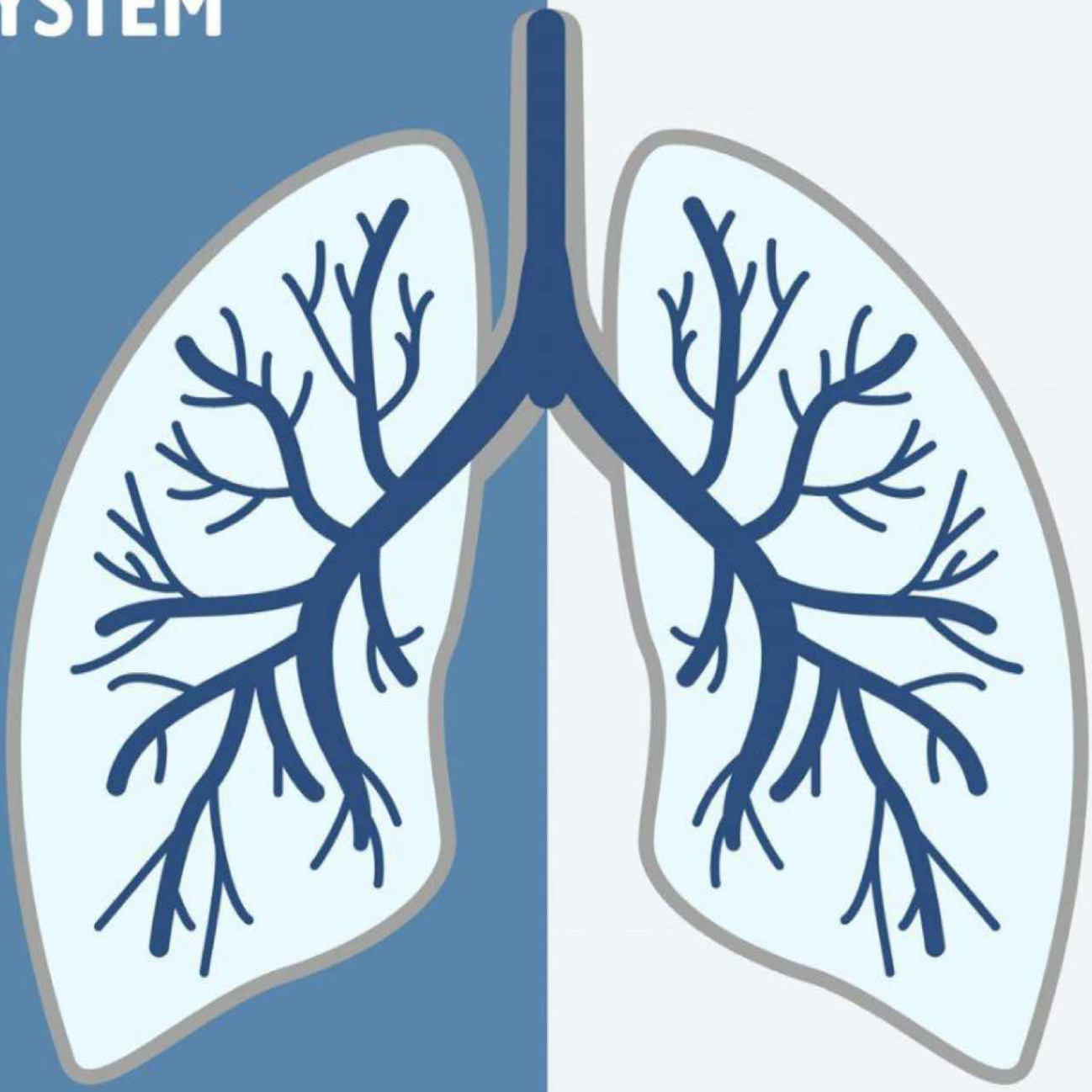
RESPIRATORY SYSTEM

PATHOLOGY



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In this lecture we are going to talk about **obstructive lung diseases**, specially: -

1- Emphysema

2- chronic bronchitis

obstructive lung diseases:-

They are 4 types (Asthma, Emphysema, Chronic Bronchitis and Bronchiectasis) they have distinct clinical and anatomical characteristics, but overlaps between asthma, chronic bronchitis, and emphysema are common.

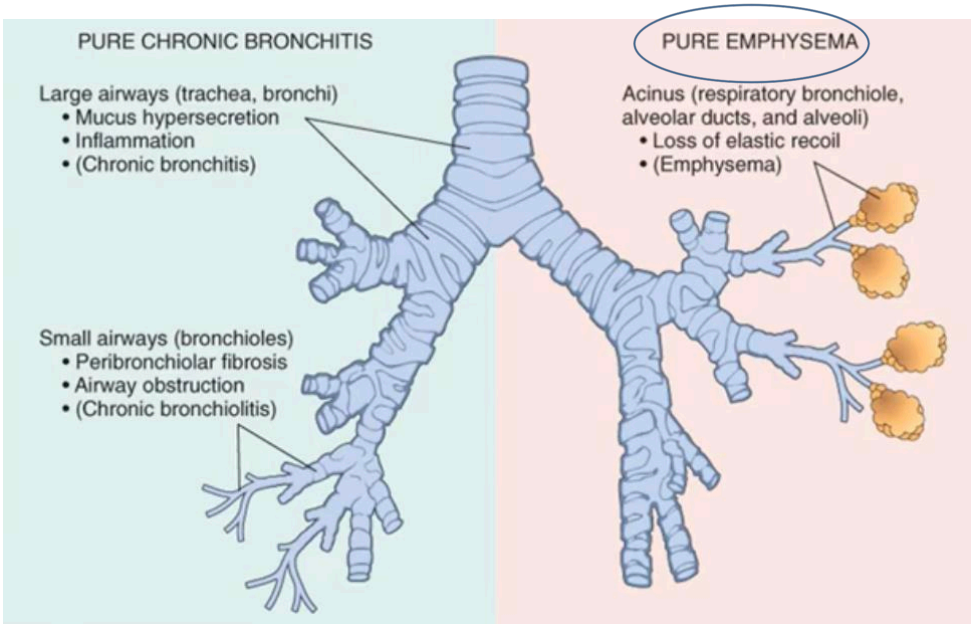
Emphysema and **chronic bronchitis** are usually diagnosed in the patient at the same time, that's why they're called together **Chronic Obstructive Pulmonary Disease (COPD).**

COPD: means that it is hard to get the air out (exhale), lungs are hyperinflated (air accumulation in the lungs) and the total lung capacity (is the volume of air in the lungs upon maximum effort of inspiration) is normal or even increased.

Imagine the lung in obstructive lung diseases as an old pair of socks or rubber band, the old ones have lax rubber and it is very easy to be expanded; since the rubber is old and damaged. Now, what happens to the rubber if you leave it expanded?

It won't return to the original size alone, so in obstructive lung diseases it is easy to inflate the lungs (get the air inside) but it is very hard to deflate it (get the air outside).

Differences between chronic bronchitis and emphysema:-



	Chronic bronchitis	Emphysema
Anatomical distribution *in severe or advanced cases of both, small airway disease (chronic bronchiolitis) is also present.	Usually involves large airways	Involves the acinus
Morphologic characteristics	Both diseases often are grouped under the rubric of chronic obstructive pulmonary diseases (COPD). The largely **irreversible** airflow obstruction of (COPD) distinguishes it from asthma, which is characterized by **reversible** airflow obstruction.	
Definition	It is defined based on clinical features.	It is defined based on morphologic and radiologic findings.

- Although emphysema may exist without chronic bronchitis (particularly in inherited alpha1 – anti – trypsin deficiency) and vice versa, the two diseases usually coexist. This is almost certainly; because cigarette smoking is the major underlying cause of both.

I. Emphysema

Permanent enlargement of the airspaces distal to the terminal bronchioles with destruction of their walls and <u>without significant fibrosis.</u> (acinus is the affected part)

Classified according to its anatomic distribution: -

<u>(1) centriacinar, (2) panacinar</u>, (3) distal acinar, and (4) irregular

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

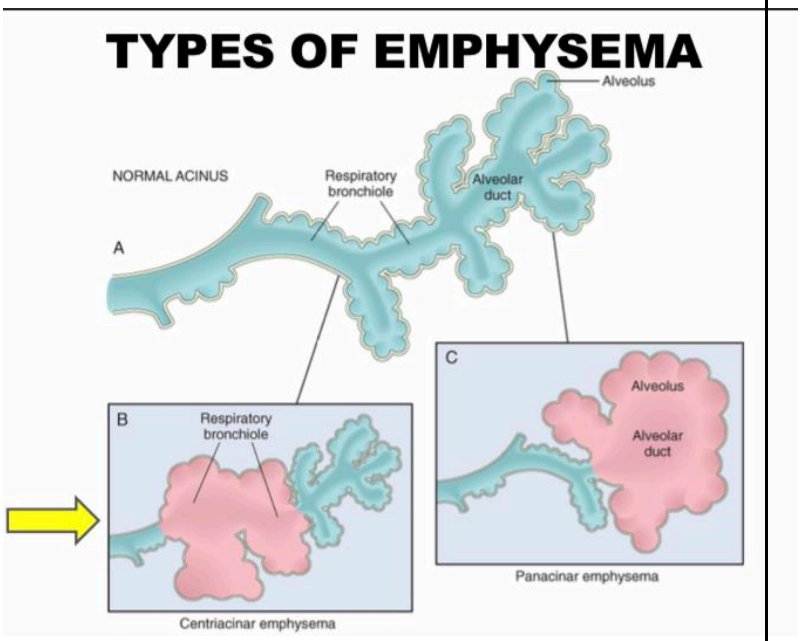
A- Centriacinar (Centrilobular) emphysema.

-affects the central or proximal parts of the acini first, formed by respiratory bronchioles, while distal alveoli are spared.

- **cigarette smokers**.

- associated with **chronic bronchitis**.

- more common and severe in the **upper lobes**, particularly in the **apical segments**.

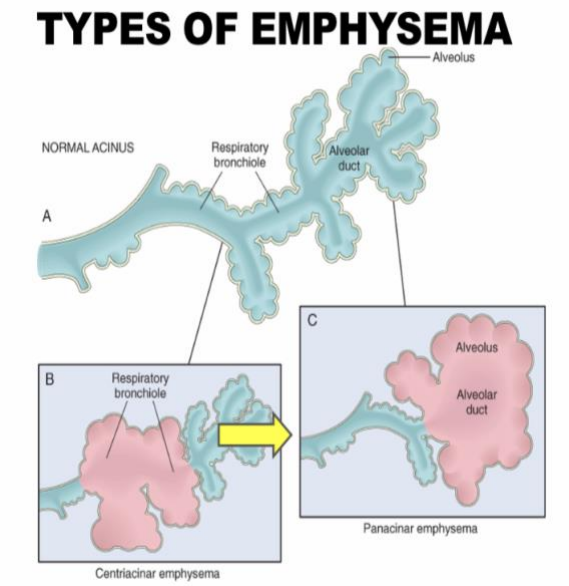


B- Panacinar (panlobular) emphysema:-

• The acini are uniformly enlarged, from the level of the respiratory bronchiole to the terminal blind alveoli.

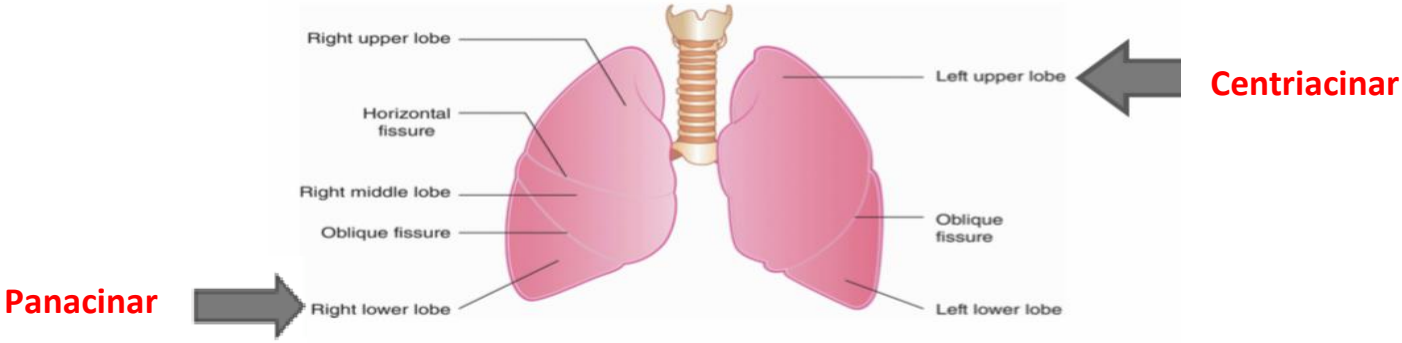
• Associated with **α1-antitrypsin deficiency**.

• More common in the **lower lung zones**.

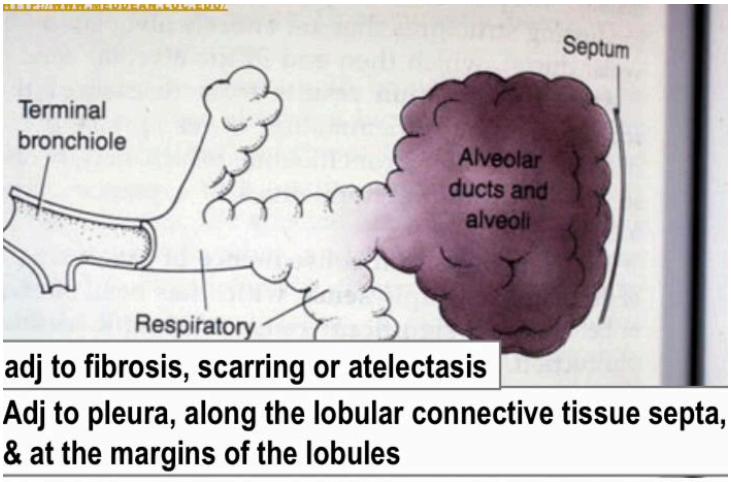


Alpha-anti-trypsin deficiency:-

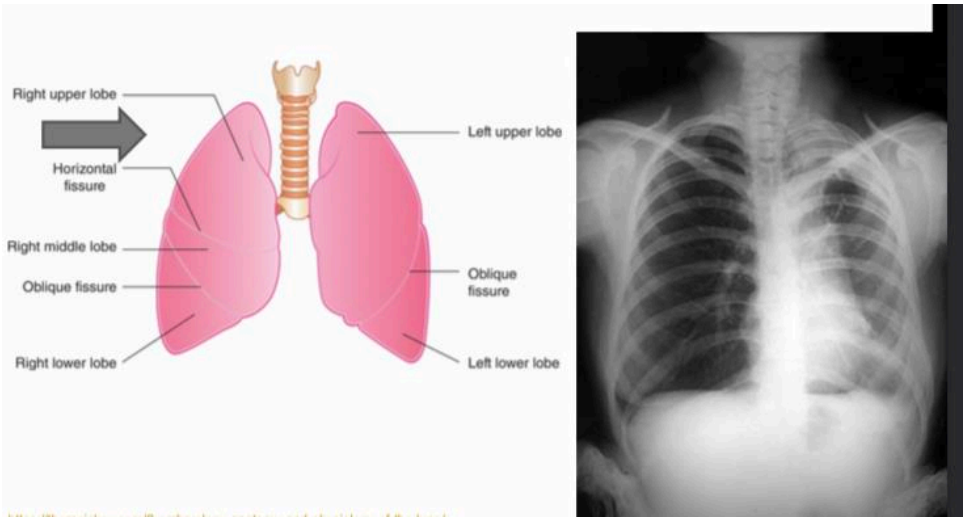
It is a genetic disorder that may result in lung disease or liver disease.



C- **Distal Acinar (Paraseptal) Emphysema:-**

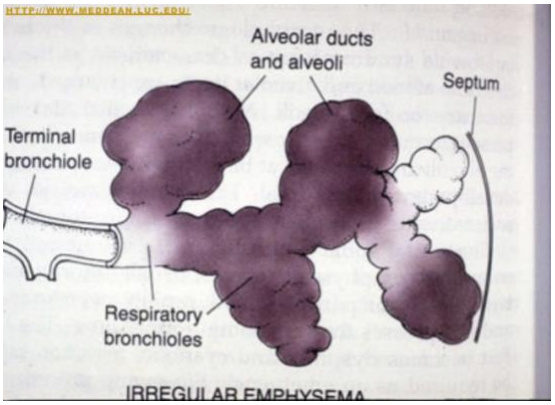


-involves the **distal** portion of the acinus while the proximal part is normal.
-present adjacent to the pleura, along the lobular connective tissue septa, at the margins of the lobules
-adjacent to fibrosis, scarring or atelectasis. more severe in the **upper half of the lungs**.
-The cause is unknown.
-The presence of multiple, enlarged air spaces (ranging in diameter from less than 0.5 cm to more than 2.0 cm) may form large cystic structures that give rise to bullae.
-The most common cause of **spontaneous pneumothorax** in young adults.



*pneumothorax can be caused by penetrating chest injury, inflammation with rupture of a bronchus into the pleura, and rupture of an emphysematous bullae.

D- Irregular emphysema:-



- The acinus is irregularly involved
- almost invariably associated with **scarring**
- clinically it's **asymptomatic**
- considered the **most common** form of emphysema.

QUESTION: - (**Clues, Answer)**

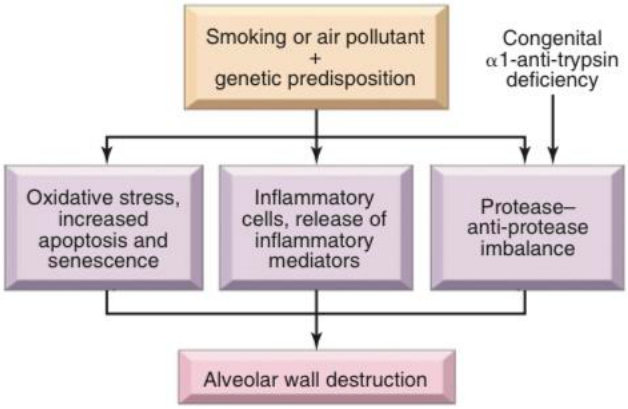
A 20-year-old, previously healthy gentleman is jogging one morning when he falls to the ground. **He suddenly becomes markedly short of breath. in ER no breath sounds audible over the Rt side of the chest. A CXR shows shift of the mediastinum from right to left. A chest tube is inserted on the right side, and air rushes out.** Which of the following underlying diseases is most likely to have produced this complication?

A. Centriacinar emphysema B. Chronic bronchitis

C. Distal acinar emphysema. D. Panlobular emphysema

Pathogenesis of emphysema:-

Inhaled cigarette smoke and other noxious particles cause lung damage and inflammation, which, particularly in patients with a genetic predisposition, result in parenchymal destruction (emphysema) and airway disease (bronchiolitis and chronic bronchitis). Factors that influence the development of emphysema include the following:-



• **Inflammatory cells and mediators:** A wide variety of inflammatory mediators have been shown to be increased (including leukotriene B4, IL-8, TNF, and others) that **attract more inflammatory cells from the circulation** (chemotactic factors), **amplify the inflammatory process** (proinflammatory cytokines), and **induce structural changes** (growth factors). The inflammatory cells present in lesions include neutrophils, macrophages, and CD4+ and CD8+ T cells. It is not known if the T cells are specific for an antigen or are recruited as part of inflammation.

• **Protease–anti-protease imbalance:** Several proteases are released from the inflammatory cells and epithelial cells that break down connective tissues. In patients who develop emphysema, there is a relative deficiency of protective anti-proteases.

• **Oxidative stress:** Reactive oxygen species are generated by cigarette smoke and other inhaled particles and **released from activated inflammatory cells such as macrophages and neutrophils. These cause additional tissue damage and inflammation**.

• **Airway infection:** Although infection is not thought to play a role in the initiation of tissue destruction, bacterial and/or viral infections cause acute exacerbations.

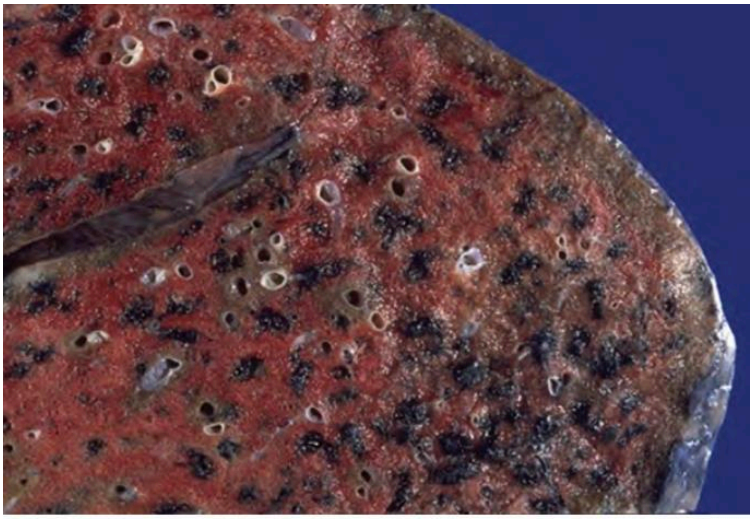
The idea that proteases are important is based in part on the observation that patients with a genetic deficiency of the anti-protease alpha1-anti-trypsin have a predisposition to develop pulmonary emphysema, which is compounded by smoking. About 1% of all patients with emphysema have this defect. Alpha1-anti-trypsin, normally present in serum, tissue fluids, and macrophages, is a major inhibitor of proteases (particularly elastase) secreted by neutrophils during inflammation.

☺ MORPHOLOGY

1- **Macroscopic:**

• **Panacinar emphysema:-** Pale, voluminous lungs

• **Centriacinar emphysema :-** Less impressive changes, Deeper pink and less voluminous lungs in late stages, the upper two-thirds of the lungs are more severely affected than the lower lung .



CENTRIACINAR EMPHYSEMA

2- **Microscopic examination of the lung:**

• destruction of alveolar walls & enlarged air spaces

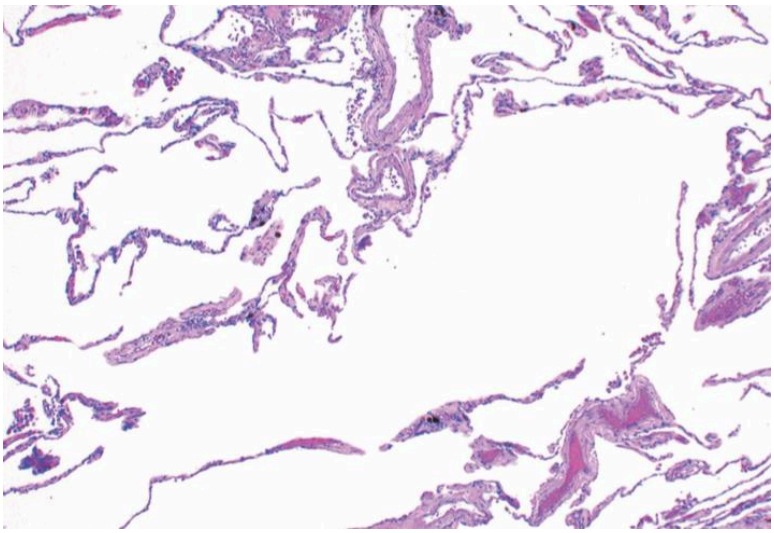
• No significant fibrosis

• small airways collapse due to loss of elastic tissue in the surrounding alveolar septa during expiration (chronic airflow obstruction).

• Bronchiolar inflammation and submucosal fibrosis in advanced cases.

Microscopic examination of **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.



THE CLASSIC PRESENTATION OF EMPHYSEMA WITH NO "BRONCHITIC" COMPONENT:

- Dyspnea (shortness of breath – first symptom)
- barrel-chested
- prolonged expiration (due to the expiratory obstruction)
- sitting forward in a hunched-over position (trying to squeeze the air out with each expiratory effort).
- Hyperventilation.
- adequate oxygenation of hemoglobin (no cyanosis).

☺ why **Pink Puffers**?? (**important**)

Pink refers to the pink face completion and **good adequate oxygenation of hemoglobin.**

Puffers because they **experience difficulty in breathing, and they breathe through burst lips during expiration**.

- Cough and wheezing if coexistent asthma and chronic bronchitis.

Barrel-chested

Due to air trapping and lung overinflation, the anterior-posterior diameter of the chest wall is increased the shape of the barrel.

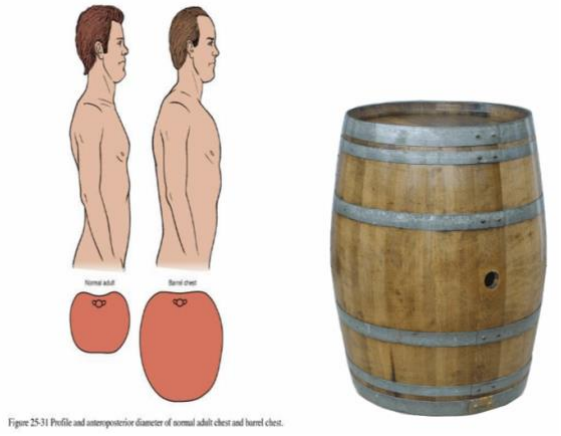


Figure 25-31 Profile and anteroposterior diameter of normal adult chest and barrel chest.

THE OTHER END OF THE SPECTRUM:

EMPHYSEMA WITH PRONOUNCED CHRONIC BRONCHITIS AND A HISTORY OF RECURRENT INFECTIONS.

1• Less dyspnea.

2• absence of increased respiratory drive —> hypoxic and cyanotic.

3• For unclear reasons, patients with chronic bronchitis tend to be obese hence the designation **"blue bloaters", why??**

Blue because —> carbon dioxide retention, hypoxia, and cyanosis.

Bloaters because —> most patients are obese.

For unknown reason

COMPLICATIONS

• Destruction of the walls distal to the terminal bronchioles (this means that the acini are the main affected parts) —> hypoxia —>Hypoxia-induced pulmonary vascular spasm —> gradual development of secondary pulmonary hypertension —> in 20-30% right-sided congestive heart failure (cor pulmonale).

• Death from emphysema is related to either respiratory failure or right-sided heart failure.

CONDITIONS RELATED TO EMPHYSEMA

Several conditions involving abnormal air spaces or accumulations of air within the lungs or other tissues also are recognized.

A• Compensatory emphysema:-

- Compensatory dilation of alveoli in response to loss of lung substance.

- As hyper-expansion of residual lung parenchyma following surgical removal of a diseased lung.

B• Obstructive overinflation:-

- Lung expands because air is trapped within it.

- Subtotal obstruction by a tumor or foreign object. (common cause)

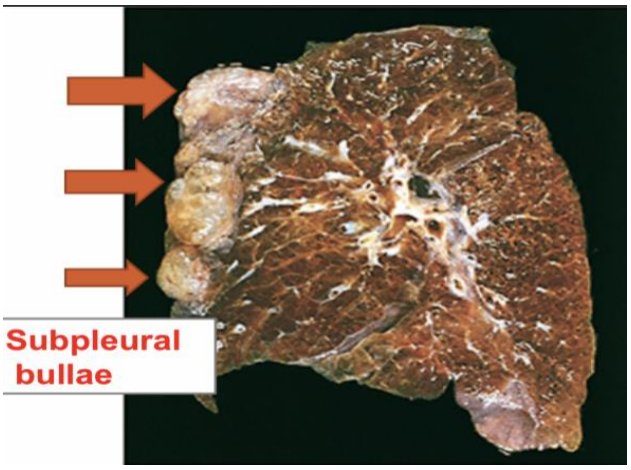
-Can be life-threatening emergency if distends sufficiently to compress the remaining normal lung.

C• Bullous emphysema:

-Any form of emphysema, most are subpleural.

- Large subpleural blebs or bullae. (the arrows in picture)

-Pneumothorax if rupture.



D• Mediastinal (interstitial) emphysema:

-Air in connective tissue of the lung, mediastinum, and subcutaneous tissue.

II. CHRONIC BRONCHITIS

• Common in **cigarette smokers**; air pollutants also contribute.

Some studies indicate that 20%-25% of men in the (40-65) years-old age group have the disease.

• Clinical diagnosis (no microscopic or radiology findings needed like in emphysema) by Persistent productive cough for AT LEAST 3 consecutive months in AT LEAST 2 consecutive years.

• In early stages, the cough raises mucoid sputum, **air flow is not obstructed**.

1 • Heavy smokers: **develop chronic outflow obstruction**, usually with associated emphysema **(COPD)**

2• in some patients, may coexist with hyperresponsive airways with intermittent bronchospasm and wheezing —> asthmatic bronchitis

PATHOGENESIS

A• hypersecretion of mucus, beginning in the **large airways**.

• **cigarette smoking**, other air pollutants (such as sulfur dioxide and nitrogen dioxide) :-

- hypertrophy of mucous glands in the trachea and bronchi.

- increase in mucin-secreting goblet cells in the epithelial surfaces of smaller bronchi and bronchioles.

- inflammation (marked by the infiltration of macrophages, neutrophils, and lymphocytes) **without eosinophils.**

B• airflow obstruction results from:

1. Small airway disease: Chronic bronchiolitis: results in early and mild airflow obstruction. Induced by mucus plugging of the bronchiolar lumen, inflammation, and bronchiolar wall fibrosis.

2. Coexistent emphysema: The cause of significant airflow obstruction.

- In general, while small airway disease (chronic bronchiolitis) is an important component of early, mild airflow obstruction, chronic bronchitis with significant airflow obstruction almost always is complicated by emphysema.

MORPHOLOGY

1- Macroscopic:-

• Mucosal lining is hyperemic and swollen **(due to the accumulation of edema fluid).**

• Layers of mucinous or mucopurulent secretions, the smaller bronchi and bronchioles also may be involved and filled with secretions

2- Microscopic:-

- **The red star represents the lumen.**
- **The yellow star represents the mucous glands.**
- **Squamous metaplasia of lung epithelium is one of the adaptive mechanisms to protect the respiratory epithelium in smokers.**

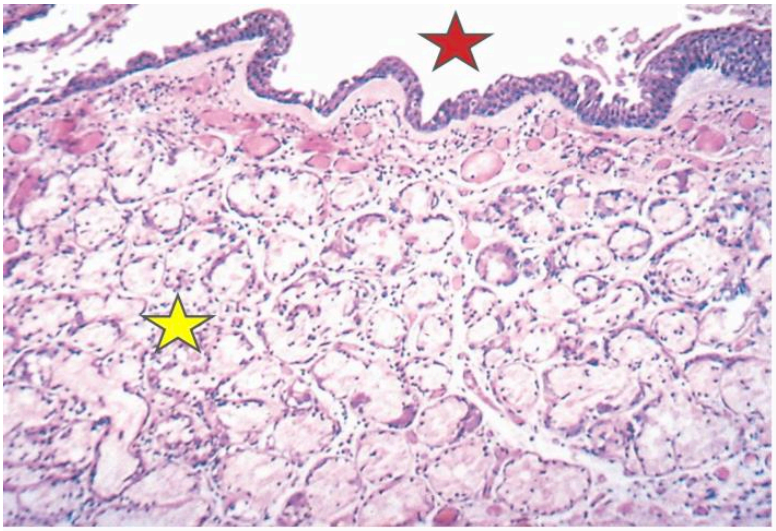


Fig. 13.9 Chronic bronchitis. The lumen of the bronchus is above. Note the marked thickening of the mucous gland layer (approximately twice-normal) and squamous metaplasia of lung epithelium. *(From the Teaching Collection of the Department of Pathology, University of Texas, Southwestern Medical School, Dallas, Texas.)*

-Enlargement of the mucus-secreting glands

-Inflammatory cells, largely mononuclear and neutrophils.

-Chronic bronchiolitis (small airway disease), characterized by goblet cell metaplasia, mucous plugging, inflammation, and submucosal fibrosis

-Changes of emphysema often co-exist.

-**Bronchiolitis obliterans** in severe cases: complete obliteration of the lumen because of fibrosis.

CLINICAL FEATURES:-

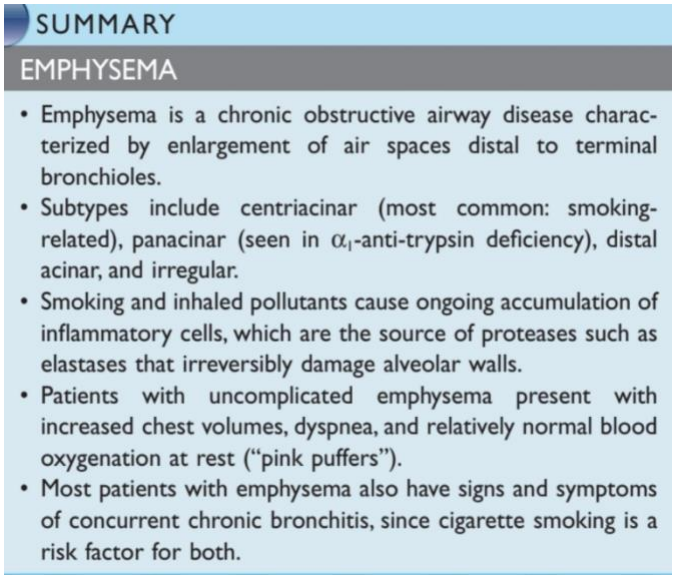
-The course of chronic bronchitis is quite variable. In some patients, cough and sputum production persist indefinitely without ventilatory dysfunction , while others develop COPD with significant outflow obstruction marked by hypercapnia, hypoxemia, and cyanosis.

-chronic bronchitis and COPD patients show frequent exacerbations, rapid disease progression, and poorer outcomes than emphysema alone.

-Progressive disease is marked by the development of pulmonary hypertension, cardiac failure, recurrent infections; and ultimately respiratory failure.

Summarize

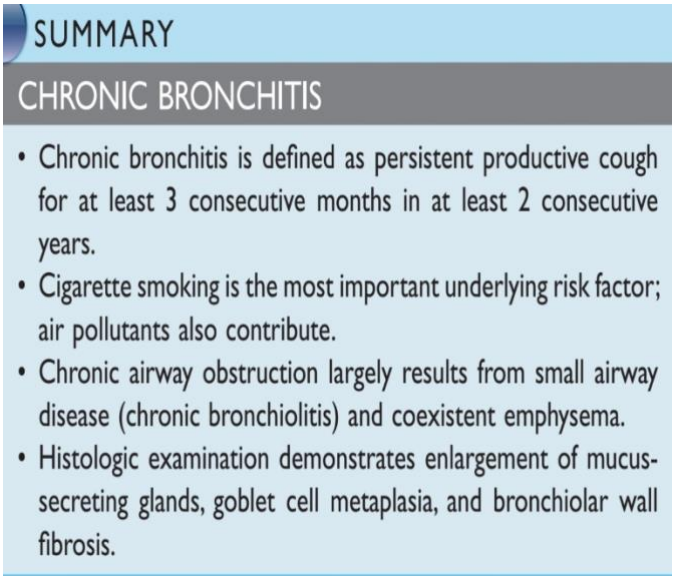
These two tables are taken from Robbins Pathology to help you revise this lecture.



SUMMARY

EMPHYSEMA

- Emphysema is a chronic obstructive airway disease characterized by enlargement of air spaces distal to terminal bronchioles.
- Subtypes include centriacinar (most common: smoking-related), panacinar (seen in α_1-anti-trypsin deficiency), distal acinar, and irregular.
- Smoking and inhaled pollutants cause ongoing accumulation of inflammatory cells, which are the source of proteases such as elastases that irreversibly damage alveolar walls.
- Patients with uncomplicated emphysema present with increased chest volumes, dyspnea, and relatively normal blood oxygenation at rest ("pink puffers").
- Most patients with emphysema also have signs and symptoms of concurrent chronic bronchitis, since cigarette smoking is a risk factor for both.



SUMMARY

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 airway obstruction 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.

Good Luck