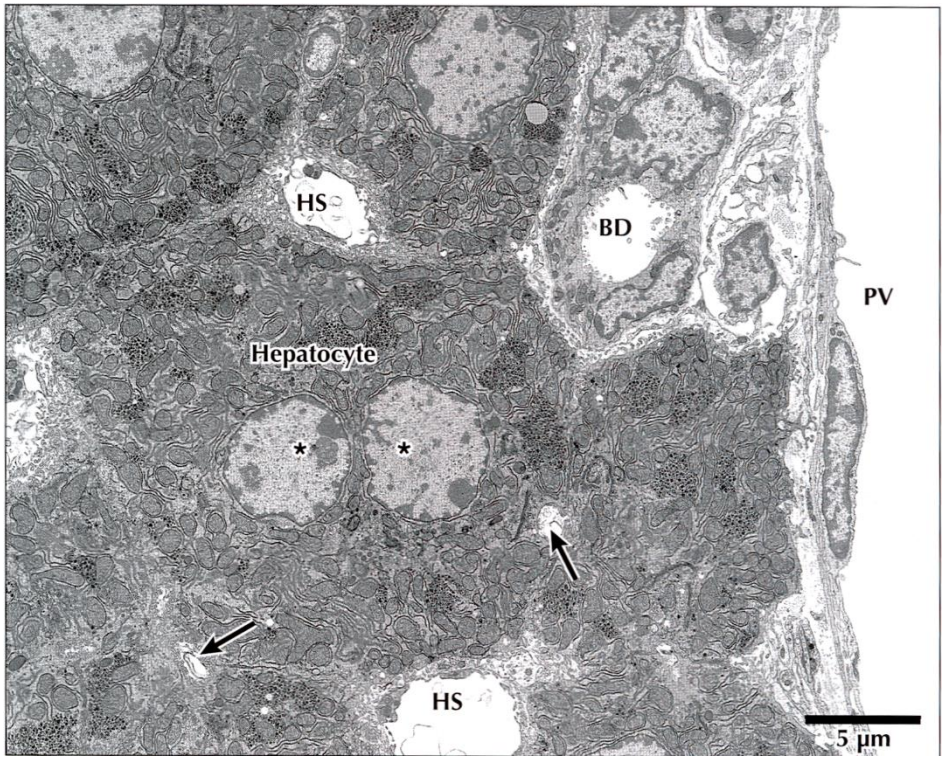


BILIARY AND BLOOD POLES OF HEPATOCYTE

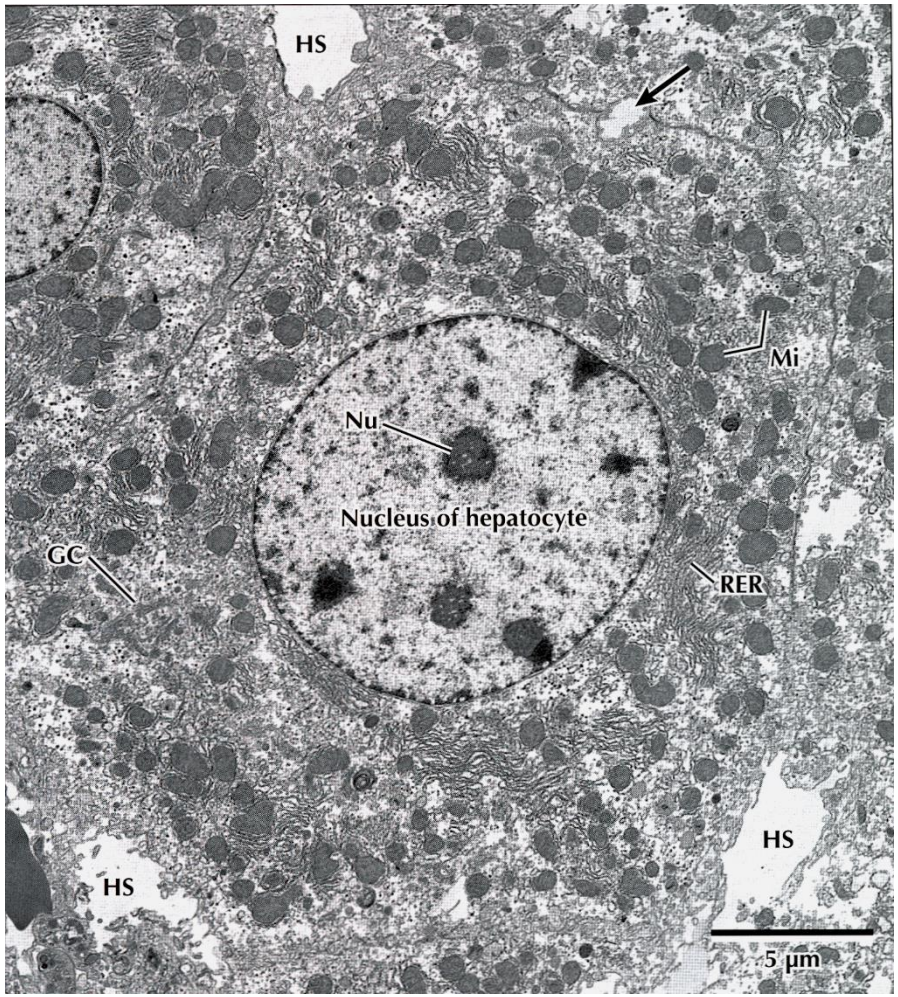




HEPATOCYTES – ULTRASTRUCTURE

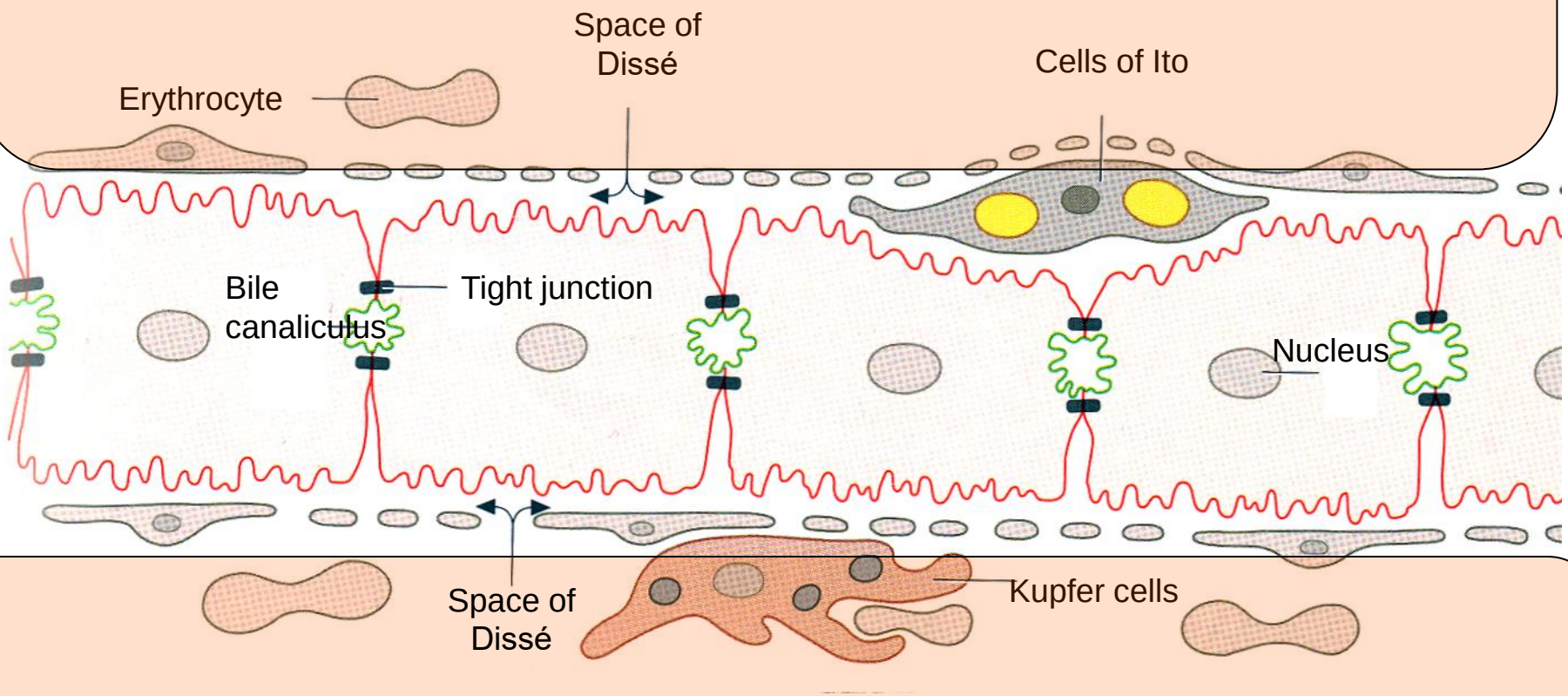


- Long mitochondria with flat or tubular cristae
- Apparent $_{R}$ER, $_{S}$ER and Golgi
- Glycogen, lipid droplets, lysosomes, peroxisomes



HEPATOCYTES – ULTRASTRUCTURE

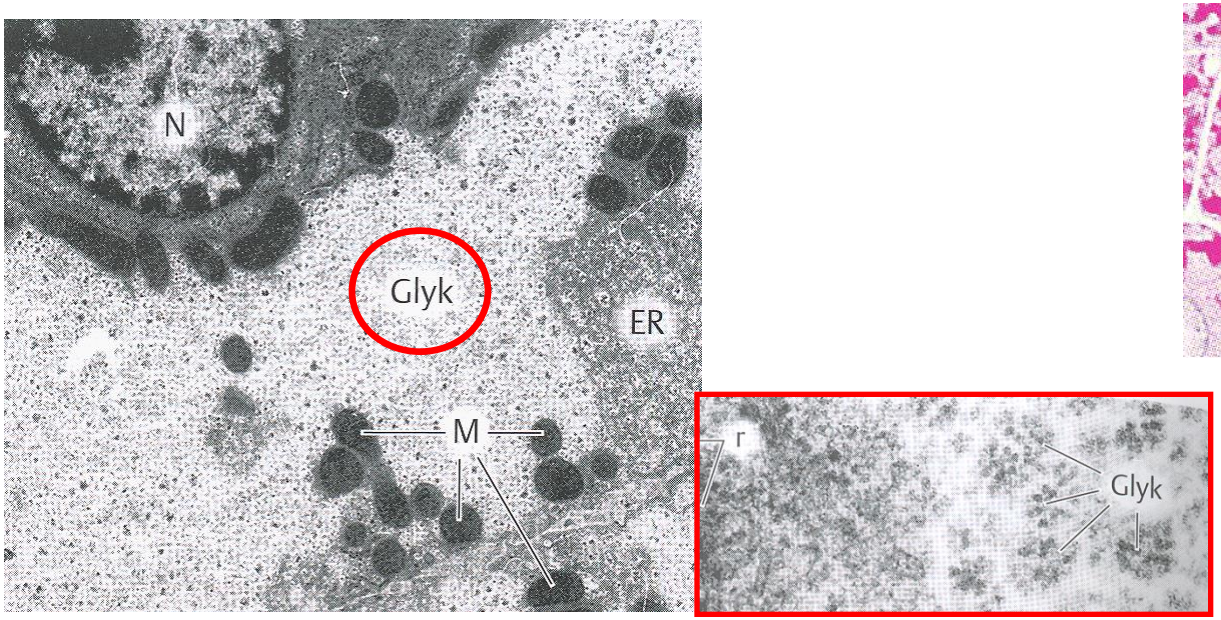
From plasma:
Glucose, aminoacids, bile acids

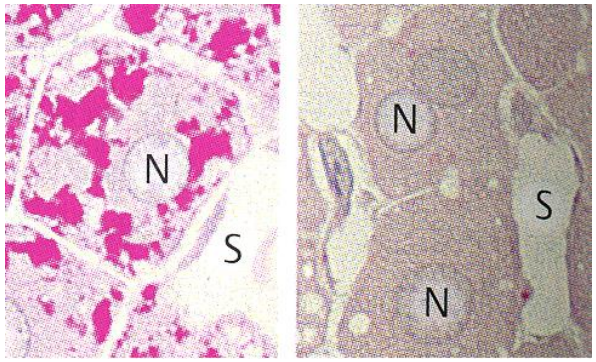


Blood proteins (serum albumin, fibrinogen, prothrombin, complement, transferrin, etc.)

- **Synthesis and metabolism**

- Proteosynthesis – $_{R}$ER + Golgi (plasma proteins – albumins, prothrombin, fibrinogen)
- Metabolisms of lipids – $_{S}$ER, peroxisomes (lipidic conversion of fatty acids and glucose, lipoprotein synthesis)
- Metabolism of glucose and saccharides - synthesis of glycogen, glycogenolysis and gluconeogenesis (insulin / glucagon)





HEPATOCYTES – FUNCTIONS

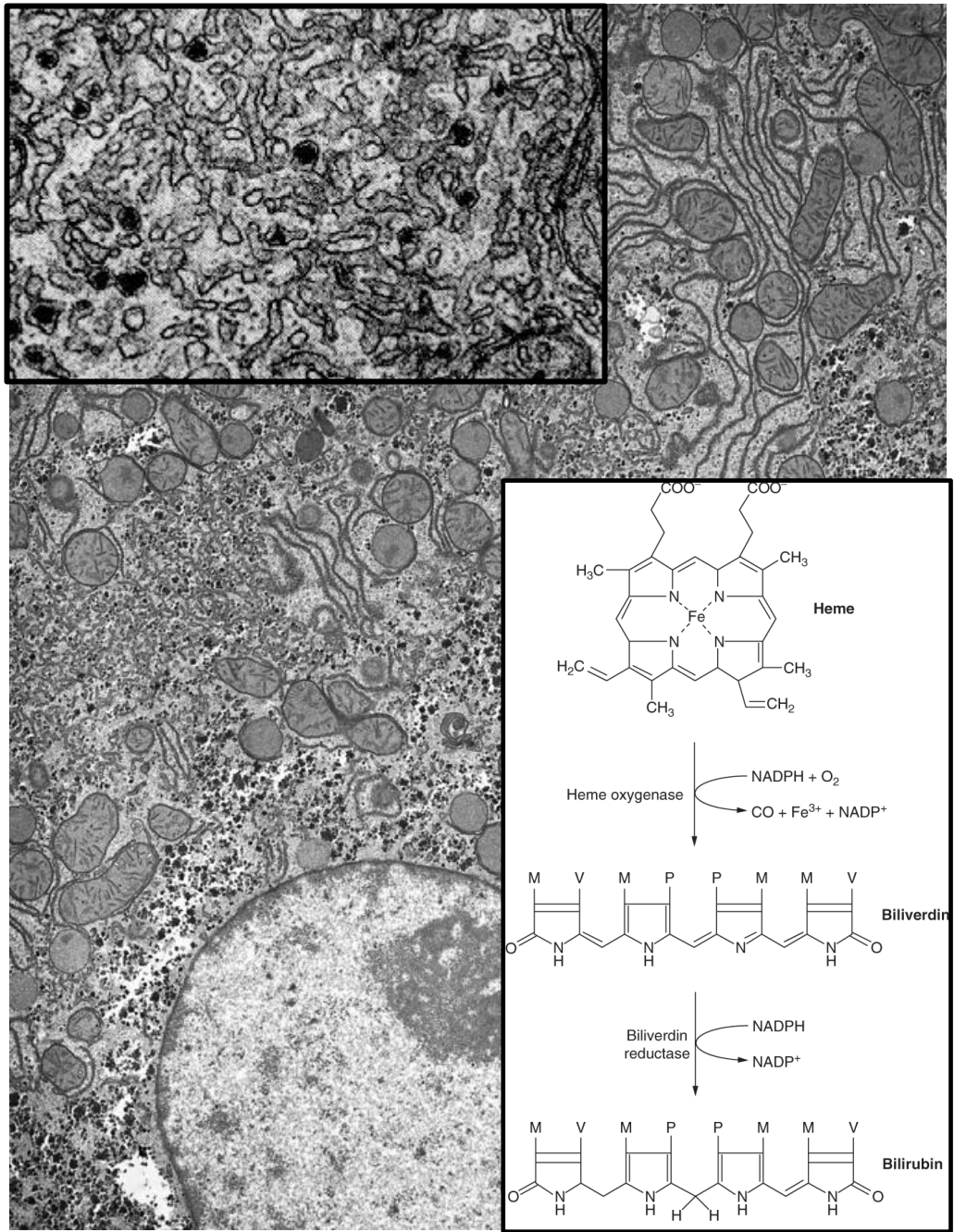
- Detoxication:

$_S$ER (steroids, barbiturates, polyaromatic, lipid soluble compounds, etc., endo- and exotoxins)

- ROS
- Peribilliary located lysosomes (autophagy, degradation of endocyted molecules)

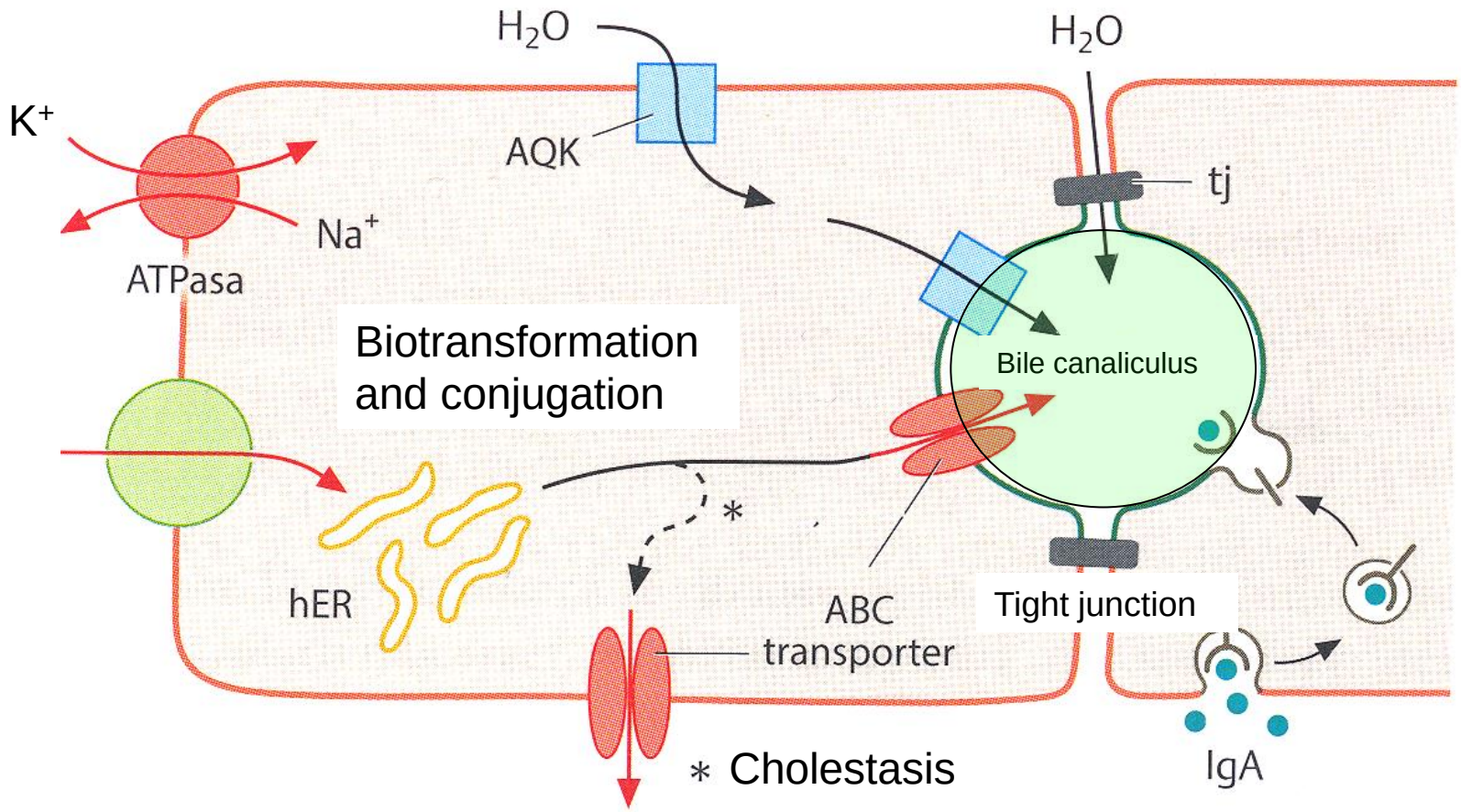
- Metabolism and deposition of vitamins and trace elements

- Bile production:
- Recycling of bile acids (90%), 10% de novo synthesis, conjugation of toxic bilirubin and glukuronic acid to nontoxic complex bilirubin-glucuronid
- $_S$ER

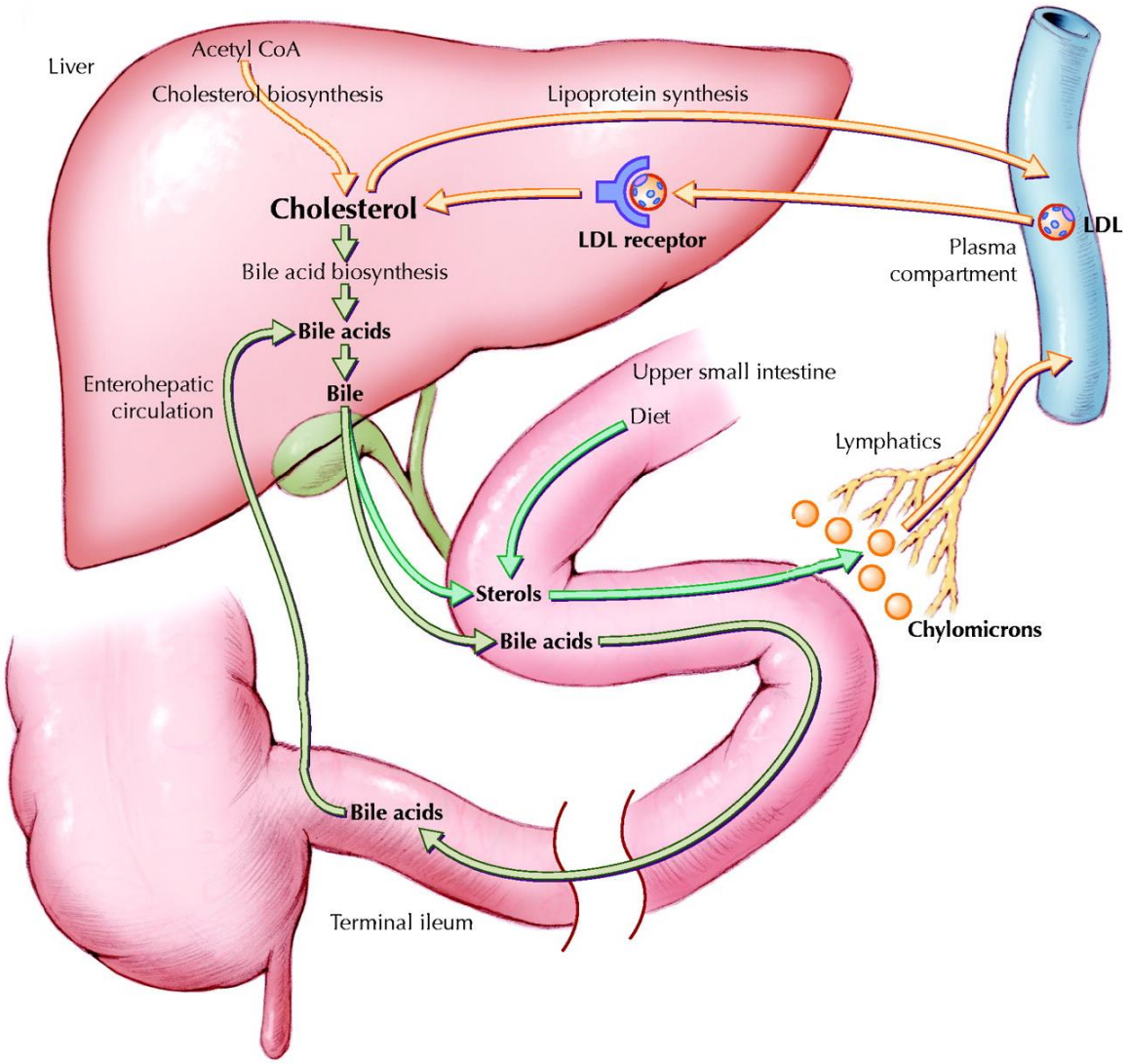


HEPATOCYTES – FUNCTIONS

Bile acids
Bilirubin
Steroids
Drugs



ENTEROHEPATIC CIRCULATION



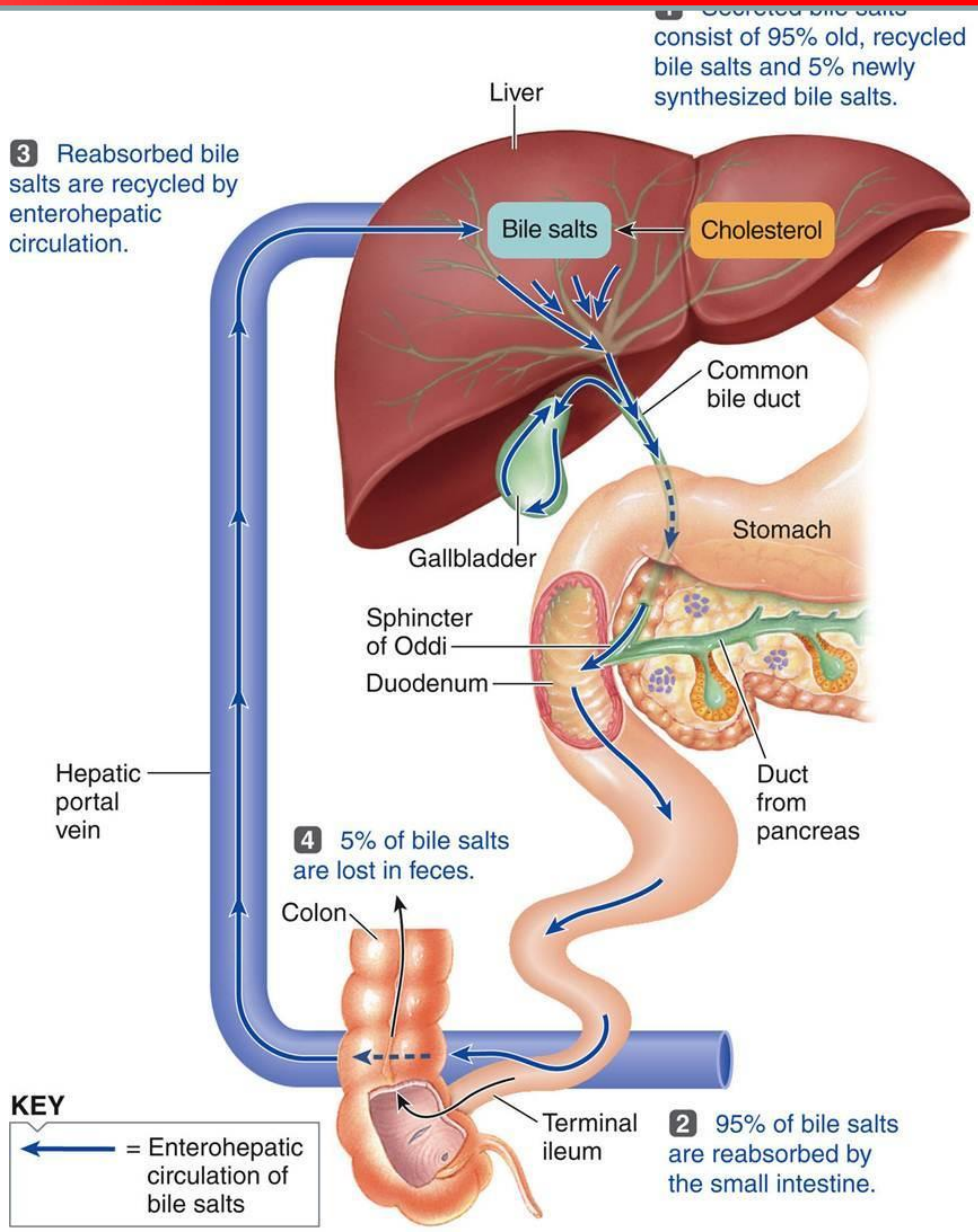
HEPATOCYTES – FUNCTIONS

ENTEROHEPATIC CIRCULATION

- Resorption in terminal ileum
- Vena portae
- Sinusoids

Hepatocytes

- Bile canaliculli
- Intra and extrahepatic ducts
- Duodenum



BILE DUCTS

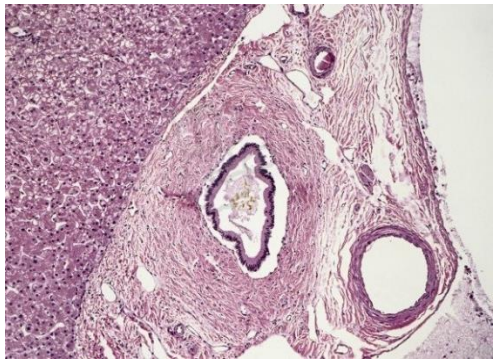
INTRAHEPATIC

Billiary canaliculli
- intercellular space between hepatocytes
- 1-2μm
- no true wall, formed by membranes of hepatocytes
- intercellular junctions

Canals of Herring
- simple squamous epithelium

Interlobular bile ducts
- cholangiocytes
- cubic or low columnar epithelium + c.t.

Lobar bile ducts
- ductus hepaticus dexter et sinister
- high simple columnar epithelium

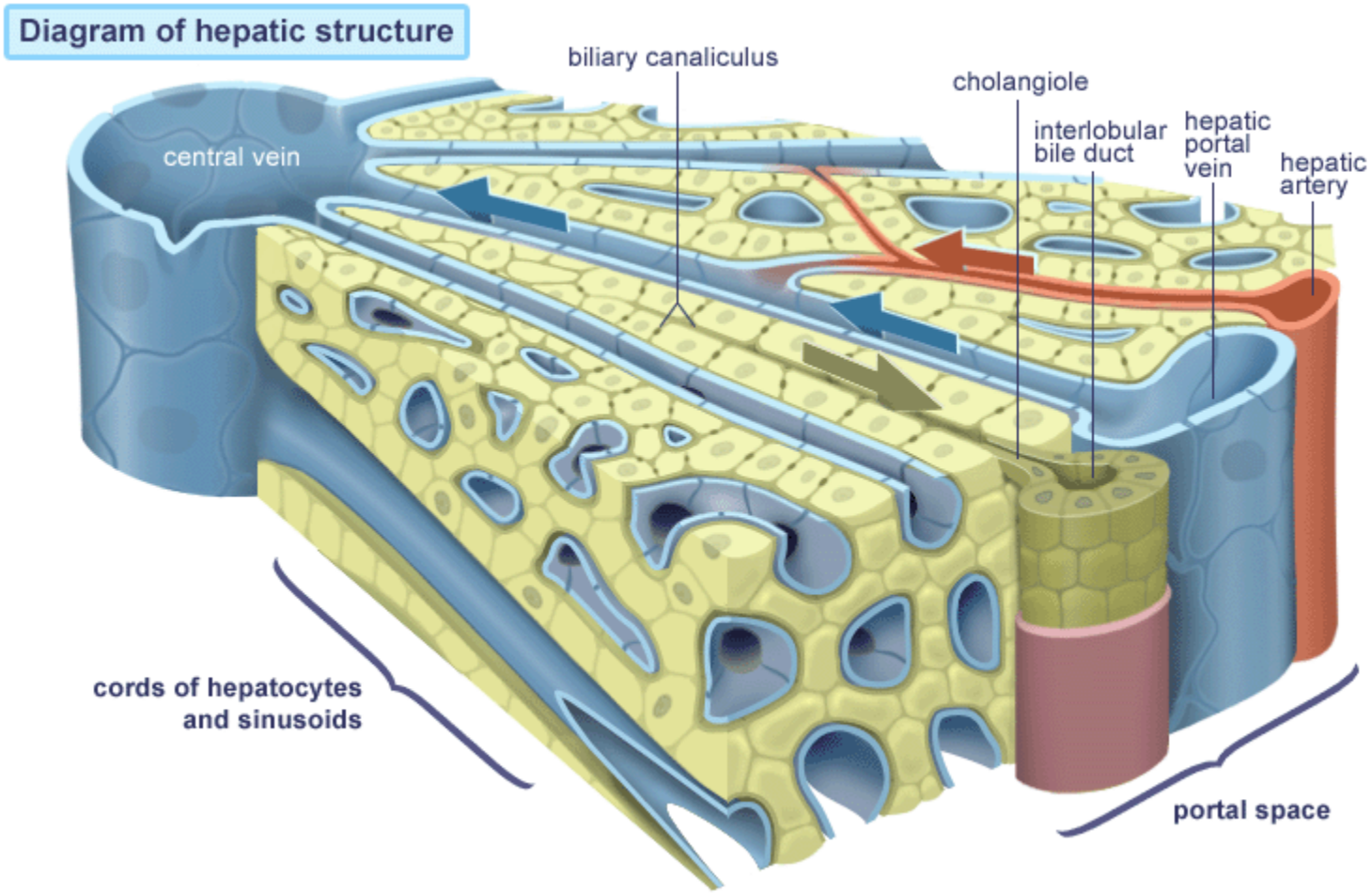


EXTRAHEPATIC

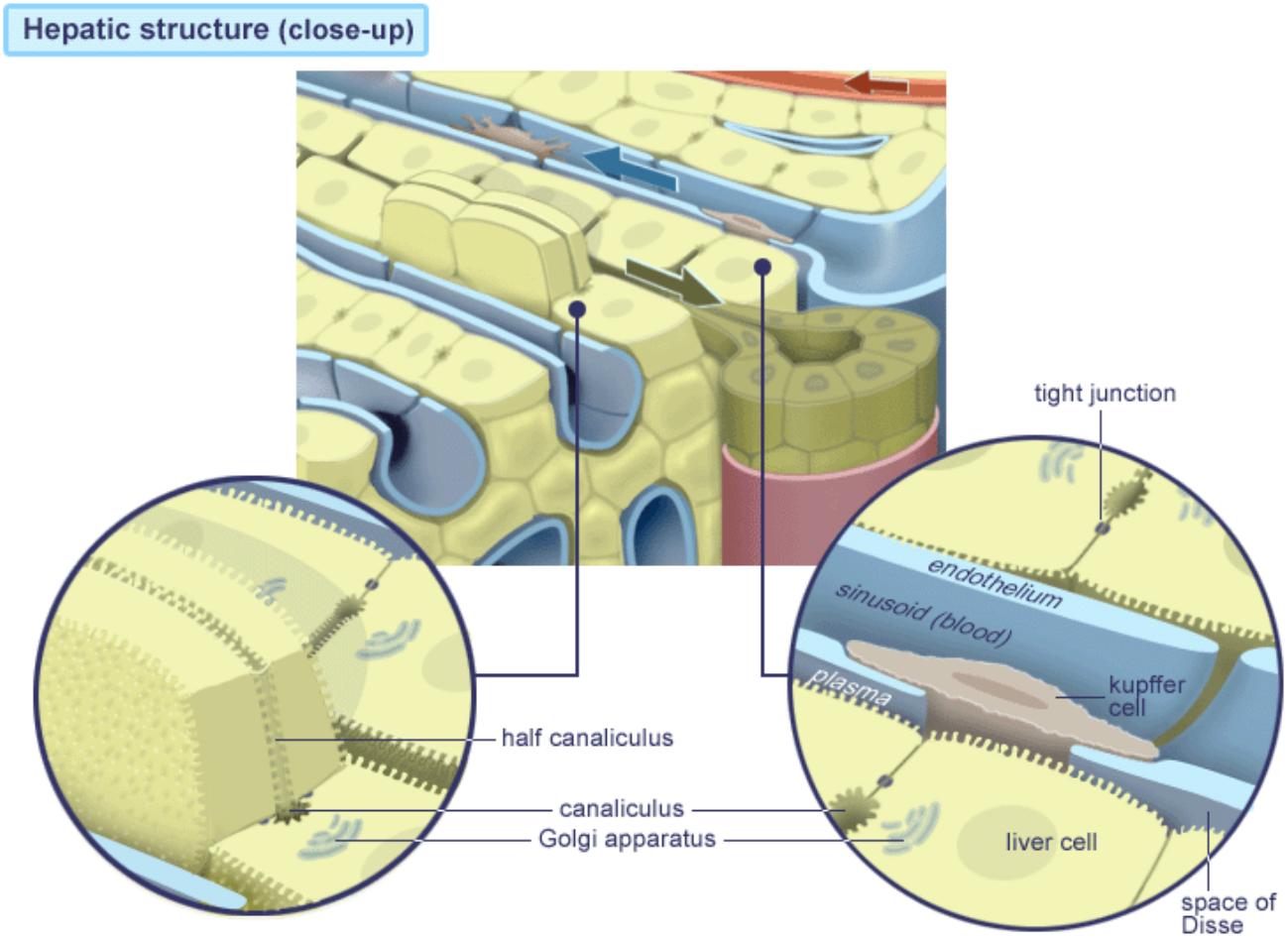
Ductus hepaticus, ductus cysticus, ductus choledochus

- mucosa
- fibromuscular layer

INTRAHEPATIC BILE DUCTS



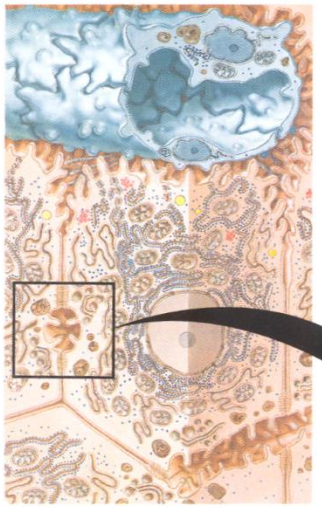
INTRAHEPATIC BILE DUCTS

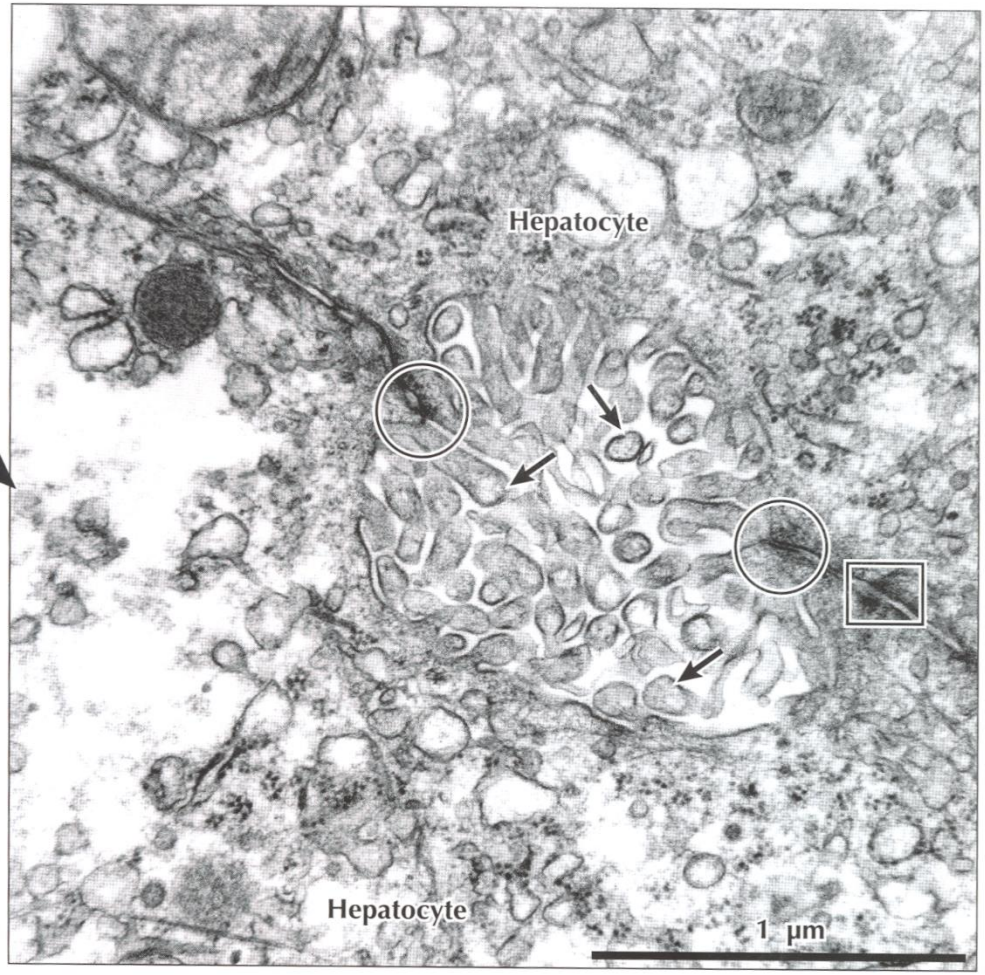


http://alexandria.healthlibrary.ca/documents/notes/bom/unit_4/unit%204%202005/L-39%202008%20%20histology%20of%20the%20pancreas.xml

INTRAHEPATIC BILE DUCTS

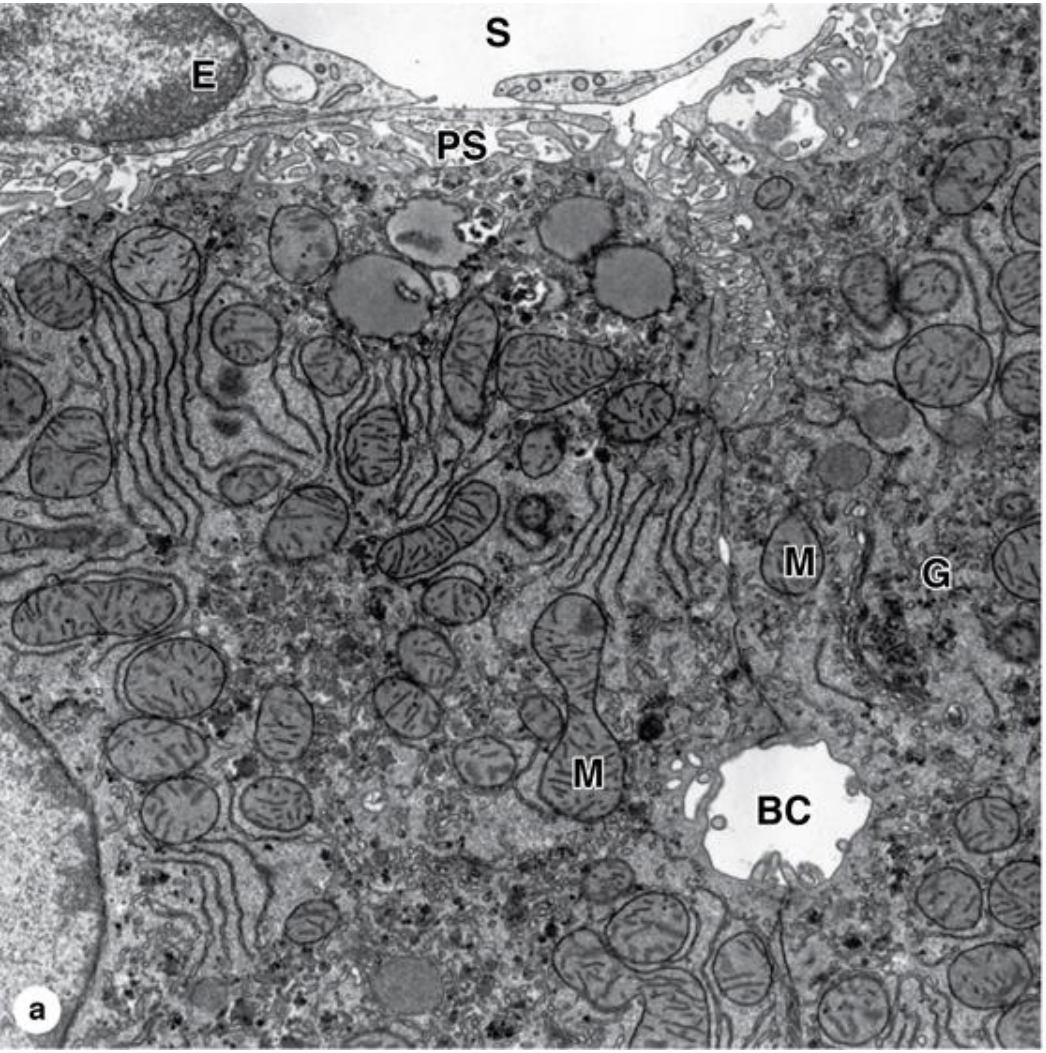
▼ The box indicates a bile canaliculus.

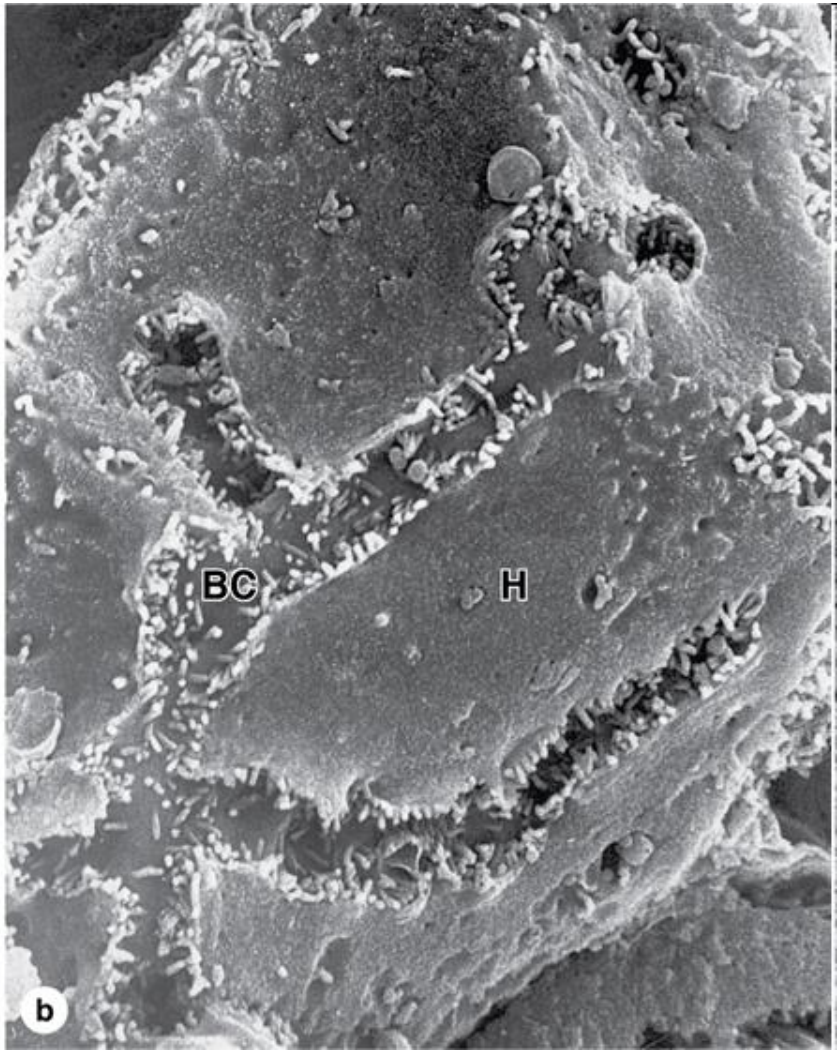




▲ **EM of a bile canaliculus in transverse section.** The lumen shows short stubby microvilli (**arrows**) of two hepatocytes. Desmosomes (**rectangle**) and tight junctions (**circles**) link cell membranes, which seals the canaliculus and prevents bile leakage to surrounding tissues. 47,000×.

INTRAHEPATIC BILE DUCTS

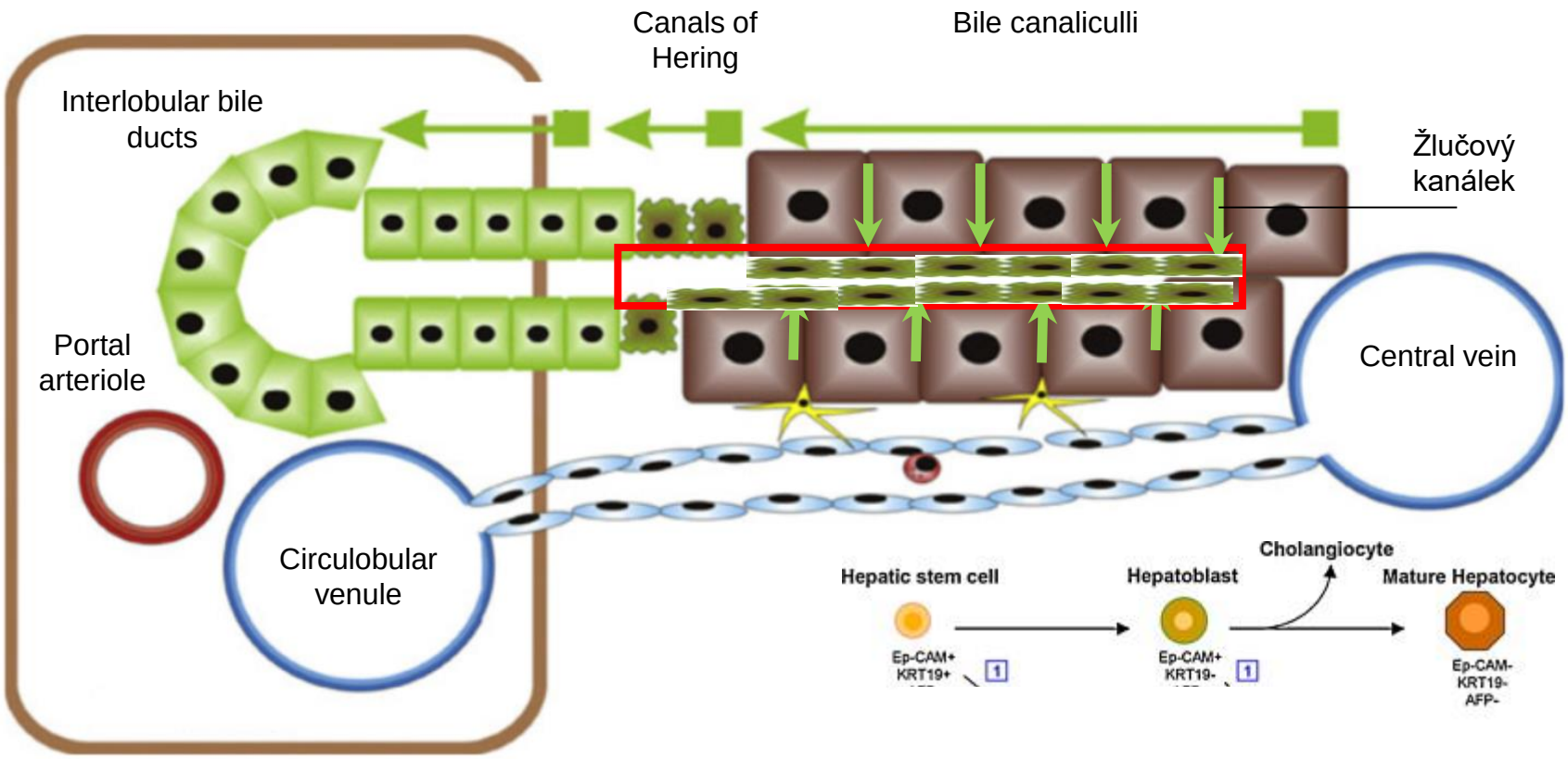




INTRAHEPATIC BILE DUCTS

CHOLANGIOCYTES

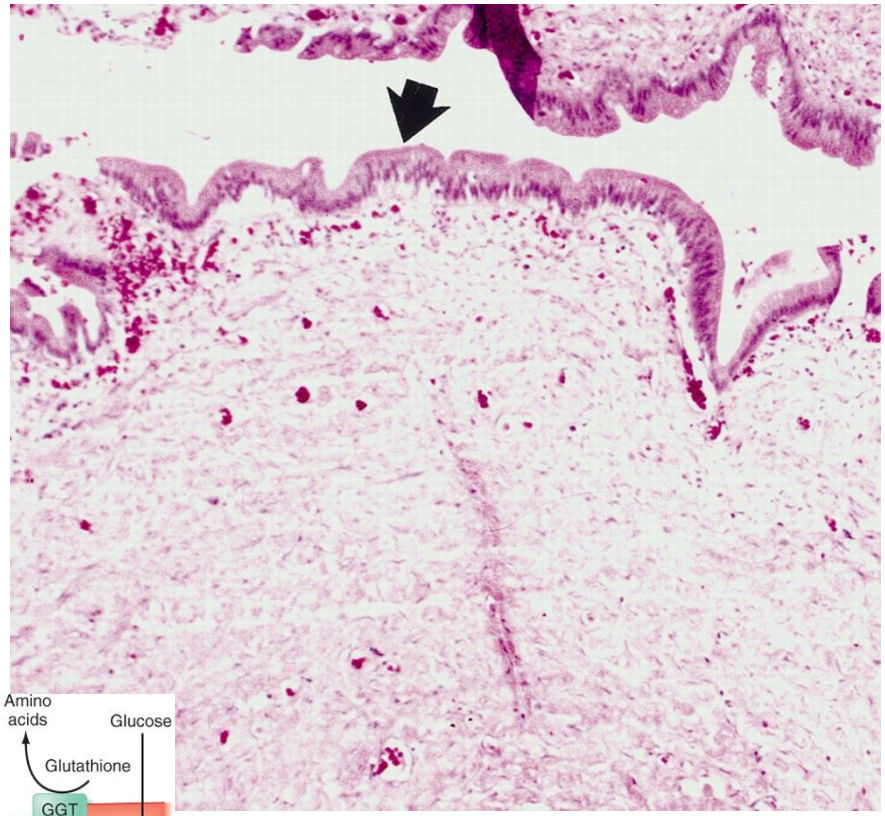
HEPATOCYTES



EXTRAHEPATIC BILE DUCTS

d. hepaticus communis + d. cysticus → d. choledochus

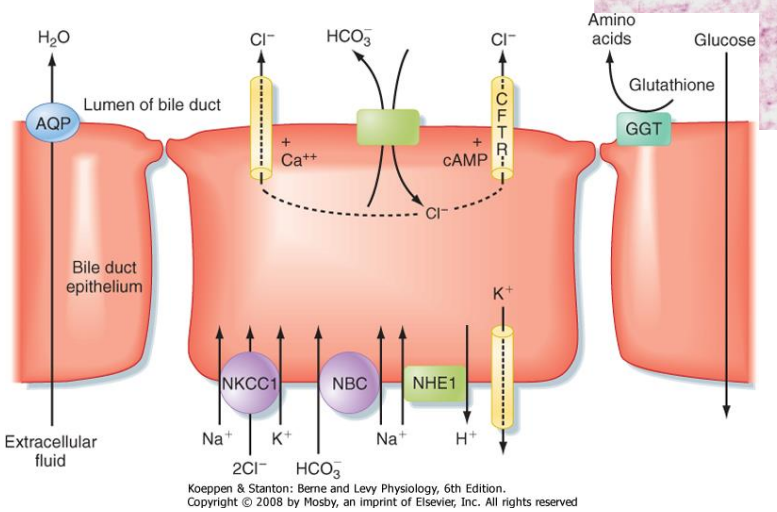
papilla duodeni major
m. sphincter ampullae hepatoduodenalis (sphincter of Oddi)



Mucosa
- lateral folds
- simple columnar epithelium (cholangiocytes)
- mucinous glands in c.t., goblet cells

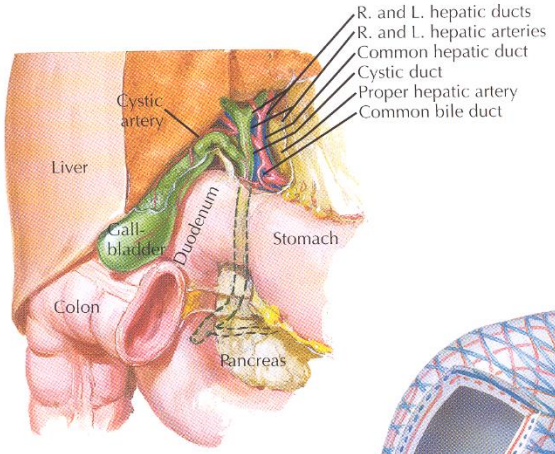
Fibromuscular layer
- dense network of collagen and elastic fibers
- leiomyocytes

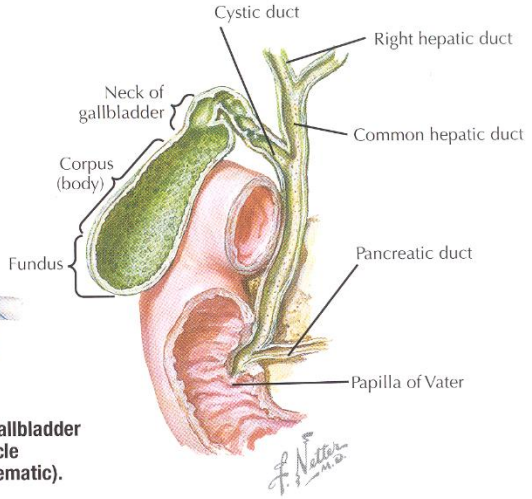
Bile modification

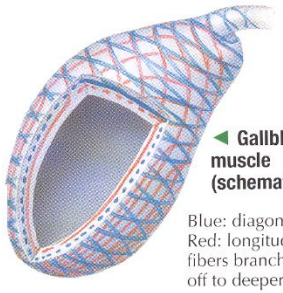


GALL BLADDER (VESICA FELLEA)

- Wall 1-2mm
  - Mucous coat
  - Muscle layer
  - Serosa/adventitia





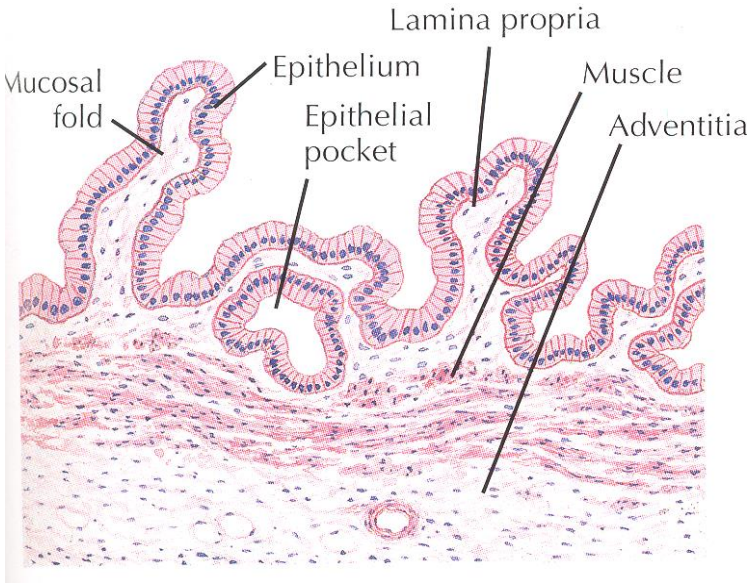


◀ **Gallbladder muscle (schematic).**

Blue: diagonal fibers
Red: longitudinal fibers branching off to deeper level

Mucosa

- mucosal folds
- 20-50μm simple columnar epithelium with microvilli
- intercellular junctions
- lamina propria mucosae - loose collagen c.t. with mucinous tuboalveolar glands
- lamina muscularis mucosae absent



Muscular layer (Muscularis propria)

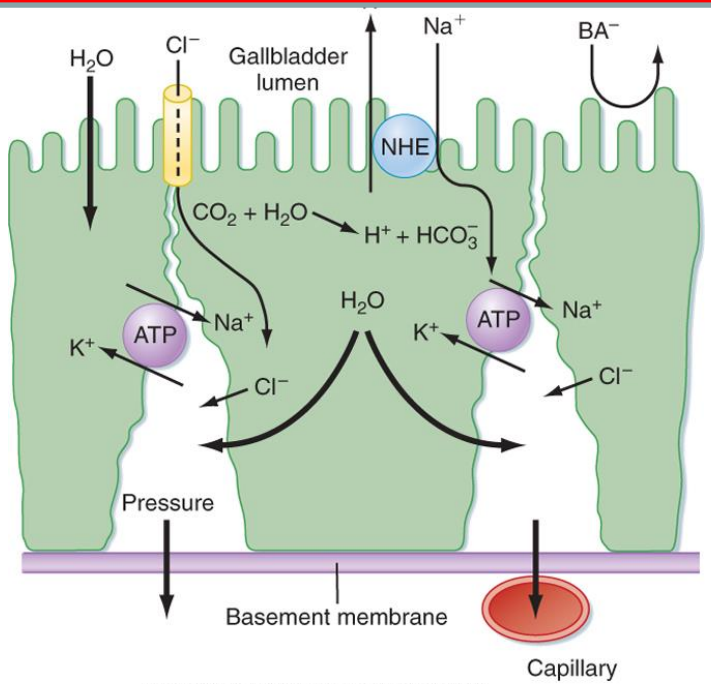
- 3D network of smooth muscle cells,
- elastic fibers

Large layer of serous c.t. (l. propria serosae)

GALL BLADDER (VESICA FELLEA)

BILE CONCENTRATION

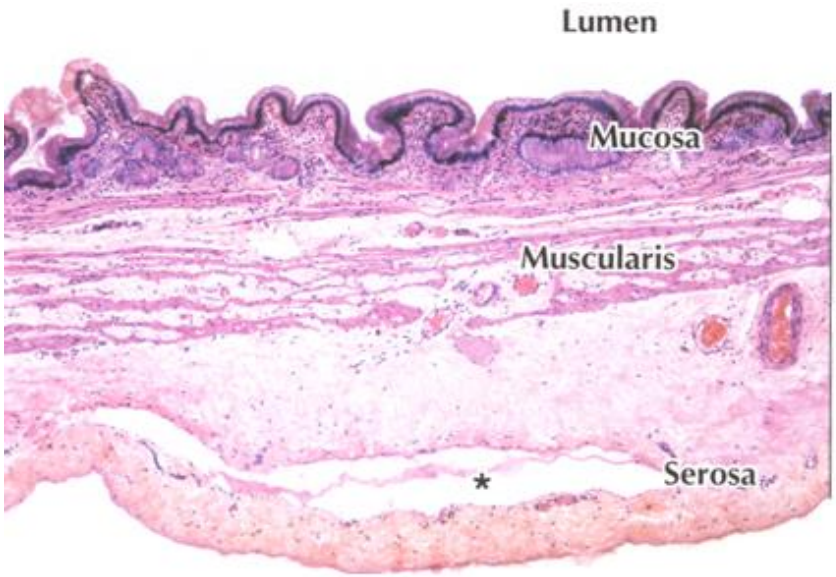
- Bile secretion by liver– ca 0,8-1l daily
- Gall bladder volume 15-60 ml
- Water resorption

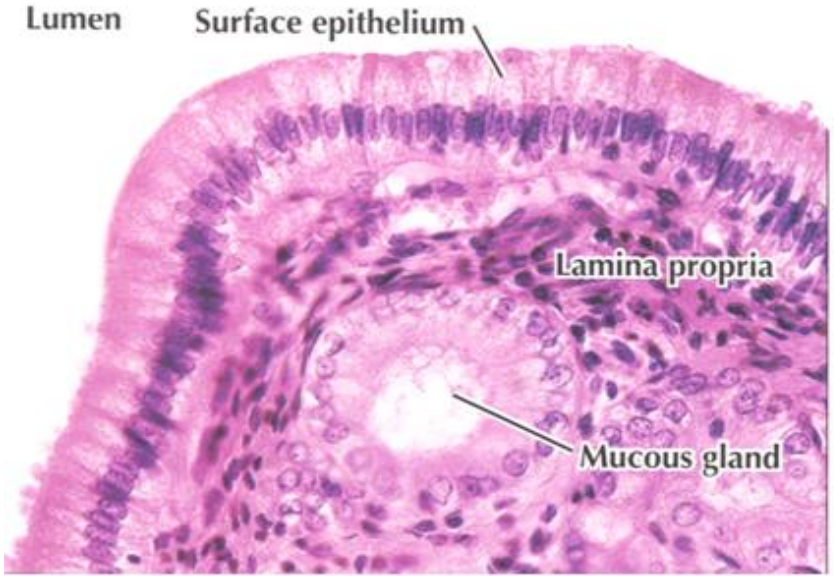


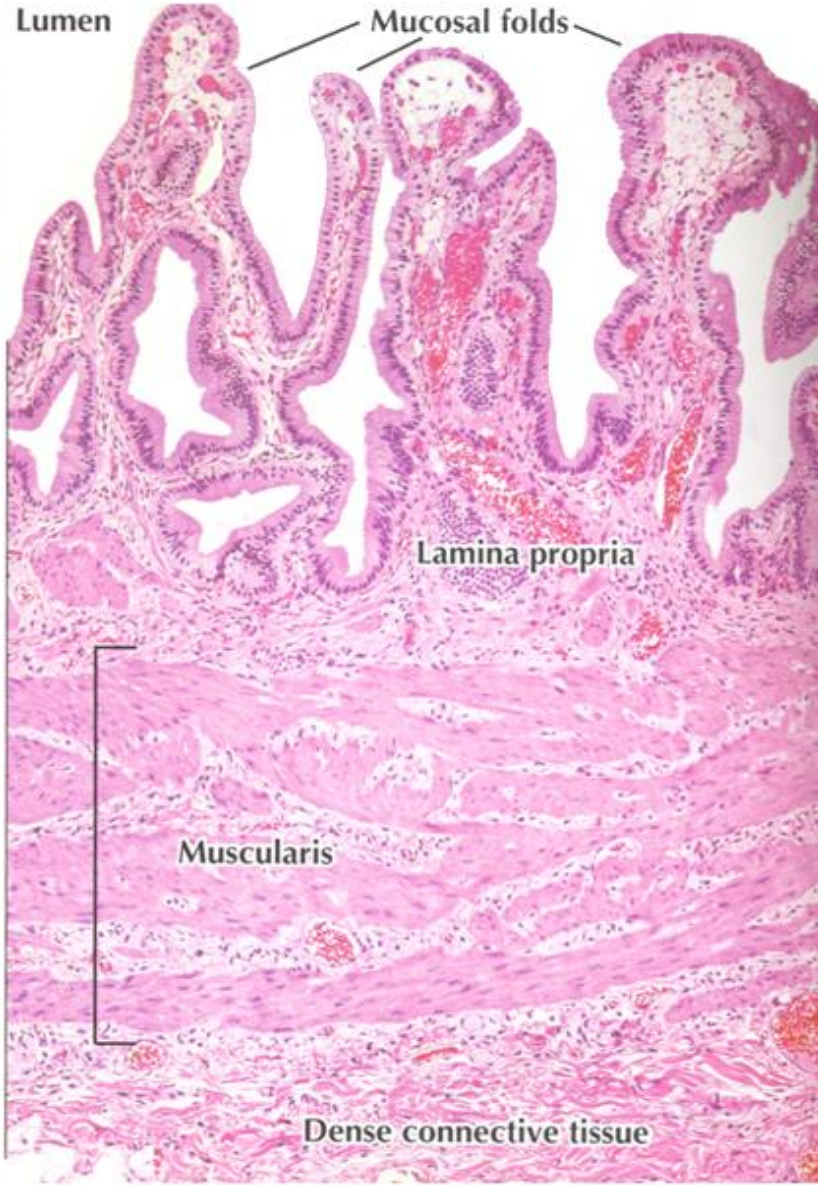
Approximate Values for Major Components of Liver and Gallbladder Bile

COMPONENT	LIVER BILE	GALLBLADDER BILE
Na^+ (mEq/L)	150	300 ↑
K^+ (mEq/L)	4.5	10 ↑
Ca^{++} (mEq/L)	4	20 ↑
Cl^- (mEq/L)	80	5 ↓
HCO_3^- (mEq/L)	25	12 ↓
Bile salts (mEq/L)	30	315 ↑
pH	7.4	6.5
Cholesterol (mg/100 mL)	110	600
Bilirubin (mg/100 mL)	100	1000

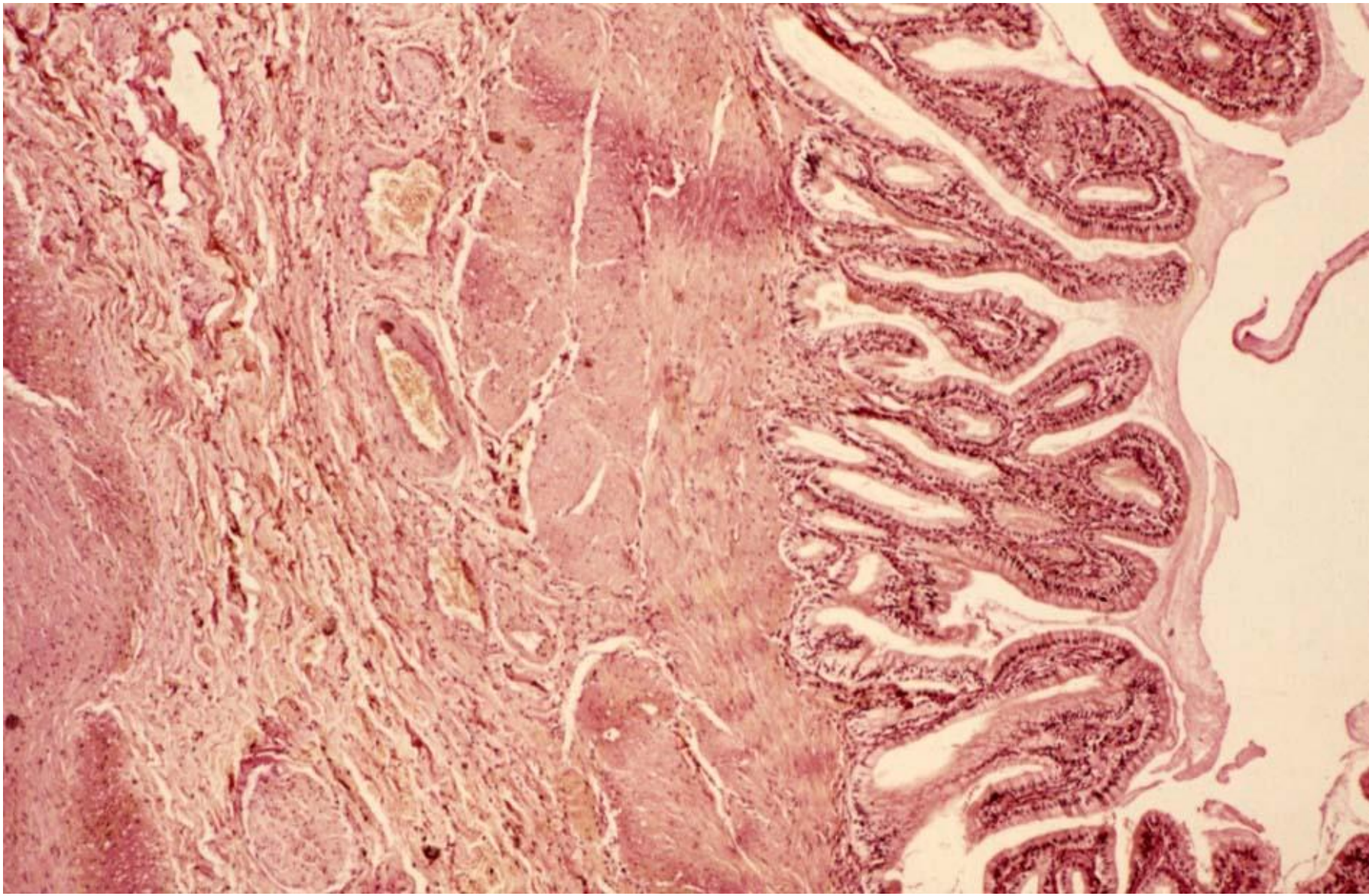
GALL BLADDER (VESICA FELLEA)



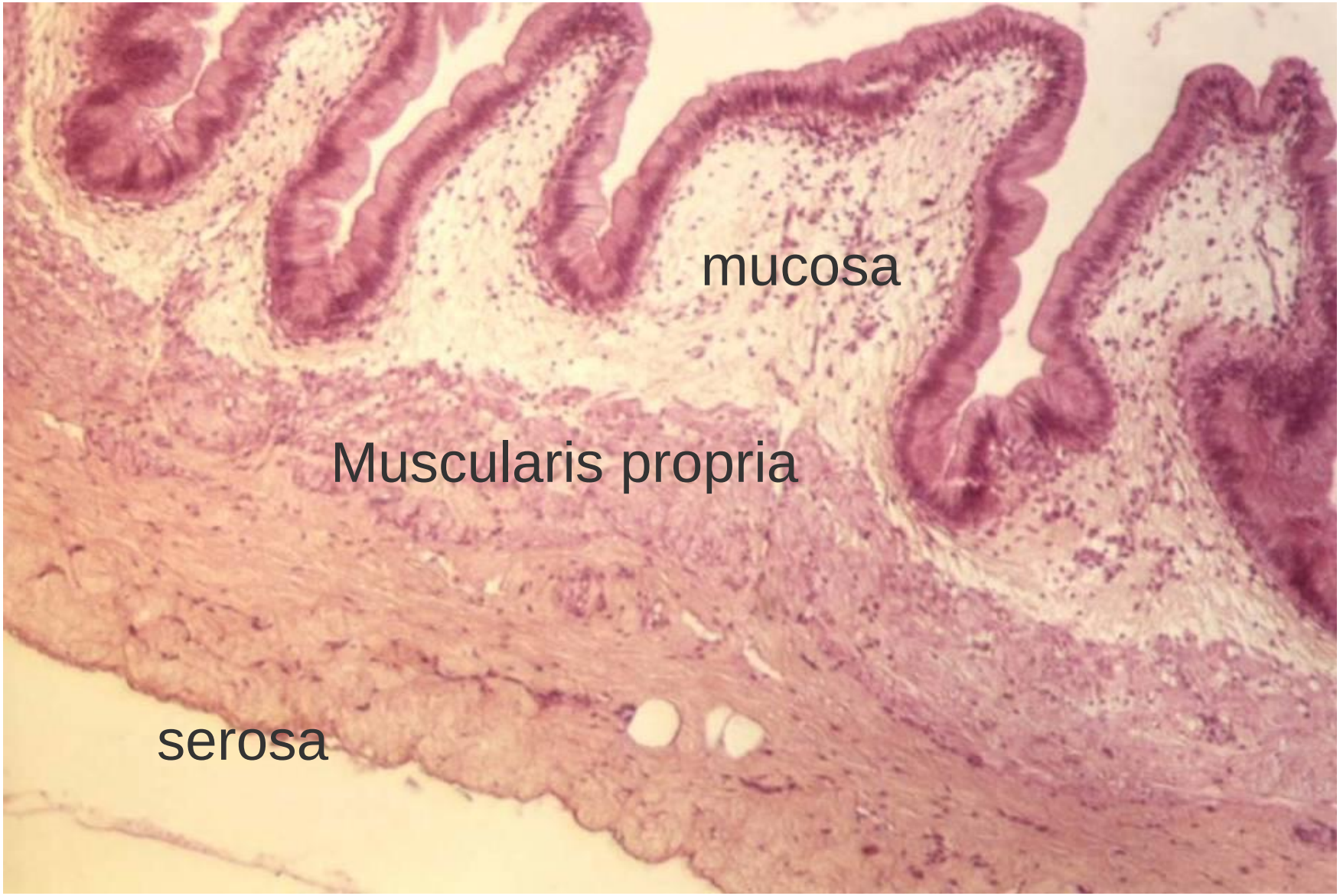




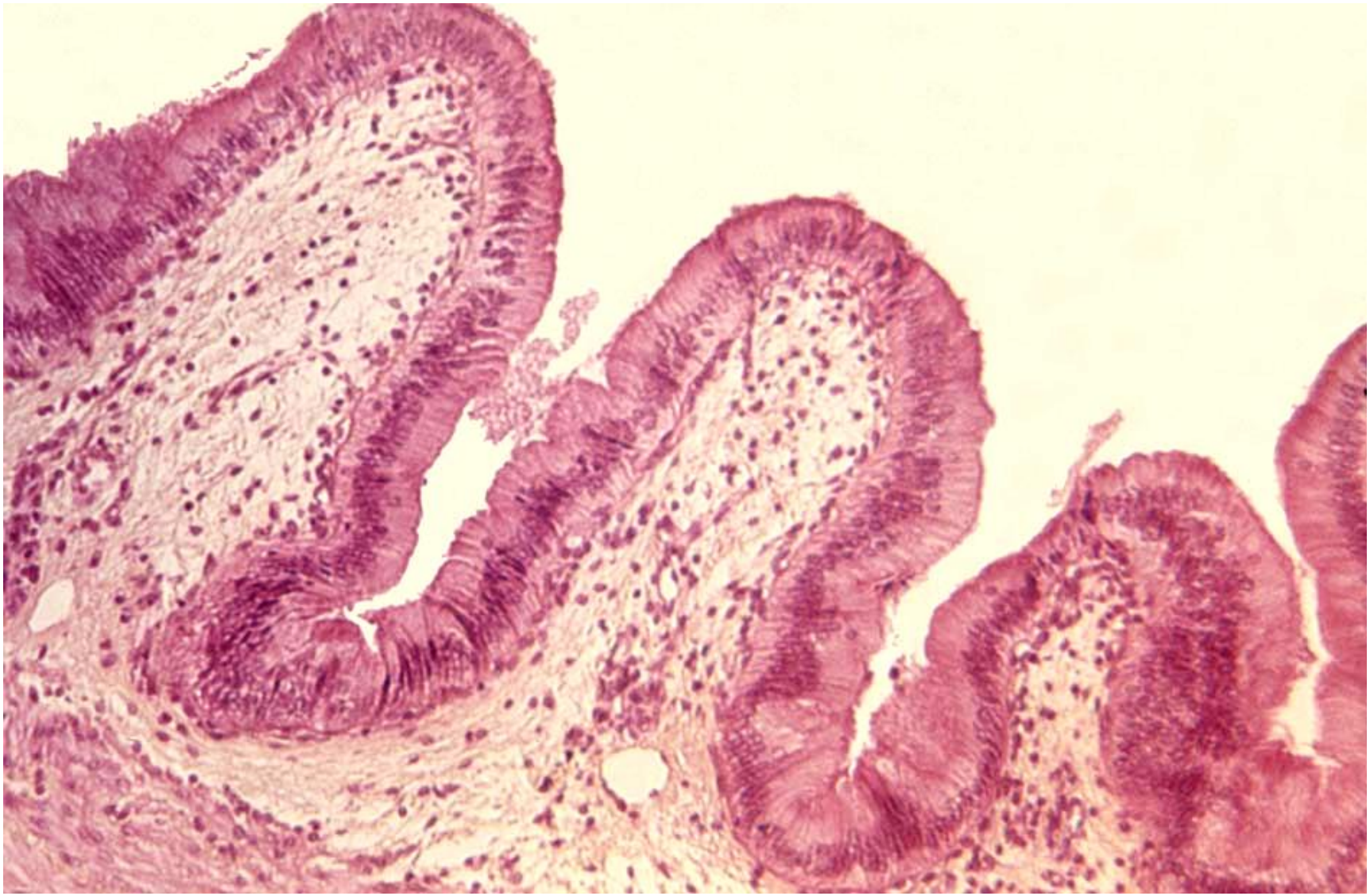
GALL BLADDER (VESICA FELLEA)



GALL BLADDER (VESICA FELLEA)



GALL BLADDER (VESICA FELLEA)



PANCREAS

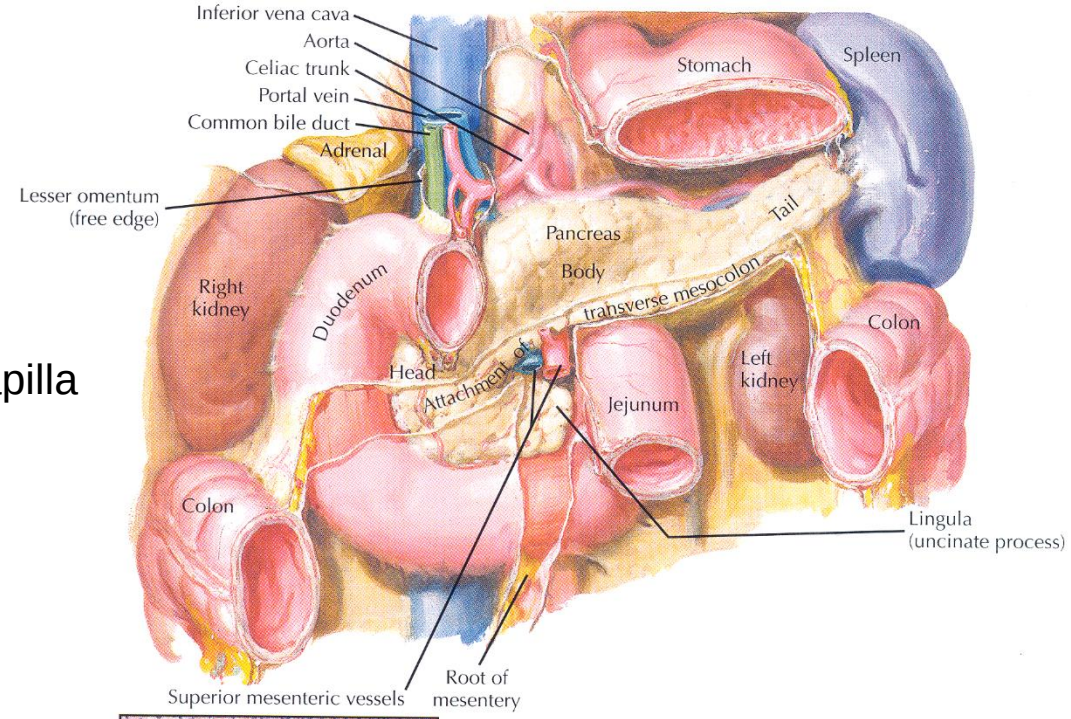
PANCREAS

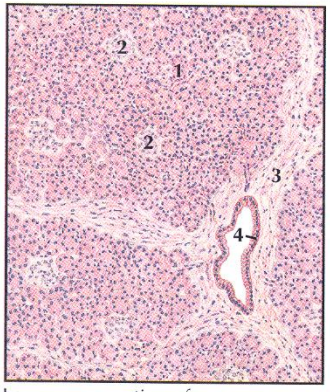
- Compound, serous, tuboalveolar gland
- **Exocrine and endocrine character**
  - pancreatic acinus
  - Islets of Langerhans

- Major duct (Wirsungi) opens to Vater papilla as a common bile and pancreatic duct

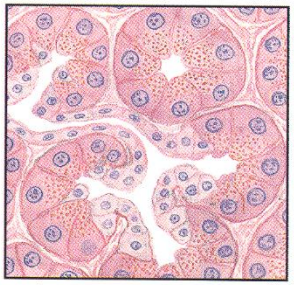
- Dense collagen c.t. capsule

- Septs – blood cells, innervation, and interlobular ducts

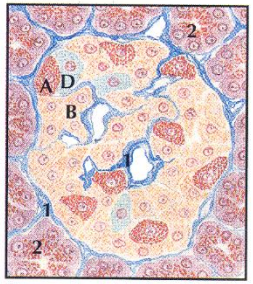




Low-power section of pancreas **1.** Acini, **2.** islet, **3.** interlobular septum, **4.** interlobular duct

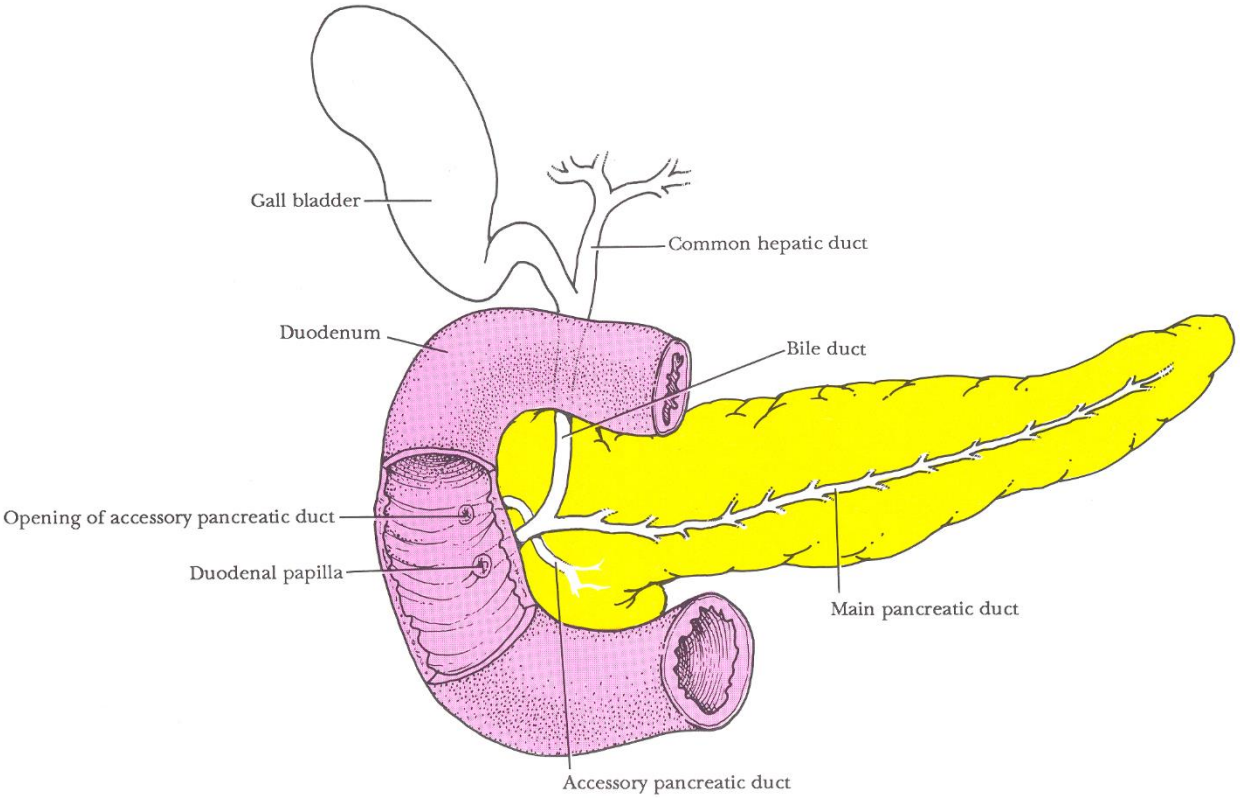


High magnification: acini, intercalated duct and zymogen granules



Pancreatic islet: **A**, **B**, and **D** cells. **1.** Reticulum, **2.** acini

PANCREAS

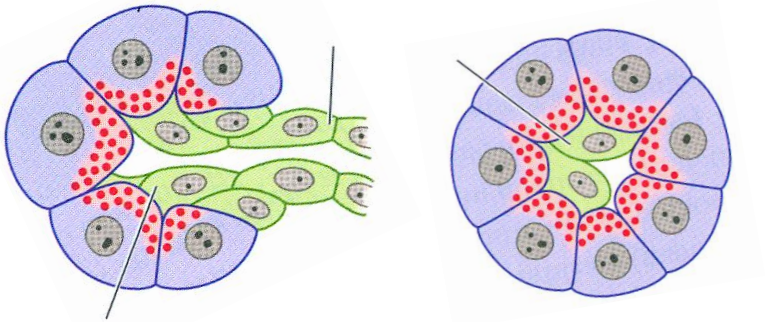

Gall bladder
Common hepatic duct
Duodenum
Bile duct
Opening of accessory pancreatic duct
Duodenal papilla
Main pancreatic duct
Accessory pancreatic duct

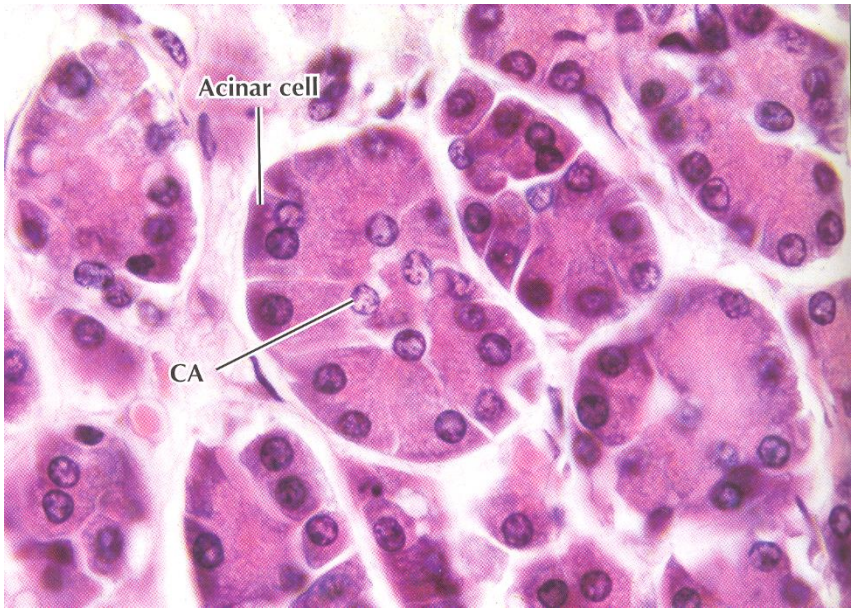
PANCREAS – PANCREATIC ACINUS

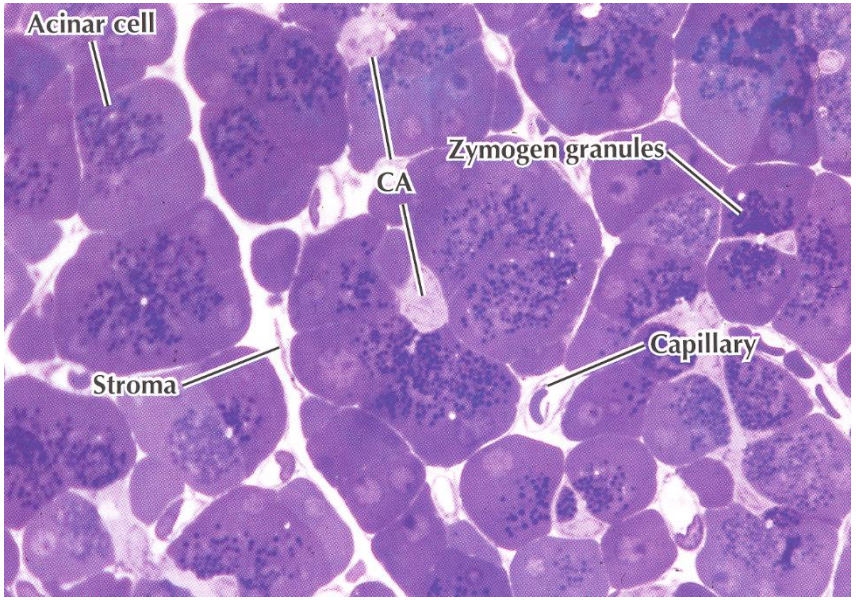
- Pyramidal epithelial cells
- Pancreatic digestive enzymes
- Intercalated ducts

- **Serous acinar cells**
  - Polarized secretory cells
  - Basophilic
  - Apex – Golgi and zymogenic granules
  - Microvilli
  - Intercellular junctions

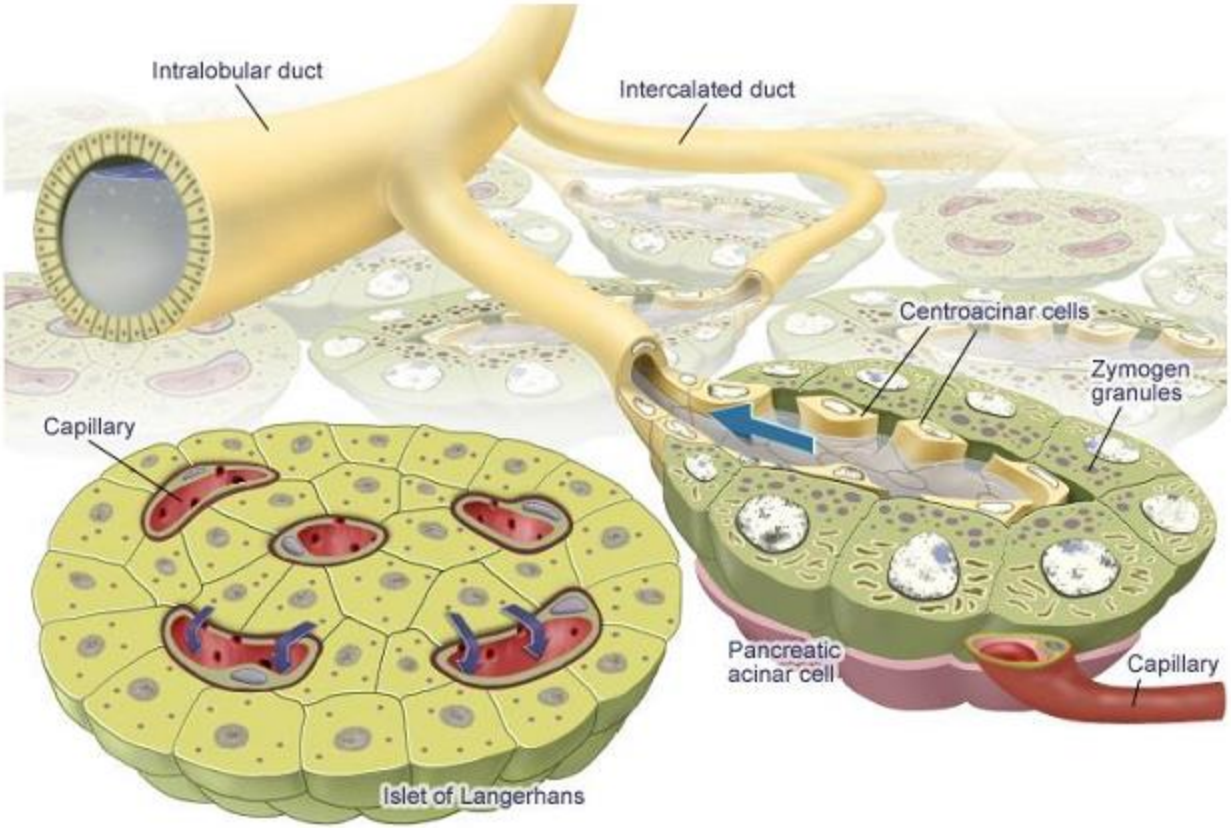
- **Centroacinar cells**
  - Centrally located nucleus, squamous character
  - Continuous with intercalated ducts



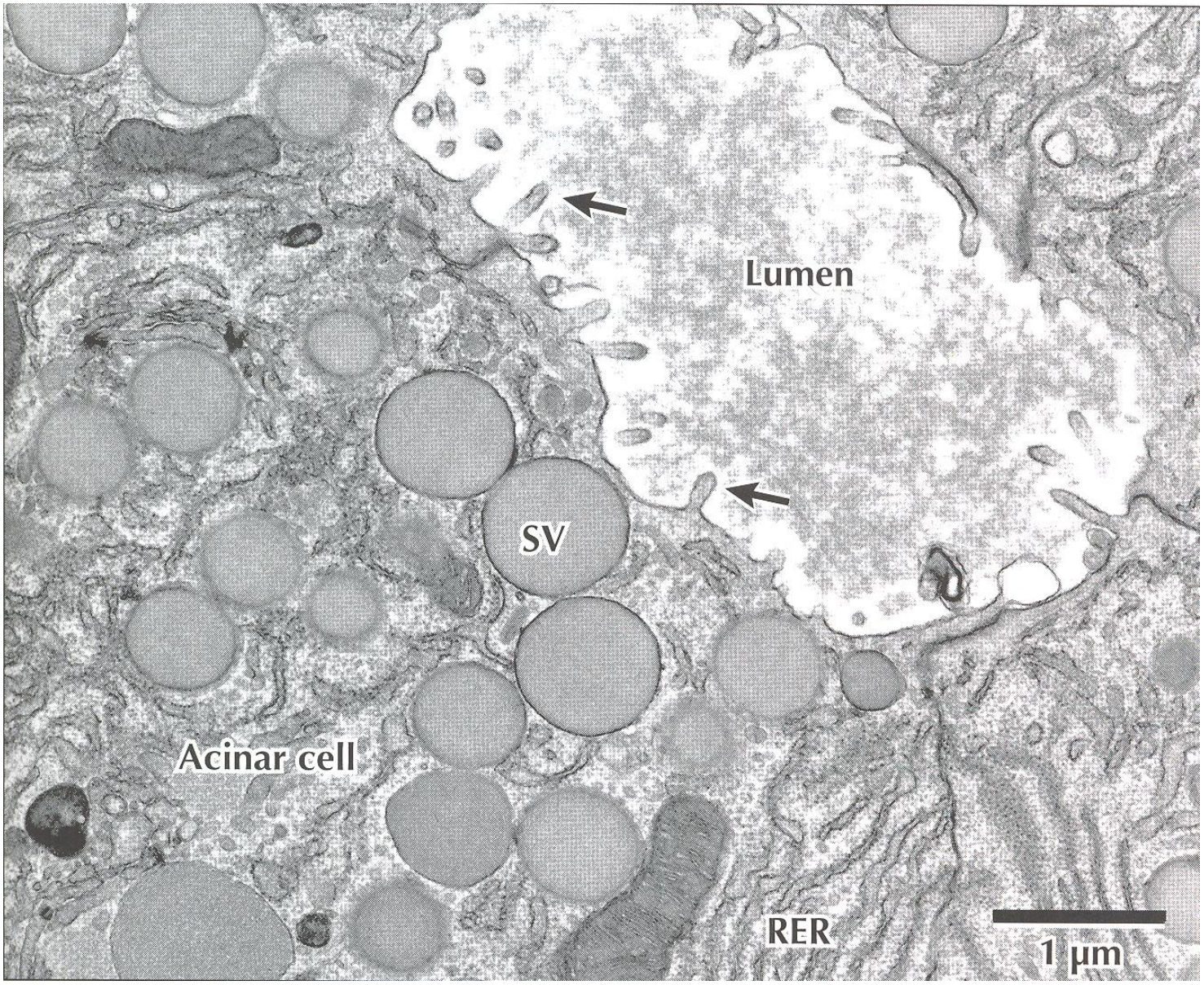




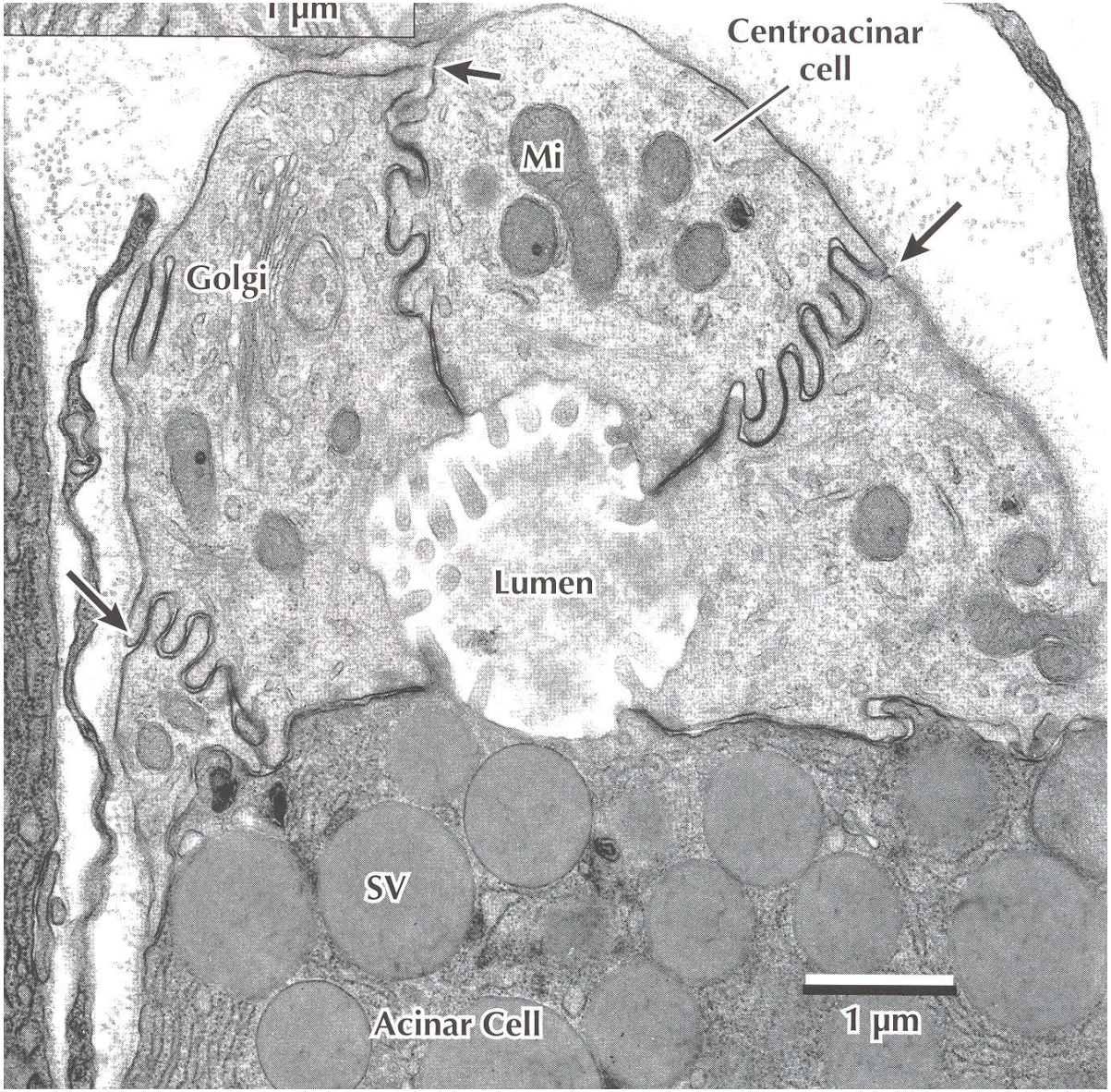
PANCREAS – PANCREATIC ACINUS



PANCREAS – PANCREATIC ACINUS



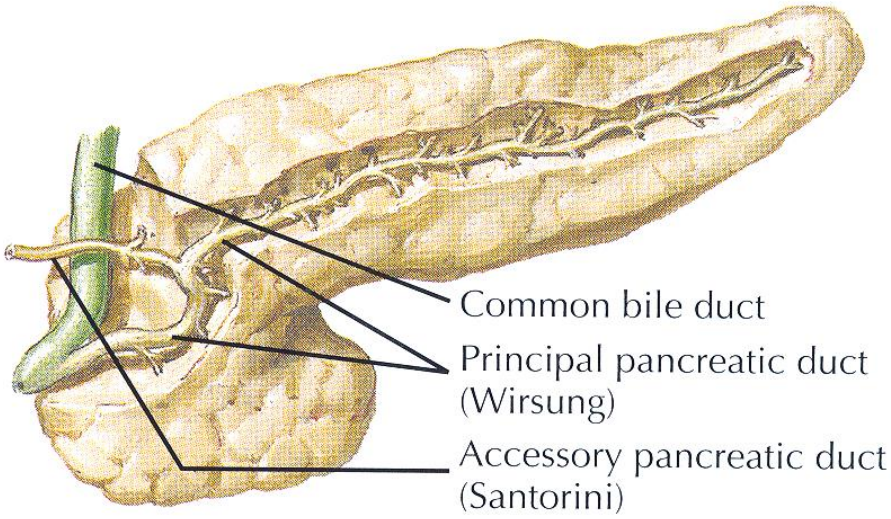
PANCREAS – PANCREATIC ACINUS

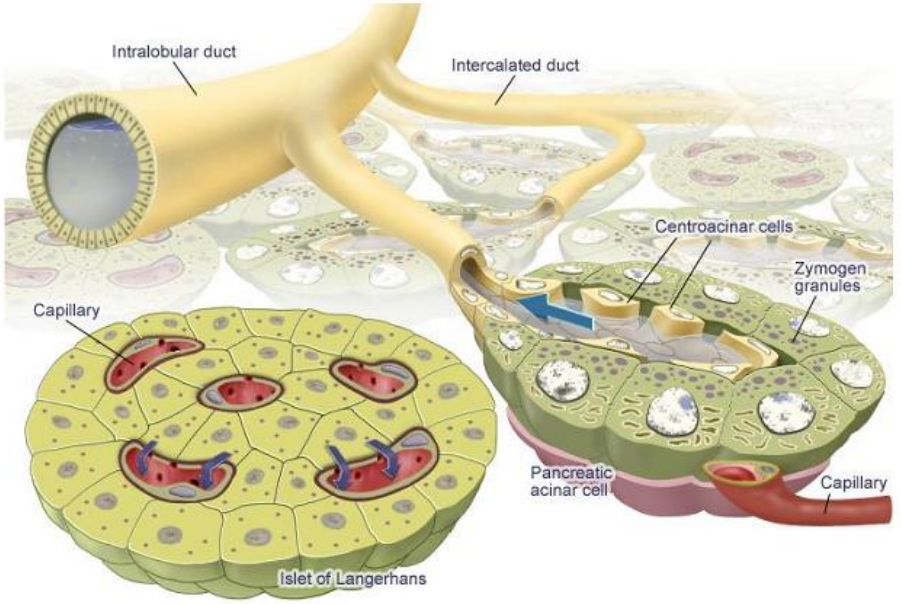


PANCREAS – PANCREATIC DUCTS

- **Centroacinar cells**
- **Intercalated ducts**
  - simple squamous epithelium + basal membrane
- **Intralobular and interlobular ducts**
  - simple cubic – low columnar epithelium

- **Major pancreatic ducts**
  - D. pancreaticus major – Wirsungi and D. pancreaticus accessorius - Santorini
  - bilayered columnar epithelium and dense collagen c.t.
  - intramural mucinous tubular glands, goblet cells, EC cells

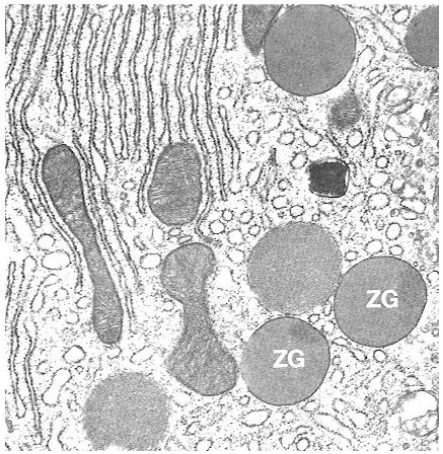


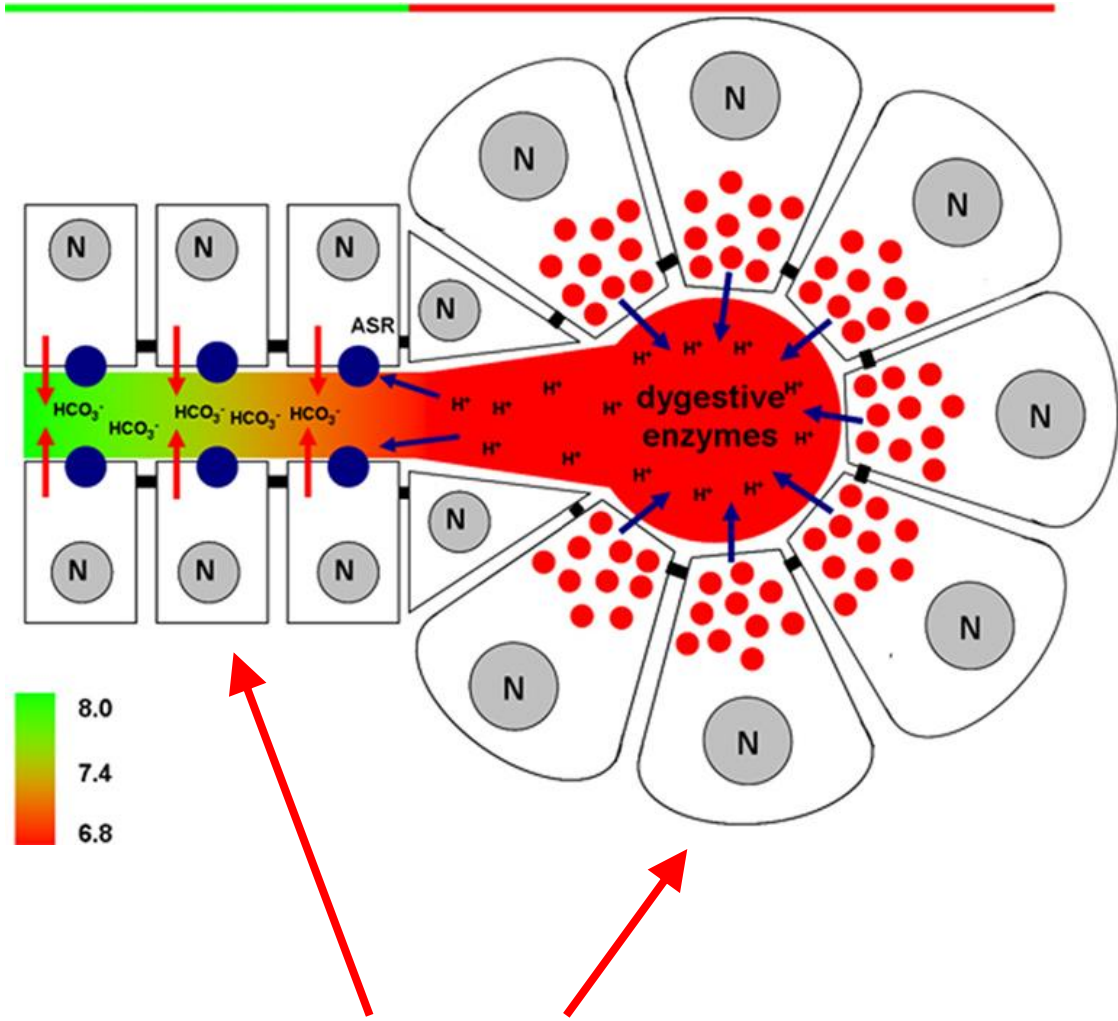


PANCREAS – EXOCRINE FUNCTION

- ca 1000-2000 ml daily
- alkalic pH (8.8), HCO_3^- (intercalated duct epithelium)
- mucin (epithelium of large ducts)

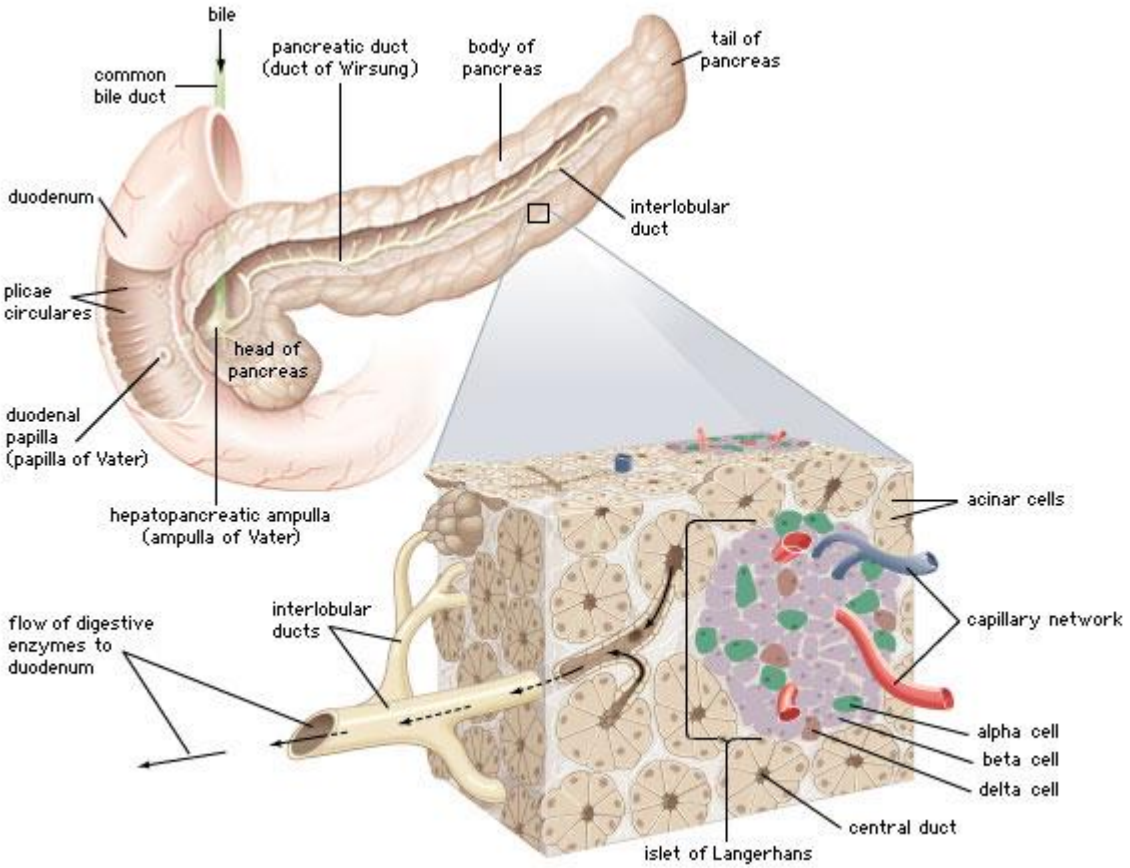
- **Hydrolases**
  - Trypsinogen
  - Chymotrypsinogen
  - Proelastases
  - Carboxypeptidases
  - Pancreatic lipase
  - Amylases
  - …





Hormonal regulation (secretin, cholecystokinin) + parasympaticus

PANCREAS – ENDOCRINE FUNCTION



Glucagon

- Glycogen consumption in tissues and muscles
- Increase of blood glucose

Insulin

- Increase of membrane permeability for glucose
- Glucose oxidation in tissues
- Decrease of blood glucose
- Synthesis of glucan in muscles and liver

Pancreatic polypeptide

- Autoregulation of pancreatic secretion

Somatostatin

- Inhibition of GIT hormones

PANCREAS – ISLETS OF LANGERHANS

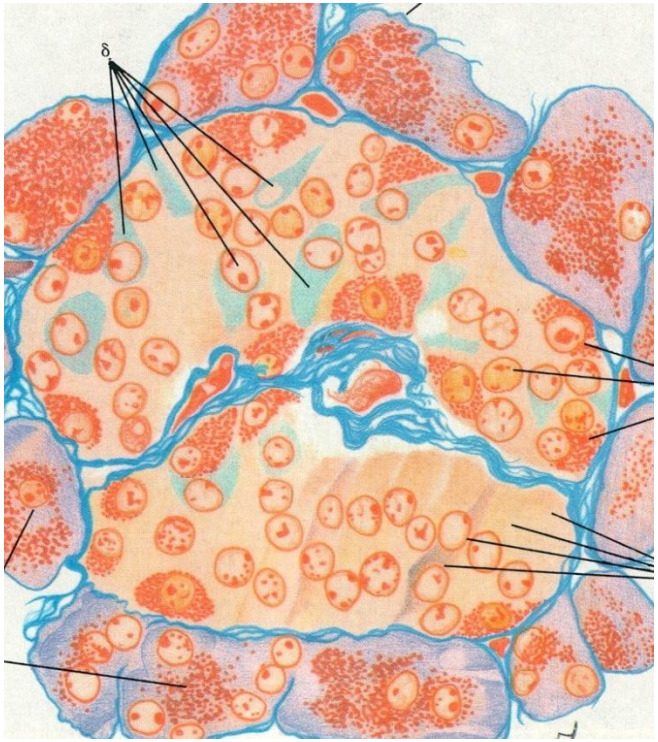
- Clusters of pale cells
- ca $1{,}5 \times 10^6$
- Thin c.t. capsule
- Cords of epithelial cells
- **No ducts**
- Sinusoids
- General characteristics of APUD cells
- A, B, D, PP cells

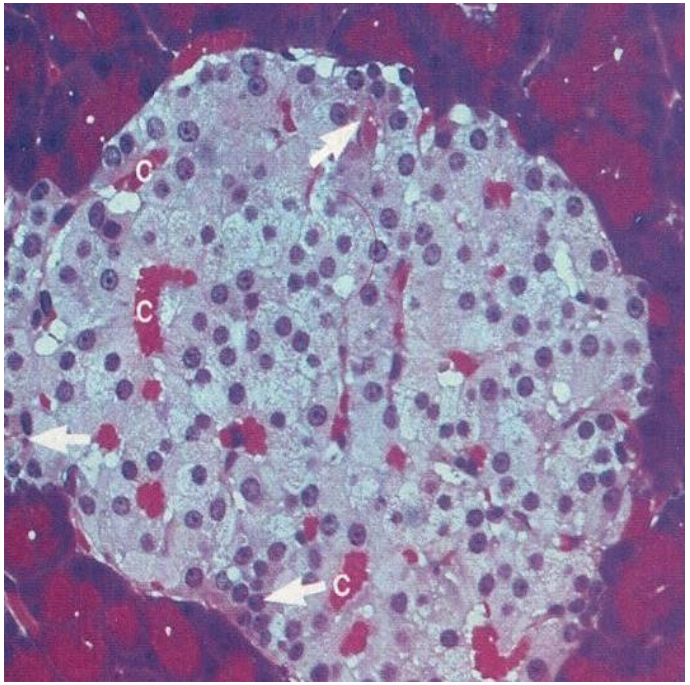
A cells: 20%, glucagon

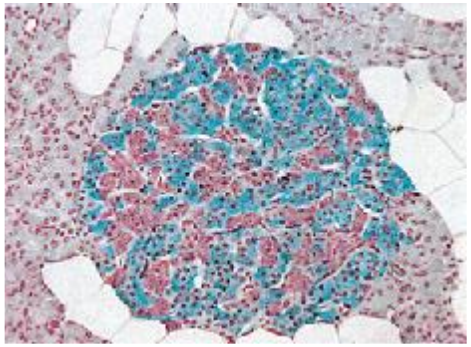
B cells: 60-70%, insulin

D cells: minor, somatostatin

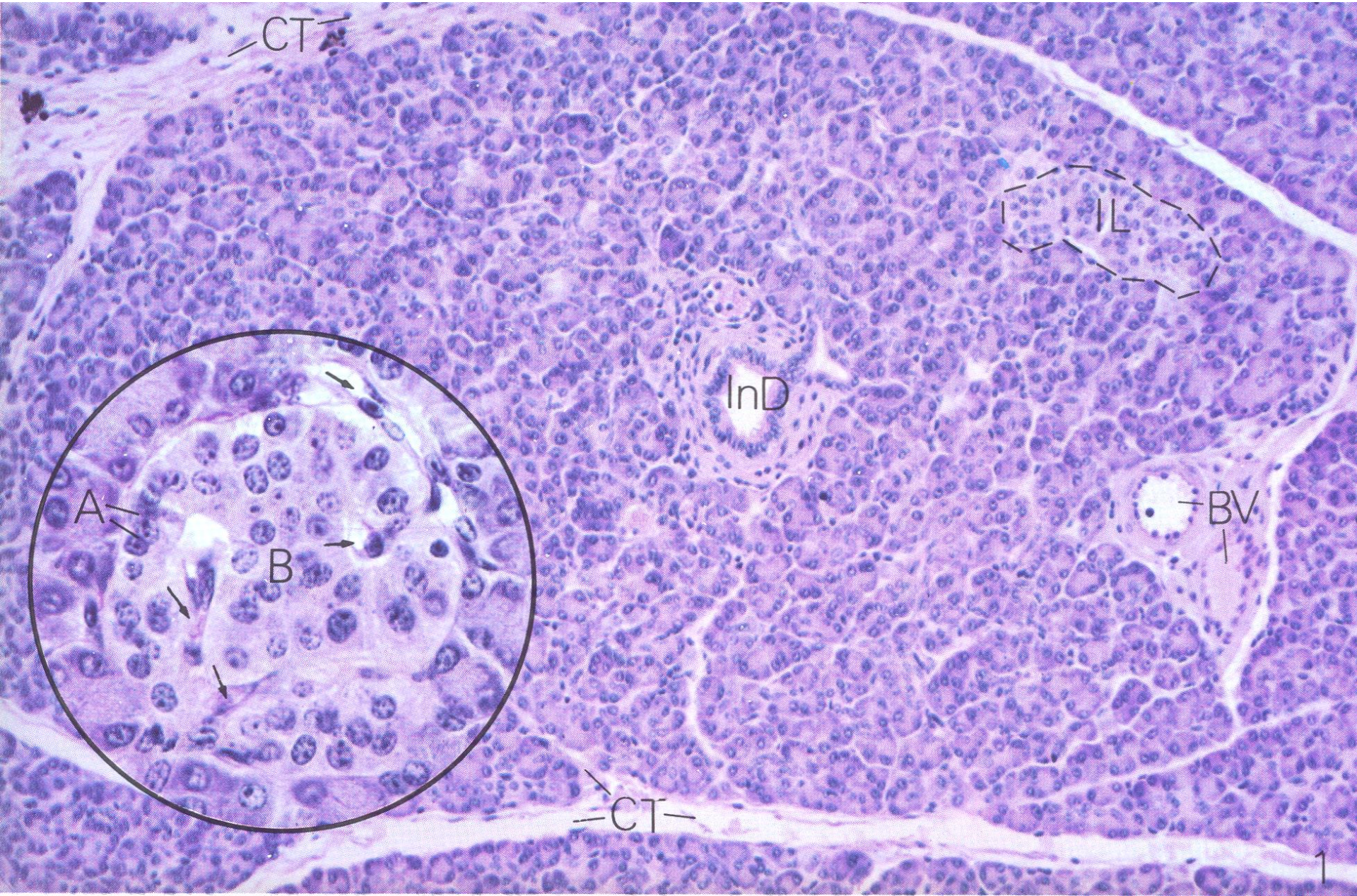
PP cells: minor, pancreatic polypeptide







PANCREAS – ISLETS OF LANGERHANS

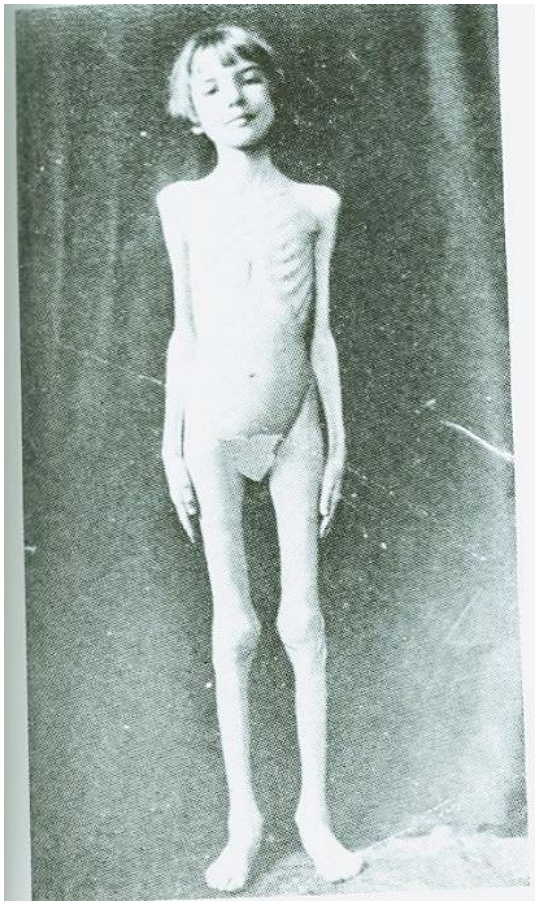


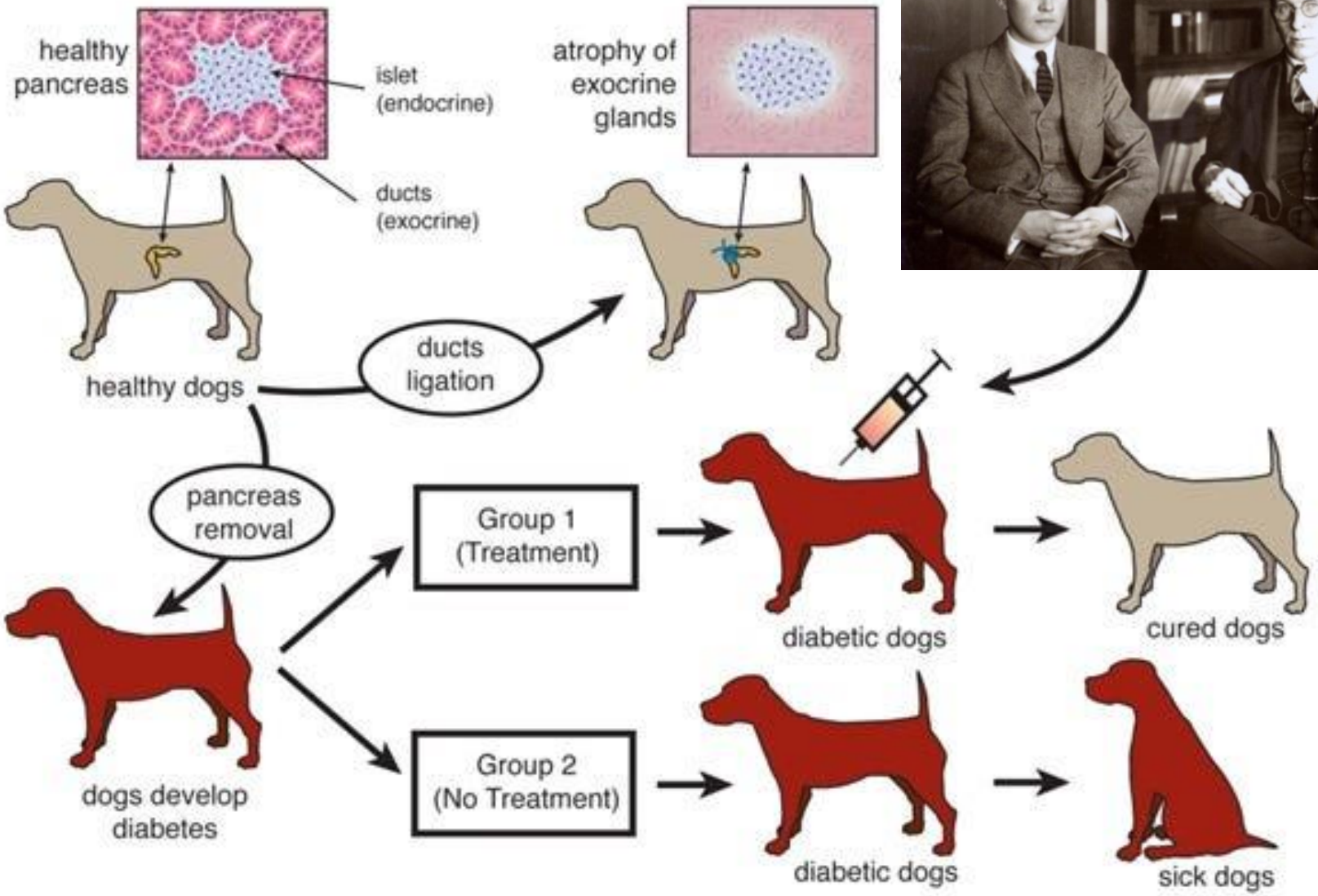
BRIEF HISTORY OF DIABETES TREATMENT

DM (I)

- Cachexy
- Vision loss
- Limb loss
- Diabetic coma
- Renal failure
- Cardiac failure
- Death

Frederick M. Allen
„starvation diet“
1921



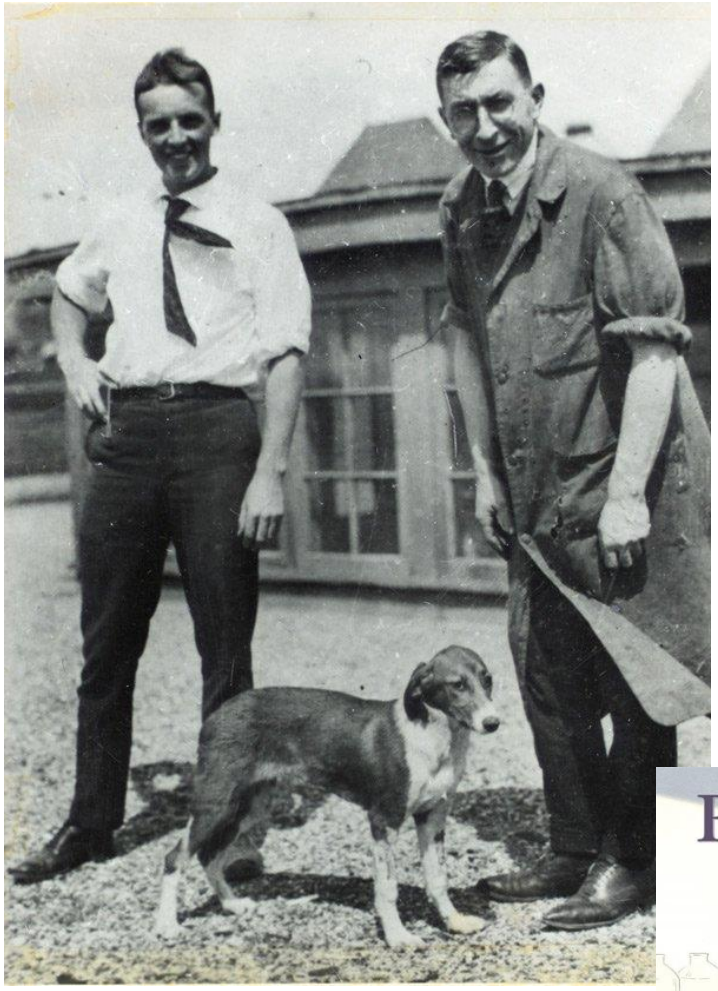

healthy pancreas
islet (endocrine)
ducts (exocrine)
atrophy of exocrine glands
healthy dogs
ducts ligation
pancreas removal
dogs develop diabetes
Group 1 (Treatment)
Group 2 (No Treatment)
diabetic dogs
cured dogs
diabetic dogs
sick dogs

BRIEF HISTORY OF DIABETES TREATMENT

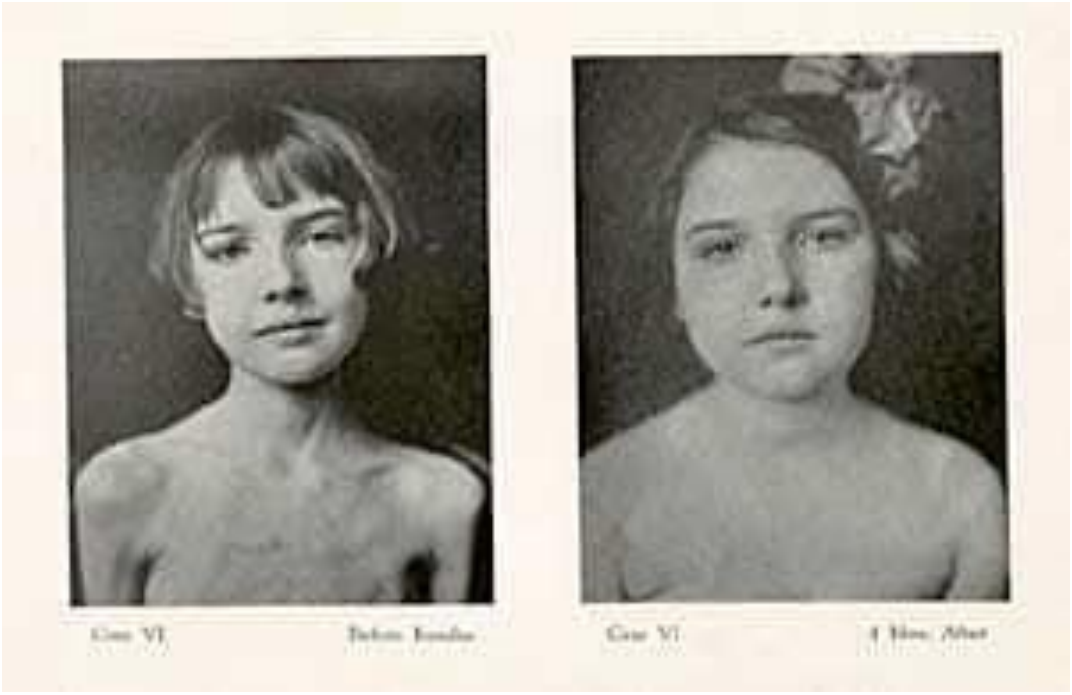
11th of January 1922, 14 year old Leonard Thompson became the first person in the world with autoimmune diabetes (type 1 diabetes) to receive insulin, isolated ("discovered") by Frederick Banting and Charles Best 27th of July 1921 (the exact date is debated). Leonard was believed to have had the disease ~3 years when his father approved the experimental trial, and had only a few days left when he was drifting in and out of diabetic coma due to his high glucose and ketoacidosis (1). Within the first 24 hours improvement was seen, but they failed. Twelve days later, the 23d of January, the team (now including biochemist James Collip) resumed the administration of the extract and finally they were was successful. Remarkable progresses was seen and Leonard left the clinic in the Spring 1922, and lived 13 more years but passed away at age 27, eventually of pneumonia

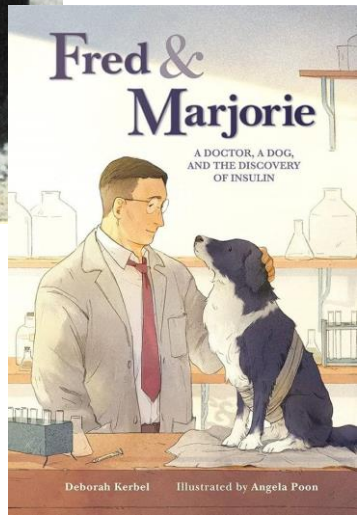
http://www.diabethics.com/science/99-years-since-first-patient-received-insulin/

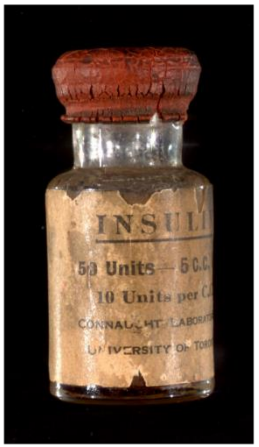
BRIEF HISTORY OF DIABETES TREATMENT



F.G. Banting, C. Best a
Pes 408
1922

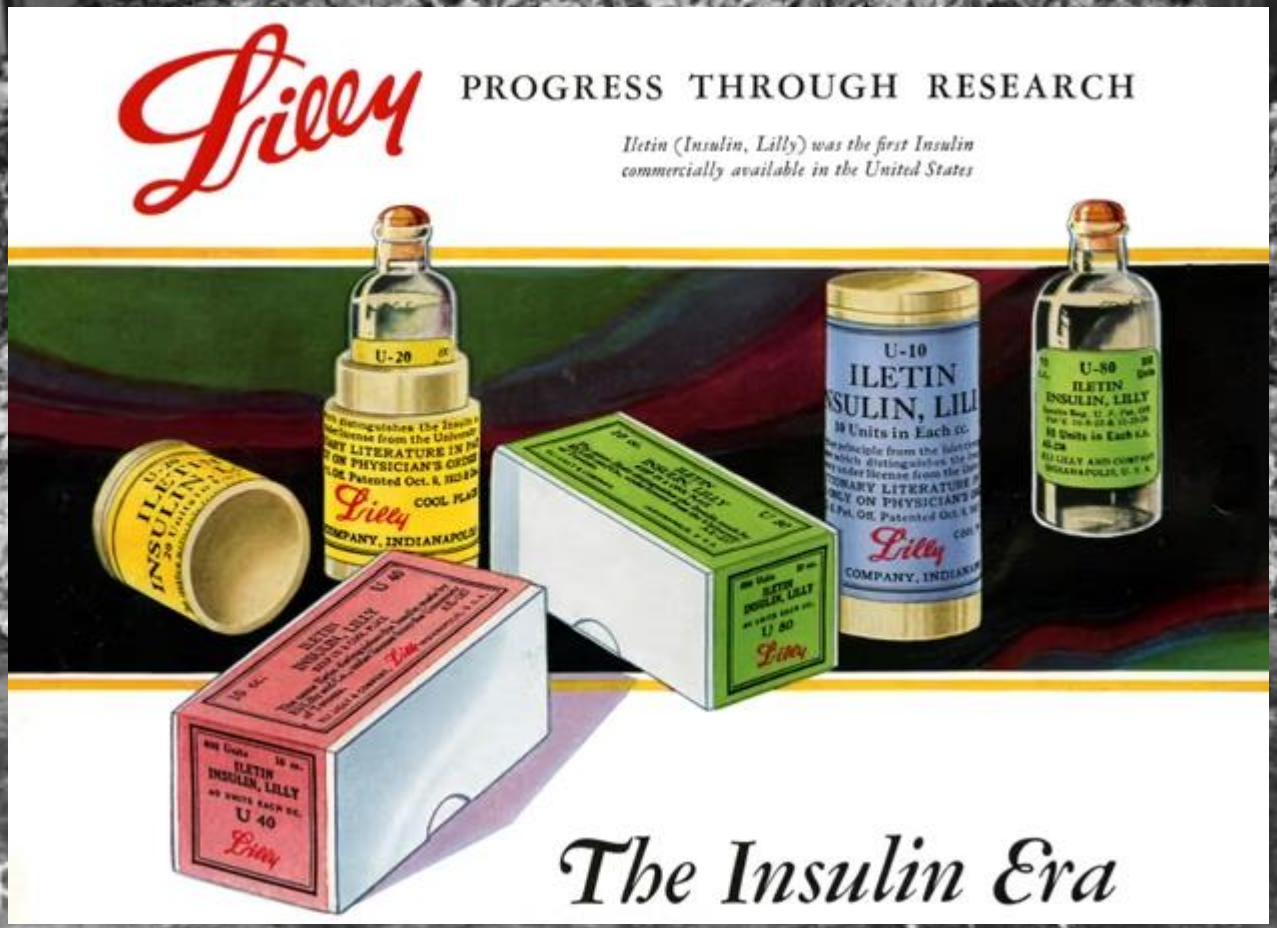




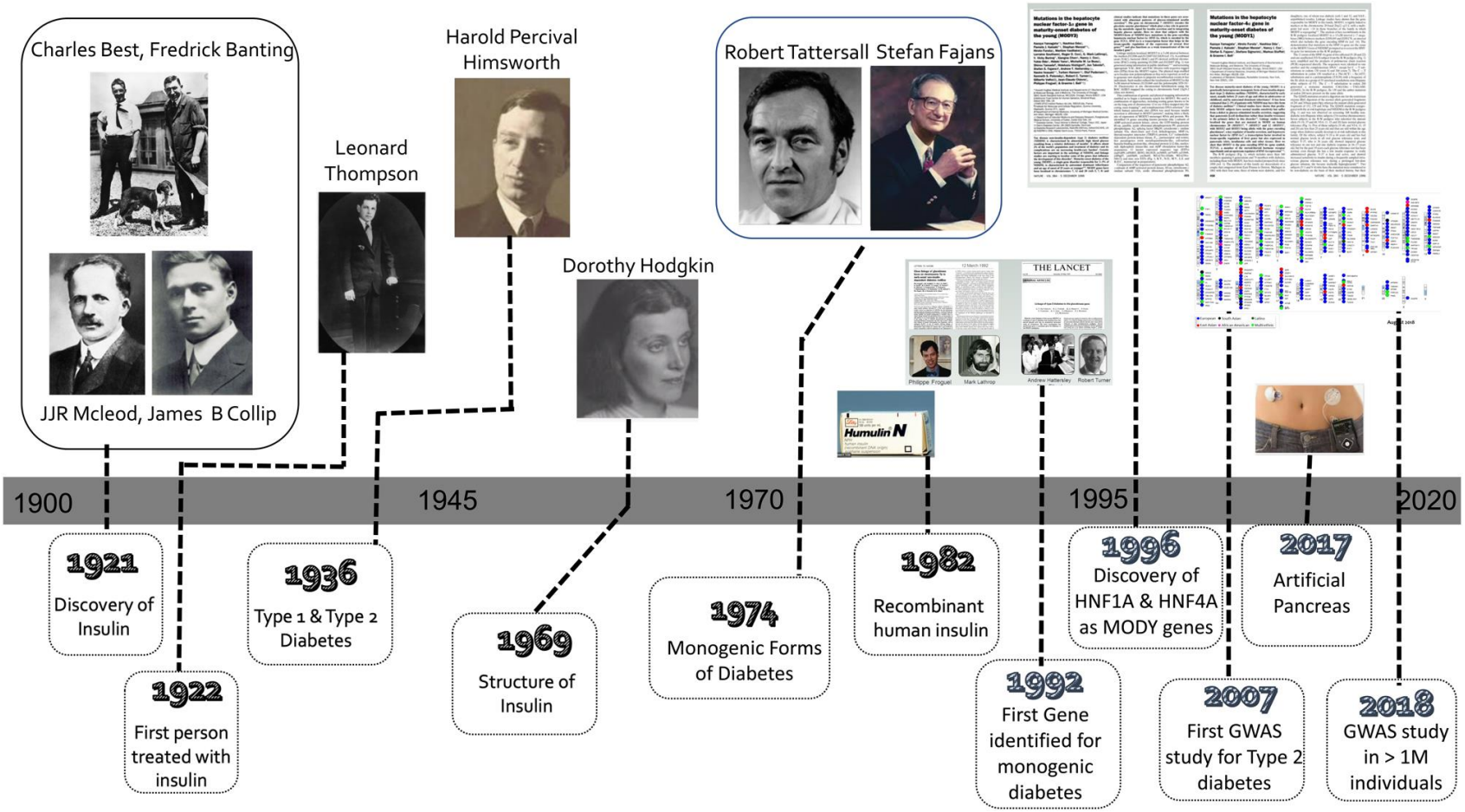


1923

BRIEF HISTORY OF DIABETES TREATMENT



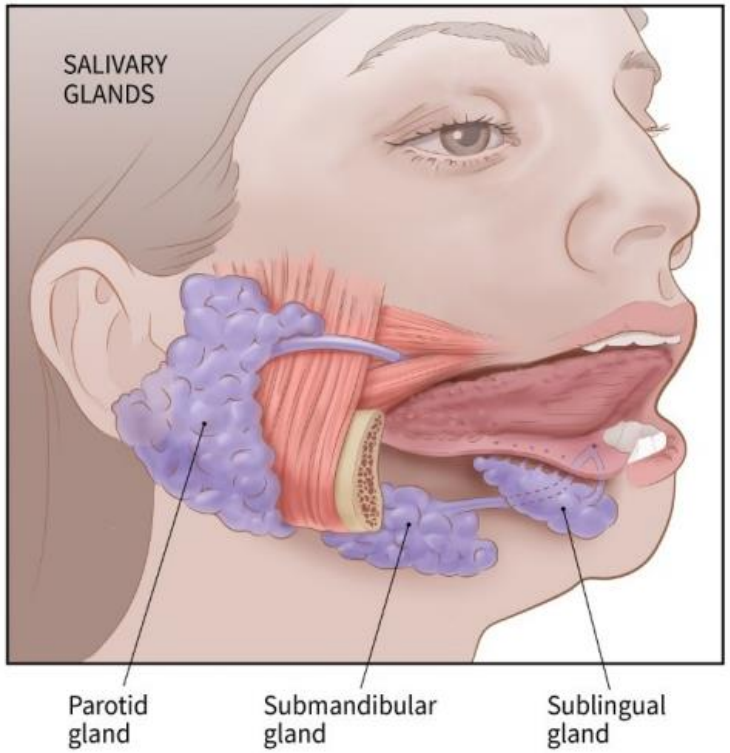
BRIEF HISTORY OF DIABETES TREATMENT



Timeline indicating key genetic discoveries in the context of our understanding of the hormone insulin and its use therapeutically.

SALIVARY GLANDS

- **small** (gll. labiales, buccales, retromolares, palatinae, gll. lingualis anterior, gll. Ebneri, gll. Weberi)
- **large** (gl. parotis, gl. submandibularis, gl. sublingualis)

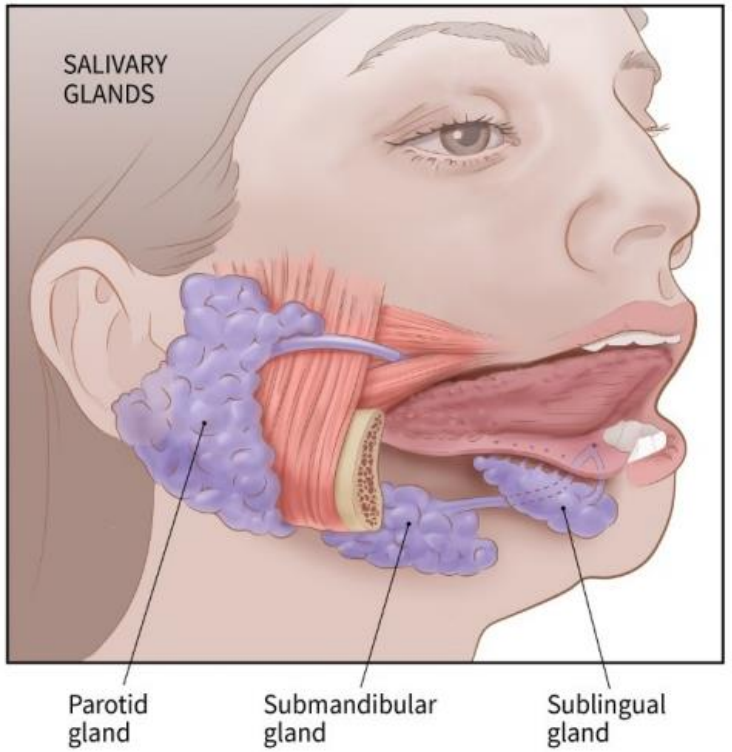


LARGE SALIVARY GLANDS

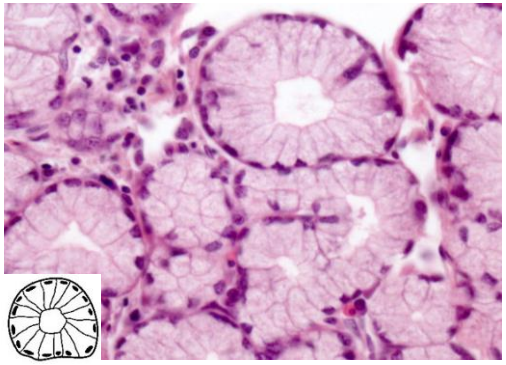
Tuboalveolar salivary galnds

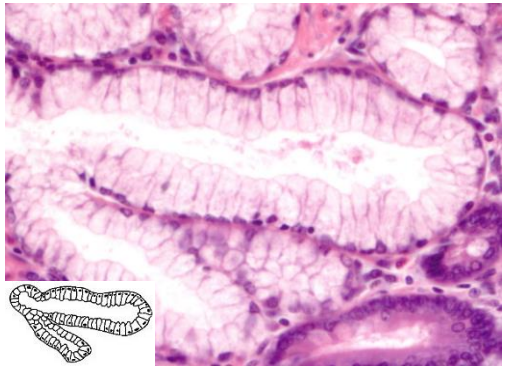
Secretory units
- Serous acini
- Serous demilunes
- Mucous tubules

Ducts
- Intercalated – striated – interlobular - main

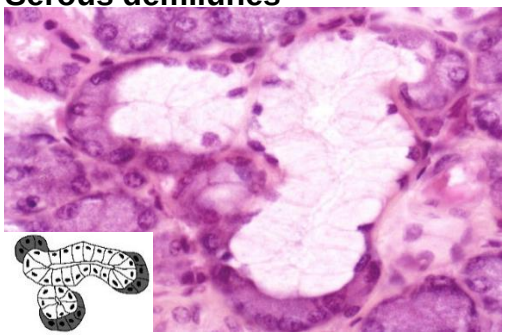


Mucous tubules

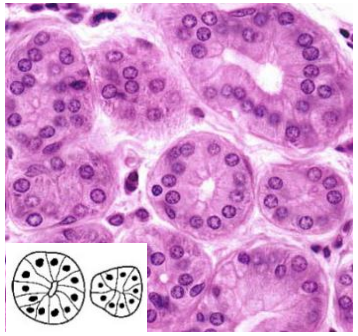




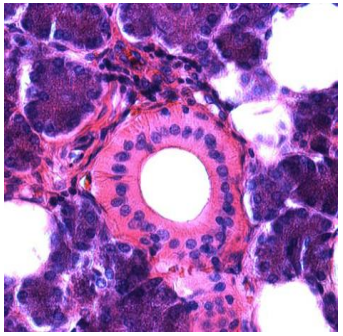
Serous demilunes



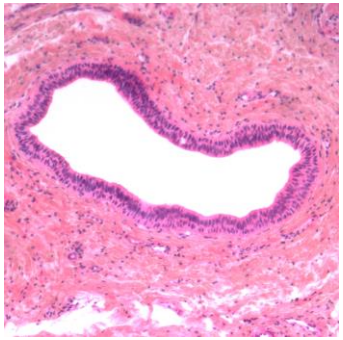
Serous acini



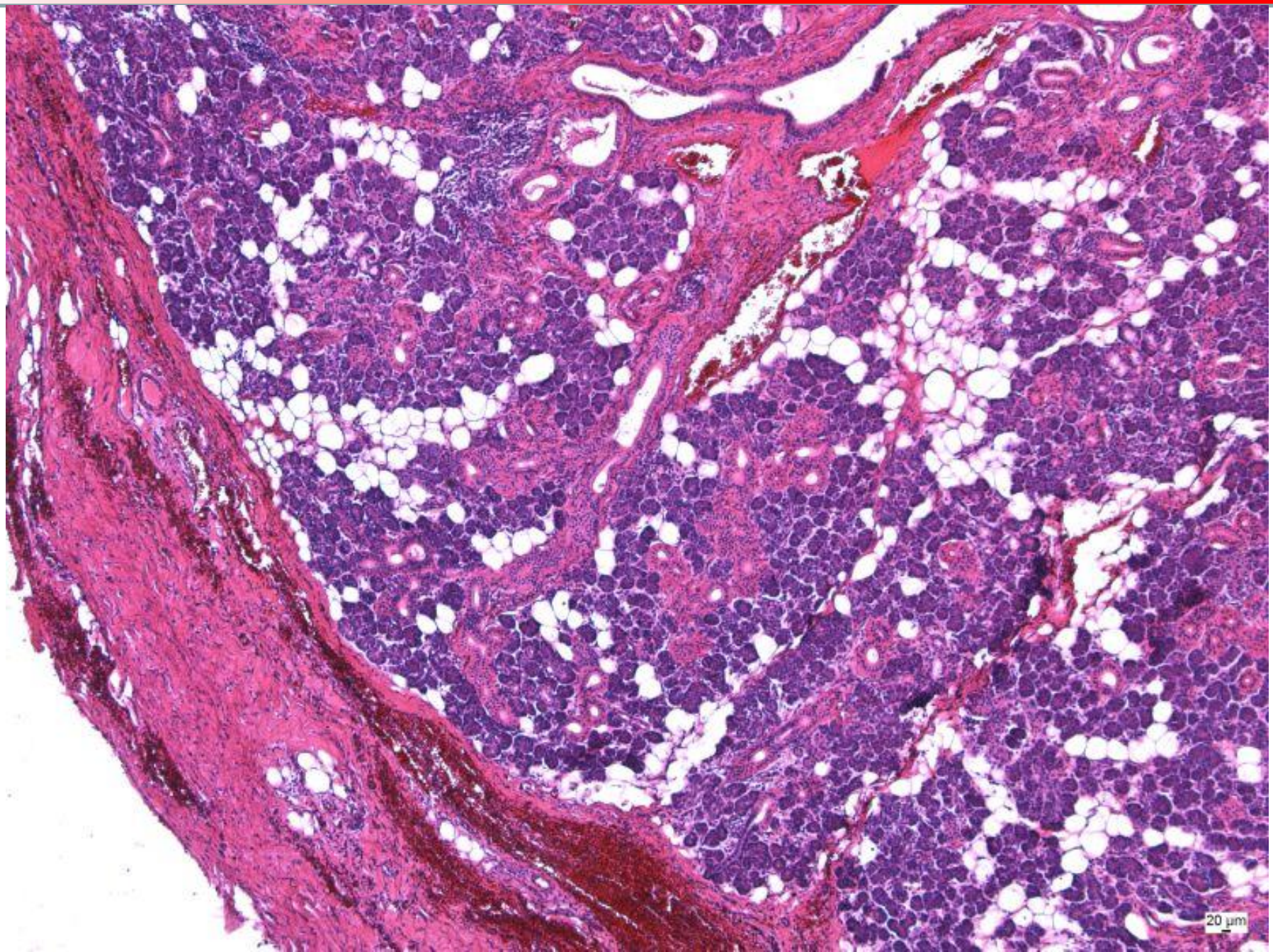
Striated duct



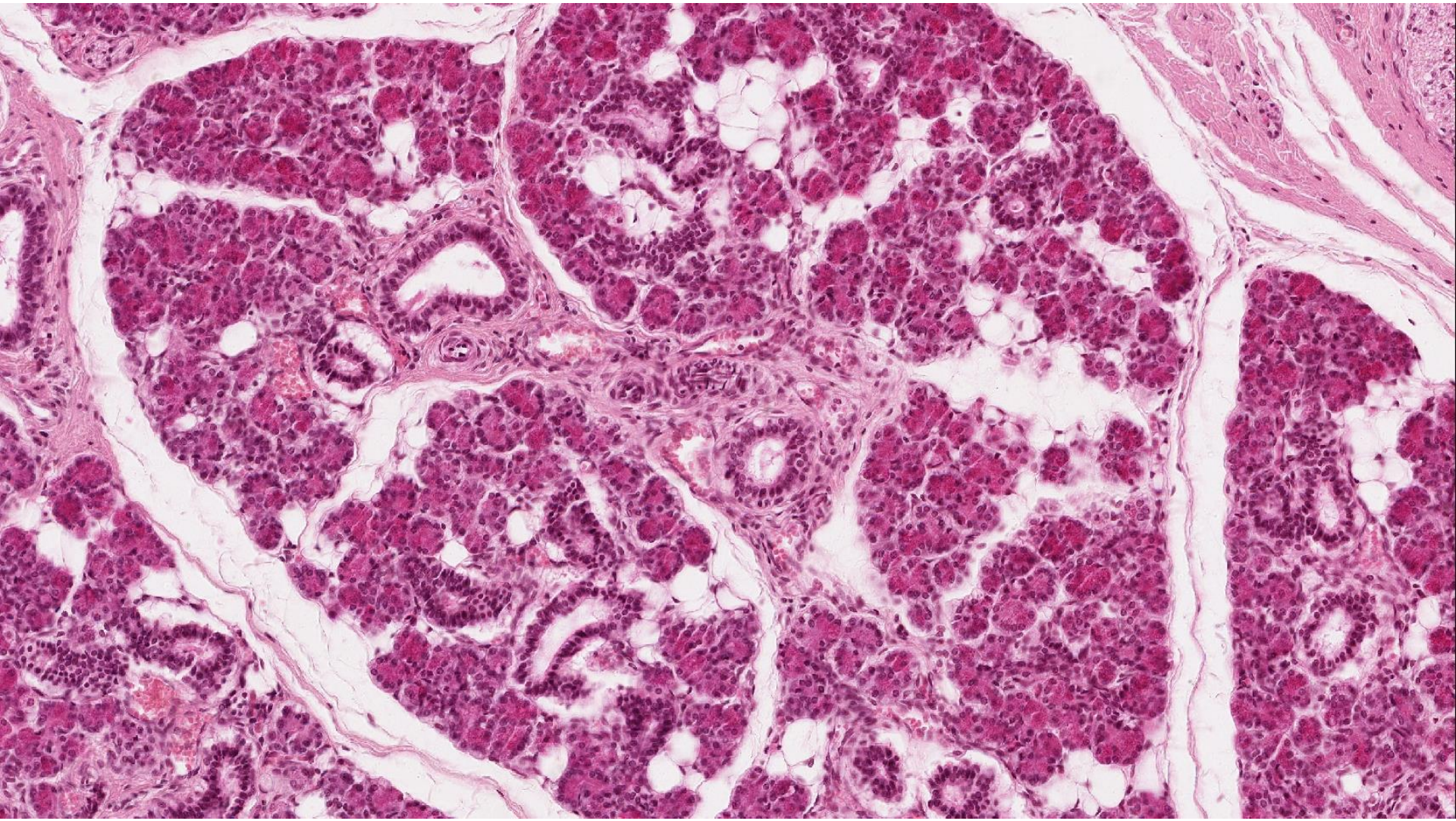
Main duct



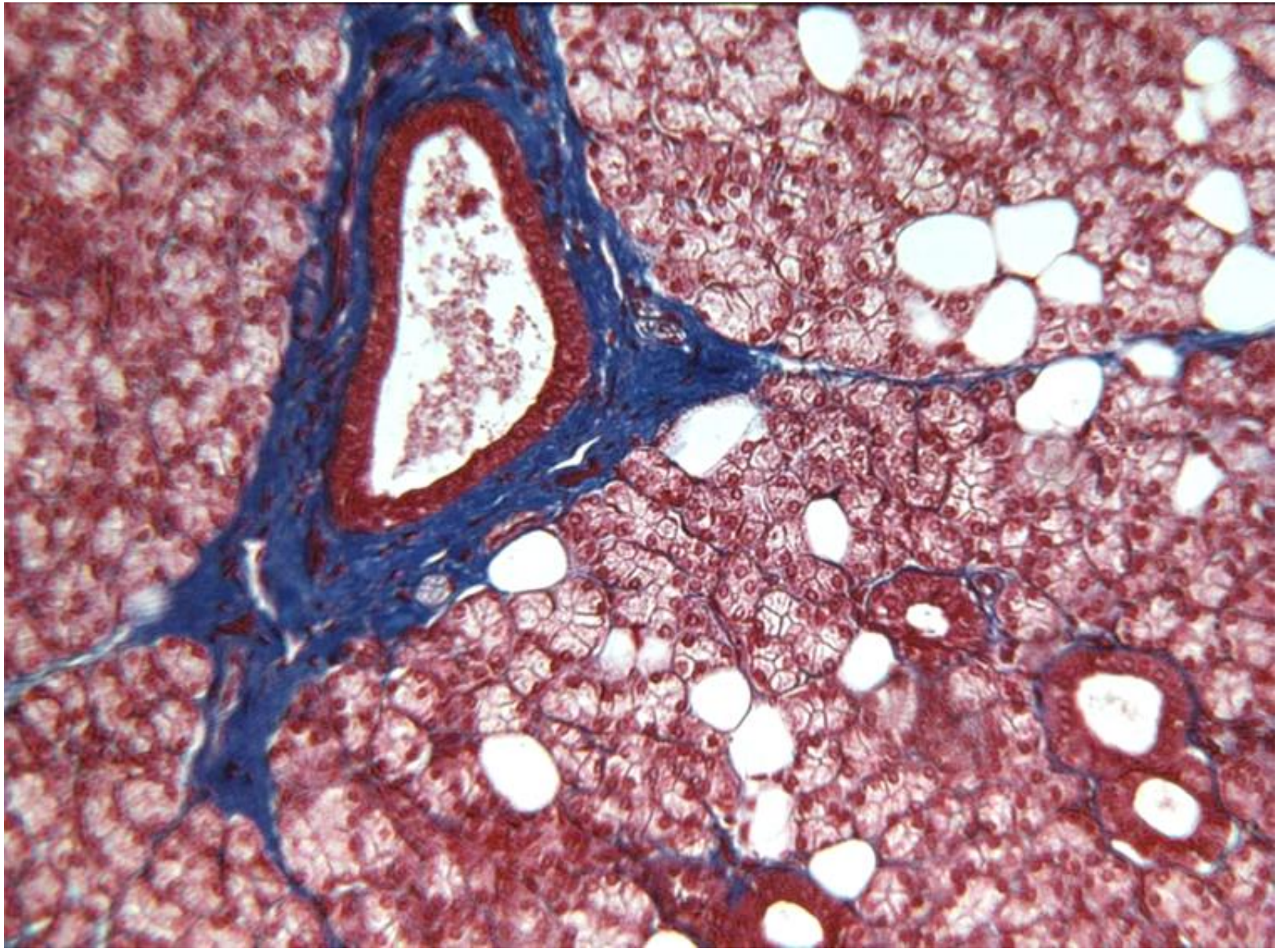
GL. PAROTIS



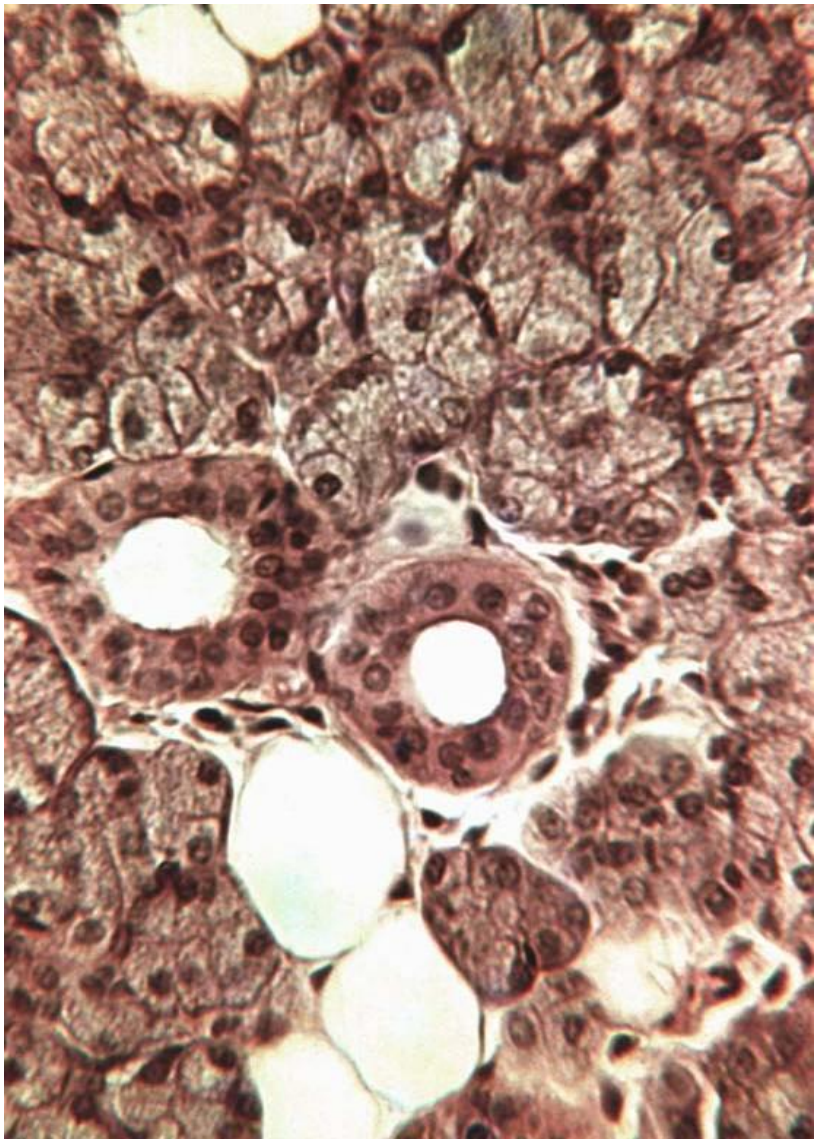
GL. PAROTIS

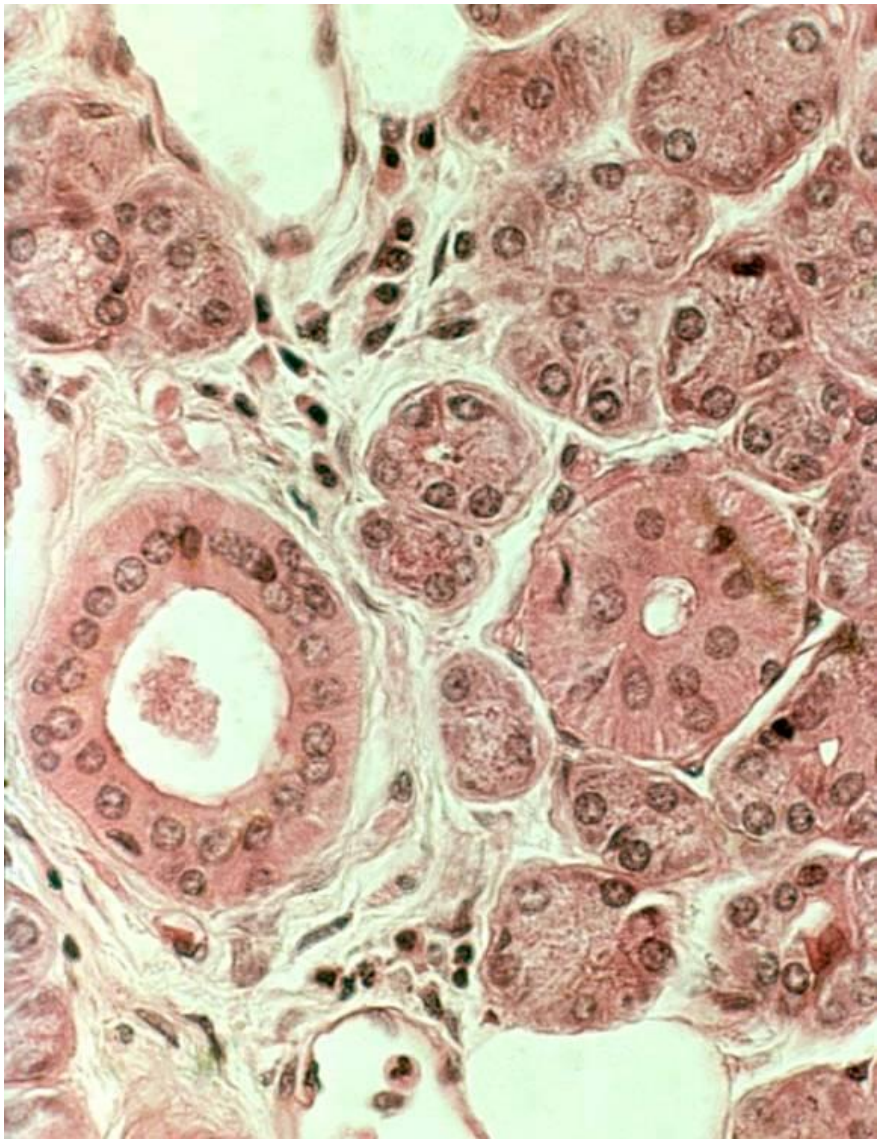


SALIVARY GLANDS – GL. PAROTIS

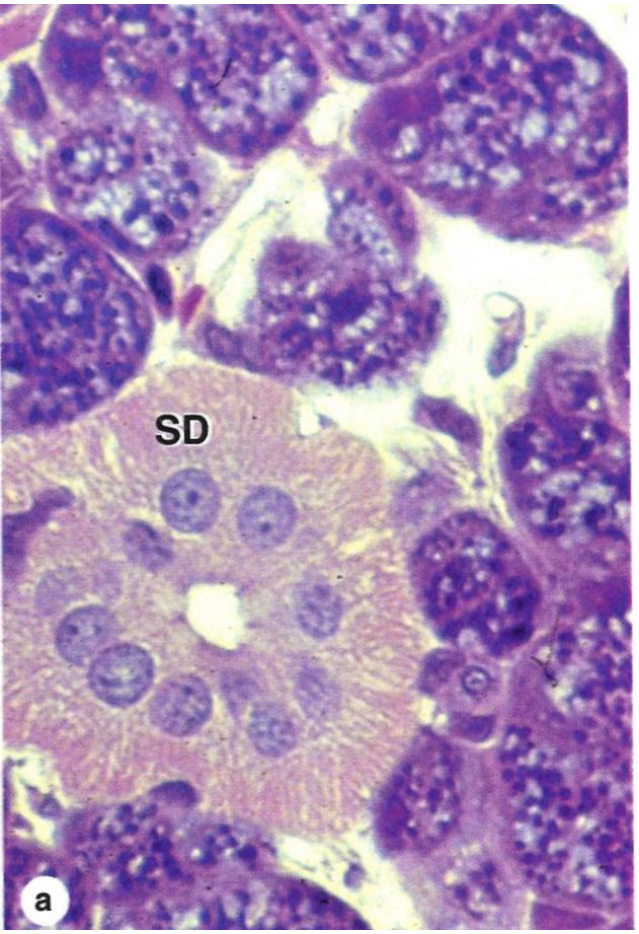


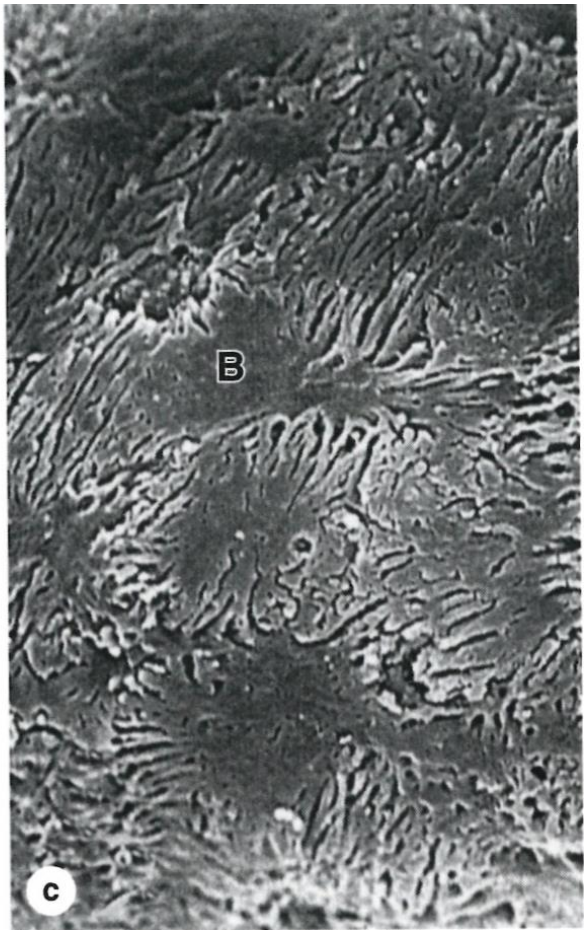
SALIVARY GLANDS – GL. PAROTIS



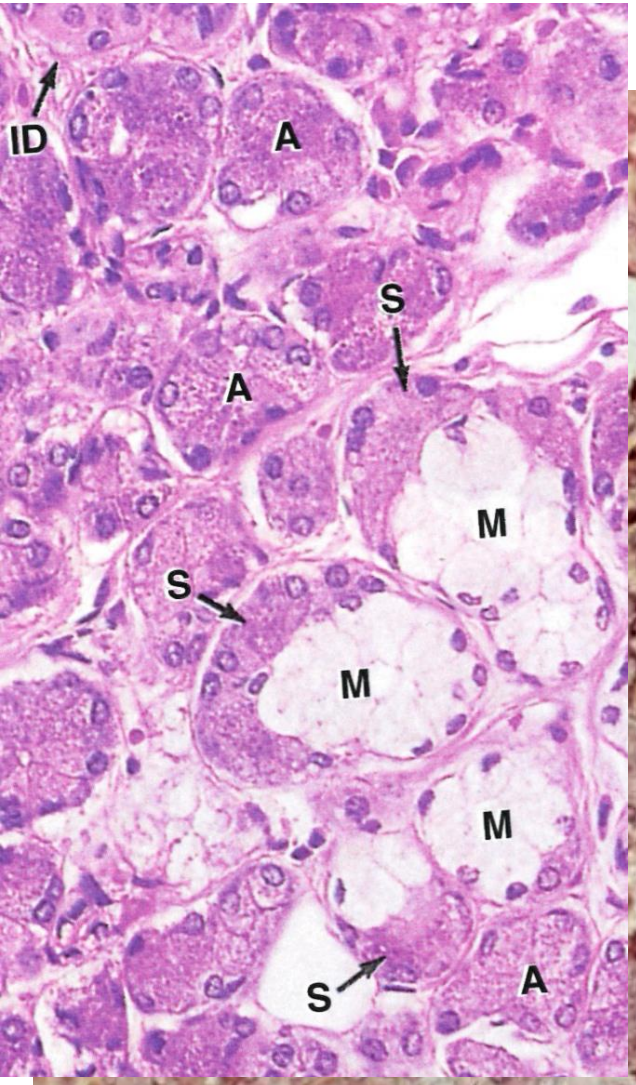


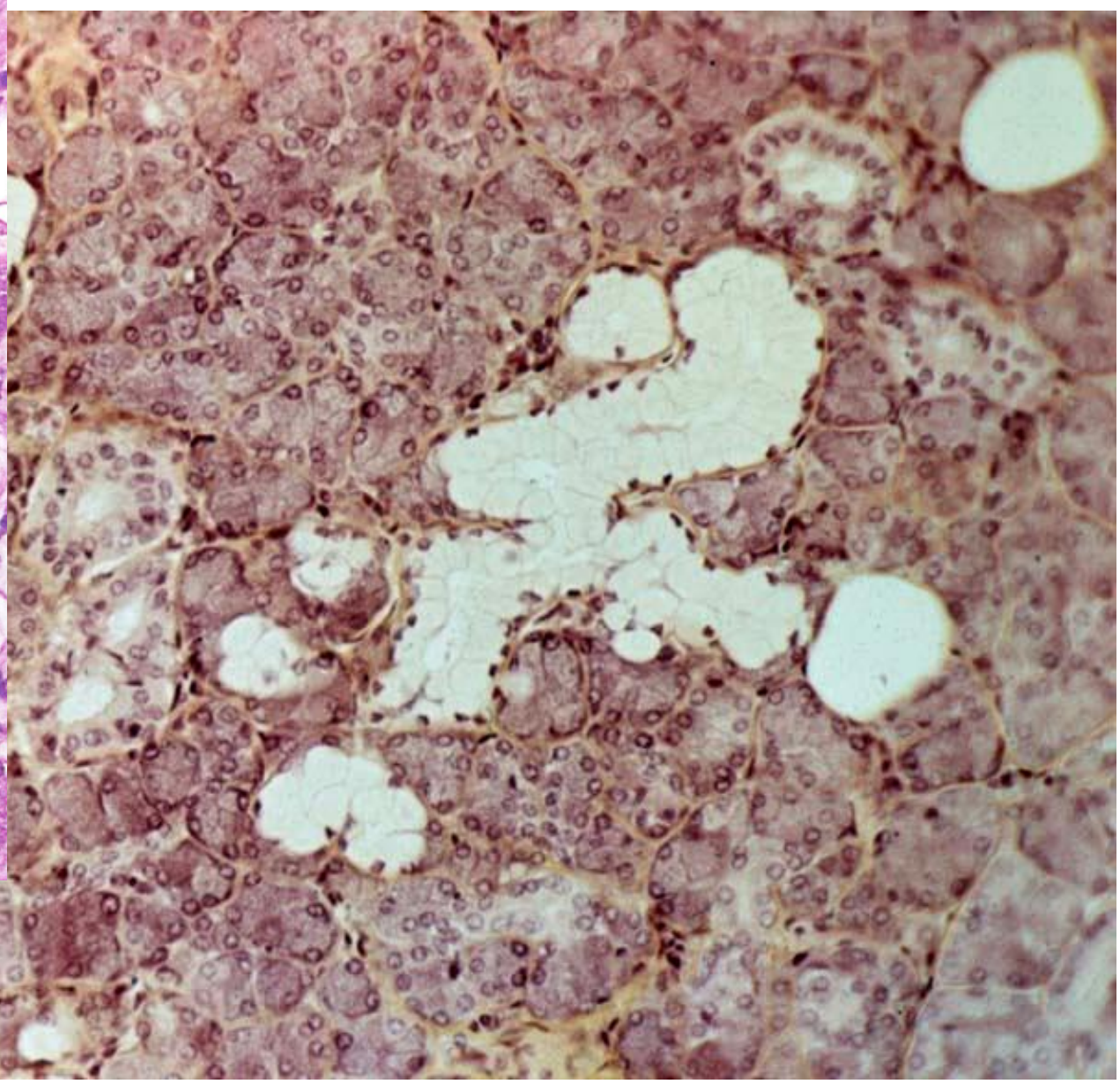
GL. PAROTIS – STRIATED DUCTS



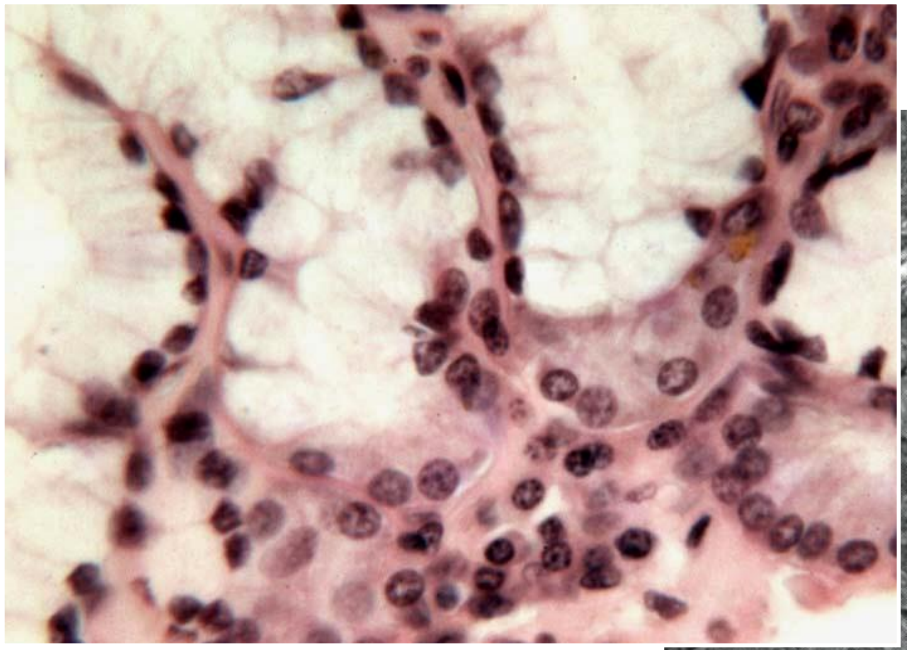


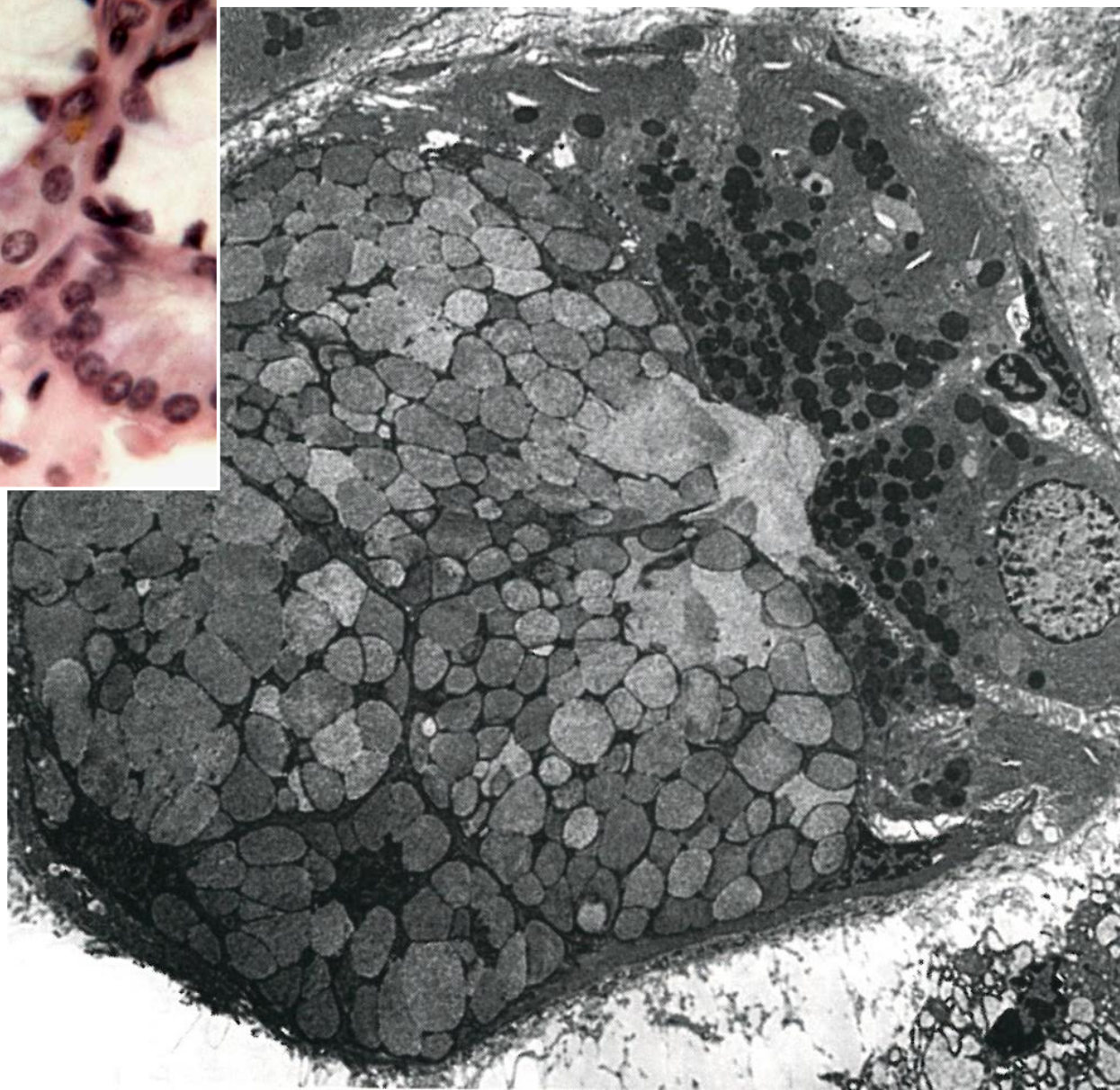
SALIVARY GLANDS – GL. SUBMANDIBULARIS



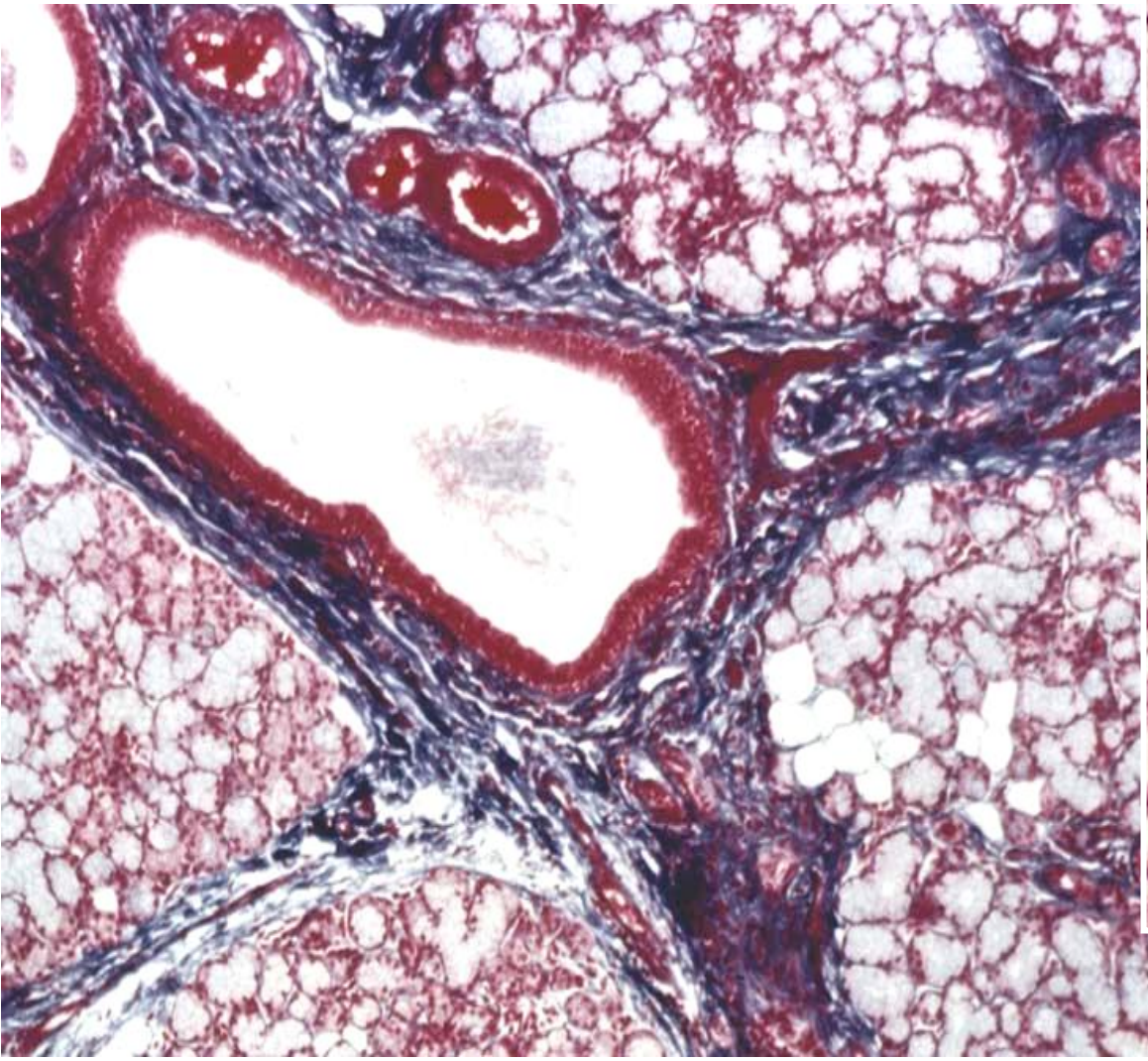


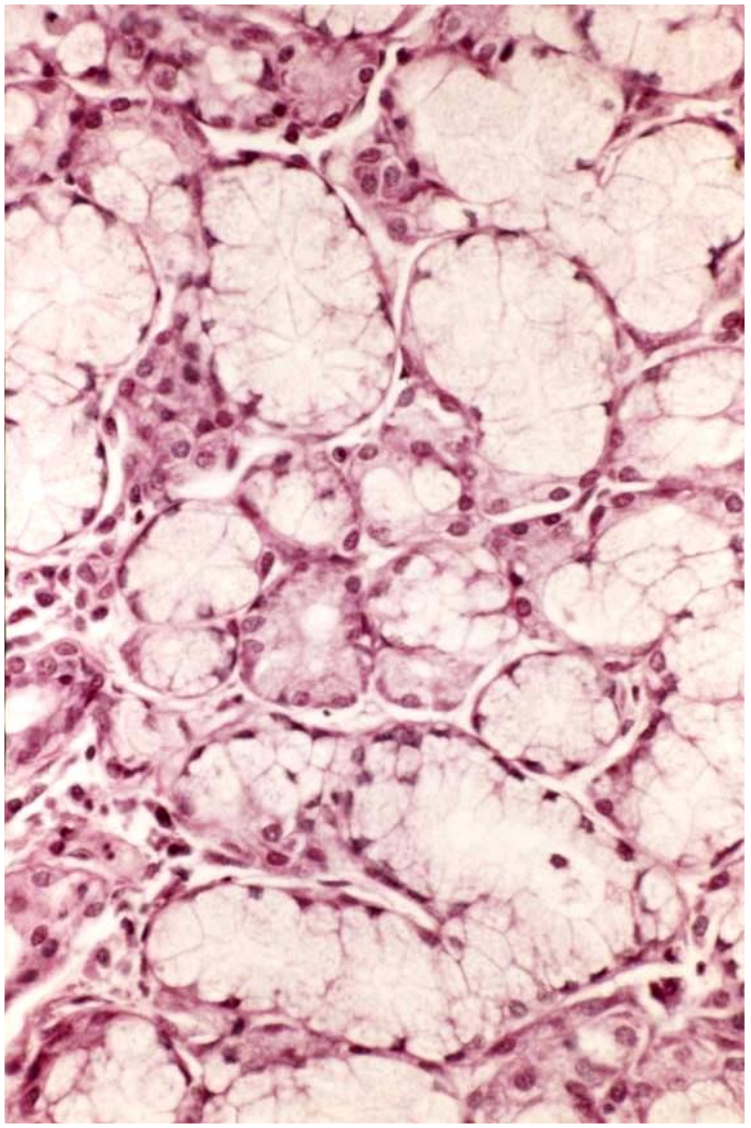
GL. SUBMANDIBULARIS – DEMILUNES OF GIANUZZI





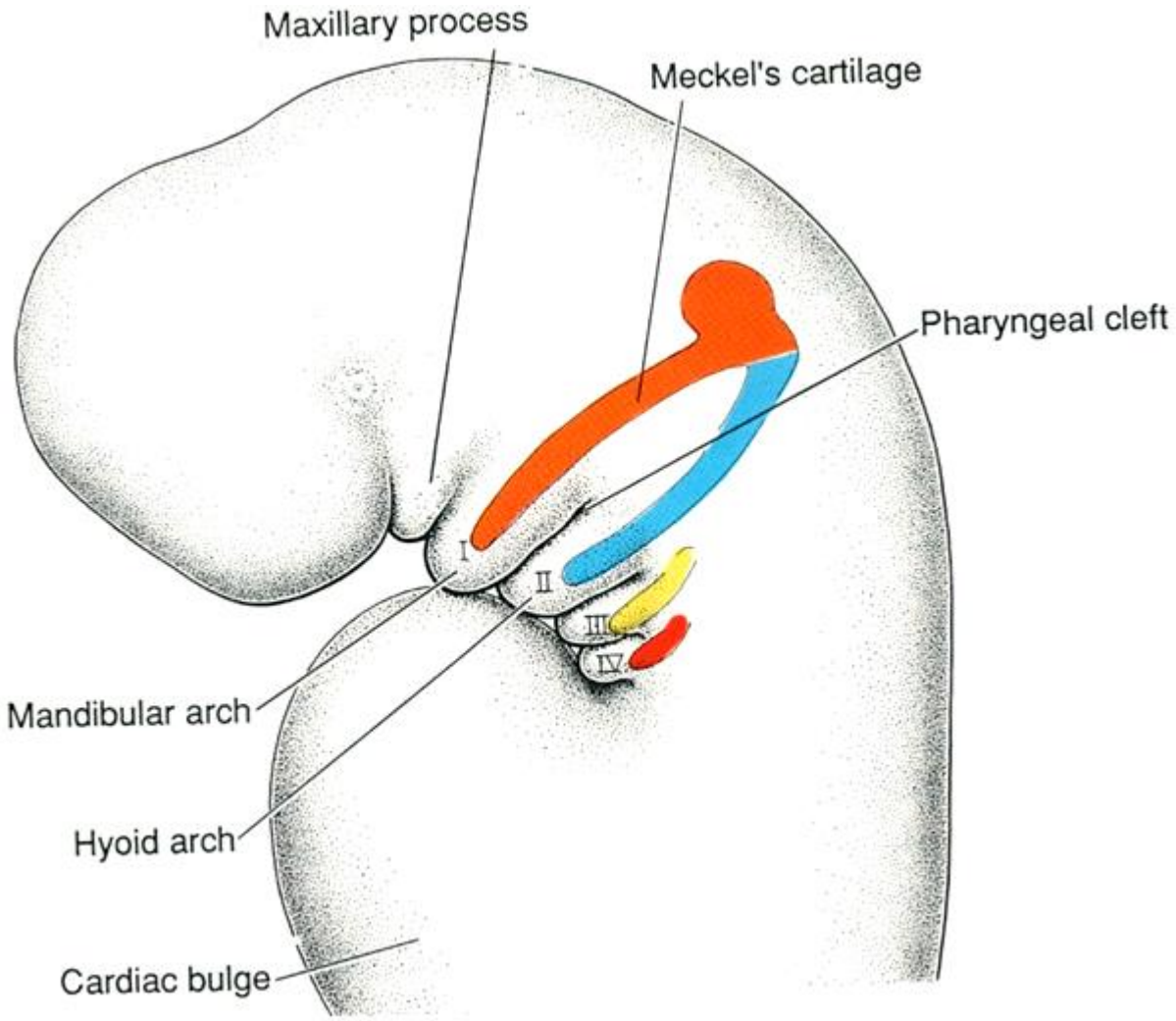
SALIVARY GLANDS – GL. SUBLINGUALIS



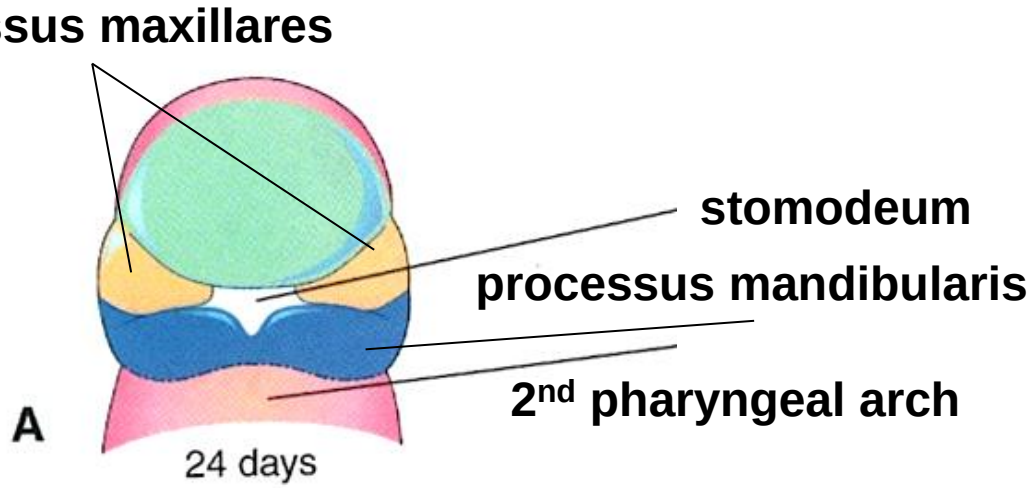


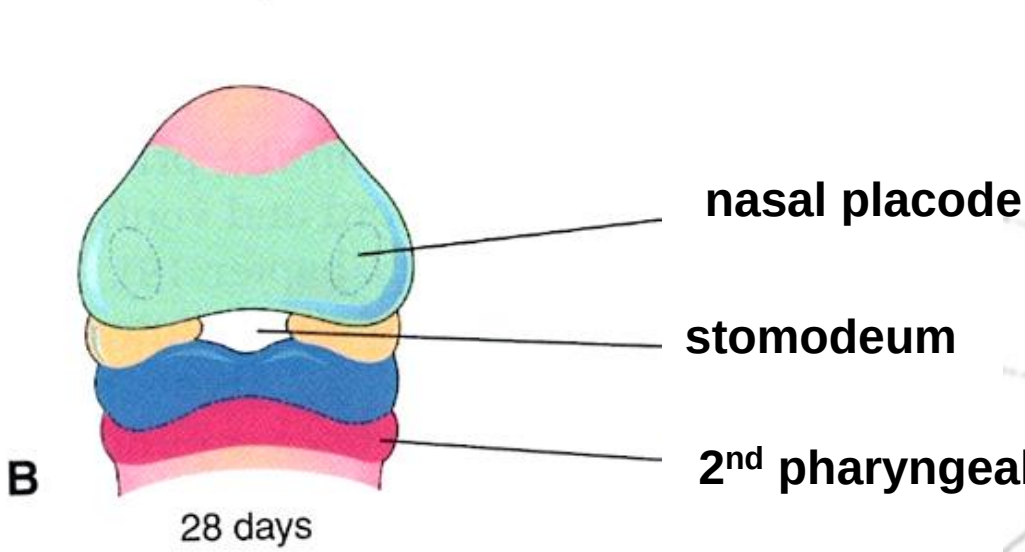
DEVELOPMENT OF GIT

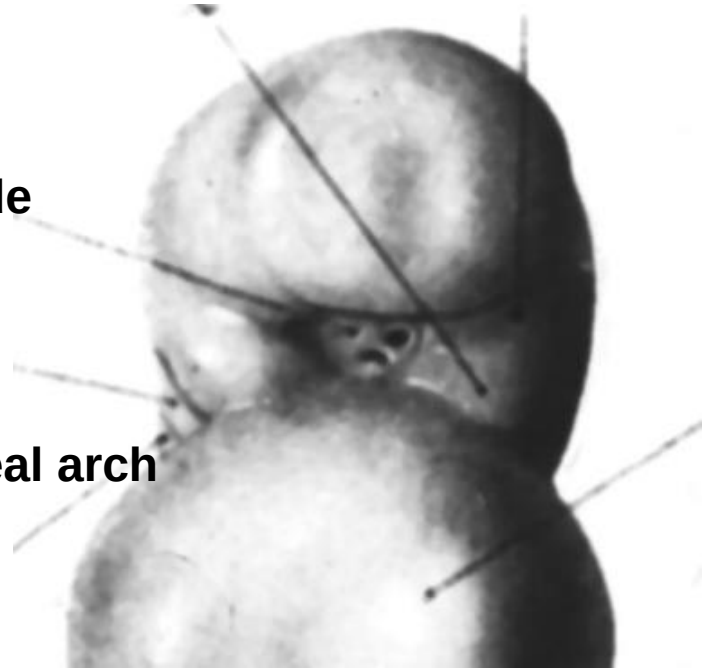
DEVELOPMENT OF FACE



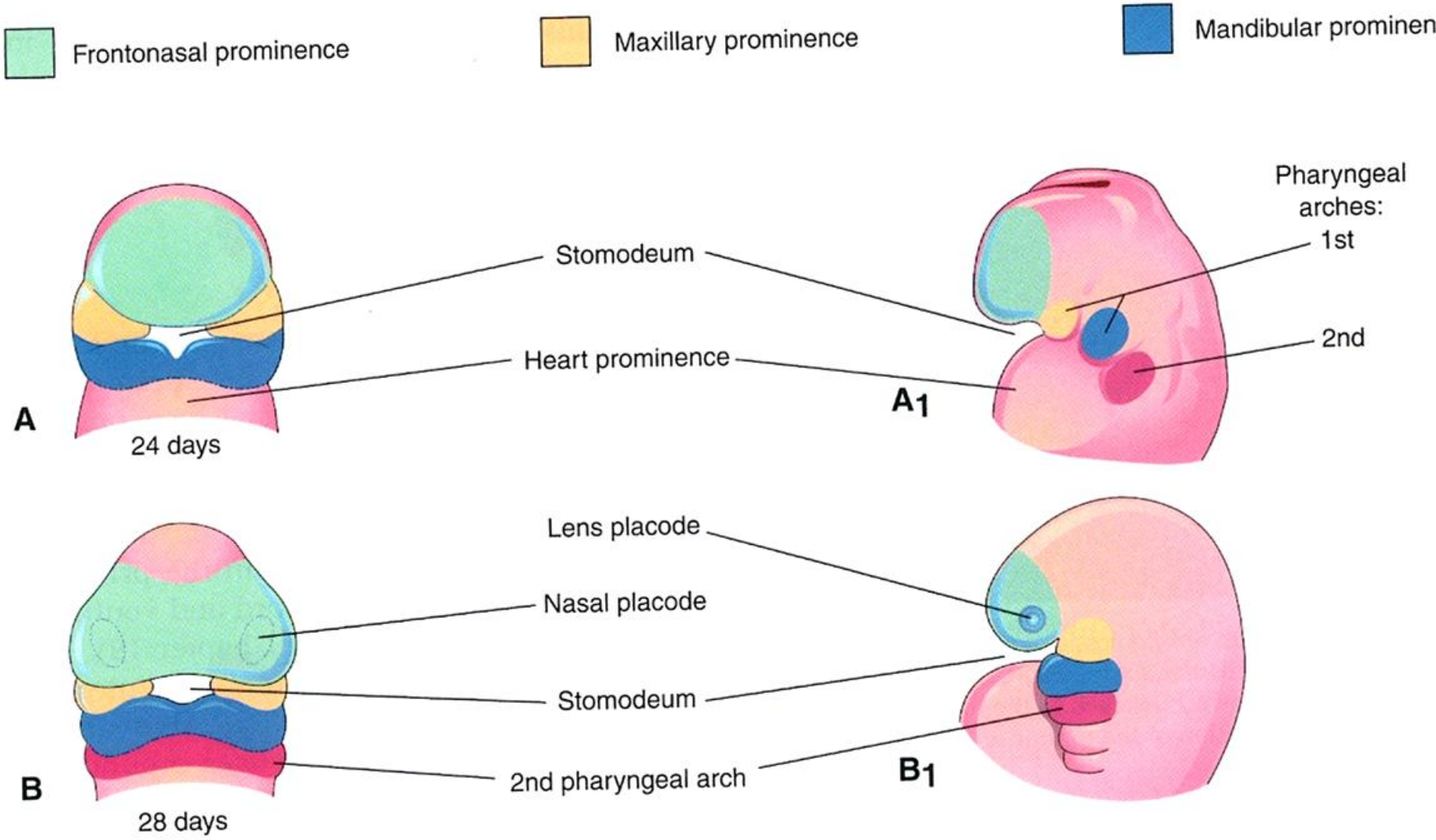
DEVELOPMENT OF FACE





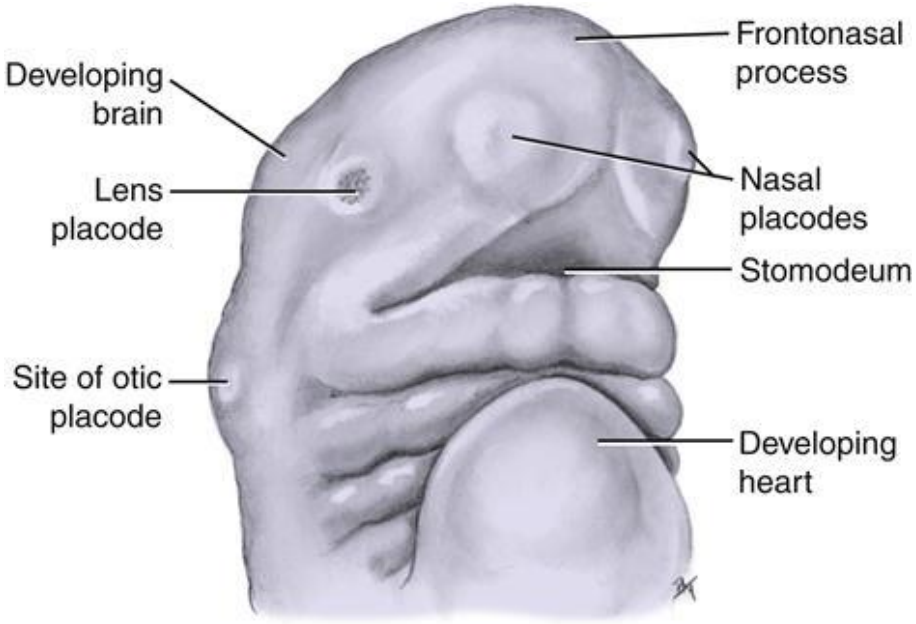


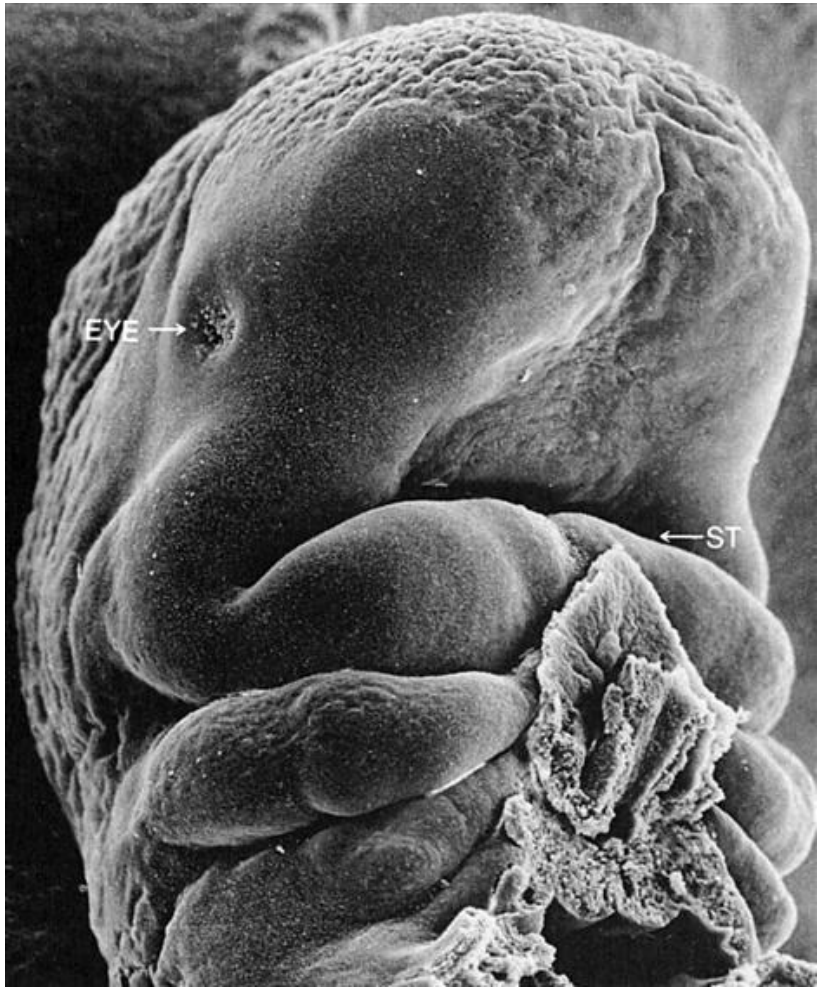
DEVELOPMENT OF FACE



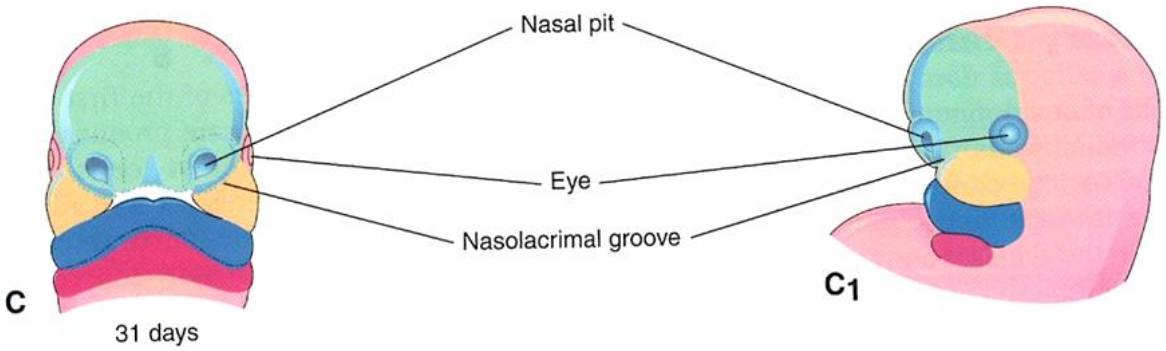
DEVELOPMENT OF FACE

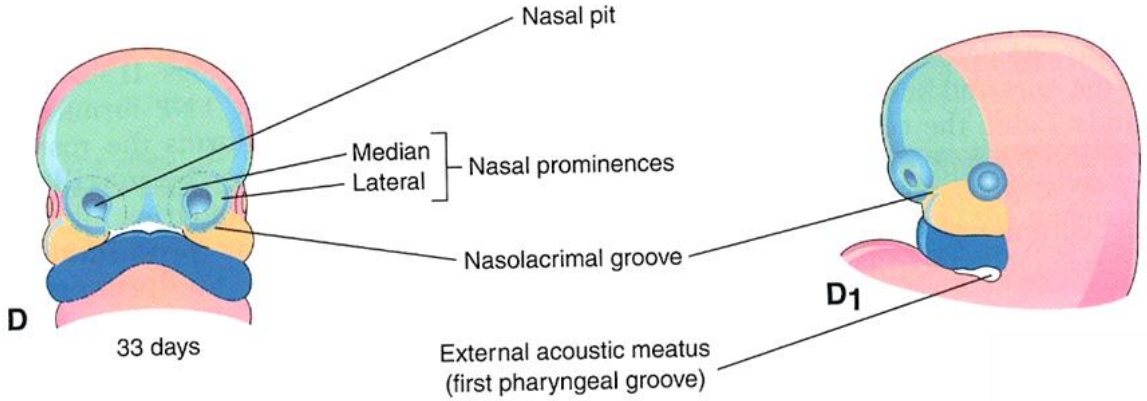
4th week

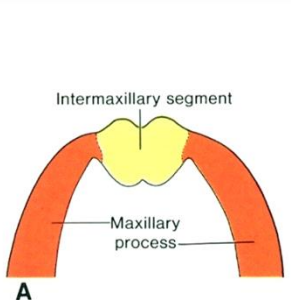


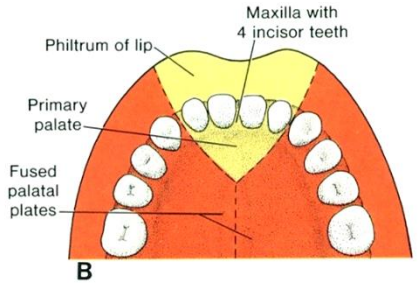


DEVELOPMENT OF FACE



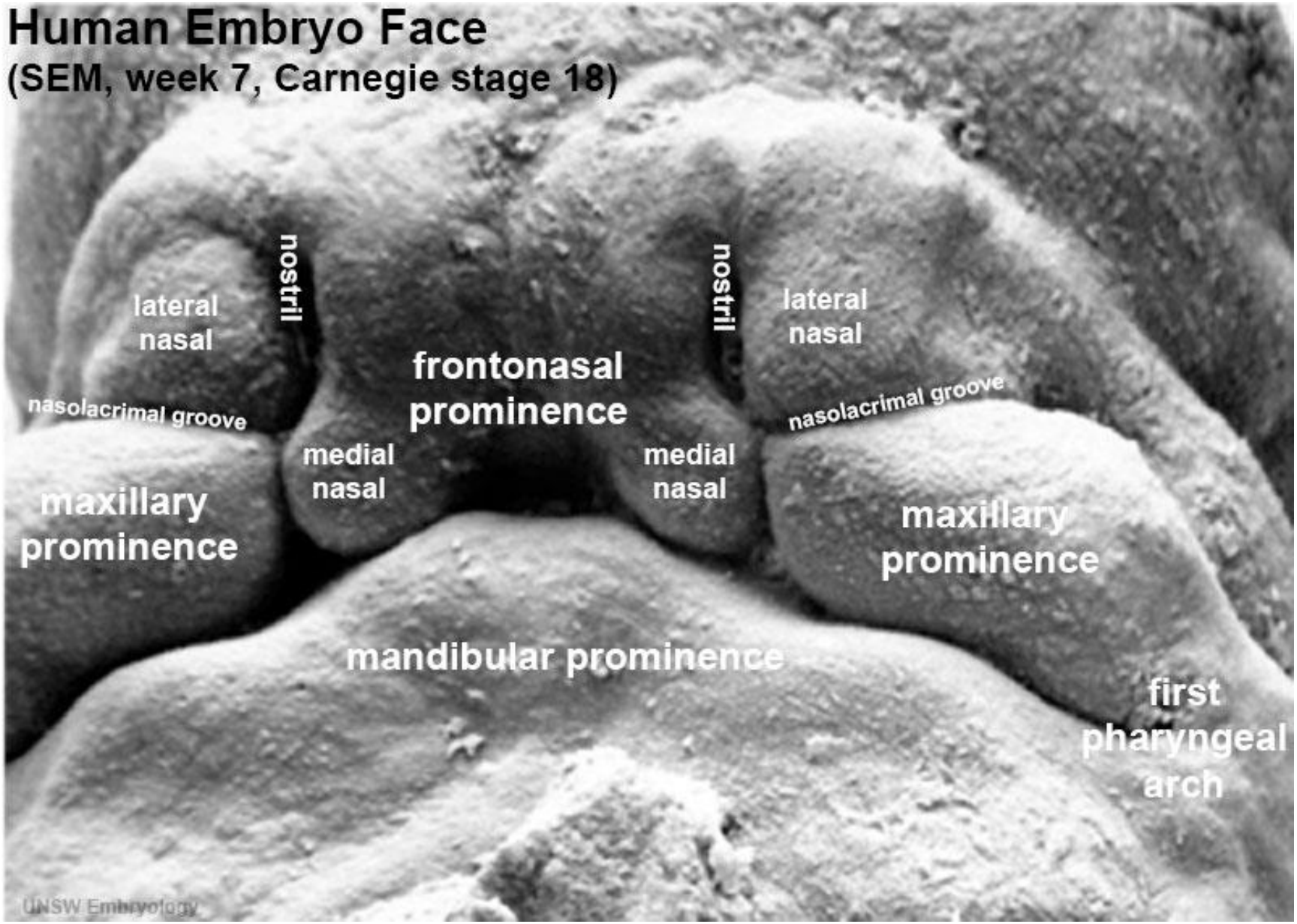




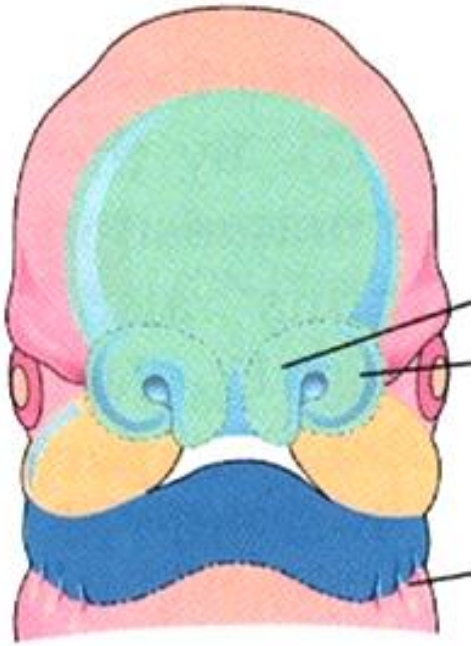


- nasal pits surrrounded by paired prominences – **medial and lateral nasal prominence**
- **area triangularis** (nose)
- **intermaxilary segment** (medial part of upper lip, part of upper jaw, primary palate)

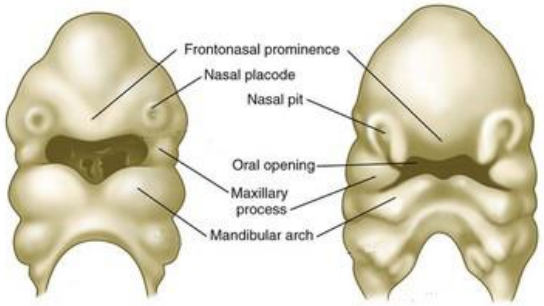
DEVELOPMENT OF FACE

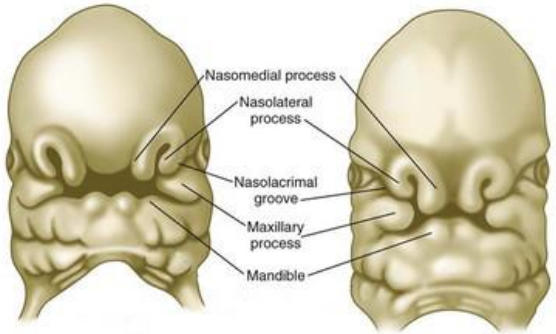


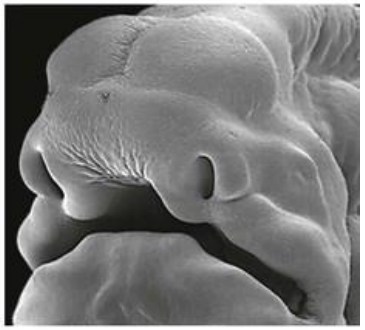
DEVELOPMENT OF FACE

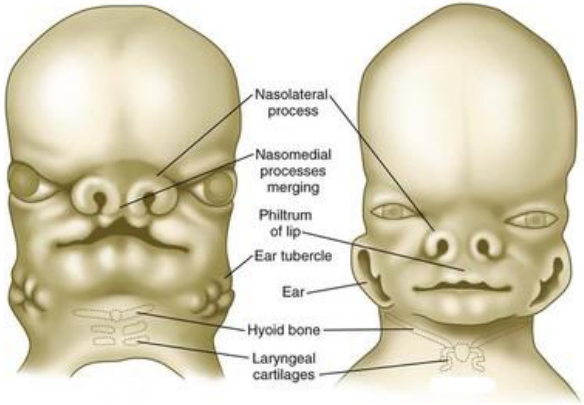


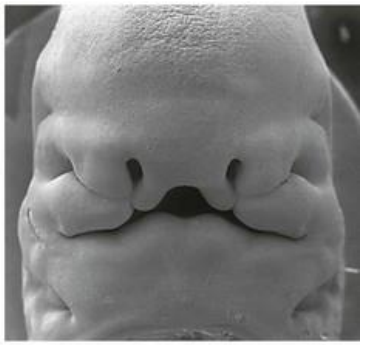
35 days







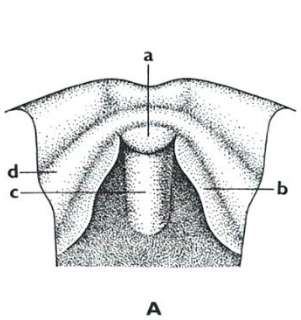




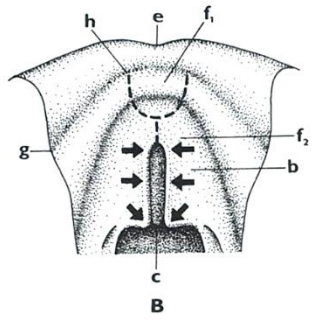
- maxillary prominences fuse with
1. intermaxillary segment
2. lateral nasal prominences
- sulcus nasolacrimalis

DEVELOPMENT OF FACE - PALATE

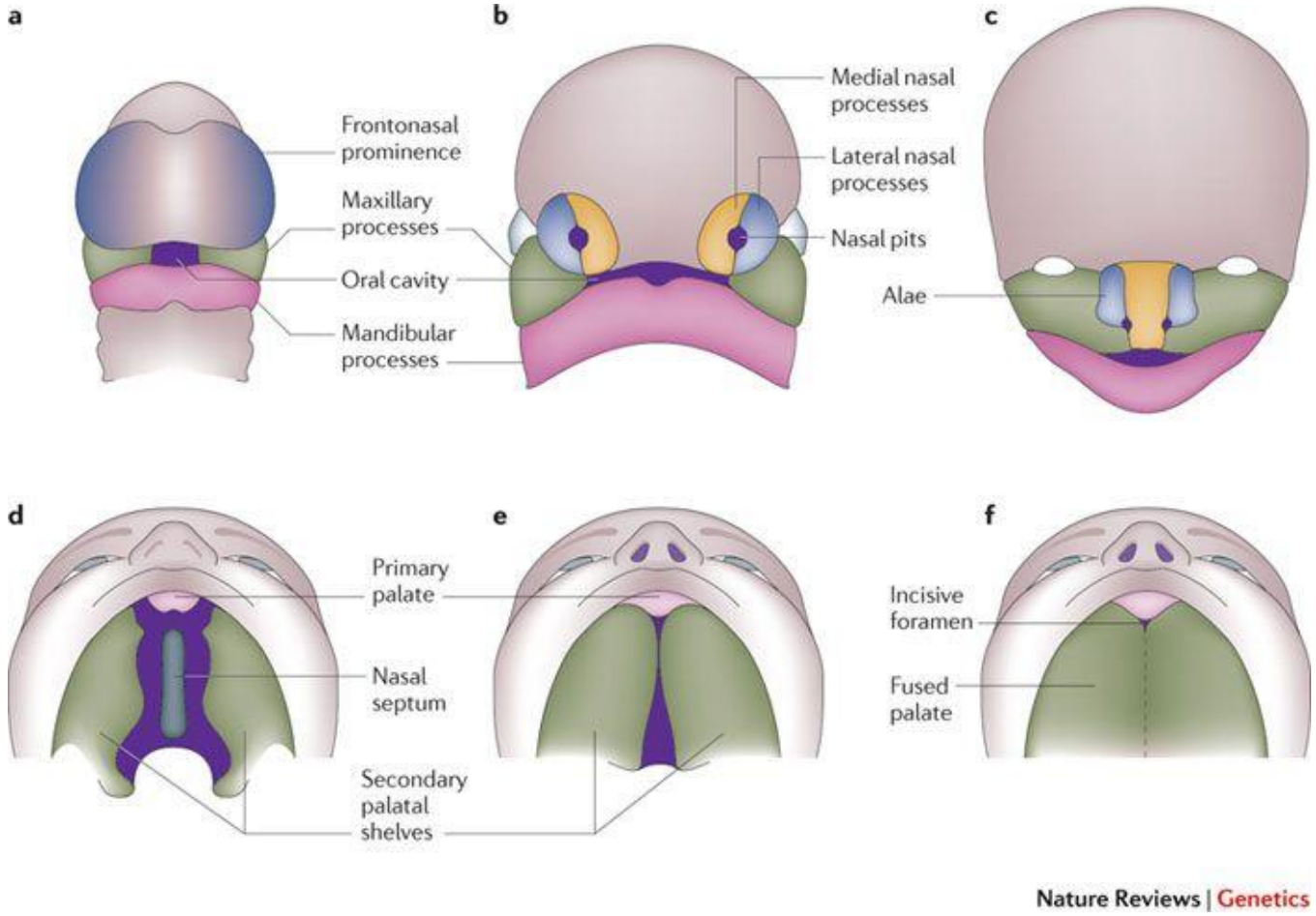
- **primary palate** (intermaxillary segment)
- **secondary palate** (lateral palate shelves)



A

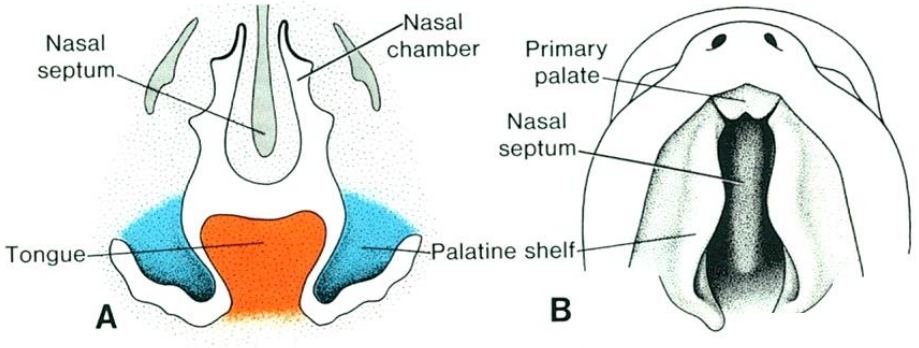


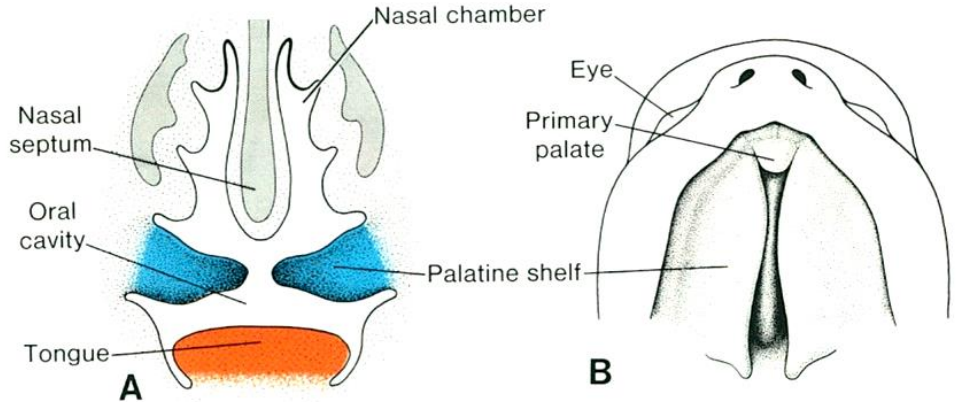
B

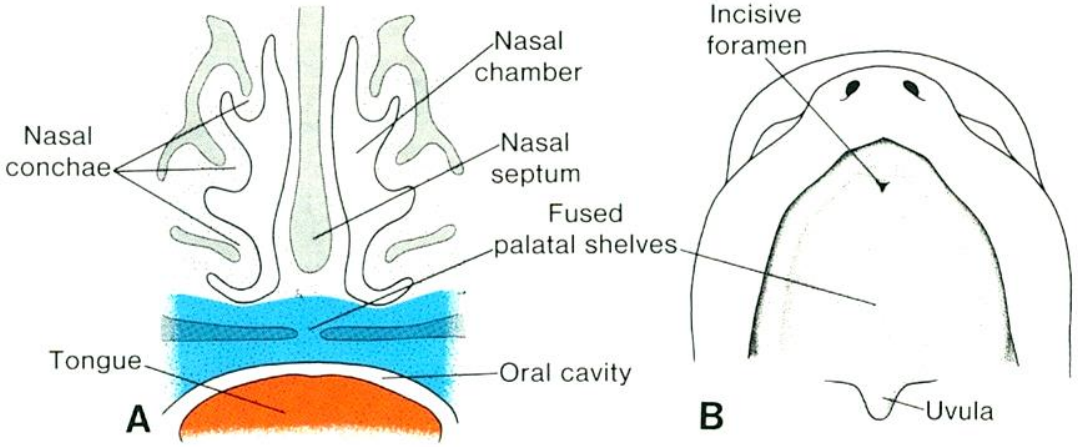


Nature Reviews | Genetics

DEVELOPMENT OF FACE - PALATE

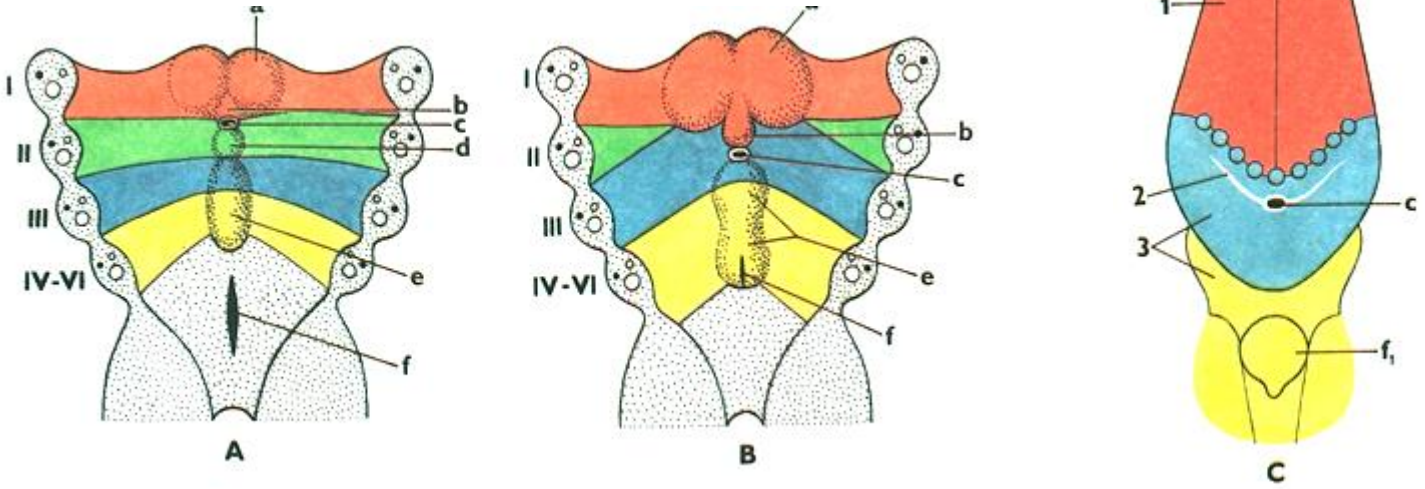






DEVELOPMENT OF TONGUE

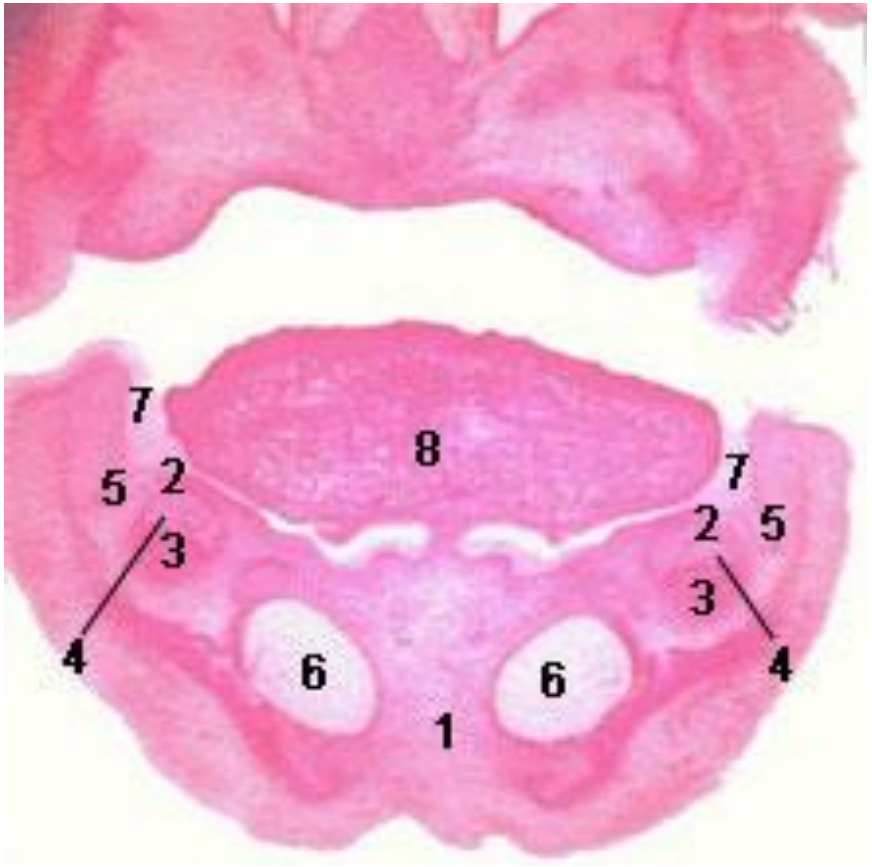
Pharyngeal arches:
I. tuberculum linguale laterale (dx. wt sin.) (paired) and tuberculum impar → **apex and corpus**
III and IV. copula and eminentia hypobranchialis → **radix**



DEVELOPMENT OF VESTIBULUM ORIS

Vestibular lamina

- Dental lamina
- Labiogingival lamina

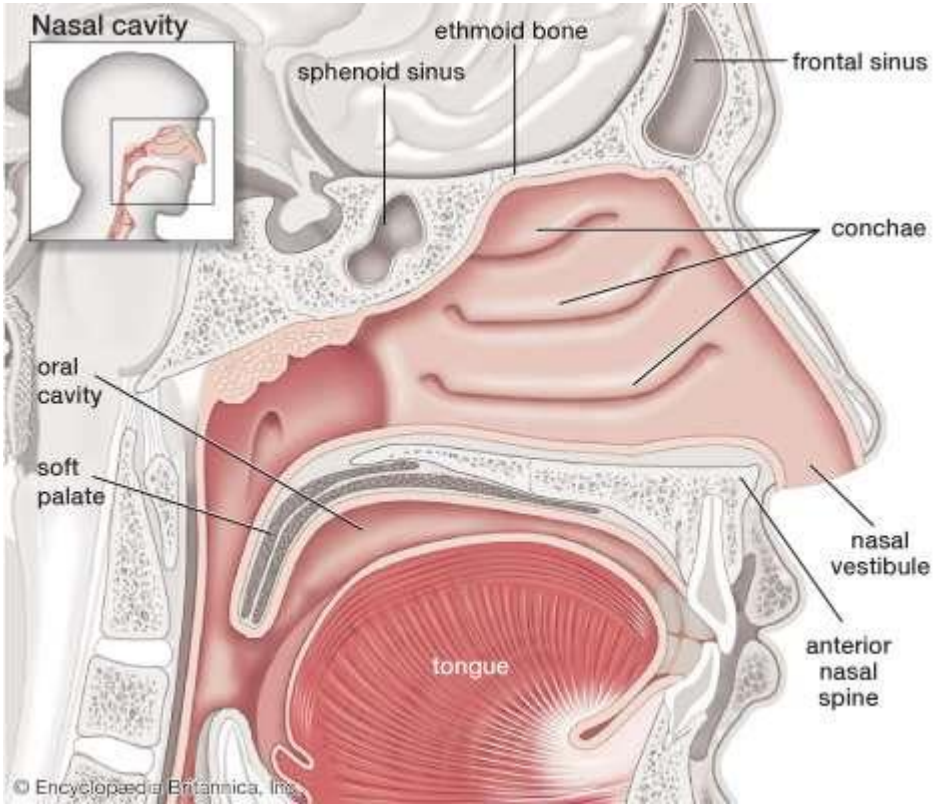


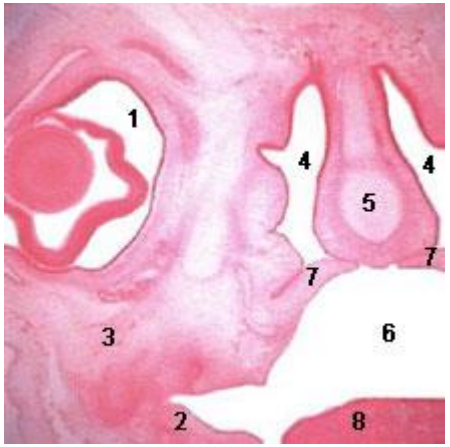
1. Mandible
2. Dental lamina
3. Dental papilla
4. Enamel organ
5. Labiogingival lamina
6. Meckel's cartilage
7. Oral epithelium
8. Tongue

http://www.chronolab.com/atlas/embryo/histo_head.htm

DEVELOPMENT OF VESTIBULUM NASI

- **Nasal canals** – primitive choans
- **Nasal septum** – from area triangularis – fusing with secondary palate

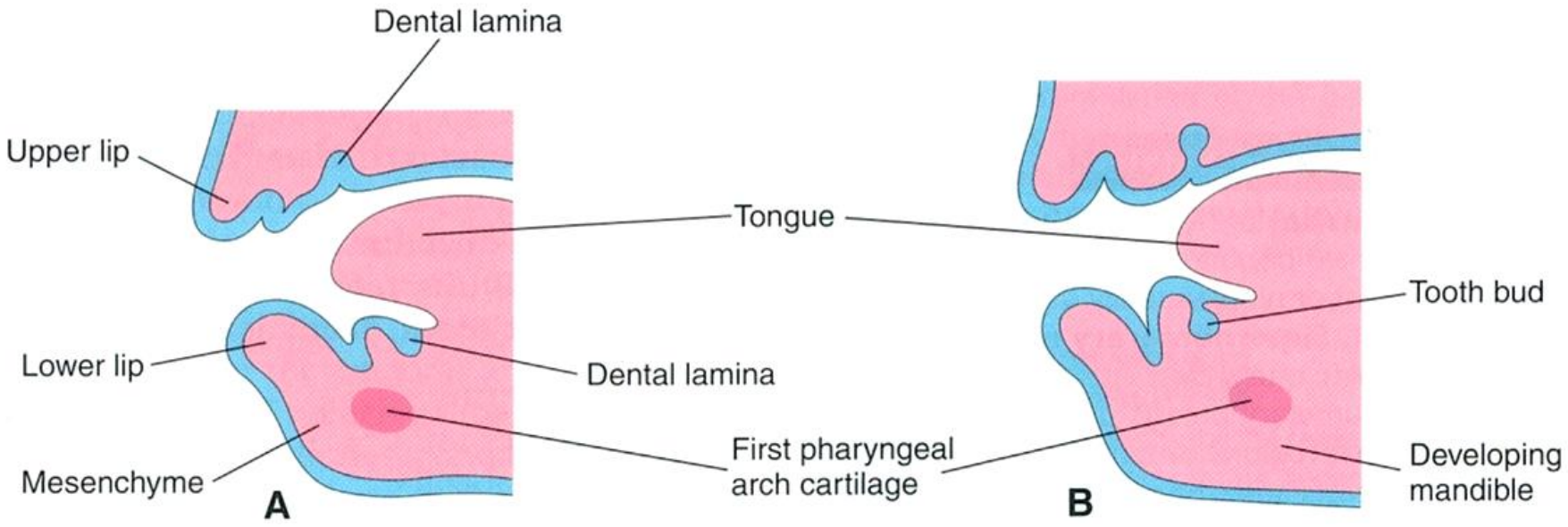




1. Eye
2. Mandibular bone
3. Maxillary bone
4. Nasal cavity
5. Nasal septum
6. Oral cavity
7. Palatine process
8. Tongue

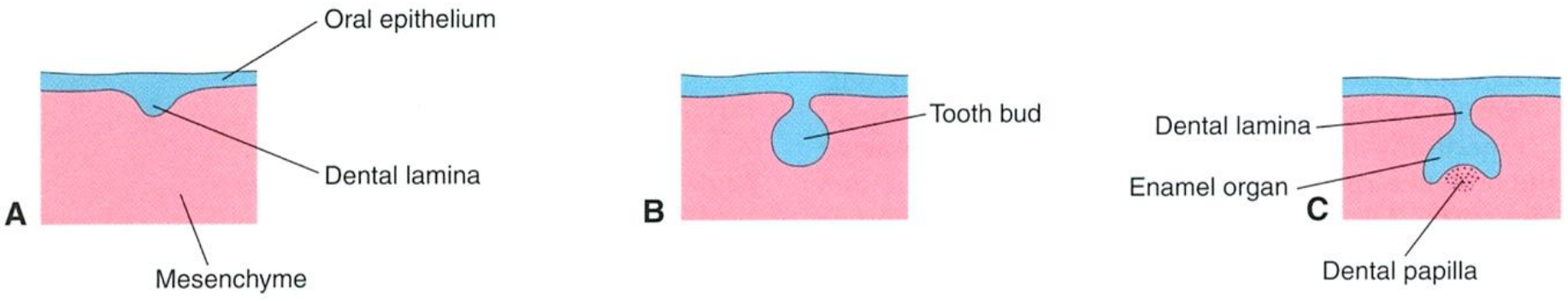
Interactions of ectoderm and mesenchyme

- primary dental lamina – teeth primordia



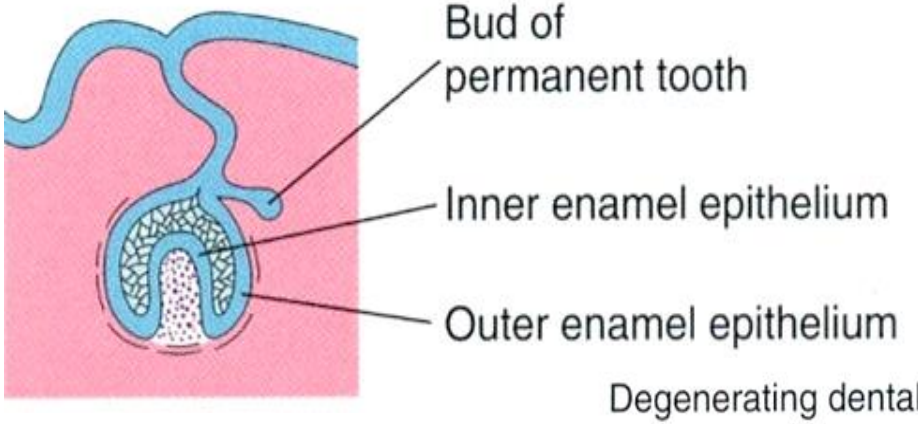
DEVELOPMENT OF TOOTH

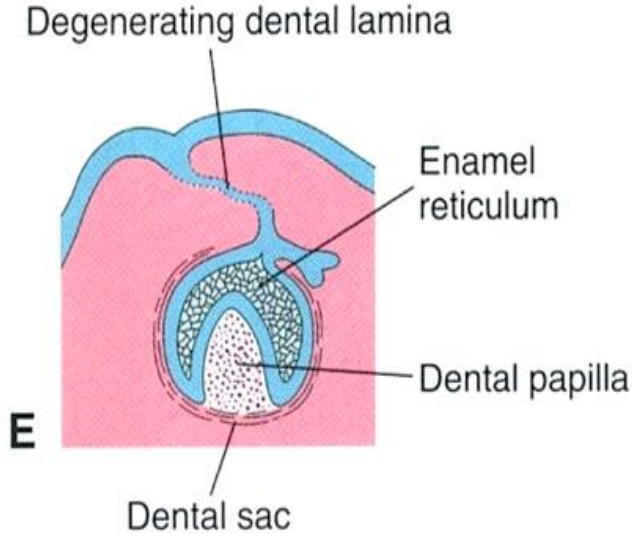
- Inititation stage
- tooth bud (primordium)
- cap stage
- bell stage (enamel organ, ectoderm), dental pulp (mesenchyme)

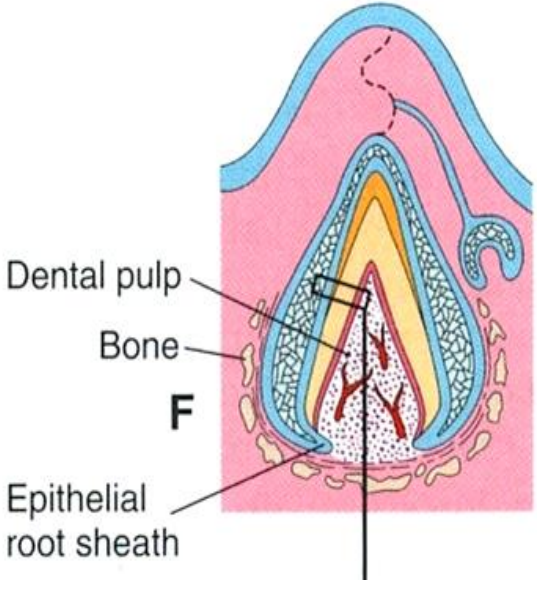


DEVELOPMENT OF TOOTH

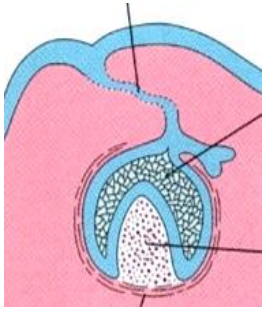
- bell stage – enamel, differentiation of odontoblasts from cells of dental pulp
- enamel prisms and dentin matrix
- dental sac

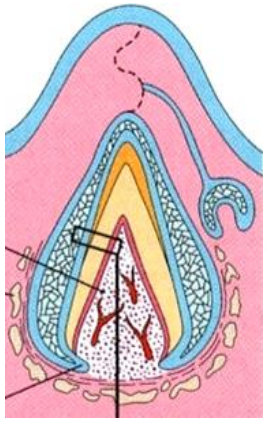




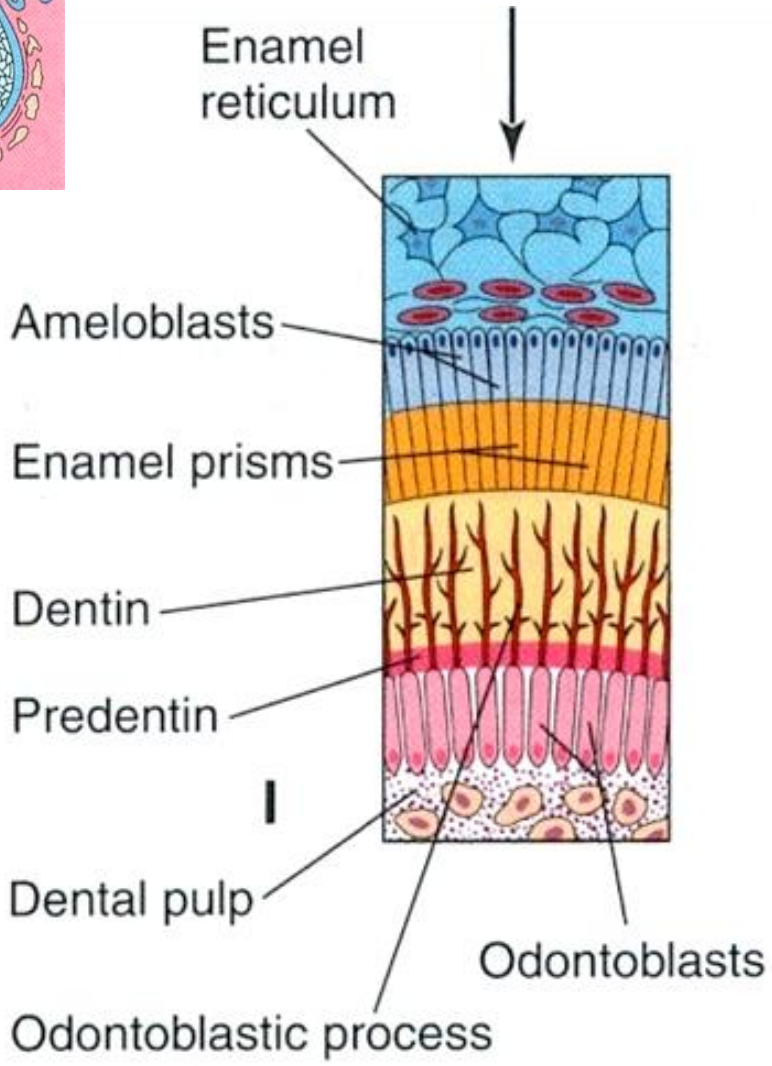


DEVELOPMENT OF TOOTH





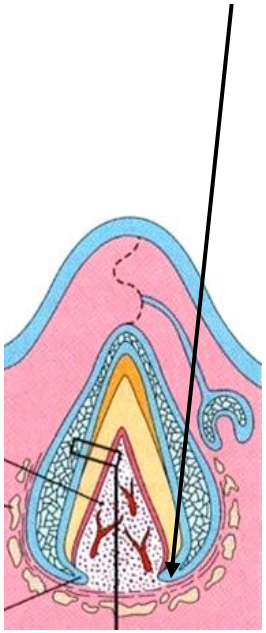
- enamel organ (inner and outer ambelobalsts, stratum intermedium stellate reticulum - pulp) – prisms
- odontoblast differentiation - dentin matrix, (processes of odontoblasts = Tomes fibers)

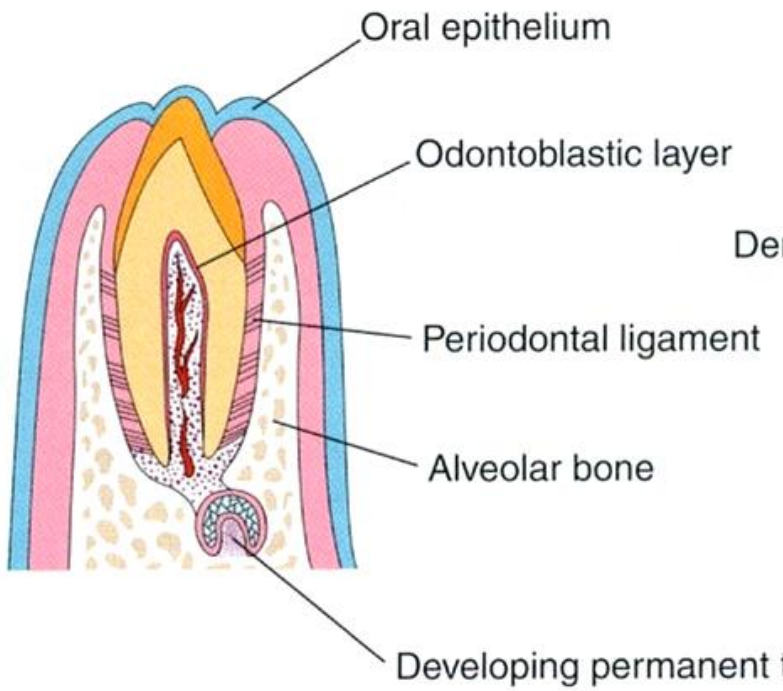


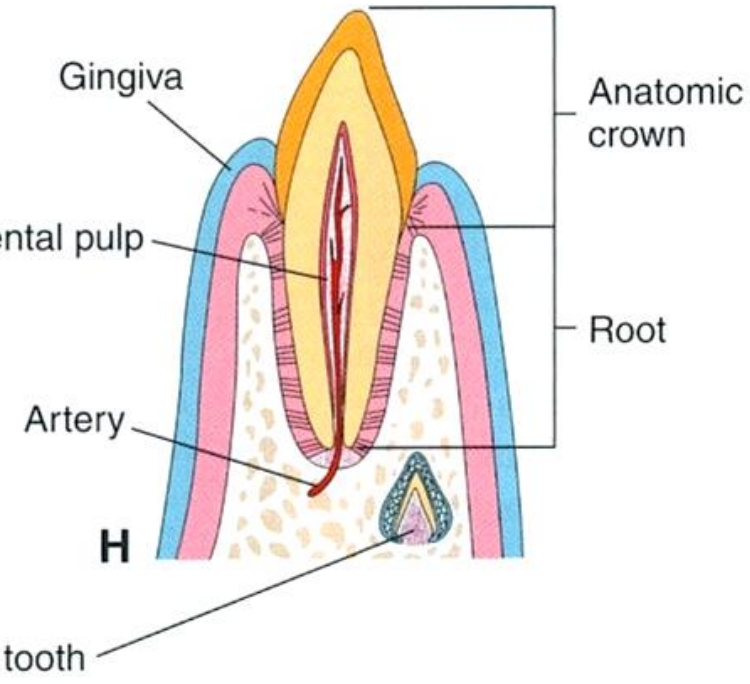
DEVELOPMENT OF TOOTH

root development – tooth eruption

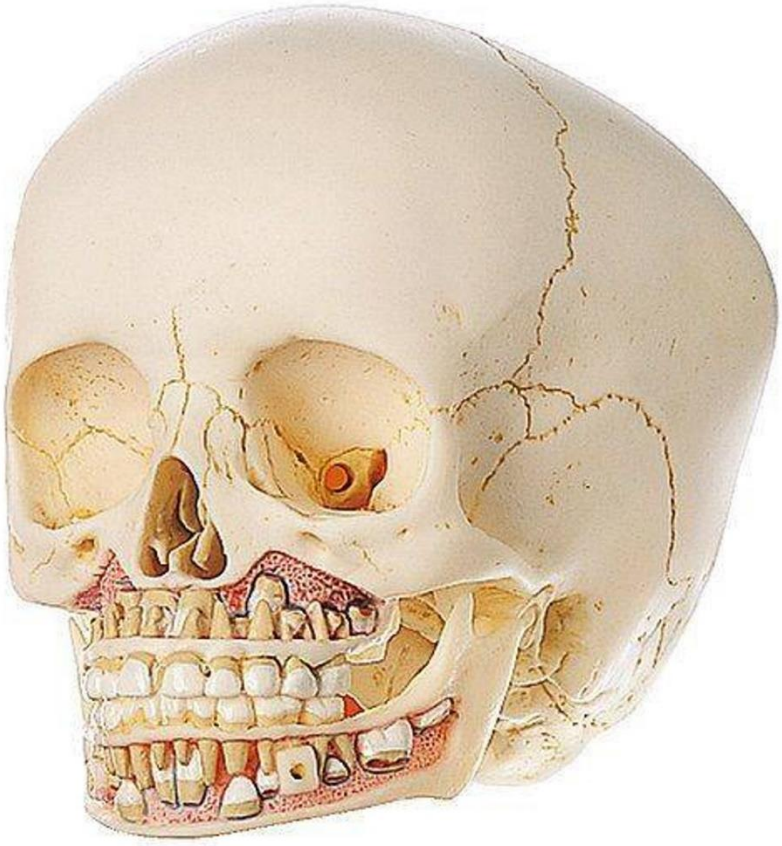
cervical loop → Hertwig epithelial root sheath

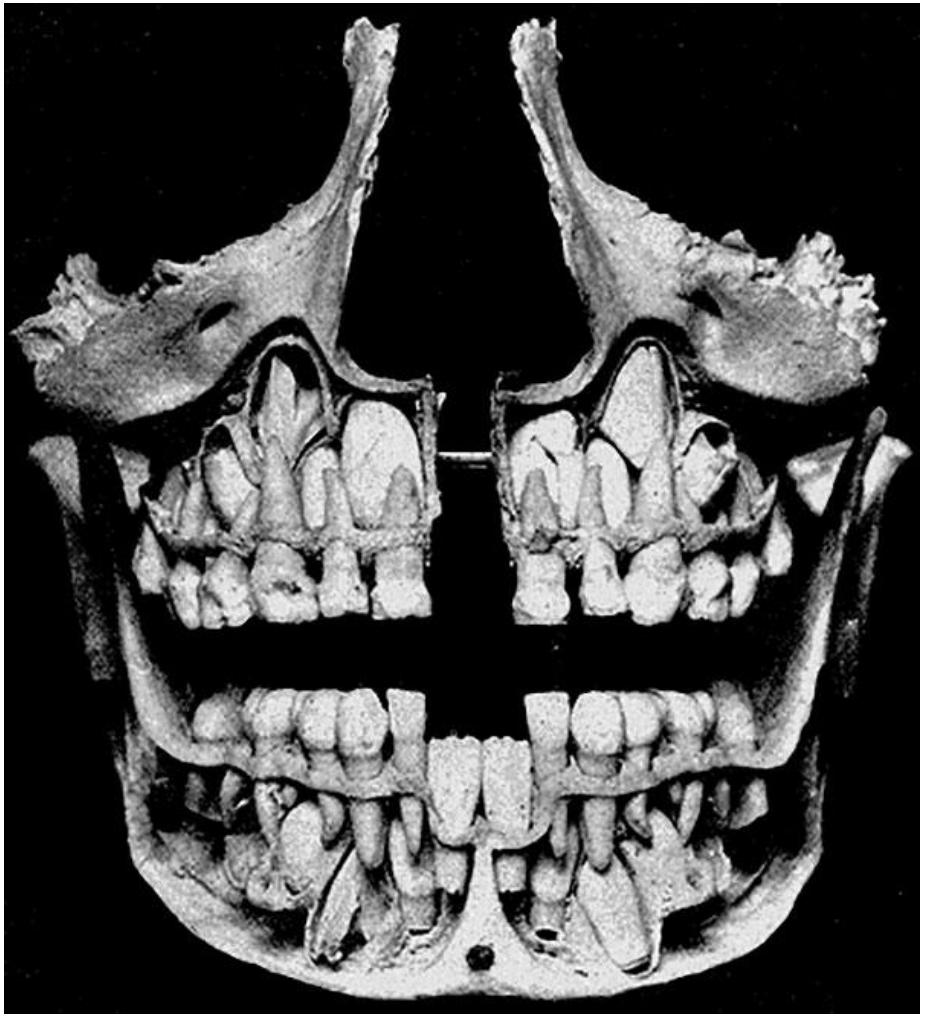




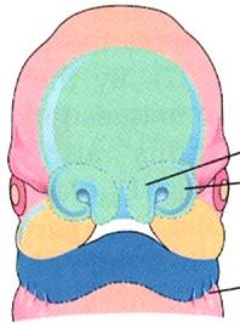


DEVELOPMENT OF TOOTH

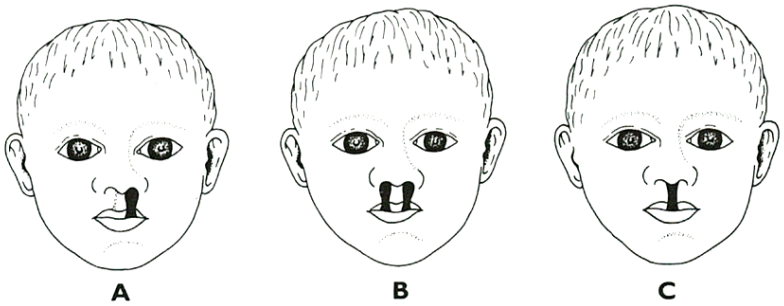




Soft tissue clefts


35 days

- upper lip (*cheiloschisis*) – lateral (uni, bi), medial
- lower lip – medial, always combined (jaw, tongue) – *gnathoschisis et cheiloschisis inf*.
- oblique cleft (*fissura orbitofacialis*)
- transferse cleft (*fissura transversa*)

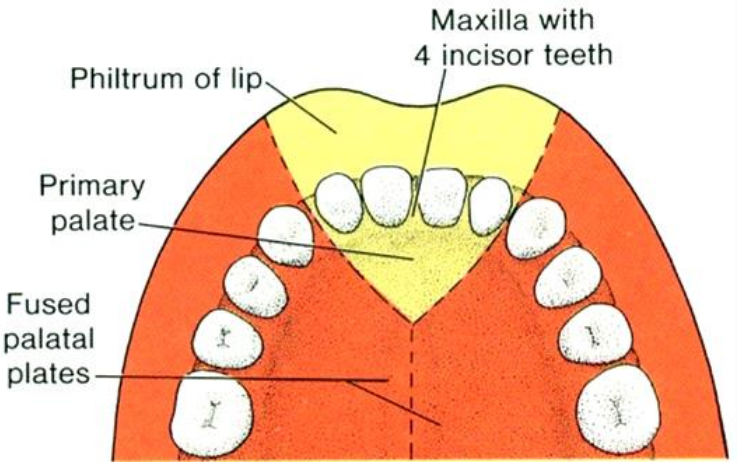


ABNORMALITIES OF FACE DEVELOPMENT - CLEFTS

Hard tissue clefts

- upper jaw
- between 2nd incisor and canine
- unilateral or bilateral
- always combined with palate cleft (cheilognathoschisis)

- palate (palatoschisis)
- primary (before foramen incisivum)
- secondary (behind foramen incisivum)
- combined: cheilognathopalatoschisis



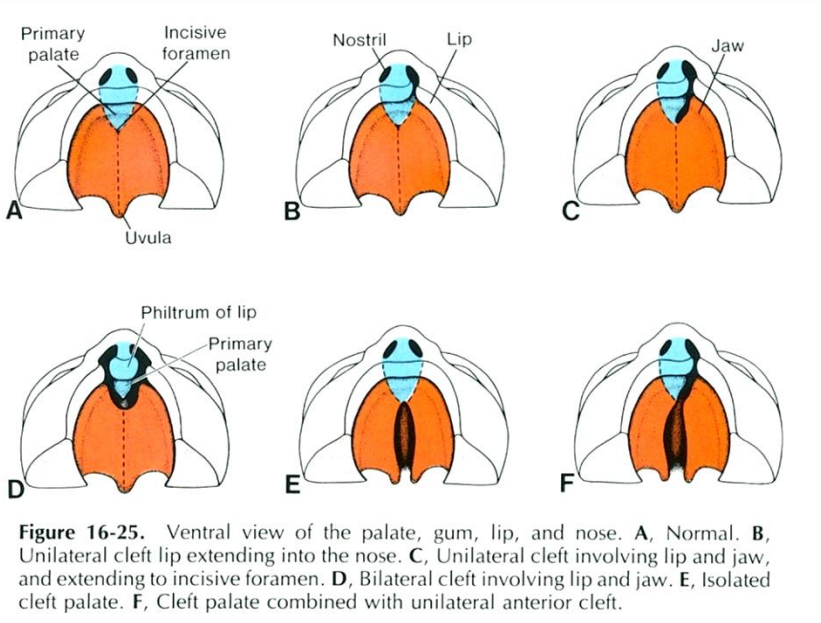


Figure 16-25. Ventral view of the palate, gum, lip, and nose. **A**, Normal. **B**, Unilateral cleft lip extending into the nose. **C**, Unilateral cleft involving lip and jaw, and extending to incisive foramen. **D**, Bilateral cleft involving lip and jaw. **E**, Isolated cleft palate. **F**, Cleft palate combined with unilateral anterior cleft.

ABNORMALITIES OF FACE DEVELOPMENT - CLEFTS

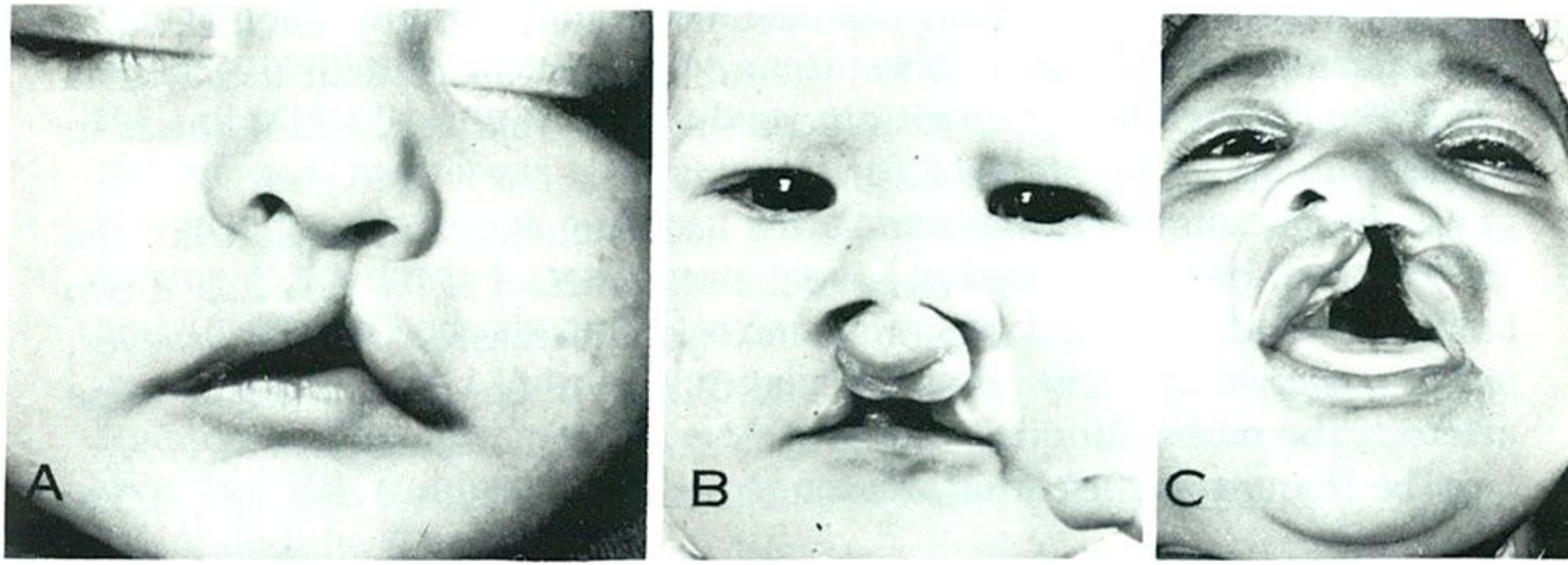
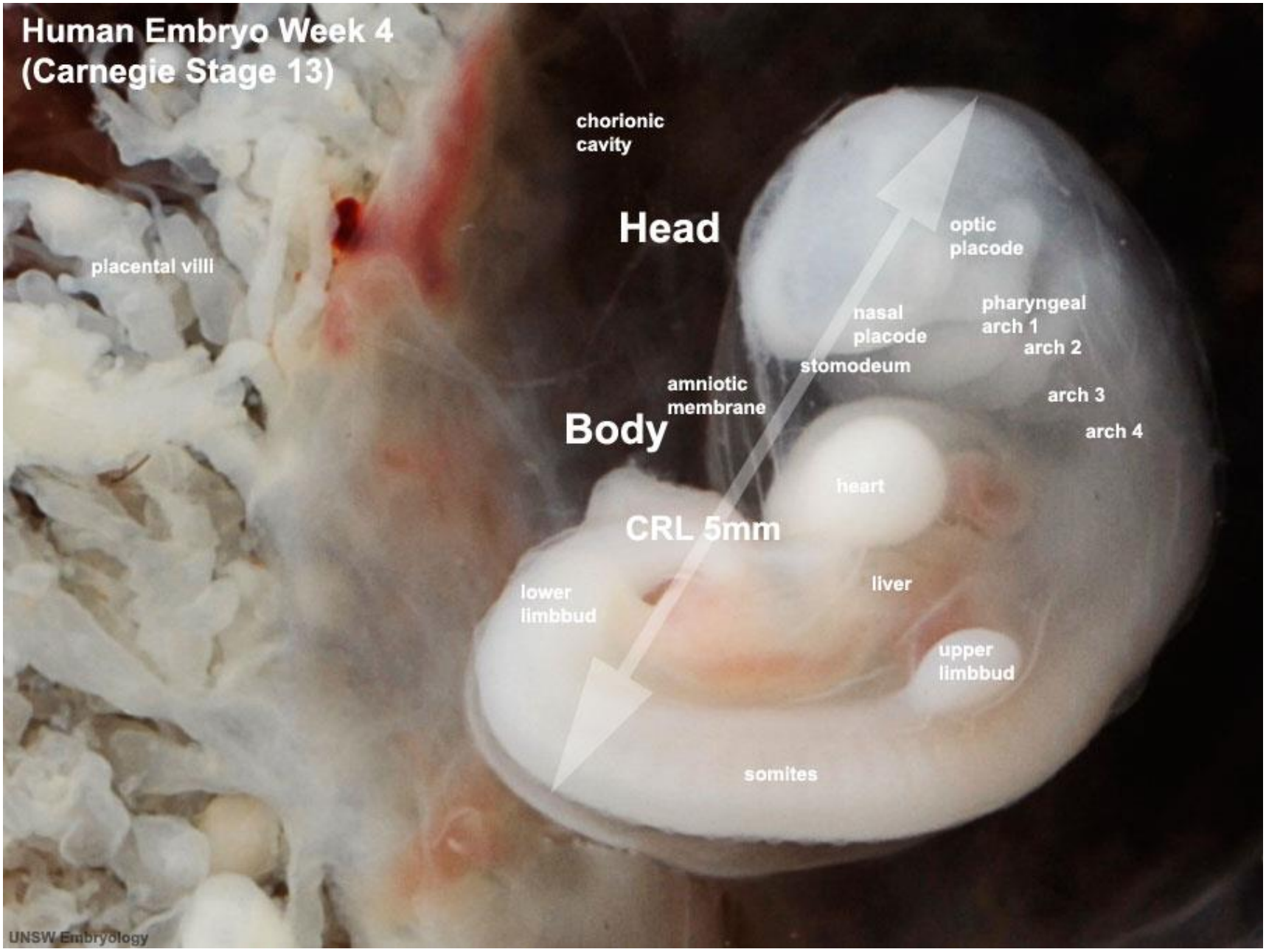


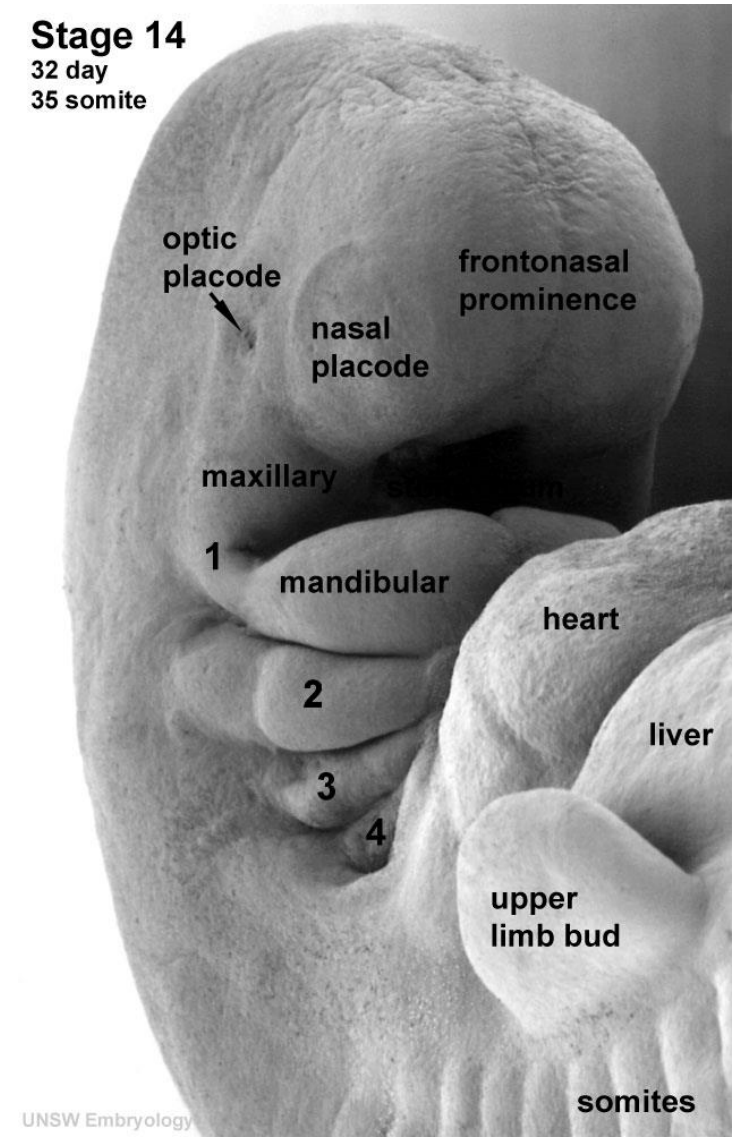
Figure 16-26. Photographs of incomplete cleft lip (**A**), bilateral cleft lip (**B**), and cleft lip, cleft jaw, and cleft palate (**C**). (Courtesy Dr. M. Edgerton, Department of Plastic Surgery, University of Virginia.)

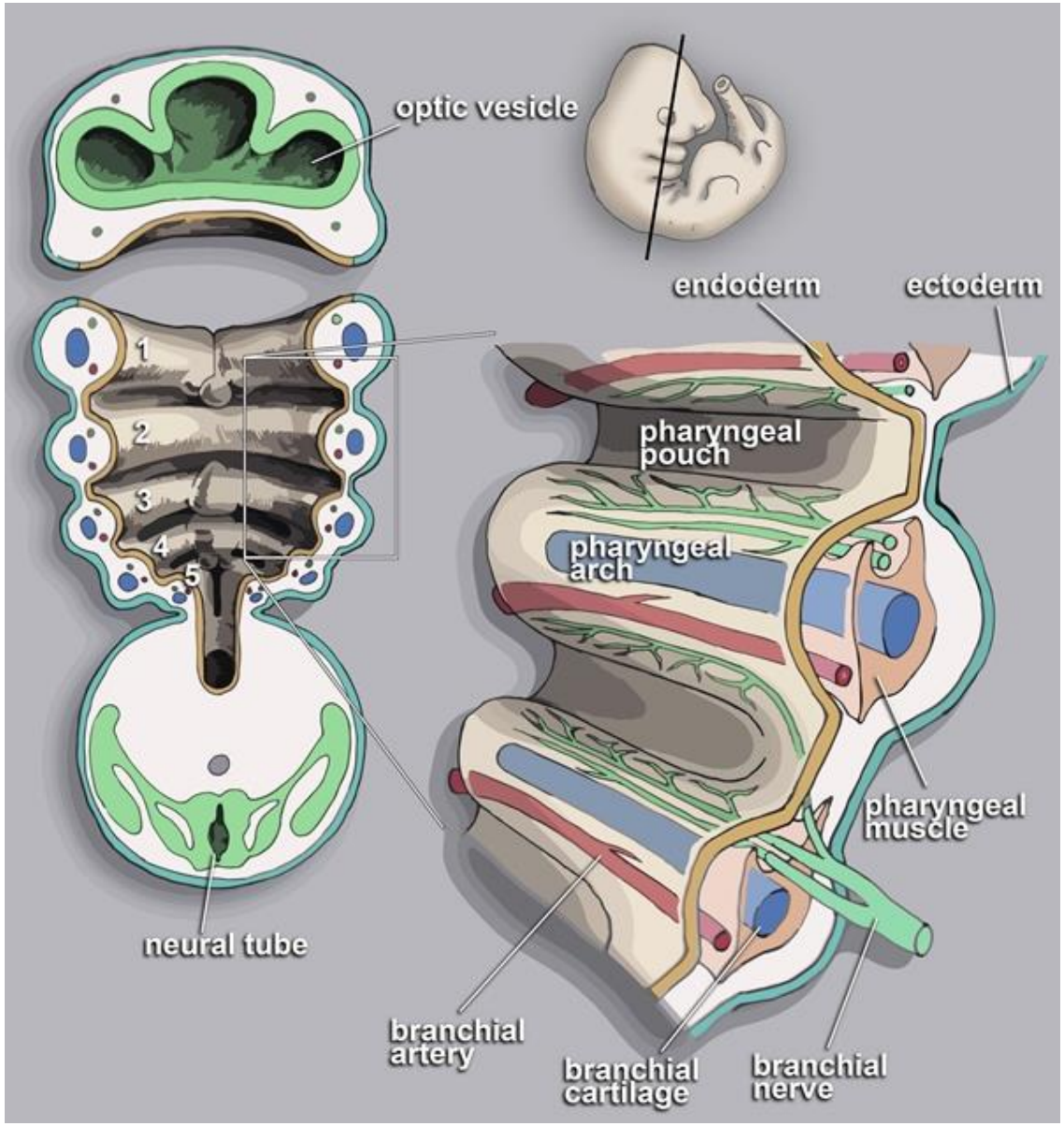
http://www.youtube.com/watch?v=agmSH8_mLz0

PHARYNGEAL APPARATUS

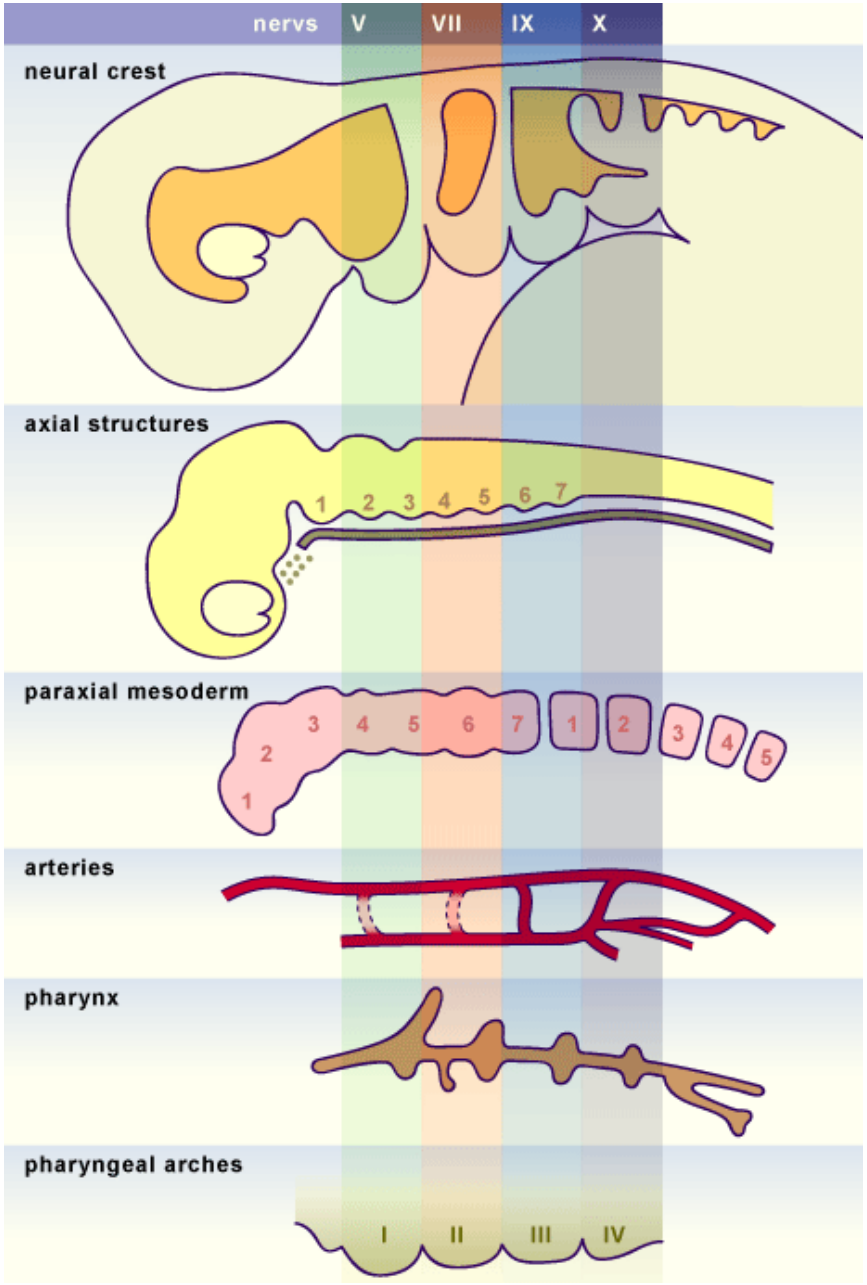


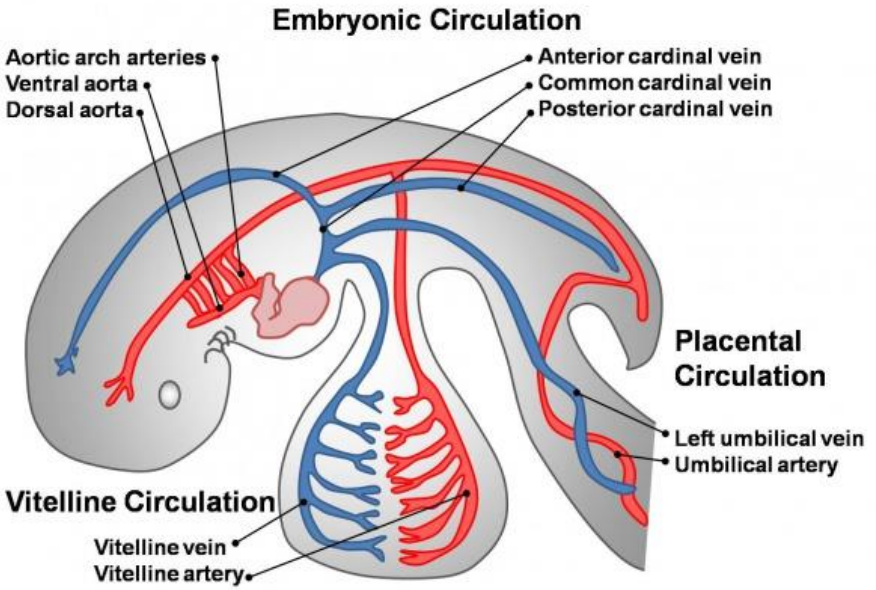
PHARYNGEAL APPARATUS



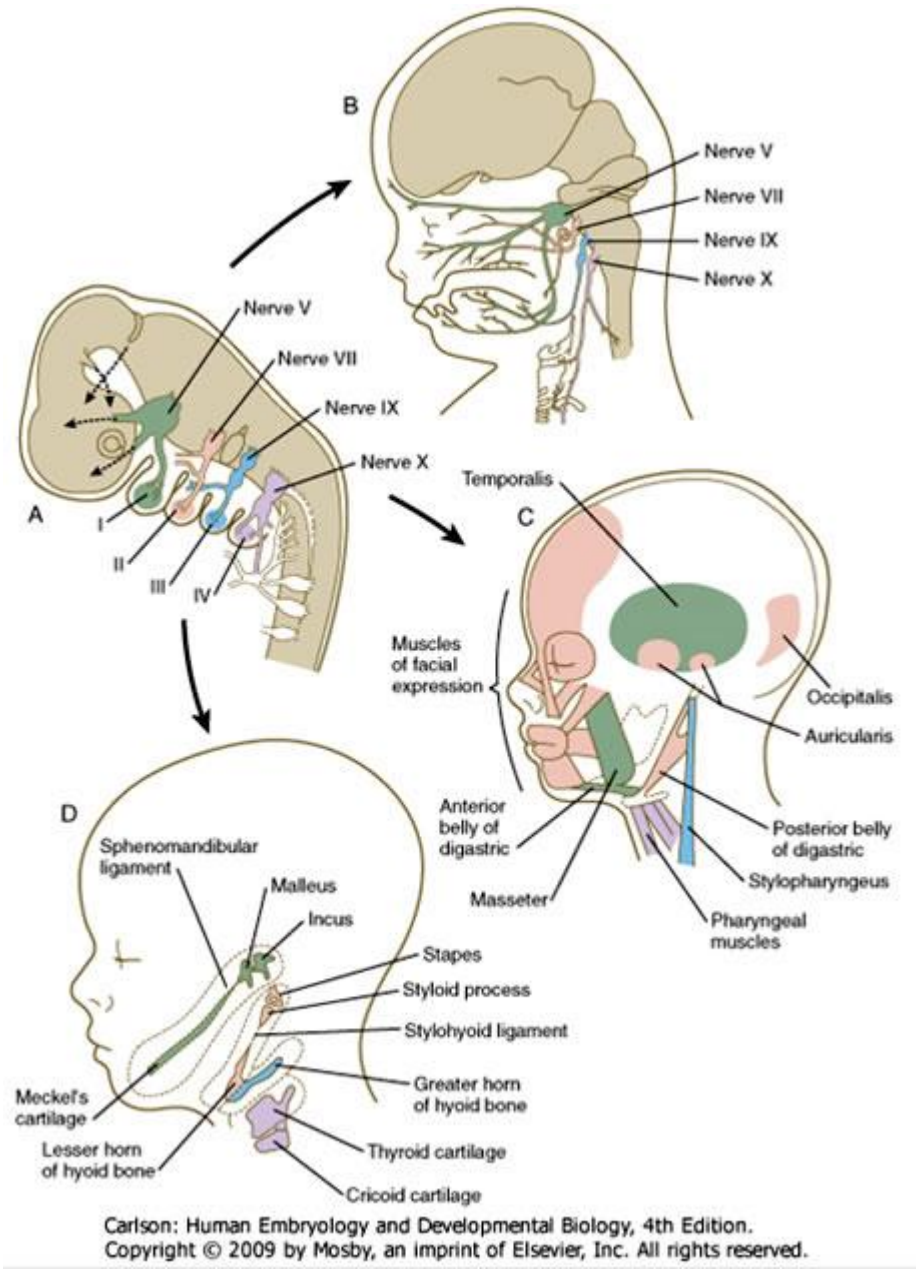


PHARYNGEAL APPARATUS





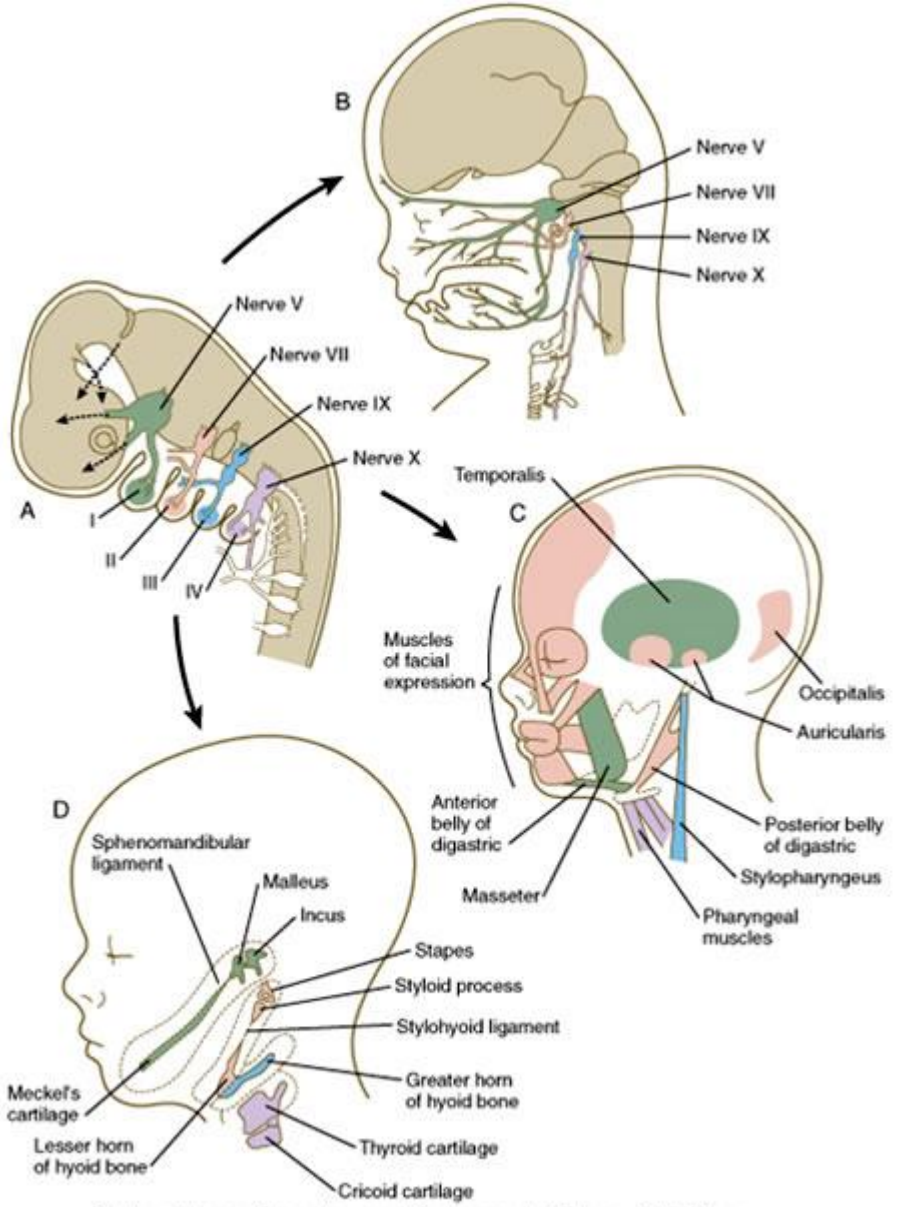
PHARYNGEAL APPARATUS



Derivatives

- Face including soft tissues
- Mimic and mastication muscles
- Tongue
- Outer and middle ear
- Hyoid bone
- Laryngeal cartilages
- Thymus
- Parathyroid glands
- Fossa tonsillaris ($\rightarrow$ t. palatina)
- Large arteries (for details see the lesson on cardiovascular systém development)

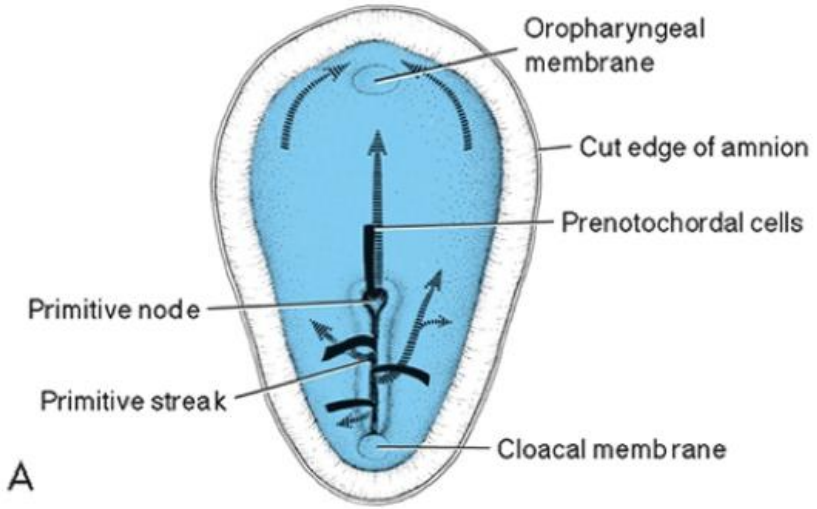
PHARYNGEAL APPARATUS

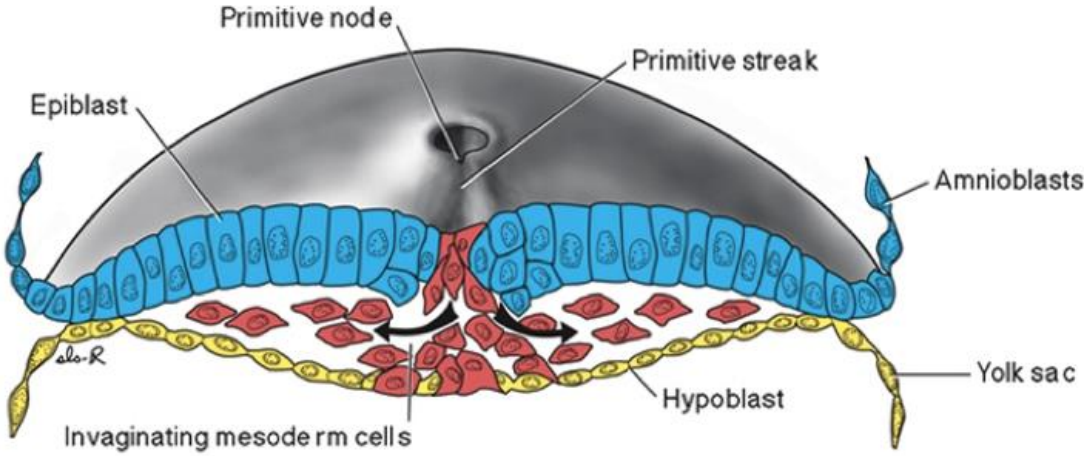


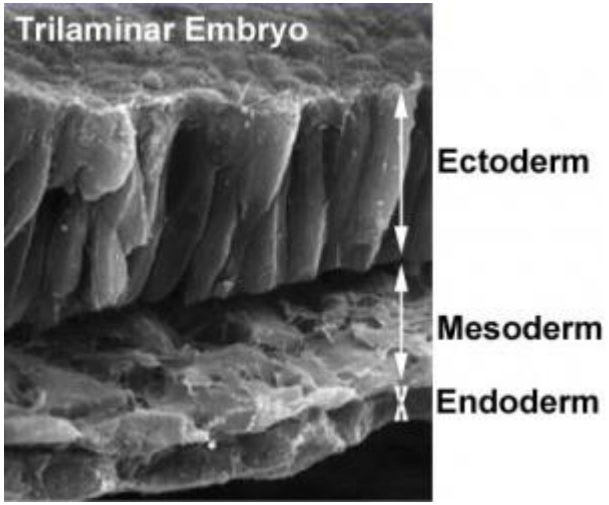
PHARYNGEAL APPARATUS

Derivative of ectodermal ridge	Pharyngeal arch	Aortic arch	Cranial nerve	Example of branchiomeric muscles	Skeletal derivatives	Derivative of endodermal pouch
1. external acoustic meatus	1 mandibular	a. maxillaris	V. trigeminus	mastica-tory	incus, maleus lig. sphenomandib. Meckel cartilage	middle ear cavity, tuba auditiva
2-4. disappear	2 hyoid	a. stapedia a. hyoidea	VII. facialis	mimic	stapes proc. styloideus, hyoid cartilage.	fossa tonsillaris
	3	a. carotis interna	IX. glosso-pharyngeus	m. stylopha-ryngeus	hyoid cartilage	thymus, parathyroid bodies (inf.)
	4	a. subclavia dx. a. arcus aortae	X. vagus	svaly faryngu a laryngu	laryngeal cartilages	parathyroid bodies (sup.)

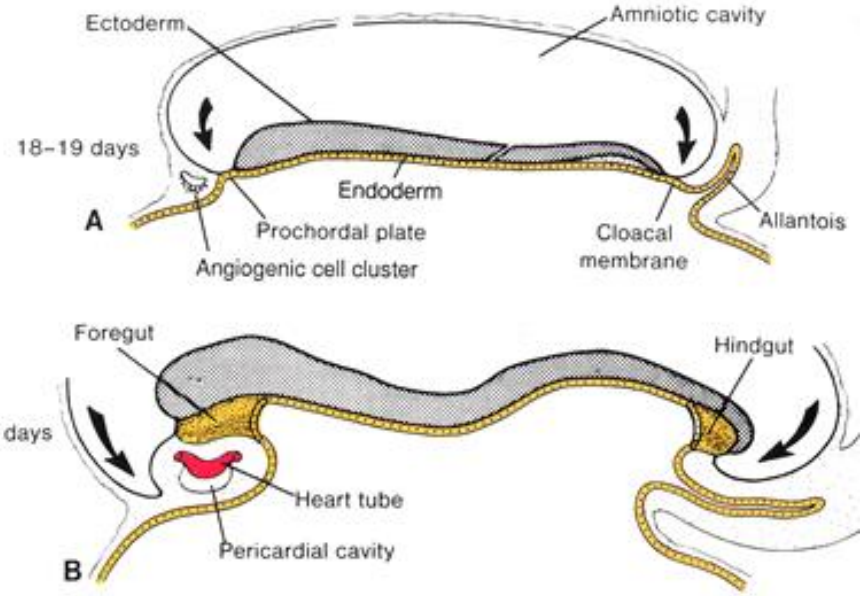
EARLY EVENTS – FROM 2TH TO 3RD WEEK

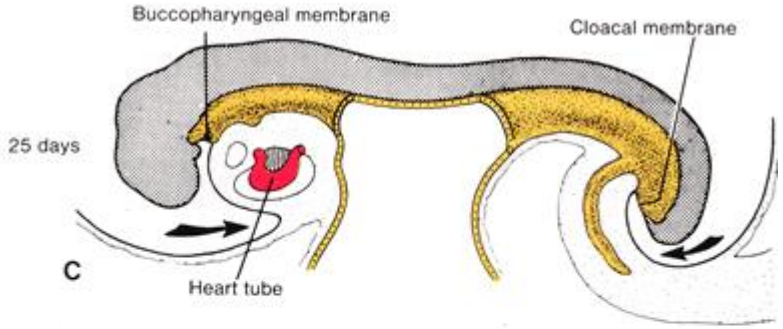


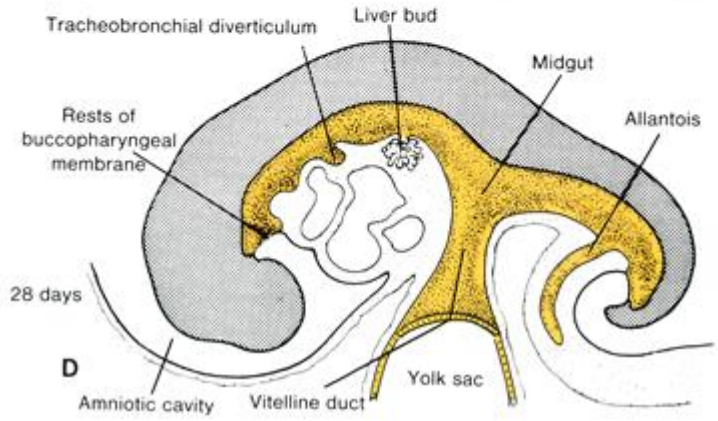




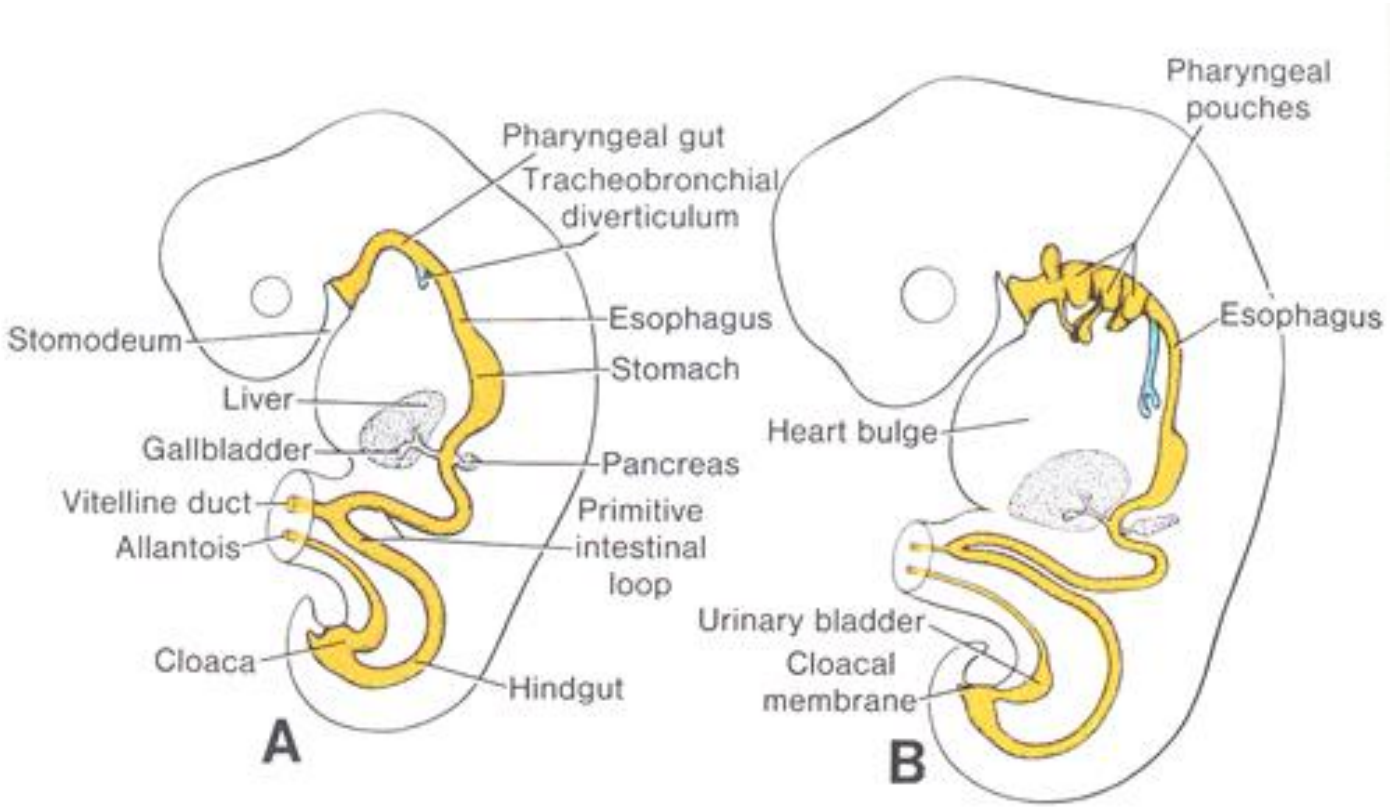
EARLY EVENTS – FROM 3RD TO 4THWEEK







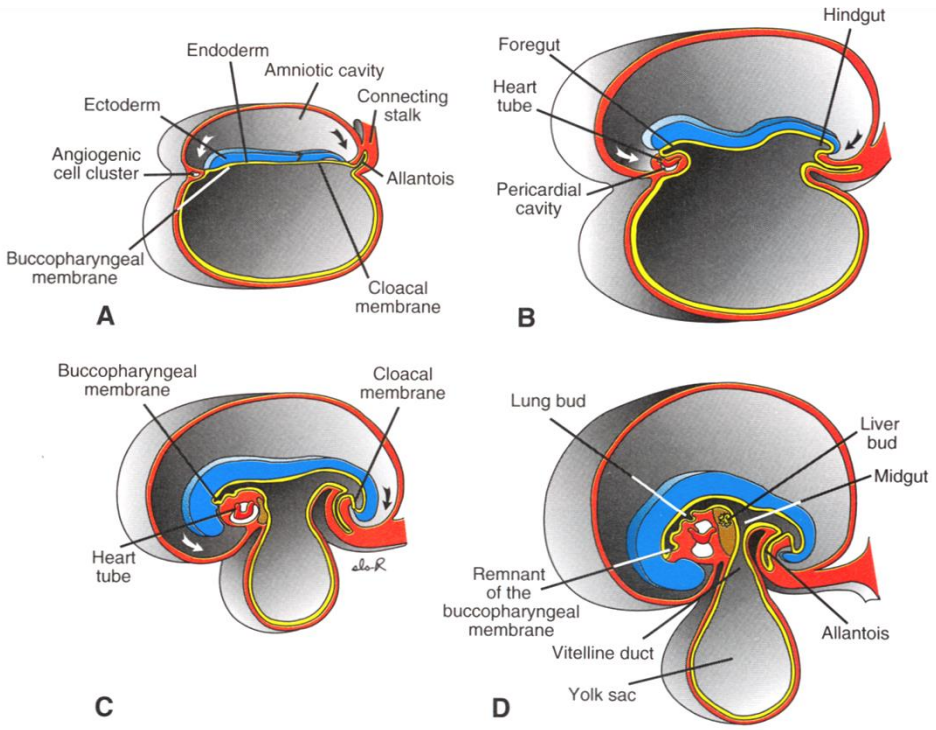
EARLY EVENTS – FROM 4TH TO 5THWEEK



EARLY EVENTS – PRIMITIVE GUT

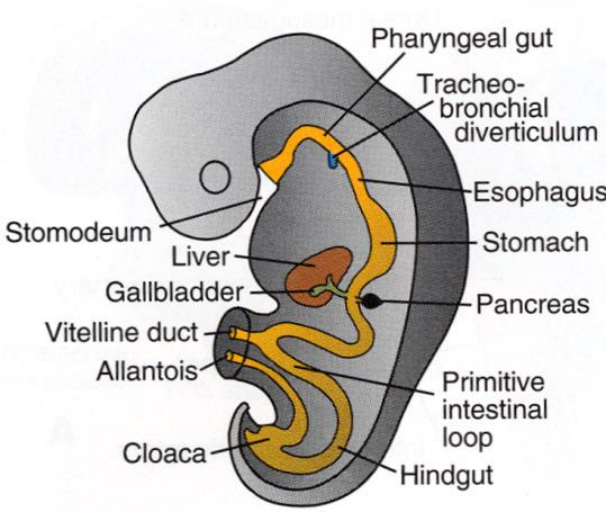
– cephalocaudal and lateral folding in 4th week

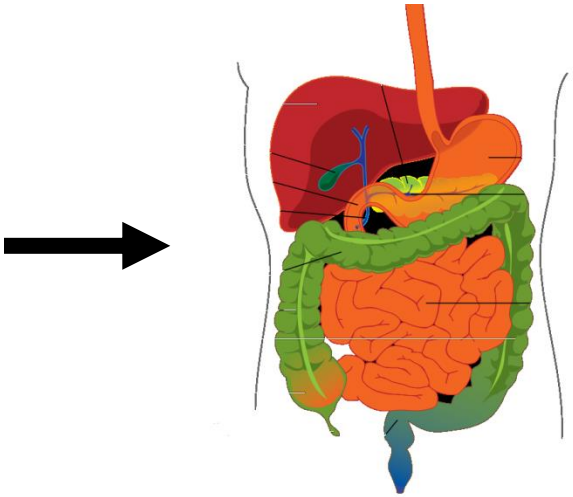
– primitive gut from buccopharyngeal membrane to cloacal membrane



Three regions of primitive gut

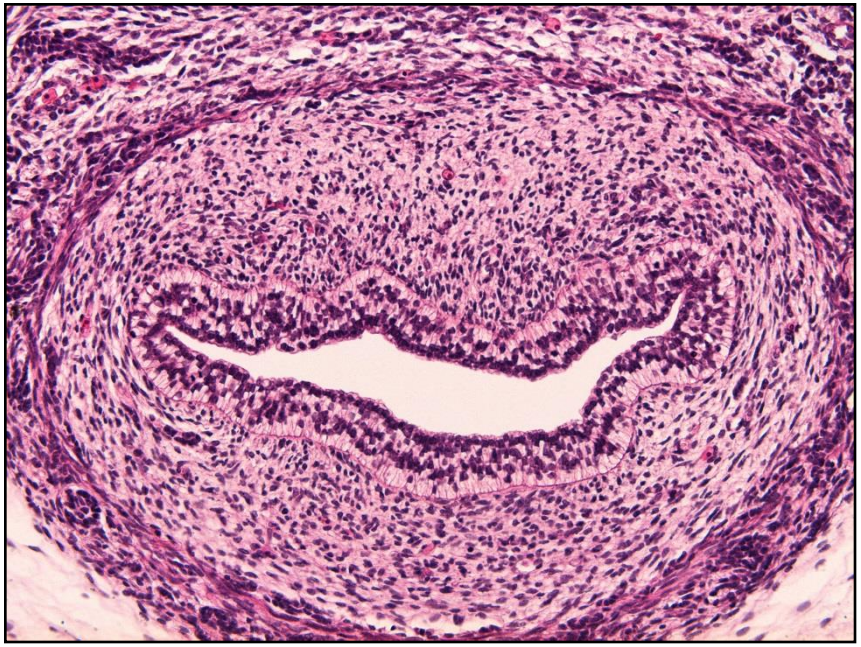
- foregut
- midgut
- hindgut



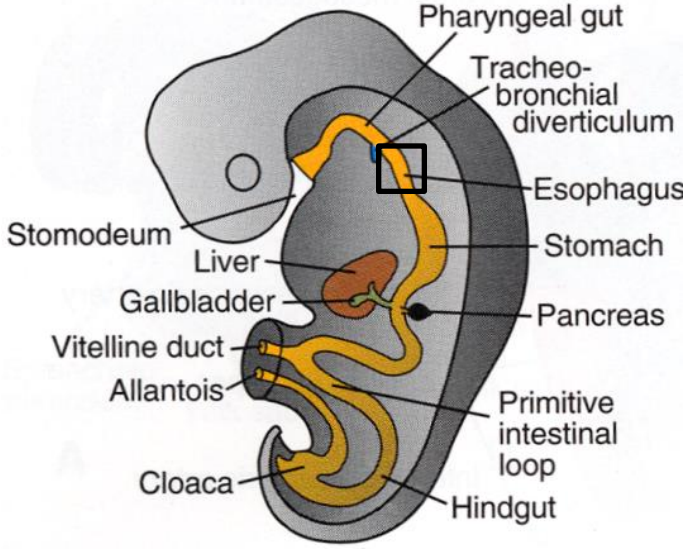


DEVELOPMENT OF ESOPHAGUS

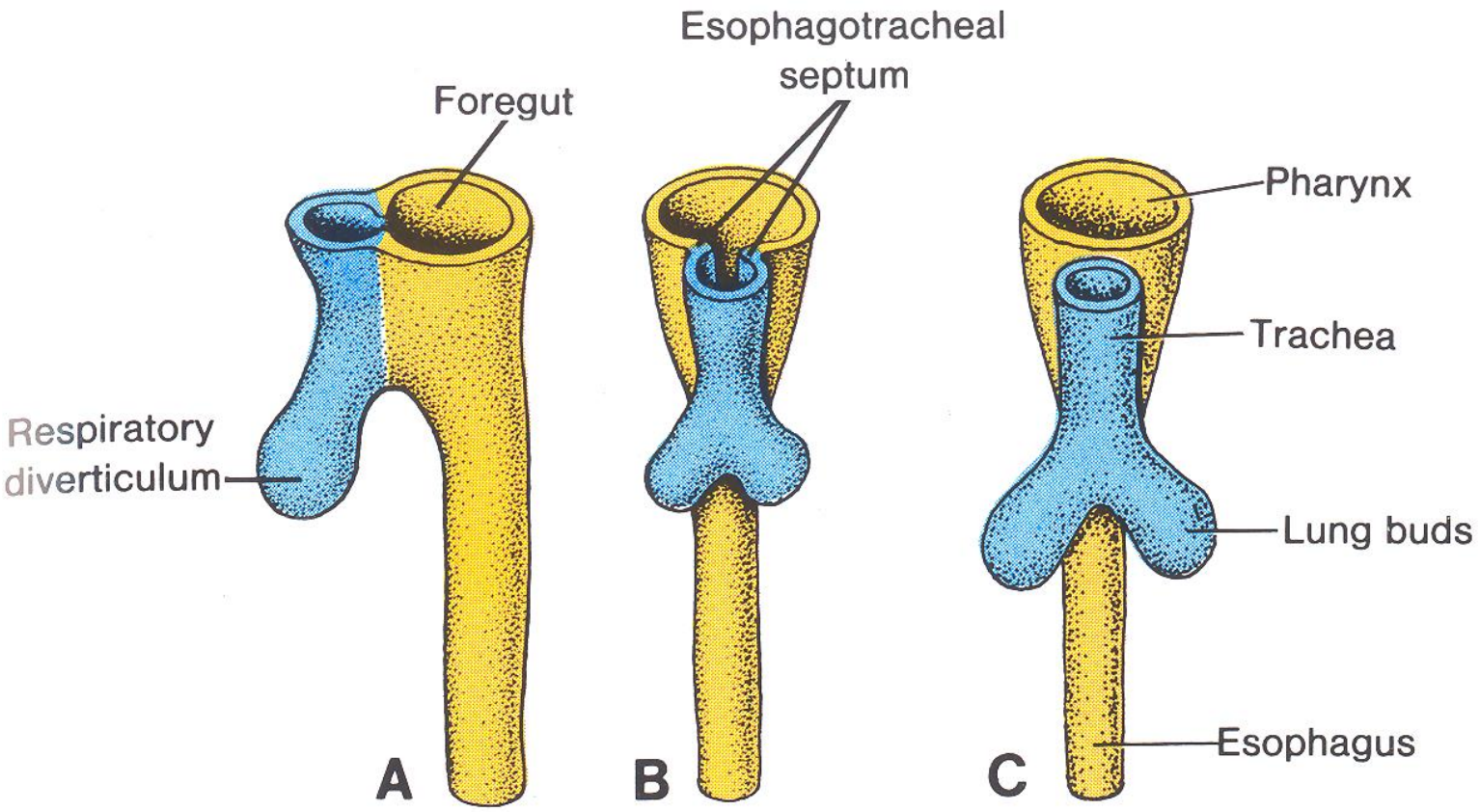
- region of foregut caudal of respiratory diverticulum
- esophagotracheal septum
- rapid elongation: 7th week - final relative length
- rapid proliferation of endoderm (epithelium and glands) that obliterates lumen – recanalization about 8th week
- connective tissue and muscle tissue – mesenchyme of caudal pharyngeal arches and splanchnic mesenchyme
- innervation by branches of *n. vagus* (caudal pharyngeal arches)



8th week

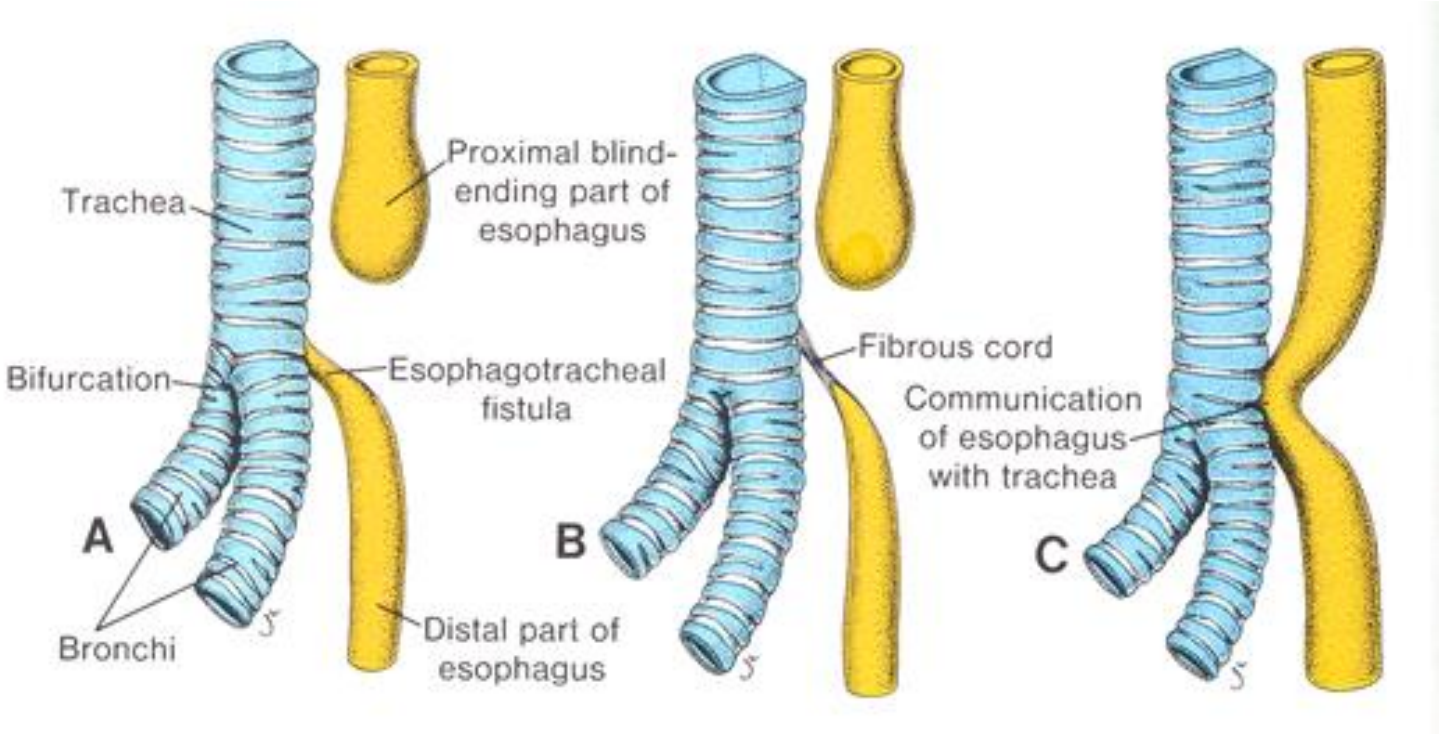


DEVELOPMENT OF ESOPHAGUS

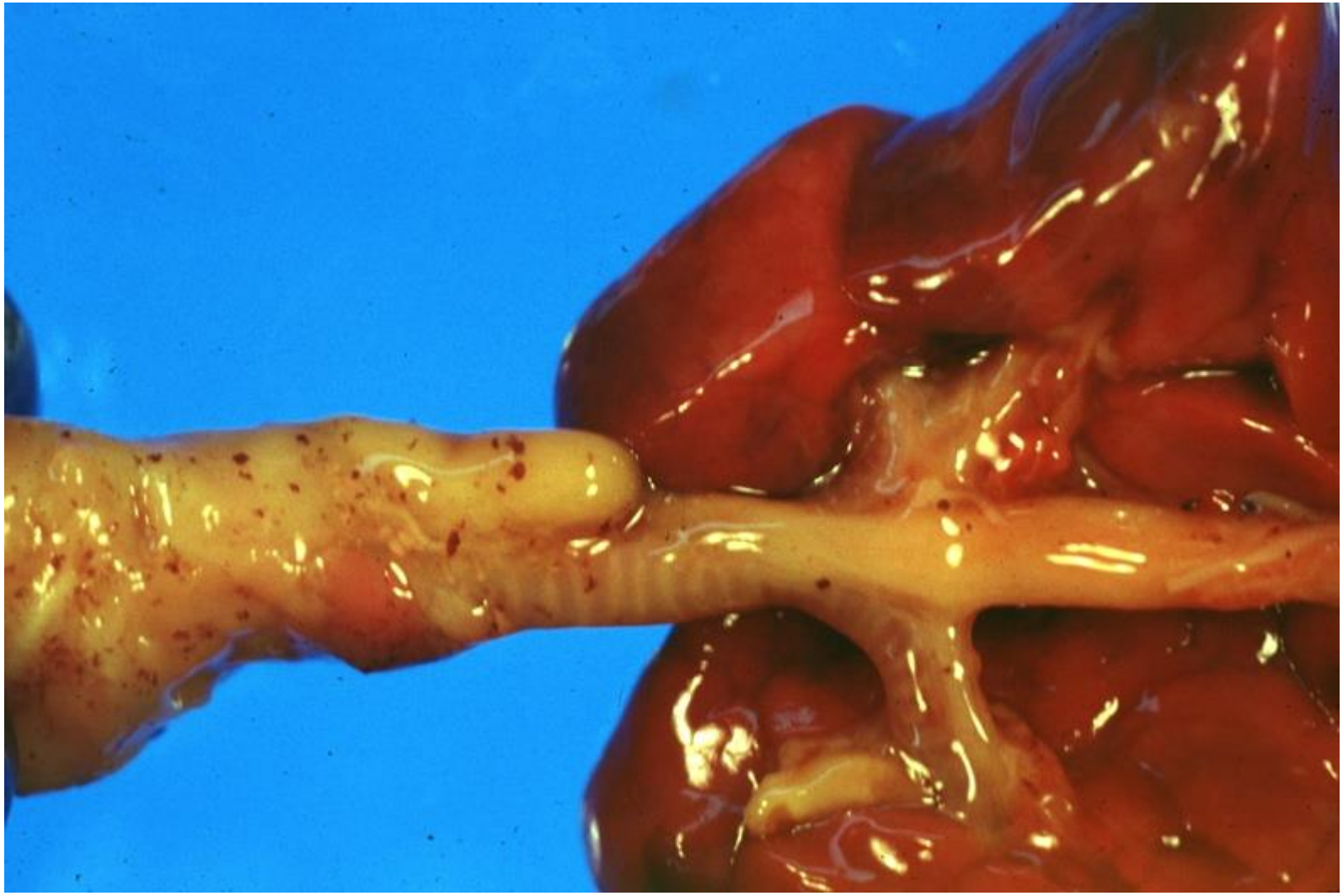


DEVELOPMENT OF ESOPHAGUS

ABNORMALITIES



DEVELOPMENT OF ESOPHAGUS - FISTULA



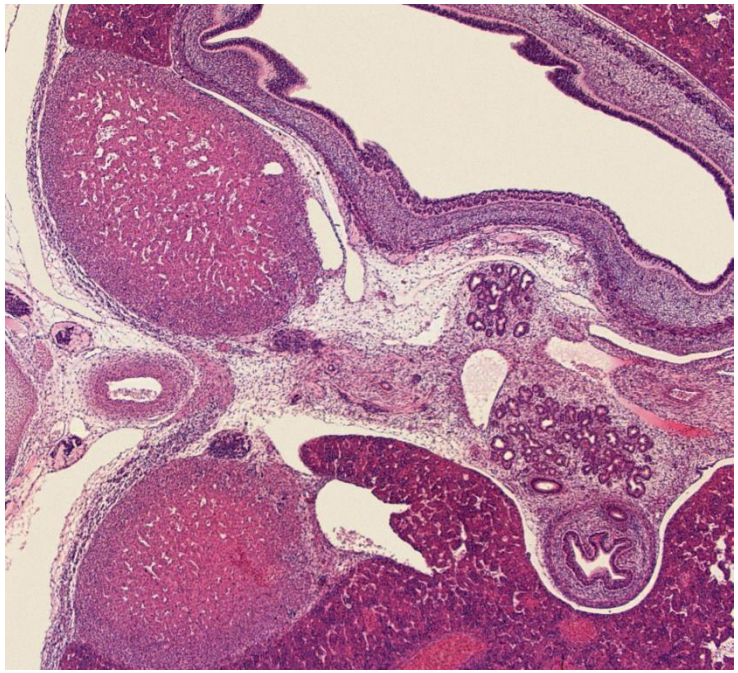
GROSS: GASTROINTESTINAL: Esophagus: Tracheoesophageal Fistula: Gross posterior view of chest contents showing blind sac of esophagus above and continuation of esophagus from carina inferiorly good example

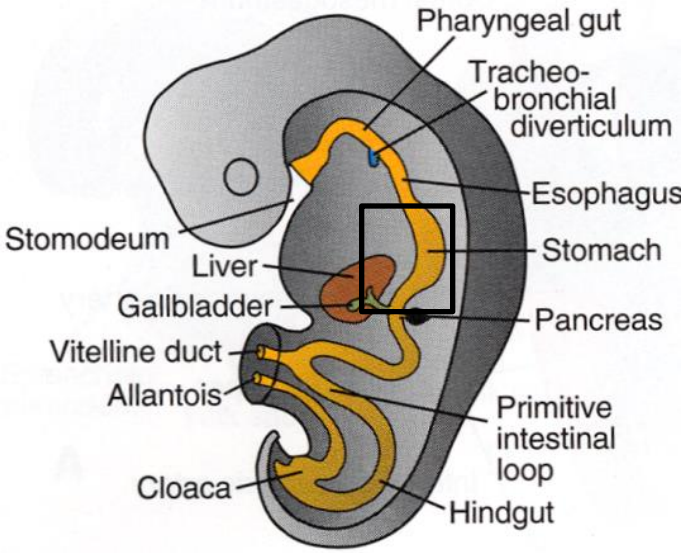
Autor
Peter Anderson

DEVELOPMENT OF STOMACH

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

8th week



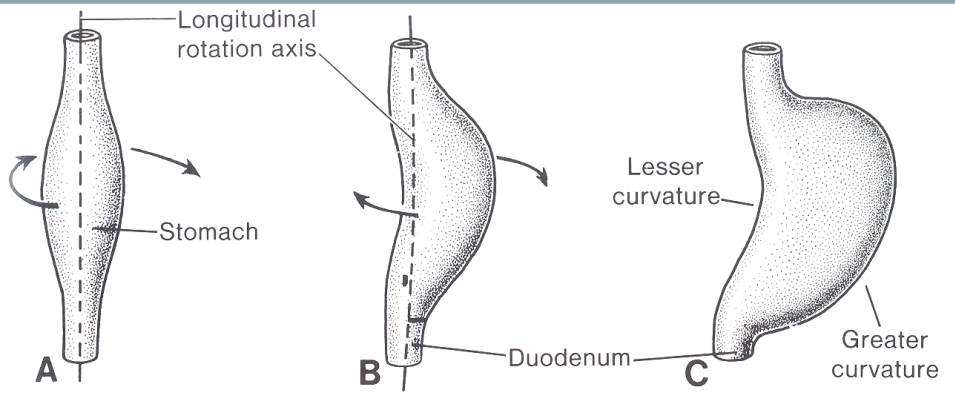


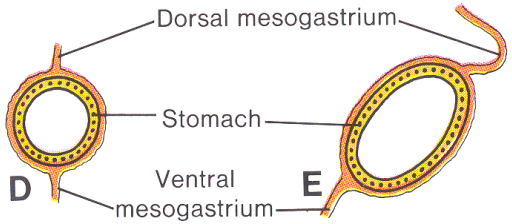
STOMACH - ROTATION

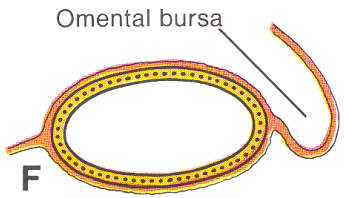
- 90°

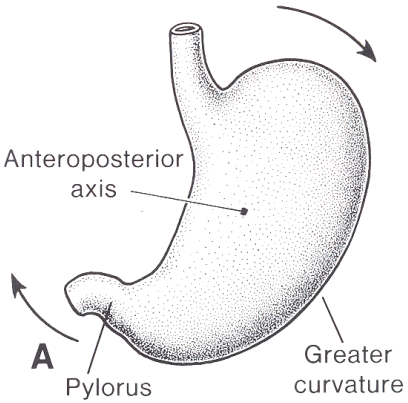
ventral lesser curvature → right
dorsal greater curvature → left
left side → ventrally
right side → dorsally
cranial part → left caudally
caudal part → right cranially

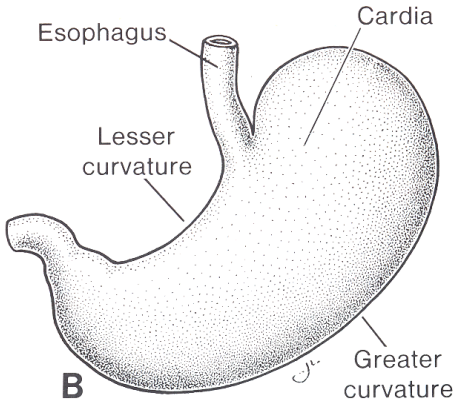
→ definitive anatomical position of left and right *nervus vagus*







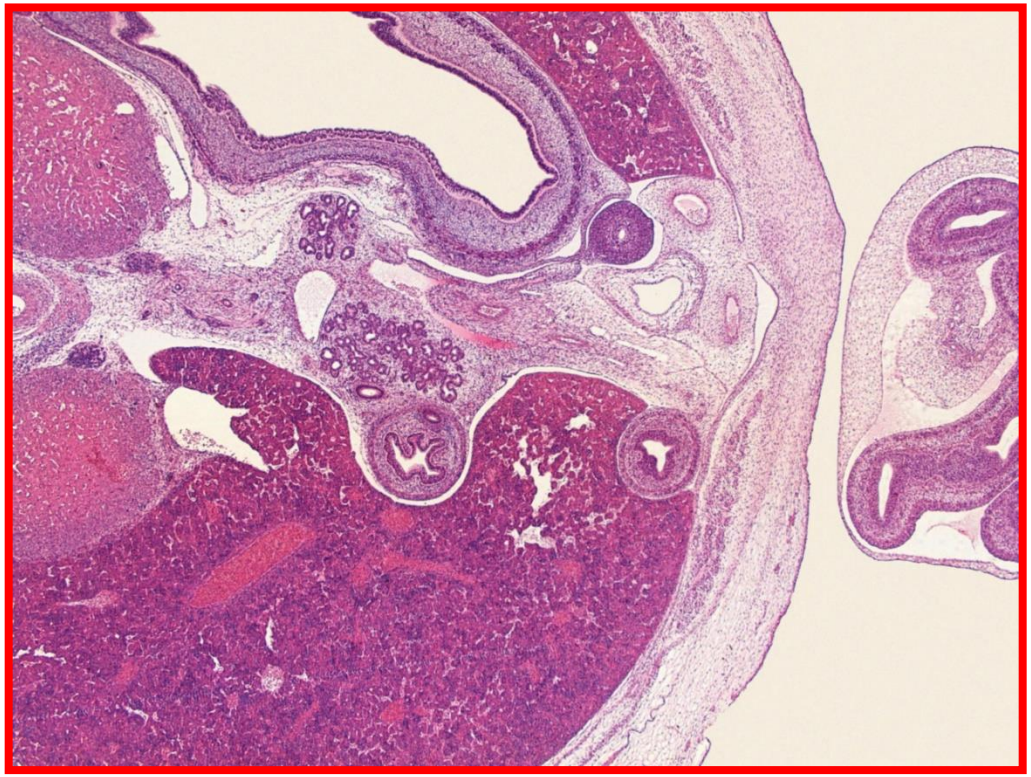


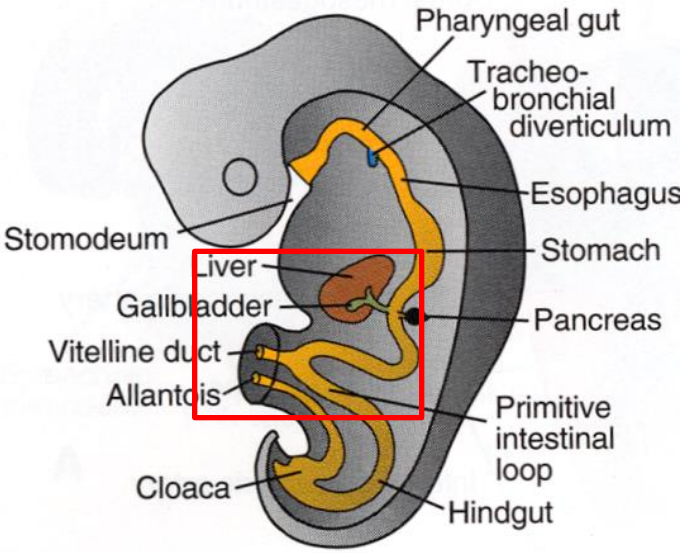


DEVELOPMENT OF INTESTINE

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

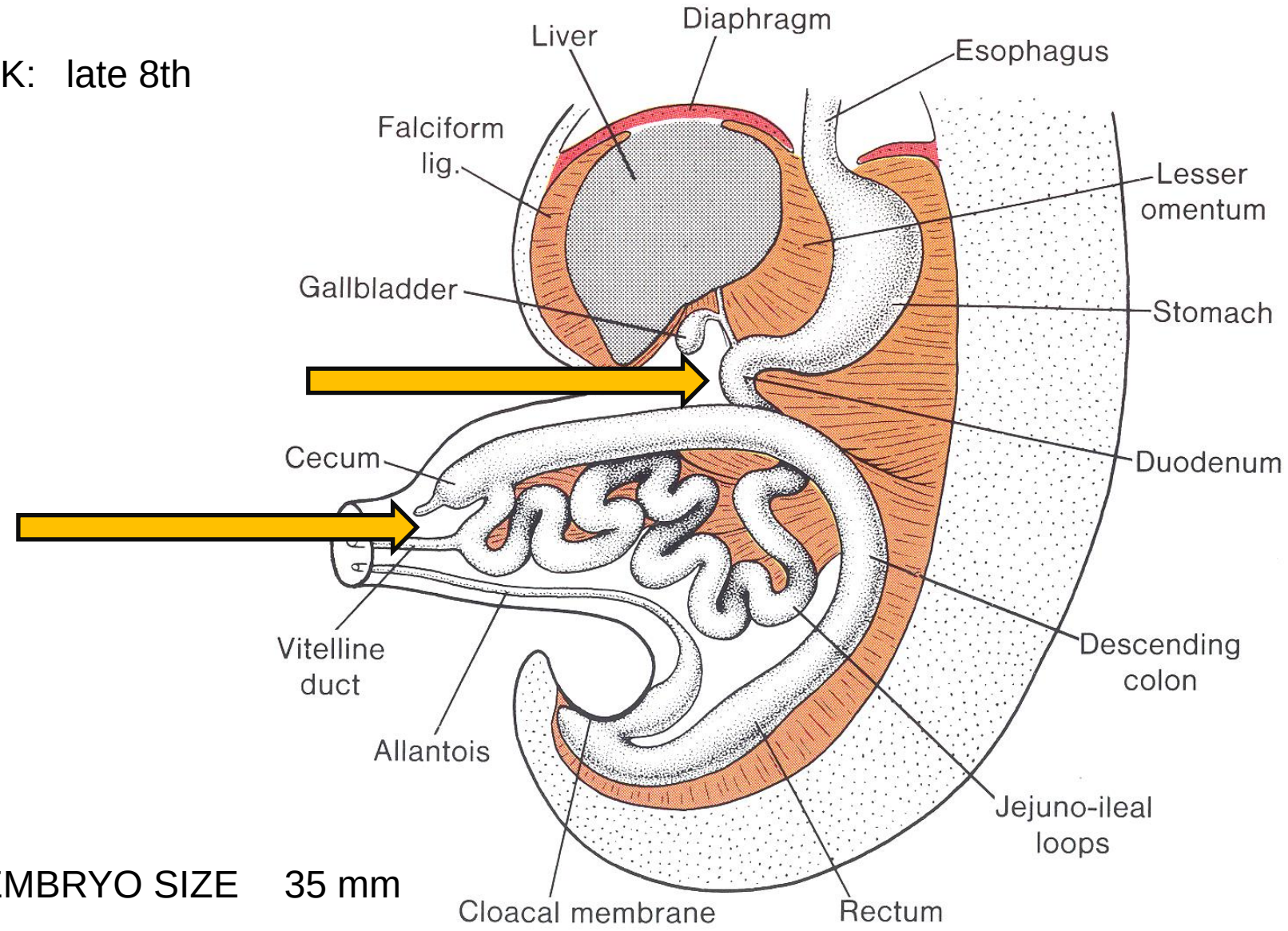
8th week





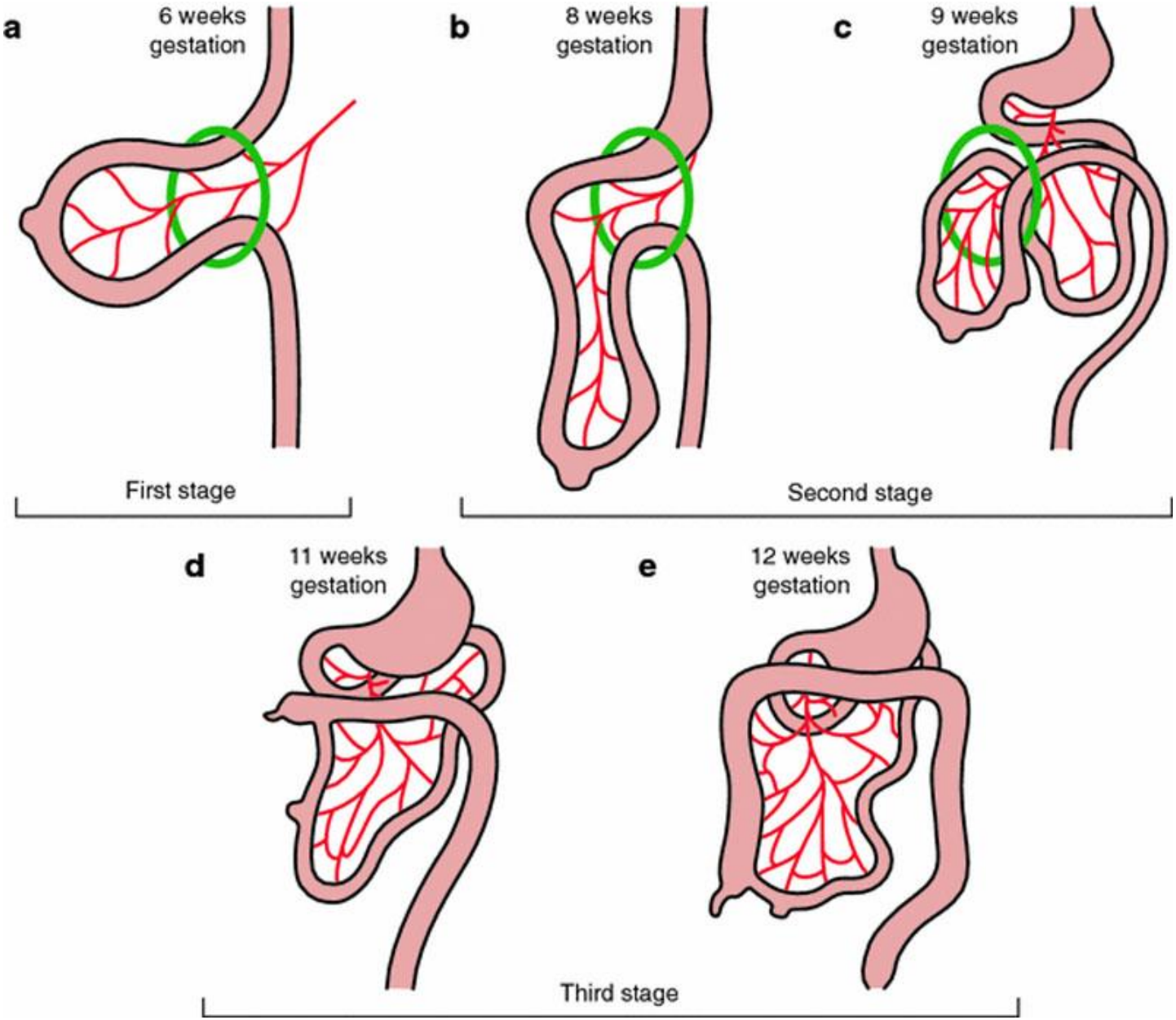
DEVELOPMENT OF INTESTINE

WEEK: late 8th

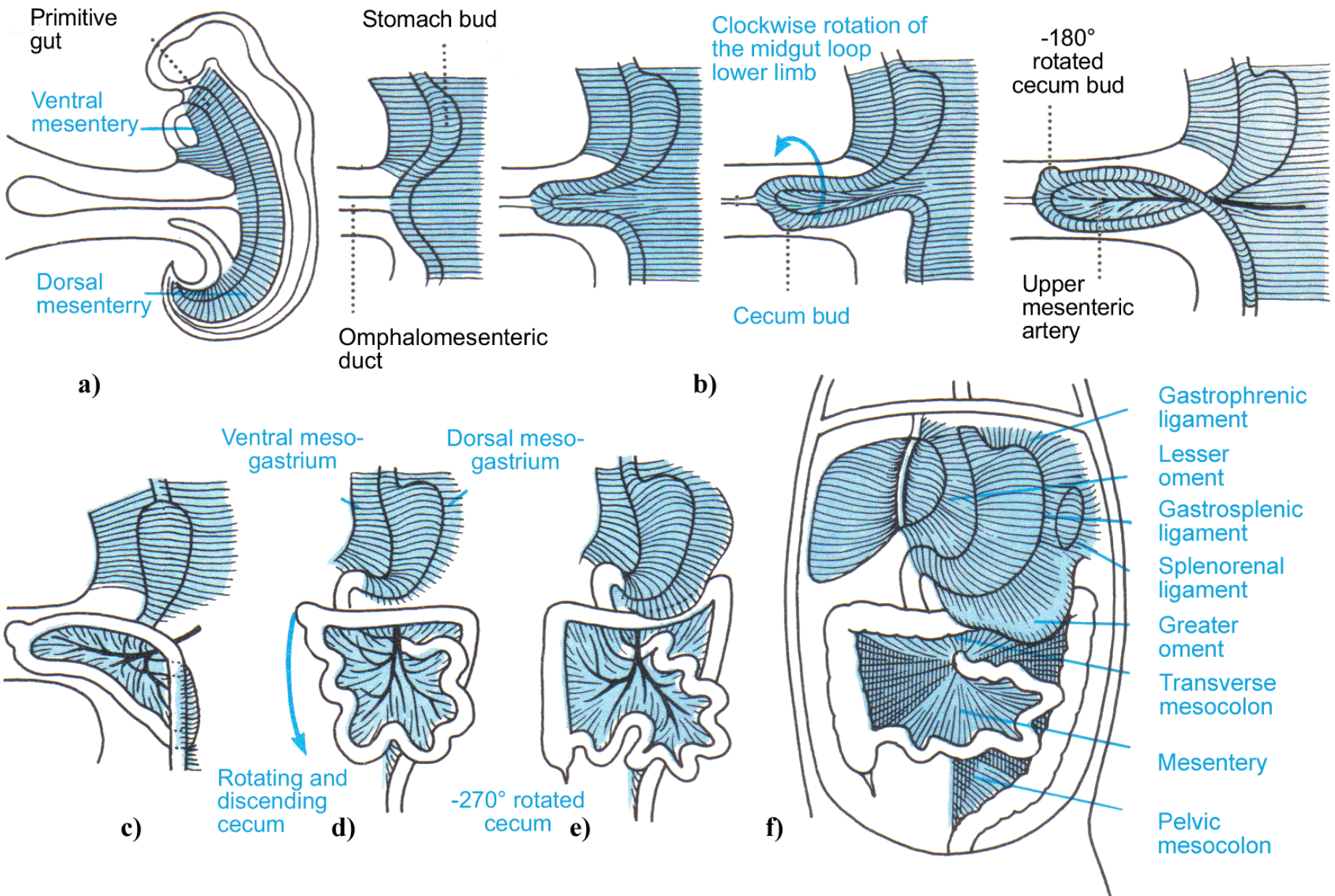


EMBRYO SIZE 35 mm

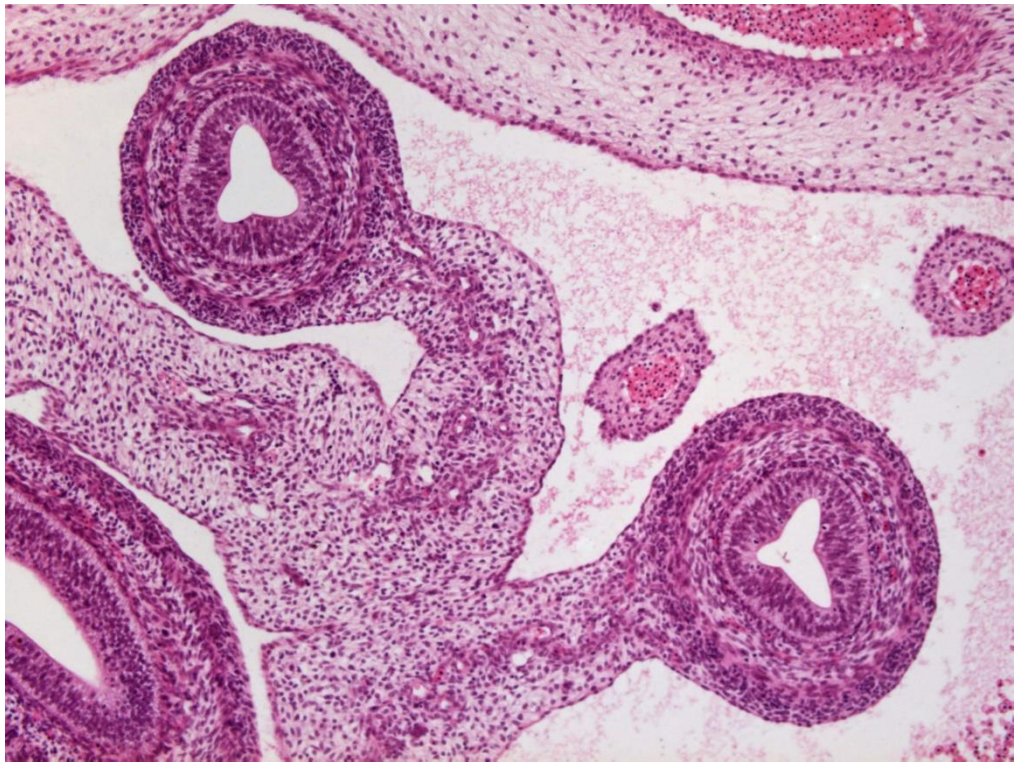
INTESTINAL ROTATION

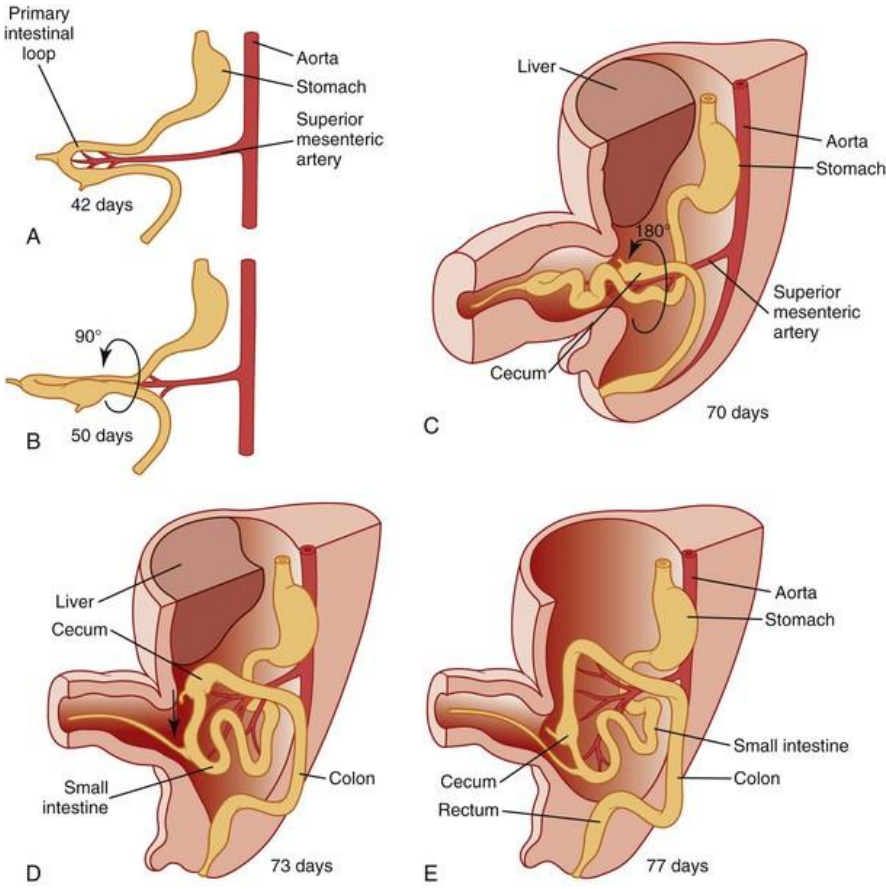


INTESTINAL ROTATION - MESENTERIES



INTESTINAL ROTATION – UMBILICAL HERNIA





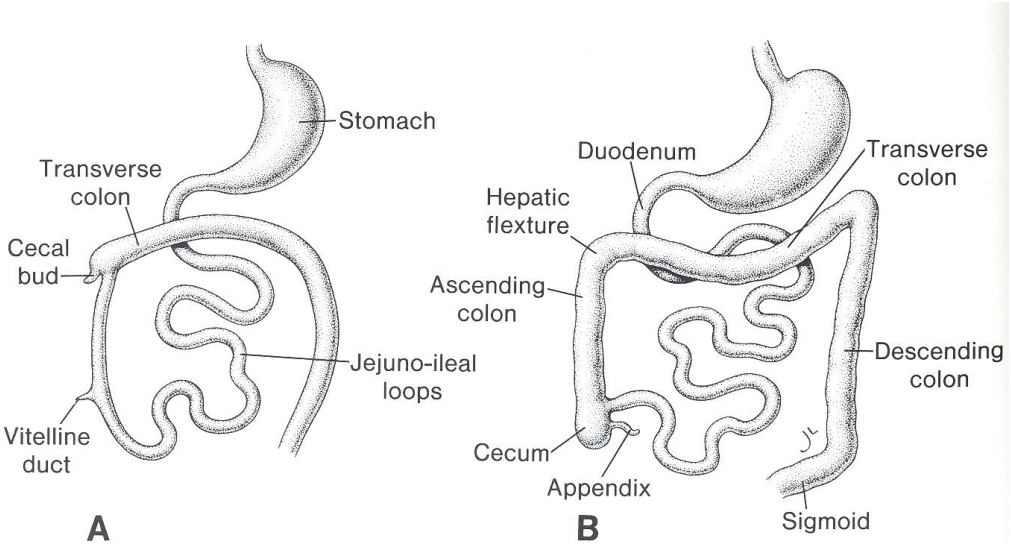
- (6-) 8th week
- Normal reposition in 10th week

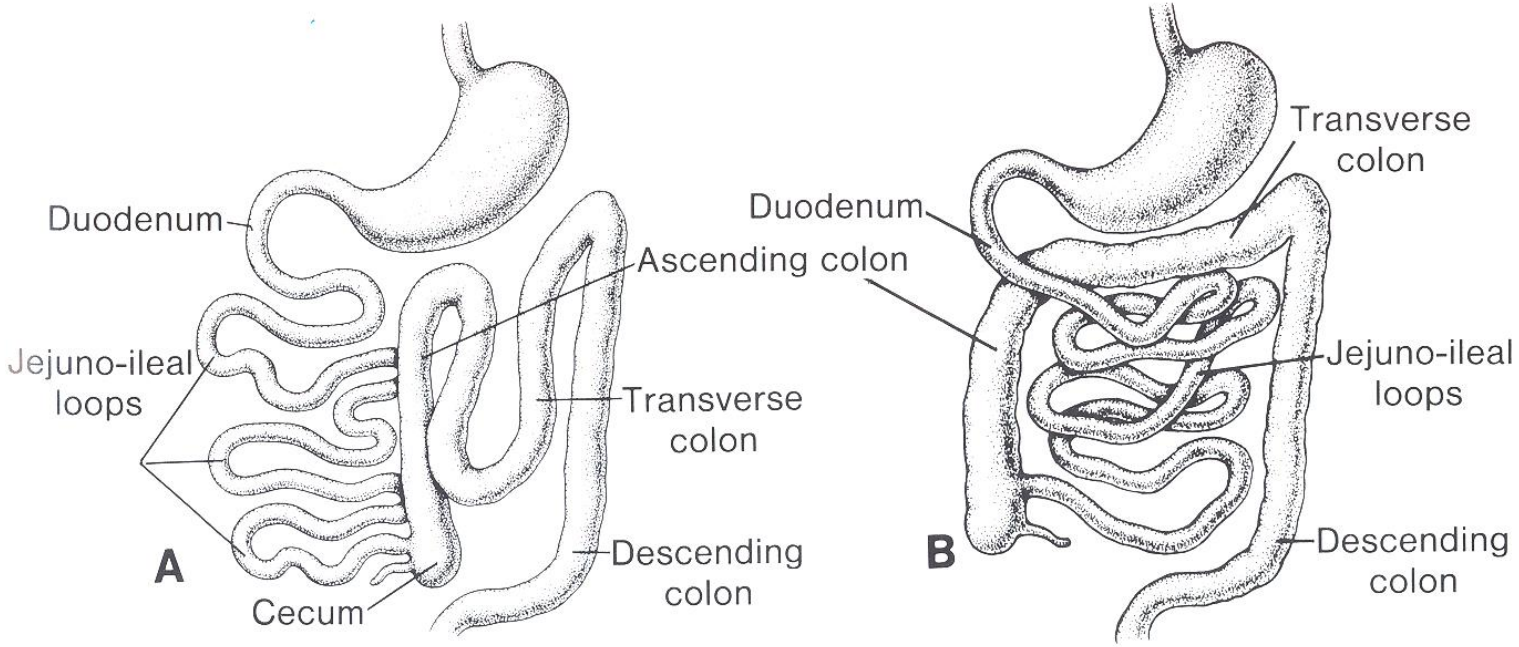
Abnormalities:

- Hernia may develop postantaly, evisceration or spontaneous reposition possible (X gastroschisis)
- Inomplete closure of umbilicus, may include omentum majus and small intestine, skin and connective tissue

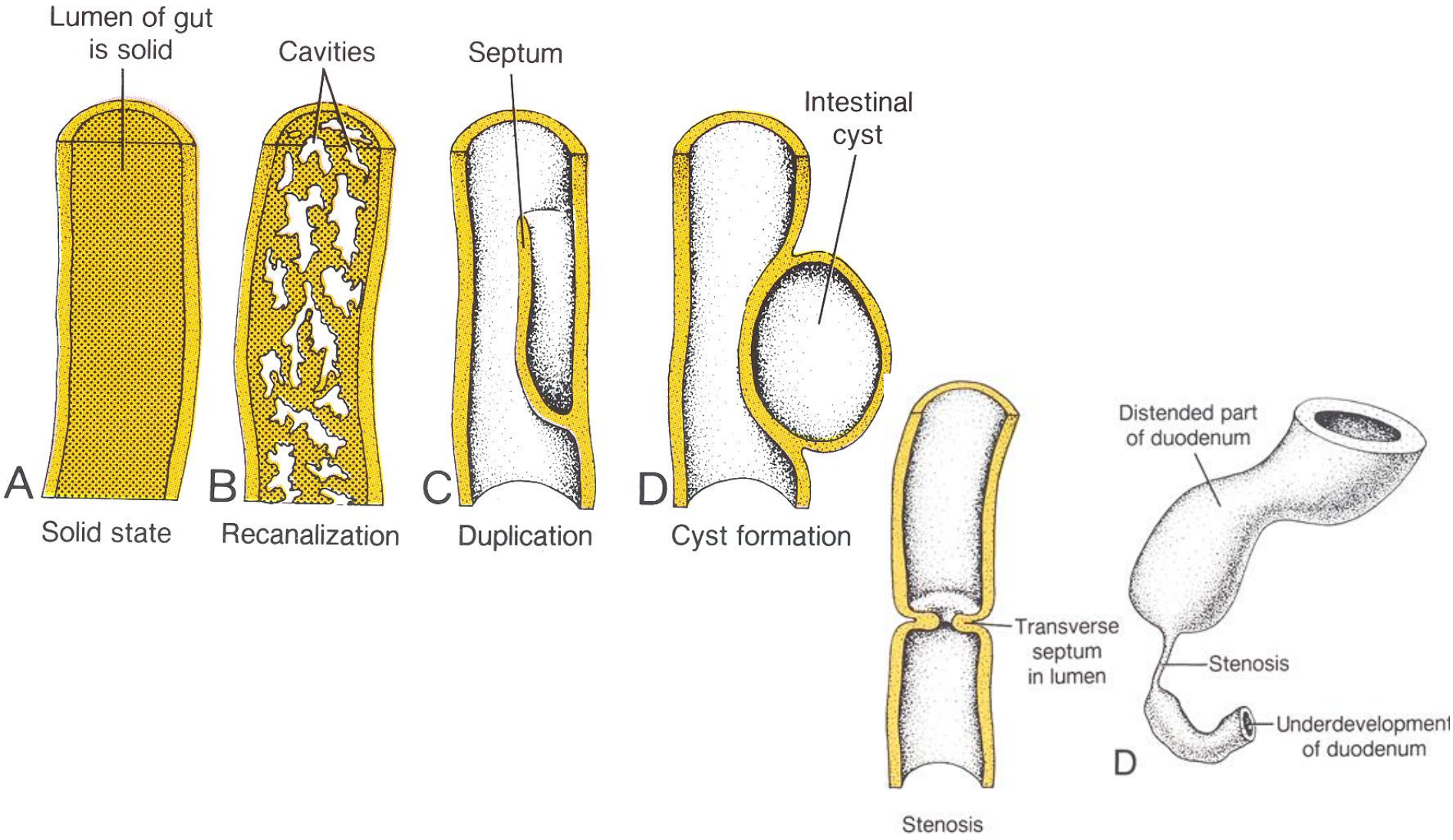
INTESTINAL ROTATION – UMBILICAL HERNIA

ABNORMALITIES



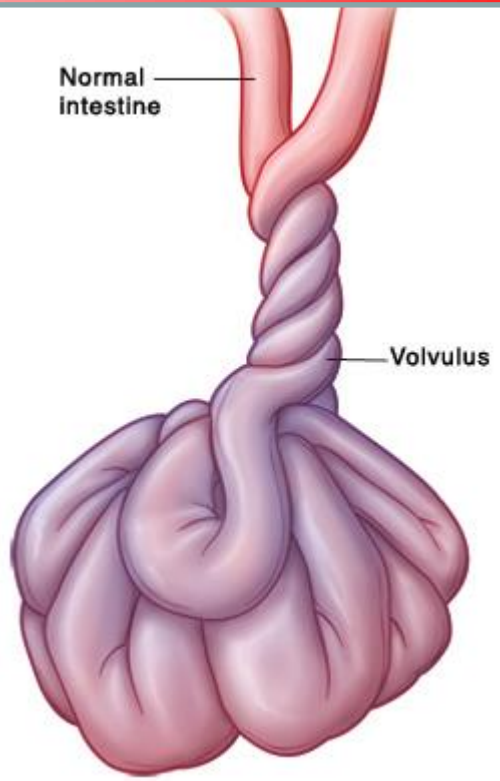


ILEUM DEVELOPMENT AND ABNORMALITIES



ILEUM DEVELOPMENT AND ABNORMALITIES

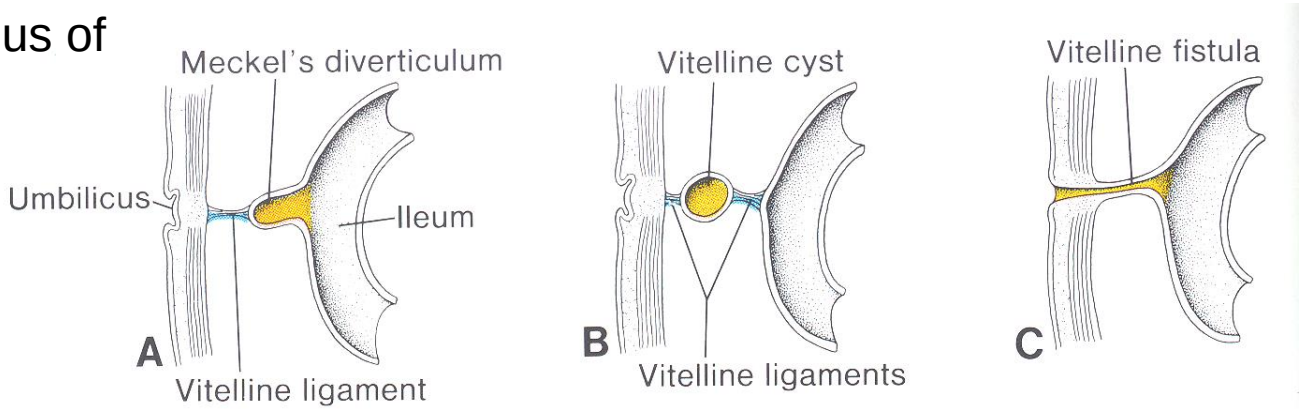
VOLVULUS



- malrotation of midgut and left colon (obstruction of a. mesenterica sup. and duodenum)
- reversed rotation (obstruction of colon)
- abnormal ahesion of caecum to liver (subhepatic caecum) - abnormal position of appendix
- caecum mobile

DIVERTICULUM MECKELI

- often phenomenon (2-4%)
- clinically relevant
- vitelline cysts, volvulus of diverticle



CLOACA AND ITS DERIVATIVES

- cloaka
- cloacal membrane - endoderm of cloaca and ectoderm of proctodeum

- septum urorectalis divides cloaca to dorsal **anorectal canal** and ventral **sinus urogenitalis**

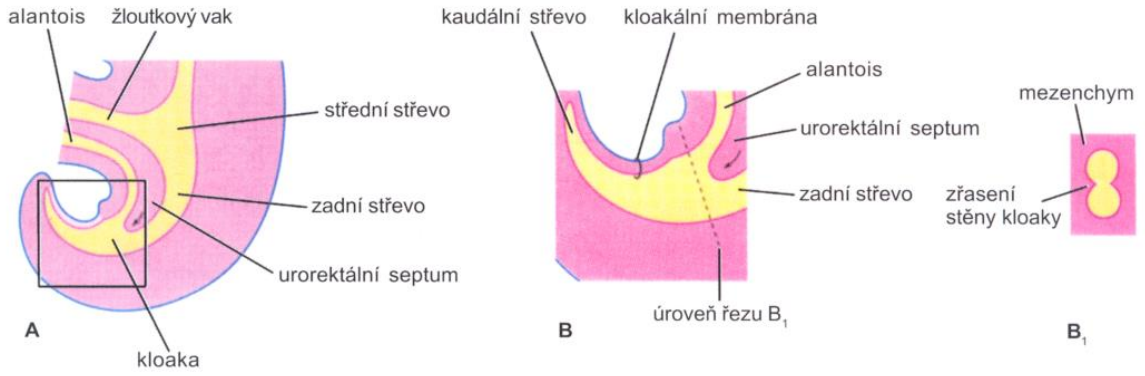
rectum

upper part of canalis analis

urinary bladder
urethra feminina
upper part of urethra masculina
vestibulum vaginae
part of prostate, other glands

- septum urorectale dividies cloacal membrane to membrana analis and membrana urogenitalis
- **perineum**

- 8th week in utero – anal membrane perforated



HIND GUT– RECTUM AND ANUS

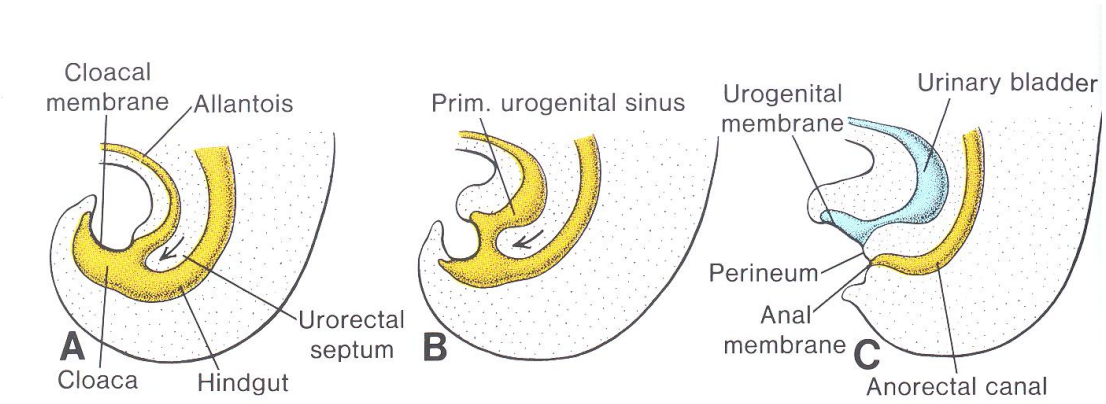
- **canalis analis**

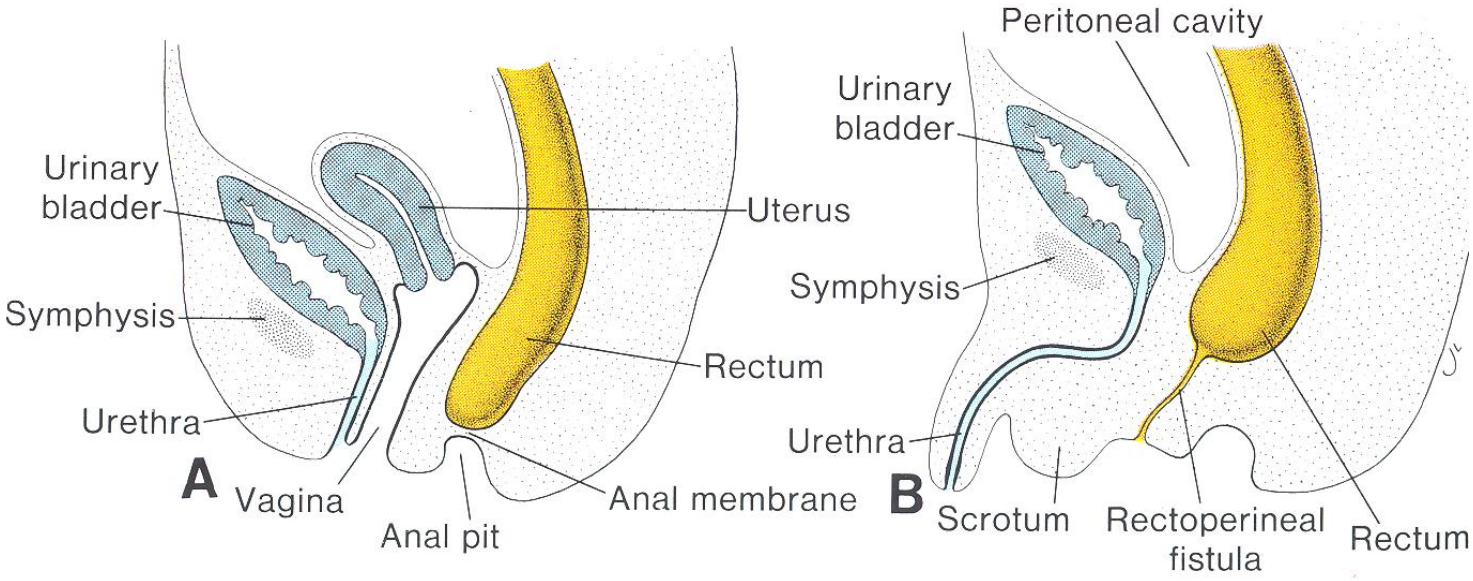
2/3 from hind gut
1/3 from **proctodeum**

linea pectinata – original position of the anal membrane

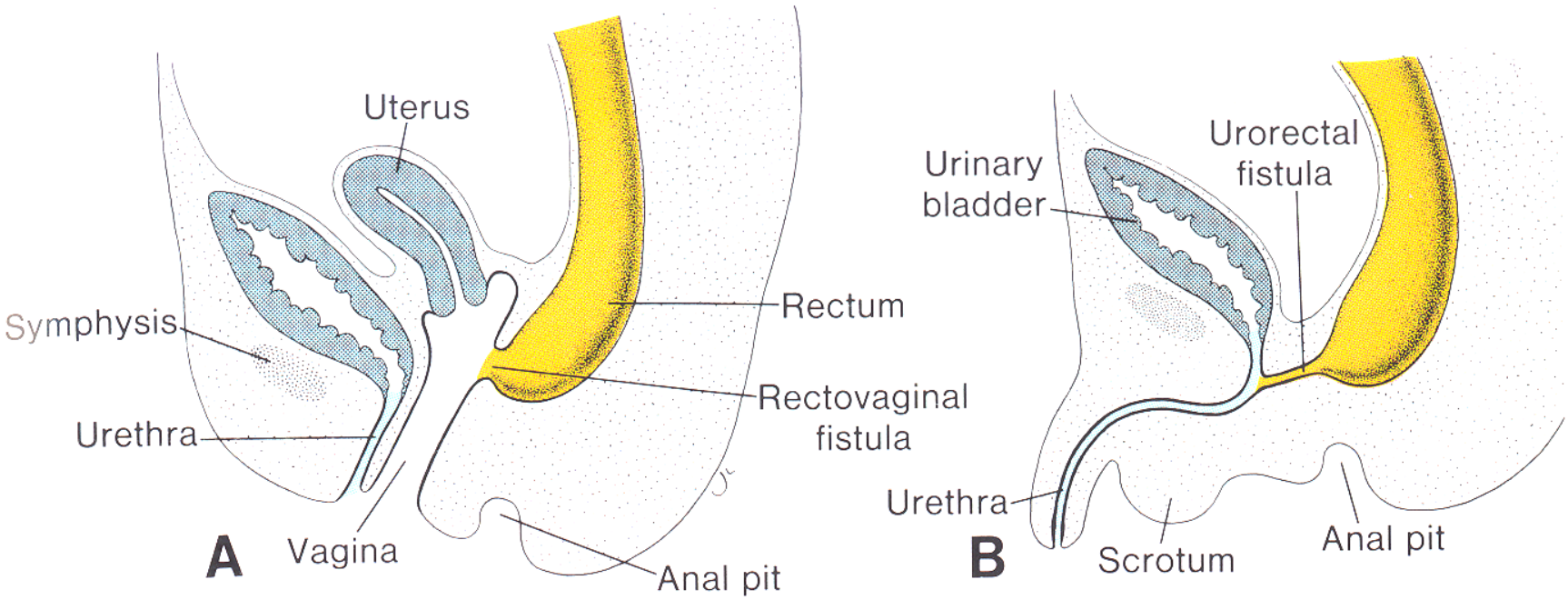
anocutaneous line – epithelium change from from non-keratinized stratified squamous epithelium to keratinized

ANUS DEVELOPMENT AND ABNORMALITIES





ANUS DEVELOPMENT AND ABNORMALITIES



PERINEAL MUSCLES

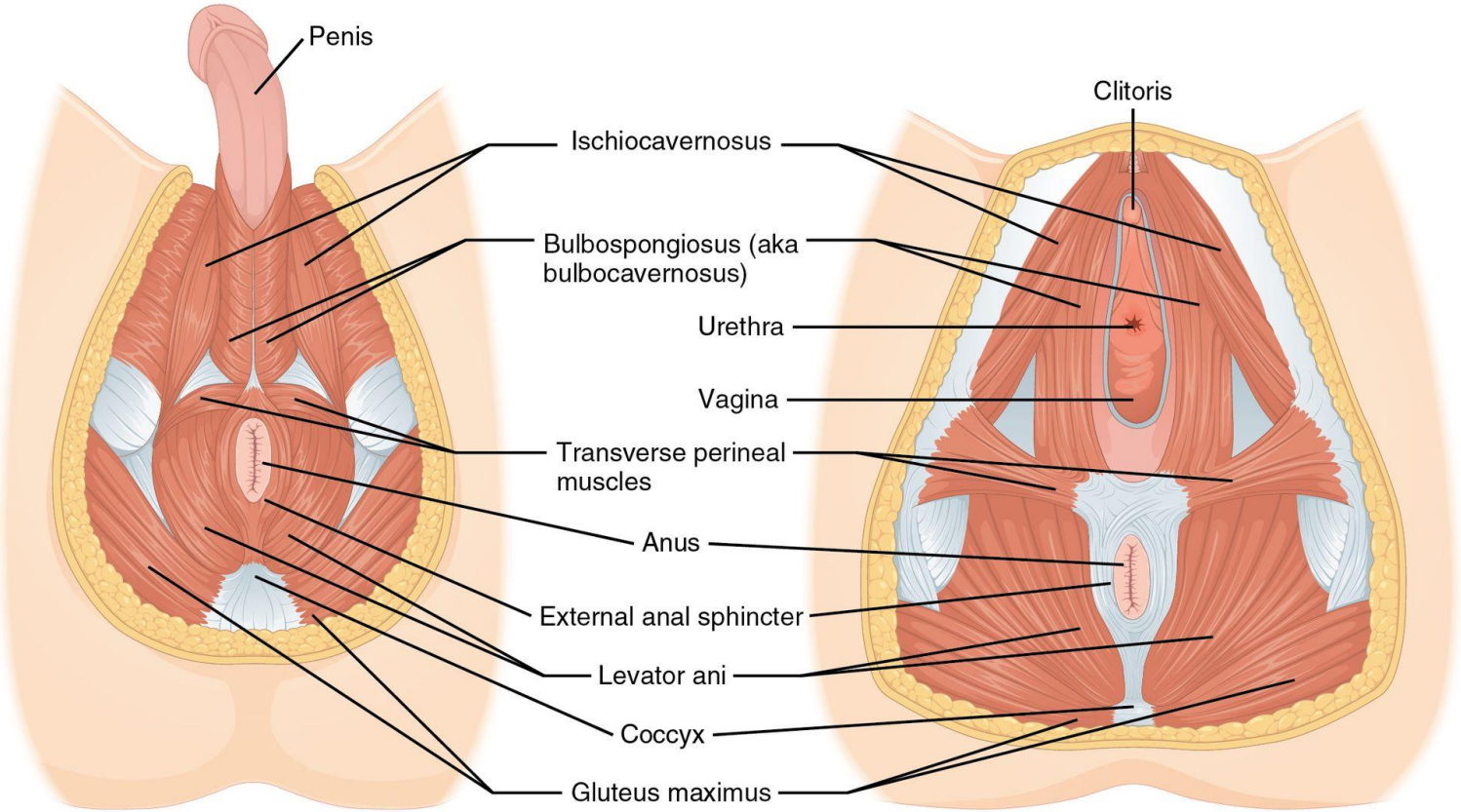
- *M. sphincter cloacae* is divided by urorectal septum to:

n. pudendus
nn. rectales inferiores

→ m. sphincter ani externus

→ m. transversus perinei superficialis
m. bulbocavernosus
m. ischiocavernosus

nn. perineales



Male perineal muscles: inferior view

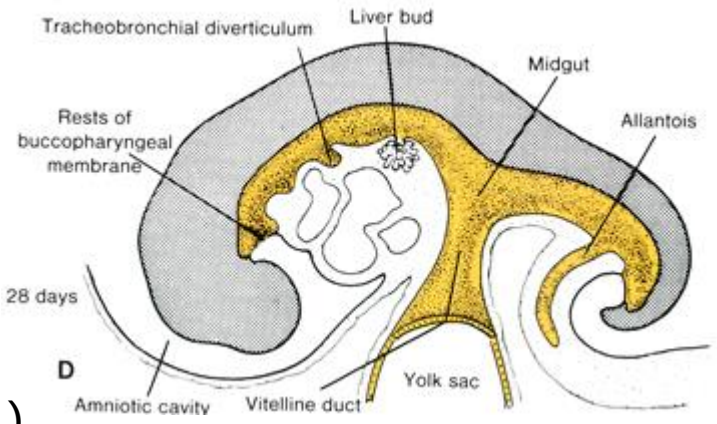
Female perineal muscles: inferior view

Primitive gut		
	Foregut	**vascularization**: *truncus coeliacus*
		derivatives: pharynx (also pharyngeal arches contribute), esophagus, stomach, proximal duodenum, liver, bile ducts and gall bladder, pankreas, trachea, bronchi and lungs
		developmental events: stomach and duodenal rotation, obliteration and recanalization of esophageal and duodenal lumen
	Midgut	**vascularization**: *a. mesenterica superior*
		derivatives: distal duodenum, jejunum, ileum, colon ascendens, 1/3-2/3 of colon transversum
		developmental events: intestinal rotation, physiological umbilical hernitation and reposition. Diverticulum Meckeli
	Hindgut	**vascularization**: *a. mesenterica inferior*
		derivatives: 1/3-2/3 of colon transversum, rectum, part of analis canalis, part of urinary bladder, part of urethra, in males part of prostate and bulbourethral glands, in females vaginal vestibulum, Skenes gll, Bartholin's gll.
		developmental events: septation of cloaca by septum urorectale, development of perineum, rectum, anus and sinus urogenitalis and its derivatives

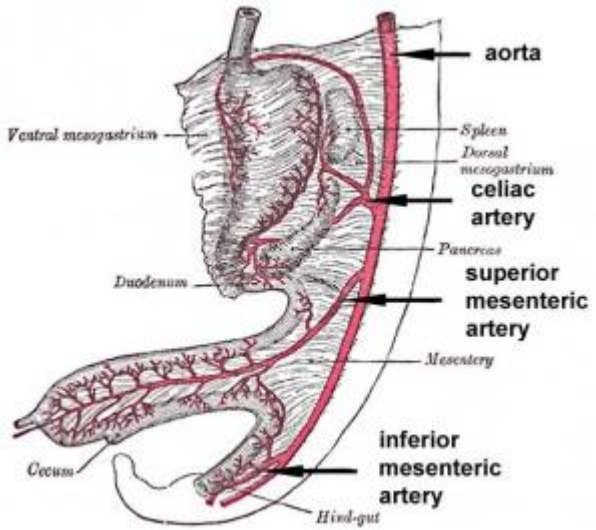
DEVELOPMENT OF LIVER, PANCREAS AND LARGE SALIVARY GLANDS

PRIMITIVE GUT

since 4th week
- oropharyngeal membrane (stomodeoum-foregut)
- cloacal membrane (hind gut-proctodeum)



Foregut
- primitive pharynx (→ and its derivatives)
- lower respiratory passages (→ laryngotracheal div.)
- liver and bile passages (→ hepatic div.)
- pancreas (→ pancreatic div.)

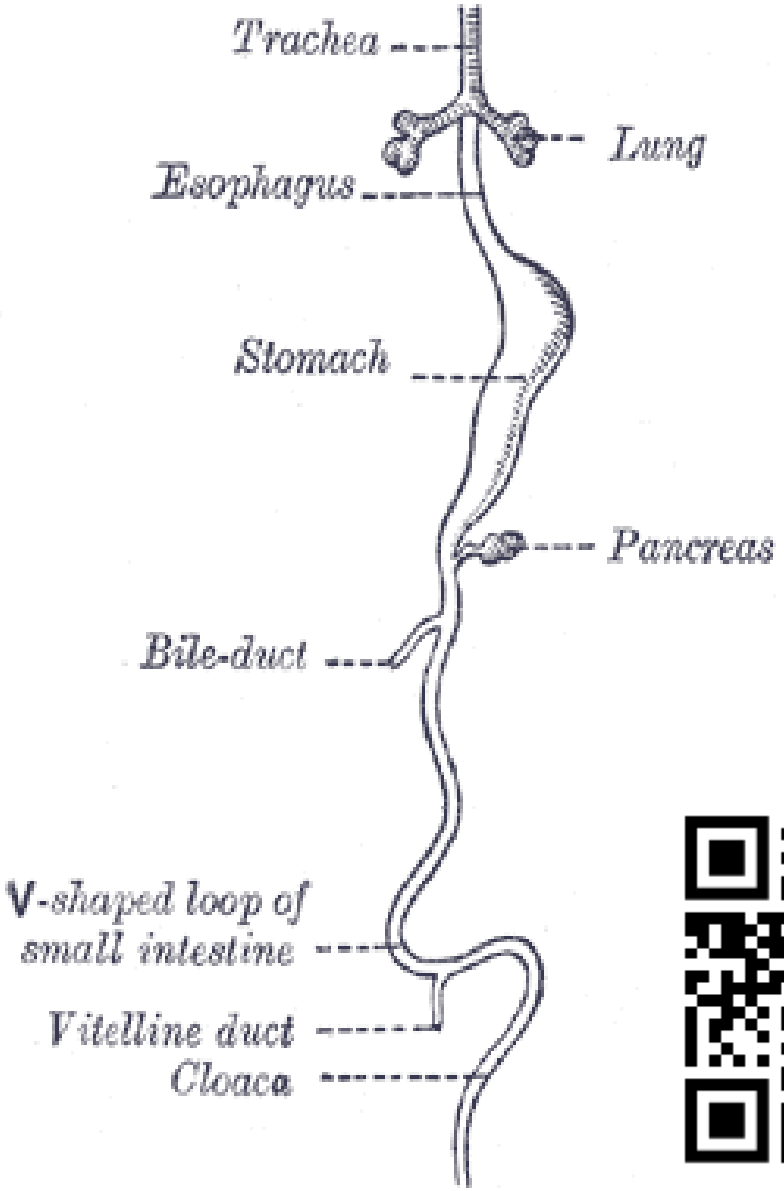


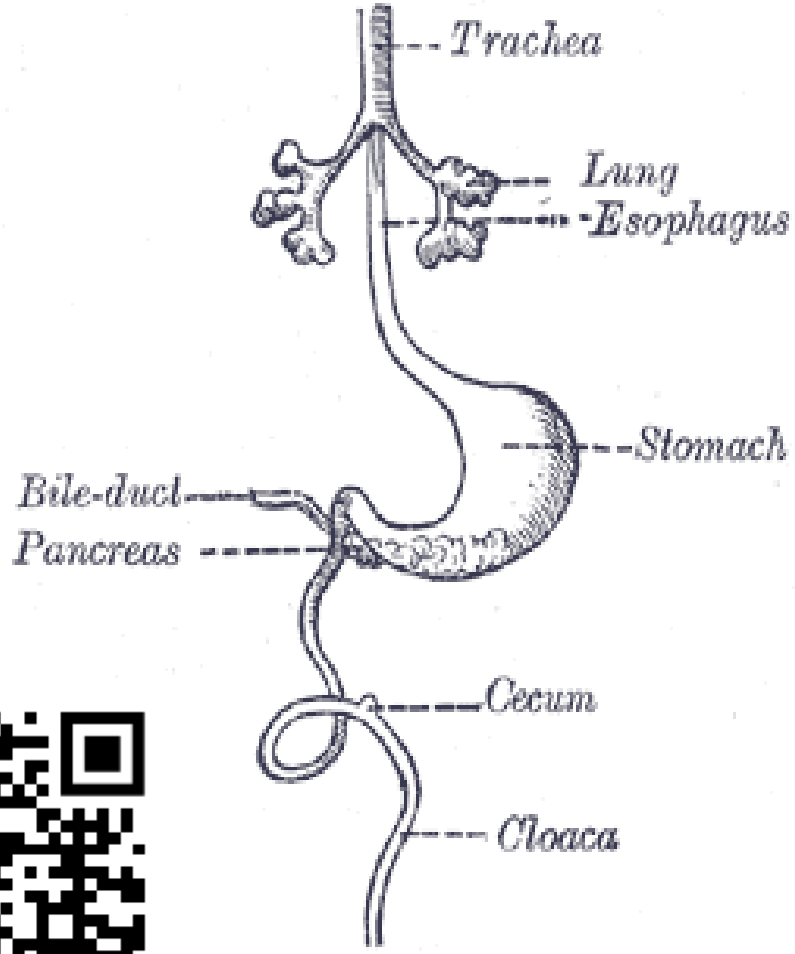
- oesophagus and stomach
- proximal duodenum

Midgut
- distal duodenum, ileum, jejunum
- caecum, appendix, colon ascendens, colon transversum (1/2-2/3)

Hindgut
- colon transversum (1/3-1/2), colon descendens, colon sigmoideum
- rectum, anal canal
- part of urinary system (derivatives of sinus urogenitalis)

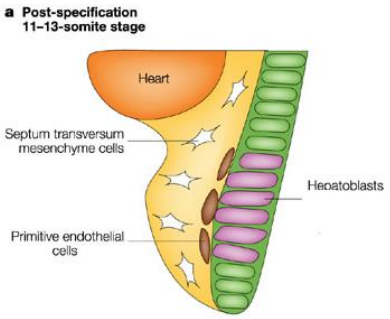
DEVELOPMENT OF DIGESTIVE TUBE

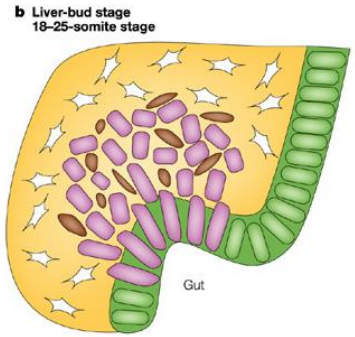


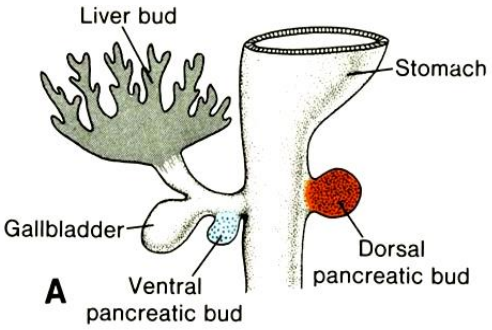


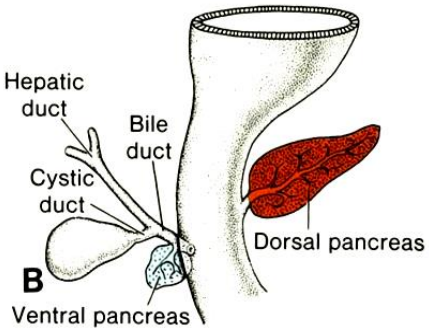
EMBRYONIC DEVELOPMENT OF LIVER

- Diverticulum of embryonic duodenum - liver diverticulum
- Pars hepatica (parenchyma + ductus hepaticus) and pars cystica (ductus cysticus + gall bladder) form d. choledochus
- Rapidly proliferating cells penetrate septum transversum (mesodermal plate between pericardial cavity and yolk sac) and growth into ventral mesentery
- liver cords – parenchyma
- Interactions between cells of liver cords and vv. omphalomesentericae induce development liver sinusoids
- C.t. , Kupffer and hematopoietic cells – from mesoderm of septum transversum
- Surface mesoderm differentiate into visceral peritoneum





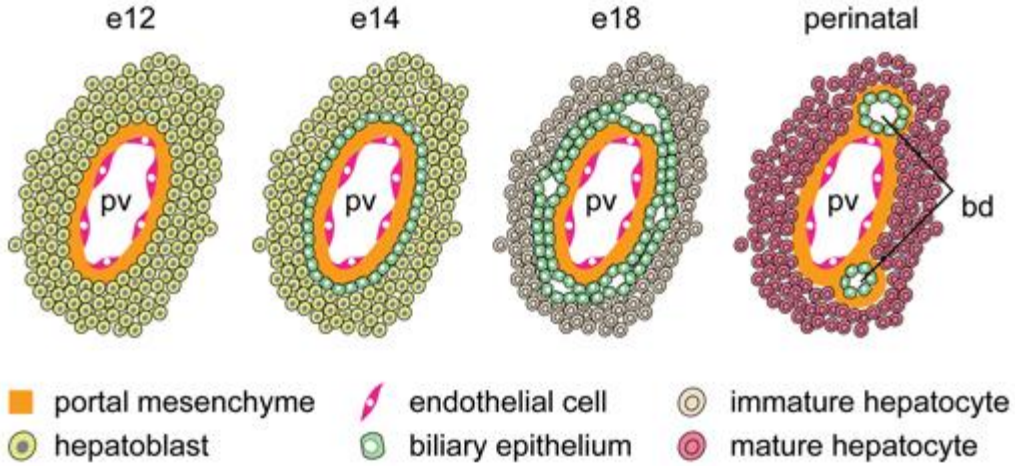


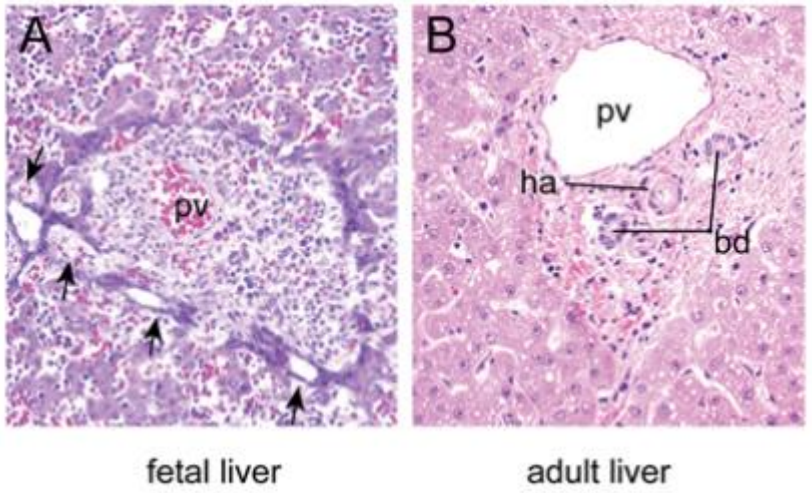


•10th week
- 10% of body volume
- hematopoiesis

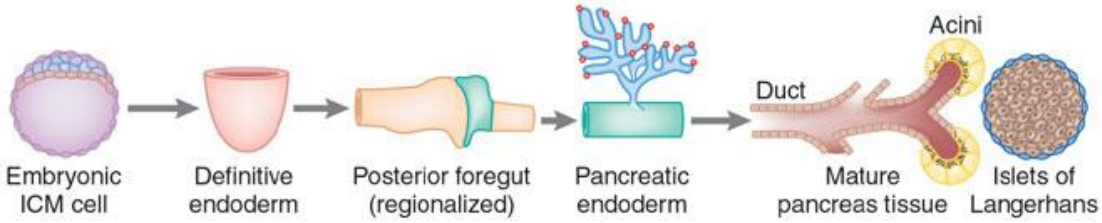
• 12th week
- bile production

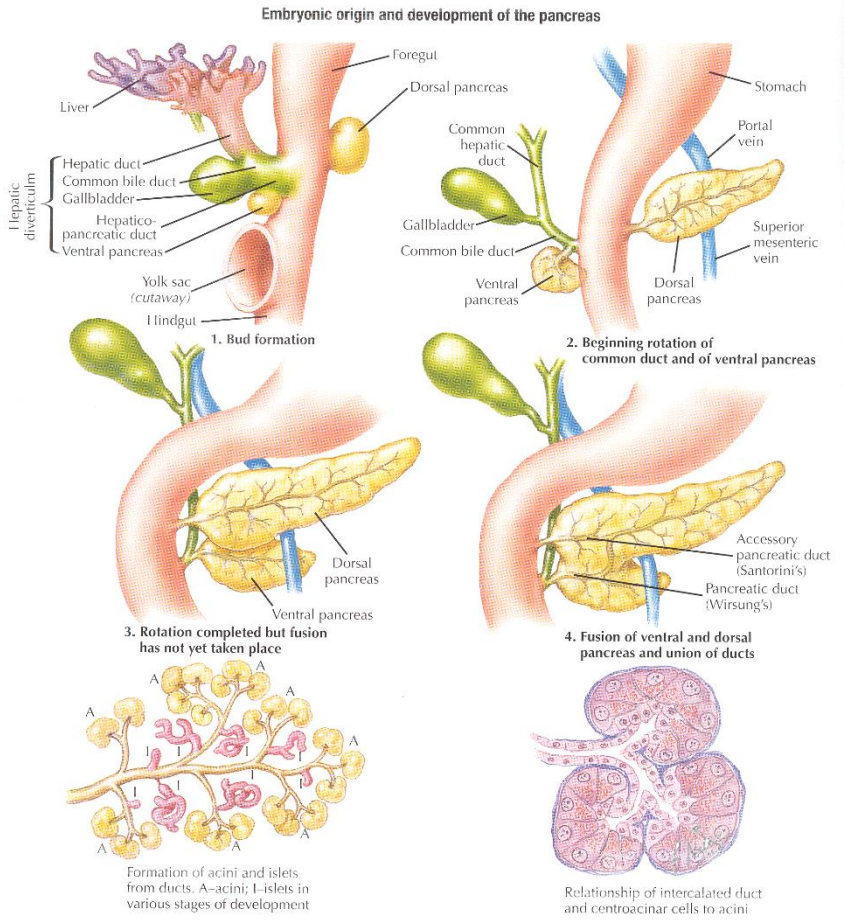
EMBRYONIC DEVELOPMENT OF LIVER





EMBRYONIC DEVELOPMENT OF PANCREAS





- 4-5th week of development: two endodermal diverticles
  - dorsal and ventral duodenal diverticle (= pancreas dorsale et ventrale)

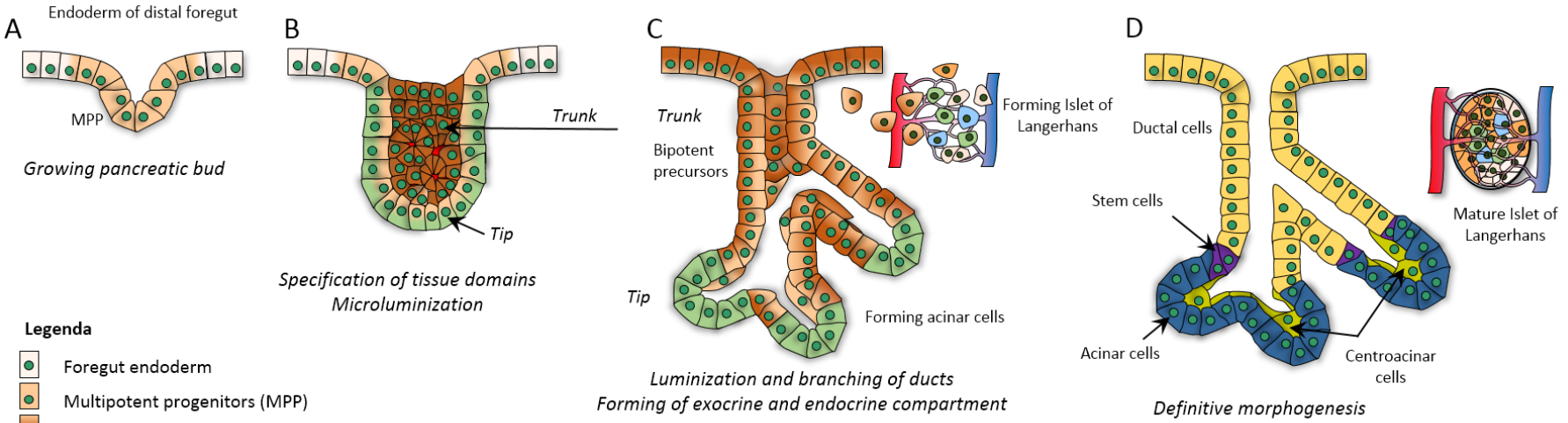
- after rotation of duodenal loop both diverticula fuse
- development of ducts:
  - ventral duct fuses with dorsal duct and divides it to proximal and distal part
  - proximal part of dorsal duct obliterates
  - ventral duct and distal part of dorsal duct form ductus pancreaticus major
  - if the proximal part of dorsal part persists, it will formsductus pancreatis accesorius

- ductal system develops first, secretory acini follow

- cells that are not part of ductal structures differentiate into Islets of Langerhans

- since 4th month in utero - secretory activity

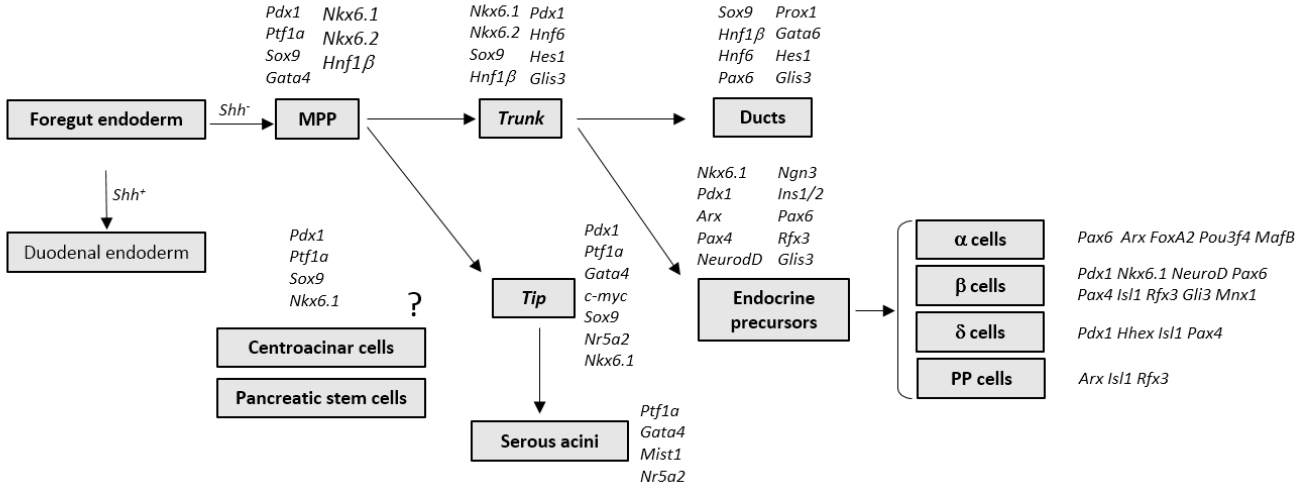
HISTOGENESIS OF PANCREAS



Legenda

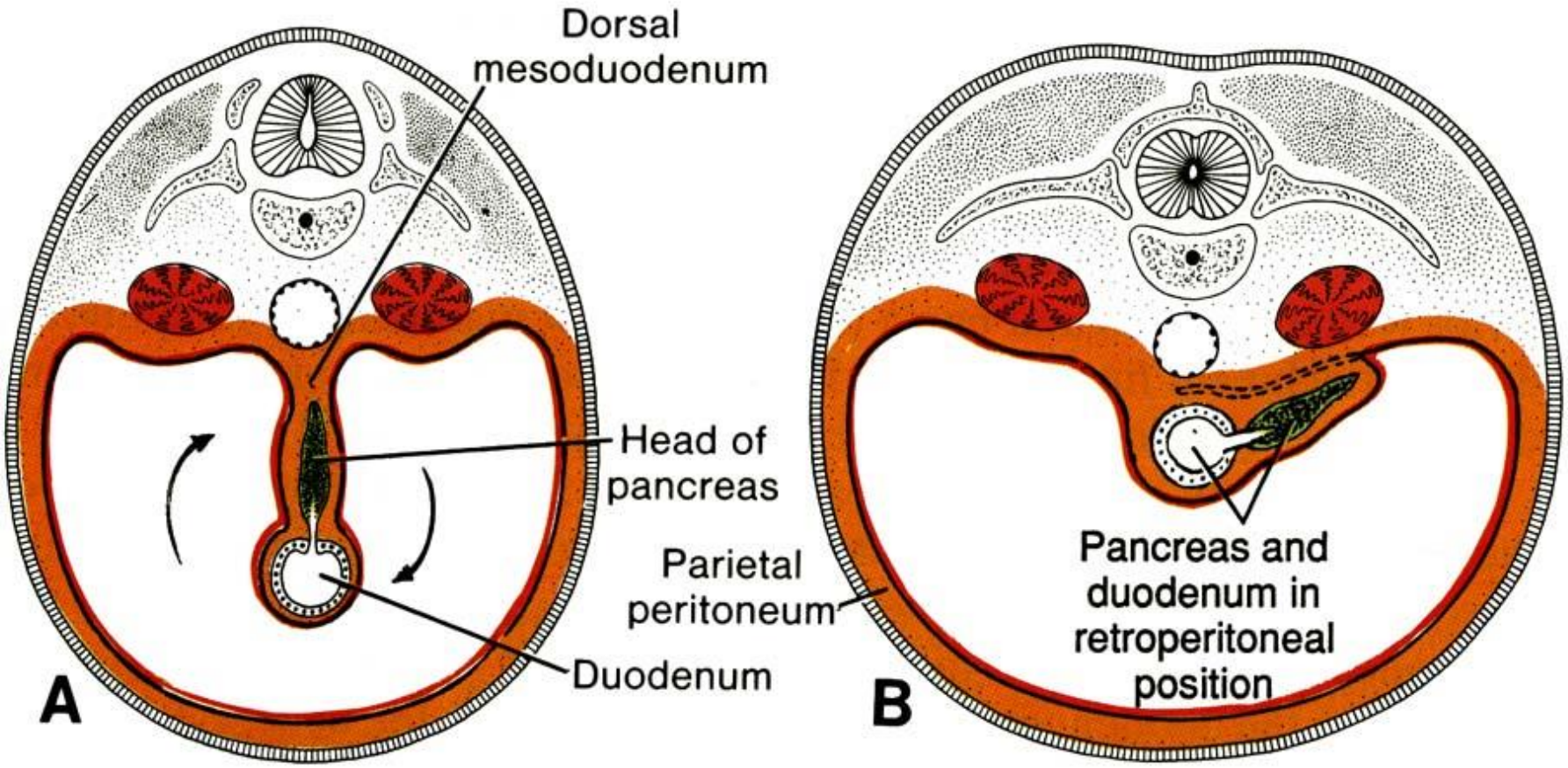
- Foregut endoderm
- Multipotent progenitors (MPP)
- Bipotent precursors of ducts and endocrine cells
- Precurzors of acinar cells
- Ductal cells
- Centroacinar cells
- Acinar cells
- Suggested pancreatic stem cells

E



ANATOMIC LOCALIZATION OF PANCREAS

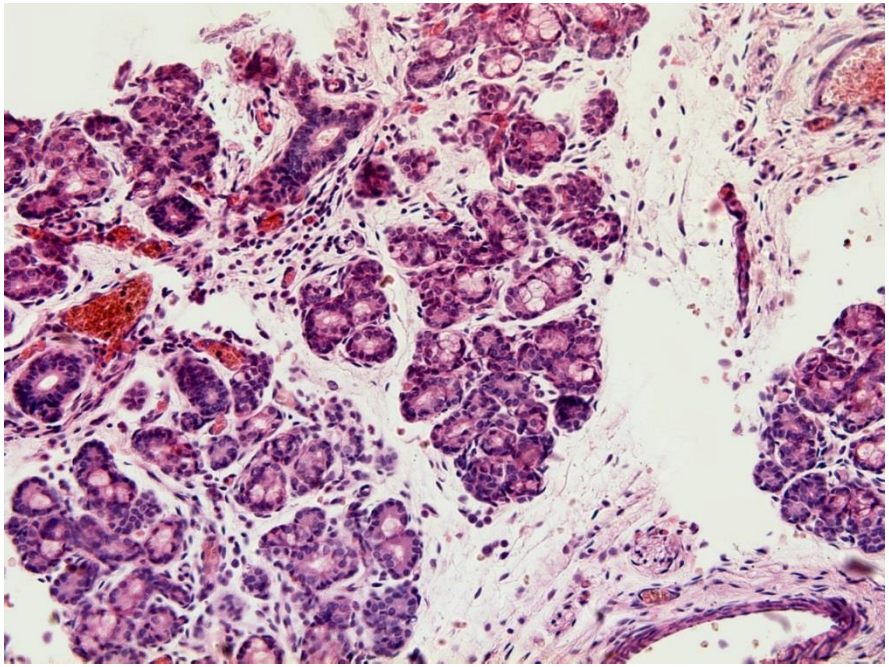
- Pancreas is secondary retroperitoneal



DEVELOPMENT OF LARGE SALIVARY GLANDS

Gl. parotis

- develops first (6th week)
- ectodermal buds from corners of stomodeum
- proliferation and branching of solid cords
- luminization and development of acini (10th week)
- vazivo - mesenchym



Gl. submandibularis

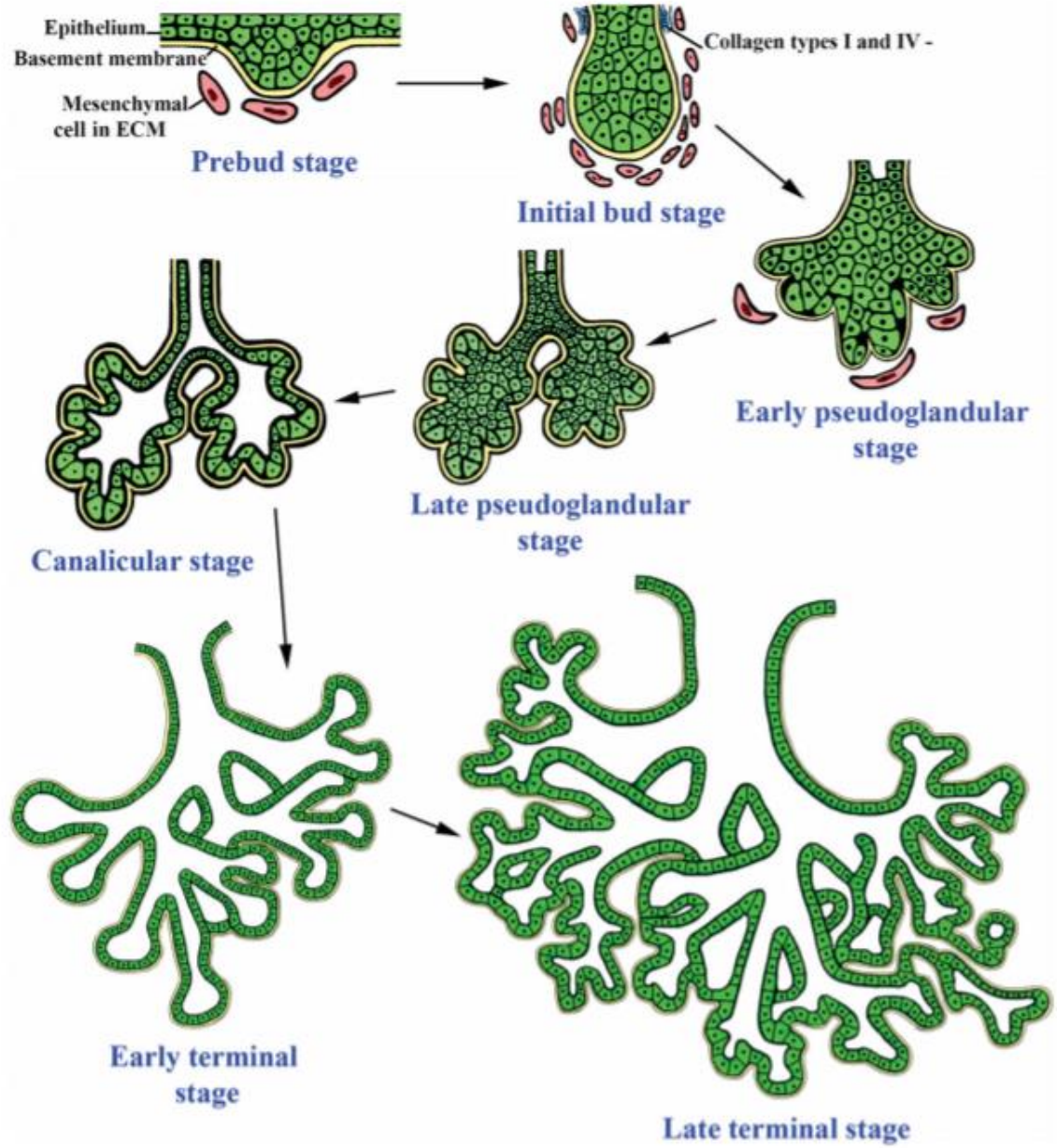
- end of 6th week
- endodermal buds from floor of stomodeum
- proliferation and branching of solid cords together with tongue development
- luminization and development of acini (12th week)
- connective tissue– mesenchym
- growths even post natally

Gl. sublingualis

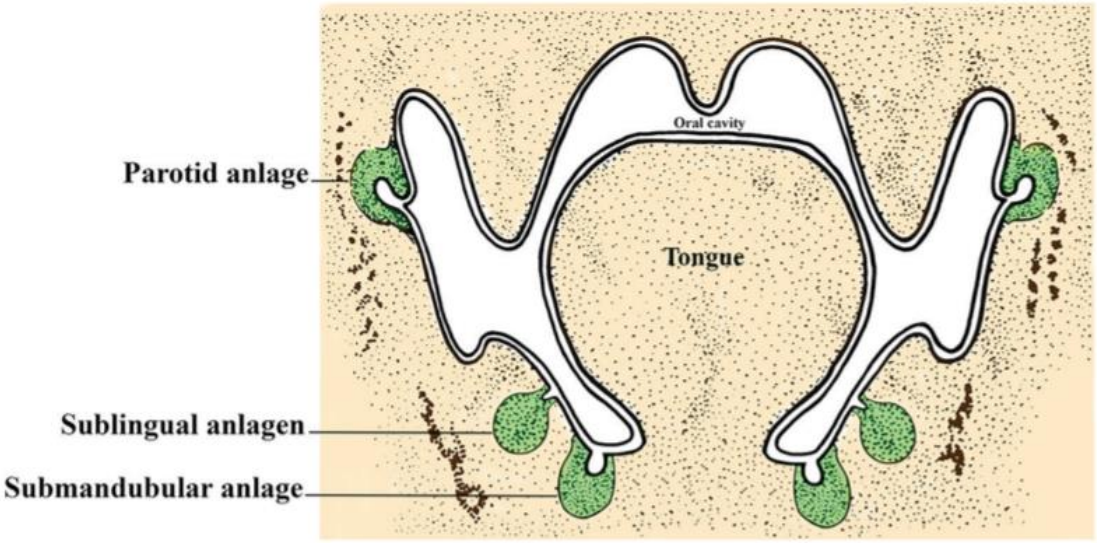
- 8th week
- multiple endodermal buds in paralingual groove
- proliferation and branching of solid cords
- luminization and development of glandular parenchyma
- connective tissue – mesenchym
- 10-12 independent ducts

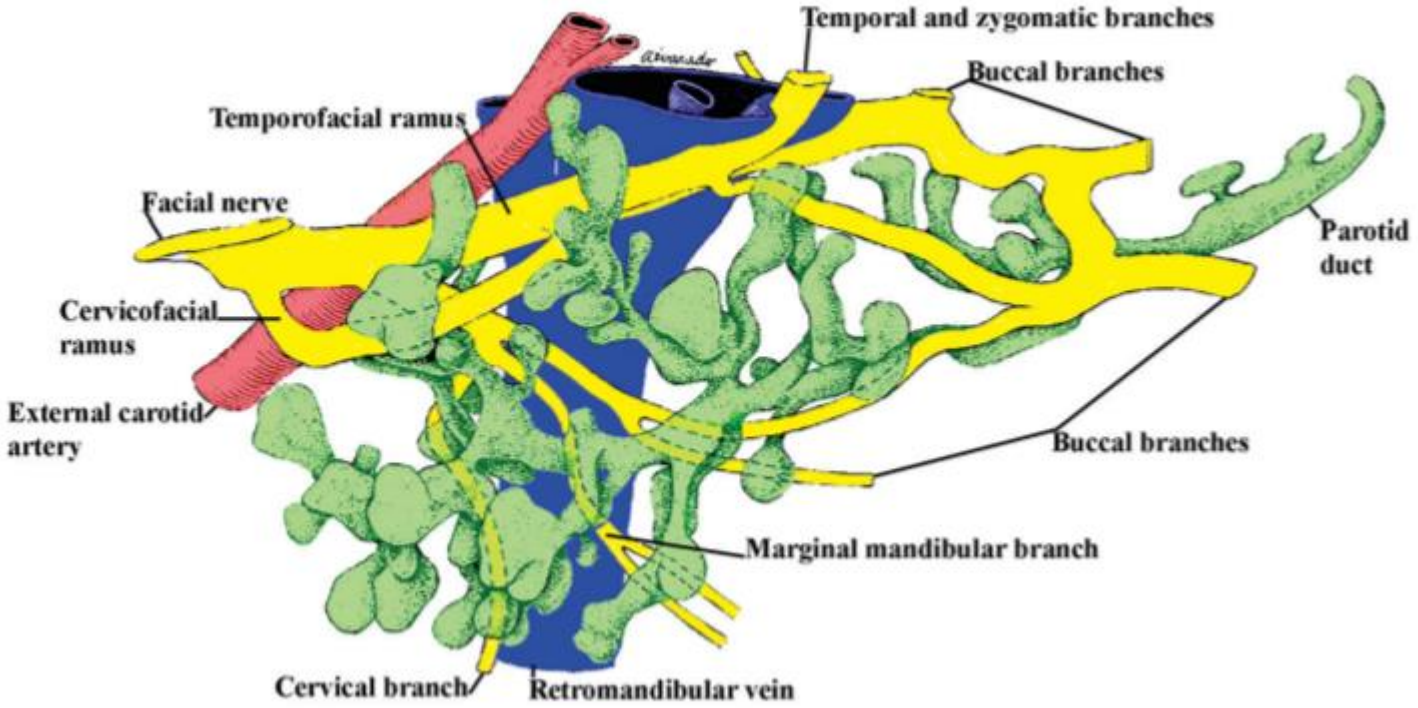
DEVELOPMENT OF LARGE SALIVARY GLANDS

DEVELOPMENT OF LARGE SALIVARY GLANDS

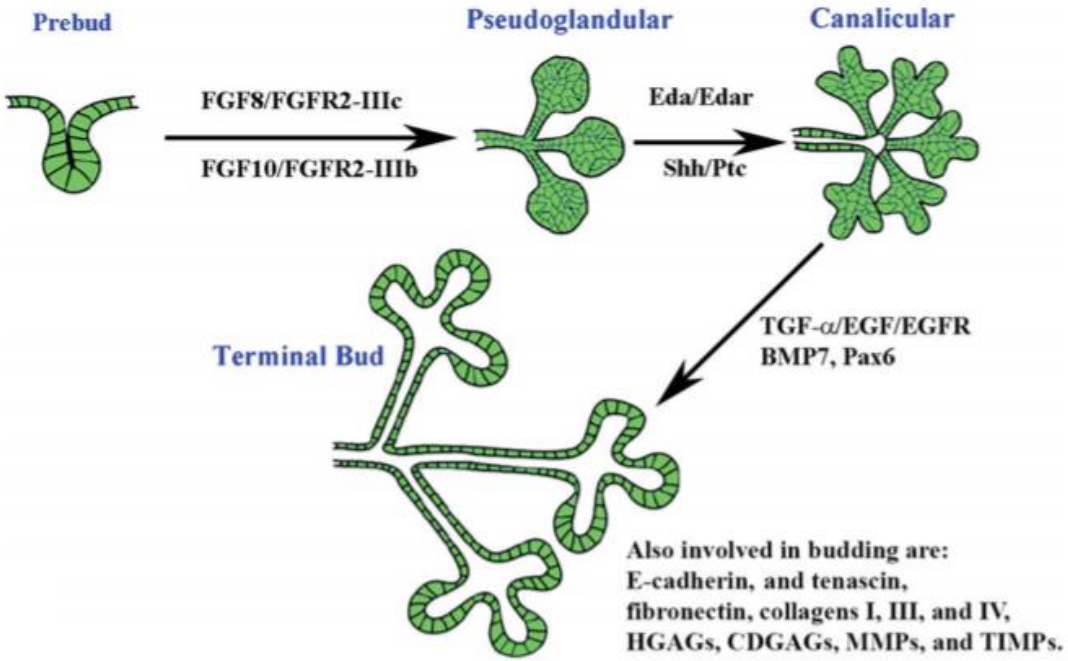


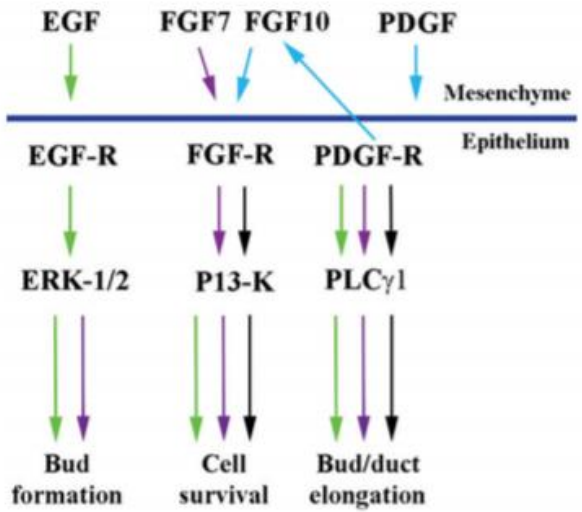
DEVELOPMENT OF LARGE SALIVARY GLANDS



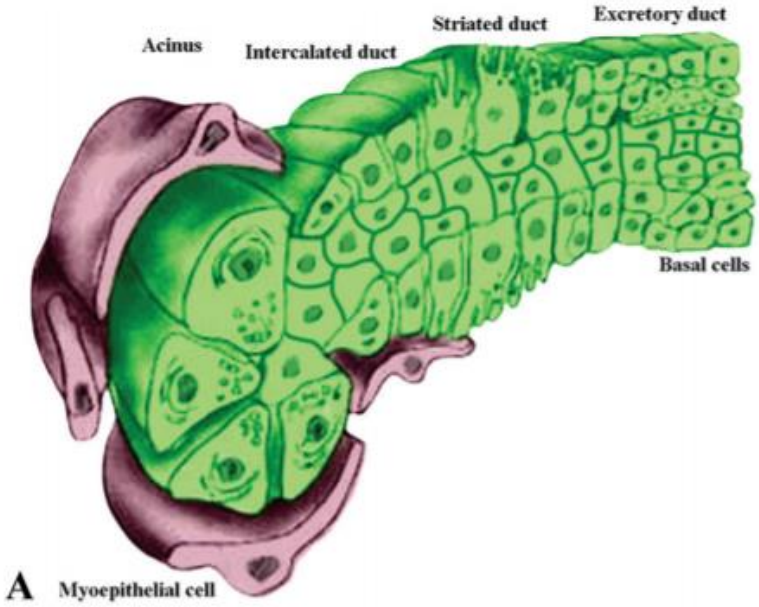


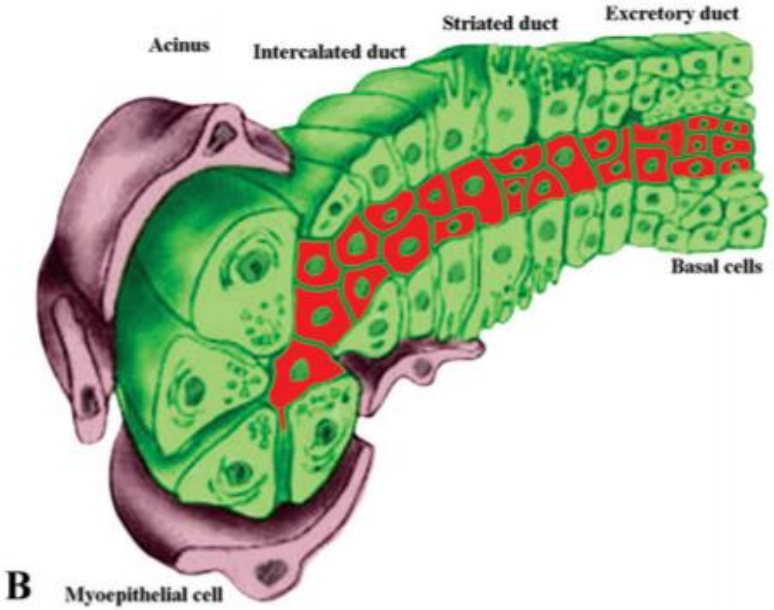
DEVELOPMENT OF LARGE SALIVARY GLANDS

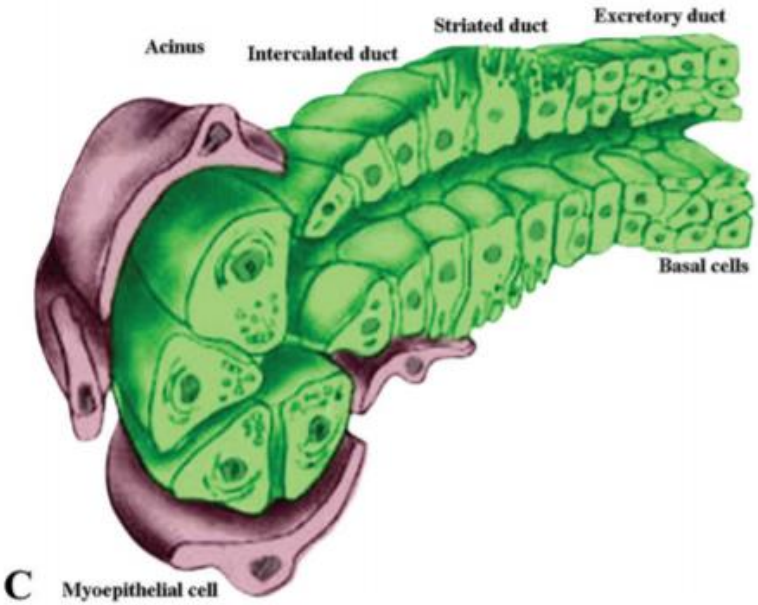




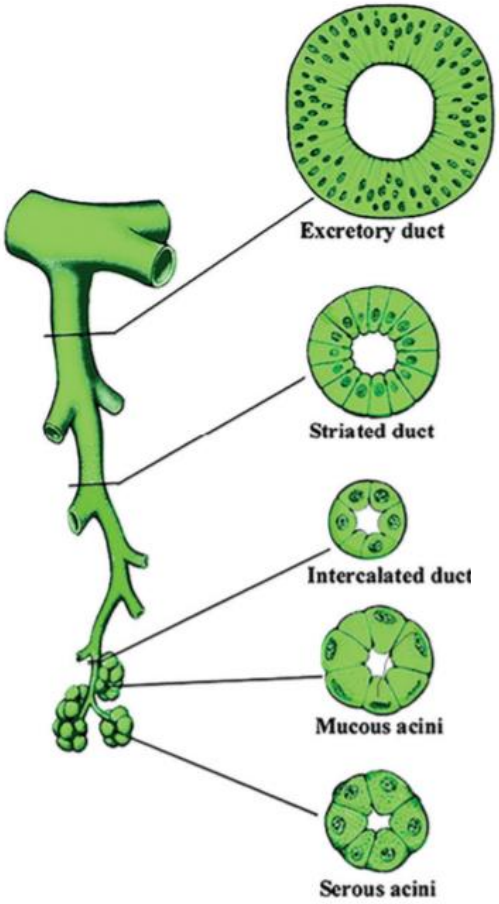
DEVELOPMENT OF LARGE SALIVARY GLANDS

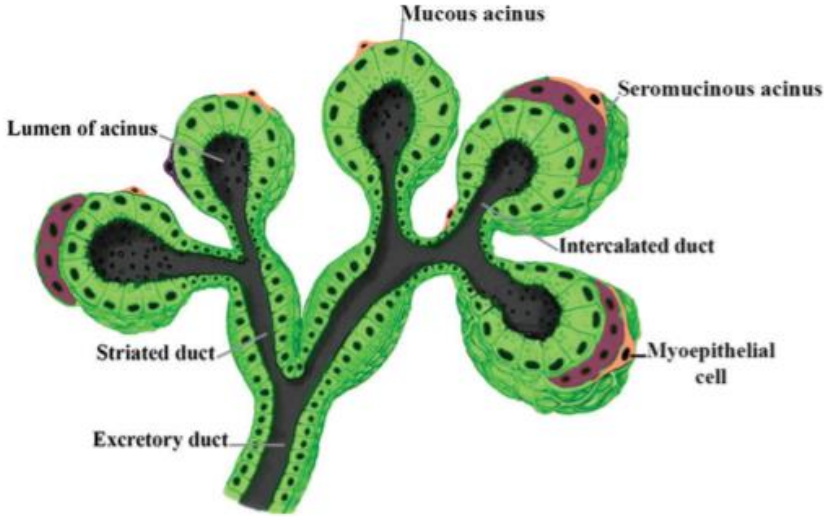


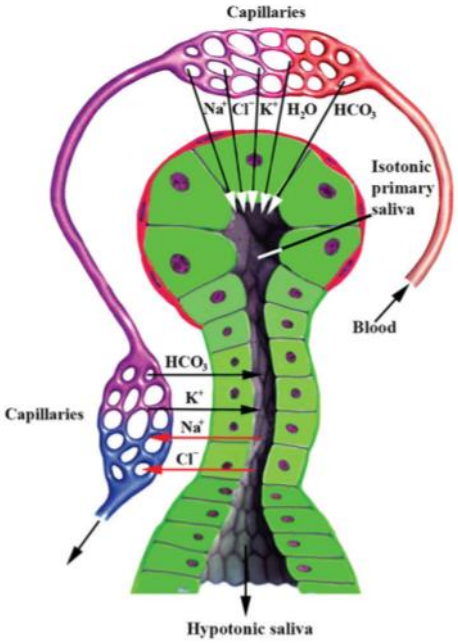


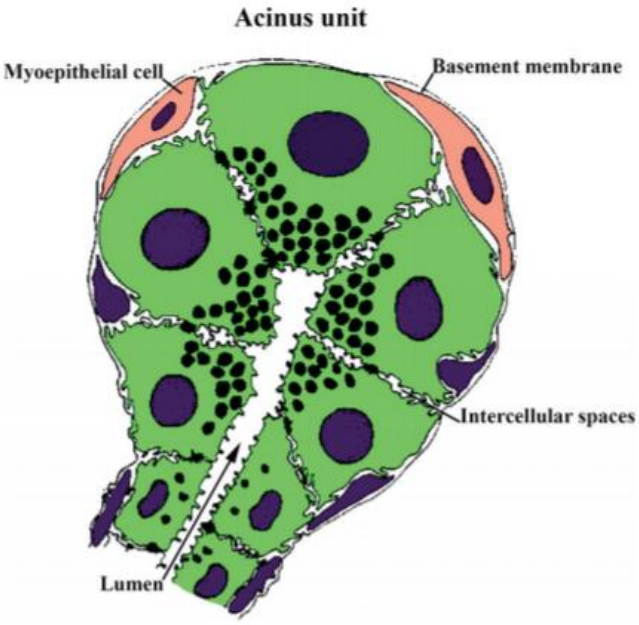


DEVELOPMENT OF LARGE SALIVARY GLANDS









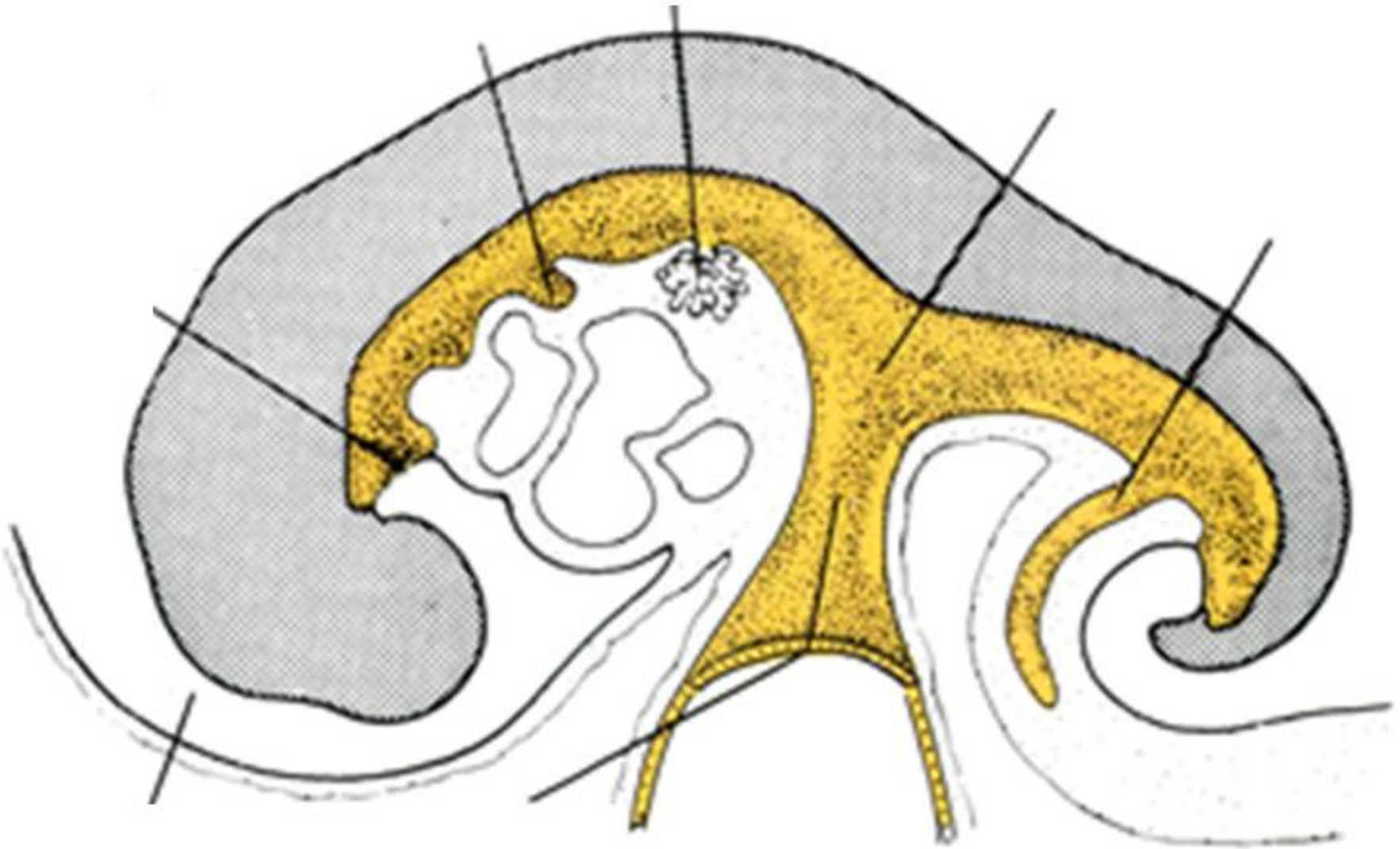
Further reading:

The Embryology of the Salivary Glands: An Update

P.M. Som and I. Miletich

Neurographics 2015 July/August; 5(4):167–177; www.neurographics.org

SUMMARY



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.

Thank you for attention

pvanhara@med.muni.cz

http://www.med.muni.cz/histology/education/