Respiratory system pathology

By

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Objectives

Emphysema(definition ,pathogenesis and clinical -1 features and morphological features)

Chronic bronchitis (definition ,pathogenesis and -2 clinical features and morphological features)

Obstructive versus Restrictive Pulmonary Diseases

Chronic noninfectious diffuse pulmonary diseases can be classified in two categories:

1) **Obstructive diseases (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. Cannot get air out**

2) **Restrictive diseases, characterized by reduced expansion of lung parenchyma and decreased total lung capacity. Cannot get air in**

Obstructive Pulmonary Disease

Under this heading come four entities:

1- Emphysema
2- Chronic bronchitis } **COPD (irreversible obstruction)**

The two diseases usually coexist with each other , under the term chronic obstructive pulmonary disease (COPD),because long-term cigarette smoking is a common underlying agent in both disorders. COPD which is one of the leading causes of death. Although chronic bronchitis may exist without emphysema, and pure emphysema may occur (with inherited α1-antitrypsin deficiency).

3- Asthma (reversible obstruction)
4- Bronchiectasis

Emphysema

It is defined as abnormal permanent enlargement of the airspaces distal to the terminal bronchioles due to destruction of alveolar wall without obvious fibrosis . and then reduces elastic recoil and after that enlargement (abnormal and irreversible) of alveoli results in bullae Significant of emphysema , expiration becomes difficult because loss of elastic recoil reduces the volume of air that can be expired passively .

Classification of emphysema is according to its anatomical distribution within the lobule

There are four major types of emphysema:

1. **Centriacinar**
2. **Panacinar**
3. **Distal acinar**
4. **Irregular**

Pathogenesis of centriacinar & panacinar forms of emphysema

1- Imbalances of protease and their inhibitors(anti-protease) , and imbalance between oxidant and antioxidant .

Individuals with hereditary deficiency of the major Protease inhibitor (i.e., α1-antitrypsin) have a marked propensity for developing emphysema , which is compounded by smoking .

α1-Antitrypsin: is a major inhibitor of proteases (particularly elastase) .

Protease :- it is mediators which secreted by neutrophils during inflammation and cause tissue destruction .

So, emphysema result from the destructive effect of high protease activity in subjects with .low anti-protease action

2-Smoking play a role in the pathogenesis of emphysema.

A-Tobacco contain nicotine which cause accumulation of neutrophils & macrophages within the alveoli through its direct chemo-attractant effects .

B-And through the reactive oxygen species contained in it (These activate the transcription factor NF-κB , which switches on genes that encode TNF and IL-8).

These, in turn, attract and activate more neutrophils.

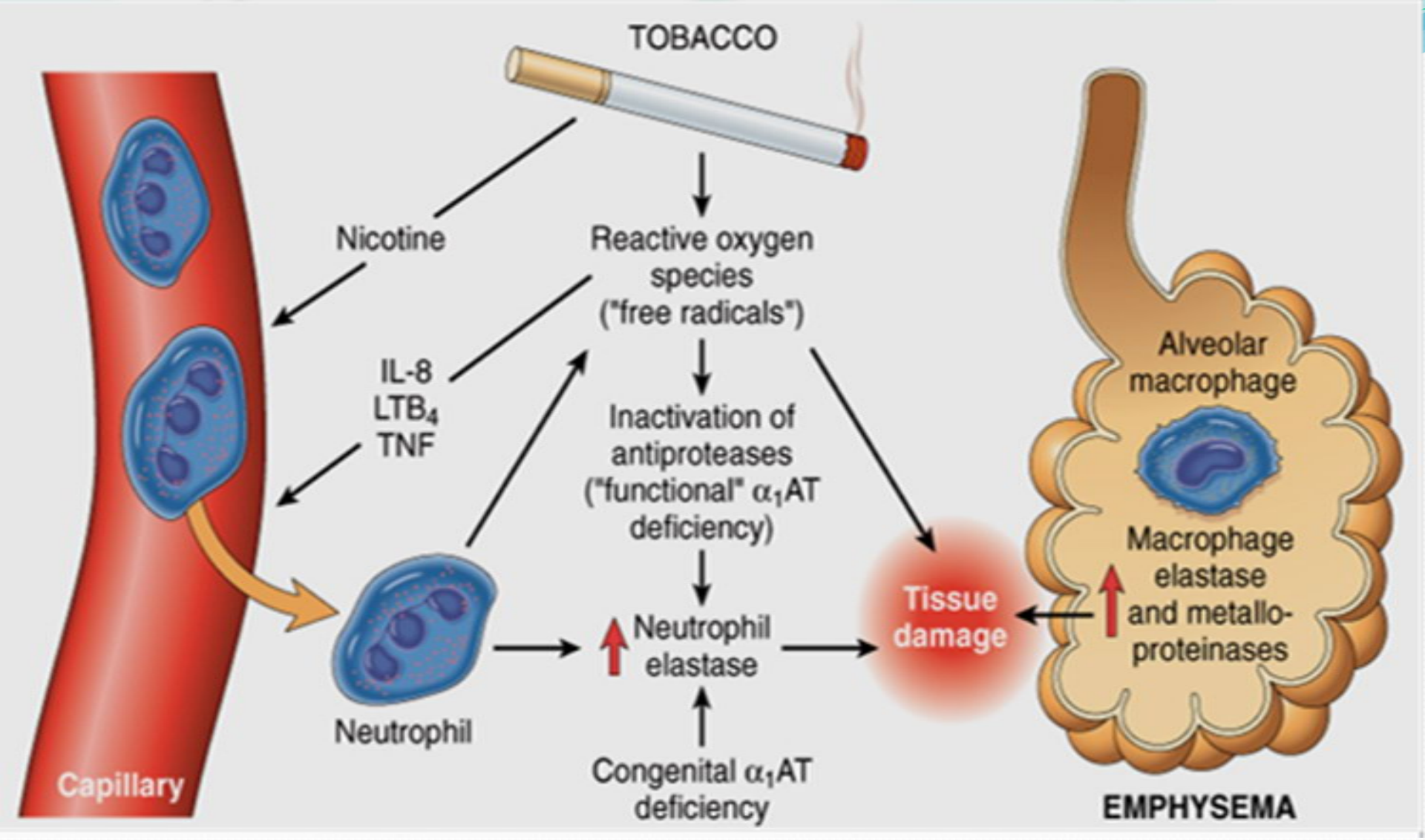
C-Accumulated active neutrophils release their granules, which are rich in a variety of proteases (elastase , proteinase, etc.) that result in tissue damage .

D-Smoking also enhances elastase activity in macrophages; this elastase is not inhibited by α1-AT ; additionally, it can digest this antiprotease.

E-Tobacco smoke contains abundant reactive oxygen free radicals, which deplete the antioxidant mechanisms, there by inciting tissue damage.

A secondary consequence of oxidative injury is inactivation
of native antiproteases , resulting in "functional“ α1-antitrypsin deficiency even in patients without enzyme deficiency.
There is increasing evidence that in addition to elastase, matrix metalloproteinases derived from macrophages and neutrophils have a role in tissue destruction.

F-Loss of alveolar elastic tissue reduces radial traction and causes respiratory bronchiole collapse during expiration ,resulting in functional obstruction .

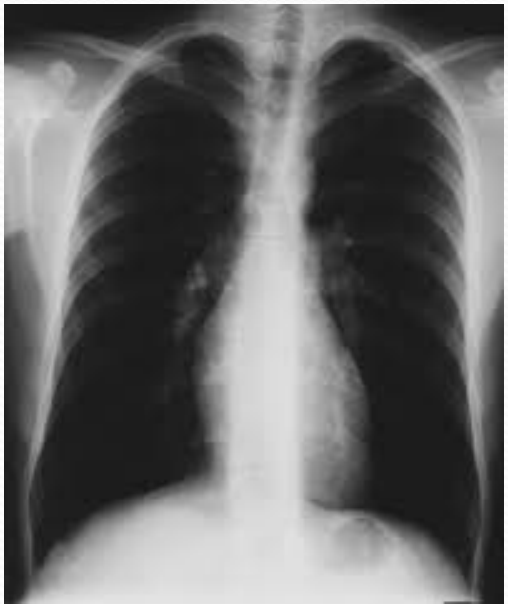


Pathogenesis of emphysema

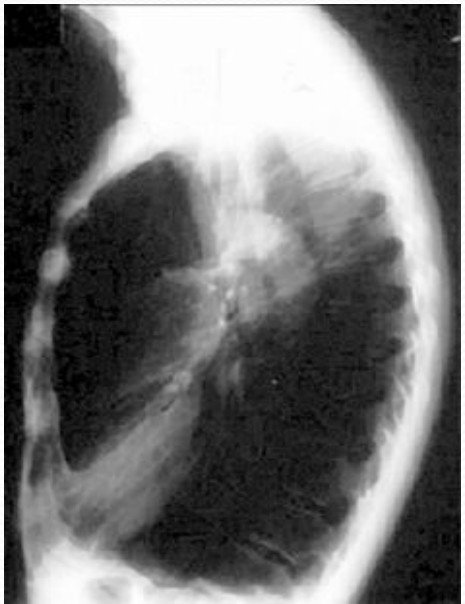
Either due to congenital α1-antitrypsin deficiency (antiprotease)or due to smoking that lead to imbalances of protease and their inhibitors(anti-protease) , and imbalance between oxidant and antioxidant .

Clinical feature

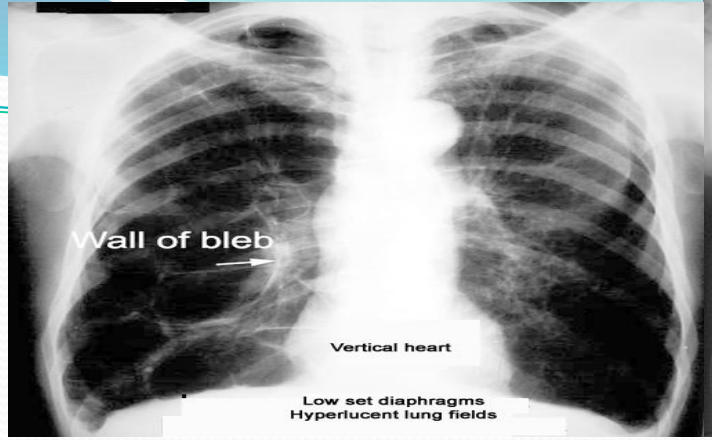
(dyspnea , wheezing ,cough) manifest when a third of the pulmonary parenchyma has been lost . Use accessory respiratory muscle, with weight loss .Patients are barrel-chest (increased anterior-posterior dimension)with obvious prolonged expiration . Classically patients over ventilate to compensate for loss of parenchyma and are typically well-oxygenated at rest . Individuals with pure emphysema are characterized as "pink puffers."

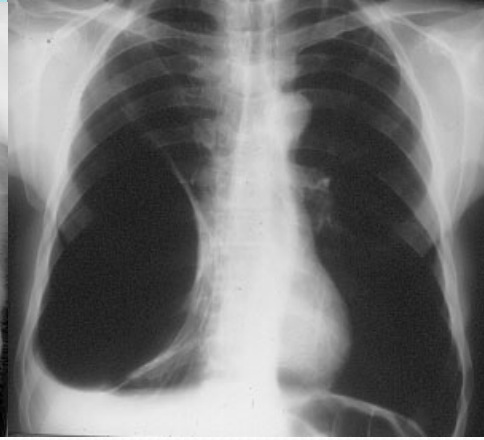


Hyperinflation, flattened diaphragm, enlarged retrosternal space

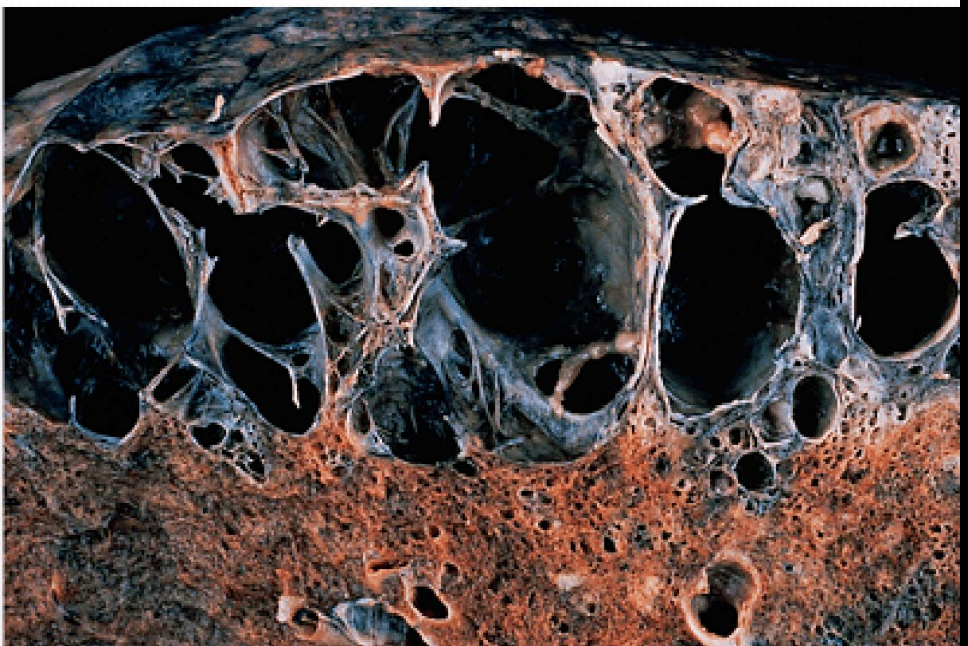


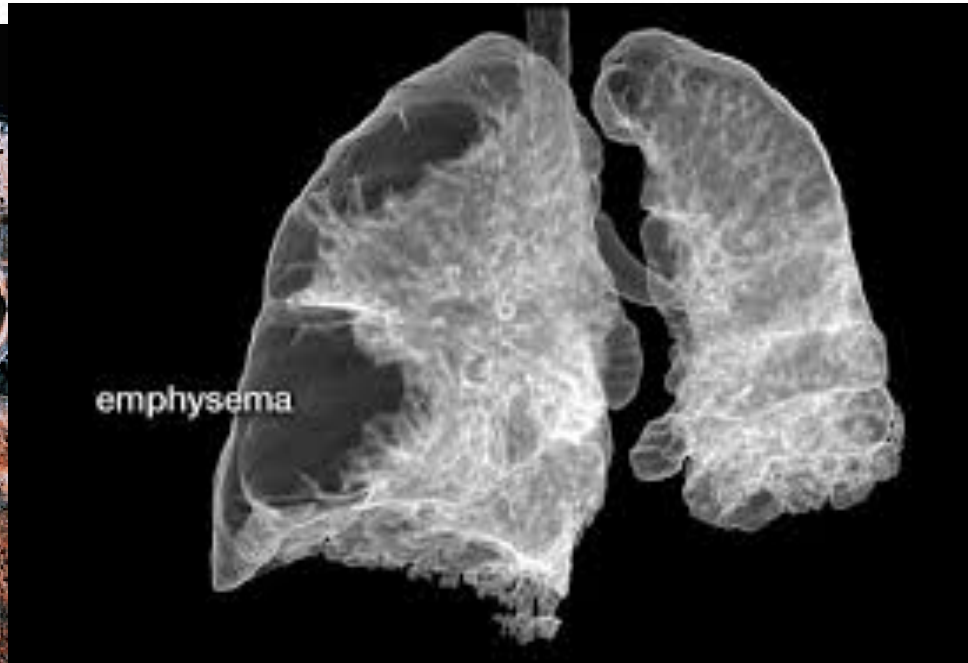
Gross features



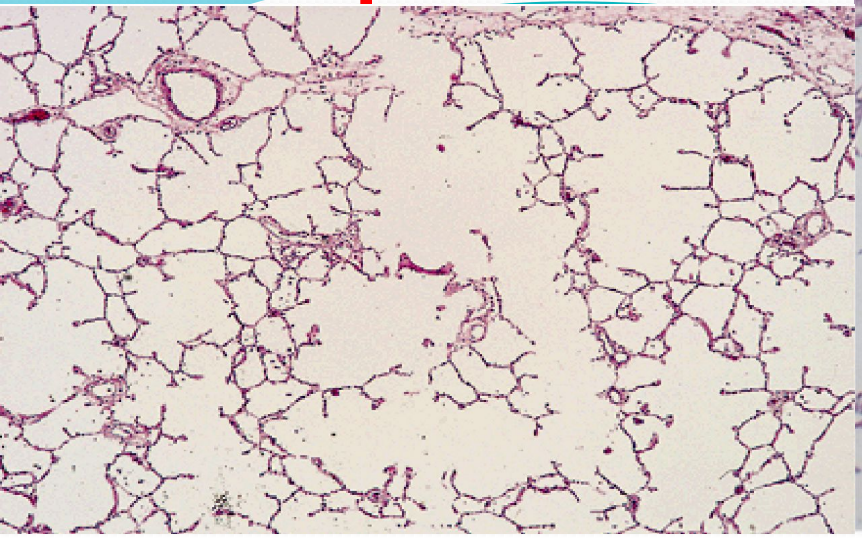


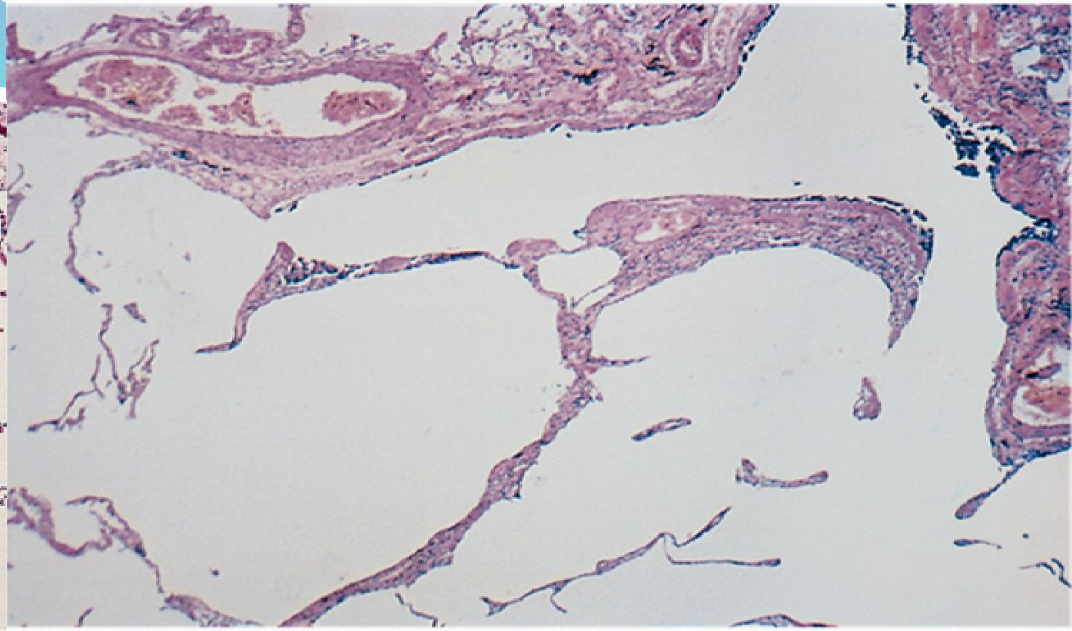
The loss of alveolar walls with advanced disease, adjacent alveoli coalesce, creating large airspaces(blebs and bullae) .



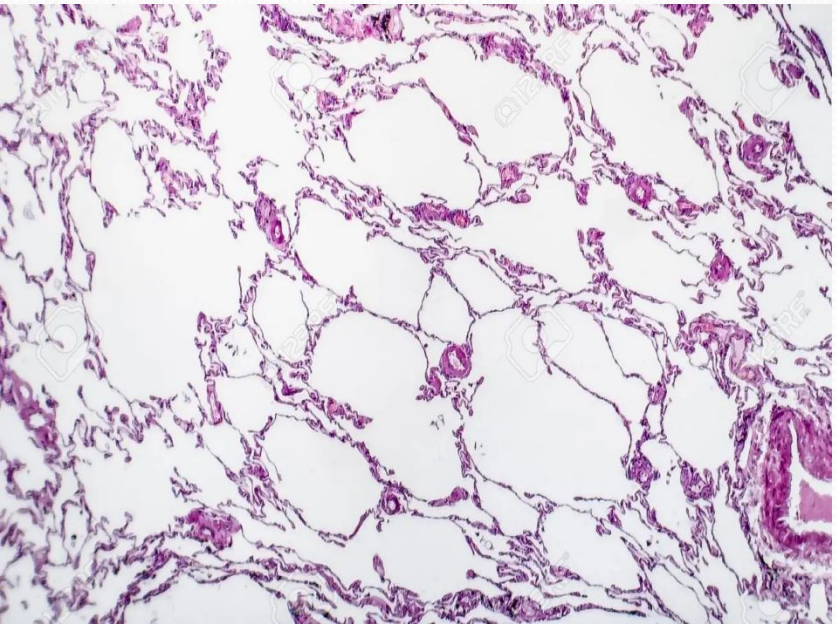


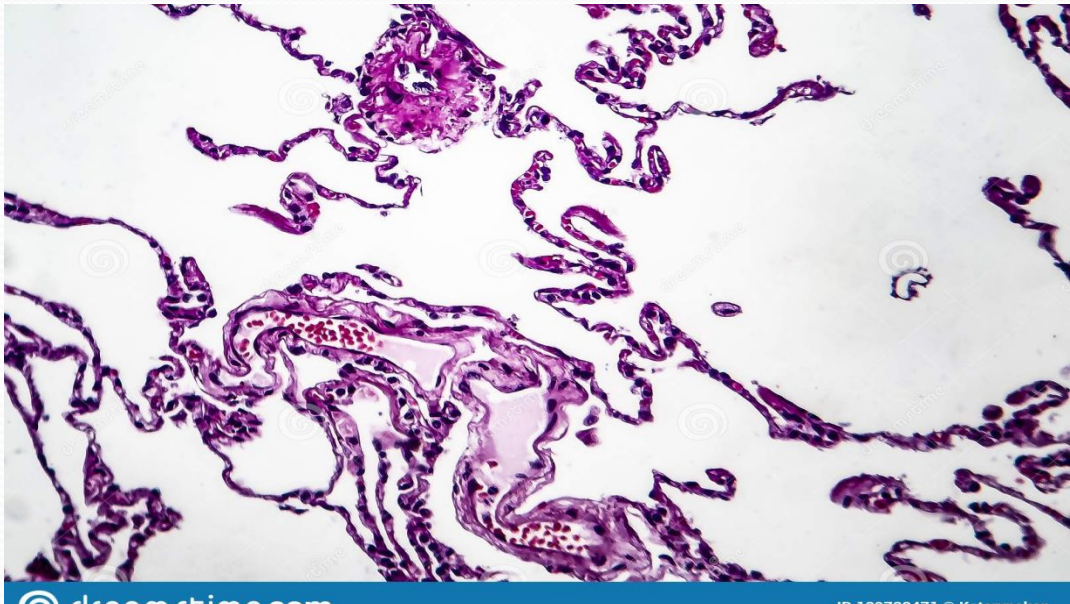
Microscopical features

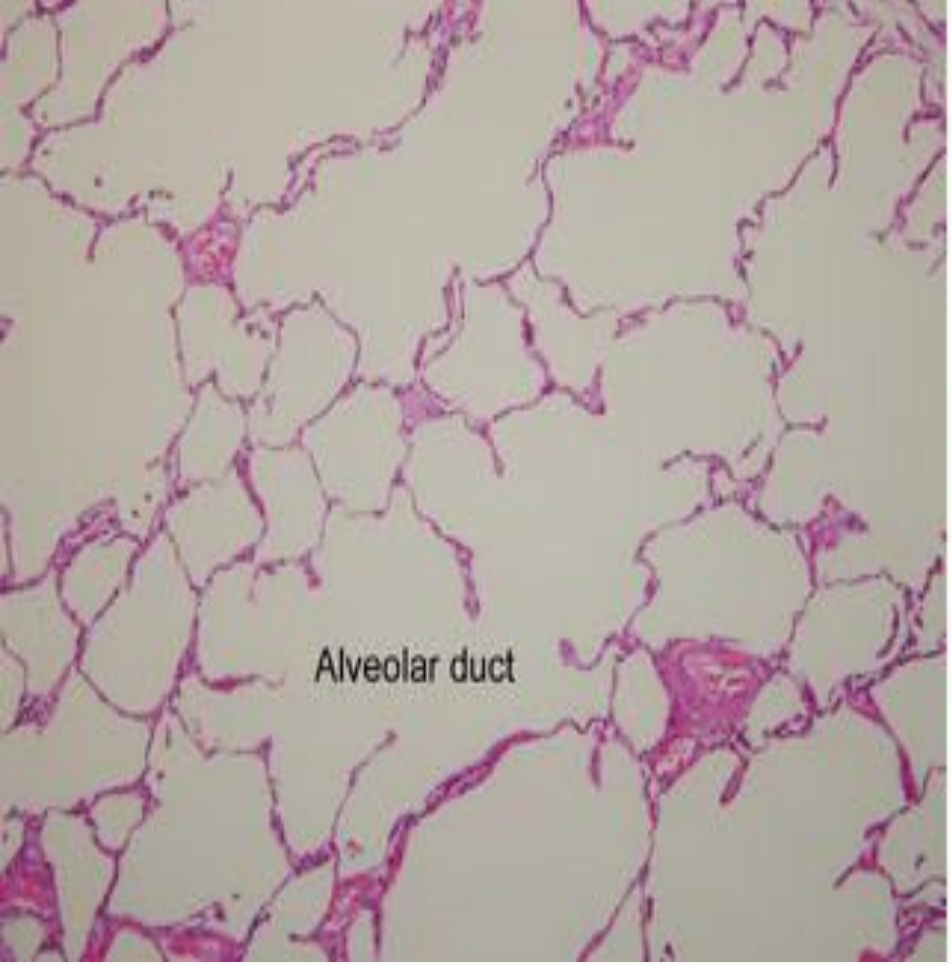


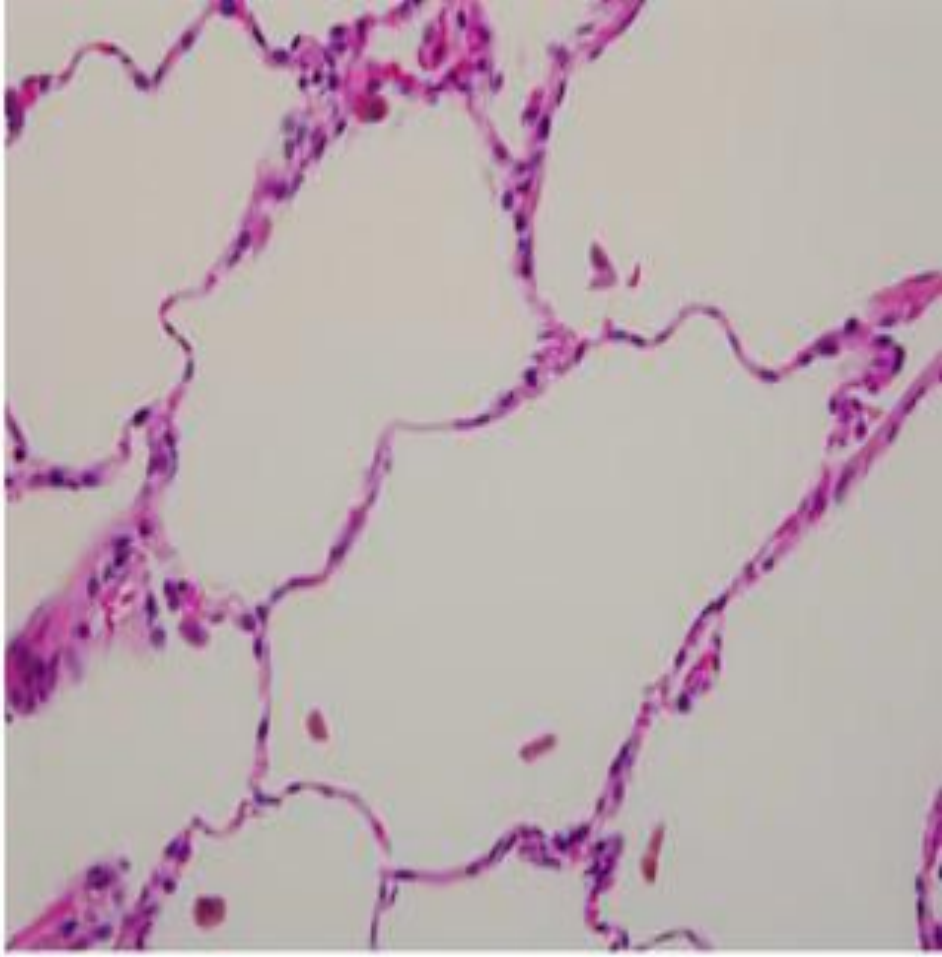


There is marked enlargement of airspaces, with thinning and destruction of alveolar walls.









There is marked enlargement of airspaces, with thinning and destruction .of alveolar walls

Other forms of emphysema

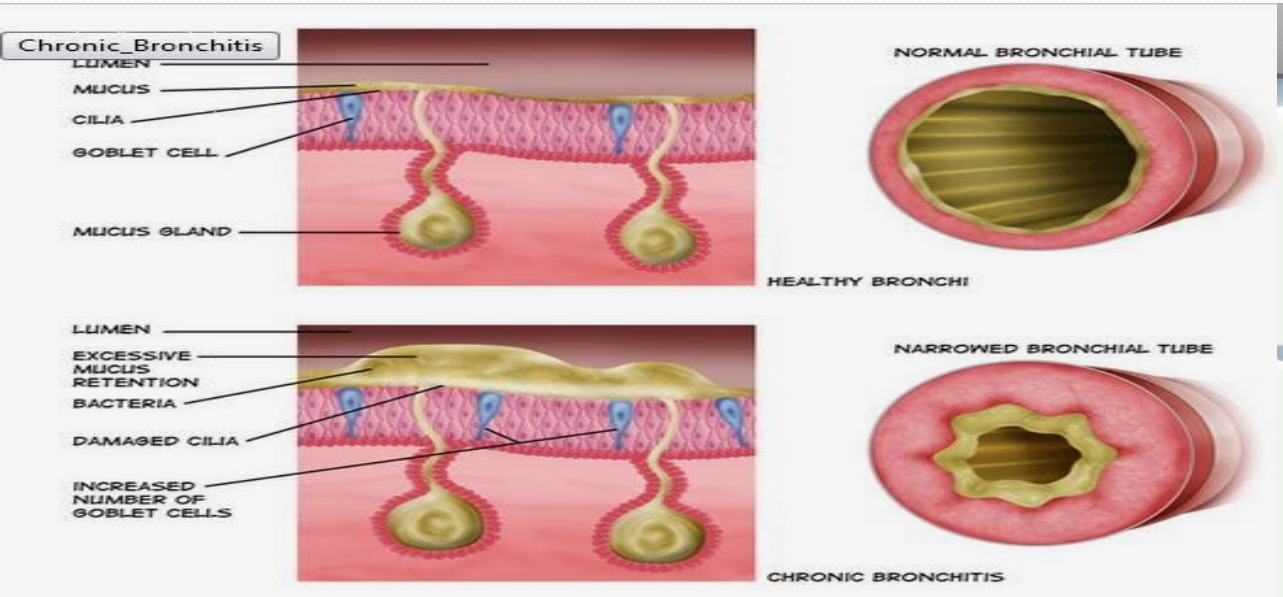
1-Compensatory hyperinflation of remaining lung after loss of pulmonary parenchyma e.g. surgical lobectomy , this type without septal wall destruction .

2-Obstructive over inflation due to subtotal obstruction of an airway ,thereby creating a ball-valve that admits air on inspiration but traps it on expiration. This type without septal wall destruction .

Mediastinal (interstitial) emphysema designates the-3 entrance of air into the connective tissue stroma of the lung, mediastinum, and subcutaneous tissue. Or This may occur spontaneously with a sudden increase in intra-alveolar pressure (as with vomiting or violent coughing) that causes a tear, with dissection of air into the interstitium. Sometimes it occurs in children with whooping cough. It is particularly likely to occur in patients on respirators who have partial bronchiolar obstruction or in persons who suffer a perforating .injury (e.g., a fractured rib)

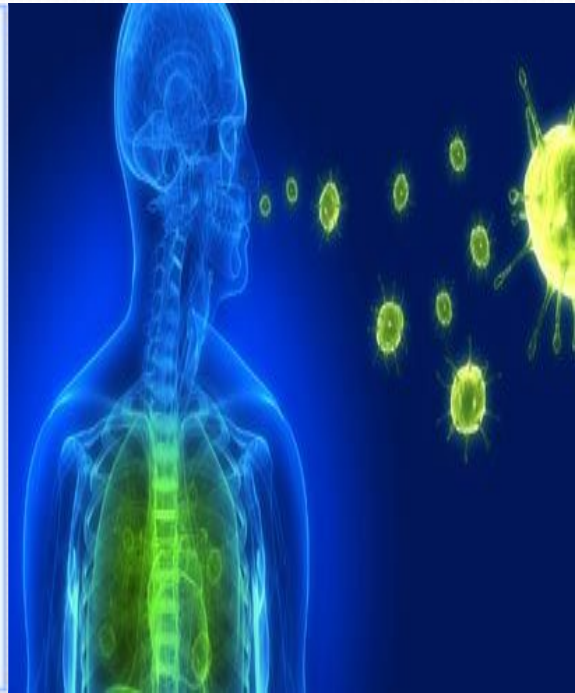
Chronic bronchitis

It is common among cigarette smokers and in smog-ridden cities . 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." but in the absence of any other identifiable cause .



Pathogenesis

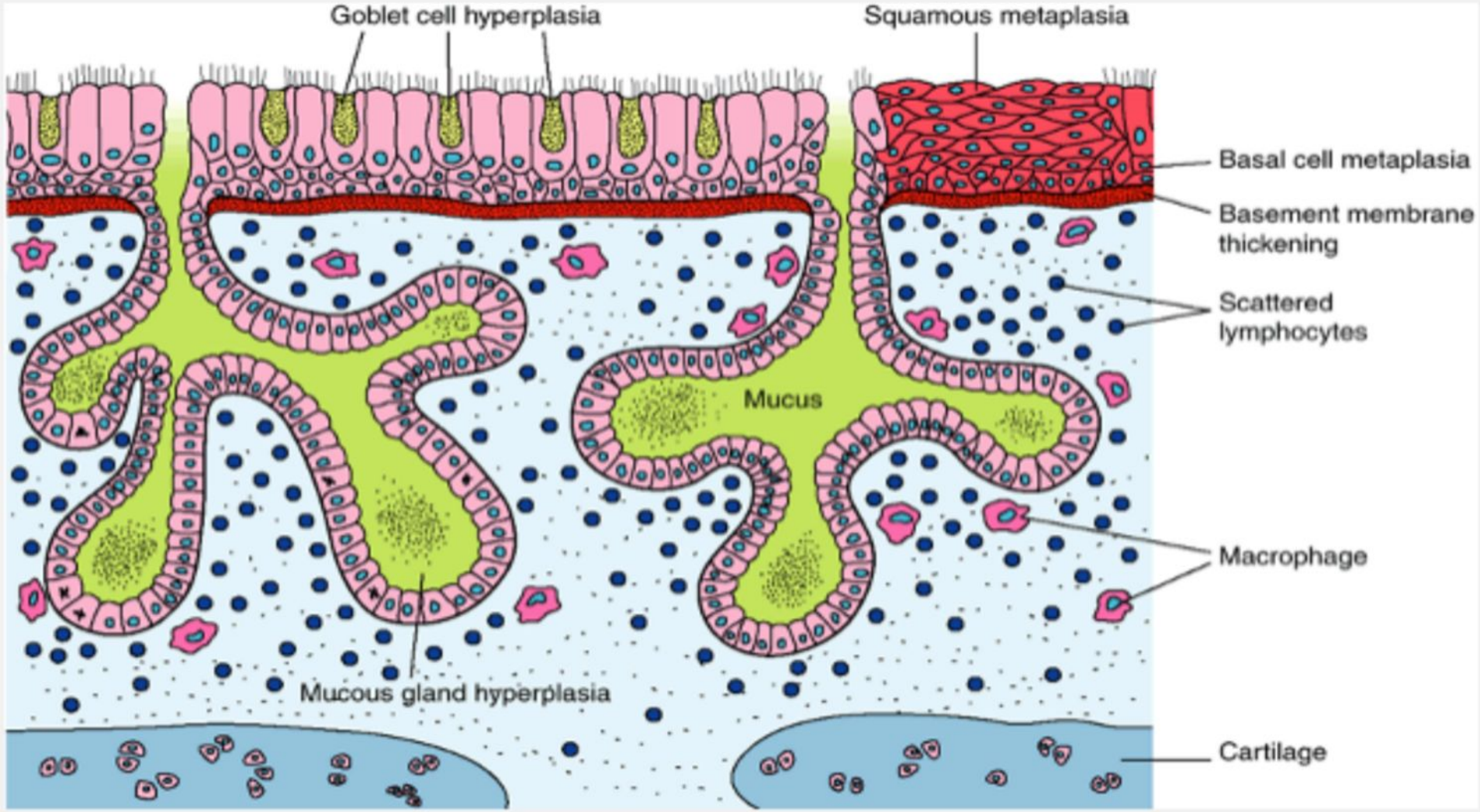
The single most important cause is cigarette smoking, and other air pollutants, such as sulfur dioxide and nitrogen dioxide, may contribute.



These environmental irritants induce hypertrophy of mucous glands in the trachea and main bronchi and a marked increase in mucin-secreting goblet cells in the surface epithelium of smaller bronchi and bronchioles . .This lead to hypersecretion of mucus

In addition, these irritants cause inflammation with infiltration of T cells, macrophages, and neutrophils.

Microbial infection is often present but has a secondary role, chiefly by maintaining the .inflammation

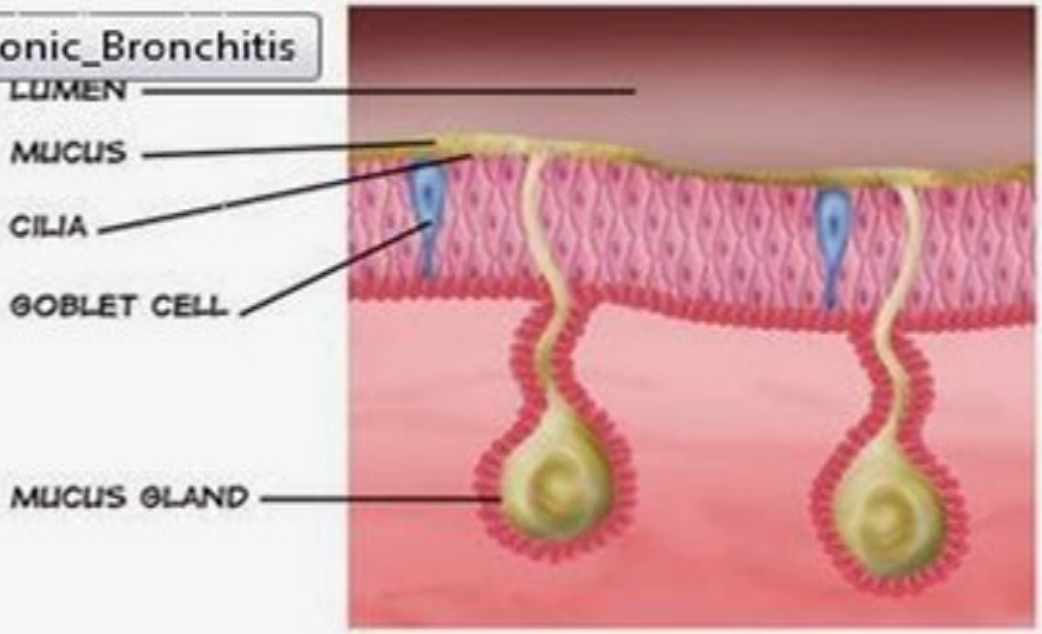


1-Hyperplasia and hypertrophy of mucous glands in the trachea and main bronchi .

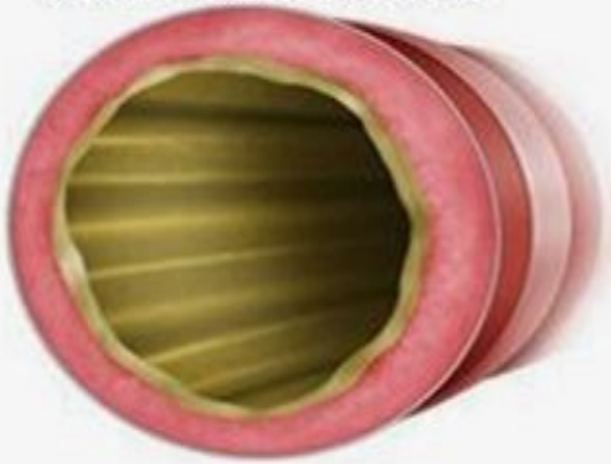
2-Hyperplasia of goblet cell in smaller bronchi and bronchioles .

3-infiltration of T cells, macrophages, and neutrophils .

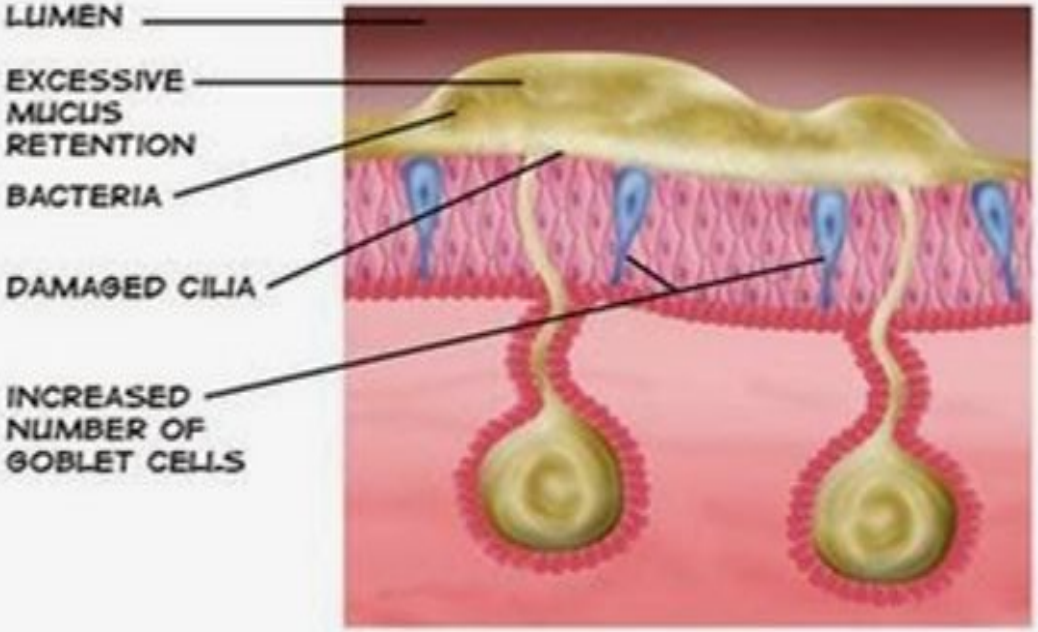
Chronic_Bronchitis



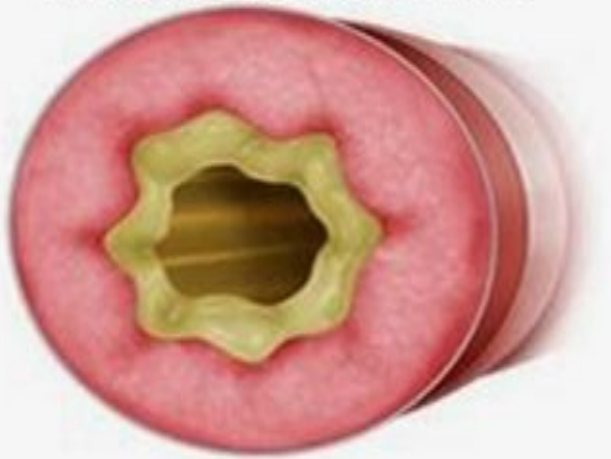
NORMAL BRONCHIAL TUBE



HEALTHY BRONCHI



NARROWED BRONCHIAL TUBE



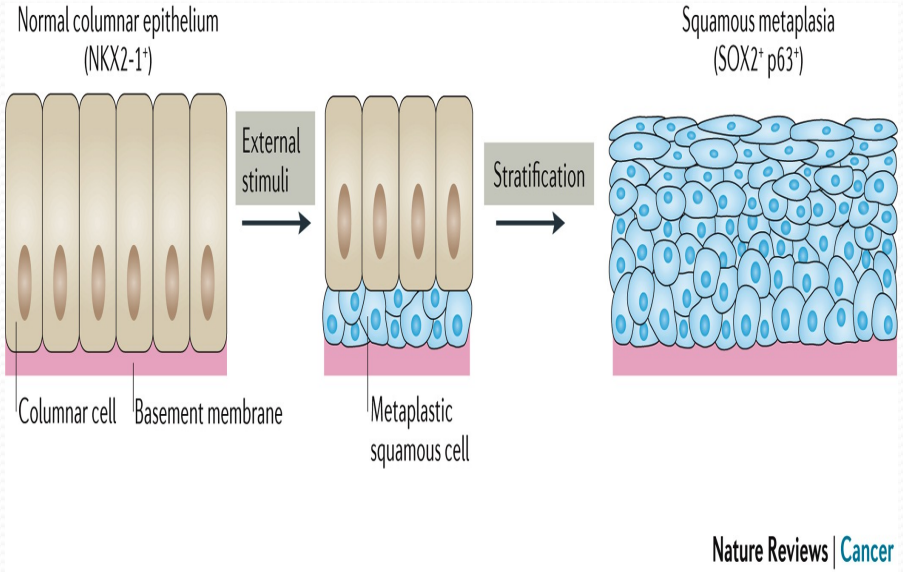
CHRONIC BRONCHITIS

Clinical features

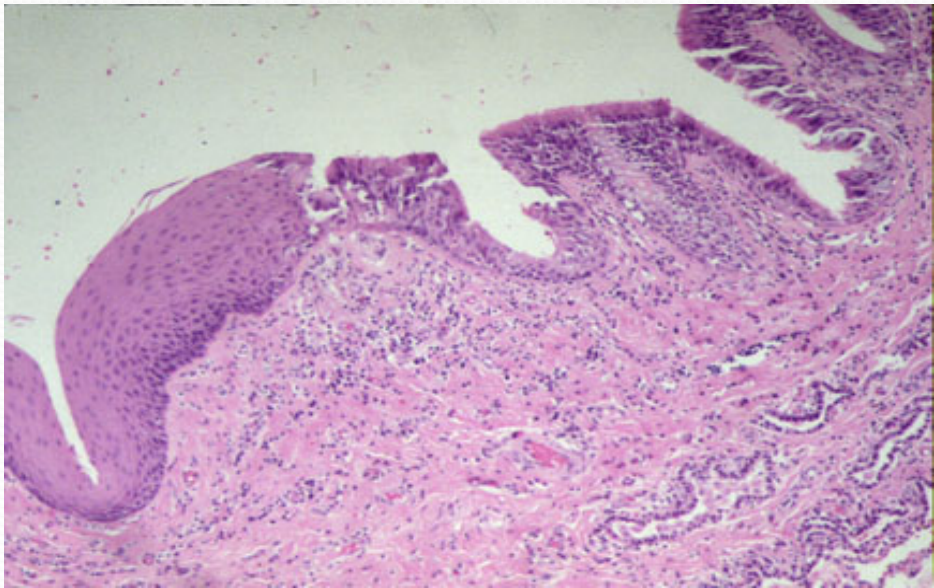
cough and sputum production , dyspnea on exertion eventually develops .

In classical cases , patients are hypoxic ,cyanotic and hypercapnic (due to retain carbon dioxide) so-called blue bloaters .

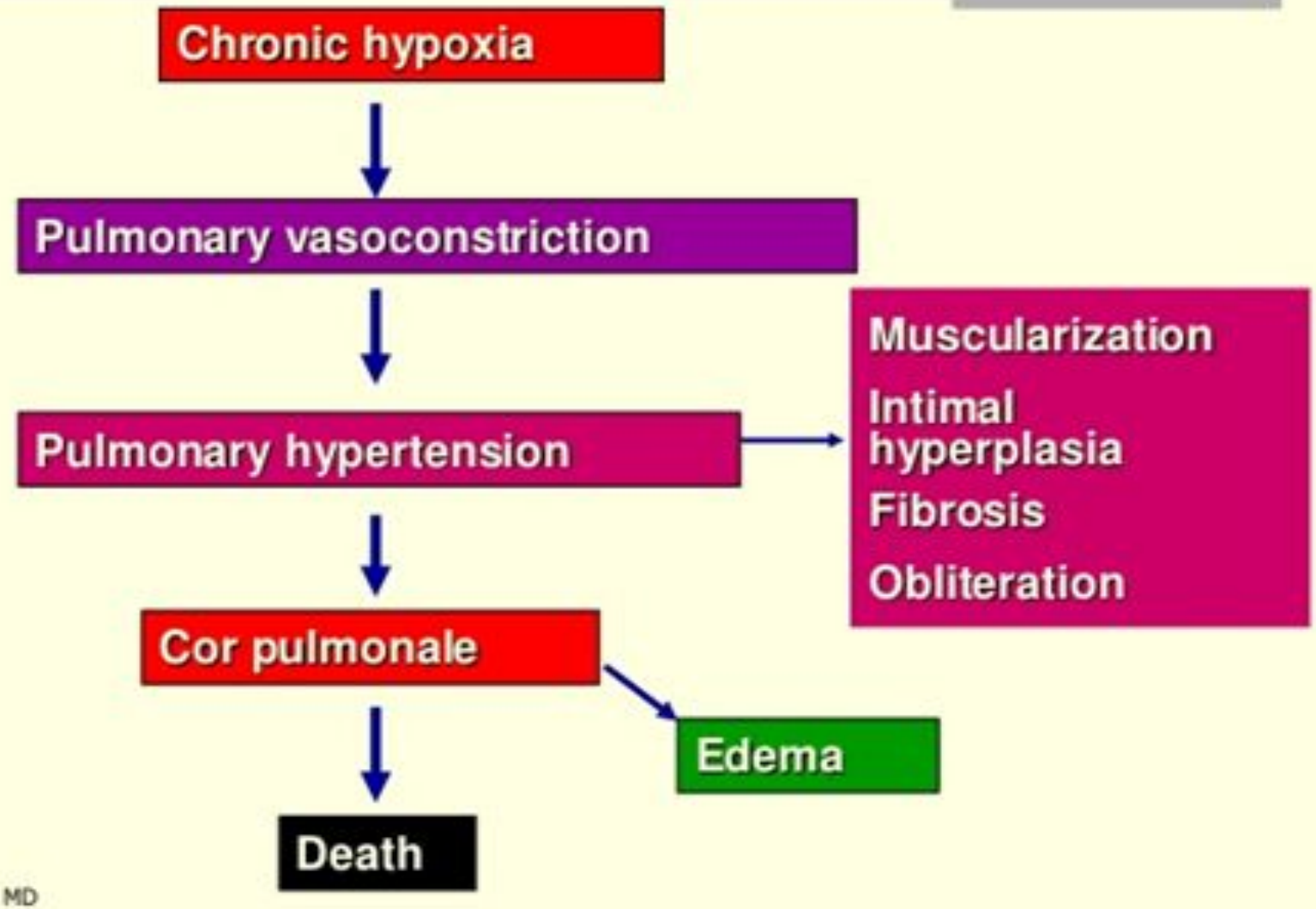
Complications include increased risk for recurrent infections; secondary pulmonary hypertension leading to right heart failure (cor pulmonale) and death .In long standing of chronic bronchitis lead to lung cancer (sq.metaplasia then dysplasia and later on lead to cancer)



sq.metaplasia



Pulmonary Hypertension in COPD

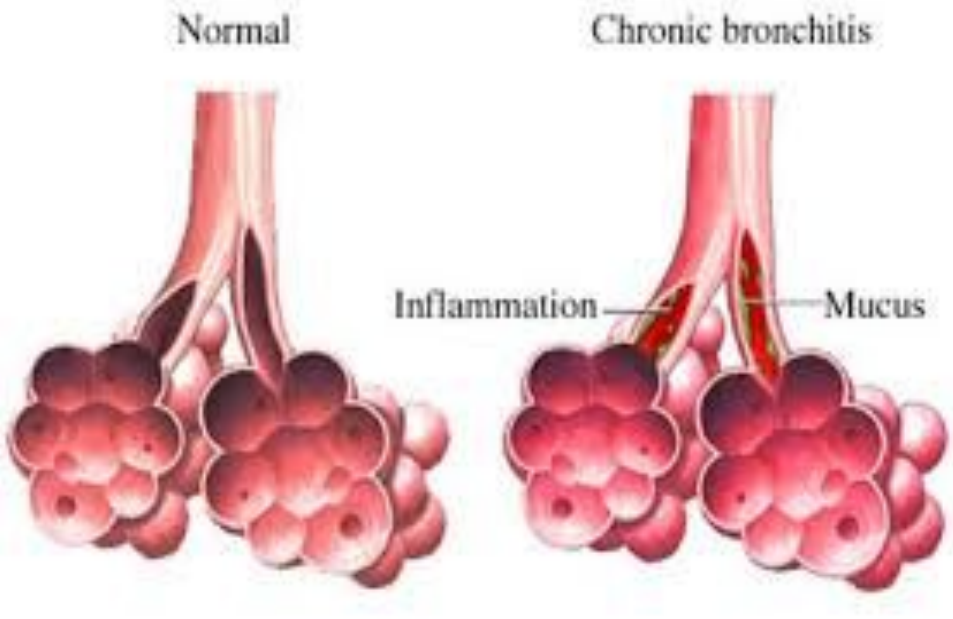


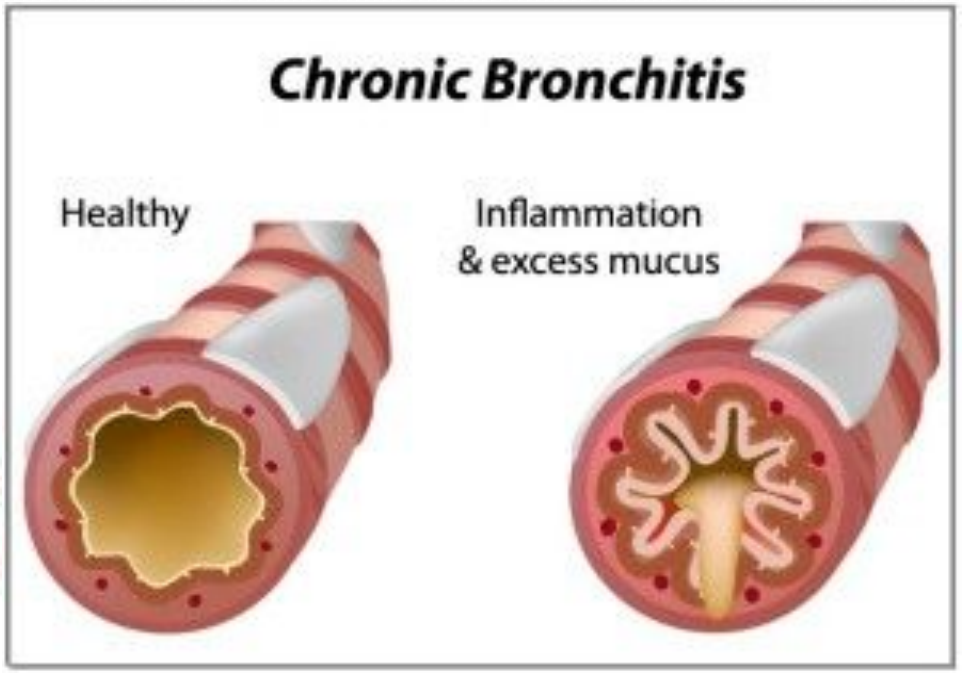
Source: Peter J. Barnes, MD

Gross features

1-The mucosal lining of the larger airways is usually hyperemic and edematous. It is often covered by a layer of mucus or mucopurulent secretions.

2-The smaller bronchi and bronchioles may also be filled with similar secretions





Microscopical features

1-The diagnostic feature of chronic bronchitis in the trachea and larger bronchi is hyperplasia and hypertrophy of the mucus-secreting glands .

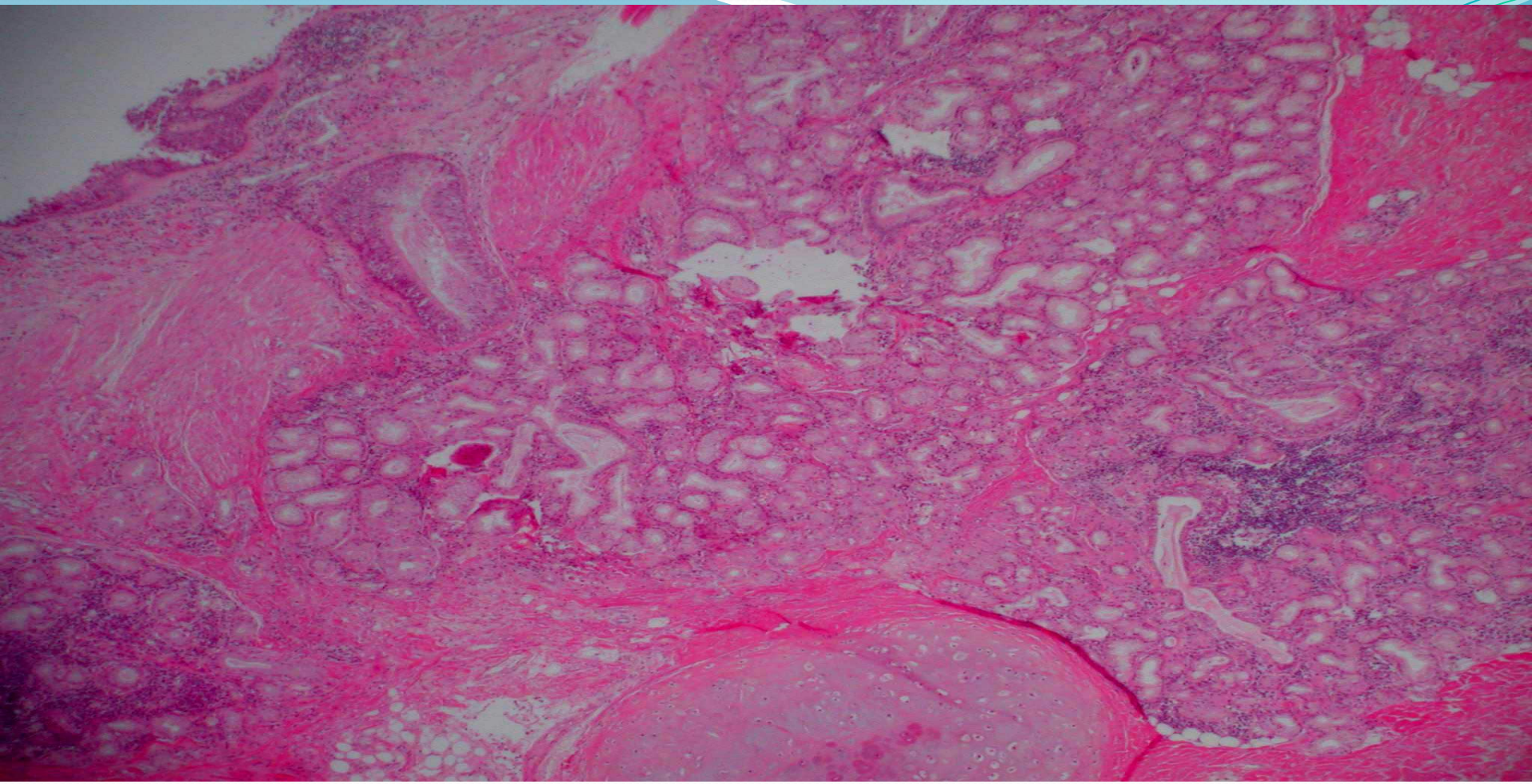
The increased in size of mucus-secreting glands can be assessed by the ratio of the thickness of the mucous gland layer to the thickness of the wall between the epithelium and the cartilage (Reid index) .
The Reid index (normally less than 0.4)is increased in chronic bronchitis , usually proportion to the severity and duration of the disease .

2-A variable density of inflammatory cells, largely mononuclear but sometimes admixed with neutrophils, is frequently present in the bronchial mucosa. Neutrophils increased markedly during superimposed acute exacerbations.

3-Chronic bronchiolitis (small airway disease), characterized by goblet cell hyperplasia, mucus plugging, inflammation, and fibrosis.

4- Destruction of cilia of bronchial epithelium .

5- Bronchial epithelium squamous metaplasia and dysplasia .



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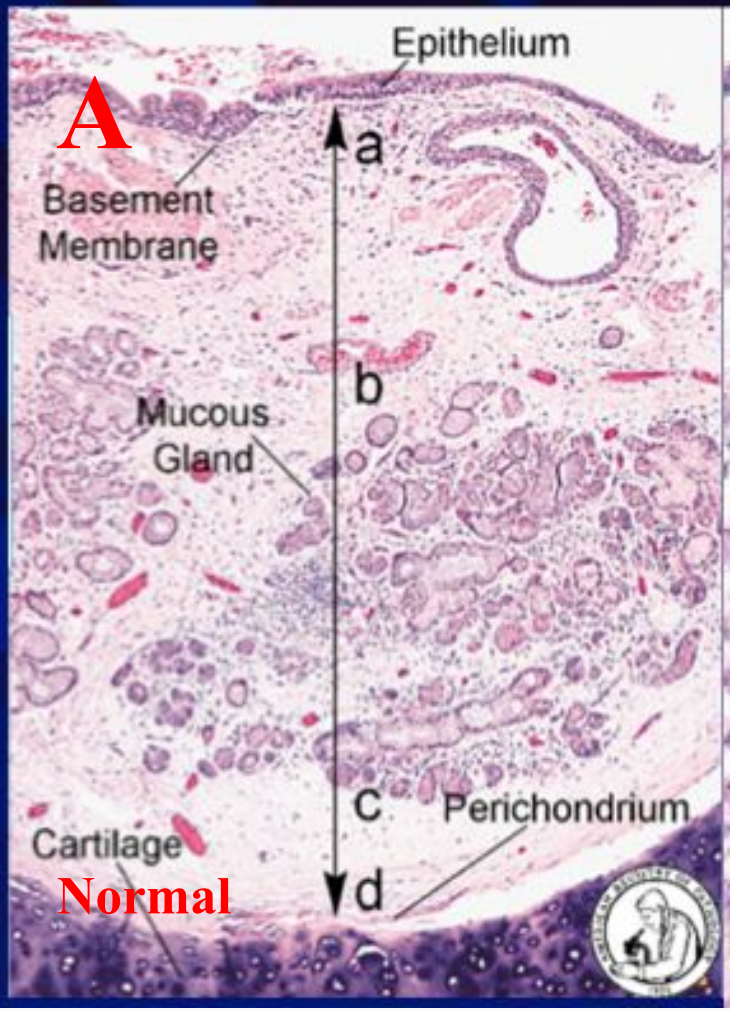
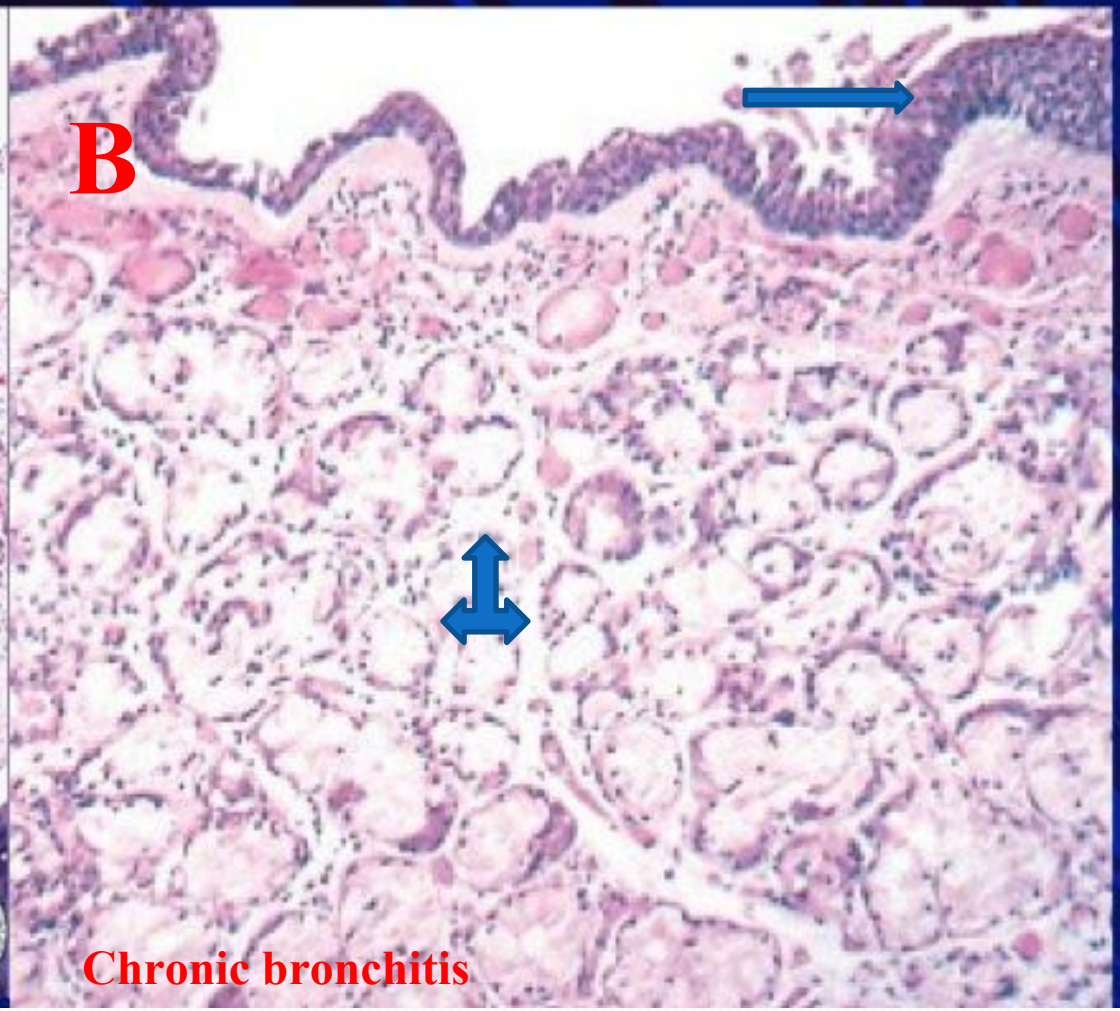
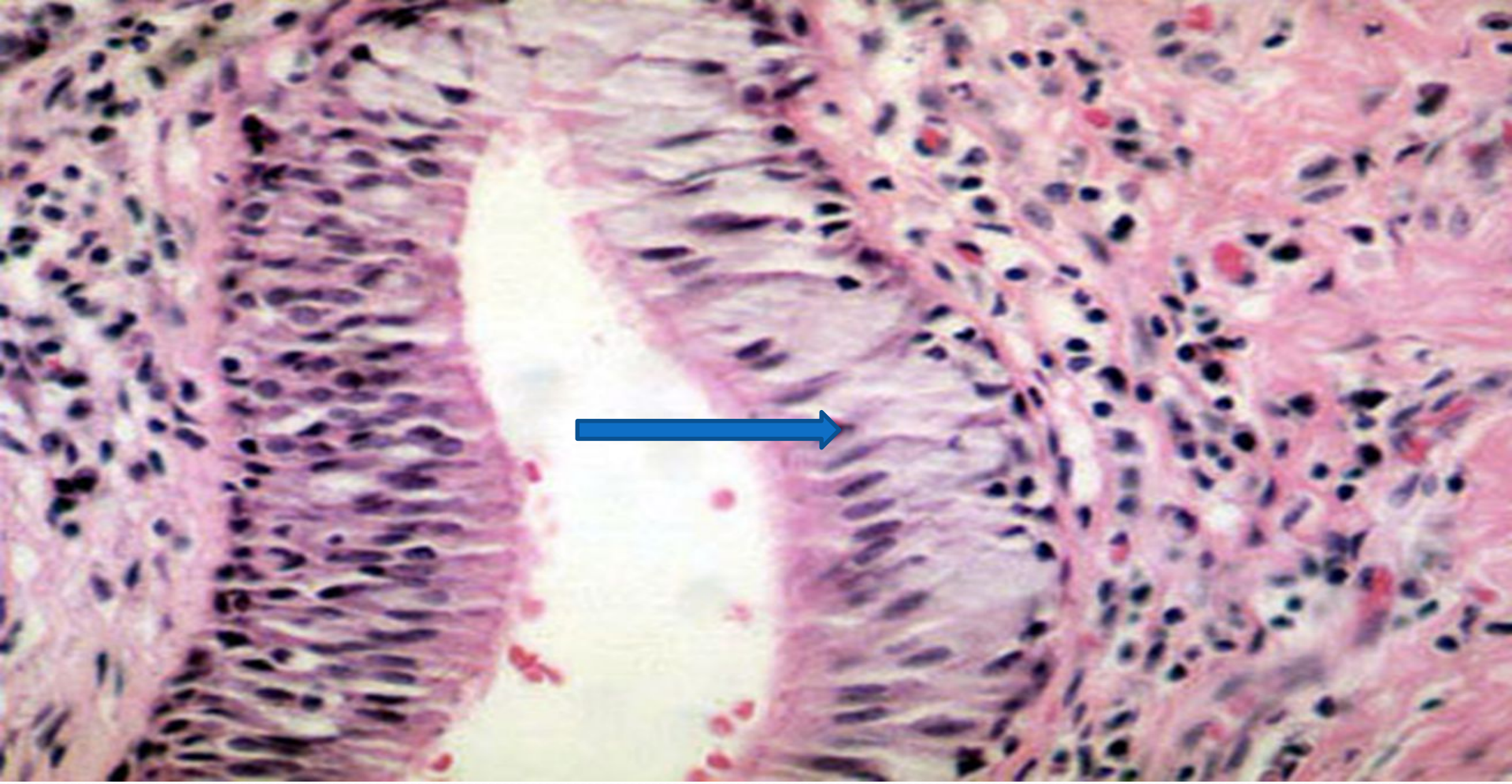




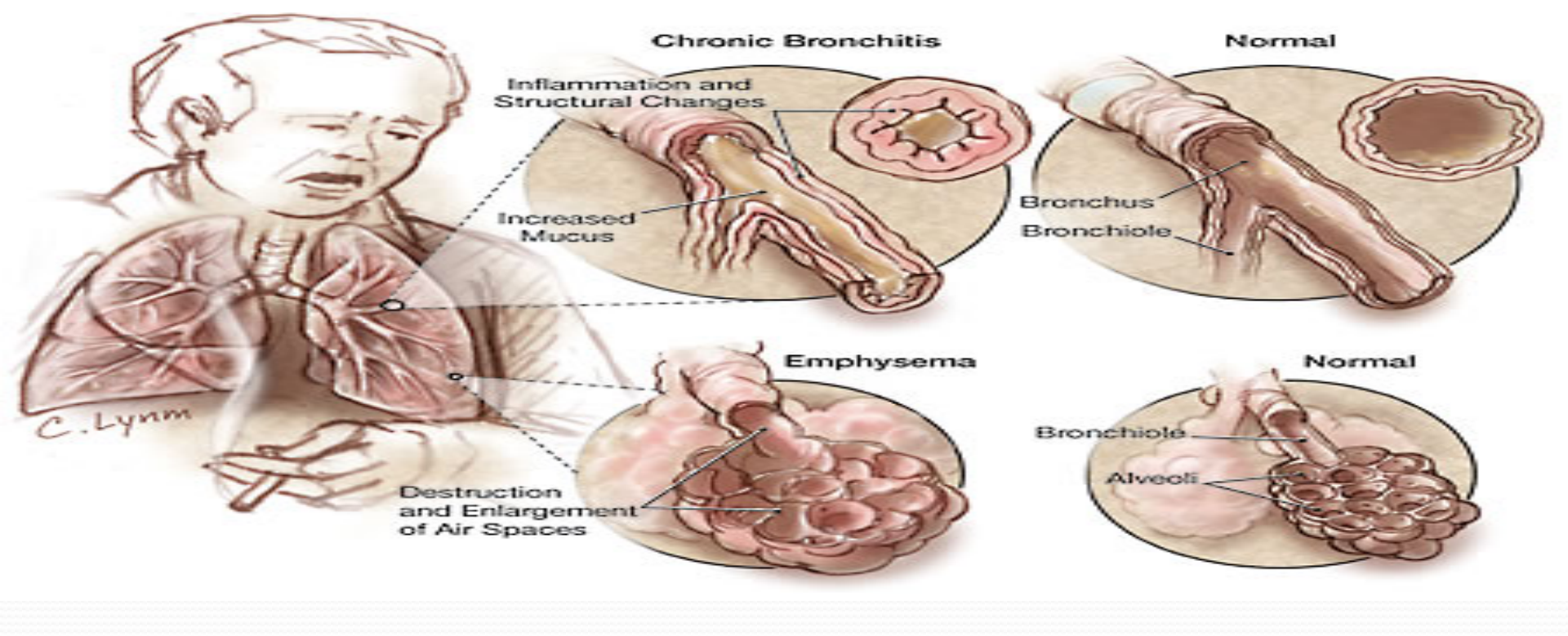
Chronic bronchitis

A- Reid index :- The ratio of the thickness of the mucous gland layer to the thickness of the wall between the epithelium and the cartilage. (normally less than 0.4) .

B-Mucous gland hyperplasia ,with bronchial inflammation and fibrosis , in advance stage the bronchial epithelium with squamous metaplasia and dysplasia .



Chronic bronchiolitis (small airway disease), characterized by goblet cell hyperplasia .



PURE CHRONIC BRONCHITIS

Large airways (trachea, bronchi)
- Mucus hypersecretion
- Inflammation
- (Chronic bronchitis)

Small airways (bronchioles)
- Peribronchiolar fibrosis
- Airway obstruction
- (Chronic bronchiolitis)

PURE EMPHYSEMA

Acinus (respiratory bronchiole, alveolar ducts, and alveoli)
- Loss of elastic recoil
- (Emphysema)

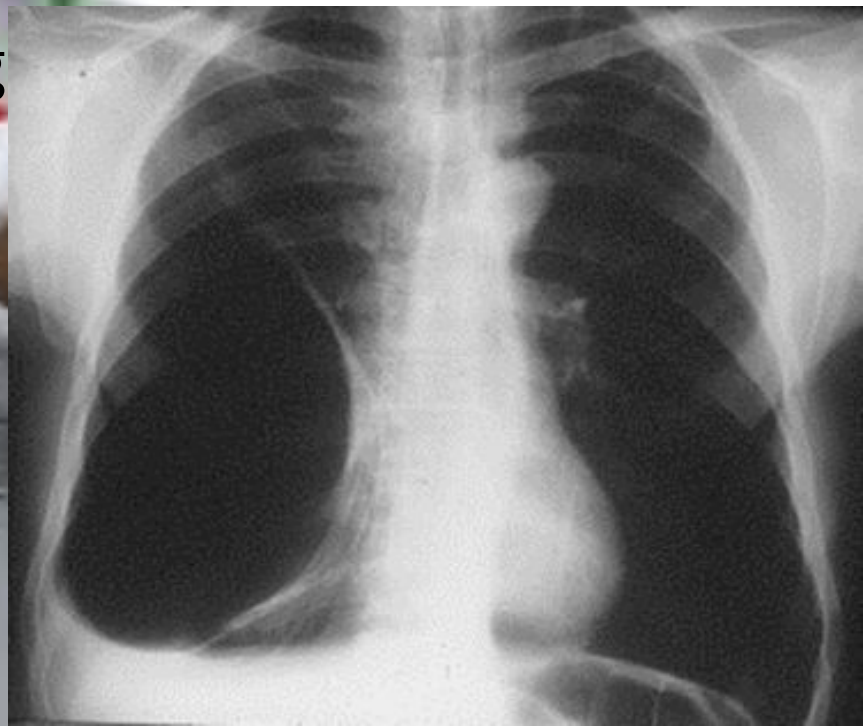
Both affected → COPD (common)


Smoking is dangerous
for your health

Case presentation

Q/A 65y-old man with a 40y history of tobacco use . Now complain from sever dyspnea . On examination ,he has barrel-shaped chest and pink puffer .
CXR reveals enlarged heart ,hyper -lucent lung fields and cystic air spaces projecting from the pleural surface .

Q1/- What is the most likely diag
Q2/- Pathogenesis ?



Case presentation

Q/A 65y-old man with a 40y history of tobacco use . Now complain from sever dyspnea , a persistent productive cough for at least 3 consecutive months in at least 2 consecutive years . On examination ,he has barrel-shaped chest and PT .

Q1/- Pathophysiology of PT ?