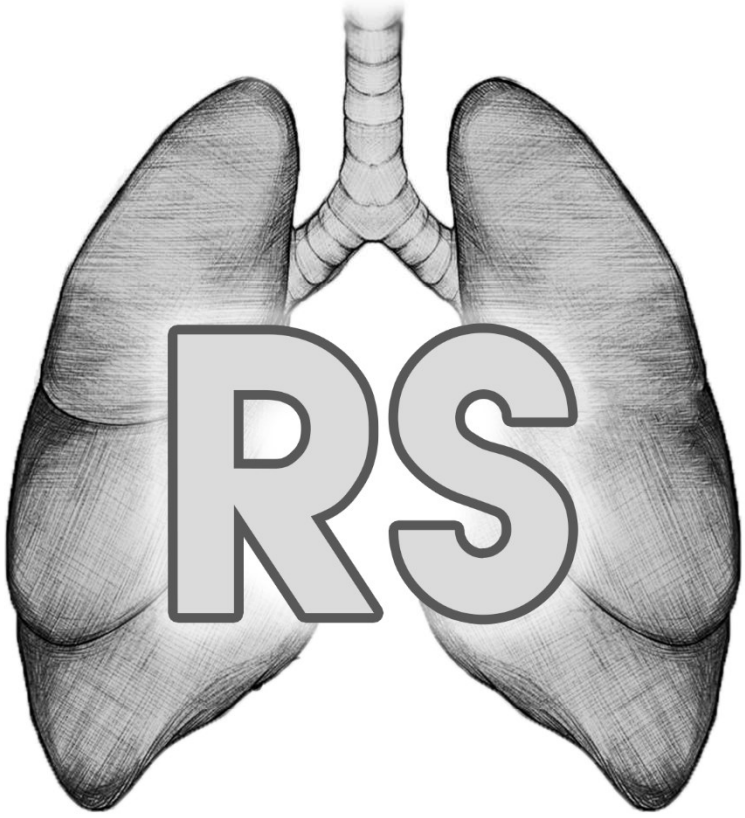

PATHOLOGY

☑ Sheet ○ Slide ○ Handout

Number

2

Subject

Generalized RS diseases & Emphysema

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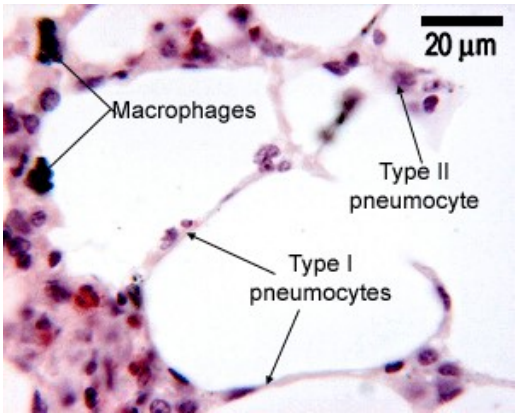
By the name of Allah the Compassionate the Merciful

- **Topics of the sheet:**
  1) Morphology of the ARDS {Adult Respiratory Distress Syndrome}
  2) Generalized Respiratory Diseases {Obstructive vs. Restrictive}
  3) Emphysema

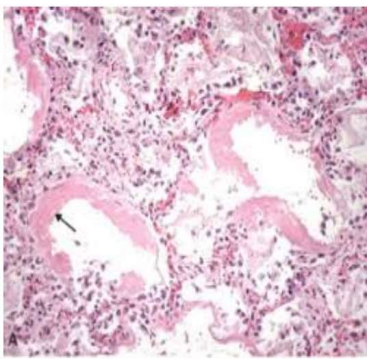
Morphology of the ARDS

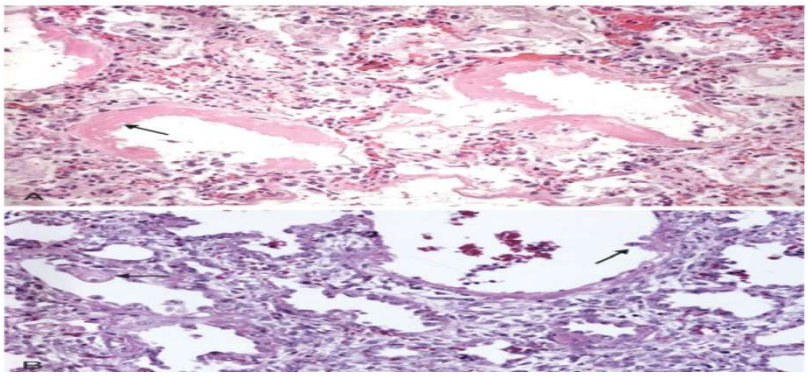
- The epithelium of the alveoli, contains two main types of cells:



  1. type I pneumocytes: large flattened cells - (95% of the total alveolar area) which present a very thin diffusion barrier for gases.
  2. type II pneumocytes (making up 5% of the total alveolar area, but 60% of cells). These cells secrete'surfactant'which decreases the surface tension between the thin alveolar walls, and stops alveoli collapsing when you breathe out & they are the main cells involved in repair.

- In ARDS, under the microscope it's **most prominent characteristic** is the hyaline membrane {which is composed of fibrin-rich edema fluid & remnants of necrotic epithelial cells and some neutrophils}. Also we would find increase in the **type II pneumocytes {increase during the regeneration}.**
- **Important note:**
  The same appearance is seen in the neonatal RDS (NRDS), although they have different pathogenesis!





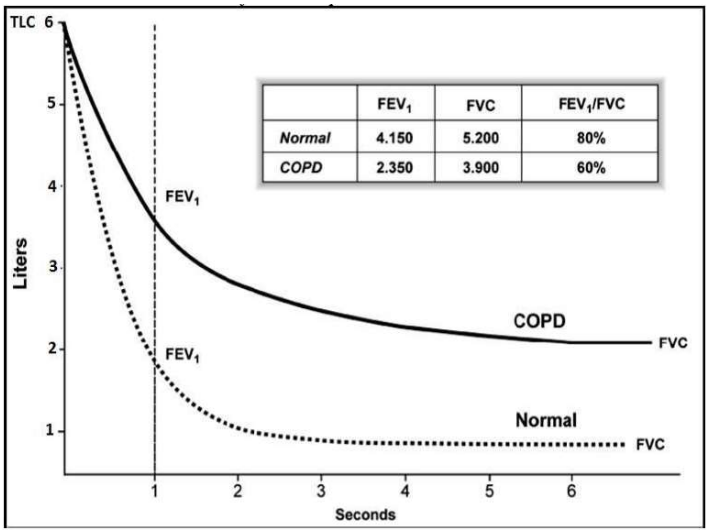
Generalized Respiratory Diseases {Obstructive vs. Restrictive}

- **Obstructive Respiratory Diseases:**
  - ***<u>Generalized "not localized"</u>*** obstruction.
  - The obstruction of the air zone at any level "may affect the respiratory zone or the conductive zone".
  - The obstruction may result either from
    1. **Structural obstruction:** Anatomic airway narrowing.
       e.g.) Asthma, Chronic bronchitis
    2. **Functional obstruction:** Loss of elastic recoil then the lung can hardly exhale the air out.
       e.g.) Emphysema.
  - Note that the obstruction here is narrowing not completely bcz the complete obstruction may lead to a lot of problems ☹!
  - Examples:
    1. COPD {Chronic Obstructive Pulmonary Disease}:
       - ✓ Emphysemas.
       - ✓ Chronic bronchitis.
    2. Bronchial Asthma.
    3. Bronchiactasis.
  - Both the inspiration and expiration are affected but the affect on the expiration is more prominent, Why?!
    The inspiration is an active process {I'm forcing the air into my RS eventhough there is an obstruction, the pressure in the pleura become more negative then that gives the RS the ability to expand, even the obstructed area then the air can enter} but the expiration is a passive process then it would be affected more {the pressure around the obstructed area may be less negative even positive in some cases then less expiration!}.

- It's important to know that not any obstruction would lead to obstructive lung diseases, the obstruction should be generalized not localized that's why cancer for example isn't considered an obstructive disease bcz it's localized!

• Restrictive Respiratory Diseases:

- As the name implies there is something that decrease the capacity of lung expansion ; "stiffness"!
- Main causes of elasticity loss:
  - 1) Chest wall disorders that decrease lung expansion like in muscle paralysis, obesity or pleural diseases {fibrosis or tumor in pleura} although the lungs are completely normal.
  - 2) Interstitial lung diseases: these are divided to acute (ARDS) and chronic (fibrosis, sarcoidosis.. etc).
- NOTE: Pleural effusion would NOT lead to restrictive diseases bcz it's transient and may not be generalized! But like pleural tumors and fibrosis are permanent.
- Trauma is not also a cause bcz it's transient.
- The capacity of expansion is affected then the inspiration is decreased, when the inspiration decrease then logically the expiration decreases by the same amount. (الكمية الي بتطلع حسب الكمية اللي بتفوت!)
- We ask the patient to fill his lung to the maximum then we ask him to empty his lung to the maximum, but as we ask him to empty his lung quickly and forcibly, if we measure what we expire in the first second (called forced expiratory volume in the 1st second (FEV1)) and what we expire in the total (Forced Vital Capacity (FVC)).

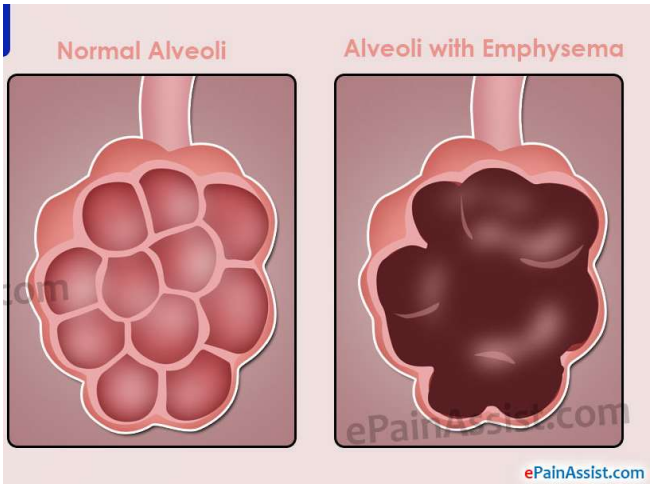


	FEV_1	FVC	FEV_1/FVC
Normal	4.150	5.200	80%
COPD	2.350	3.900	60%

- Measure the FEV / FVC then it should be normally 80%, in the restrictive lung diseases it remains the same,,, How come?!
  Bcz the vital capacity, inspiration and expiration are reduced!
- But in the obstructive diseases, the expiration is affected more than the inspiration {as mentioned before}, then expiration would take more time.
  FVC >>> remain the same. FEV >>> decrease.
  Then the FEV/FVC >>> decrease!

Emphysemas "انتفاخ الرئة":

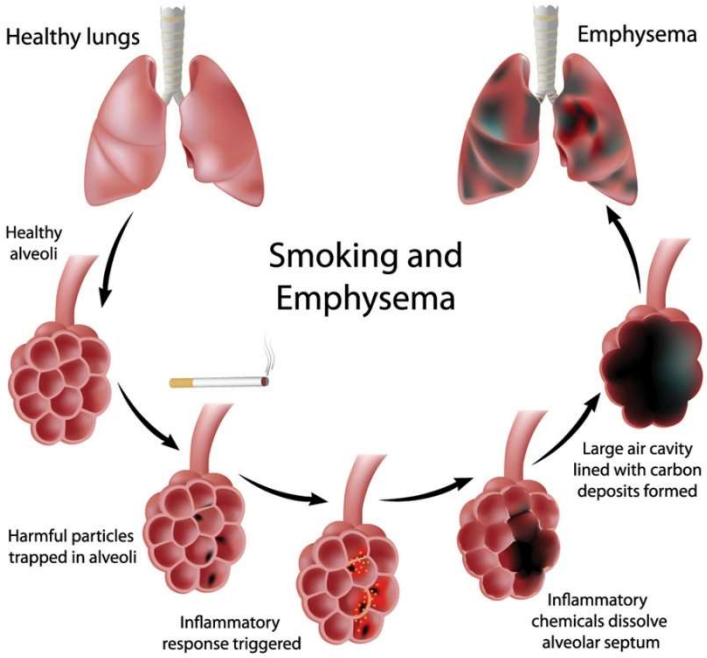
- **Definition**
  - ✓ One of the obstructive respiratory diseases.
  - ✓ Irreversible Destruction of the alveolar wall without fibrosis, resulting in increase the volume of the alveoli and decrease the surface area also decrease the vascular capillaries in the alveoli.



  - ✓ In other words, the emphysema is permanent irreversible enlargement of the alveoli due to the destruction of the alveolar-capillary walls without fibrosis.
    - ⇨ Very very very Important :P
      the destruction is NOT accompanied with fibrosis

- **The etiology of the emphysema: (Causes)**
  1. Toxins (Smoking & air pollutents).
  2. α -1 antitrypsin deficiency.

- **Pathogenesis:**
  - ❖ **How does the smoking lead to emphysema**:
    - Exposure to toxic substances such as tobacco smoke then that would stimulate the macrophages!
    - Macrophages secrete cytokines then stimulate neutrophils, more macrophages & lymphocytes. {it's a chronic process of accumulation}
    - These inflammatory cells secrete:-
      chemical mediators, proteases, elastases, matrix metalloproteinases {MMPs}, ROS.



    - Then that will lead to death of the cells;
      - ROS kill the endothelium of the capillaries, type I and II pneumocytes.
      - Elastases degrade elastin of the walls.
      - MMPs degrade the ECM ,,, ➔ The Wall at whole is lost **without fibrosis (no healing of wounded alveoli!)** then several alveoli merge together and produce one large alveolus. that of course result in losing the surface area!

        There is defect in the anti inflammatory process, as this large damage fibrosis should occur but here no fibrosis, How come?!
        - ➢ Bcz the mesenchymal cells in the alveolar walls don't respond to this damage!
        - ➢ normally they should proliferate, produce TGF-beta & thus ECM, but in the emphysema, these cells die by apoptosis, don't produce ECM {its their main job} and don't secrete TGF-beta which is also the most important fibrogenic agent!

    ⇨ So we can think of emphysema as a problem in repair!

- ❖ Not all smokers would develop emphysema some may develop fibrosis of the lung instead, others may not develop any of these!
    - Depending on the genetic polymorphism (SNPs).
    - Our DNA have about 3 billion nucleotides, we all share 99.9% "the difference is really large it's out of 3 billion"!
    - The variation resulted from a lot of things, one of them is **SNPs** "single nucleotide polymorphisms".
      This genetic predisposition makes some smokers susceptible to develop emphysema, others develop fibrosis and others aren't susceptible
    - in the **emphysema**, they patients have certain polymorphism in **TGF-beta gene** makes the mesenchymal cells unable to **produce the TGF-beta {most important}**, also, polymorphism in the **α -1 antitrypsin gene**. As well as they should have certain polymorphism in **the genes of MMPs {9, 12}**
    - Note: MMP 12 deficiency >>> never having emphysema!

❖ Types of emphysema:

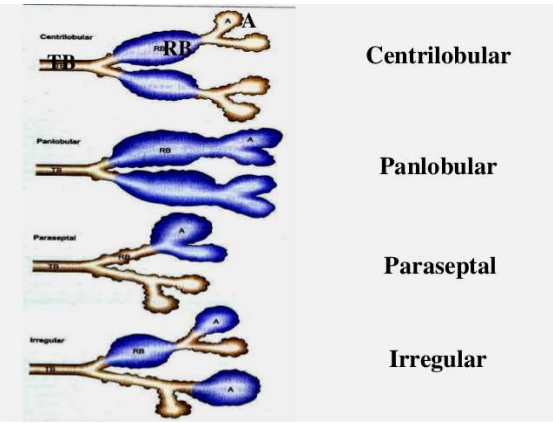
Emphysema only affects the lower airway (respiratory zone), starting from respiratory bronchioles to the alveolar ducts and alveolar sacs {So, emphysema only affects acini}. And according to the affected area, there are 3 types of emphysema:

1. Centriacinar (Centrilobular) Emphysema
    - ❖ At the middle & proximal parts of the acini
    - ❖ Caused by the smoking.
    - ❖ Affect the upper acinar lobules.
    - ❖ Can progress into the panacinar emphysema.

2. Panacinar (Panlobular) Emphysema
    - ❖ Caused by the α -1 antitrypsin deficiency.
    - ❖ Affect the while acinus, but more prominently, the lower lobules.
    - ❖ Occurs around regions of fibrosis

3. Irregular Emphysema:
    - ❖ Occurs around regions of fibrosis.
    - ❖ The most common type, although it's asymptomatic.

4. **Distal Acinar (Paraseptal)** Emphysema:
    - ❖ It involves the distal part of the acinus.
    - ❖ The proximal portion of the acinus is normal
    - ❖ It's risky bcz alveolus may enlarge and become a bullus, these bullae may exploded, leading to pneumothorax .
    - ⇨ So, The most common cause of pneumothorax is **Distal Acinar (Paraseptal) emphysema.**



❖ Signs and symptoms:

- **Dyspnea** usually is **the first symptom** which begins insidiously but is steadily progressive.
- The patient has enlarged alveoli with decrease the surface area and loss of elasticity then the patient inspires normally but labor for expiration, leading to enlarged lung and this changes the shape of chest. **{Barrel-chest}.**
- They inspire more through mouth, becoming more susceptible to infections.
- Sitting forward in a hunched-over position, attempting to squeeze the air out of the lungs with each expiratory effort, then they are called puffers. (as shown in the figure!)

- Weight loss is common and may be so severe as to suggest a hidden malignant tumor, that can be explained by:
  1. They use the mouth for expiration then changing the taste >>> loss of appetite.
  2. Taking a lot of antibiotics also may change the taste and result in losing the appetite
  3. The enlarged stomach can compress the lung and vice versa, then the dyspnea increase with eating
  4. Muscle wasting, so there is mass loss.

- The blood gases {O2 and CO2} >>> Normal! bcz the inspiration is normal then the oxygen is also normal, the problem in the expiration but the patient labor to expire then the CO2 also is normal

- Ventilation perfusion mismatch (V/Q mismatch) >>>
  - ✓ when there is V/Q mismatch then this indicates cyanosis; the blood the enter the blood doesn't take the proper amount of oxygen {not all completely ventilated}
  - ⇨ In case of emphysema alone, the ventilation decreases as well as blood vessels then both the ventilation and perfusion are decreased BUT EVERY COMING RBC GETS VENTILATED! then no mismatch {it's minimal}, then these patients get enough hemoglobin, so they are pink. Also using many muscles for expiration makes the patient even more pink (Pink puffers) (NO cyanosis).

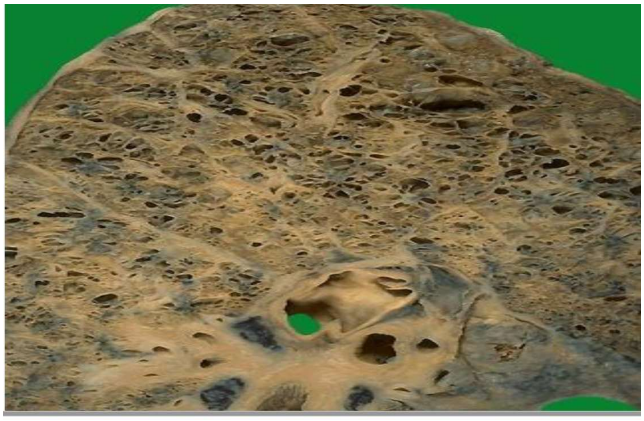
NOTE: These are symptoms of pure emphysema, but COPDs usually accompanied by each other (emphysema + chronic bronchitis);
These patients DO show cyanosis!

✓ Complications:

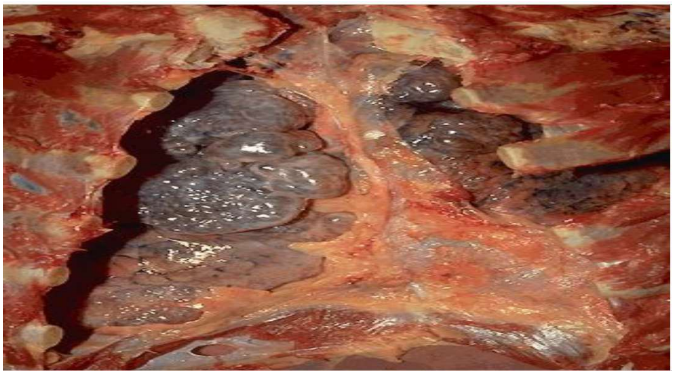
1. Tiredness and fatigue
2. Anorexia and weight loss
3. Infections
4. Cor pulomanle (right-sided heart failure)

✓ Morphology :

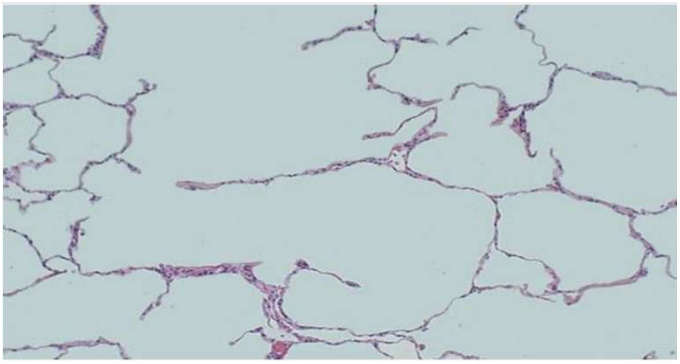
Emphysema is diagnosed by it's MORPHOLOGY (grossly, under the microscope, or even more commonly by X-ray).



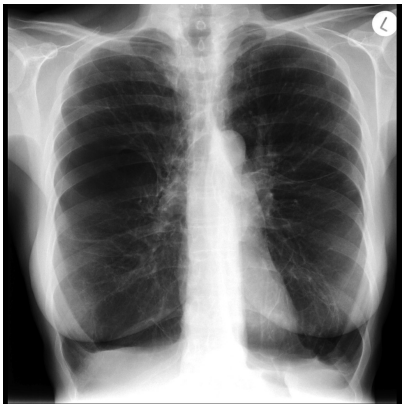
1. Grossly, normally, the alveoli are very tiny that we cannot see them but in the emphysema they are enlarged and obviously seen.



2. This balloon like structure is the bullus, indicating paraseptal emphysema.(It's rupture will lead to pneumothorax)



3. Under the microscopealveolar spaces are very large, NO fibrosis.



4. Chest X-ray >>> enlarged alveoli as circles

Wish you all best of luck ^^