Pathology of Chronic obstructive pulmonary disease

OBJECTIVES:

- ✓ Understand that this group of disorders is characterized by increase to airflow, owing to partial or complete obstruction at any level of the bronchial/bronchiolar.
- ✓ Know that the major obstructive disorders are chronic bronchitis, emphysema, asthma and bronchiectasis.
- ✓ Be aware that the symptom common to all these disorders is “dyspnea” (difficulty in breathing) but each have their own clinical and anatomical characteristic.
- ✓ Know that chronic bronchitis and emphysema almost always coexist.

Editing File

Black: original content.
Red: Important.
Green: AlRikabi’s Notes.
Grey: Explanation.
Blue: Only found in boys slides.
Pink: Only found in girls slides.

INTRODUCTION

Diffuse pulmonary diseases can be classified into two categories:

Obstructive airway diseases

Characterized by **limited airflow**, usually resulting from an increase in resistance caused by partial or complete obstruction at any level.

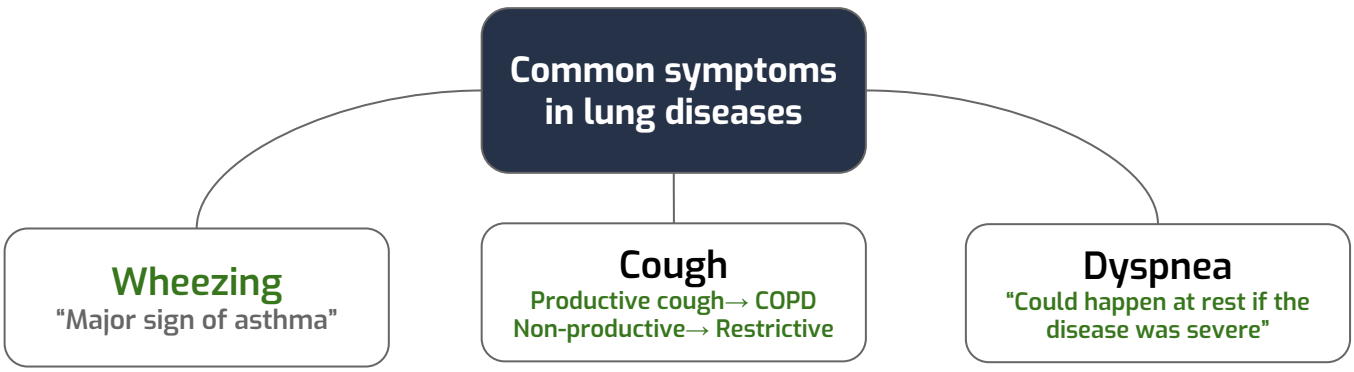
Obstruction → Air trapped in lungs, Airway close prematurely at high volume

Restrictive airway diseases

Characterized by **reduced expansion** of lung accompanied by decreased total lung capacity.

Restriction is due to stiffness inside lung tissue or chest wall cavity→ inability to Reach full volume

	Obstructive	Restrictive
Forced Vital Capacity(FVC)	Normal or slightly Decreased	Decreased
Forced Expiratory volume in 1 SEC (FEV1)	Decreased	Normal or Decreased
(FEV1/FVC)	Decreased	Normal or Increased



In this lecture we will discuss Chronic obstructive pulmonary diseases (COPD) which includes:

1- **Chronic bronchitis.** "Inflammation of the bronchi"
2- **Emphysema.**
3- **Bronchiectasis.** "Dilatation of bronchi"
4- **Bronchial asthma.** "We've already discussed it in the previous lecture"

Chronic Bronchitis

Definition

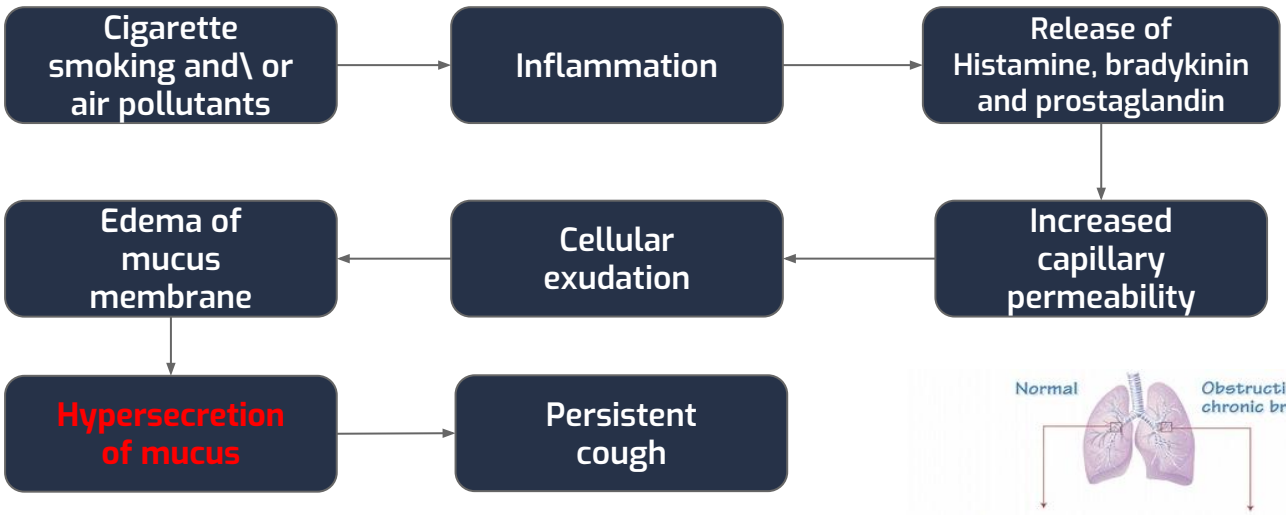
A chronic obstructive airway disease characterized by the presence of chronic productive cough that Persists for at least 3 consecutive months in at least 2 consecutive years.

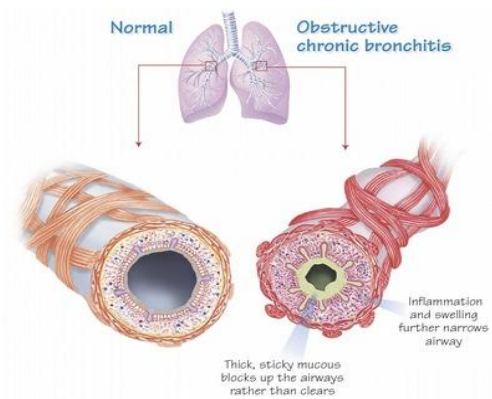
Etiology

- Cigarette smoking and pollutants (sulfur dioxide, nitrogen dioxide).
- Infection (due to mucus and sputum excessive production)
- Genetic factors e.g. cystic fibrosis.

Pathogenesis:

The distinctive feature of chronic bronchitis is hypersecretion of mucus, beginning in the large airways.





Chronic Bronchitis (Cont.)

Clinical presentation:

- Persistent productive cough
- Hypercapnia and Hypoxemia
- Cyanosis in severe cases
- Dyspnea
  "Shortness of breath"

Patients suffering of this disease may be called Blue Bloaters! Why?

1- Blue[1] is because of Cyanosis is one of the presenting symptoms.

2- Bloater Because he's bloated "منتفخ" due to the obstruction of his airways by excessive mucus, inflammatory cells and the thickened mucus glands, therefore he will not be able to expire air so the air will be trapped in his lungs.

Complications

- **Cor pulmonale.**
  " heart failure caused by chronic lung diseases, usually it is right sided heart failure."
- Increase the incidence of infections due to excessive mucus production.
- Death due to further impairment of respiratory functions after superimposed acute bacterial infections.
- **Emphysema**
  "Usually coexist with Chronic bronchitis"
- **Acute exacerbation of chronic bronchitis:** severe symptoms which includes: Dyspnea, Productive cough(purulent mucus"contain pus") and sometimes with fever.

How can a lung disease cause heart failure "Cor pulmonale"?

Accumulation of mucus in the lumen of bronchi → Hypoxemia → Increase resistance in pulmonary blood vessels → increase pressure in the pulmonary artery → Pulmonary hypertension (pulmonary pressure is higher than 25 mmHg) → increase pressure inside the right side of the heart → Heart failure "Cor pulmonale".

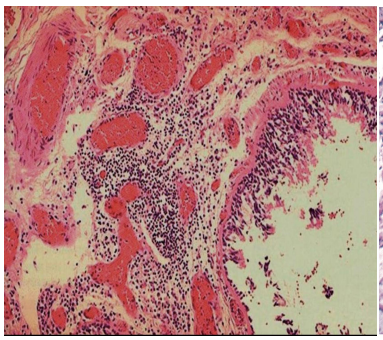
[1] Because he doesn't have enough oxygen due to accumulation of mucus in the lumen of bronchi → increased PCO2(Acidosis) and decreased PO2 → Blue.

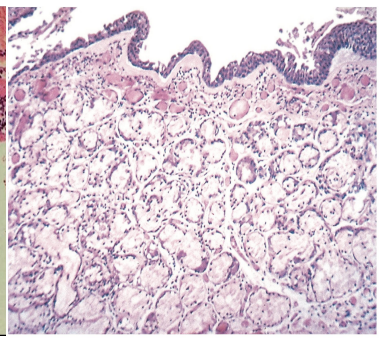
Chronic Bronchitis (Cont.)

Morphology

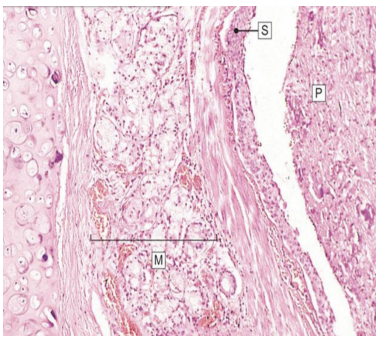
- **Goblet cell hyperplasia**: increase in their number.
- Presence of **mucus bulges & mucosa** contains pus with neutrophils, mucus, and bacteria.
- **Hypertrophy** and **Hyperplasia** of mucosal and submucosal glands leads to overproduction of mucus.
- Increase in thickness of subepithelial mucus glands. This will lead to an increase in the **Reid Index**.

Reid Index:
Is a mathematical relationship comparing the thickness of the mucus glandular tissue versus the distance from the epithelium to the level of the cartilage.
We don't use it for diagnosis therefore **no biopsy will be needed in the diagnosis.**





Chronic bronchitis. The lumen of the bronchus is above. Note the marked thickening of the mucous gland layer (approximately twice-normal) and squamous metaplasia of lung epithelium.



Abnormal amount of mucus causes plugging of the airway lumen (P)

In contrast with asthma; there is no eosinophils in chronic bronchitis.
Remember there are 2 major types of asthma:
1- Extrinsic asthma→ IgE and eosinophils levels are elevated.
2- Intrinsic asthma→ IgE and eosinophils levels are normal.

EXTRA

- In the early stages of the disease, the productive cough raises mucoid sputum, but airflow is not obstructed. Some patients with chronic bronchitis may demonstrate hyperresponsive airways with intermittent bronchospasm and wheezing. If a culture is done to the sputum we will find lots of bacteria because the sputum is favorable environment for the bacteria to grow and this will lead to increase the incidence of infections.

-The patients will use the accessory muscles to help in breathing, and this will make the muscles stiff , In order to expel the trapped air he/she will shorten his neck to using the sternomastoid muscles

Emphysema

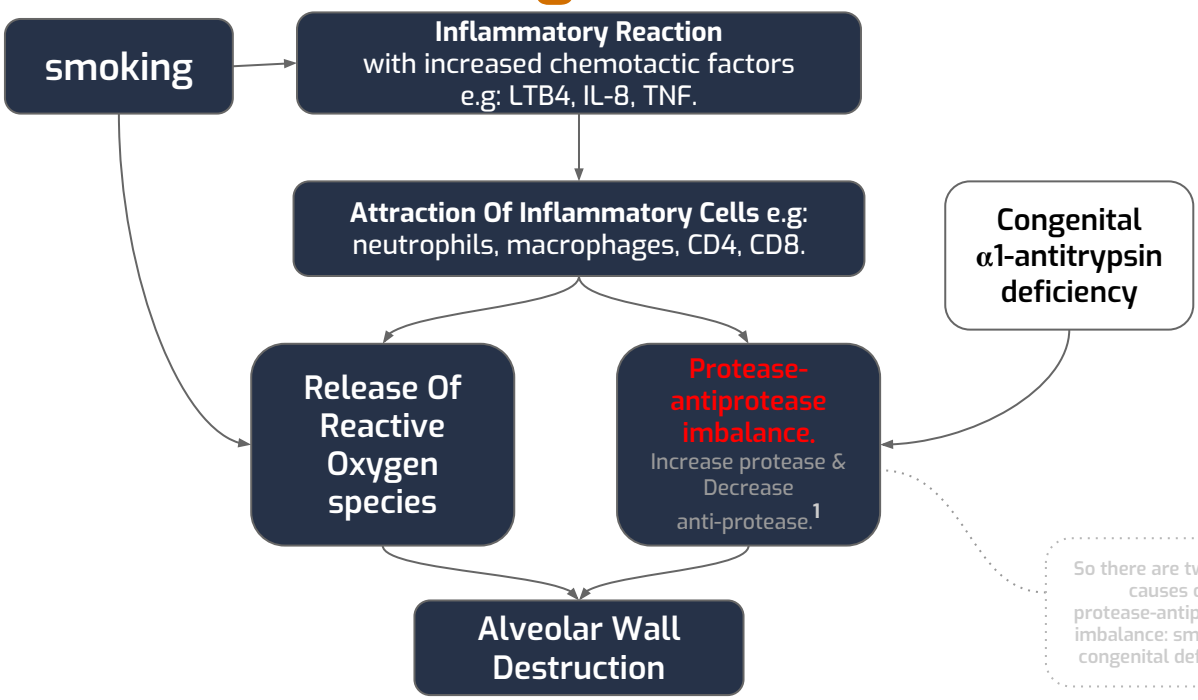
Definition

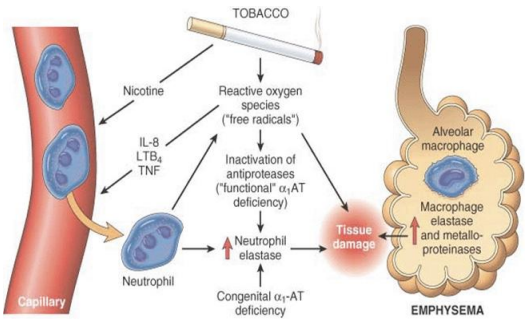
Permanent enlargement of the airspaces distal to the terminal bronchioles accompanied by destruction of their walls, without obvious fibrosis.
(Associated with loss of recoil and support of small airways —> tendency to collapse with obstruction)

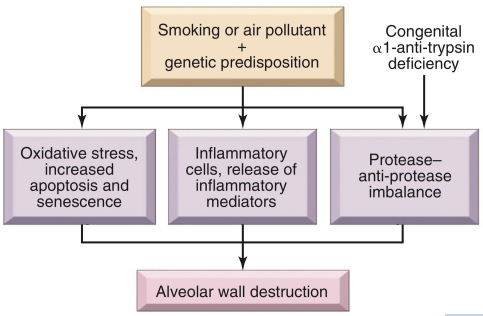
Etiology

- Smoking, (causes chemical inflammation).
- Inhaled pollution.
- Congenital deficiency of the anti-protease enzyme (α1-anti-trypsin)

Pathogenesis:







[1] **Protease**(e.g. Elastase): a proteolytic enzyme that breaks down the elastic tissue of the alveolar wall, it's produced by neutrophils and macrophages.
Anti-protease(e.g.α1-antitrypsin) : Inhibits proteases, normally present in serum, in tissue fluids and macrophages, The gene is located on the long arm of the 14 chromosome (14q32.1), we can call the locus it's found on Pz or Pi.

Emphysema (Cont.)

Types of Emphysema

	Centriacinar (centrilobular) "Most common"	Panacinar (panlobular)	Distal acinar (paraseptal)	Irregular
Location	Central or Proximal alveoli of the acini.	Uniform injury, total damage of the alveoli.	The distal alveoli of the acinus.	Can affect any part of the respiratory tract.
Cause	Smoking	Genetic condition: Alpha-1 antitrypsin deficiency	Unknown seen often in cases of spontaneous pneumothorax in young adults.	Invariably associated with scarring such as that resulting from healed inflammatory diseases.
Features	Common in upper Lobes.	Common in lower lobes.	- Occurs adjacent to areas of fibrosis or atelectasis. - More severe in the upper half of the lungs	Asymptomatic.

There is an extra type called Mediastinal (interstitial) emphysema which is caused by entry of air into the interstitium of the lung, from where it may track to the mediastinum and sometimes the subcutaneous tissue.

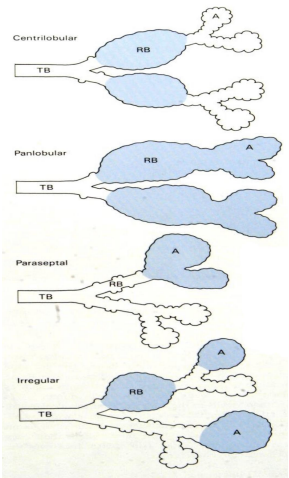
Till now we took 3 cases of acute medical emergency:

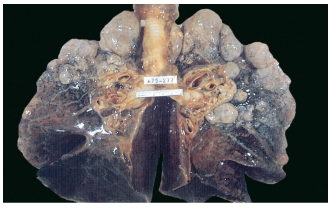
1- Status asthmaticus: persistent, irreversible asthma that lasts days, the patient should be admitted to the intensive care unit.

2- Acute exacerbation of chronic bronchitis: severe symptoms which includes: Dyspnea, Productive cough(purulent mucus"contain pus") and sometimes with fever.

3- Pneumothorax: accumulation of excessive air in the pleural cavity which will lead to increase pressure exerted on lungs → lung collapse"Atelectasis"

- Symptoms:
  - very severe dyspnea
  - Can't hear any breathing sounds by stethoscope (Why? Because he has an air barrier.)
- Diagnosis: By portable chest x-ray.
- Management: Tube thoracostomy "inserting a chest tube to the chest to drain air."

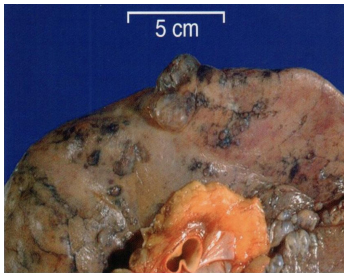




Bullous emphysema with large apical and subpleural bullae.

A smoker lung, he has centriacinar emphysema.

Why is it black?
Because he has a lot of carbon in his alveolar macrophage.
Anthracosis: accumulation of carbon in the lungs.



Distal acinar (paraseptal emphysema) forming multiple cyst-like structures with spontaneous pneumothorax.

Emphysema (Cont.)

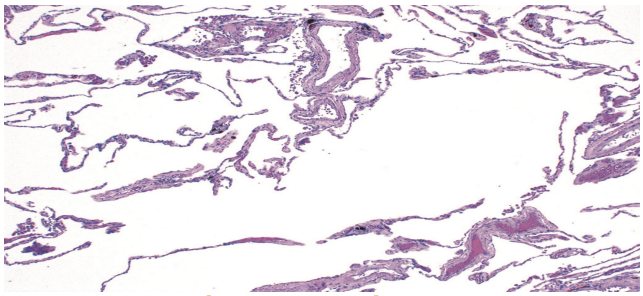
Morphology

Histological features

- Large airspaces.
- Loss of elastic tissue.
- Reduced radial traction on the small airways.
- Diminished alveolar capillaries.

Gross features

- Voluminous lungs. "In panacinar emphysema only"
- Pale lungs. "In panacinar emphysema only"



Pulmonary emphysema

There is marked enlargement of the air spaces, with destruction of alveolar septa but without fibrosis. Note the presence of black anthracotic pigment.

Clinical features

- Dyspnea (Fish-mouth breathing)
- Barrel chest."Increase in anteroposterior diameter of the chest" due to: 1- air-trapping with inflammation. 2- hypersecretion of viscid contraction in the small airways.
- Patients are known as "Pink Puffers".
- Usually coexist with Chronic bronchitis.

Complications

- Pneumothorax.
- Cor pulmonale
- Death may occur either due to Pulmonary failure with respiratory acidosis[1] or due Pulmonary hypertension[2]

[1] A patient with emphysema who also has pronounced chronic bronchitis and has a history of recurrent infections. Dyspnea will usually be less prominent, and in the absence of increased respiratory drive the patient will retain carbon dioxide(Acidosis), becoming hypoxic and often cyanotic.

[2] Due to destruction of small capillaries in alveolar wall and hypoxia lead to pulmonary vascular spasm

Bronchiectasis

Definition		• Permanent **Dilation of the Bronchi and the Bronchioles** caused by destruction of the smooth muscle and the supporting Elastic tissue.
Characteristics		• typically results from or is associated with chronic necrotizing infections. • **It is not a primary disorder**, as it always occurs secondary to a variety of conditions.
Etiology	*Bronchial obstruction*	• **Localized:** Tumors,Foreign bodies or mucous impaction. • **Systemic:** Bronchial Asthma and Chronic bronchitis.
	Congenital or Hereditary	• Congenital bronchiectasis • **Cystic Fibrosis** • **Primary Ciliary Dyskinesia** • Intralobar sequestration of lung • Immunodeficiency
	Suppurative Pneumonia	• Klebsiella spp. • Staphylococcus aureus

Kartagener Syndrome
(Immotile Cilia syndrome or Ciliary Dyskinesia)

Definition: Autosomal Recessive disease characterized by the absence of outer and inner Dynein Arms causing immotile cilia.

Characteristics: It causes a malfunction in the cilia therefore loss of defense in the Upper respiratory tract

Diagnosis:
- Genetic Study.
- Electron Microscope.

Complications:

1- Recurrent respiratory tract infections, e.g. Sinusitis "Because the cilia can't function to take the sputum out of the lung (which contains a lot of bacteria)"

2- Infertility in Males."Because the spermatozoa requires cilia to move to fertilize the ovum."

3- Deafness(Can't hear)."To transmit the sound there are ciliated cell inside the ear so they have to move to transmit the sound"

Electron micrograph of cilia from a person with recurrent chest infections since childhood. The outer dynein arms are absent and there are abnormal single microtubules (M), which prevent normal motility.

Cystic Fibrosis
(Mucoviscidosis)

Definition: An inherited Disease causing thicky, sticky mucous secretion to build up in the lung and digestive tract causing Bronchiectasis.

Usually theses patients present with:
1-Pancreatitis.
2-Malabsorption.
3-Upper respiratory tract infections.
4-Bronchiectasis

Diagnosis:
By sodium test (Sweat test): usually they have low sodium in sweat.

Bronchiectasis (CONT.)

Pathogenesis:

Two intertwined processes that contribute to Bronchiectasis Obstruction and Chronic Infection:

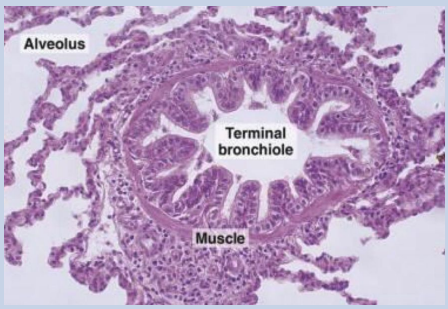
Step 1	Step 2	Step 3	Step 4
A foreign Body enters the body leading to obstruction.	**Impaired mucociliary clearance, mucus stasis and accumulation which in turn further makes the airways susceptible to microbial colonization**	**The persistence of the pathology with superadded infection leads to a "vicious circle" of inflammation and tissue damage**	Inflammatory damage to the bronchi which will lead to **irreversible** dilation and loss of elasticity of the alveolar wall leading to **Bronchiectasis**.

Clinical features	• Severe persistent cough with sputum (Mucopurulent sputum) and sometimes with blood, the sputum has bad smell. • Clubbing of fingers. • Fever, hypoxemia, hypercapnia. • dyspnea, rhinosinusitis, and hemoptysis.
Complications	• If severe, obstructive pulmonary function develop. • Lung abscess. • Rare complications: metastatic brain abscess and amyloidosis(Chronic inflammation → amyloidosis) . • Infection/ Necrotizing pneumonia caused by TB, staphylococci or mixed infection.

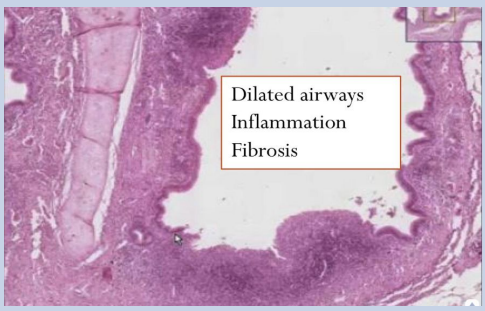
Bronchiectasis (CONT.)

Morphology

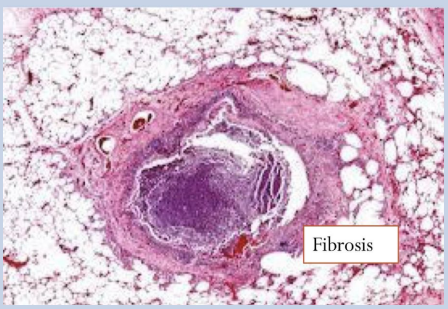
- Dilated airways up to four times, reaching the pleura.
- Inflammation
- Fibrosis



Normal



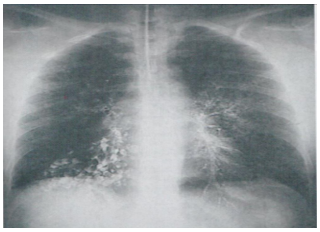
Bronchiectasis



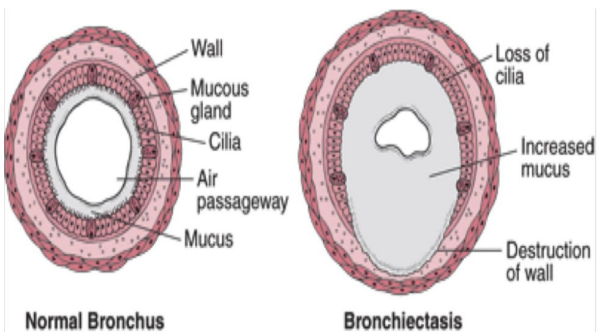
Bronchiectasis

X- Ray: Small dense(purulent) nodule-like areas (dilated bronchi) in lower/ middle lobes, also there is increased bronchovascular shadowing.

Grossly : Large purulent dilated bronchi.



Bronchiectasis, Chest radiograph



Summary

Chronic Obstructive Pulmonary Diseases

	Anatomical site	Pathologic changes	Etiology	Signs/Symptoms
Emphysema	Acinus	- Air space enlargement. - Wall destruction.	Tobacco smoke.	Dyspnea.
Chronic bronchitis	Bronchus	Mucous gland hypertrophy, hyperplasia and hypersecretion.	-Tobacco smoke. -Air pollutants.	-Cough. -Sputum Production.
Asthma	Bronchus	- Smooth muscle hypertrophy, & hyperplasia. - Excessive mucus. - Inflammation.	Immunologic or undefined causes.	- Episodic wheezing. - Cough. - Dyspnea.
Bronchiectasis	Bronchus	Airway dilation and scarring.	Persistent or severe infection.	- Cough. - Purulent. - Sputum. - Fever.
Small airway disease, bronchiolitis	Bronchus	- Inflammatory scarring. - partial obliteration of bronchioles.	-Tobacco smoke. -Air pollutants.	- Cough. - Dyspnea.

	Predominant Bronchitis	Predominant Emphysema
Appearance	"Blue bloaters"	"Pink Puffers"
Age	40-45	50-75
Dyspnea	Mild, late	Severe, early
Cough	Early, copious sputum	Late, scanty sputum
Infection	Common	Occasional
Cor pulmonale	Common	Rare, terminal
Airway resistance	Increased	Normal or slightly increased
Elastic recoil	Normal	Low
Chest radiography	Prominent vessels, large heart	Hyperinflation, small heart
$PaCO_2$	Increased	Normal to decreased
Cyanosis	Present	Absent

Dr. AlRikabi's notes

Diseases are defined either Clinically or pathologically or by etiology.

Chronic bronchitis

Definition (Clinical): Persistent chronic productive cough for a period of 3 months over 2 consecutive years.

Etiology: Almost all patients are smokers."usually coexist with emphysema"

Symptoms:

1- Dyspnea.
2- Productive cough.
3- Wheezing "sometimes not always" due to obstruction of the lumen of the bronchi by excessive mucus production.

Histological presentations:

1- Mucus secreting bronchial glands become hypertrophic/hyperplastic therefore there thickness will increase and will occupy a lot of space in the bronchial wall.
2- Congested blood vessels."when there is inflammation there is vasodilation → increased vascular permeability"
3- Submucosal edema.

Emphysema

Definition (Pathological): Chronic obstructive airway disease characterized by abnormal dilation and destruction of the airspaces distal to the terminal bronchioles (which includes the Respiratory bronchioles, alveolar duct and alveoli).

Etiology: Smoking."usually coexist with chronic bronchitis"

Symptoms:

1- Dyspnea.
2- Productive cough.
3- If advanced the patient will have Honeycomb lung appearance and barrel chest "due to increase in the anteroposterior diameter of the thoracic cavity."
4- Pink puffer."Pink because he has no cyanosis and puffer because he blows air out"

Types of emphysema

Centriacinar	Panacinar	Distal acinar	Irregular
-Only the respiratory bronchioles are dilated. -Common in smokers.	-Respiratory bronchioles, alveolar duct and acini are dilated. -Common in patients with α1-antitrypsin deficiency.	-Dilatation of the distal part of the acini. -Causes bullae" if the bullae rupture it will cause pneumothorax" -common in Non-smokers and Young people.	-Can affect any part. -Usually in inflammatory conditions"patients with previous pneumonia, old TB"

Bronchiectasis

Definition: Chronic obstructive airway disease characterized by abnormal and permanent dilatation of bronchi and bronchioles associated with inflammation and fibrosis and pus formation.

Etiology: Bronchial obstruction or due to congenital abnormalities.

Symptoms:

1- Dyspnea.
2- Productive cough (purulent, copious sputum with bad smell due to anaerobes.)

Quiz

A) A 20-year-old, previously healthy man is jogging on morning when he trips and falls to the ground. He suddenly becomes markedly short of breath. On examination in the emergency room there are no breath sounds audible over the right side of the chest. A chest radiograph shows shift of the mediastinum from right to left. A chest tube is inserted on the right side, and air rushes out. Which of the following underlying diseases is most likely to have produced this complication?

1) Asthma
2) Bronchiectasis
3) Centriacinar emphysema
4) Chronic bronchitis
5) Distal acinar emphysema
6) Panlobular emphysema

B) A 45-year-old man has smoked two packs of cigarettes per day for 20 years. For the past 4 years, he has had a chronic cough with copious mucoid expectoration. During the past year, he has had multiple respiratory tract infections diagnosed as "viral flu." He has also developed difficulty breathing, tightness of the chest, and audible wheezing. His breathing difficulty is relieved by inhalation of a β-adrenergic agonist and disappears after the chest infection has resolved. Which of the following pathologic conditions is most likely responsible for his clinical condition?

1) α1-Antitrypsin deficiency with panlobular emphysema
2) Centrilobular emphysema with cor pulmonale
3) Chronic asthmatic bronchitis
4) Cystic fibrosis with bronchiectasis
5) Hypersensitivity pneumonitis with restrictive lung disease
6) Emphysema

C) A 55-year-old man is admitted to the hospital with increasing shortness of breath and dry cough for the past few years. He smokes 1.5 packs of cigarettes and drinks about four bottles of beer a day. He is constantly "gasping for air" and now walks with difficulty because he becomes breathless after only a few steps. Prolonged expiration with wheezing is noted. Physical examination shows a barrel chest, hyperresonance on percussion, and clubbing of the digits. The patient's face is puffy and red, and he has pitting edema of the legs. A chest X-ray discloses hyperinflation, flattening of the diaphragm, and increased retrosternal air space. Which of the following is the appropriate diagnosis?

1) Asthma
2) Chronic bronchitis
3) Emphysema
4) Hypersensitivity pneumonitis
5) Usual interstitial pneumonia
6) Restrictive pulmonary disease

D) A 48-year-old man with a history of heavy smoking presents with a 3-year history of persistent cough and frequent upper respiratory infections, associated with sputum production. Physical examination reveals prominent expiratory wheezes and peripheral edema. Analysis of arterial blood gases reveals hypoxia and CO2 retention. Which of the following is the appropriate diagnosis?

1) Atelectasis
2) Chronic obstructive pulmonary disease
3) Goodpasture syndrome
4) Hypersensitivity pneumonitis
5) Usual interstitial pneumonia
6) Restrictive pulmonary disease

E) A 16-year-old boy is rushed to the emergency room after sustaining a stab wound to the chest during a fight. Physical examination reveals a 1-cm entry wound at the right 5th intercostal space in the midclavicular line. His temperature is 37°C (98.6°F), respirations are 35 per minute, and blood pressure is 90/50 mm Hg. A chest X-ray shows air in the right pleural space. Which of the following pulmonary conditions is the expected complication of pneumothorax arising in this patient?

1) Atelectasis
2) Chylothorax
3) Diffuse alveolar damage
4) Empyema
5) Pyothorax
6) Restrictive disease

F) A 28-year-old woman with cystic fibrosis presents with increasing shortness of breath and production of abundant foul-smelling sputum. The sputum in this patient is most likely associated with which of the following pulmonary conditions?

1) Atelectasis
2) Bronchiectasis
3) Emphysema
4) Pneumothorax
5) Pyothorax
6) Chronic bronchitis

Answer Explanation File

A- 5 | B- 3 | C- 3 | D- 2 | E- 1 | F- 2

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Thank you

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