Lecture 12

Respiratory system

- Functions
- Epithelial lining
- Nasal cavity
- Larynx
- Pharynx
- Trachea
- Lungs + Bronchial tree
- Blood-air barrier
- Development of the respiratory system
- Lung regeneration

Brno, September 2019

Respiratory system – Functions

Respiratory function

supply of O_2 + elimination of CO_2

Respiration = overall exchange of gasses between atmosphere and cells

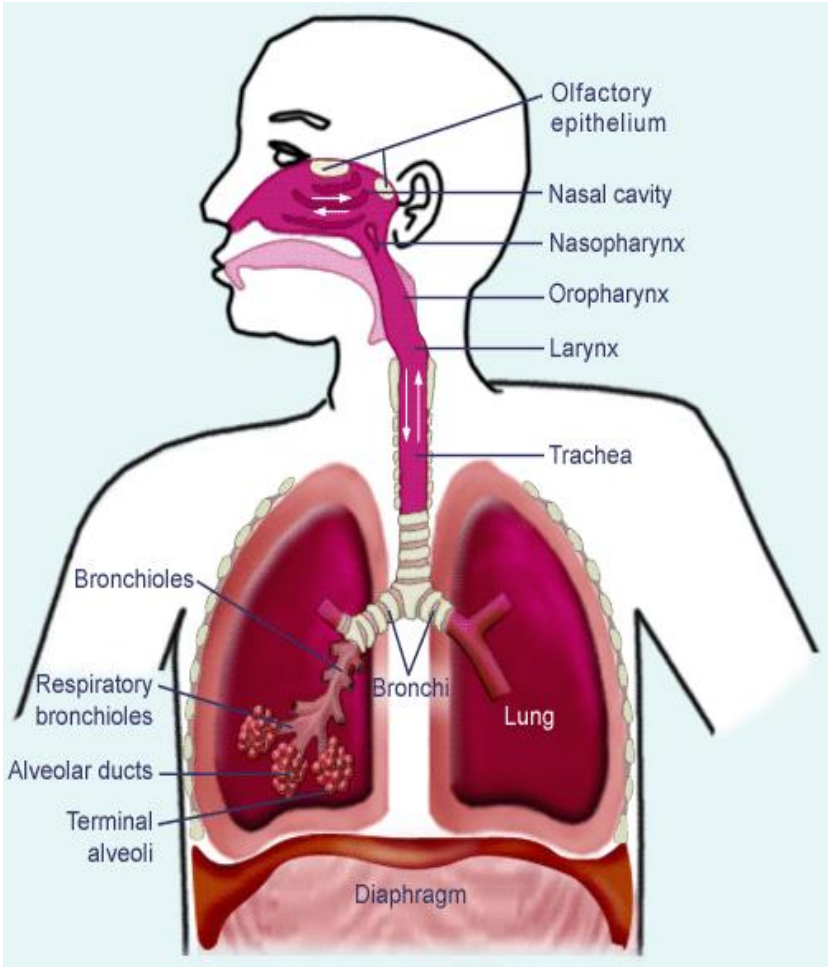
Involves:

- pulmonary ventilation
- gas exchange: External + Internal respiration
- gas transport

Non-respiratory functions:

- synthesis, activation and inactivation of vasoactive substances, hormones, neuropeptides, eicosanoids, lipoprotein complexes.
- hemostatic functions (thromboplastin, heparin)
- lung defense: complement activation, leucocyte recruitment, cytokines and growth factors
- speech, vomiting, defecation, childbirth

Respiratory system – Overall composition



Anatomic

Functional

Upper respiratory tract — **Conducting portion**
- nasal cavity
- *paransal sinuses*
- nasopharynx
- oropharynx

Lower respiratory tract
- larynx
- trachea
- bronchi (extra- + intrapulmonary)
- bronchioles (up to terminal)

Respiratory portion
- respiratory bronchioles
- alveolar ducts
- alveolar sacs
- alveoles

Conducting portion – General features

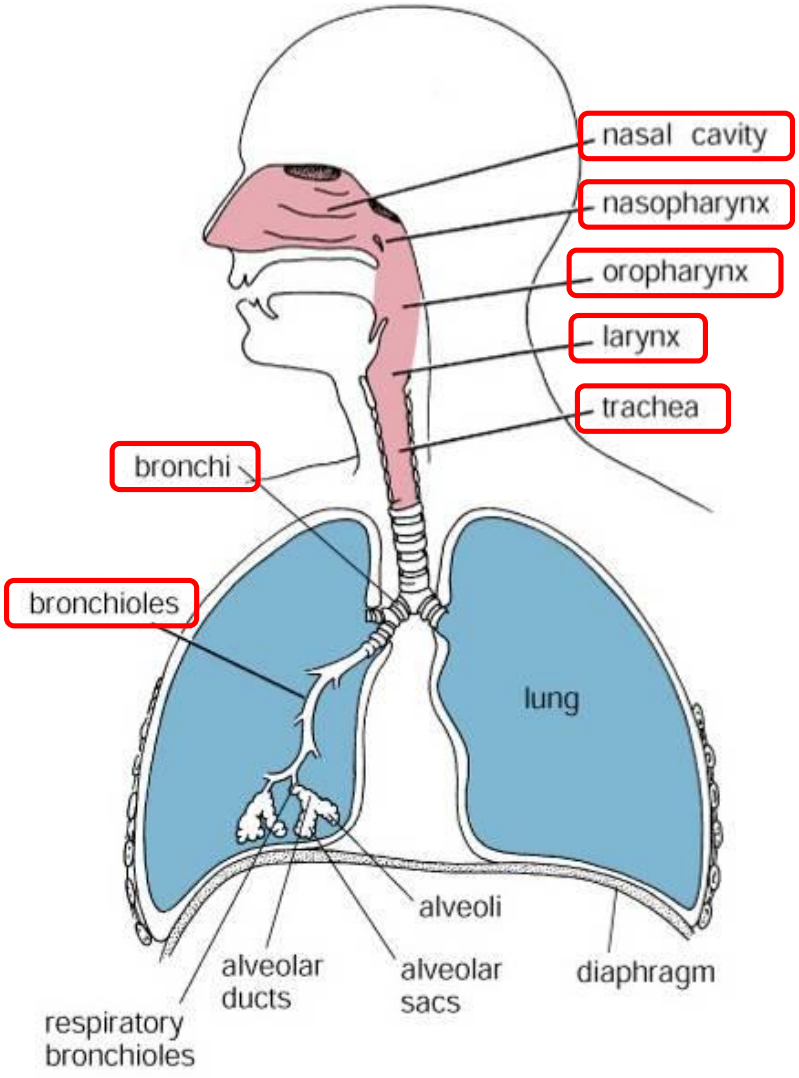


Figure 18.1. **Diagram of respiratory passages.**

Function

- Transport
- Moistening
- Filtering
- Warming

Composition

Bone and/or **cartilage**
(mechanical support)

Mucosal lining
- Epithelium
- Lamina propria

Conducting portion – Nasal cavity + Paranasal sinuses

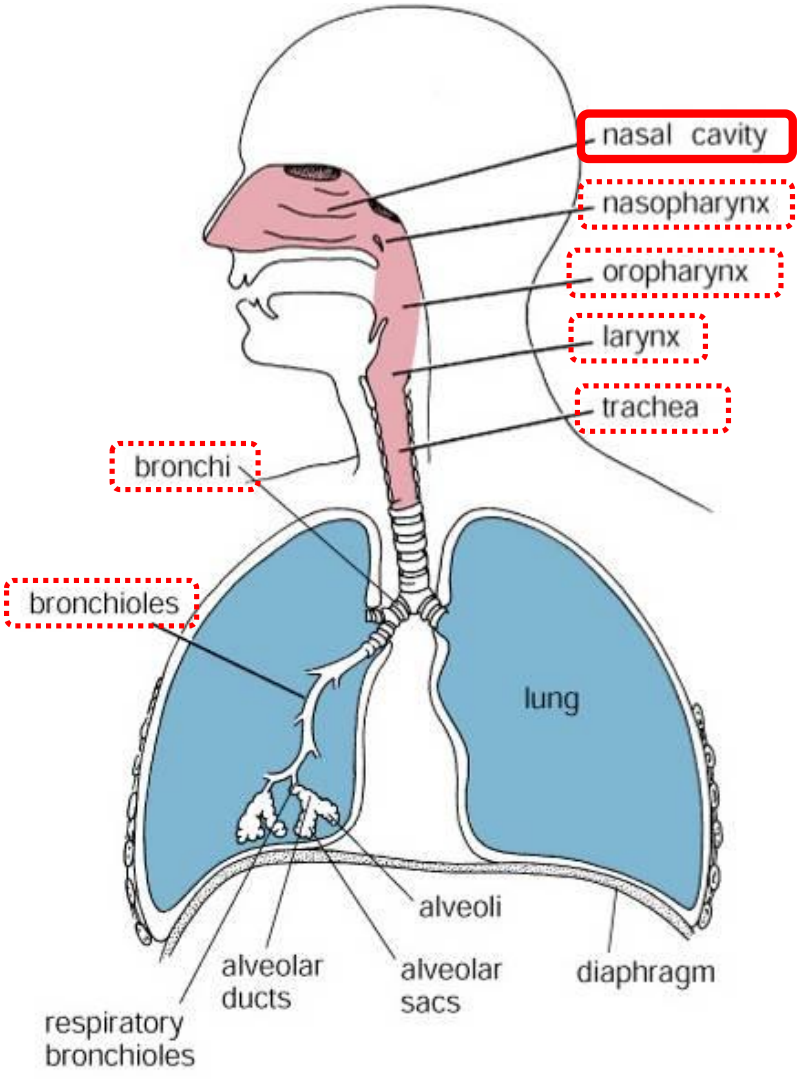
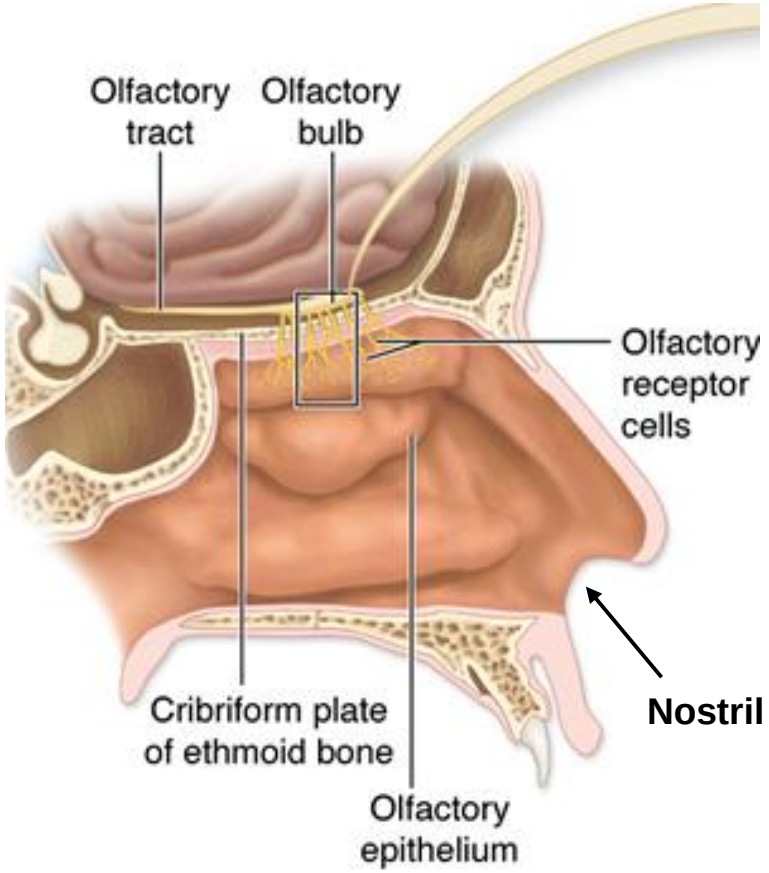


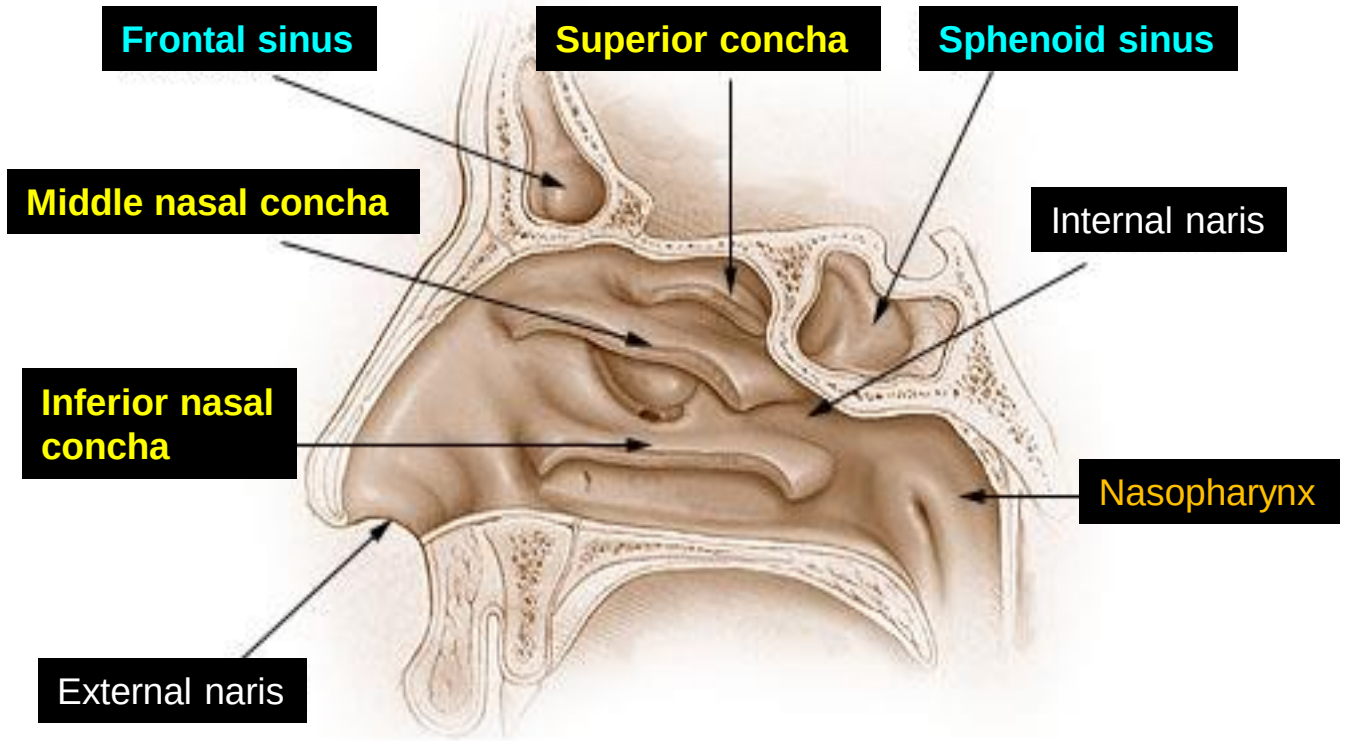
Figure 18.1. **Diagram of respiratory passages.**

Left + Right nasal cavity

(separated by osseous/cartilagineous nasal septum)



Conducting portion – Nasal cavity + Paranasal sinuses



Lining of the nasal cavity

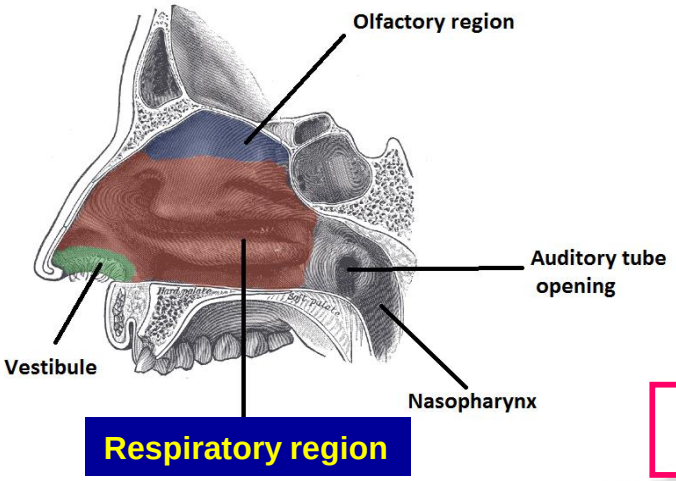
Roof + Superior concha	Nostrils + Vestibule	Remaing surfaces
Olfactory epithelium	Dermis	Airway mucosa
	• keratinizing squamous ep. • hairs • sweat + sebaceous glands • in vestibule transits to airway ep.	„respiratory“
Olfactory region		Respiratory region

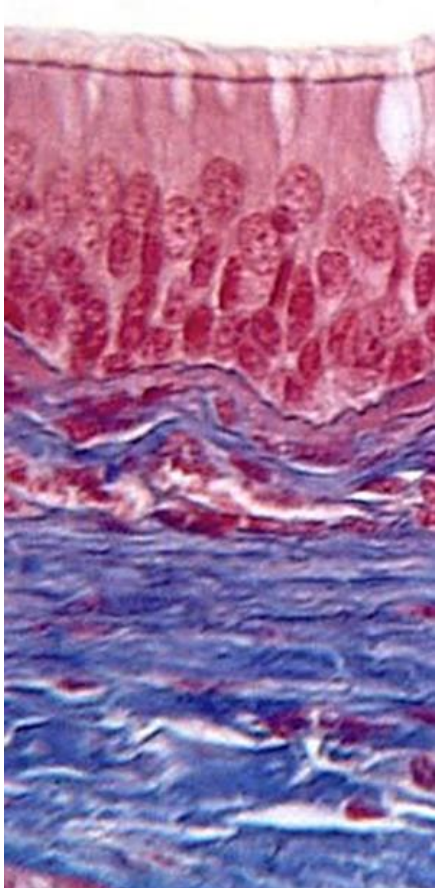
Support: bone and/or cartilage

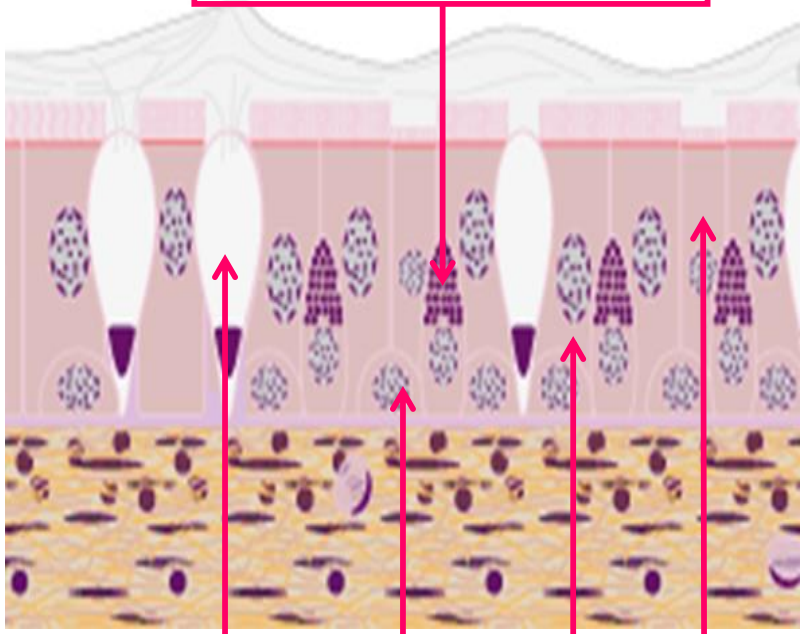
No submucosa and/or hypodermis

Nasal cavity - Airway musosa

= respiratory mucosa – lines most of the conducting portion of the respiratory system







Small granule cells (Kulchitsky)
DNES – diffuse neuroendocrine system

Mucous layer

Ciliated pseudotratified collumnar epithelium
(min. 5 types of cells)

Basal cells
(stem cells)

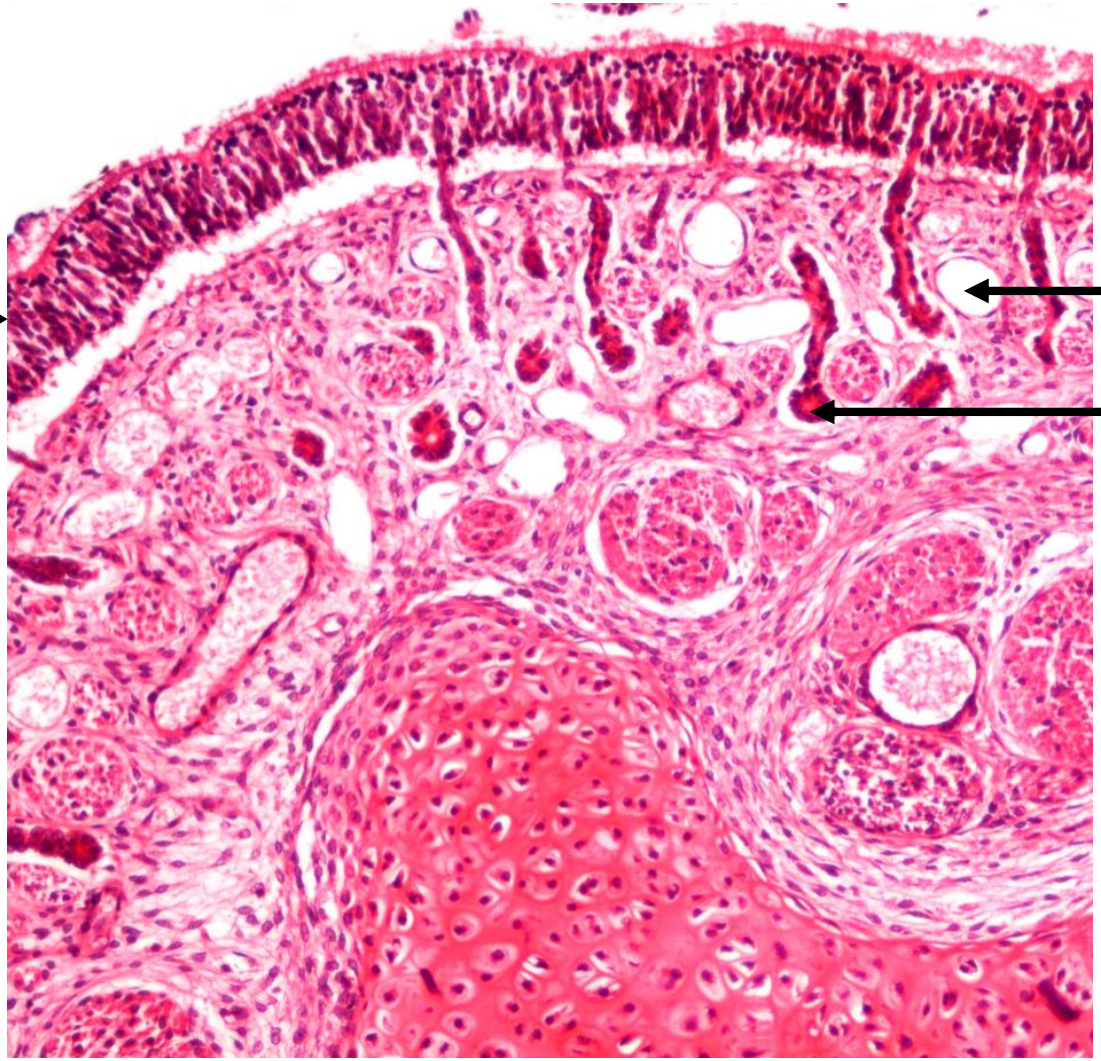
Brush cells
(chemosensory)
(similar to cells of taste buds)

Goblet cells
(mucin)

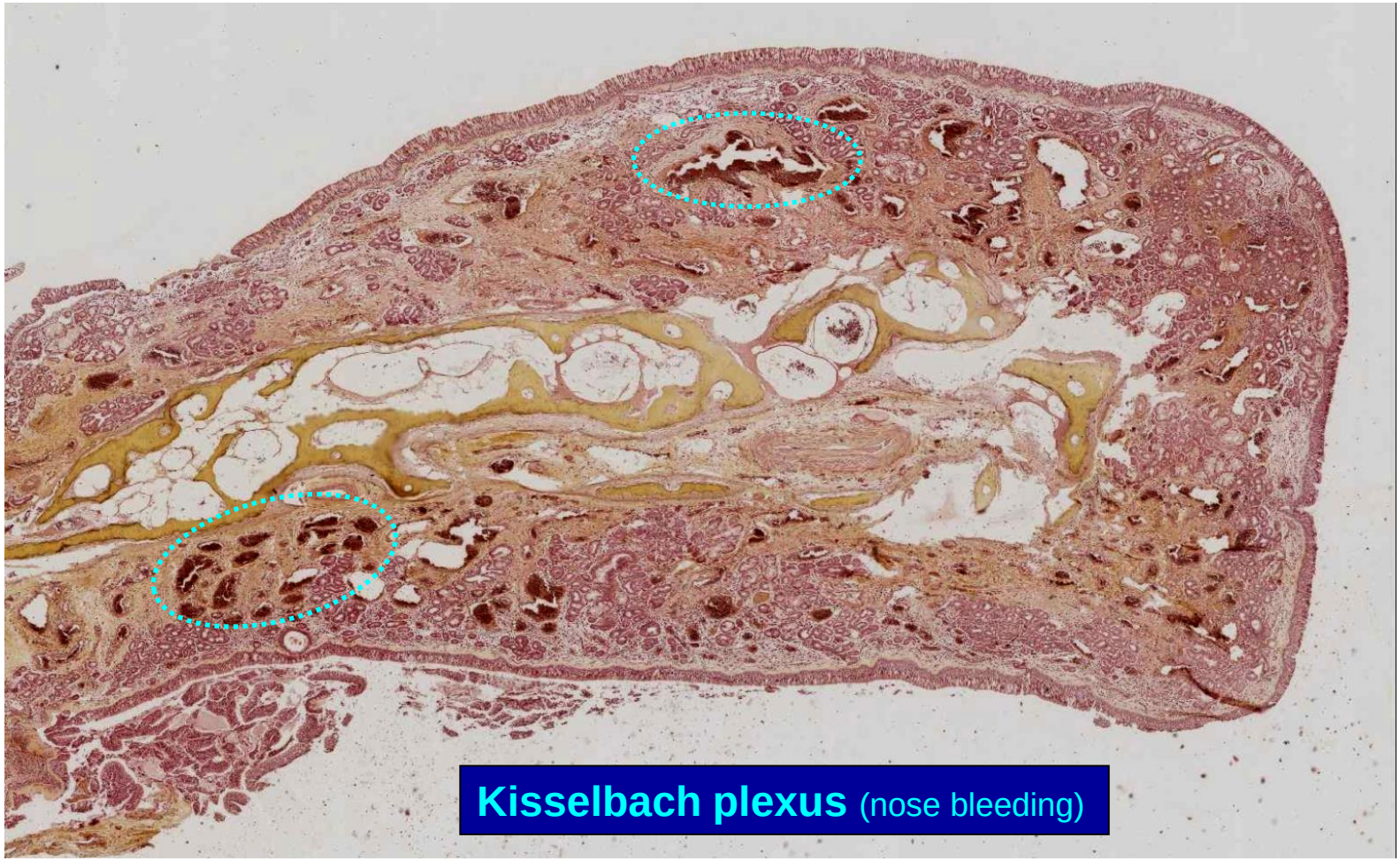
Ciliated cells
(most abundant)

Lamina propria mucosae
- loose connective tissue
- arterial and venous plexuses
- many seromucinous glands
- abundant lympoid elements (nodules, mast cells, plasma cells)

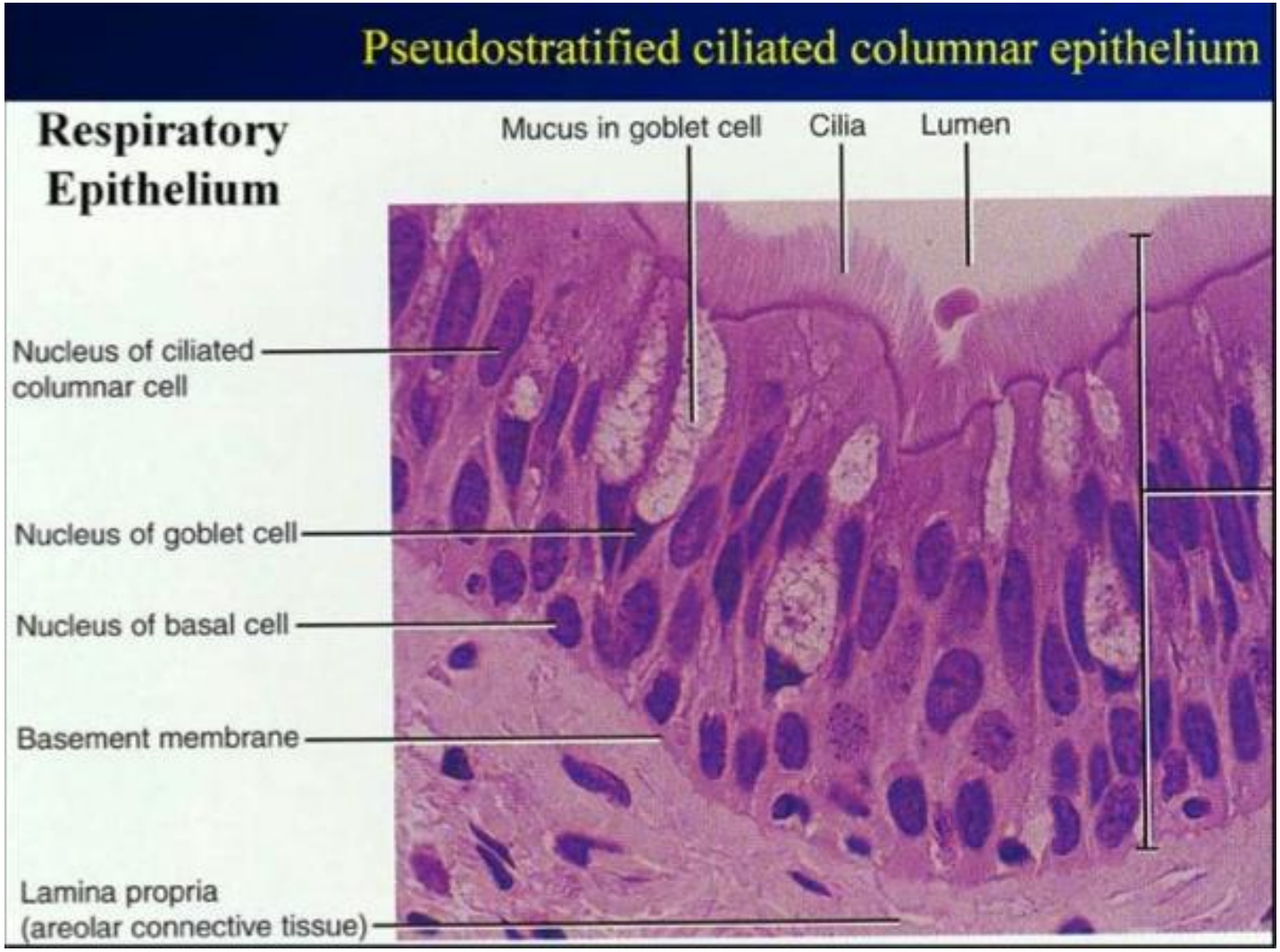
Airway mucosa



Airway mucosa – Nasal concha (Concha nasi)



Airway mucosa - Epithelium

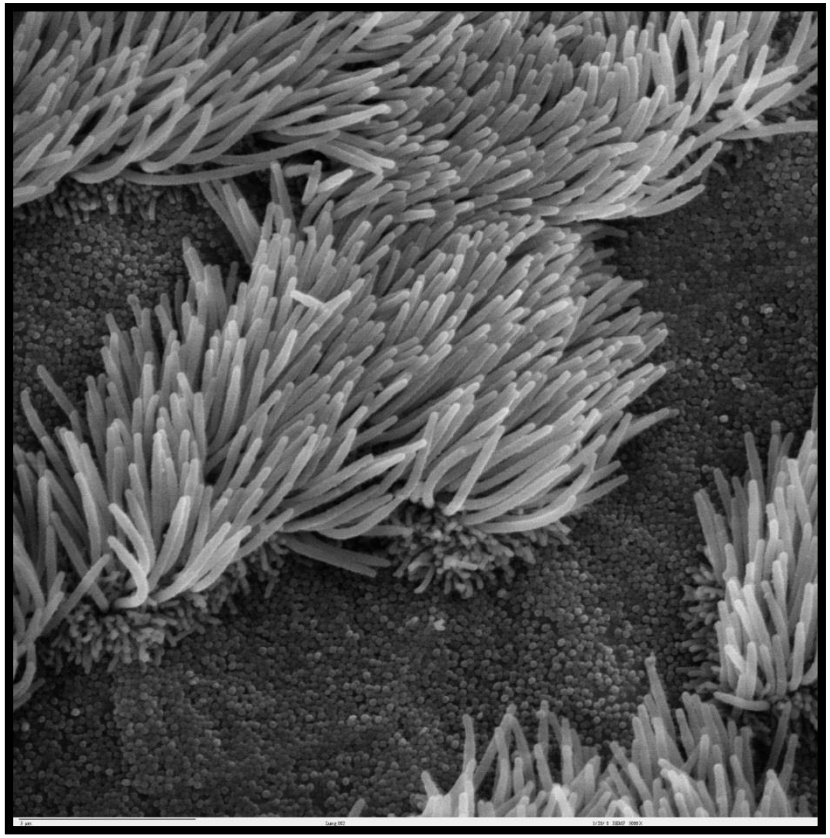


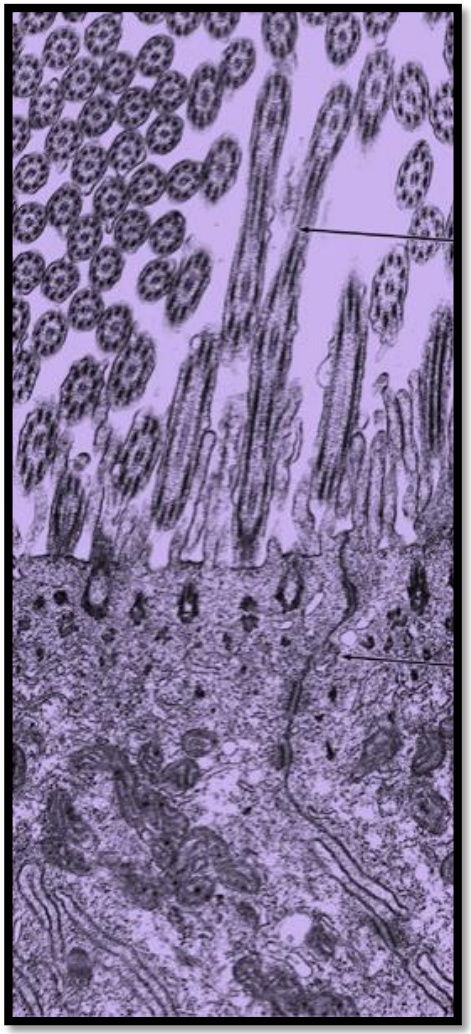
Exposure to toxic compounds

Squamous metaplasia

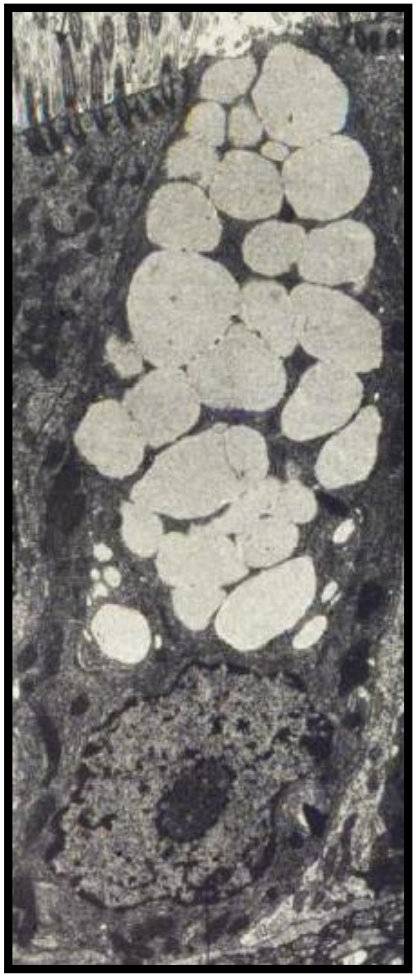
- **pseudostratified cilliated collumnar** ep. changes to **squamous stratified** ep.
- may develop into cell dysplasia (precancerous)

Airway mucosa - Epithelium

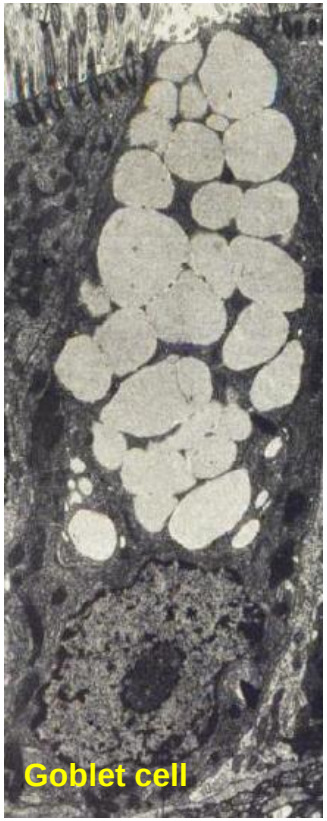




Ciliated cells



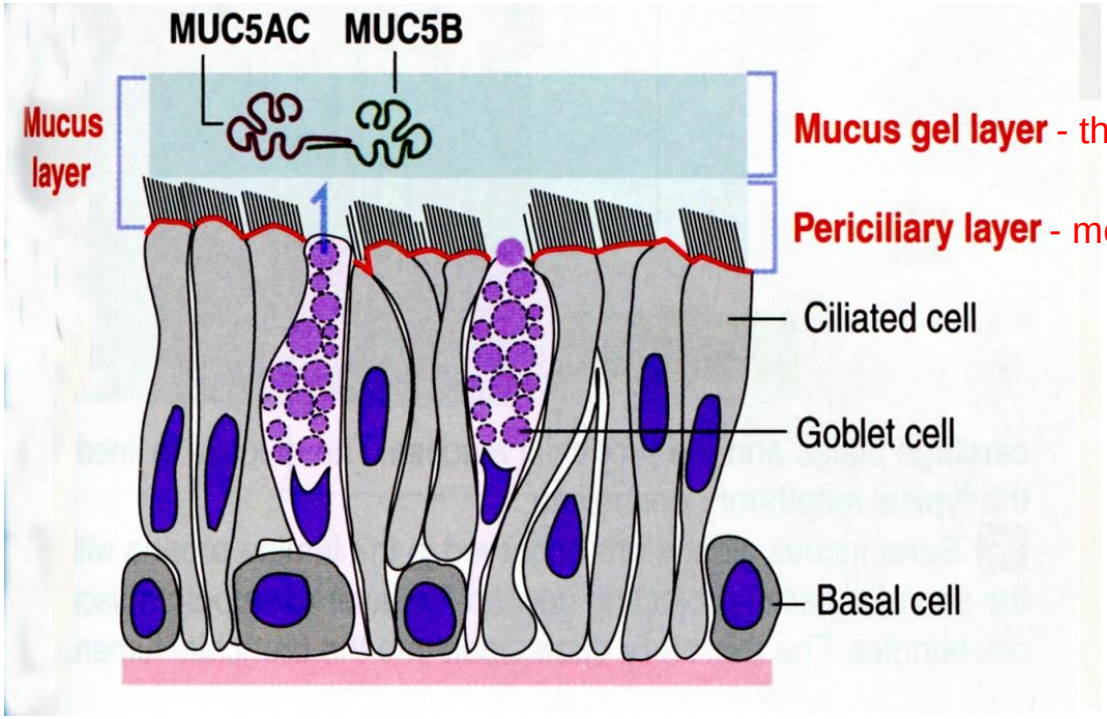
Goblet cell



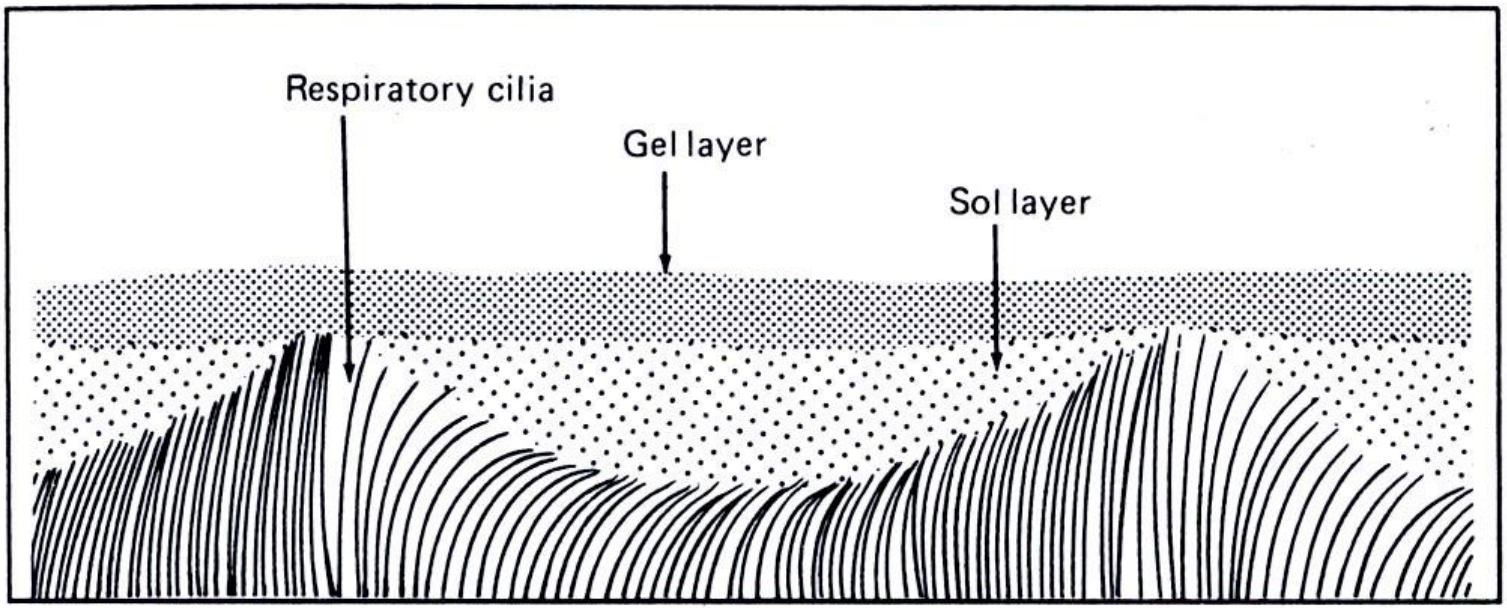
Airway mucosa - Mucus

Mucus

- mainly glycoproteins in water
- ensures moisturing od mucosa and air
- contains IgA immunoglobulins (mucosal immunity)
- traps airborne particles (dust etc)
- helps selfcleaning of the airways

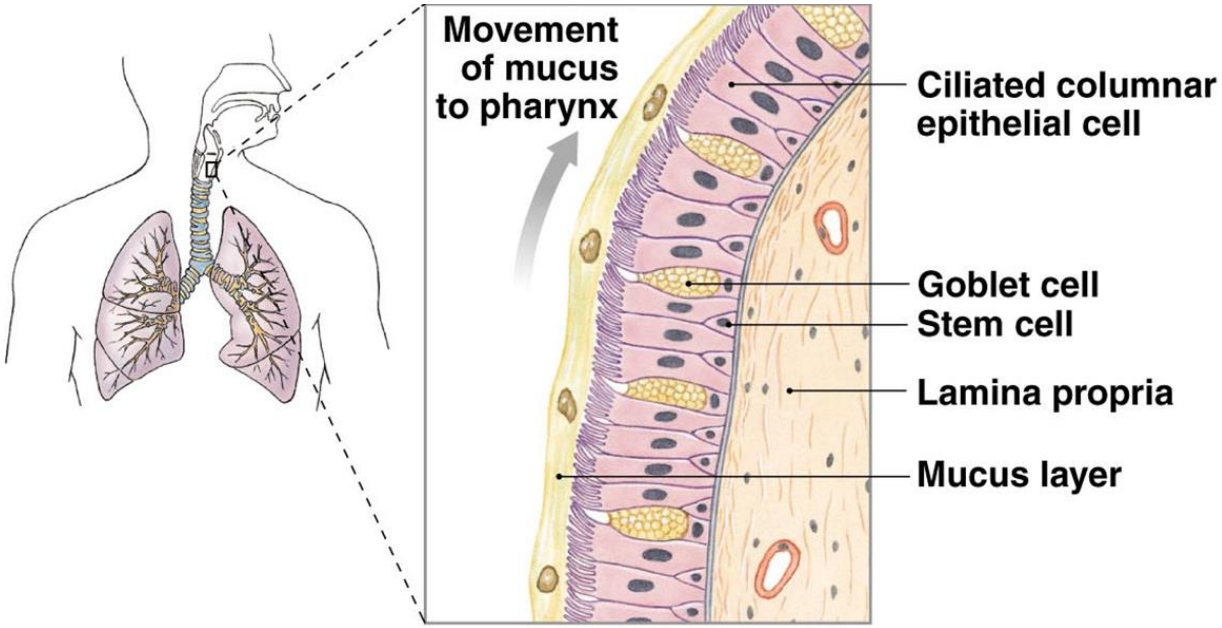


Airway mucosa - Mucus



Respiratory cilla are bathed in the sol portion of the mucus layer above them. Their power strokes allow mucus movement by contacting the viscous gel layer, always in the same direction. (From Martin DE and Youtsey JW: Respiratory anatomy and physiology, St Louis, 1988, The CV Mosby Co.)

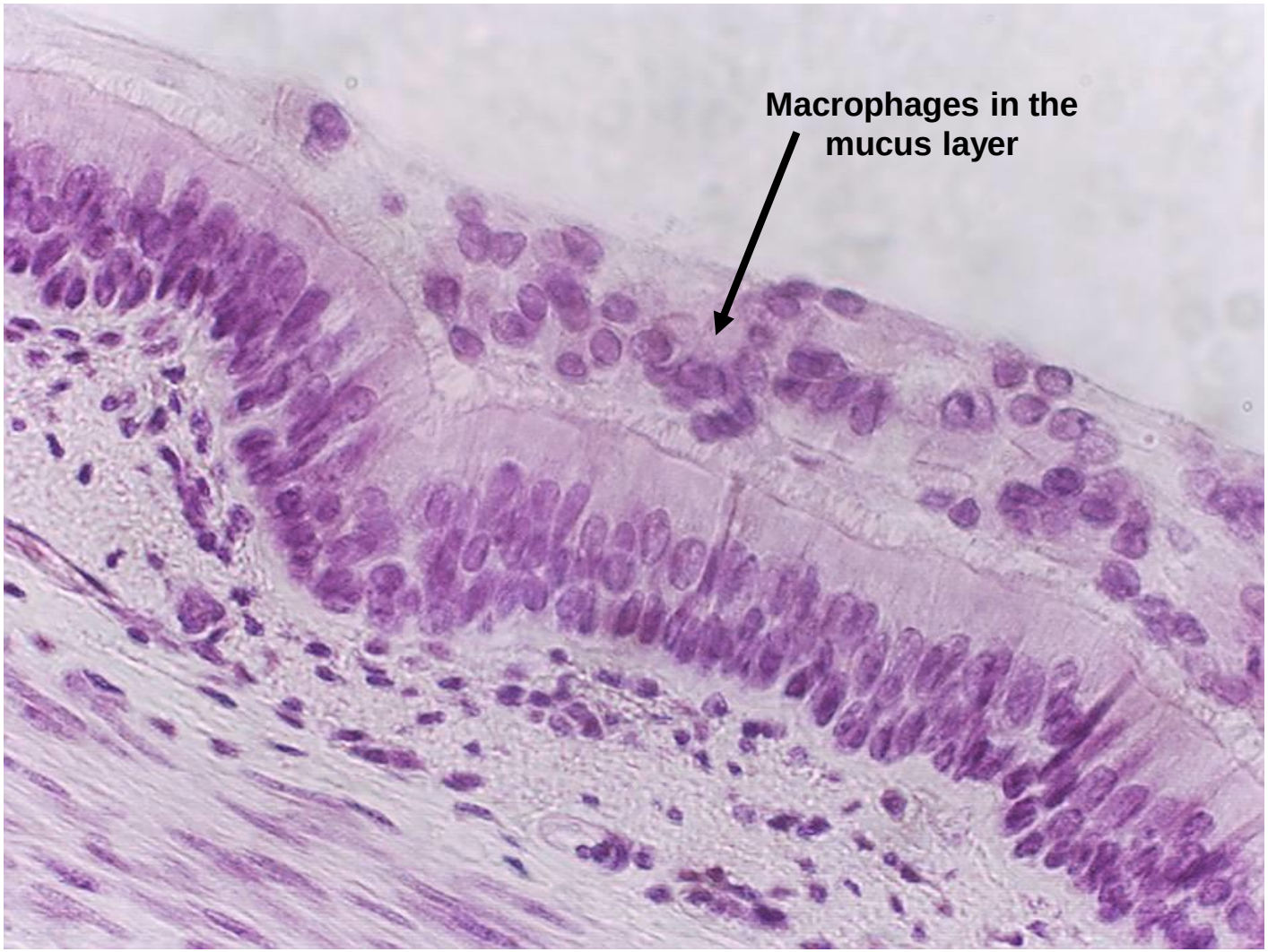
Airway mucosa - Mucus



Cilia movement drives mucus towards pharynx.

Speed of mucocilliary transport - 5 mm / minute.

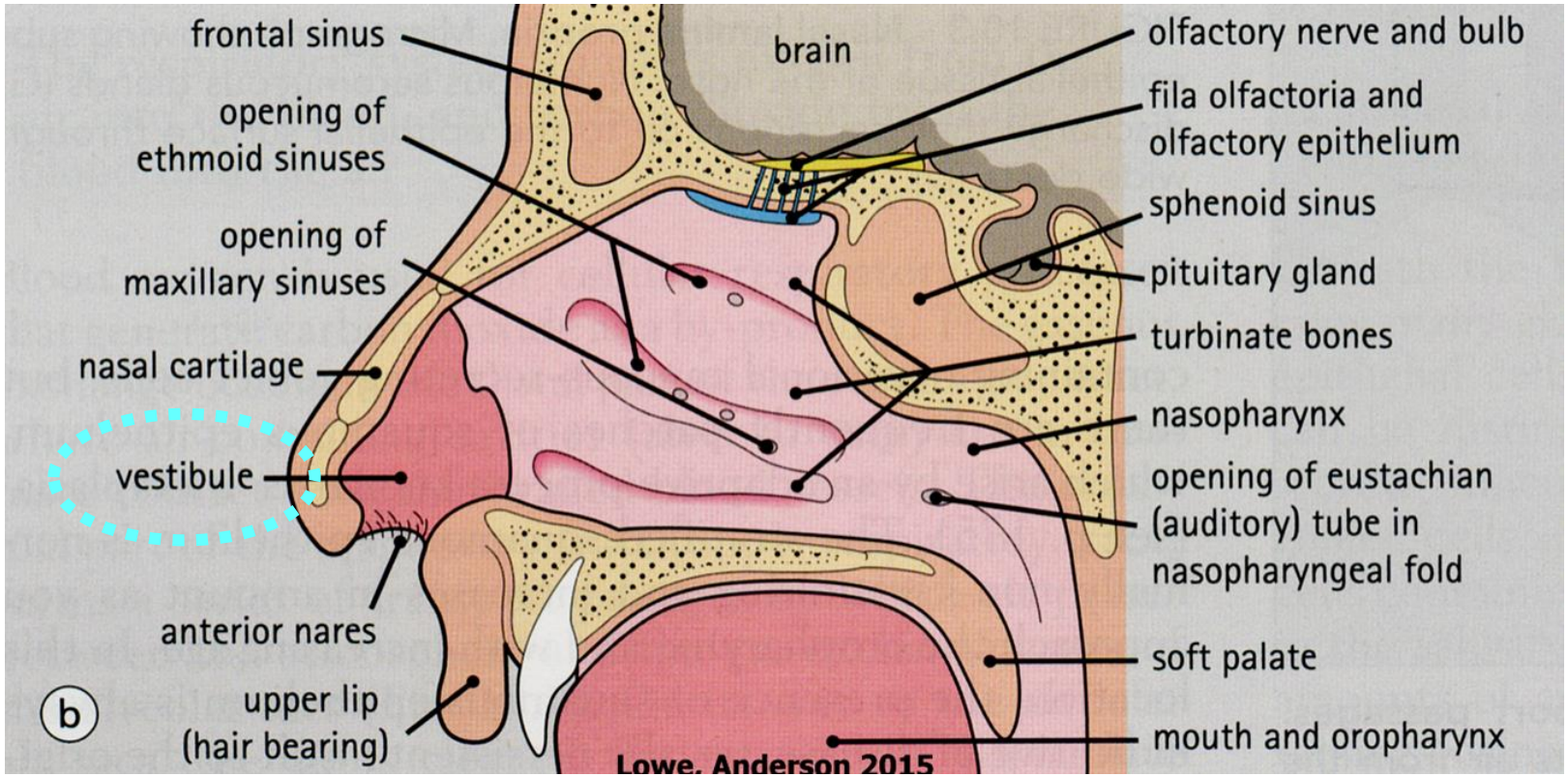
Airway mucosa - Mucus



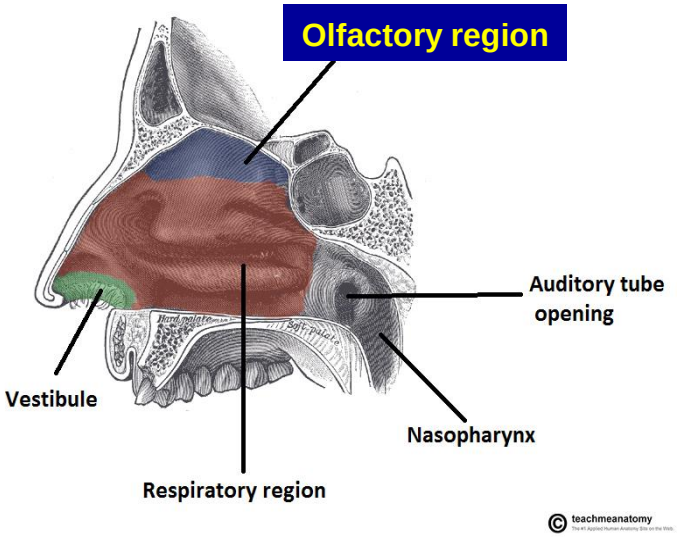
Nasal cavity – Vestibule (Vestibulum nasi)

Location: 5 – 6 mm wide zone at the edge of nostrils

Lining: transition of dermis to respiratory mucosa – hairs with sebaceous glands



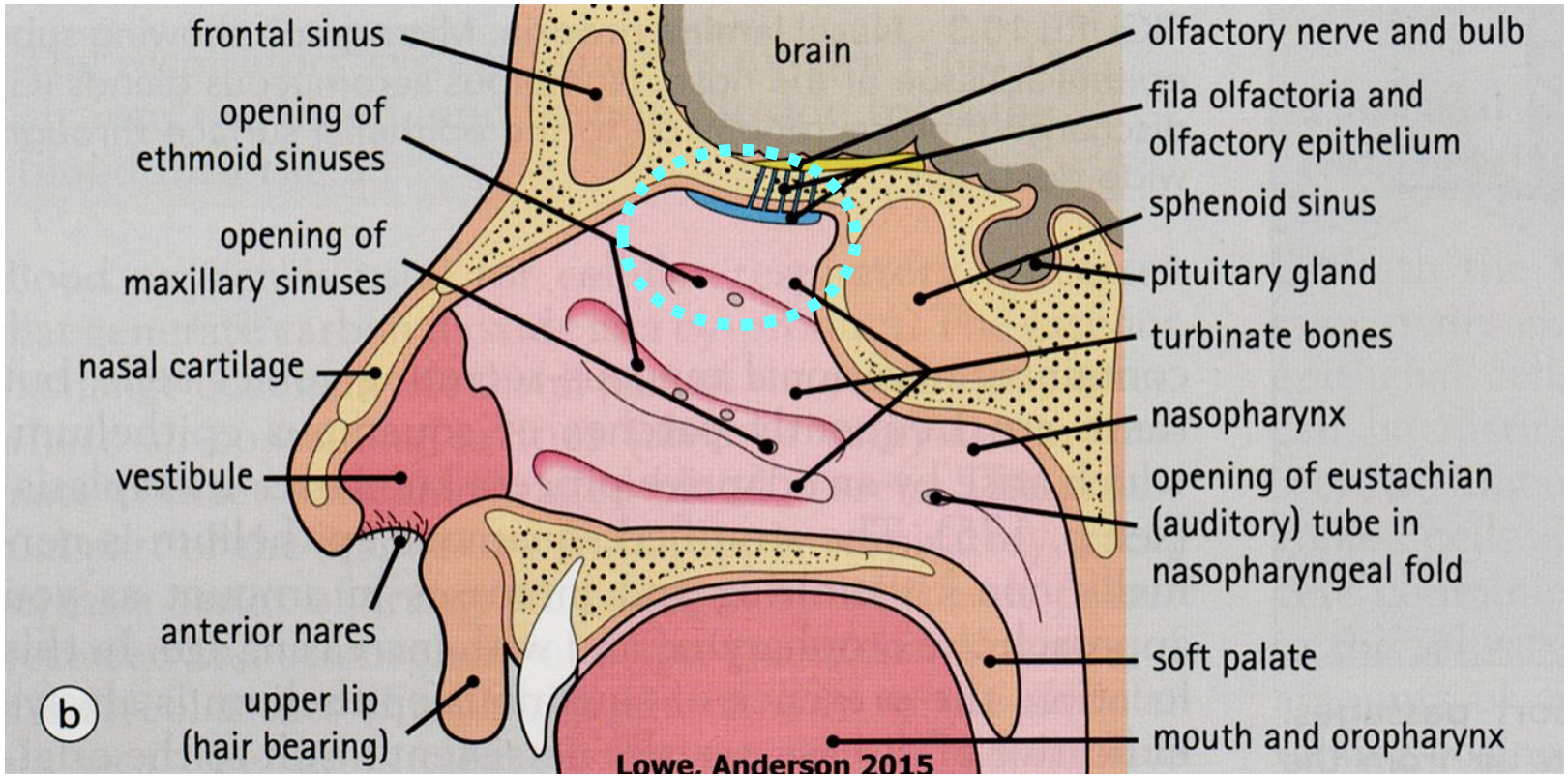
Nasal cavity – Olfactory epithelium



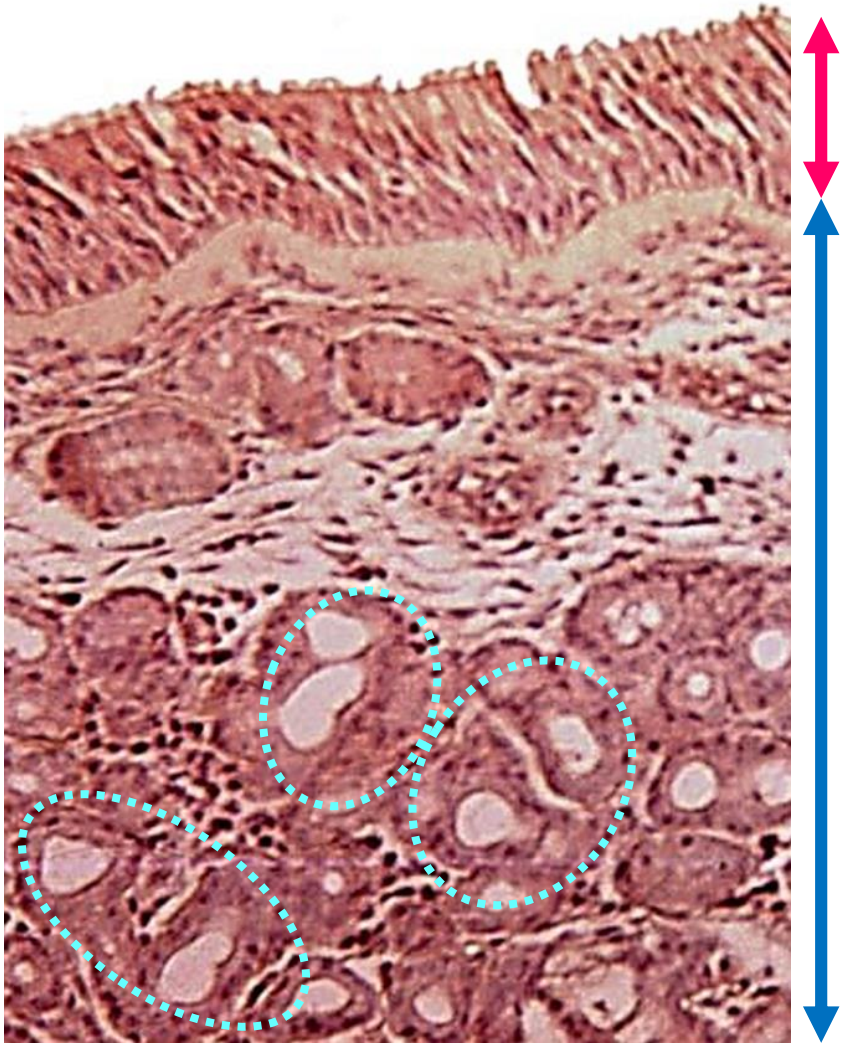
Location:
- rooof of the nasal cavity
- superior aspect of nasal septum
- superior concha

Colour: yellow

Size: approx. 7-10 cm^2



Nasal cavity – Olfactory epithelium



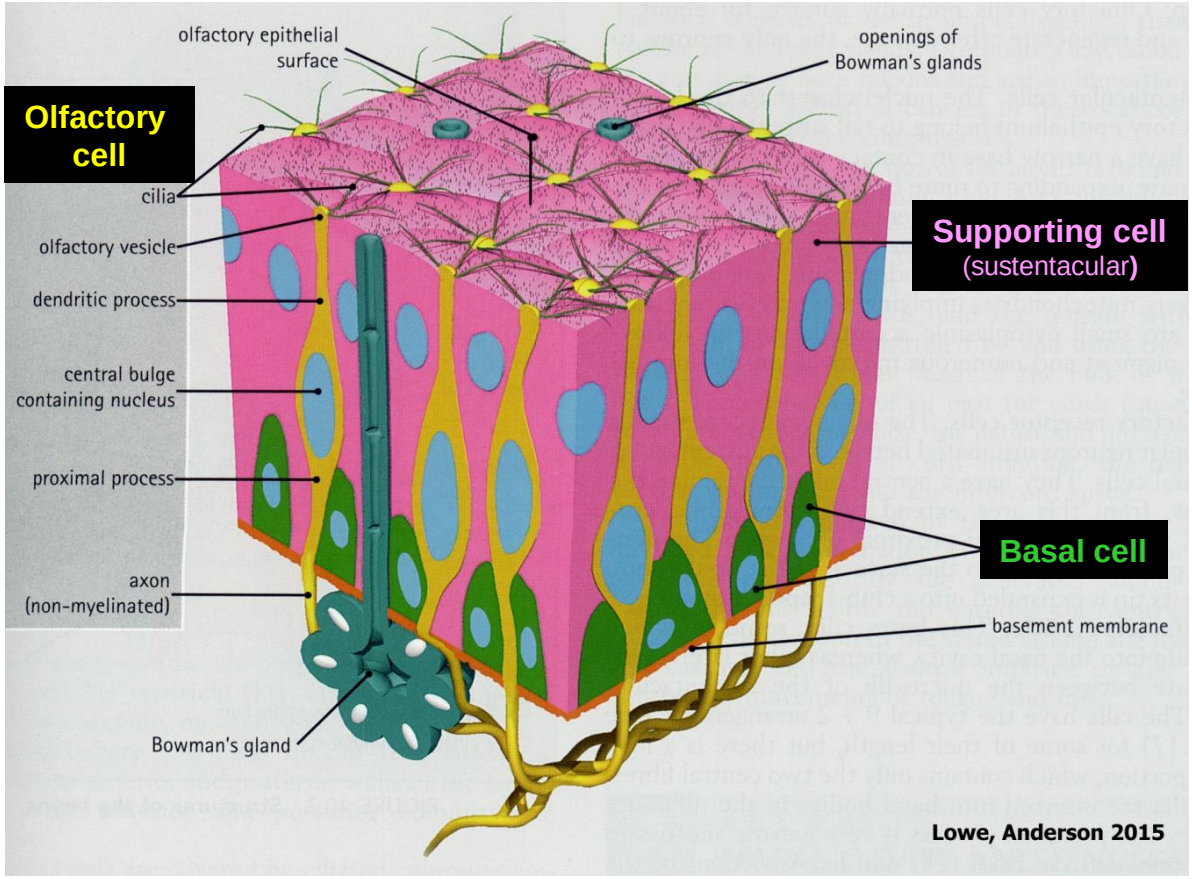
Pseudotratified columnar epithelium

- 70 – 100 μm thick
- 3 types of cells

Lamina propria mucosae

- loose connective tissue
- arterial and venous plexuses
- axons of sensory cells
- Bowman´s glands
  (tubular, branched, serous)

Nasal cavity – Olfactory epithelium



Olfactory cell

- bipolar neuron apical aspect – dendrite - olfactory vesicle
- 10-20 nonmotile cilia emerge from one vesicle
- modified cilia contain the odorant receptors
- basal aspect - axon

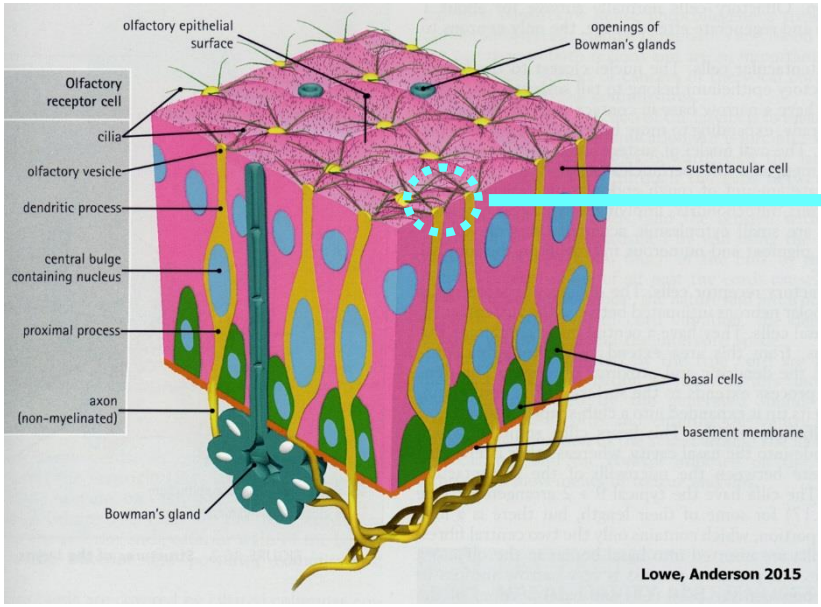
Supporting cell (sustentacular)

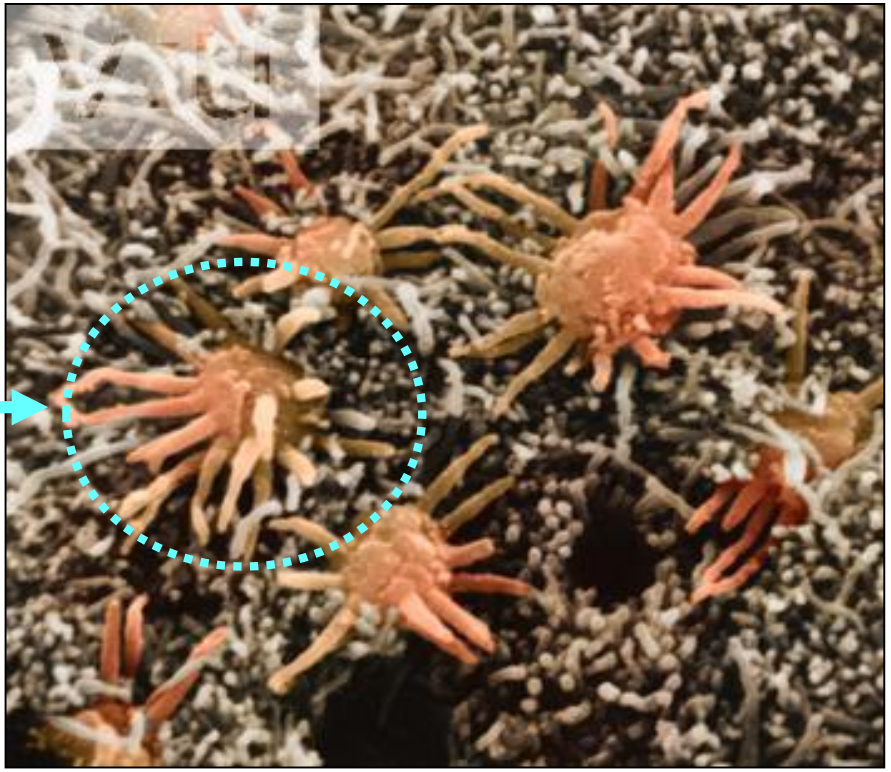
- striated border - microvilli
- secretory granules
- provide physical support + nourishement

Basal cell

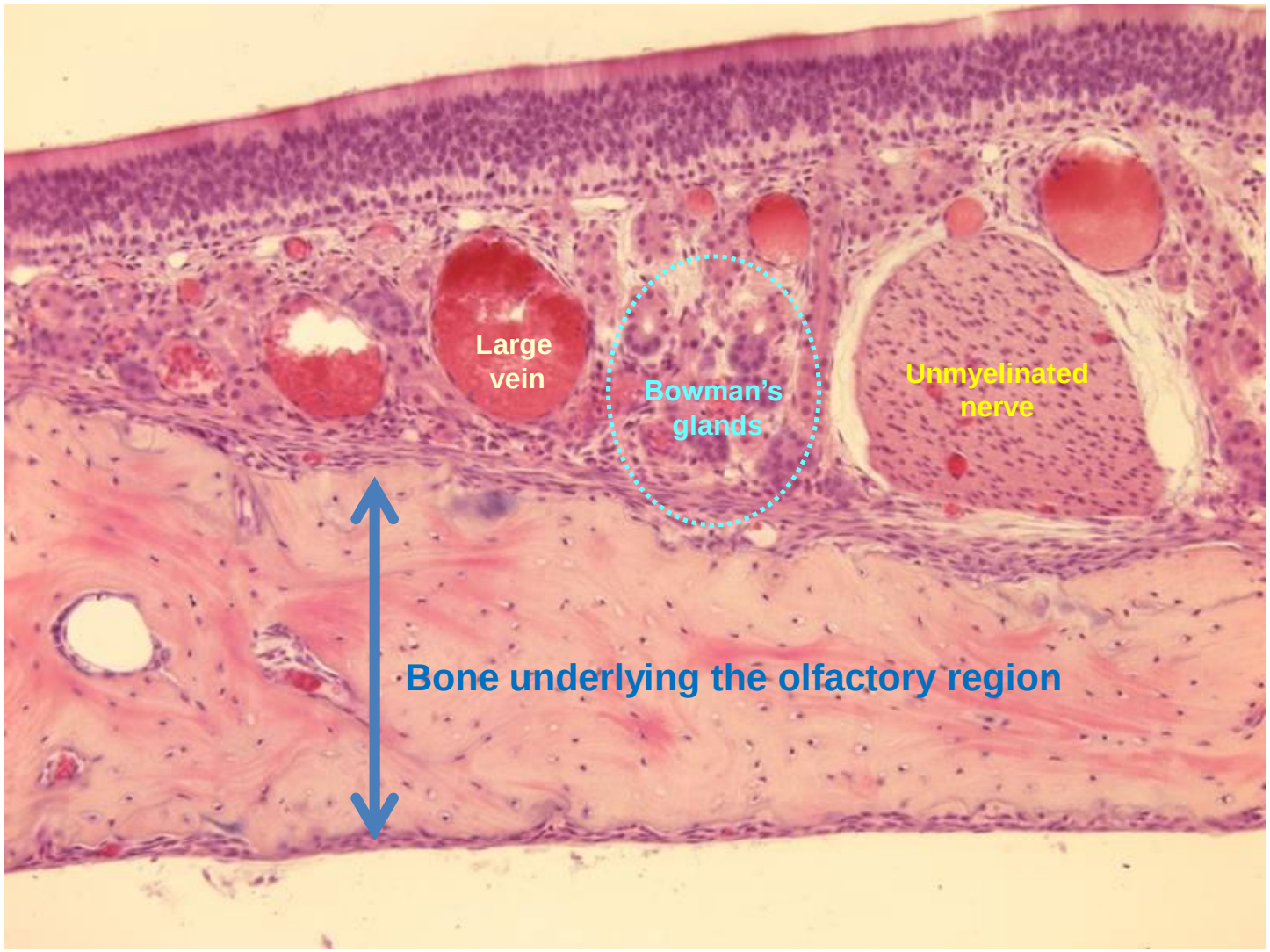
- short basophilic
- stem cells to supporting and olfactory cells *(regeneration of neurons !!!)*

Nasal cavity – Olfactory epithelium





Nasal cavity – Olfactory epithelium



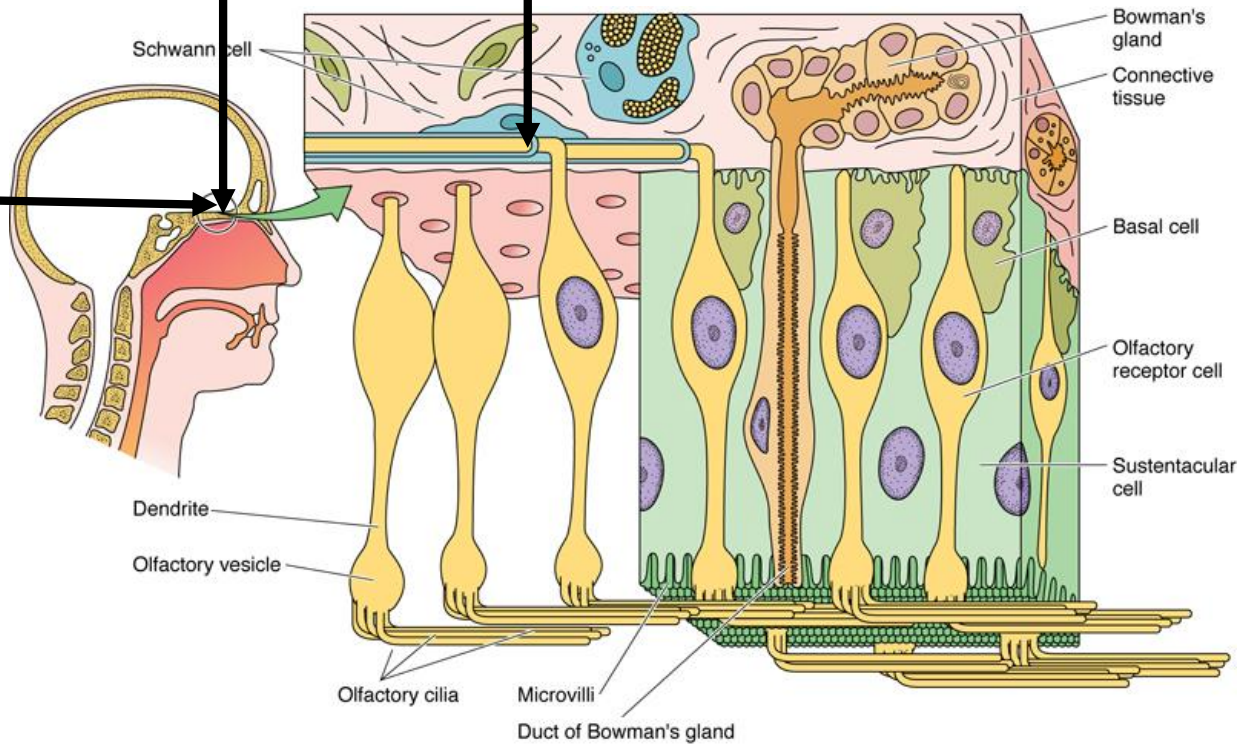
Nasal cavity – Olfactory epithelium

Flipped upside down compared to all previous pictures **!!!**

Axons of olfactory cells (Fila olfactoria)

Passage through the cribriform plate

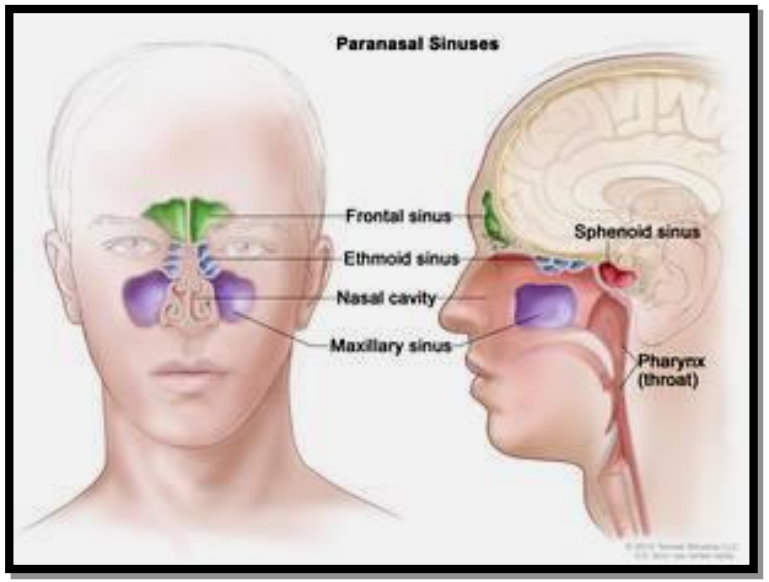
Synapse with secondary neurons in the olfactory bulb (N. olfactorius)

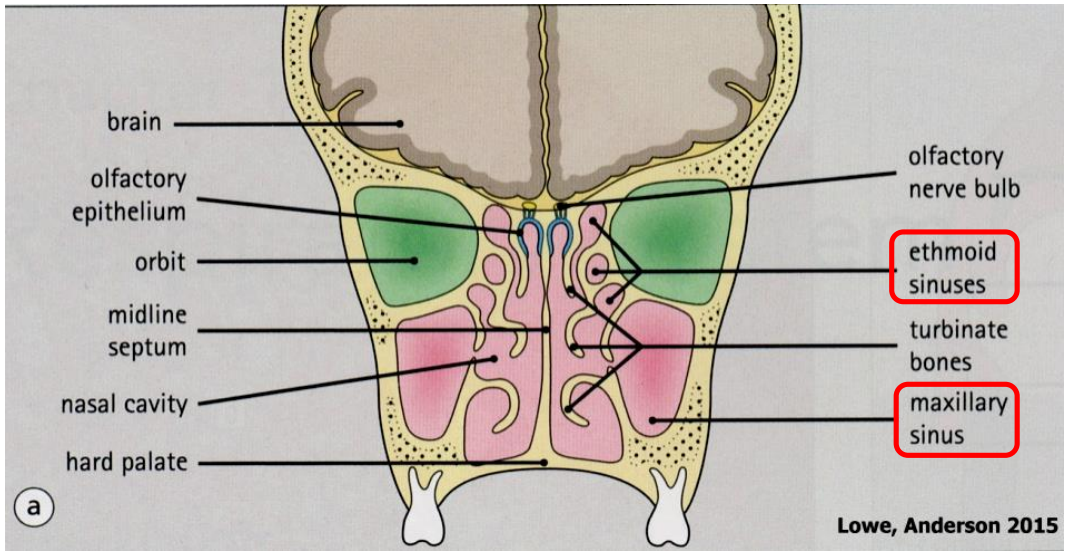


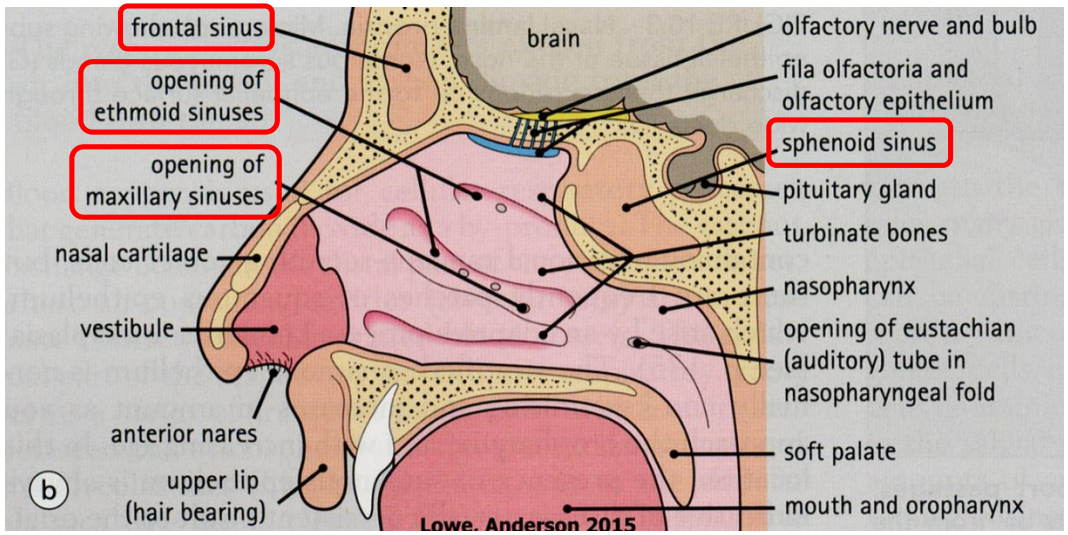
Nasal cavity – Paranasal sinuses (Sinus paranasales)

- **sinus maxillaris (15-25 cm^3)**
- sinus ethmoidalis
- sinus frontalis
- sinus sphenoidalis

Mucous lining
- similar to airway mucosa
- thinner
- less glands
- no sumbmucosa







Nasopharynx (Pars nasalis pharyngis) + Oropharynx (Pars oralis pharyngis)

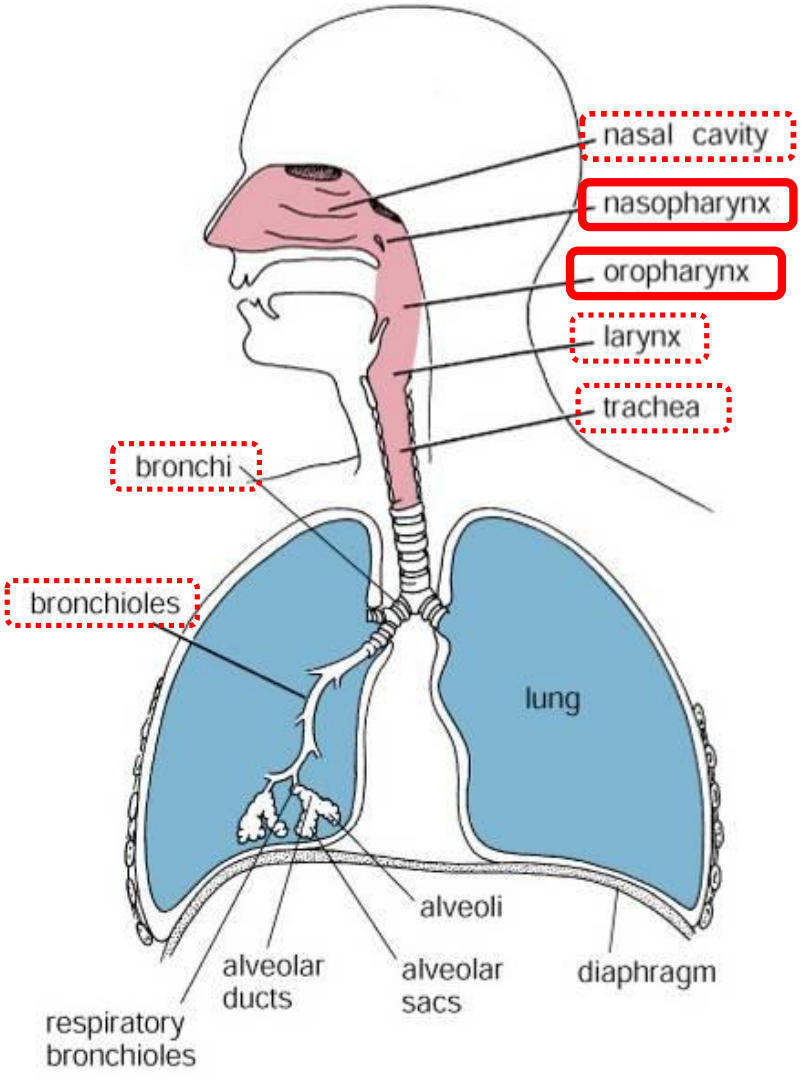


Figure 18.1. **Diagram of respiratory passages.**

Junction of respiratory and digestive tracts

Nasopharynx

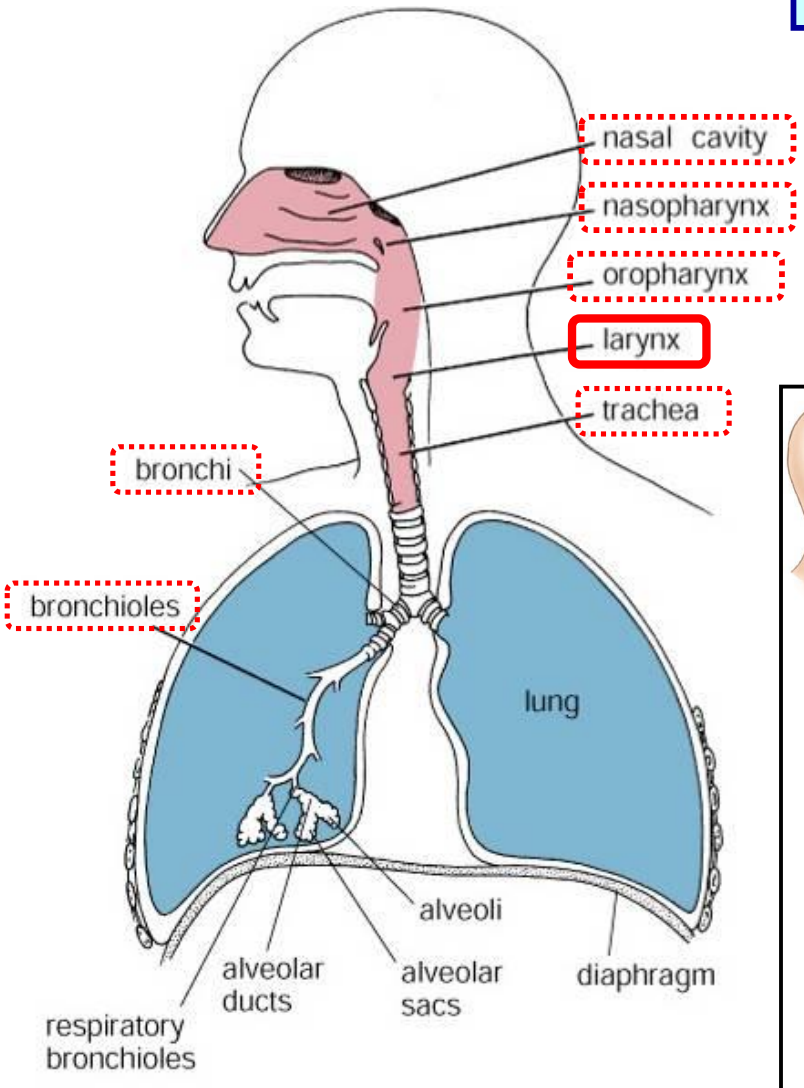
- pseudostratified cilliated columnar epithelium
- tonsila pharyngea – infiltration of lamina propria by lymphocytes
- entry of Eustachian tube

Oropharynx

- stratified squamous epithelium

Larynx

Voicebox - responsible for phonation



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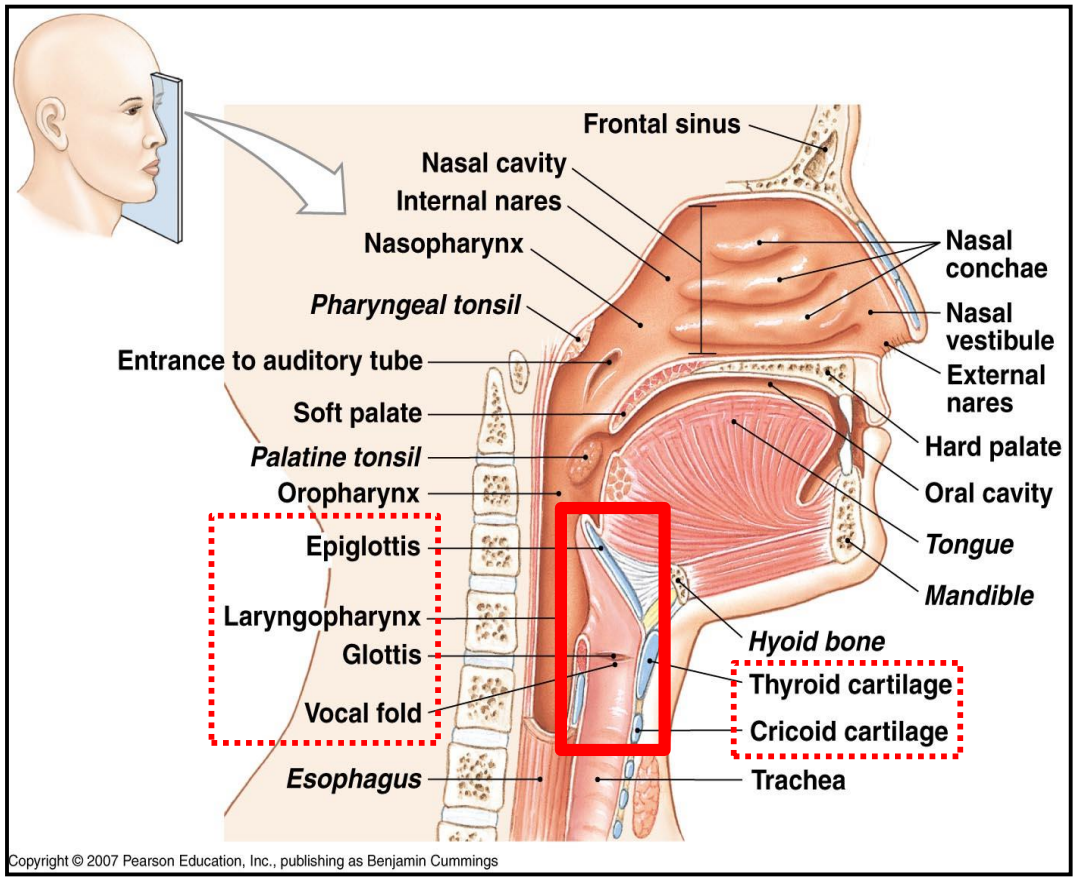
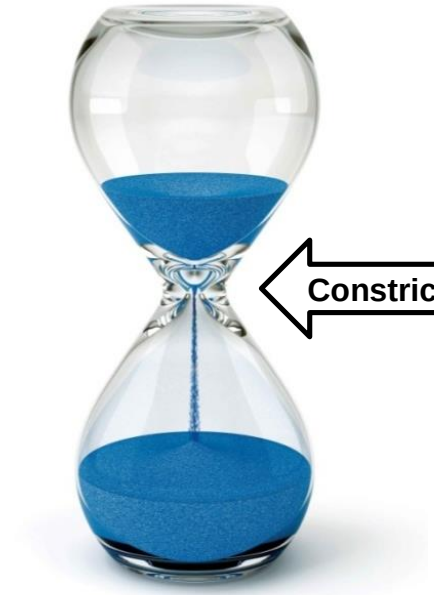


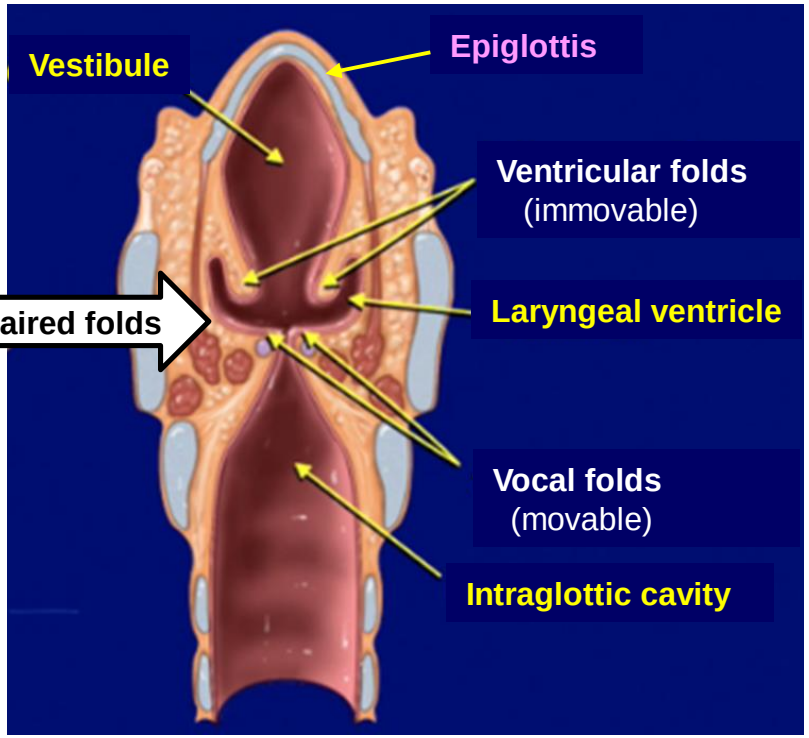
Larynx – Overall anatomy



Shape of sand-glass

Constriction = paired folds

Frontal section



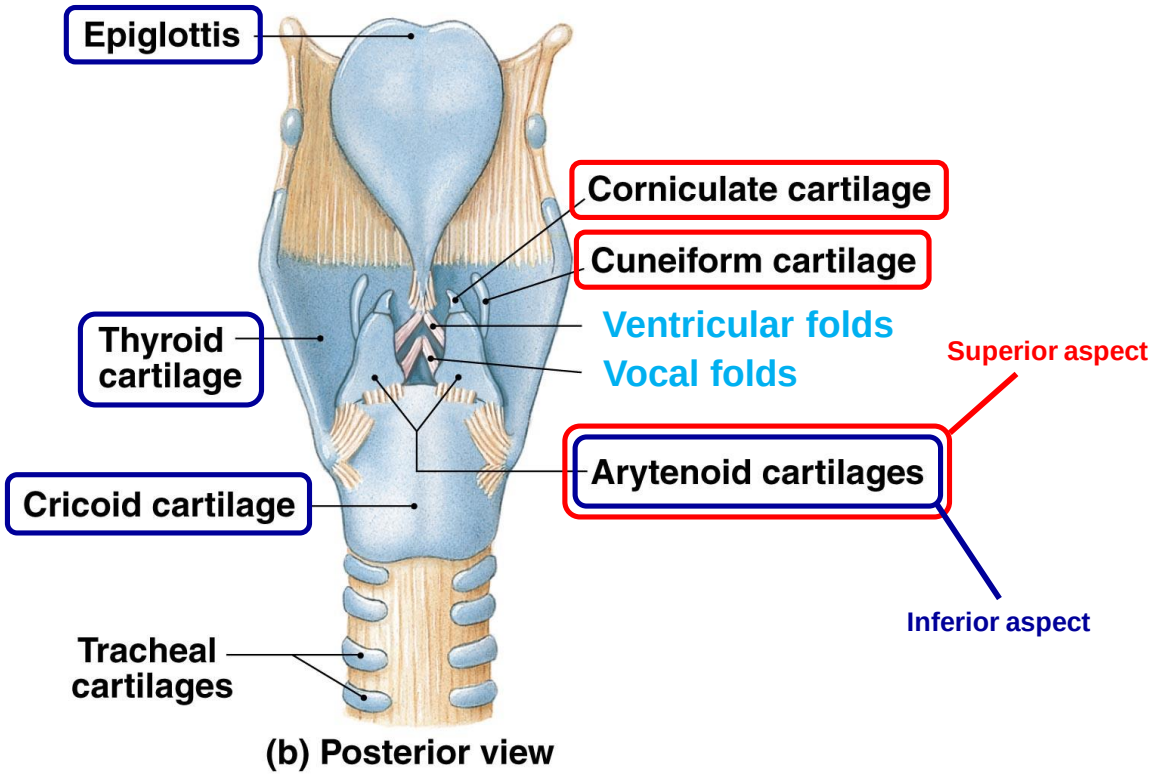
Approx. 4 cm

Larynx – Reinforecemnt

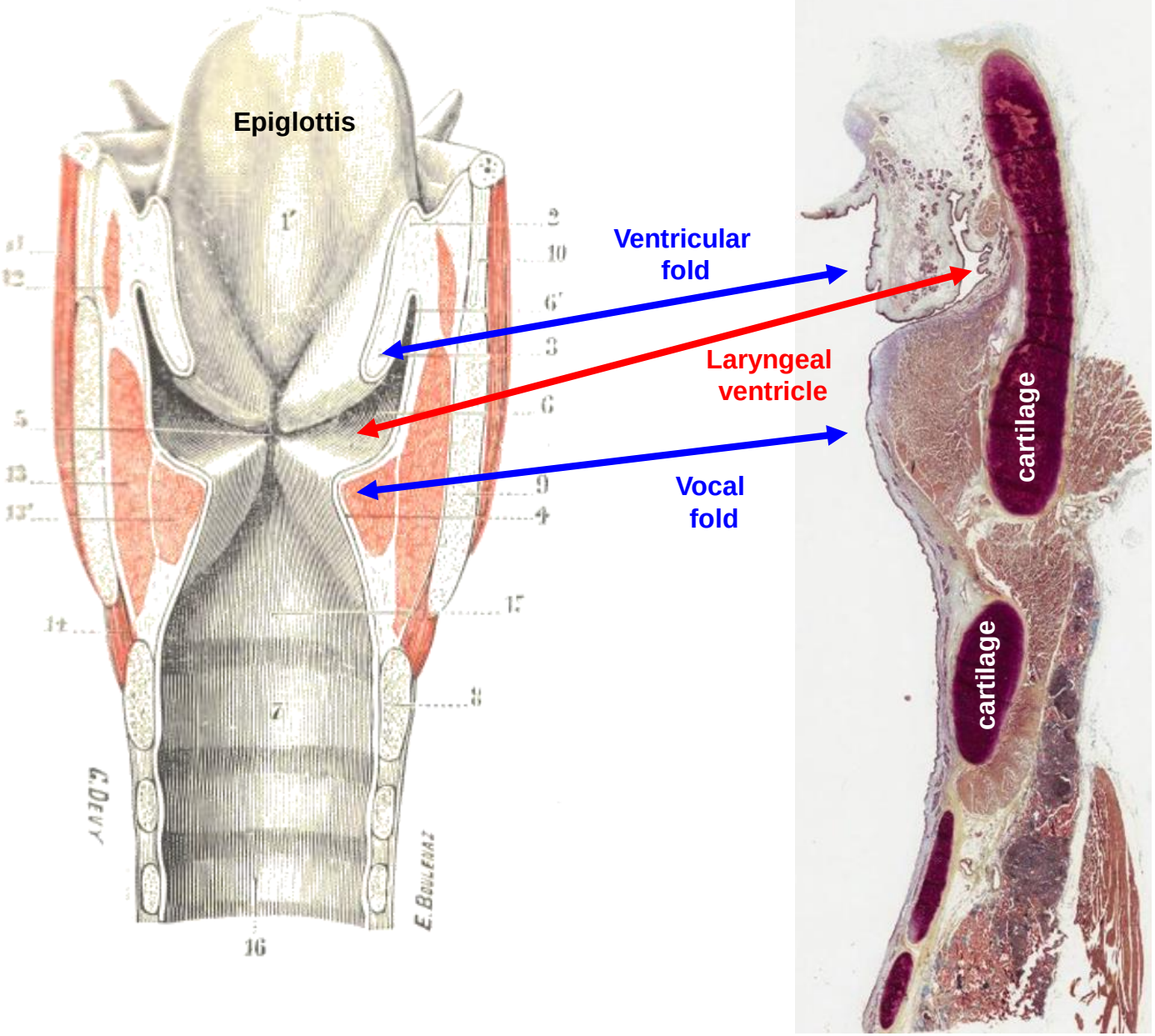
Cartilages

joint by ligaments and operated by muscles

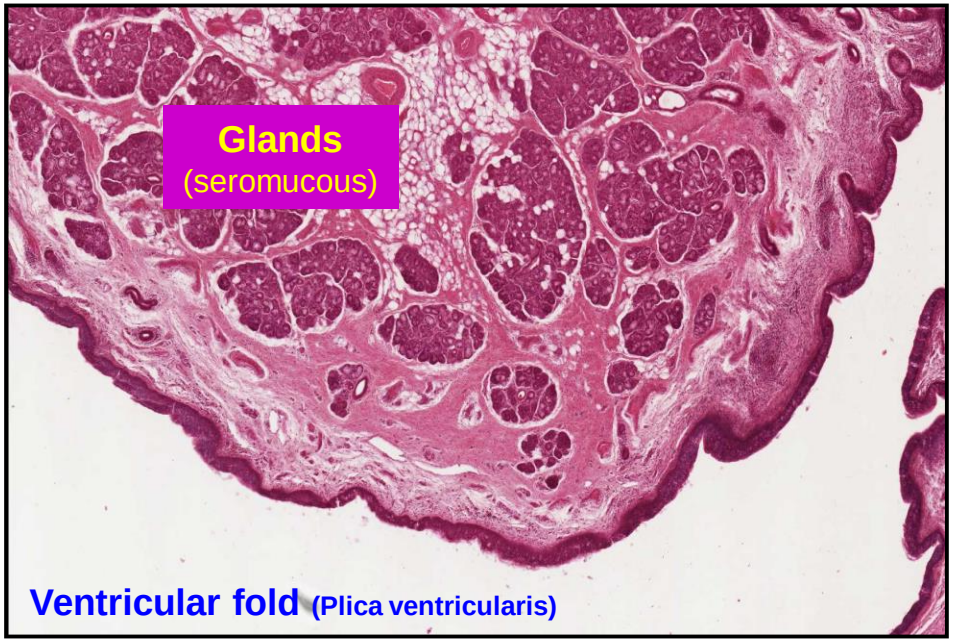
- **Hyaline**
- **Elastic**



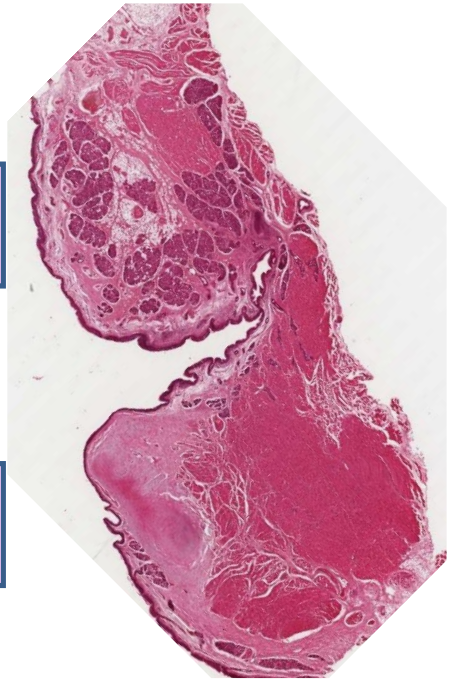
Larynx

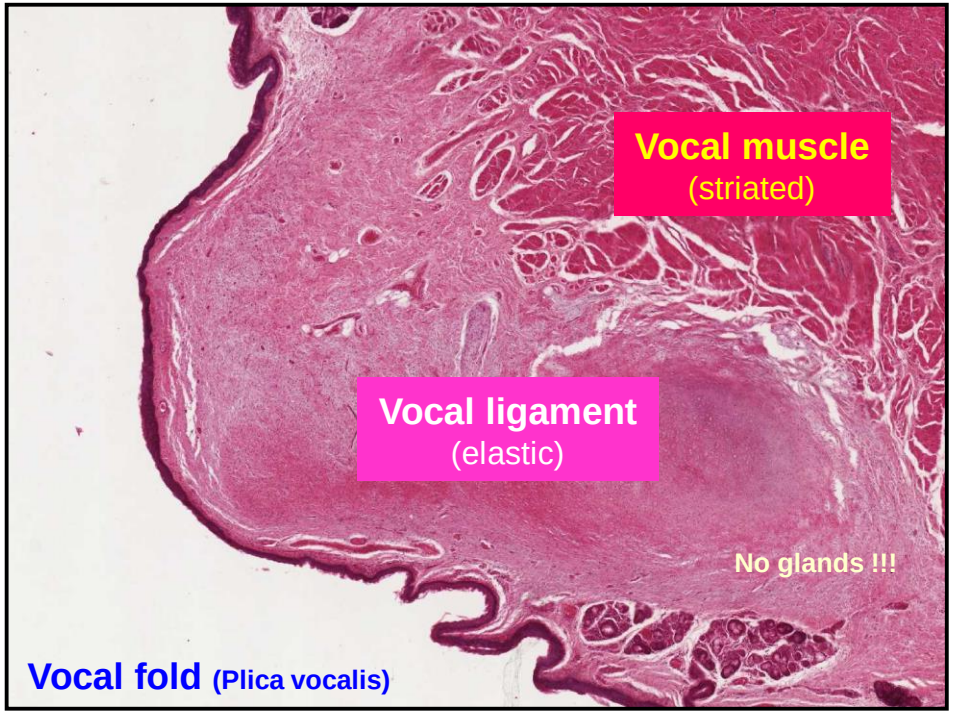

Epiglottis
Ventricular fold
Laryngeal ventricle
Vocal fold
cartilage
cartilage

Larynx – Histology



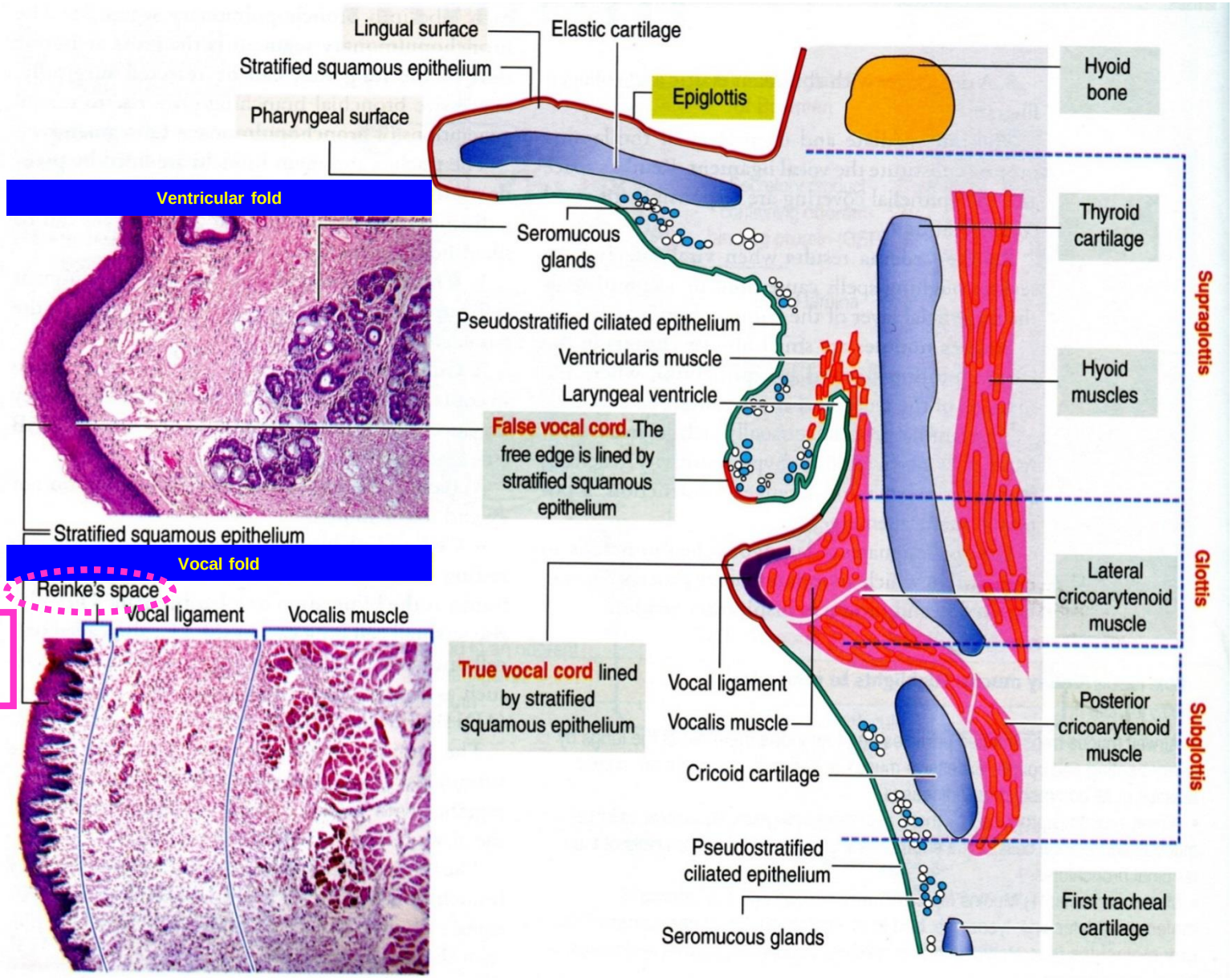
Pseudostratified ciliated collumnar ep.





Stratified squamous ep.

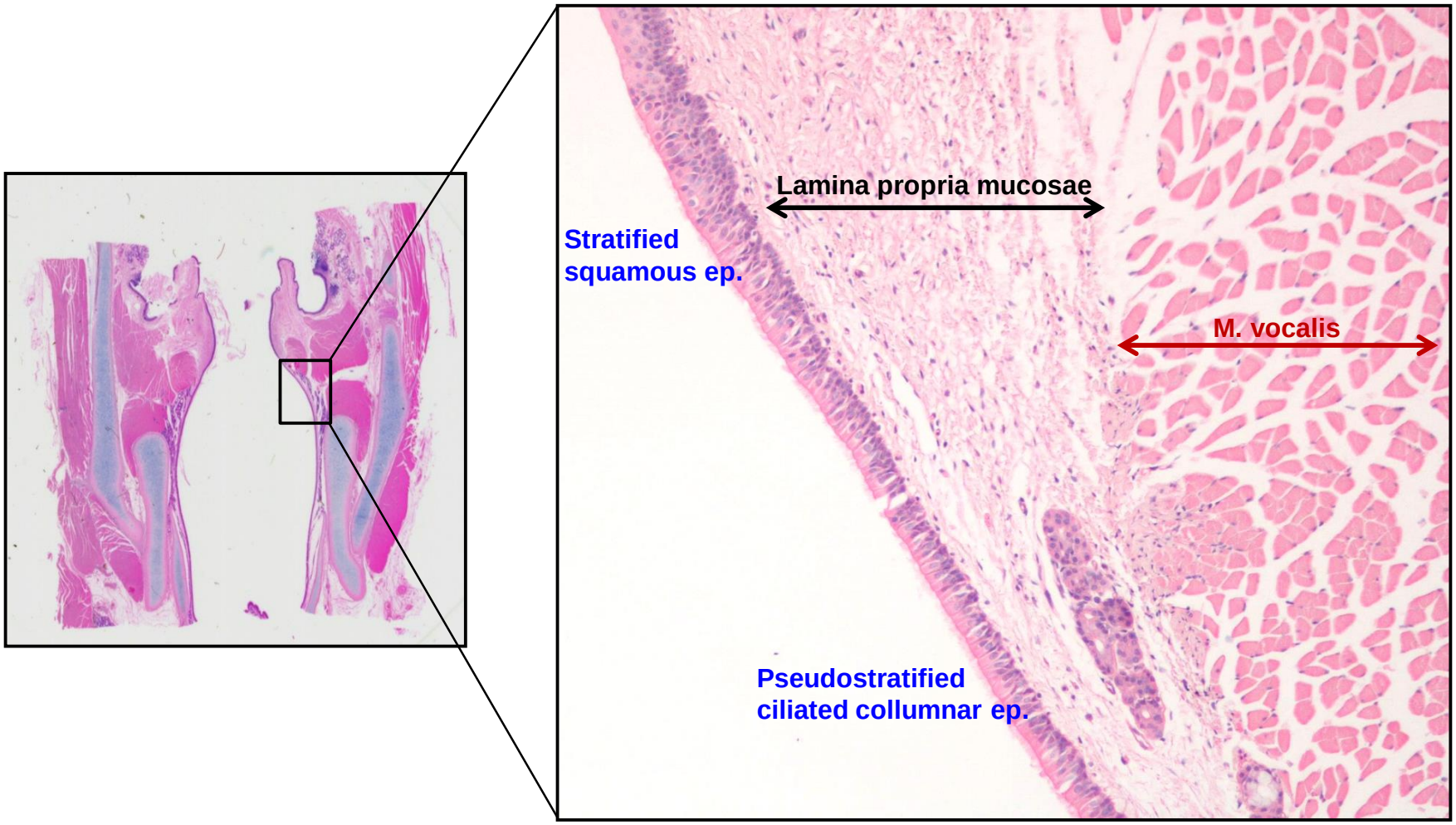
Larynx – Mucosal lining



Reinke´s oedema
exudate in Reinke´s space
= hoarse voice

Larynx

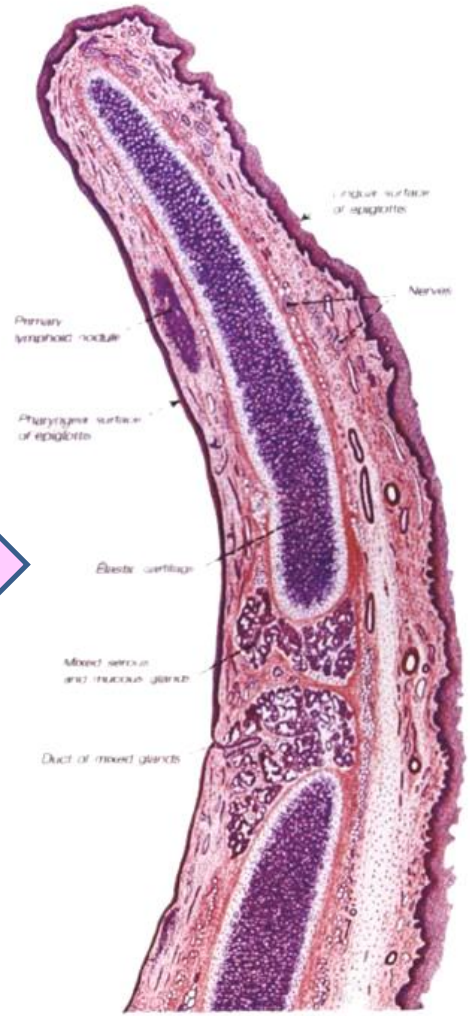
Transition of epithelia on inferior aspect of vocal fold



Larynx - Epiglottis

Laryngeal surface

Lingual surface



Pseudostratified ciliated collumnar ep.

Stratified squamous ep.

Trachea

Conducting portion
Extrapulmonary position

Length approx.: 12 cm
Diameter approx.: 2 cm

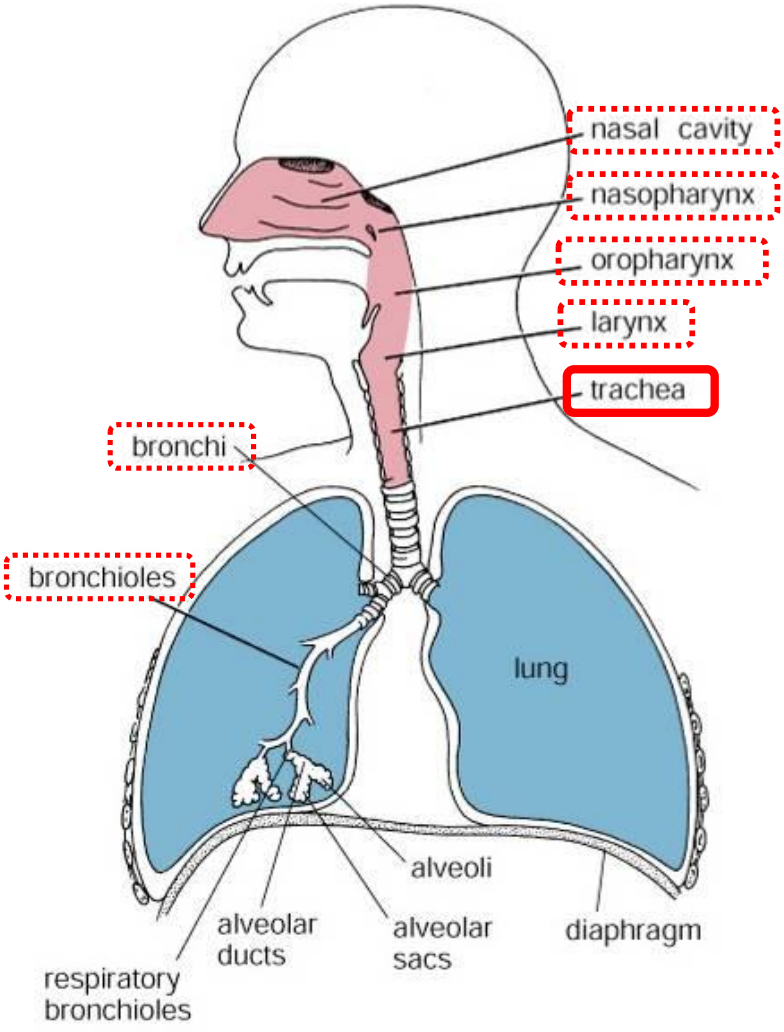
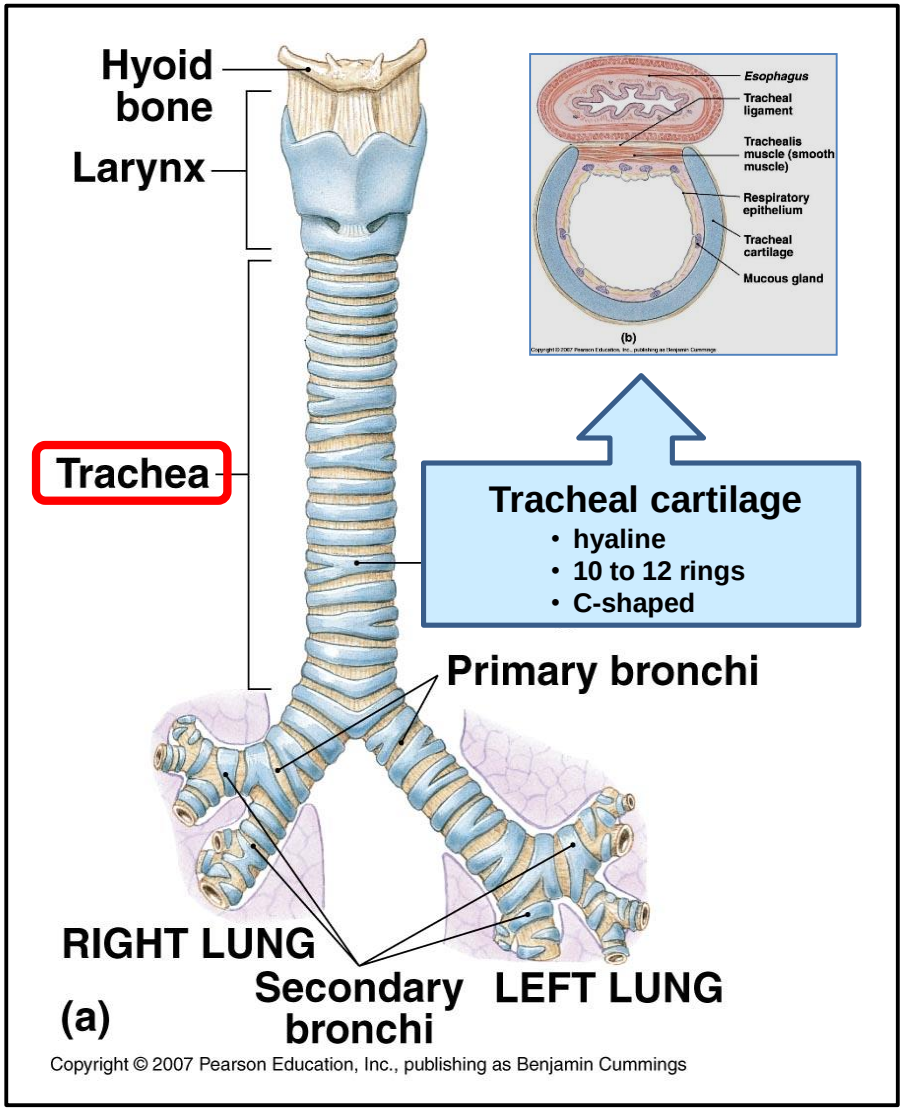
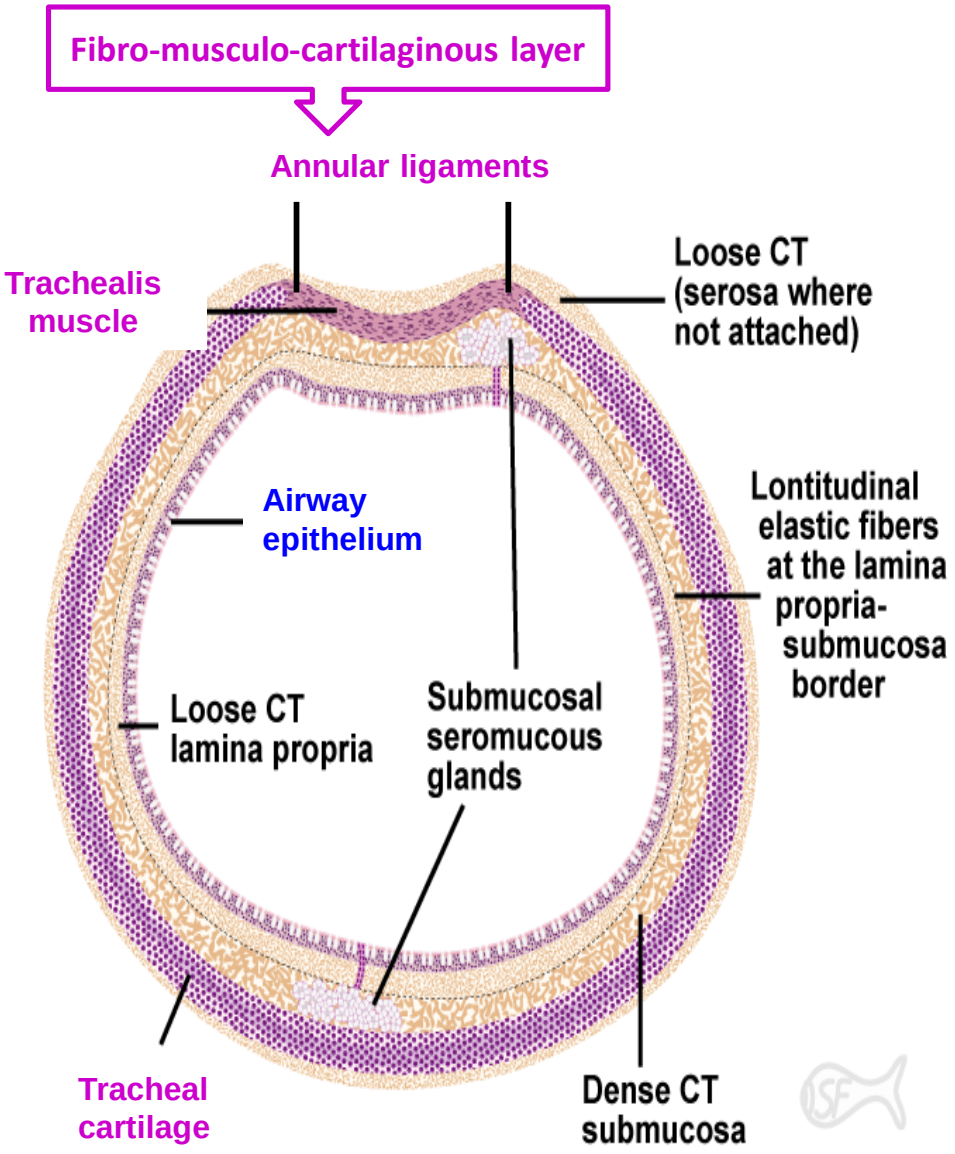


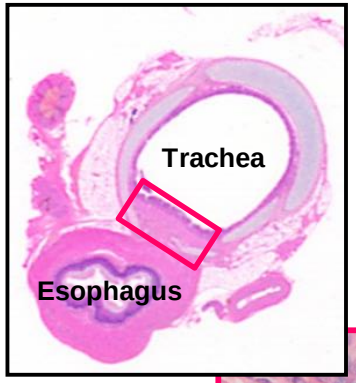
Figure 18.1. **Diagram of respiratory passages.**

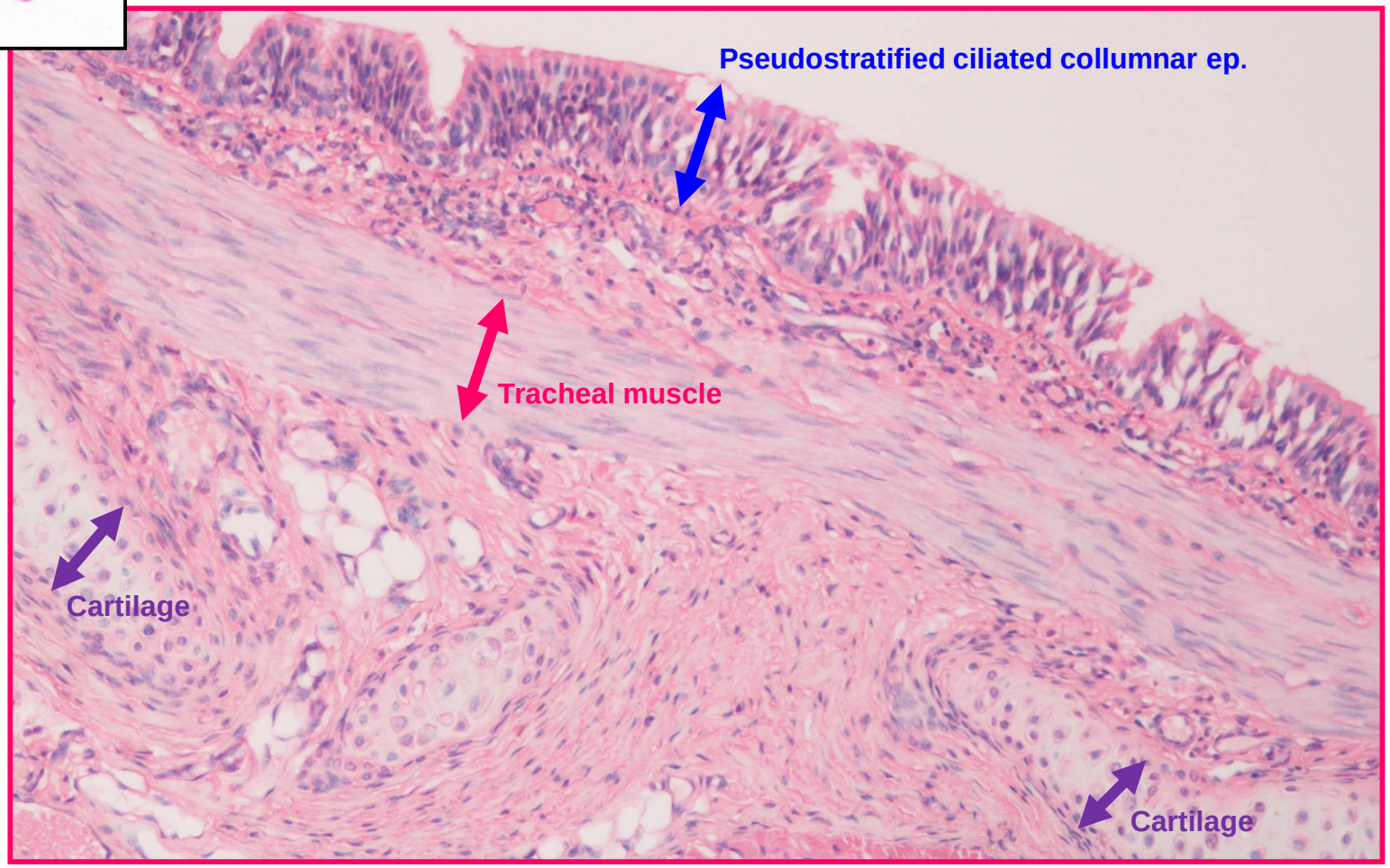


Trachea - Crossection

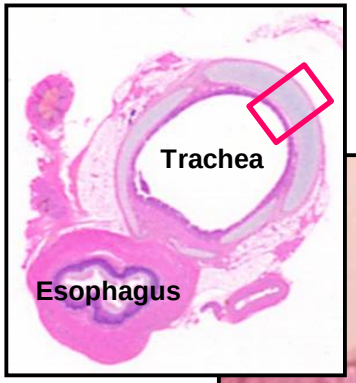


Trachea - Wall





Trachea - Wall



Pseudostratified ciliated collumnar ep.

Lamina propria mucosae
- fibroelastic connective tissue + lymphoid cells

Submucosa
- thick, dense fibroelastic connective tissue
- numerous seromucous glands – Tracheal glands
- rich blood and lymph supply

Perichondrium

Cartilage

Adventitia
- fibroelastic connective tissue

Bronchial tree

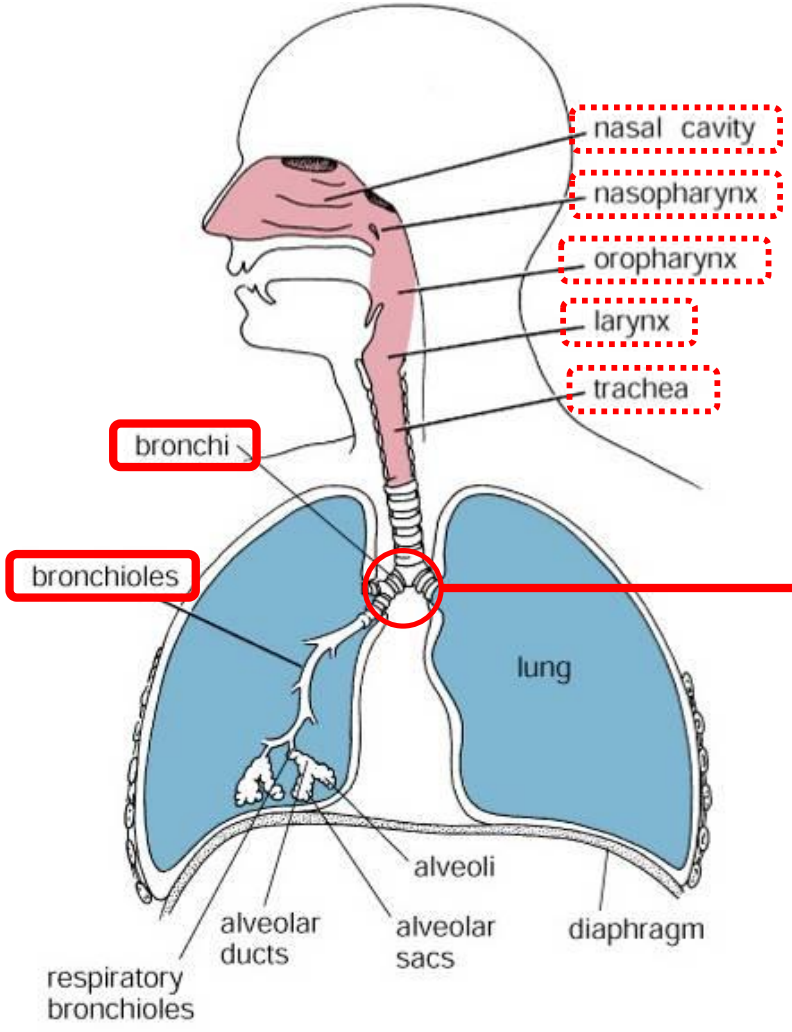


Figure 18.1. **Diagram of respiratory passages.**

Begins at bifurcation of trachea

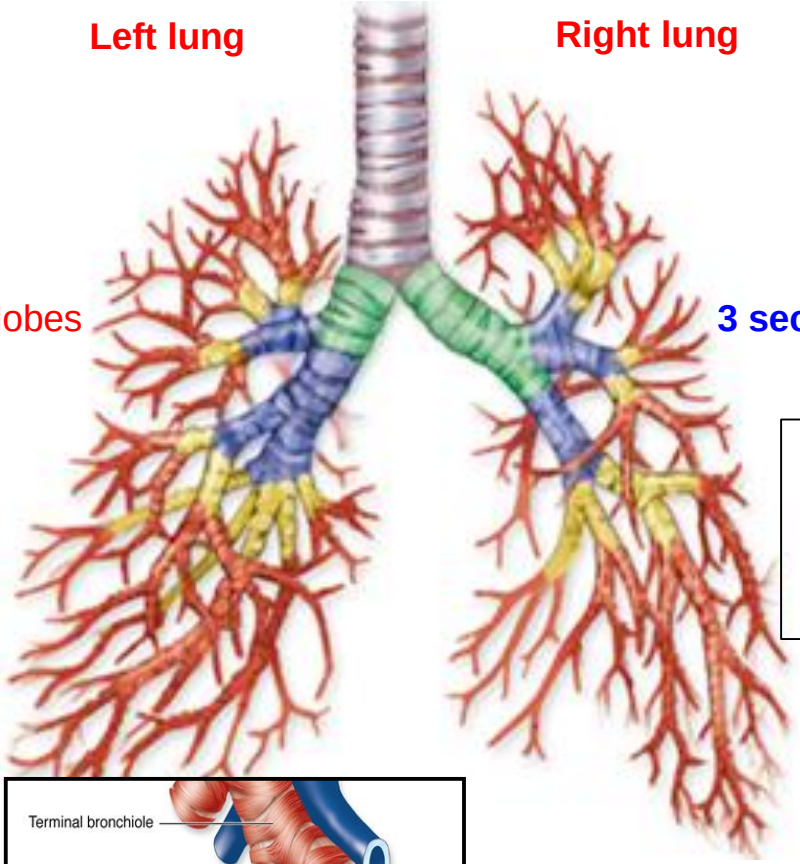
Primary bronchi – Extrapulmonary

- the same structure as trachea
- smaller diameter then trachea
- accompanied by the pulmonary arteries, veins, and lymphatics

Bronchial tree

18 to 25 dichotomic divisions in total

Left lung **Right lung**



2 secondary bronchi – 2 lung lobes
(Lobar bronchi**)**

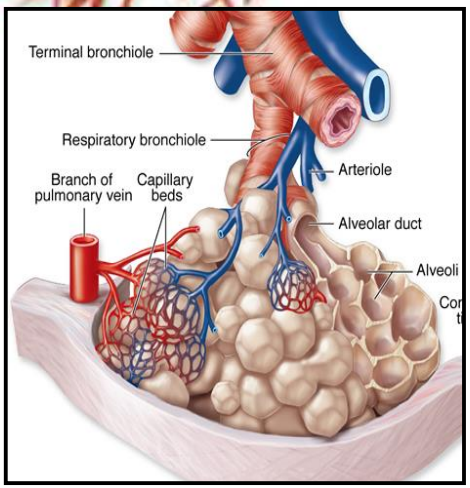
3 secondary bronchi – 3 lung lobes
(Lobar bronchi)

Tertiary bronchi
(Segmental bronchi)
- total number of 10
- diameter about 8 mm
- further ramification 8x - 10x

Medium + Small bronchi
- diameter down to 1 mm
- cartilage in their wall

Primary bronchioles
- diameter about 1 mm
- no cartilage
- one PB serve one **pulmonary lobule**

Terminal bronchioles
- 5 – 7 TB branched from one PB
- diameter about 0,5 mm

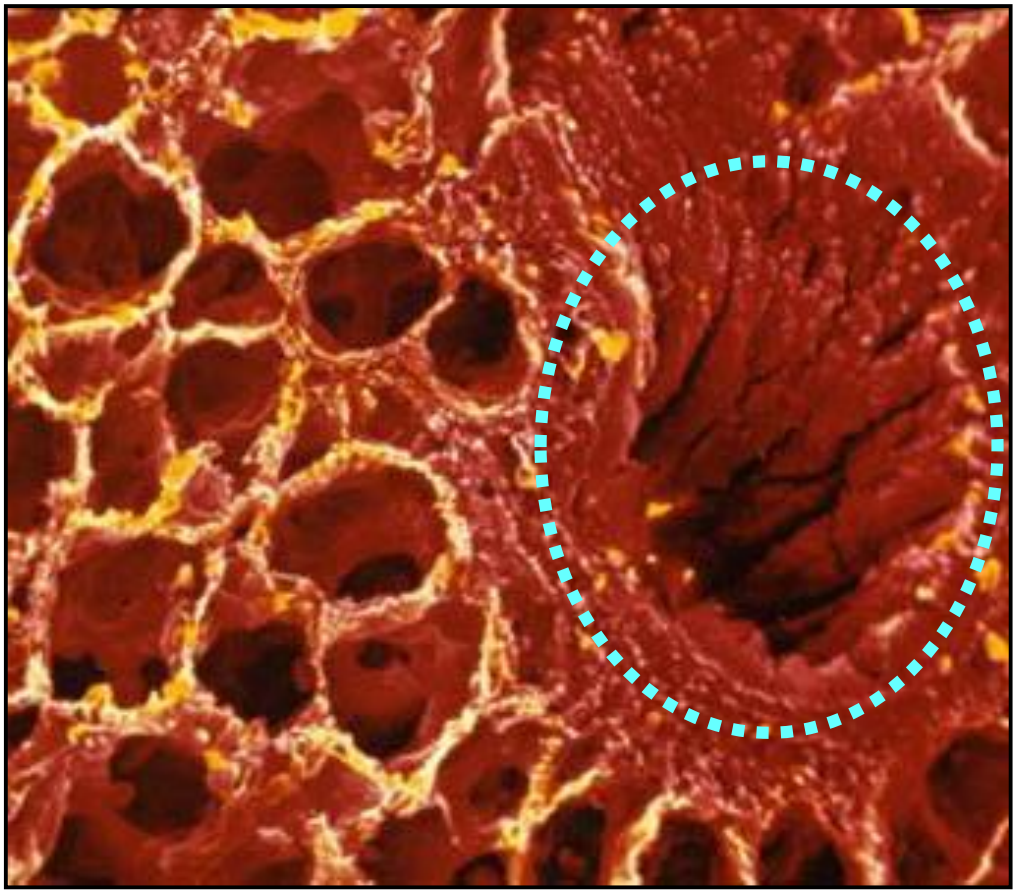


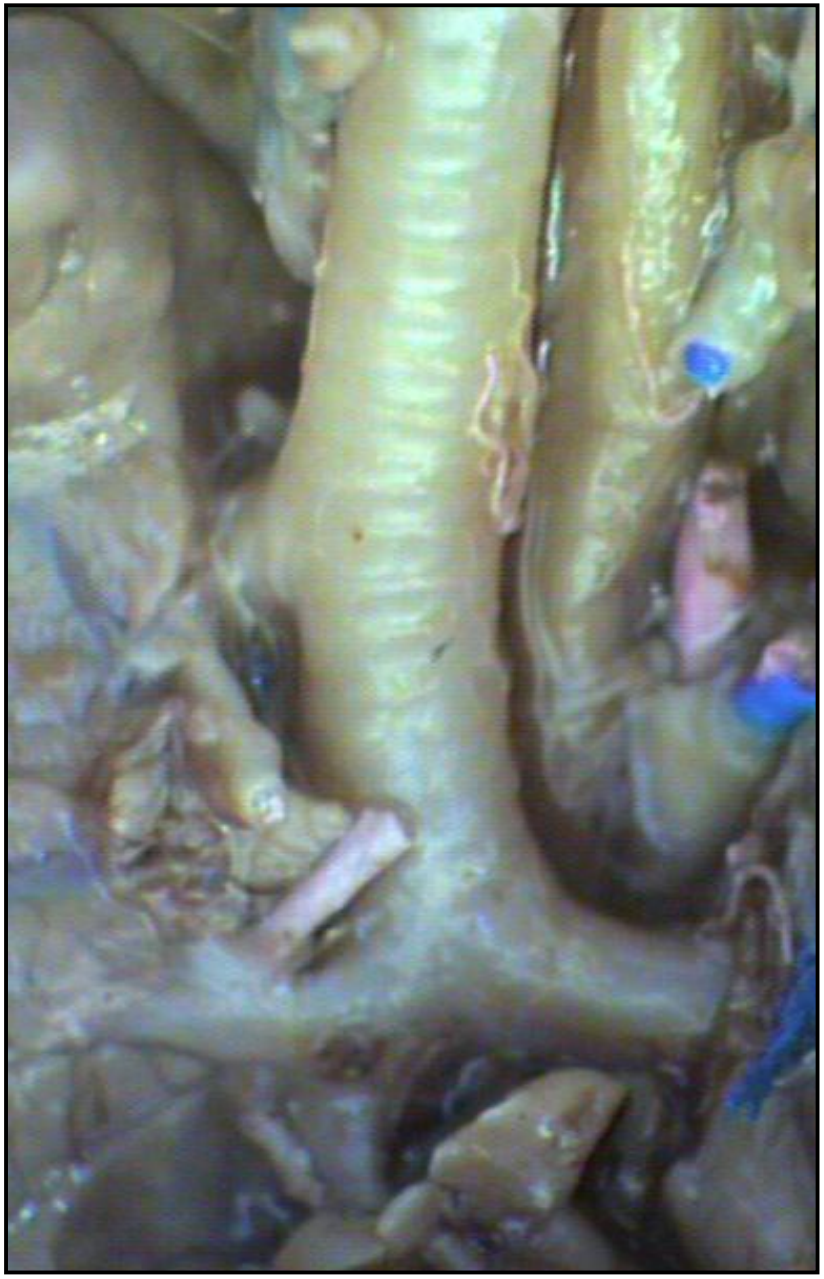
Bronchopulmonary segment
- about 10 % of lung
- own vasculature
- enclosed in fibrous capsula
- used in surgery

DO NOT MIX !!!

Pulmonary lobule
- pyramidal shape
- surrounded by very thin fibrous capsule
- volume 1 – 2 cm^3

Bronchi
macroscopic picture





Bronchial tree – Bronchi (Lobar to Small)

Mucosa
- typical airway epithelium (or bilayered collumnar)
- elastic fibers in lamina propria
- bronchial glands in LP
- BALT in LP (bronchi-associated lymphoid tissue)

✚

Submucosa
- contains fewer glands
- discontinuous layer of smooth muscle separates from lamina propria mucosae
- muscle becomes more prominen in smaller size bronchi

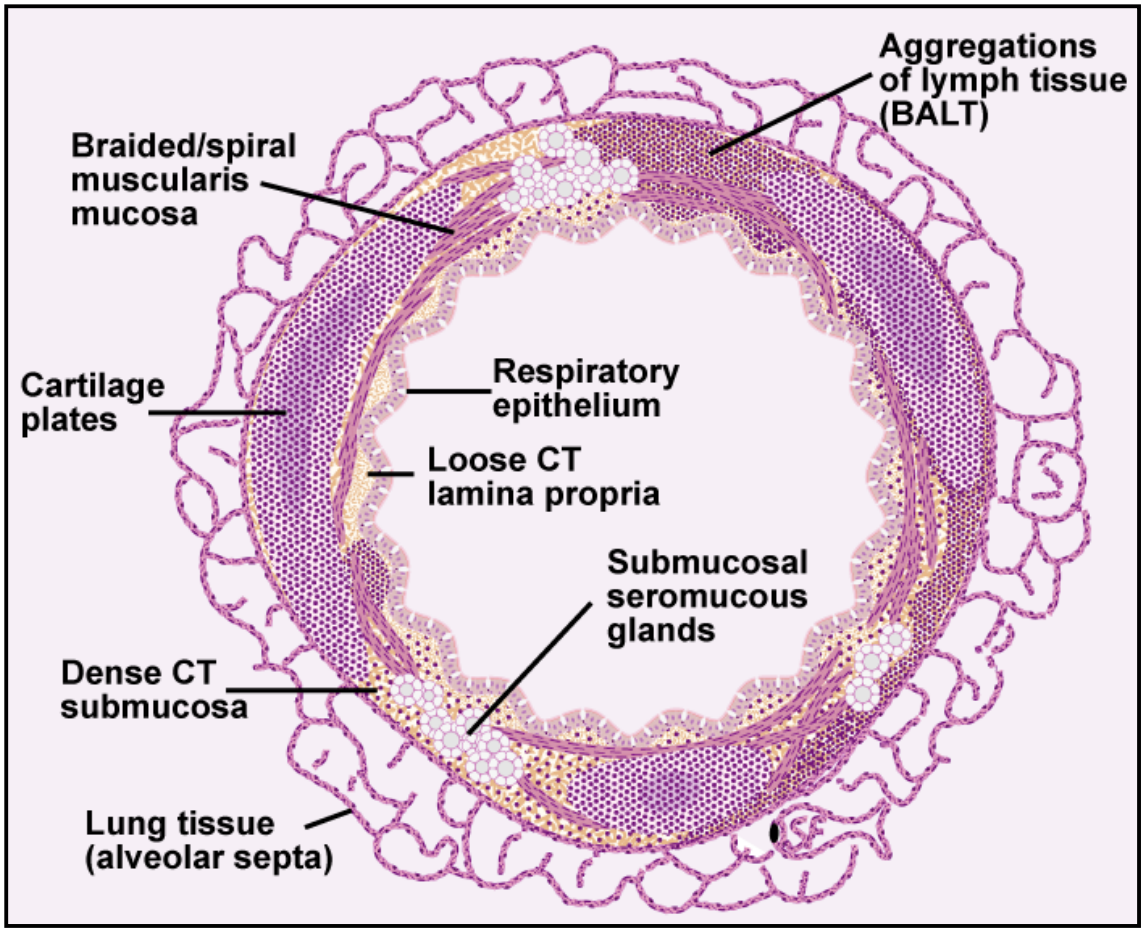
✚

Fibrocartilaginous layer
- cartilaginous plates

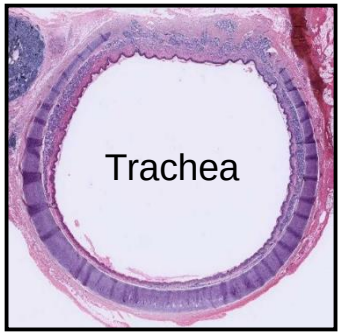
Diametr of bronchi

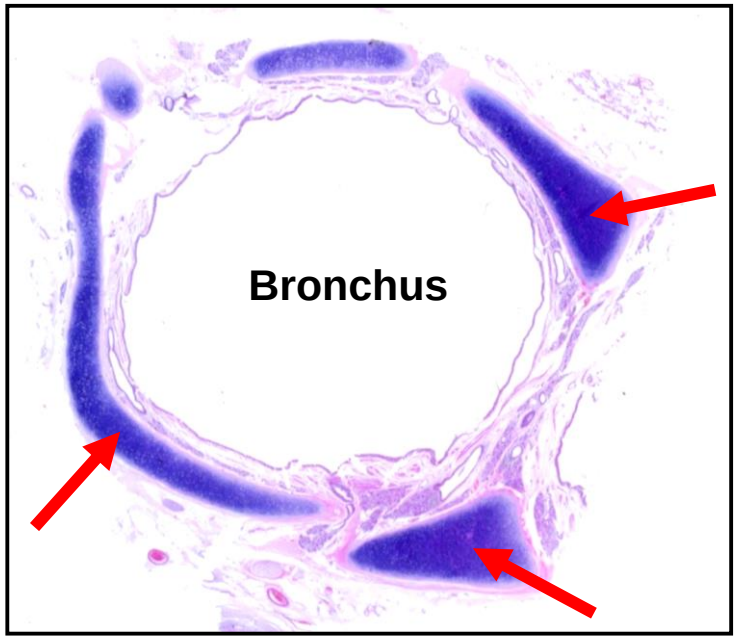
- cartilage
- glands
- goblet cells
- height of epithelium

- elastic fibres
- smooth muscle

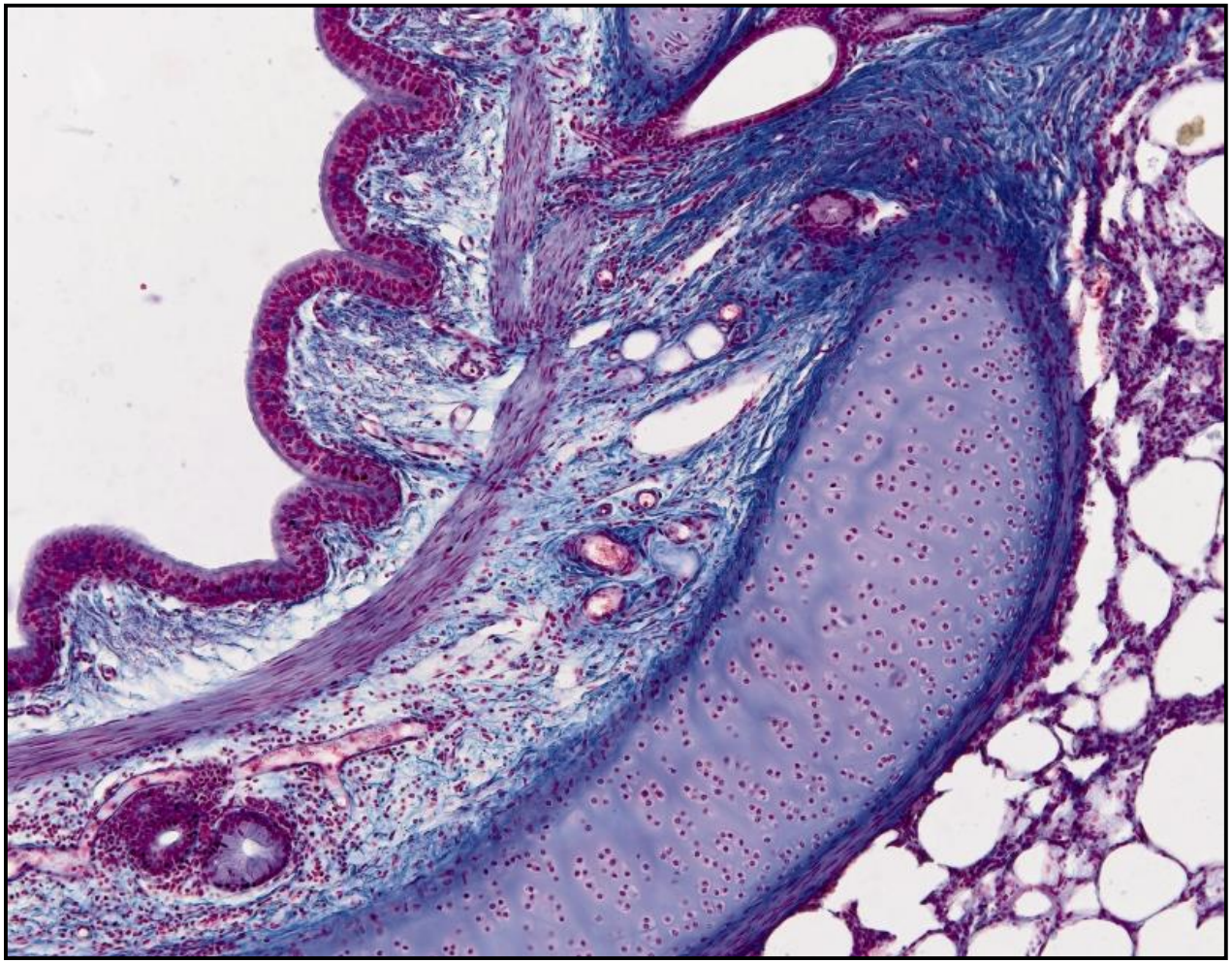


Bronchus – Cartilaginous plates

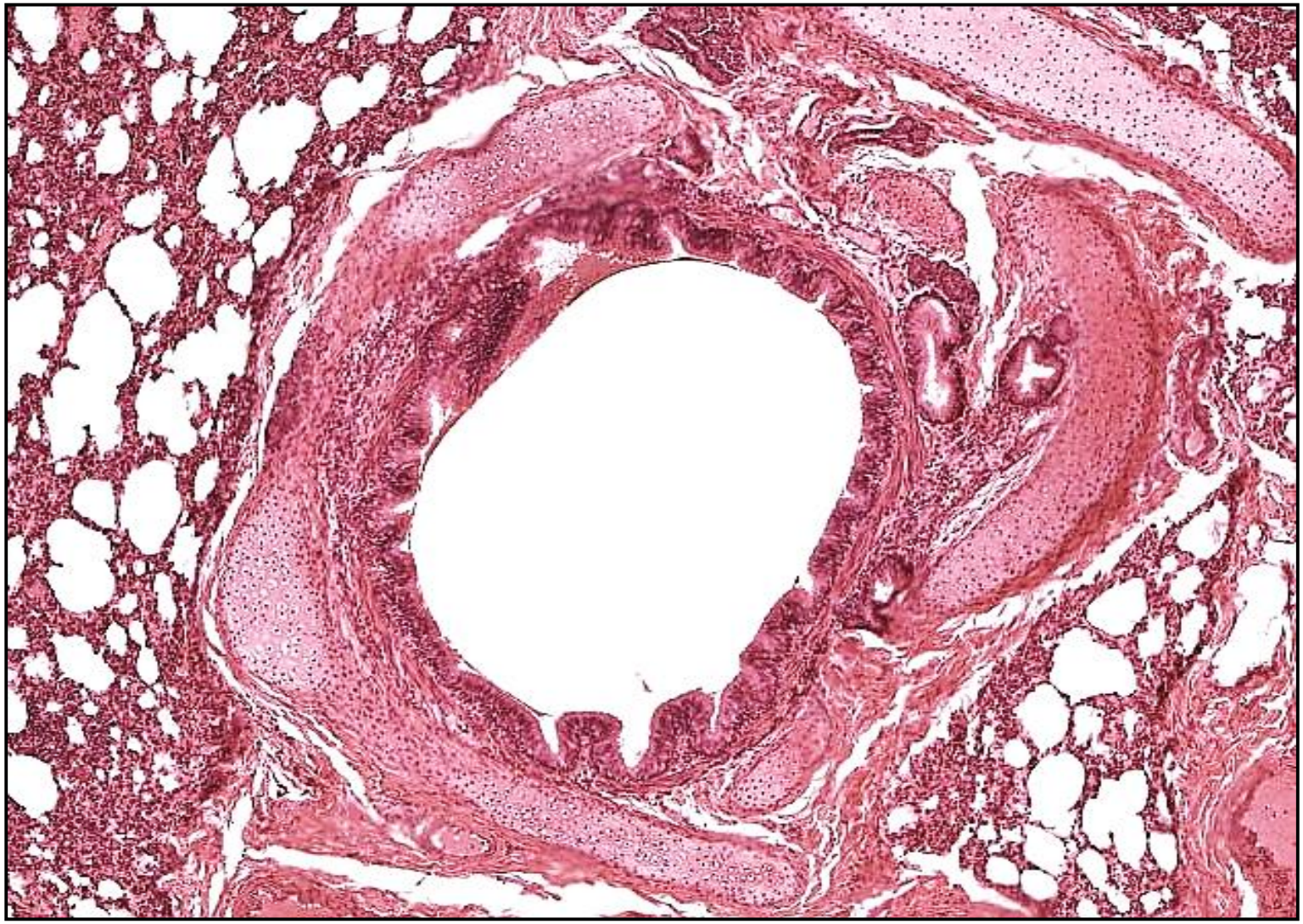




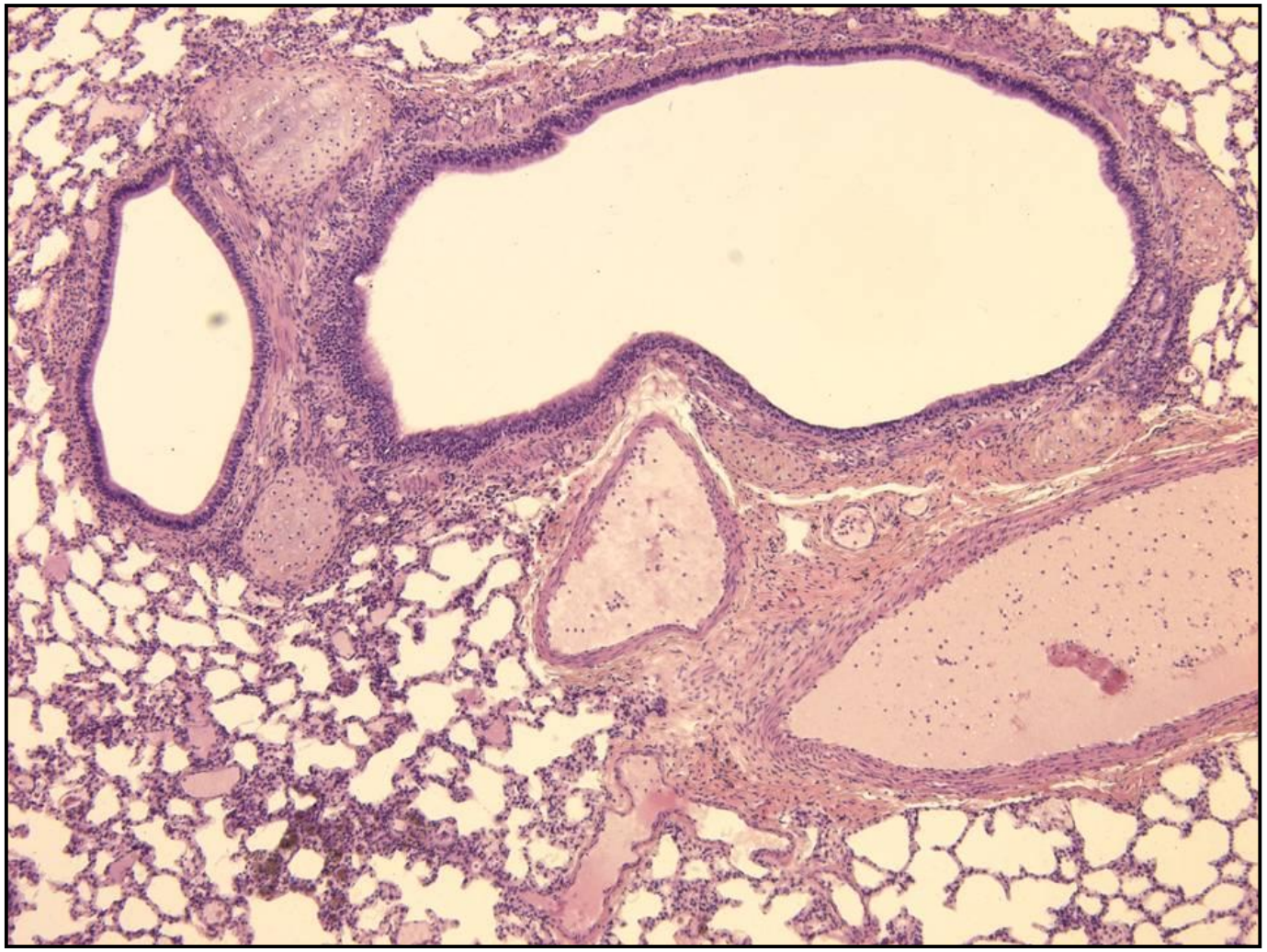
Bronchus - Intrapulmonary



Bronchus - Intrapulmonary



Bronchus - Intrapulmonary

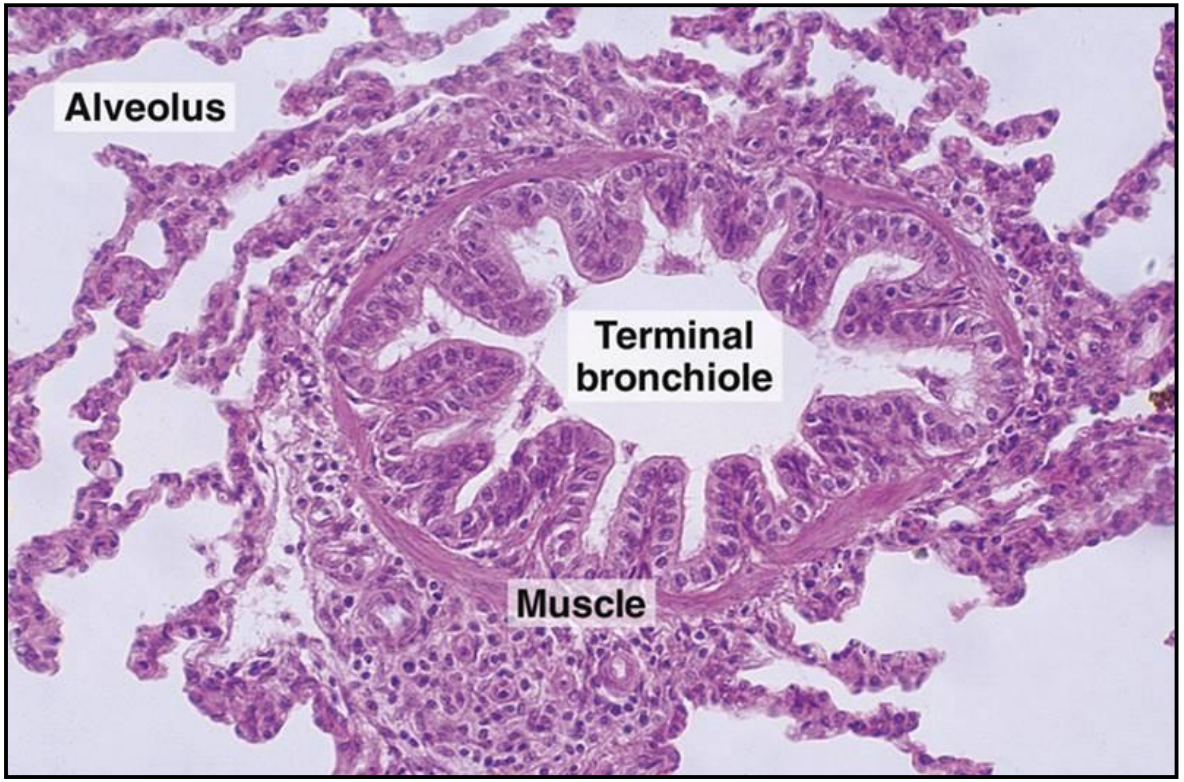


Bronchioles - Primary + Terminal – General features

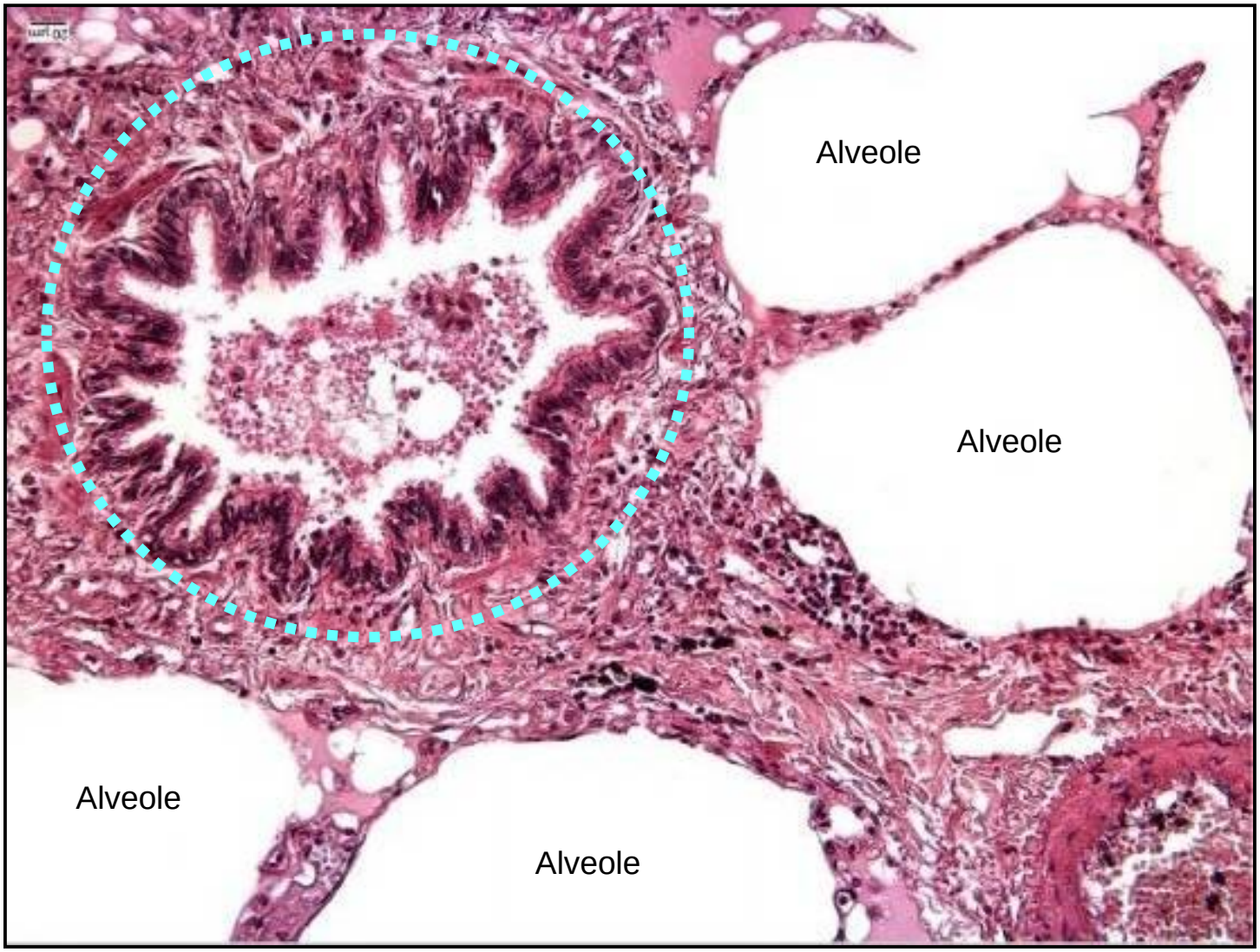
Wall
- mucosa + muscle layer (bundles) + elastic and colagen fibers
- NO cartilage
- NO glands

Epithelial lining
- simple collumnar to simple cuboidal ep.
- many epithelial cells have cilia
- NO Goblet cells
- Club cells (formerly Clara cells)

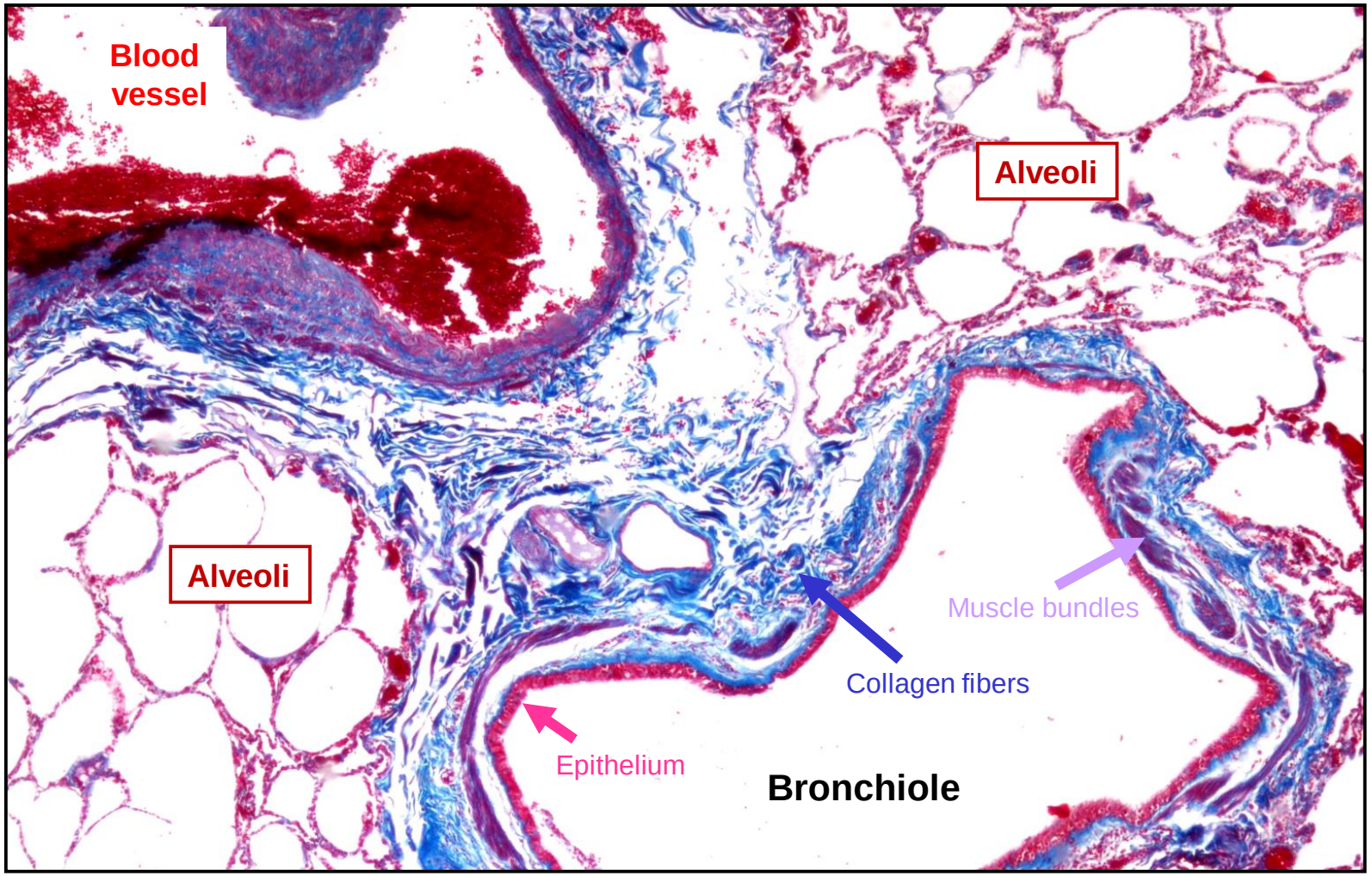
Club cells
- dome-shaped
- apex with microvili
- secretions
(antimicrobials, surfactant-like material)
- P450 enzyme (detoxification)
- stem cells to the area



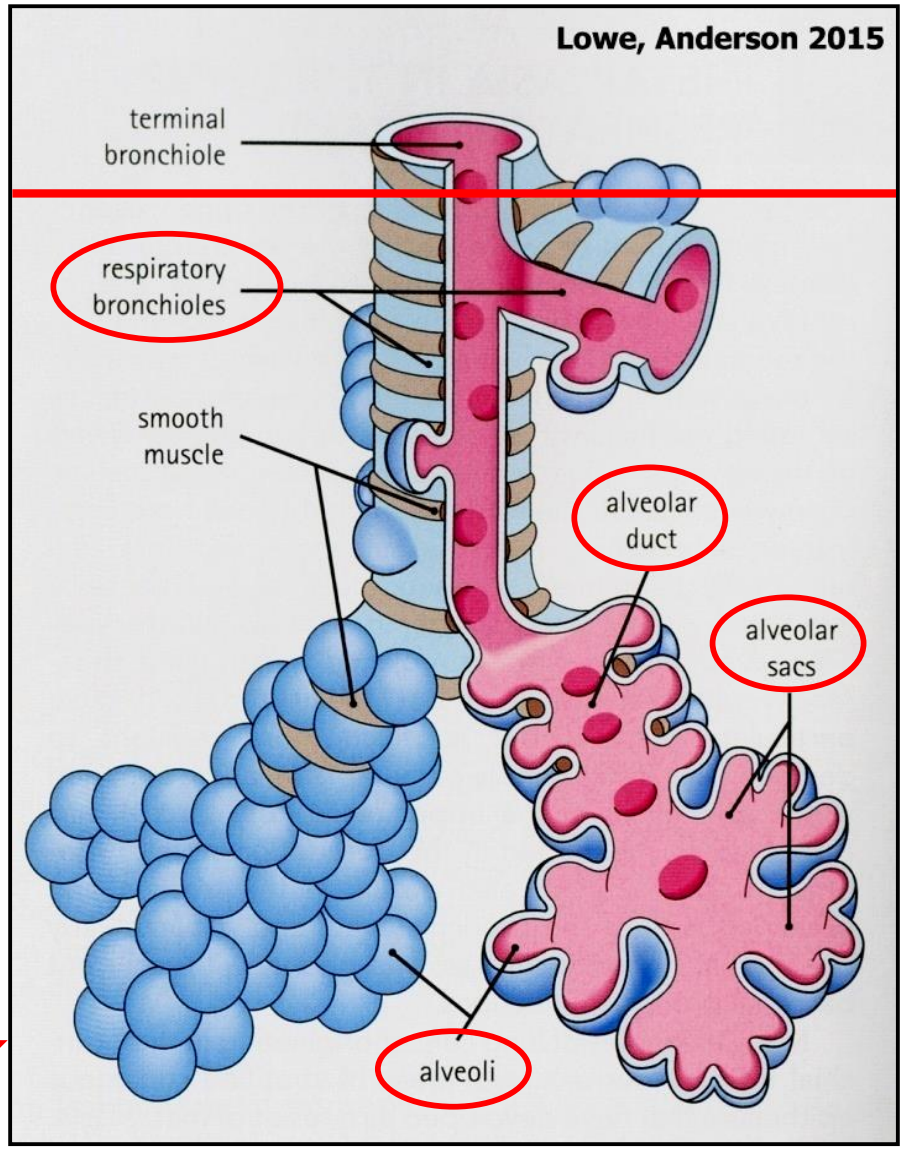
Bronchiole



Bronchiole


Blood vessel
Alveoli
Alveoli
Muscle bundles
Collagen fibers
Epithelium
Bronchiole

Respiratory portion



Respiratory portion

Terminal bronchiole

NO alveoli

Respiratory bronchiole

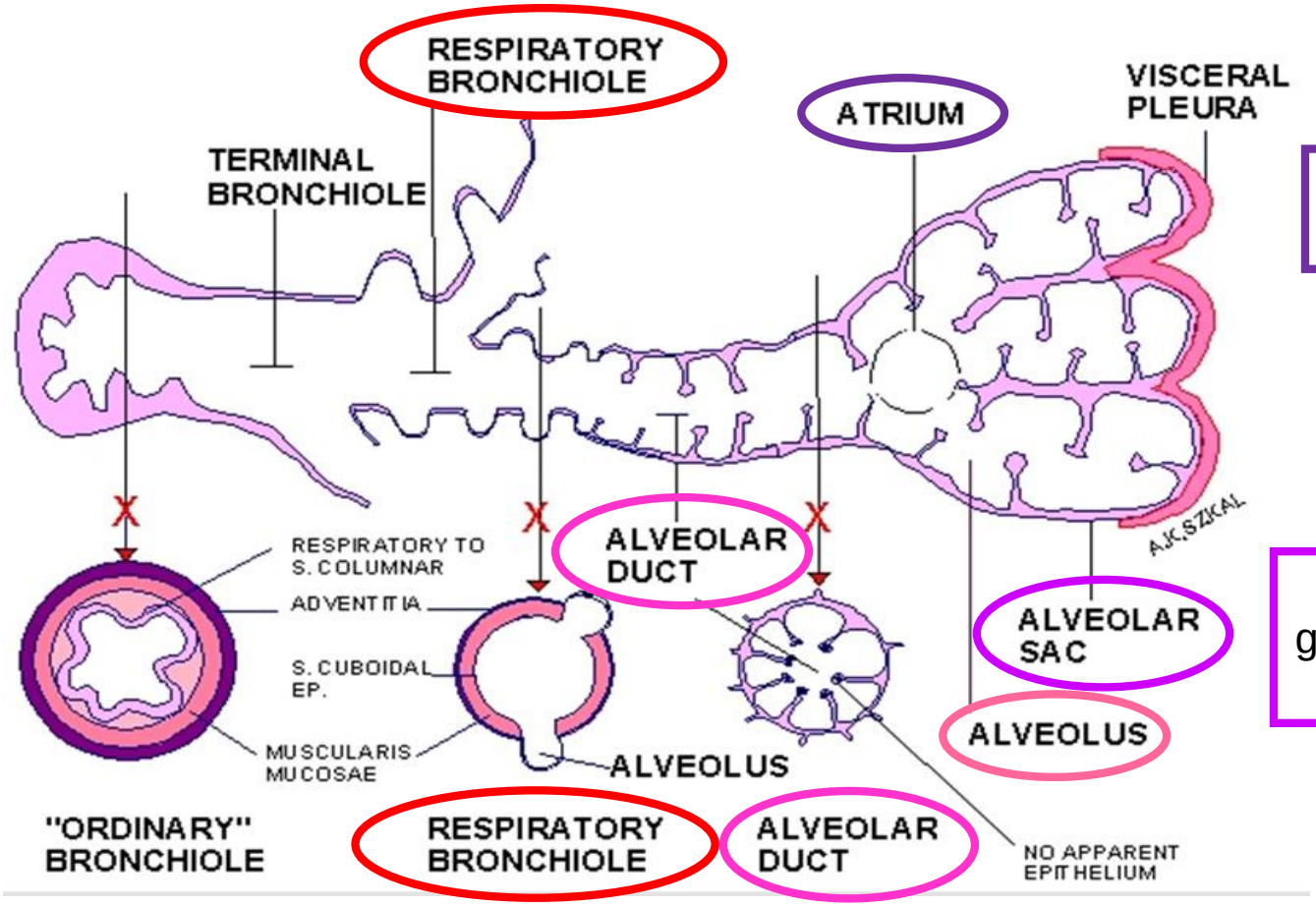
Outpocketing alveoli

REMINDER

Pulmonary lobule

- **defined by ONE primary bronchiole**
- **Include 5 to 7 Terminal bronchioles**
- pyramidal shape
- surrounded by very thin fibrous capsule
- volume 1 – 2 cm^3

Respiratory portion



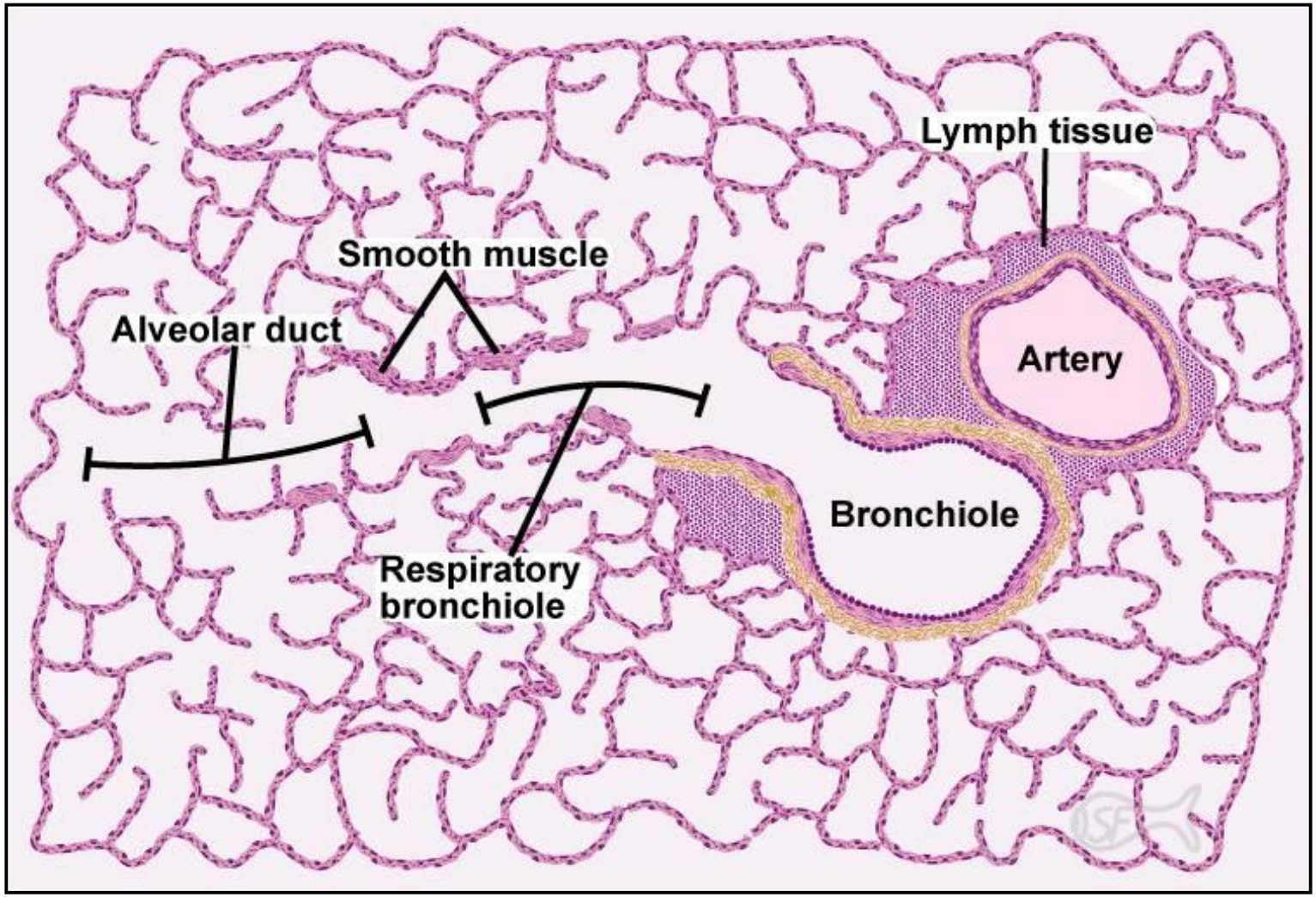
Atrium
entry into alveolar sac

Alveolar sac
group of alveoles opened into common atrium

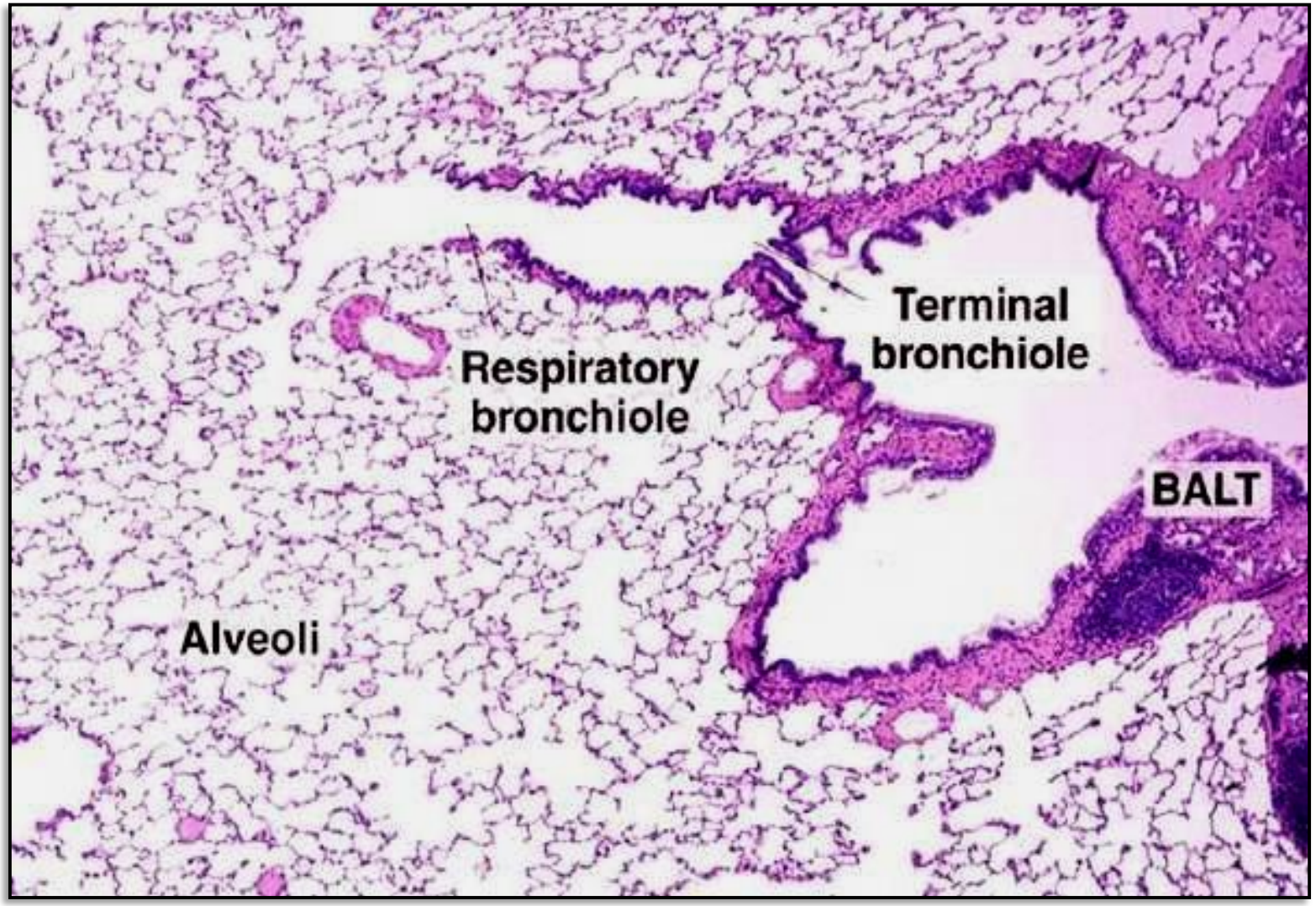
Alveolar duct - wall made by:

- groups of cuboidal cells
- individual alveoli
- elastic fibers
- smooth muscle cells surrounding alveolar entries

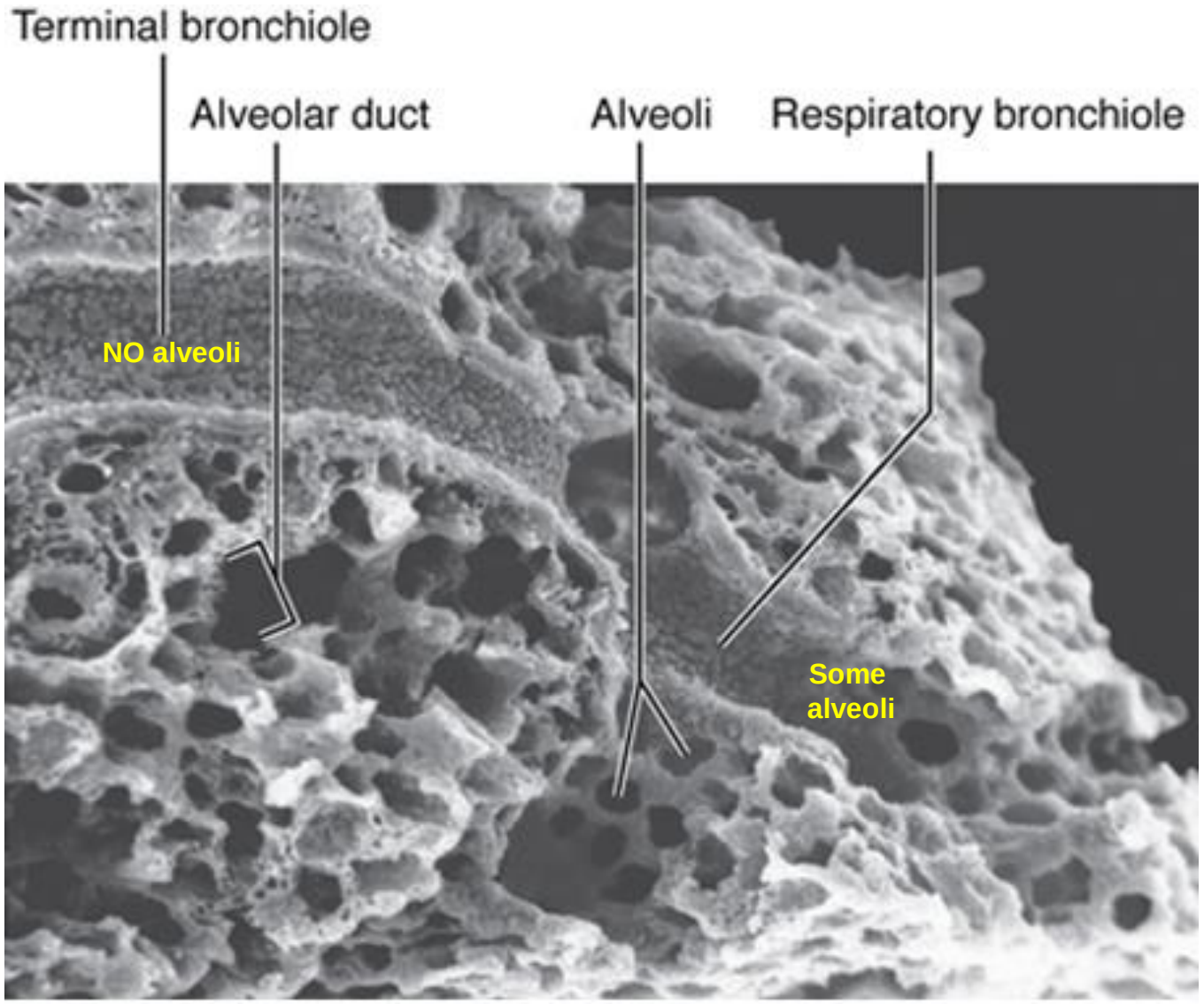
Respiratory portion



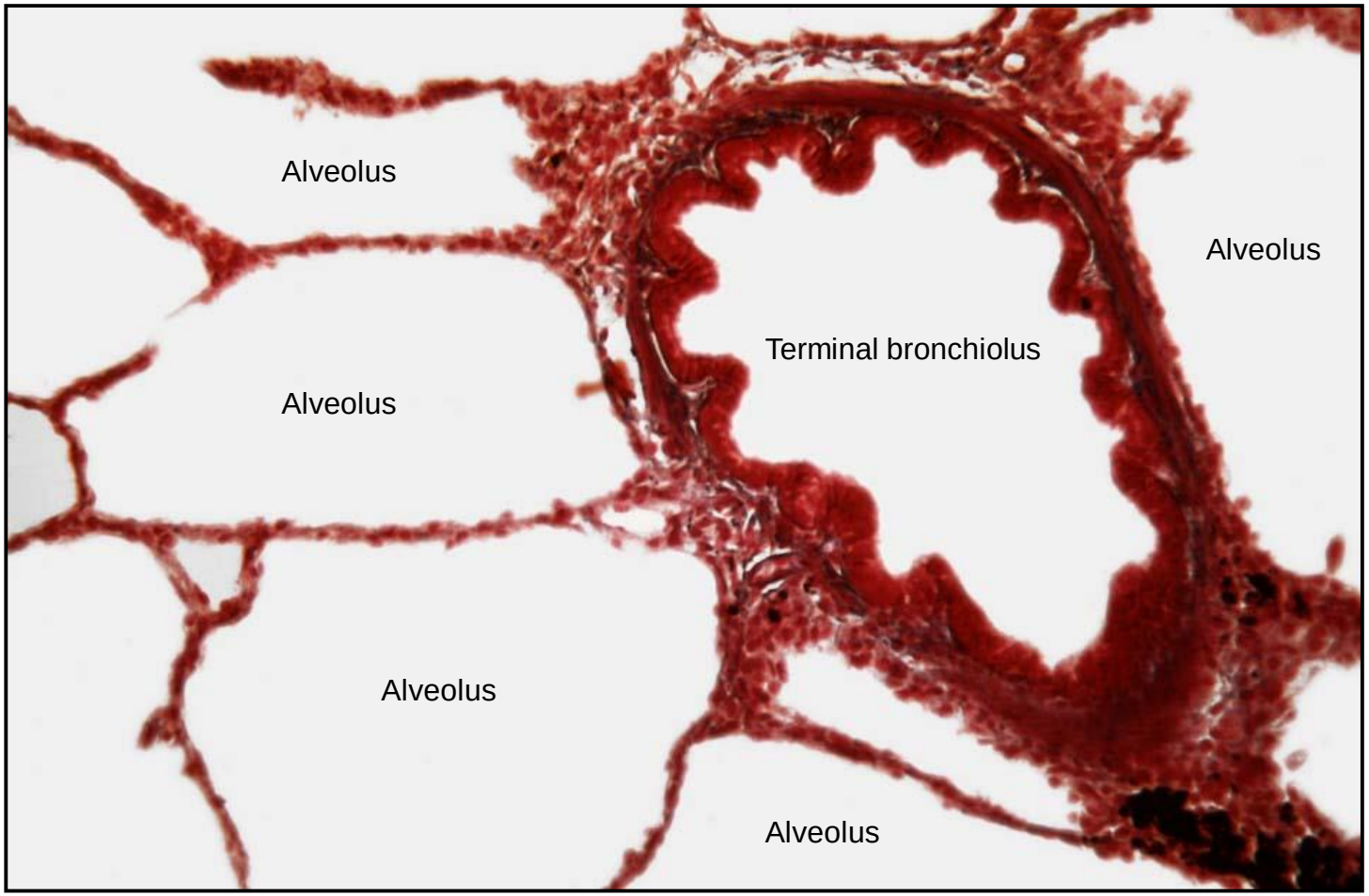
Respiratory portion



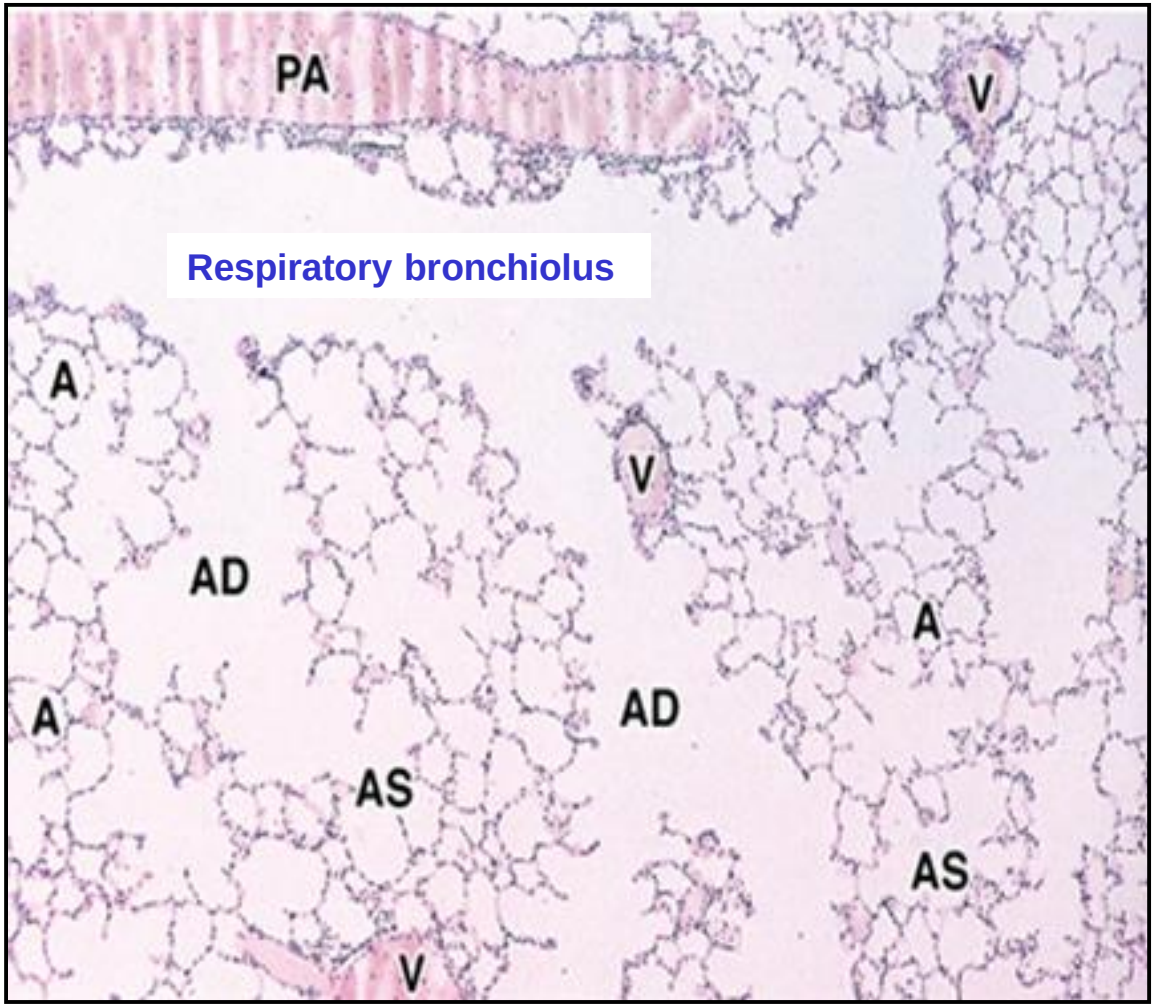
Respiratory portion



Terminal bronchiolus – NO connection into alveoli

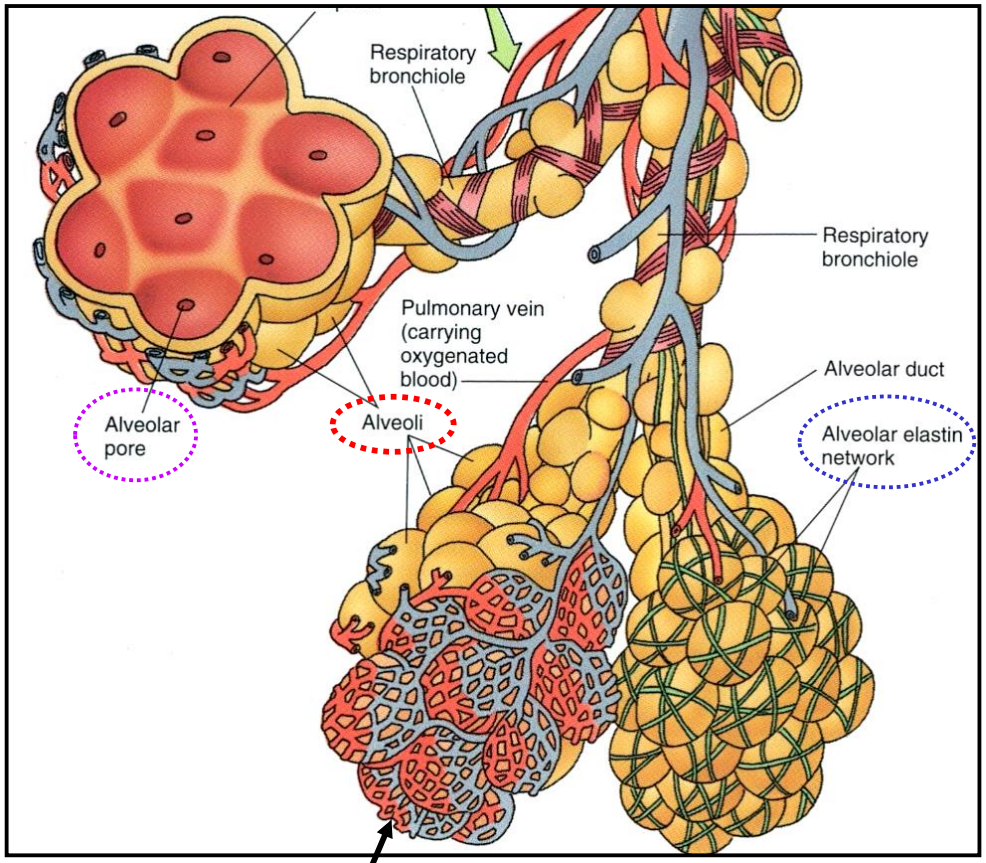


Respiratory bronchiolus – openings into alveoli



AD - Alveolar duct **AS** – Alveolar sac **A** - Alveolus **V** – Vein **PA** – Perialveolar artery

Alveoli

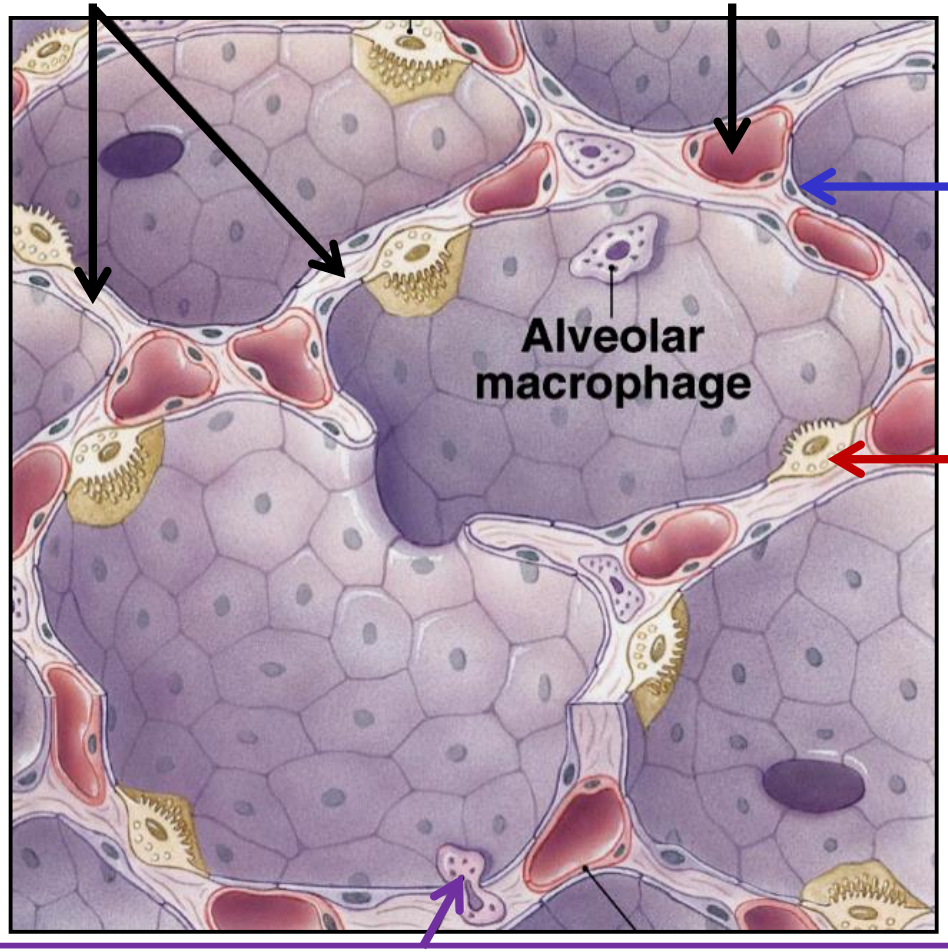


Place of gas exchange

Features

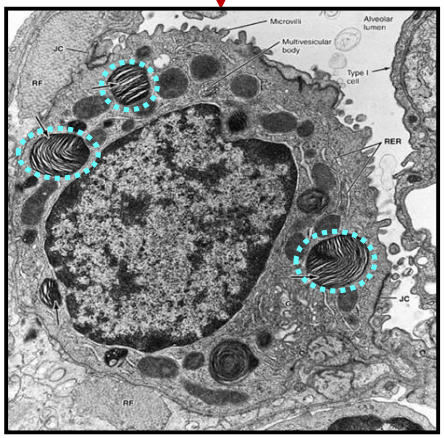
- diameter approx. 200 μm
- total number approx. 300 millions
- total surface about 100 – 140 m^2
- interalveolar septa (elastin + type III collagen)
- alveolar pores (Kohn´s; 8 – 60 μm diameter)

Alveoli



Type I Pneumocyte
(membranous)
- very flat – about 80 nm thickness
- occluding junctions
- about 95% of alveolar surface

Type II Pneumocyte
(granular)
- cuboidal (10 μm)
- more numerous than type I pneumocytes
- lamellar bodies – surfactants SP-A, -B, -C, -D
- stem cells to alveolar lining (type I and II pneu.)

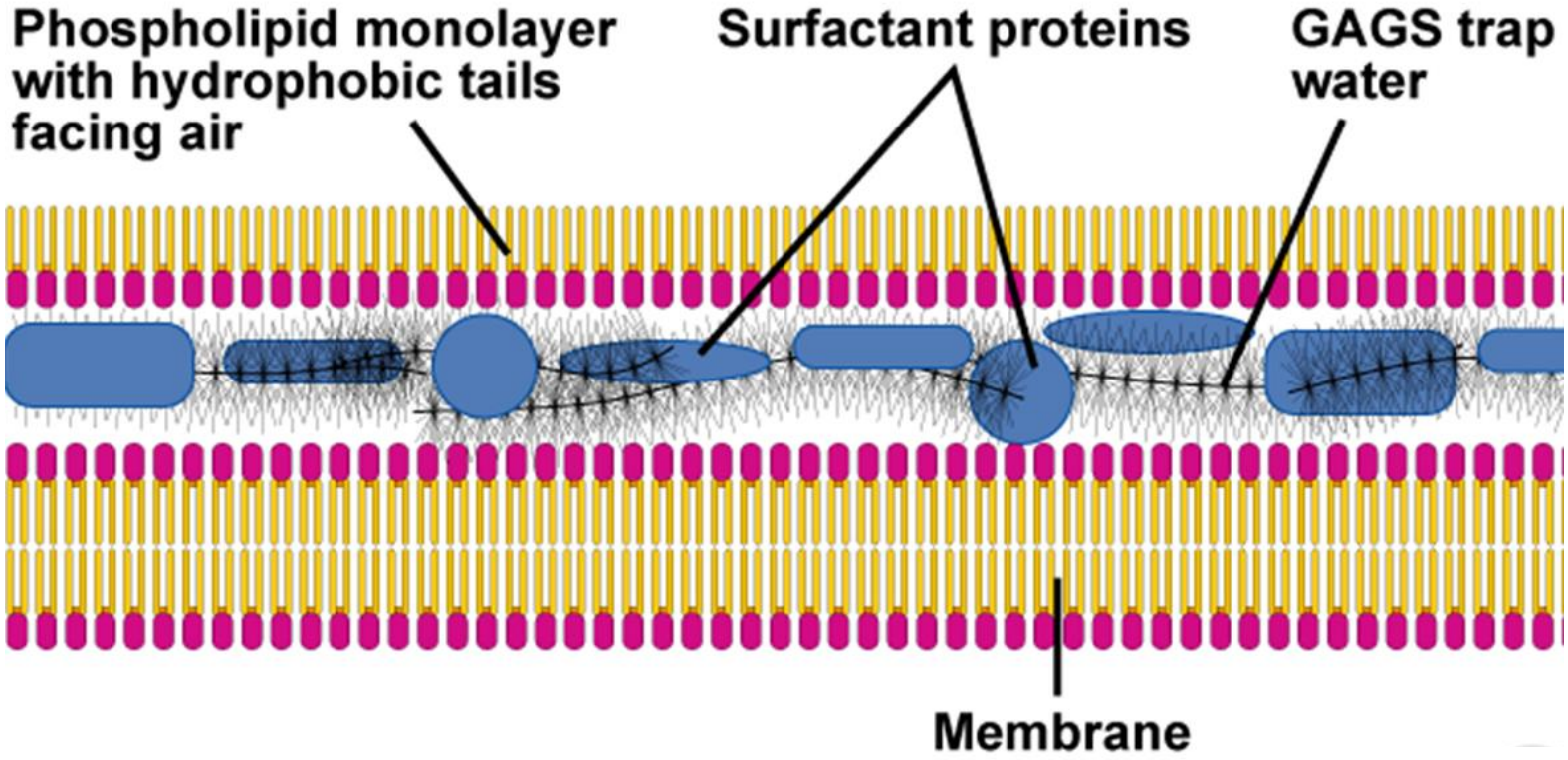


Alveolar macrophage – „dust cell“
- migratory
- some migrate up to pharynx and get swallowed/expectorated
- some migrate via lymph vessels
- some become resident in lungs

RDS (Respiratory Distress Syndrome of neonates)
lack of surfactants in premature born - collapse of alveoli

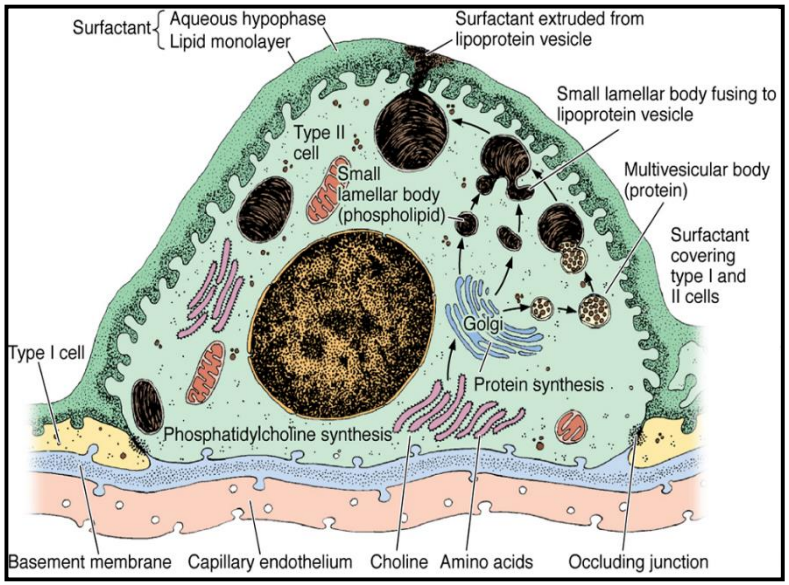
Alveoli - Surfactant

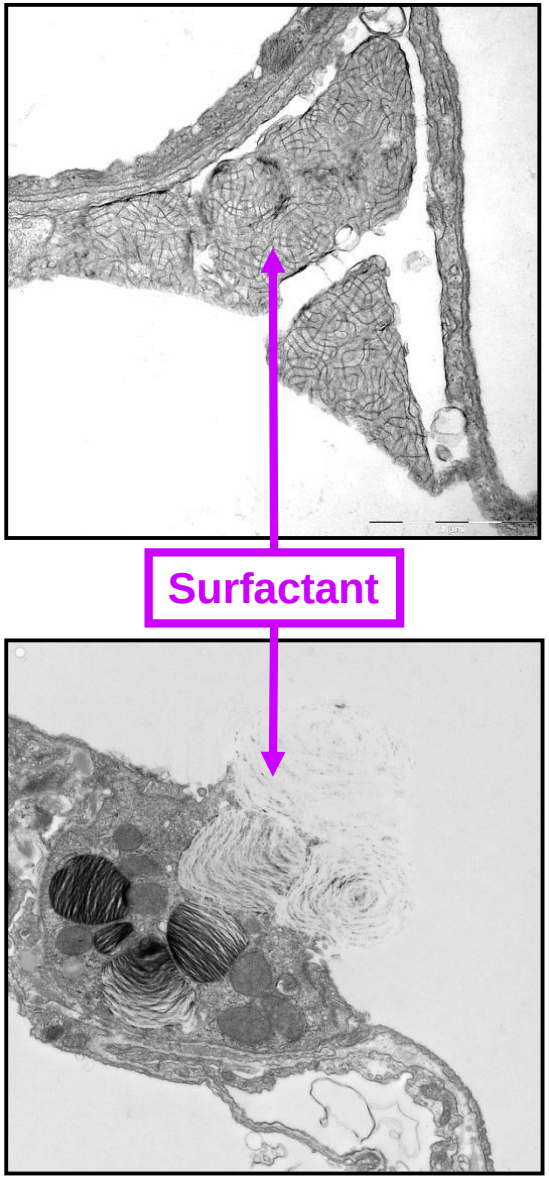
Lumen of alveolus



Cytoplasm of type I pneumocyte

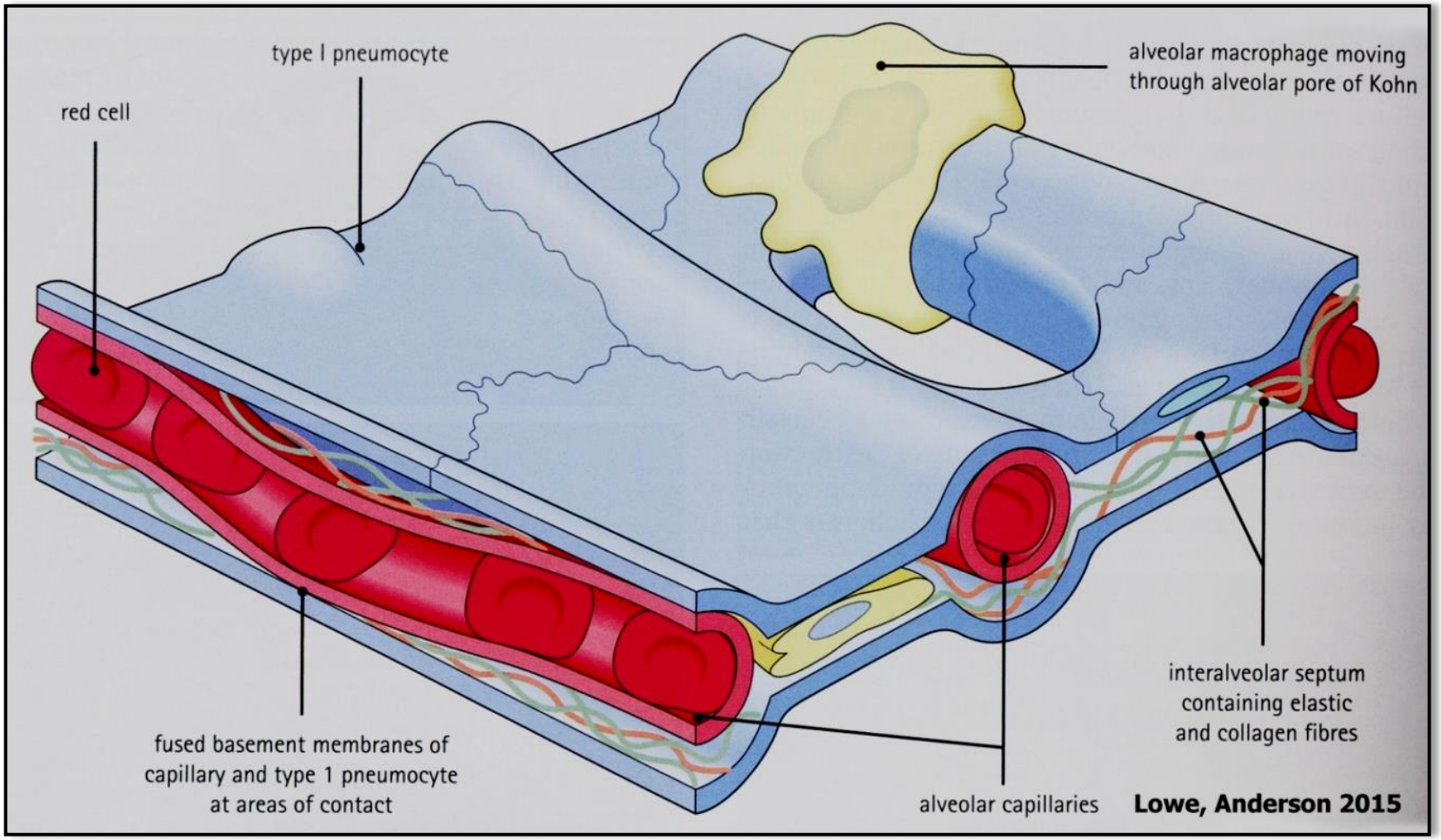
Alveoli - Surfactant





Alveoli – Macrophages

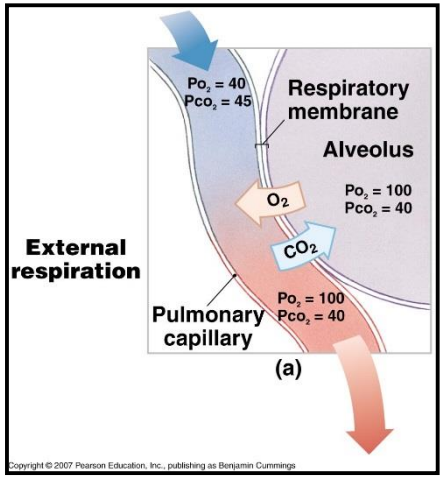
Alveoli – Interalvealar septum

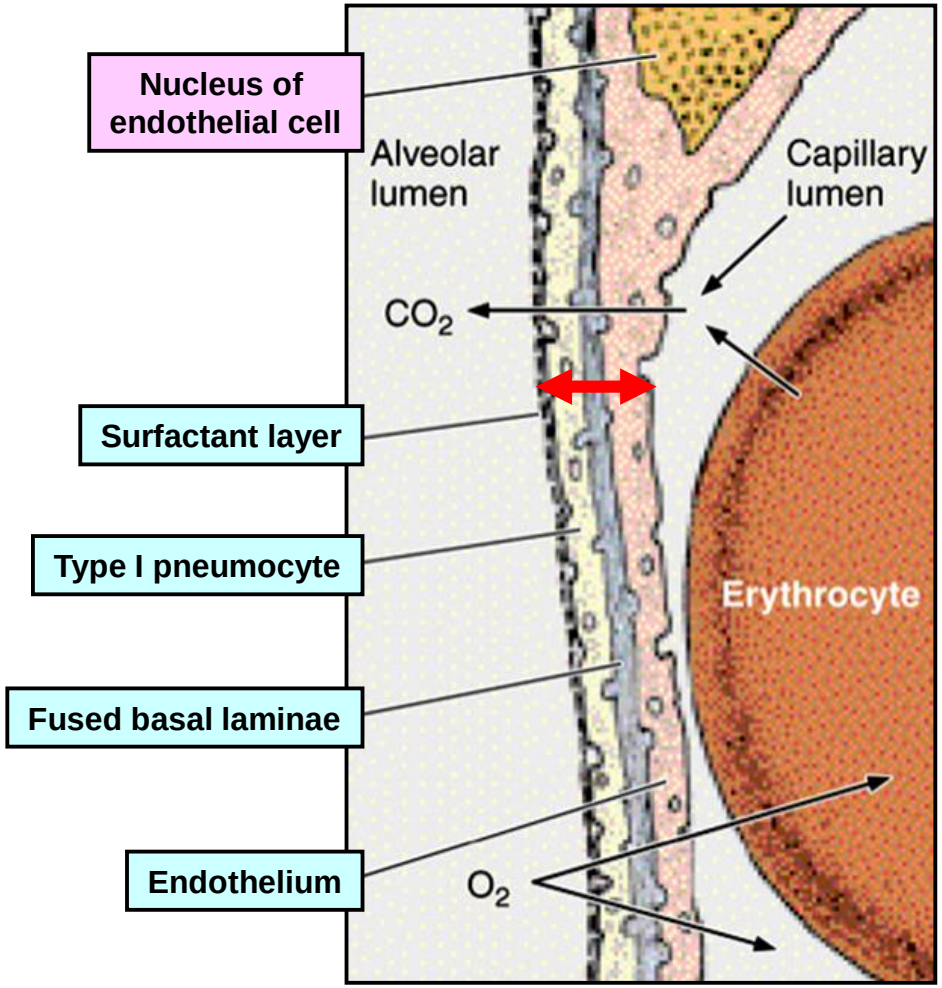


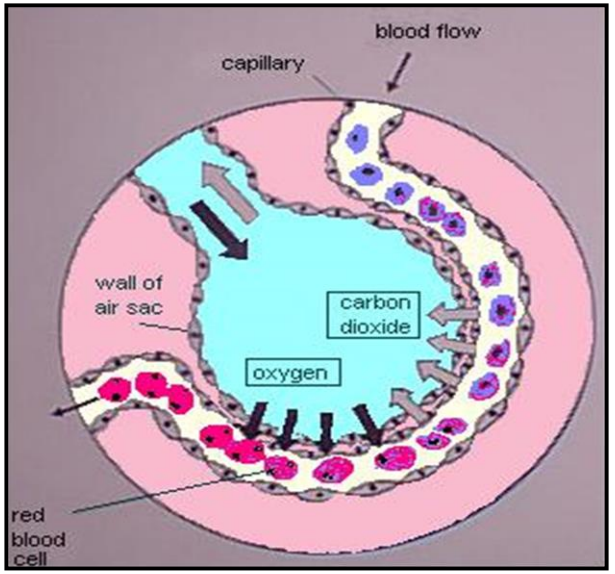
Alveoli – Blood-Air barrier

Thickness: 0,1 – 1,5 μm

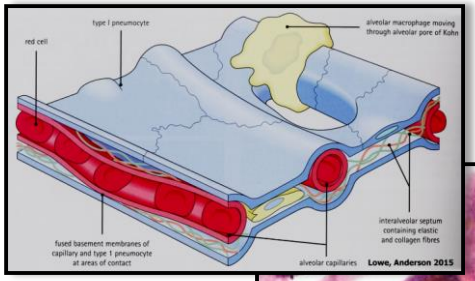
Exchange of gasses: passively by diffusion based on gradient

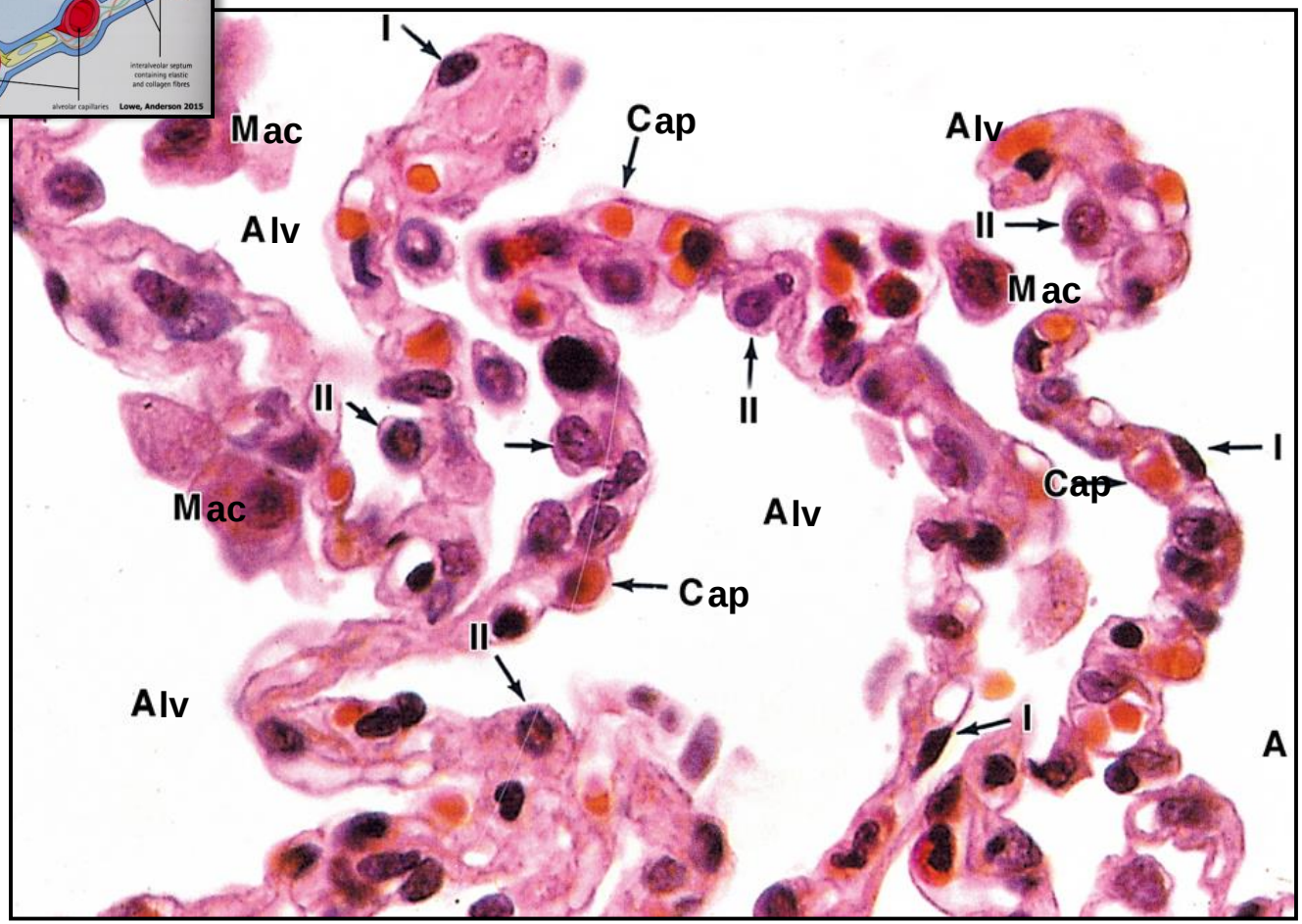






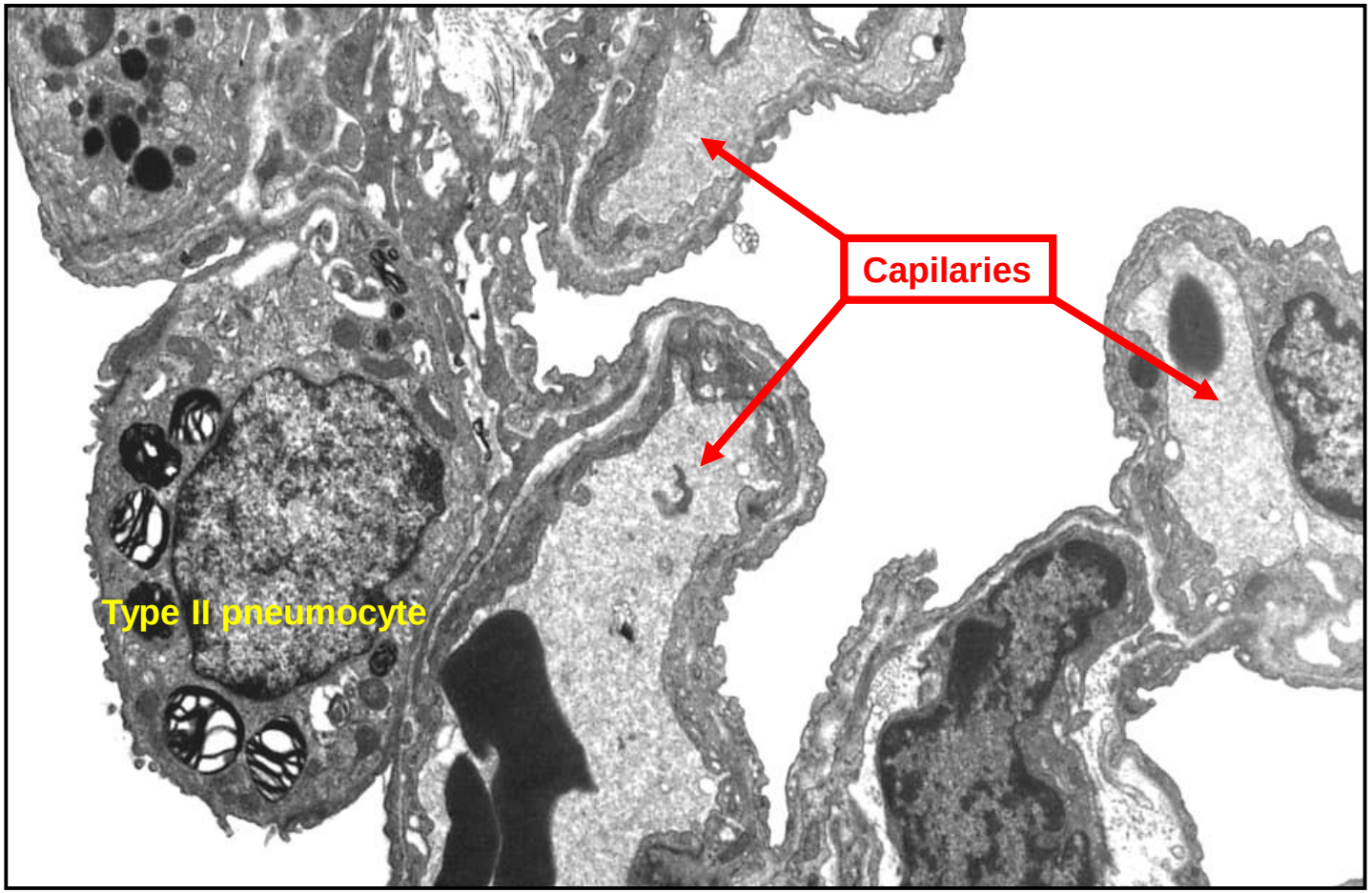
Alveoli – Blood-Air barrier



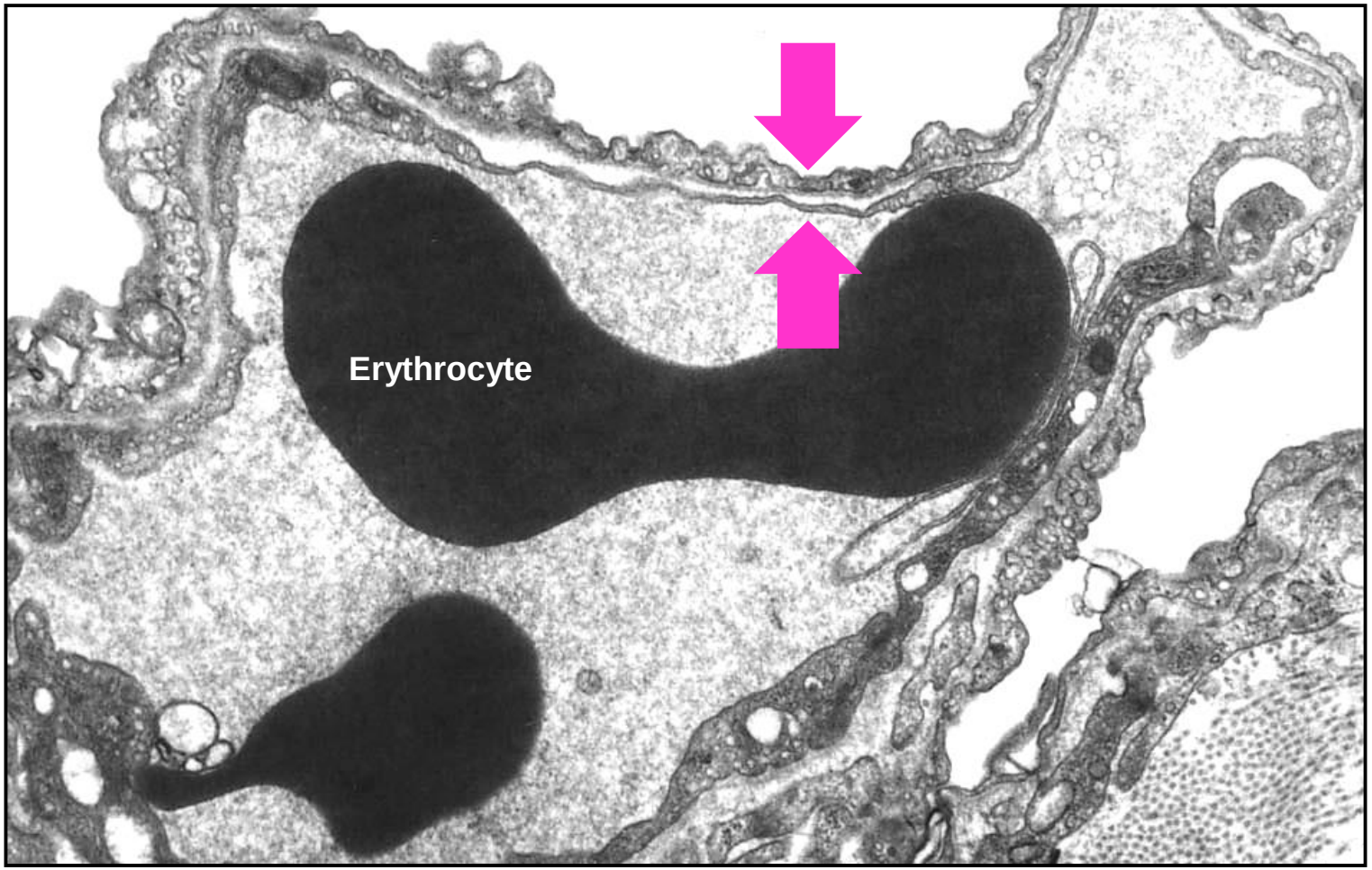


I - Type I pneumocyte **II** - Type II pneumocyte **Alv** - Alveolus **Cap** - Capillary **Mac** - Macrophage

Alveoli – Blood-Air barrier

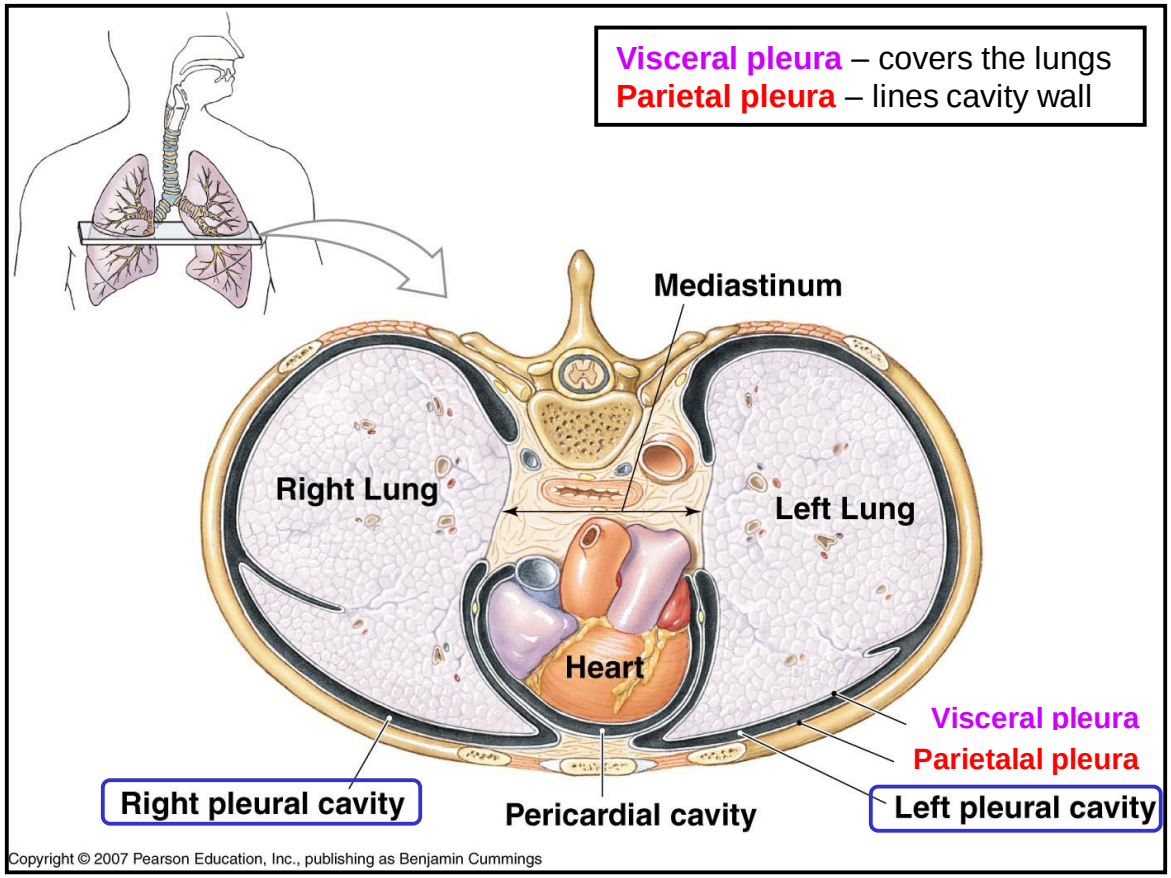


Alveoli – Blood-Air barrier

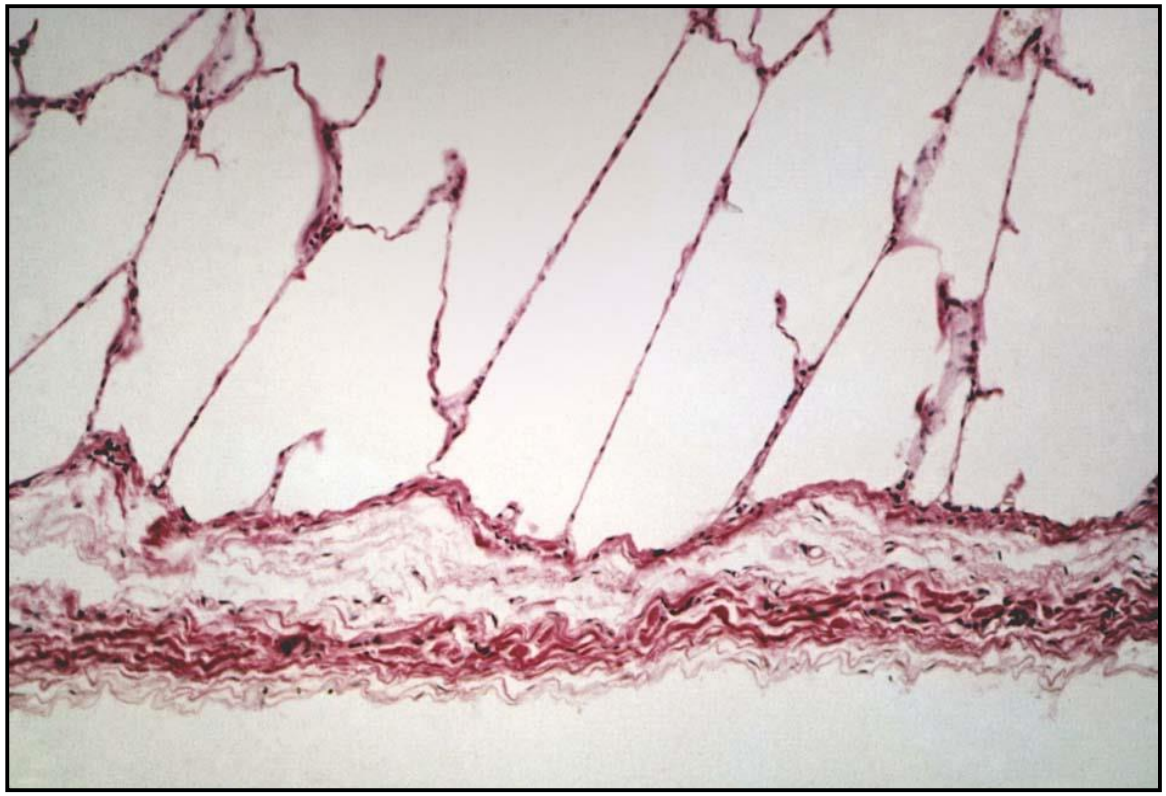


Pleura

Sheet that lines pleural cavities (left and right)



Pleura



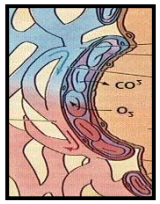
Mesothelium (simple squamous ep.)

Connective tissue (about 1 mm)

Blood supply

Pulmonary circulation „functional“ ✚ **Bronchial circulation** „nutritive“

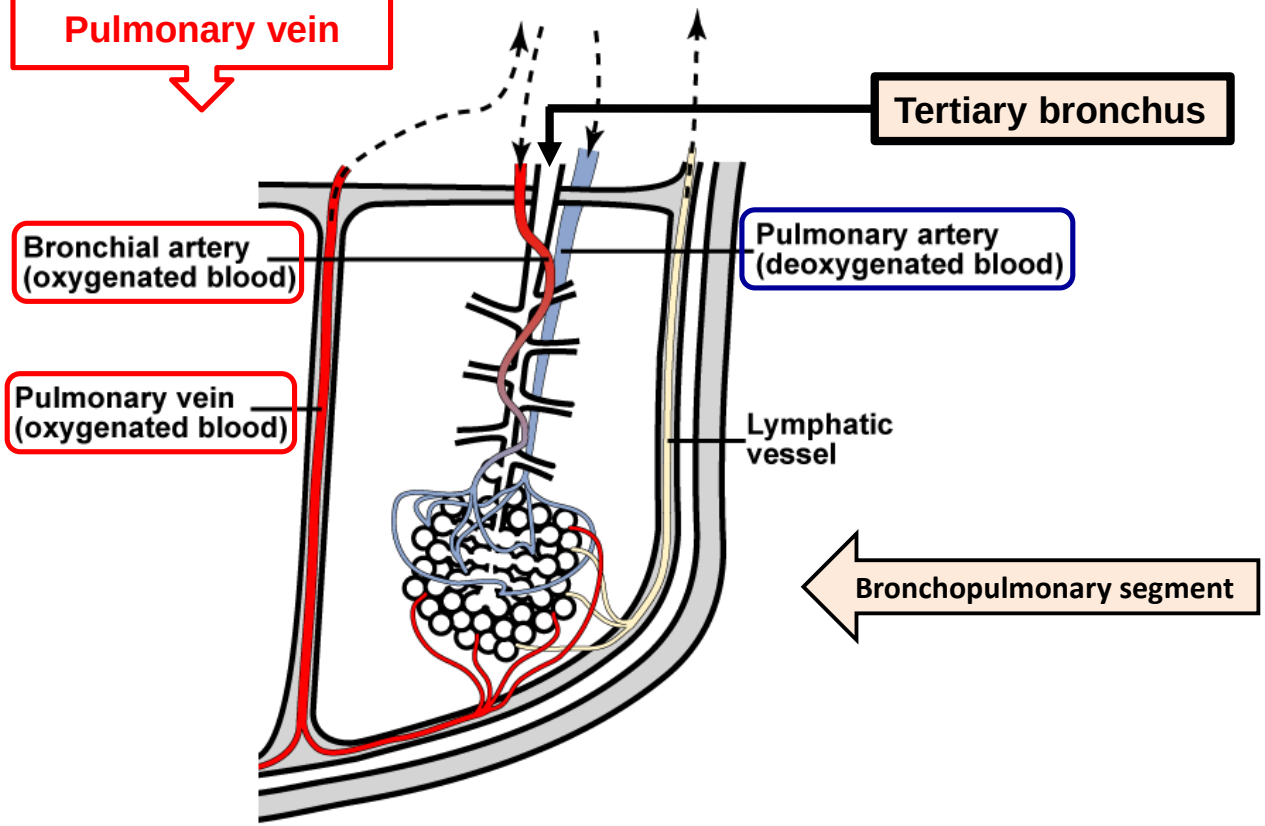
Pulmonary artery



Bronchial artery

Bronchial capilaries

Pulmonary vein

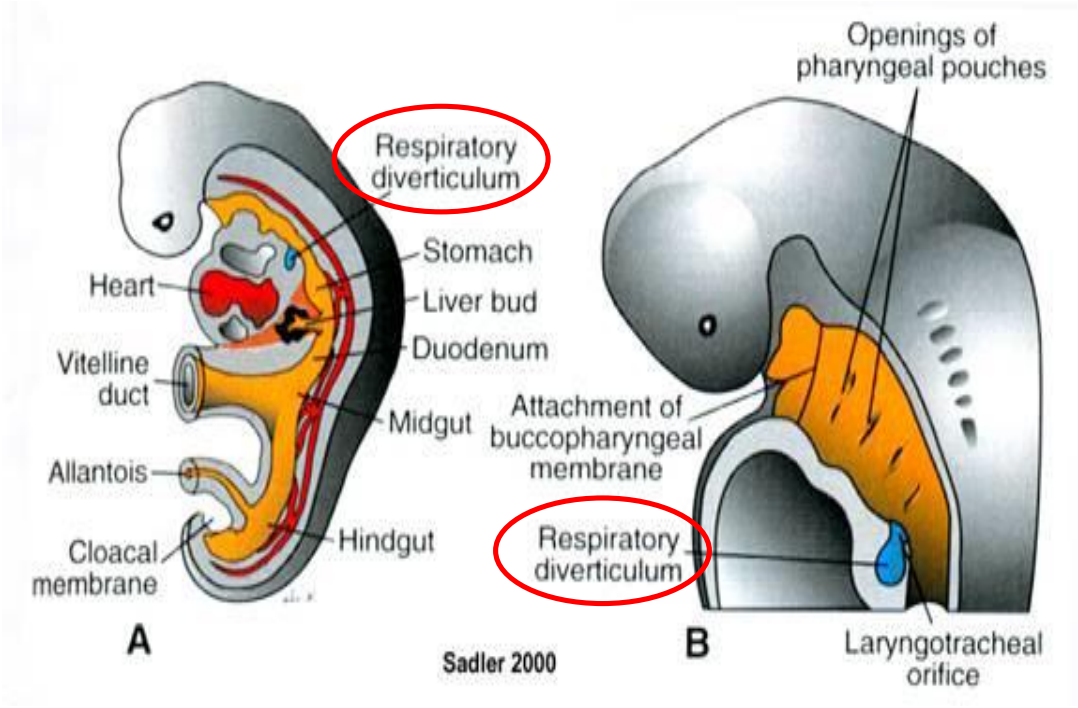


Lung development

Endoderm
- epithelium
- glands

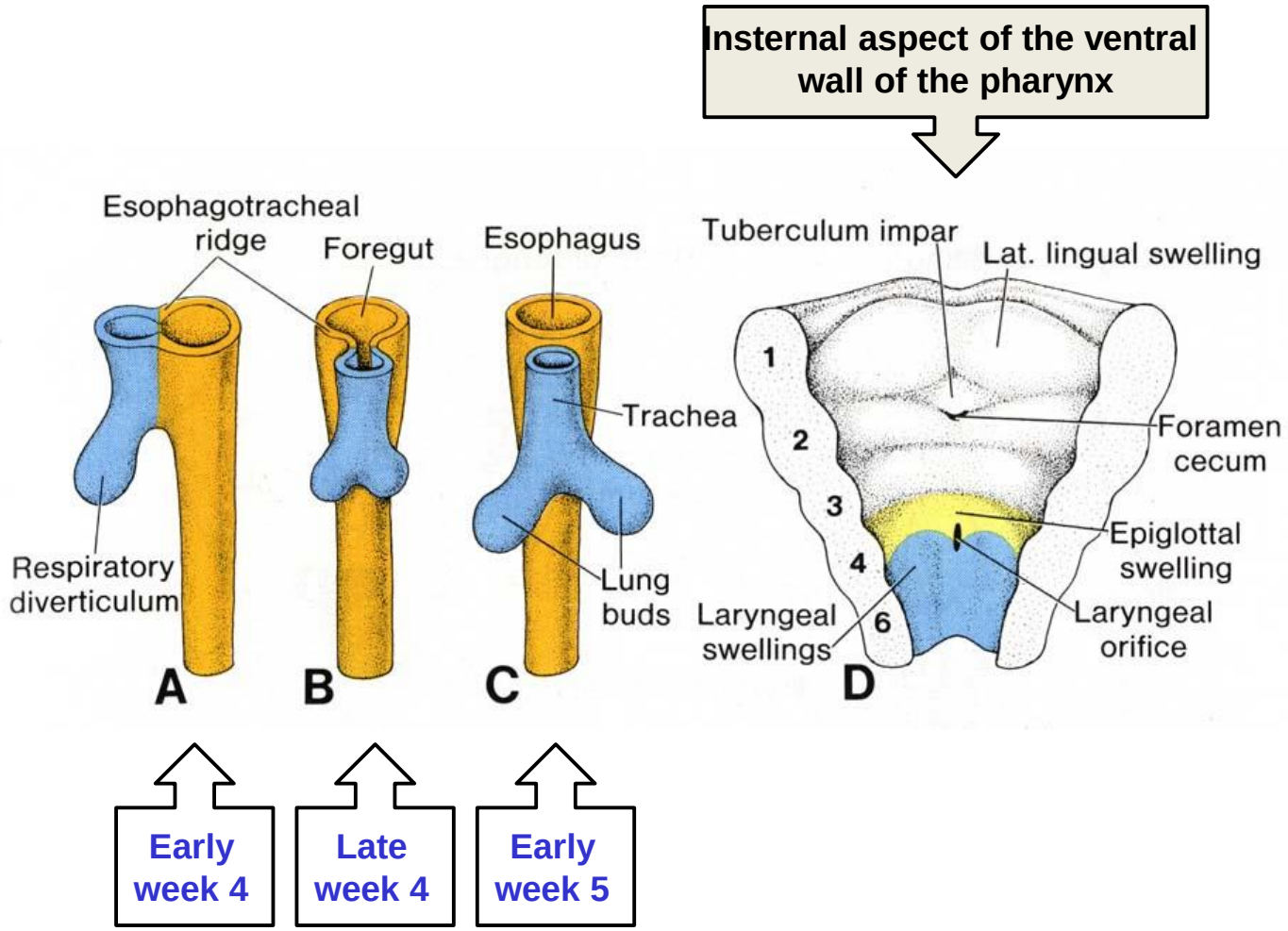
+

Mesenchyme
- connective tissue
- cartilage
- muscles



Early week 4: **Respiratory** (laryngotracheal) **diverticulum of the foregut** (ventral aspect)

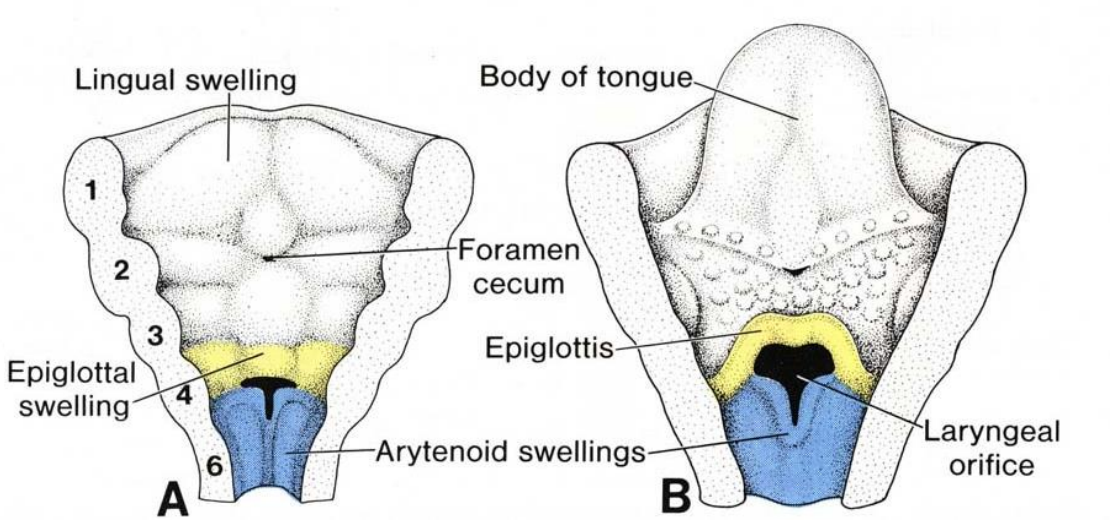
Lung development



Intricate interactions with the surrounding mesoderm

Lung development

Inside aspect of the ventral wall of the pharynx



week 6

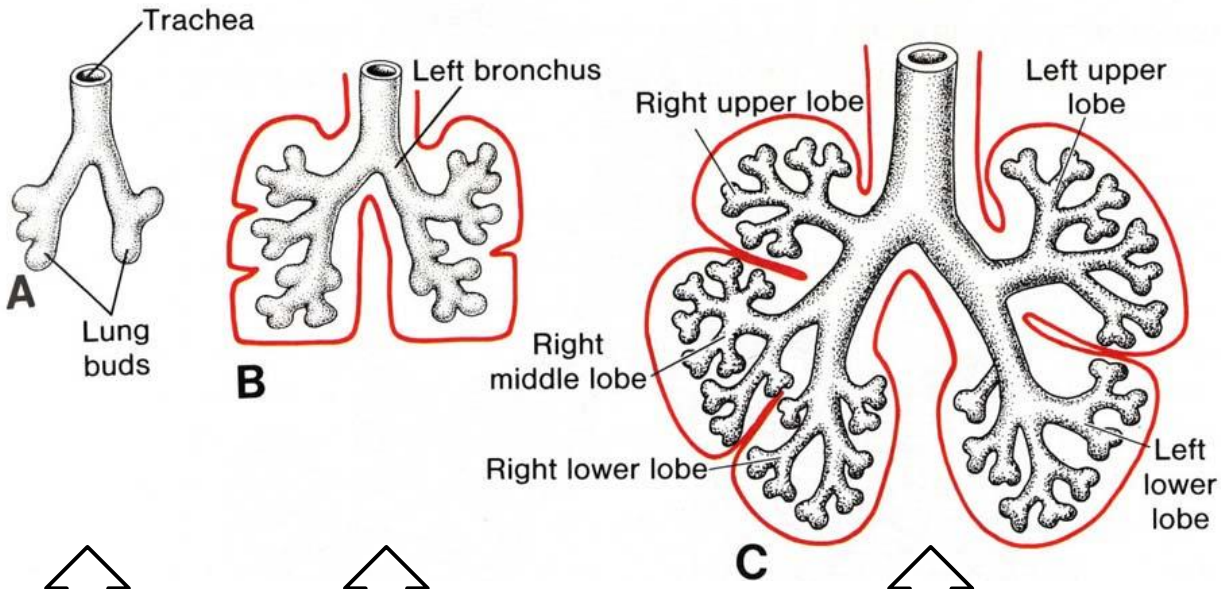
week 12

- **Lumen** first obliterate and then **recanalize**
- **Pharyngeal ventricle + Ventricular and Vocal plicas** develop
- **Pharyngeal cartilages + Ligaments + Muscles** develop (from 4. and 5. pharyngeal arch)

Lung development – Further branching of bronchi

Total number of branchings

Before birth - 18 x + **After birth - 7x**
until 8 years of age

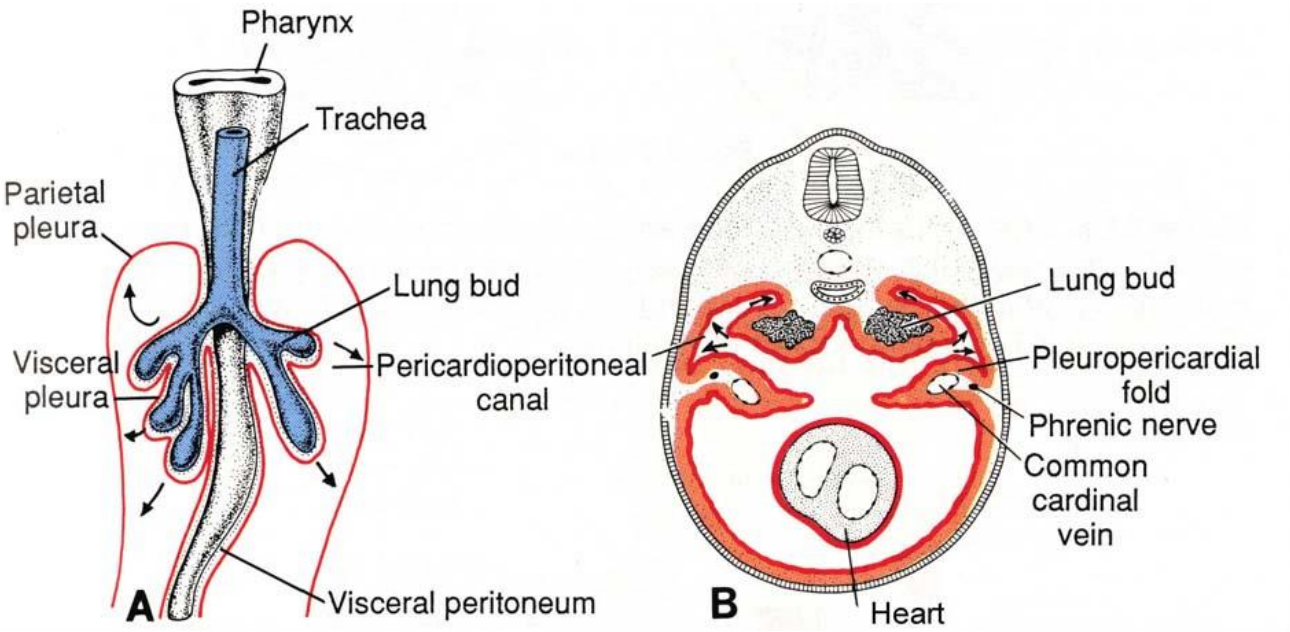


Late week 5

Late week 6

Late week 8

Lung development – Development of pleuro-pericardial folds

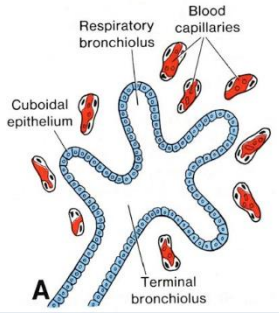


- by subsequent growth in caudal and lateral directions, the bronchial buds penetrate into **primitive pleural cavities**
- the splanchnic mesoderm, which covers the outside of the lung, is transformed into the **visceral pleura**
- the somatic mesoderm, covering the body wall from the inside, becomes the **parietal pleura**
- the space between the parietal and visceral pleura is the **pleural cavity**

Lung development – Lung histogenesis (maturation)

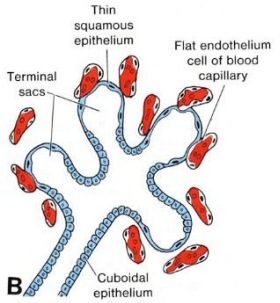
Pseudoglandular period (week 5 to 17)

- terminal bronchioles are formed
- blindly ended terminal bronchioles - resemble gland
- cuboidal epithelial lining (endodermal)
- **NO respiratory bronchioles and/or alveoli**



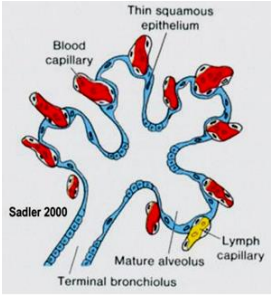
Canalicular period (week 13 to 25)

- development of respiratory bronchioles, sacs, and vascularisation
- respiration and survival is possible but only with intensive
- **still severe non-maturity**



Terminal sac period (week 24 to birth)

- considerable increase of terminal sacs and alveoli with well differentiated pneumocytes
- **sufficiently formed blood-air barrier**
- **since week 26 - survival without intervention is possible** (fetal weight about 1000 g)



Alveolar period (week 32 – 8 years)

- longest period
- development of lungs becomes finalized

Thank you for your attention !

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