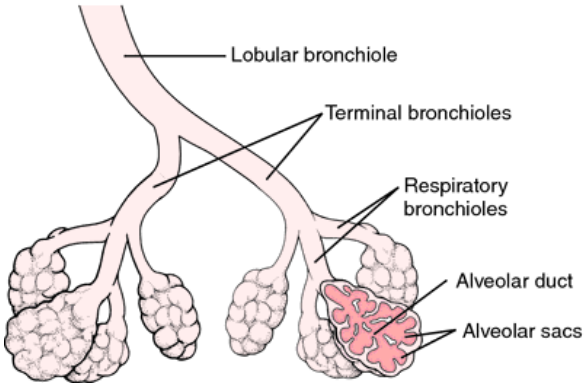
Today lecture we will discuss 3 subject :

1- Structure and function of the respiratory system
2- Atelectasis
3- Adult respiratory distress syndrome

What is the structure of R.S ?

R.S it's a pipe , this pipe start as large trachea and then branch to bronchus (large bronchi , small bronchi and then become smaller which we called them bronchioles) then it end as alveolar sacs (this is the terminal part of bronchiole alveolar system) .



The lobular bronchiole (we call it lobular because it give a lobule) , lobule means several asinie

What is the asinus ? (if we follow the pic from down to up)

The end or the last sac is called alveolus and this alveolus have alveolar sac and then a bronchiole called respiratory bronchiole , the respiratory bronchiole and all the alveolus called asinus .

Simple asinus together are called lobule , so we need to know the different between asinus and lobule :

- **Asinus is anything under the terminal bronchiole and it consists of respiratory bronchioles and alveoli**
- **Lobule is a simple asinus usually 3-4 asini**

The alveoli is the site for gas exchange , there is no gas exchange in the bronchiole or trachea the only site for exchange is alveoli .

The alveolus very rich in blood supply it has arteriole and venule , and the exchange of O2 and CO2 occur in the endothelium and epithelium of alveolus .

Within (inside) the alveolus there is air and cell which is macrophage (dust cell) .

The lining epithelium is type 1 and type 2 pneumocytes (they line the alveolus not inside it).

Type 1 is a thin epithelium cells which line the alveoli and form a barrier , why we need a barrier? If there is no barrier the fluid inside the blood will go to alveoli and the exchange of gases will be impaired , so we need barrier to prevent fluid from entering the alveoli (it important note to remember when we talk about ARDS) .

So type 1 pnumocytes are the majority , they consist about 95% , and they act as a barrier .

Type 2 pnumocytes produce surfactant , they're only 5% , also they have other function which is division for regeneration and repair .

Type 1 >>> 95% >>> barrier

Type 2 >>> 5% >>> produce surfactant and repair

We said that alveoli is the site for gas exchange , exchange of gas occur due to diffusion , diffusion depends on :

1- Surface area
2- Solubility
3- Pressure gradient
4- Thickness of membrane
5- Molecular weight

The alveoli have very large surface area , this surface area is almost as large as half of tennis-court ; they also rich in blood supply and this important for keeping the gradient for O2 and CO2 ; the membrane is very thin so the diffusion is excellent , so any thing that effect these will cause disease in diffusion .

lets go to **atalectasis** , this is the first disease about the lung , what atelactasis means ?

Lung collapse

What can case atelectasis ?

1- An obstruction at any point , the area supplied by that point will not be aerated so this area will collapse.

The cause is obstruction and we call that >>> resorption atelectasis

2- Other case that if we have something that compress the lung , here the problem is not in the lung itself but from outside , the lung is surrounded by pleura , there is very little fluid in pleura for lubrication , now if this fluid increase it will compress the lung .

3- The third thing if we have fibrosis at certain area the lung will contract and will not be aerated .

Again 3 types of atelectasis :1- resorption caused by obstruction 2- compression 3- contraction caused by fibrosis

1- **Resorption atelectasis :**

Caused by obstruction , what are the causes of obstruction :

1- **Mucus >>> the most important case**
2- Tumor
3- Foreign body

What are the causes of mucus that cause obstruction ?

1- Cystic fibrosis
2- Chronic bronchitis
3- Asthma
4- **Post-op** <<<< it's very important cause , people after operation can't get rid of mucus because they can't cough (that's why we do physiotherapy)

Sum up by Dr : the resorption atelectasis caused by obstruction and mucus is the most common cause of obstruction and it happens after operation due to accumulation of mucus .

2- **Compression atelectasis :**

It's something accumulated in pleura and compress the lung like :

1- **Fluid** due to inflammation , injury , liver problem , heart problem , cardiac edema

We call the fluid that accumulate in pleura >>> **pleural effusion**

2- **Blood** >>> **haemothorax**
3- **Air** >>>> **pneumothorax**

All these three can cause compress atelectasis

3- **contraction atelectasis :**

Caused by **fibrosis**

Now is atelectasis reversible ? it depends on the type

Contraction atelectasis <<< irreversible

The others are <<<< reversible (Dr said there is Q in exam about atelectasis)

ARDS : adult respiration distress syndrome

Acute lung injury can progress to ARDS

let's start talking about acute lung injury :-

- The lung its susceptible to be injury by disease in the lung itself or by systemic disease , if there is sever disease in the lung itself it can be effected by inflammatory mediators , which is life treating , that's what acute lung injury is .

- It has to be **bilateral pulmonary damage** >> to be acute lung injury it needs to be **bilateral** (as in unilateral damage the normal lung will compensate for the damage one thus no acute lung injury) .

- **Endothelium and epithelium damage** >> the **barrier is lost** (which is the main problem) , if the chemical mediators and the inflammatory cells cause damage to endothelium or epithelium or both this will cause loss of barrier and the fluid in the blood will go to alveoli and cause INSUFFICIENCY .

- Its caused by direct or indirect injuries .

- Clinically defined as acute dyspnea , hypoxemia (which not response to oxygen supply) , bilateral pulmonary infiltrate **without** primary heart disease .

- **Acute lung injury can progress to ARDS .**

  The most 2 common direct cause :
  1- Pneumonia
  2- Aspiration

  The most 2 common indirect cause :

  1- Sepsis
  2- Sever trauma with shock

(Dr said this might be a Q in exam so it important)

ARDS clinical features :

1- Respiratory insufficiency
2- Cyanosis >> because there is no oxygen
3- Hypoxemia
4- Can be progress to multisystem organ failure and cause death

What is the pathogenesis of this disease ?

- We said impaired of barrier which cause the fluid to move to alveoli and impair gas exchange .

- Also it's caused by inflammatory mediators that cause damage to epithelium , these inflammatory mediators like (cytokines , platelet aggregation factor , kinin system etc ..)
- **The first one to be released or secreted is IL-8** , just within half hour of injury the IL-8 is released .
- IL-8 will cause chemotaxis and activation of neutrophil , the neutrophil will come to lung , that's why in histology we see a lot of neutrophil inside alveoli , and these neutrophil will cause more damage to endothelium and epithelium and lose of barrier .
- IL-8 synthesis from alveolar macrophage
- Cytokines are the most important mediator mainly IL-8 , IL-1 , TNF .

(Dr ask which cytokines are anti-inflammatory >> IL-10)

- Cytokine cause inflammation and also up-regulation of the anti-inflammatory mediator to make balance .
- What are anti-inflammatory mediators (IL-10 , TGF-b , anti proteases e.g. a1 antitrypsin , antioxidants) .
- All these are up regulated to reduce the effect of inflammation , **it's the balance between the inflammatory and anti-inflammatory which will determines the degree of injury .**
- So what is the outcome of ARDS :

- It can be resolved (rare)
- It can end as fibrosis or death (60%, in USA reduced to 40%)

What is the morphology of ARDS :-

1- Due to fluid in lung it must be **heavy**
2- **Airless** because there is no gas exchange
3- Firm
4- **Red** due to hemorrhage

Under the microscope what we see ?

1- Neutrophil inside alveoli
2- Capillary congestion
3- Hemorrhage
4- Intra-alveolar edema
5- Interstitial edema
6- Necrosis
7- **Hyaline membranes >>> this is the hallmark of ARDS** .

Hyaline membranes consist of edema rich in fibrin and necrotic cell

Now if someone has ARDS what is expected to happen , as we said he might die 40% , but who survived what happens to them , they might resolve completely which is rare and it will take from 6-12 months , the majority of survival will have long term problem caused by organization .

What we mean by **organization** ? it's **<u>healing by fibrosis .</u>**

So the majority will have healing by fibrosis , the edema fluid will be reabsorbed and then regeneration of endothelium and epithelium , but it's incomplete regeneration due to fibrosis , and the fibrosis cause thickening of alveoli wall and diffusion will be effected (respiratory insufficiency) .

Again long term survival will have **organization** :

- **Increase in type 2 pneumocytes** (responsible for repair and regeneration)
- **Fibrosis in alveoli** (cause thickening in alveoli wall) and end as respiratory insufficiency.

Clinical features :

- 80% will develop ARDS within 72 hours of the insult << mean if someone has sepsis , and this sepsis is severe and is not treated , so within 3 days will develop ARDS .
- 60-40% will die .
- Treatment : anti-inflammatory might reduce the symptoms but the most important thing is to support the lung (to give it chance to heal itself) .
- Poor prognosis is associated with :
  1- Old age
  2- Sepsis
  3- Multisystem failure

Outcome of ARDS :

- The survived ones end with diffuse interstitial fibrosis
- The interstitial is between alveoli and blood vessel
- What interstitium consist of ? **Collagen and elastin**

- Elastin is very important in lung because the alveoli take the air and release it again so it needs elasticity for that , so if we have disease that affect the elastic fibers it will reduce the elasticity and case insufficiency of ventilation .
- These patient , the fibrosis is irreversible and they will suffer from respiratory insufficiency for rest they life .
- Fibrosis can cause to them other disease which is >> contraction atelectasis
- Now if they not have fibrosis they need from 6 to 12 months to go bake to normal function

(Dr said there're 2 Qs in exam one about atelectasis and the other about ARDS)

Sorry for any mistakes

Done by : mohamed alaqra