

Respiratory System

RS

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Diffuse Pulmonary Diseases:

1. Obstructive Diseases:

- Characterized by an increase in resistance to airflow caused by partial or complete obstruction at any level.

2. Restrictive Diseases:

- Characterized by a reduced expansion of lung parenchyma and decreased total lung capacity.

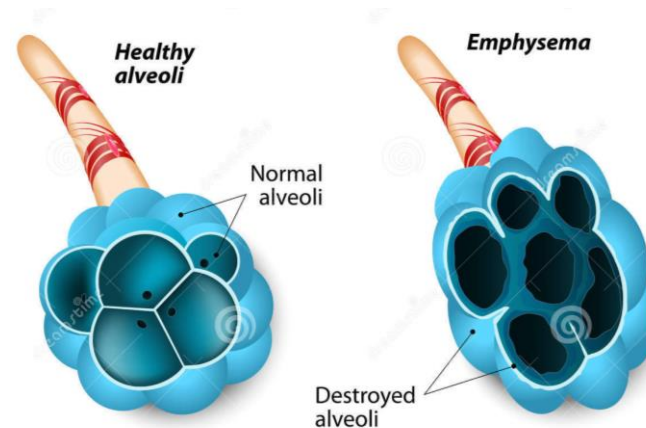
Obstructive lung diseases

1. Emphysema

-Defined based on morphologic and radiologic features.

Definition:

-Abnormal **permanent enlargement** of the air spaces **distal** to the terminal bronchioles (in the acinus), associated with the **destruction of the wall** of acini but **without obvious fibrosis**.



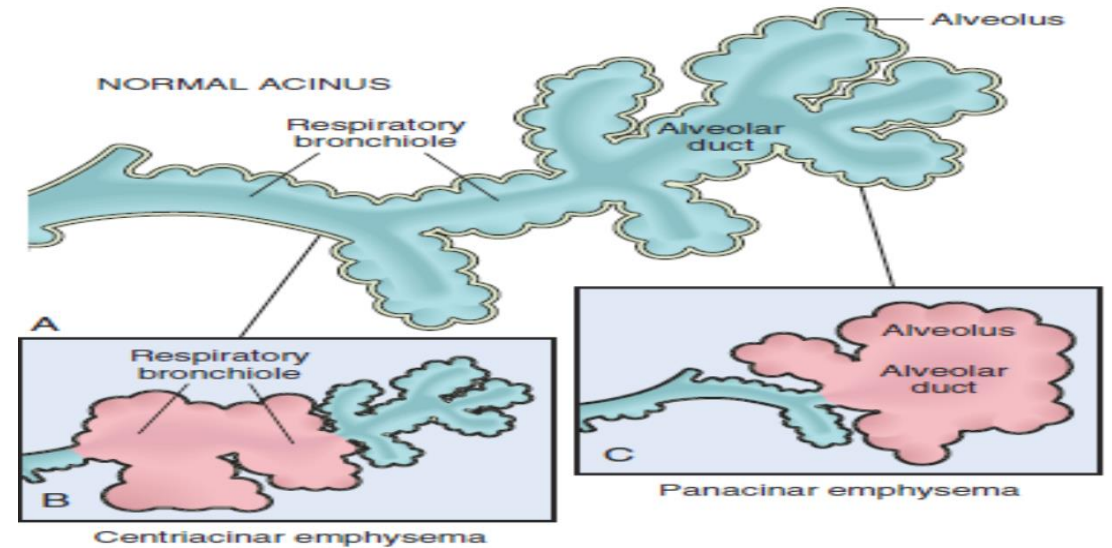
Types of emphysema:

1. Centriacinar (centrilobular) Emphysema:

- The central or the **proximal part** of the acini, formed by the respiratory bronchioles, are **affected**, while the distal alveoli are spared.
- The lesions are more common & severe in the **upper lobes**
- Most commonly due to **cigarette smoking**, often in association with chronic bronchitis.

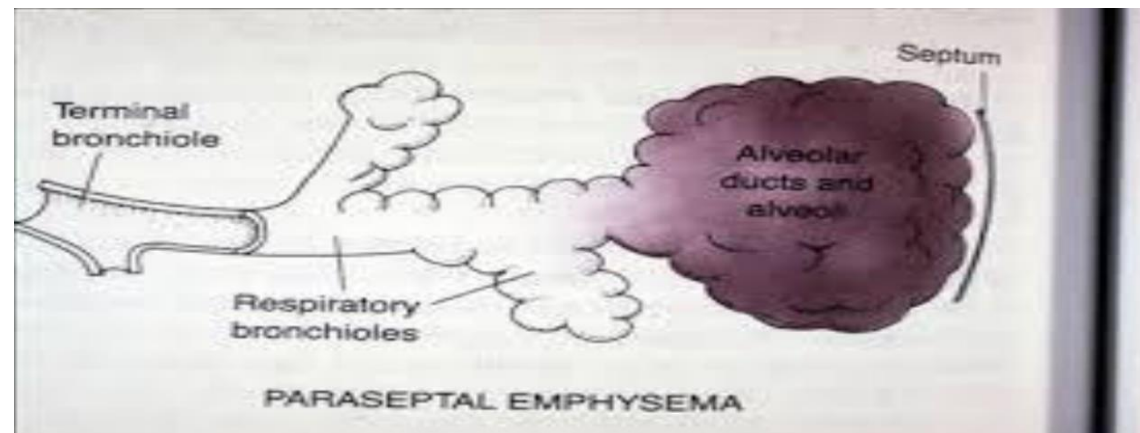
2. Panacinar (Panlobular) Emphysema :

- The **acini** are **uniformly enlarged** from the level of the respiratory bronchioles to the terminal blind alveoli.
- It tends to occur in the **lower lung zones**.
- Occurs in **alpha- 1 anti-trypsin deficiency**.



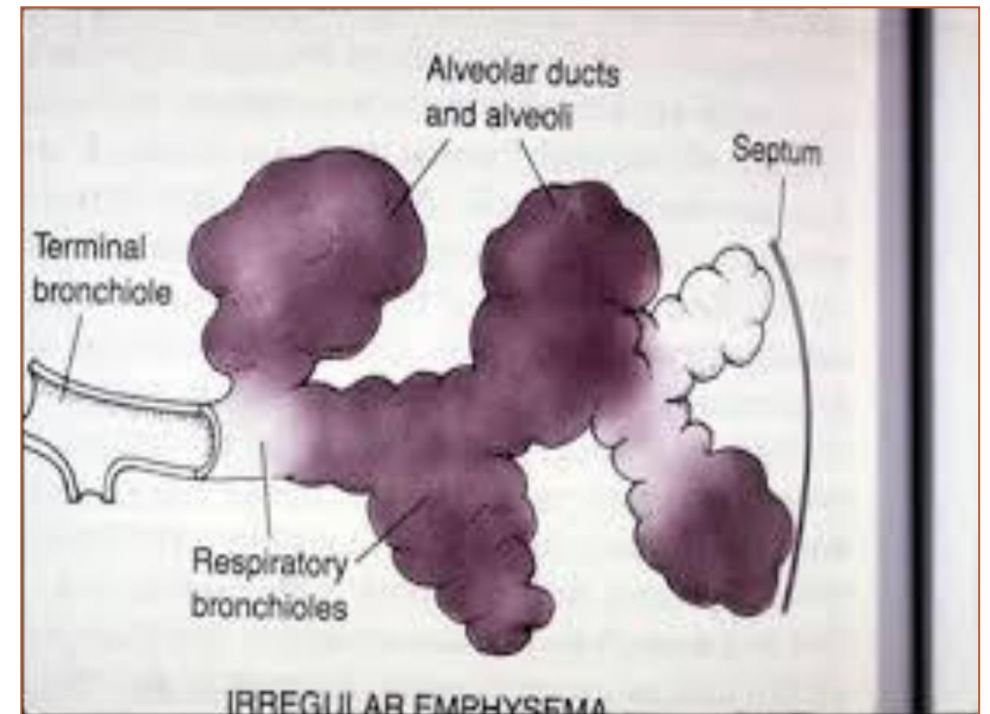
3. Distal acinar (Paraseptal) emphysema:

- The proximal portion of the acinus is normal, but the **distal part** is primarily **involved**.
- More severe in the **upper half** of the lungs.
- The emphysema is more striking **adjacent to the pleura** and **along** the lobular connective tissue **septa**.
- It occurs adjacent to areas of fibrosis or atelectasis.



4. Irregular Emphysema:

- The acinus is irregularly involved; it is associated with scarring in healed inflammatory diseases.
- Although clinically **Asymptomatic**, it is the **most common form of emphysema**.



Pathogenesis:

Two Pathways are involved :

1- PROTEASE -ANTIPROTEASE imbalance.

2- OXIDANT – ANTIOXIDANT imbalance

- Such imbalances almost always coexist.

- Complex interactions between inflammatory mediators and inappropriate activation of repair mechanisms may result in tissue destruction without fibrosis.

- **α 1- antitrypsin** is a major inhibitor of protease, particularly elastase, which is secreted by **neutrophils** during inflammation.

- Exposure to toxic agents such as tobacco induces ongoing inflammation with infiltration of neutrophils, macrophages & lymphocytes in lung tissue

➔ **Elastases, cytokines & oxidants are released by these cells, causing epithelial injury, and unless inhibited by antitrypsin, anti-elastase, and antioxidants, the cycle of inflammation & proteolysis of ECM continues.**

Decrease in these protective mechanisms produce damage.

Decrease in antiprotease activity may be :

i- Genetic: α 1- antitrypsin deficiency

ii- Acquired: Smoking

- More than 80% of patients with congenital α 1- antitrypsin deficiency develop symptomatic panacinar emphysema.
- A secondary consequence of oxidative injury caused by smoking is the inactivation of a native anti-protease, resulting in functional α 1- antitrypsin deficiency even in normal individuals.
- Tobacco smoke contains abundant ROS (free radicals), which deplete anti-oxidant mechanisms
- Activated neutrophils add to the pool of ROS in the alveoli

How does obstruction occur?

- Small airways are normally held open by the elastic recoil of the lung parenchyma, and the loss of elastic tissue in the walls of alveoli that surround respiratory bronchioles reduces radial traction and thus causes the respiratory bronchioles to collapse during expiration → **functional airflow obstruction despite the absence of mechanical obstruction.**

Clinical Features :

- Dyspnea (progressive).
- Weight loss (**thin**).
- Without concomitant chronic bronchitis usually presents with a **barrel chest**, dyspnea, and **prolonged expiration, sitting forward in a hunched-over position**.
- Hyperventilation.
- The blood gases stay normal very until late in the disease due to hyperventilation, and there is adequate oxygenation of the blood.
- Patients are called **Pink-puffers**.



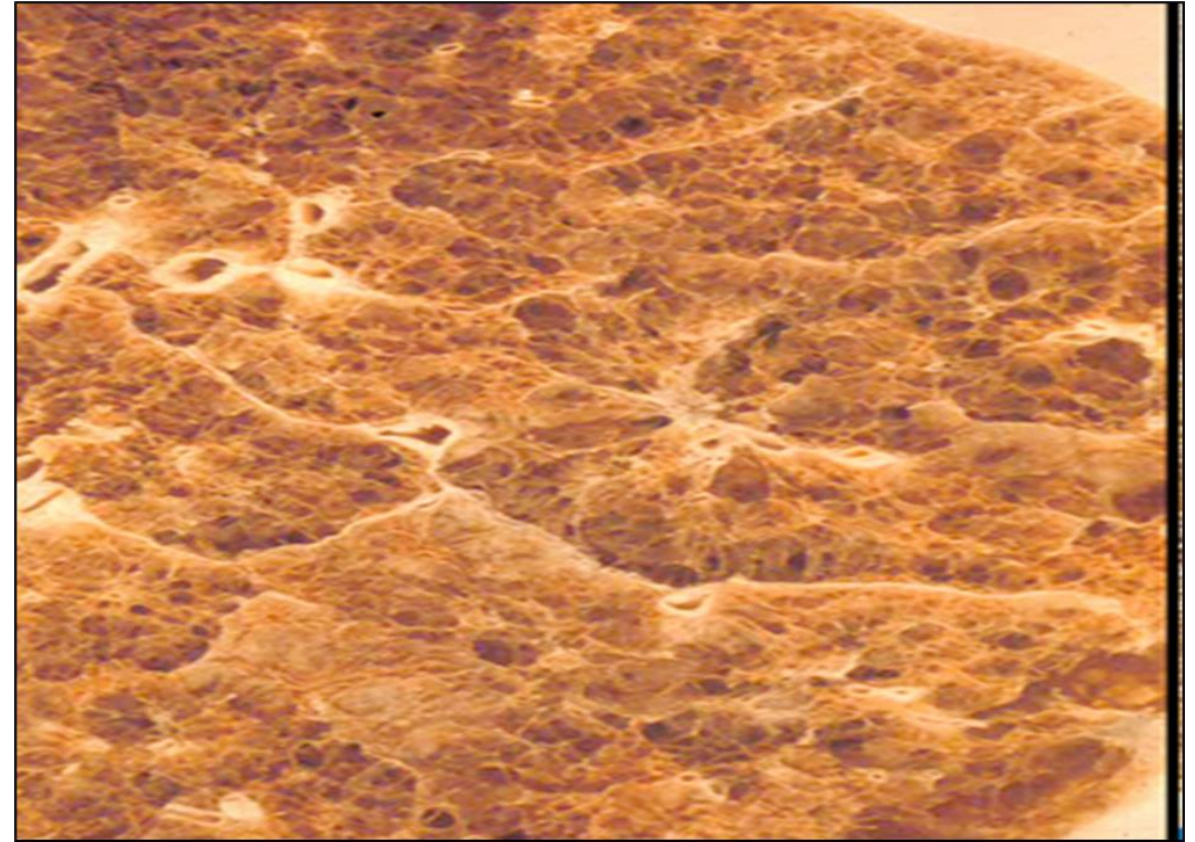
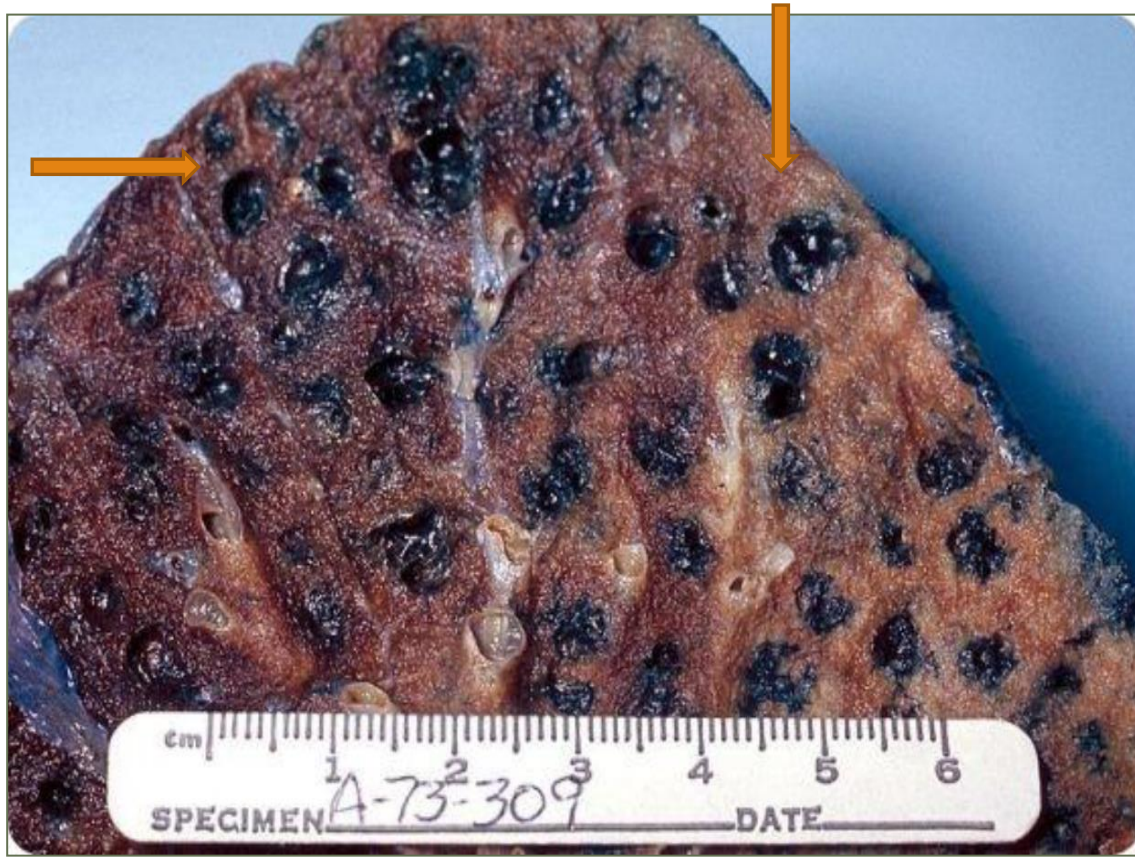
Morphology of Emphysema:

Grossly:

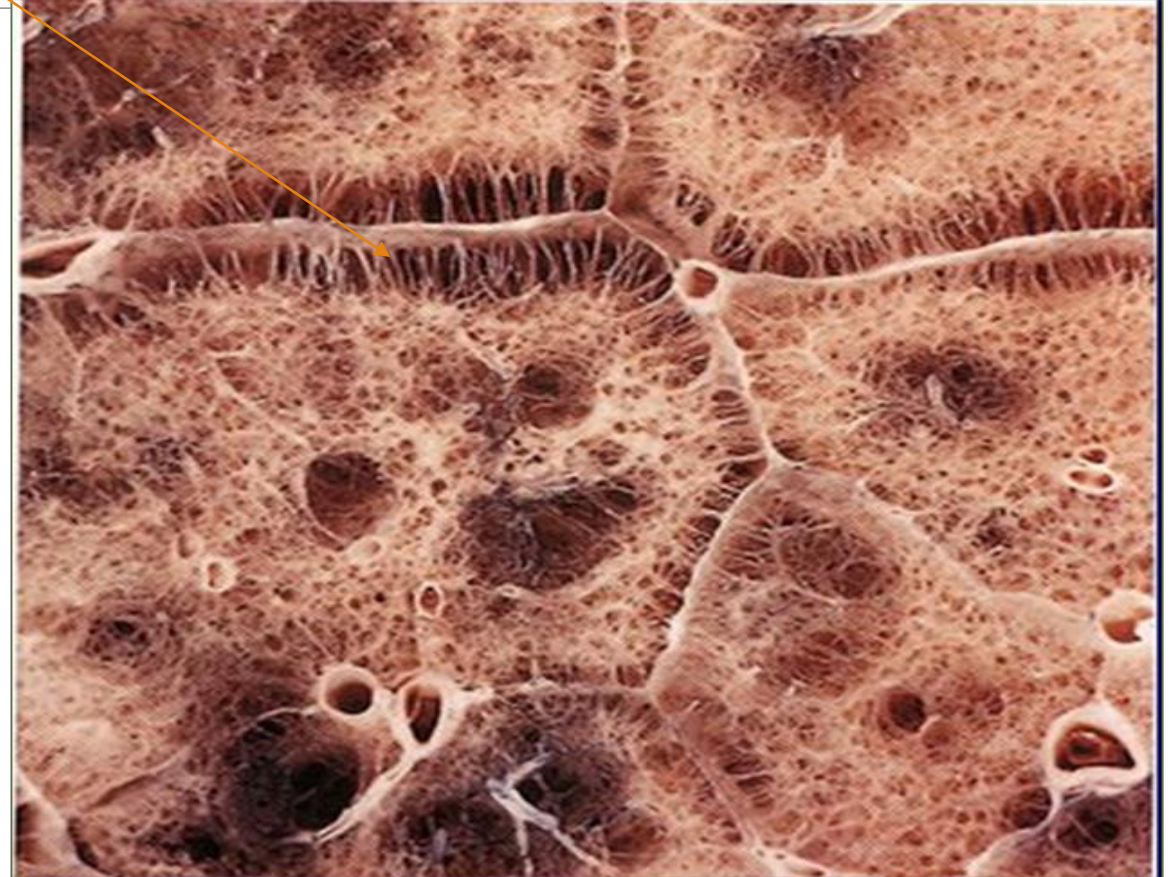
- The diagnosis & classification of E . depend on the macroscopical appearance of the lung.
- In pan-acinar E. the lungs are pale voluminous hyperinflated and obscure the heart.
- In centriacinar E. the features are less impressive, the lung look deeper pink than in pan-acinar E., and less voluminous.

Centriacinar emphysema : centrilobular dilatation surrounded by normal lung tissue, with black color due to carbon particles (smokers).

Panacinar emphysema: the expansion is diffuse throughout each affected acinus



Paraseptal & centriacinar emphysema



Peripheral cystic bullae

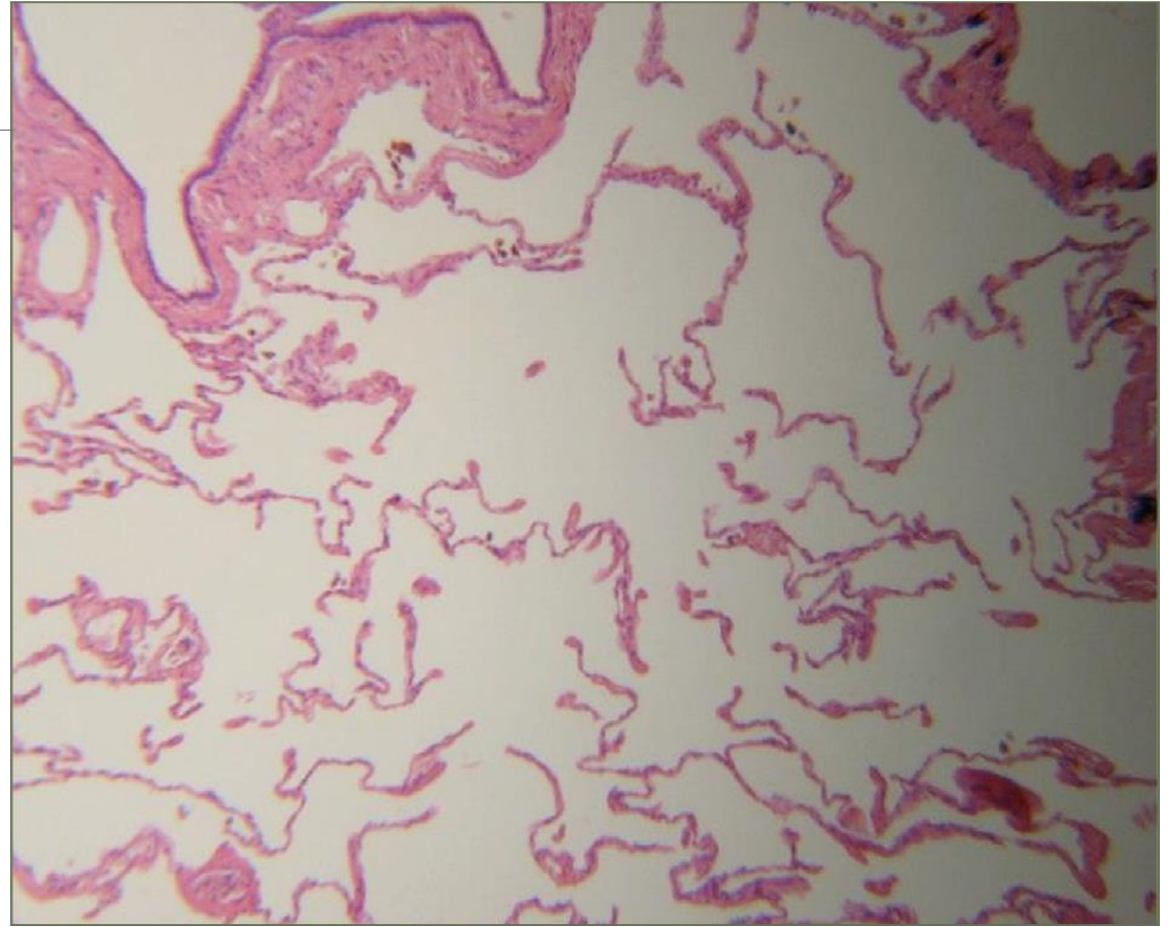
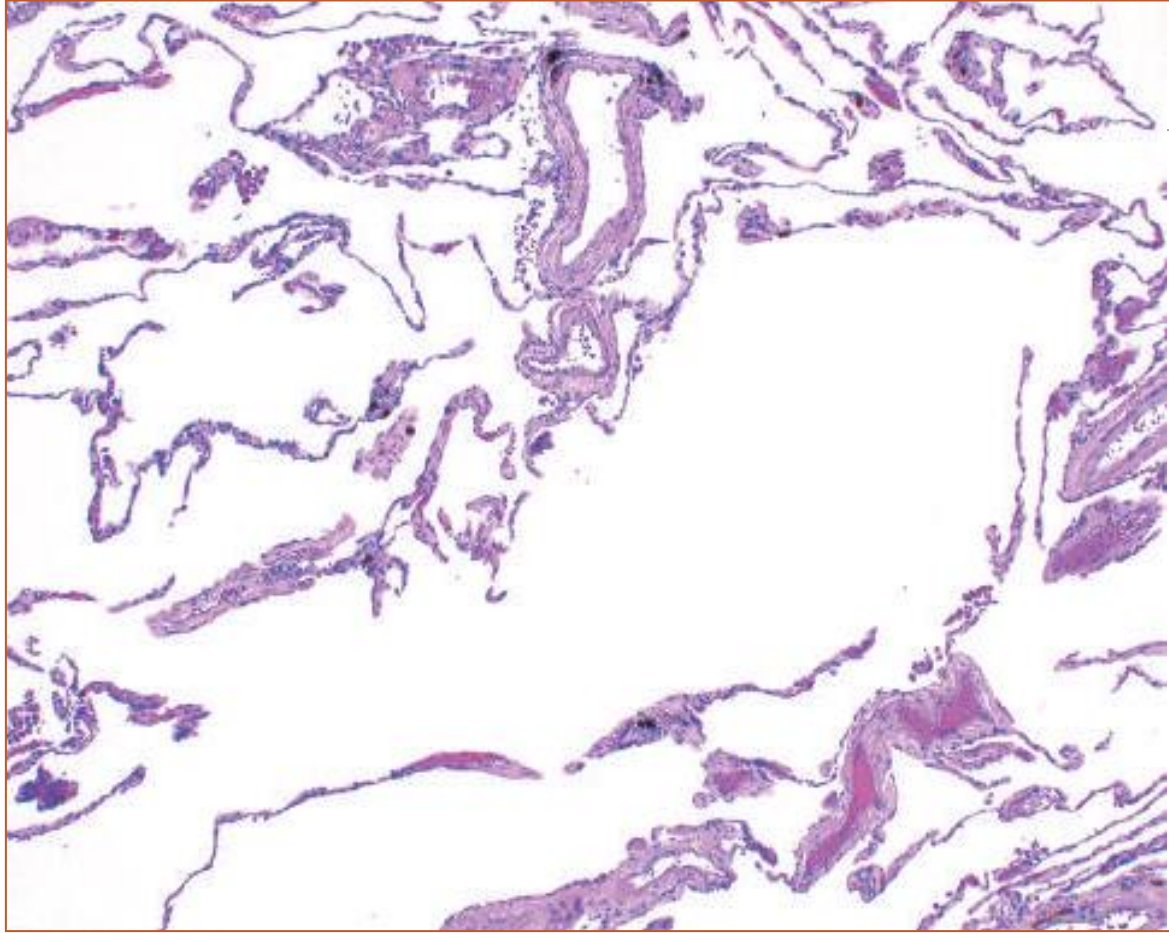
Bullous emphysema :

- Any form of emphysema that produces large subpleural blebs or bullae i.e. air spaces larger than 1cm., when rupture leads to **pneumothorax**



Histologically :

- ❑ Thinning & destruction of alveolar walls; with advanced disease, the adjacent alveoli create large air spaces.
- ❑ Terminal & respiratory bronchioles may be deformed
- ❑ Alveolar capillaries are diminished.
- ❑ Bronchiolar inflammation and submucosal fibrosis are consistently present in advanced disease



2. Chronic Bronchitis :

Chronic bronchitis is defined based on clinical features.

Definition :

- A clinical condition characterized by a persistent productive cough for at least **three** consecutive months in at **least two consecutive years** (WHO)
- It is common among **cigarette smokers** and **urban dwellers**.

Chronic bronchitis can occur in several forms :

1- Simple chronic bronchitis :

-Patients have a productive cough with mucoid sputum, but airflow is not obstructed.

2- Asthmatic bronchitis :

- Patients may demonstrate hyper-responsive airways with intermittent bronchospasm and wheezing.

3- Chronic obstructive bronchitis :

- Including heavy smokers who develop frank chronic outflow obstruction, usually with associated emphysema.

Pathogenesis :

- ❑ Hypersecretion of mucus, **beginning in the large airways** as major bronchi.
- ❑ In advanced disease, even small bronchioles are involved.
- ❑ The environmental irritants induce hypertrophy of mucus glands in the bronchi & goblet cell metaplasia, which leads to a marked increase in mucus-secreting goblet cells in the bronchi & bronchioles.
- ❑ In addition to inflammation with infiltration of lymphocytes, macrophages & neutrophils.
- ❑ **Eosinophils are NOT seen in chronic bronchitis.**
- ❑ Microbial infection is often present but has a secondary role chiefly by maintaining the inflammation.

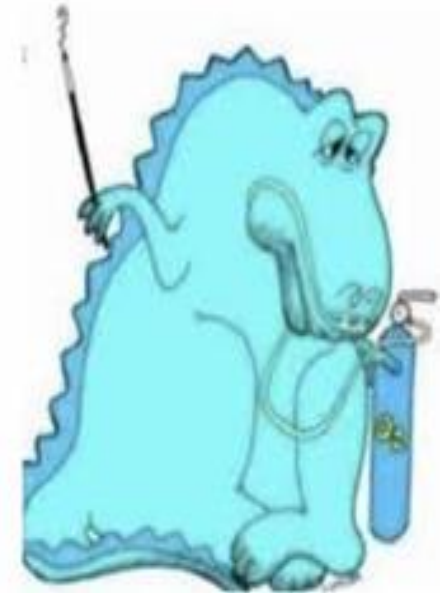
Whereas the defining **mucus hypersecretion** is primarily a reflection of the involvement of **large bronchi**, the **airflow obstruction** in chronic bronchitis results from:

- 1- So called **small-airways disease** induced by **goblet-cell metaplasia** with mucus-plugging of the bronchiolar lumen, inflammation, and fibrosis.
- 2- **Co-existent emphysema.**

Clinical features and course :

- Cough with the production of excessive mucoid or mucopurulent sputum
- Some patients may develop COPD with outflow obstruction; this is accompanied by hypercapnia, hypoxemia & in severe cases, **cyanosis**.
- For unknown reasons, they tend to be **obese**.

called **blue bloater**



Morphology:

Grossly:

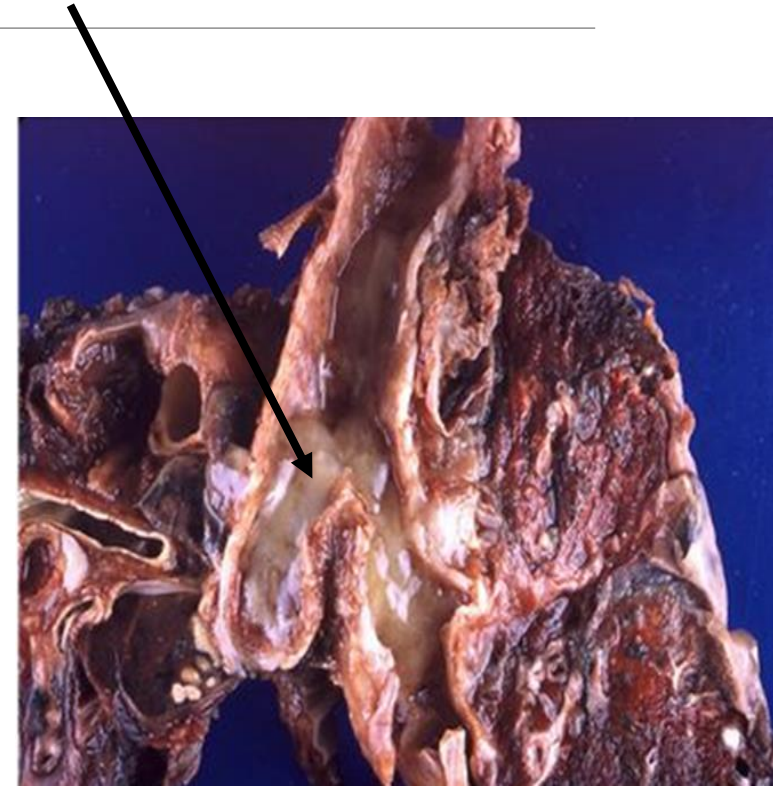
- ❖ The mucosal lining of larger airways is usually hyperemic & swollen by edema and covered by a layer of mucopurulent secretion.
- ❖ The smaller bronchi & bronchioles may also be filled with similar secretions.

Histologically:

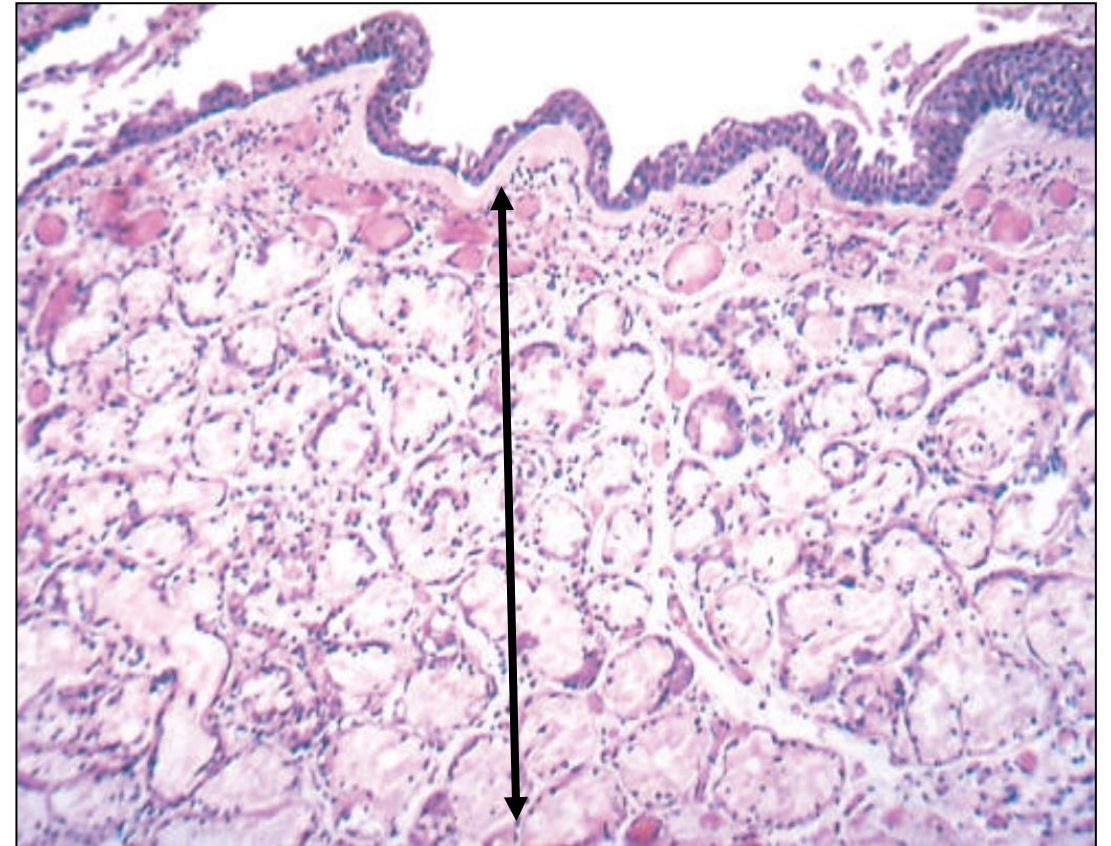
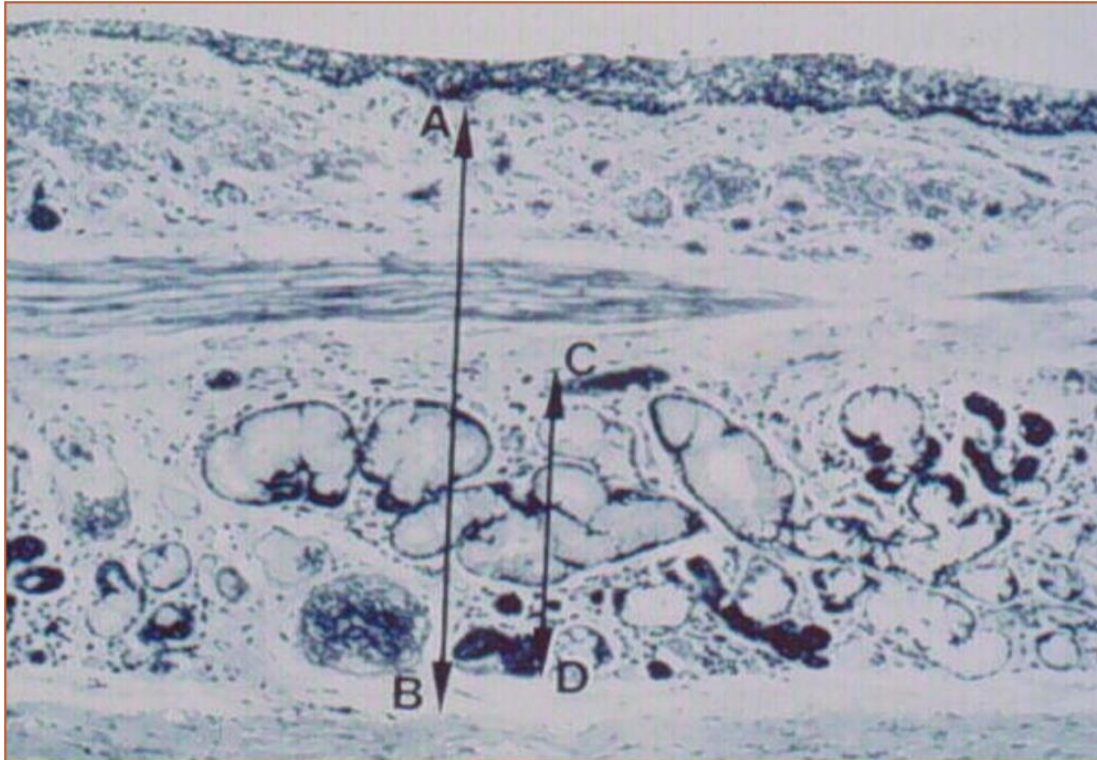
- ❖ The larger bronchi: **goblet cell metaplasia of bronchial epithelium** and **hyperplasia of submucosal mucus-secreting glands**.

The magnitude of the increase in size is assessed by the ratio of the thickness of the submucosal gland layer to that of the bronchial wall from the epithelial layer down to the cartilage

This ratio is called the Reid index, which normally is (0.4)



Measuring Reid index, normal 0.4; in chronic bronchitis, it is increased by 1/1.



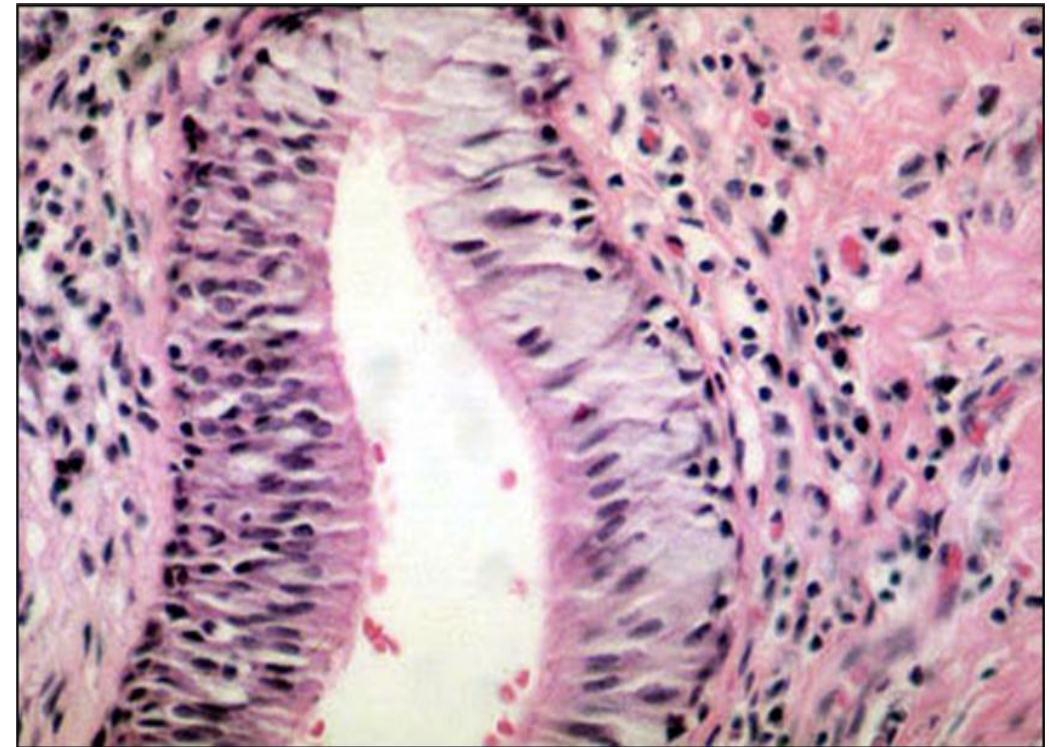
- Variable inflammatory cells, largely mononuclear cells but sometimes with neutrophils, are present in the bronchial mucosa.

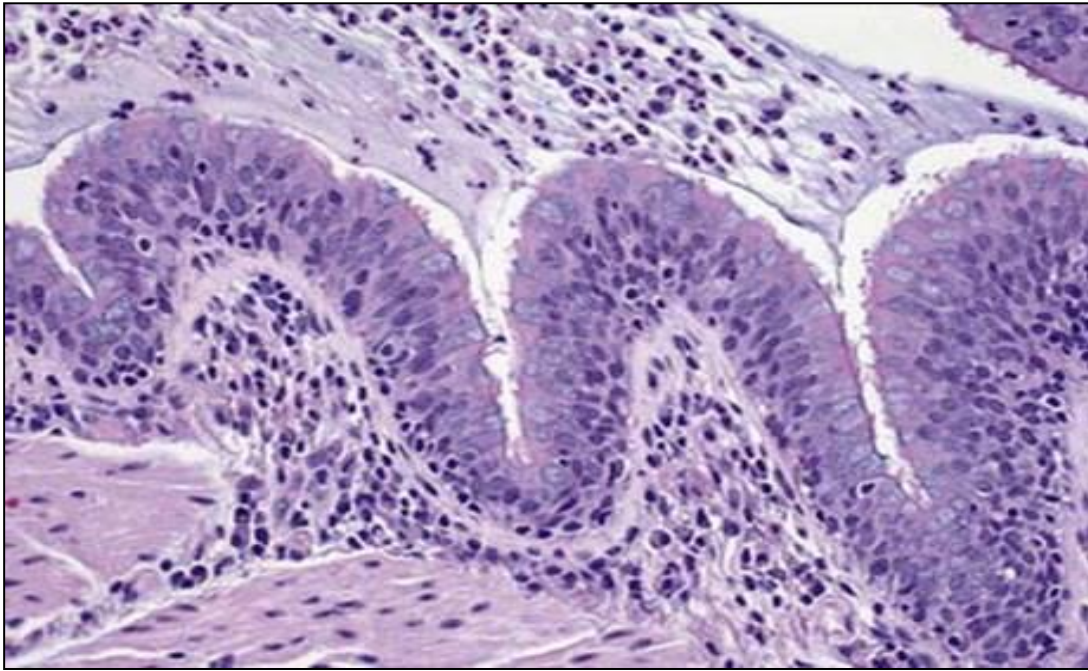
- **Chronic bronchiolitis** is inflammation of small bronchioles, showing **goblet cell metaplasia, mucus plugging inflammation & fibrosis.**

- In severe cases narrowing and obstruction with complete obliteration of the lumen due to fibrosis called **bronchiolitis Obliterans.**

- Squamous metaplasia ± DYSPLASIA

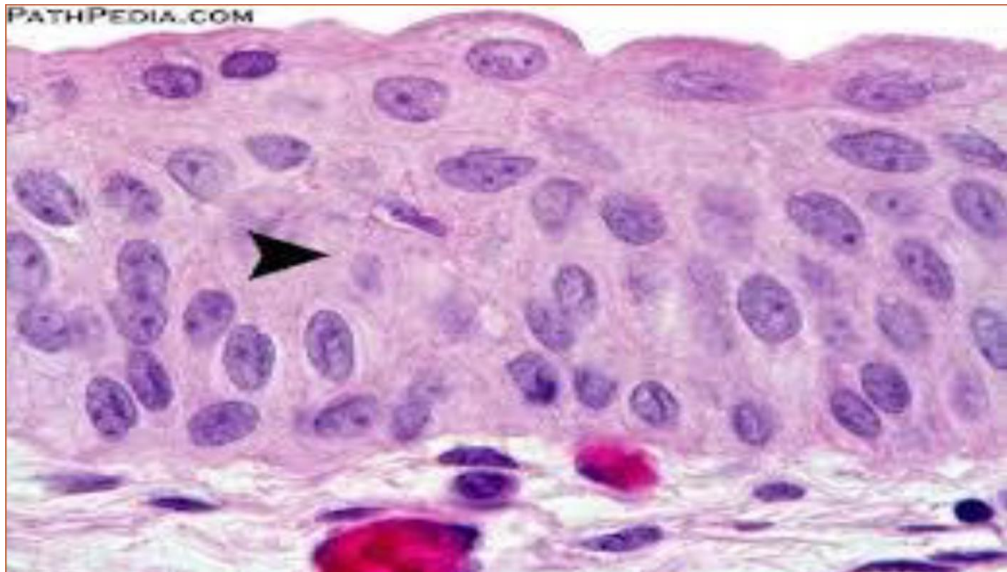
Goblet cell metaplasia (right) of the bronchiolar epithelium (left) with inflammatory cells infiltrate in surrounding tissue .





Chronic bronchitis:

- Goblet cell hyperplasia and chronic inflammation in the submucosa, and acute inflammation mixed with intraluminal mucus.



Bronchial mucosa showing squamous metaplasia



Thank You