MUNI MED

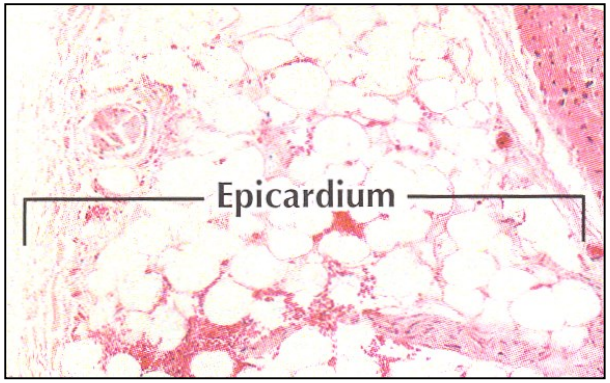
Ústav histologie a embryologie

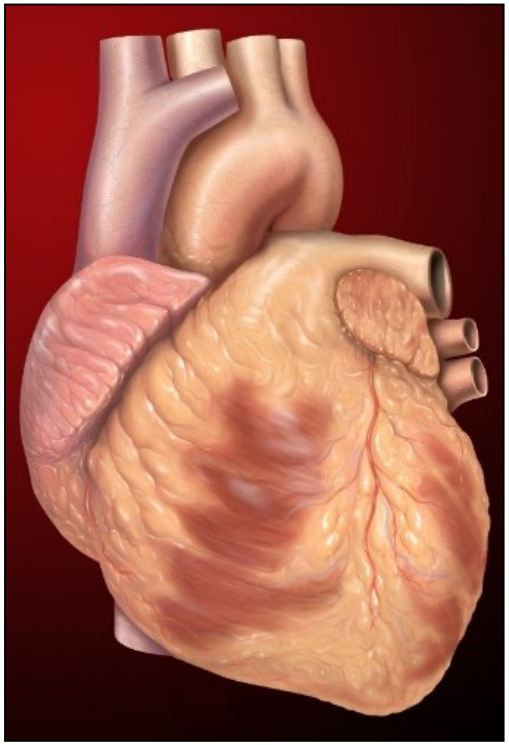
- **Tissue concept and classification**
- **Epithelial tissue**

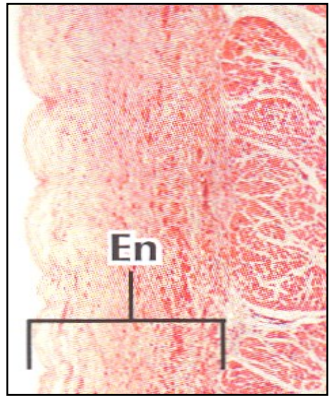
Petr Vaňhara

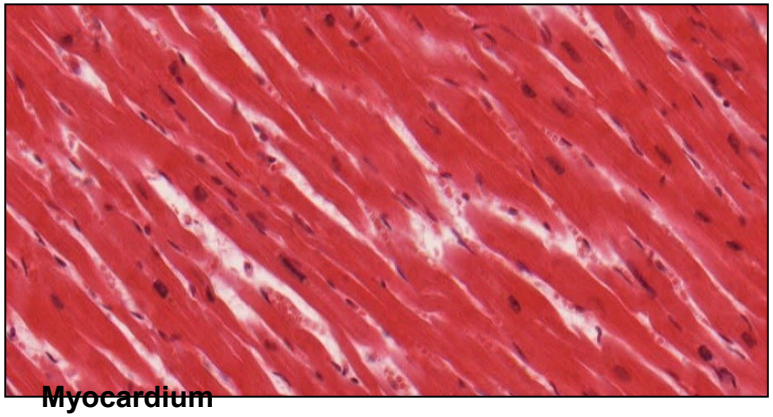
TISSUES AND ORGANS

- 6×10^{13} CELLS of 200 different types
- cells form functional, three-dimensional, organized aggregations of morphologically similar cells and their products and derivatives - TISSUES
- tissues constitute ORGANS and organ systems







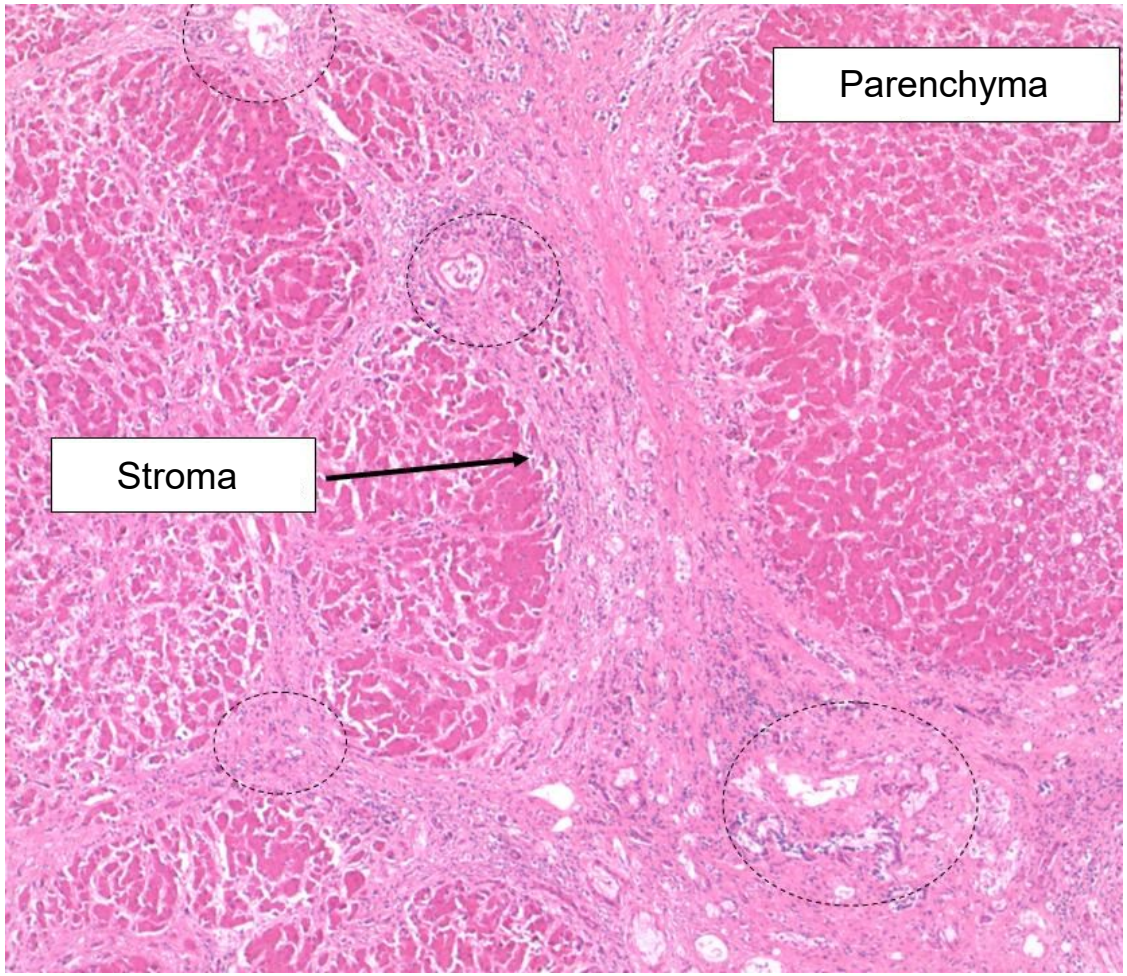


Myocardium

TISSUES AND ORGANS

Parenchyma: functional component of a tissue (liver, lung, pancreatic, kidney parenchyma)

Stroma: surrounding, supportive tissue



LIVER

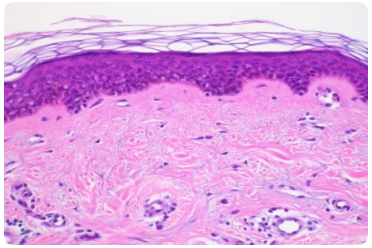
Parenchyma:
- Hepatocytes
- Sinusoids and adjacent structures

Stroma:
- Connective tissue and adjacent structures
- Vessels
- Nerves
- Bile ducts

CONTEMPORARY TISSUE CLASSIFICATION

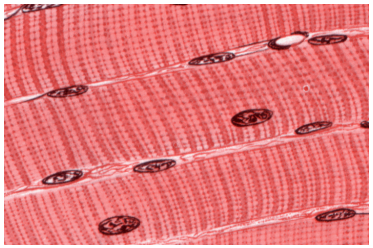
Based on morphology and function:

Epithelium



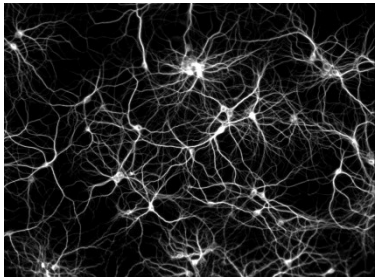
Continual, avascular layers of cells with different function, oriented to open space, with specific junctions and minimum of ECM and intercellular space.
Derivates of all three germ layers

Muscle



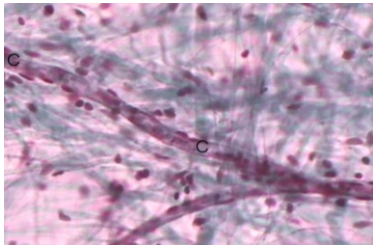
Myofibrils → contraction
Mesoderm – skeletal muscle, myocard, mesenchyme – smooth muscles
Rarely ectoderm (eg. m. sphincter a m. dilatator pupillae)

Nerve



Neurons and neuroglia
Reception and transmission of electric signals
Ectoderm, rarely mesoderm (microglia)

Connective

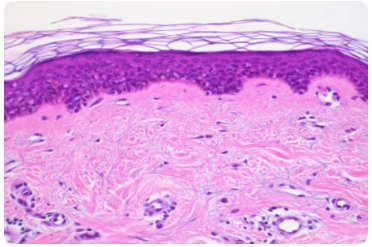


Dominant extracellular matrix
Connective tissue, cartilage, bone…
Mesenchyme

CONTEMPORARY TISSUE CLASSIFICATION

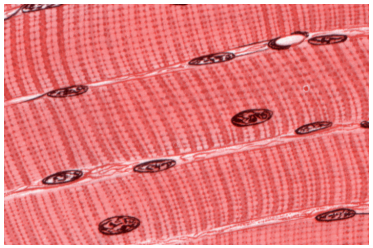
Based on morphology and function:

Epithelium



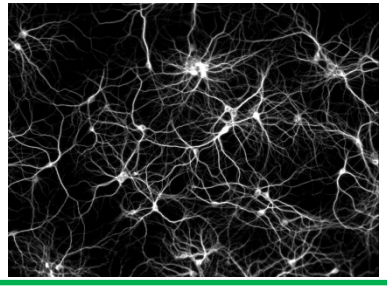
Continual, avascular layers of cells with different function, oriented to open space, with specific junctions and minimum of ECM and intercellular space.
Derivates of all three germ layers

Muscle



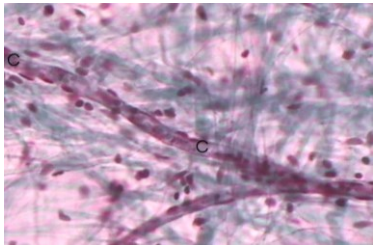
Myofibrils → contraction
Mesoderm – skeletal muscle, myocard, mesenchyme – smooth muscles
Rarely ectoderm (eg. m. sphincter a m. dilatator pupillae)

Nerve



Neurons and neuroglia
Reception and transmission of electric signals
Ectoderm, rarely mesoderm (microglia)

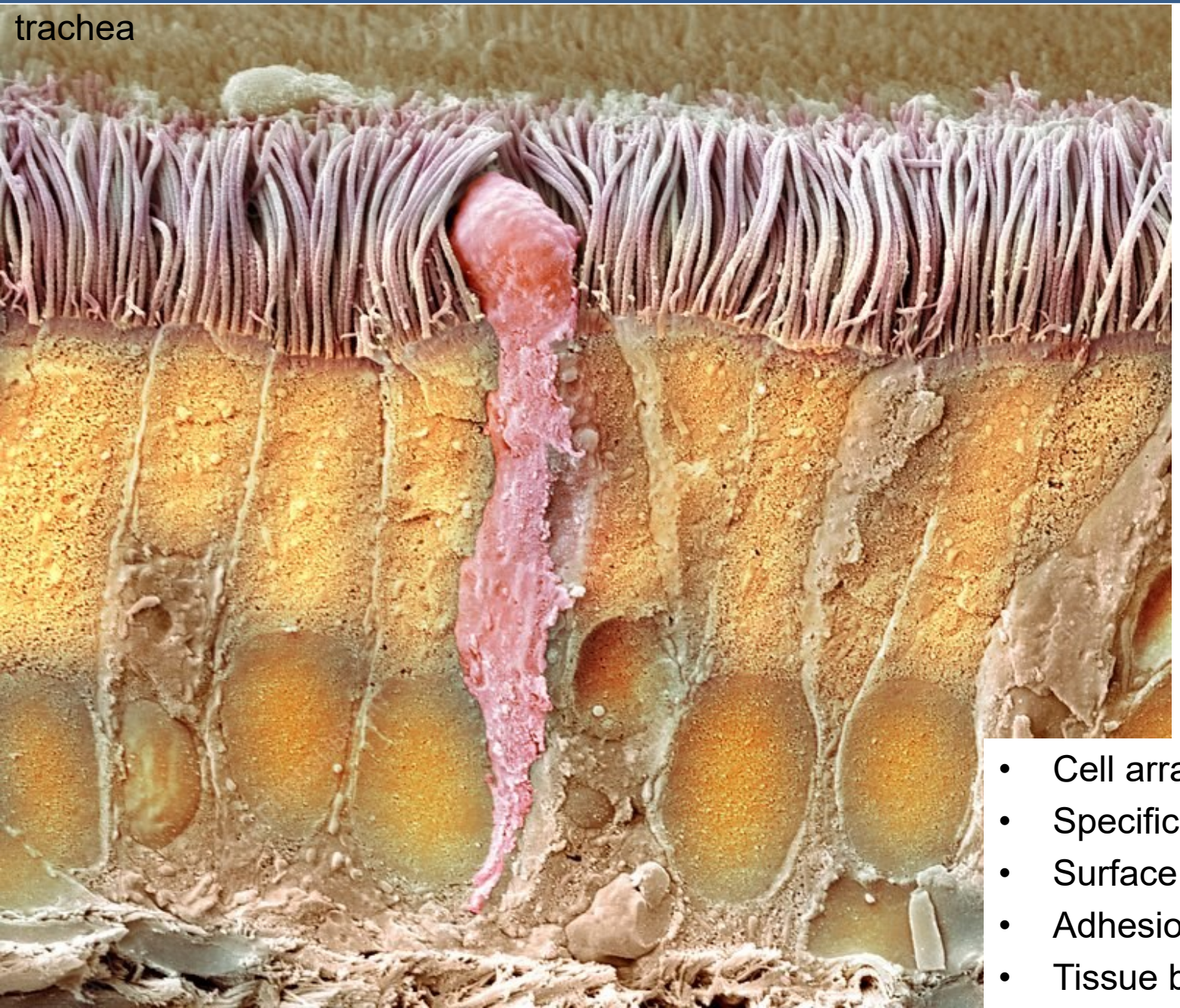
Connective



Dominant extracellular matrix
Connective tissue, cartilage, bone…
Mesenchyme

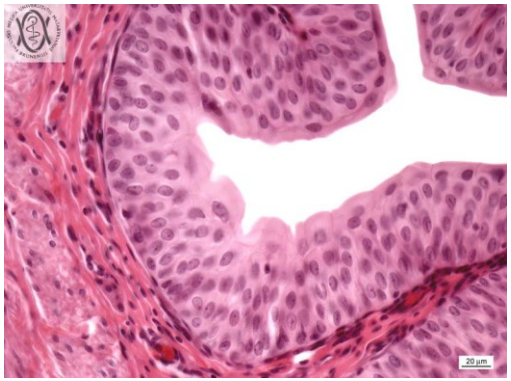
General characteristics

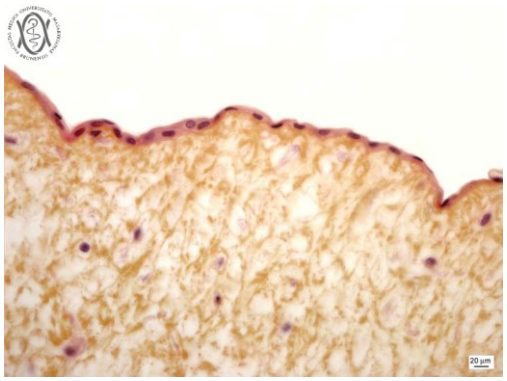
EPITHELIUM

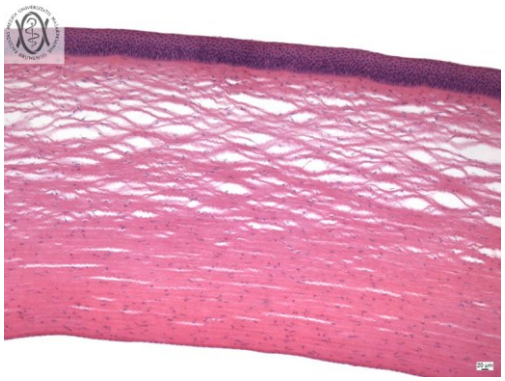


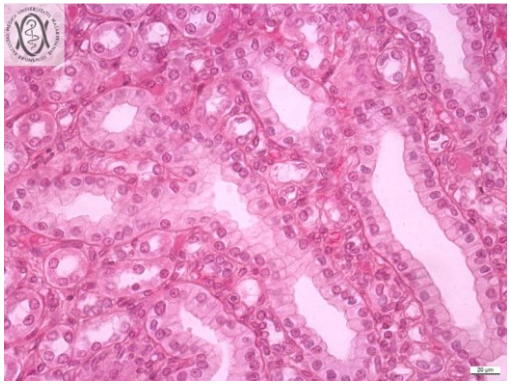
- Cell arrangement
- Specific morphology
- Surface modifications
- Adhesion
- Tissue barriers

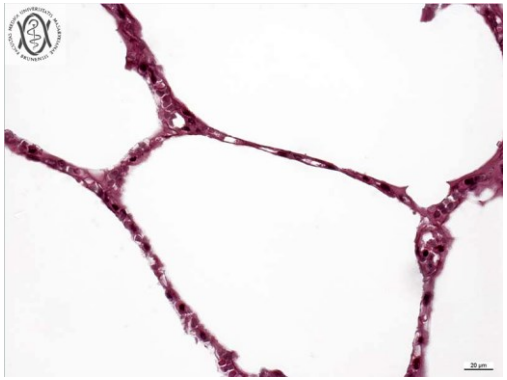
EPITHELIAL VARIABILITY IN HUMANS

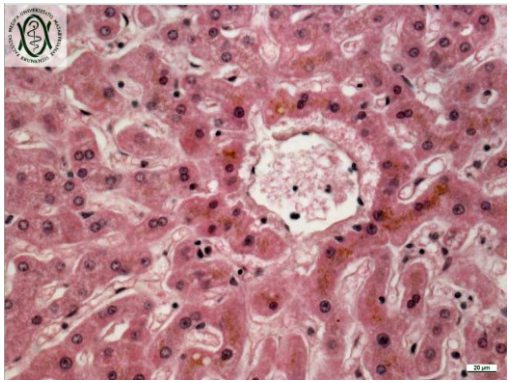


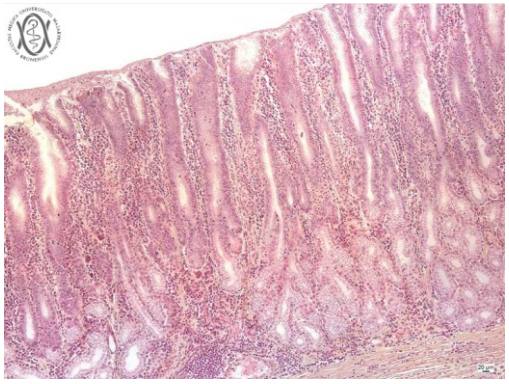


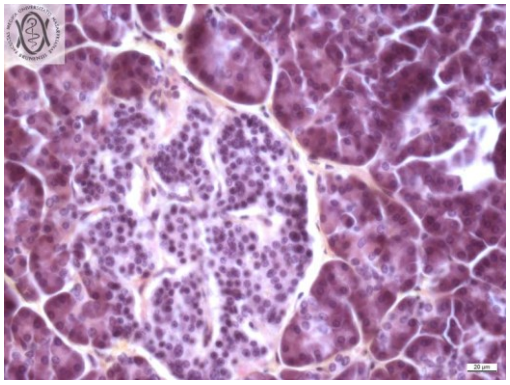










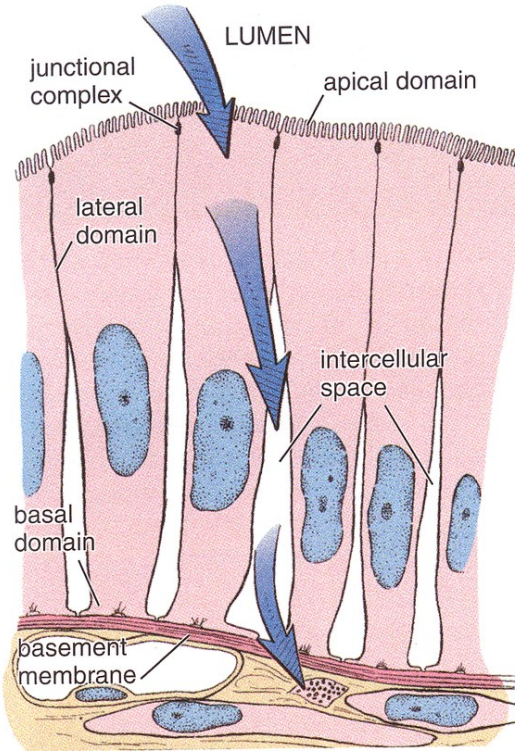


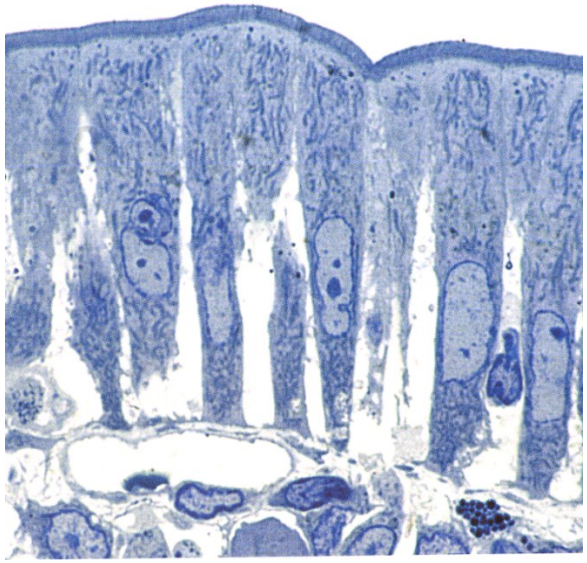
GENERAL CHARACTERISTICS OF EPITHELIAL TISSUE

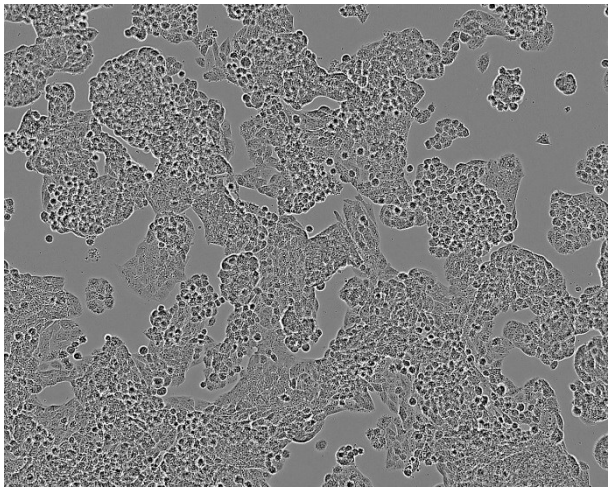
- **Avascular** (without blood supply) – nutrition by diffusion from a highly vascular and innervated area of loose connective tissue (*lamina propria*) just below the basement membrane

- **Highly cellular** – cohesive sheet or groups of cells with no or little extracellular matrix

- Typical **morphology** and **cell connections**





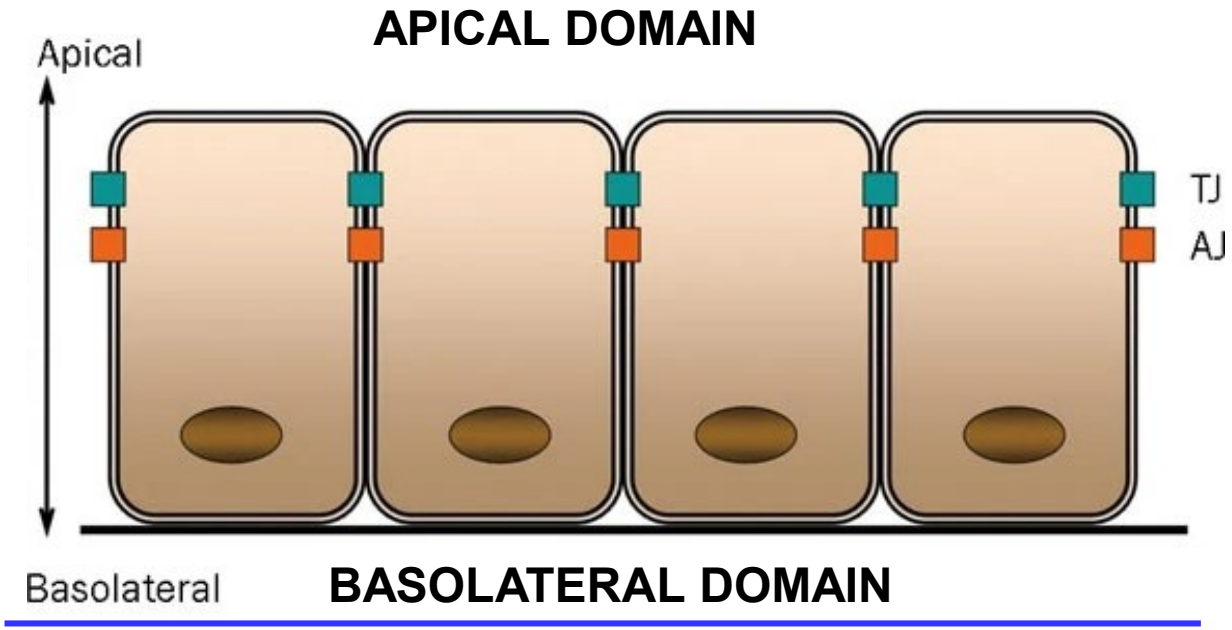


CELL POLARITY

EPITHELIUM

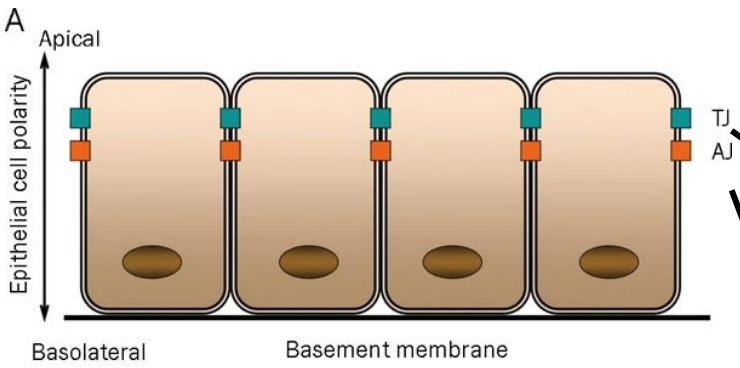
vs.

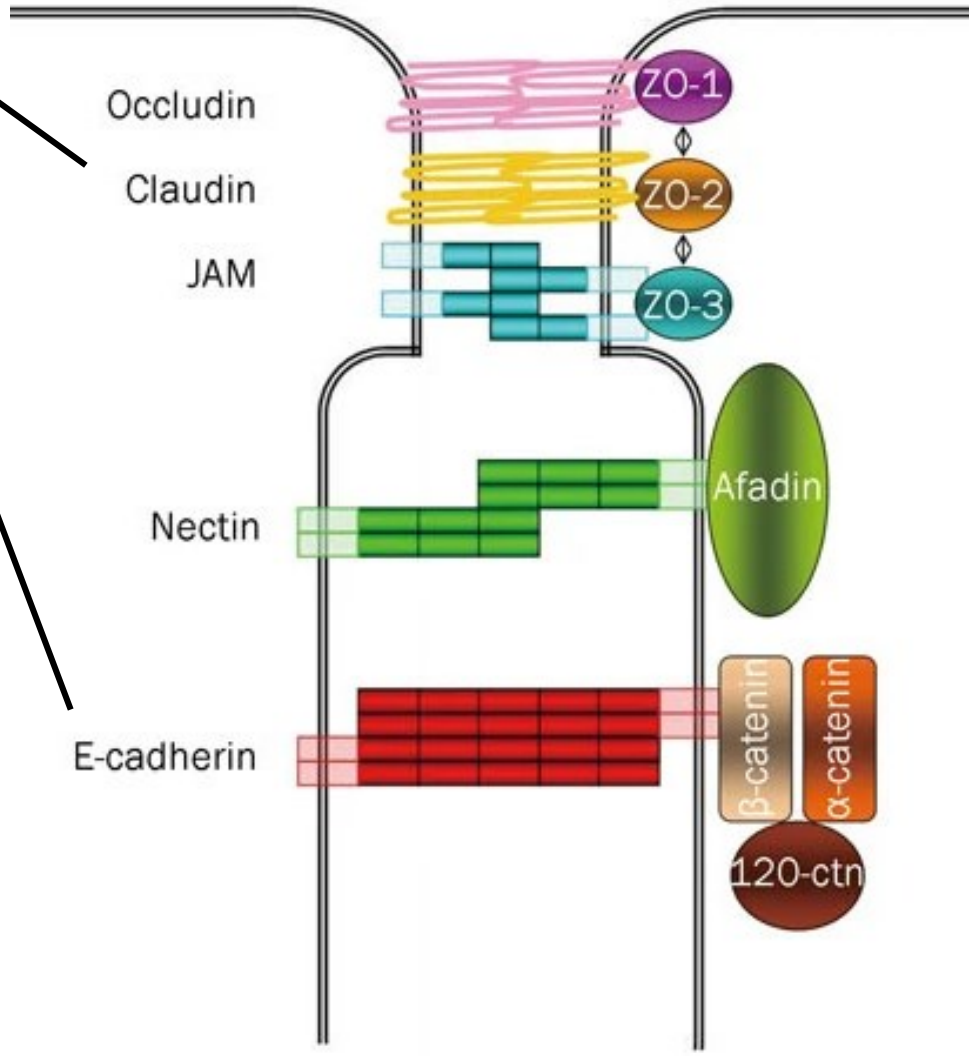
MESENCHYME



https://doi.org/10.1038/aps.2011.20

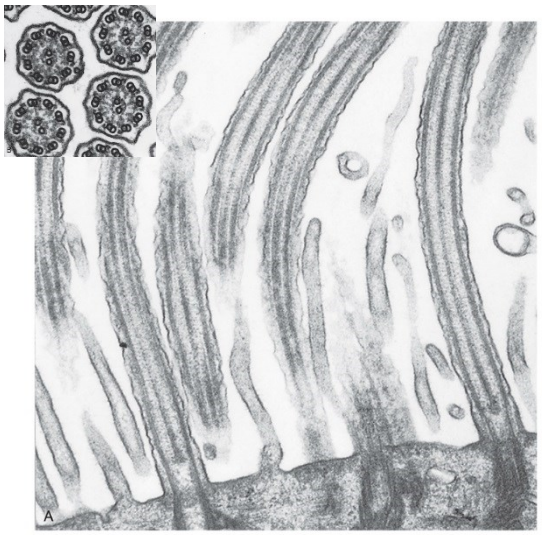
CELL POLARITY



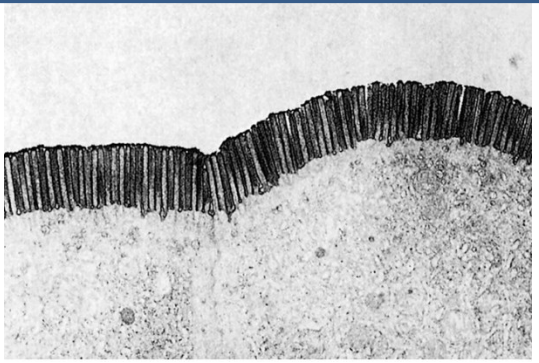


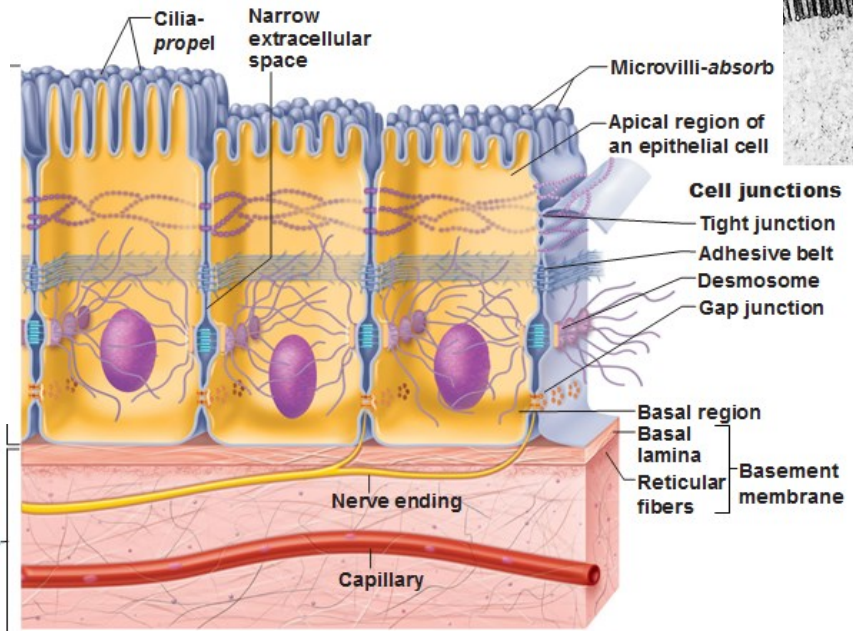
https://doi.org/10.1038/aps.2011.20

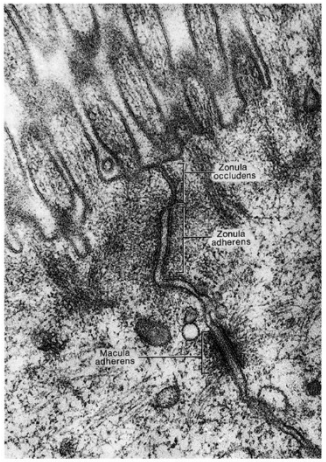
HALLMARKS OF A TYPICAL EPITHELIAL CELL

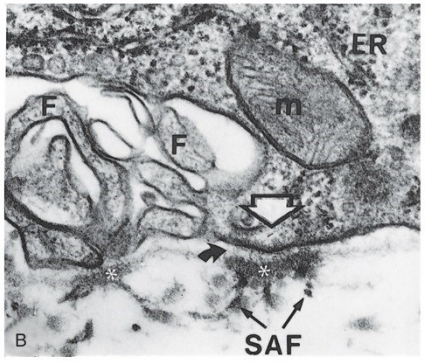


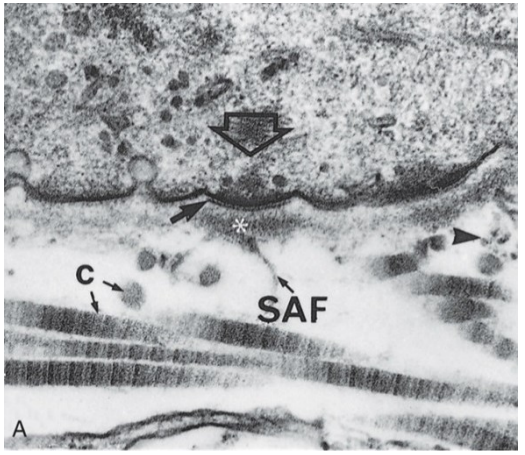
From Leeson TS, Leeson CR, Paparo AA. *Text/Atlas of Histology*. Philadelphia: WB Saunders; 1988.





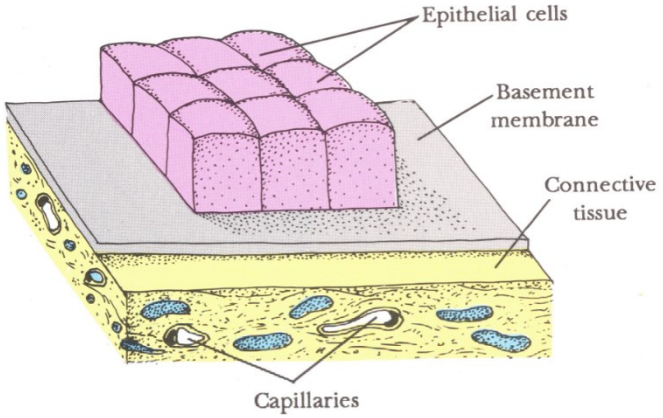


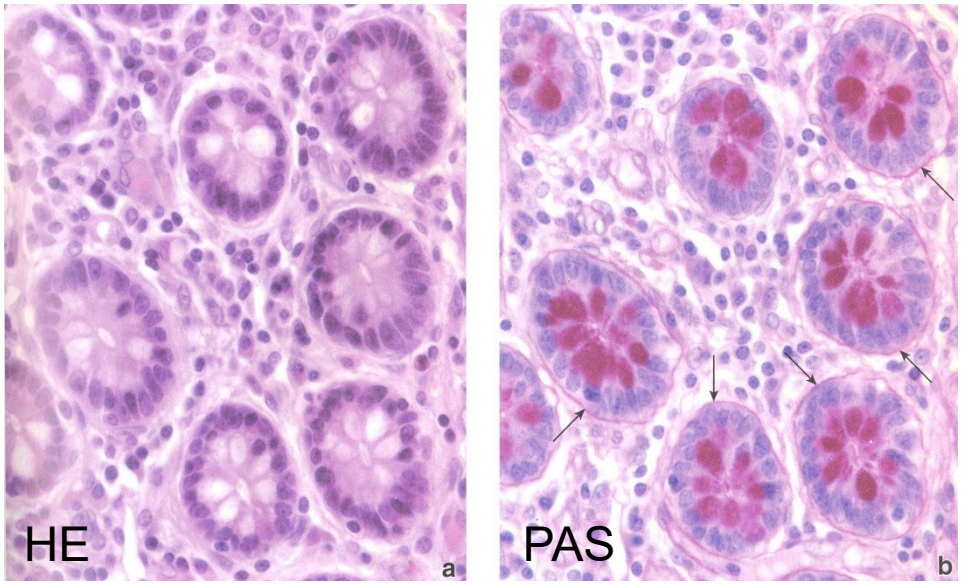


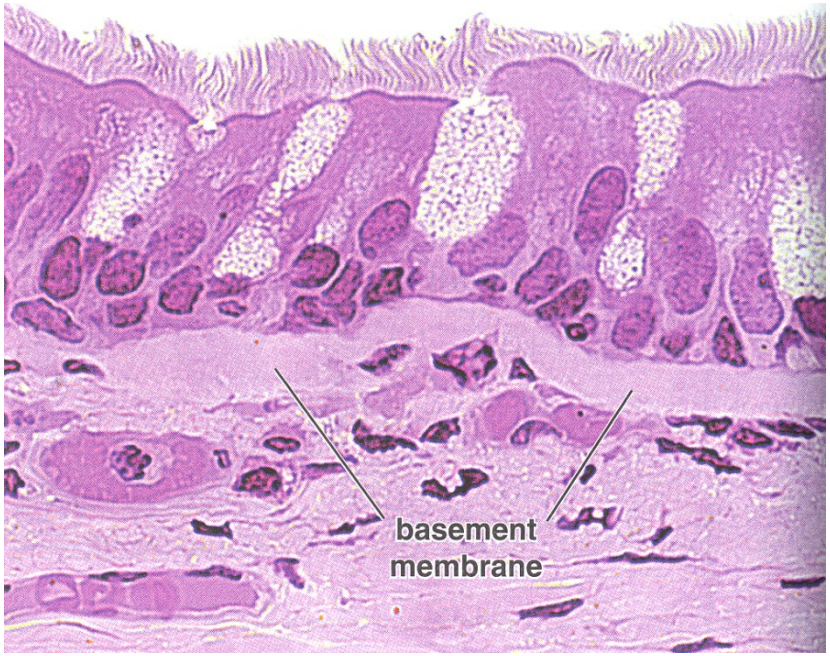


BASEMENT MEMBRANE

- Attachment of epithelium to underlying tissues
- Selective filter barrier between epithelial and connective tissue
- Communication, differentiation

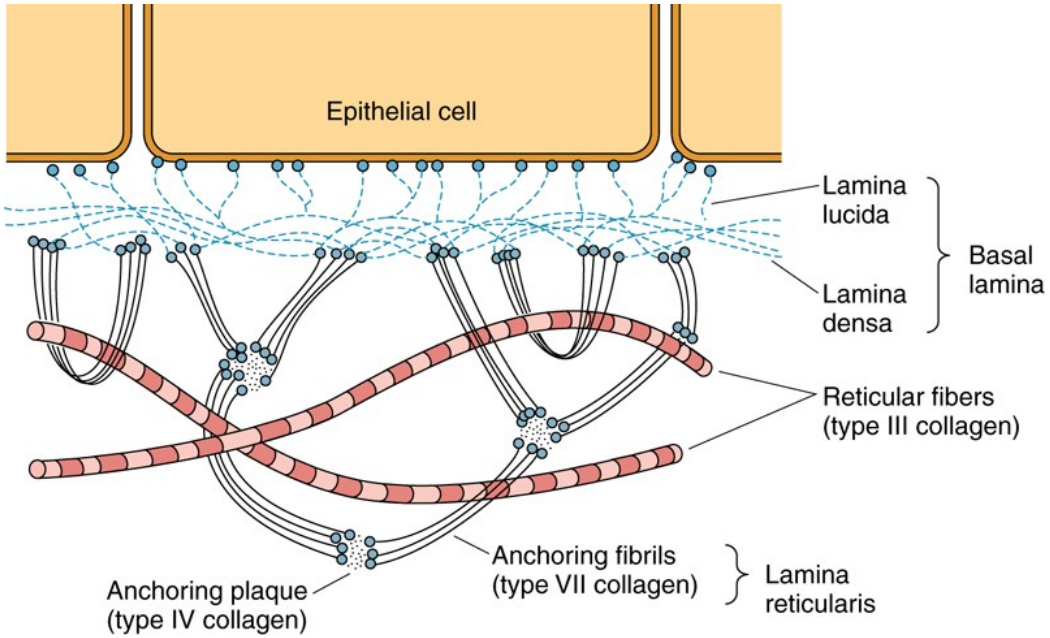


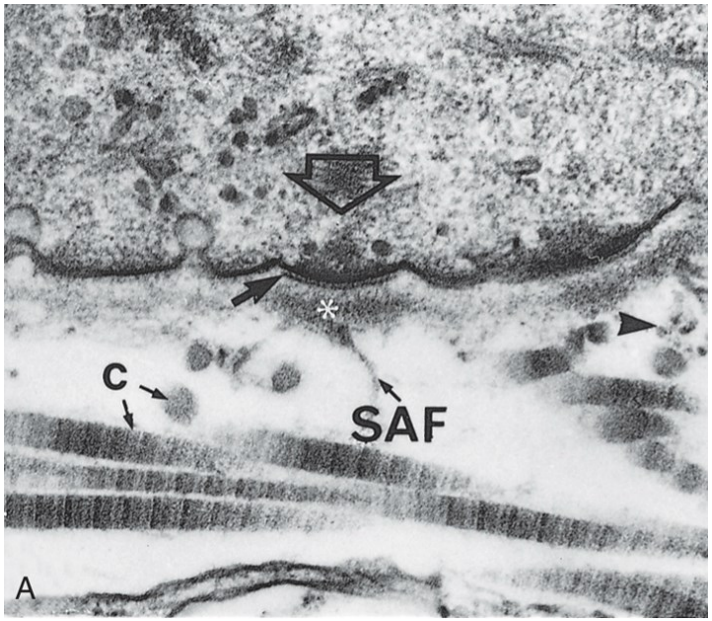




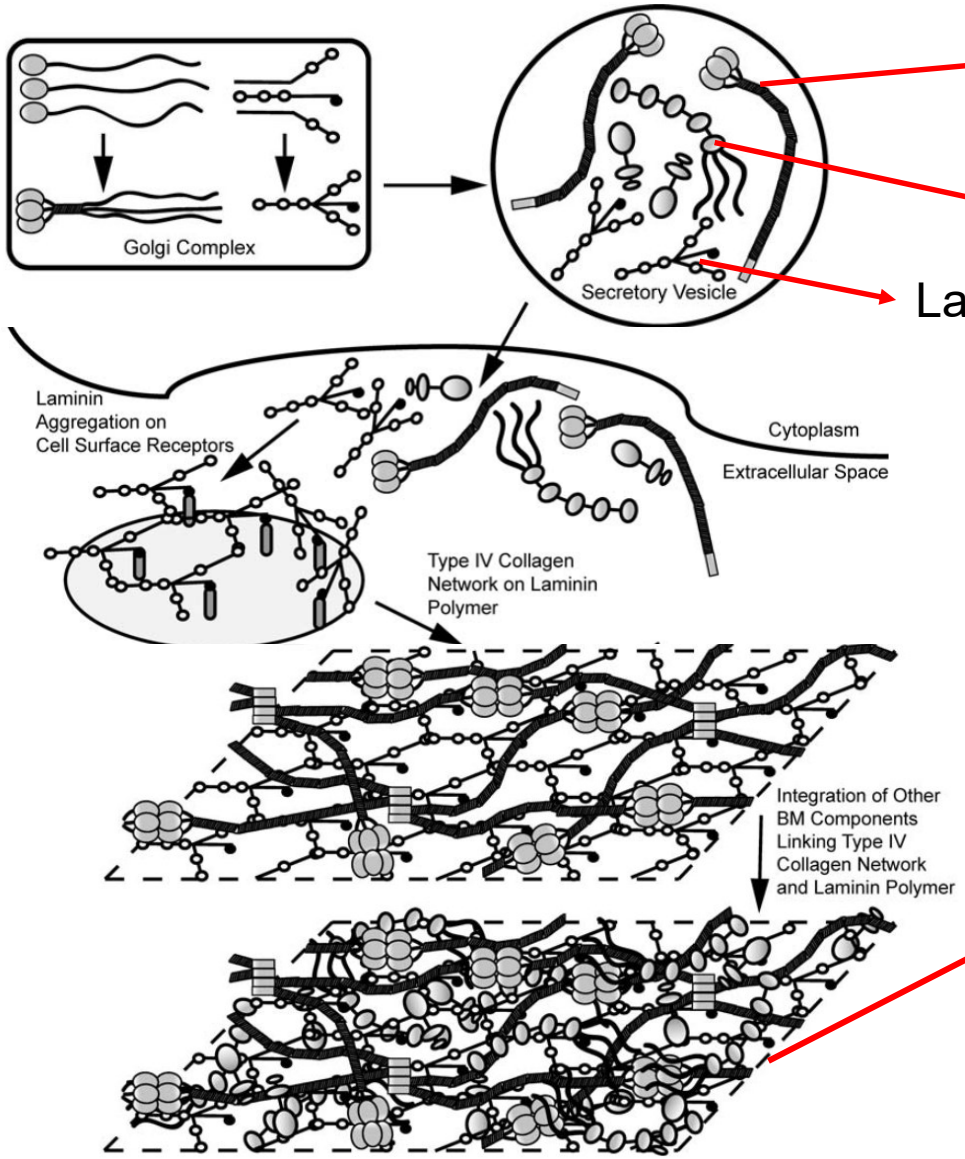
BASAL LAMINA vs. BASEMENT MEMBRANE

- 50-100nm
- Glycosaminoglycans – heparansulfate
- Laminin, collagen III, IV, VI,
- Nidogen/entactin
- Perlecan
- Proteoglycans





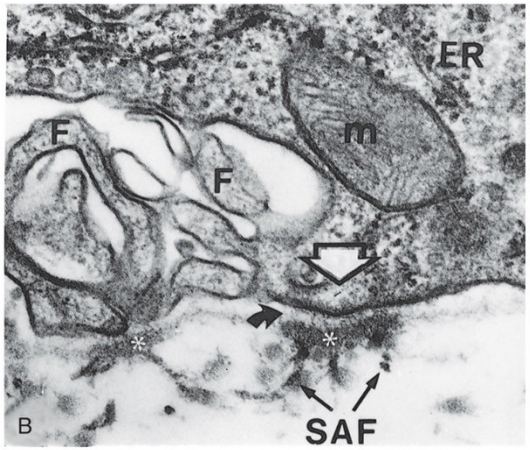
BASEMENT MEMBRANE

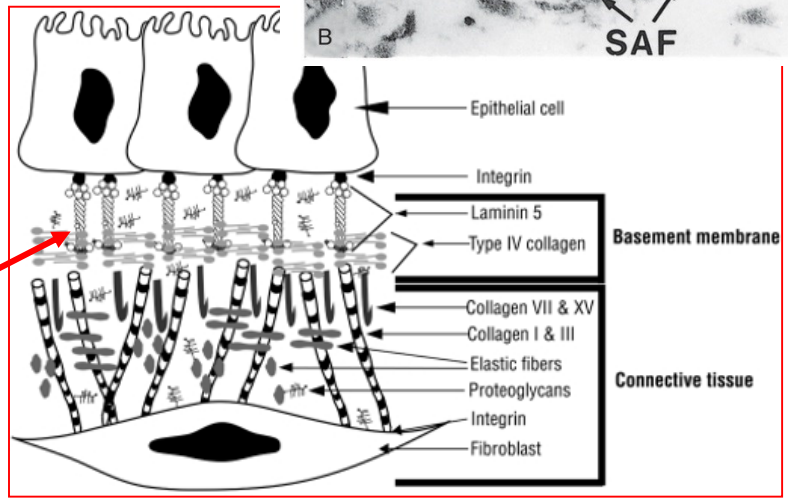


Kolagen IV

Perlecan,
Nidogen/Entactin

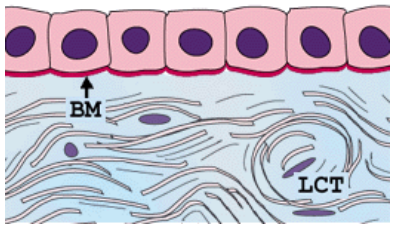
Laminin



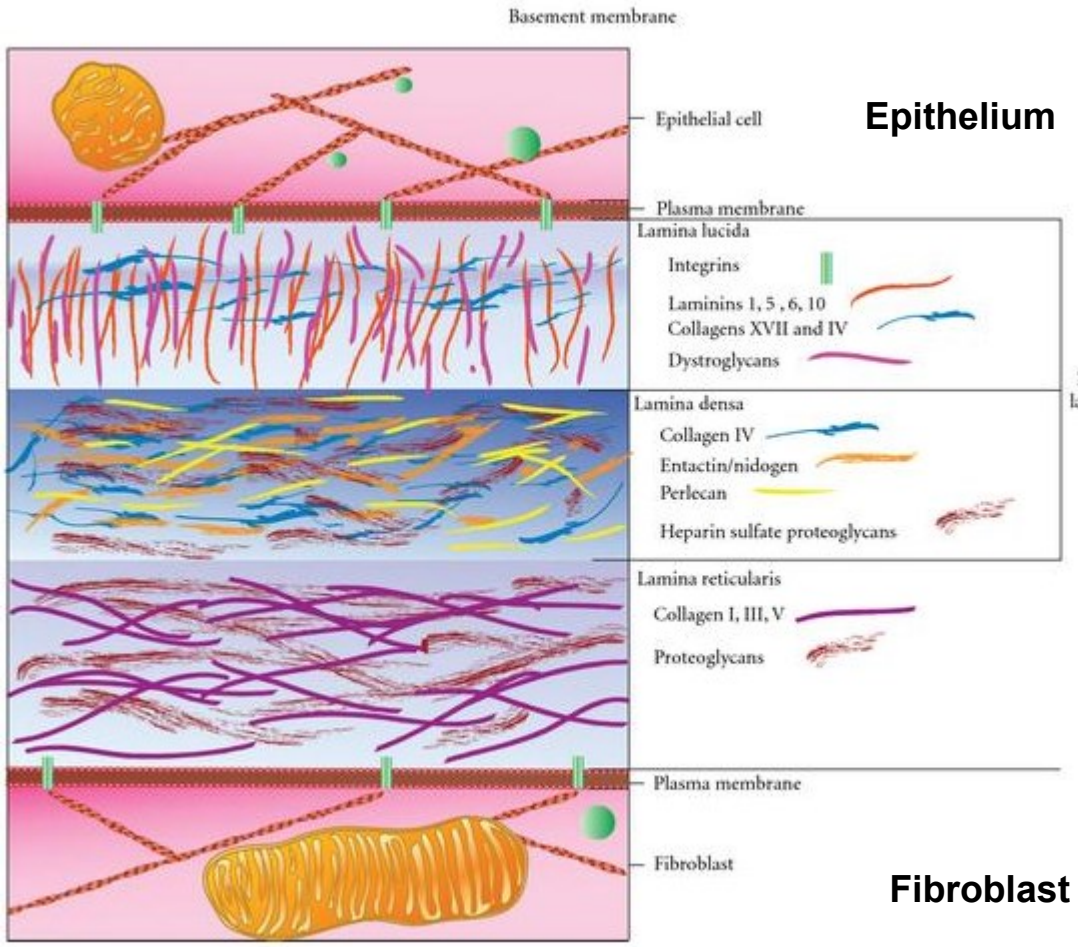


Dunsmore SE, Chambers RC, Laurent GJ. 2003. Matrix Proteins. Figure 2.1.2. In: Respiratory Medicine, 3rd ed. London. Saunders, p. 83; Dunsmore SE, Laurent GJ. 2007. Lung Connective Tissue. Figure 40.1. In: Chronic Obstructive Pulmonary Disease: A Practical Guide to Management, 1st ed. Oxford. Wiley-Blackwell, p. 467.

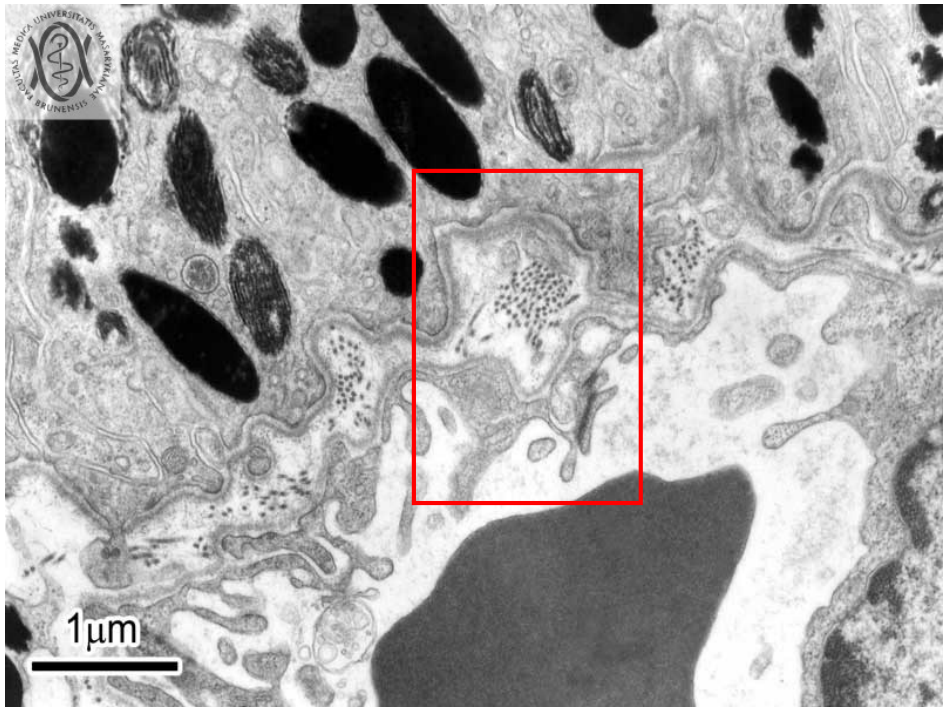
ARCHITECTURE OF BASEMENT MEMBRANE

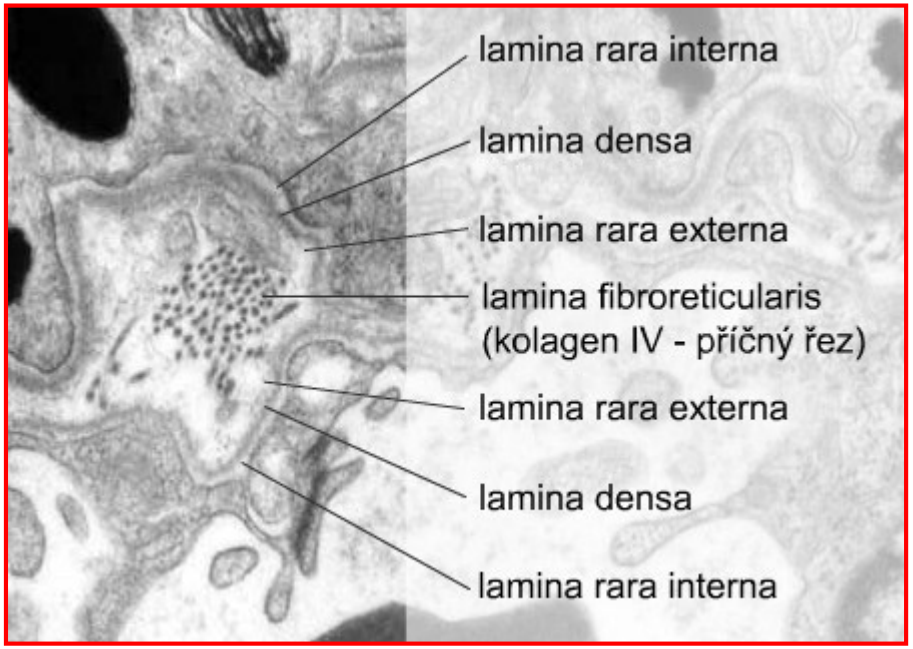


BM



MODIFICATIONS OF BASEMENT MEMBRANE





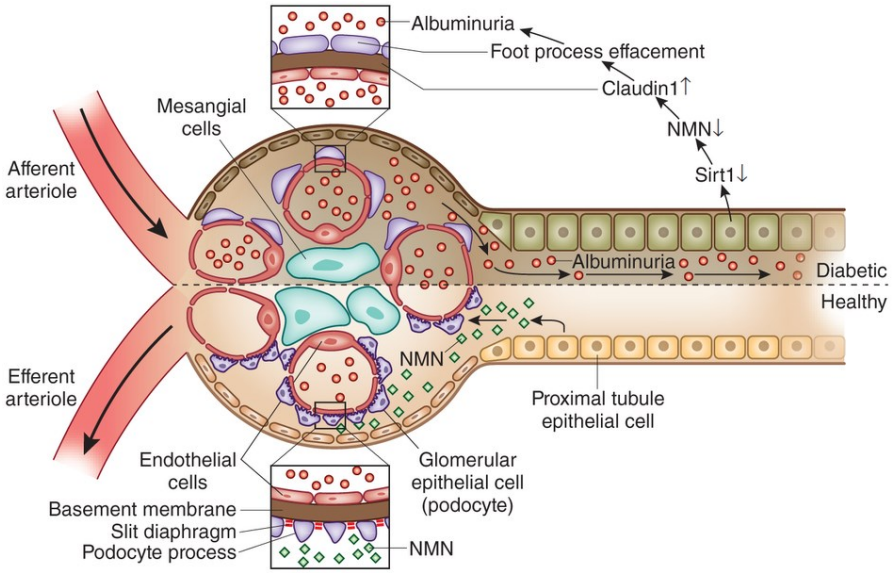
- **Two basic layers of basement membrane**
  - lamina basalis
  - lamina fibroreticularis

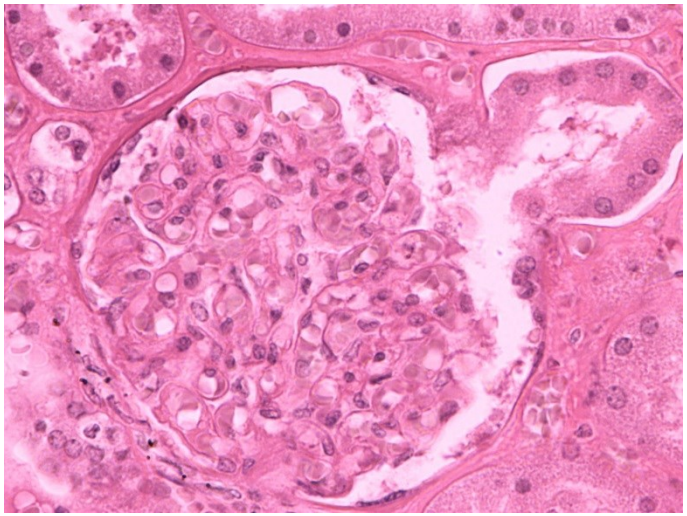
- **Contact of two epithelia (or with endothelium)**
  - fusion of laminae basales
    - lamina densa
    - lamina rara (lucida) ext. et int.

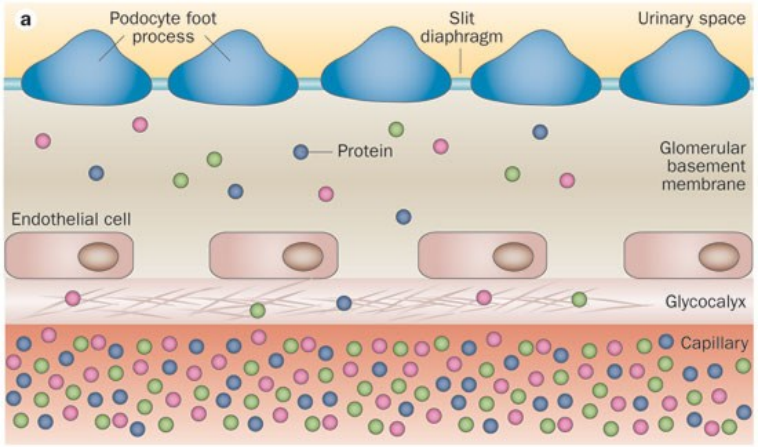
- **Tissue specific modifications**
- Descemet membrane (cornea)
- Glomerular BM (Bowman's capsule)
- Part of Bruch's membran of retina

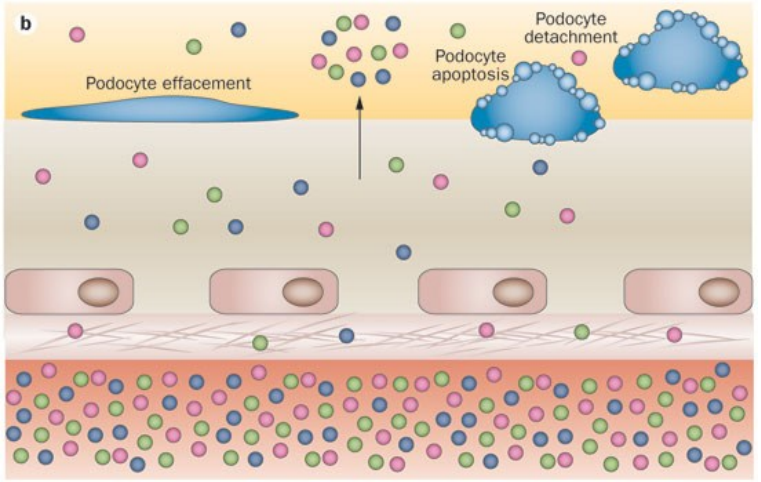
…

BASEMENT MEMBRANE IN CORPUSCULUM RENIS





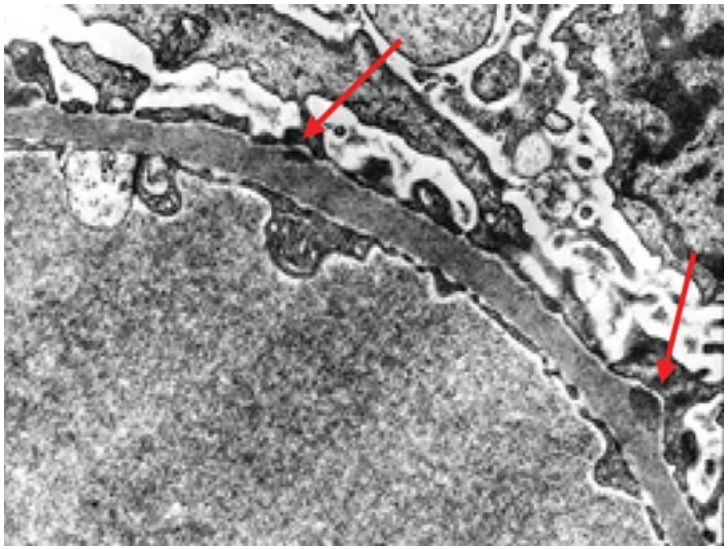


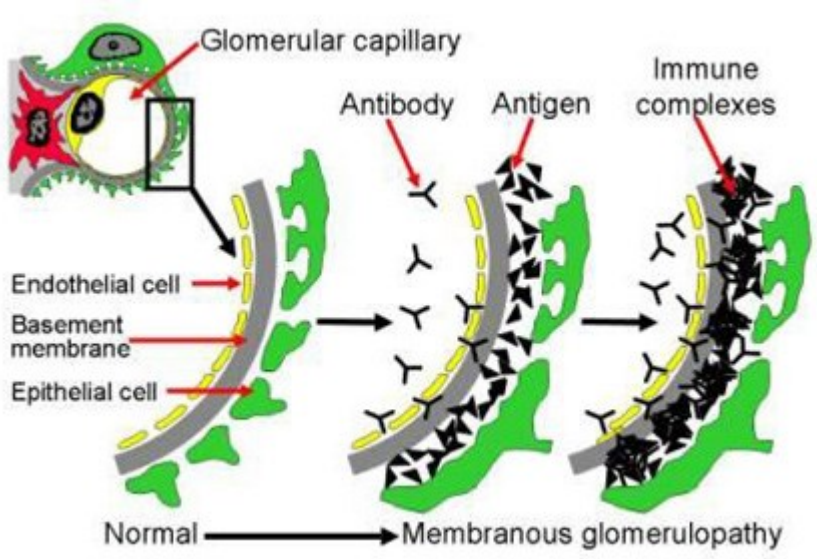


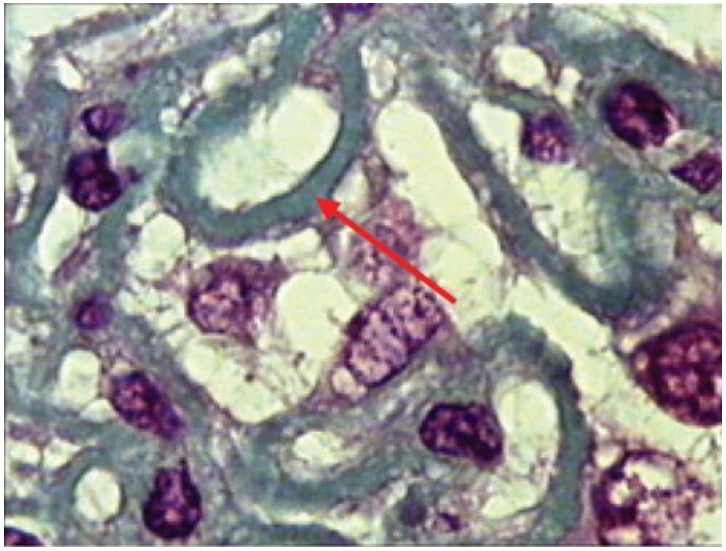
BASEMENT MEMBRANE IN CORPUSCULUM RENIS

- **Clinical correlations – *membranous glomerulonefritis***

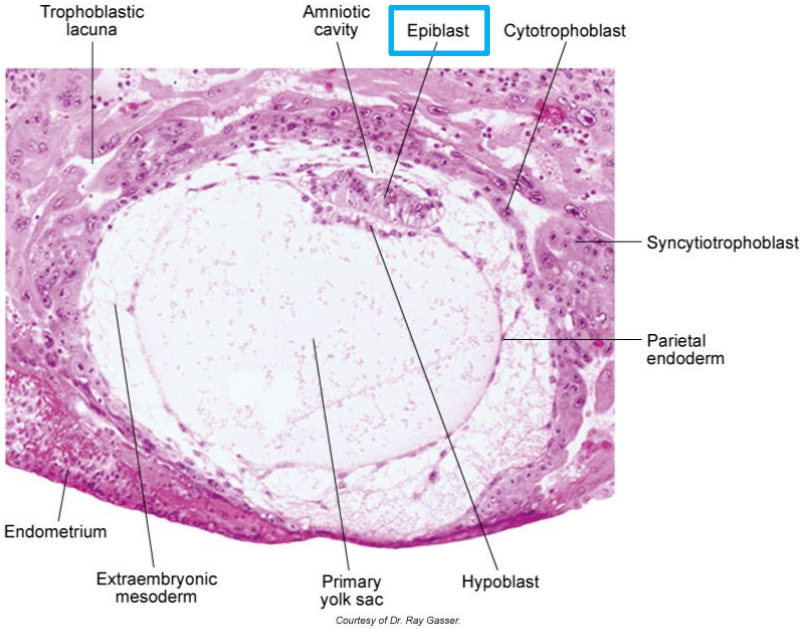
- circulationg Abs bind to BM of capillary wall
- complement (C5b-C9) attacks glomerular endothelial cells
- filtation barrier compromised
- proteinuria, edema, hematouria, renal failure







EMBRYONIC ORIGIN OF EPITHELIAL TISSUE



Courtesy of Dr. Ray Gasser.

Fig. 5-3. Digital photomicrograph of a 12-day human embryo (Carnegie No. 7700) taken just as implantation within the endometrium is completed.

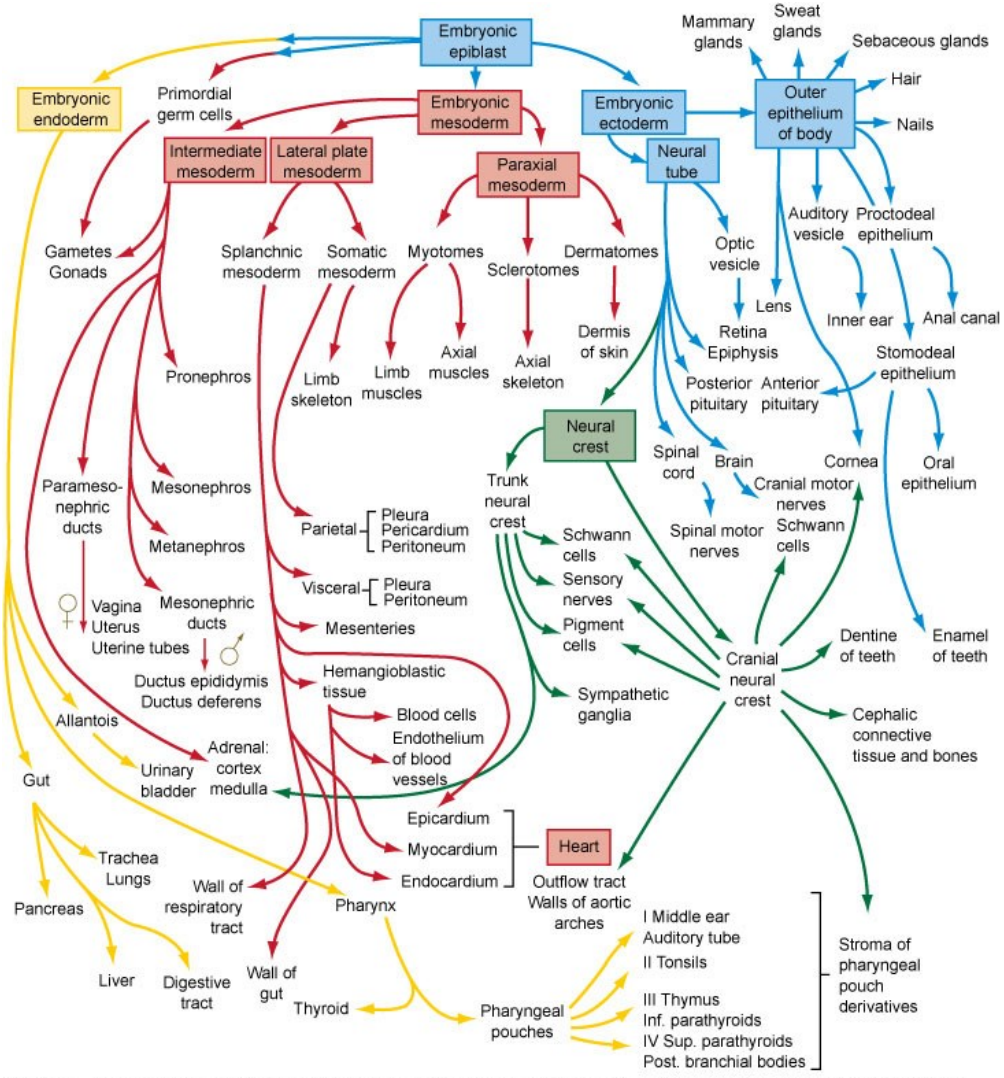


Fig. 6-27. **Flow chart showing the formation of the organs and tissues of the embryo from the fundamental germ layers.** The *arrows* are color-coded according to the germ layer of origin of the structure (see Fig. 4-1 for color code).

EMBRYONIC ORIGIN OF EPITHELIAL TISSUE

- **derived from all three germ layers**

Germ layer	Epithelial derivatives
Ectoderm	1. Epidermis (stratified squamous keratinized epithelium) 2. Sweat glands and ducts (simple and stratified cuboidal epithelium) 3. Oral cavity, vagina, anal canal (stratified squamous non-keratinized epithelium)
Mesoderm	1. Endothelium of blood vessels (simple squamous epithelium) 2. Mesothelium of body cavities (simple squamous epithelium) 3. Urinary and reproductive passages (transitional, pseudostratified and stratified columnar epithelium, simple cuboidal and columnar epithelium)
Endoderm	1. Esophagus (stratified squamous non-keratinized epithelium) 2. GIT (simple columnar epithelium) 3. Gall bladder (simple columnar epithelium) 4. Solid glands (liver, pankreas) 5. Respiratory passages (ciliated pseudostratified columnar epithelium, ciliated simple columnar epithelium, cuboidal, squamous epithelium) 6. Part of urinary system (cloaca-derived)

CLASSIFICATION OF EPITHELIAL TISSUE

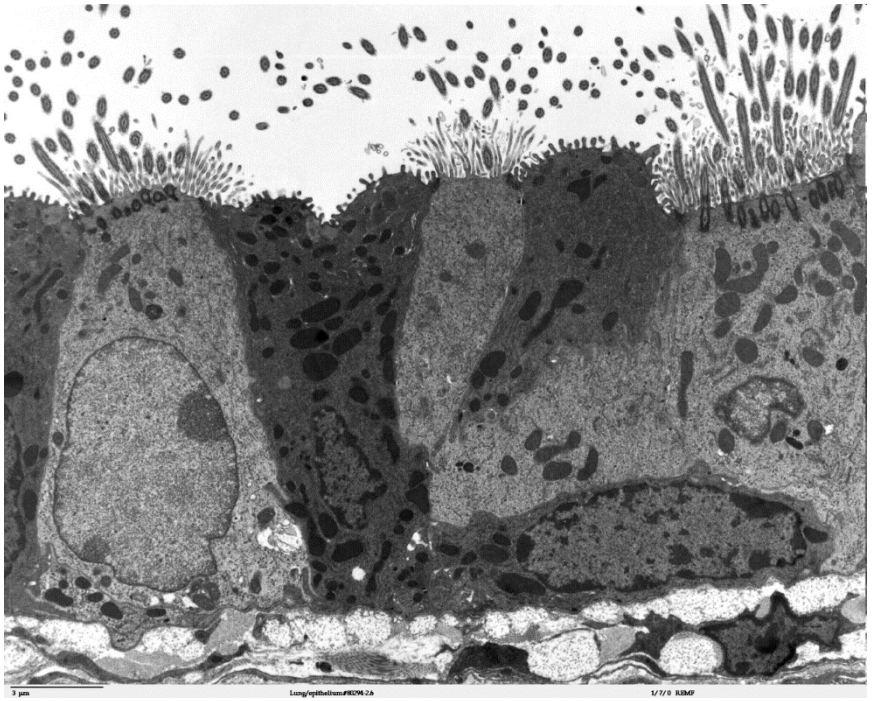
According to

1) morphology

- Covering (sheet) epithelium
- Trabecular epithelium
- Reticular epithelium

2) function

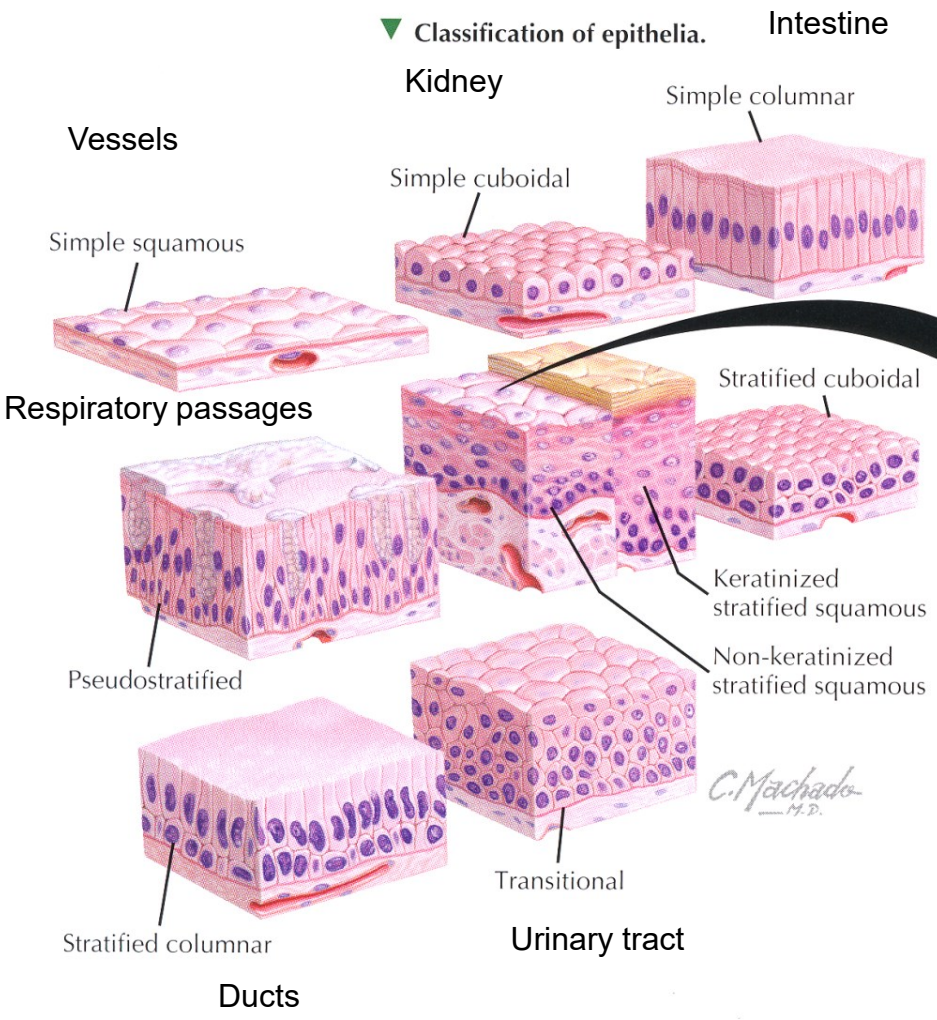
- Covering
- Glandular
- Resorption
- Sensory
- Respiratory
- Alveolar
- Germinal
- ...

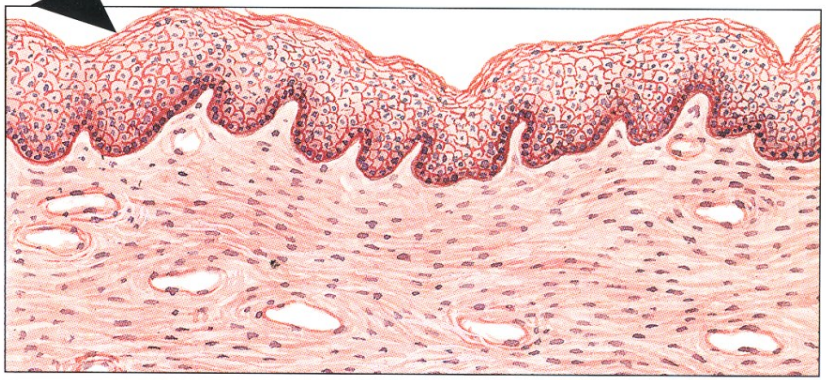


Classification by morphology

CLASSIFICATION OF EPITHELIAL TISSUE

1) Covering (sheet) epithelia

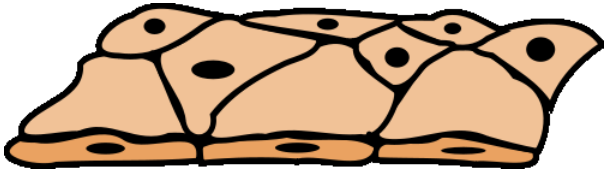




▲ **Schematic of nonkeratinized stratified squamous epithelium as seen with the light microscope.** The epithelium acts as a protective barrier and is typical of wet surfaces—linings of the oral cavity, esophagus, anal canal, part of the urethra, and vagina. It also covers the cornea.

CLASSIFICATION OF EPITHELIAL TISSUE

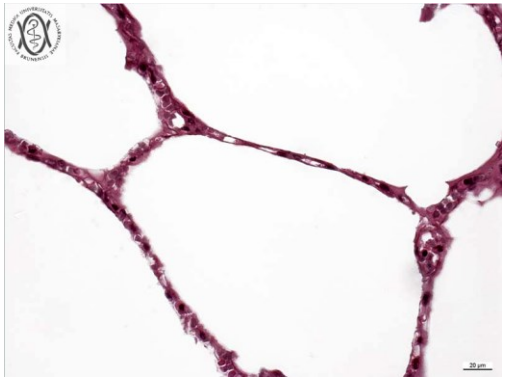
▪ Simple squamous epithelium



– Single layer of flat cells with central flat nuclei

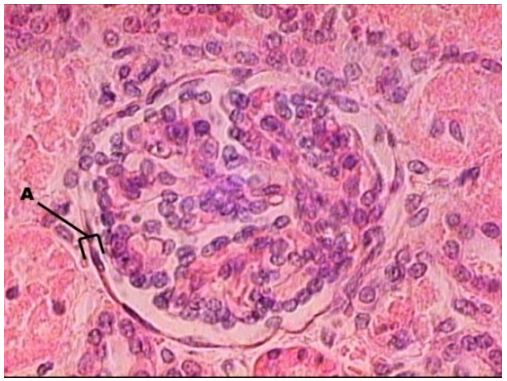
– Capillaries
– Lung alveolus
– Glomerulus in renal corpuscle

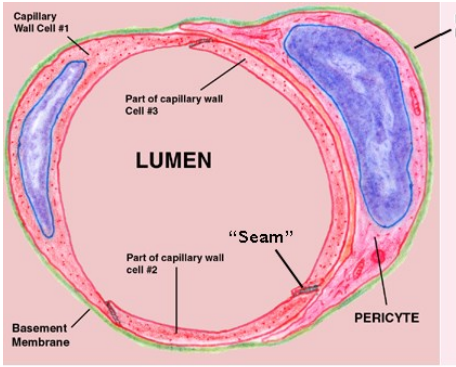
Selective permeabilty



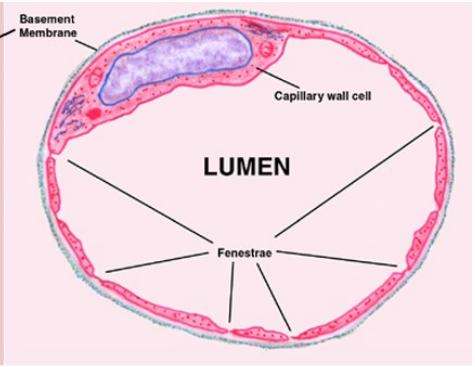
Endothelium
heart, blood, and lymphatic vessels.

Mesothelium
serous membranes - body cavities





Closed or Continuous Capillary



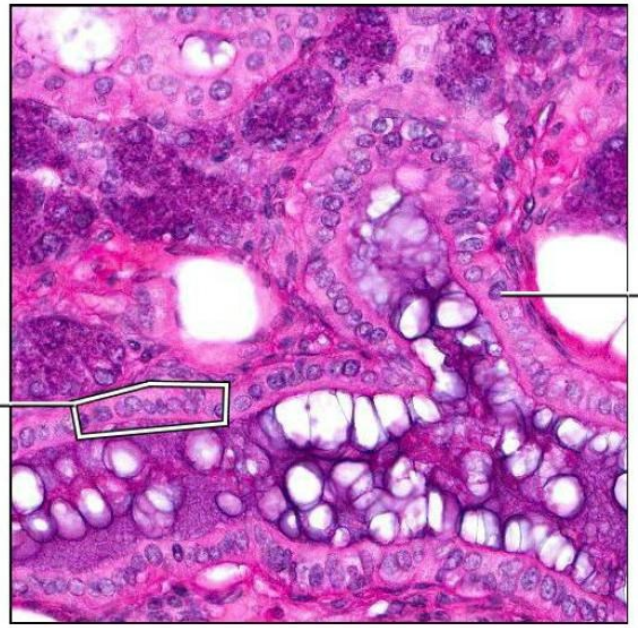
Fenestrated Capillary

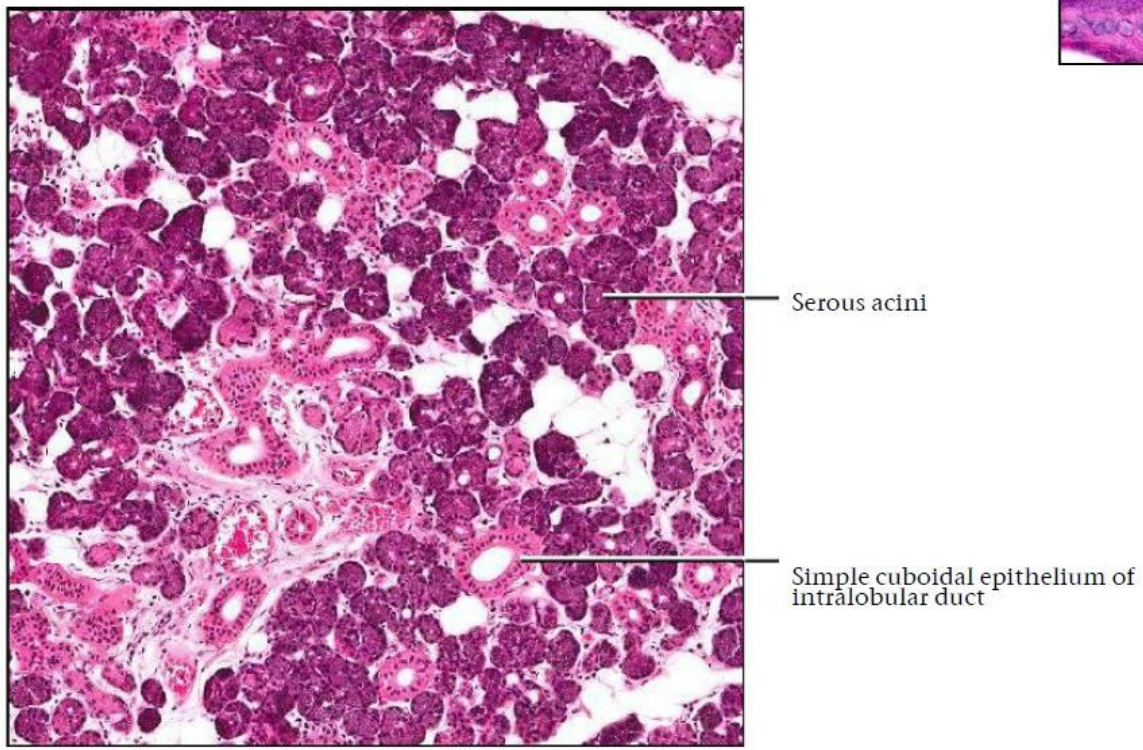
CLASSIFICATION OF EPITHELIAL TISSUE

CLASSIFICATION OF EPITHELIAL TISSUE

Simple cuboidal epithelium

- Single layer of cuboidal cells with large, spherical central nuclei
- Secretion or resorption



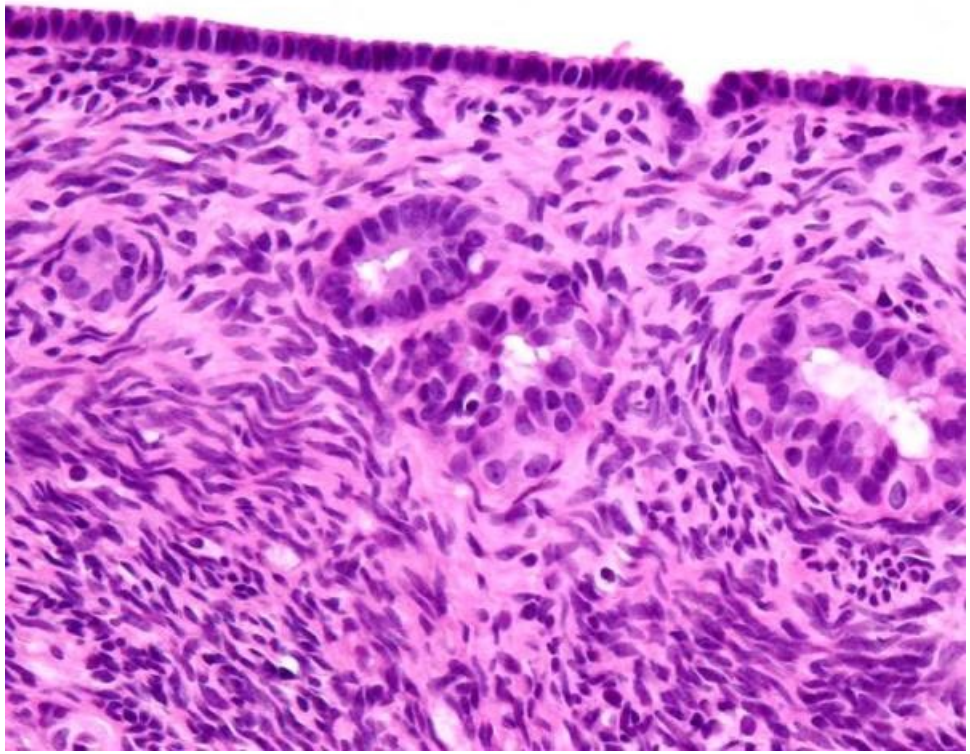


Examples:

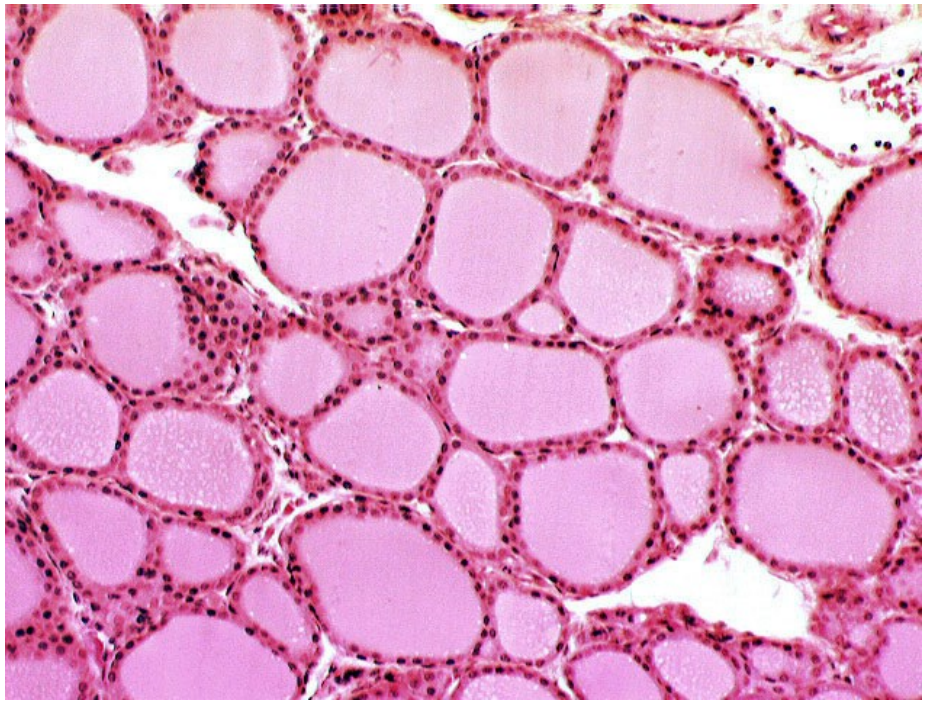
- Ovarian surface epithelium
- Renal tubules
- Thyroid
- Secretion acini

CLASSIFICATION OF EPITHELIAL TISSUE

Ovarian surface epithelium



Thyroid follicles

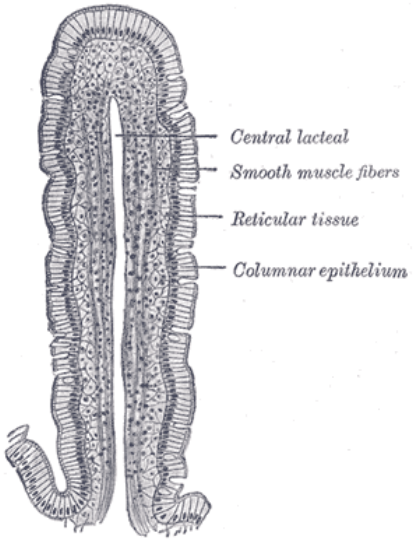


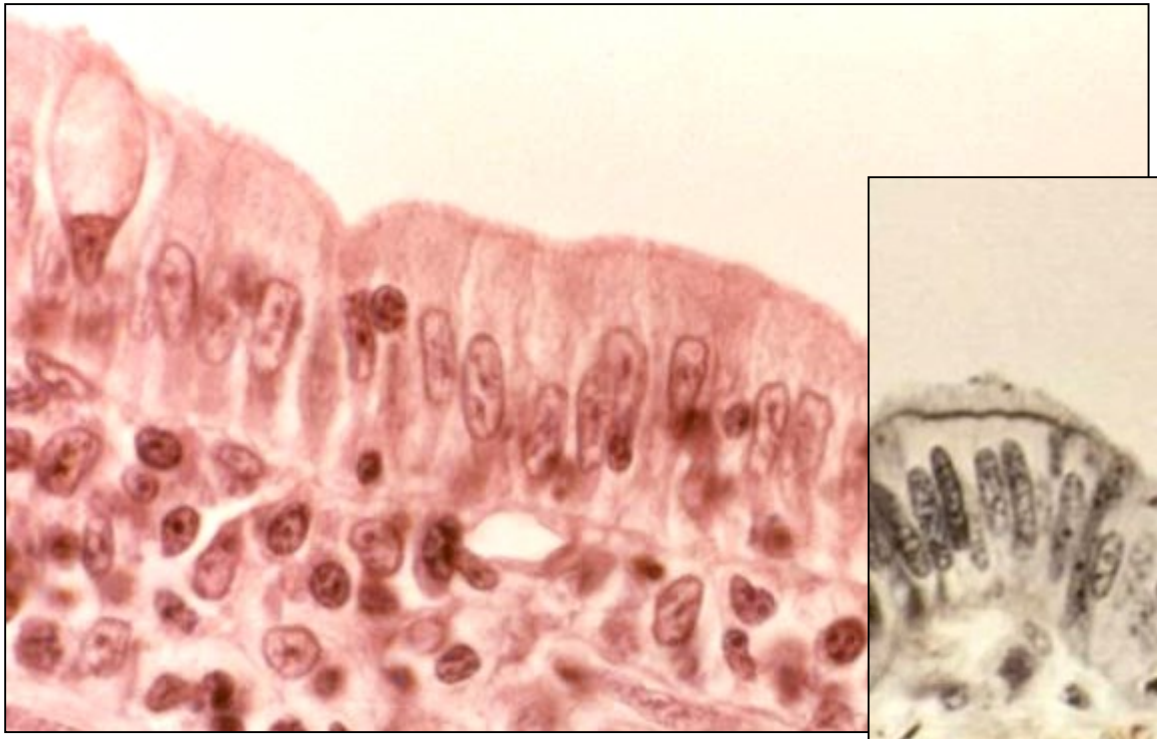
CLASSIFICATION OF EPITHELIAL TISSUE

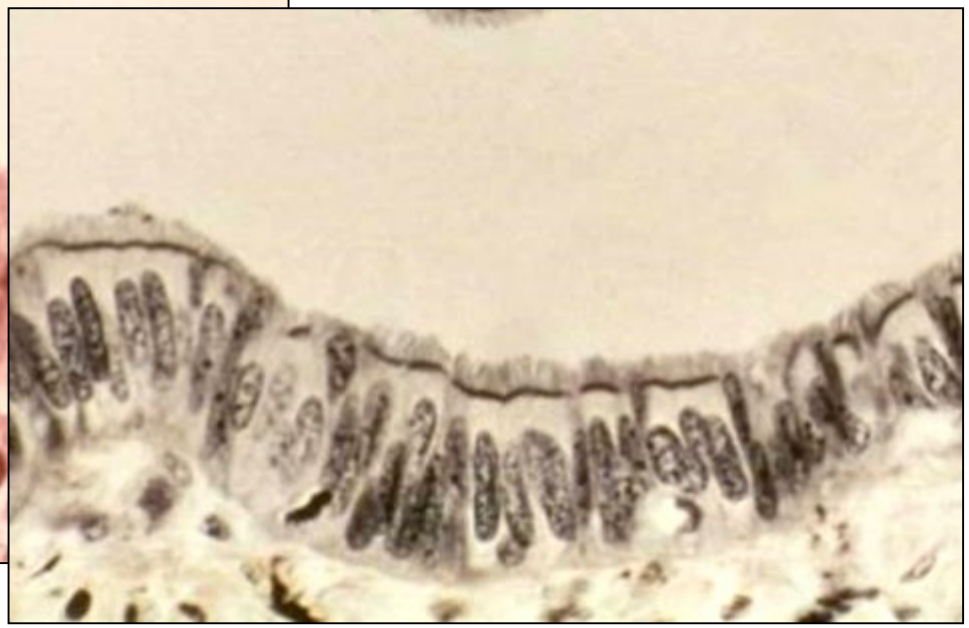
▪ Simple columnar epithelium

– Single layer of columnar cells with large, oval, basally located nucleus

– **Typicall epithelium of GIT**
  - stomach
  - small and large intestine
  - gall bladder



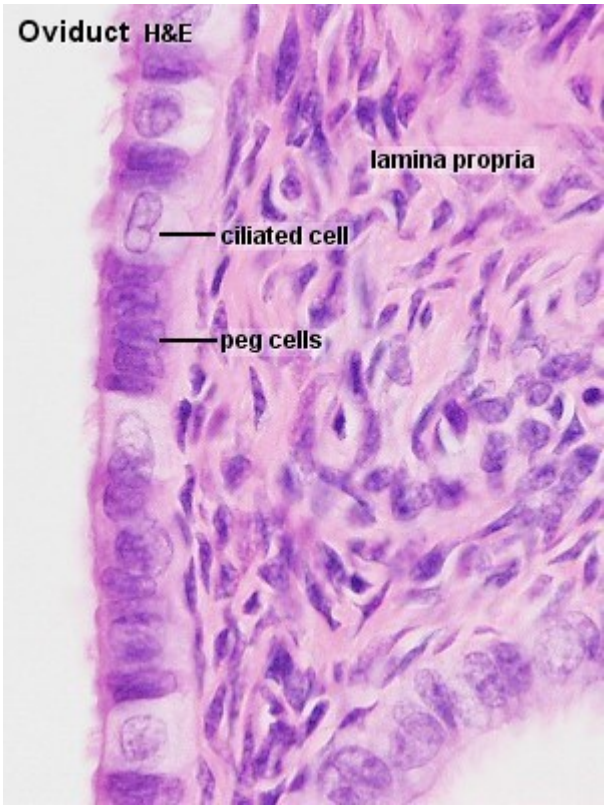


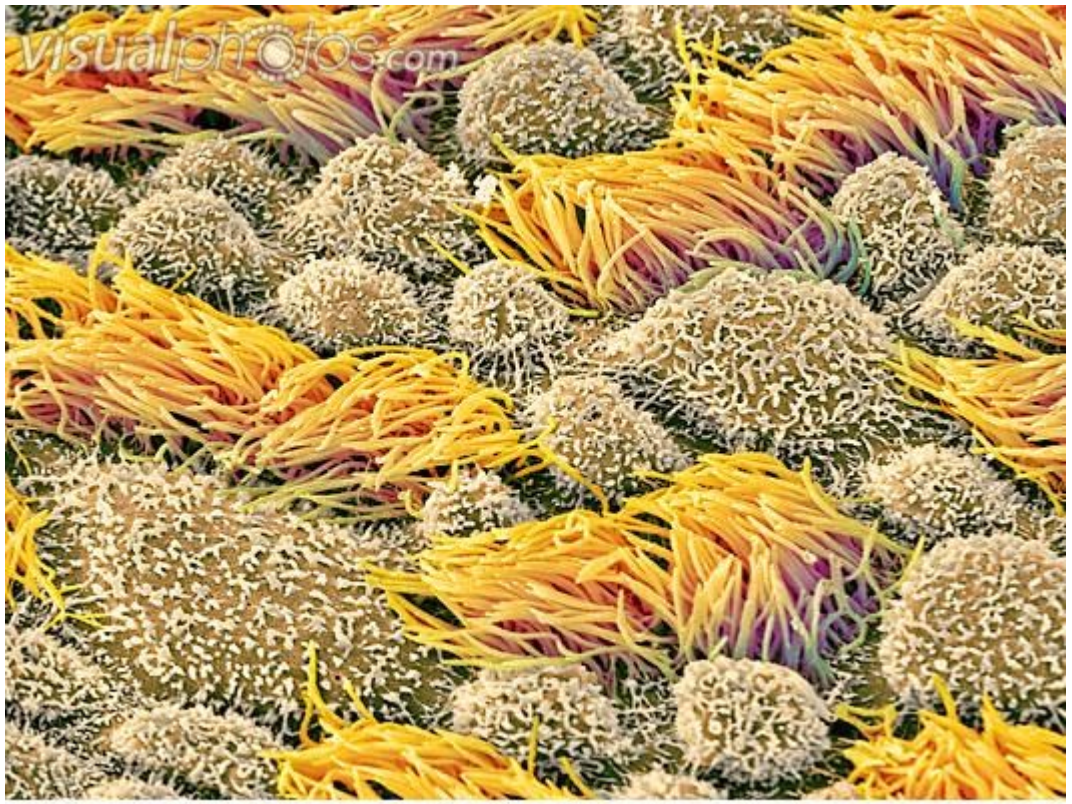


- **Simple columnar epithelium with kinocilia**

Uterine tube

– flow of the oocyte towards the uterus



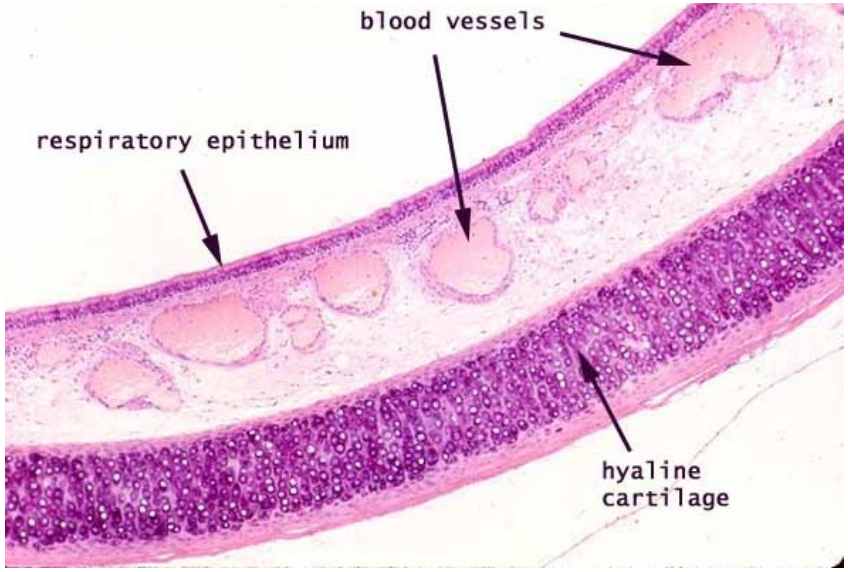


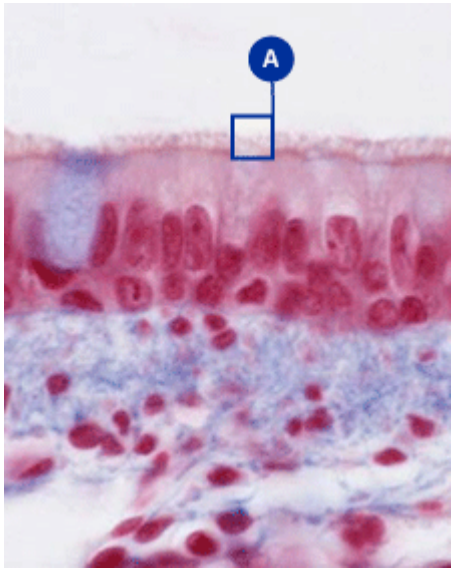
CLASSIFICATION OF EPITHELIAL TISSUE

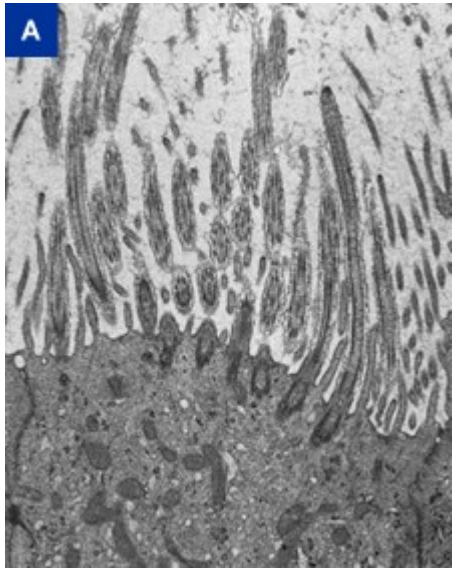
- **Pseudostratified columnar epithelium with kinocilia and goblet cells**

Upper respiratory passages

– Removal of mucus produced by epithelial glands



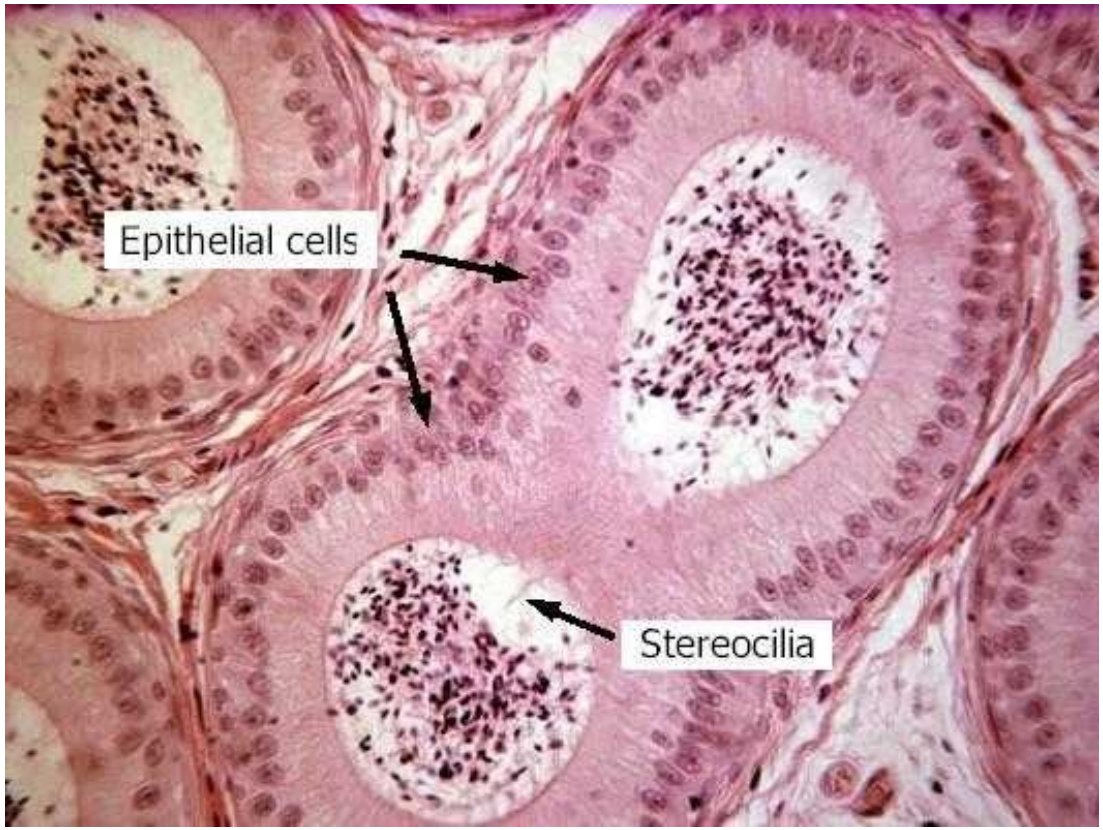




- **Pseudostratified columnar epithelium with stereocilia**

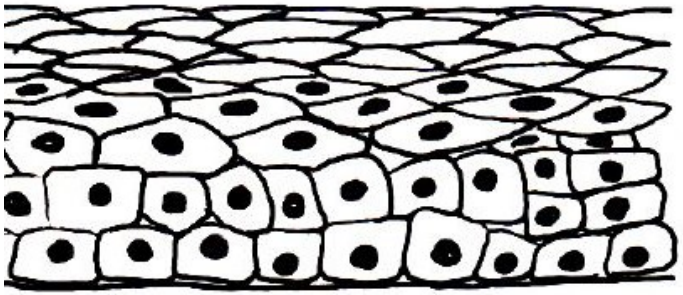
Male reproductive passages

– Epididymis
– Ductus deferens

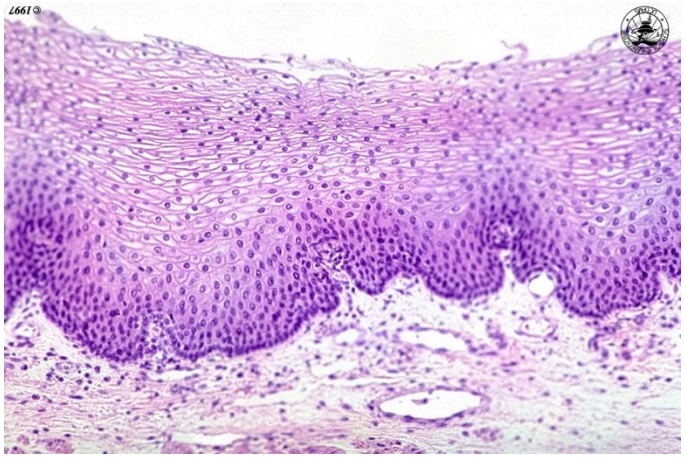


Non-keratinized stratified squamous epithelium

- Multiple layers of cubic cells with centrally localized nuclei, flattening towards surface
- Cells in the superficial layer viable
- First layer in contact with BM, last layer – squamous



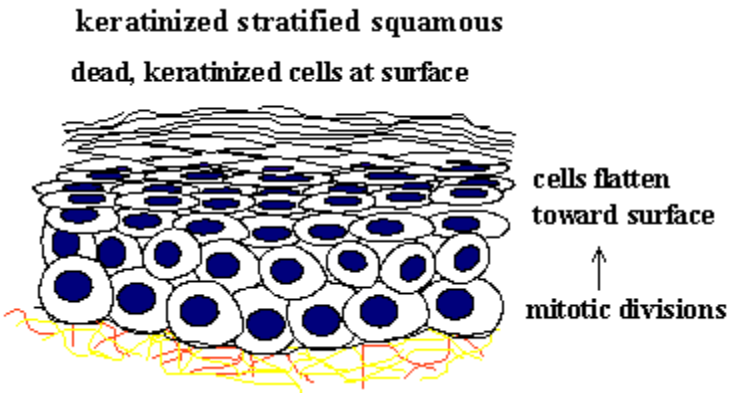
- Constant abrasion
- Mechanical resilience
- Protection from drying
- Rapid renewal



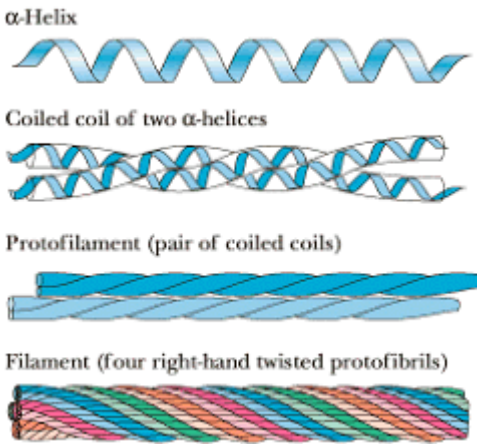
Examples:

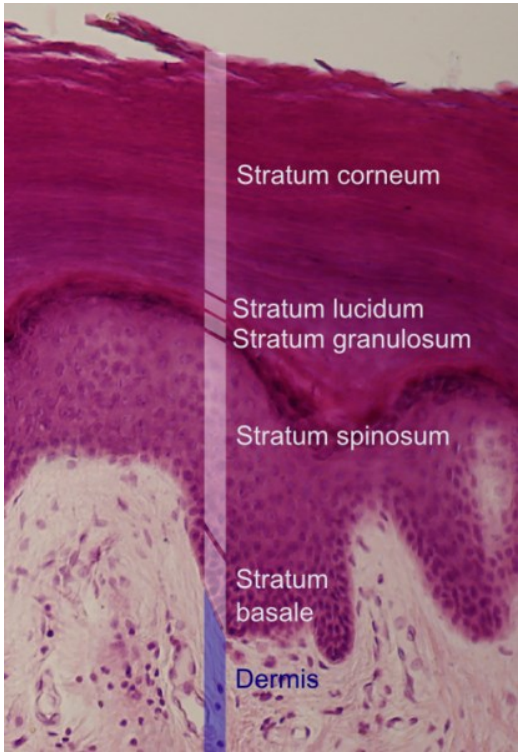
- Cornea
- Oral cavity and lips
- Esophagus
- Anal canal
- Vagina

Keratinized stratified squamous epithelium



- Cell in the superficial layer dead
- Skin (epidermis)
- Nail
- Keratins
  - Fibrous proteins, ~ 40 types
  - Intermediate filaments
  - Very stable, multimeric
  - Disorders of keratin expression – variety of clinical symptoms
  - e.g. Epidermolysis bullosa simplex (mutations in the genes encoding keratin 5 or keratin 14)

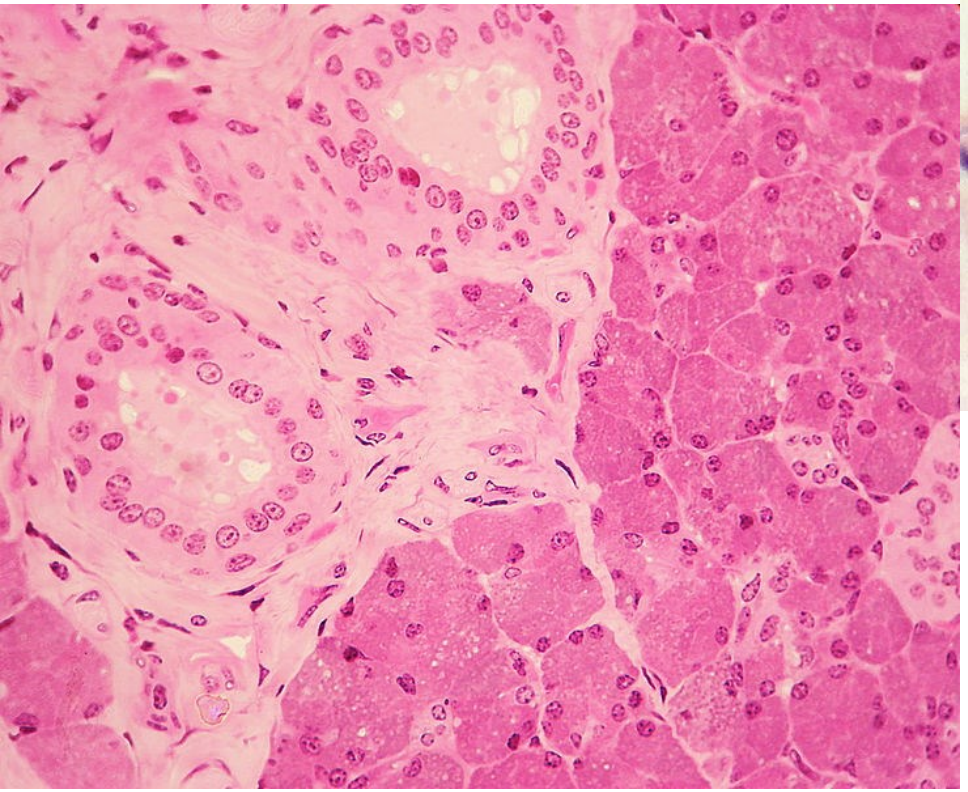


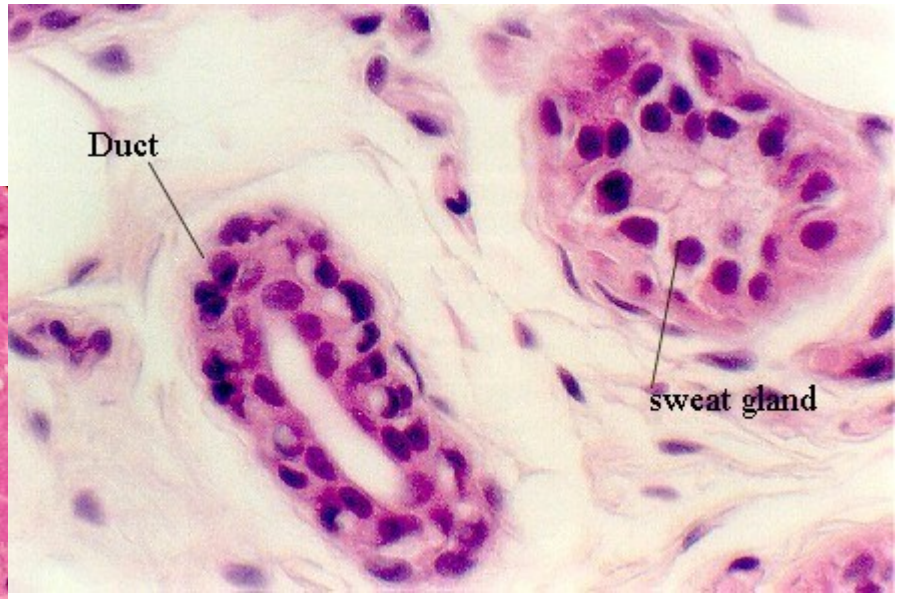


- **Stratified cuboidal epithelium**

Large ducts of:

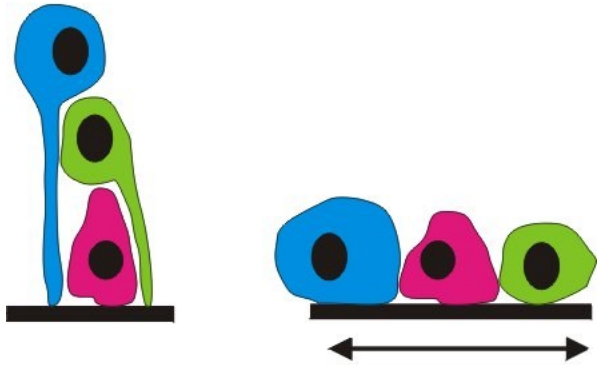
– sweat glands
– mammary glands
– salivary glands





Transitional epithelium (urothelium)

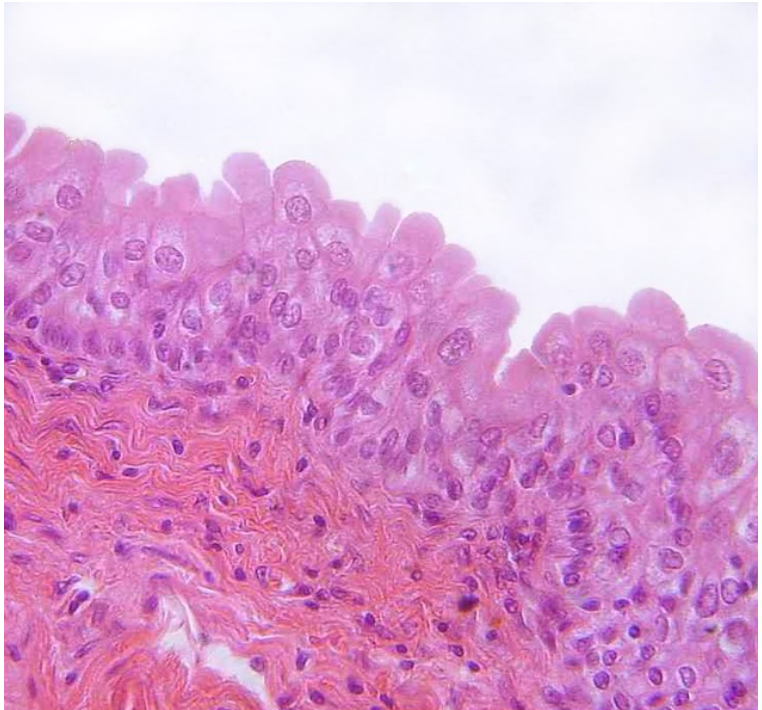
- fluctuation of volume
- organization of epithelial layers
- membrane reserve
- protection against hyperosmotic urine



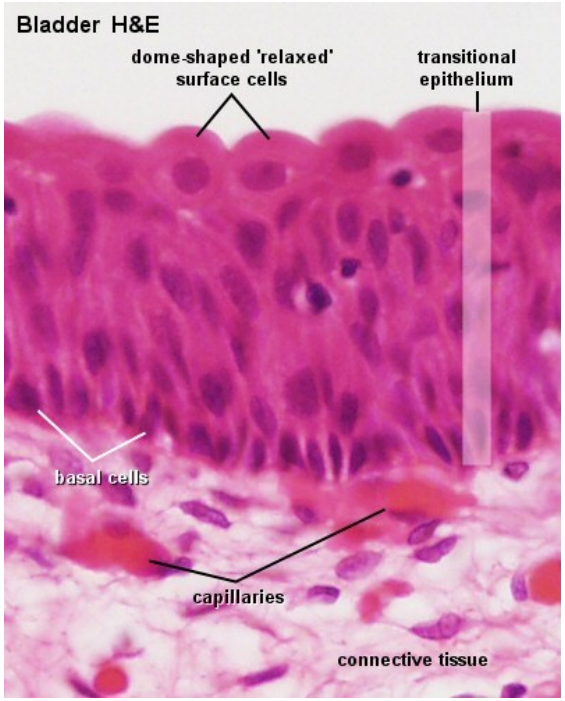
Urinary system

- urinary bladder, ureters, renal calyx and pelvis

Empty (relaxed): rather cuboidal cells with a domed apex
Full: flat,stretched

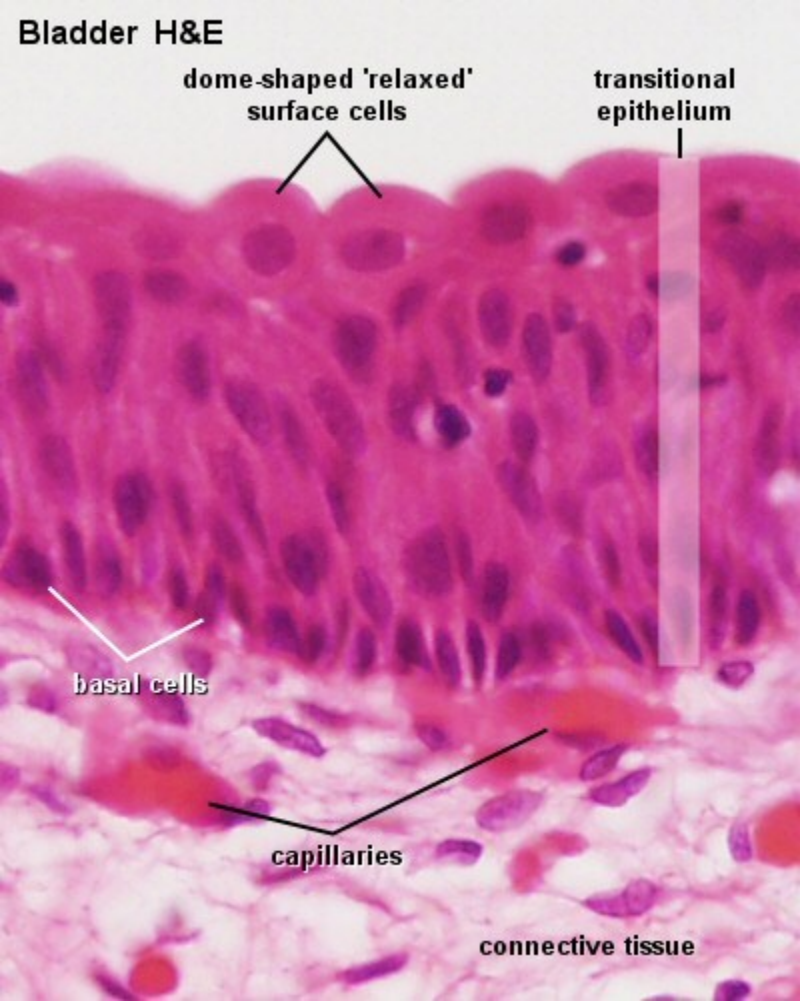


- Basal cells
- Intermediate layer
- Surface cells



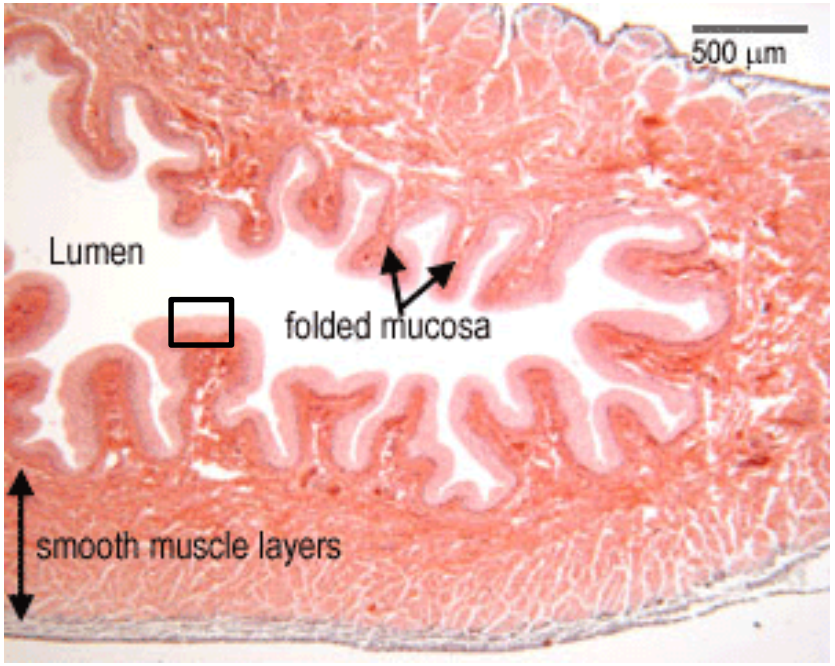
Transitional epithelium (urothelium)

- glycosaminoglycan layer (GAG) on the surface
- osmotic barrier
- antimicrobial properties



Barrier architecture:

- GAG-layer
- surface cells (tight junctions), uroplakins proteins in the apical cell membrane
- subepithelial capillary network

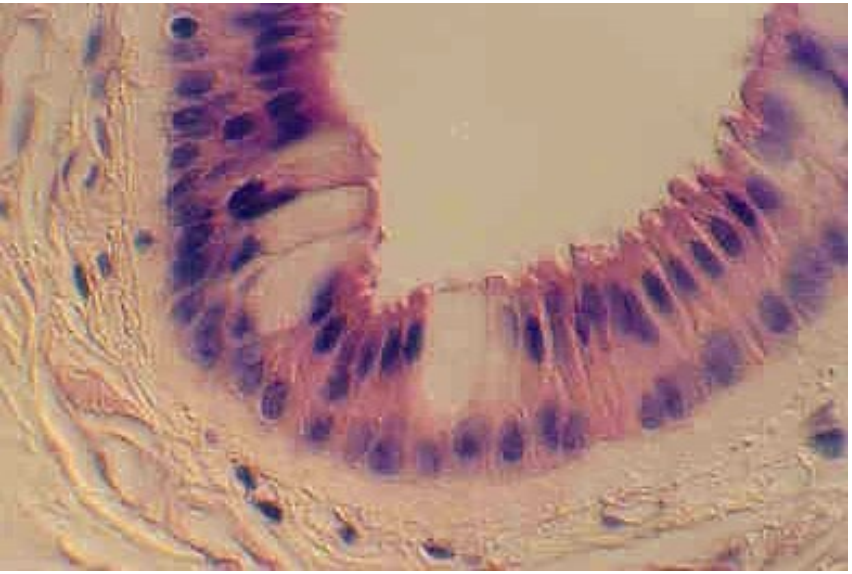


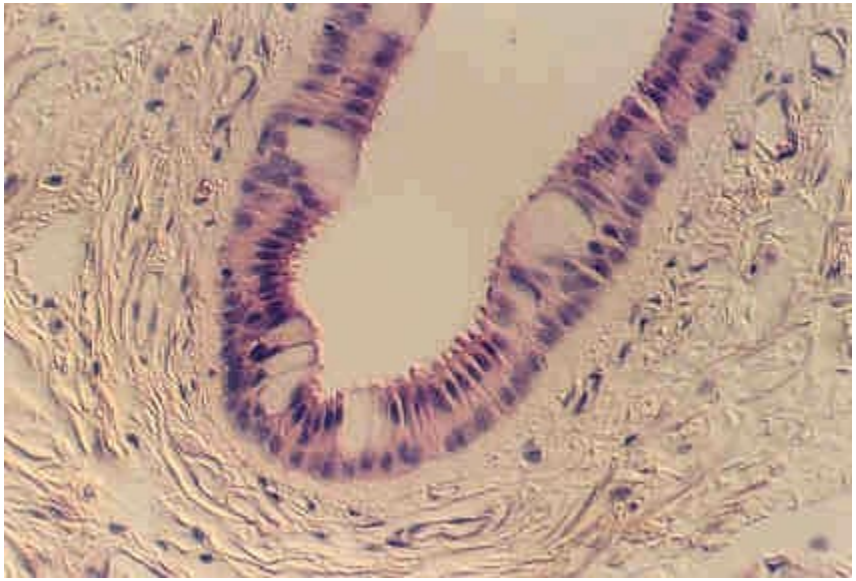
CLASSIFICATION OF EPITHELIAL TISSUE

Stratified columnar epithelia

- several layers of columnar cells
- secretion / protection

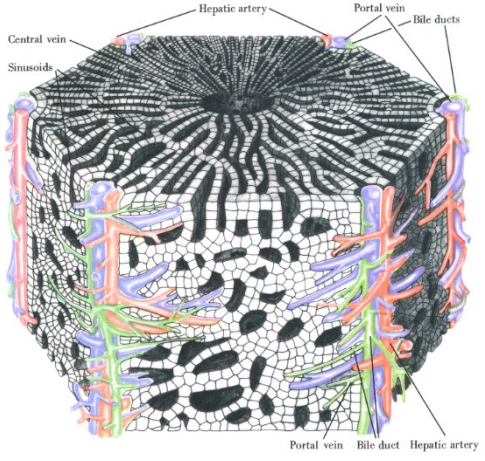
- occular conjunctiva
- pharynx, anus – transitions
- male urethra, vas deferens
- large ducts of salivary glands

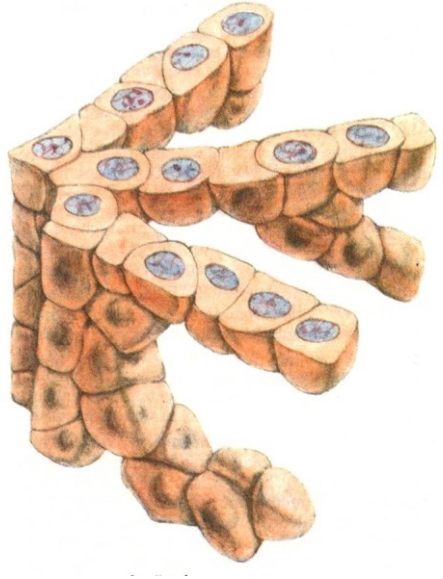


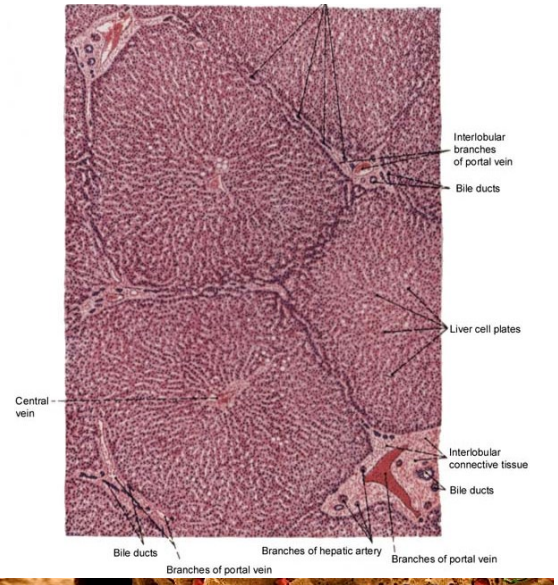


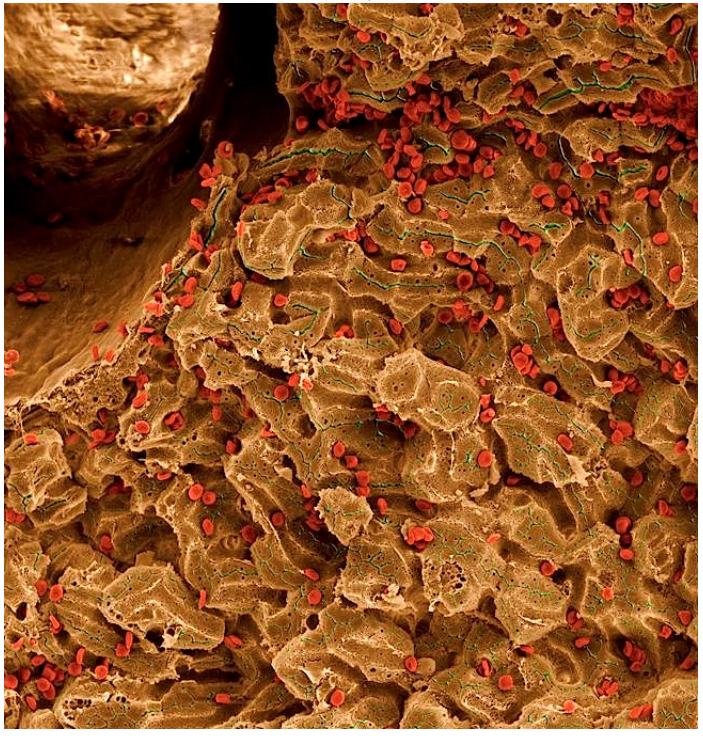
©http://www.cytochemistry.net/microanatomy/epithelia/salivary7.jpg

2) Trabecular epithelium





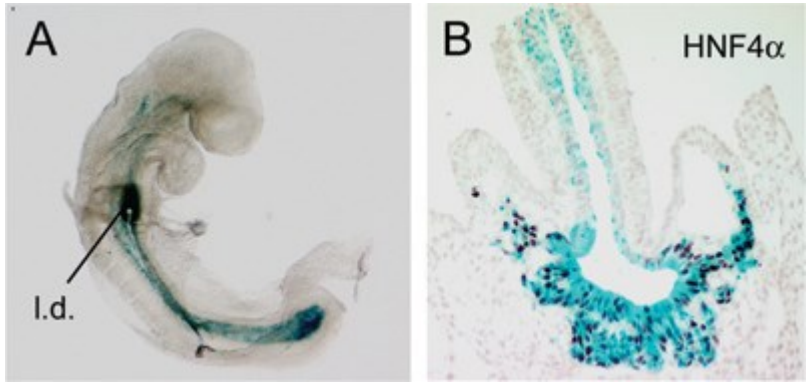


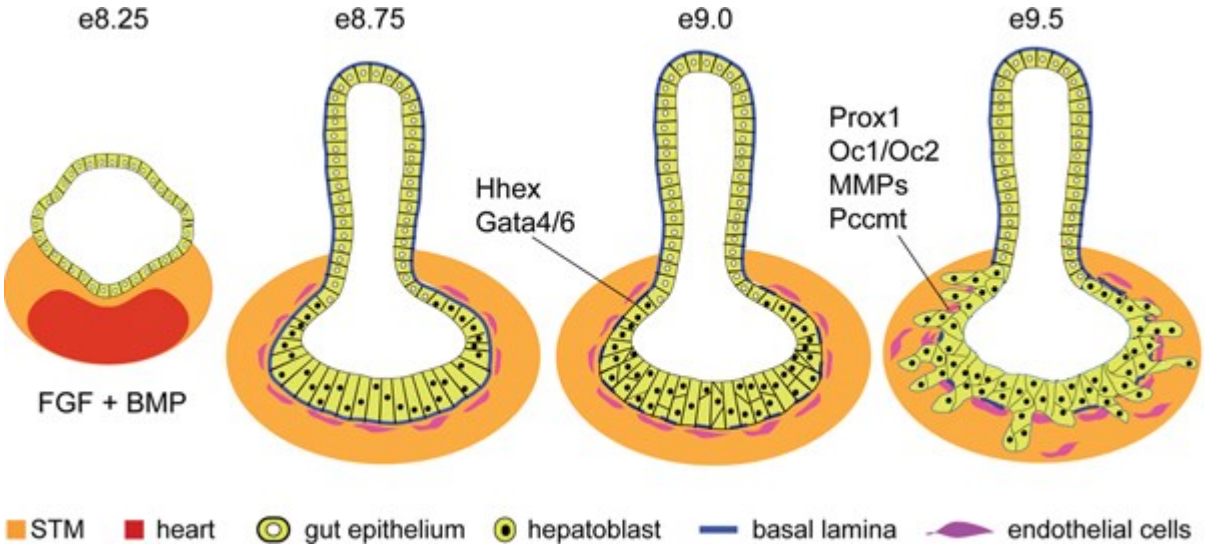


CLASSIFICATION OF EPITHELIAL TISSUE

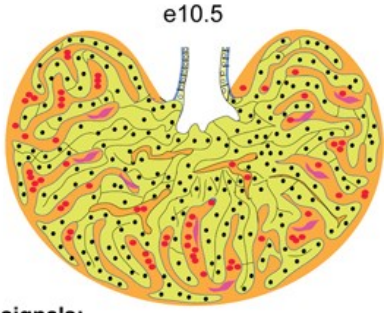
- **Liver**

Trabecules of hepatocytes develop from sheet epithelial layer of primitive gut lining





hepatoblasts:
BMPR, FGFR, c-Met, TGFR,
Pi3K, Sek1/JNK, Elf5, Arf6, Raf1
Smad2/3, β-catenin, c-jun, Tbx3, NFκβ
Foxm1b, Xbp1, Mtf-1



mesenchyme signals:
BMP, FGF, HGF, Wnt, TGFβ, RA
Gata4, WT1, N-myc, Hlx, Lhx2

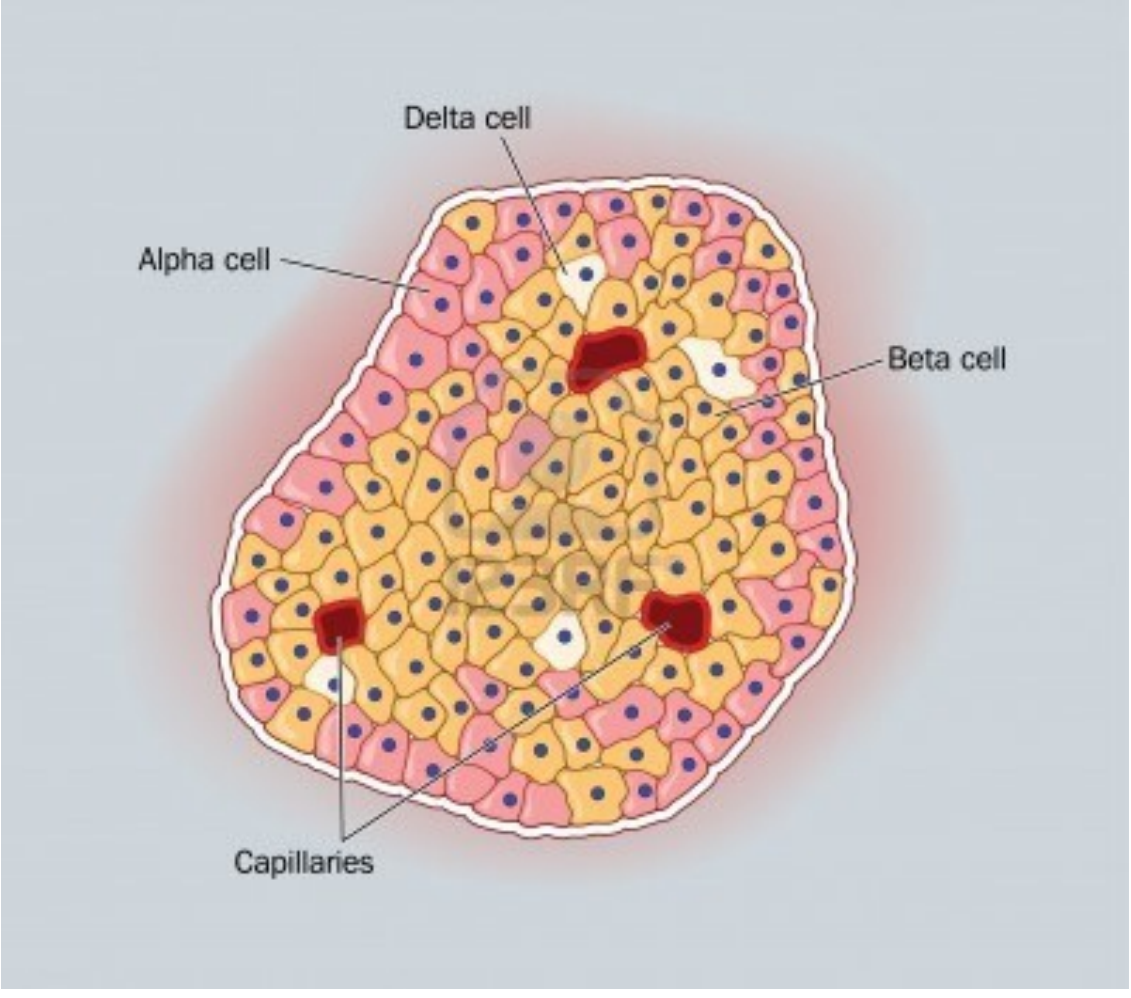
STM hepatoblast blood cells endothelial cells

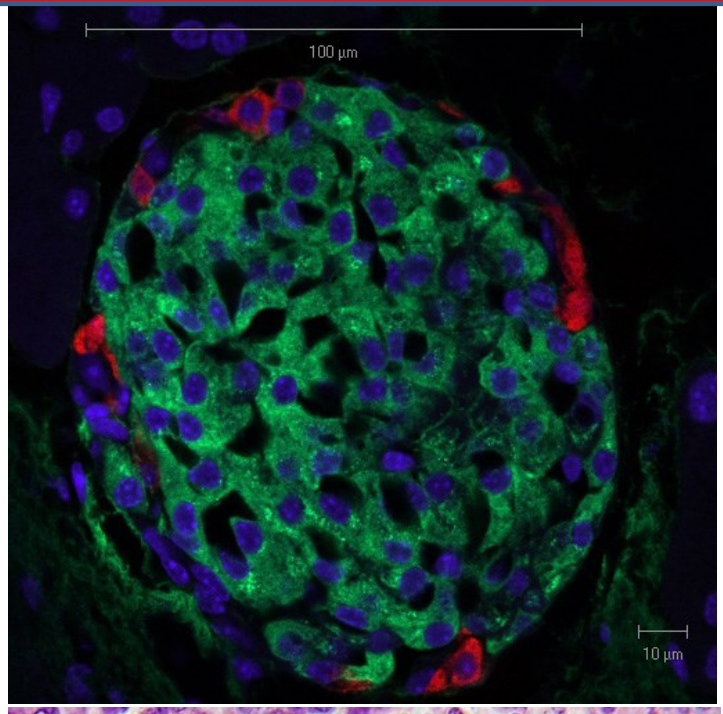
CLASSIFICATION OF EPITHELIAL TISSUE

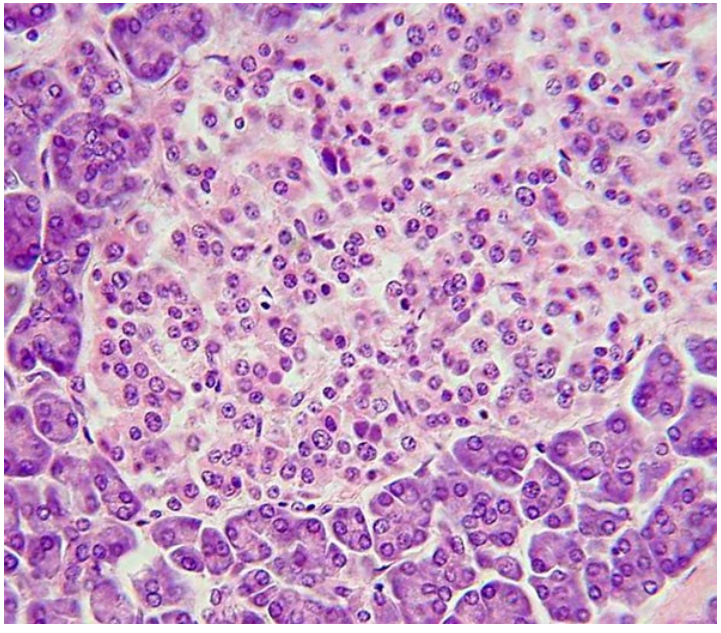
- **Endocrine glands**

  Islets of Langerhans

  Cords of endocrine active cells





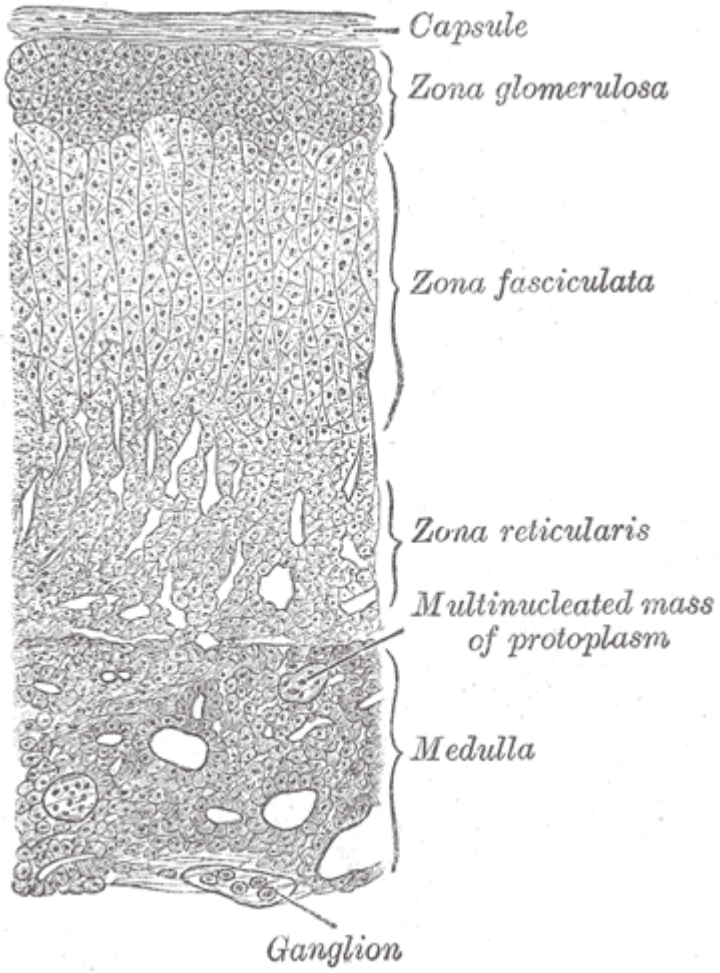


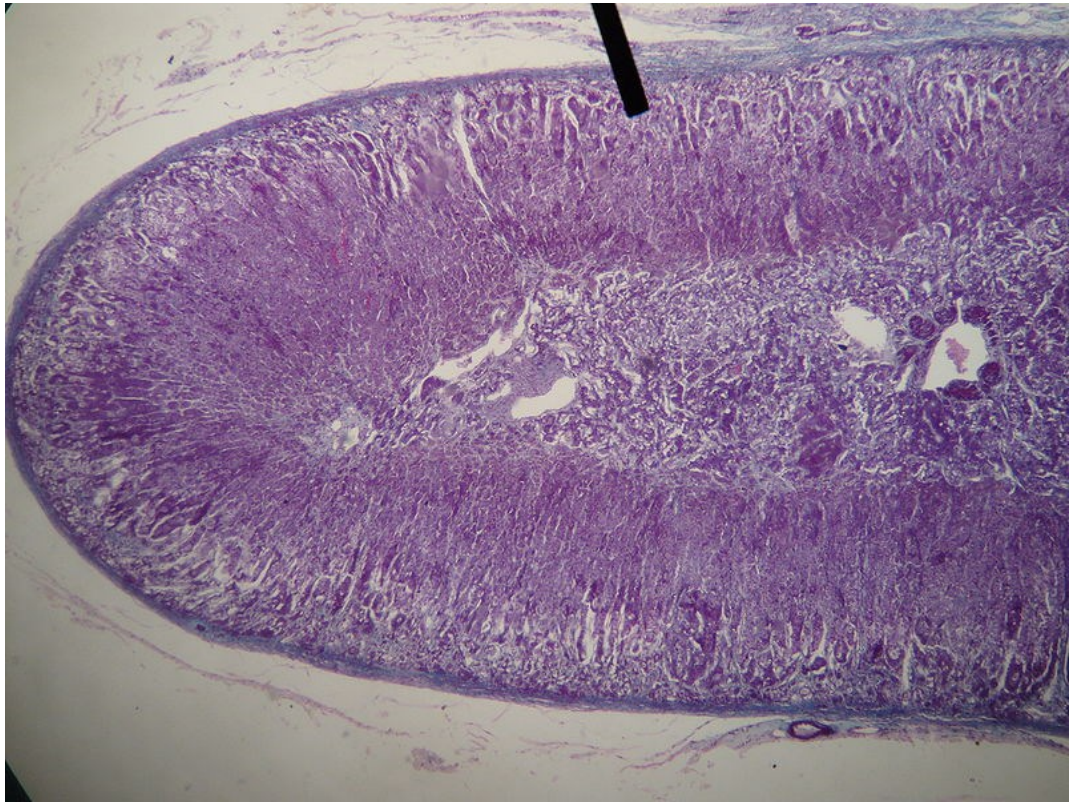
CLASSIFICATION OF EPITHELIAL TISSUE

- **Endocrine glands**

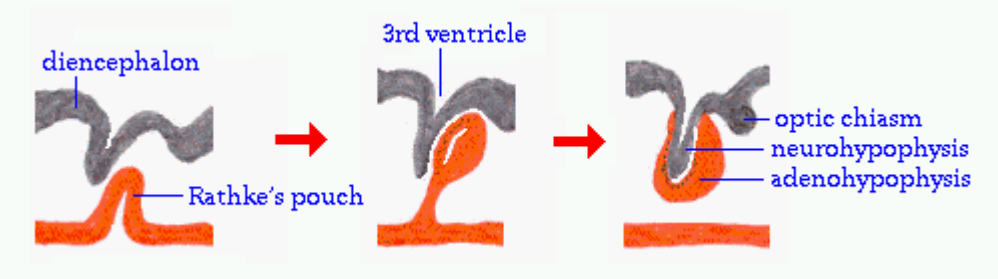
Adrenal cortex

Cortex of adrenal gland – epithelial cells in cords secreting corticoid



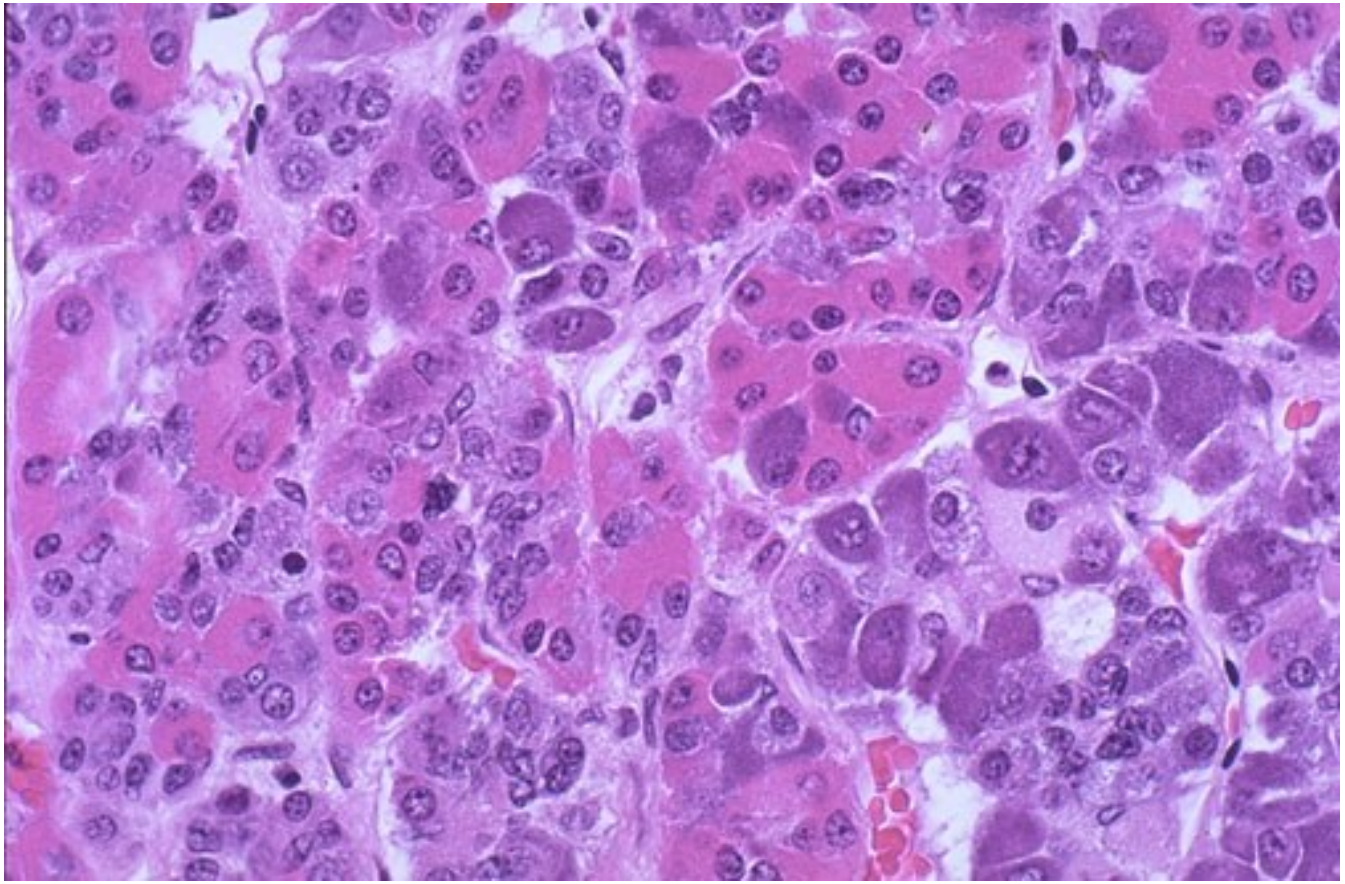


CLASSIFICATION OF EPITHELIAL TISSUE



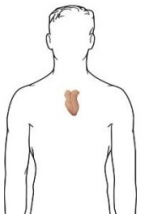
- **Endocrine glands**

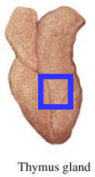
Adenohypophysis – anterior pituitary

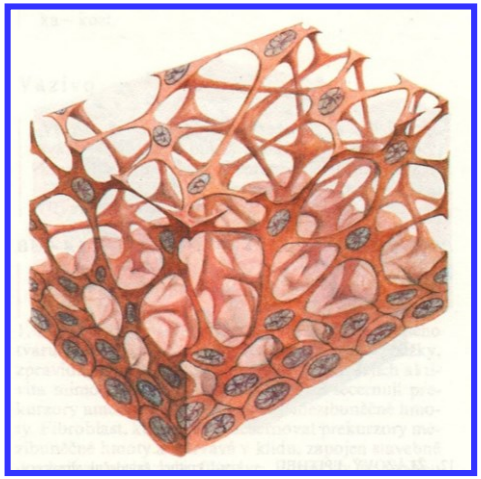


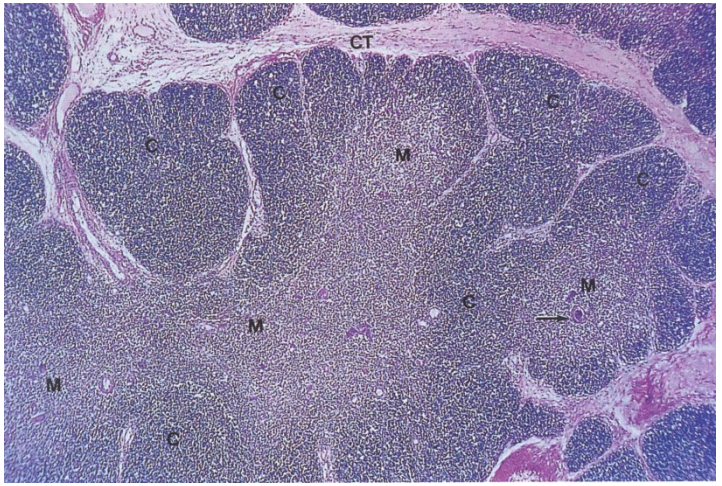
CLASSIFICATION OF EPITHELIAL TISSUE

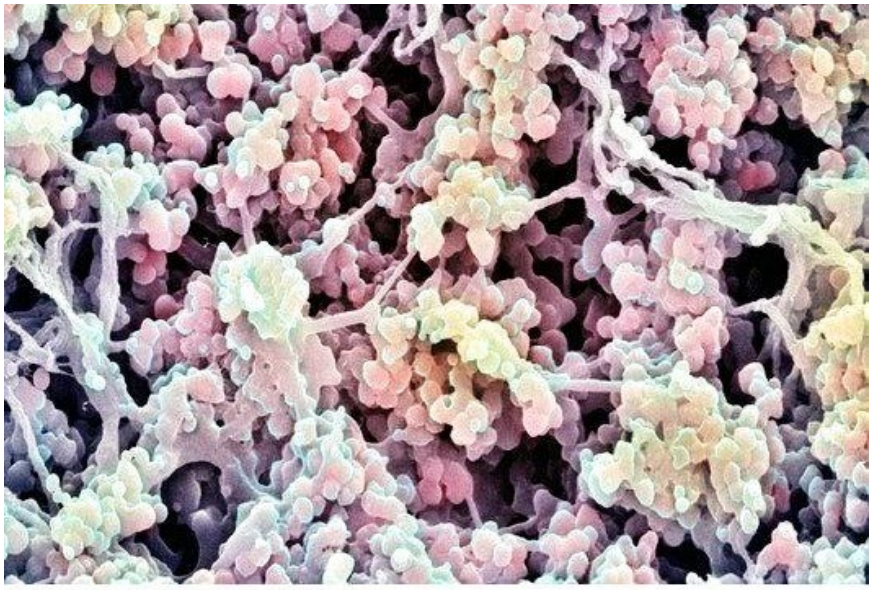
Thymus - cytoretikulum

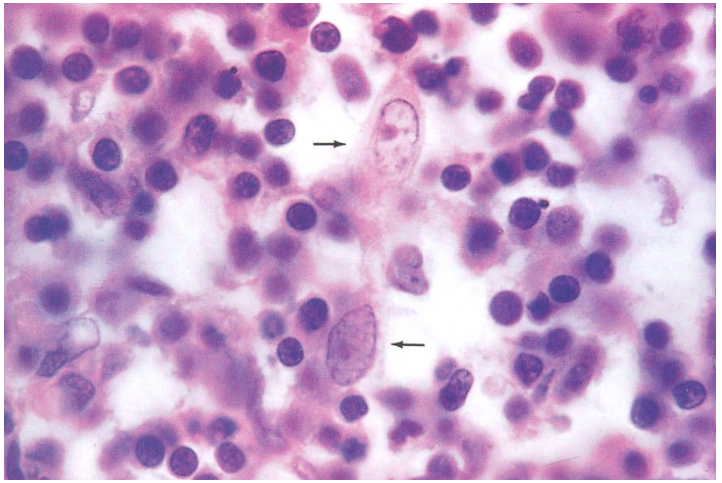






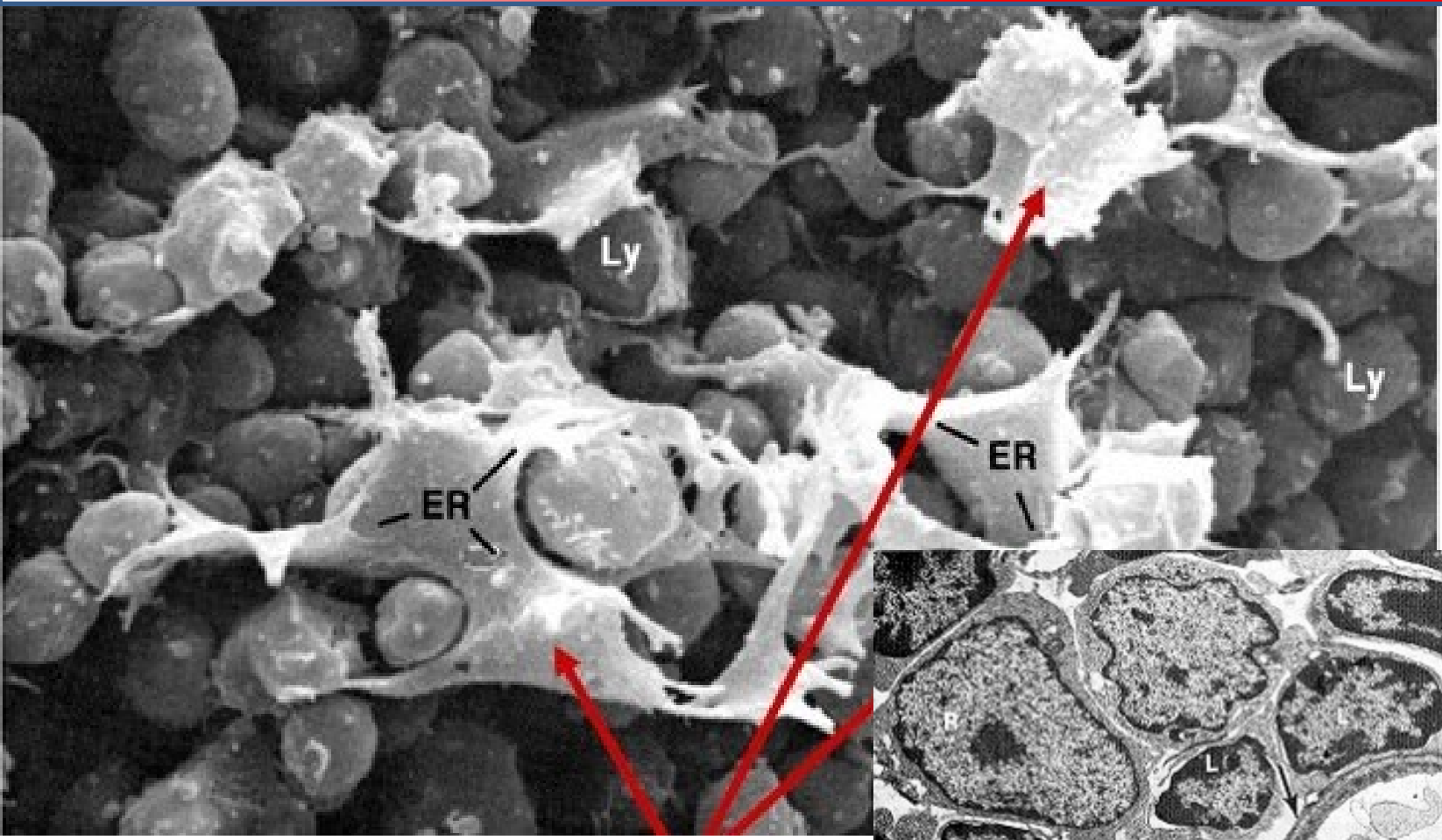


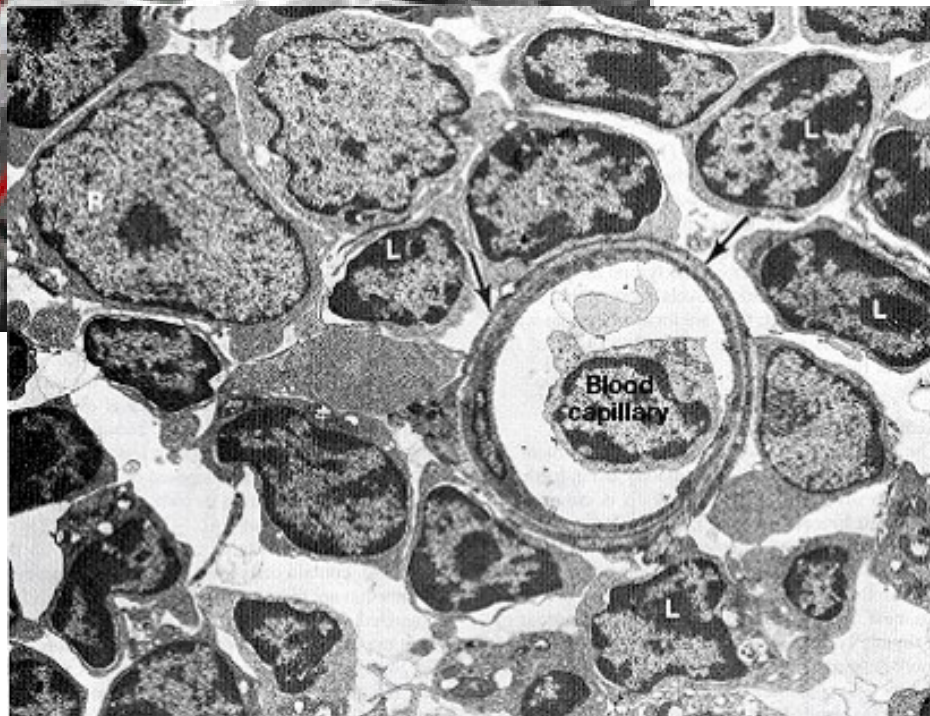




- Compartments and microenvironment for T-cell development and selection
- Blood-thymus barrier

CLASSIFICATION OF EPITHELIAL TISSUE

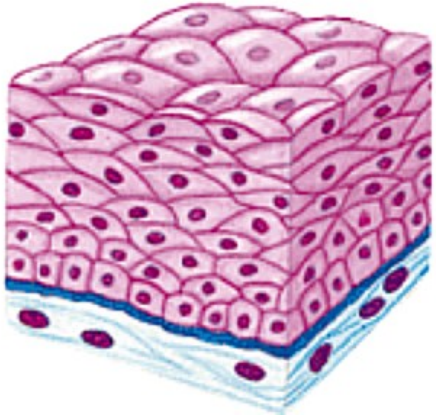




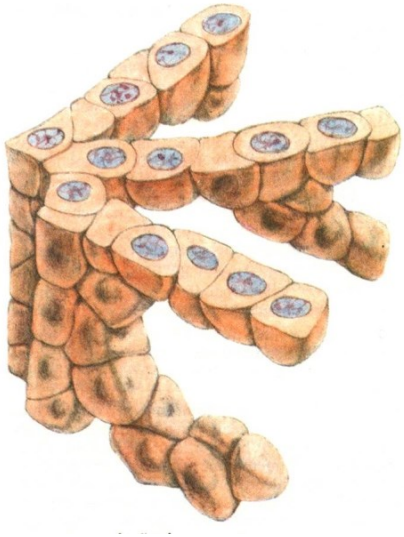
Epithelial reticular (epithelioreticular) **cells**:

Structural and functional support for developing T-lymphocytes

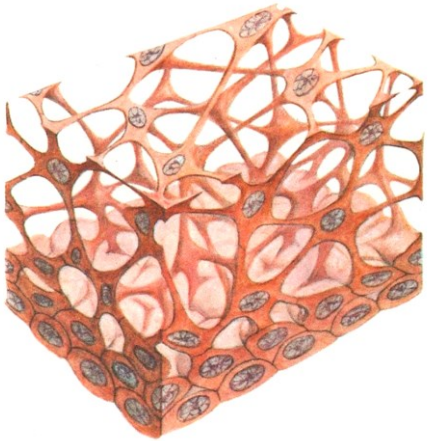
SUMMARY



Sheet



Trabecular

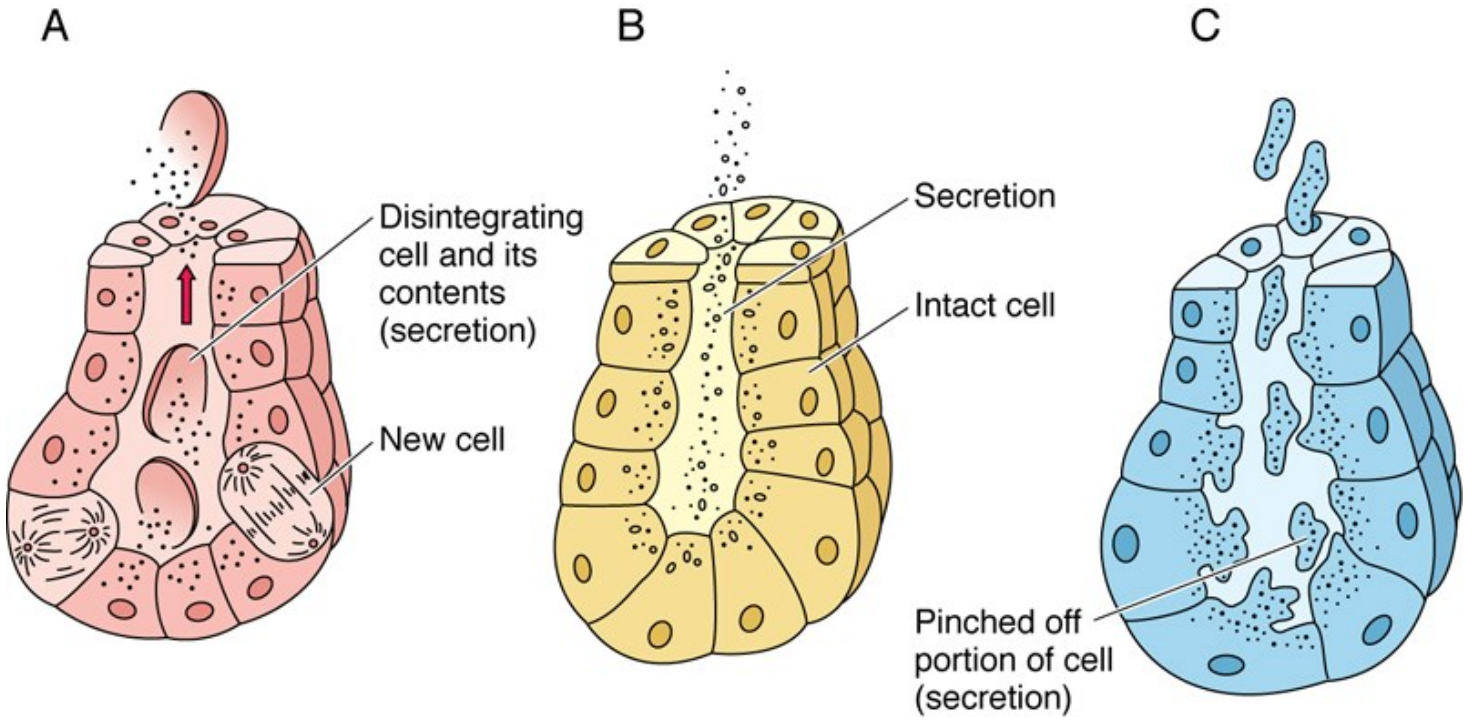


Reticular

Classification by function

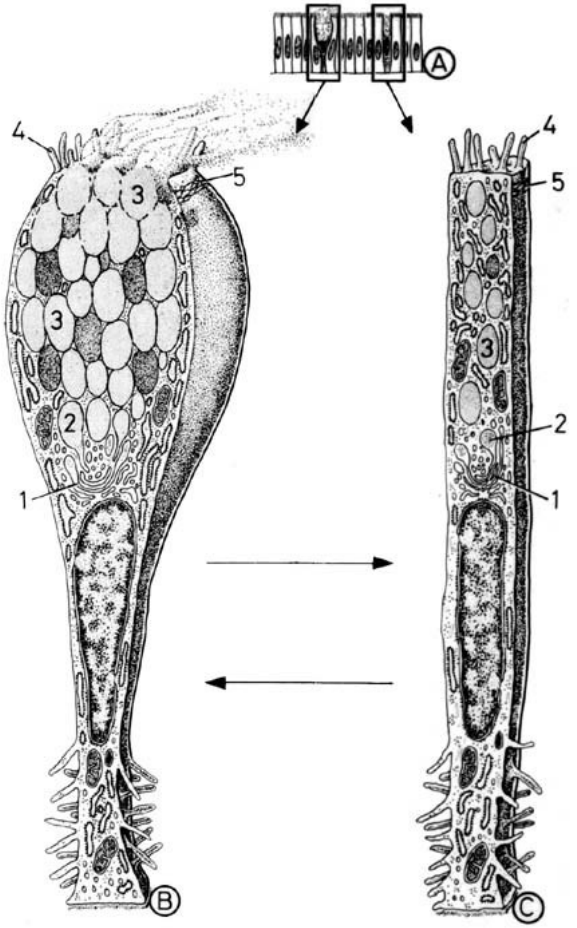
Ways of secretion

- Secretion ↔ excretion
- Process of secretion:



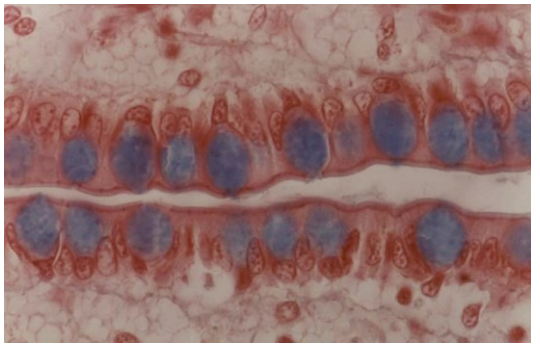
Holocrine × Merocrine × Apocrine

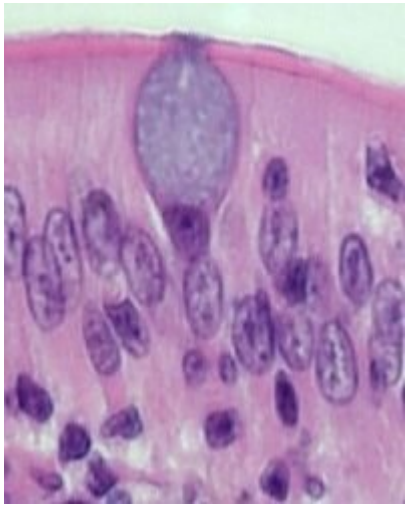
- **Single cell glands**
  - Goblet
  - Enteroendocrine

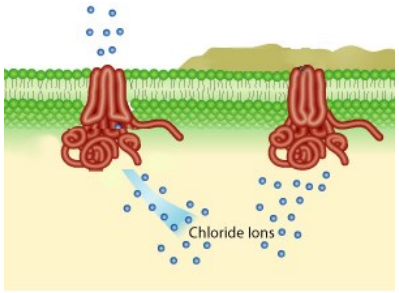


Goblet cells

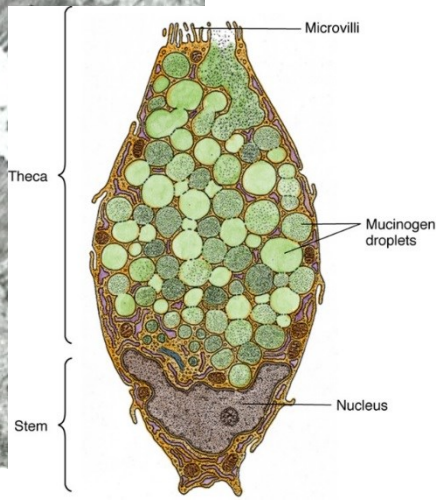
- Mainly respiratory and intestinal tract
- Produce mucus = viscous fluid composed of electrolytes and highly glycosylated glycoproteins (mucins)
- Protection against mechanic shear or chemical damage
- Trapping and elimination of particular matter
- Secretion by secretory granules constitutive or stimulated
- After secretion mucus expands extremely – more than 500-fold in 20ms
- Dramatic changes in hydration and ionic charge
- Chronic bronchitis or cystic fibrosis – hyperplasia or metaplasia of goblet cells





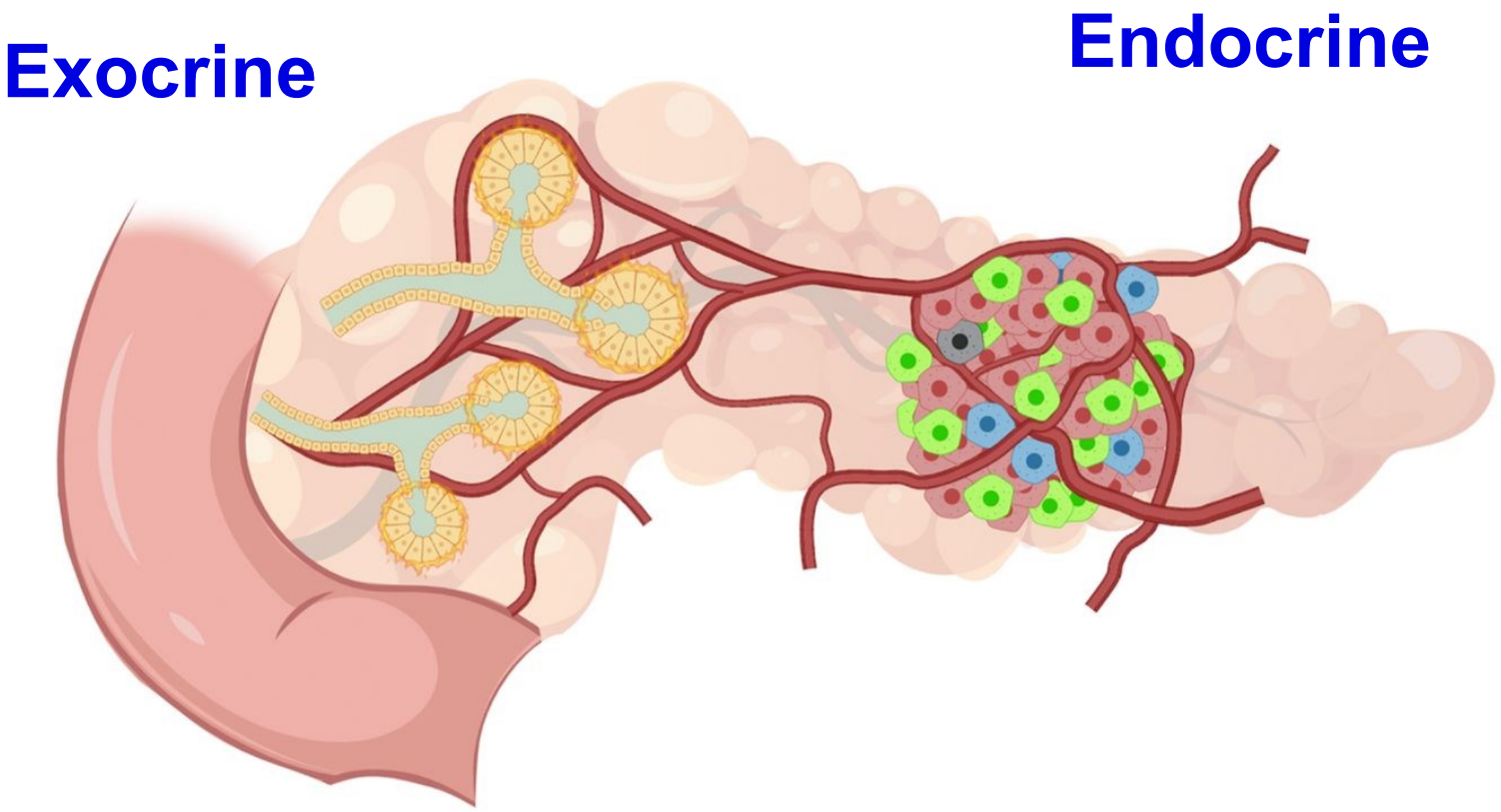


GOBLET CELL

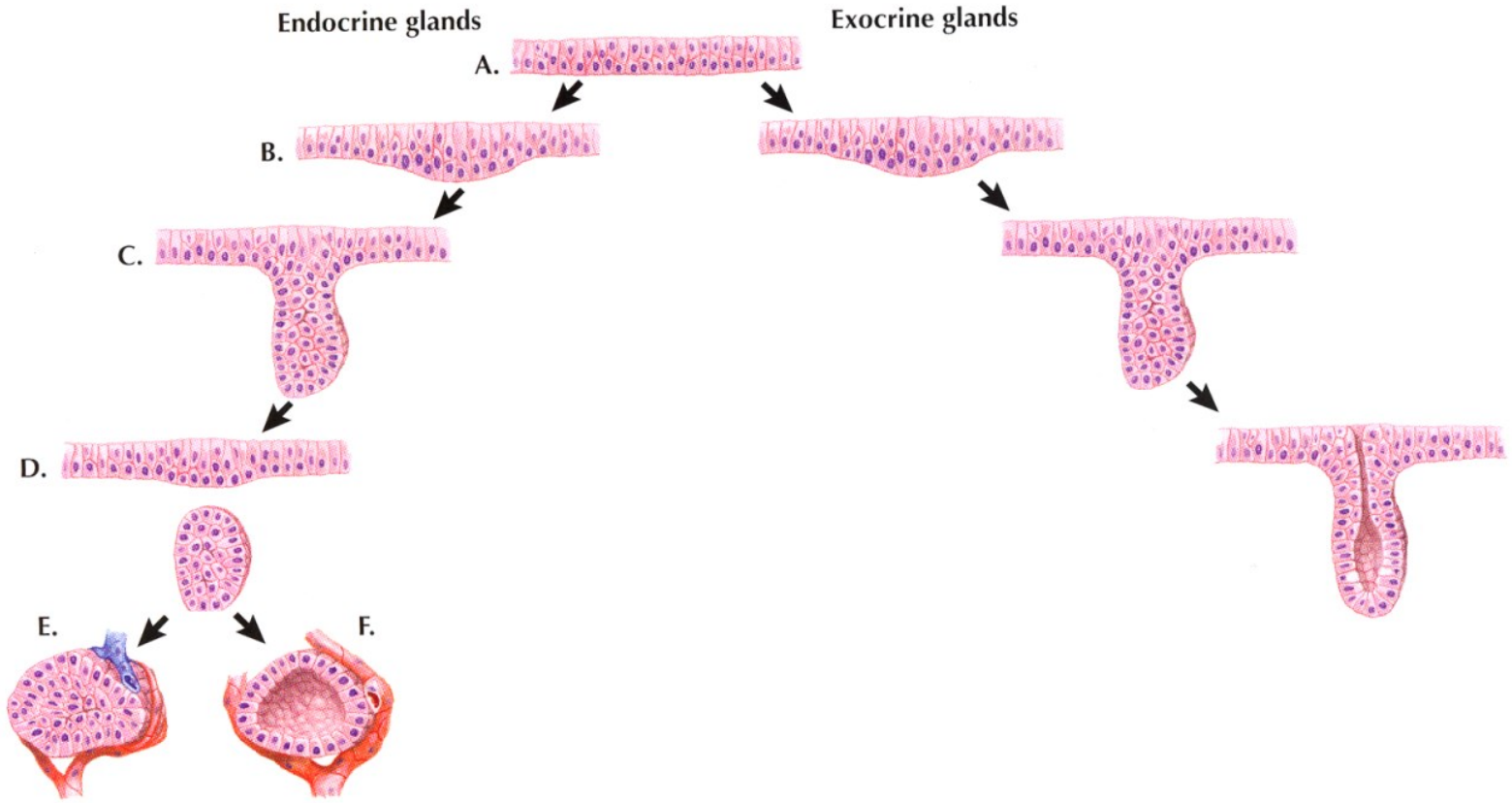


GLANDULAR EPITHELIUM

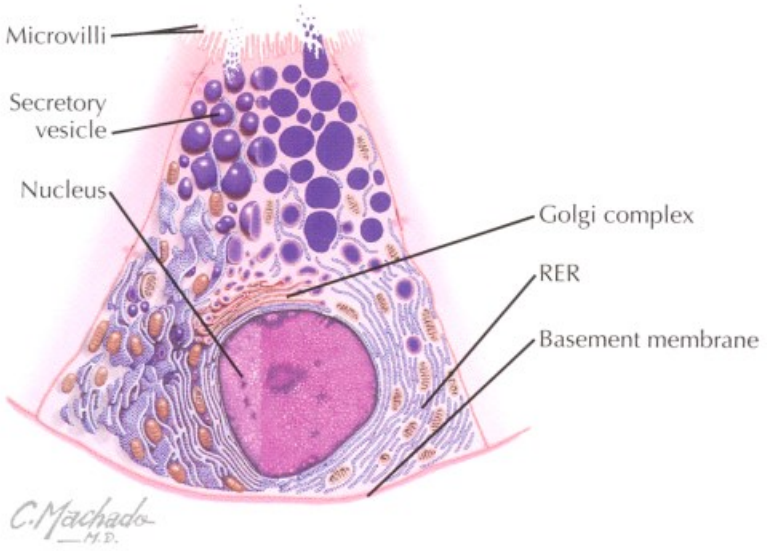
- **Multicellular glands**



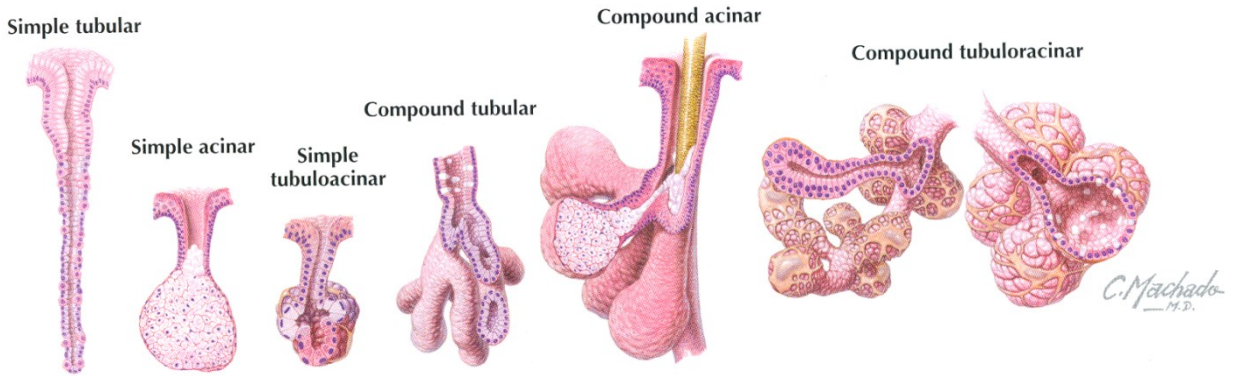
- **Development of multicellular glands**
  - Endocrine vs. exocrine



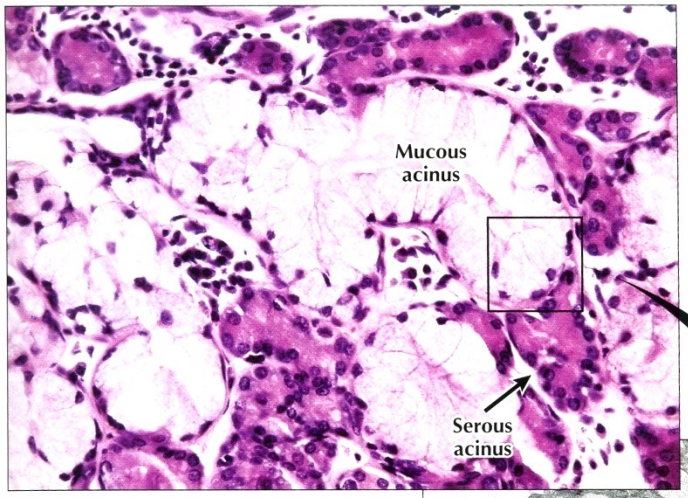
Exocrine multicellular glands



- Shape of secretion part
  - Alveolar (acinar)
  - Tubular
  - Tubuloalveolar (tubuloacinar)
- Branching
  - Simple
  - Branched
  - Compound
- Secretion
  - Mucous
  - Serous
  - Compound



Mucous glands

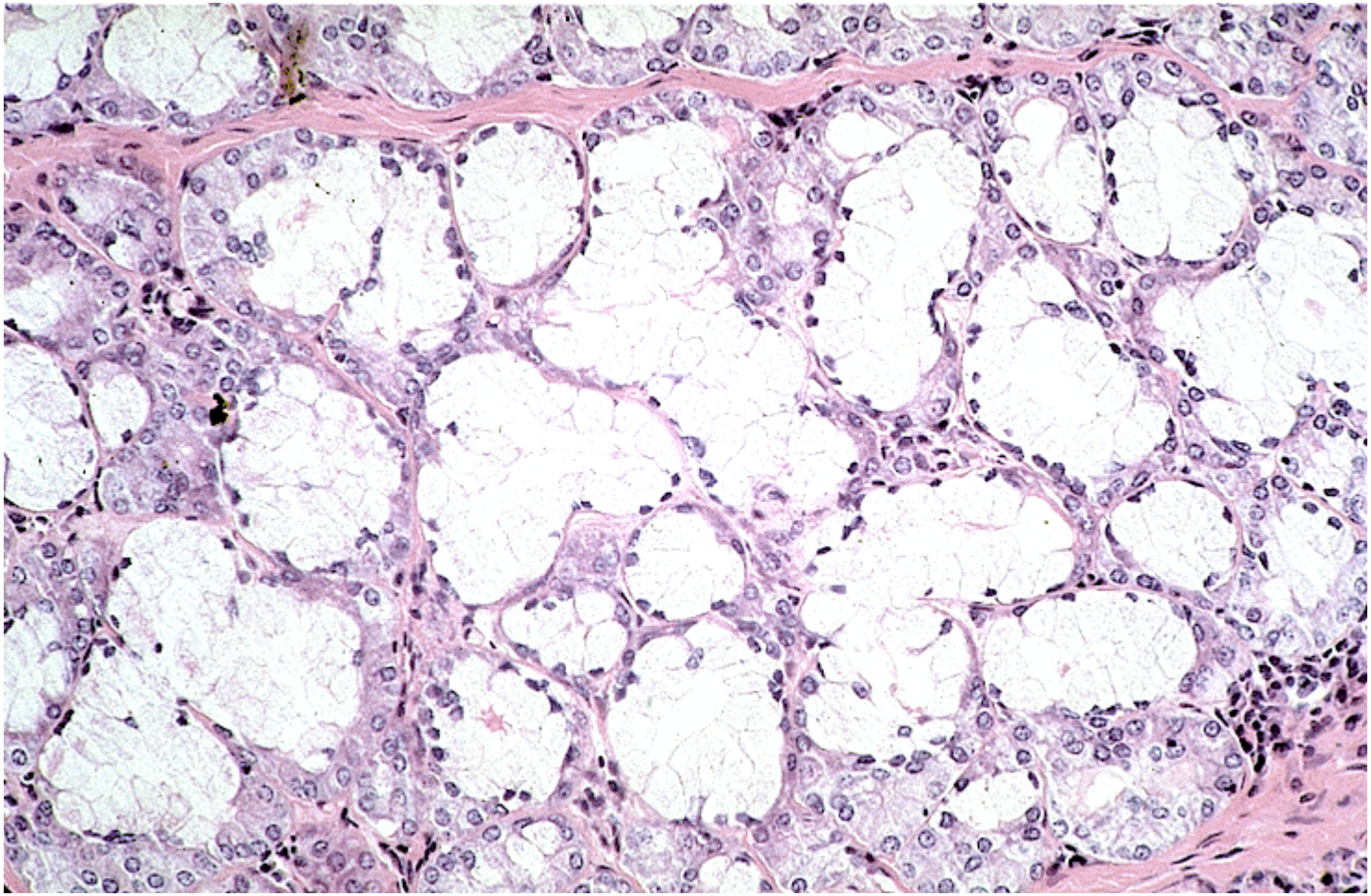


◀ **LM of part of a mixed seromucous gland in the trachea.** Several mucous acini with pale-stained mucous cells are seen. The basal nuclei are flat, and cells appear washed out because mucous droplets dissolved during specimen preparation. Darker stained serous cells in adjacent acini have more rounded basal nuclei. Serous cells are smaller than mucous cells. The square outlines the area of interest seen in the EM below. 295×. *H&E.*

▶ **EM of part of a mucous acinus in a mixed salivary gland.** Parts of three mucous cells line the acinus lumen (*). Euchromatic basal nuclei have prominent nucleoli. Basal cytoplasm contains many profiles of rough endoplasmic reticulum (**RER**). Many large, electron-lucent secretory vesicles (**SV**) dominating the remaining cytoplasm are discharged by exocytosis into the acinus lumen. 5400×.

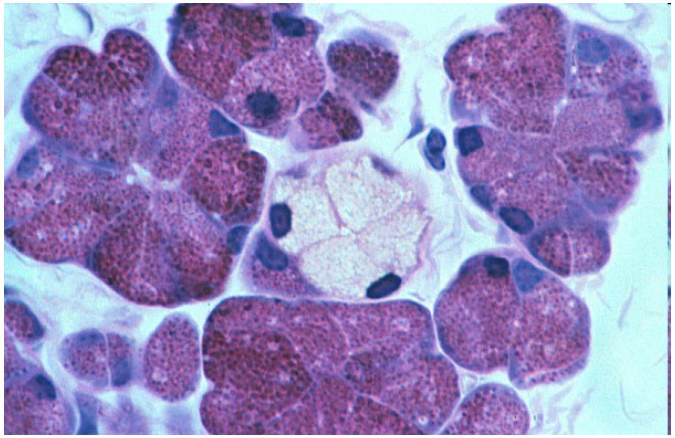
GLANDULAR EPITHELIUM

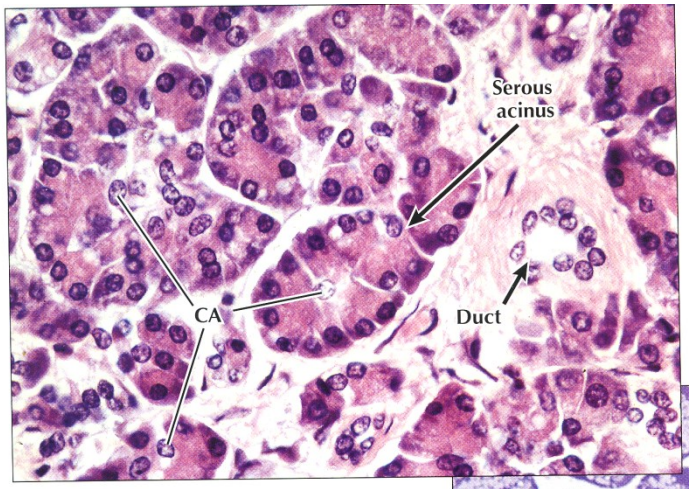
- **Mucous glands**



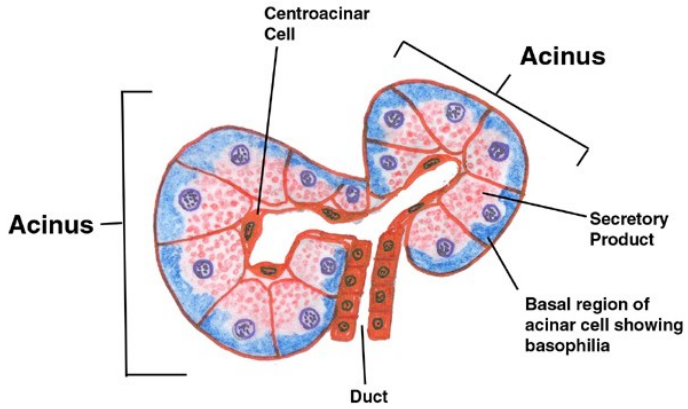
GLANDULAR EPITHELIUM

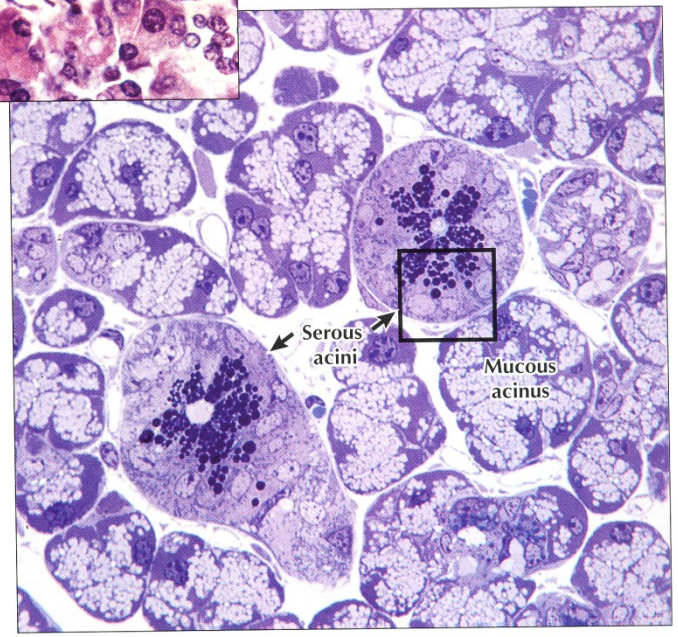
- **Serous glands**





◀ **LM of part of the exocrine pancreas.** The exocrine part of the gland consists of closely packed spherical or pear-shaped serous acini. Several columnar to pyramidal acinar cells, with round basal nuclei, face a small central lumen in each **serous acinus**. Basal cytoplasm is basophilic; apical cytoplasm is more eosinophilic. Small clear centroacinar cells (**CA**) in acini centers help distinguish this purely serous gland from others, such as the parotid salivary gland. A small **duct**, in the connective tissue stroma, conveys secretions from acini to larger pancreatic ducts. 385×. *H&E.*

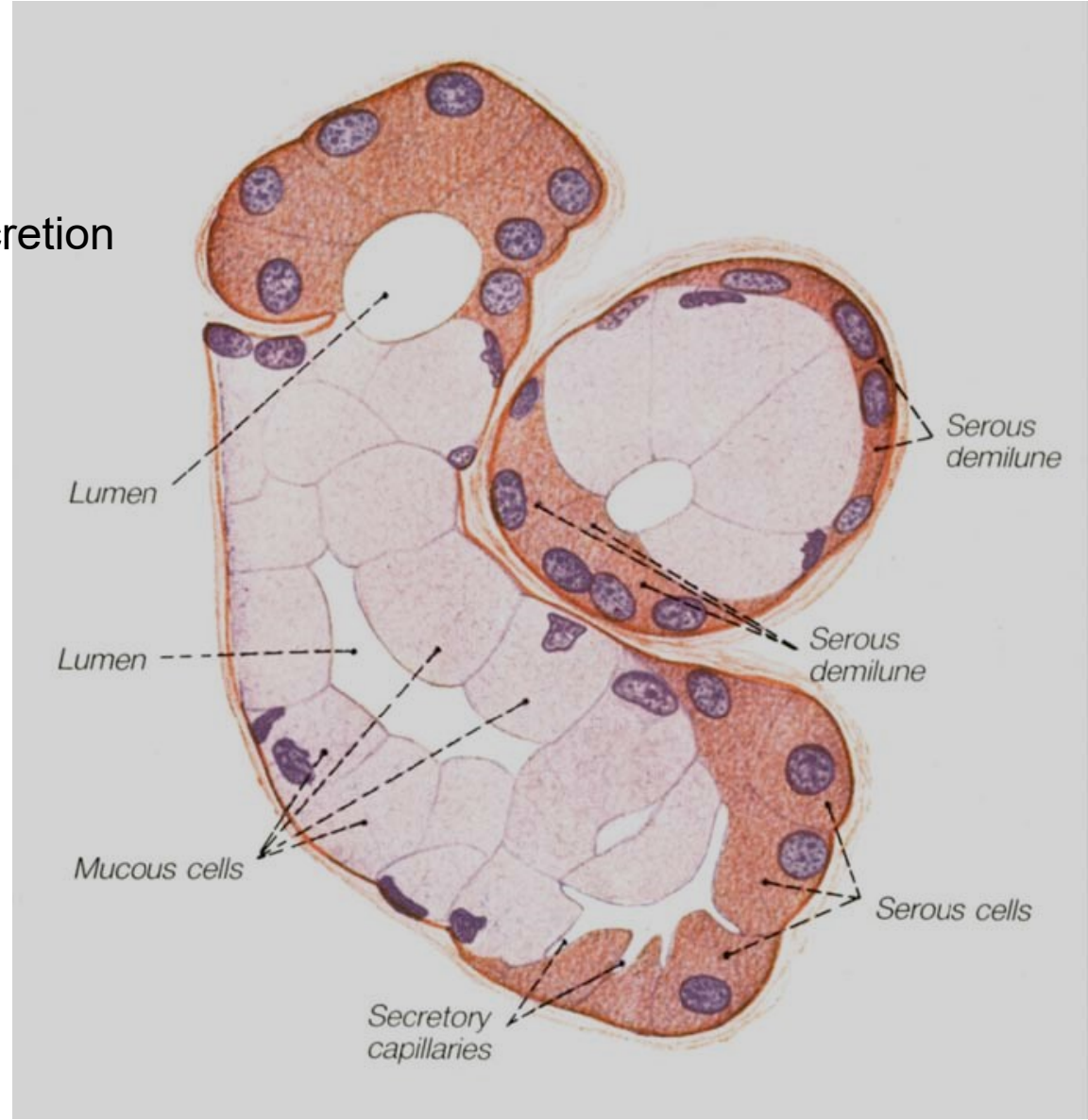




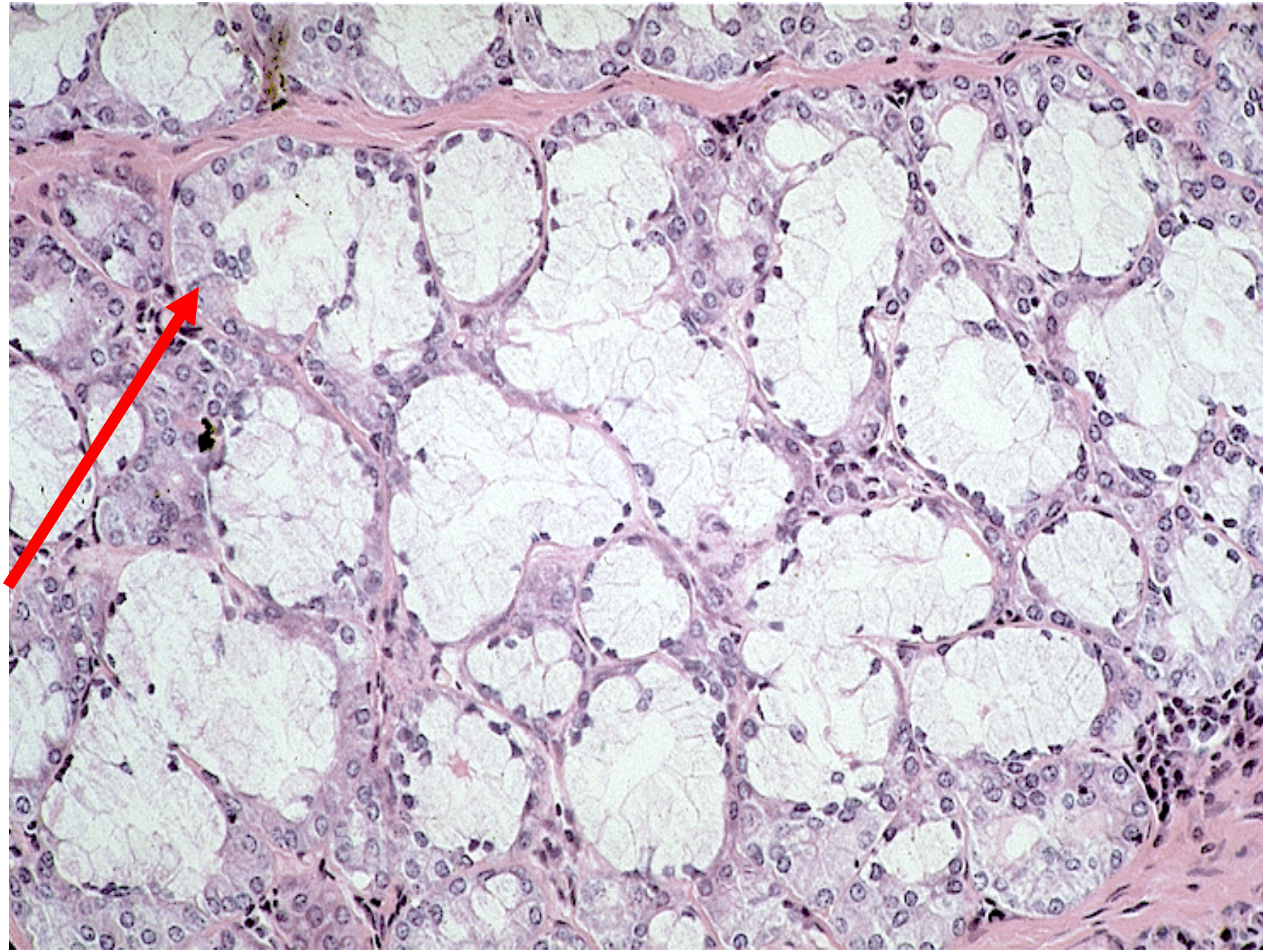
▶ **LM of part of a mixed salivary gland.** Several pale **mucous acini** surround two round **serous acini**. Serous cells have conspicuous, dark-stained secretory vesicles; mucous cells look vacuolated and washed out. EM in 2.15 shows the area in the square in detail. 600×. *Toluidine blue, plastic section.*

- **Mixed glands**

  - mixed serous and mucous secretion

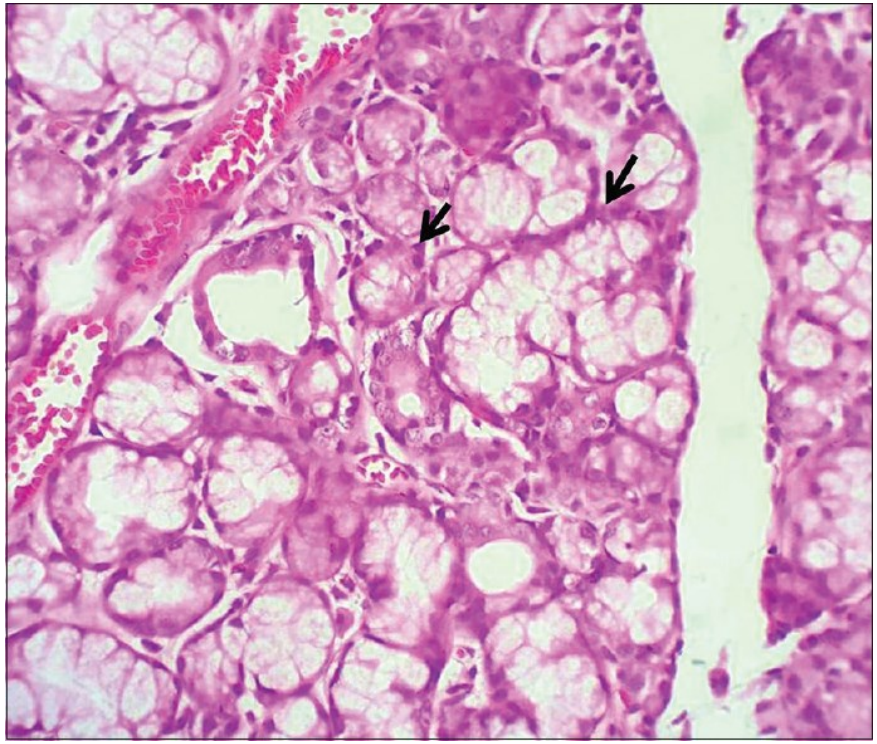


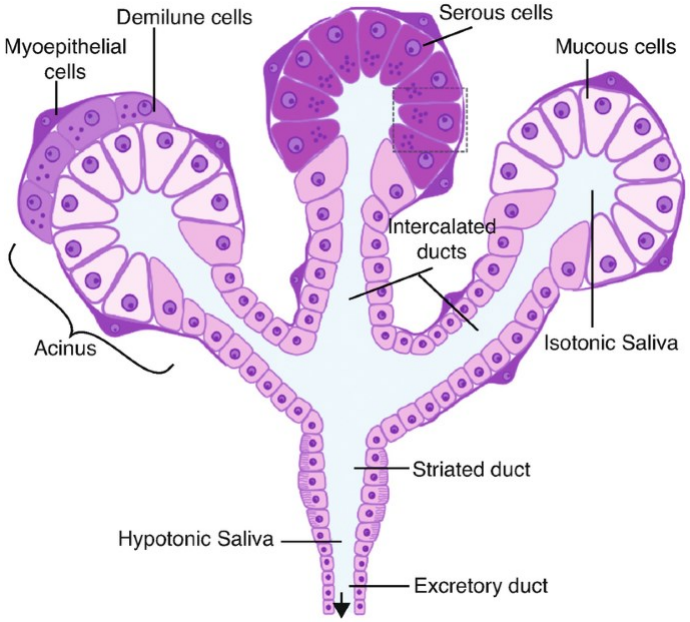
GLANDULAR EPITHELIUM



Myoepithelium

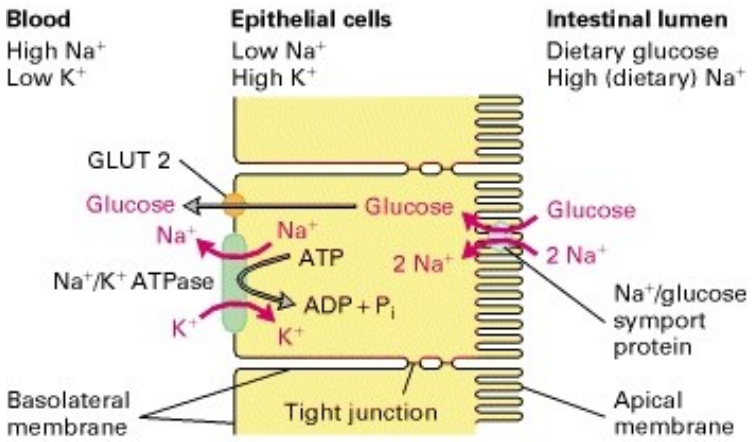
- star-like or spindle cells
- connected by nexus and desmosomes
- actin microfilaments, myosin and tropomyosin
- contraction
- sweat and salivary glands – enhancing secretion



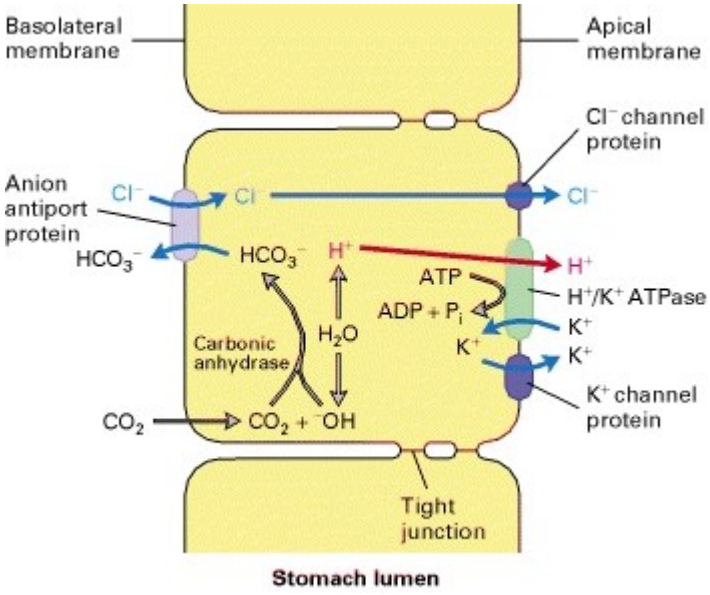


DOI: 10.4103/0973-029X.190952

Transcellular transport through epithelial cells is driven by concentration and/or charge gradients



Glucose transport



HCl secretion in stomach

http://www.ncbi.nlm.nih.gov/books/NBK21502/

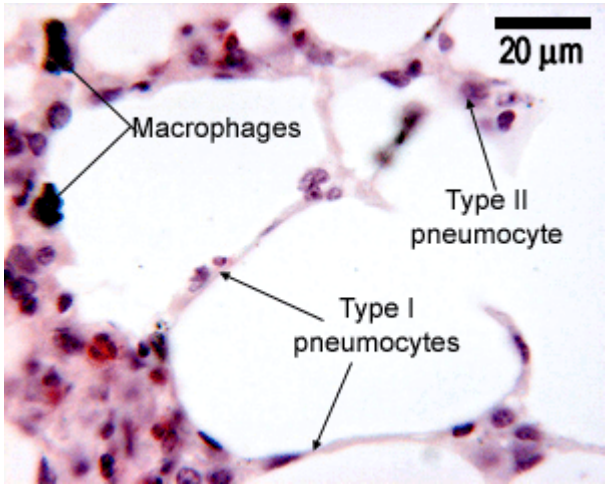
Respiratory epithelium

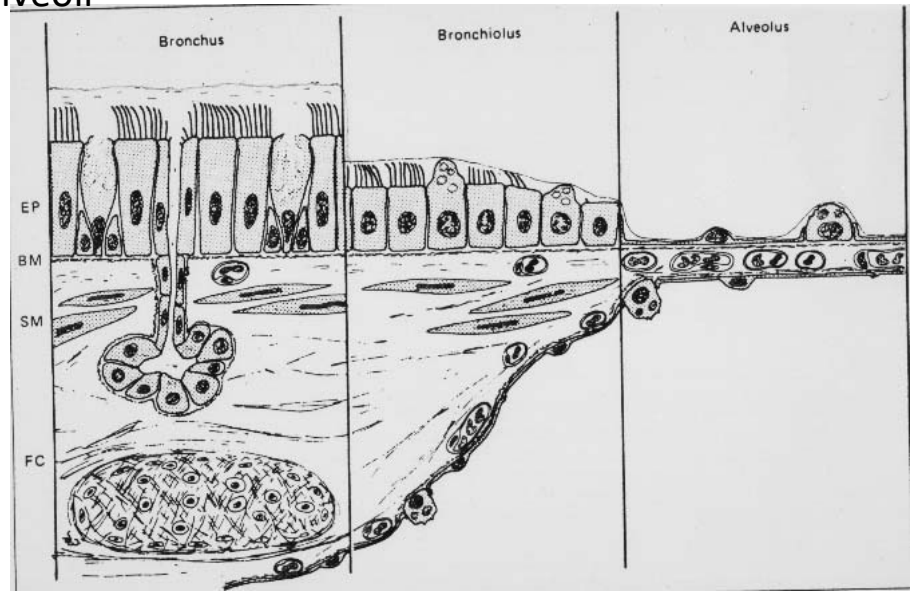
Epithelium of respiratory passages

- Moistening and protection against injury and pathogens
- Remove particles by mucociliary clearance
- Pseudostratified columnar epithelium with cilia
- Basal cells → epithelium renewal

Alveolar epithelium

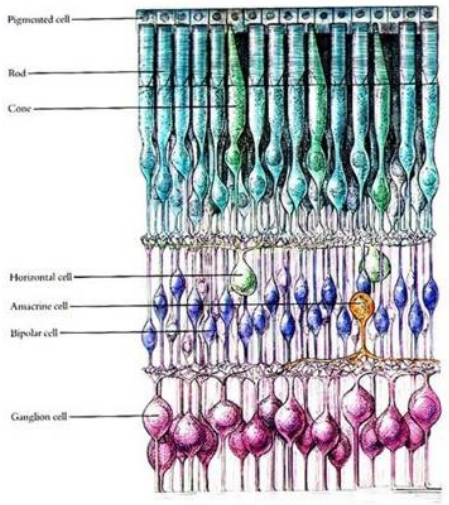
- Gas exchange
- Surfactant
- Respiratory bronchioles, alveolar passages and alveoli
- Type I and II pneumocytes





Sensory epithelium

– Supportive and sensory cells

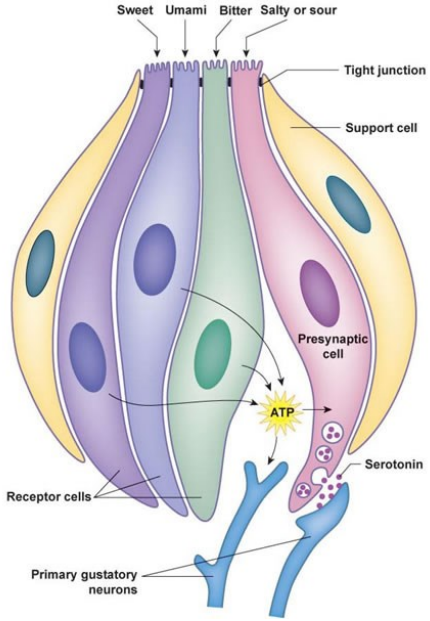


Primary sensory cells

– directly convert stimuli to membrane potential
– receptor region, body, axonal process
– olfactory epithelium (*regio olfactoria nasi*), rods and cones

Secondary sensory cells

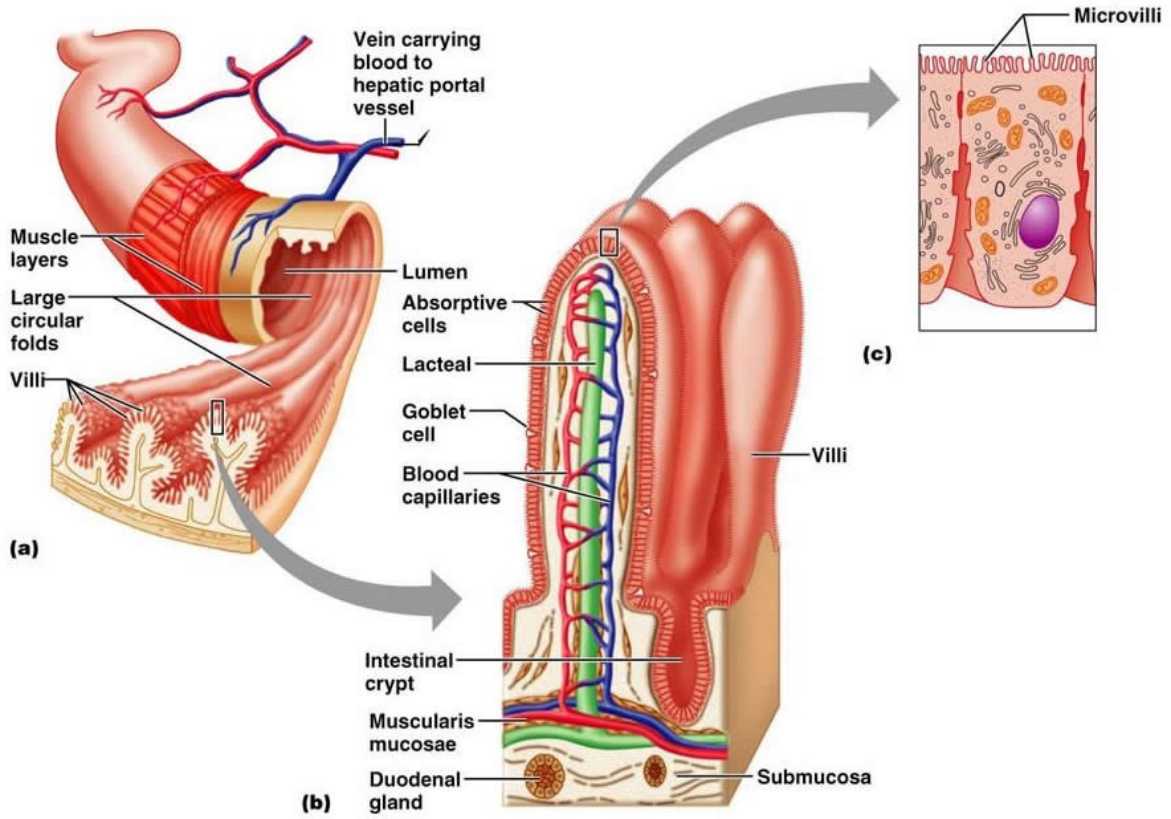
– receptor region and the cell body
– signal is transmitted by adjacent neurons terminating on secondary sensory cell
– taste buds, vestibulocochlear apparatus



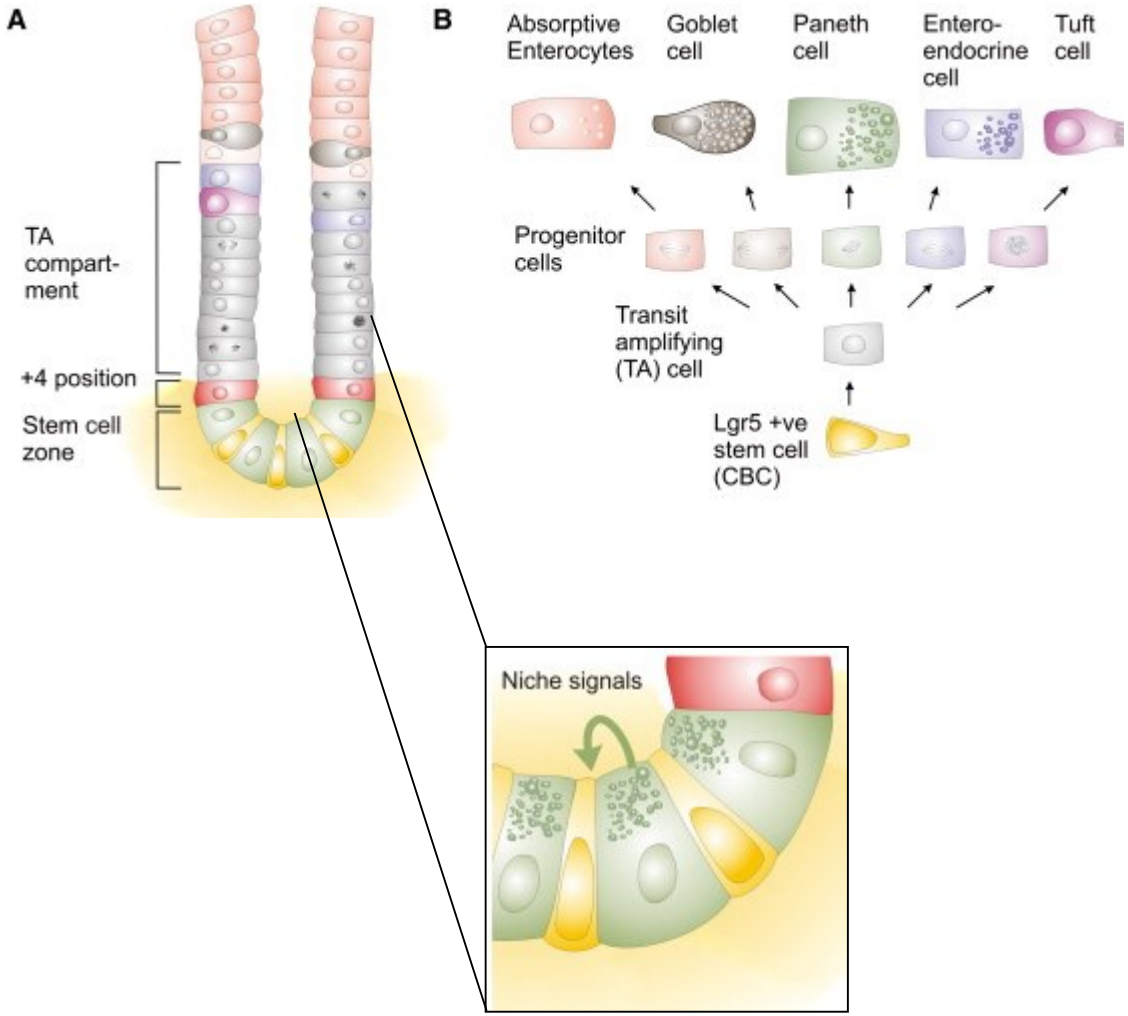
Renewal of epithelium

- different regenerative potential (epidermis × sensory epithelium of inner ear)
- multi- and oligopotent stem cells
- microenvironment – *stem cell niche*

Example: Regeneration of intestine epithelium



Example: Regeneration of intestine epithelium

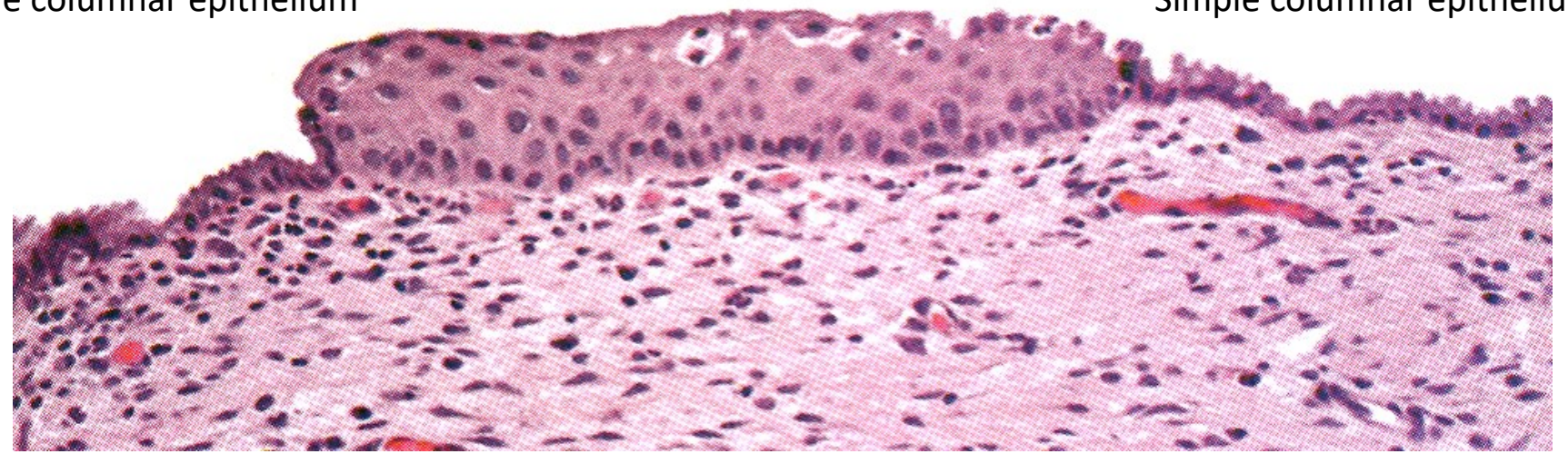


Abnormal renewal: metaplasia

Stratified squamous epithelium

Simple columnar epithelium

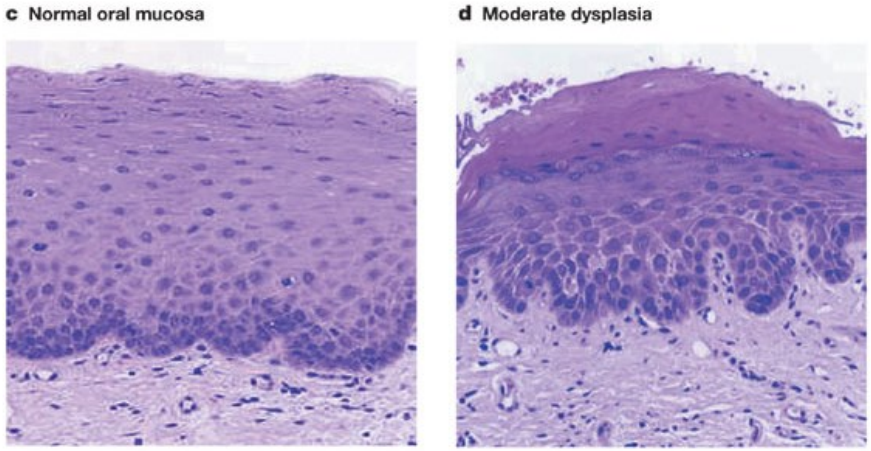
Simple columnar epithelium

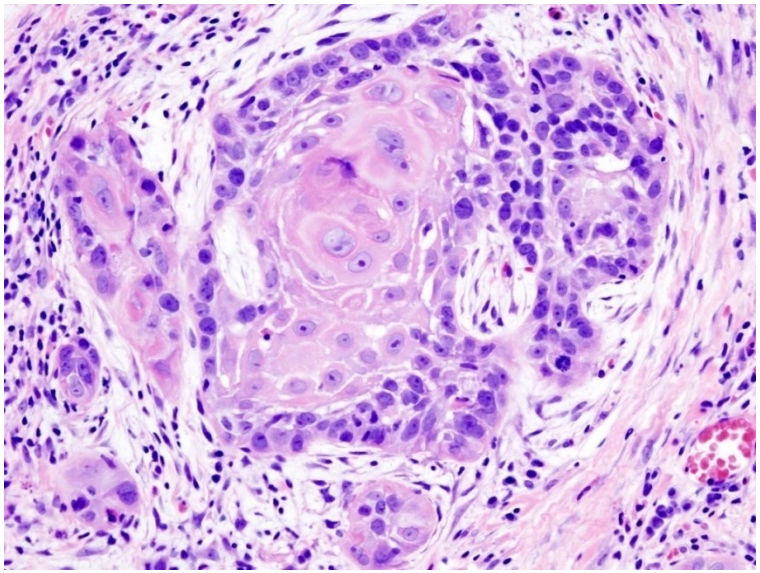


- squamous metaplasia of cervix uteri
- respiratory passages

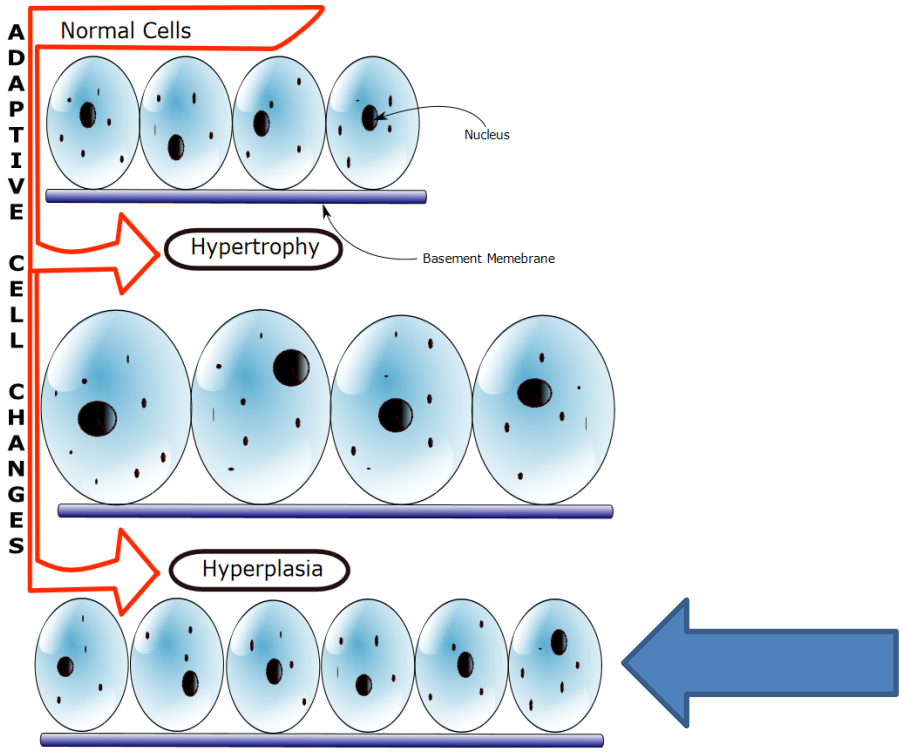
Abnormal renewal: metaplasia

- risk of development of precancerous lesions

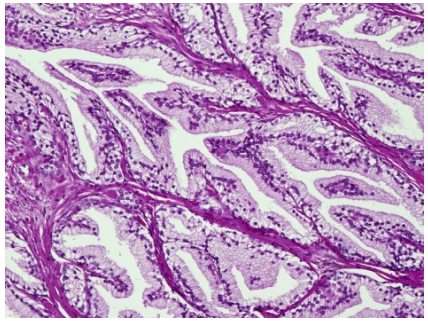




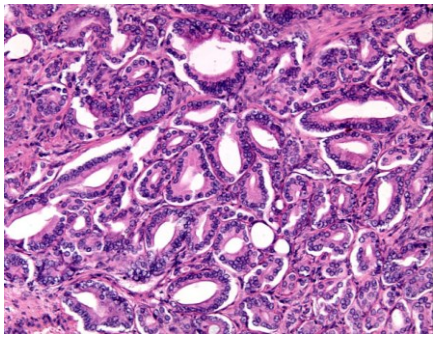
Abnormal renewal: hyperplasia



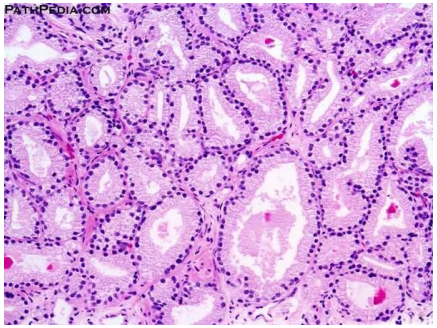
Normal prostate



Hyperplasia of prostate glandular epithelium



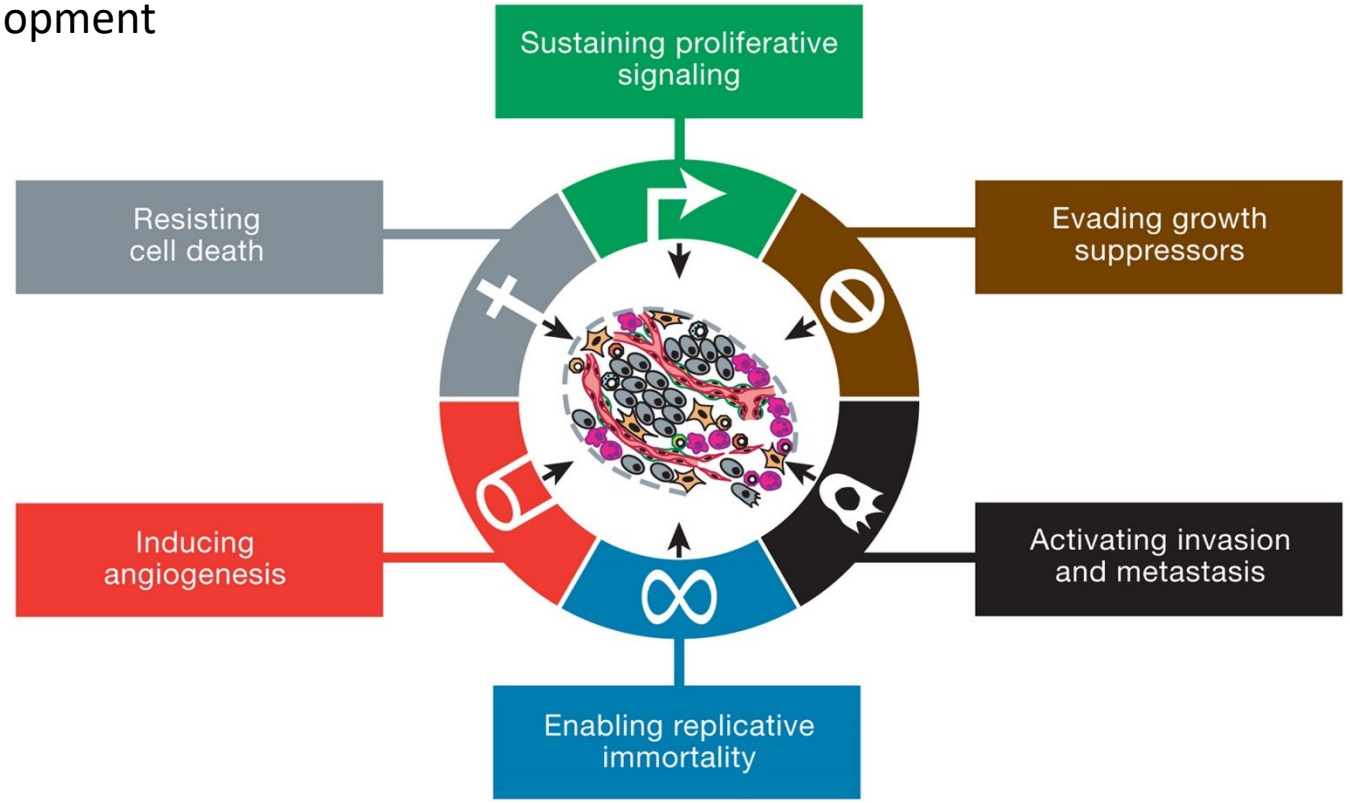
Prostate adenocarcinoma



Wikipedia.org; http://radiology.uchc.edu

Abnormal renewal: dysplasia and neoplasia

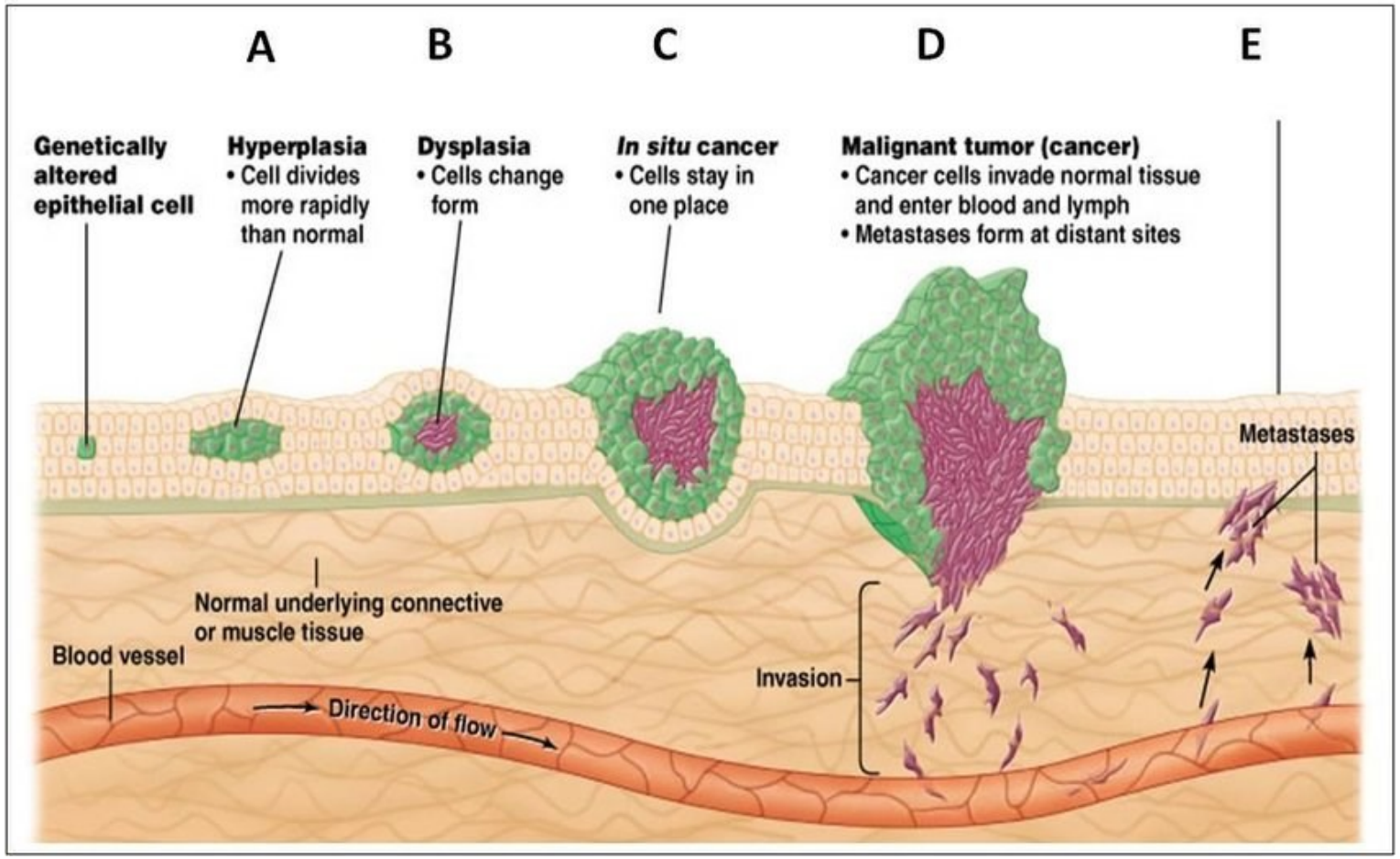
- uncoupling from regulatory mechanisms
- change in morphology and acqusition of new biological properties
- tumor development



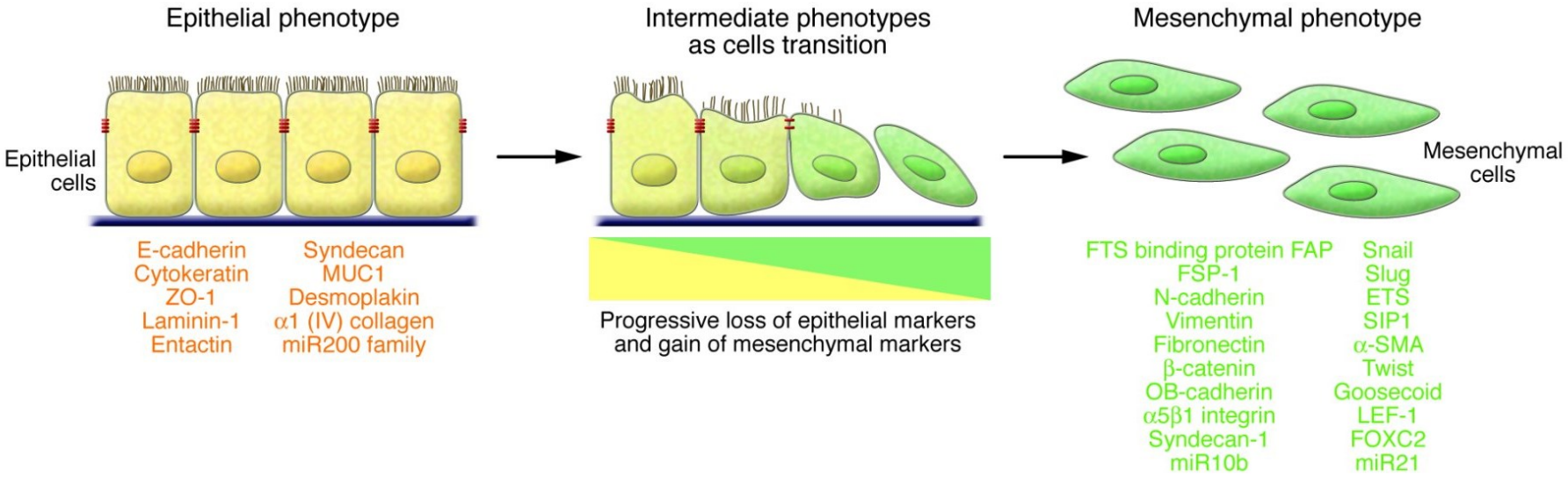
Hanahan & Weinberg, Cell 2011. The six hallmarks of cancer.
https://doi.org/10.1016/j.cell.2011.02.013

Abnormal renewal: neoplasia

- uncoupling from regualtory mechanisms
- tumor development

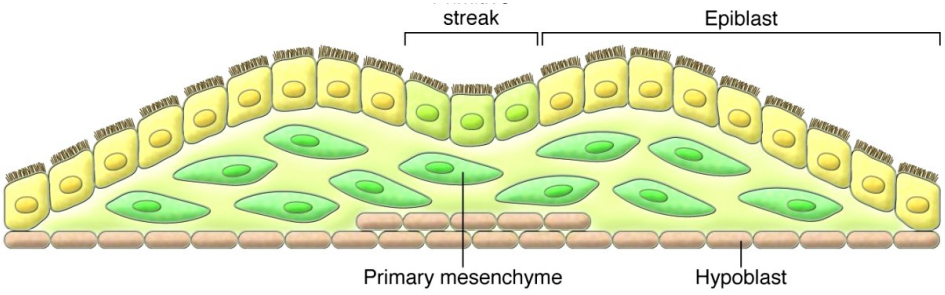


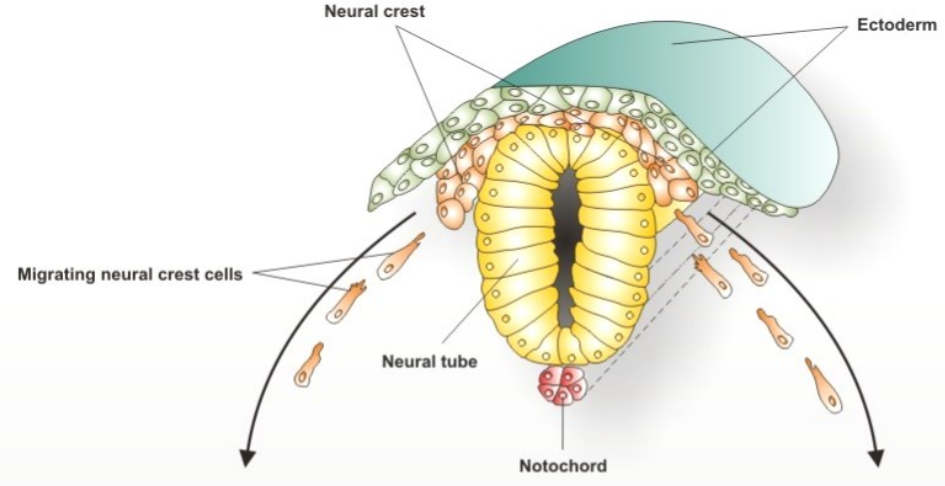
Epithelial to mesenchymal transition (EMT)

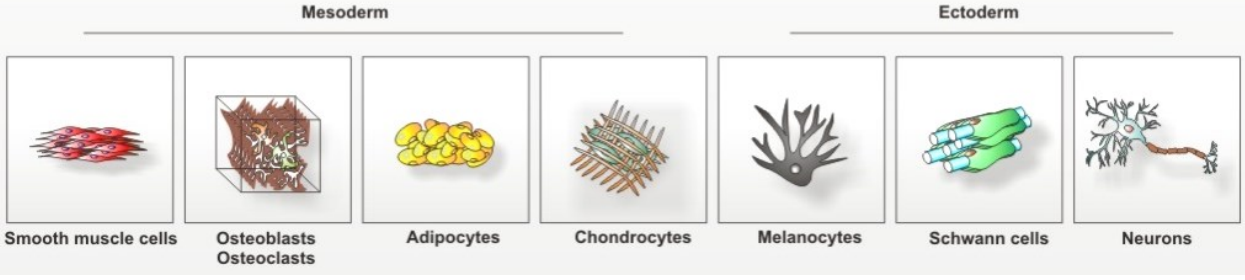


J Clin Invest. 2009;119(6):1420–1428. doi:10.1172/JCI39104.

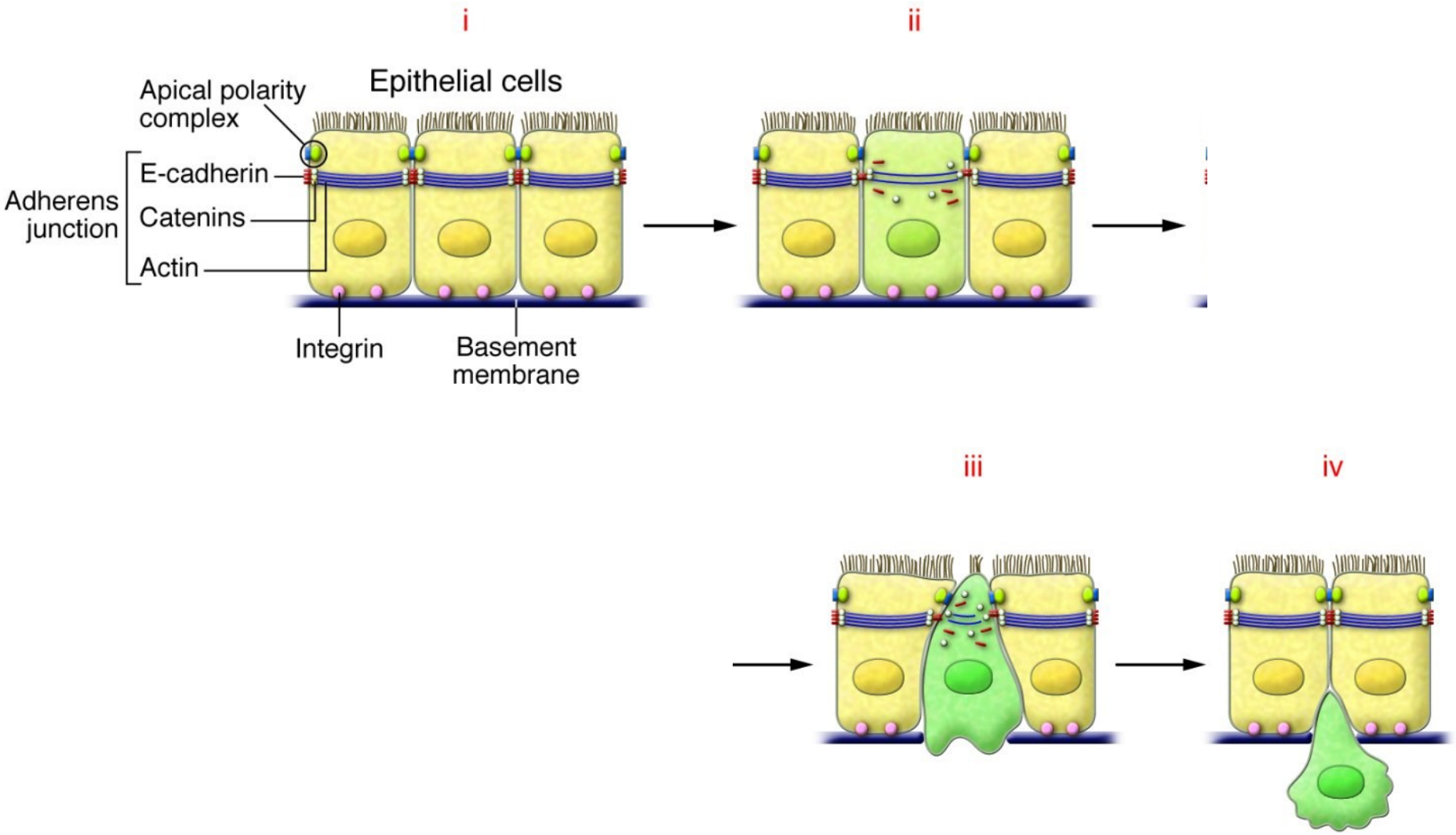
EMT in embryonic development



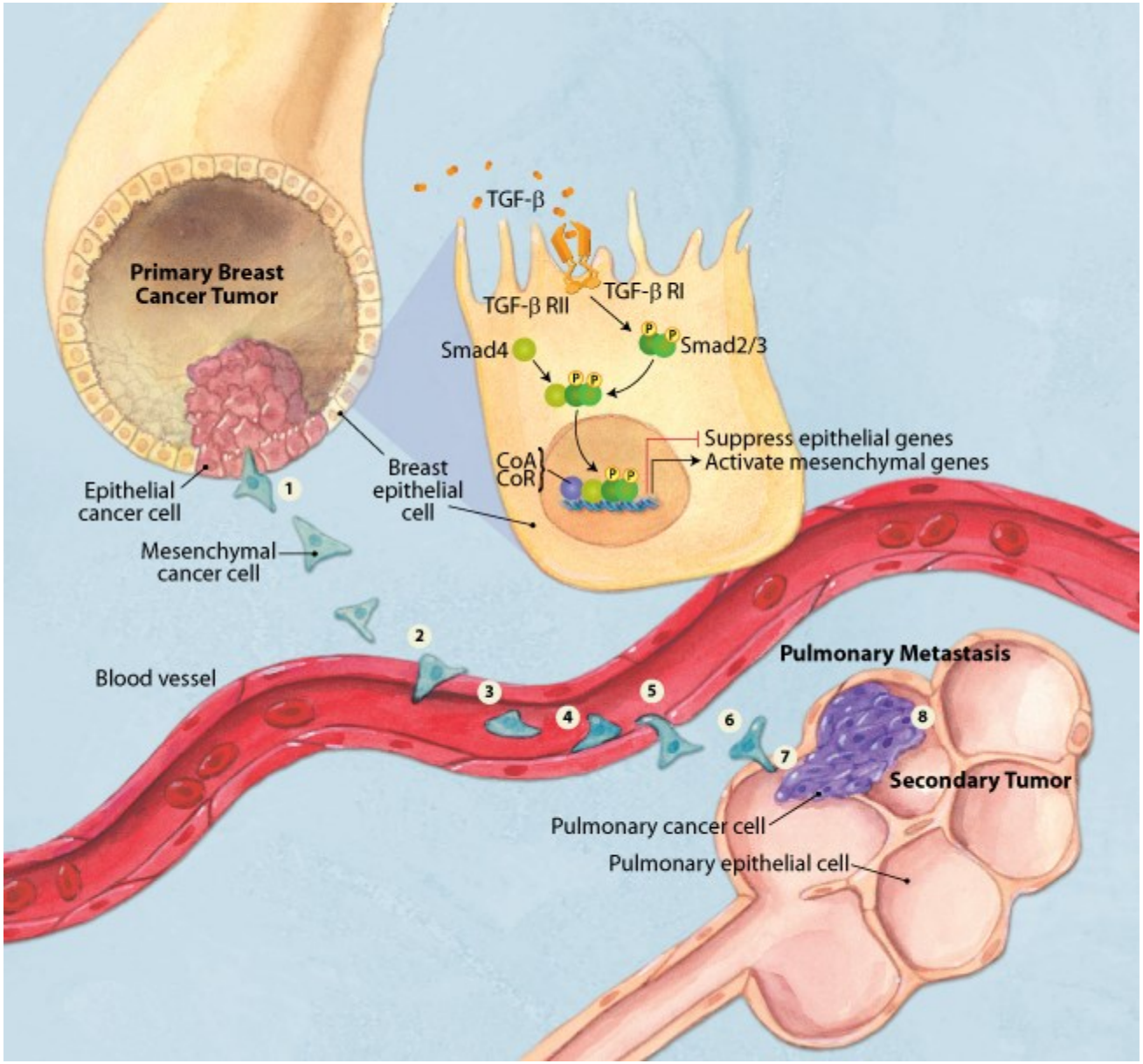




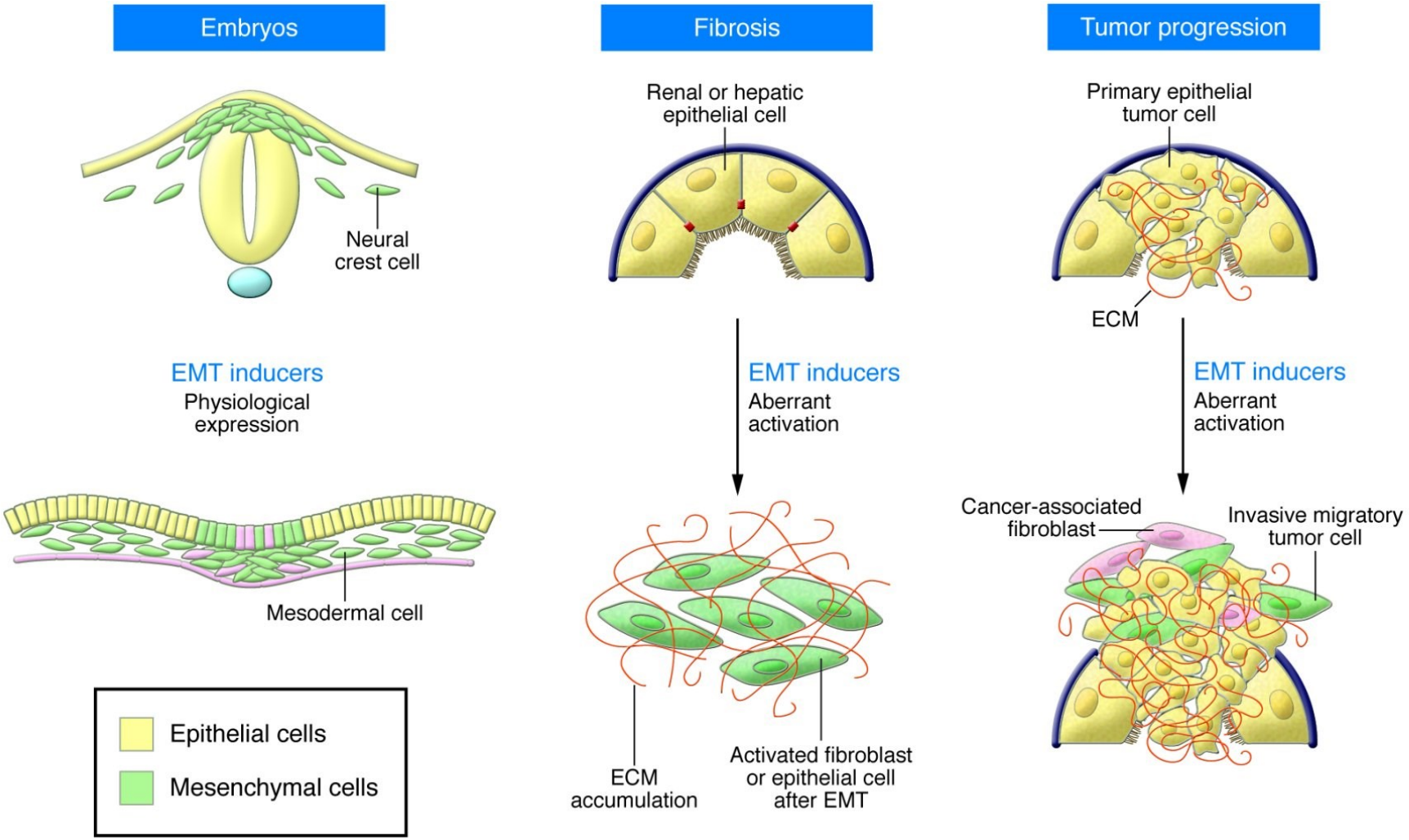
EMT in tumor dissemination



PLASTICITY OF EPITHELIAL TISSUES

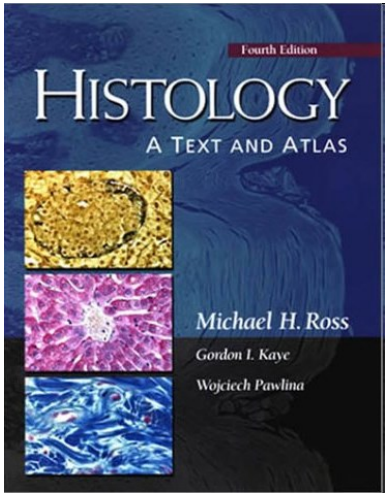


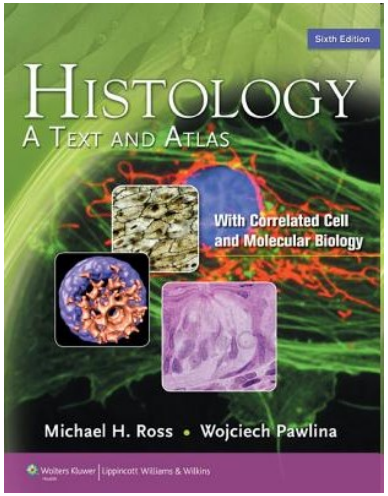
EMT overview

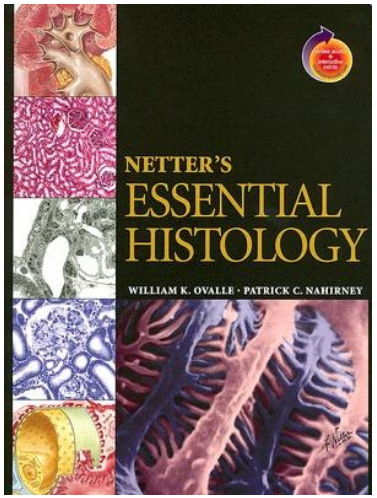


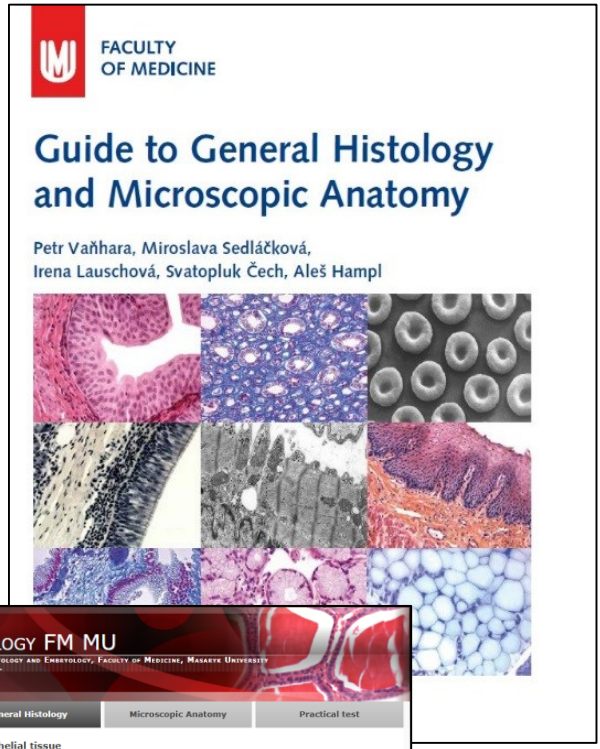
J Clin Invest. 2009;119(6):1438–1449. doi:10.1172/JCI38019.

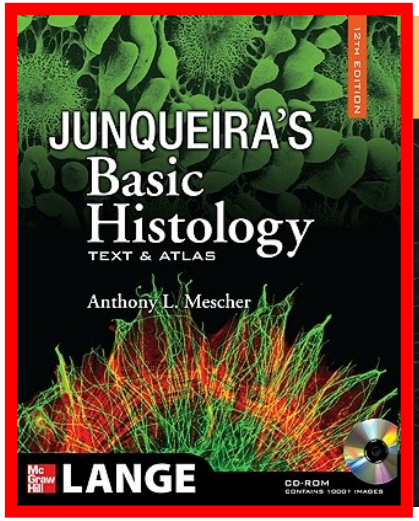
FURTHER STUDY

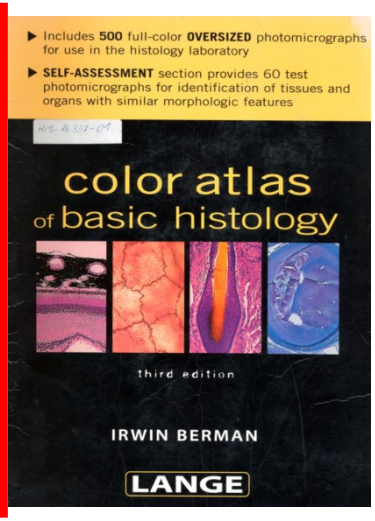


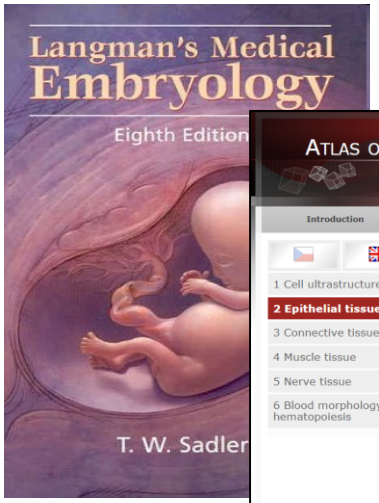








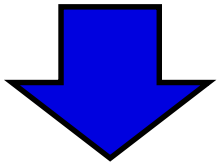




http://www.histology.med.muni.cz/

Thank you for attention

Questions? Comments?



pvanhara@med.muni.cz

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