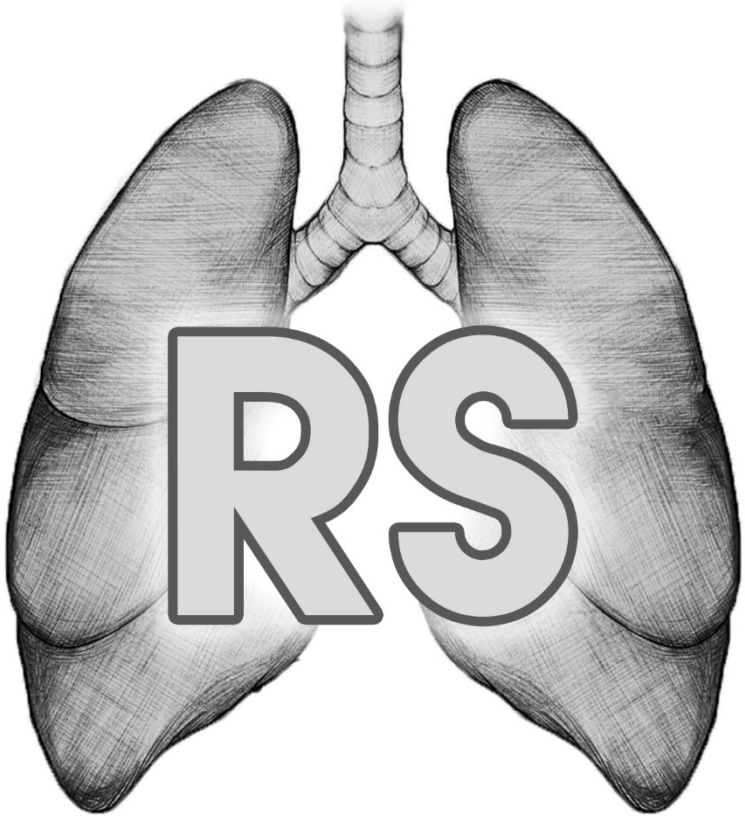

PATHOLOGY

☑ Sheet ○ Slide ○ Handout

Number

1

Subject

Atelectasis & ARDS

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Price:

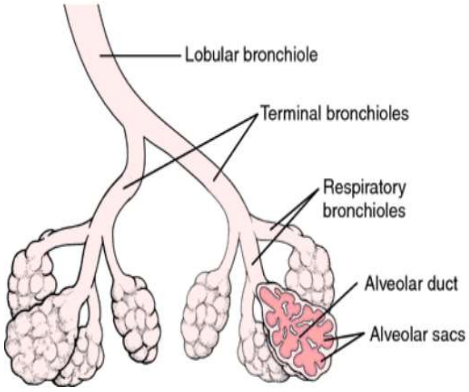
بسم الله الرحمن الرحيم

The main source for studying this course for the sake of exam are the slides. 🤔

Dr.Heyam suggested Robbins' book, since it's really helpful and it'll help you understand the lectures.

In this sheet we are going to discuss three main topics:

1. Basics about the physiology, anatomy and histology of the respiratory system.
2. Atelectasis.
3. Acute lung injury and ARDS (adult respiratory distress syndrome).



❖ **Structure of the respiratory system**

- The respiratory passages (pathway of the air):
Trachea ⟶ main bronchi ⟶ bronchioles ⟶ Terminal bronchioles ⟶ Respiratory bronchioles ⟶ Alveolar duct ⟶ Alveolar sacs.

- What's the main difference "histologically" between the bronchus and bronchioles?
* Bronchi walls contains cartilage & mucus secreting glands * Bronchiole walls lack boths.

- So, when we say that we have a disease that's secreating mucus, it'll be a bronchi problem.
- When we are going to discuss diseases affecting the respiratory system we'll find diseases affecting only the large bronchi, and others affecting smaller bronchioles and some of them affecting respiratory bronchioles and other smaller parts "the most distal part of these passages".
- so anything distal to terminal bronchioles is called an **acinus (**Respiratory bronchioles, Alveolar duct & Alveolar sacs**).**
- The Acinus are important for distribution of some diseases, for example some types of emphysema are called panacinar emphysema, others are called centriacinar emphysema …
- Every 3-5 acini form a **lobule**.

❖ Main function of the lung?
- Gas exchange (that happens in the respiratory zone & mainly in the **Alveoli)**.

Alveoli:

Lined by epithelium that is called pneumocytes.

- Type I pneumocytes (occupies 95% of the alveolar surface)
  - Simple squamous epithelium
  - For gas exchange

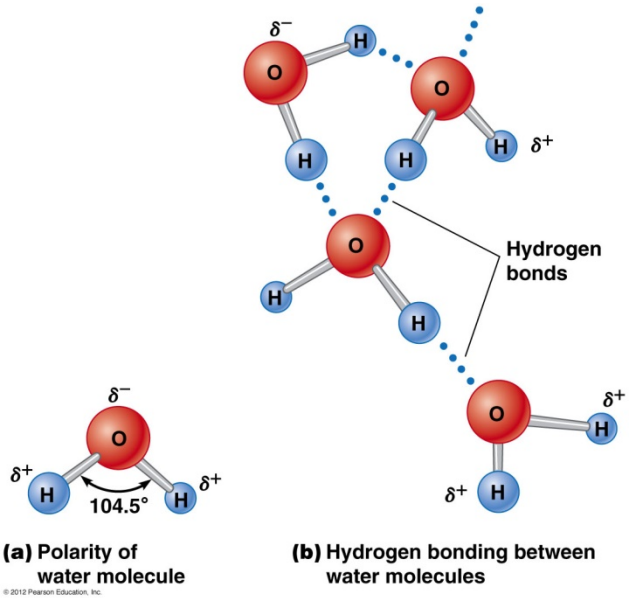
- Type II pneumocytes (occupies 5%) in between type I.
  - Bigger & cuboidal
  - Secrete surfactant & are the main cells involved in **repair** after injury of type I

⇨ **Surfactant:**

- Lowers the surface tension inside the alveolar membrane to prevent them from collapsing during exhalation.
- It's a lipoproteins (part of it is hydrophilic and the other is hydrophobic).

Surface tension:

The alveolus is filled with air and it's lubricated by mucus, this mucus is mainly water (H_2O) and hydrogens in this case are able to make bonds whith oxygens of other water molecules (**Hydrogen bonds)** And that explains why water has (relatively; since H_2O is a small molecule) a very high boiling temprature (100^0C) . Each hydrogen bond on its own is weak but when they are backed together they become relatively strong.



(a) Polarity of water molecule

(b) Hydrogen bonding between water molecules

➔ Water molecules on the lung surface (facing air) are attached to water molecules under them by H-bonds and no bonds with air, and that produces surface tension. Those H2O molecules on the surface are tensed together, producing a thin skin layer.
If the surface tension increases during expiration (reduce the volume of the alveoli, then the radius is reduced too), we have a relation between radius and tension, so if we reduced the radius without changing the surface tension in the alveoli, the alveolus will collapse.
And here comes the function of surfactants, forming bonds with water molecules (those facing the air) reducing H-bonds and thus surface tension is reduced.

❖ Diffusion of gases:

- Oxygen & CO2 exchange happens through diffusion, and simple diffusion depends on:
  1. Concentration gradient.
  2. Thickness of the diffusion membrane.
  3. Surface area.
     Note: the permeability of the membrane is constant.

→ So, in order to maximize the diffusion I need HIGH surface area, THIN diffusion membrane and HIGH concentration gradient. And those are the characteristics of the alveoli:

- We have about 300 million alveoli in our lungs and they make a huge surface area
- Its diffusion membrane is composed of alveolar epithilium (pneumocytes) and endothelial cells at the capillaries' side. "very thin membrane"
- Concentration gradient kept to maximum because of the rich blood supply. *

ATELECTASIS = LUNG COLLAPSE
(الانْخِماص)

- Inadequate expansion of the air spaces.

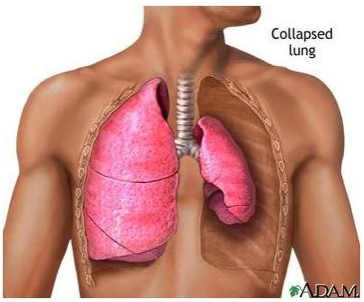
- **<u>Types of atelectasis:</u>**

❖ ***Resorption atelectasis***: (relieved by releasing of the obstructed bronchus)

The alveoli is an air space, so if the bronchus get closed and obstruction of it was induced, we'll end up having no air entering the alveoli, and the already filled air will be resorbed outside through diffusion, so we will have a non-expanded alveoli.

The level of obstruction will determine how much of the lungs will be collapsed; e.g.) small or large part, one lobe or more, etc… (depending on which bronchus is affected).

- Clinical case:
  A 70 years old male (<u>elderly</u>) admitted for sigmoidectomy after being diagnosed with sigmoid adenocarcinoma, he had a history of heavy <u>smoking</u> and <u>chronic bronchitis (compromised respiratory function)</u>. The operation was long; the anaesthetist gave morphine intraoperativly to reduce pain (the doctor by that suppressed respiration and other functions). After the operation the patient had breathing difficulty and his oxygen levels were low. X-ray showed lung infiltrate diagnosed as atelectasis.



- The above underlined signs are risk factors for atelectasis post operatively:
    1. Elderly.
    2. Compromised respiratory function.
    3. Smoker.
    4. Lung disease.
    5. Long term operations “since the patient is breathing through the tube; he’s not breathing normally; he’s not getting rid of mucus”.
    6. Morphine. (causes depression of the respiratory function)

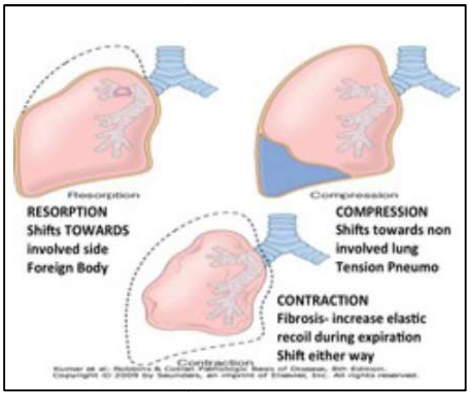
- Obstruction by:
    a. Mucous or mucopurulent plug; in cases of bacterial infection, cystic fibrosis, bronchial asthma, mucus-secreting tumor, post-operative (most common cause).
    b. Foreign body.
    c. Tumor.

❖ **Compression atelectasis:** (relieved by removing of the compression factor)

1. **Compression by the diaphragm**:
   In the above mentioned patient who was intubated for a long time is that the diaphragm will be raised (its movement during expiration and inspiration “up and down” is lost), and it can compress part of the lungs; causing atelectasis.
2. **Fluid**: Plural effusion “anything between the plura and the lungs will cause compression”.
3. **Pneumothorax**; accumulation of air between the pleura and the lungs and it’s caused by:
   a) When the alveoli itself expands to an abnormal level, its wall won’t be protected by collagen or elastic fibers, so it might <u>spontaneously</u> rupture (not traumatic).

   b) **Iatrogenic (خطأ طبي)** ; if your patient was having Haematothorax for example and you tried to save him by inserting a tube to drain the blood, if you pushed the tube hard you might perforate the alveoli and the air will get out causing Pneumothorax, consequently atelectasis.

   c) Trauma; for example, perforating the alveolus by a punctured rib.



4. **Haematothorax**; accumulation of blood between the pleura and the lungs caused for example by <u>trauma</u>.

P.S.) Points 2, 3 & 4 are all within the pleural cavity.

❖ **Contraction atelectasis: (The only irreversible type!)**

Fibrosis of the lung tissue. So, it can't open or close.

It's not a must that the whole lung will be fibrotic, it could be only a segment of it.

✓ **What causes lung fibrosis?**

- Ischemia - it's really uncommon in the lung since it has rich blood supply.
- Inflammation (commonly casued by Asbestosis).

Adult respiratory distress syndrome

متلازمة الضائقة التنفسيَّة (ARDS)

We have Neonatal respiratory distress syndrome (NRDS) caused by primary deficiency of surfactant; premature babies have no surfactant ➡ the lungs will collapse.

- It affects adults.
- Respiratory distress: the patient is unable to breath.
- It can be a complication of many different diseases.
- Acute lung injury "severe injury of the lungs" includes a spectrum of bilateral (both lungs) pulmonary damage of capillary endothelium & alveolar epithelium.
- ARDS patients are usually hospitalized (having severe problems) and they are having severe damage to the lungs, this indicates that ARDS can't be caused spontaneously and to a healthy person.

❖ **Causes of ARDS:**

Swine flu (انفلونزا الخنازير) patients die secondary to complication by ARDS.

➢ **Direct lung injury**

A) Common causes:

- Pneumonia (most common cause)
- Aspiration of gastric content

B) Uncommon cause:

- Pulmonary contusion.

➢ **Indirect lung injury (secondary to a systemic damage)**

A) Common causes:

- **Sepsis** (most important indirect cause)**;** bacteria is inside the blood and it can reach any tissue in the body including the lungs ➡ Damage the lung.
- **Severe trauma with shock & multiple blood**
- **Hypovolemia** ➡ certain ischemic effects ➡ Damage the lung.

C) Uncommon cause:

- **Acute pancreatitis**
- **Kidney failure**

❖ The acute consequences of ARDS

The alveoli are lined by epithelial cells "pneumocytes", and the blood vessels are lined by endothelial cells. This endothelial-epithelial barrier will prevent the fluid in the blood from moving toward the alveoli. So, if this barrier was damaged (damage of the endothelial cells and/or the epithelial cells), the fluid will move according to its concentration gradient from the blood to the alveoli via osmosis. So, the patient will have difficulty in breathing, and he will feel like he's drowning in the water. So, even if we have oxygen in outer air, the patient can't utilize it since the diffusion capacity gets disrupted. (The alveoli is filled by fluid)
Those patients are refractory to oxygen (it's even one of the modalities of treatment, since our problem is not the oxygen shortage, the problem here is the disturbed barrier allowing fluid to enter and this fluid doesn't allow exchange of gases).

So even if you have O2 there's no enough exchange

❖ Pathogenesis 🤔

- If we have any damaged tissue (cell injury), Alveolar Macrophages will sense this cell injury through its receptors, and then it will release inflammatory factors.
- The first inflammatory factor to be released during the first 30 minutes of the severe injury is **IL-8**, it's a very potent chemotactic agent, it'll attract neutrophils. The alveoli will get filled by neutrophils; it could induce further damage through initiating oxidative burst by making oxygen radicals "ROS" and releasing proteases and other cytokines and mediators (mediators attack everything), and that will cause inflammation and consequently further damage to the epithelial cells (Type I & II pneumocytes) & endothelial cells; so the whole barrier will be disturbed.

- However, as we have inflammatory mechanisms we have anti-inflammatory mechanisms too. The oxygen radicals can be scavenged by antioxidant mechanisms. In addition to that we have anti-proteases such as α1-antitrypsin secreted by tissue surrounding the alveoli. Some cytokines are anti-inflammatory such as IL-10.

The pulmonary infiltrates with fluid in acute lung injury are caused by damage to the alveolar capillary membrane, rather than by left-sided heart failure, so ARDS is an example of *non-cardiogenic pulmonary edema (effusion).*

- Macrophages, neutrophils & the tissue itself can start an anti-inflammatory process.
- So, we have inflammatory and anti-inflammatory mediators working at the same time;
  ➔ It's the balance between proinflammatory & anti-inflammatory mediators that will determine the severity of ARDS.

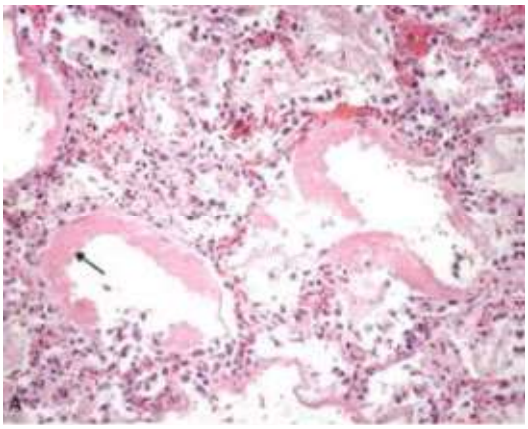
❖ Clinical Manifestations (bilateral disease)

1. Severe dyspnea (due to congestion of fluid/pulmonary edema).
2. Low PO2, patients are refractive to oxygen therapy. (hardly responsive)

❖ **Morphology:**

- Under the microscope the lung will look heavy and congested.
- The alveolus is surrounded by fibrin-rich fluid with neutrophils and neutrophilic debri that will form a membrane "red membrane" and this forms a hyaline membrane that looks exactly the same of the hyaline membrane of respiratory distress of new born. (ARDS aqnd NRDS have similar morphology but different pathogenesis).

⇨ **Hyaline membrane is most characteristic for RDS.**



❖ **Outcomes:**

- Mortality rate of 50%. (It was 60% but with better treatments it decreased to 40%).
- The majority ends with fibrosis (remember: It's a severe injury).
- Minority will recover completely, but they need around 6-12 months for full recovery.

❖ **Treatment:**

- Supportive treatment. (corticosteroids → antiinflammatory)
- We put the patient in the ICU.
- Intubation; in order to supply him with oxygen with a higher pressure (eventhough the patient is refractory to oxygen therapy, but we cannot totally deprive him from oxygen.)
  * Keep in mind that if the oxygen was under a very high pressure it'll cause Barotrauma, so you need to balance between high and low pressure oxygen doses.
- ECMO **(Extracorporeal** "outside the body" **membrane oxygenation) we use it as a last line therapy;** in this case I take the blood outside the patient's body, and we apply it on a diffusion membrane and we do oxygenation "like renal dialysis to some extant".

The End
Sorry for any mistakes.