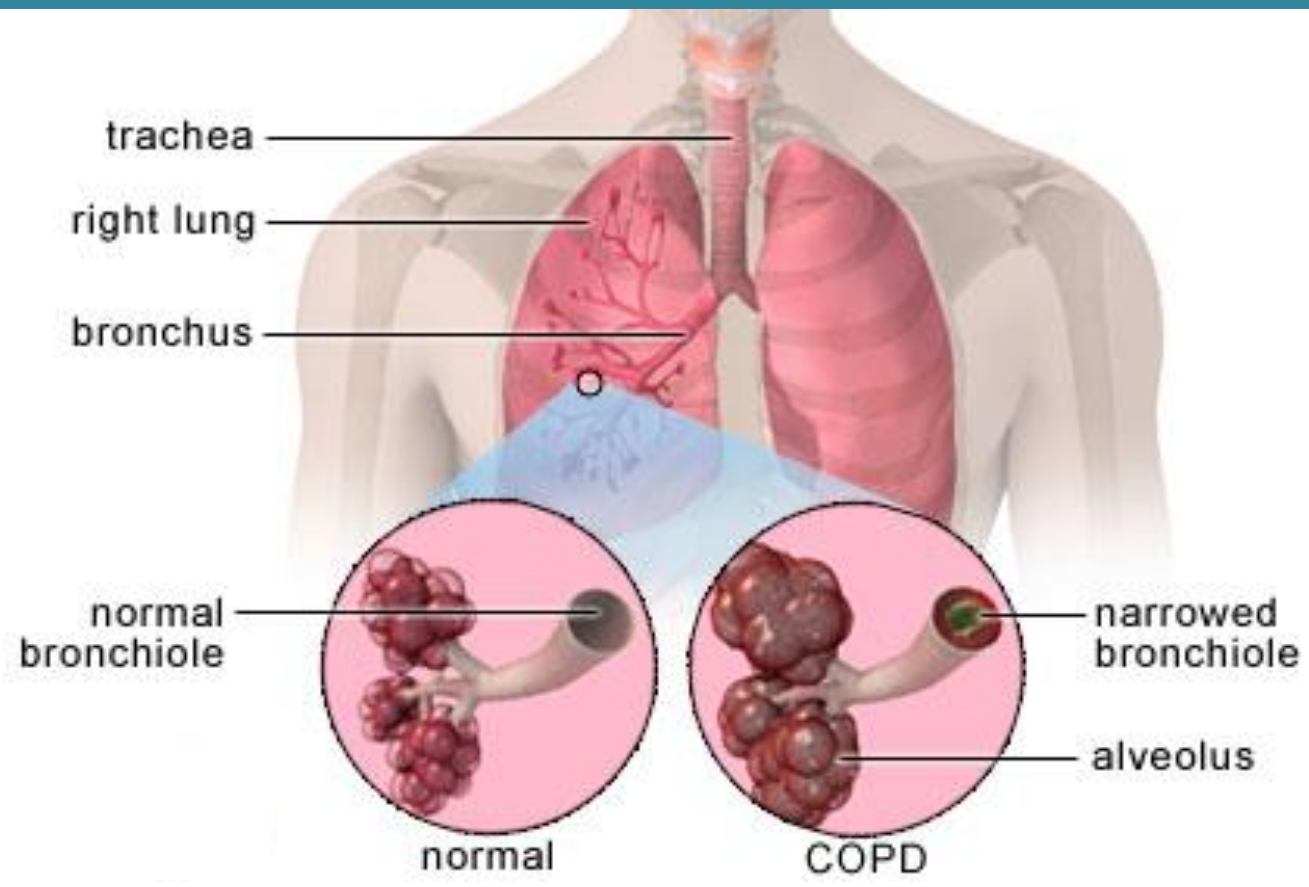

Lecture Two

COPD Part 2

Pathology and pathogenesis of:

Chronic Bronchitis, Emphysema** and **Bronchiectasis

*432 **Pathology** Team*

Done By:

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***Ammar** Naji, **Ibrahim** Abunohaiah*

Respiratory Block

B- Chronic Bronchitis

Chronic bronchitis is a **persistent productive** cough for at least 3 consecutive months in at least 2 consecutive years.

NOTE: productive cough is a cough with sputum.

Symptoms of chronic bronchitis:

1- **Productive cough.**

2- **Dyspnea.**

Clinical Presentation:

Most if not all of the Patient with Chronic bronchitis has Emphysema

Chronic bronchitis is clearly linked to lung Emphysema because (etiology); the patient come pink (pink puffer) or blue (blue bloater) depending on whether there is hypoxemia or not.

He is always puffing (ينفخ) and he leans forward (ينحني للأمام) because he is using his accessory muscles to get rid of the air.

In blue bloater (hypoxemic patient) the color is changed mostly in the lips and some times in the eye.

Etiology:

Chronic bronchitis is clearly linked to **cigarette smoking** and is also associated with air pollution, infection and genetic factors.

The symptoms becomes worse with flu

In severe cases it may lead to Cor Pulmonale:

Cor Pulmonale is a Heart failure from pulmonary lung disease is associated with right ventricular failure. Its pathogenesis is due increasing the pressure of the pulmonary circulation (caused by fibrosis of the lung and inflammatory reaction) → increase load in the right ventricle → the right ventricle dilate → once we have right, we get left ventricle dilate as well → heart failure.

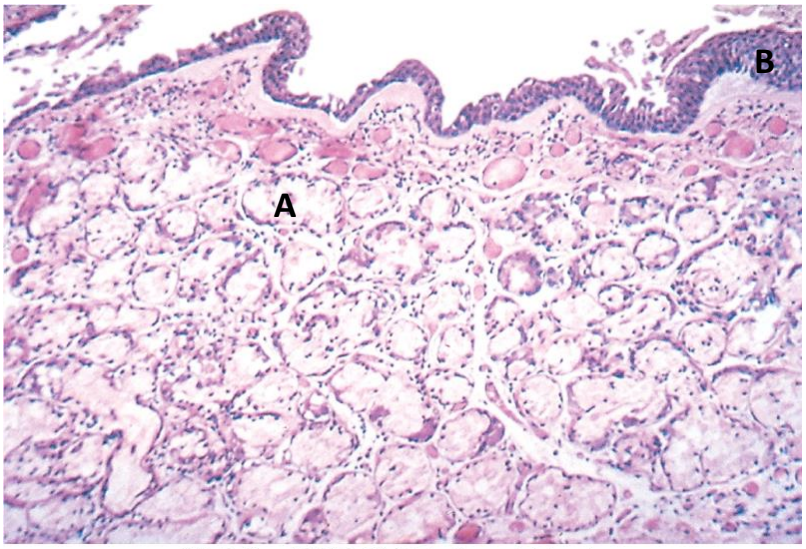
NOTE: (It can happen also in chronic asthma, Emphysema)

Pathology:

Biopsy (rare used)

Typical characteristics include:

1- **Hypersecretion** of mucus due to:
2- Marked **hyperplasia of mucus-secreting sub mucosal glands.**



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NOTE: If we measure the ratio of bronchial gland to the full thickness of the bronchial wall it will be abnormal (Reid index).

PICTURE: *The lumen of the bronchus is above. Note the marked thickening of the mucous gland layer (A) (approximately twice normal) and squamous metaplasia of lung epithelium (B).*

The mucus in **chronic bronchitis** is green or yellow because it's **purulent** (has pus).

Inside the lumen of the bronchus there is: (pus, mucus neutrophils, cellular debris bacterial colonies …)

The patient come **pink** (pink puffer) or **blue** (blue bloater) depending on wither there is **hypoxemia** or not.

He always **puffing** (ينفخ) and he **leans forward** (ينحني للأمام) because he is using his **accessory muscles** to get rid of the air.

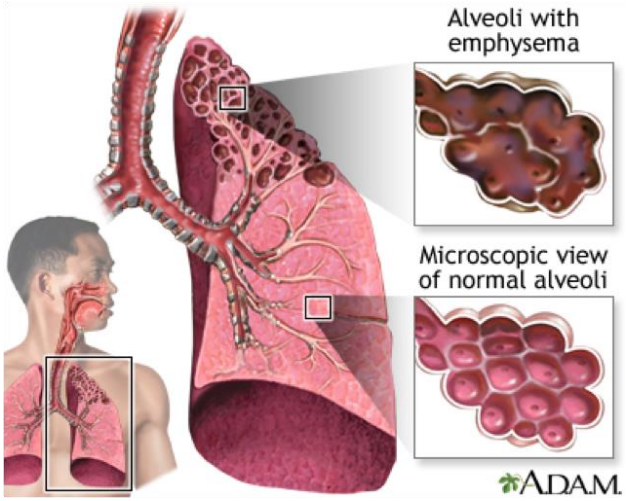
In blue bloater (hypoxemic patient) the color is changed mostly in the lips and some times in the eye.

Asthma	Chronic Bronchitis
• Late stages increase in the number of goblet cells.	• The mucus glands increase and thicken.

Summary:

Chronic Bronchitis: is defined as persistent productive cough for at least 3 consecutive months in at least 2 consecutive years. Cigarette smoking is the most important underlying risk factor; air pollutants also contribute. Chronic obstructive component largely results from small airway disease (chronic bronchiolitis) and coexistent emphysema. Histology demonstrates enlargement of mucus-secreting glands, goblet cell metaplasia, and bronchiolar wall fibrosis.

C- Emphysema (pulmonary emphysema) (إنتفاخ الرئة)

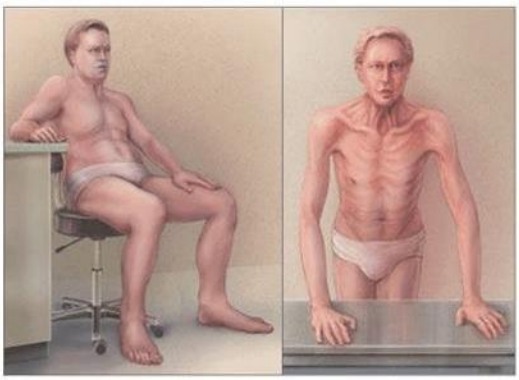


Emphysema is an abnormal dilatation of the airways which are distal to the terminal bronchiole (affect respiratory bronchiole, alveolar duct and alveoli (acinus of the lung) associated with destruction later on of pulmonary acinus or the affected areas within the acinus (respiratory bronchiole, alveolar duct and alveolus).

Causes of Emphysema:

1- **Hereditary alpha 1 antitrypsin (an enzyme) deficiency:**
   Rare cases present early in the patient life. Usually, they come with liver and lung problems related to congenital emphysema.
2- **Cigarette smoking or live in polluted area (the majority of patients):**
   Usually, they have emphysema and chronic bronchitis at the same time.

Clinical presentation:



1- Patient come with **hyper-inflated chest** (barrel chest), lungs are over inflated with air. Increased anteroposterior diameter of the chest (Barrell chest); increased total vital capacity; hypoxia, cyanosis and respiratory acidosis.
2- Patient is also present with dyspnea, sometimes appears blue bloater or pink puffer. Also, they may have symptoms of chronic bronchitis (productive cough and secondary heart failure in advanced case).

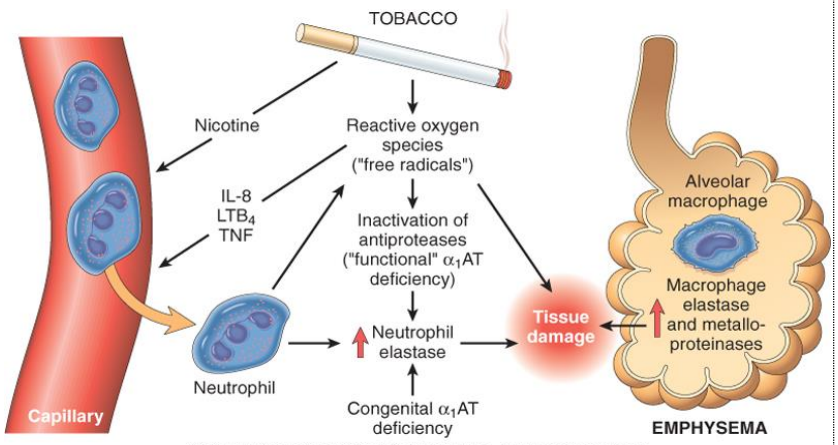
Pathogenesis:

Emphysema may result from action of **proteolytic** enzymes such as elastase on the alveolar wall. **Elastase** can induce destruction of elastin unless neutralized by the anti-proteinase-anti-elastase activities of α1-antitrypsin which can be deficient in cases of emphysema.

As mentioned: It can be **congenital** (born with α_1-AT inactive), or **acquired** (especially in smokers).

Congenital: the patient doesn't have elastase inhibitor → elastase destroys the wall of the acini (acinus), respiratory bronchiole and alveolar duct → emphysema.

Acquired (Smokers): irritating the lung and bronchial tree (by the smoke) → inflammatory reaction → migration of neutrophils and macrophages to inflamed site → releasing of elastase → destruction and dilatation of alveolar wall → **Emphysema**



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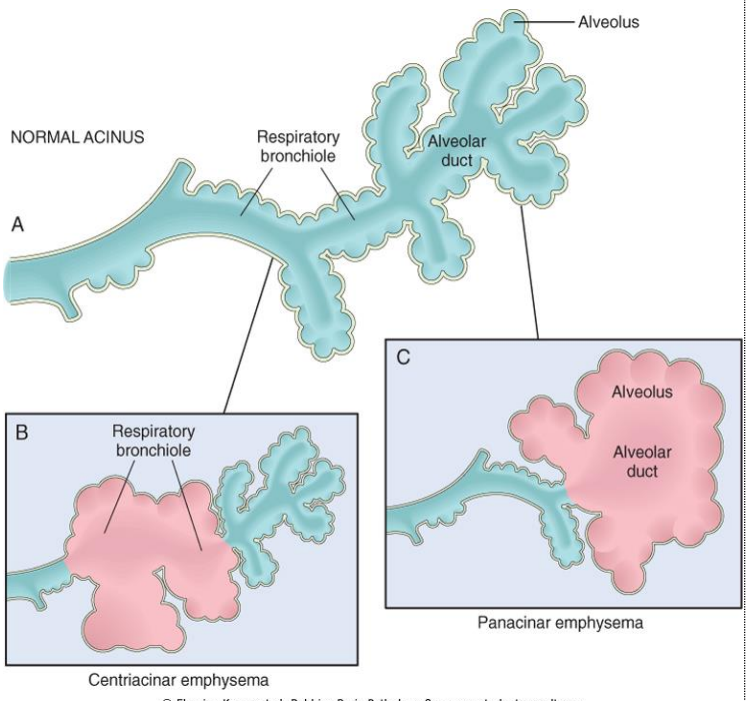
Types of emphysema:

1- **Centrilobular (Centriacinar) emphysema:** (only the respiratory bronchiole is dilated. Quite common in smokers. ***See figure (B)***

2- **Panacinar emphysema** (pan=كلي): respiratory bronchiole, alveolar duct, alveolar sacs and alveoli all of them are **dilated** and the wall may be **destroyed** by **elastases**. There is associated **inflammation** around them. Also, there is chronic bronchitis. **This type of emphysema which occur in α_1 antitrypsin deficiency.** ***See figure (C)***



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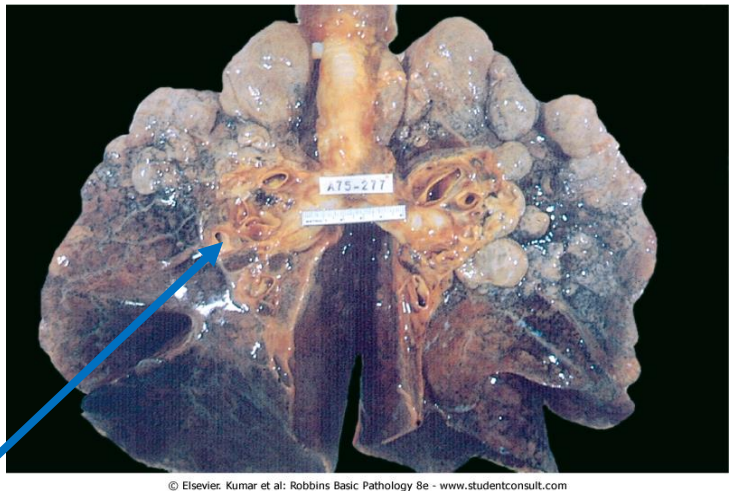
3- **Paraseptal (peripheral) emphysema:** Usually cause emphysema in the distal part and mostly in the peripheral part of lungs then in sub-pleural areas.
When it is in sub-pleural areas, it is more commonly associated with **pneumothorax**.



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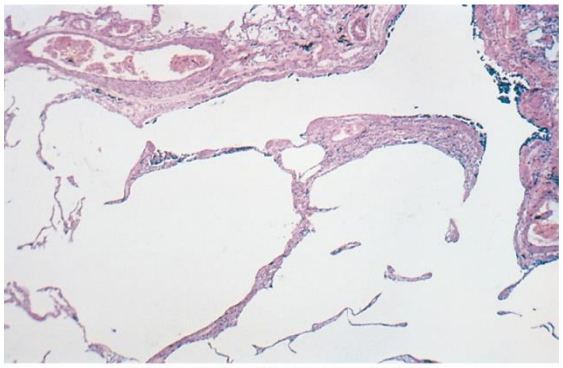
Picture: Bullous emphysema with large apical and sub-pleural bullae.

4- **Irregular emphysema:** it affects various places (an area with alveolar duct dilatation and another one with respiratory bronchi dilatation and so on). It happens in chronic inflammatory conditions. Old tuberculosis, old ammonia, old fibrosis in the lung for any reason.



PICTURE: Pulmonary emphysema. There is marked enlargement of airspaces, with thinning and destruction of alveolar septa.

Complications of Emphysema:

1- **Cor Pulmonale.**
2- **Pneumothorax:** especially in Paraseptal (peripheral) emphysema →formation of emphysematous bullae (group of emphysematous areas which coalition together) → rupture of the bullae → Pneumothorax.
It is source of a very common medical emergency.
3- **Interstitial emphysema:** when emphysema and air is ruptured to the mediastinum, and sometimes underneath the skin → we get air in the mediastinum or subcutaneous area.
4- **Status asthmaticus.**
5- **Respiratory failure.**

More details about Pneumothorax which mentioned in the lecture:

- Sub-pleural emphysema when they become large they called sub-pleural bullae (فقاعة), they destroy the wall of alveoli → amalgamated (دمج) → form a big cavity
- When one of those bullae have ruptured→ air go to pleural cavity (pneumothorax) → pleural cavity filled with air → compress the lung and cause collapse the lung (atelectasis) → patient may die unless he treated.
- Treatment put chest tube (lower down) in his pleural cavity → air come out and he is saved.

SUMMARY:

- **Emphysema**: is a chronic obstructive airway disease characterized by permanent enlargement of airspaces distal to terminal bronchioles.
- Subtypes include Centriacinar (most common; smoking related), Panacinar (seen in α_1-antitrypsin deficiency), distal acinar, and irregular.
- The two key pathogenic mechanisms are an excess of cellular proteases with low antiprotease levels (protease-antiprotease imbalance), and an excess of reactive oxygen species (oxidant-antioxidant imbalance).
- The accumulated inflammatory cells are the source of proteases and oxidants; together, they cause tissue injury and inactivate antiproteases.
- Most individuals with emphysema demonstrate elements of chronic bronchitis concurrently, since cigarette smoking is an underlying risk factor for both; individuals with pure emphysema are characterized as "*pink puffers*."

Any medical terminology with (ectasis) means dilatation and stagnation(توسع و ركودة)

D- Bronchiectasis

Bronchiectasis is characterized by permanent and abnormal dilatation of the bronchi because of accumulation of mucopurulent (صديدي) secretions. Usually associated with inflammation and in later stages there is destruction in the bronchial wall and formation of abscesses.

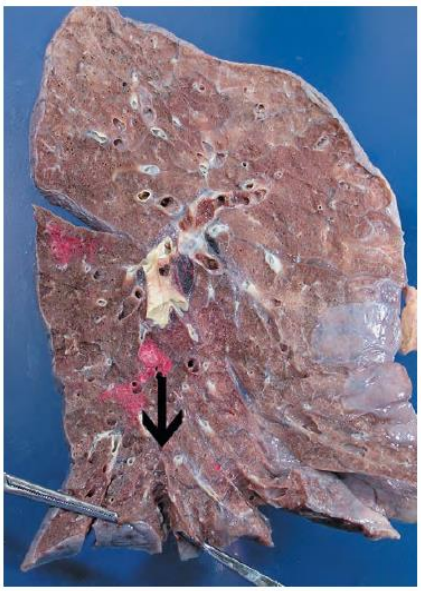
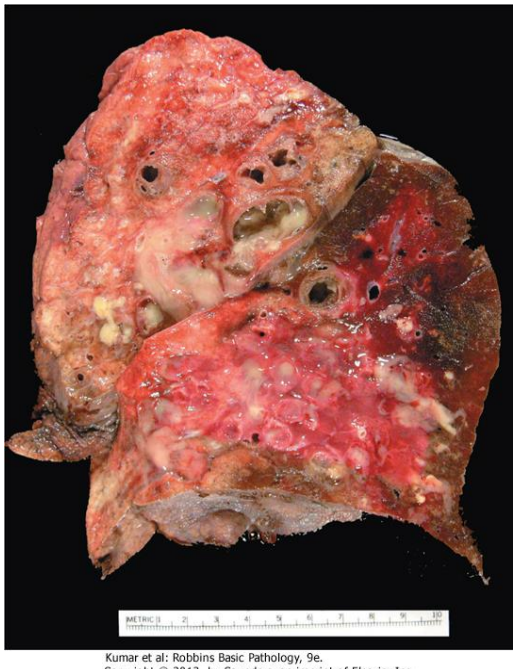


Figure 13-4. Bronchiectasis. In the lower lobe of this lung, the bronchi can be traced to the pleural surface (*arrow*).

Causes of Bronchiectasis:

1- **Congenital:** due inherited diseases.
   For example: cystic fibrosis and ciliary dyskinesia.
2- **Acquired**: caused by something obstructing an area (in the lung) and area after it is dilated.

Clinical presentation:



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- The patient presents with a lot of **cough**, a lot of **sputum** and rarely with dyspnea. So, the main symptom is **reproductive cough** with large amount of copious (لزج و كثيف) purulent sputum, sometimes is fetid (bad smelling). Also these patients may come with hemoptysis and fever (because their recurrent pulmonary infections which lead to lung abscesses).
- This disease likes to affect the base of the lung (lower lobes), gradually it moves to the superior lobes. Thus, in advanced cases all the lobes are affected.
- **On the x-ray we see:** dilatation of the bronchial shadows and the wall of those bronchi are also dilated (train traces appearance) and full with secretion.

Pathogenesis:

Acquired: This obstruction usually caused by: mucus plugs *(in case of cystic fibrosis which is a congenital disease characterized by deficiency of the enzymes controlling certain secretion → increased in the sodium of the sweat).* Also, it may be caused by ciliary dyskinesia, foreign bodies, tumors (most often), thickening in mucous plugs or anything can obstruct will associated with secondary or acquired bronchiectasis.

Congenital: Affected children come with recurrent sinusitis, chest infection, pneumonia, rhinitis, tonsillitis or adenitis. They always have upper respiratory infections.

These children may have a congenital disease which stops the cilia from moving. Movement of cilia is very important to stop bacteria and foreign bodies to enter into the lungs.

This disease has many names: immotile cilia syndrome, ciliary dyskinesia (سكون) and Kartagener syndrome.

When we examine the cilia under the electron microscope, usually there are doublets (9-doublets one in the c) which formed of microtubules. These microtubules have outer dynein arms and inner dynein arms. Normally dynein arms move → cilia moves.

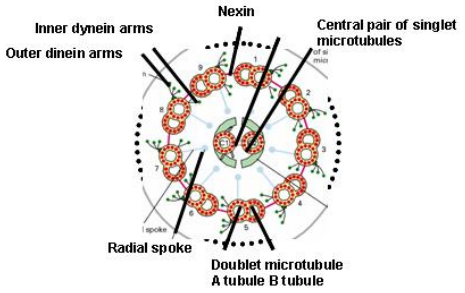
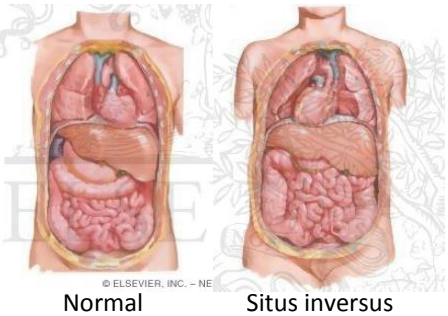


Diagram of ciliary structure

Others symptoms of ciliary dyskinesia:

- **When they grow up they become infertile** (عقم). *Because the tail of the sperm is like cilia so it won't move to the ovary).*
- **They can't hear.** *Because cilia is responsible for hearing.*
- **Situs inversus:** dislocation of the pulmonary artery, the pulmonary arch and dislocation of the heart to the right side (مقلوب بوجوده في الجهة اليمنى بدلا من اليسرى).

These symptoms may be presented all in the patient (uncommon) or just some of them.



Normal Situs inversus

Kartagener syndrome → Bronchiectasis, sinusitis, rhinitis, otitis medial.

In those patients they have absence of dynein arms → their cilia doesn't move → they cannot stop bacteria and particle from entering to their nose, bronchial tree and sinuses → they get infection. Also, they may have less number of doublets.

Treatment of acquired Bronchiectasis:

- We give the patient **mucolytic substances** (مواد مميعة للقشع) to help them cough and get rid of the sputum. (Some old patient cannot cough because of other diseases. So, physiotherapist helps them) → we culture the sputum (patient sputum usually abundant, foul or bad smelling (because of an infection by anaerobic bacteria) and mucopurulent) → we treat them if they have infection → if there is no response → we excise that part of the lung.

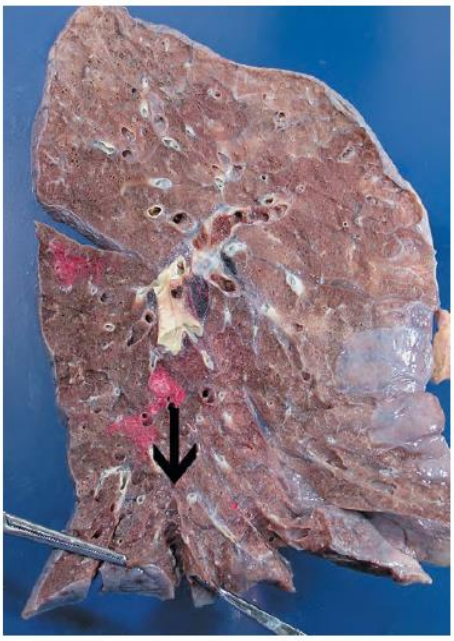


Figure 13-4. Bronchiectasis. In the lower lobe of this lung, the bronchi can be traced to the pleural surface (*arrow*).

Sputum *enables us to diagnose asthma, do bacterial culture, and recognize malignant cells and other things.*

Complications of Bronchiectasis:

1- **Abscesses:** (in X-ray, it may looks like a lung tumor)
   a. **Lung abscess**
   b. **Migrating abscesses** (brain abscess, renal abscess or other organs)
2- **Amyloidosis.**
3- **Respiratory failure.**

E- Respiratory Bronchiolitis

Respiratory Bronchiolitis is a chronic inflammation of the bronchioles characterized by **dyspnea** and **little coughs** due to ***smoking*** but not that much productive.

SUMMARY of chronic obstructive pulmonary diseases COPD:

Clinical Term	Anatomic Site	Major Pathologic Changes	Etiology	Signs/Symptoms
Chronic bronchitis	Bronchus	Mucus gland hyperplasia, hypersecretion	Tobacco smoke, air pollutants	Cough, sputum production
Bronchiectasis	Bronchus	Airway dilation and scarring	Persistent or severe infections	Cough, purulent sputum, fever
Asthma	Bronchus	Smooth muscle hyperplasia, excessive mucus, inflammation	Immunologic or undefined causes	Episodic wheezing, cough, dyspnea
Emphysema	Acinus	Airspace enlargement, wall destruction	Tobacco smoke	Dyspnea
Small-airway disease, bronchiolitis	Bronchiole	Inflammatory scarring, obliteration of bronchioles	Tobacco smoke, air pollutants	Cough, dyspnea

432 Pathology Team

*Good Luck ^_^*