Obstructive Lung Diseases

@pathology434

Objectives:

- Understand that this group of disorders is characterized by an increase in resistance 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.
- Is aware that the symptom common to all these disorders is "dyspnea" (difficulty in breathing) Chronic bronchitis and emphysema almost always coexists.

Important note: During the previous blocks, we noticed some mistakes just before the exam and we didn't have the time to edit the files. To make sure that all students are aware of any changes, please check out this link before viewing the file to know if there are any additions or changes. The same link will be used for all of our work: **Pathology Edit**

Introduction.

There are four disorders in this group: emphysema, chronic bronchitis, asthma, and bronchiectasis.

- Emphysema and chronic bronchitis often are clinically grouped together under the name of ***chronic obstructive pulmonary disease*** (**COPD**). COPD affects more than 10% of the U.S. adult population and is the fourth leading cause of death in this country.

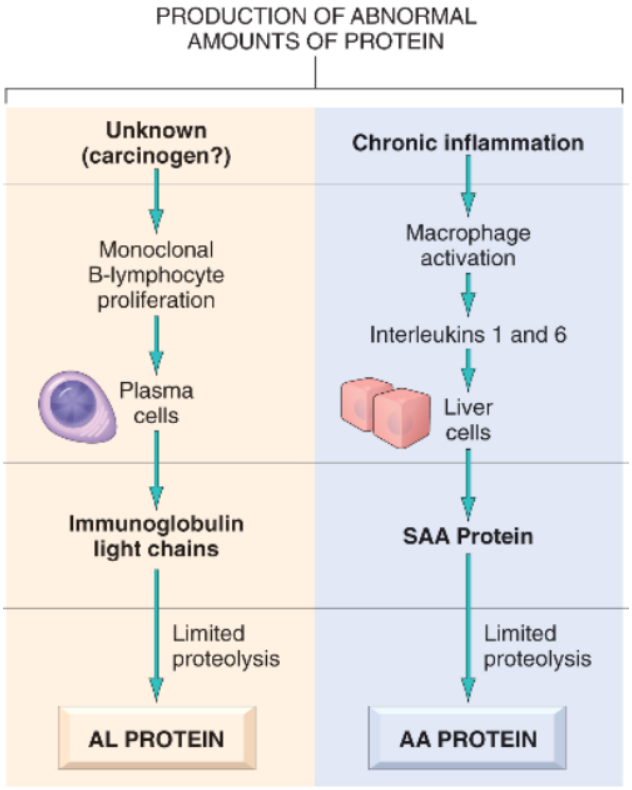
What's the difference between Asthma & COPD?
Asthma is reversible, while COPD is irreversible.

Before we start with specific diseases we would like to start by talking about amyloidosis, a complication of chronic diseases. (For full information: Robbins p153)

Amyloidosis: is a condition in which extracellular deposits of misfolded proteins lead to tissue damage.
There are several forms of amyloidosis. Two of them are of interest in our lesson: **AA** & **AL**

- **AA:** This is the one that is increased in chronic inflammation. During inflammation, macrophages release cytokines that affect the liver cells. This makes hepatocytes synthesize **SAA** which is a precursor to **AA** leading to amyloidosis of chronic diseases.
- **AL:** This is produced by plasma cells (antibody secreting cells). If there is a type of cancer that affects B lymphocytes, such as multiple myeloma[1], increased amounts of **AL** will be created & this leads to amyloidosis.

Diseases that cause amyloidosis: Rheumatoid arthritis, Bronchiectasis, TB.



Clinical Entity	Anatomic Site	Major Pathologic Changes	Etiology	Signs/Symptoms
Chronic bronchitis	Bronchus	Mucous gland hypertrophy and 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 hypertrophy and hyperplasia, excessive mucus, inflammation	Immunologic or undefined causes	Episodic wheezing, cough, dyspnea
Emphysema	Acinus	Air space enlargement, wall destruction	Tobacco smoke	Dyspnea
Small airway disease, bronchiolitis*	Bronchiole	Inflammatory scarring, partial obliteration of bronchioles	Tobacco smoke, air pollutants	Cough, dyspnea

[1] a malignant tumor of the bone marrow.

Chronic Bronchitis

It is a chronic obstructive airway disease characterized by presents of **chronic productive cough**. Productive cough means that it will produces **mucus** and **sputum**[2] and it will be present in patients during at least **3 consecutive months** over at least **2 consecutive years**.

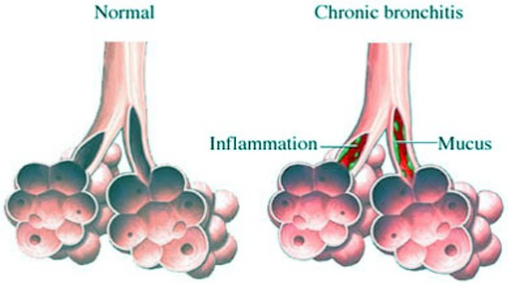
In early stages of the disease, the productive cough raises mucoid sputum, but airflow is *not* obstructed. Some patients with chronic bronchitis may demonstrate hyperresponsive airways with intermittent bronchospasm and wheezing.

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** ·

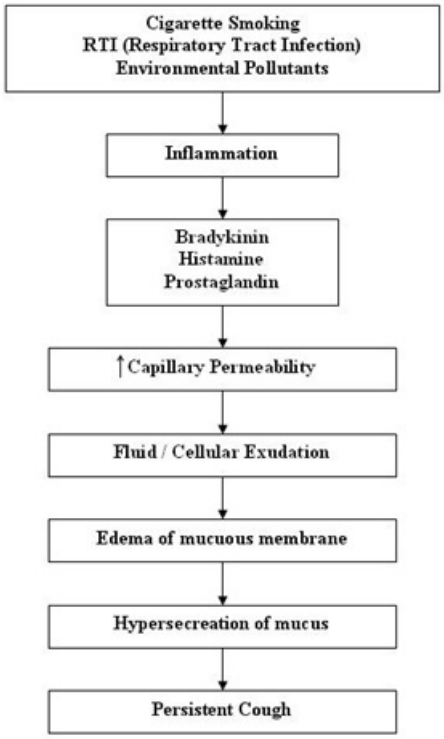
Etiology.

Chronic bronchitis is clearly linked by **cigarette smoking** and also associated with **air pollution**, **infections** (due to mucus and sputum excessive production) and **genetic factors.**

The patients will use the **accessory muscles** to help in breathing, and this will make the muscles stiff[3], In order to expel the trapped air he/she will shorten his neck to using the **sternomastoid muscles**.



Pathogenesis.



[2] a mixture of saliva and mucus coughed up from the respiratory tract
[3] rigid

Clinical presentations.

- inflammation
- Auscultation reveals crepitations (crackling sound made when breathing with an excessive mucus secretion)
- Dyspnea (shortness of breath)
- hypercapnia[4] and hypoxemia
- bronchiolar wall fibrosis
- Cyanosis in severe cases (bluish discoloration in mucosal lining)

Patients suffering of this disease may be called Blue Bloaters. Why?
1) **Blue** is because of cyanosis is one of the presenting symptoms.
2) **Bloater** because The patient has difficulties **expiring** air out of lungs causing excessive air in lungs.

Histological presentations.

- Hypertrophy and hyperplasia of mucosal and submucosal glands leads to overproduction of mucus
- Presence of mucus bulges[5] & mucosa contains pus with neutrophils, mucus, bacteria
- **Goblet cell metaplasia:** increase in their number
- Increase in the thickness of subepithelial mucus glands. This leads to an increase in the **Reid index**.
    - in contrast with asthma, there is **no eosinophils** in chronic bronchitis.

What is Reid index?
A mathematical relationship comparing the thickness of the mucous glandular tissue versus the distance from epithelium to the level of cartilage.

$$RI = \frac{gland}{wall}$$

- Biopsy NOT needed for diagnosis"

Complications of the disease.

- Increase the incidence of **infections** due to excessive mucus production.
- The patient may also be present with inward pressure in the intercostal muscles appearing contracted with bluish discoloration in very severe cases.
- Because there is inadequate ventilation, pulmonary capillaries undergo **vasoconstriction**, This process leads to **pulmonary hypertension**, which leads to **cor pulmonale** (Pulmonary heart disease)**.**

Cor pulmonale: is a heart failure caused by chronic lung diseases, usually it is right sided heart failure.

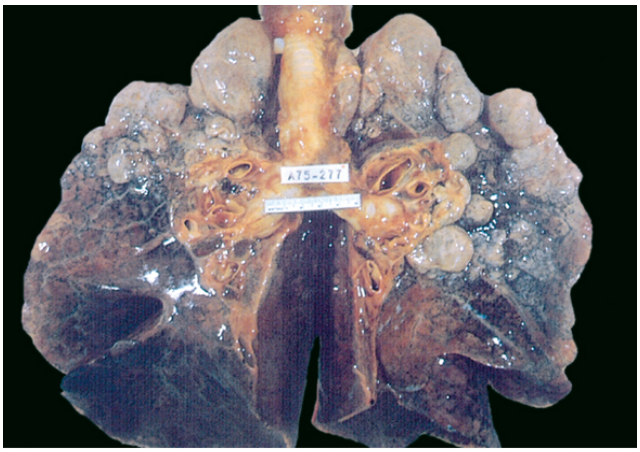
Chronic Bronchitis

- 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.
- Histologic examination demonstrates enlargement of mucus-secreting glands, goblet cell metaplasia, and bronchiolar wall fibrosis.

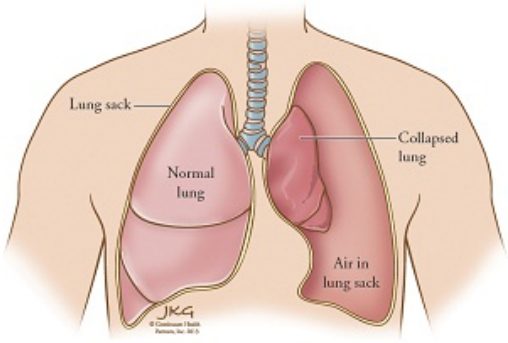
[4] excessive carbon dioxide in the bloodstream
[5] bulge is a rounded swelling which distorts an otherwise flat surface

Emphysema.

It is a permanent[6] –usually irreversible- dilation of the small airways which are distal to the terminal bronchioles.



Damage of large areas of the alveoli cause emphysematous bullae[7].



A common complication emphysema that it could be the cause of **Secondary Spontaneous Pneumothorax** (A sudden collapse of the lung) caused by emphysematous bullae, which is considered as a threatening medical emergency.

- ➔ Primary pneumothorax → without an apparent cause.
- ➔ Secondary pneumothorax → Caused by lung disease (For example: COPD).

Management: **Tube thoracostomy** → inserting a chest tube to the chest to drain air, fluid, pus.. etc

Presentation.

- Dyspnea
- Usually associated with chronic bronchitis. **Why?** Because smoking is a common etiologic factor
- Increase in anteroposterior diameter of the chest "**Barrel shape**" over expiation of lung parenchyma
- Patients with this disease are described as "**Pink Puffers**[8]"

Etiology: Smoking cause chemical inflammation, Pollution, Congenital.

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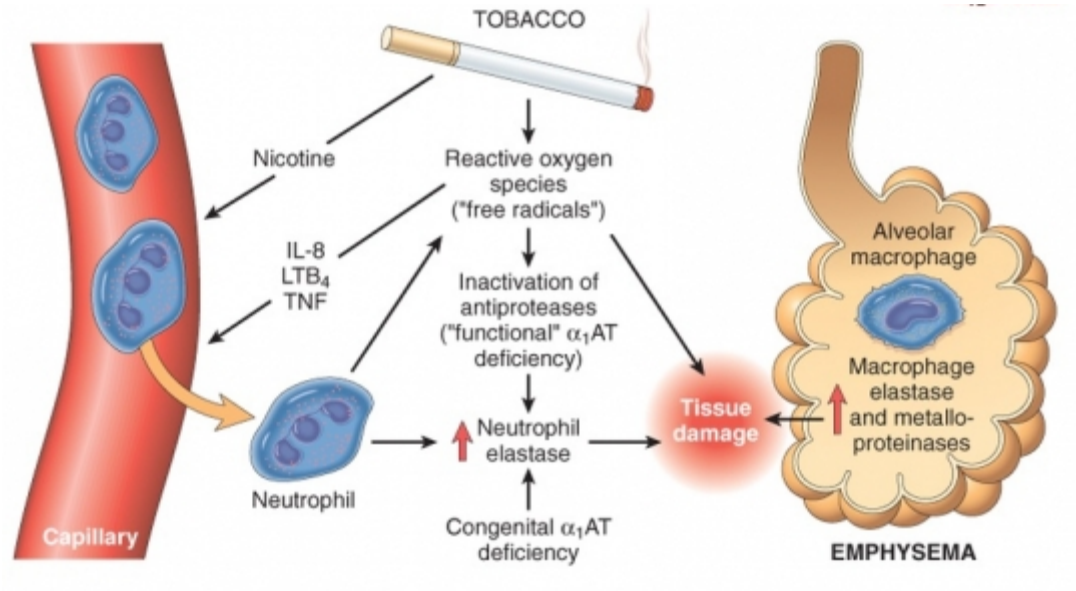
[6] دائم

[7] bullae = فقاعات

[8] Because the emphysema drastically increases the effort required to inhale and exhale, causing facial flushing (pinkish coloration) and obviously labored breathing (puffing).

Pathogenesis of smoking induced emphysema.
Chronic irritation by cigarettes → inflammation → chemotaxis → inflammatory cells (such as neutrophils) release proteolytic enzymes such as elastase & proteases that cause destruction of alveolar walls → emphysema.

There is an enzyme in the lung called **alpha-1 antitrypsin** (This enzyme is responsible of inactivating proteolytic enzymes). Alpha- 1 antitrypsin gene is autosomal recessive. Deficiency causes *congenital* emphysema.

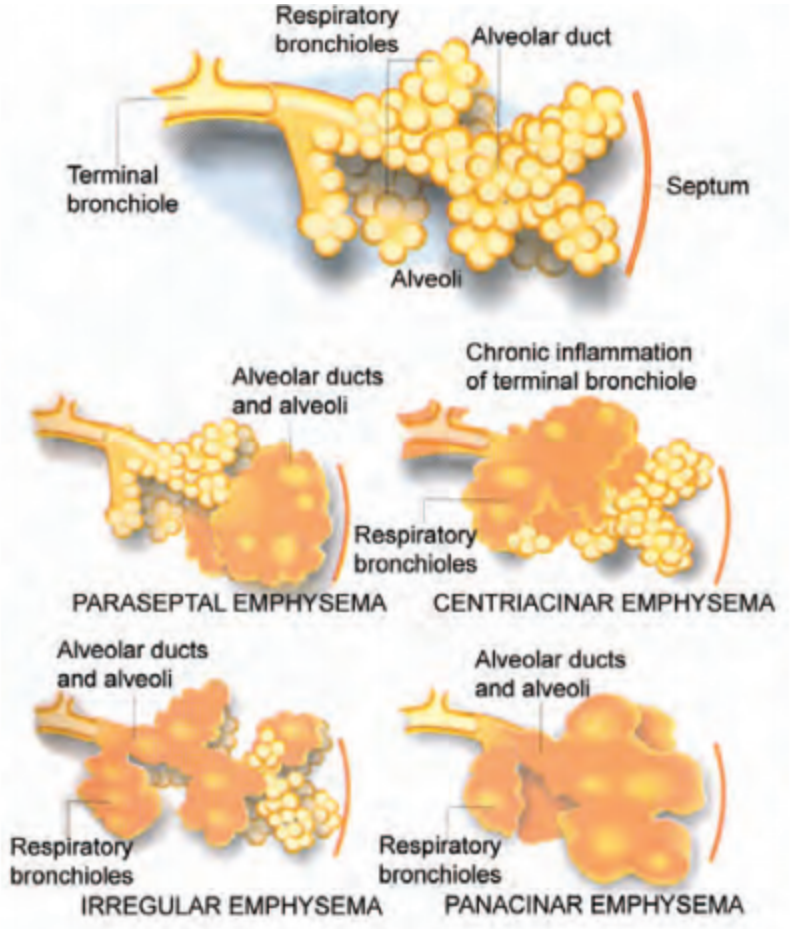


Types of emphysema.

Type	Location	Causes
Centriacinar (Centrilobular)	The central or proximal parts of the acini	Smoking
Panacinar (Panlobular)	Uniform injury	Alpha- 1 antitrypsin deficiency
Distal Acinar (Paraseptal)	effect peripheral parts (dilate) alveolar duct and alveoli	unknown; seen often in cases of spontaneous pneumothorax in young adults.
Irregular	Multiple site of acini	healed inflammatory diseases

- Irregular Emphysema is more common is Saudi Arabia usually caused by infection like T.B.
- There is an extra type called Intestinal Emphysema it happens after surgeries or accidents due to rupture in the lung making air escape to intestinal, and subcutaneous tissues.

Only the first two types cause clinically significant airway obstruction, with centriacinar emphysema being about 20 times more common than panacinar disease.



Complications:

- Cor pulmonale.
- Respiratory acidosis[9].
- Chronic Bronchitis.

Emphysema

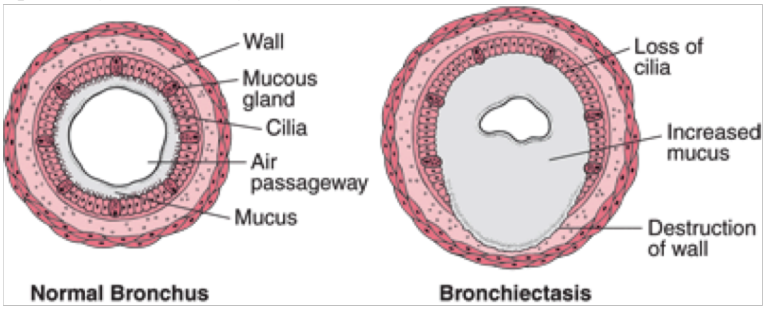
- Emphysema is a chronic obstructive airway disease characterized by permanent enlargement of air spaces distal to terminal bronchioles.
- Subtypes include centriacinar (most common; smoking-related), panacinar (seen in α_1-antitrypsin deficiency), distal acinar, and irregular.
- Smoking and inhaled pollutants cause ongoing accumulation of inflammatory cells, releasing elastases and oxidants, which destroy the alveolar walls without adequate mesenchymal repair response.
- Most patients with emphysema demonstrate elements of chronic bronchitis concurrently, since cigarette smoking is an underlying risk factor for both; patients with pure emphysema are characterized as “pink puffers.”

[9] an excessively acid condition of the body fluids or tissues.

Bronchiectasis.

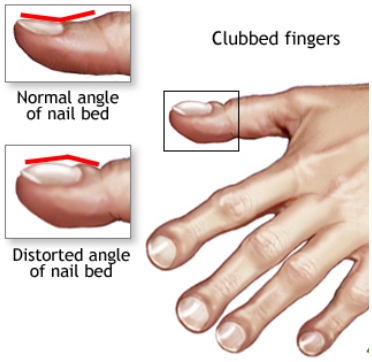
[Bronchiectasis Animation - What is Bronchiectasis?]

It is chronic necrotizing infection and inflammation of bronchi and bronchioles leading to abnormal Permanent and irreversible **dilation** of bronchial walls (airways). It usually affects the **lower parts of the lung,** and rarely affects upper parts (lower lobe).



Clinical feature :

- Severe persistent cough with sputum (has bad smell and sometimes with blood) **why?** Anaerobic bacteria "cilia is damaged,so it cannot let bacteria out"
- Fever, hypoxemia and hypercapnia.
- clubbing of fingers[10].
- **If severe:** obstructive pulmonary function develope (may lead to lung abscess).



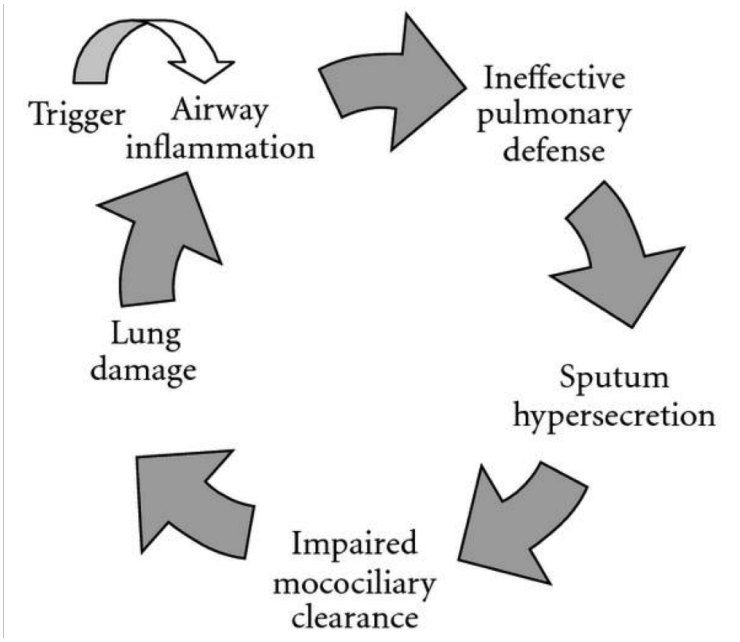
Bronchiectasis is a result of chronic inflammation compounded by an inability to clear mucoid secretions. Conditions commonly associated with Bronchiectasis are as follows:

Pathogenesis of Bronchiectasis.

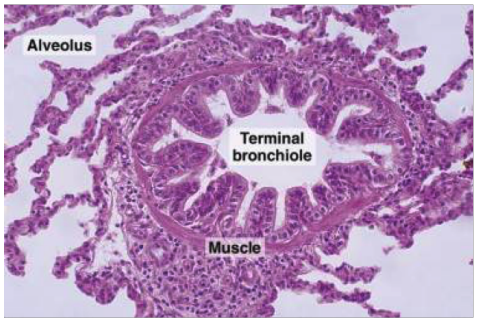
Any of the previously mentioned conditions can cause damage to the airways resulting in impaired mucociliary clearance, mucus stasis and accumulation which in turn further makes the airways susceptible to microbial colonization. The persistence of the pathology with superadded infection leads to a "**vicious circle**" of inflammation and tissue damage.

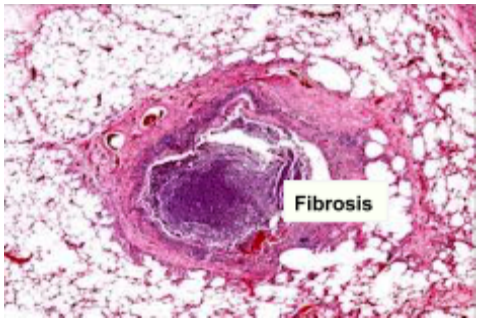
Inflammation results in progressive destruction of the normal lung architecture, in particular the elastic fibres of bronchi.
Neutrophils are thought to play a central role in the pathogenesis of tissue damage that occurs in bronchiectasis.

[10] Clubbed fingers is a symptom of a disease of the heart or lungs 'often'. diseases that cause chronically low blood levels of oxygen.



NORMAL **Bronchiectasis**





Cavities (dilated bronchi) dilated airways up to four times of normal, reaching the pleura.

Congenital or hereditary conditions:

- Conginital bronchiectasis.
- Kartagener's Syndrome (immotile cilia).
- Cystic fibrosis.
- Immunodeficiency status.
- Intralobar sequestration of lung → Congenital condition caused by a piece of tissue that develops in the lung but isn't attached to the blood supply.

Obstruction of bronchi:

- localized: tumor, foreign bodies or mucus impaction
- Generalized: Bronchial asthma , chronic bronchitis

Cystic Fibrosis.

It is an inherited disease causes thick, sticky viscous mucus to build up in lungs and digestive tract.
thick mucosal secretion causing bronchiectasis.

Immotile cilia syndrome/ Kartagener syndrome.

An autosomal recessive condition characterized by absence of outer and inner dynein[11] arms causing immotile cilia & therefore loss of defense in upper Respiratory Tract causing sinusitis, Infertility in males, daphnis "can't hear".

- increased risk of infection → Cause the cilia can't function to take the sputum out of the lung (which contains a lot of bacteria).

Diagnosis of ICS (Immotile Cilia syndrome):

- Genetic study
- Electron microscope

Complications:

- **Lung abscess**
- **Rare complications: metastatic brain abscess and amyloidosis.**
- **If severe, obstructive pulmonary function develop.**
- **Infection/ Necrotizing pneumonia** caused by TB, staphylococci or mixed infection.
- Chronic inflammation → amyloidosis (as we have explained in the beginning)

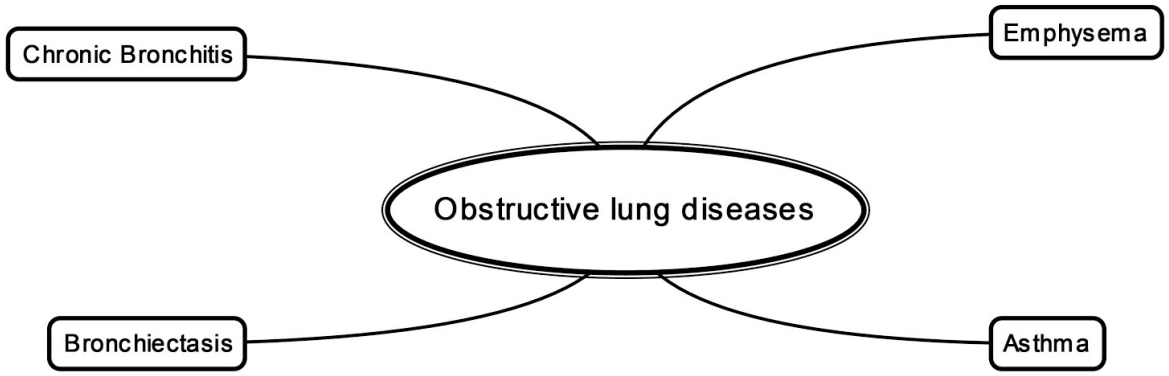
If there is a lot of pus formation (chronic inflammation), it is better to do spectomy taking the affected lobe of the lung.

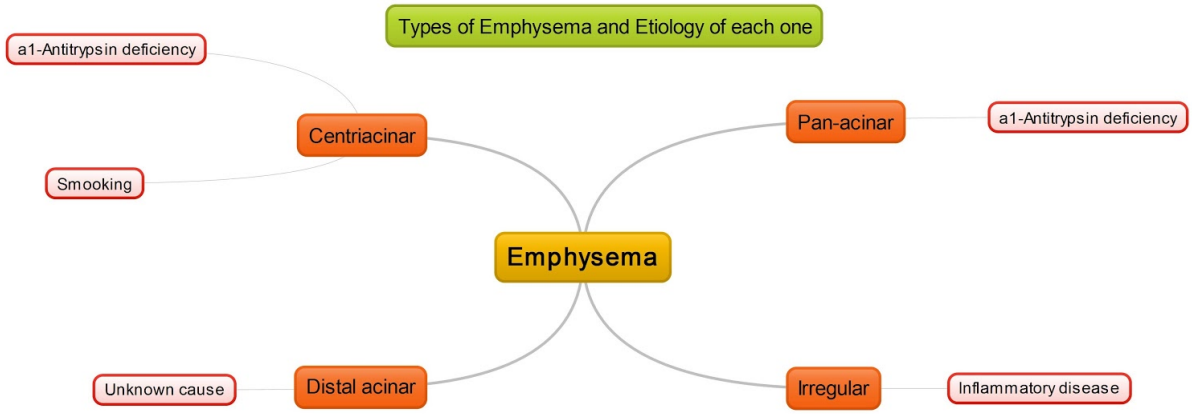
Why bronchiectasis is considered obstructive lung disease although there is not any actual blocking of airways?

Loss of the elasticity[12] of the alveolar wall cause resident to air flow.

[11] Dynein: a type of ATpase, provides energy for microtubules sliding.
[12] flexibility

Summary.


Chronic Bronchitis
Emphysema
Obstructive lung diseases
Bronchiectasis
Asthma


Types of Emphysema and Etiology of each one
a1-Antitrypsin deficiency
Centriacinar
Smooking
Pan-acinar
a1-Antitrypsin deficiency
Emphysema
Unknown cause
Distal acinar
Irregular
Inflammatory disease

MCQ's.

1.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 several episodes of respiratory tract infections that were diagnosed as "viral flu," and he developed difficulty breathing, tightness of the chest, and audible wheezing. His breathing difficulty was relieved by inhalation of a β-adrenergic agonist and disappeared after the chest infection had resolved. Which of the following pathologic conditions best describes these clinical findings?

(A)Cor pulmonale
(B) Chronic bronchitis with asthmatic bronchitis
(C) Emphysema
(D) Bronchiectasis

Ans:(B) Smoking is one of the causes of Chronic asthmatic bronchitis(diseases' overlap). He has had persistent cough with sputum production for at least 3 months in 2 consecutive years.

2. A 50-year-old man comes to the physician with gradually increasing dyspnea and a 4-kg weight loss over the past 2 years. He admits to smoking two packs of cigarettes per day for 20 years, but states that he has not smoked for the past year. Physical examination shows an increase in the anteroposterior diameter of the chest ("barrel chest"). Auscultation of the chest shows decreased lung sounds. A chest radiograph shows bilateral hyperlucent lungs; the lucency is especially marked in the upper lobes. Pulmonary function tests show that the FEV1 is markedly decreased, but the FVC is normal,and FEV1/FVC ratio is decreased. Which of the following is most likely to contribute to the pathogenesis of his disease?

(A) Impaired hepatic release of α1-antitrypsin
(B) Release of elastase from neutrophils
(C) Abnormal epithelial cell chloride ion transport
(D) Decreased ciliary motility with irregular dynein arms

Ans:(B) The patient's findings are predominantly those of an obstructive lung disease—emphysema—with a centrilobular pattern of predominantly upper lobe involvement. Smoking is a major cause of this disease. The inflammation that can accompany smoking leads to increased neutrophil elaboration of elastase and elaboration of macrophage elastase that not inhibited by the antiprotease action of α1-antitrypsin.

3. 21 A 20-year-old, previously healthy man is jogging one morning when he trips and falls to the ground. He suddenly becomes markedly short of breath. His jogging partner brings him to the emergency department where on examination there are no breath sounds audible over the right chest. A chest radiograph shows shift of the mediastinum from right to left. A right chest tube is inserted, and air rushes out. Which of the following types of obstructive lung disease is the most likely diagnosis?

(A) Bronchiectasis
(B) Centriacinar emphysema
(C) Chronic bronchitis
(D) Distal acinar emphysema

Ans:(D) Distal acinar (paraseptal) emphysema is localized, beneath pleura typically in an upper lung lobe, and may occur in an area of fibrosis or scar formation. It could cause pneumothorax. α1-antitrypsin deficiency is the most likely antecedent.

4. Asthma's cough differs from Chronic Bronchitis in:

A. Dry cough in Chronic Bronchitis.
B. productive cough in Asthma.
C. cough with sputum in Asthma.
D. productive cough in Chronic Bronchitis.

Ans:D

5. All of the following related to Chronic Bronchitis, except:

A. The ratio of FEV1 to FVC is reduced.
B. Increase sleepiness.
C. Secondary polycythemia due to chronic hypoxia.
D. Right ventricular dilation and hypertrophy.

Ans:A

6. Patient came to the clinic with increased anteroposterior diameter of the chest, increased total vital capacity and hypoxia. What is the diagnosis :

A. emphysema.
B. restrictive pulmonary diseases.
C. bronchial asthma.
D. Bronchiectasis.

3- Which one of emphysema types is tend to localize subjacent to the pleura and interlobular septa:

A. irregular emphysema.
B. panacinar emphysema.
C. paraseptal emphysema.
D. centrilobular emphysema

Ans:C

7.An enzyme that destroys elastic fibers from the wall of alveoli:

A. Elastase.
B. Amylase
C. Alpha 1 antitrypsin.
D. IL6

Ans:A

8.The difference between the location of Centrilobular emphysema and Bronchiectasis:

A. Bronchiectasis is in the upper part of the pulmonary lobes.
B. Centrilobular is in the lower part of the pulmonary lobes.
C. whole the pulmonary lobes are involved in Bronchiectasis
D. Centrilobular is in the upper part of the pulmonary lobes.

Ans:D

9. A 33-year-old man has had increasing dyspnea for the past 8 years. On examination, there are decreased breath sounds over all lung fields. A chest radiograph shows flattened diaphragms and increased lucency in all lung fields. Pulmonary function tests show decreased FEV1 and increased FVC. A sibling is similarly affected. What is the most likely mechanism for his pulmonary disease?
(A) Atopy with IgE binding to mast cells
(B) Increased neutrophil proteases
(C) Prior infection with tuberculosis
(D) Reduced antielastase activity
Ans: D He is having Emphysema.The major antielastase is α1-antitrypsin deficiency leads to increasing of proteases (elastase). D is more specific than B.

10- Which enzyme is inactivated by alpha-1 antitrypsin?

A. ACE 2
B. Elastase
C. Proteases
D. Both B,C

Ans:D

11. Ahmad 21 years old came to hospital, because he had productive cough for last 8 months, also he is smoker. We did sputum culture, we found macrophages full of carbon, and a lot of neutrophil. What is the diagnosis?
A.Chronic bronchitis
B. Emphysema
C.Chronic asthma
D.Bronchiectasis
Ans:A

12.Which of the following is causing infertility?
A.Bronchiectasis
B.Emphysema
C.kartagener syndrome
D.pneumothorax
Ans:C

Direct questions:

1. **What are Chronic Obstructive Pulmonary Diseases?**

group of disorder is characterized by an increase in resistance to airflow, owing to partial or complete obstruction at any level of the bronchial/bronchiolar.

- Chronic Bronchitis, Emphysema, Asthma, Bronchiectasis.

2. **The diagnosis of chronic bronchitis is based on what?**

Based on clinical features. Persistent productive cough (with sputum) for at least 3 consecutive months in 2 consecutive years (at least).

3. **What are the complications in Chronic Bronchitis?**

- Pulmonary failure with respiratory acidosis, hypoxia and coma.
- Cor-pulmonale

4. **Where is the site of dilation in Emphysema?**

Distal to terminal bronchiole. (include: respiratory bronchiole, alveolar duct ,"alveolar sac and alveoli" acinus)

5. **Paraseptal Emphysema could lead to pneumothorax?**

Accumulation of air in pleural cavity lead to (acute medical emergency), it will compress the lung and collapse it.

6. **What is the etiology of Kartagener Syndrome?**

Defect in the motility of respiratory, auditory, and sperm cilia, due to absence of outer and inner dynein arms.

Dynein=a type of ATPase, provides energy for microtubules to move.

7.What are the possible complications of Bronchiectasis?

- Lung Abscess
- Rare complications: metastatic brain abscess and amyloidosis.

True and false:

1.Bronchiectasis is a primary permanent and abnormal bronchial dilatation.
2.Neutrophils is source of elastase and attracts by cigarette smoking.
3. The acinus is irregularly involved, associated with scarring in Panacinar (panlobular) emphysema.
4. Emphysema characterized as anatomical pulmonary obstructive disease.

Anc:
1.F, not 1ry. It is 2ry to chronic inflammation, infection…
2.T
3.F,in irregular emphysema
4.F,physiological pulmonary obstructive disease

Contact us on: Pathology434@gmail.com
Twitter: **@Pathology434**

Good Luck!

عمر الرهبيني
محمد الخراز
أحمد الصالح

مها الربيعة
هديل السلمي
ريما الرشيد
ريم لبني
نوف الحربي
نجلاء الدريويش