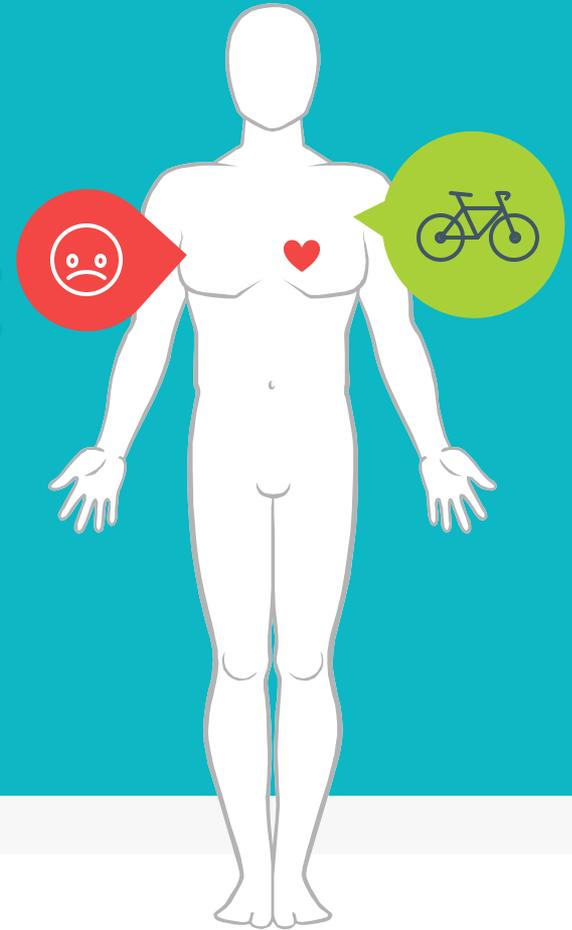


# Respiratory System Pathology: Obstructive Lung Disease I

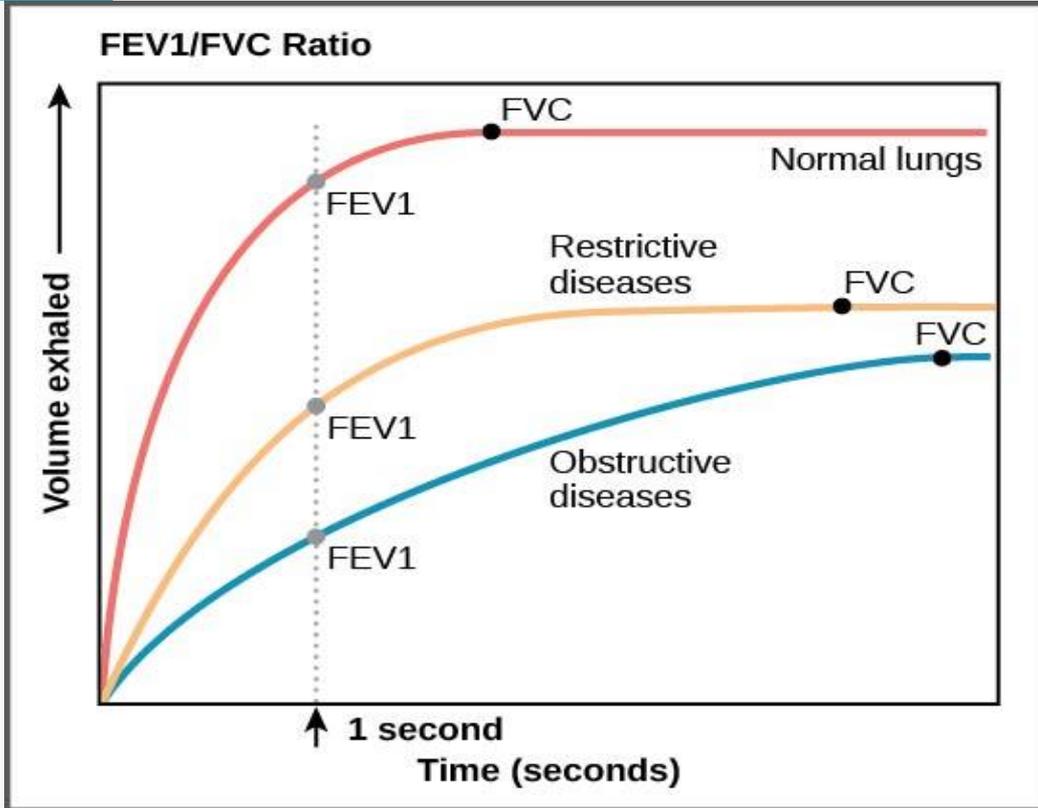


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**Diffuse pulmonary diseases** can be classified into two categories:

1. **Obstructive (airway) disease:** an increase in resistance to airflow due to partial or complete obstruction at any level (trachea → larger bronchi → terminal & respiratory bronchioles).
2. **Restrictive disease:** reduced expansion of lung parenchyma and decreased total lung capacity.

# Obstructive vs. Restrictive



- ▶ Forced expiratory volume at 1 second (FEV1)/forced vital capacity (FVC); FEV1/FVC ratio of less than 0.7 → Obstructive
- ▶ proportionate decreases in both total lung capacity & FEV1 → normal FEV1/FVC ratio → Restrictive

# OBSTRUCTIVE LUNG (AIRWAY) DISEASES

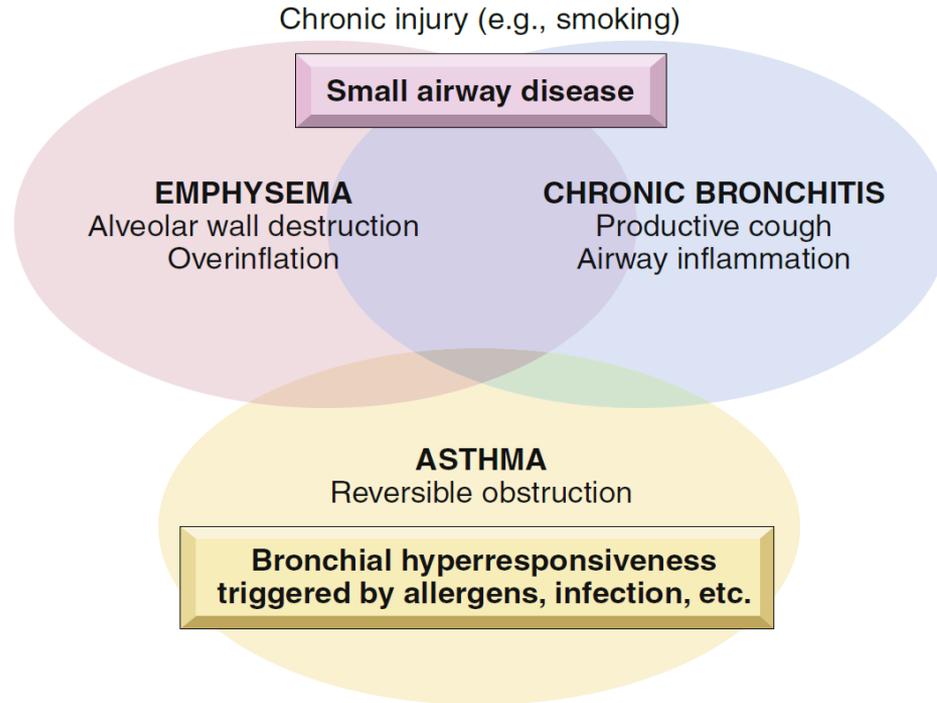
- ▶ Four main disorders with distinct clinical & anatomic characteristics

Clinical Entity	Anatomic Site	Major Pathologic Changes	Etiology	Signs/Symptoms
Emphysema	Acinus	Air space enlargement, wall destruction	Tobacco smoke	Dyspnea
Chronic bronchitis	Bronchus	Mucous gland hypertrophy and hyperplasia, hypersecretion	Tobacco smoke, air pollutants	Cough, sputum production
Bronchiectasis	Bronchus	Airway dilation and scarring	Persistent or severe infections	Cough, purulent sputum, fever
Asthma	Bronchus	Smooth muscle hypertrophy and hyperplasia, excessive mucus, inflammation	Immunologic or undefined causes	Episodic wheezing, cough, dyspnea
Small airway disease, bronchiolitis <sup>a</sup>	Bronchiole	Inflammatory scarring, partial obliteration of bronchioles	Tobacco smoke, air pollutants	Cough, dyspnea

<sup>a</sup>Can be present in all forms of obstructive lung disease or occur by itself.

# OBSTRUCTIVE LUNG (AIRWAY) DISEASES

## overlap sometimes

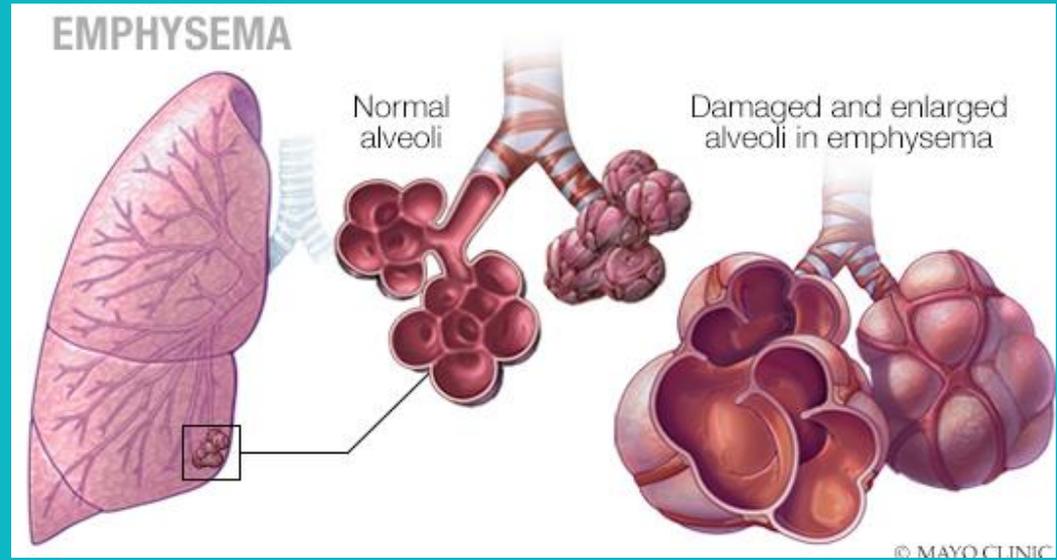


- ▶ Emphysema & chronic bronchitis often coexist → grouped together as **chronic obstructive pulmonary disease (COPD)**
- ▶ The irreversible airflow obstruction of COPD distinguishes it from asthma (characteristic reversible airflow obstruction)

# Chronic obstructive pulmonary disease (COPD)

- ▶ Majority of patients have features of both Emphysema & chronic bronchitis.
- ▶ Certainly, because both share a major trigger → cigarette smoking.
- ▶ 40-50% of heavy smokers develop COPD, 80% of COPD is due to smoking.
- ▶ Other risk factors: environmental & occupational pollutants, airway hyperresponsiveness & genetic polymorphisms.
- ▶ Emphysema may exist without chronic bronchitis (particularly in inherited  $\alpha$ 1-anti-trypsin deficiency).

# 1. Emphysema

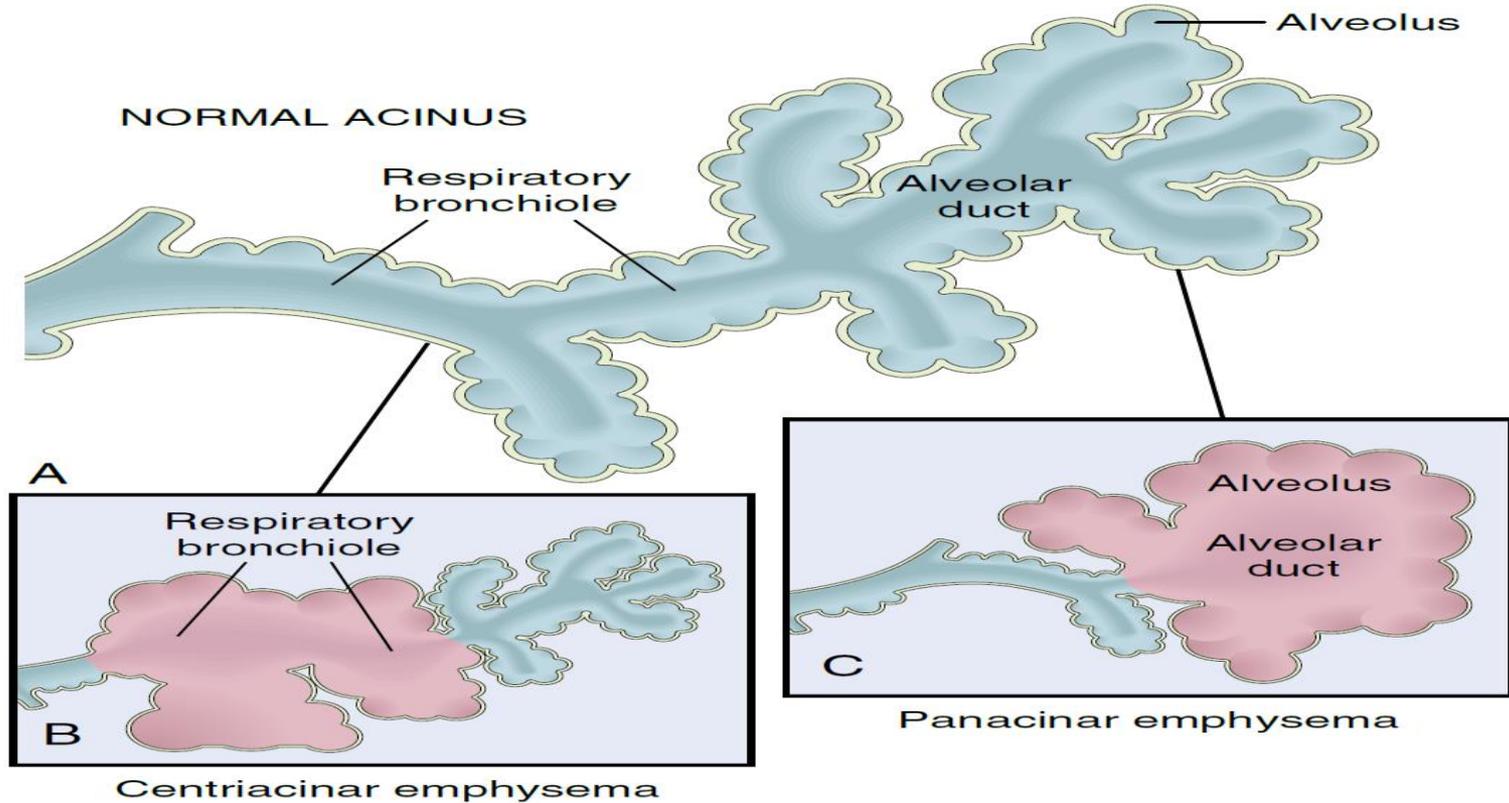


Characterized by **permanent** enlargement of the air spaces **distal** to the terminal bronchioles, accompanied by **destruction** of their walls without significant fibrosis.

# Emphysema - subtypes

- ▶ Emphysema is classified According to its **anatomic distribution within the lobule** (a lobule is a cluster of 3 to 5 acini; an acinus is the part of the lung distal to terminal bronchiole):
  1. **Centriacinar emphysema**: in the upper lobes, most common type in cigarette smokers (**central or proximal parts of the acini, distal alveoli are spared.**)
  2. **Panacinar emphysema**: in the lower lung zones & associated with  $\alpha$ 1-anti-trypsin deficiency. (**the acini are uniformly enlarged** from the level of the respiratory bronchiole to the terminal blind alveoli).

# Clinically significant patterns of emphysema



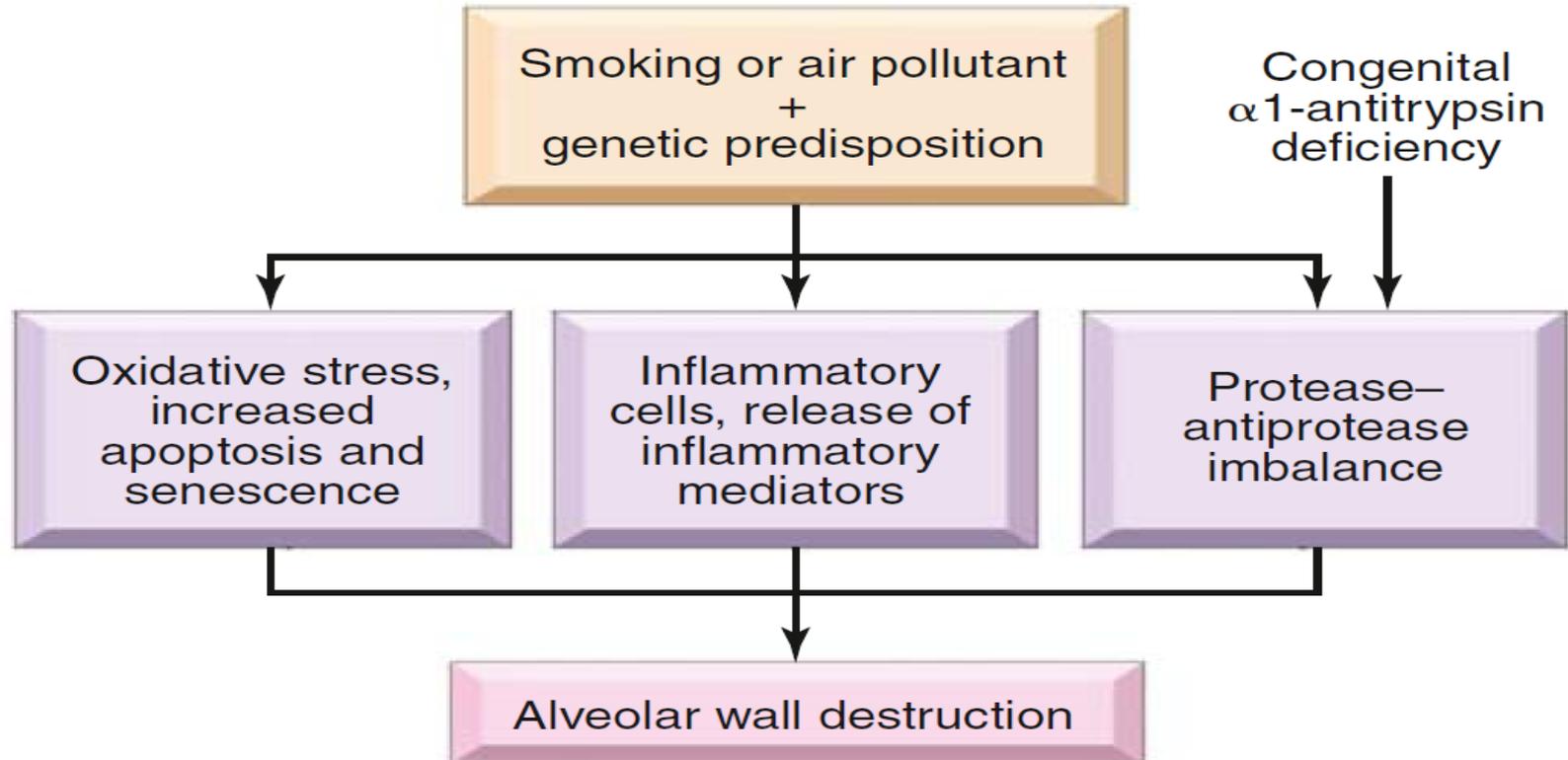
# Emphysema - subtypes

3. **Distal acinar emphysema:** often in young adults who present with spontaneous pneumothorax, (**the proximal portion of the acinus is normal, but the distal part is primarily involved**)
4. **Irregular emphysema:** clinically asymptomatic, (**the acinus is irregularly involved, is almost invariably associated with scarring**)

# Emphysema - Pathogenesis

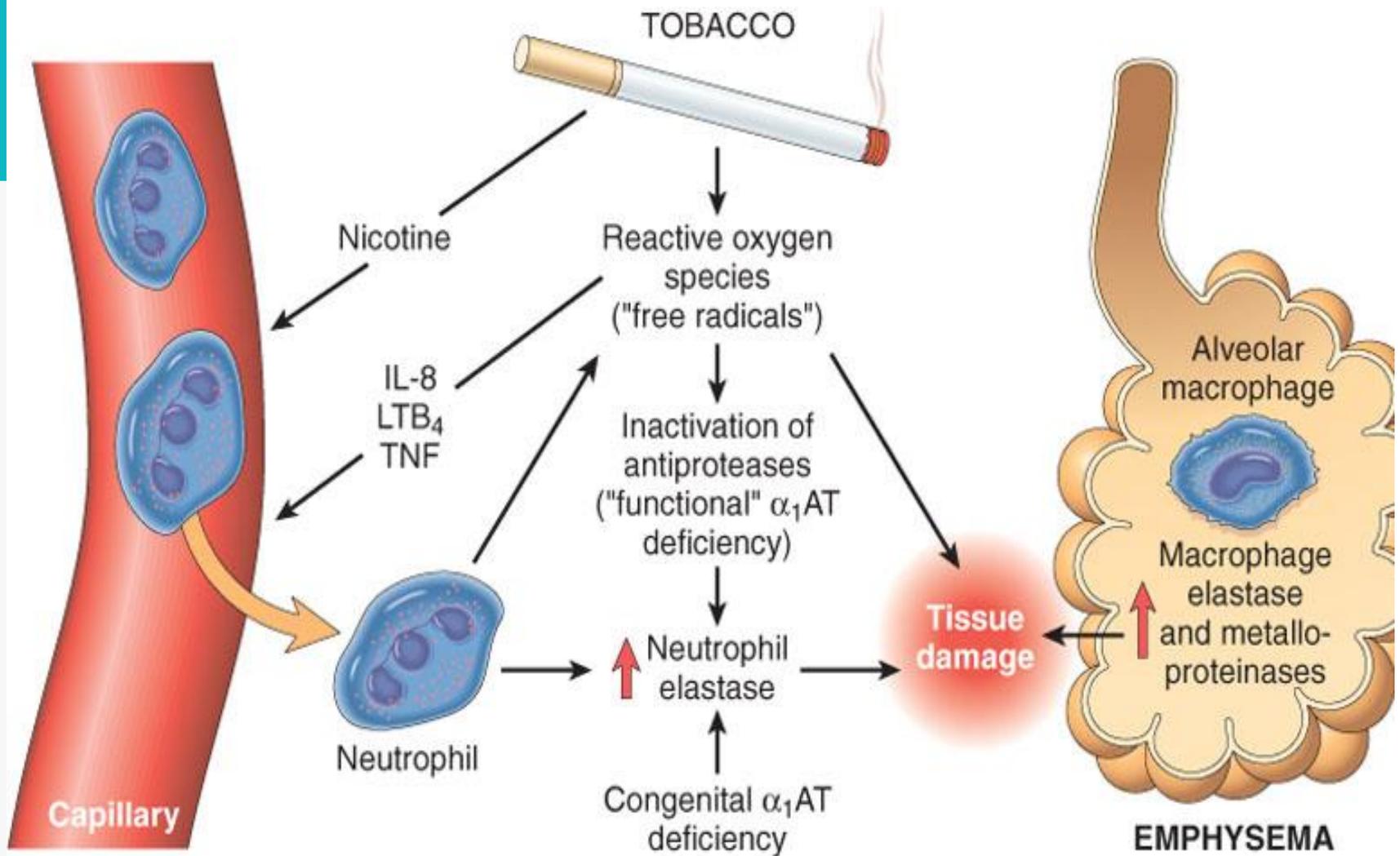
- ▶ (1) Inhaled cigarette smoke & other noxious particles cause lung damage and inflammation, particularly in patients with (2) a genetic predisposition. Other factors that influence emphysema development:
  1. *Inflammatory cells and mediators.*
  2. *Protease-anti-protease imbalance.*
  3. *Oxidative stress; Reactive oxygen species.*
  4. *Airway infection, worsen the picture.*

# Emphysema - Pathogenesis



# Emphysema - Pathogenesis

- ▶ **Observation** → patients with a genetic deficiency of anti-protease  $\alpha$ 1-anti-trypsin have a predisposition to develop emphysema, (compounded by smoking) **led to the idea** → **Protease-mediated damage of extracellular matrix has a central role in the airway obstruction seen in emphysema.**
- ▶  $\alpha$ 1-anti-trypsin, normally present in serum, tissue fluids, and macrophages, it is a major inhibitor of proteases (particularly **elastase**) secreted by neutrophils during inflammation.



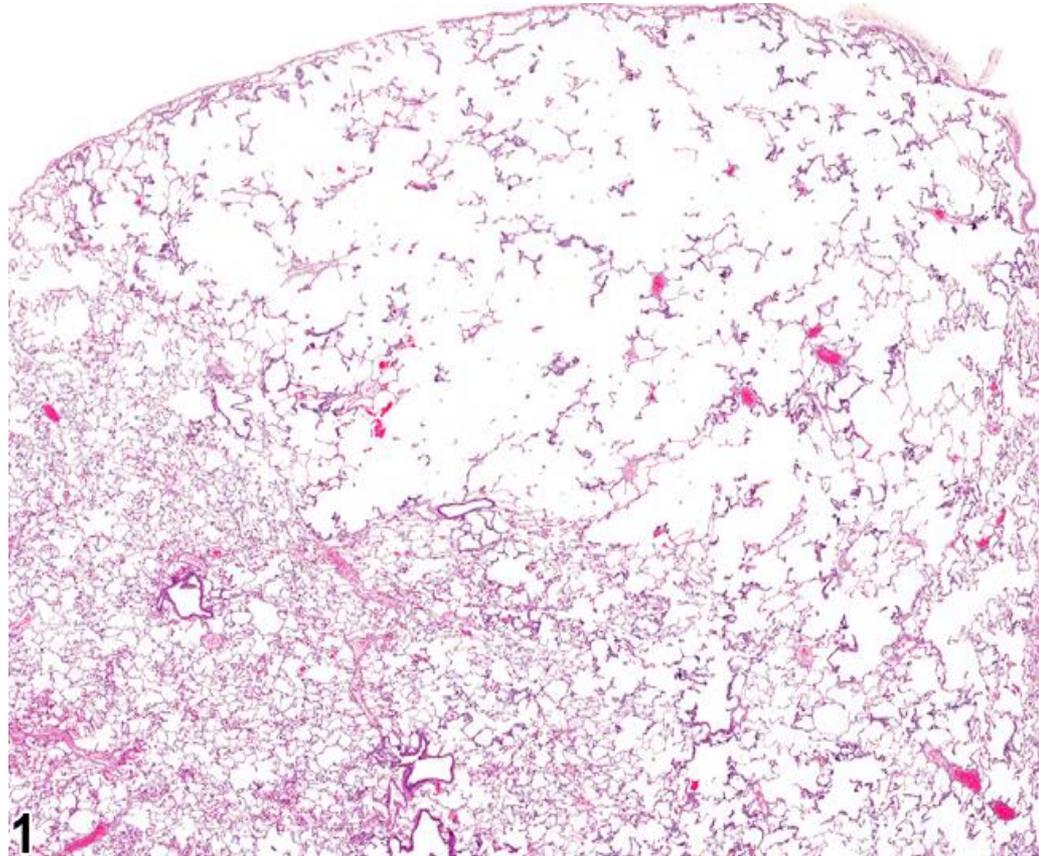
# Emphysema - Morphology

- ▶ **Panacinar:** **B** pale, voluminous lungs that often obscure the heart.
- ▶ **Centriacinar:** **A** less impressive. Until late stages, the lungs are a deeper pink than in panacinar emphysema and less voluminous



# Emphysema - Morphology

- ▶ **destruction of alveolar walls without fibrosis, leading to enlarged air spaces**, alveolar capillaries is diminished.
- ▶ With the **loss of elastic tissue** in the alveolar septa, radial traction on the small airways is reduced → collapse during expiration → chronic airflow obstruction functional

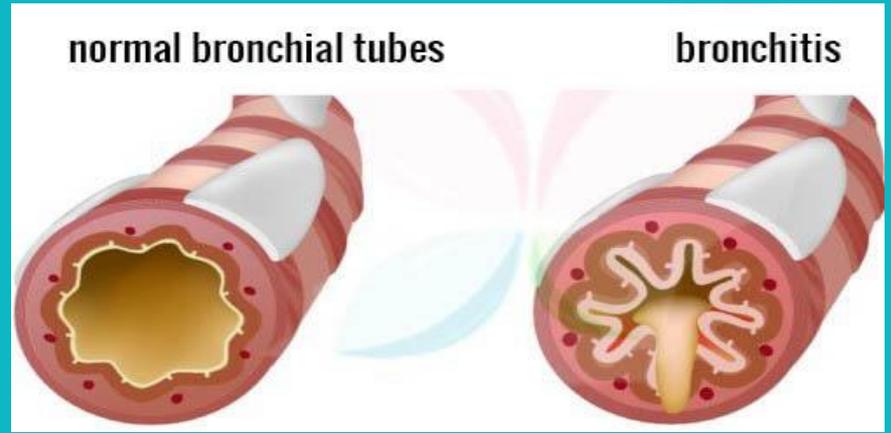


# Emphysema – Clinical features

- ▶ Dyspnea usually first symptom; insidious but progressive.
- ▶ Weight loss is common
- ▶ PFT: reduced FEV1 with normal or near-normal FVC ~ FEV1/FVC ratio is reduced.
- ▶ **Classic presentation:** barrel-chested + dyspneic, sitting forward in a hunched-over position. Dyspnea and hyperventilation are prominent, so that until very late in the disease, gas exchange is adequate and blood gas values are relatively normal → **“pink puffers.”**

## 2.

# Chronic Bronchitis



Diagnosed based on clinical grounds → defined by the presence of a **persistent productive cough** for at least 3 consecutive months in at least 2 consecutive years.

# Chronic Bronchitis - Pathogenesis

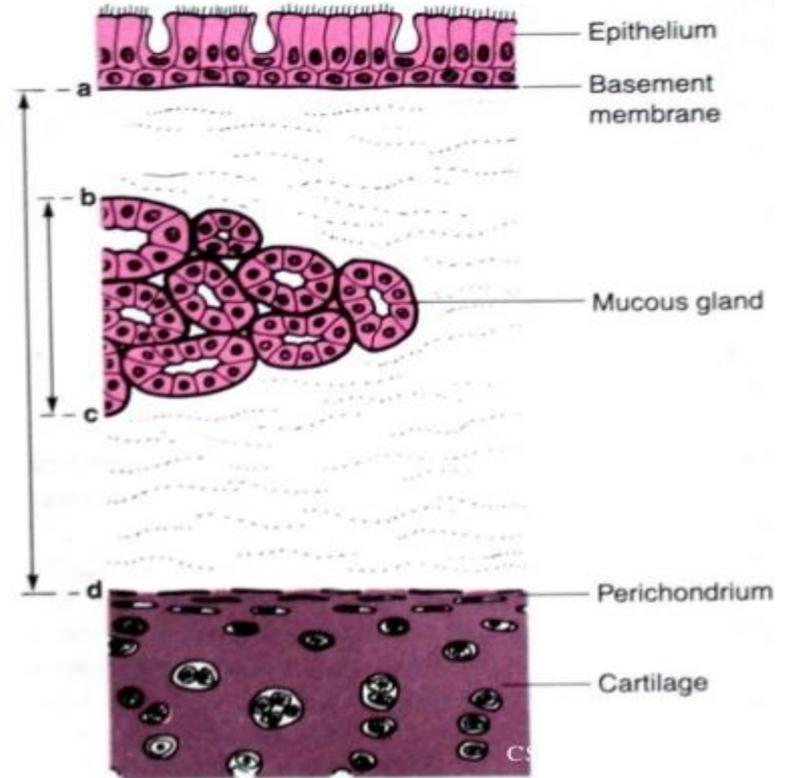
- ▶ Initiating (primary) factor is exposure to irritating inhaled substances such as tobacco smoke (90% of patients are smokers), dust, cotton, or silica:
- 1. **Mucus hypersecretion:** earliest feature, beginning in the large airways: inflammatory mediators (histamine and IL-13) → submucosal gland hypertrophy & increase in goblet cells as a protective reactions against tobacco smoke or other pollutants

# Chronic Bronchitis - Pathogenesis

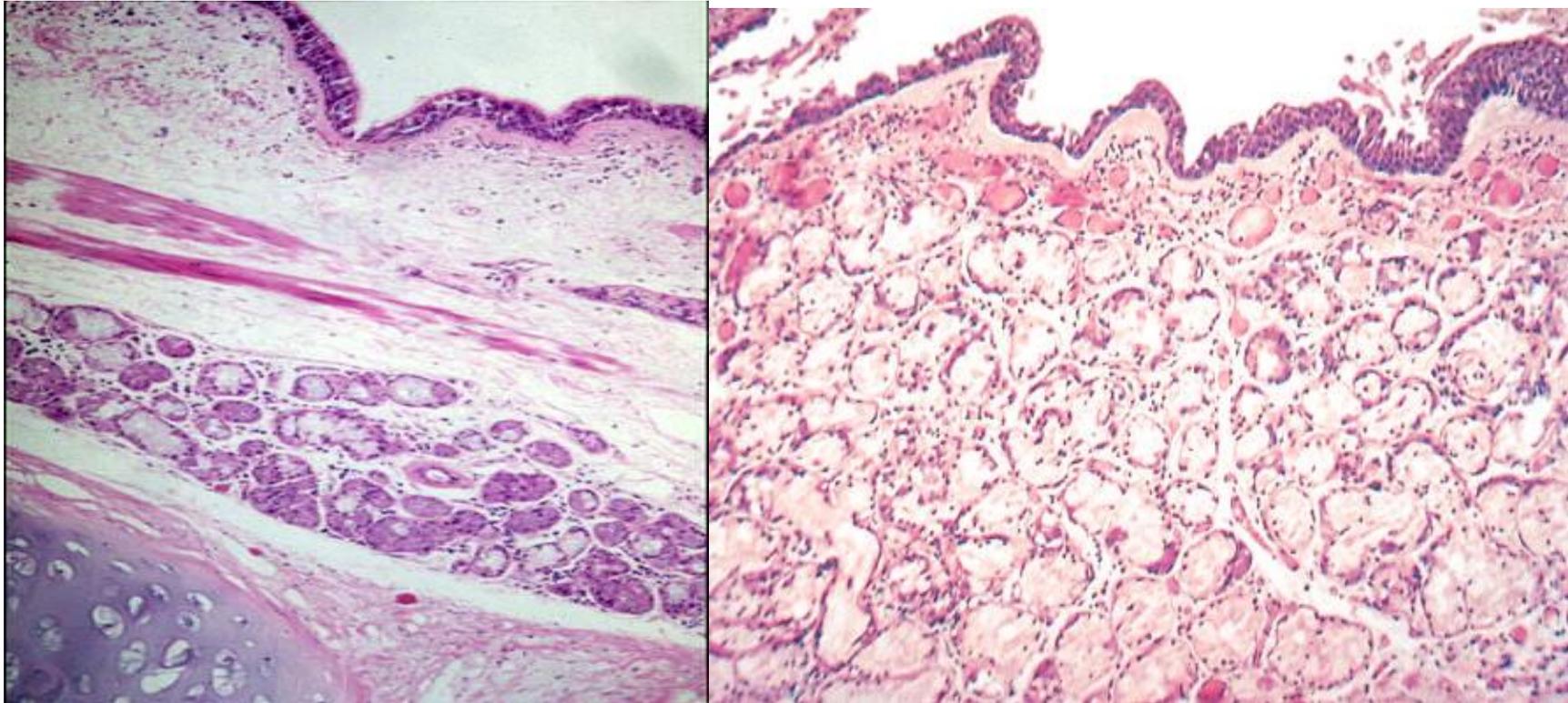
- 2. *Inflammation*:** Inhalants that induce chronic bronchitis cause cellular damage. Long-standing inflammation & accompanying fibrosis involving small airways → chronic airway obstruction.
- 3. *Infection*:** Infections does not initiate chronic bronchitis but producing **acute exacerbations**
- 4.** Cigarette smoke also **interferes with the ciliary action of the respiratory epithelium**, preventing the clearance of mucus and increasing the risk of infection.

# Chronic Bronchitis - Morphology

- ▶ **Enlargement of the mucus secreting glands in trachea and larger bronchi.**
- ▶ assessed by the ratio of the thickness of the submucosal gland layer to that of the bronchial wall (**the Reid index—normally 0.4**).



# Chronic Bronchitis - Morphology



# Chronic Bronchitis - Morphology

- ▶ Inflammatory cells: lymphocytes, macrophages, & maybe neutrophils
- ▶ **Chronic bronchiolitis** (small airway disease): goblet cell metaplasia, mucous plugging, inflammation, & fibrosis. In severe cases, fibrosis → obliteration of the → **(bronchiolitis obliterans)**
- ▶ Emphysematous changes often coexist.

# Chronic Bronchitis – Clinical features

- ▶ **Cardinal symptom:** persistent productive cough (earliest)
- ▶ For many years no respiratory impairment → eventually dyspnea on exertion develops.
- ▶ With time & continued smoking, other elements appear hypercapnia, hypoxemia, & mild cyanosis (*“blue bloaters”*).
- ▶ Long-standing severe chronic bronchitis commonly leads to cor pulmonale and cardiac failure.
- ▶ Death: impairment of respiratory function due to superimposed acute infections.

# Chronic Bronchitis vs. Emphysema

- ▶ Differentiation of pure chronic bronchitis from that associated with emphysema can be made in the classic case, but many patients with COPD have both conditions

	Predominant Bronchitis	Predominant Emphysema
Age (yr)	40-45	50-75
Dyspnea	Mild; late	Severe; early
Cough	Early; copious sputum	Late; scanty sputum
Infections	Common	Occasional
Respiratory insufficiency	Repeated	Terminal
Cor pulmonale	Common	Rare; terminal
Airway resistance	Increased	Normal or slightly increased
Elastic recoil	Normal	Low
Chest radiograph	Prominent vessels; large heart	Hyperinflation; small heart
Appearance	Blue bloater	Pink puffer

**‘The only safer cigarette is your  
last one.’**

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