Histology of the Respiratory System

MEDEMIA ACADEMY

Learning Objectives

- Recognize & describe the cellular components of respiratory epithelium
- Understand the structure & function of conchae
- Recognize & describe the cellular components of olfactory epithelium
- Describe components of the vocal cords
- Recognize & understand function of epiglottis
- List the tubes that make up the conducting and respiratory portions
- Distinguish between a bronchus, bronchioles & respiratory bronchiole
- List all components that make up the interalveolar septum
- Distinguish between type I & type II alveolar cells, macrophage and endothelium

Objectives of studying the RS

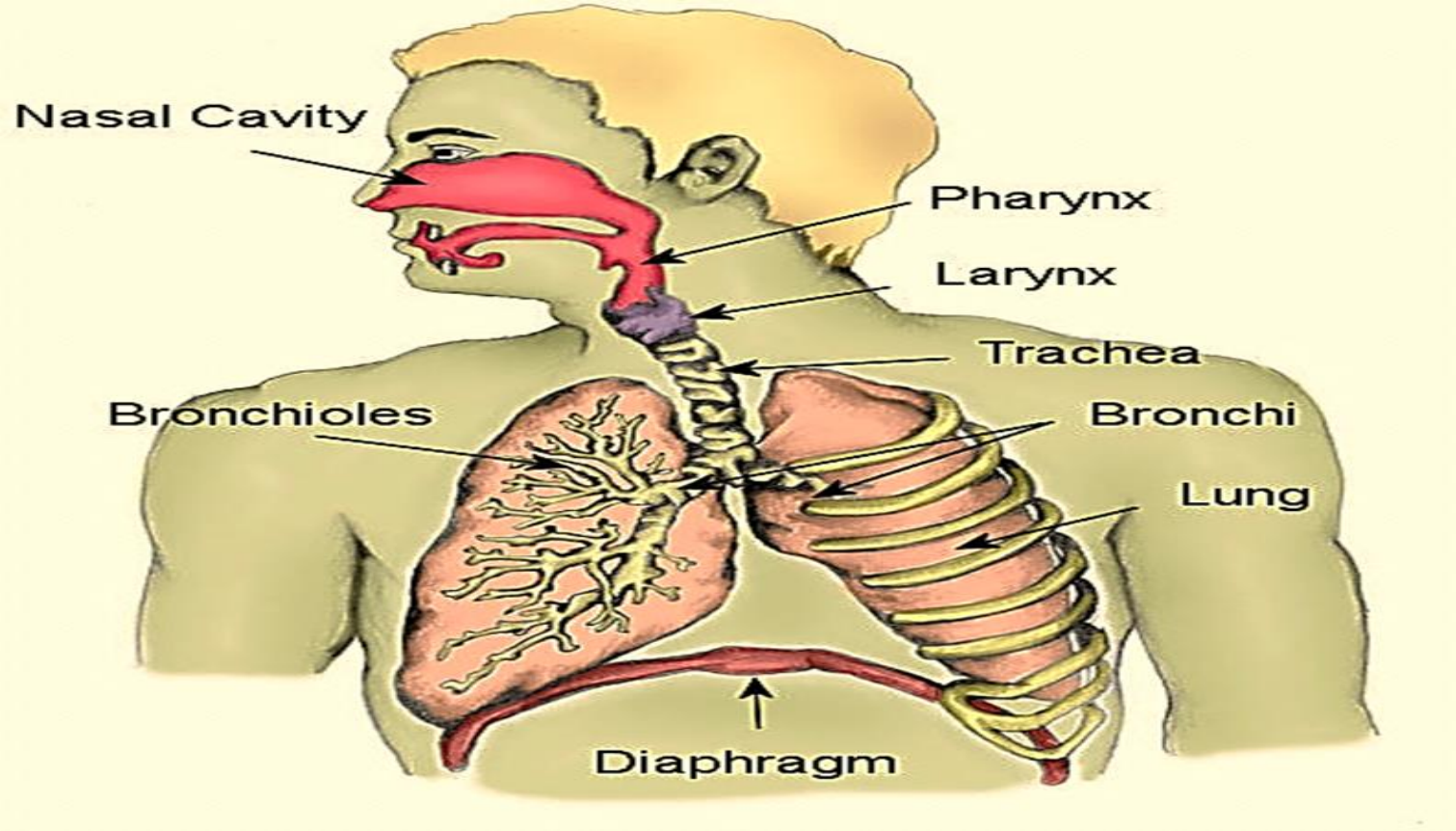
- Understand the structure and function of air ways, lungs, and the role of their lining epithelium in clearing the inspired air and in gas exchange

- Understand the structure of chemoreceptors involved in the sense of smell

- Understand structures responsible for production of sounds (Phonation)

Respiratory System Portions

Conducting portion	Respiratory portion
Conduct, filters, warms & moistens air	Gas exchange & secretion of Surfactant

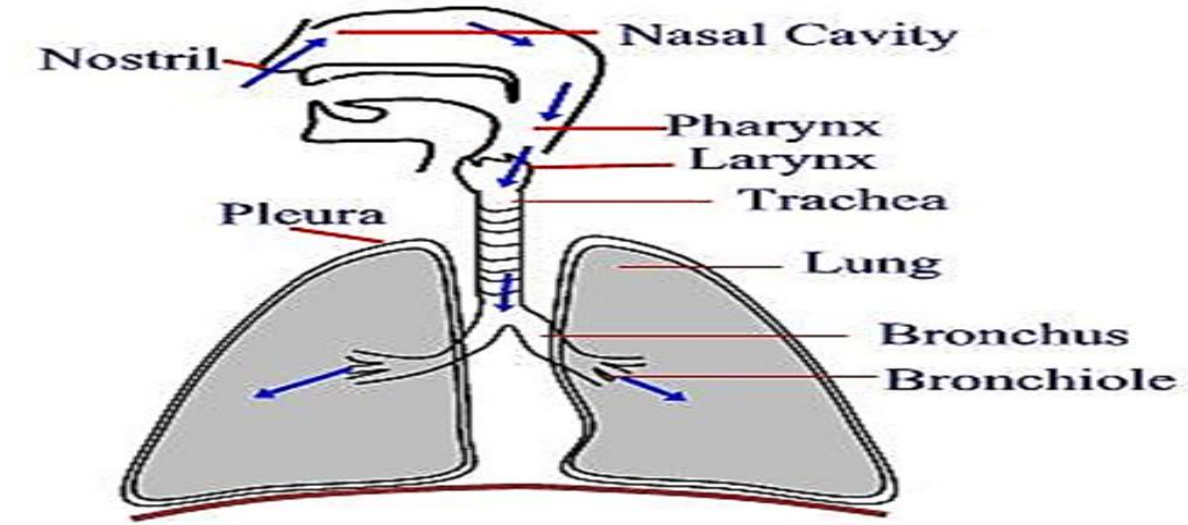


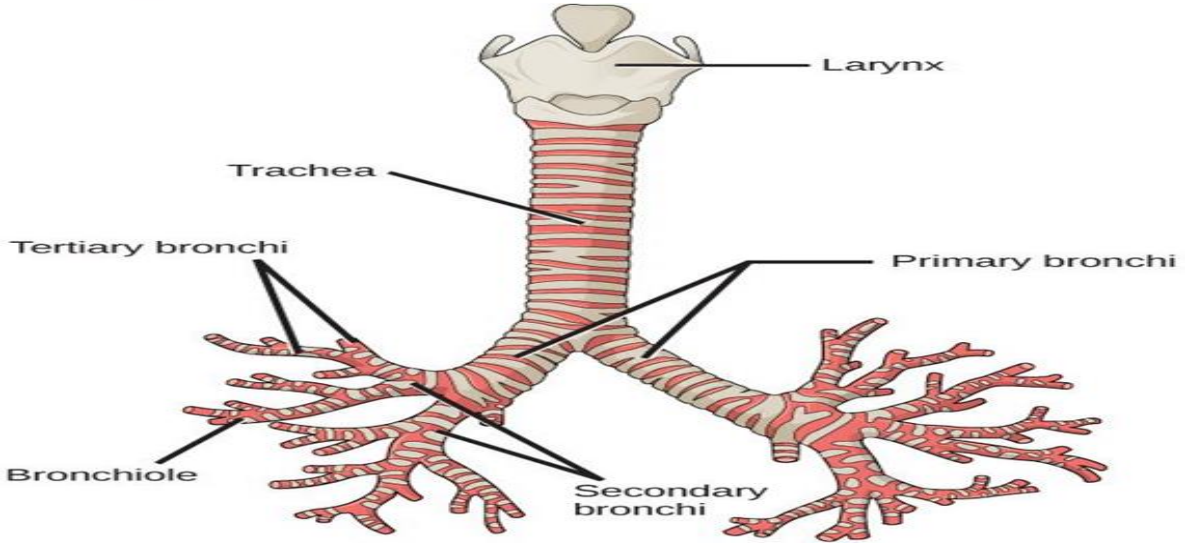
Types of epithelium in the RS

- **Non-keratinized stratified squamous epithelium:** Found at nostrils, lingual surface of epiglottis, & true vocal cords
- **Respiratory epithelium:** Cover most of the conducting portion of the respiratory tract
- **Olfactory epithelium:** Contains chemoreceptors of smell sensation → superior conchae
- **Alveolar epithelium:** Found in Respiratory portion / alveoli where gas exchange

Parts of the Conducting portion

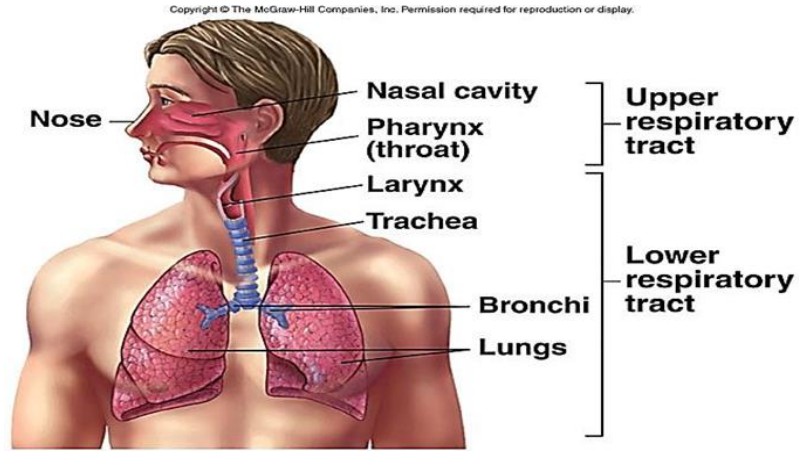
- Nasal cavities & sinuses
- Nasopharynx
- Larynx
- Trachea
- Bronchi (right and left)
- 2ry and 3ry bronchi
- Bronchioles
- Terminal bronchioles

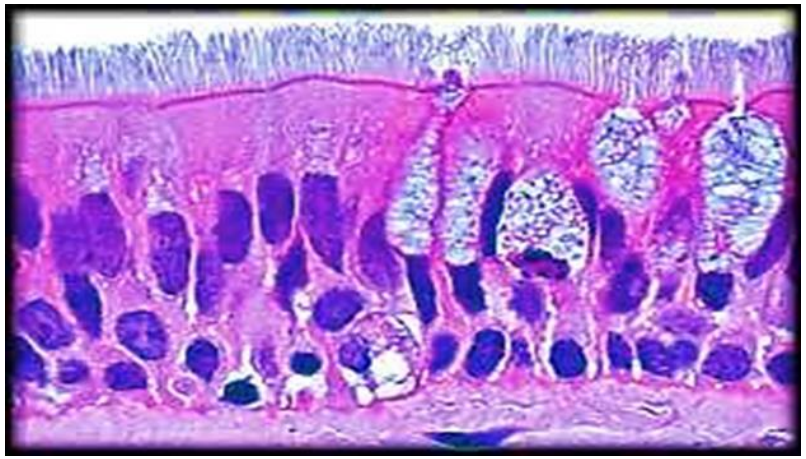




Structure / Function relation in Conducting portion

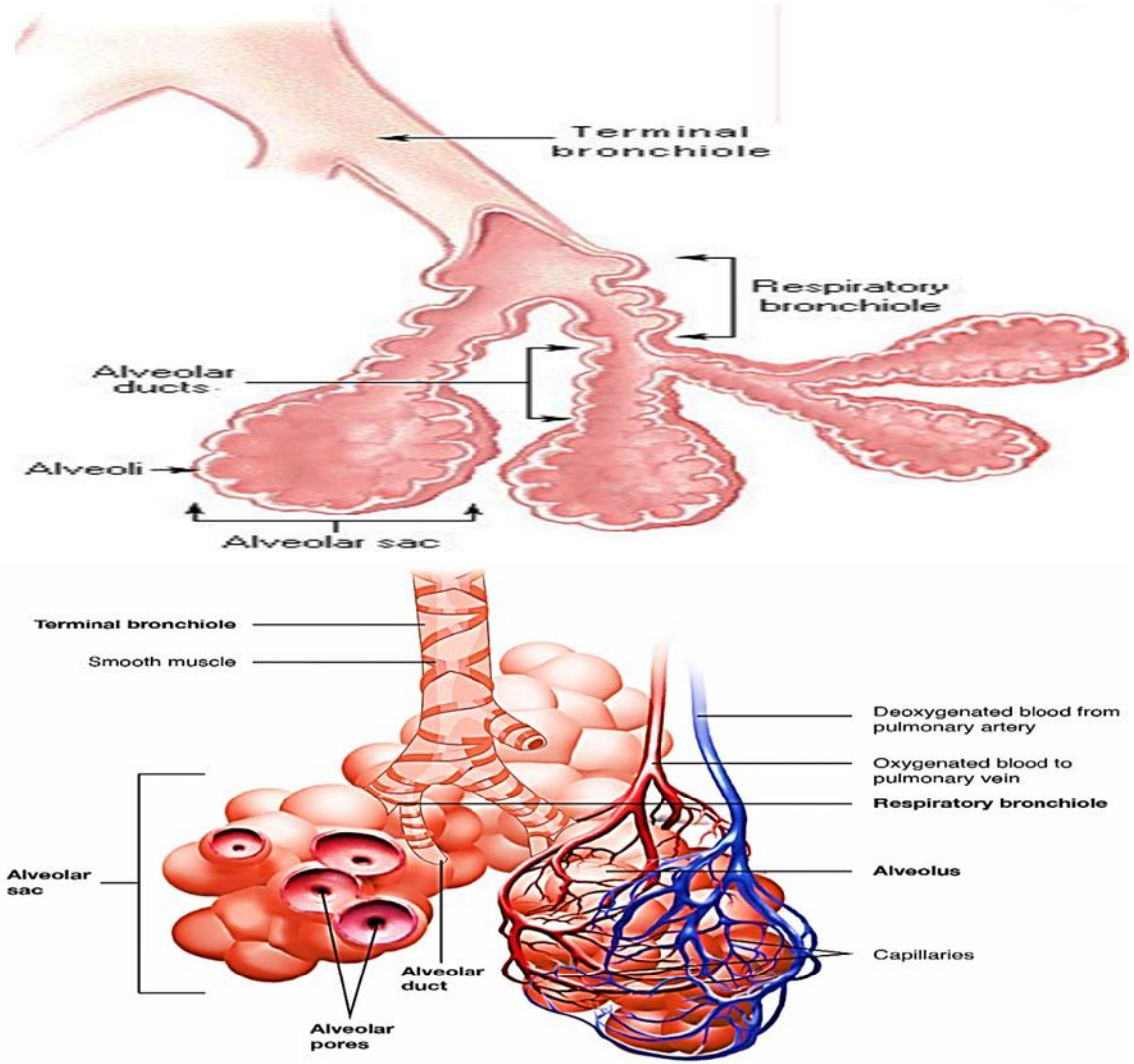
- Cartilage to prevent collapse → Maintain an open lumen
- Elastic fibers & smooth muscle fibers for flexibility → Ability to accommodate expansion & contraction
- Respiratory epithelium → Filtering, moisturizing & warming of inspired air

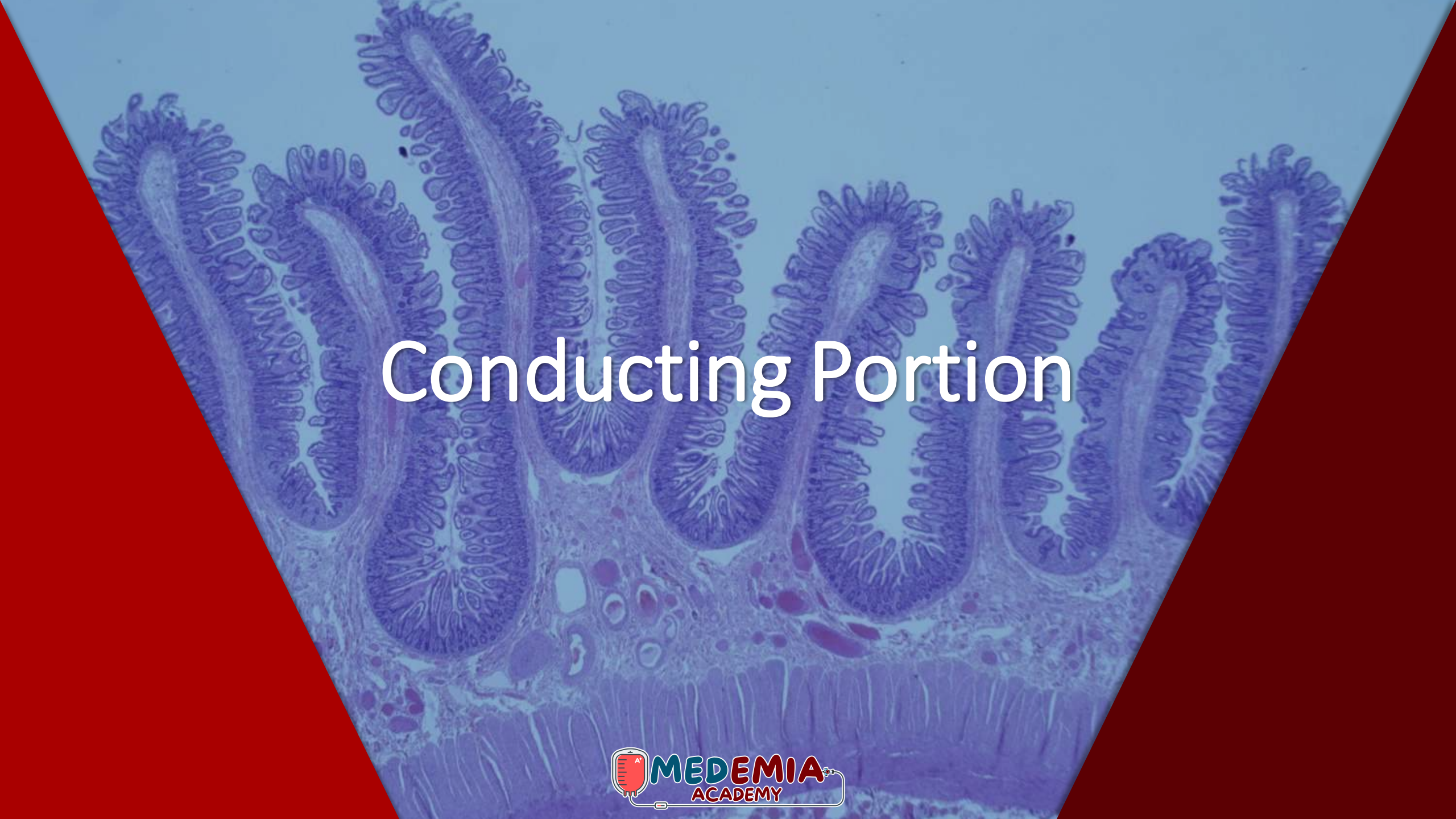




Parts and Function of the Respiratory portion

- Parts:
  - Respiratory bronchioles
  - Alveolar ducts
  - Alveolar sacs
  - Alveoli
- Function:
  - Gas (O_2/CO_2) exchange between blood & inspired air
  - Production of surfactant





Conducting Portion

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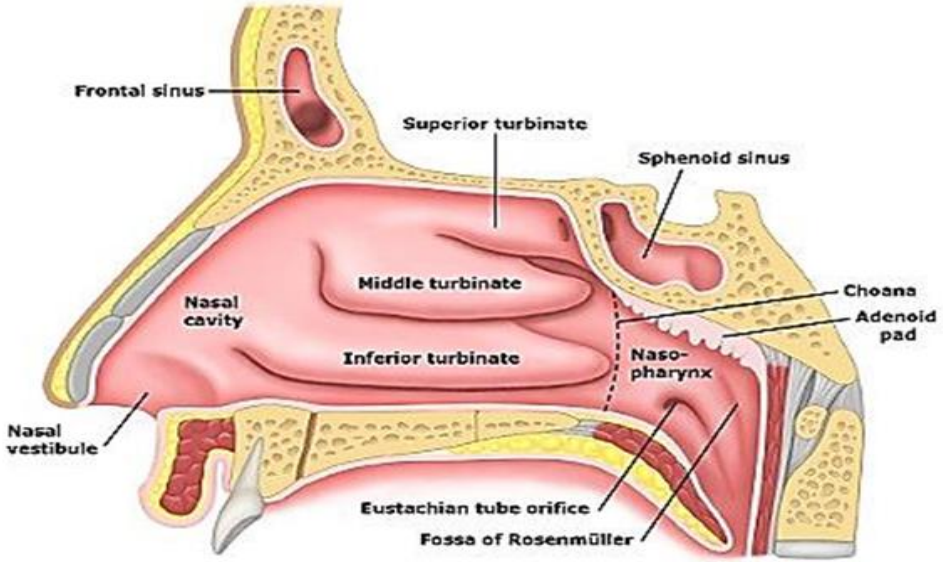
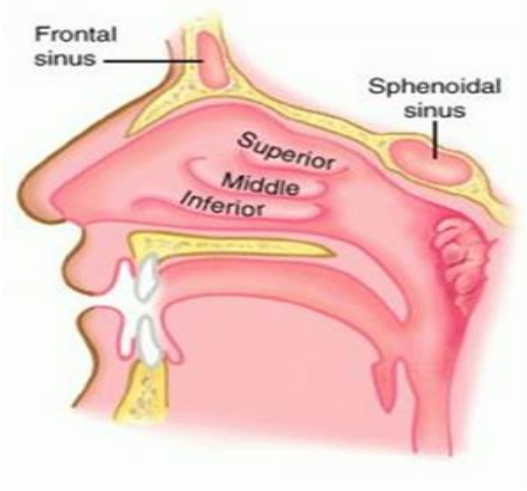
Nasal Cavity

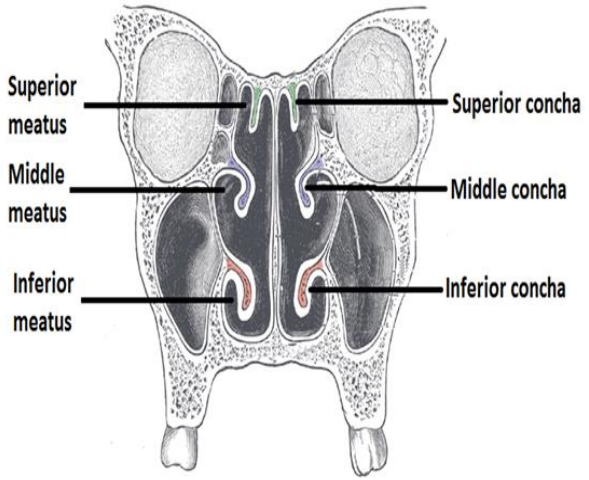
- Nasal cavities: Separated by a septum (cartilaginous & bony) parts each consists of:
  - Vestibule
    - Is the anterior part
    - Lined with thin skin
    - Deeper changes → non-keratinized stratified squamous epithelium
    - Hair filters out large dust particles

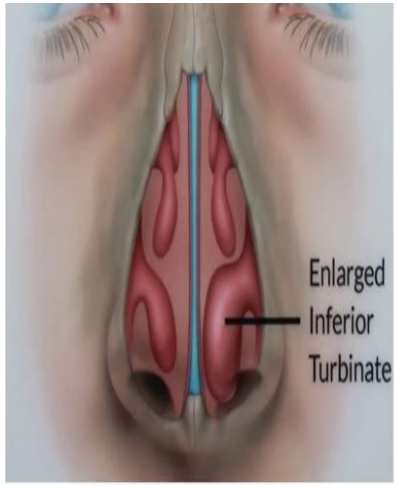


Nasal Cavity

- Nasal cavities: Separated by a septum (cartilaginous & bony) parts each consists of:
  - Nasal fossa
    - Their lateral walls contain three bony projections (conchae) superior, middle, and inferior
    - Superior one covered with Olfactory epithelium
    - Middle & inferior covered with respiratory epithelium
    - The conchae slow flow of air & increase the surface area of respiratory epithelium for conditioning of the inspired air
    - lamina propria beneath respiratory epithelium rich with superficial venous plexus (swell bodies)



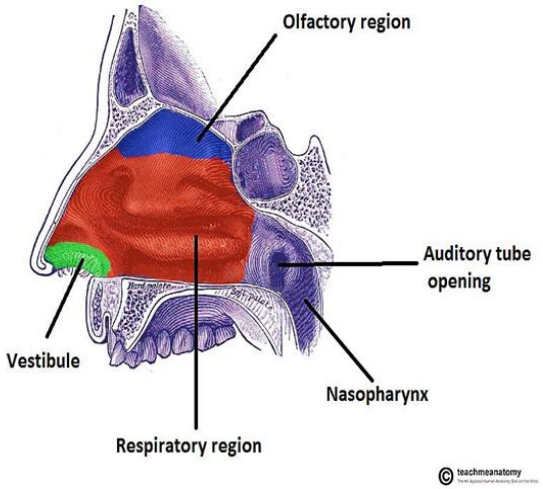




Enlarged Turbinates

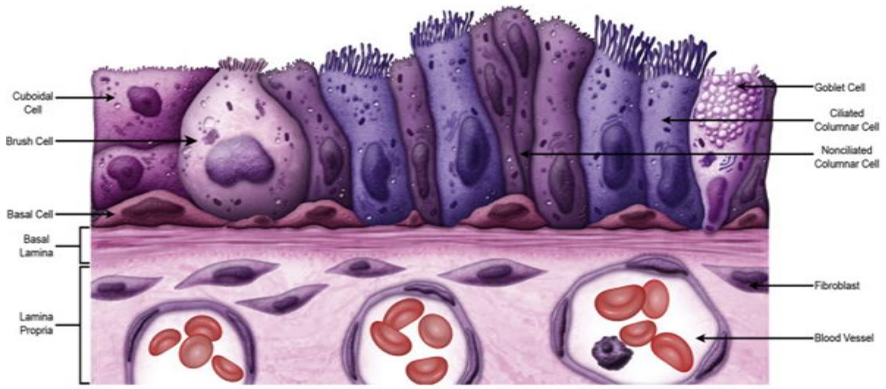
- Allergies
- Concha Bullosa

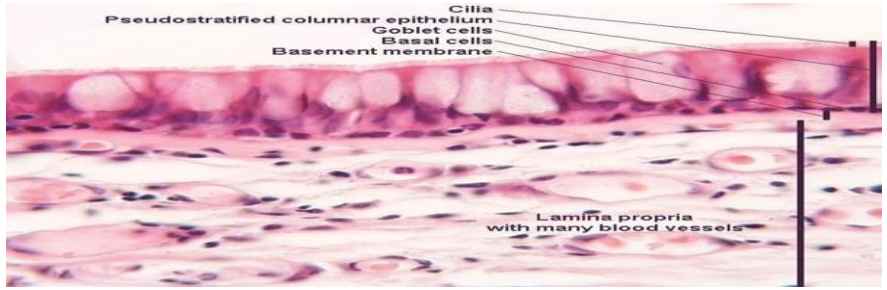
Symptoms

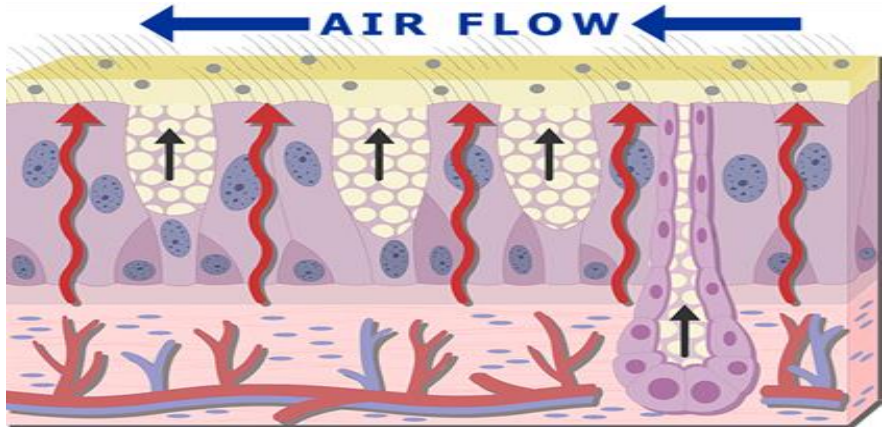


Swell Bodies

- Loops of venous plexus located in of lamina propria of the respiratory epithelium of the nasal cavities
  - Important for conditioning & warming of inhaled air → "counter current flow"
  - Due to their thin wall & proximity to the surface, nosebleed occurs so common
  - Responsible for nasal cycle
  - Allergic reactions & inflammation can cause sever engorgement of swell bodies in both fossa

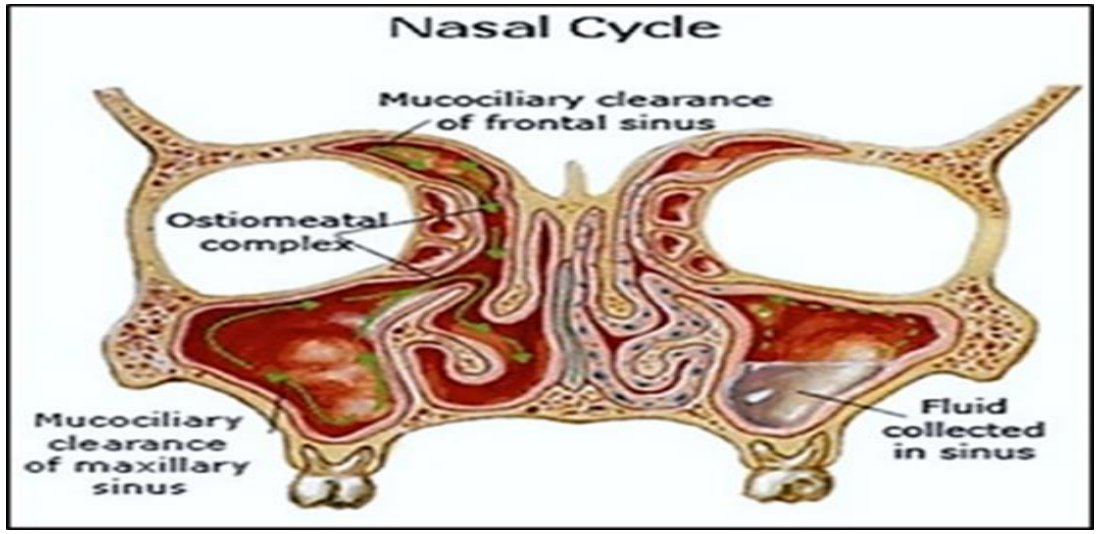


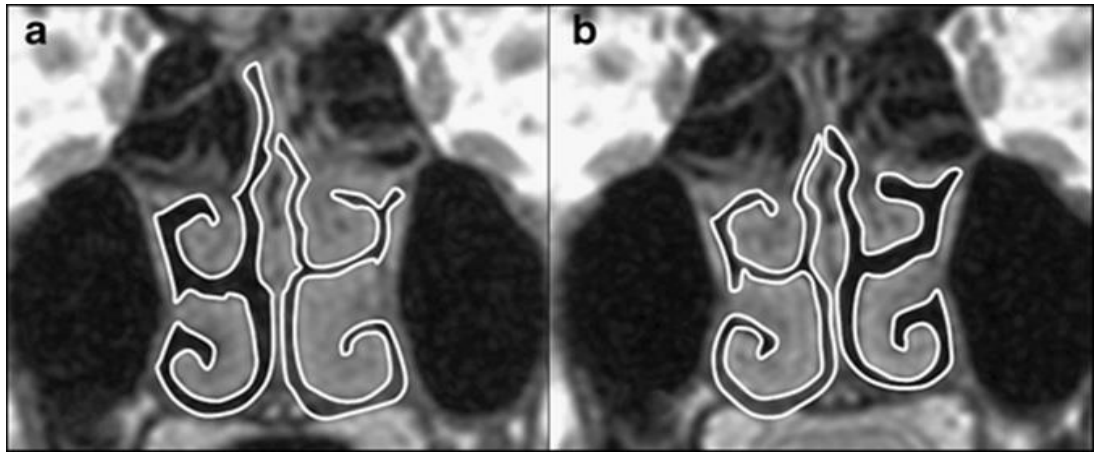




Nasal Cycle

- Every 20-30 minutes, rhythmic cycles of physiological congestion & decongestion occurs in the mucosa of the nasal cavities.
- Normally we are not aware of it
- When Swell bodies in lamina propria of one nasal cavity become engorged with blood → distention of conchal mucosa → decrease flow of air → allowing the engorged respiratory epithelium to recover from dehydration
- The cycle under the control of autonomic nervous system





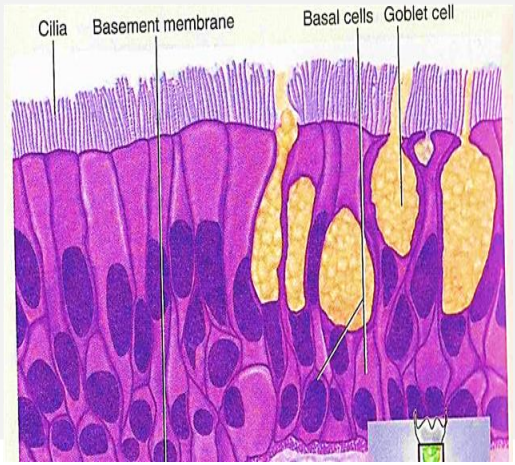
Nasal cycle using MRI imaging

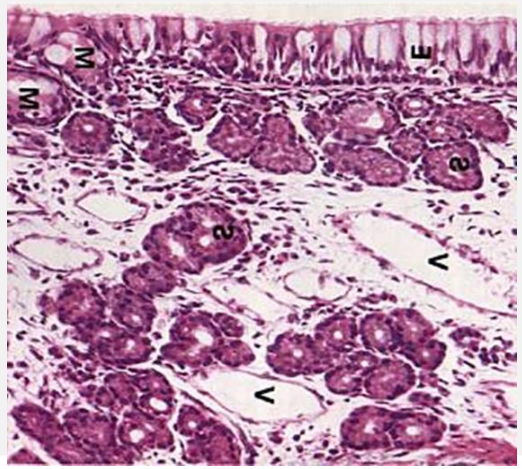
Brain Freeze

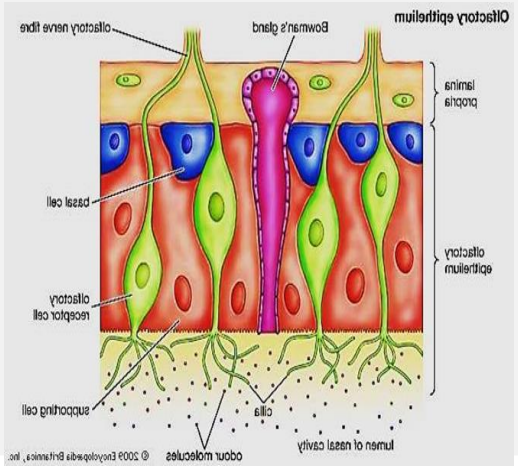
- Why eating ice-cream causing pain & headache ?
  - It is also called “Brain Freeze”, or cold neuralgia or sphenopalatine ganglio-neuroalgia
  - You experience this pain in the head or behind your eyes, it usually lasts less than five minutes
  - Happen when the cold substance like ice or ice-cream touches the palate cause drop in the temperature which subsequently cause vasoconstriction of the blood vessels which ultimately re-open up again to restore the normal temperature
  - Pain receptors near the blood vessels sense the discomfort and send the message along tiny nerve fibers to a larger nerve (the trigeminal nerve), which forwards it to the brain. The trigeminal nerve also carries pain signals from the face. The brain reads the cold-stimulus sensations as coming from the head rather than the mouth — a phenomenon called referred pain.

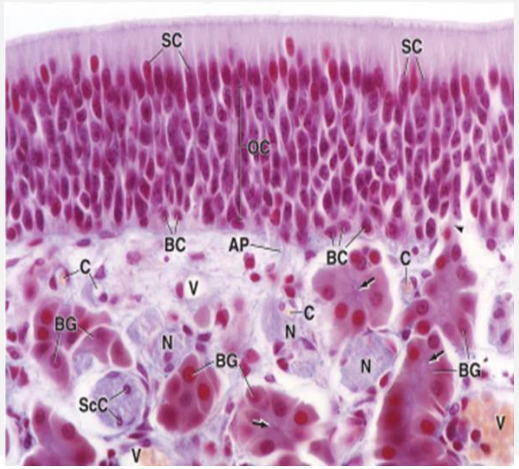
Respiratory and Olfactory Epithelium

Respiratory Epithelium	Olfactory Epithelium
Pseudostratified columnar ciliated epithelium with goblet cells	Pseudostratified columnar e chemoreceptors and No goblet cells
❖ Epithelium ❖ Lamina propria • Nasal glands (Mucous & Serous) • Blood vessels	❖ Epithelium ❖ Lamina propria • Olfactory glands (Serous only) • Blood vessels







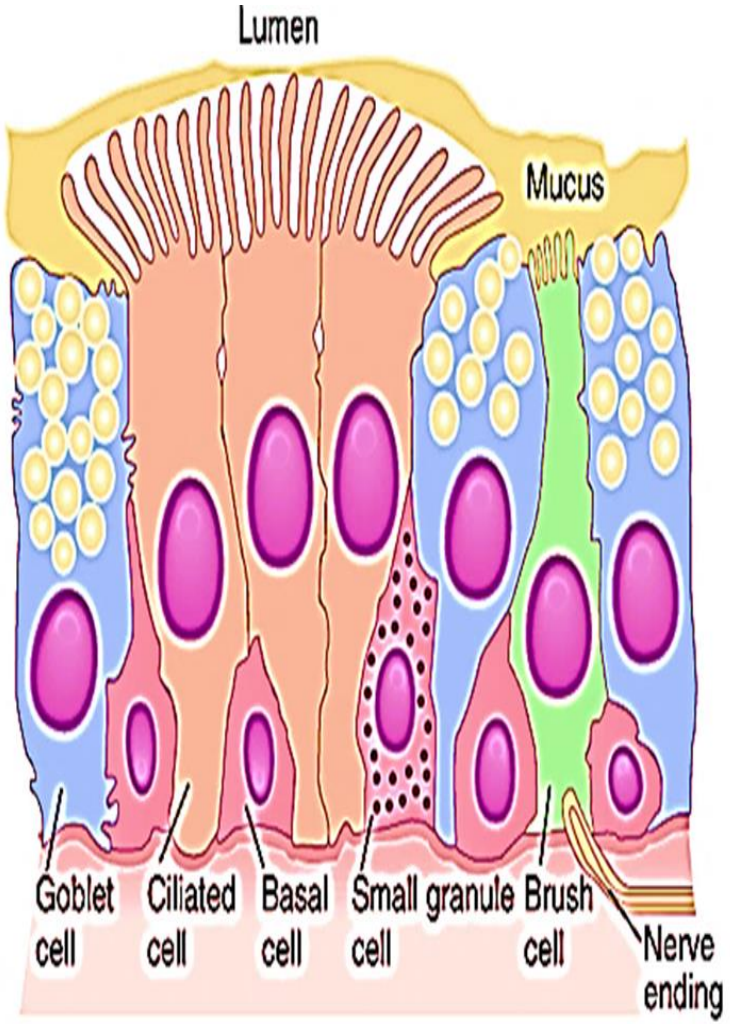


Respiratory Epithelium

- The respiratory epithelium lines most of the conducting portion
- 5 types of cells are present:
  - **Columnar ciliated cells:** most cells, have motile cilia (300) on apical surface (unidirectional beating)
  - **Goblet cells:** secrete mucus, cover surface to trap bacteria & dust
  - **Brush cells:** columnar cells e apical microvilli, have basal afferent nerve endings that communicate e trigeminal nerve 5th → give sensory information about the mucosa = (chemosensory receptors i.e. O_2 & Co_2 levels)
  - **Basal (stem) cells:** small cells, act as stem cells
  - **Granule cells** (diffuse neuroendocrine cells): have basal cytoplasmic granules, secret hormones (serotonin & catecholamine) → regulate the caliber & secretions of airways

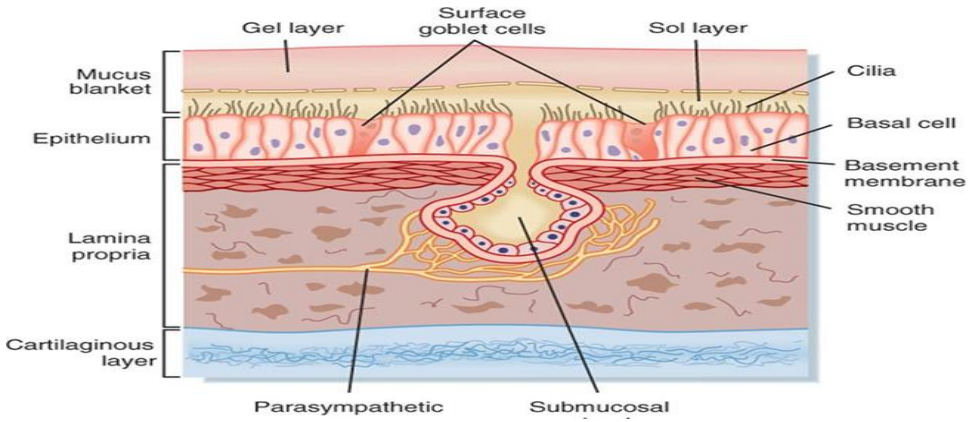
Granular cells

- During development they exert a local mitogenic effect, they influence the lengthen of the individual airway branches.
- In adult they provide local regulation of bronchial or vascular muscle tone in response to hypoxia or hypercapnia
- Serotonin is a cilio-stimulatory (i.e. increase ciliary beat frequency (CBF))
- Serotonin induces the release of Ach from columnar ciliated cells → release of Ca & ATP → ↑CBF .
- Serotonin cause increase in periciliary liquid & thus facilitate mucociliary clearance
- Serotonin induces vasoconstriction in pulmonary vasculature → role in Pulmonary hypertension

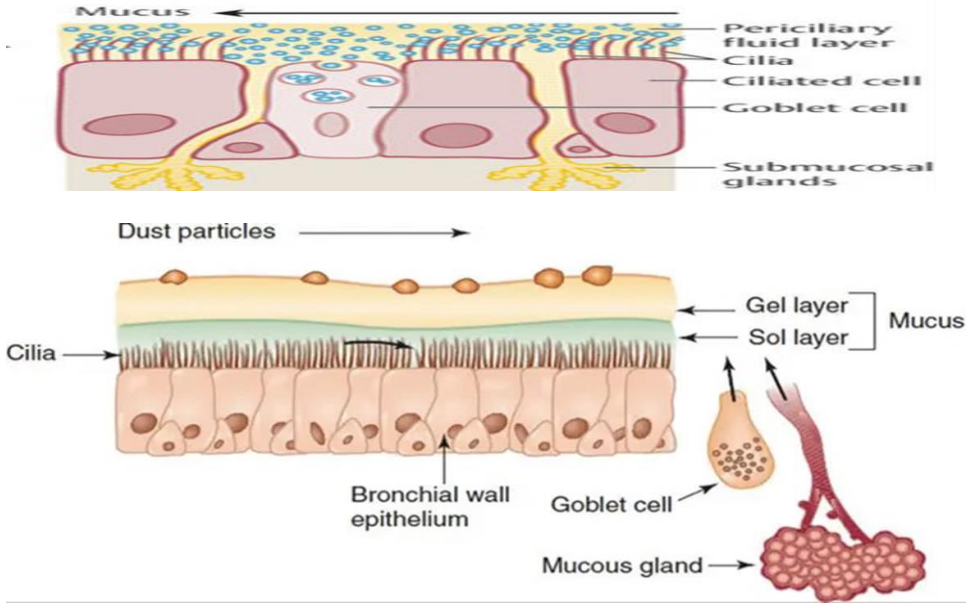


Respiratory Mucosa

- The respiratory epithelium rests on lamina propria contain many nasal glands (serous & mucus) + blood vessels + immune cells
- The serous glands secretions serve to facilitate movement of cilia
- The mucous glands secretions serve to catch inhaled dirt & bacteria particles inhaled & prevent dryness of RS mucosa
- Both secretions form the mucous blanket
  - The Gel layer is mucous, and the Sol layer (peri-ciliary) is liquid
  - In cystic fibrosis disease this mucus become dehydrated, thick & sticky that the cilia become unable to propel the mucus out of the lung



Mucociliary Escalator

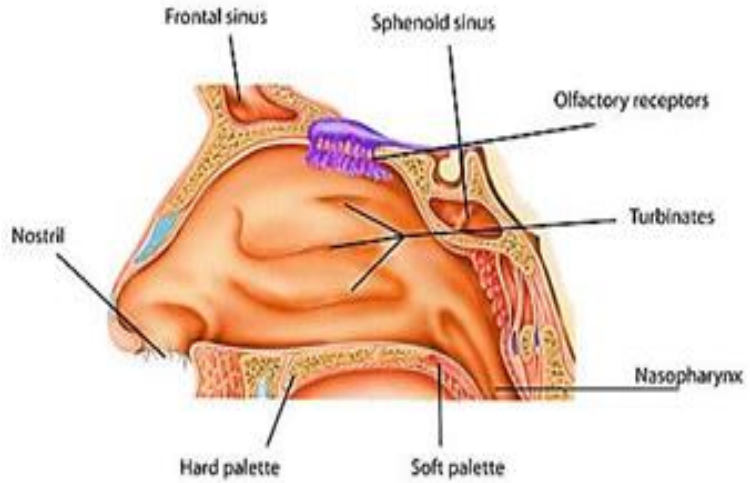


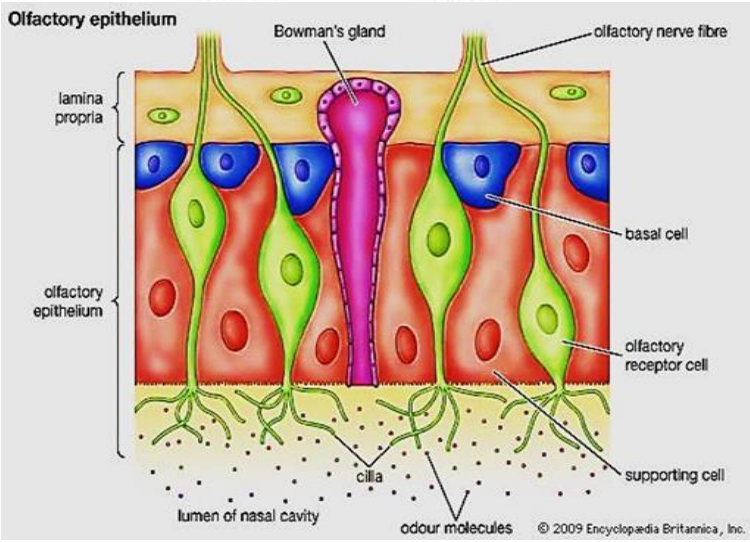
Respiratory Mucosa

- Lamina propria contains many immune cells (e.g. mast cells, plasma cells & lymphoid nodules) as part of mucosa associated lymphoid follicles (MALT) to protect the RS from the microbes inhaled with air (explains the allergic reactions in upper respirator tract)
- The blood vessels serve to warm the inspired air (humidity of the lung can be maintained)
  - Mechanism is called counter-current exchange
- In smokers the proportion of ciliated cells to goblet cells is altered (increase goblets) to trap gaseous pollutants

Olfactory Epithelium

- The olfactory epithelium covers the roof of nasal cavities & superior conchae.
- Contains chemoreceptors of smell
- 3 types of cells are present:
  - Olfactory neurons
  - Supporting (sustentacular) cells
  - Basal cells
- The olfactory epithelium rests on lamina propria contains:
  - Blood vessels and olfactory nerve fibers
  - Bowman's glands secrete constant flow of serous fluid → surface → facilitate dissolve of odoriferous substance

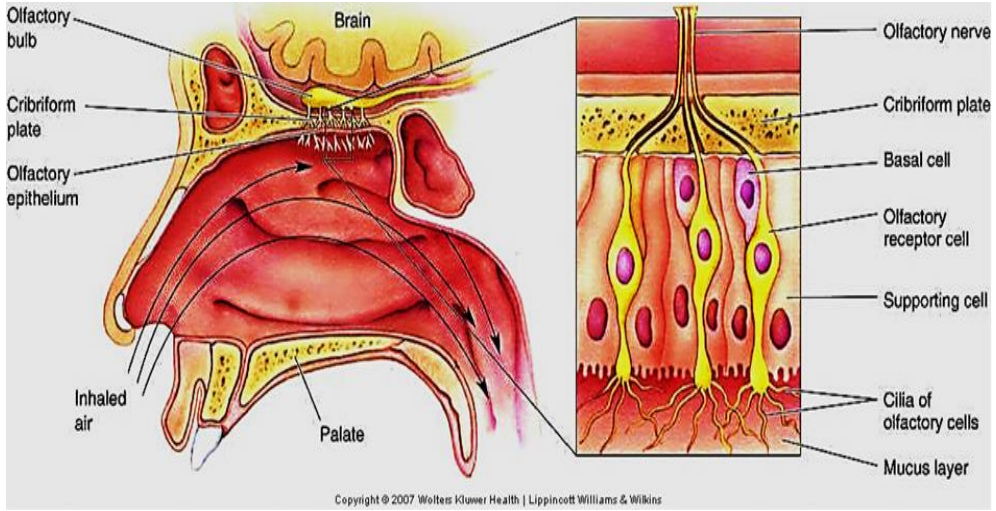


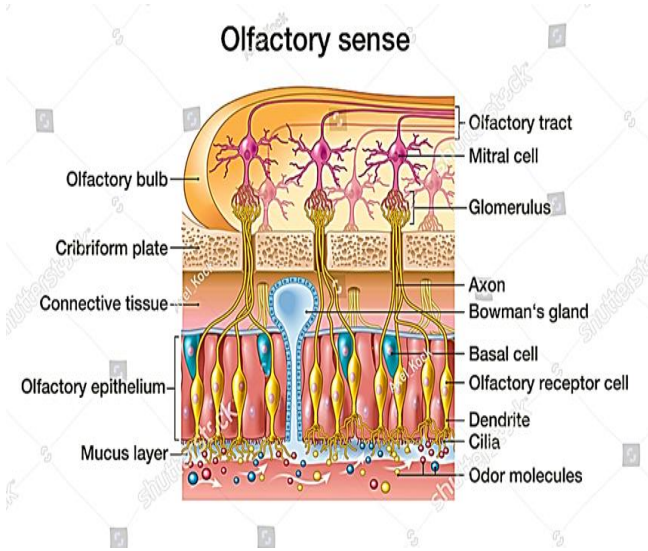


Olfactory Epithelium

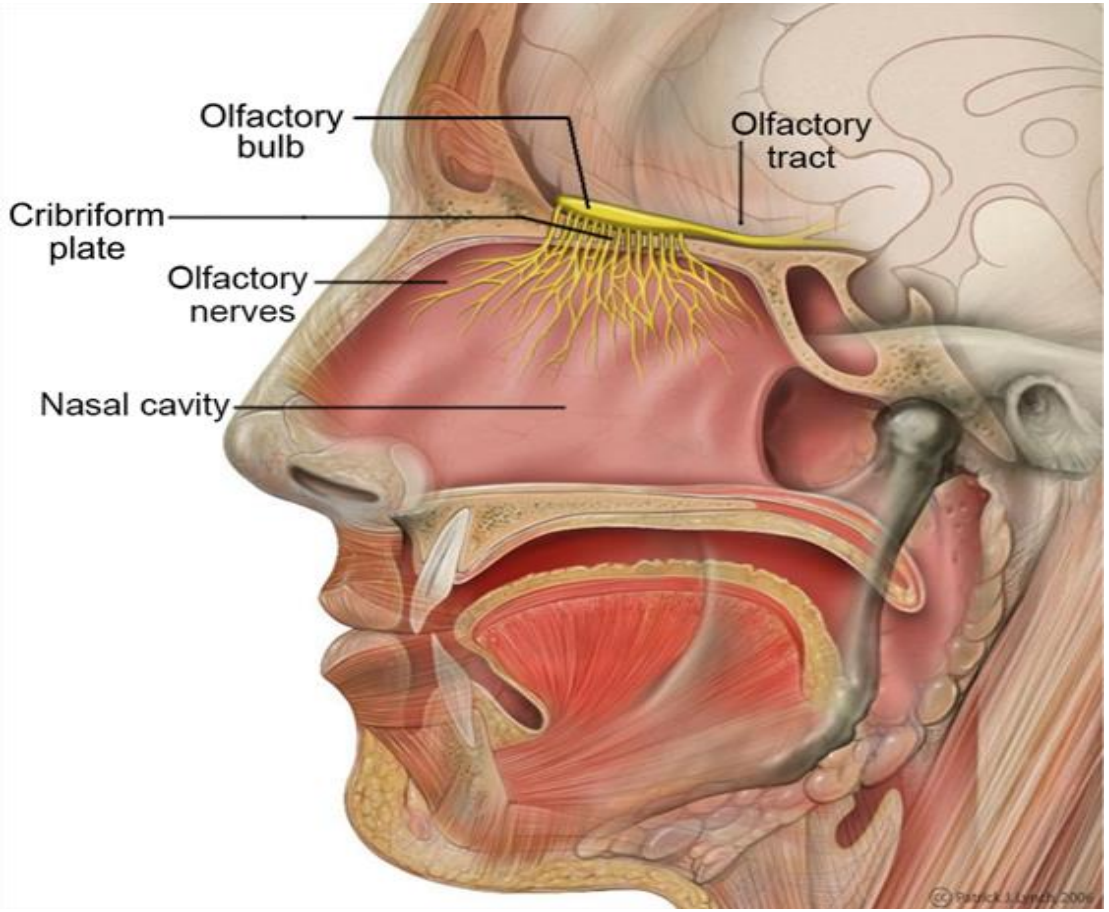
❖Olfactory Neurons

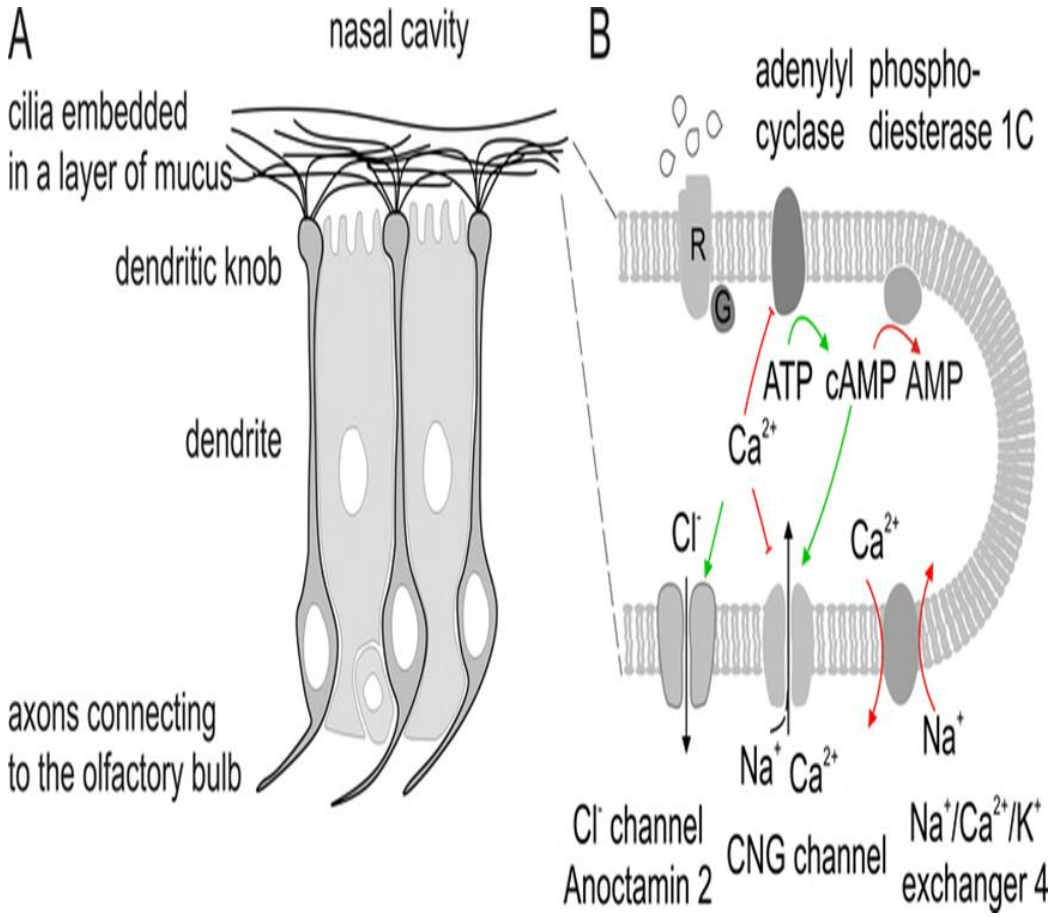
- Bipolar nerve cells (renew 30- 60 days)
  - regenerative neuronal tissue!
- Their dendrites extend toward surface → end in swellings (olfactory vesicles) from which cilia arise
- These cilia (10-20) are very long & non motile.
  - It provides large surface for transmembrane chemoreceptors
- Their axons pass to lamina propria to form olfactory nerve fibers





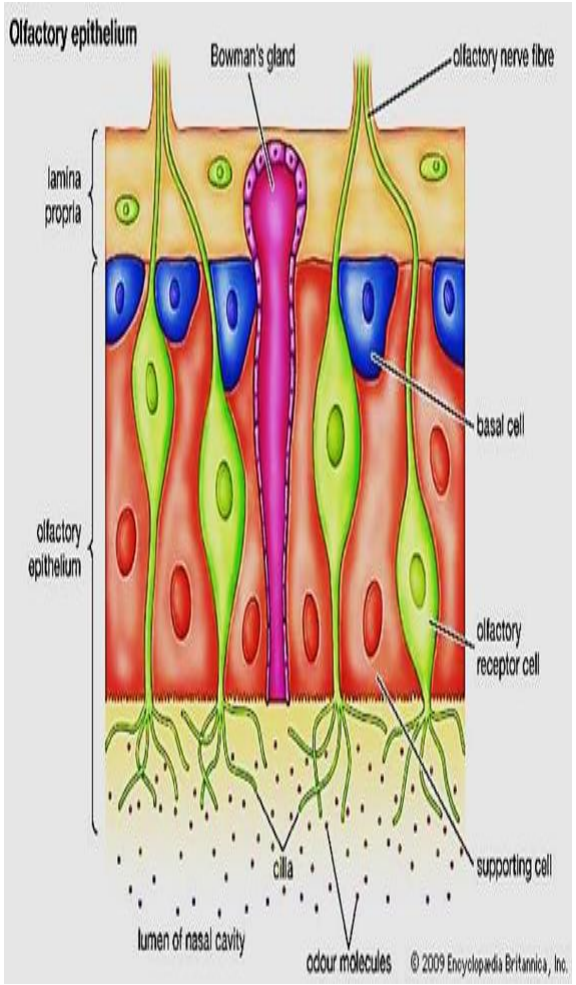
Schematic illustration of the of the olfactory epithelium with olfactory receptors





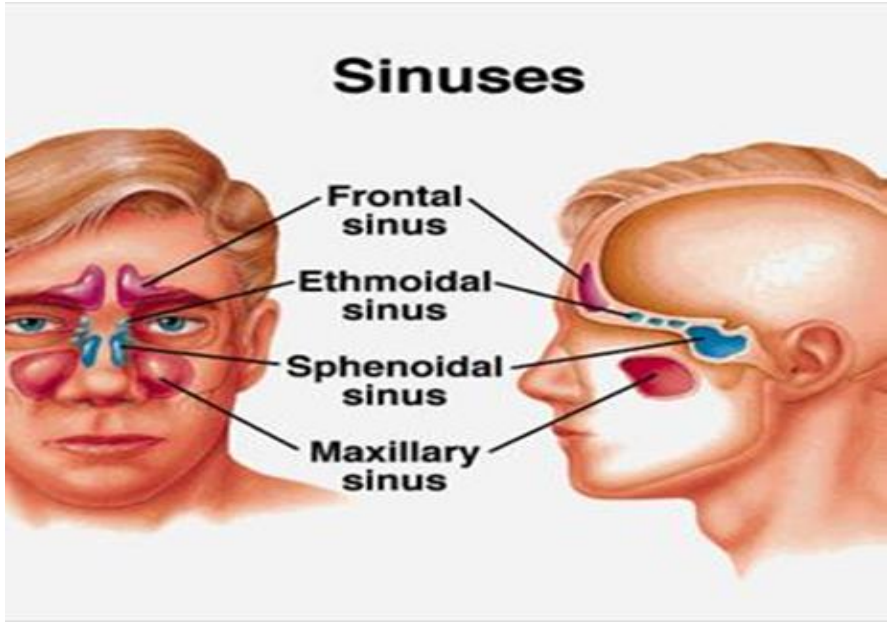
Olfactory Epithelium

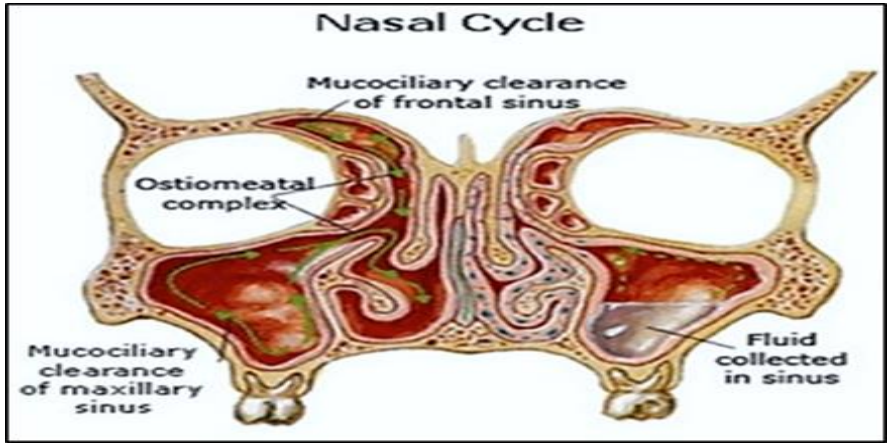
- **Supporting cells (neuroglia)**
  - Tall columnar cells with wide apex and narrow base
  - Their free surface has microvilli
  - Tight junctions bind these cells with olfactory cells.
  - They secrete odorant binding proteins & express abundant ion channels → role in signal conduction of smell sensation .
  - These cells play role in smell loss (anosmia) in COVID 19
- **Basal cells**
  - Small pyramidal cells with basophilic cytoplasm
  - Act as stem cells for both olfactory & supporting cells



Paranasal Sinuses

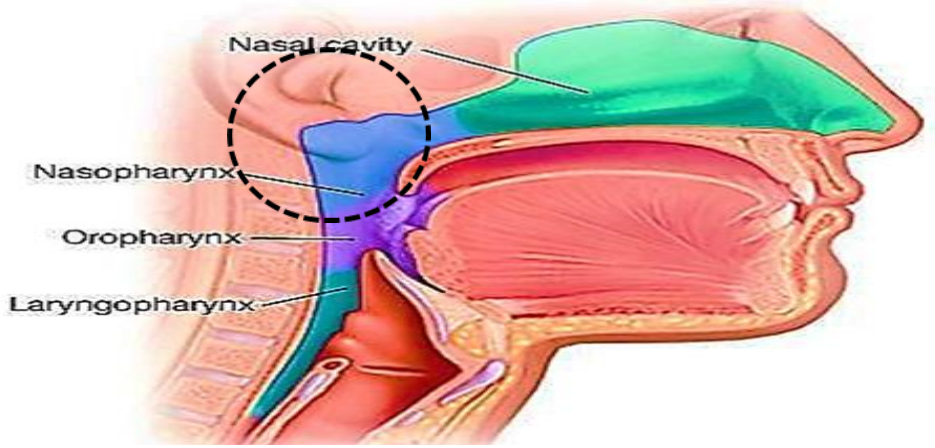
- Bilateral frontal, ethmoidal, sphenoidal, and maxillary
- These cavities open in nasal cavities
- Lined with thin respiratory epithelium with few goblet cells
- Chronic sinusitis = immotile cilia syndrome

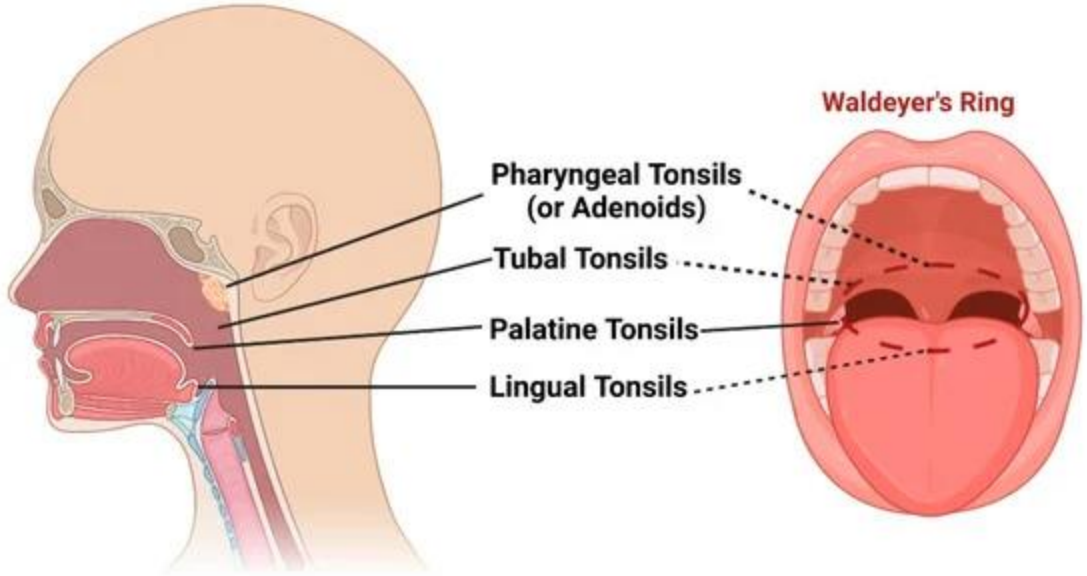


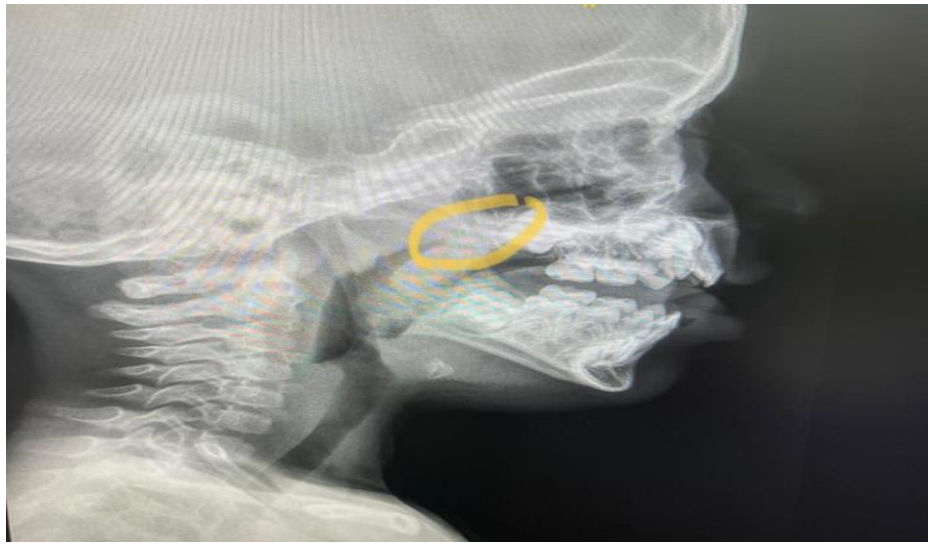


Nasopharynx

- Lined with respiratory epithelium
- Its lamina propria contains:
  - Pharyngeal tonsil
  - Openings of Eustachian tubes



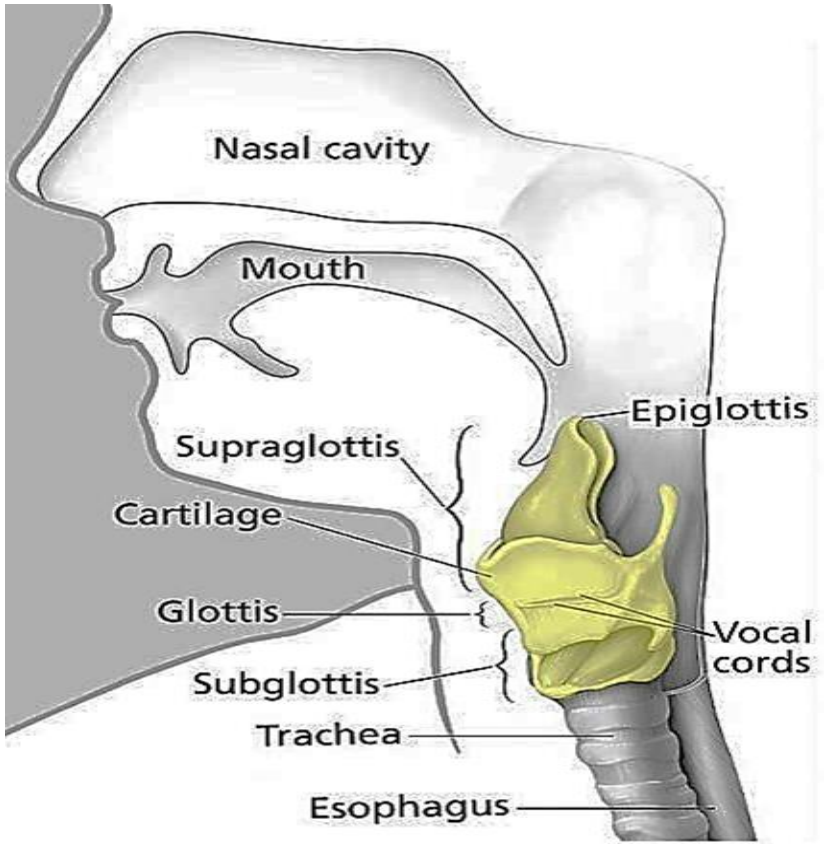




Enlarged pharyngeal tonsil = adenoids

Larynx

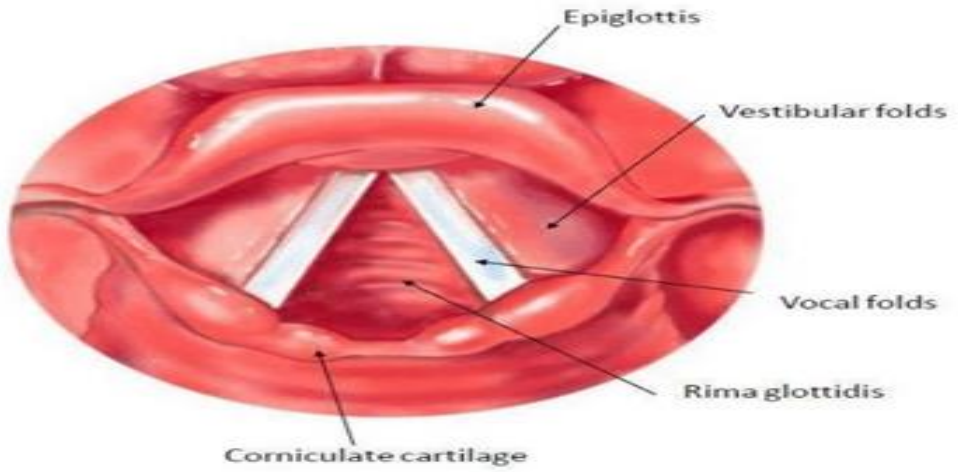
- At the beginning of trachea (4x4cm)
- Its beginning is guarded by epiglottis
- Has 2 functions:
  - production of voice via vocal cords
  - Prevent food & fluid from entering the trachea through the epiglottis which has elastic cartilage
- It is lined with respiratory epithelium

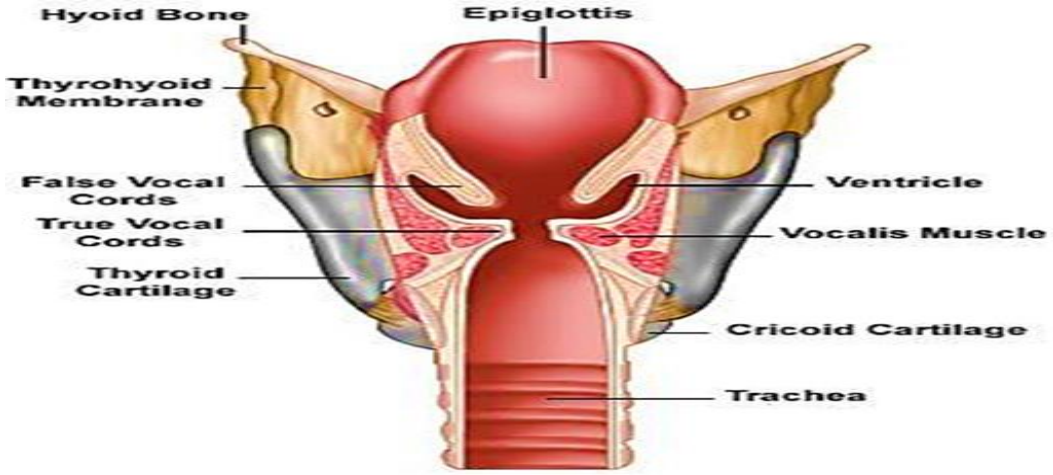


Vocal Cords

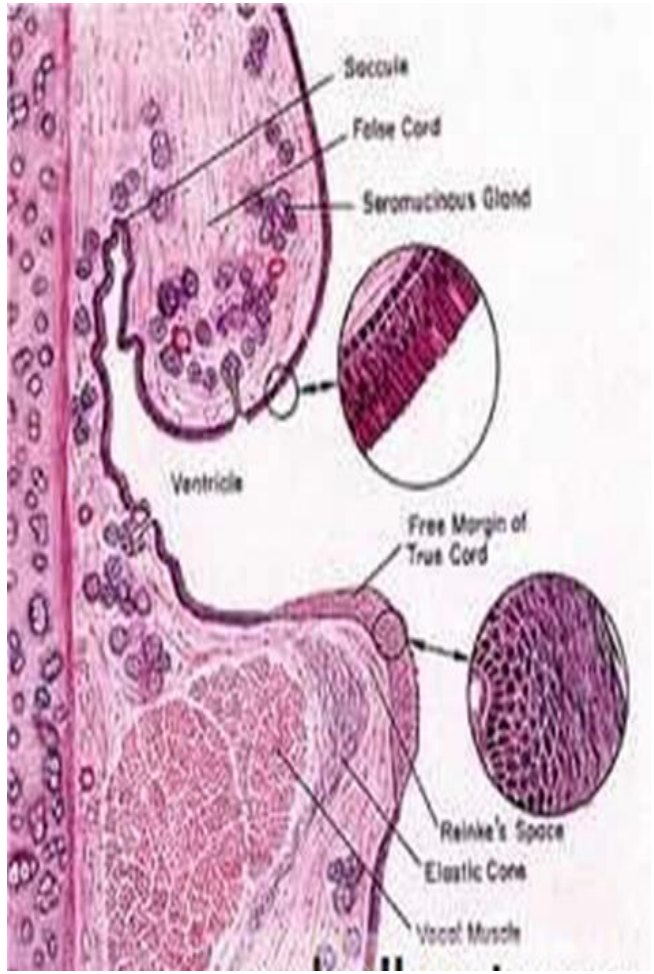
❖Two pairs of mucosal folds extend in lumen of larynx

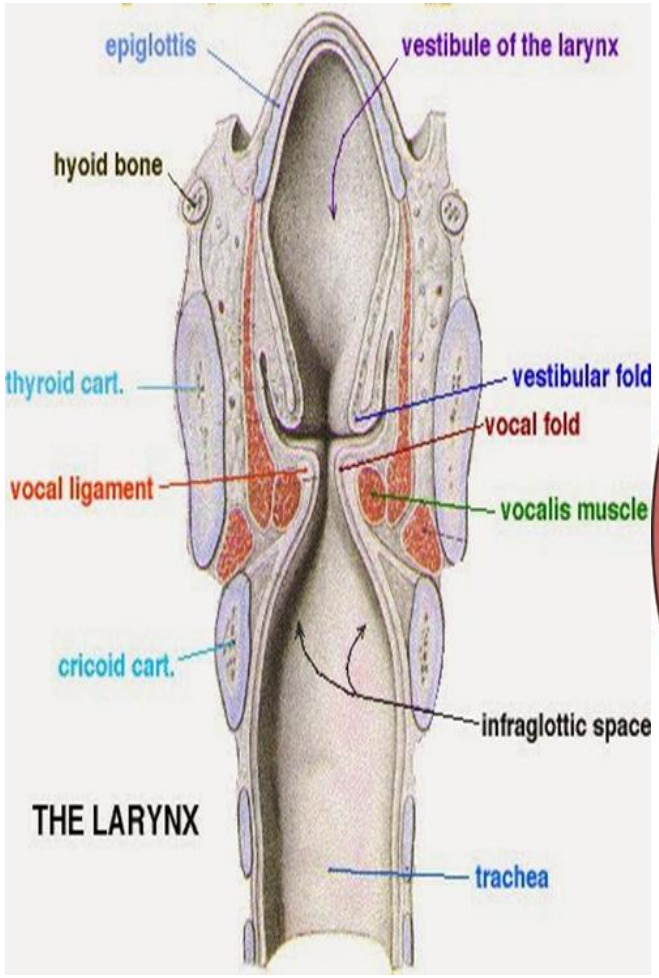
False Vocal Cords (upper pairs)	True Vocal Cords (lower pairs)
covered with respiratory epithelium	Covered with non-keratinized stratified squamous epithelium
Called vestibular folds (made of vestibular ligament)	Made of ligaments (vocal ligaments) & skeletal muscles (Vocalis muscle)
Guard against entrance of food into larynx	Tension of cords & distance between them produce sound

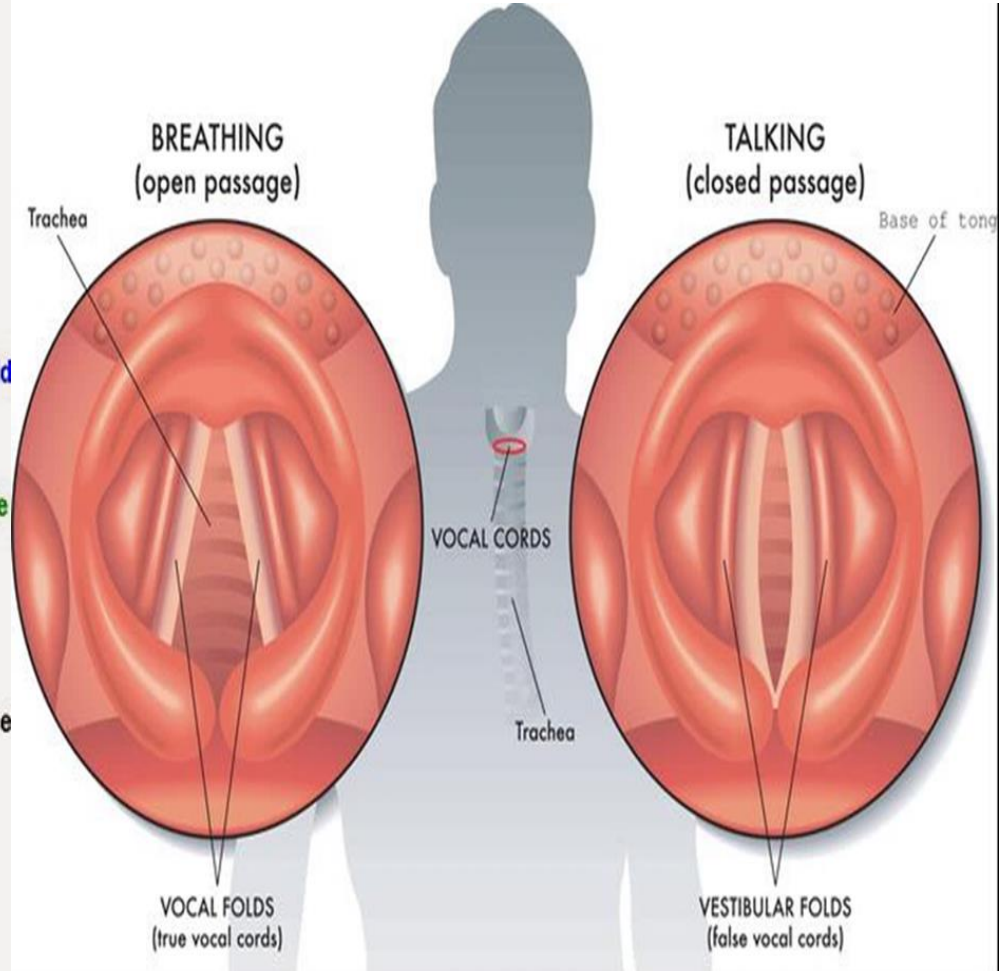




True and false vocal cords and the importance of the ventricle

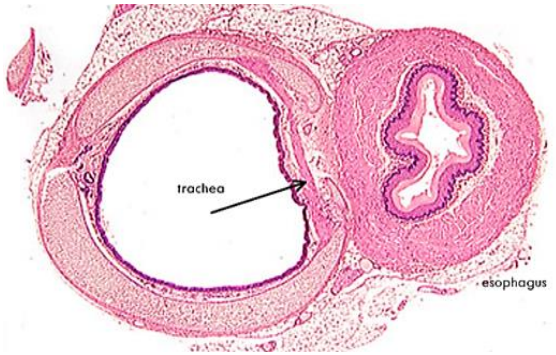


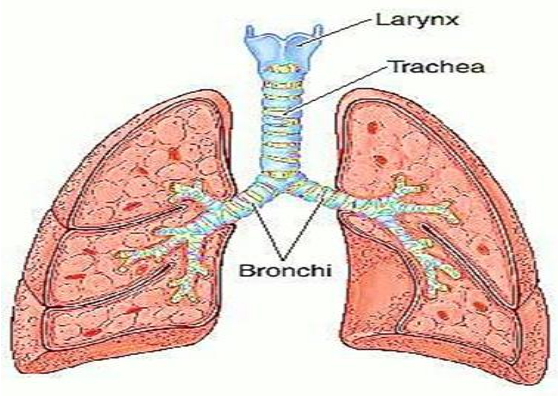


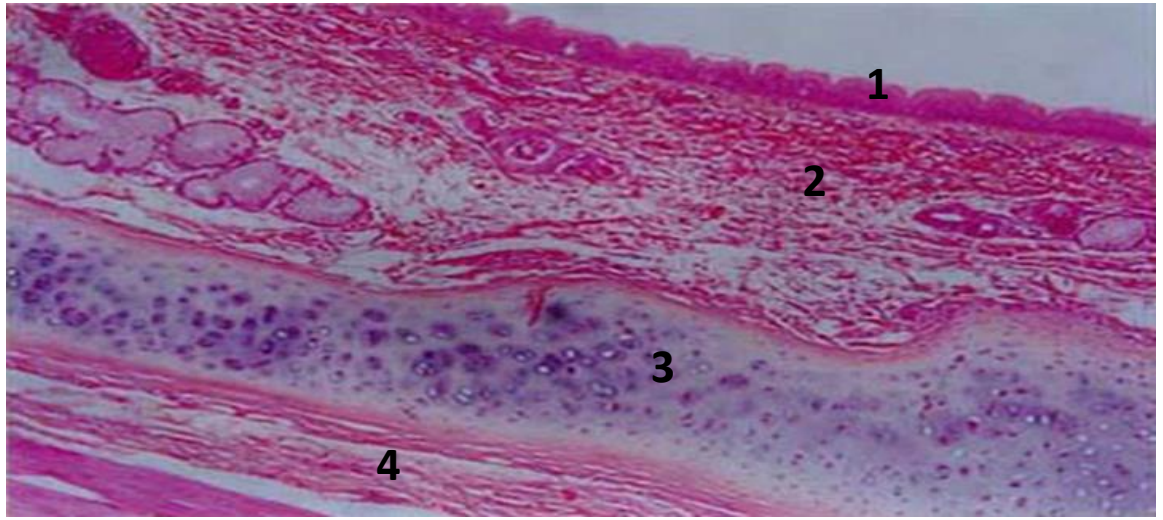


Trachea

- Tube (12- 14 cm) extends from larynx to bifurcation of bronchi
- Kept open by about 20 C-shaped (horse shoe) cartilage rings (hyaline cartilage)
- Its wall is formed of 4 layers:
  1. Mucosa
  2. Submucosa
  3. Hyaline cartilage
  4. Adventitia

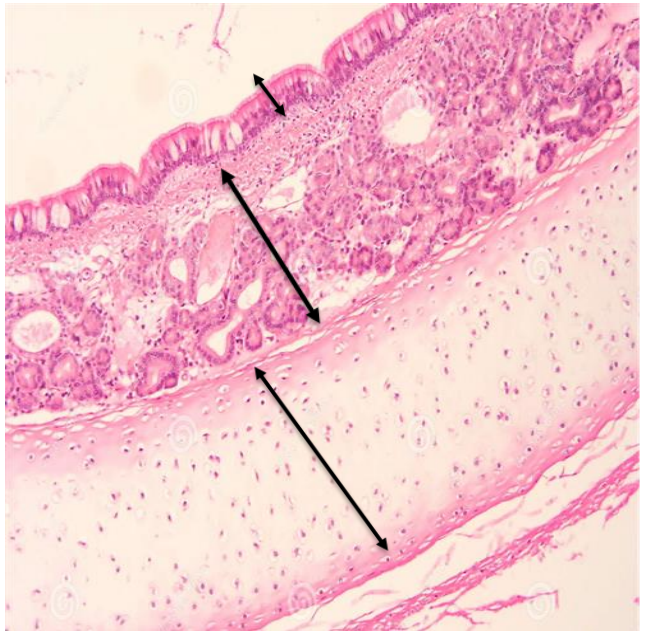


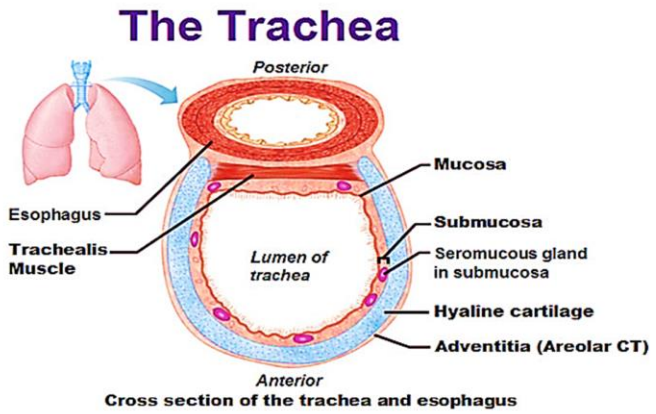




Trachea

- Wall of trachea:
  - **Mucosa:** epithelium – lamina propria – elastic fibers
    - Epithelium: respiratory epithelium
  - **Submucosa:** loose connective tissue, blood vessels, nerves, lymphoid nodules, tracheal glands
  - **Cartilage layer:** C- shaped cartilage rings, the gap between cartilage ends connected by elastic ligament & trachealis muscle (smooth muscle)
    - Contraction of the trachealis muscle is important for the Cough Reflex
    - Contraction → narrowing the tracheal lumen → increase the velocity of the expelled air → squeezed out → cough
  - **Adventitia:** loose connective tissue

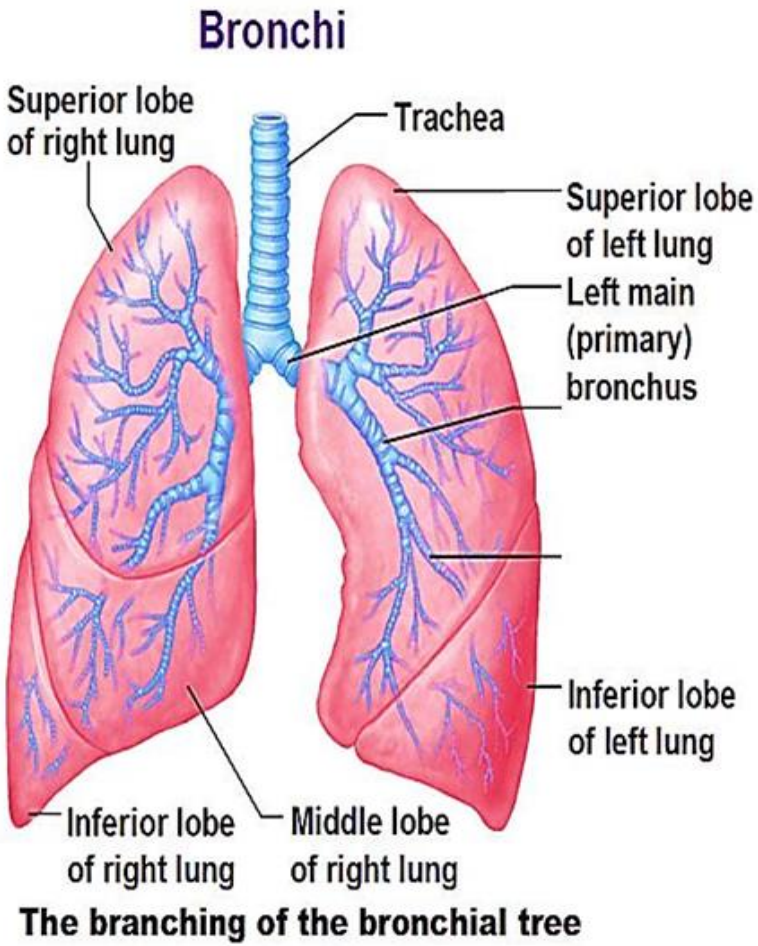




Cross section of the trachea and esophagus

Bronchial Tree

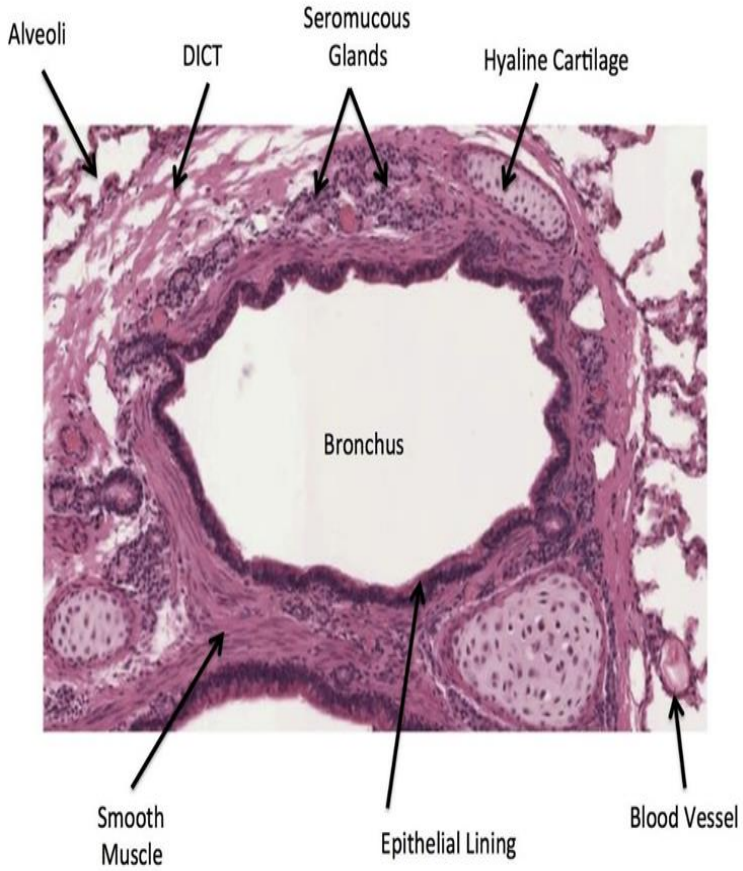
- Primary (Extra pulmonary) bronchi
  - RT & LF→ similar to trachea (but cartilage is a complete ring)
- Secondary (Intra-pulmonary) bronchi
  - within the lung → divide into 3ry bronchi
  - Its wall is formed of 4 layers (No submucosa):
    - Mucosa
    - Musculosa
    - Cartilage plates (isolated plates)
    - Adventitia
- Bronchioles
- Terminal bronchioles



The branching of the bronchial tree

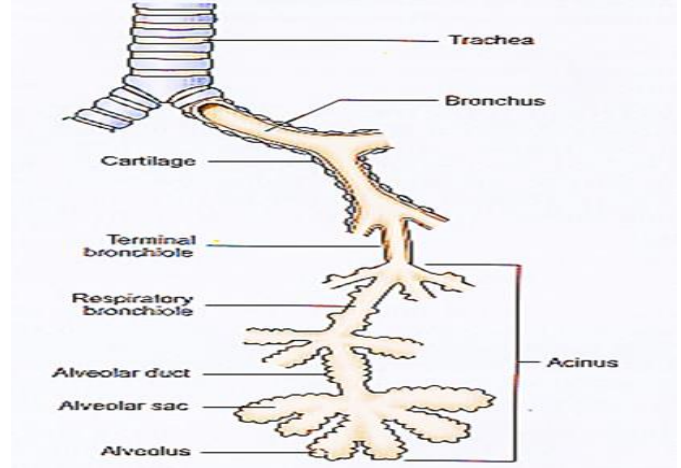
Bronchial Tree

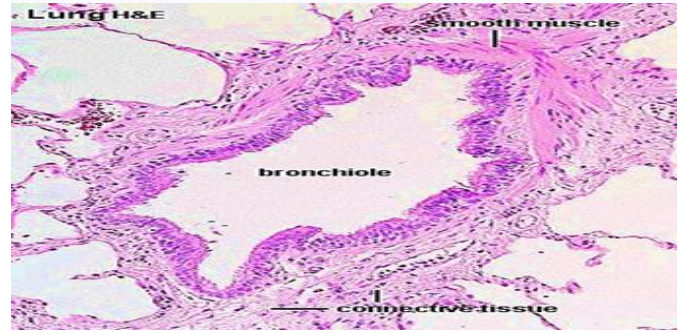
- Wall of secondary bronchi:
  - **Mucosa:**
    - Increase folded, respiratory epithelium, decrease goblet cells, lamina propria has elastic fibers & MALT (mucosa associated lymphatic tissue)
  - **Musculosa:**
    - Spiral layers of smooth muscles encircling the mucosa
  - **Cartilage plates:**
    - Muco-serous glands & lymph nodules found between cartilage plates
  - **Adventitia**

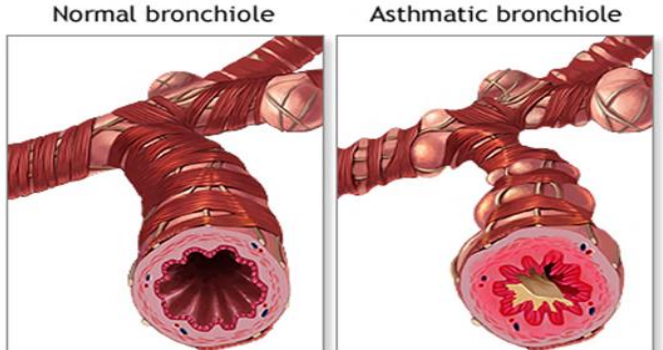


Bronchial Tree

- Bronchioles:
  - Small airways ≤5 mm
  - Its wall has (No submucosa, No cartilage, No glands, No lymphatic nodules)
  - Its wall formed of 3 layers
    - **Mucosa:** simple columnar ciliated epithelium with Clara cells, neuroendocrine cells, & neuroepithelial bodies (chemosensory receptors → O_2 level)
    - **Musculosa:** complete layer of circularly arranged smooth muscle (Asthma attacks)
    - **Adventitia**

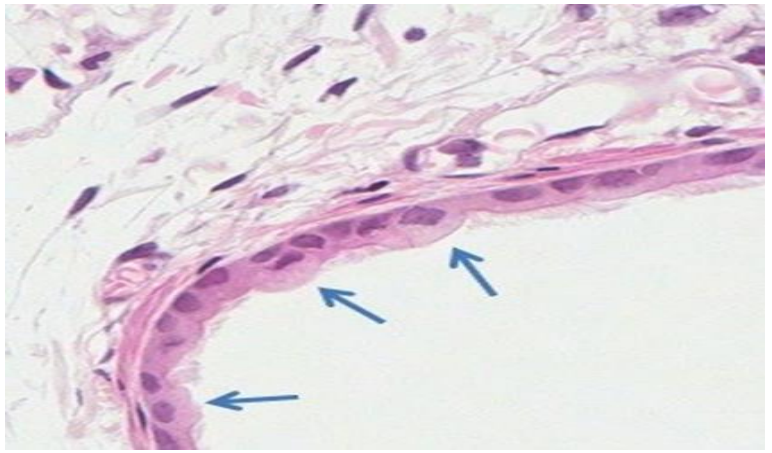






Bronchial Tree

- **Clara cells** (Also called club cells or bronchiolar exocrine cells):
  - Dome- shaped, non- ciliated,
  - Cytoplasm has lots of secretory granules (not mucus) basal rough ER, apical smooth ER
  - Function:
    - Defensive role: glycoprotein granules (contain proteolase, oxidase & cytokines)
    - Degradation of inhaled toxins (smooth ER)
    - Secretion of surfactant-like substance to prevent collapse of bronchioles
    - Act as stem cells
  - Mutation → adenocarcinoma of lung



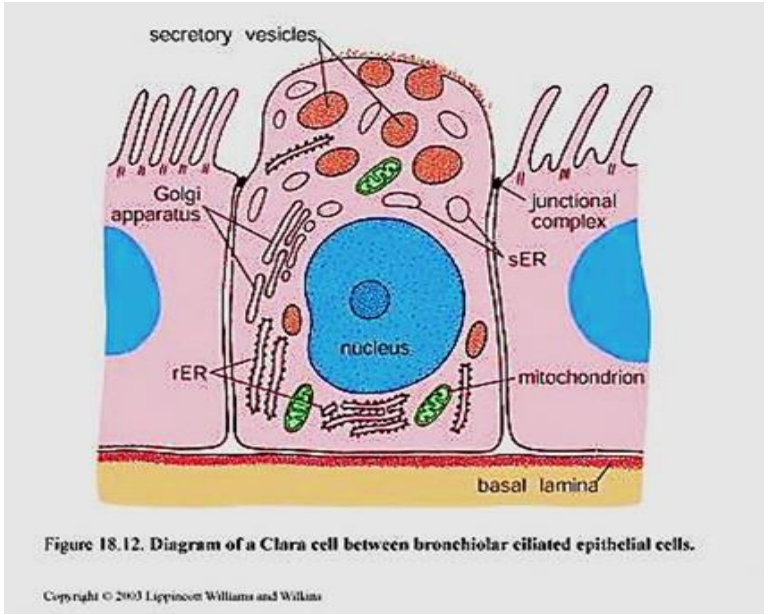
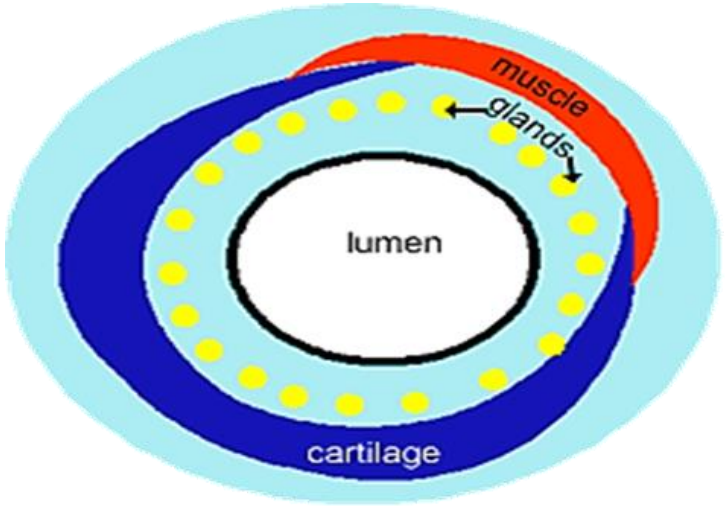
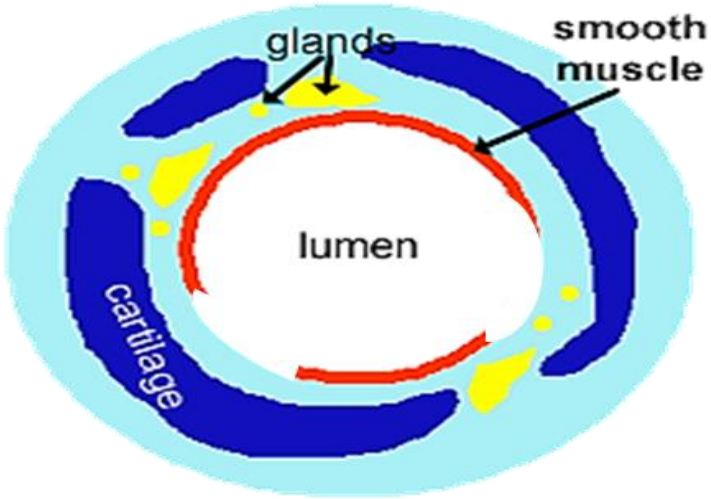


Figure 18.12. Diagram of a Clara cell between bronchiolar ciliated epithelial cells.

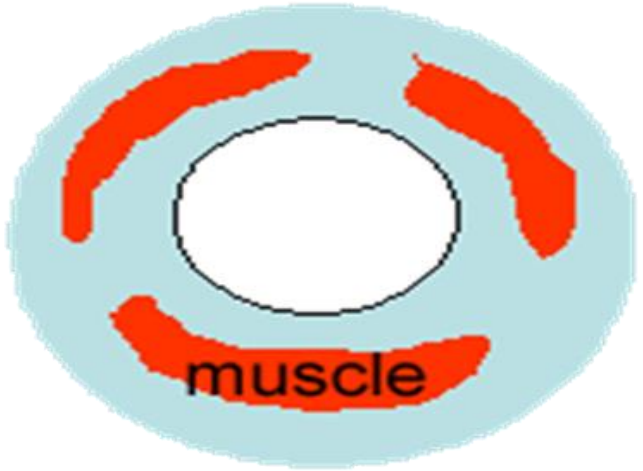
Differences between Trachea, Bronchi , and Bronchioles



Trachea



Intra pulmonary bronchus



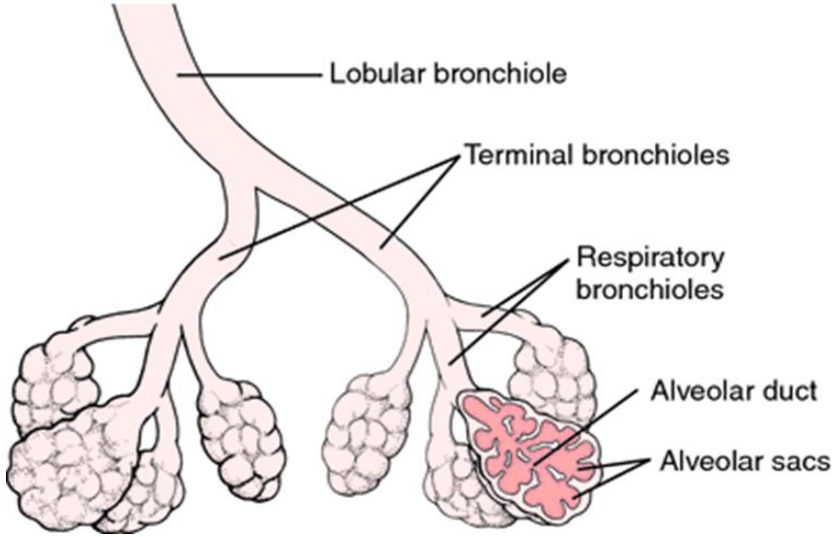
Bronchiole

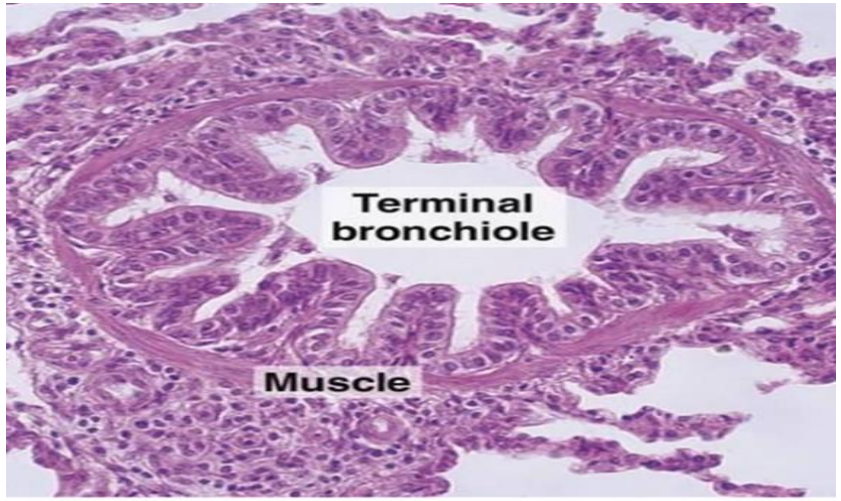
N.B. Smooth muscle component increases in proportion and continuity as the air passage decreases in size. Then decrease again till disappear in the respiratory portion

N.B. If cartilage is present, it is a "bronchus“, but if cartilage is absent the airway is a "bronchiole“.

Bronchial Tree

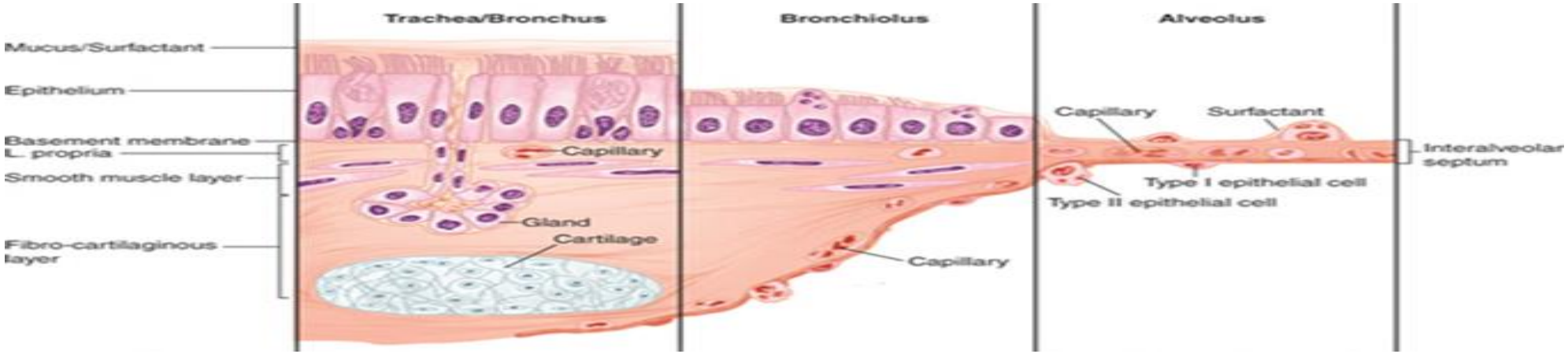
- Terminal Bronchioles:
  - The smallest & last part of conducting portion
  - Lining epithelium: Simple cubical ciliated with Clara cells
  - **Secondary pulmonary lobule:**
    - Is the lobule supplied by a terminal bronchiole that branches into respiratory bronchioles.





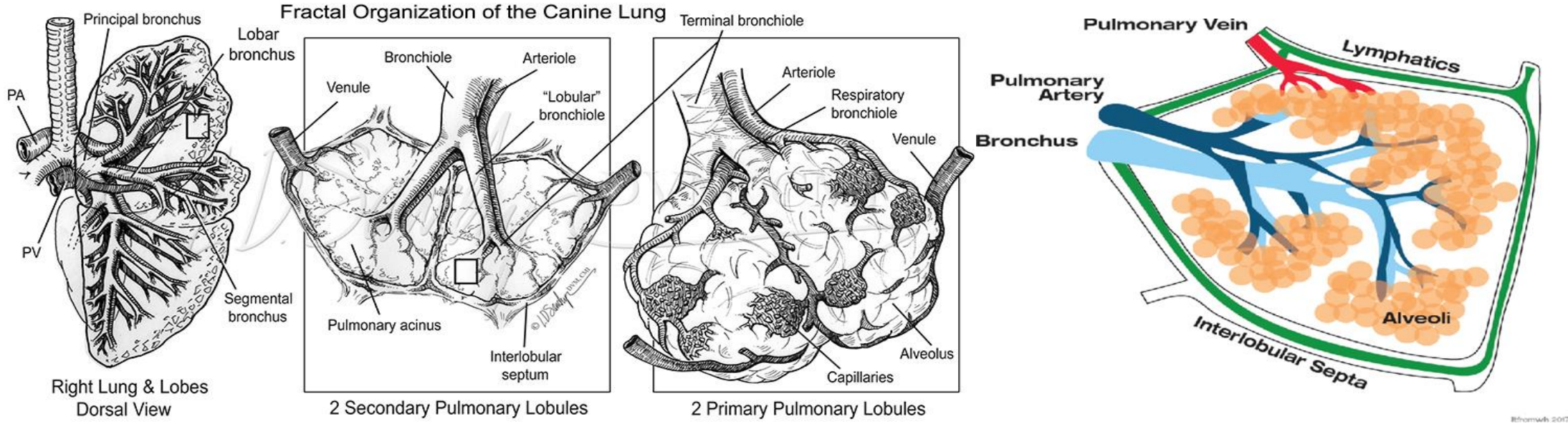
Histological changes across the conducting portion

- Bronchial tree can be as small as 0.5 mm diameter and as they get smaller some changes occur.
- First, the glands disappear, then goblet cells.
- There is also an epithelial transition from the pseudostratified RE to simple columnar, then to a low cuboidal type.
- Along the way ciliation disappears.
  - Why secretion ends before ciliation does?



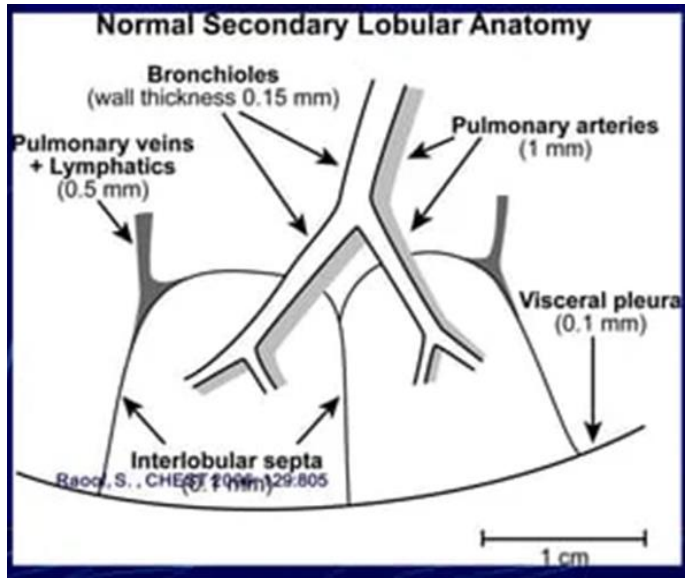
Pulmonary Lobules vs. Pulmonary Acinus

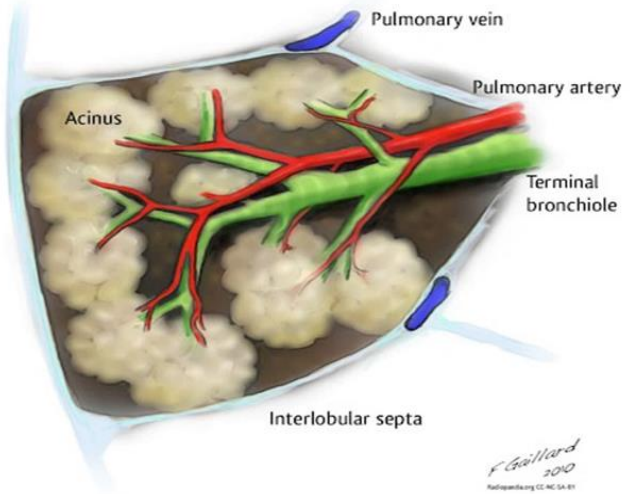
Primary Pulmonary Lobule	Secondary Pulmonary Lobule	Pulmonary Acinus
Smaller than acinus, includes lung unit distal to respiratory bronchioles, alveolar ducts, sacs ,and alveoli	Bigger, lung unit supplied by 3-5 terminal bronchioles, derived from single bronchus & surrounded by connective tissue (3- 12 acini & 30- 50 primary pulmonary lobule)	Lung unit distal to single terminal bronchiole includes respiratory bronchioles, alveolar ducts, sacs, and alveoli

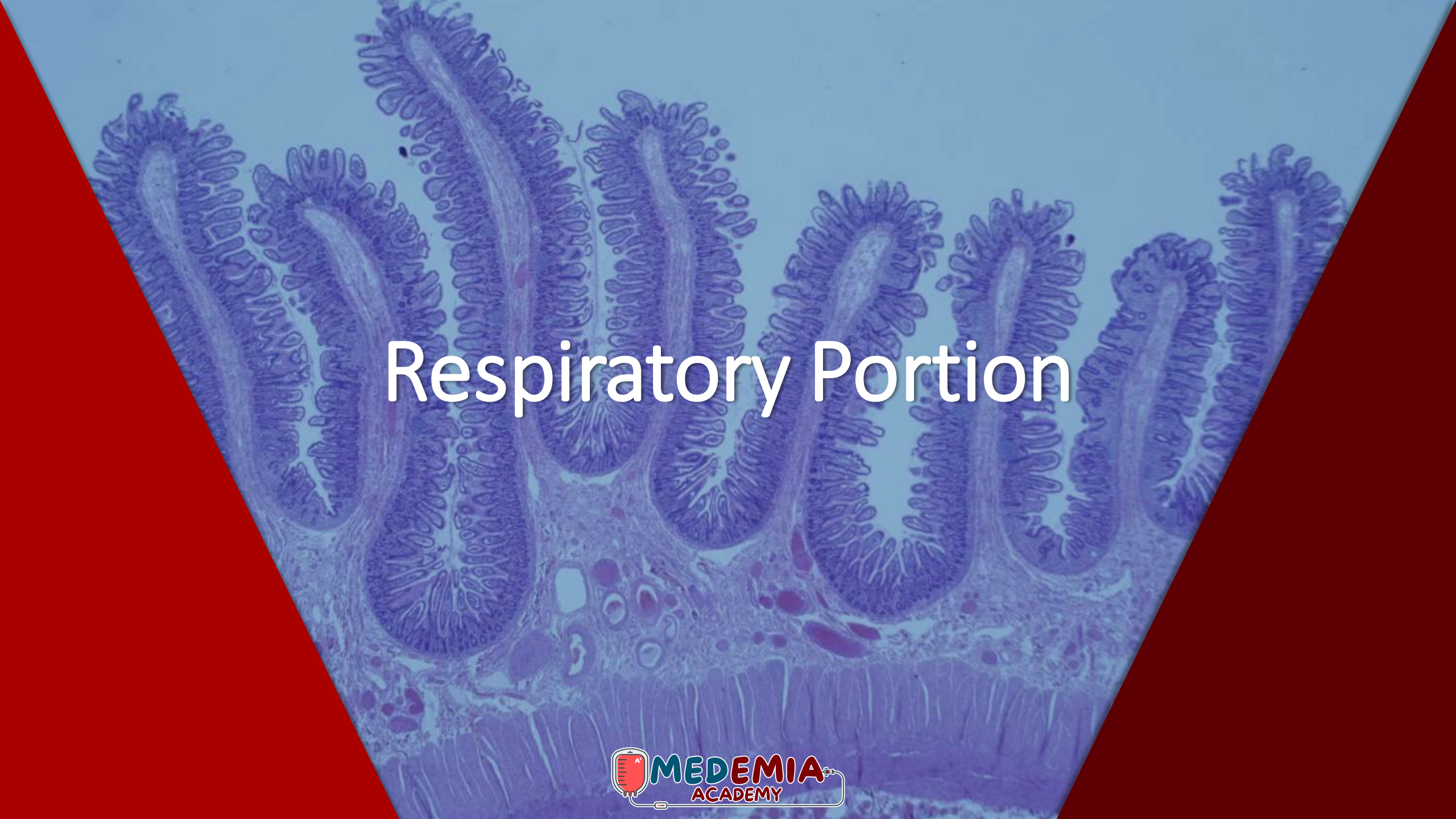


Secondary Pulmonary Lobules

- The secondary pulmonary lobule is a fundamental unit of lung structure, and it represents the lung in miniature. Airways, pulmonary arteries, veins, lymphatics, and the lung interstitium are all represented at the level of the secondary lobule. Several of these components of the secondary lobule are normally visible on thin-section computed tomographic (CT) scans of the lung. The recognition of lung abnormalities relative to the structures of the secondary lobule is fundamental to the interpretation of thin-section CT scans. Pathologic alterations in secondary lobular anatomy visible on thin-section CT scans include interlobular septal thickening and diseases with peripheral lobular distribution, centrilobular abnormalities, and panlobular abnormalities. The differential diagnosis of lobular abnormalities is based on comparisons between lobular anatomy and lung pathology.





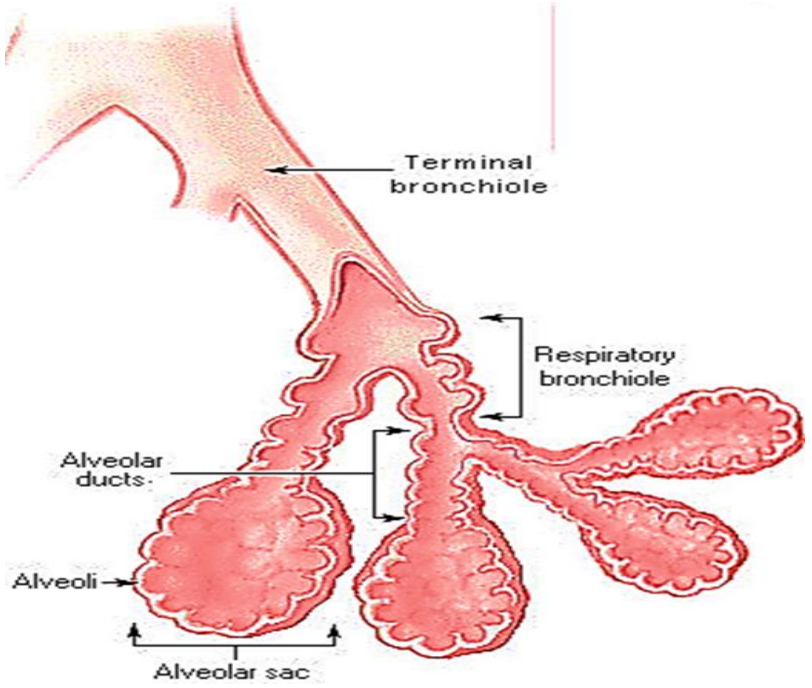


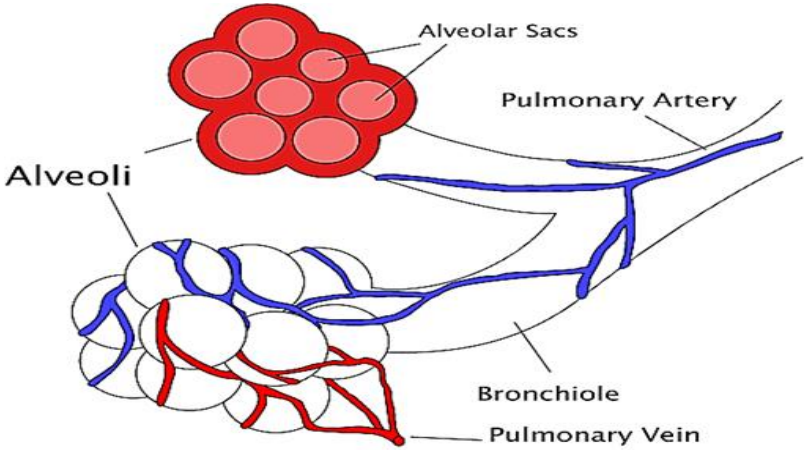
Respiratory Portion

MEDEMIA ACADEMY

Respiratory Portion

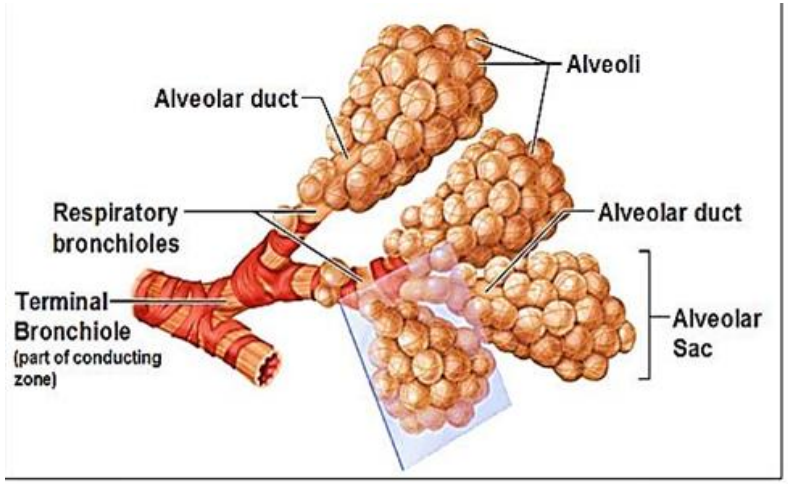
- Is where gas exchange takes place
- Includes:
  - Respiratory bronchioles
  - Alveolar ducts
  - Alveolar sacs
  - Alveoli

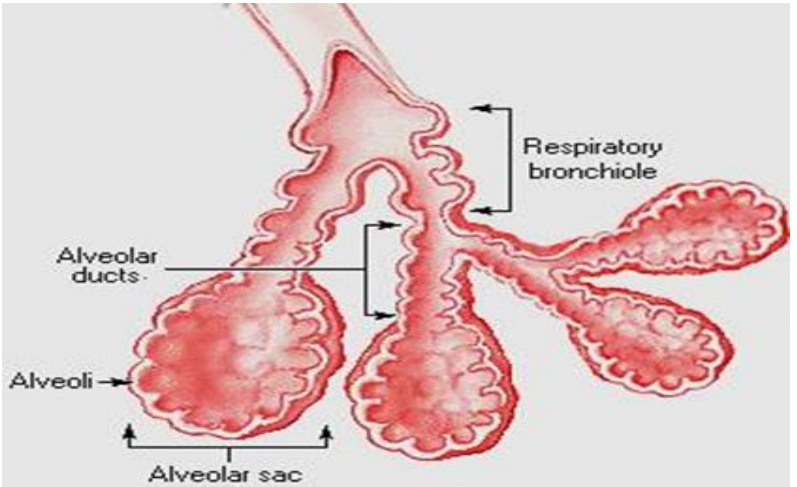


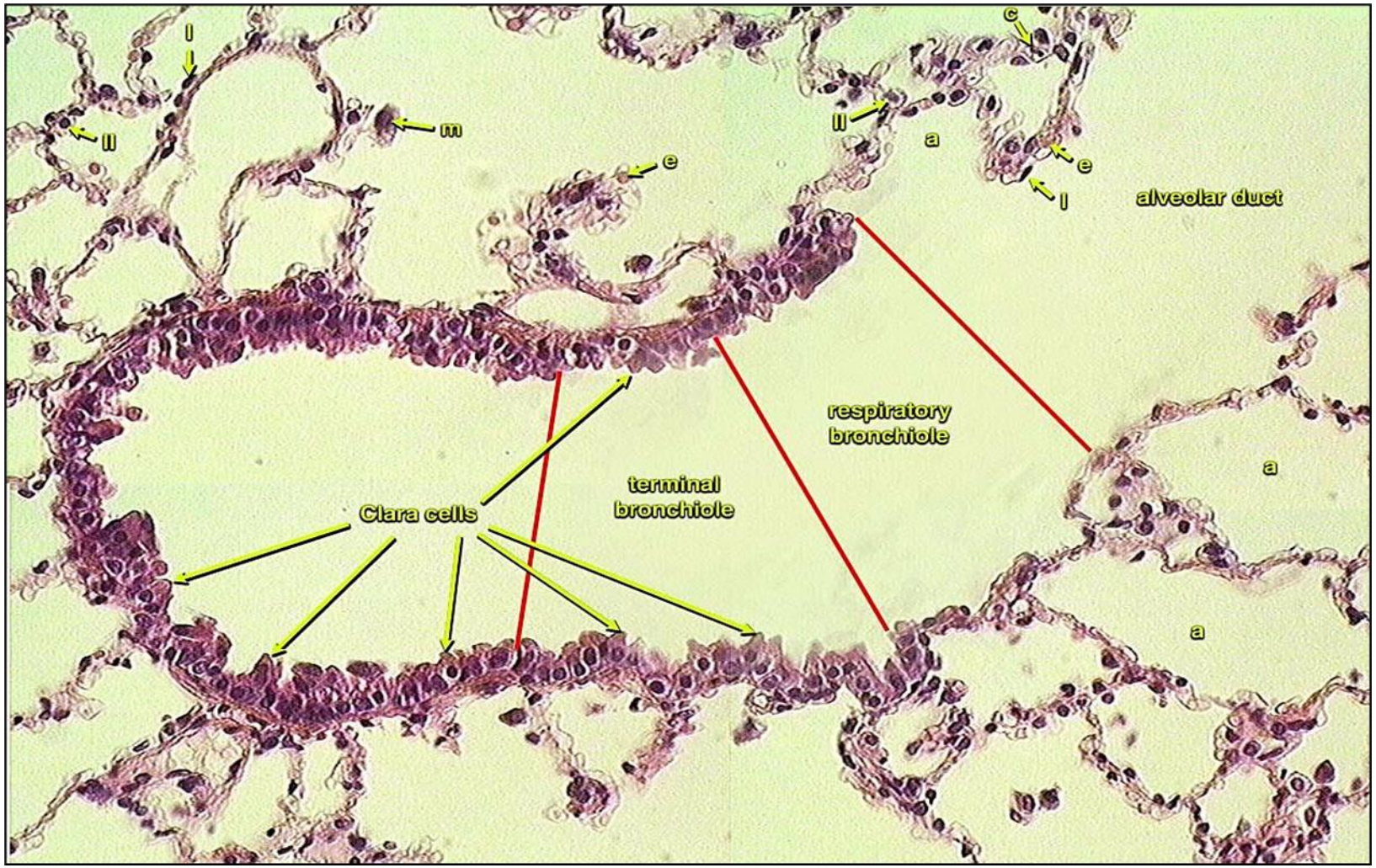


Respiratory Portion

- Respiratory bronchioles (RB):
  - Transitional part between conducting & respiratory portions, still bronchiole but shorter & thinner
  - Lined with simple cubical ciliated with Clara cells with Some alveoli open in its wall
- Alveolar ducts (AD):
  - Alveoli open along its wall
  - Lined with squamous alveolar cells
  - At the distal end of AD smooth muscles disappear, elastic & collagen fibers provide the only support



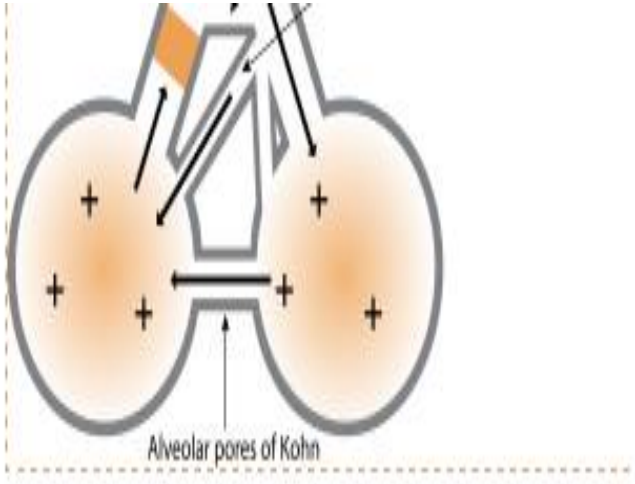


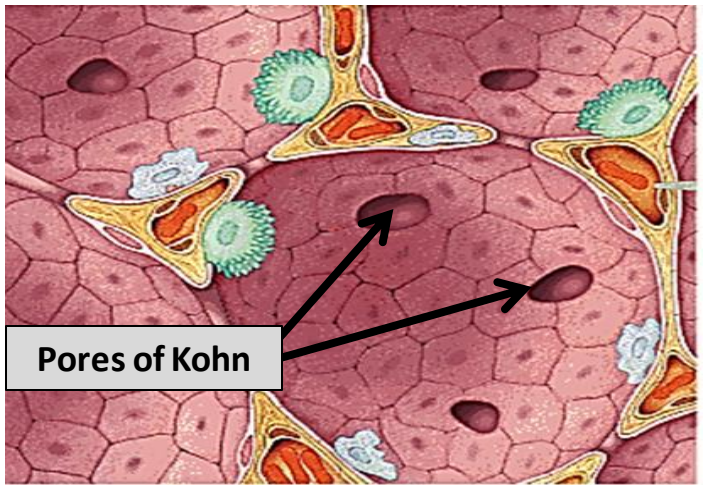


Section is showing terminal bronchiole and parts of the respiratory portion

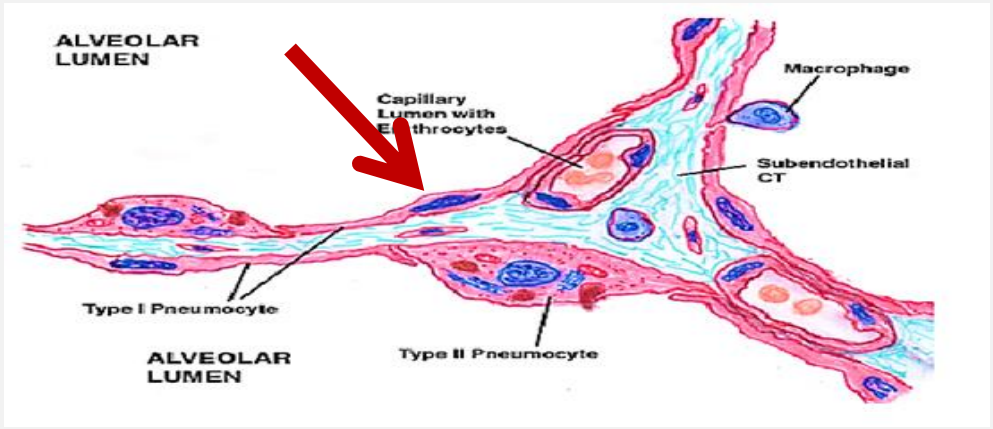
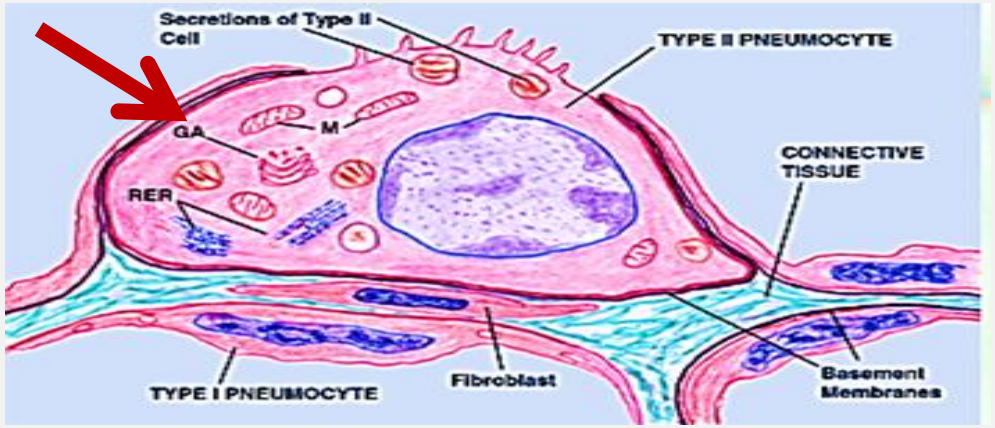
Respiratory Portion

- Alveolar sacs (AS):
  - Group of alveoli opens into common central space
  - Lined with squamous alveolar cells
- Alveoli:
  - Structural & functional units of lung (gas exchange)
  - Alveoli found open into RB, AD, AS
  - They separated by inter-alveolar septa
  - Alveolar pores of Kohn present in walls between alveoli (collateral ventilation)
    - Normally they are nonfunctioning
    - Play an important role in case of airway obstruction to ventilate the collapsed area
  - Lined with alveolar epithelium formed of 2 types of cells
    - type I & type II pneumocytes

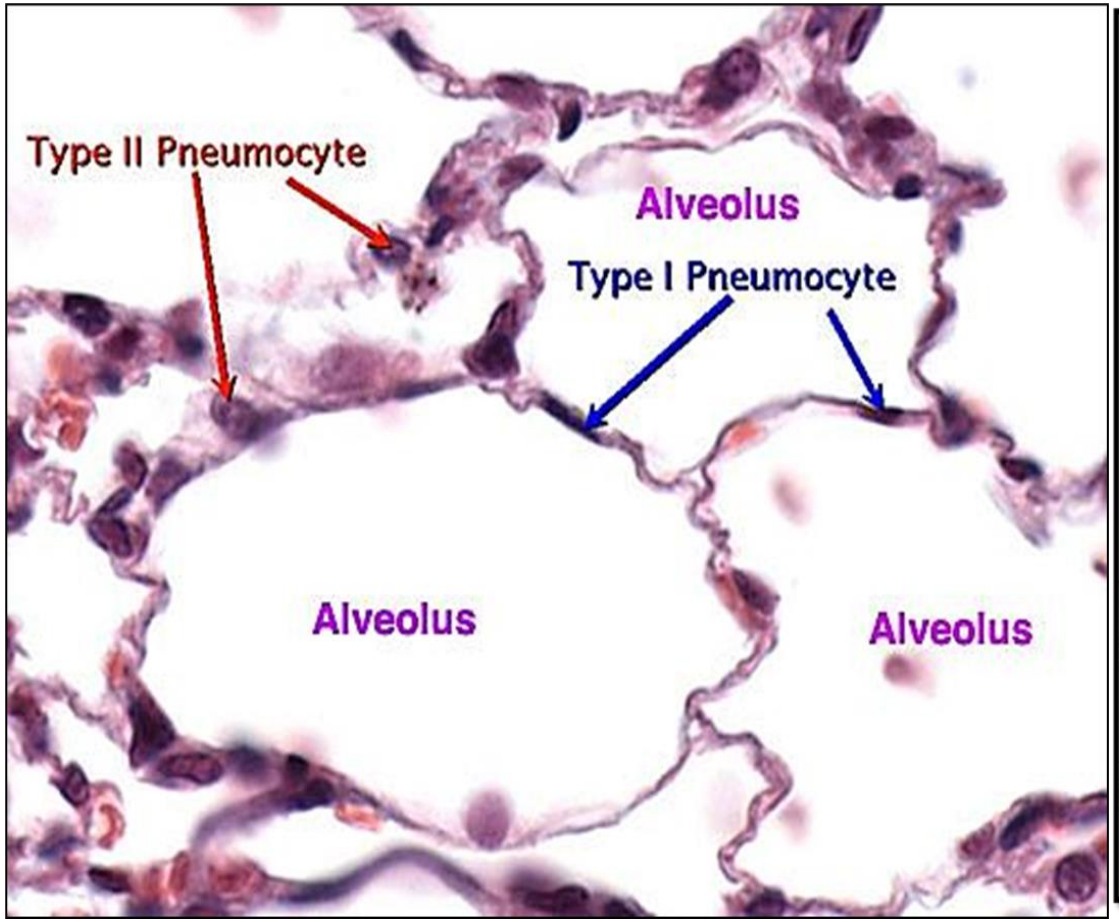


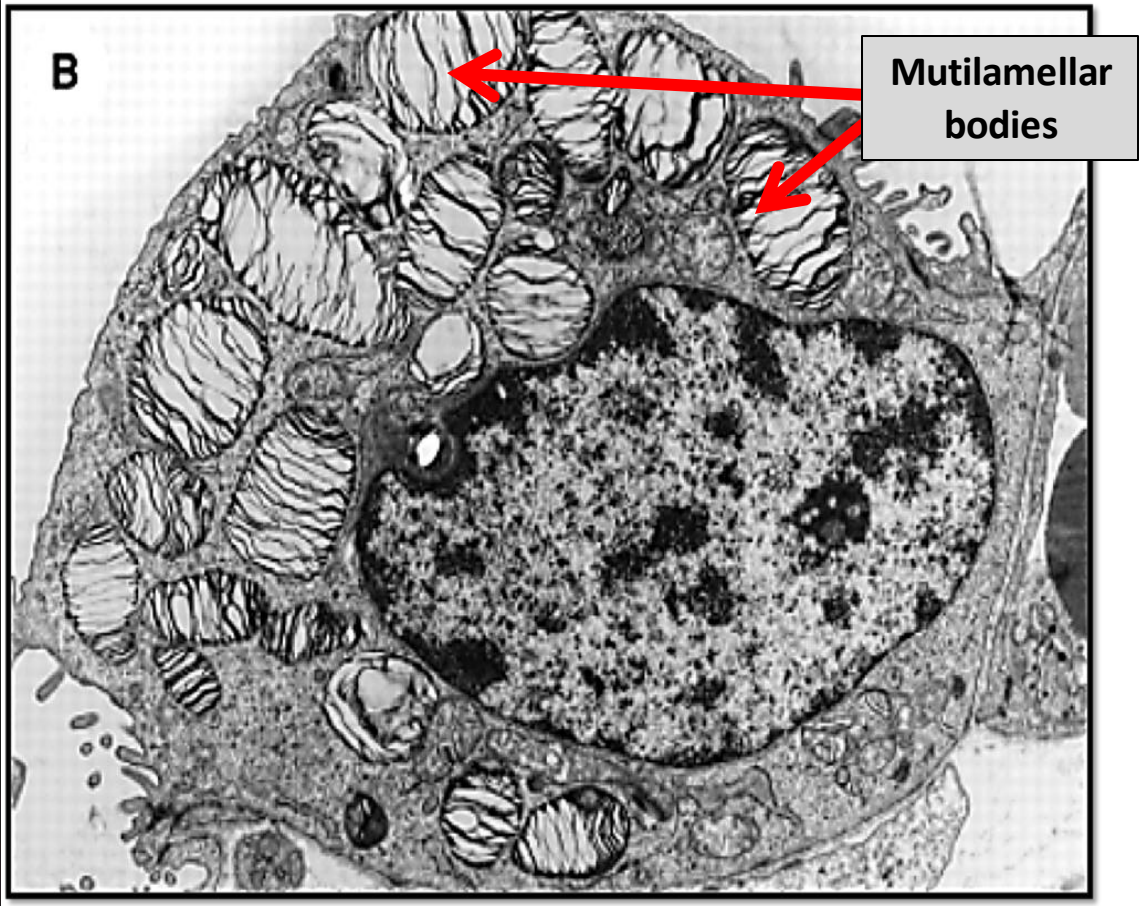


Lining Epithelium of the Alveoli

Type I pneumocytes	Type II pneumocytes
Cover 97% of alveolar surface Flat simple squamous cells with flat nuclei Cytoplasm has few organelles Cells joined together by tight junctions Gas exchange occurs through them	Cover 3% of alveolar surface Cuboidal cells with central nuclei & foamy cytoplasm Free surface has short microvilli Cytoplasm rich in organelles, multilamellar bodies Secrete surfactant (decrease tension & bactericidal) Act as stem cells Have ACE2 receptors where Covid-19 spikes attack
	

Lining Epithelium of the Alveoli



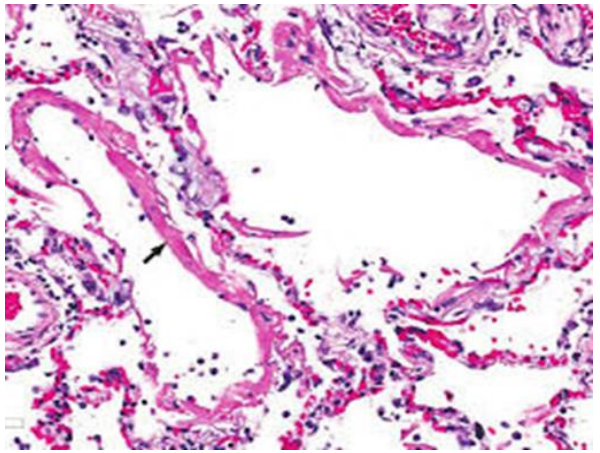


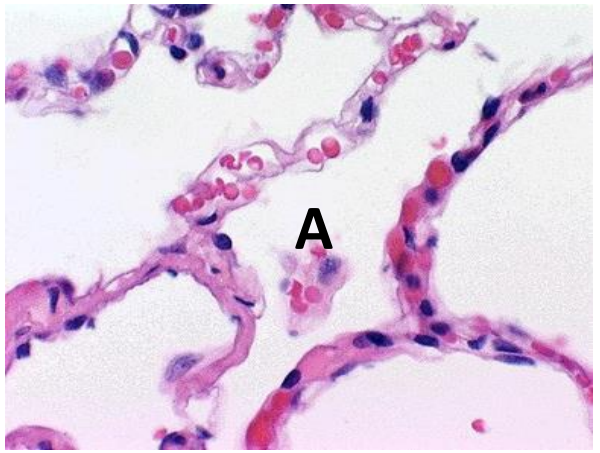
(E/M of type II pneumocyte)

Respiratory Distress Syndrome (RDS): **occurs In premature babies because surfactant appears in last weeks of gestation**

Intra-alveolar Septa

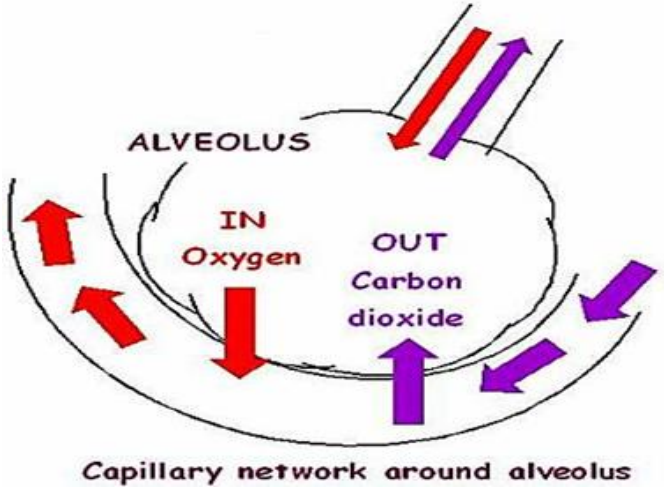
- Delicate walls separate adjacent alveoli
- Have richest capillary network
- Where gas exchange take place
- Contains Blood-Air barrier
- Rich in elastic and reticular fibers
  - Support and prevent over expansion
- No smooth muscle cells
- Contains extravasated leucocytes (monocytes), which will migrate through the wall → to the lumen and become alveolar macrophages (A)
- This septa is destructed in emphysema and Covid - 19

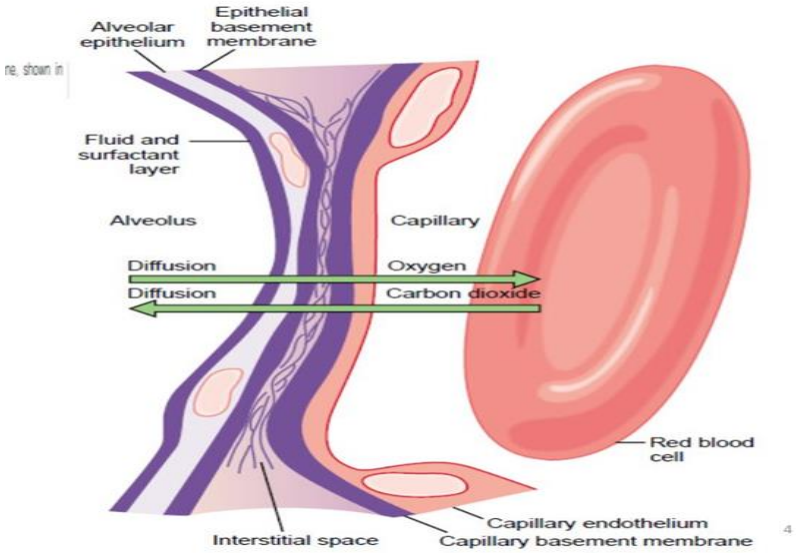




Blood-Air Barrier

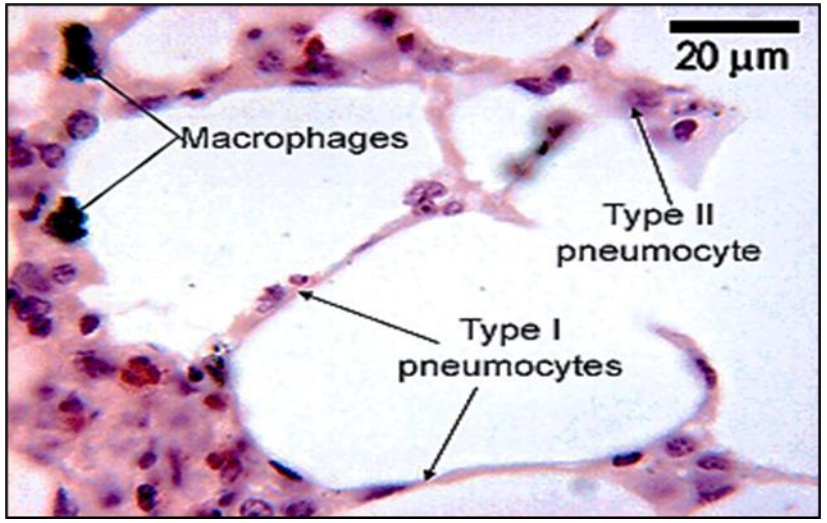
- Also known as Blood-Gas barrier or respiratory membrane
- Its where O_2 and CO_2 cross for exchange
- Composed of 4 layers:
  - Thin film of surfactant on the surface
  - Cytoplasm of type I pneumocyte
  - Fused basal lamina of type I pneumocytes + capillary endothelia cells
  - Cytoplasm of endothelial cells



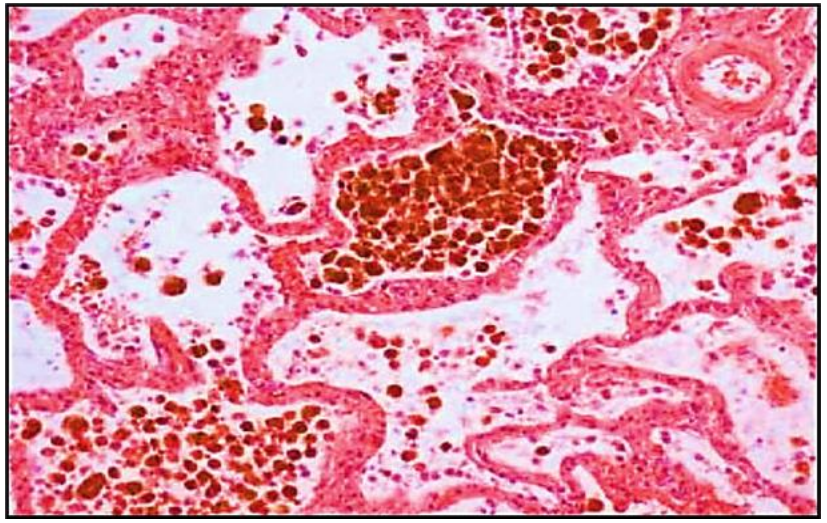


Alveolar Phagocytes

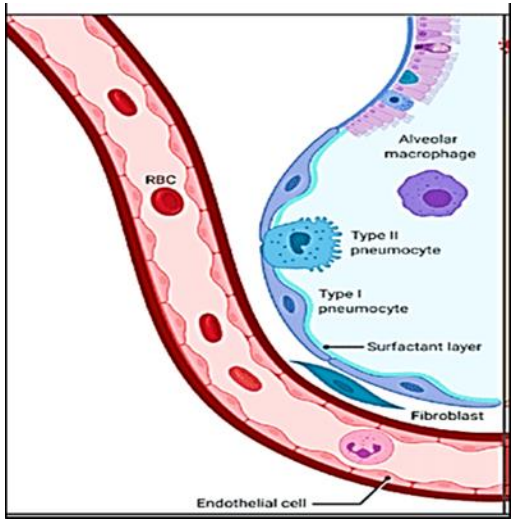
- Blood monocytes → Connective tissue in alveolar septa →lumen of alveoli→ macrophages
- 2 types of alveolar macrophages:
  - **Dust cells:** macrophages engulfing dust particles
  - **Heart failure cells:** macrophages engulfing erythrocytes (hemosiderin granules) found in congestive heart failure



Dust cells

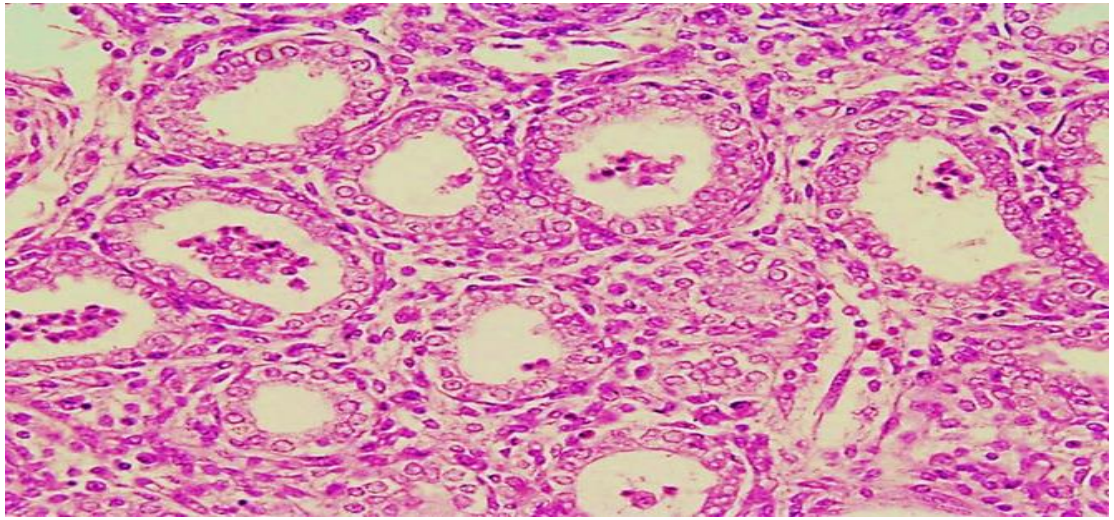


Heart failure cells

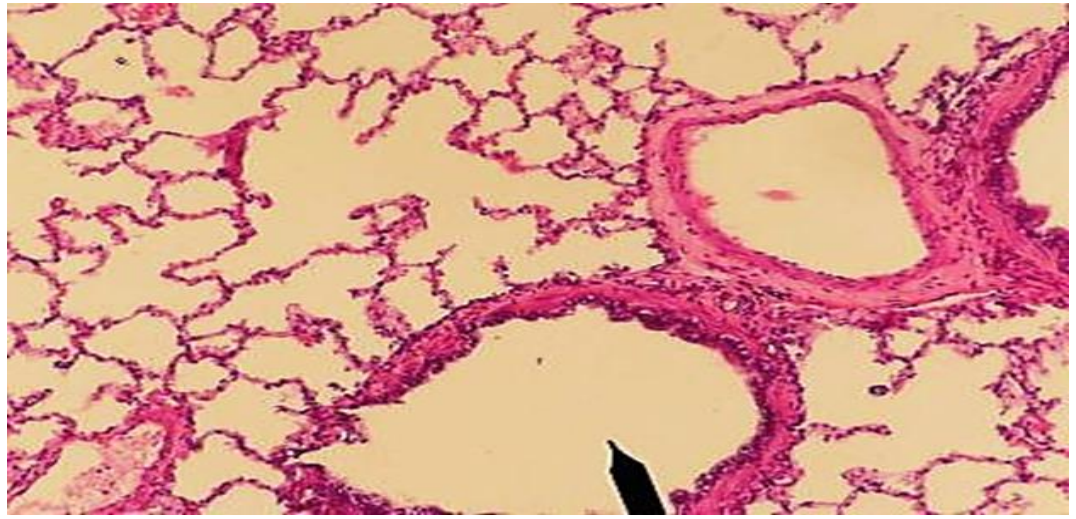


Fetal Lung

- Lobulation is clear due to thick connective tissue septa
- Fetal lung similar to gland in histological section
- Alveoli collapsed lined with simple cubical epith.
- Pulmonary blood vessels are congested
- Whole lung sinks in water



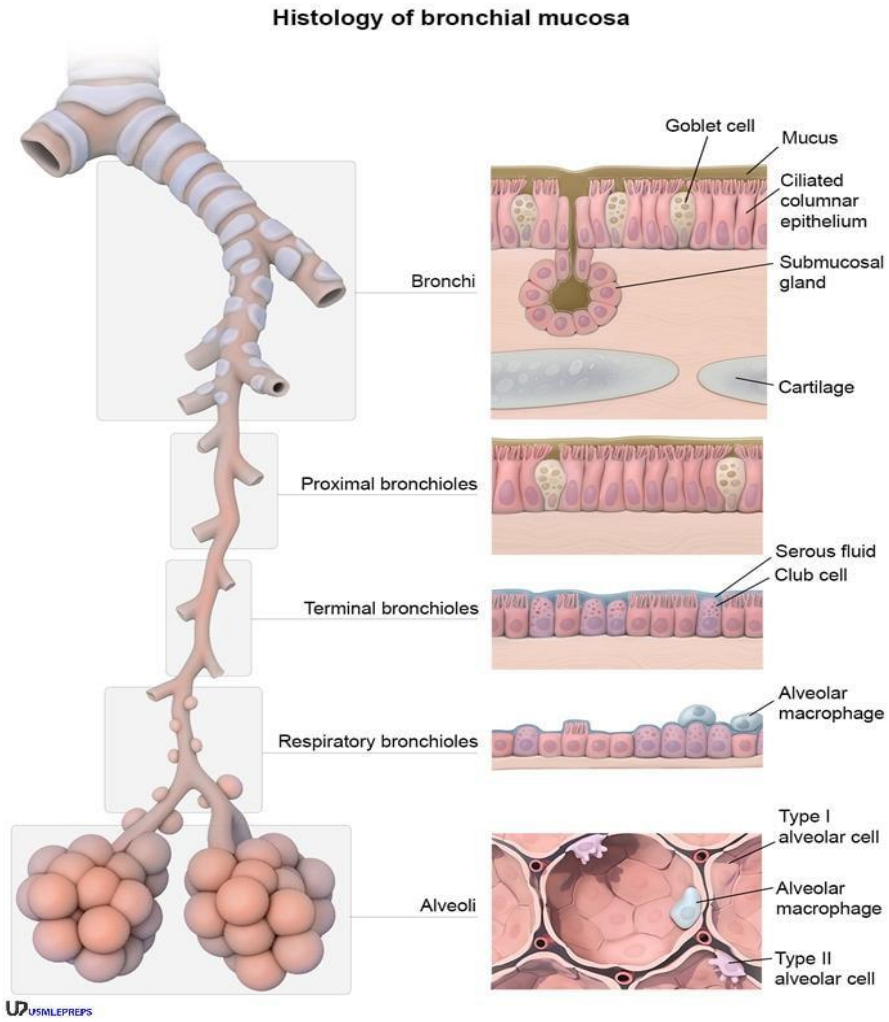
Fetal Lung



Normal Lung

Recap

- Hyaline cartilage in Trachea (C-shape)
- Complete ring of cartilage in Primary Bronchi
- Cartilaginous (isolated) plate in Secondary Bronchi
- No submucosa in Secondary Bronchi
- No cartilage , No mucoserous glands, No lymphatic nodules, and No goblet cells at the level of Bronchioles
- Clara cells appear at the level of Bronchioles
- Cilia terminate in Respiratory Bronchioles
- Airway smooth muscle cells extend to the end of Terminal Bronchioles and become sparse beyond this point till disappear



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MEDEMIA ACADEMY

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- Which of the following statements about the olfactory epithelium is CORRECT?

  A. Olfactory receptor cells provide large surface area to adapt the transmembrane chemoreceptors

  B. Basal cells express abundant ion channels which play role in signal transduction

  C. Supporting cells divide to replace worn out olfactory receptor cells

  D. Olfactory receptor cells synthesize and secrete odorant binding proteins

  E. Supporting cells are provided with basal afferent nerve fibers that send sensory information to the trigeminal (5th) nerve

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❖A 25- year old pregnant female who is 24 weeks gestation presented to the labor and delivery ward. She has no underlying medical problems. She was 5 cm dilated and having continuous contractions. The newborn (700 gram) was delivered 10 hours later. Shortly after birth the neonate manifested with fast breathing. fast heart rate, chest contractions and blue discoloration of the skin. He was admitted to the neonatal ICU and placed on conventional ventilator. The condition is most probably due to _____ ?

A. Damage of type | pneumocytes by Covid -19 virus

B. Lack of oxygen due to insufficiency of type II peumocytes

C. The alveoli are loaded with dust cells

D. lmmaturity of type II pneumocytes

E. Inadequate alveolar collateral ventilation

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❖All of the following statements about the respiratory system are correct EXCEPT?

A. Clara cells are found only in the bronchiolar epithelium

B. Most of the inside surface of alveoli is lined with type I pneumocytes

C. The surfactant lining of the alveoli is produced by type II peumocytes

D. The larynx contains hyaline cartilage, smooth muscle and stratified squamous epithelium

E. Mucociliary clearance involves goblet cells, ciliated epithelial cells and submucosal glands

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❖How are bronchioles histologically different from bronchi?

A. Bronchi lining epithelium contains Clara cells

B. Bronchiole walls have smooth muscle

C. Bronchi have mucosa associated lymphoid tissue

D. Bronchiole walls have hyaline cartilage

E. Bronchi are different from bronchioles based on size alone

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❖Choose the WRONG statement from the followings?

A. Alveolar duct is the first part of the respiratory tract that does not contain cilia

B. Fusion of the epithelial and endothelial basal laminae are important adaptation in the blood-air barrier

C. Presence of cartilage plates is a histological feature of bronchioles

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❖Wrong about Blood-Air barrier?

A. Thick

❖Mismatch:

Terminal bronchioles lined with Clara and goblet cell

❖Mismatch:

Type 1 pneumocytes --- Phagocytosis