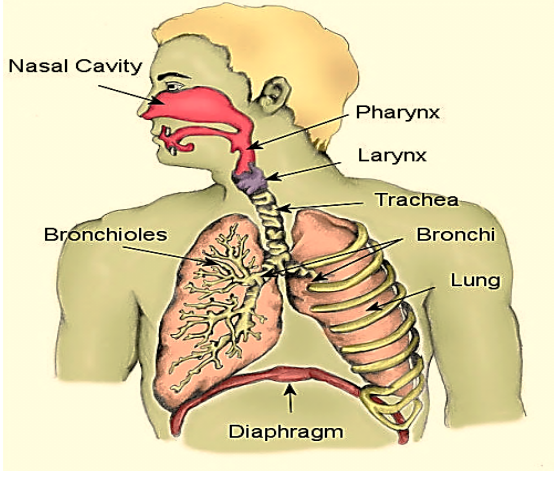
The respiratory system



Objectives of studying the respiratory system:

- Structures involved in inspiration / expiration of air & gas exchange

- Structures of chemoreceptors involved in sense of smell

- Phonation

Learning objectives:

1- Recognize & describe the cellular components of respiratory epithelium

2- Understand the structure & function of conchae

3- recognize & describe the cellular components of olfactory epithelium

4- Describe components of the vocal cords

10 Recognize & understand function of epiglottis

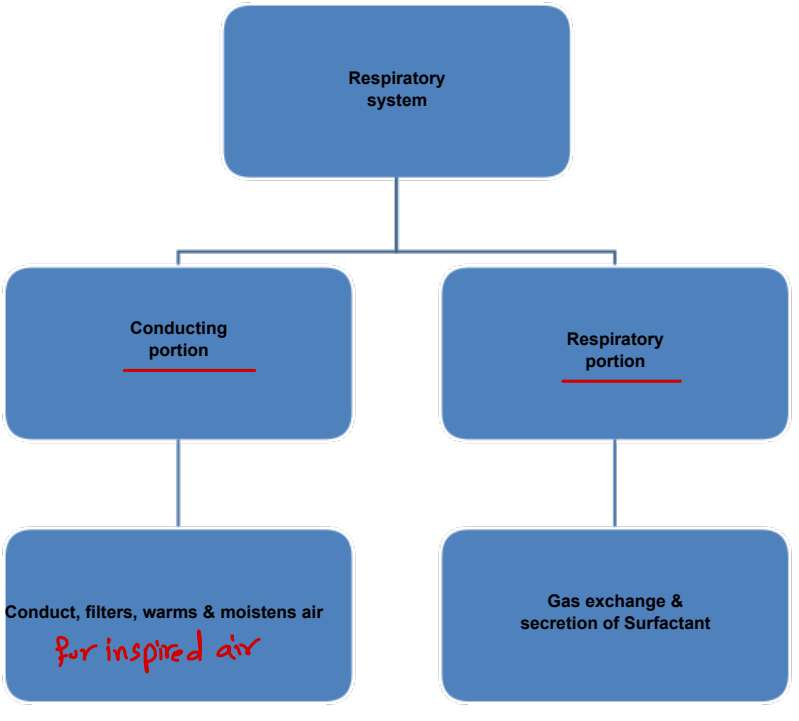
5-List the tubes that make up the conducting and respiratory portions

6- Distinguish between a bronchus , bronchioles& respiratory bronchiole

7- List all components that make up the interalveolar septum

8- Distinguish between type I & type II alveolar cells , macrophage and endothelium

9- Describe the two separate blood supplies to the lung & understand their function


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

- **Types of epithelium in the respiratory system:**

1- Non- K stratified squamous epith. → found at nostrils, lingual surface of epiglottis, & true vocal cords

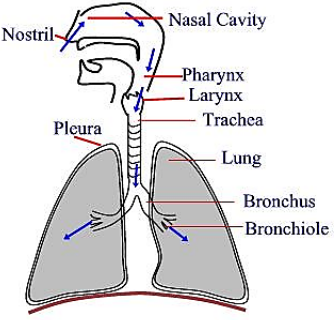
2- Respiratory epith. Cover most of the conducting portion of the respiratory tract

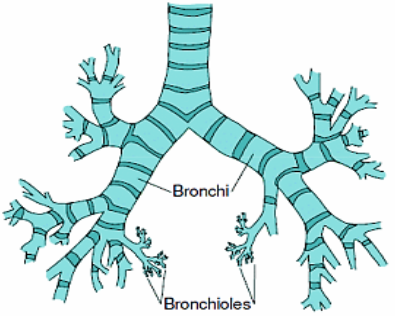
3- Olfactory epith. Contains chemoreceptors of smell sensation → superior concha

4- Alveolar epith. → Respiratory portion / alveoli where gas exchange

➢ **A- The conducting portion includ**

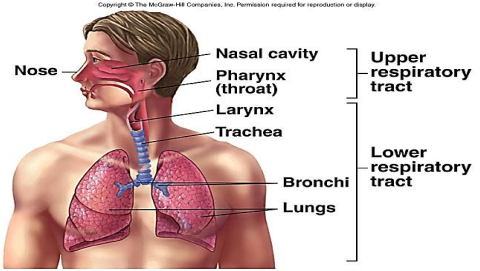
- Nasal cavities & sinuses
- Nasopharynx
- Larynx
- Trachea
- Bronchi (Rt & Lf) → outside the lung
- 2ry , 3ry bronchi → inside the lung
- Bronchioles
- Terminal bronchioles

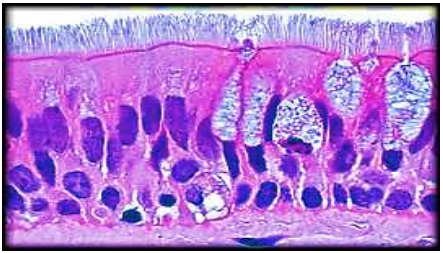




Structure / Function relation in Conducting portion

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

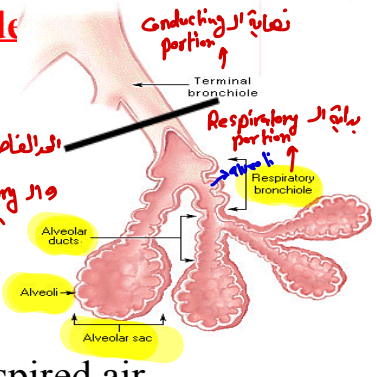




Respiratory epithelium

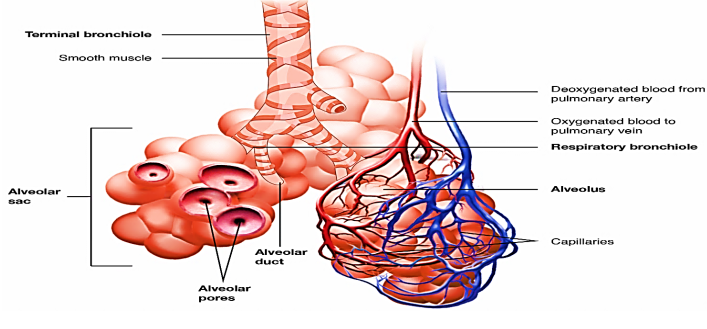
➢ B- The respiratory portion include

- Respiratory bronchioles
- Alveolar ducts
- Alveolar sacs
- Alveoli



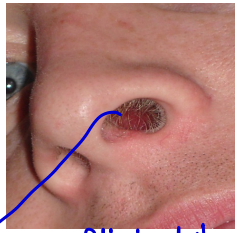
Function of respiratory portion:

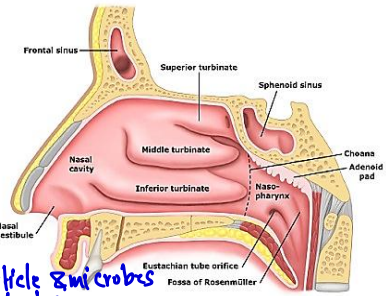
O_2/CO_2 exchange between blood & inspired air



A- Conducting portion

Nasal cavities: separated by a cartilaginous & bony septum anterior posterior
each consists of: vestibule & nasal fossa





Vestibule:

- Is the anterior part
- Lined e thin skin فيه ⟹ (hair follicles, sweat glands, sebaceous gland)
  deeper changes → non - keratinized st. squ. epithelium

filtrate dust particle & microbes on inspired air

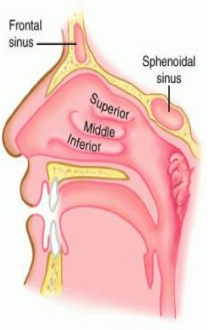
- hair filters out large particles

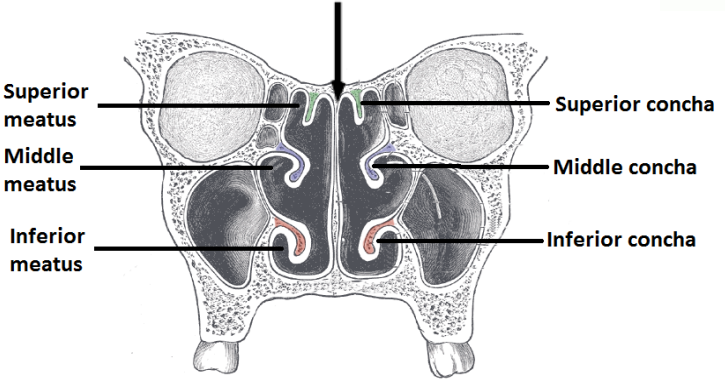
Nasal fossae:

- 2 cavities separated by nasal septum

- Their lateral walls contain 3 bony projections (conchae) superior, middle, inferior

Shelfs رفوف





- Superior one covered e Olfactory epithelium

يعني مسؤول عن الـ Smell sensation

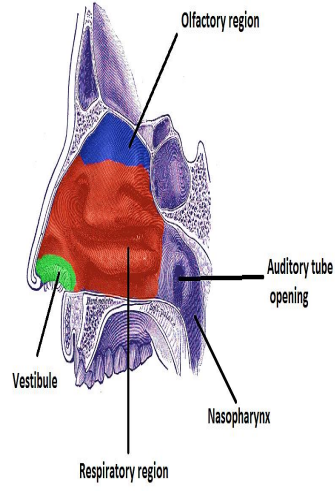
- Middle & inferior covered e respiratory epithelium

- The conchae slow flow of air & increase the surface area of respiratory epithelium for conditioning of the inspired air

to enter the lung at optimum conditions

- lamina propria beneath RS epith. rich with superficial venous plexus (swell bodies)

Respiratory tract اللي بيأدي لـ RS epith وكمان موجودة بـ nasal cavity بس اللي بـ

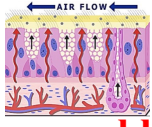


Swell bodies:

Loops of venous plexus located in of lamina propria of the respiratory epithelium of the nasal cavities

1- Important for conditioning & warming of inhaled air → "counter current flow"

الهواء إله إتجاه والدم عكسها بتاعه لذلك هذا النوع يكون أفضل لـ Conditioning



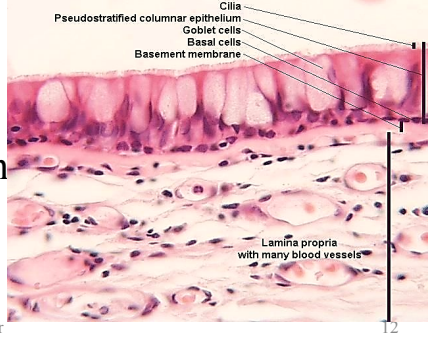
2- Due to their thin wall & proximity to the surface **nosebleed** occurs so common

B.V of lamina propria

3- Responsible for **nasal cycle**

4- Allergic reactions & inflammation can cause sever engorgement (احتقان) of swell bodies in both fossa

B.V of lamina propria



Nasal cycle:

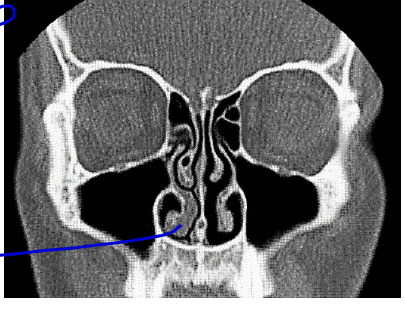
- Every 20-30 min. rhythmic cycles of physiological congestion & decongestion occurs in the mucosa of the nasal cavities. Normally we are not aware of it → بنحس فيها لما نتمرض

2 cavities بوصة من الـ — 2 cavities مثال بوصة

- When Swell bodies in lamina propria of one nasal cavity become engorged with blood → distention of conchal mucosa → ↓ flow of air → allowing the engorged Res. Epith. To recover from dehydration.

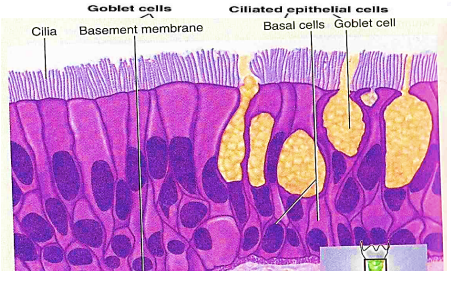
والجزء الثاني اللي ما حارله engorged بنتنفس فيه

- The cycle under the control of autonomic nervous system

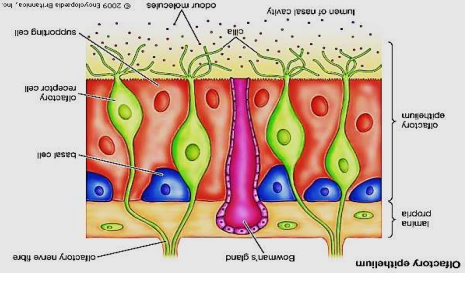


Q:What is the difference between the respiratory & olfactory epithelium?

RESPIRATORY



OLFACTORY



The respiratory epithelium:

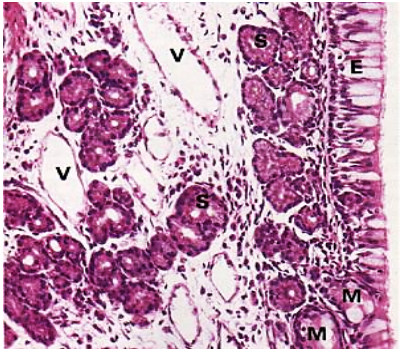
- Pseudostratified columnar ciliated e goblet cells

The olfactory epithelium:

- Pseudostratified columnar e chemoreceptors & NO goblet cells

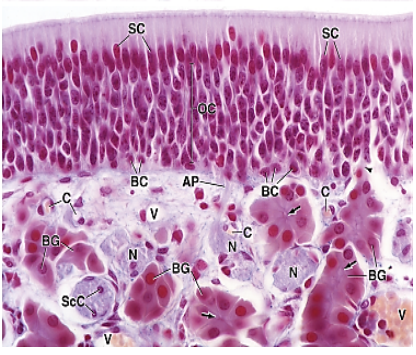
Respiratory mucosa

- Epithelium
- Lamina propria
- Nasal glands
- Blood vessels



Olfactory mucosa

- Epithelium
- Lamina propria
- Olfactory glands
- Blood vessels



The respiratory epithelium

- Lines most of the **conducting portion**

- **5 types of cells** are present:

1- Columnar ciliated cells

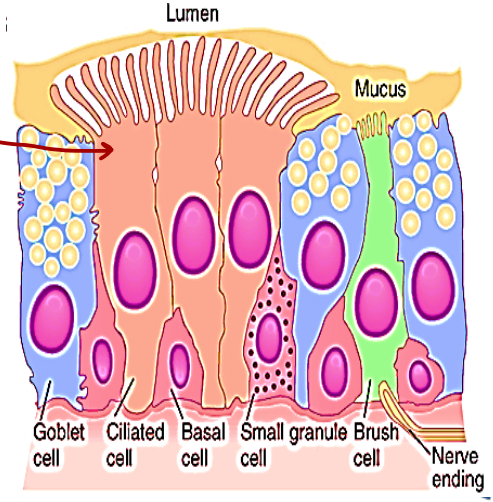
2- Goblet cells

3- Brush cells

4- Basal (stem) cells

5- Granule cells (NE cells)

Neuro endocrine



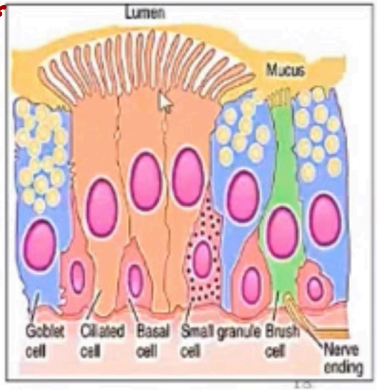
1- Columnar ciliated cells : most cells, have **motile cilia** (300) on apical surface (unidirectional beating)

2- Goblet cells: secrete mucus, cover surface to trap bacteria & dust

3- 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)

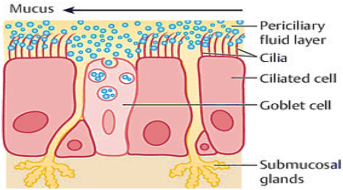
4- Basal cells: small cells, act as stem cells

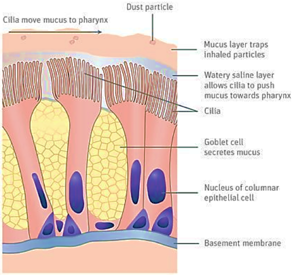
5- Granule cells: (neuro-endocrine cells): have basal cytoplasmic granules, secret hormones (serotonin & catecholamine) →regulate the caliber & secretions of airways



- 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 airway hypoxia or hypercapnia
- Serotonin is a cilio- stimulatory i.e. increase ciliary beat frequency (CBF)
- Serotonin induces the release of Ach from epithelial cells → release of Ca & ATP → ↑CBFSerotonin cause ↑in periciliary liquid & thus facilitate mucociliary clearance
- Serotonin cause ↑in periciliary liquid & thus facilitate mucociliary clearance
- serotonin induces vasoconstriction in pulmonary vasculature → contraction of airway (role in Pulmonary hypertension)

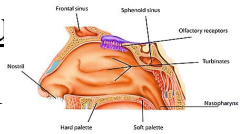
- The respiratory epithelium rests on lamina propria contain many glands serous & mucus (Nasal glands) + BV
- The secretion of the glands (+ goblet cells) serve to catch any particles & bacteria inhaled (Mucociliary escalator)





- The blood vessels serve to warm the inspired air (humidity of the lung can be maintained)
- In smokers the proportion of ciliated cells to goblet cells is altered (↑ goblet) to trap gaseous pollutants

The olfactory epitheliu

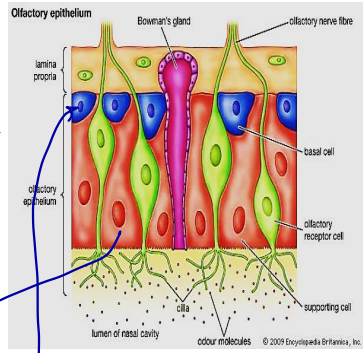


- Covers the roof of nasal cavities & superi conchae.

- Contains **chemoreceptors of smell**

Stypes ← RS epith

- **3 types of cells** are present:
  - Olfactory neurons
  - Supporting (sustentacular) cells
  - Basal cells

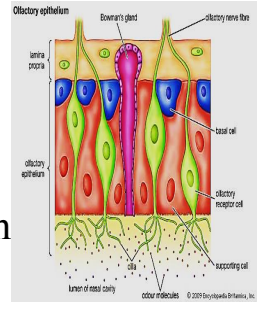


olfactory epithelium → lamina propria → B.V nerve fibers nasal gland

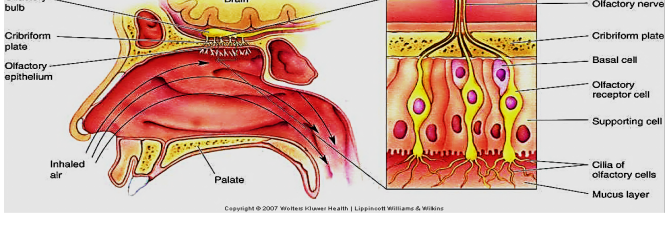
- The olfactory epithelium rests on lamina propria contains:
  - ✓ BV & olfactory nerve fibers
  - ✓ Bowman's glands, secrete constant flow of serous fluid → surface → facilitate dissolve of odoriferous substance

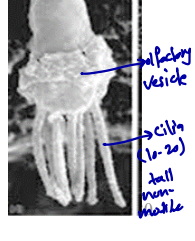
1- Olfactory neurons:

- Bipolar nerve cells (renew 30- 60 days) i.e (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
- The axons pass to lamina propria to form olfactory n. fibers

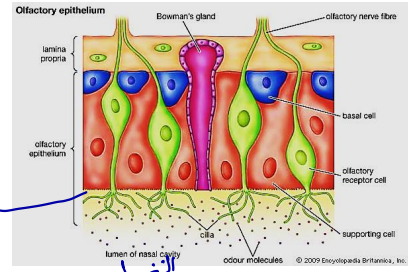




for olfactory epithelium

2- Supporting cells (neuroglia):

- Tall columnar cells e wide apex narrow base
- Their free surface has **microvilli**
- Tight junctions bind these cells e olfactory cells.
- They secrete **odorant binding proteins &** express **abundant ion channels** → role in smell conduction → تنقل signal transduction



صغيرة بجر

الخضراء

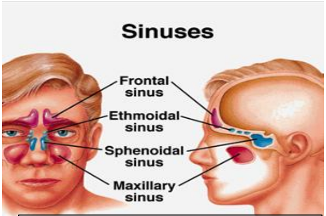
3- Basal cells:

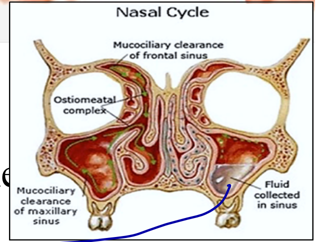
- Small pyramidal cells e basophilic cytoplasm
- Act as stem cells for both olfactory & supporting cells

Paranasal sinuses (Bilateral)

- Frontal, Ethmoidal, Sphenoidal
  Maxillary
- These cavities **open in nasal cavities**
- Lined e thin respiratory epith.
  e few goblet cells → لأنهم حركات متكررة
  فلما نربط تنفرز فيهم مخاط كتير وينحبس

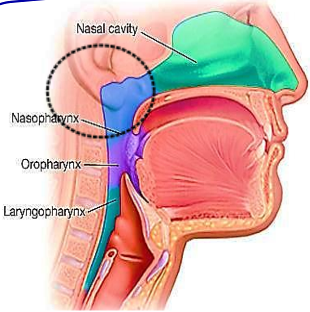
Chronic sinusitis = immotile cilia syndrome
الـ cilia تتخرب فتبطل تطلع الإفرازات من هاي الجيوب





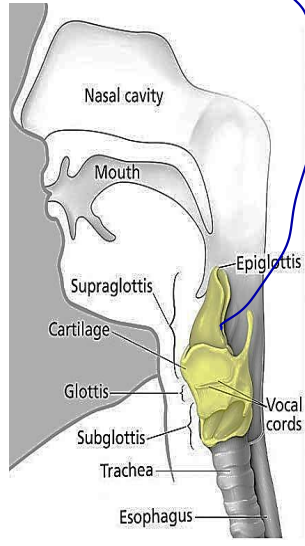
Nasopharynx

- Lined e respiratory epithelium
- Its lamina propria contains
  pharyngeal tonsil & openings of
  Eustachian tubes → بتوصل الـ middle ear بالـ nasal cavity
  لما تبلع عشان تفتح ولما تطلع طيارة فالضغط يزيد بتنسد فينغلق أو ينقفل



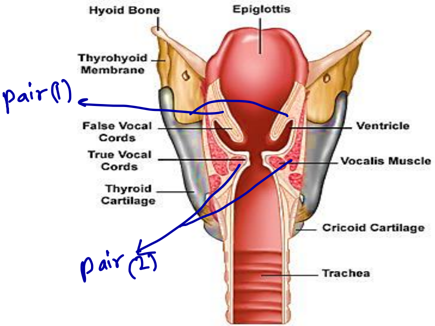
Larynx:

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



Vocal cords:

- 2 pairs of mucosal folds extend in lumen of larynx



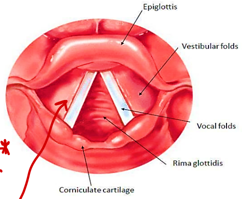
- False vocal cords (Upper pair)

➢ called (**vestibular folds**)

➢ covered e **respiratory epith.**

➢ guard against entrance of food into larynx (made of vestibular ligament)

wall of false vocal cord موجود بال



* لما نكون ناكل وتفوت قطعة أكل بال larynx هنول الاطراف بينقبضوا ويتفج عشان نطلع الأكل العالق → initiate cough reflix

- True vocal cords (Lower pair)

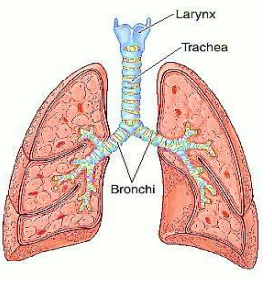
➢ covered e **non-keratinized stratified squamous epith.**

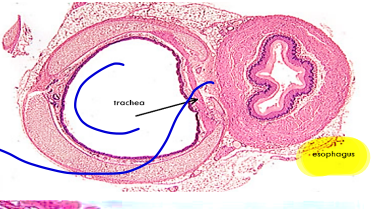
➢ made of **ligaments (vocal lig.)** & **skeletal ms. (Vocalis ms.)** (skeletal muscle)

➢ tension of cords & distance between them produce sound

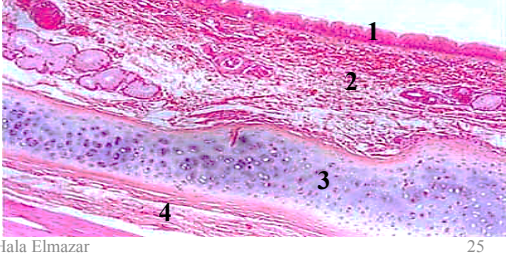
Trachea

- 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:
  - Mucosa
  - Submucosa
  - Hyaline cartilage
  - adventitia



Wall of trachea:

- **Mucosa**: epithelium – lamina propria – elastic fibers

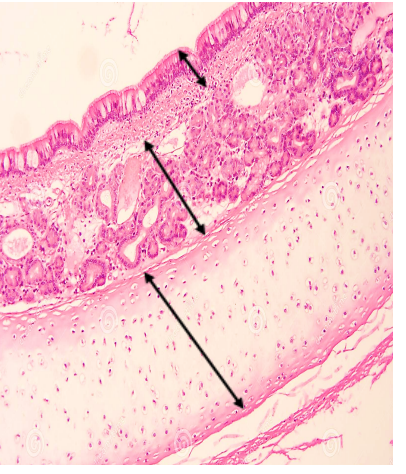
  RS epithelium

  Epithelium: respiratory epithelium

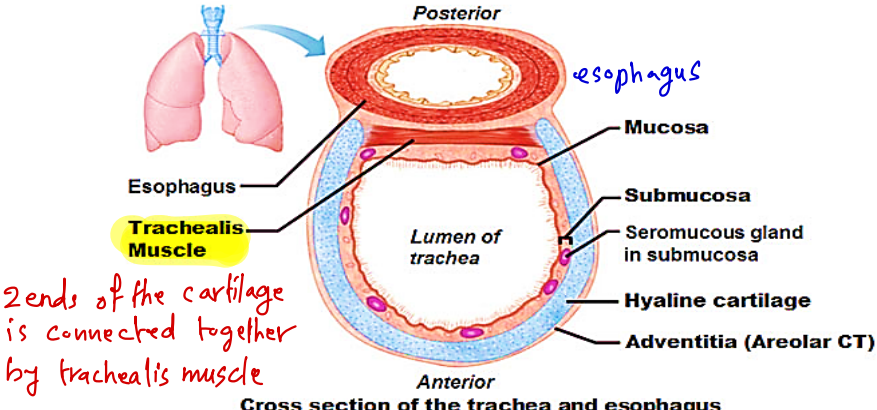
- **Submucosa**: loose CT. BV, nerves, Lymphoid nodules, Tracheal glands

  Hyaline cartilage

- **Cartilage layer**: C- shaped cartilage rings, the gap between cartilage end connected by elastic ligament & **Trachealis *ms*** *(smooth ms)*



The Trachea



2 ends of the cartilage is connected together by trachealis muscle

Cross section of the trachea and esophagus

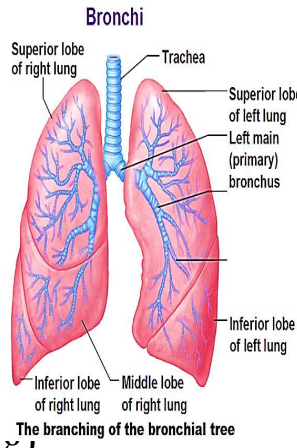
Contraction of the trachealis ms. is important for the cough reflex

Contraction → narrowing the tracheal lumen → ↑ the velocity of the expelled air → squeezed out

Cough reflex

Bronchial tree

- Primary (Extra pulmonary) bronchi
- Secondary (Intra-pulmonary) bronchi
- Bronchioles
- Terminal bronchioles → ناقلة الـ Conducting portion



The branching of the bronchial tree

- **1ry bronchi**: RT & LF→ similar to trach
  (but cartilage is a complete ring)

- **2ry bronchi**: within the lung → divide into 3ry bronchi
  Its wall is formed of 4 layers (NO Submucosa):

- Mucosa
- Musculosa

• cartilage plates (isolated plates)
• Adventitia

بدلها طبقة musculosa

- **Mucosa**: ↑folded, respiratory epith.,↓goblet cells, lamina propria has elastic fibers & MALT (mucosa associated lymphatic tissue)

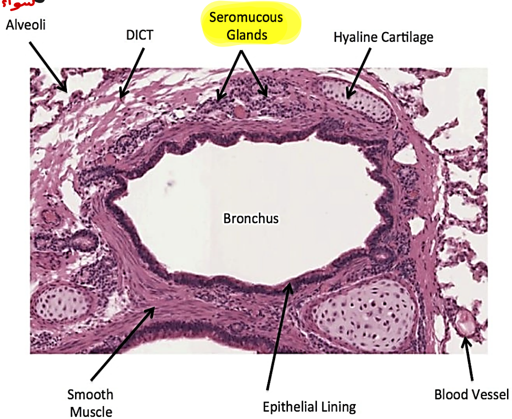
سواء كانت diffuse أو follicles

بسبب وجود cartilage plates ↑

رزنه لما فيه جزء من الـ wall

حلزونية ← فيها cartilage يعني الـ muscle مش محيطة من كل الجهات

- **Musculosa**: spiral layers of smooth ms. encircling the mucosa



Structure of 2ry, 3ry bronchi

- **Cartilage plates:**

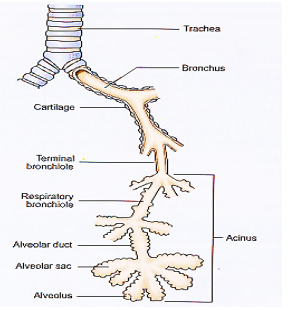
muco-serous glands &

lymph nodules found between cartilage plates

* يعني مجرد أشوف شوية cartilage بالـ wall معناه أنا لسا بالـ bronchus مش bronchioles

- Adventitia

- **Bronchioles**
- Small airways 5 - ↓ mm (أقل)
- Its wall has (**No** *submucosa,* **No** *cartilage,* **No** *glands,* **No** *lymphatic nodules*)
- Its wall formed of 3 layers

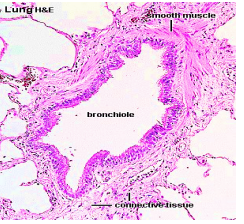


Mucosa: (R.S.epith يعني مبش)

- **Simple columnar ciliated** epithelium e

Clara cells & NE cells & neuroepithelial bodies (اختفت الـ goblet cells وظهرت بدلها)

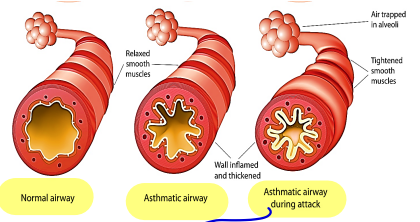
(chemosensory receptors → O_2 level)



Musculosa:

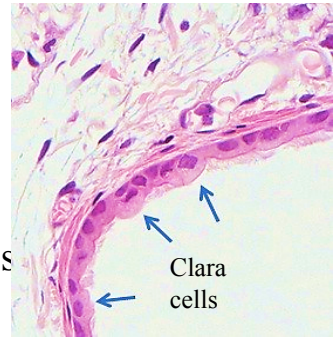
complete layer of circularly arranged smooth ms. (Asthma attacks)

Adventitia



Clara Cells:

- Also called club cells or bronchiolar exocrine cells
- Dome- shaped, non- ciliated,
- Cytoplasm has lots of secretory granules (not mucus) basal rER, apical sER
- Function:



كتير

لها دور في المناعة

Defensive role :glycoprotein granules (contain proteolyase & oxidase & cytokines

2. Degradation of inhaled toxins (sER)
3. Secretion of surfactant-like substance to prevent collapse of bronchioles
4. Act as stem cells
5. Mutation ⟶ adenocarcinoma of lung.

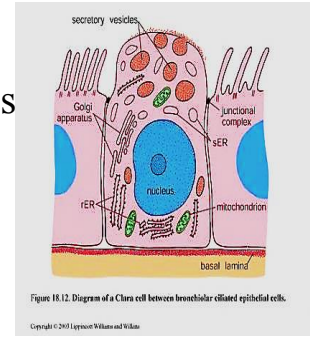
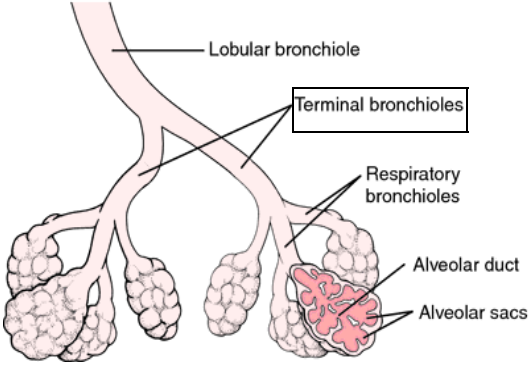
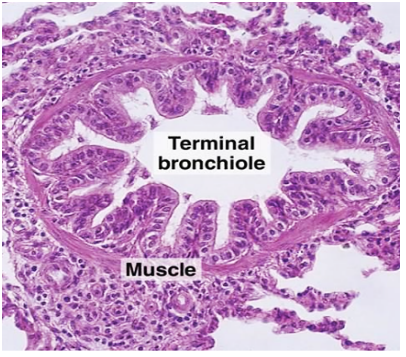


Figure 18.12. Diagram of a Clara cell between bronchiolar ciliated epithelial cells.

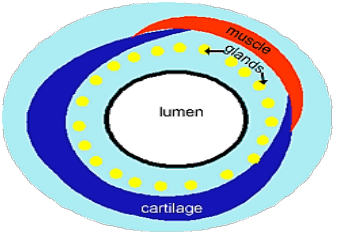
- **Terminal bronchioles:**



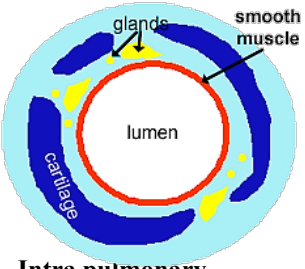


- The smallest & last part of conducting portion
- Lining epithelium: Simple cubical ciliated e Clara cells
- Secondary pulmonary lobule: is the lobule supplied by a terminal bronchiole that branches into respiratory bronchioles.

Difference between structure of wall of trachea vs. Wall of intra-pulmonary bronchi & bronchiole

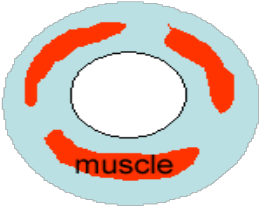


Trachea



Intra pulmonary bronchus

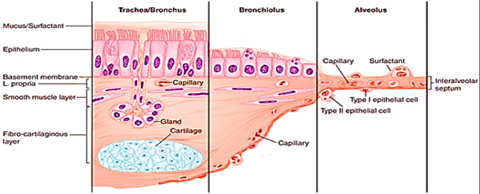
N.B: Smooth muscle component increases in proportion and continuity لغاية ماريصير دائري **as the air passage decreases in size. Then decrease again till disappear in the respiratory portion**



Bronchiole

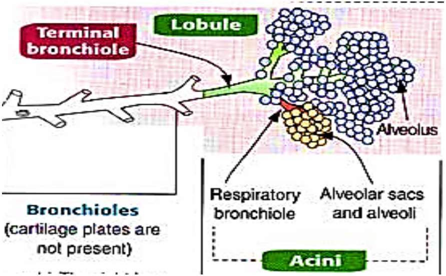
N. B: if cartilage is present, it is a "bronchus," but if cartilage is absent the airway is a "bronchiole."

Changes occur in the epith. of conducting portion as it branches



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. **secretion ends before ciliation does. Why?** لأنه لو بالأول خلصت الـcilia) مين رح يدفع الـmucus لبرا

Pulmonary lobule vs pulmonary acinus



2ry Pulmonary lobule:
one terminal bronchiole divides into a number of Respiratory bronchioles, alveolar ducts, sacs & alveoli

Pulmonary acinus:
respiratory bronchiole divides into alveolar ducts, sacs, & alveoli

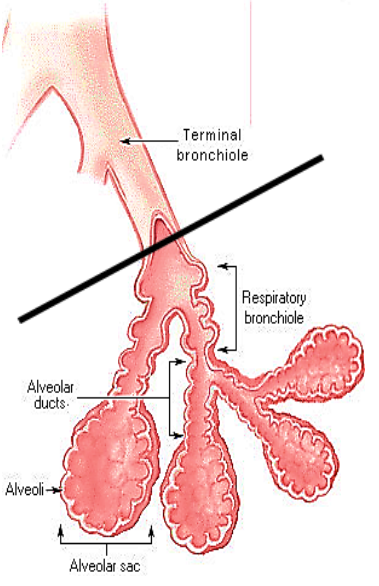
1ry pulmonary lobule : part of the acinus that include alveolar ducts, sacs & alveoli

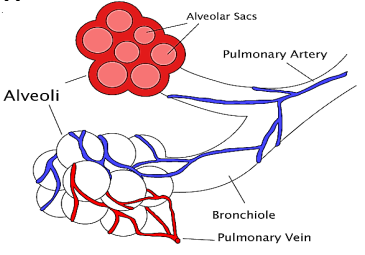
B- respiratory portion

- Is where gas exchange takes place

- Includes:

1. Respiratory bronchioles
2. Alveolar ducts
3. Alveolar sacs
4. Alveoli

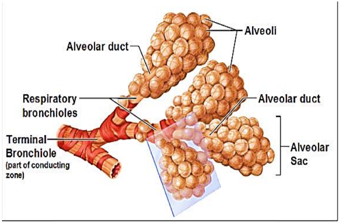




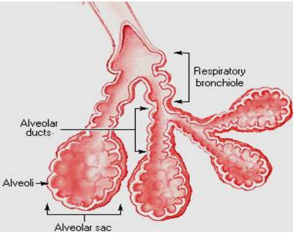
Respiratory bronchioles (RB):

هون إختفت ال smms

- Transitional part between conducting & respiratory portions, still bronchiole but shorter & thinner
- Lined with **simple cubical ciliated e Clara cells with Some alveoli open in its wall**

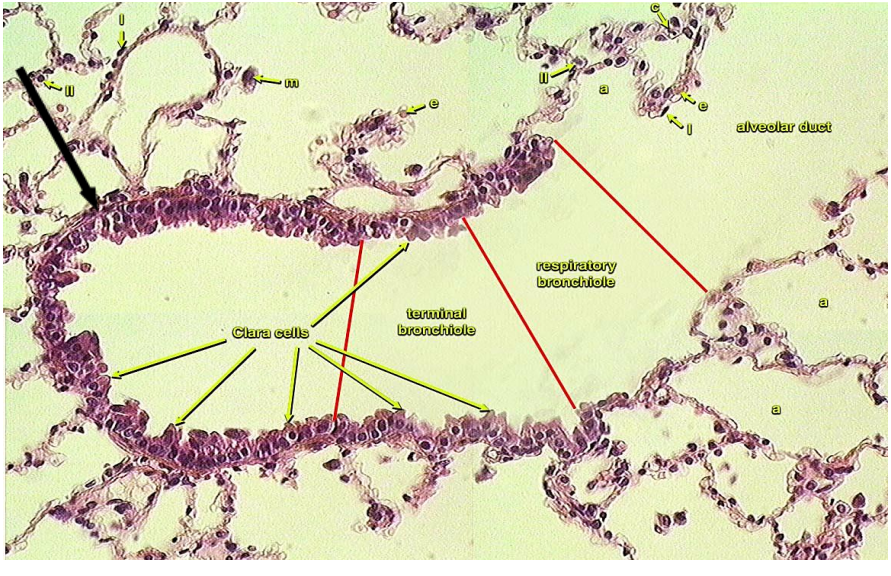


alveolar duct



Alveolar ducts (AD):

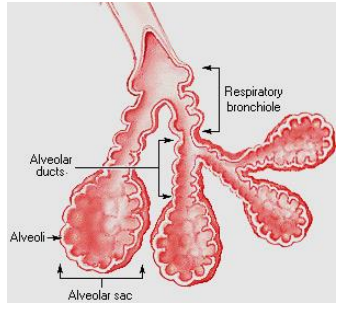
- **Alveoli open along its wall**
- Lined e **squamous alveolar cells** (gas exchange الخلايا اللي بتعمل)
- At the distal end of AD smooth m. disappear, elastic & collagen fibers provide the only support



Section is showing terminal bronchiole and parts of the respiratory portion

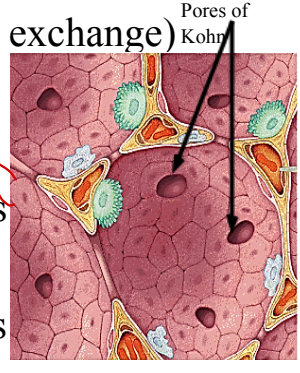
Alveolar sacs (AS):

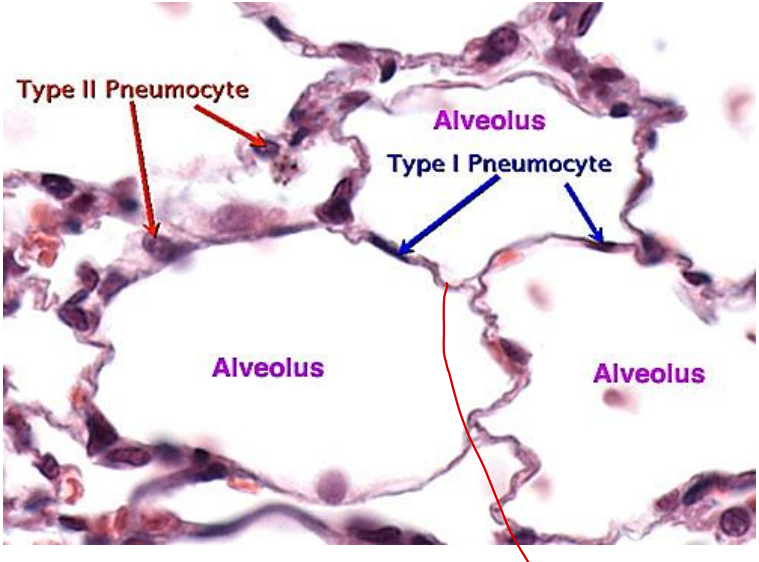
- Group of alveoli opens into common Central space
- Lined e **squamous alveolar cells**



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 ??)
- Lined e **alveolar epith**. formed of **2** types of cells **type I & type II pneumocytes**

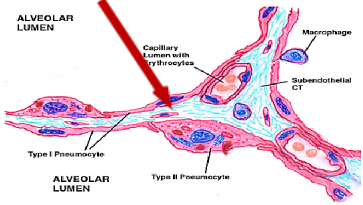




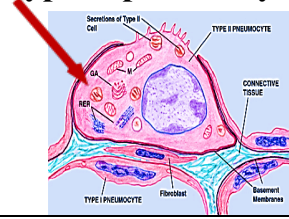
Type I and type II pneumocytes

Lining epithelium of alveoli

Type I pneumocytes



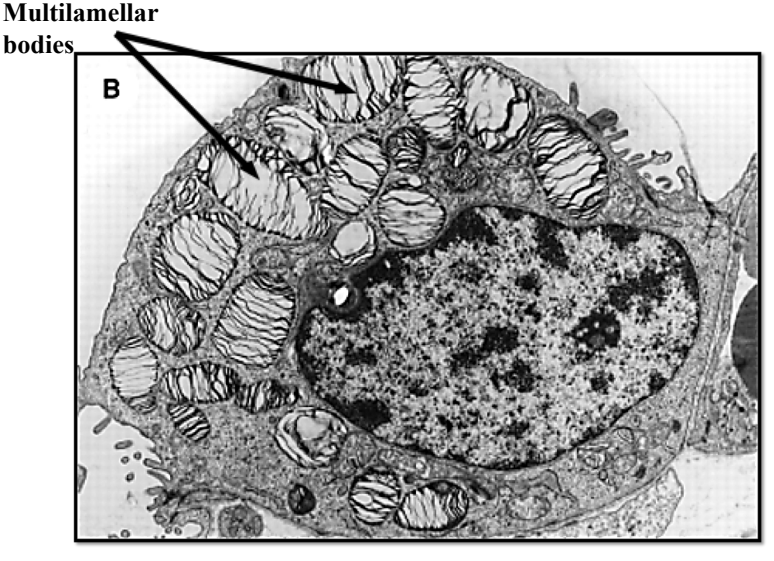
Type II pneumocytes



- Cover **97%** of alveolar surface
- **Flat** simple squamous cells e flat nuclei
- cytoplasm has **few organelles**
- Cells joined together by **tight junctions**
- **Gas exchange** occurs through

- Cover **3%**
- **Cuboidal ce**lls e central nuclei & foamy cytoplasm
- Free surface has **short microvilli**
- Cytoplasm rich in **organelles, multilamellar bodies**
- **Secrete surfactant** (↓ tension & bactericidal)
- Act as stem cells

• Has ACE2 receptors where covid-19 spikes attack

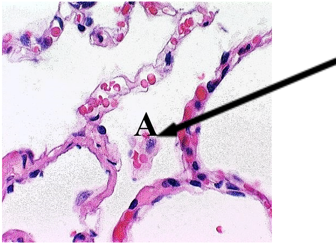


(E/M of type II pneumocyte)

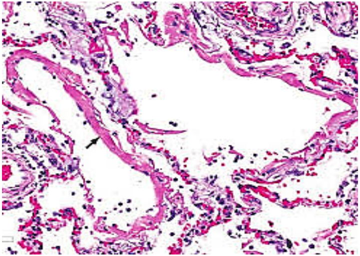
Respiratory Distress Syndrome (RDS): occurs In premature babies because surfactant

appears in last weeks of gestation

Interalveolar septa:



- Delicate walls separate adjacent alveoli
- Have **richest capillary network**
- **Rich in elastic & reticular fibers** (support & prevent over expansion)
- No smooth ms. 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 & Covid - 19



ويشوما أعطيته أكسجين ما رح ينفع لأنه الـ machinary تا الـ alveoli خرب

Alveolar phagocytes

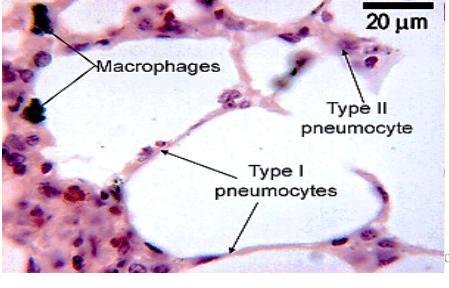
- Blood monocytes → CT in alveolar septa→ lumen of alveoli→ **macrophages**

- **2 types** of alveolar macrophages:

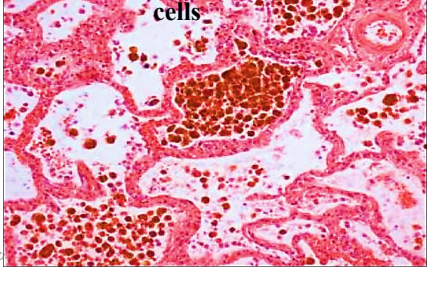
Dust cells: macrophages engulfing dust particles → وحيا لونها أسود

Heart failure cells: macrophages engulfing erythrocytes (hemosidren granules) found in congestive heart failure

Dust

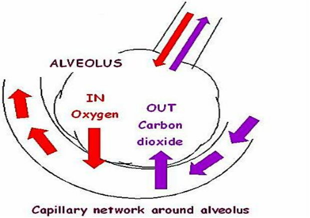


Heart failure cells

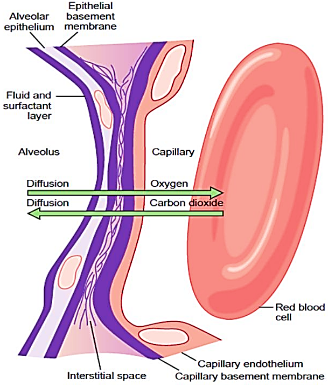


Blood- air barrier (respiratory membrane)

- Its where O_2 & 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

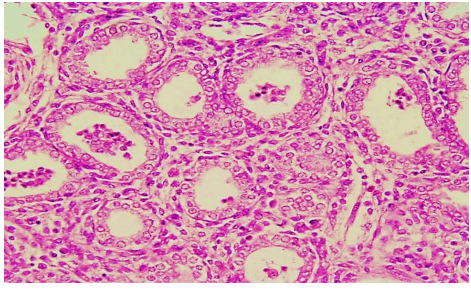
pulmonary capillaries lesi

- Cytoplasm of **endothelial cells** (Continuous type)

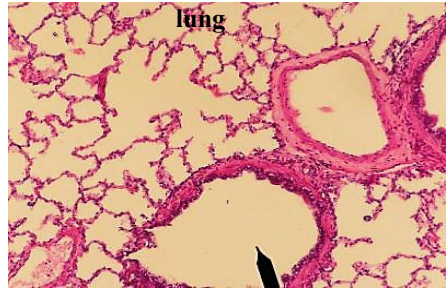
Fetal Lung

- **Lobulation** is clear due to thick CT septa
- Fetal lung **similar to gland** in histological section
- **Alveoli collapsed** lined e simple cubical epith.
- Pulmonary BV are congested
- Whole lung sinks in water

Fetal



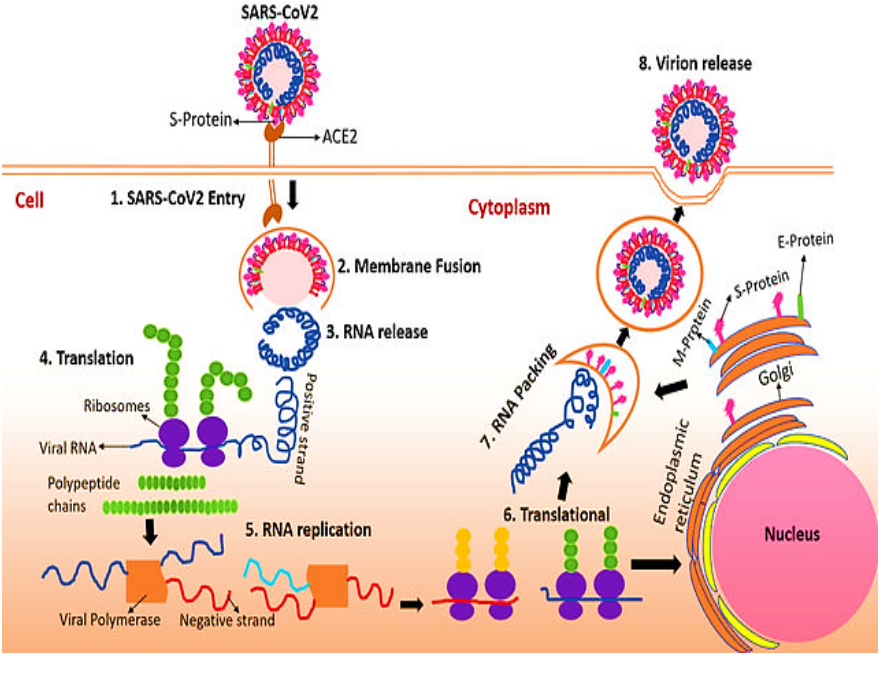
Normal lung



type 2 pneumocyte target on **Covid -19**

- Virus transmitted by respiratory droplets & and also through aerosol (airborne)
- It gets into the mucosa of our mouth , nose & eyes
- The virus attach to cells of our body through ACE2 receptors
- The receptors are located on certain cells of our body (tongue , nose , back of throat, lungs,…..etc

- In the lungs located on type II Pneumocytes
- Virus spikes attach to ACE2 receptors → get inside the cell → copies of its m-RNA → use cell machinery to make its proteins → replicate itself → attack another type II pneumocytes
- this will trigger a cascade of reactions called cytokine storm
- Pneumocytes II will release interleukins IL (1,6,8,29)


SARS-CoV2
S-Protein
ACE2
Cell
1. SARS-CoV2 Entry
2. Membrane Fusion
3. RNA release
4. Translation
Ribosomes
Viral RNA
Polypeptide chains
Positive strand
5. RNA replication
Viral Polymerase
Negative strand
6. Translational
7. RNA Packing
Cytoplasm
8. Virion release
E-Protein
S-Protein
M-Protein
Golgi
Endoplasmic reticulum
Nucleus

- Neutrophils in the blood are attracted to interleukins secreted by pneumocytes type II
- Neutrophils will leave the blood & enter the alveolar space
- Neutrophils in the alveolar space release more chemicals (leukotrienes)
- Macrophages will act to destroy the invader which will lead to destruction of the alveolar wall & endothelial cells → leakage of fluids into the alveoli (alveoli filled with fluid)
- The nucleus will down regulate ACE2 receptors which will cause shift toward formation of more angiotensin II (vasoconstrictor & pro-fibrotic) and less angiotensin 1,7 (vasodilator & antifibrotic) which will cause pulmonary hypertension

- Endothelial damage will lead formation of anti-phospholipids antibodies → these antibodies will trigger the formation of blood clots in the pulmonary capillaries (patients given Blood thinner

- The cytokine storm that develop releases chemokine (Rath) that binds to receptors on CD4 & CD8 lymphocytes → lymphocytes will infiltrate those are of inflammation (that was the reason for low CD4 & CD8 in sever covid-19 patients

- Diffuse alveolar damage + hyaline membrane formation + massive pulmonary embolism → Acute respiratory distress syndrome (ARDS) /Shock and multi-organ failure seen in Covid - 19