Respiratory block
2018
Pathology

Chronic obstructive pulmonary disease (COPD)

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Objectives:

- Give introduction for diffuse lung disease
- Explain why emphysema and bronchitis are both considered to be examples of chronic obstructive pulmonary disease (COPD).
- Compare and contrast the major clinical and functional differences between predominant chronic bronchitis versus predominant emphysema in patients with COPD

Chronic Bronchitis

a. Define chronic bronchitis.
b. Describe the pathogenesis and the morphology of chronic bronchitis.
c. Describe the mechanism of airway obstruction in a patient with chronic bronchitis.
d. Understand that when severe obstruction is present in chronic bronchitis, significant emphysema is nearly always present

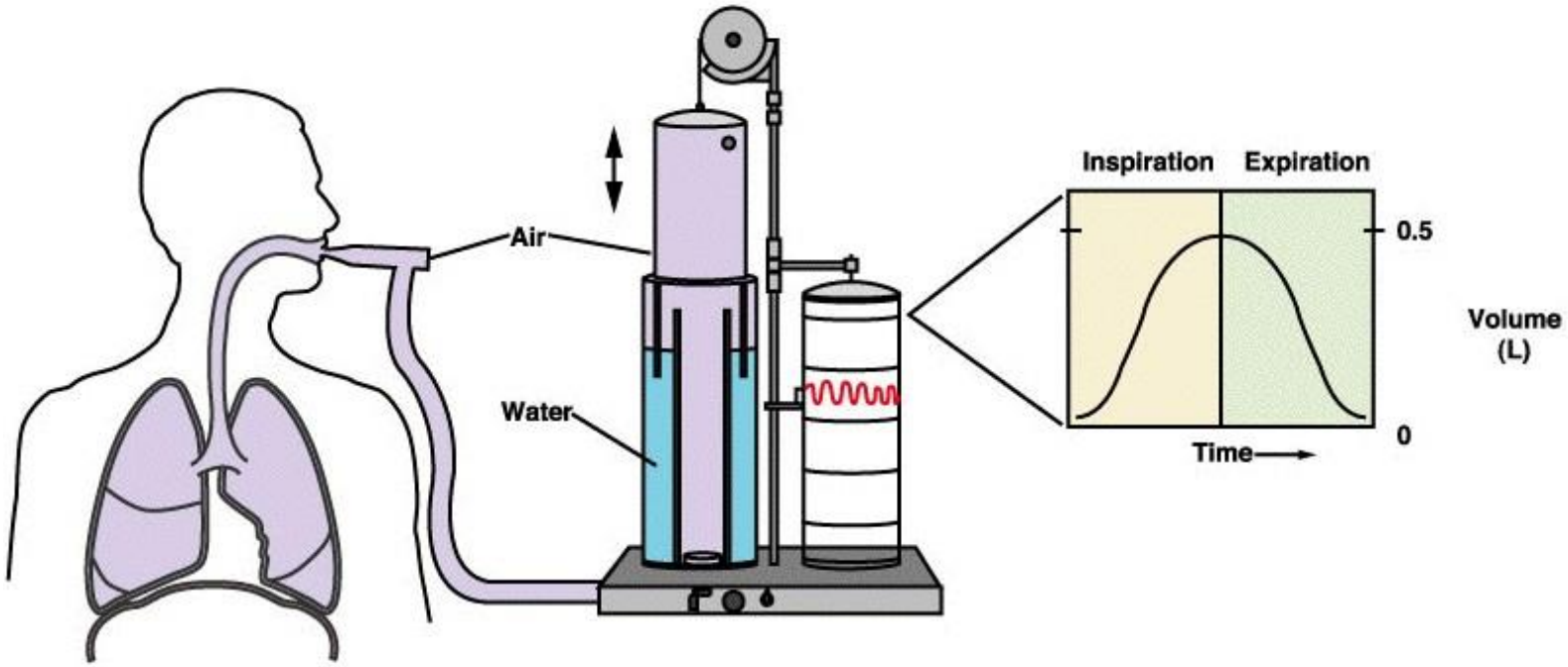
Emphysema

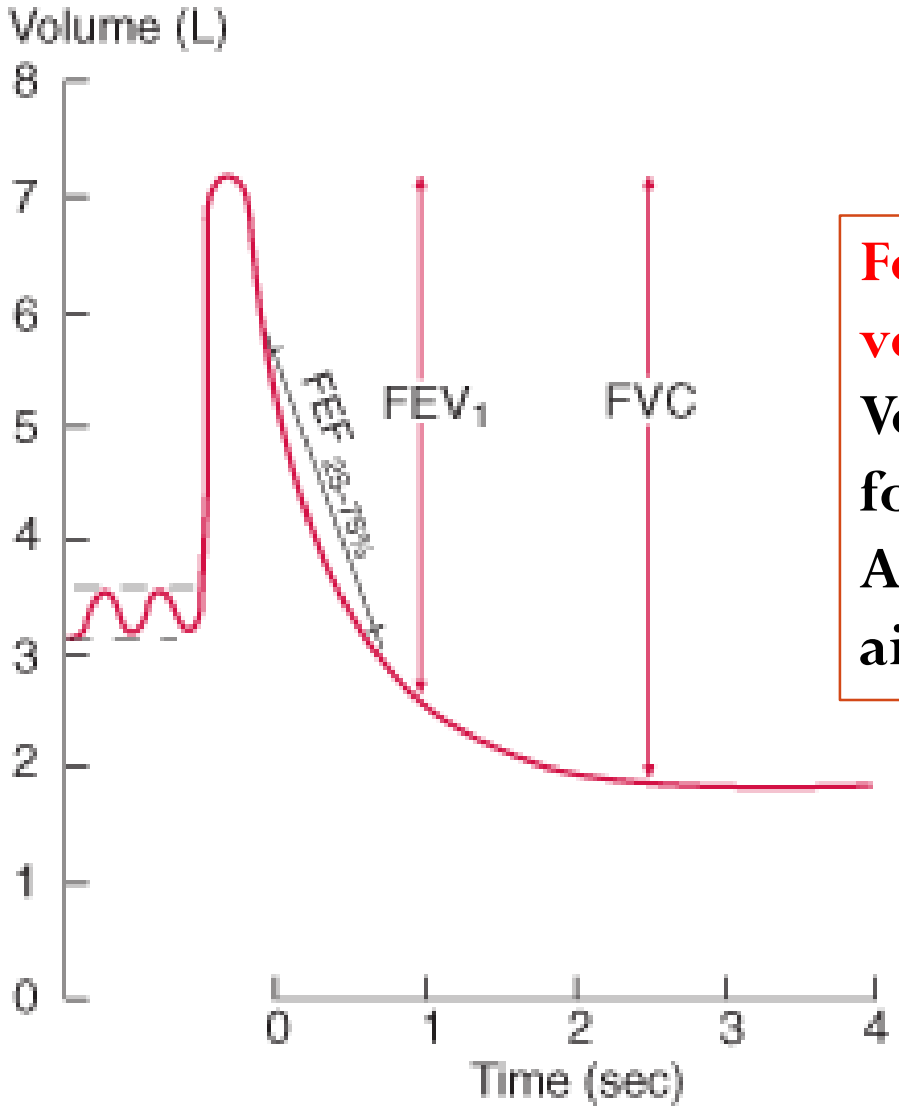
a. Define emphysema.
b. Describe the gross and microscopic changes in emphysema.
c. Discuss the typical clinical presentation and causes of death.
d. Describe the most likely mechanism of emphysema (the protease-antiprotease mechanism).
e. Describe the pathophysiologic mechanisms of emphysema

- Define Bronchiectasis and its causes, presentation, morphology and significant.

Spirometer

- is an equipments used for measuring the volume of air inspired and expired by the lungs (Pulmonary Function Tests)





Forced expiratory volume (FEV1):
Volume of air blown out forcibly in 1 second.
A function of large airways.

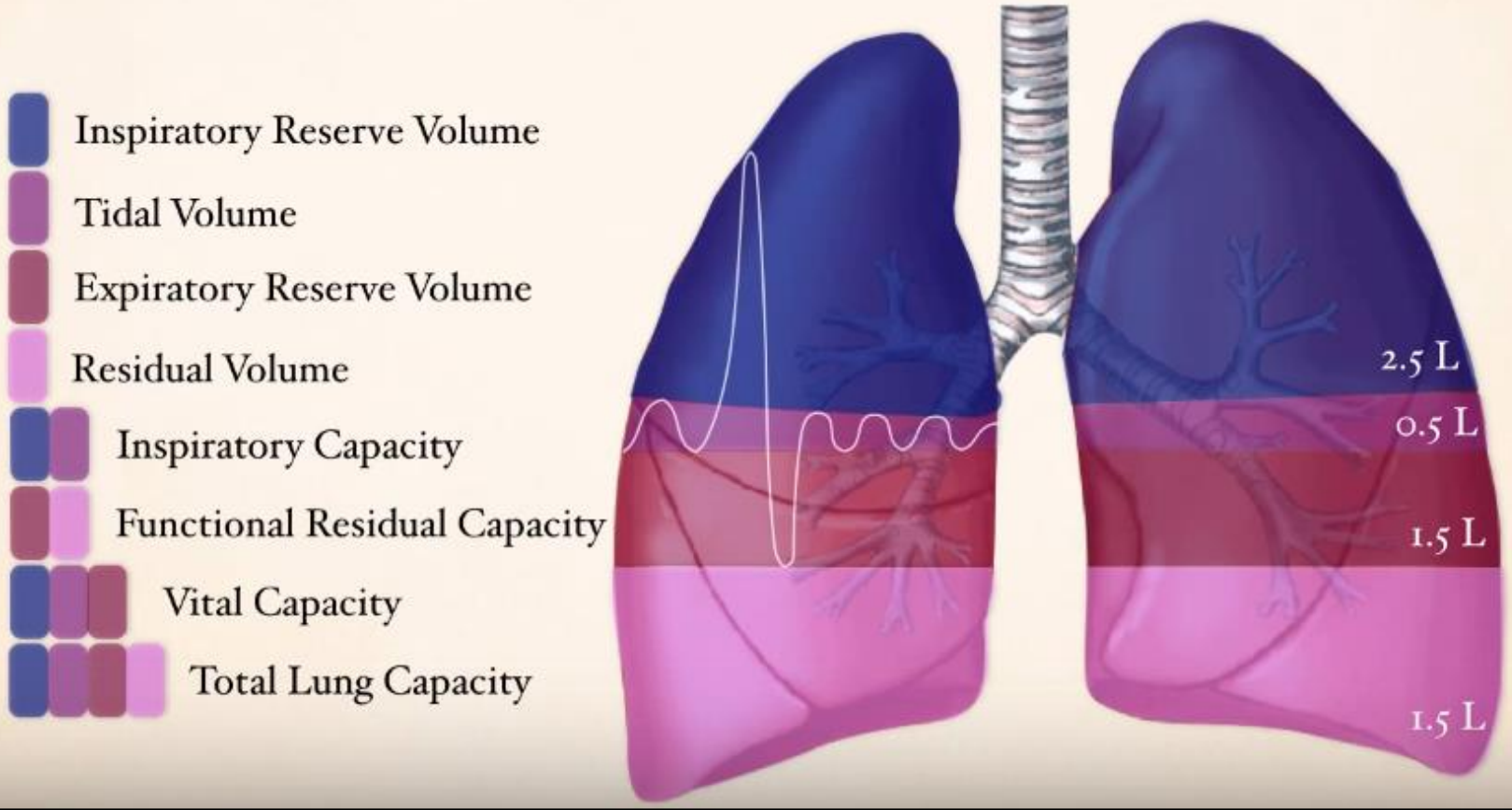
Obstructive and Restrictive Pulmonary Diseases

- Diffuse pulmonary diseases are divided into:

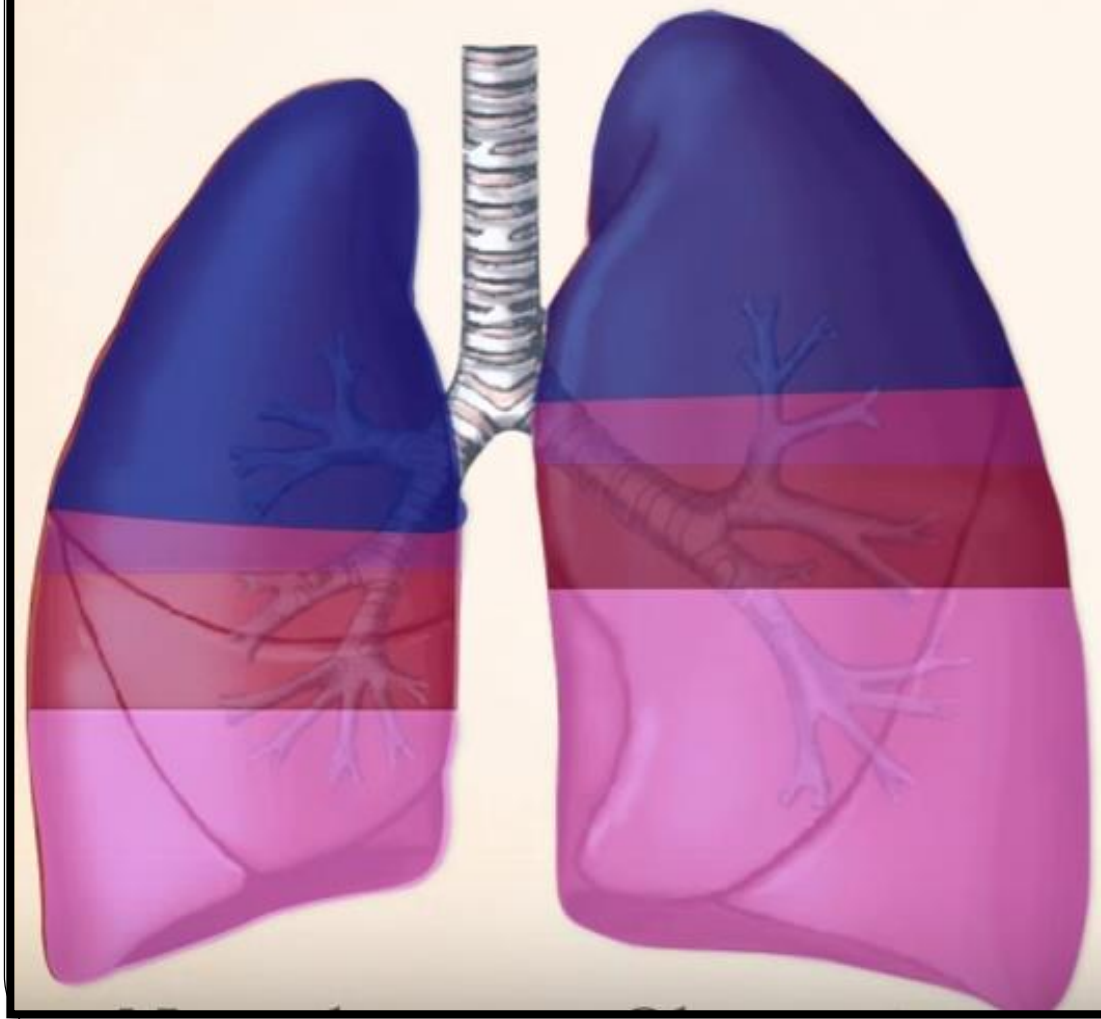
1. Obstructive disease:
characterized by limitation of airflow owing to partial or complete obstruction at any level from trachea to respiratory bronchioles.
Pulmonary function test: limitation of maximal airflow rate during forced expiration (FEVI).

2. Restrictive disease:
characterized by reduced expansion of lung parenchyma with decreased total lung capacity while the expiratory flow rate is near normal.
Occur in:
1. Chest wall disorder.
2. Acute or chronic, interstitial and infiltrative diseases,
e.g. ARDS and pneumoconiosis.

INTRODUCTION
LUNG VOLUMES AND CAPACITIES



OBSTRUCTIVE



Forced Expiratory Volume in 1sec ↓↓

Forced Vital Capacity ↓

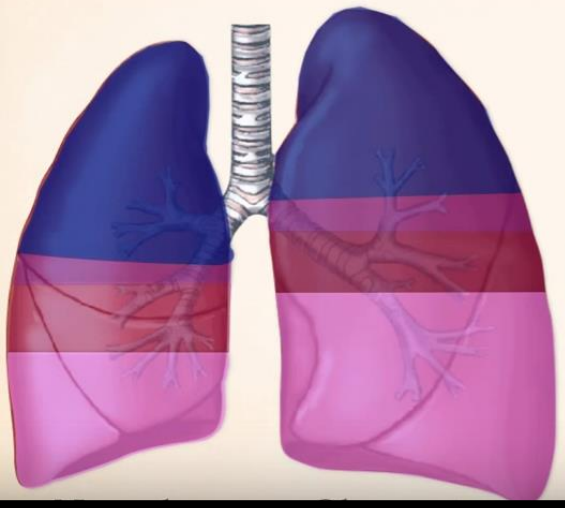
FEV1 / FVC ↓↓

Total Lung Capacity ↑

Residual Volume ↑↑

Introduction for diffuse lung disease

OBSTRUCTIVE



Forced Expiratory Volume in 1sec ↓

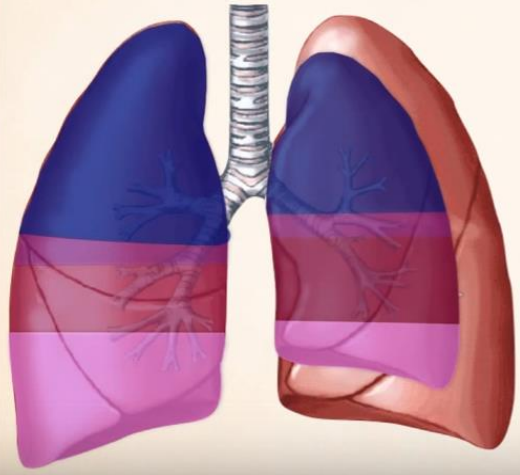
Forced Vital Capacity ↓

FEV1 / FVC ↓↓

Total Lung Capacity ↑

Residual Volume ↑↑

RESTRICTIVE

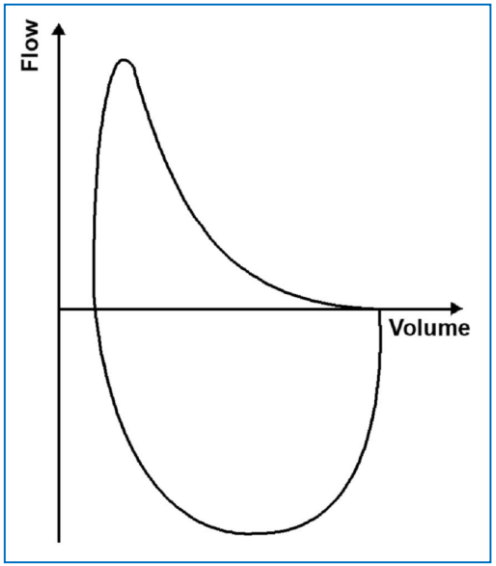


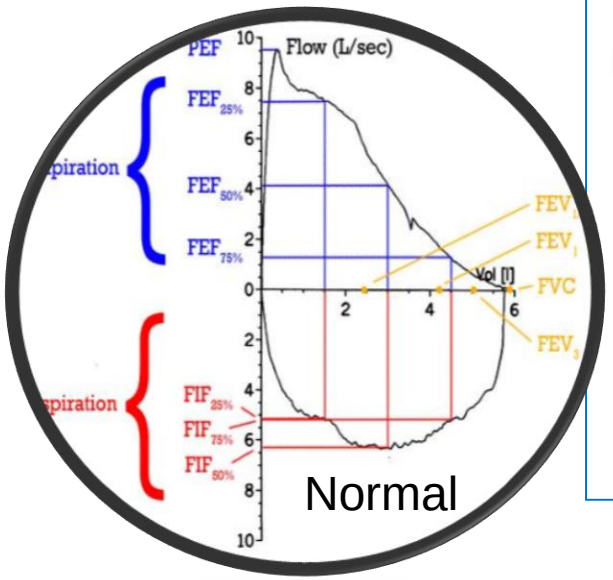
Forced Expiratory Volume in 1sec ↑

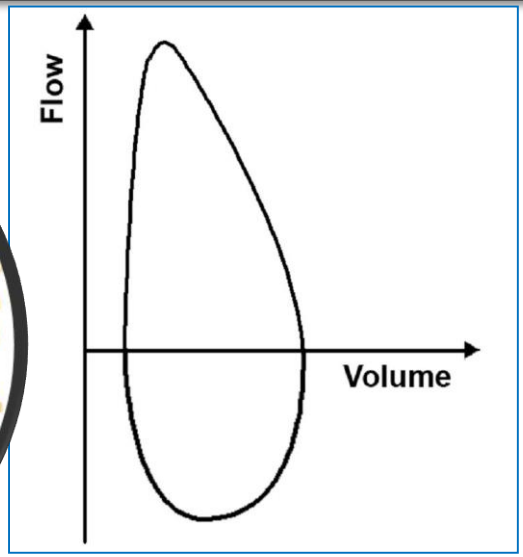
Forced Vital Capacity ↓↓

FEV1 / FVC ↑

Total Lung Capacity ↓↓







Chronic obstructive Pulmonary Disease (COPD)

=Chronic obstructive airway disease (COAD)
=Chronic obstructive lung disease (COLD)

COPD:

- Irreversible obstruction to airflow out of the lungs
- Cigarette smoking is the principal cause of COPD
- Greater than 10% of the population >45 years old has airflow obstruction.
- Majority of patients with COPD have both emphysema (air space destruction) and chronic bronchitis

Obstructive Lung Diseases

(diffuse)

1) Bronchial Asthma

Common symptoms in lung disease

- **Dyspnea: difficulty with breathing**
- **Cough**
- **Hemoptysis**

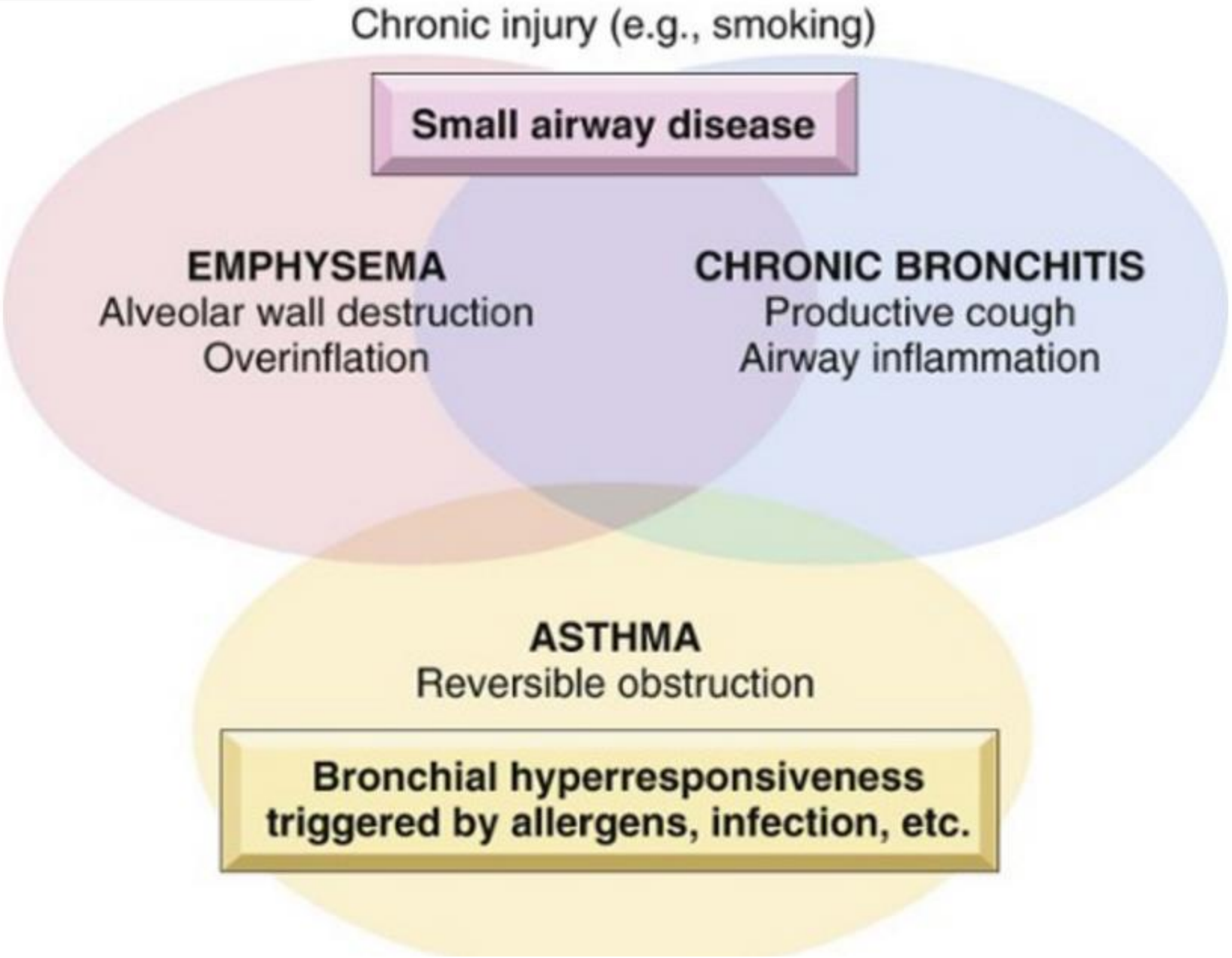
2) **Chronic obstructive pulmonary disease (COPD)** **They are of two types:**

   a) Chronic bronchitis

   b) Emphysema

3) Bronchiectasis

Obstructive lung disease



Chronic Bronchitis

a. Define chronic bronchitis.
b. Describe the pathogenesis and the morphology of chronic bronchitis.
c. Describe the mechanism of airway obstruction in a patient with chronic bronchitis.
d. Understand that when severe obstruction is present in chronic bronchitis, significant emphysema is nearly always present

Chronic Bronchitis

- The definition of chronic bronchitis is based on clinical features
- **Persistent productive cough (with sputum) for at least 3 consecutive months in at least 2 consecutive years**

Chronic bronchitis

Causative factor are:

- Cigarette smoking and pollutants. Most patients are smokers
- Infection
- Genetic factors e.g. cystic fibrosis
- Age: 40 to 65

Chronic bronchitis

Pathogenesis

Chronic irritation of inhaled substances or microbial infection leads to:

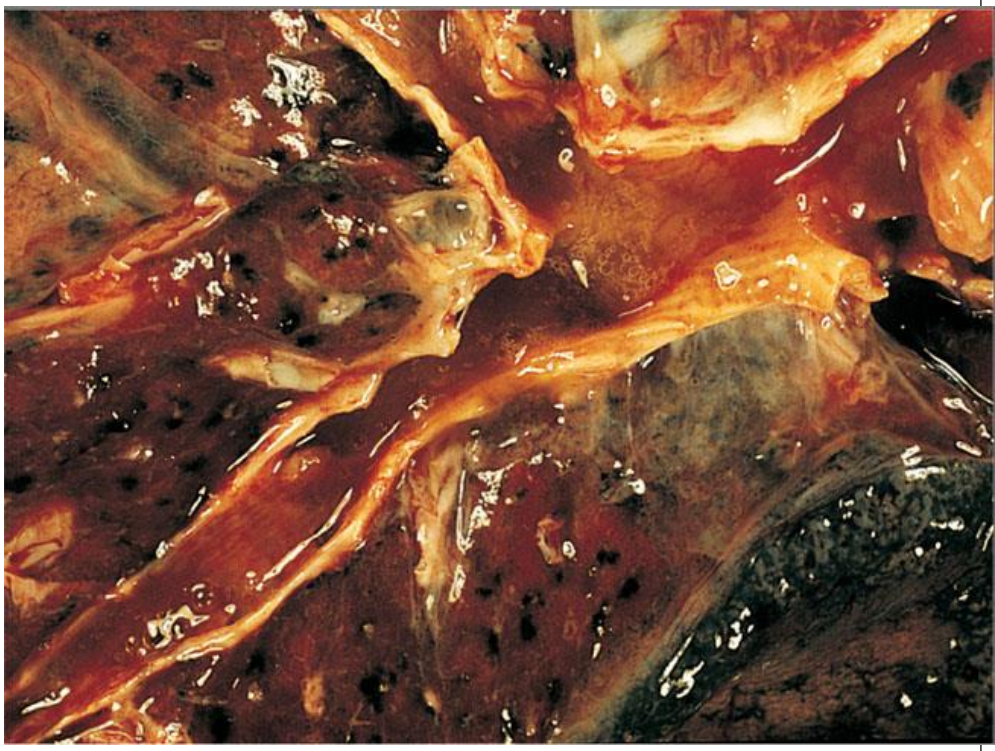
- Hypersecretion of mucus that starts in the large airways with associated hypertrophy of the sub-mucosal glands and inflammation.

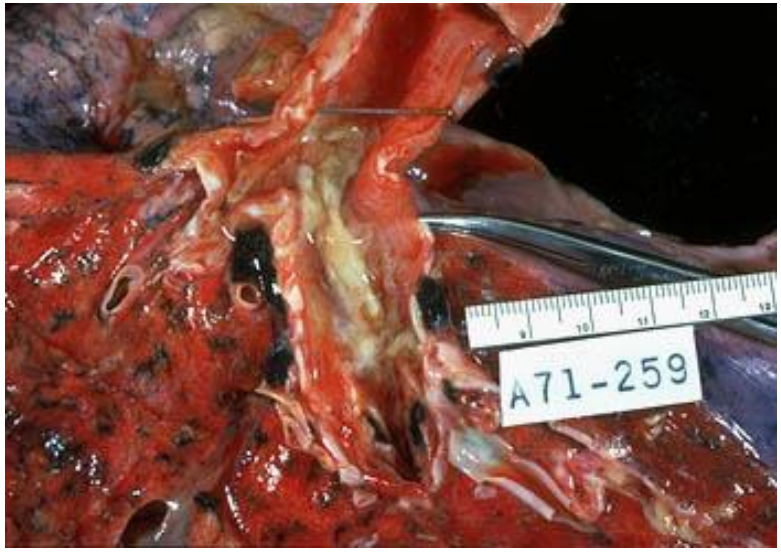
- Infection. Infection does not initiate chronic bronchitis, but is probably significant in maintaining it and may be critical in producing acute exacerbations.

- As chronic bronchitis persists the small bronhi and bronchioles also get affected leading to irreversible bronchiolar wall fibrosis

Chronic bronchitis: Pathologic findings

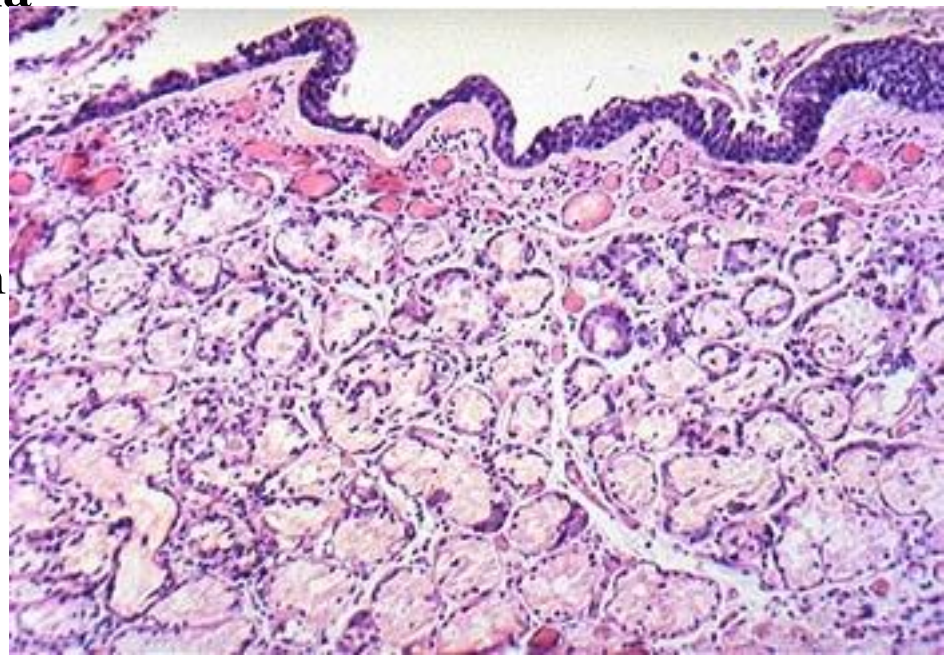
- Chronic bronchitis does not have characteristic pathologic findings
- In bronchitis the airway mucosa is red and edematous





Chronic bronchitis: morphology

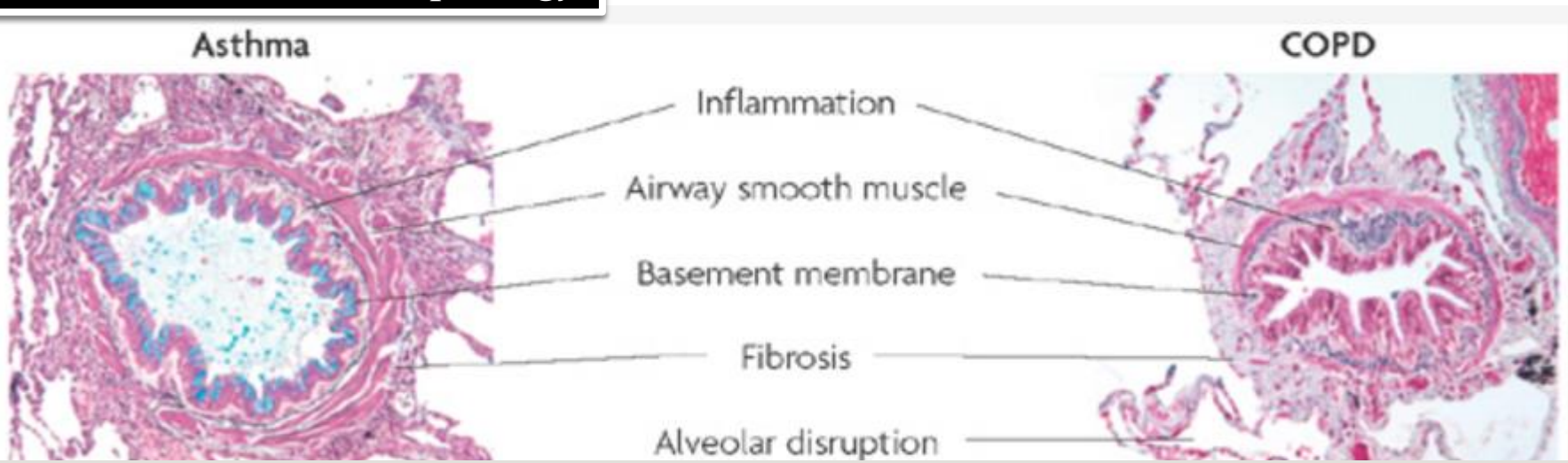
- **Inflammation of airways,** fibrosis and narrowing of bronchioles
- **Hypertrophy and hyperplasia of mucus producing cells** increased number of goblet cells
- **Squamous metaplasia** which can progress to dysplasia and even invasive carcinoma
- **Injury to cilia with** loss of ciliated epithelial cells
- Coexistent emphysema



How do these changes differ from the changes seen in a typical case of allergic asthma?

A typical allergic asthma, which also has mucous gland hyperplasia, the bronchial wall has an inflammatory infiltrate in which eosinophils are prominent. There is also hypertrophy and hyperplasia of smooth muscle cells in asthma.

Chronic Bronchitis: Morphology



Inflammation	+++	+++
Airway smooth muscle	+++	+
Basement membrane	++	–
Fibrosis	+ (subepithelial)	+++ (peribronchiolar)
Alveolar disruption	–	+++
Airway vessels	++	No change
Mast cells	++ (and activated)	Normal
Dendritic cells	++	ND
Eosinophils	++	Normal
Neutrophils	Normal	++
Lymphocytes	T_H2 type	T_H1 and T_C1 type
Epithelium	Often shed	Pseudostratified
Goblet cells	++	++

Chronic bronchitis: Clinical Course

- Prominent cough and the production of sputum.
- Hypercapnia, hypoxemia and cyanosis.
- Patients with severe chronic bronchitis are termed blue bloaters.
- Patients can have:
  - increased sleepiness due to CO_2 narcosis
  - cyanosis due to very poor oxygenation
  - elevated red cell counts (secondary polycythemia) as a result of chronic hypoxemia
  - Cardiac failure (Cor pulmonale/right heart failure): diseases of the lung or pulmonary vasculature leads to pulmonary hypertension which leads to right ventricular dilation and hypertrophy (right heart failure).

Patients with chronic bronchitis and COPD have frequent exacerbations, more rapid disease progression, and poorer outcomes than those with emphysema alone

Chronic Bronchitis: SUMMARY

Chronic Bronchitis: defined as persistent productive cough for at least 3 consecutive months in at least 2 consecutive years

Causes

- Cigarette smoking is the most important risk factor; air pollutants also contribute

Features

- enlargement of mucous-secreting glands, goblet cell hyperplasia, chronic inflammation, and bronchiolar wall fibrosis.

Complications

- Persistent reproductive cough. dyspnea on exertion, hypercapnia, hypoxemia, cyanosis and cor pulmonale
- Death may result from further impairment of respiratory function due to superimposed acute infections.

Emphysema

Permanent enlargement of all or part of the respiratory unit

a. Define emphysema.
b. Describe the gross and microscopic changes in emphysema.
c. Discuss the typical clinical presentation and causes of death.
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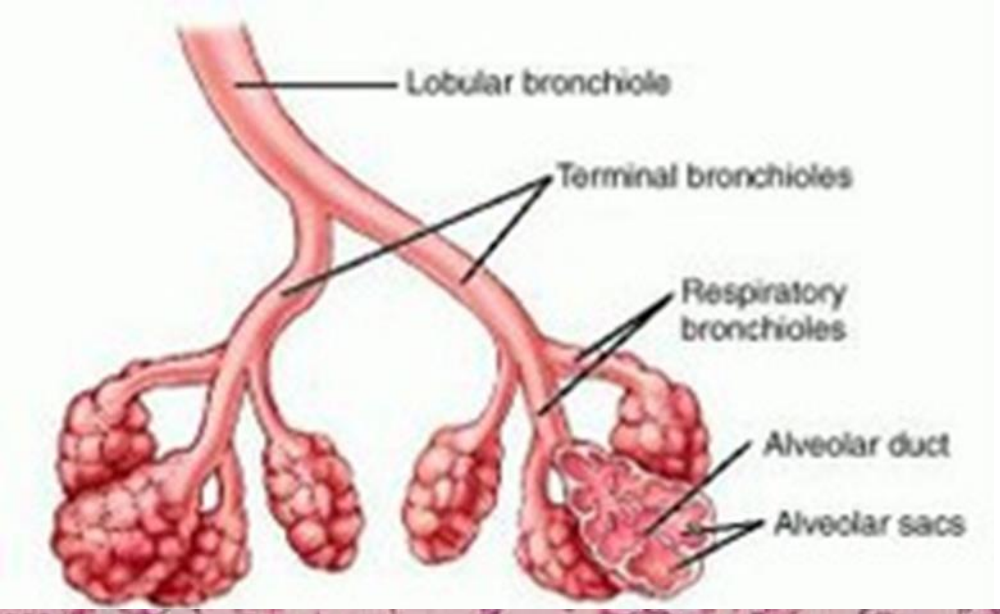
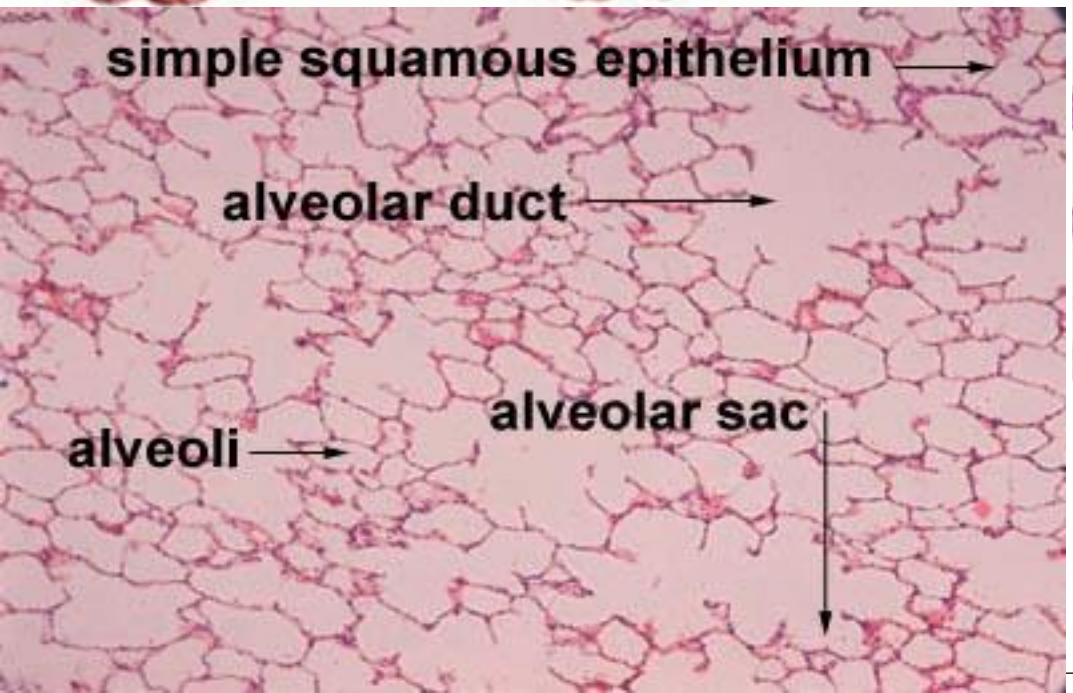
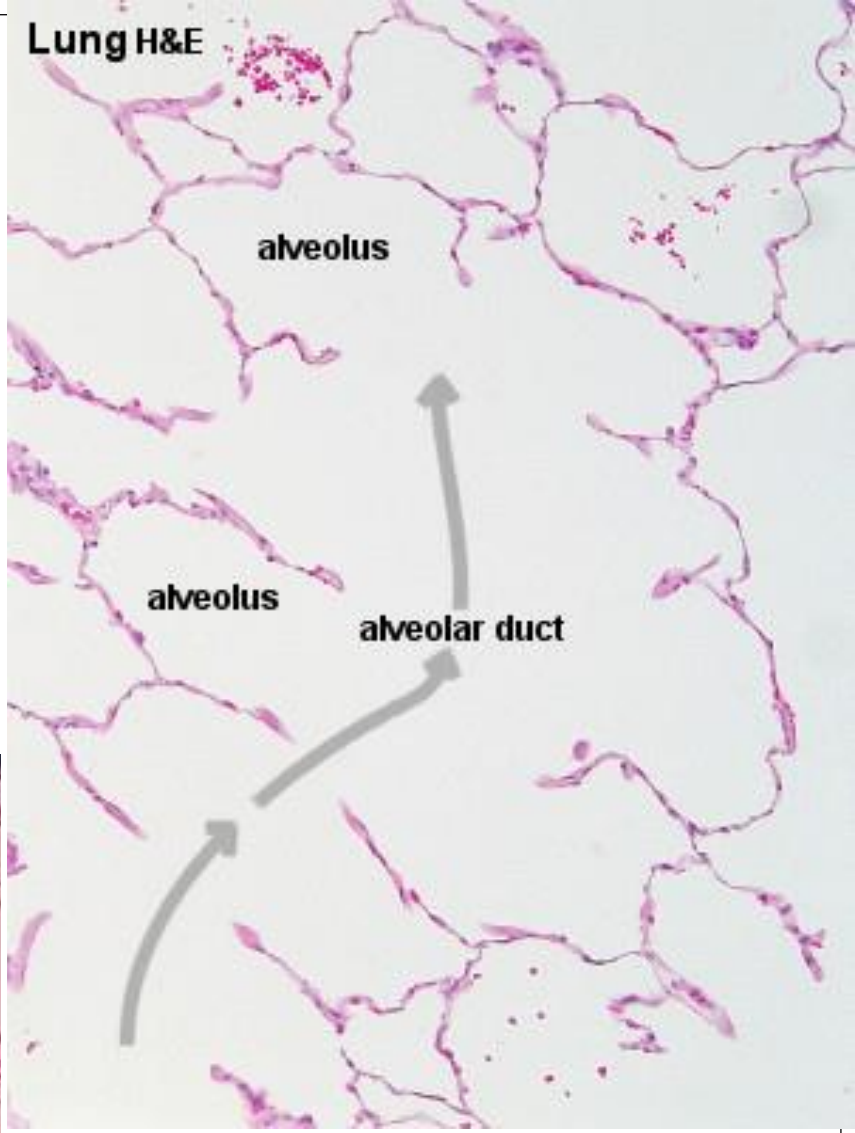
Emphysema

normal







Emphysema

- Is abnormal permanent enlargement of the airspaces distal to the terminal bronchioles accompanied by destruction of their walls, without obvious fibrosis
- Element of chronic bronchitis coexists
- "Dilatation" is due to destruction and loss of alveolar walls (tissue destruction)
- Appears as "holes" in the lung tissue
- Emphysema Impairs respiratory function:

- Diminished alveolar surface area for gas exchange (decreased Tco)

- Loss of elastic recoil and support of small airways leading to tendency to collapse with obstruction

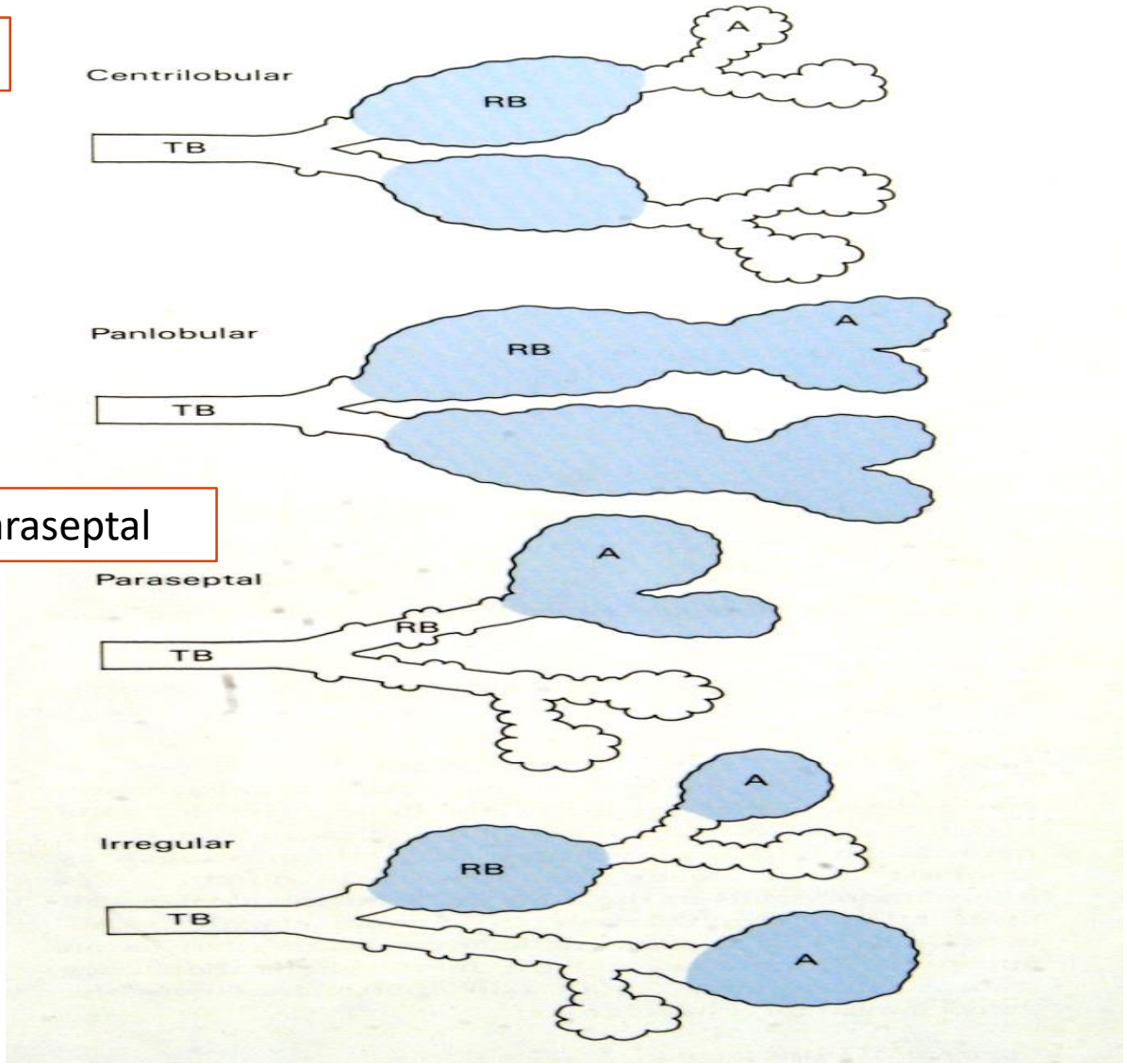
Types of emphysema:

1. Centriacinar

2. Panacinar

3.Distal acinar /paraseptal

4. Irregular

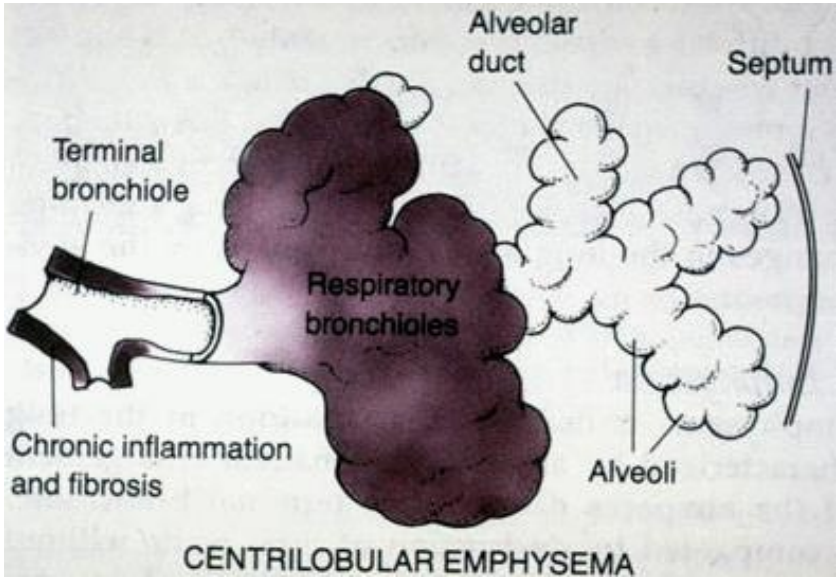


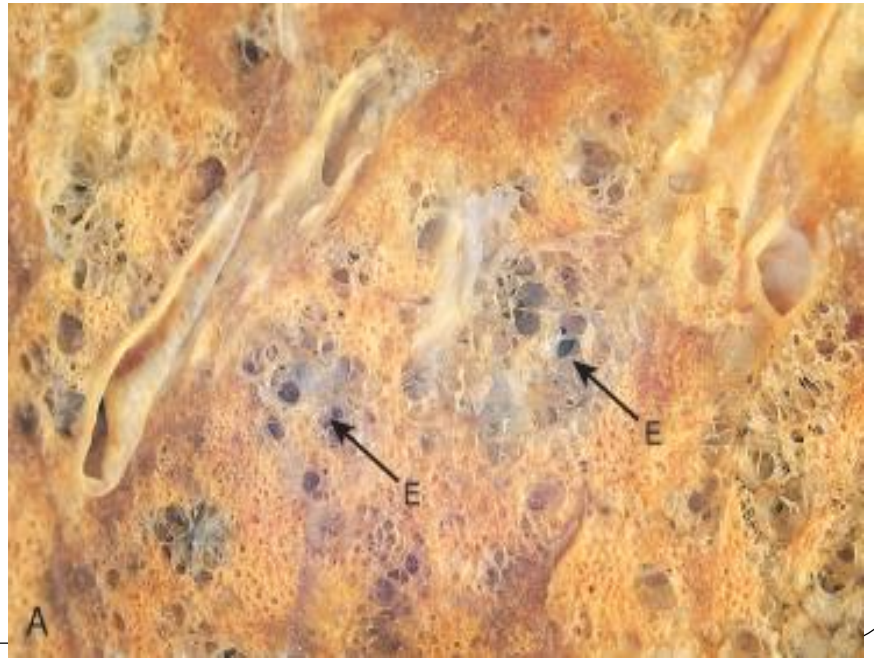
Centriacinar (centrilobular) emphysema

- Occur in heavy smoker in association with chronic bronchitis
- The central or proximal parts of the acini are affected, while distal alveoli are spared
- More common and severe in upper lobes (apical segments)
- The walls of the emphysematous

space contain black pigment.

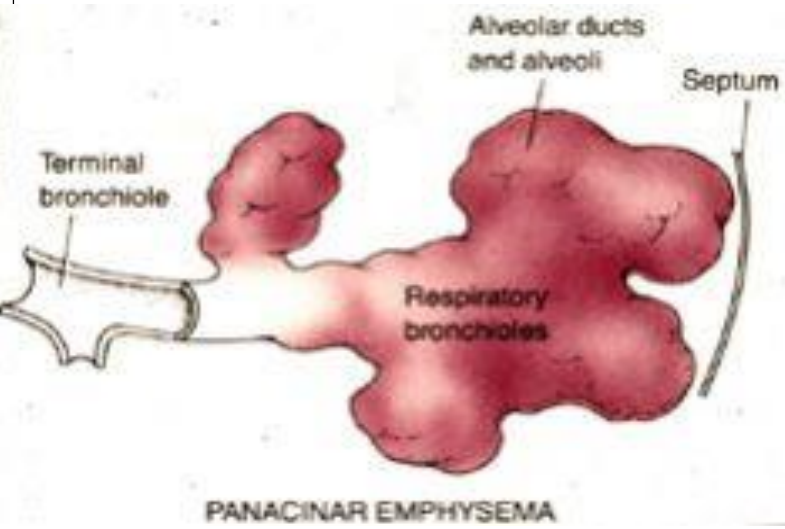
- Inflammation around bronchi & bronchioles.

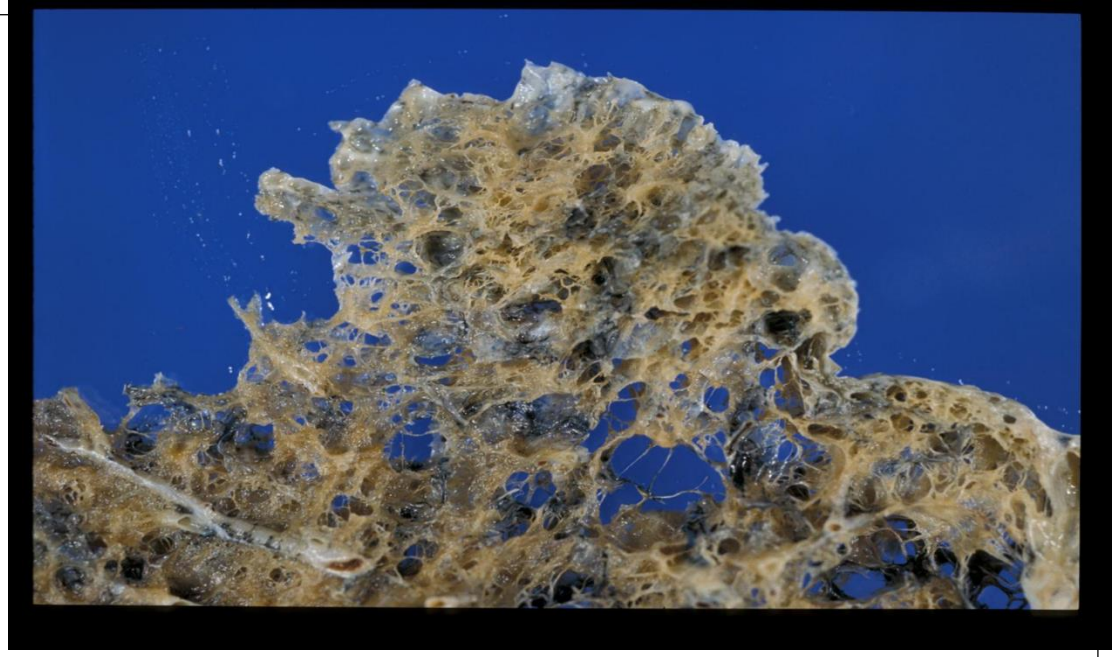


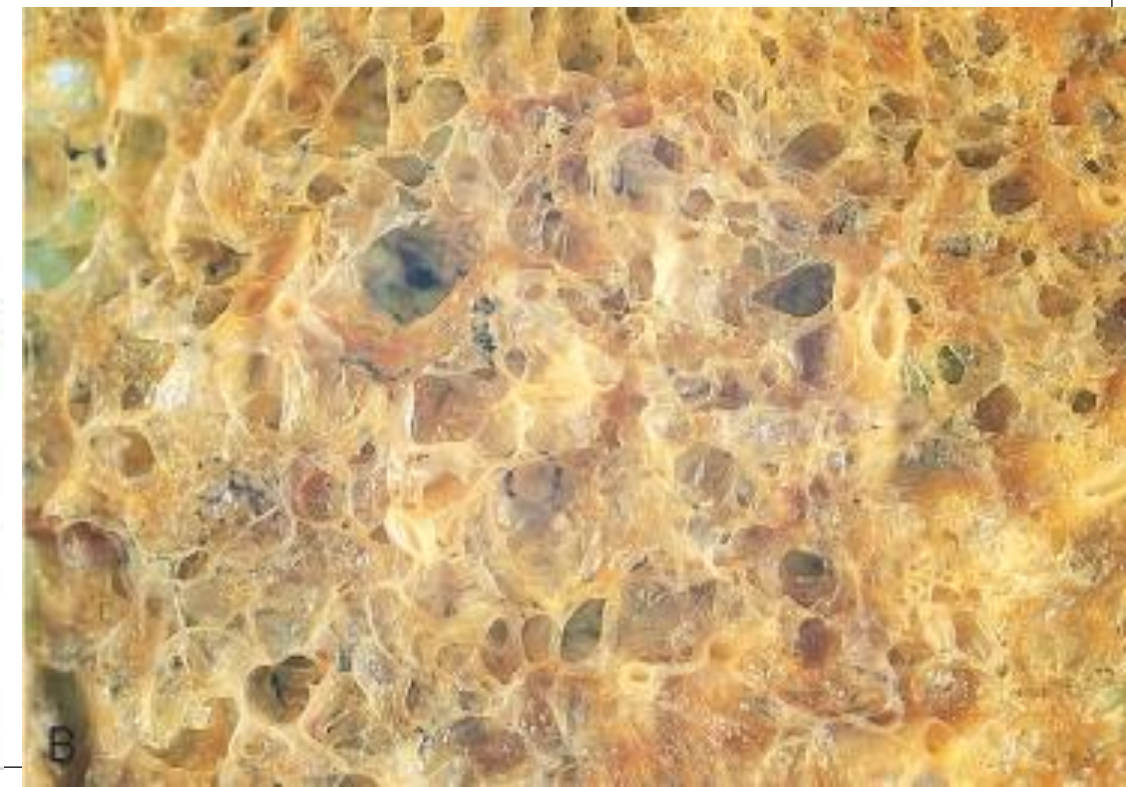


Panacinar (panlobular) emphysema

- Cause :Occurs in α_1-anti-trypsin deficiency.
- **Uniform injury:** Acini are uniformly enlarged from the level of the respiratory bronchiole to the terminal blind alveoli.
- More commonly in the lower lung zones.

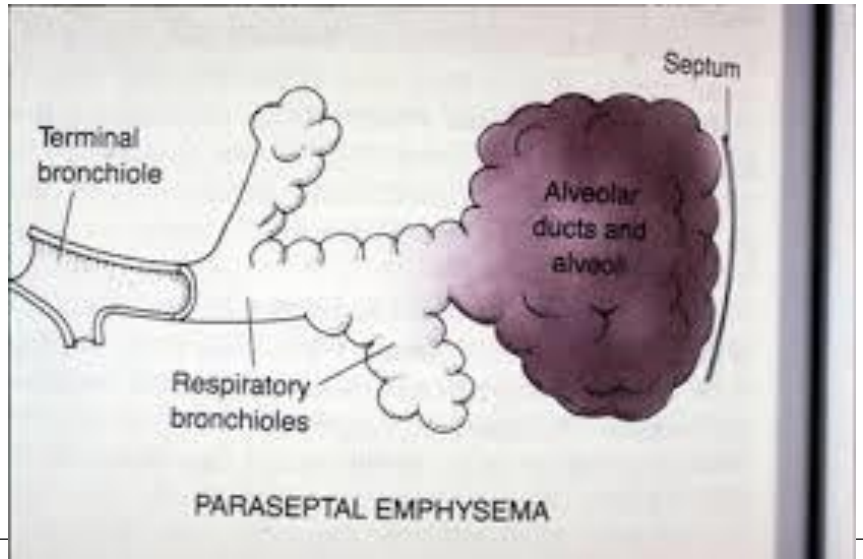


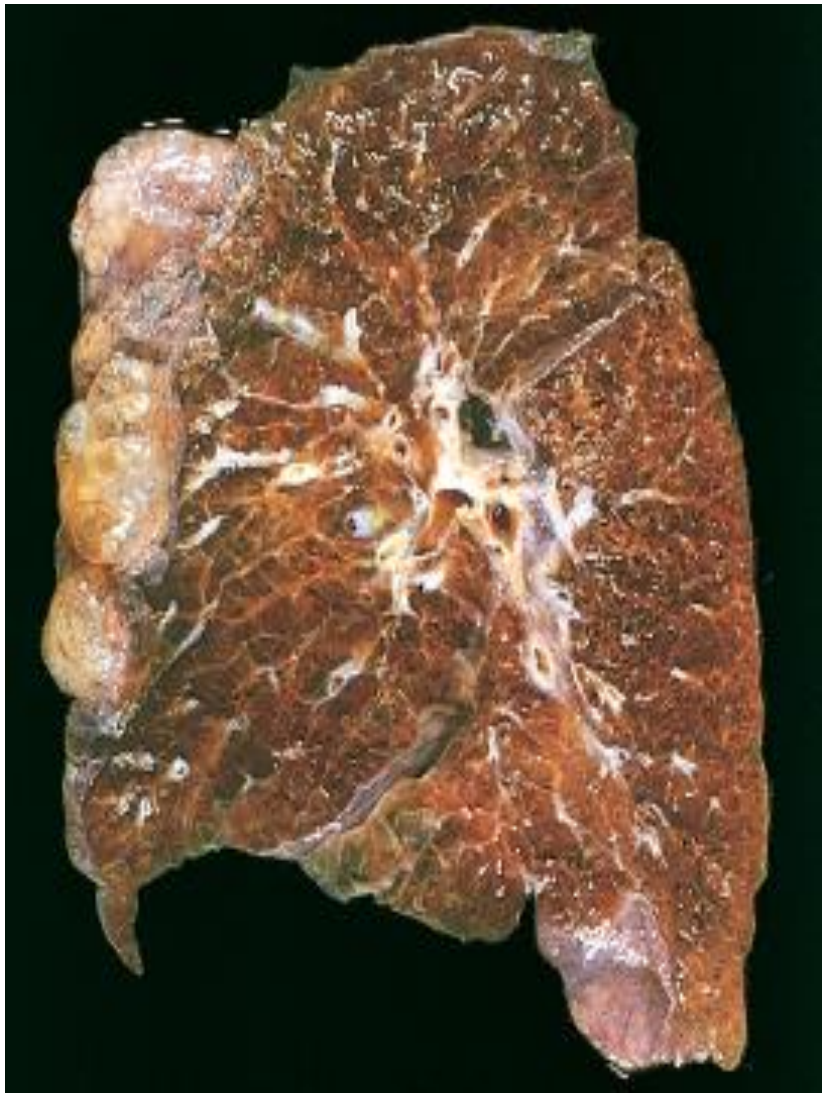




Distal acinar (paraseptal) emphysema

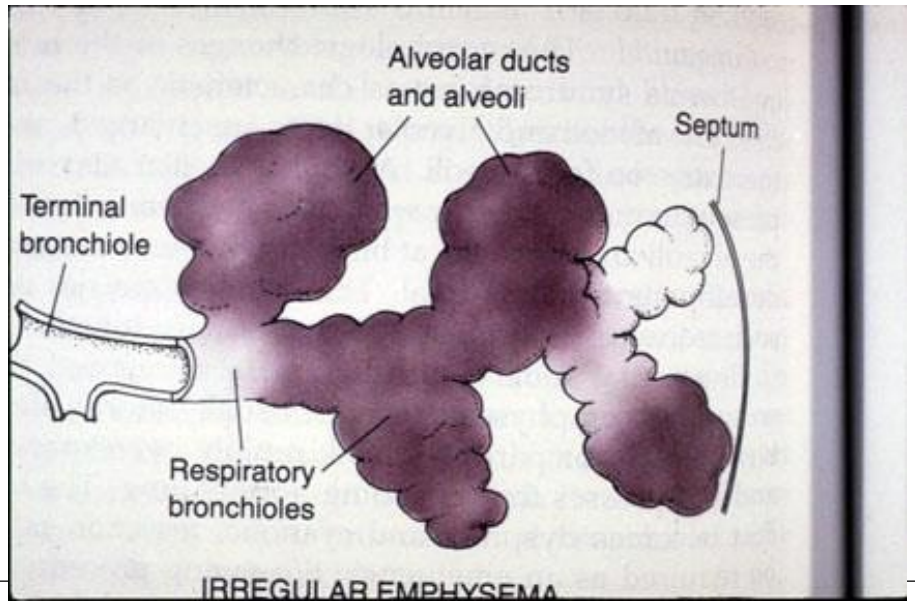
- The proximal portion of the acinus is normal but the distal part is dominantly involved.
- Occurs adjacent to areas of fibrosis, scarring or atelectasis.
- More severe in the upper half of the lungs.
- Sometimes forming multiple cyst-like structures with spontaneous pneumothorax.





Irregular Emphysema

- The acinus is irregularly involved, associated with scarring.
- Most common form found in autopsy.
- Asymptomatic.
- usually a complication of various inflammatory processes including chronic pulmonary tuberculosis



Pathogenesis of Emphysema

- **Is not completely understood**
- **Elastic tissue of the alveolar wall is broken down by action of proteolytic enzymes like protease (e.g.elastase).**
- **Protease is produced by neutrophils and macrophages.**

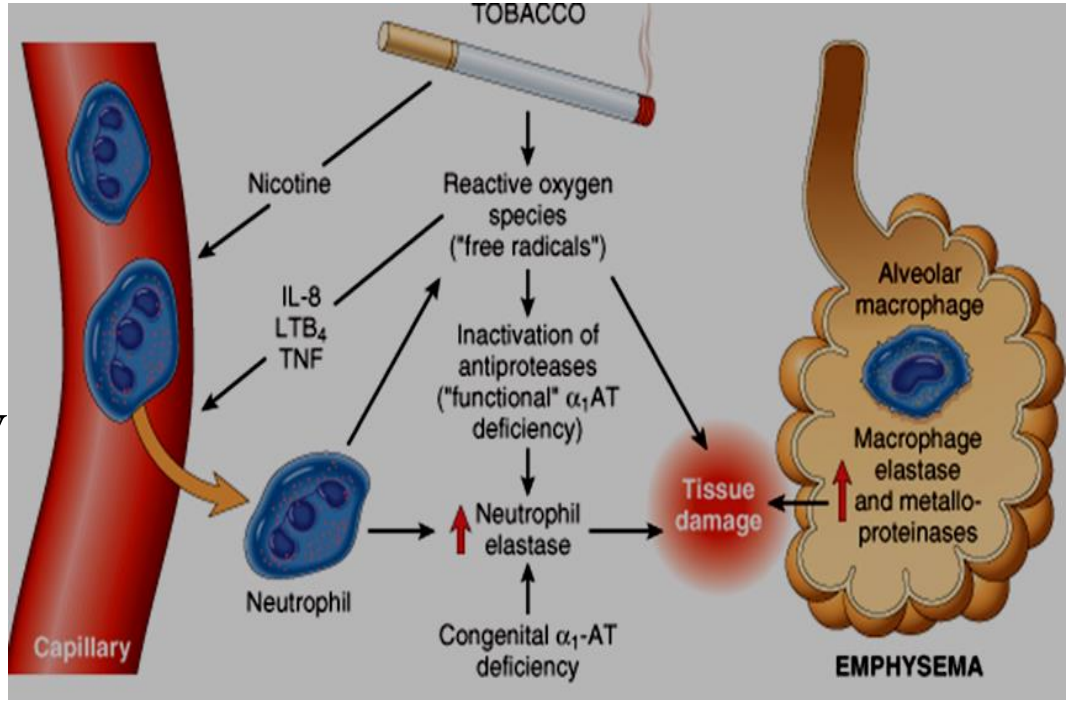
Pathogenesis in α1-anti-trypsin deficiency:

- **Alpha 1 antitrypsin is an anti-protease (anti-elastase)**
  - **is a major inhibitor of proteases.**
  - **is normally present in the serum, in tissue fluids and in macrophages.**
  - **Normally there is a balance between protease and anti protease activity.**
- **More than 80% of people with genetic deficiency of the α1-anti-trypsin (encoded by a gene in the proteinase inhibitor (Pi) locus on chromosome 14) develop panacinar emphysema.**

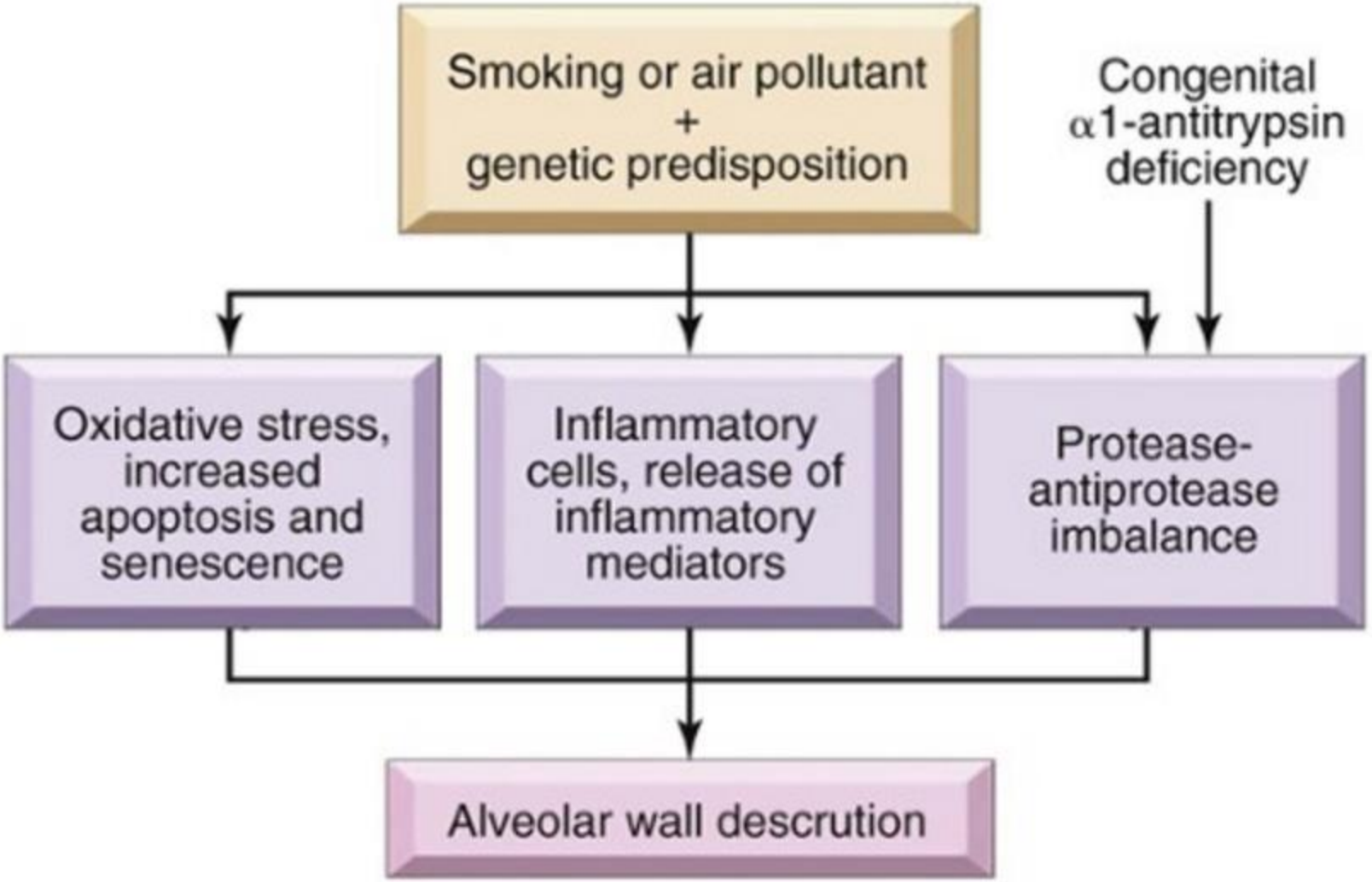
Pathogenesis of Emphysema

- **The protease-antiprotease hypothesis explains the effect of cigarette smoking in the production of centriacinar emphysema**

- **Smokers have increases number of neutrophils and macrophages in their alveoli (increase chemical mediators)**
- **Smoking stimulates release of elastase and enhances elastase activity in macrophages.**
- **Smoking Inhibits alpha 1 antitrypsin.**
- **Tobacco smoke contains reactive oxygen species with inactivation of anti-proteases.**



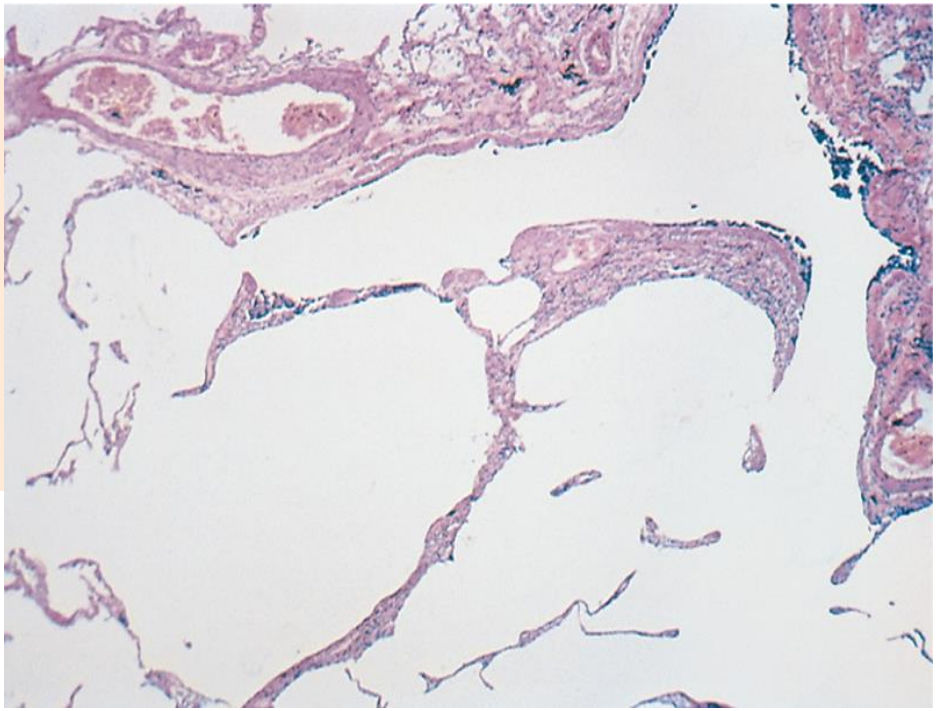
Pathogenesis of Emphysema



Emphysema: Morphology

- The lungs are pale, voluminous.
- Histologically, thinning and destruction of alveolar walls creating large airspaces.

- Loss of elastic tissue.
- Reduced radial traction on the small airways.
- Alveolar capillaries is diminished.
- Accompanying bronchitis and bronchiolitis.



Clinical course

- Cough and wheezing
- Weight loss
- Barrell chest

(increased anteroposterior diameter of chest)

- Pulmonary function tests reveal reduced FEV1
- Advanced: hypoxia, cyanosis, respiratory acidosis
- Patients are known as pink puffers

Complications

- Coexistent chronic bronchitis
- Interstitial emphysema in which air escapes into the interstitial tissues of the chest from a tear in the airways.
- may also be complicated by rupture of a surface bleb with resultant Pneumothorax
- Death from emphysema is related to::

1. Pulmonary failure with respiratory acidosis, hypoxia and coma.
2. Cor pulmonale : (Right-sided heart failure induced by pulmonary disease)

Emphysema: SUMMARY

Emphysema: Dilated air spaces beyond respiratory arteriols

Types

- Centriacinar: Smoking
- Panacinar: deficiency of α1 AT
- Paraseptal
- Irregular: scar

Clinical features

- Cough and wheezing. Respiratory acidosis
- Weight loss
- Pulmonary function tests reveal low FEV1

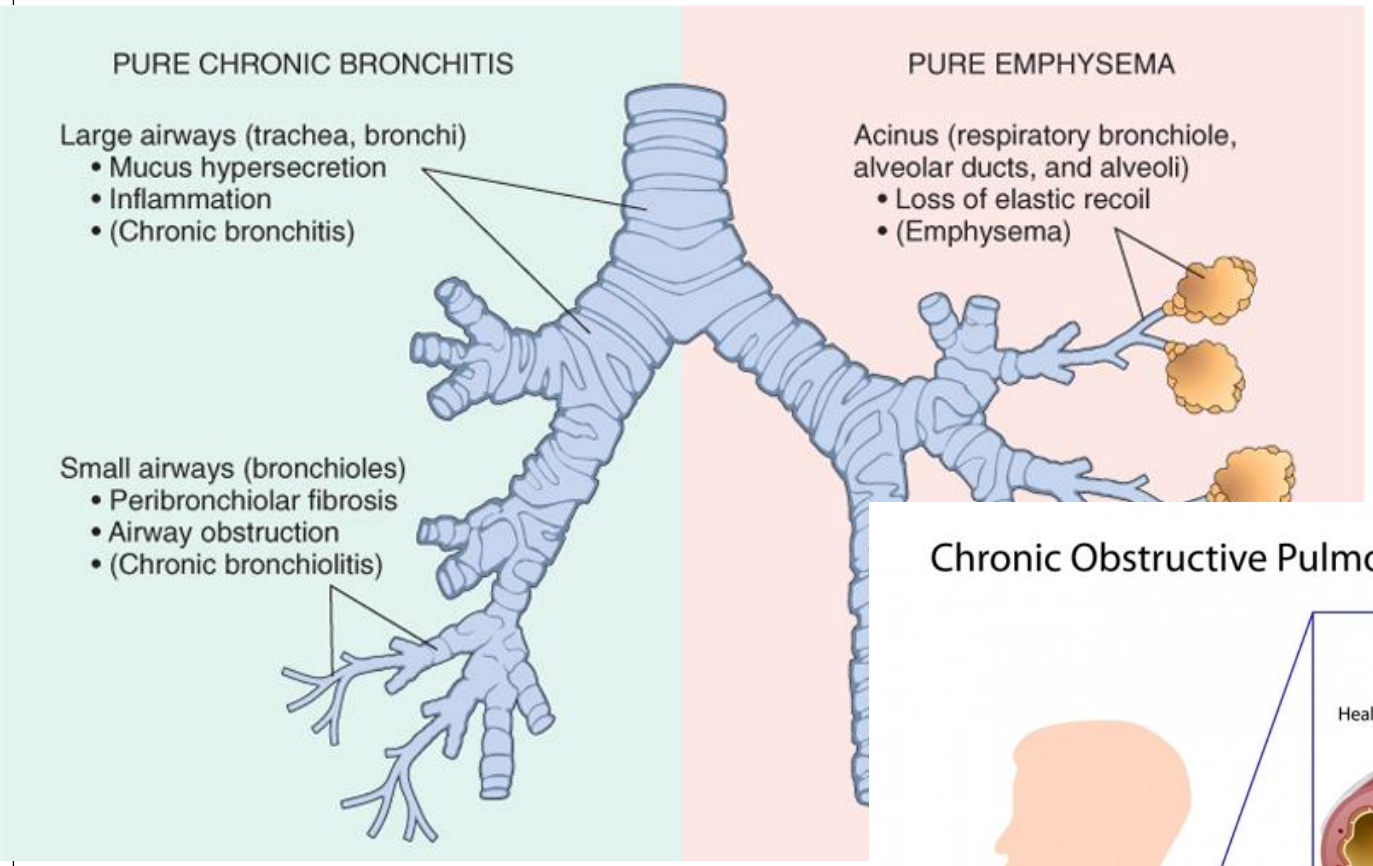
Complications

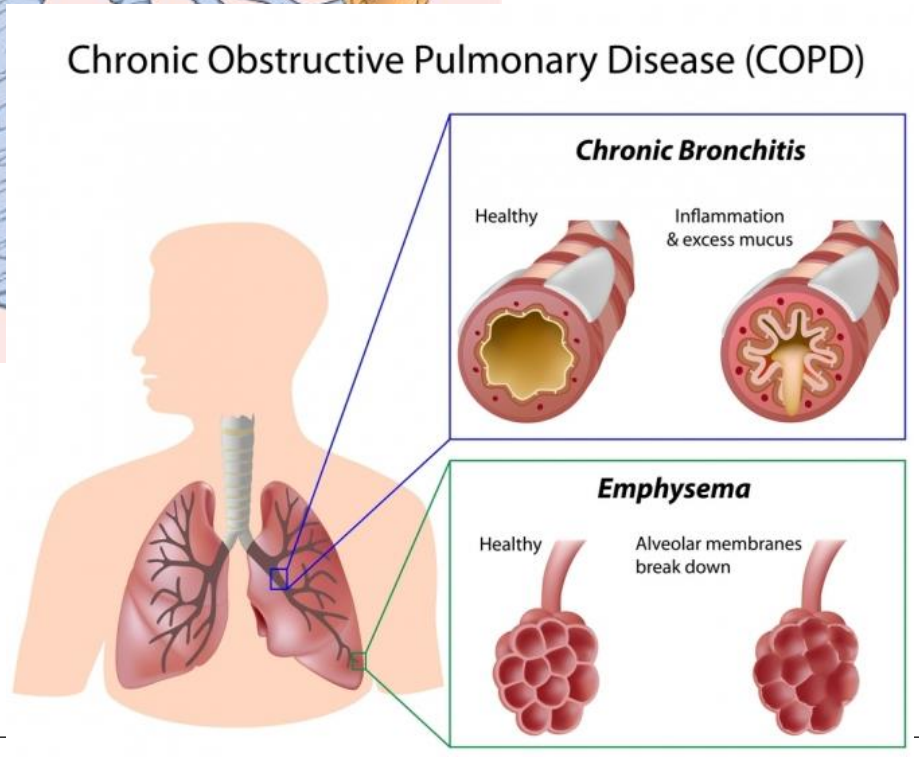
- Pneumothorax
- Death from emphysema is related to:
  - Pulmonary failure with respiratory acidosis, hypoxia and coma.
  - Right-sided heart failure (Cor pulmnale)

Emphysema and Chronic Bronchitis

	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

Chronic bronchitis vs. Emphysema



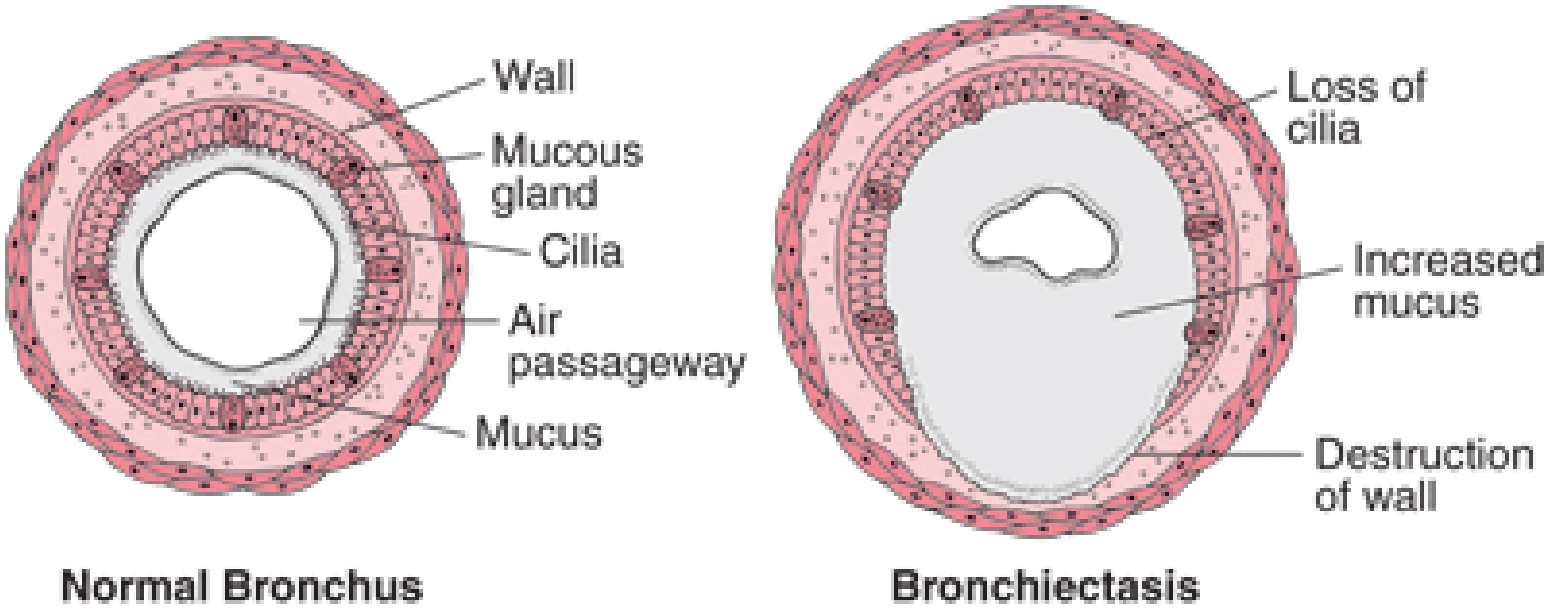


Bronchiectasis

Define Bronchiectasis and its causes, presentation, morphology and significant

Bronchiectasis

- is chronic necrotizing infection and inflammation of the bronchi and bronchioles leading to abnormal permanent dilation of these airways. It represents the end stage of a variety of pathologic processes that cause destruction of the bronchial wall.
- most often involves the lower lobes of both lungs.
- is characterized by fever and cough with production of copious purulent foul smelling sputum,
- and recurrent pulmonary infection that may lead to lung abscess.



Bronchiectasis

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

1. Bronchial obstruction

Localized:
- tumor, foreign bodies or mucous impaction

Generalized:
- bronchial asthma
- chronic bronchitis

2. Congenital or hereditary conditions:

- Congenital bronchiectasis
- Cystic fibrosis.
- Intralobar sequestration of the lung.
- Immunodeficiency status.
- Immotile cilia and kartagner syndrome

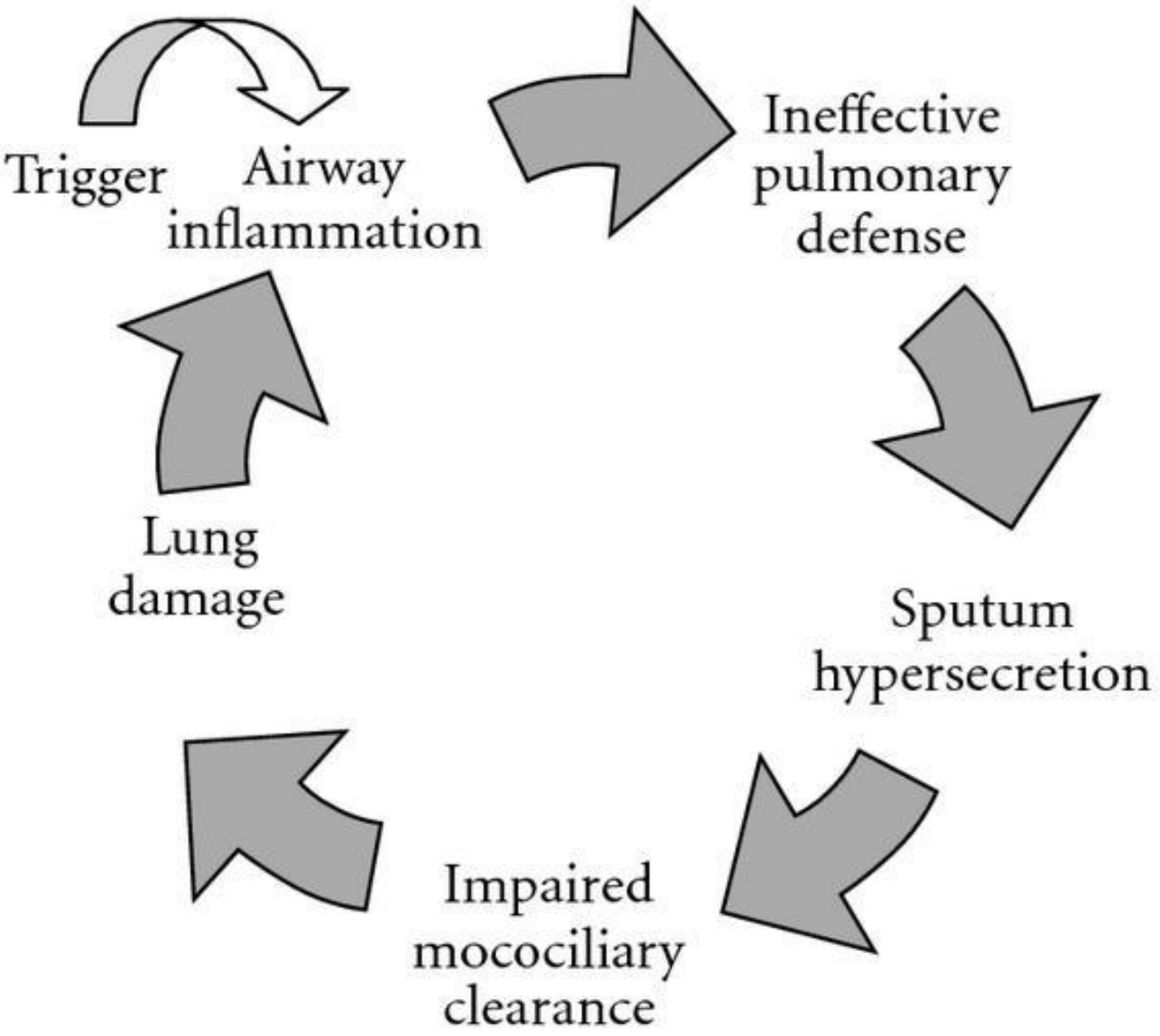
3. Chronic or severe infection / necrotizing pneumonia

Caused by TB, staphylococci or mixed infection.

Pathogenesis

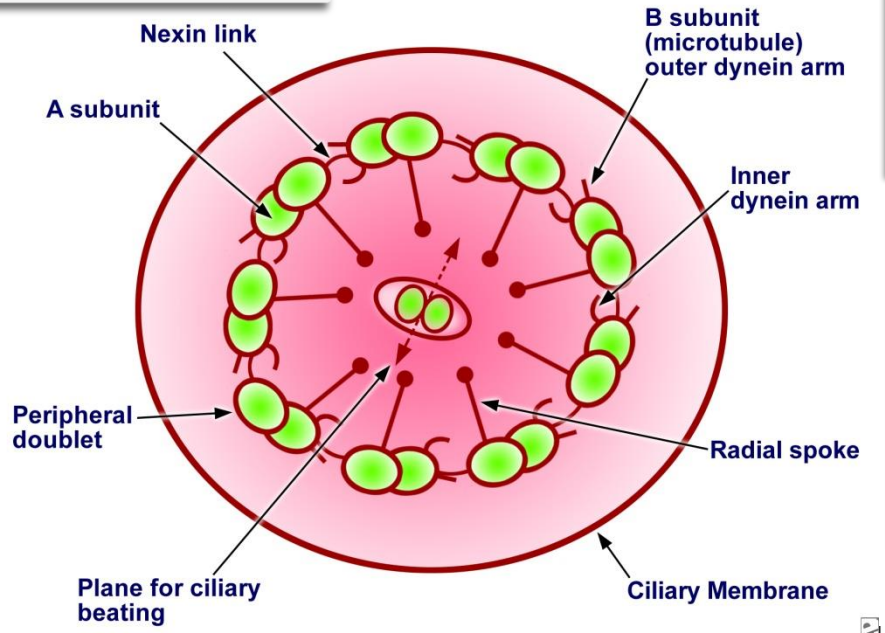
- Any of the previously mentioned conditions can cause damage to the airways resulting in **impaired mucociliary clearance, mucus stasis and accumulation**
- The airways become susceptible to microbial colonization lead to a "vicious circle" of inflammation and tissue damage.
- Inflammation results in 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.

Pathogenesis of bronchiectasis



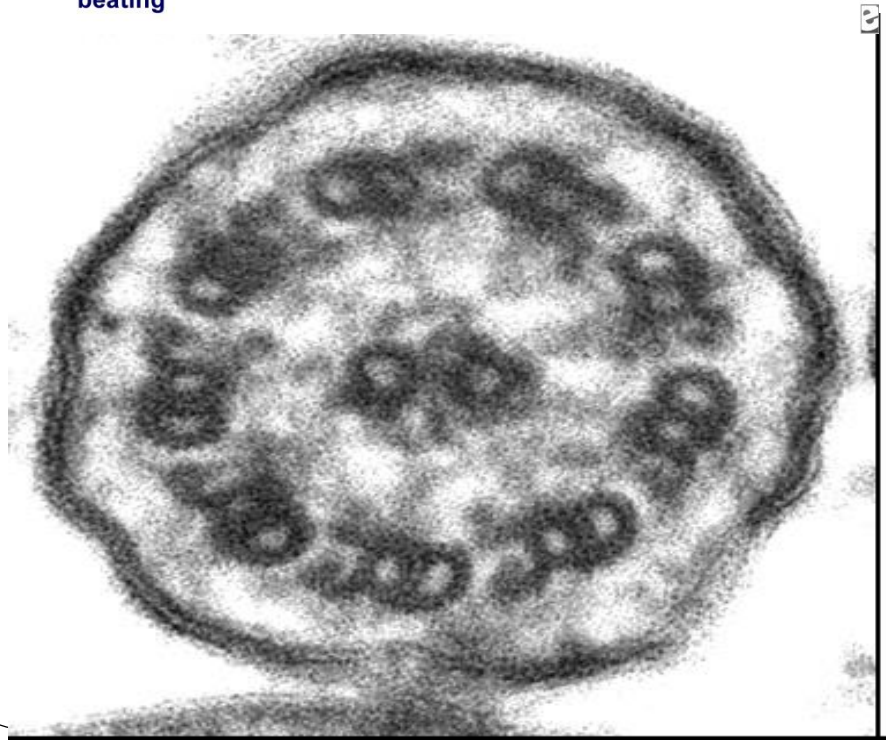
Kartagener Syndrome/ immotile cilia syndrome

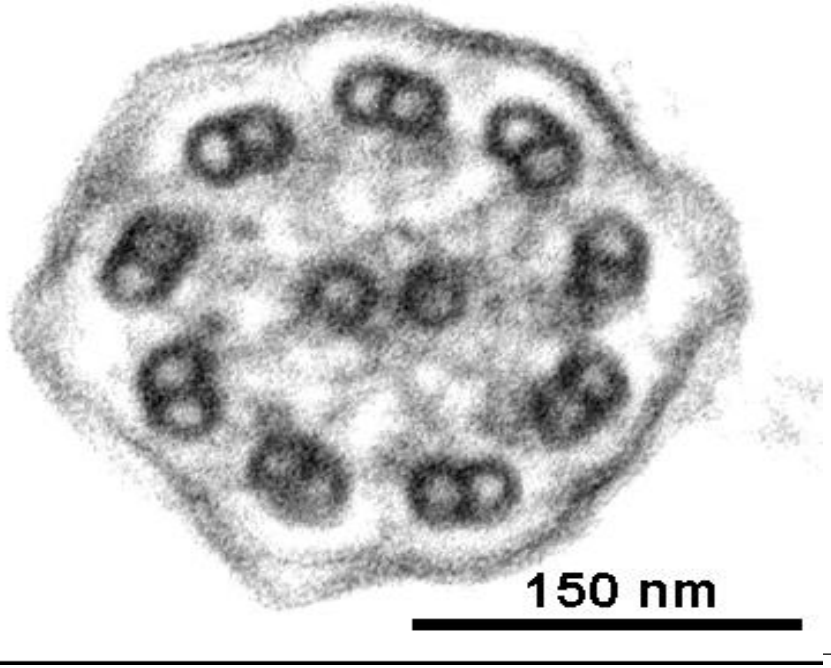
- It is a genetic condition resulting in the failure to clear sputum (Primary ciliary dyskinesia) caused by a defect in the motility of respiratory, auditory, and sperm cilia.
- Inherited as autosomal recessive trait.
- Patient develop bronchiactasis, sinusitis and situs invertus sometimes with hearing loss and male sterility.
- Lack of ciliary activity interferers with bronchial clearance of mucus.



absence of outer and inner dynein arms in a patient with primary ciliary dyskinesia.

Dynein, a type of ATPase, provides energy for microtubule sliding and the longitudinal displacement of adjacent microtubular doublets, resulting in ciliary bending.



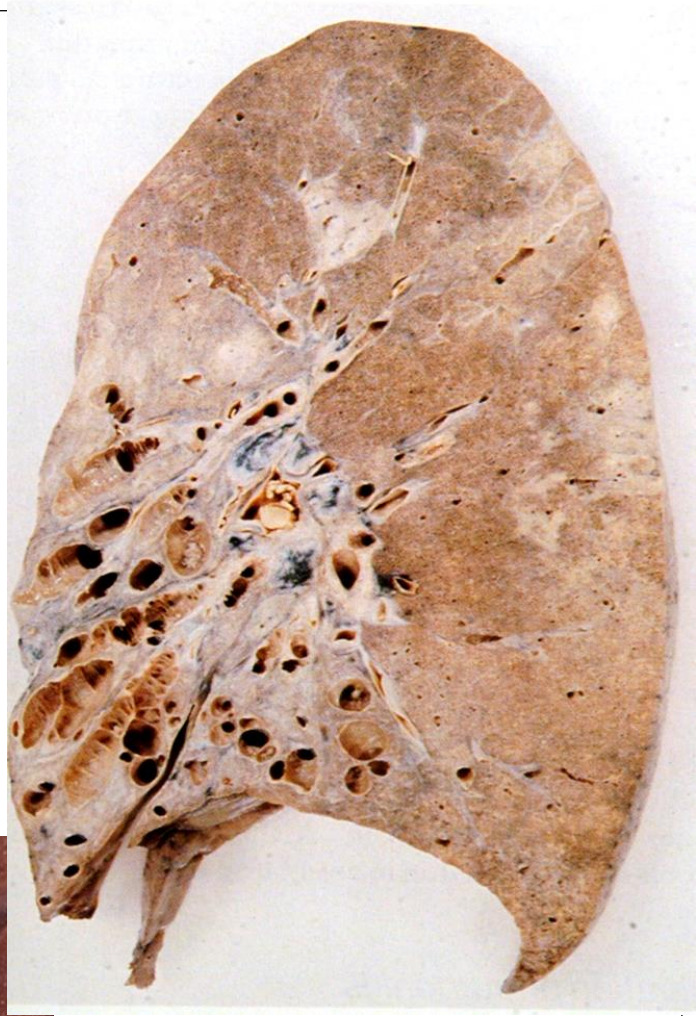


Cystic fibrosis

- **Cystic fibrosis is an inherited disease that causes thick, sticky viscus mucus to build up in the lungs and digestive tract. It is one of the most common chronic lung diseases in children and young adults, and may result in early death.**
- **It may lead to bronchiectasis.**

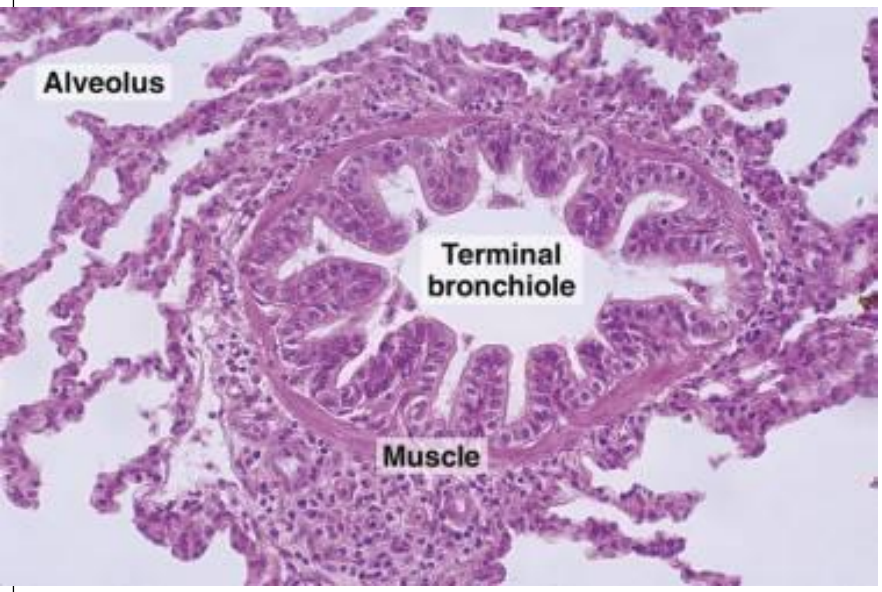
Morphology of Bronchiectasis

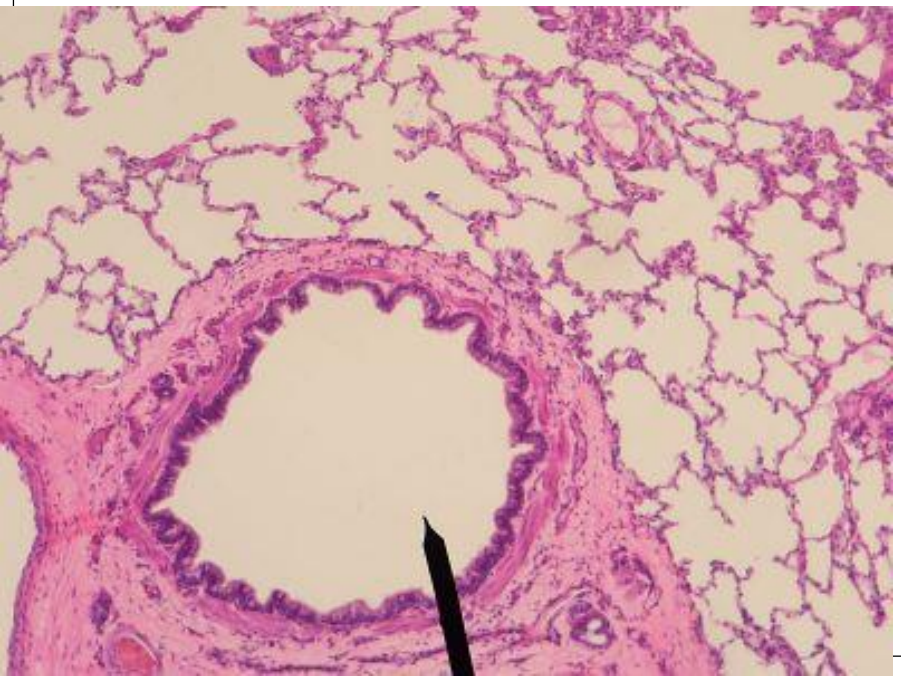
- Usually affects lower lobes bilaterally (vertical airways).
- Dilated airways up to four times of normal, reaching the pleura.
- Acute and chronic inflammation (neutrophils, lymphocytes, histiocytes and plasma cells)
- Necrosis and ulceration in the wall of the bronchi and bronchioles with loss of cilia, squamous metaplasia and fibrosis.



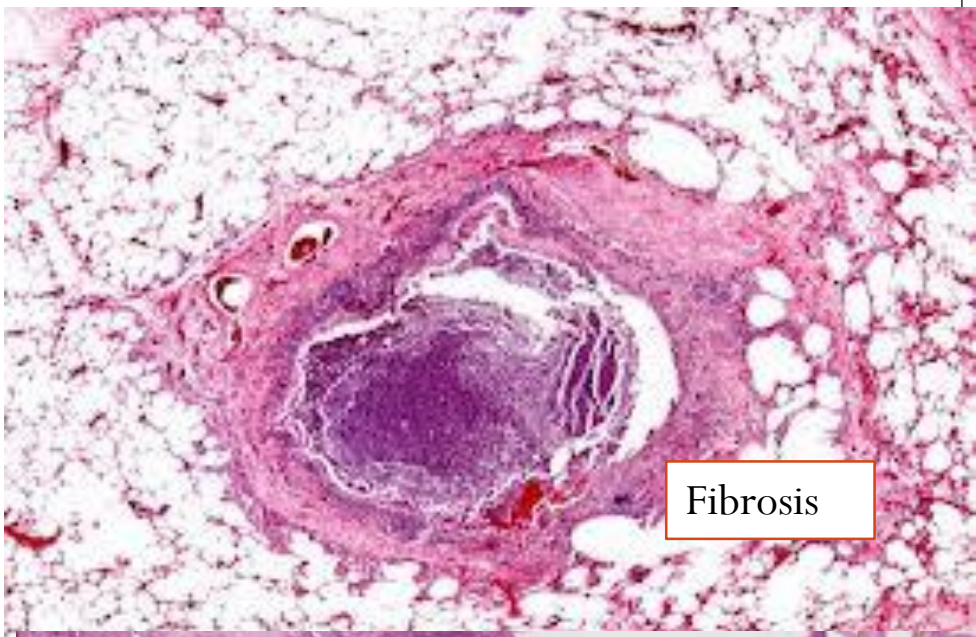
Bronchiectasis

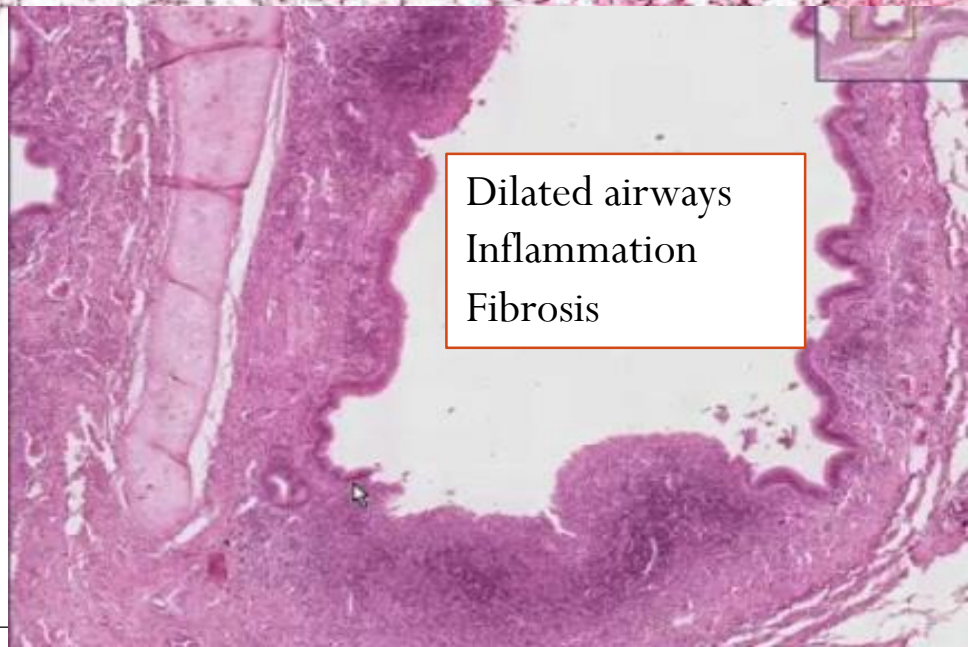
- Normal





- bronchiectasis





Bronchiectasis

- **Clinical course:**
  - Sever persistent cough with sputum (mucopurulent, fetid sputum) sometime with with blood.
  - Clubbing of fingers.

- **Complication:**
  - If sever, obstructive pulmonary function develop.
  - Other complications: metastatic brain abscess and amyloidosis

Bronchiectasis:

Dilatation of bronchi and bronchioles secondary to chronic inflammation and obstruction

Causes

- Infection/ Necrotizing pneumonia
- Obstruction
- Congenital (Cystic fibrosis, Kartagener's Syndrome)

Clinical features

- Sever persistent cough with sputum (mucopurulent sputum) sometime with blood.
- Clubbing of fingers.

complications

- If sever, obstructive pulmonary function develop.
- Lung Abscess
- Rare complications: metastatic brain abscess and amyloidosis.