PATHOLOGY TEAM
439

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Introduction To COPD

Objectives:

- Give introduction for diffuse lung disease.
- Compare and contrast the major clinical and functional differences between predominant chronic bronchitis versus predominant emphysema in patients with COPD.
- Define Chronic bronchitis, its causes, pathogenesis, morphology.
- Describe mechanism of airway obstruction in patients with chronic bronchitis.
- Understand that when severe obstruction is present in chronic bronchitis, significant emphysema is nearly always present.
- Define Emphysema, its gross and microscopic changes, pathological mechanism, typical clinical presentation, cause of death.
- Describe the most likely mechanism of Emphysema (protease-antiprotease mechanism)
- Define Bronchiectasis, its causes, presentation, morphology and significant.

Rikabi's content

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Extra Information

Chronic Bronchitis

Diffuse disease

Definition

Defined as persistent productive cough for at least 3 consecutive months in at least 2 consecutive years, involves the Bronchus.
This definition based on clinical features

Etiology

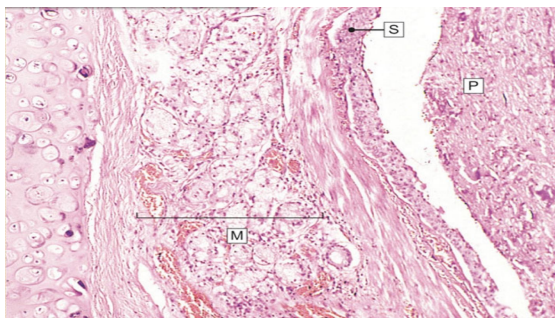
- Cigarette smoking is the most important risk factor (emphysema Usually coexist with Chronic bronchitis, both usually caused by smoking)
- Air pollutants
- Cystic fibrosis: congenital disorder characterized by thick secretion accumulated in the lung, might cause superadded infection.

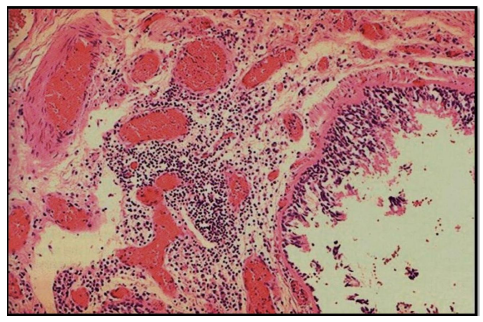
Morphology

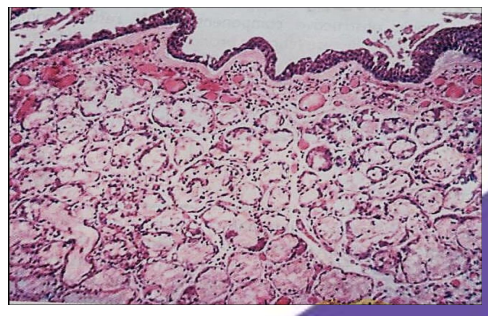
1- enlargement of mucous-secreting glands
2- goblet cell hyperplasia
3- chronic inflammation:
(Presence of lymphocytes and macrophage)
4- bronchiolar wall fibrosis.

Hypertrophy and **hyperplasia** of mucosal And submucosal glands leads to overproduction of mucus. this will lead to having **mucosal plug (سدادات مخاطية)**

Increase in thickness of subepithelial mucus glands, this will lead to an increase in the **"Reid Index"**: which 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.







In chronic bronchitis the main abnormality is secretion of abnormal amounts of mucus, causing plugging of the airway lumen (P).

Chronic Bronchitis

Clinical presentation

Persistent productive cough (with flames = sputum)

The patient can come leaning forward and use his accessory muscles "intercostal muscles + sternocleidomastoid muscle"
(remember?)In order to make forced breathing

Hypercapnia, hypoxemia, cyanosis

Dyspnea on excretion

Patients suffering of chronic Bronchitis may be called Blue Bloaters (mucus is not red) **Why?**
1- **Blue** 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."
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".
vasoconstriction due to hypoxia → increase in pulmonary BP causing weakness in the right side of the heart and edema.

Emphysema (As we said it Usually coexist with Chronic bronchitis)

Death due to further impairment of respiratory functions after superimposed acute bacterial infections. (50-60 years old)

Acute exacerbation of chronic bronchitis (purulent mucus + high symptom severity)

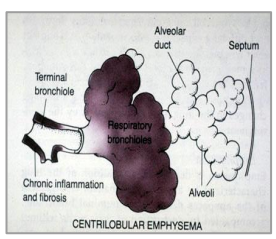
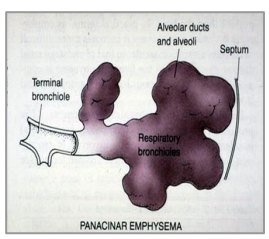
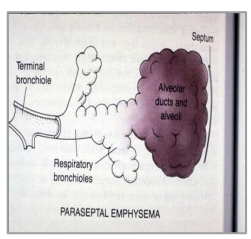
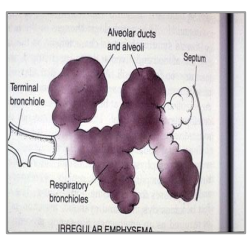
Emphysema (diffused disease)

Definition

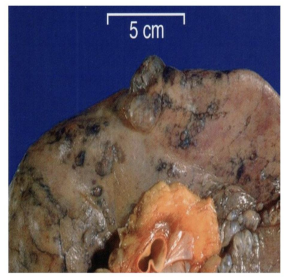
Abnormal Permanent enlargement of all or part of the respiratory unit: (gas exchange area known as "acinar" which contains respiratory bronchiole, alveolar duct and alveoli) accompanied by destruction of their walls. (functional obstruction, not actual anatomical obstruction because bronchial tree is normal)
other definition: permanent destruction of alveolar septae distal to terminal bronchioles
Associated with loss of elastic recoil and support of small airways leading to tendency to collapse with obstruction. (the collapsing will be in another area not the injured one by emphysema because of the pressure)

Etiology

1- Smoking
2- Air pollutant
3- α1-anti-trypsin deficiency (congenital) rare. Explanation: α1-anti-trypsin inhibit the action of protease and elastase (they cause destruction to the alveolar wall) so when they are deficient it causes emphysema. α1-anti-trypsin Found in the long arm of chromosome 14

Types of emphysema	Centriacinar (most common)	Panacinar	Distal acinar/ paraseptal/ Bullous	Irregular
Cause	Smoking, mostly heavy smokers	α1-anti-trypsin deficiency	Unknown (most often in young males who present with spontaneous pneumothorax due to bullous rupture	associated with scarring, e.g. TB
Location	proximal part of the acini (respiratory bronchiole)	the whole acinar	Distal alveoli of the acinus, in peripheral part of the lung near pleura	Can affect any part of the acinar
Features	severe in the upper lobes, Main pathology is in the respiratory bronchioles, the rest is fine but may have collapsed.	Common in both lower lobes (zones)	occurs adjacent to areas of fibrosis, scarring, or atelectasis and is more severe in the upper half of the lungs. might form subpleural bullae and cyst-like structures (atelectasis is managed via tube thoracostomy)	Asymptomatic, no clinical significance. common in 50% of people
Pictures	 CENTRILOBULAR EMPHYSEMA	 PANACINAR EMPHYSEMA	 PARASEPTAL EMPHYSEMA	 IRREGULAR EMPHYSEMA

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



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

Those emphysematous bullae might rupture when they do the air will go to the pleural cavity, this cause a medical emergency called pneumothorax. Symptoms: 1-severe dyspnea 2-hypercapnia. Usually affect young adult. When we use stethoscope we can't hear anything,why? Because of air barrier.

Emphysema

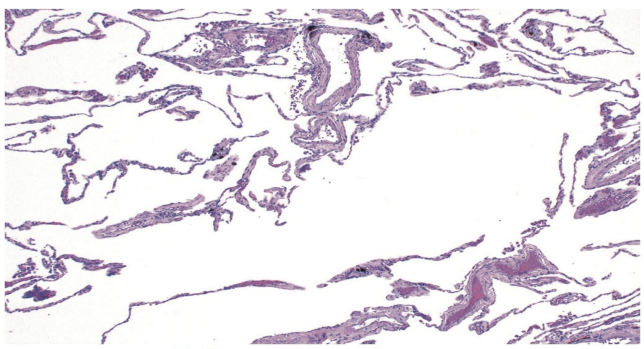
- **Pathogenesis :**

01 — Tabaco could releases the nicotine and reactive oxygen (free redials) leading to oxidative stress (irritating the bronchial tree)

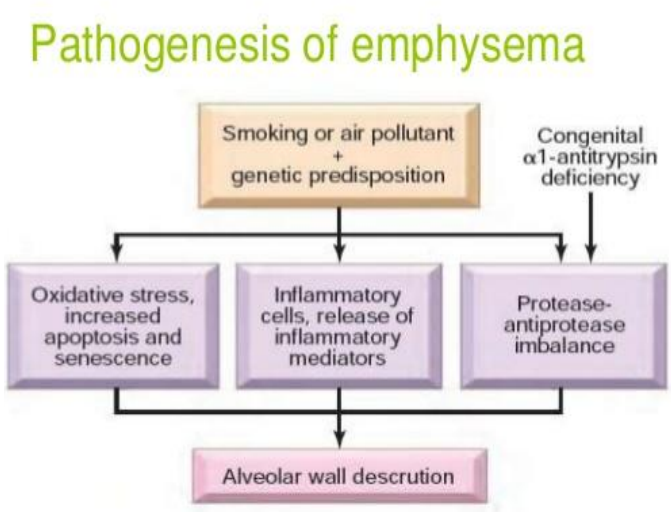
02 — Nicotine will active and recur more neutrophils (induce inflammation) that produce protease while the free radicals inhibit the activation of Anti-protease result in (functional anti-protease deficiency)

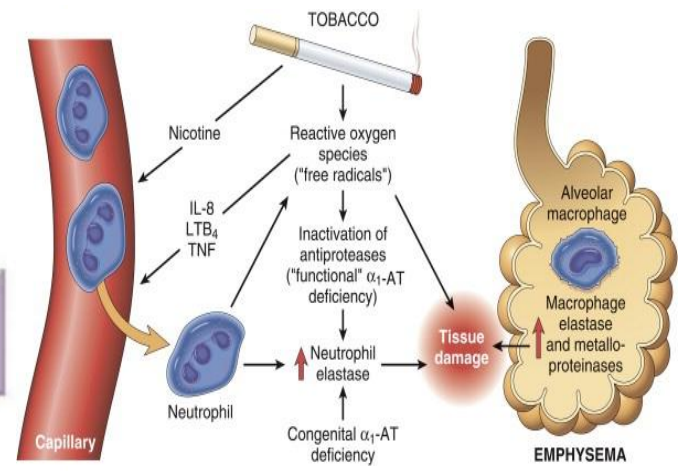
03 — **Leading to imbalance protease-antiprotease**
'Minimal inflammation in emphysema because few inflammatory cells can lead to this imbalance

04 — Congenital alpha1-antitrypsine Deficiency cause directly imbalance.
Leading to damage of alveolar wall



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

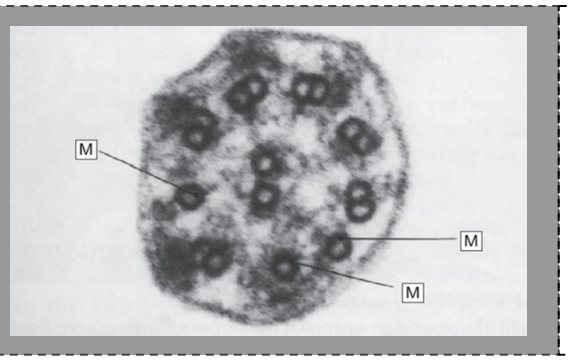
- Cough and wheezing. Respiratory acidosis
- weight loss (smoking suppress appetite and because breathing uses so much energy)
- pulmonary function tests reveal low FEV1
- Barrel chest (is the increasing in Anterior posterior diameter = transverse diameter due to hyperventilation result from:1- air trapping and inflammation. 2-if it associates with chronic bronchitis hypersecretion of viscid contraction in the small airways.)
- Patient are known as pink puffers(Breathing may be assisted by pursed lips(keep their lips nearly closed or closed)

Complications

Pneumothorax (medical emergency)
Death from emphysema is related to:
1- Pulmonary failure with respiratory acidosis, hypoxia and coma.
2- Pulmonary hypertension.
3- Right-sided heart failure (Cor pulmonale)

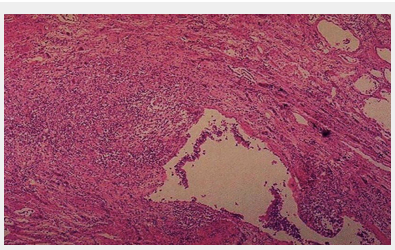
Bronchiectasis (localized disease)

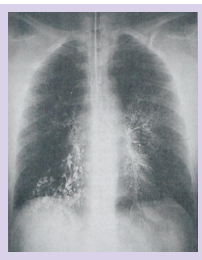
Definition	• permanent "irreversible" dilation of bronchi with destruction of their walls. • It is a result of chronic inflammation, and/or infection associated (with obstruction due to hypersecretion of thick mucus) with an inability to clear mucoid secretions/ excessive secretions,		
Etiology	**Bronchial obstruction:** **Localized :** tumor, foreign bodies or mucous impaction, mucous plug **Generalized :** Bronchial asthma. chronic bronchitis Fibrosis	• Congenital bronchiectasis(in babies 👶) • Cystic fibrosis (also called mucoviscidosis caused by a gene in chromosome 7. where the formation of thick,sticky mucus which is difficult to cough it so it accumulates in the lung ,characterized by chronic pancreatitis and increased secretions. diagnosed by sweat test) • Intralobar sequestration of the lung(congenital) • Immunodeficiency status (due to low immunity the patient will have repeated infections leading to permanent damage of Bronchial tree) • Immotile cilia/ kartagener syndrome	**Chronic or severe infection / necrotizing pneumonia:** Caused by **TB** , Staphylococci or mixed infection (The infection causes damage to bronchial tree with necrosis)



Ciliary dysmotility syndrome:
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.
Normally The outer dynein arms will get rid of abnormal single microtubules

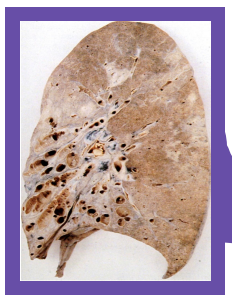
histologically.
Inflammatory infiltrate, fibrosis and dilated airways

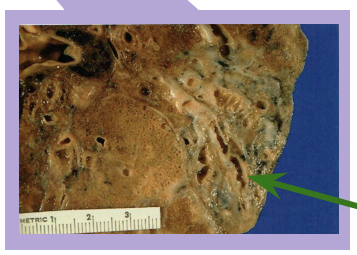




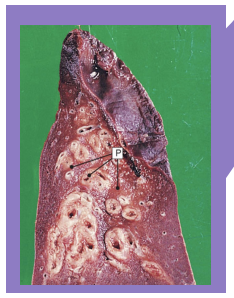
Chest radiograph.
in x-ray we see it as bilateral, with inflammation around the dilated bronchi with purulent (small dense(areas

Dilation of bronchi with destruction/ ulceration of bronchial walls.





Gross .
Normally, the bronchial tree should stop at the midpoint, but here it is continuous to the pleura. we see secretions and abscess



This is a lower lobe of lung surgically resected for bronchiectasis.

Bronchiectasis

- **Pathogenesis :**

01 — A trigger will lead to air inflammation

02 — Ineffective pulmonary defense will lead to hypersecretion of mucus.

03 — With superimposed bacterial infection such as necrotizing pneumonia will leading to

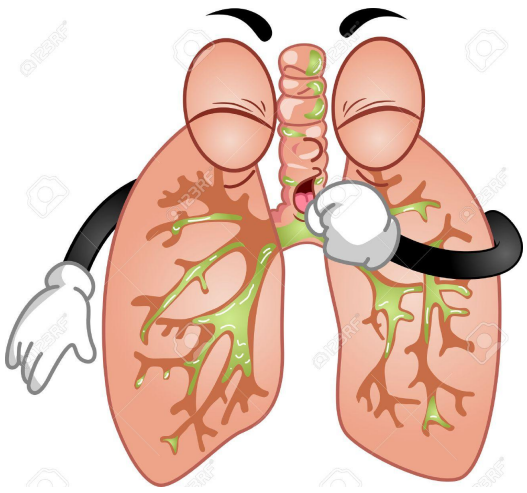
04 — Permanent destruction of the bronchial tree (Bronchus , bronchiole)

Clinical features

- Severe persistent cough with sputum (Mucopurulent sputum) and sometimes with blood (hemoptysis), the sputum has bad smell
- Clubbing of fingers (due to chronic hypoxia, growth of the tissue occurs below the nails)
- Productive cough with foul smell because of the pus (because, if we look at it histologically, we see a mixture of bacteria including anaerobes that cause it)

Complications

- If severe, obstructive pulmonary function develope.
- Lung abscess
- Rare complications: metastatic brain abscess (cerebral abscess) and amyloidosis (causes include: chronic bronchiectasis, chronic osteomyelitis, migratory abscesses).
- Septicaemia
- Infection/Necrotizing pneumonia caused by TB , staphylococci or mixed infection.



Summary

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COPD

Disease	Definition	Etiology	Morphology	Clinical Symptoms	Complications
Chronic bronchitis	Persistent productive cough for 3 consecutive months for 2 years	Smoking Air pollution	enlargement of mucous-secreting glands Goblet cell hyperplasia chronic inflammation, bronchial wall inflammation fibrosis.	Persistent productive cough Cyanosis (severe case) Dyspnea Blue Bloater	Emphysema Acute exacerbation of chronic bronchitis Death may result from further impairment of respiratory function due to superimposed acute infections. Blue Bloater
Emphysema	Permanent enlargement of the airspaces in the acinus due to destruction of alveolar wall (Centriacinar: Smoking · Panacinar: deficiency of α1 AT · Paraseptal: Occurs adjacent to areas of fibrosis or atelectasis. ·Irregular: scar)	Smoking Air pollution α1-anti-trypsin deficiency	large air spaces and loss of elastic tissue Voluminous lungs and pale lungs (Panacinar only)	Productive cough Barrel Chest Pink Puffers (respiratory acidosis) Weight loss wheezing. Respiratory acidosis	Pneumothorax Death from emphysema is related to: · Pulmonary failure with respiratory acidosis, hypoxia and coma. · Pulmonary hypertension. · Right-sided heart failure (Cor pulmnale)
Bronchiectasis	Dilatation and destruction of bronchi ، bronchioles secondary to chronic inflammation and obstruction	Infection/ Necrotizing pneumonia · Obstruction · Congenital (Cystic fibrosis, Kartagener's Syndrome)	Dilated airways Fibrosis Large purulent dilated bronchi grossly	Severe persistent cough with sputum (mucopurulent sputum) sometime with blood. Clubbing of fingers	Obstructive pulmonary function Lung abscess metastatic brain Amyloidosis(rarely)

Quiz

1- Is permanent "irreversible" dilation of bronchi with destruction of their walls:			
a- Bronchial Asthma	b- Chronic bronchitis	c- Emphysema	d- Bronchiectasis
2- A 34-year-old man who used to smoke two packs of cigarettes per day for 14 years. For the past 2 years, he has had a chronic productive cough that usually lasts for 3.5 month for each year. The patient came to the clinic complaining from shortness of of breath and tightness of the chest. The Clinical presentation showed audible wheezing. a biopsy that has been taken showed enlargement of mucous secreting glands causing plugging of the airway lumen (P). Which of the following pathologic conditions is most likely responsible for his clinical condition?			
a- Emphysema	b- bronchiectasis	c- chronic bronchitis	d- asthma
3- A 21 years old man came to the hospital with very severe dyspnea and a fever of 39.2 C. when Dr.Mohamed alquhidan used his stethoscope he couldn't hear anything. Which of the following is most likely the diagnosis?			
a- chronic bronchitis	b-emphysema	c- pneumothorax	d- bronchiectasis
4-: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?			
a- Atelectasis	b- Bronchiectasis	c- Empyema	d- Pyothorax
5- 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 CO 2 retention. Which of the following is the appropriate diagnosis?			
a- Atelectasis	b- Usual interstitial pneumonia	c- Hypersensitivity pneumonitis	d- Chronic obstructive pulmonary disease
6- A 55-year-old man was admitted to the hospital with a chief complaint of increasing shortness of breath over the past several years. The patient was a heavy smoker over the past 40 years. Physical examination reveals cyanosis, elevated jugular venous pressure, and peripheral edema. A high-resolution CT scan shows bullae over both lungs. Chronic intra-alveolar exposure to which of the following proteins is most likely associated with the pathogenesis of chronic obstructive pulmonary disease in this patient?			
a- α1-Antitrypsin	b- Elastase	C- Collagenase	D-Alkaline phosphatase

1- d
2-c
3-c
4-b
5-d
6-b

special thanks for
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