Pathology of respiratory system

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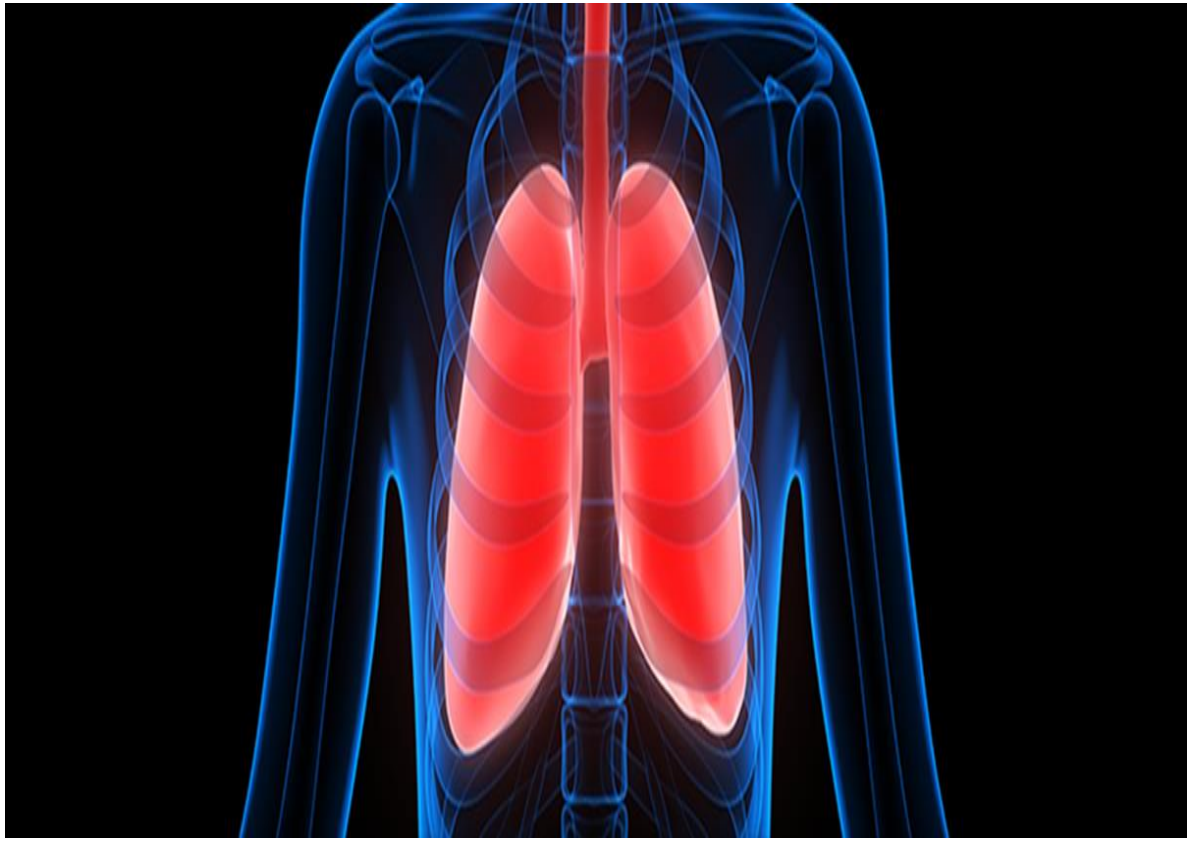


Lung Pathology Outline

- Congenital anomalies
- Atelectasis
- **Obstructive lung diseases**
- Restrictive lung diseases
- Infections
- Carcinoma

- **Chronic obstructive pulmonary diseases(COPD)**

Pulmonary Function Tests measures:

- **Tidal volume (TV).** This is the amount of air inhaled or exhaled during normal breathing.
- **Residual volume.** This is the amount of air left in the lungs after exhaling as much as possible.
- **Total lung capacity(TLC).** This is the total volume of the lungs when filled with as much air as possible.
- **Forced vital capacity (FVC).** This is the amount of air exhaled forcefully and quickly after inhaling as much as you can.
- **Forced expiratory volume (FEV1).** This is the amount of air expired during the first second of the FVC test.

- In individuals with diffuse obstructive disorders, **pulmonary function tests show: decrease maximal airflow rates during forced expiration, usually measured by forced expiratory volume at 1 second.**
-
- In contrast, restrictive diseases **are identified by a reduced total lung capacity, and an expiratory flow rate that is normal or reduced proportionately.**

- Obstructive & Restrictive Pulmnary diseases
- Depending on the **pulmonary function test**, chronic noninfectious diffuse pulmonary diseases can be classified into two categories:
- **Obstructive diseases (OPD),** (or **airway diseases**), characterized by an increase in resistance to airflow due to partial or complete obstruction at any level, from the trachea and larger bronchi to the terminal and respiratory bronchioles.

- FVC: normal or slightly decreased.
- **FEV1: significantly decreased**.
- *Forced expiratory volume at 1 second (**FEV1**): measure how much air person can exhale during a forced breath , can measured during one second of breath.*
- *Forced vital capacity (**FVC**):It is total amount of air that can be forcibly exhale from the lungs after taking deepest breath in FEV test.*

- An **FEV1/FVC ratio** of less than 0.7 generally indicates obstructive disease.
- **Normal ratio is 0.8**

- **Restrictive diseases (RPD), characterized by reduce expansion of the lung parenchyma,** with decrease total lung capacity.
- **FVC: reduced**
- **FEV 1: normal or reduced**
- **Decrease Total lung capacity:** maximum amount of air that can full the lungs.
- FEV1/FVC ratio remains normal.
- **Examples of restrictive diseases:**
- 1) **Chest wall disorders**:(e.g., severe obesity, pleural diseases, kyphoscoliosis, and neuromuscular diseases such as poliomyelitis)
- 2) chronic interstitial and infiltrative diseases, such as pneumoconiosis and interstitial fibrosis.
- .

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

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Under this heading come four entities

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

Chronic Obstructive Pulmonary Disease(COPD)

Emphysema and **chronic bronchitis** are often clinically grouped together under the term **chronic obstructive pulmonary disease (COPD),** which is one of the leading causes of death.

The irreversibility of airflow obstruction of COPD distinguishes it from **asthma (reversible obstruction)**

The hallmark is a decreased expiratory flow rate, usually measured by forced expiratory volume at 1 second (FEV_1)

-Total lung capacity and forced vital capacity (FVC) … • normal .

The ratio of FEV_1 \ FVC is characteristically decreased.

- Emphysema
- **abnormal permanent enlargement of the airspaces distal to the terminal bronchioles, accompanied by destruction of their walls .**
- Overinflation: enlargement of airspaces is NOT accompanied by destruction. For example, compensatory overinflation in opposite lung in patient with unilateral pneumonectomy.

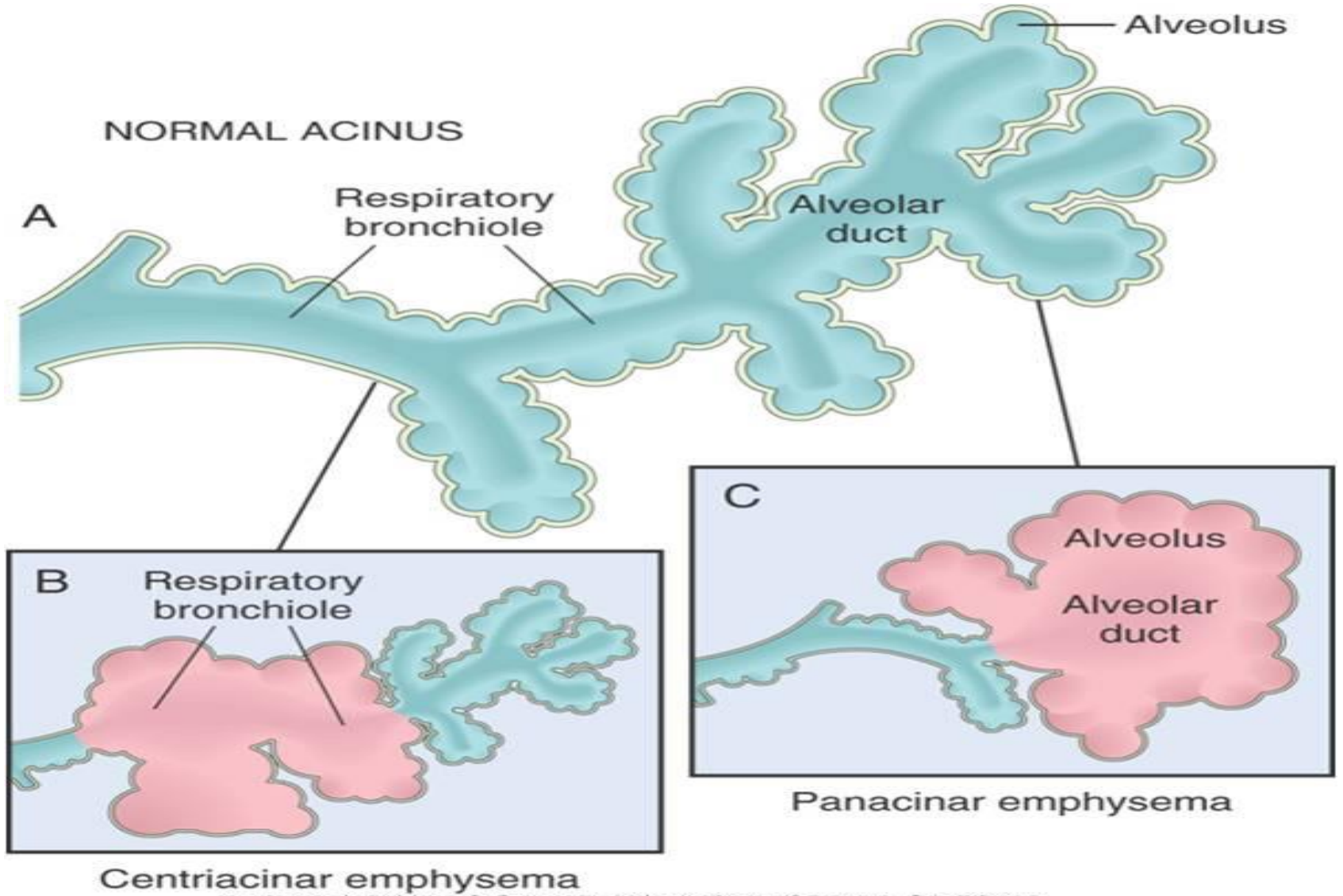
- The relationship between chronic bronchitis and emphysema is complicated.
- Usually coexist because the major pathogenic mechanism, cigarette smoking, is common to both

Types of Emphysema:

- According to the anatomic distribution in the lobule:
- ***Note**: the acinus is the structure distal to terminal bronchioles, and a cluster of 3 to 5 acini is called a lobule*
- **1- centriacinar.**
- **2-Panacinar.**
- **3-distal acinar (Paraseptal).**
- **4-Irregular.**

- **1- Centriacinar emphysema :**
- involve the **central or proximal** parts of the acini (formed by the respiratory bronchioles), sparing the distal part.
- More common in the **upper lobes.**
- This type is most commonly associated with **heavy cigarette smoking** often in association with chronic bronchitis.
- The wall often contains large amount of black pigment.

Respiratory Acinus



2- Panacinar:

- the acini are uniformly enlarged from the level of the respiratory bronchiole to the terminal blind alveoli.
- More commonly in the **lower zone** of the lung, and most severe in the bases.
- Associated with **alpha1 antitrypsin deficiency**

3- Distal acinar:

- The **distal part** is predominantly involved.
- Occur adjacent to the areas of **fibrosis, scarring, or atelactasis**.
- Characteristically, there are multiple, adjacent, enlarged airspaces up to 2 cm or more in diameter, sometimes forming cystic structures referred to as bullae. This type of emphysema probably underlies many of the cases of **spontaneous pneumothorax** in young adults due to **bullae rupture.**

irregular emphysema:

- Acinus irregularly involved.
- Airspaces enlargement with fibrosis
- Almost invariably associated with scarring.
- Usually asymptomatic and insignificant.

- **Pathogenesis:**
- Emphysema is associated with **heavy cigarette smoking.**
- The current theory favors emphysema arising as a consequence of **two coexisting imbalances**
- **1-Proteases—antiproteases imbalance.**
- **2- Oxidant------Antioxidant imbalance.**
-
- **Proteases:** are enzymes which digest the tissue.
- Normally proteases secreted by neutrophils and macrophages
- Most important one is **elastase.**
- **Anti-proteases**: are the counteracting enzymes that stop the action of digestion, important one is **antielastase (α-1 atnitrypsin**), which is normally present in serum, tissue fluids, & macrophages.

- So the development of emphysema occurs:
- When there is **increase in elastase** activity as in smoking.
- When there is **decrease in anti-elastase** activity as in:
- 1**-Hereditary** α-1 anti- trypsin deficiency.
- **2-Acquired** as in smokers due to the effect of nicotine, O2 free radicals that inhibit the release of anti-elastase.

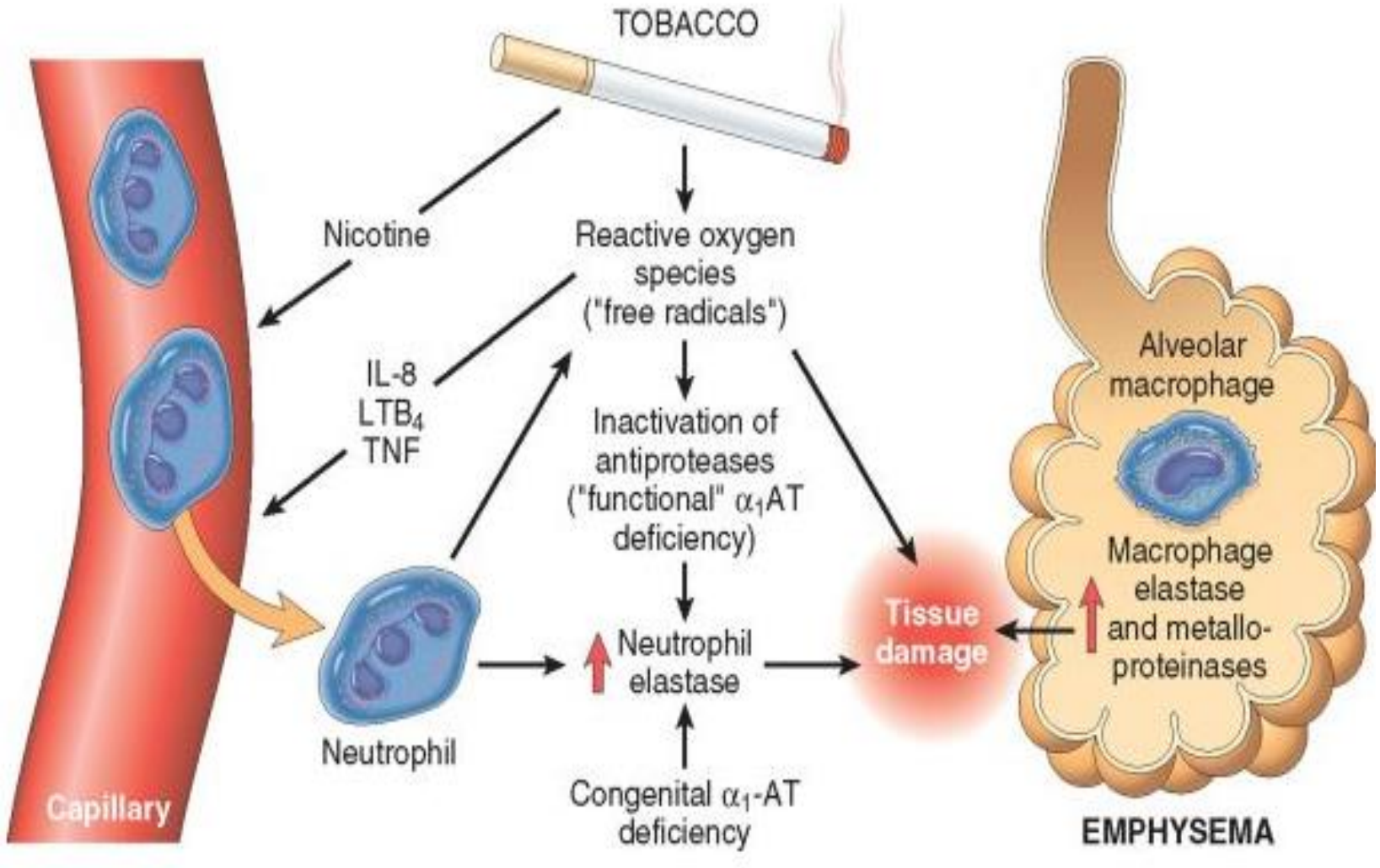
Pathogenesis of Emphysema

- **α-antitrypsin** present normally in the serum prevents digestion of lung tissue by proteolytic enzyme released from WBC and alveolar macrophages.
- Absence of this enzyme allow digestion of lung tissue leading to **panacinar emphysema**

The effect of smoking in the development of emphysema:

- 1-Smoking both **increased elastase availability** and **decreased antielastase activity** occur in smokers because :
- **Nicotine** is a **chemotactic substance** for neutrophils…. increased the no. of neutrophils, macrophages, in the alveoli…. stimulates the elastase activity.
- **The oxidants** in the smoke and the **free radicals** from the accompanying neutrophils → inhibit the secretion of anti-elastase.
- **2**-Smoking also cause **oxidant- antioxidant imbalance**, tobacco smoke contains abundant amount of free radicals (reactive oxygen species) which deplete antioxidant mechanisms in the lung, therefore inciting tissue damage

Pathogenesis of emphysema

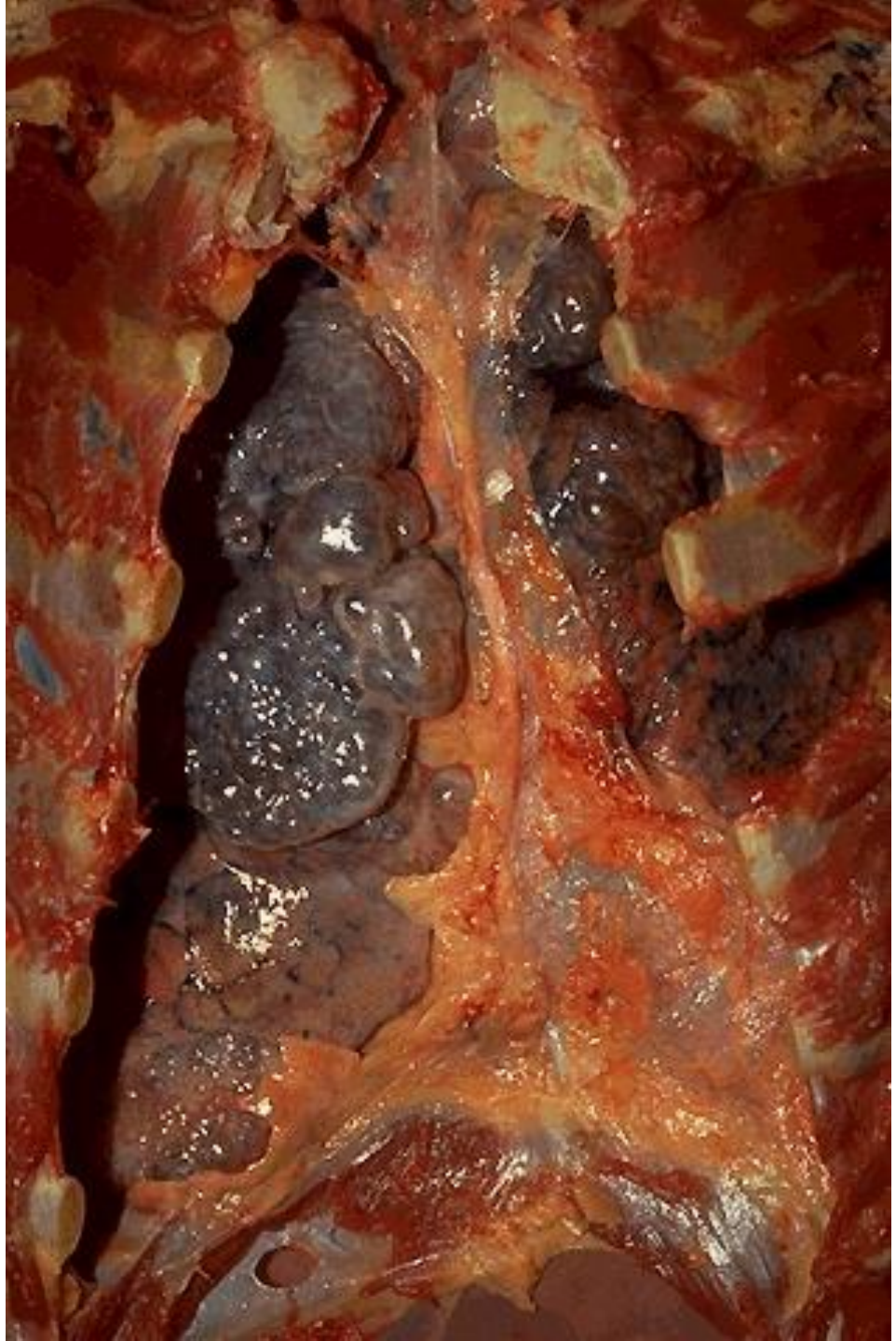


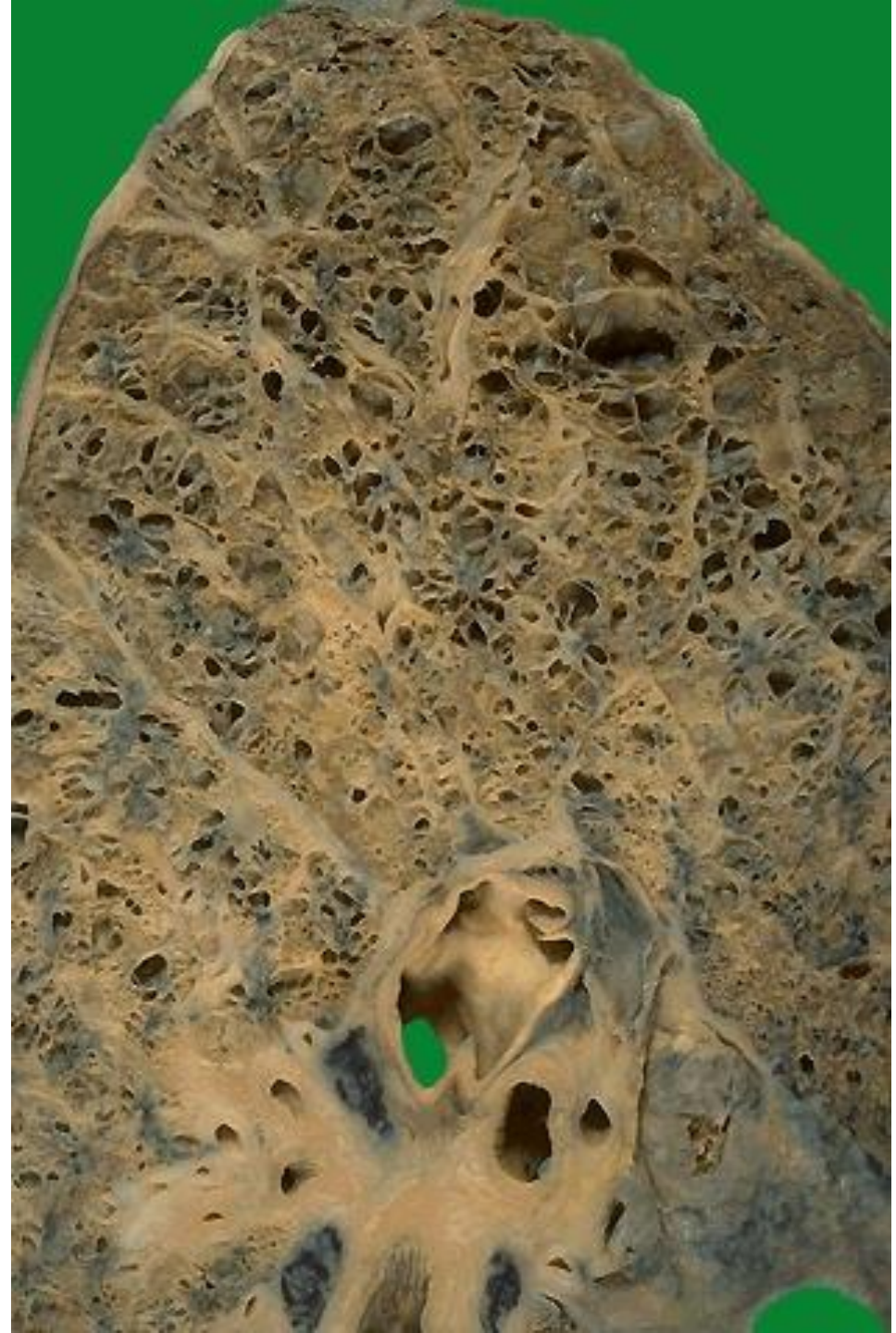
Pathogenesis of emphysema. Excessive protease activity and ROS are additive in their effects to tissue damage. α1-antitrypsin (α1-AT) deficiency can be either congenital or "functional" as a result of oxidative inactivation.

- **MORPHOLOGY:**
- **GROSS:** voluminous lung that obscure the heart at autopsy , large blebs or bullae may be seen.
- **MIC:**
- There is marked **enlargement** of the air spaces,
- with **thinning** and **destruction** of alveolar wall
- With advanced disease, adjacent alveoli coalesce, creating large airspaces.

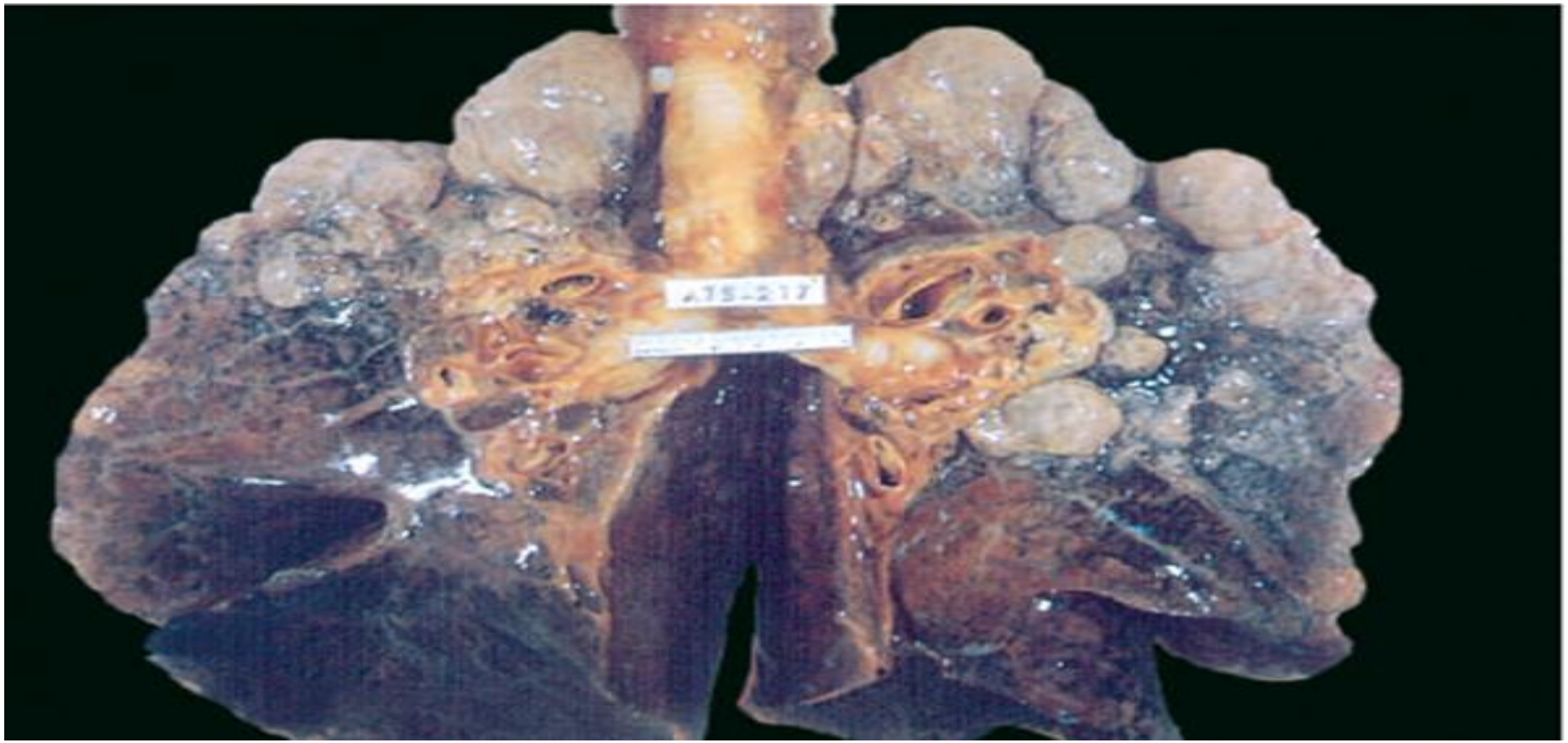
- **Course & prognosis**
- The eventual outcome of emphysema is the **gradual** development of **secondary pulmonary hypertension.**

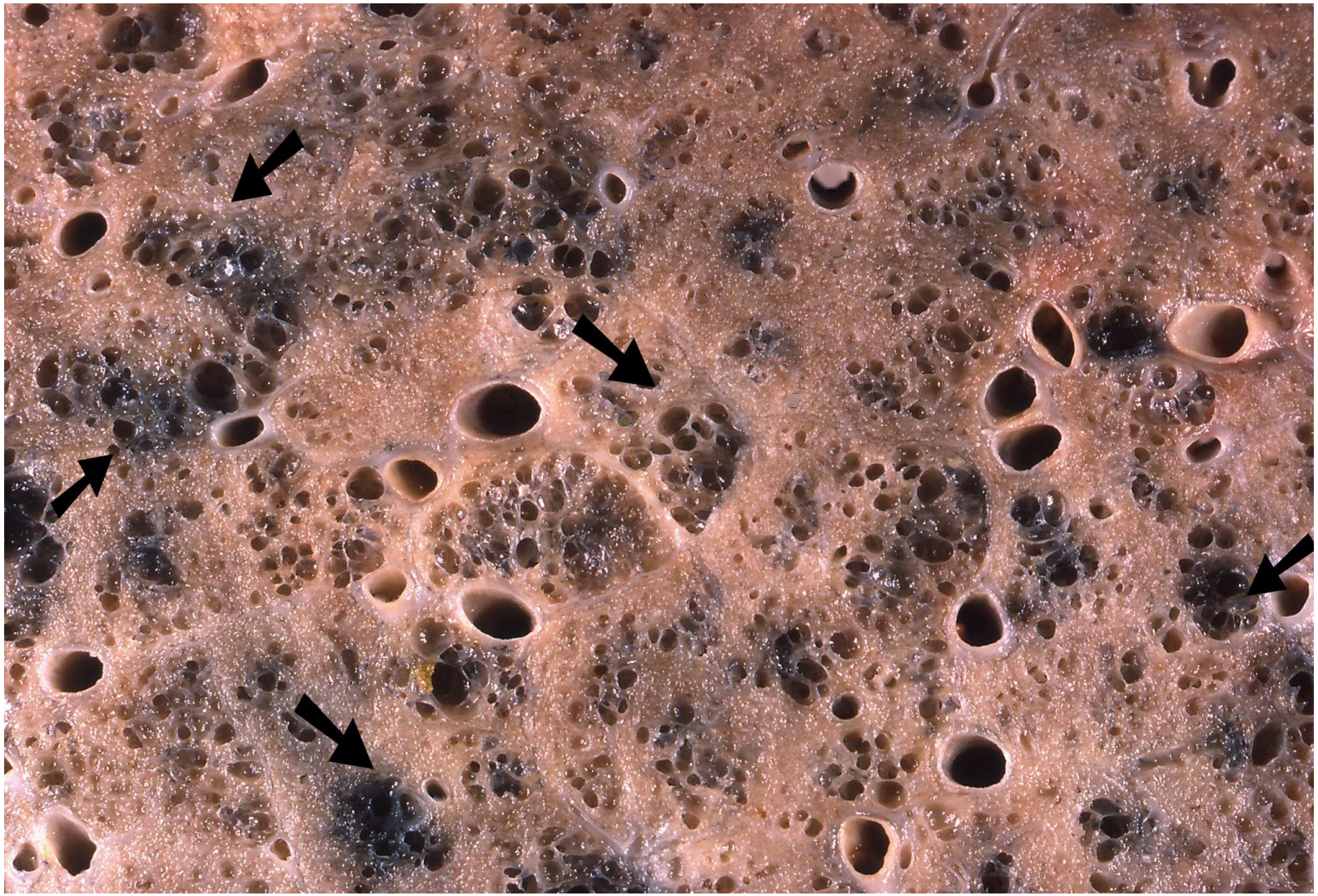
- **Death from emphysema is related to**:
- either **respiratory failure**, or
- **right-sided heart failure (cor pulmonale).**



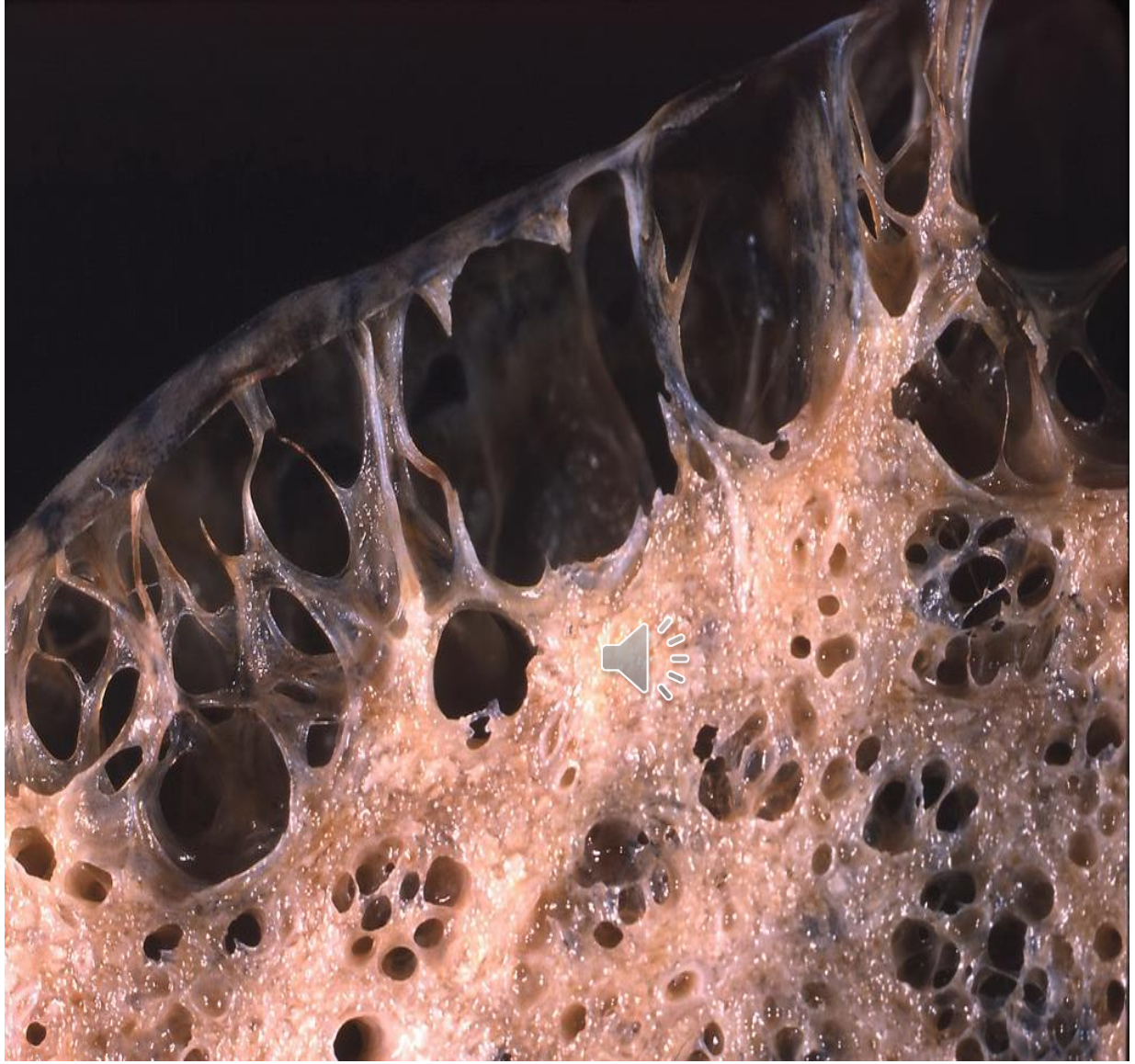


Bullous emphysema with large apical and subpleural bullae



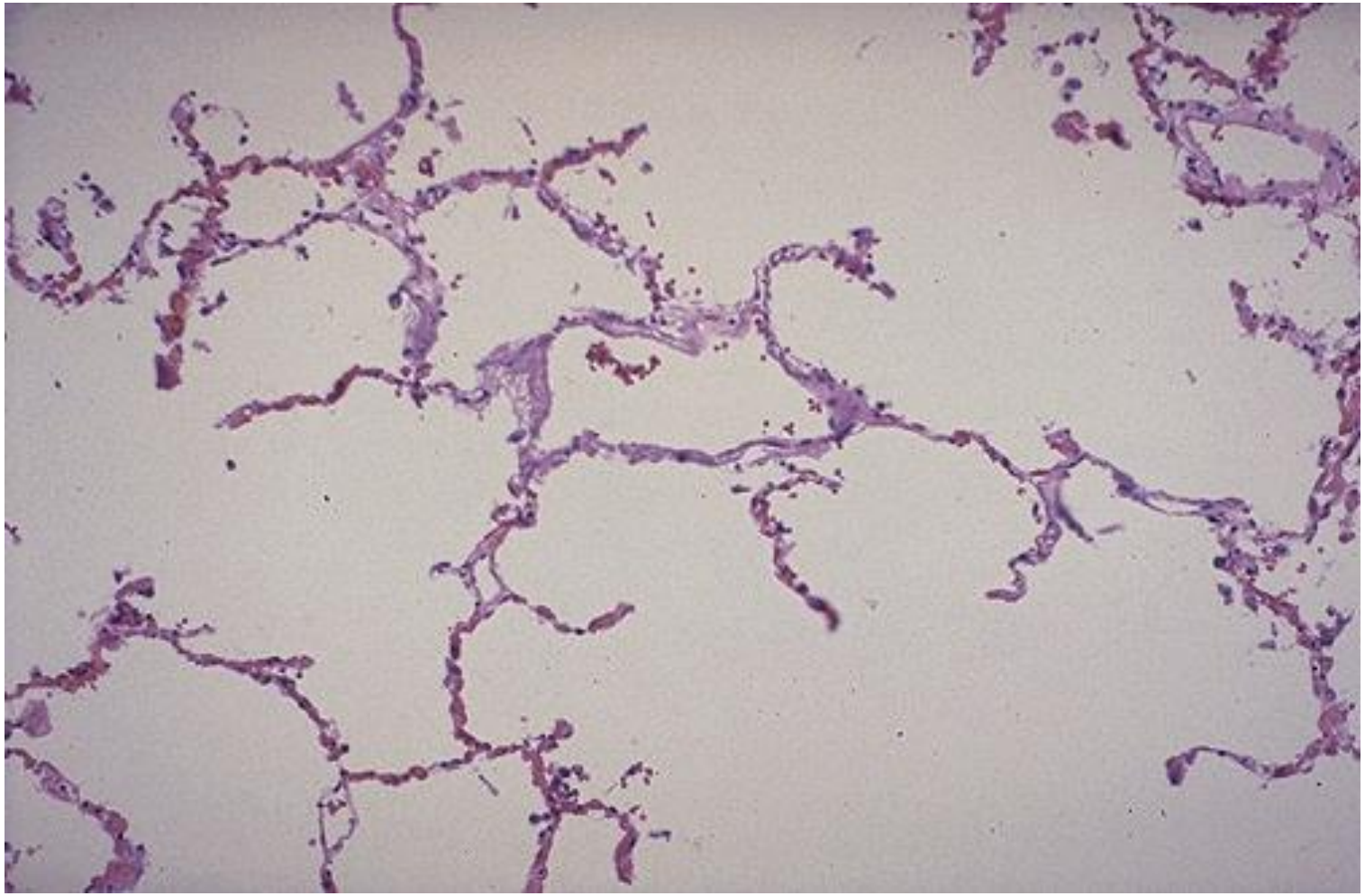


Emphysema centrelobular



Emphysema with **bullae**, subpleural in location

Mic. Pulmonary emphysema. There is marked enlargement of the air spaces, with thinning and destruction of alveolar wall



CHRONIC BRONCHITIS

- Chronic bronchitis is common among **cigarette smokers.**
- The diagnosis of chronic bronchitis is **clinical**; it is defined **as "a persistent productive cough for at least 3 consecutive months in at least 2 consecutive years." in the absence of any other identifiable cause".**

Pathogenesis

Two distinctive etiological factors of chronic bronchitis:

1. Chronic irritation by smoking, air pollutants

(sulfur dioxide, nitrogen dioxide which result in followings

- I.**Hypersecretion of mucus due to hypertrophy of submucosal mucus glands & goblet cells……. Excess mucin production** that contributes to airway obstruction.
- It is thought that both the enlargement of submucosal glands and the increase in numbers of goblet cells are protective reactions against tobacco smoke or other pollutants
- **II.** These irritants also cause **acute and then chronic inflammation** marked by the infiltration **of inflammatory cells neutrophils ,MQ, &lymphocytes ……** (In contrast with asthma, **eosinophils are not seen** in chronic bronchitis).**. Continuous inflammation……. Tissue destruction.** Long-standing inflammation and accompanying **fibrosis** can also lead to **chronic airway obstruction**

2. Microbial infection

Infection **does NOT initiate** chronic bronchitis, but it play a significant role in maintaining it and may be critical in producing acute exacerbations

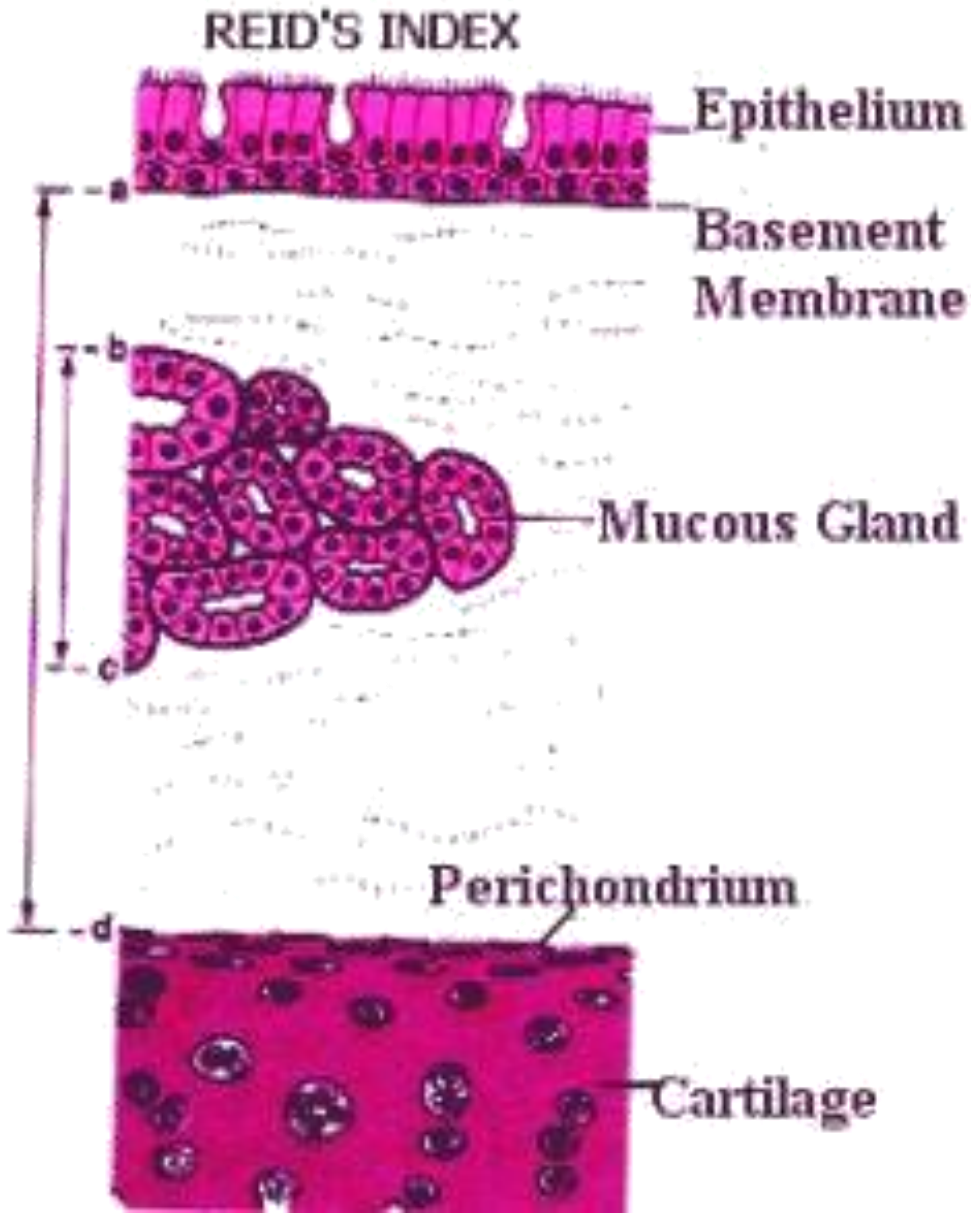
- **Role of cigarette smoke in chronic bronchitis pathogenesis:**
- 1- It damage airway-lining cells, leading to chronic inflammation.
- 2-it interferes with the ciliary action of the respiratory epithelium, preventing the clearance of mucus and increasing the risk of infection.

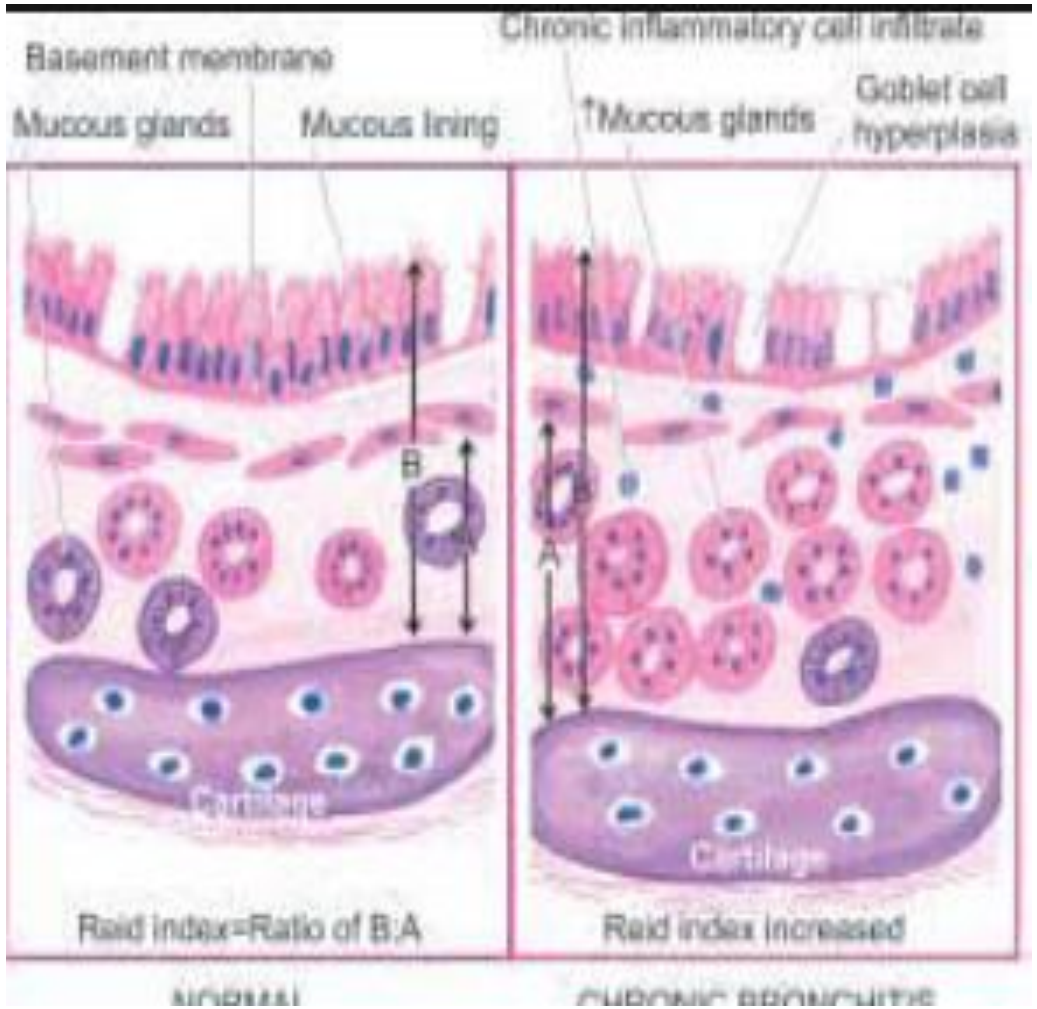
- Morphological features
- **Grossly**, airways are **hyperemia, swelling and edema** of the mucous membranes
- with excessive mucinous or mucopurulent secretions on the epithelial surfaces.
- **MIC.:**
- **The characteristic histologic features of chronic bronchitis are:**
- ◘ **chronic inflammation of the airways** (predominantly lymphocytes and macrophages)
- ◘ **Enlargement of the mucus-secreting glands** of the trachea and bronchi.

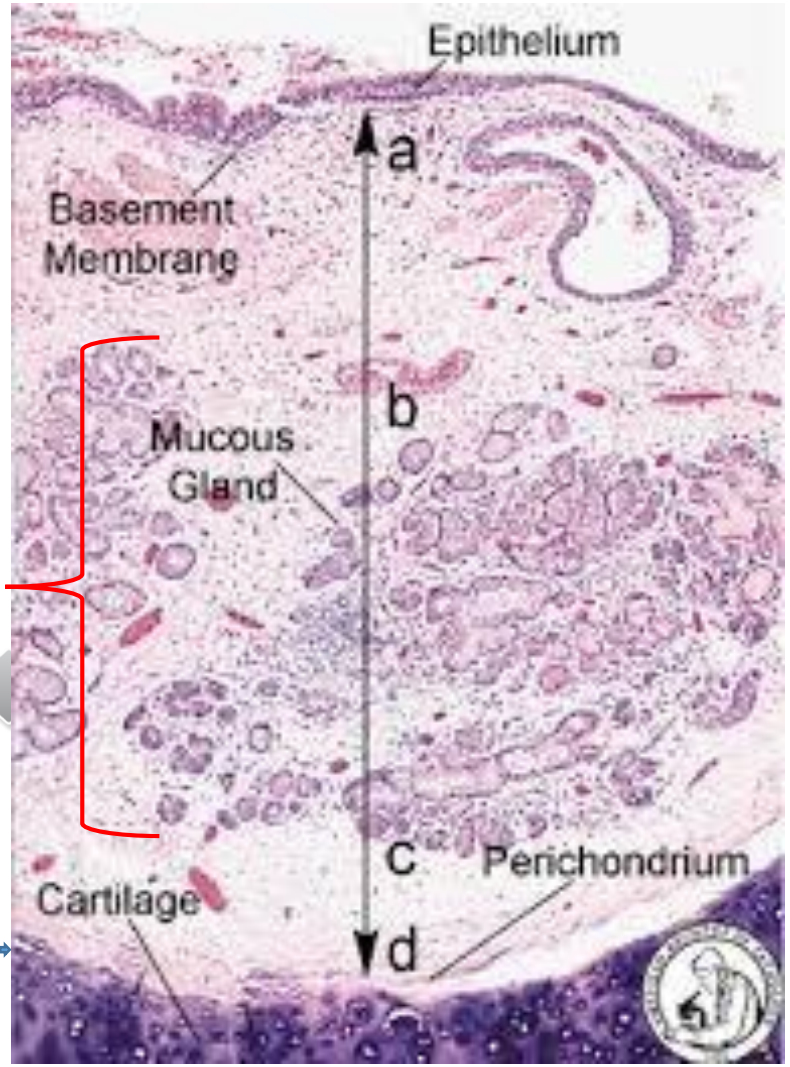
- The most striking change is an increase in the size of the mucous glands.
- This increase can be assessed by the **ratio of the thickness of the mucous gland layer to the thickness of the wall between the epithelium and the cartilage (Reid index).**
- The Reid index (normally 0.4) is increased in chronic bronchitis.
- ◘Although the numbers of goblet cells increase slightly, the major increase is in the size of the mucous glands.
- ◘The bronchial epithelium may show **squamous metaplasia** and **dysplasia** due to the irritating and mutagenic effects of substances in tobacco smoke.
- ◘There is marked narrowing of bronchioles caused by **goblet cell metaplasia**, **mucus plugging**, i**nflammation**, and **fibrosis.**

Reid index:

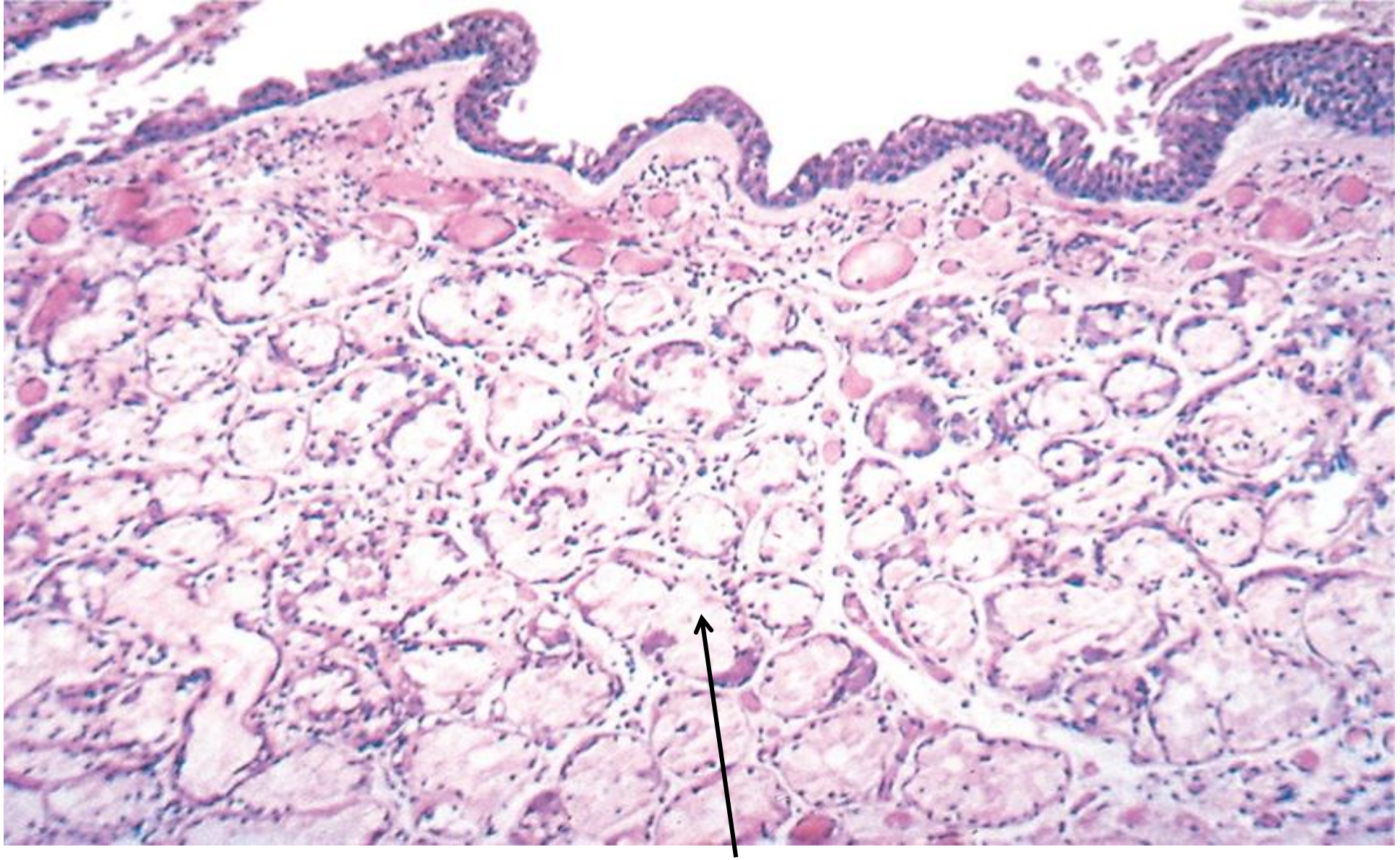
- It is the ratio of the thickness of the mucous gland layer / thickness of the wall between the epithelium and the cartilage.
- Normally it is 0.4 , it increases in chronic bronchitis.


REID'S INDEX
Epithelium
Basement Membrane
Mucous Gland
Perichondrium
Cartilage
a
b
c
d



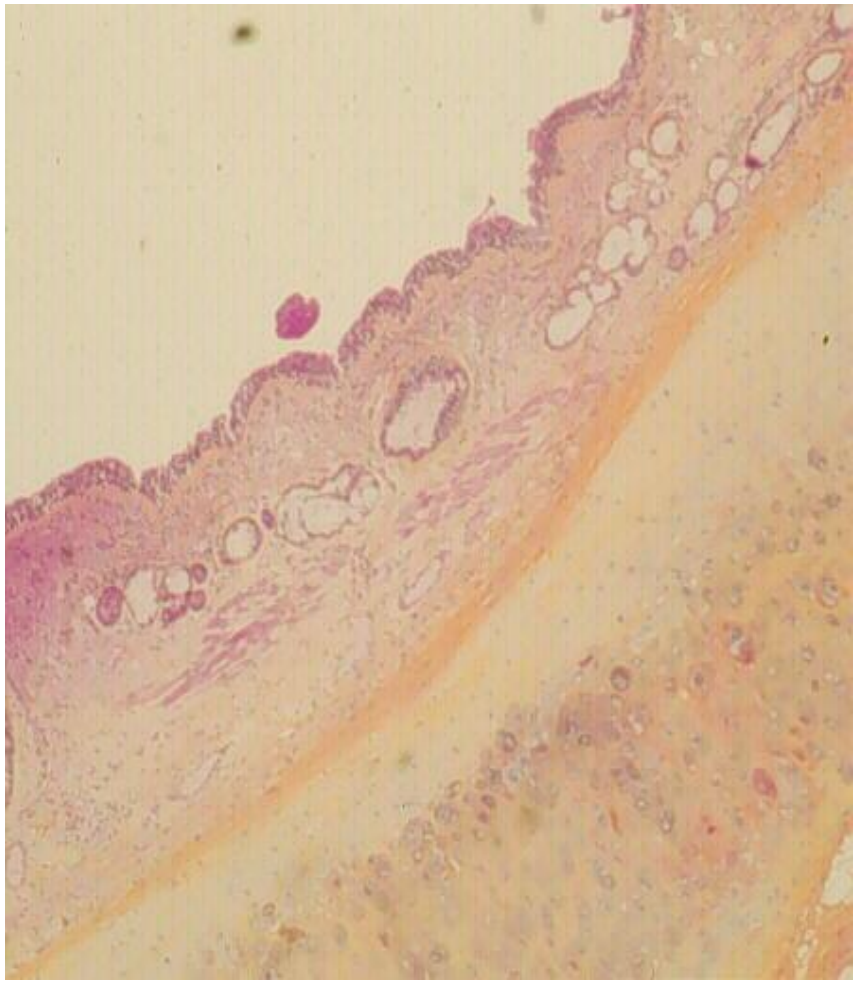


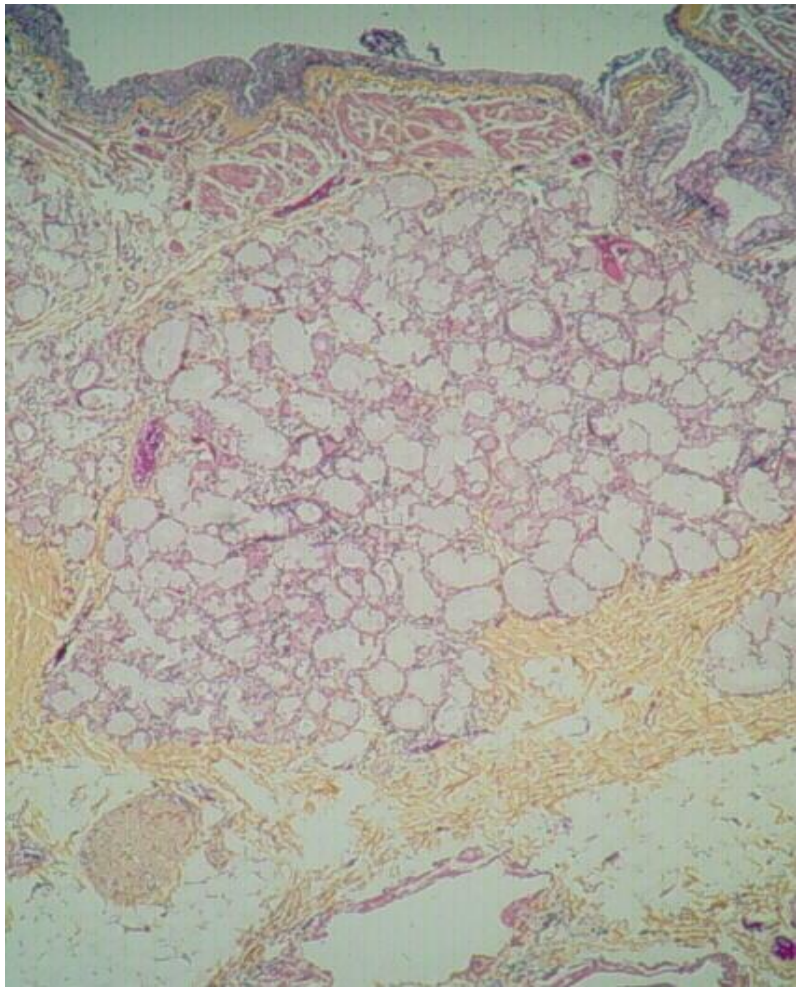
Chronic bronchitis: Reid index increased to more than 0.5 (normally less than 0.4) due to seromucinous glands enlargment



Chronic bronchitis. marked thickening of the mucous gland layer (twice-normal) and squmous metaplasia of lung epithelium.

Increase Ried index





- **Clinical features:**
- The cardinal symptom of chronic bronchitis is a **persistent productive cough** ….**after years** .. dyspnea on exertion develops .

- **With time**, and usually with continued smoking, other features may appear, including **hypercapnia**, **hypoxemia**, and **mild cyanosis**.
- With progression, chronic bronchitis is complicated by **pulmonary hypertension** and **cardiac failure**.
- Recurrent infections and respiratory failure are constant threats.

BRONCHIECTASIS:

Ectasia: dilatation

- Define as "**the permanent dilation of bronchi and bronchioles caused by destruction of the muscle and elastic supporting tissues, resulting from or associated with chronic necrotizing infections.**"
- To be considered bronchiectasis, dilation should be permanent.
- Because reversible bronchial dilation often accompanies viral and bacterial pneumonia.

- **Clinical features**:
- severe, persistent cough;
- expectoration of copious amounts of foul-smelling, mucopurulent sputum.
- sometimes **bloody sputum**; **dyspnea** and orthopnea in severe cases
- Because of better control of lung infections, bronchiectasis is now an uncommon condition.
- But may still develop in association with certain conditions
- **Etiology and Pathogenesis.**
- **It is NOT a primary disease, is secondary to persisting infection or obstruction caused by a variety of conditions**.

***Predispose conditions to Bronchiectasis* include the following:**

- The disease is secondary ***to persisting infection or obstruction*** caused by a variety of conditions.
- **1- Severe necrotizing or Suppurative pneumonia** caused by bacteria, viruses, or fungi; this may be a single severe episode or recurrent infections.
- **2- Bronchial obstruction**, due to tumor, foreign bodies, and occasionally mucus impaction.
- **3-Congenital or hereditary conditions**: that predispose to chronic infections, like :

. ***In cystic fibrosis***: *viscid mucus lead to obstruction & pulmonary infection which end with bronchiectasis.*

- ***In immunodeficiency states* e.g. immunoglobulin deficiencies result in repeated bacterial infections and bronchiectasis.**
- ***Kartagener syndrome***, an *autosomal recessive disorder*, develop *impair mucociliary clearance in the airways & reduce mobility of spermatozoa* leading to persistent infections and *bronchiectasis, and sterility in male*

- Diagnosis: depends on an appropriate **history** along with **radiographic demonstration** of bronchial dilation.

Morphology:

Gross features

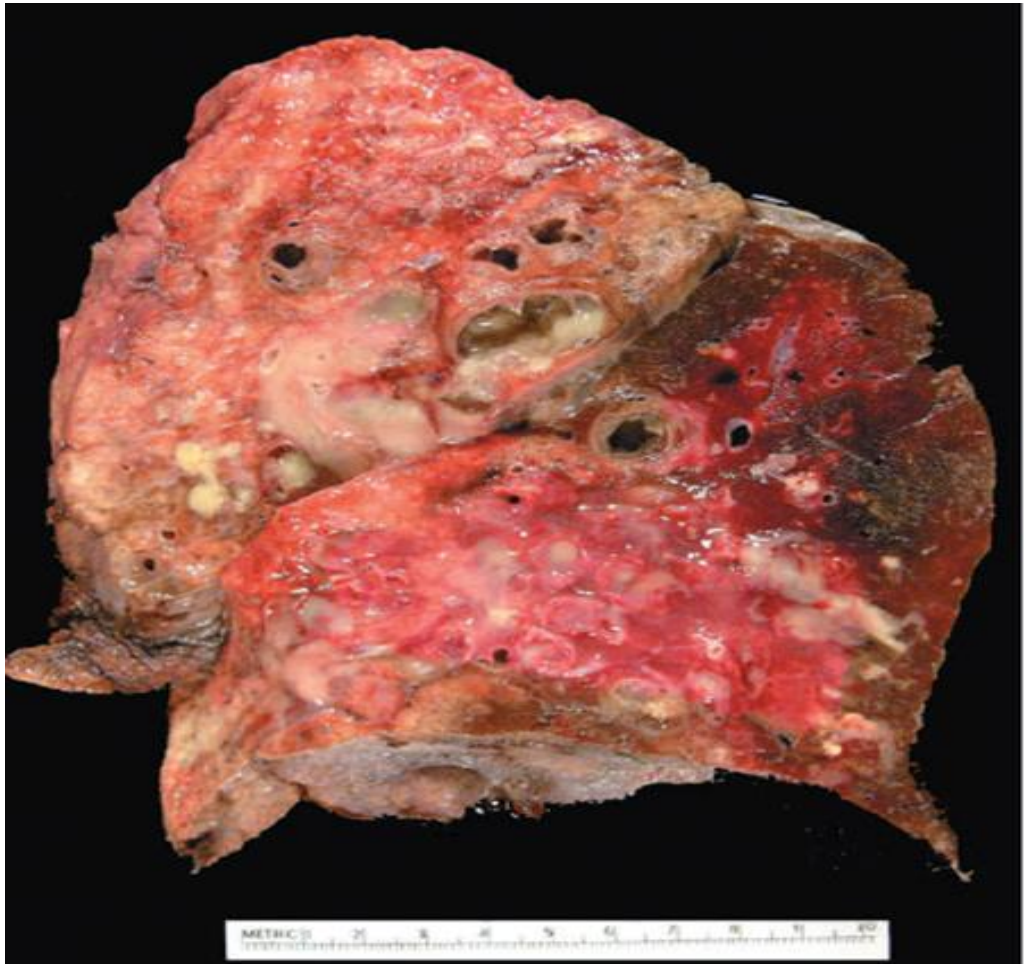
- The airways are **dilated (cylindroid, fusiform or saccular distention)** up to 4 times their usual diameter.
- On the cut surface of the lung, the transected dilated bronchi appear as **cysts filled with mucopurulent secretions**

- **Microscopic features**
- vary with the activity and chronicity of the disease
- **Active case**:
- 1- There is intense **acute and chronic inflammatory exudate** within the walls of the bronchi and bronchioles.
- 2-**desquamation** of the lining epithelium and extensive areas of **necrotizing ulceration.**
- There may be **squamous metaplasia** of the remaining epithelium.
- **In chronic cases** there **is fibrosis** of the bronchial and bronchiolar walls and peribronchiolar areas.

Complications:

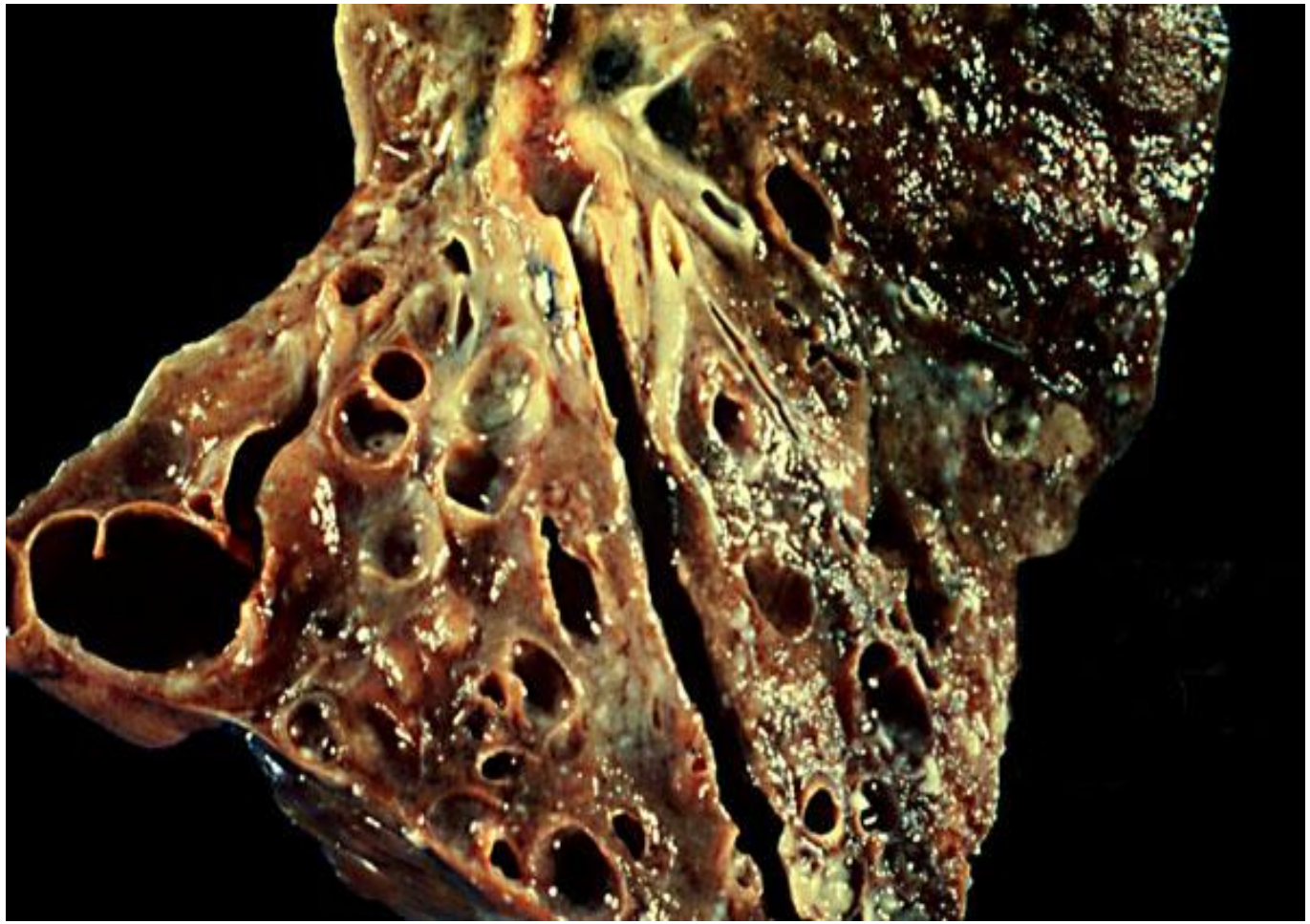
- 1-In some instances, the necrotizing inflammation destroys the bronchial or bronchiolar walls and forms a **lung abscess**.
- 2-In cases of severe, widespread bronchiectasis **hypoxemia, hypercapnia, pulmonary hypertension,** and (rarely) **cor pulmonale occur**.
- 3- **Metastatic brain abscesses** and **reactive amyloidosis** are other, less frequent complications.
- current treatments with better antibiotics and physical therapy have improved outcomes considerably

Bronchiectasis
Dilated airway involving lower part of lung

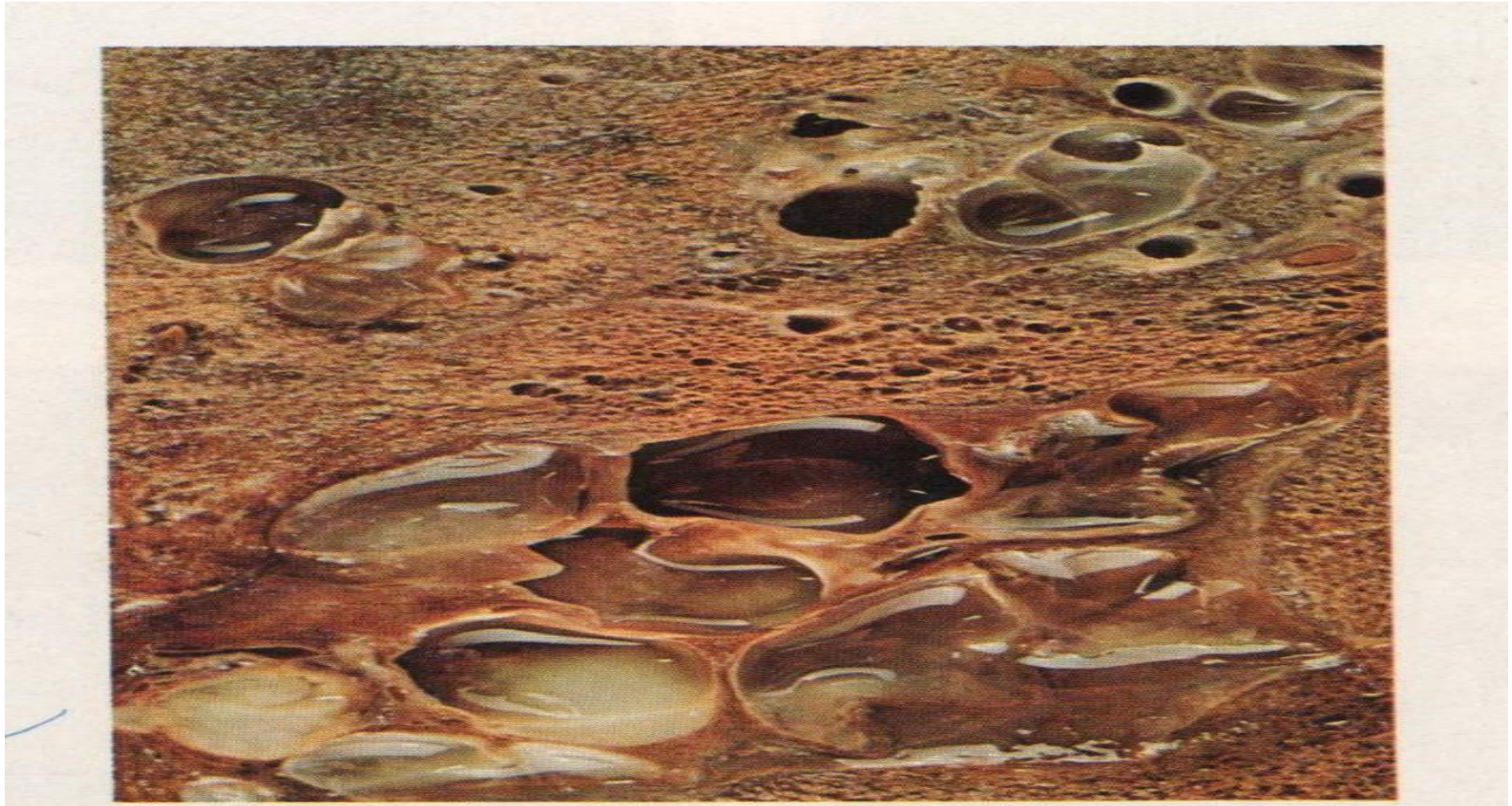


- Bronchiectasis in a patient with cystic fibrosis who underwent lung resection for transplantation. Cut surface of lung shows markedly dilated bronchi filled with purulent mucus that extend to subpleural regions

Bronchiectasis : gross



Grossly: Bronchiectasis



7.17 Bronchiectasis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Thank you