Diseases of the respiratory system lecture 2

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Obstructive versus restrictive lung diseases

Obstructive lung diseases: limitation of airflow due to partial or complete obstruction. Expiration affected more than inspiration.

Expiratory obstruction may result either from

A. **Anatomic** airway narrowing, such as in asthma and chronic bronchitis

B. **Loss of elastic recoil** (functional obstruction)characteristic of emphysema

- Restrictive lung diseases: reduced expansion of the lungs and decreased total lung capacity.
- Caused by:

1. Chest wall disorders that decrease lung expansion like in obesity or pleural diseases
2. Interstitial lung diseases: these are divided to acute (ARDS) and chronic (fibrosis, sarcoidosis.. Etc)

Obstructive versus restrictive lung diseases

Obstructive vs restrictive lung diseases	
Obstructive	**restrictive**
characterized by limitation of airflow due to partial or complete obstruction	characterized by reduced expansion of lung parenchyma accompanied by decreased total lung capacity.
Eg are emphysema, chronic bronchitis, bronchiectasis, and asthma	Eg are ILD like Fibrosing alveolitis, idiopathic pulmonary fibrosis, interstitial pneumonia, Pneumoconiosis,Sarcoidosis; and chest wall neuromuscular diseases
total lung capacity normal	decreased
forced vital capacity (FVC) normal	reduced
decreased expiratory flow rate, measuerd as forced expiratory volume at 1 second (FEV_1)	Normal or reduced
FEV1/FVC ratio < 0.80	normal

OBSTRUCTIVE VS. RESTRICTIVE

Obstructive disorders	Restrictive disorders
• **Characterized by:** reduction in airflow. • So, shortness of breath → in exhaling air. (the air will remain inside the lung after full expiration) 1. COPD 2. Asthma 3. Bronchiectasis	• **Characterized by** a reduction in lung volume. • So, Difficulty in taking air inside the lung. (DUE TO stiffness inside the lung tissue or chest wall cavity) 1. Interstitial lung disease. 2. Scoliosis 3. Neuromuscular cause 4. Marked obesity

Obstructive pulmonary diseases

1. Emphysema,
2. Chronic bronchitis,
3. Bronchiectasis,
4. Asthma.

COPD= chronic obstructive pulmonary disease

- = Chronic bronchitis and emphysema
- These two are distinct diseases but they overlap and coexist in the same patient because both are caused by smoking.

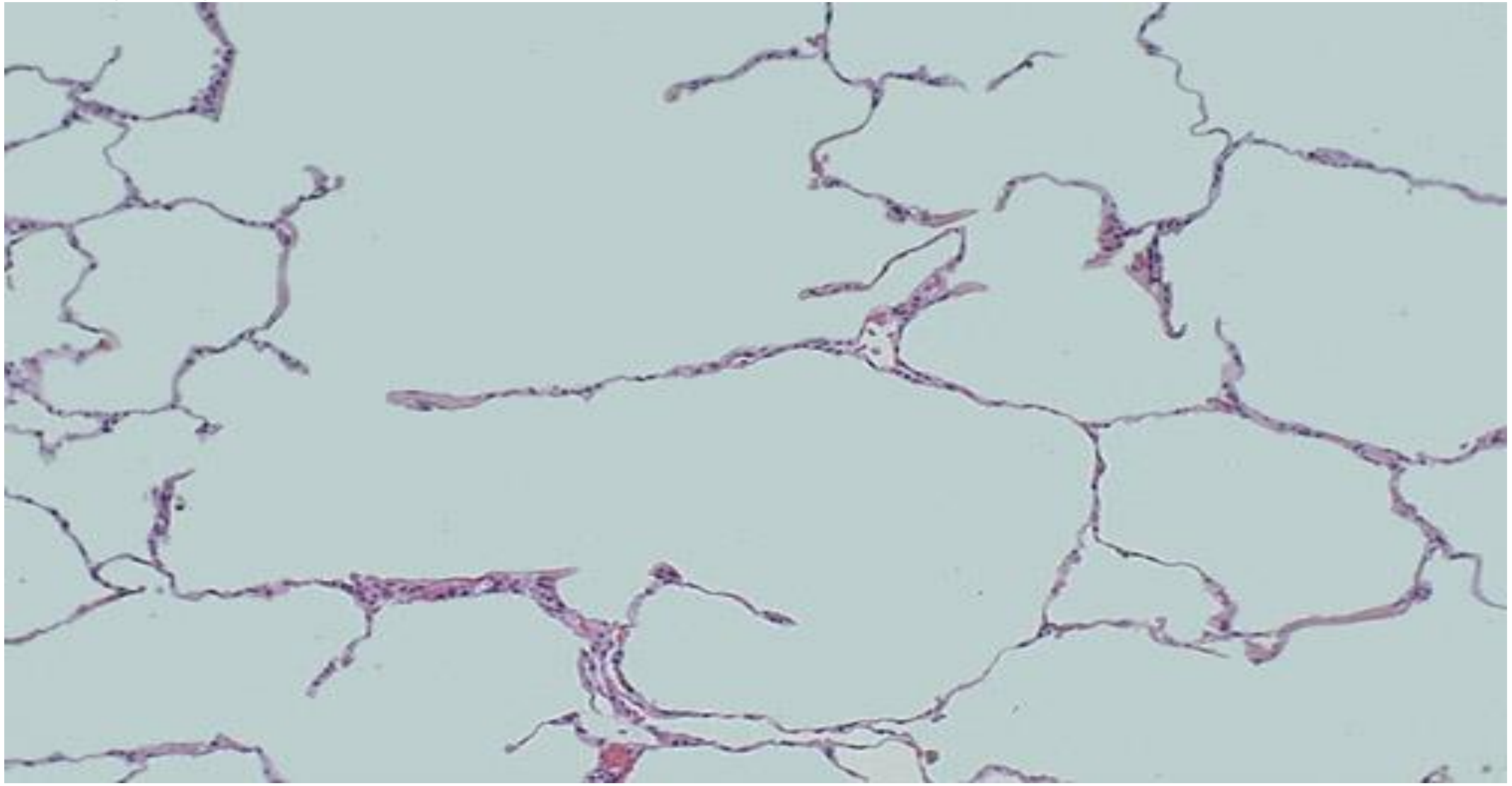
Differences between chronic bronchitis and emphysema

- The definition of emphysema is morphologic, whereas chronic bronchitis is defined on the basis of clinical features
- The anatomic distribution is different; chronic bronchitis initially involves the large airways, whereas emphysema affects the acini.
- Clinical presentation differs (details later)

Emphysema: definition

- Abnormal **permanent enlargement** of the air spaces **distal to the terminal bronchioles** accompanied by **destruction of their walls without fibrosis**

Emphysema



Types of emphysema

- Emphysema is classified according to its anatomic distribution within the lobule, the acinus is the structure distal to terminal bronchioles, and a cluster of three to five acini is called a lobule

-There are four major types of emphysema:

(1) Centriacinar,

(2) Panacinar

(3) Distal acinar,

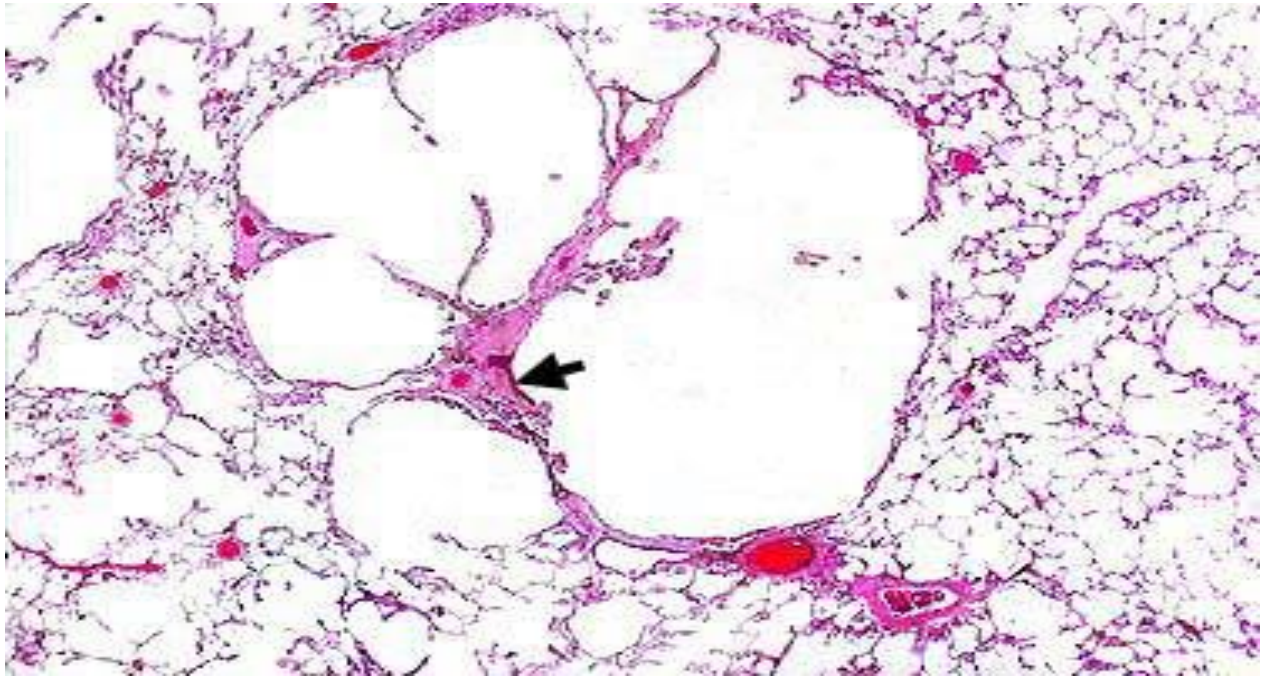
(4) Irregular.

Types of emphysema

1. Centriacinar (Centrilobular) Emphysema

- The central or proximal parts of the acini, formed by respiratory bronchioles, are affected, while distal alveoli are spared
- Both emphysematous and normal air spaces exist within the same acinus and lobule

Centriacinar emphysema



CENTRIACINAR EMPHYSEMA

-The lesions are more common and severe in the upper lobes.

- This type of emphysema is most commonly caused by smoking

2. Panacinar (Panlobular) Emphysema

- *The acini are uniformly enlarged,* from the level of the respiratory bronchiole to the terminal blind alveoli
- Tends to occur more commonly in the lower lung zones
- It occurs in α_1-antitrypsin deficiency.

3. Distal Acinar (Paraseptal)

- It involves the distal part of the acinus.
- The proximal portion of the acinus is normal
- Is more striking adjacent to the pleura, along the lobular connective tissue septa

PARASEPTAL EMPHYSEMA

- It occurs adjacent to areas of fibrosis
- The characteristic finding is the presence of multiple, enlarged air spaces ranging in diameter from less than 0.5 mm to more than2.0 cm, sometimes forming cystic structures that, with progressive enlargement, are referred to as *bullae*
- Ruptured bullae cause spontaneous pneumothorax especially in young adults.

4. Irregular Emphysema

- The acinus is irregularly involved,
- Is almost invariably associated with scarring, such as that resulting from healed inflammatory diseases.
- Although clinically asymptomatic, this may be the **most common** form of emphysema.

PATHOGENESIS/ 1

- Exposure to toxic substances such as tobacco smoke and inhaled pollutants induces ongoing inflammation with accumulation of neutrophils, macrophages and lymphocytes in the lung.
- Neutrophils release elastases, cytokines (including IL-8) and oxidants causing epithelial injury and proteolysis of the extracellular matrix (ECM).

PATHOGENESIS/ 2

-Unless checked by antielastases (e.g., α_1-antitrypsin) and antioxidants, the cycle of inflammation and ECM proteolysis continues.

- More than 80% of patients with congenital α_1-antitrypsin deficiency develop symptomatic panacinar emphysema, which occurs at an earlier age and with greater severity if the affected person smokes .

PATHOGENESIS/ 3

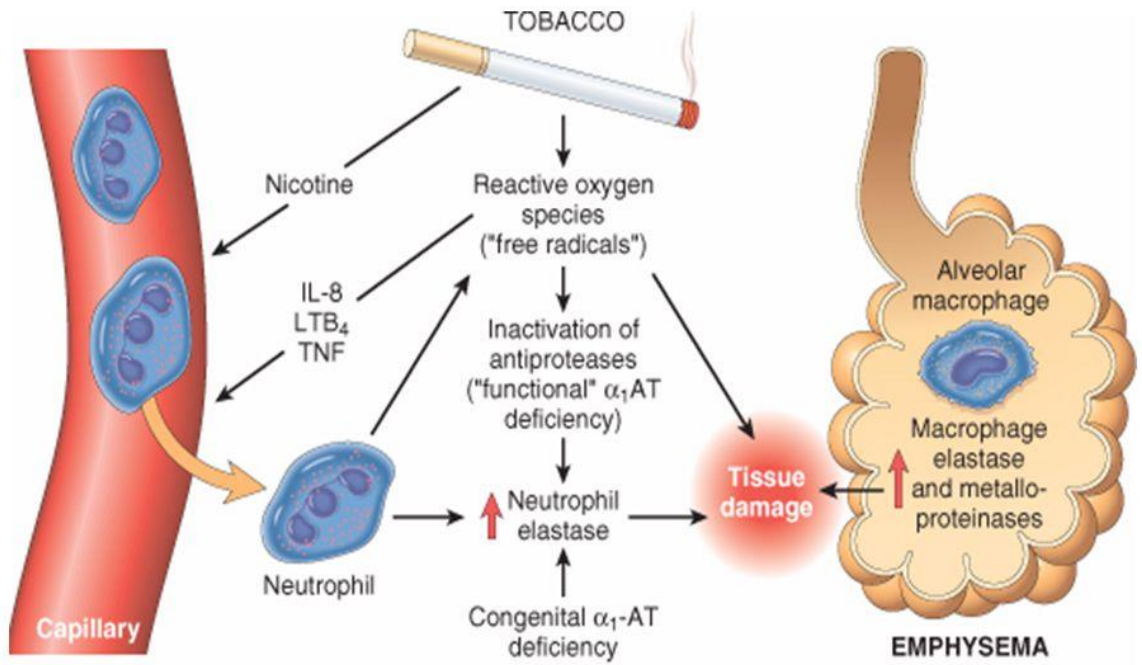
In emphysema there is loss of not only epithelial and endothelial cells but also **mesenchymal cells**, leading to **lack of extracellular matrix**, the scaffolding upon which epithelial cells would have grown.

- *Thus,* ***emphysema can be thought of as resulting from insufficient wound repair*****.**

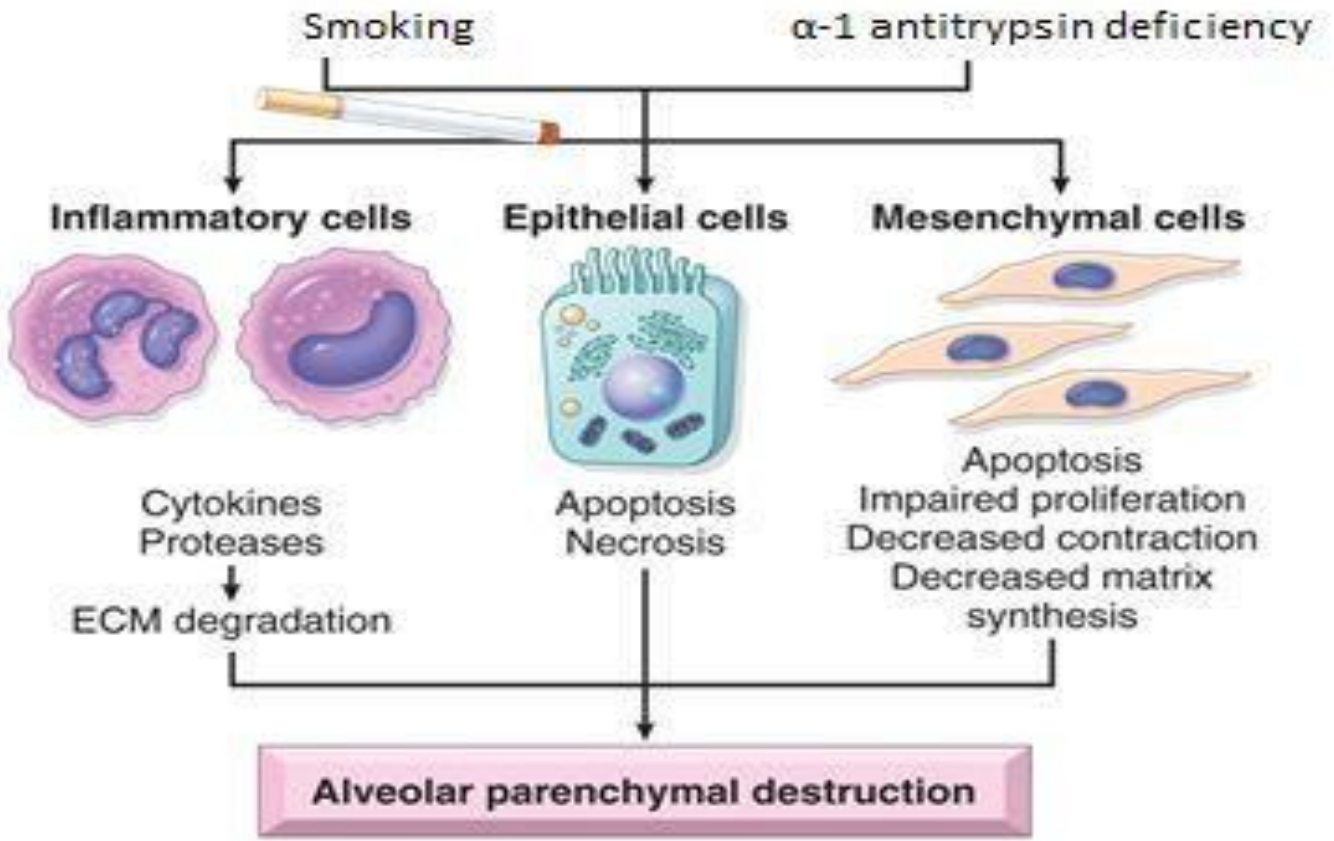
- With the **loss of elastic tissue** in the surrounding alveolar septa, radial traction on the small airways is reduced.
- As a result, they tend to collapse during expiration-an important cause of chronic airflow obstruction in severe emphysema.

Pathogenesis of Emphysema

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



Pathogenesis of emphysema



GENETIC FACTORS

-Multiple genetic factors control the response to injury after smoking.

-The ***TGFB* gene** exhibits **polymorphisms** that influence susceptibility to the development of COPD by **regulating the response of mesenchymal cells to injury.**

with certain polymorphisms, mesenchymal cell response to TGF-β signaling is reduced, which results in inadequate repair of elastin injury caused by inhaled toxins

Genetic factors

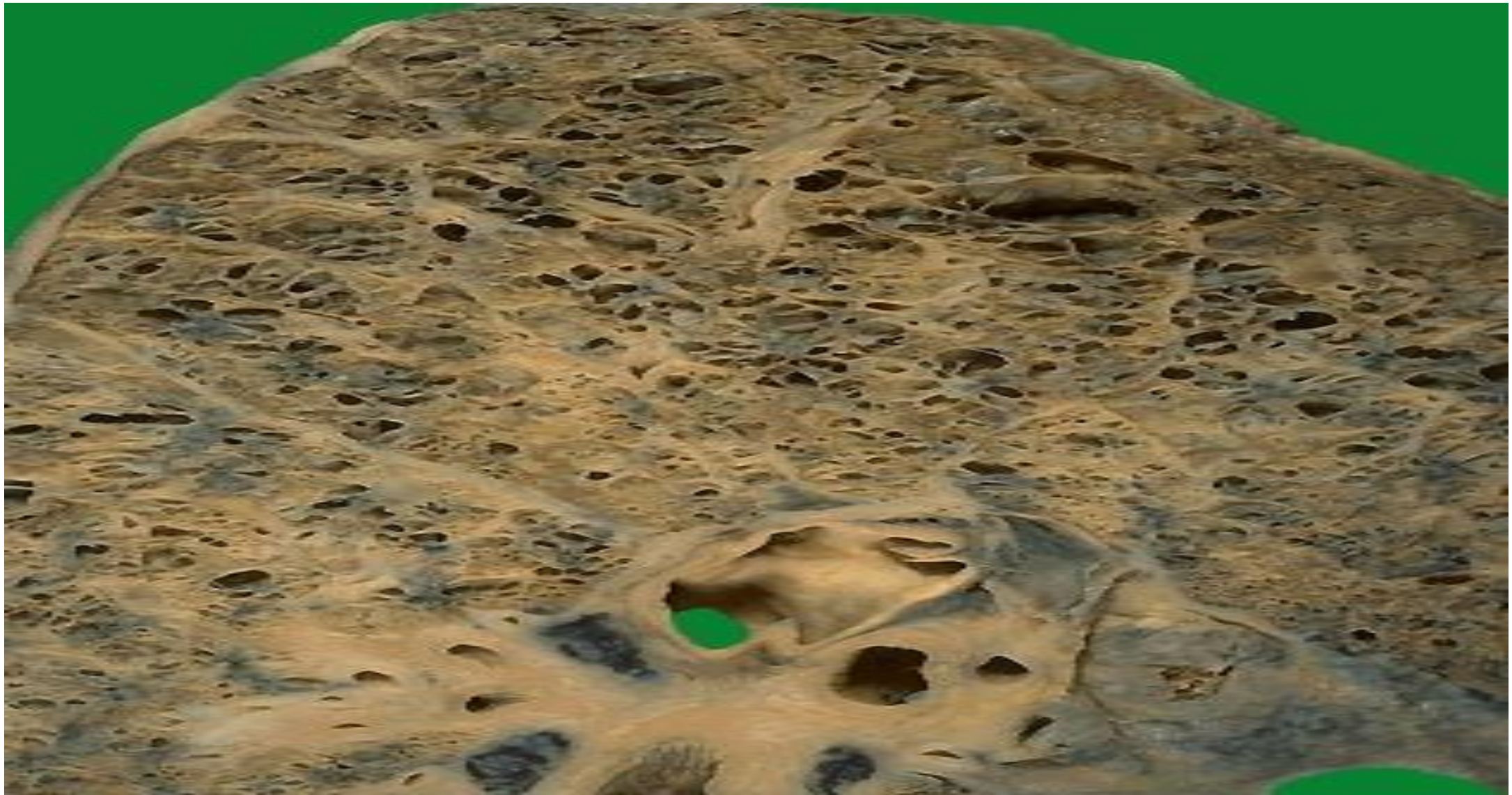
- metalloproteinases play a role: MMP-9 gene polymorphisms and higher levels of both MMP-9 and MMP-12 have been found in some emphysema patients.
- Moreover, MMP-12-deficient mice are protected from cigarette smoke-induced emphysema.

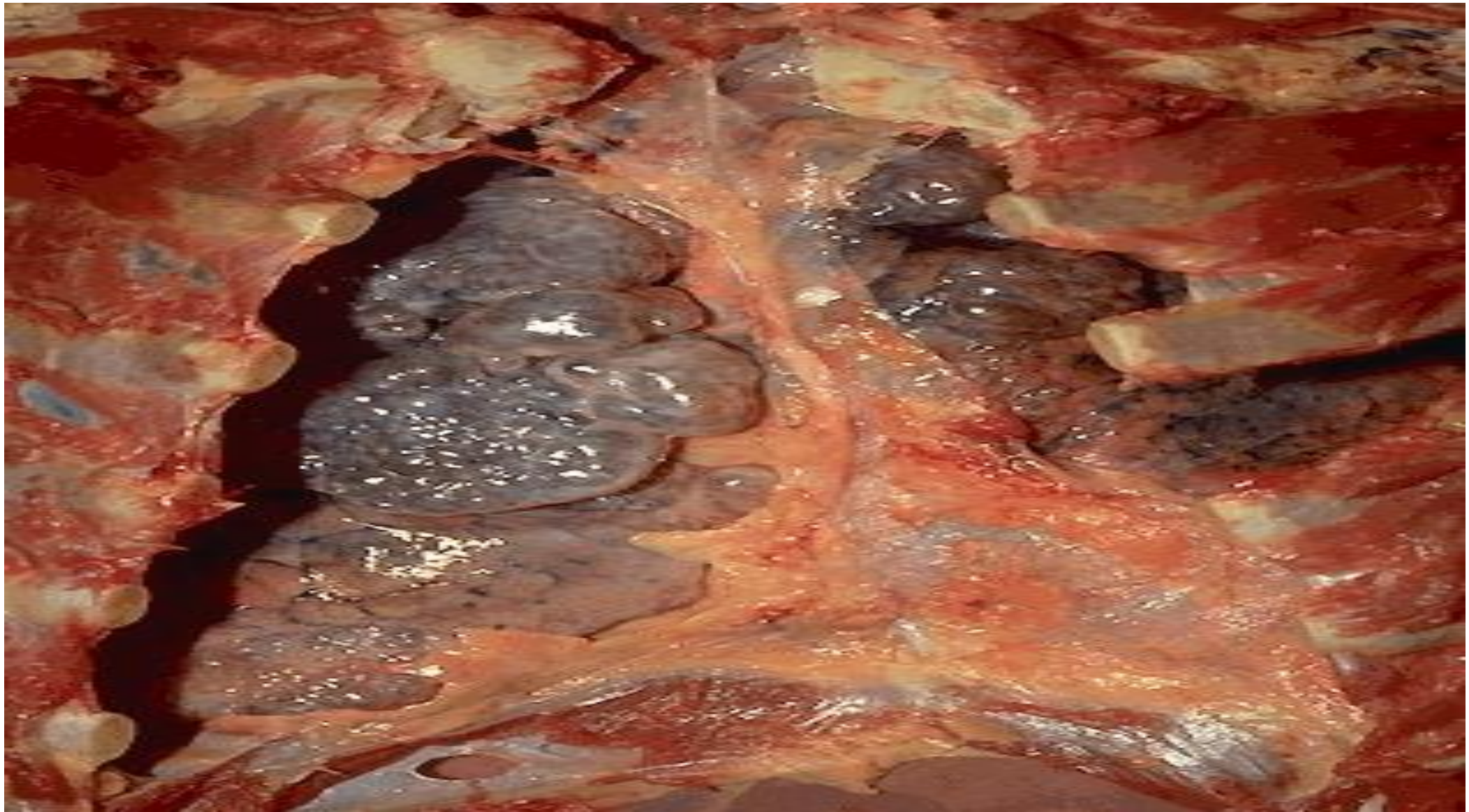
Histologic examination reveals :

a. Destruction of alveolar walls without fibrosis, leading to enlarged air spaces

b. The number of alveolar capillaries is diminished.

Emphysema





Clinical Features

- Dyspnea usually is the first symptom which begins insidiously but is steadily progressive.

-Weight loss is common and may be so severe as to suggest a hidden malignant tumor.

- The classic presentation in emphysema with no "bronchitic" component is one in which the patient is

a. Barrel-chested and dyspneic,

b. with obviously prolonged expiration,

c. Sitting forward in a hunched-over position, attempting to squeeze the air out of the lungs with each expiratory effort.

Clinical features:

-Dyspnea and hyperventilation are prominent, so that until very late in the disease, gas exchange is adequate and blood gas values are relatively normal.

- Because of prominent dyspnea and adequate oxygenation of hemoglobin, these patients sometimes are called **"pink puffers**."

Pink puffers