Obstructive Lung Diseases

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Learning outcomes

Emphysema

Chronic bronchitis

Asthma

Bronchiectasis

Define

Etiology

Pathogenesis

Morphology

Clinical features

Conditions related to the disease

Definition of Obstructive Lung Disease

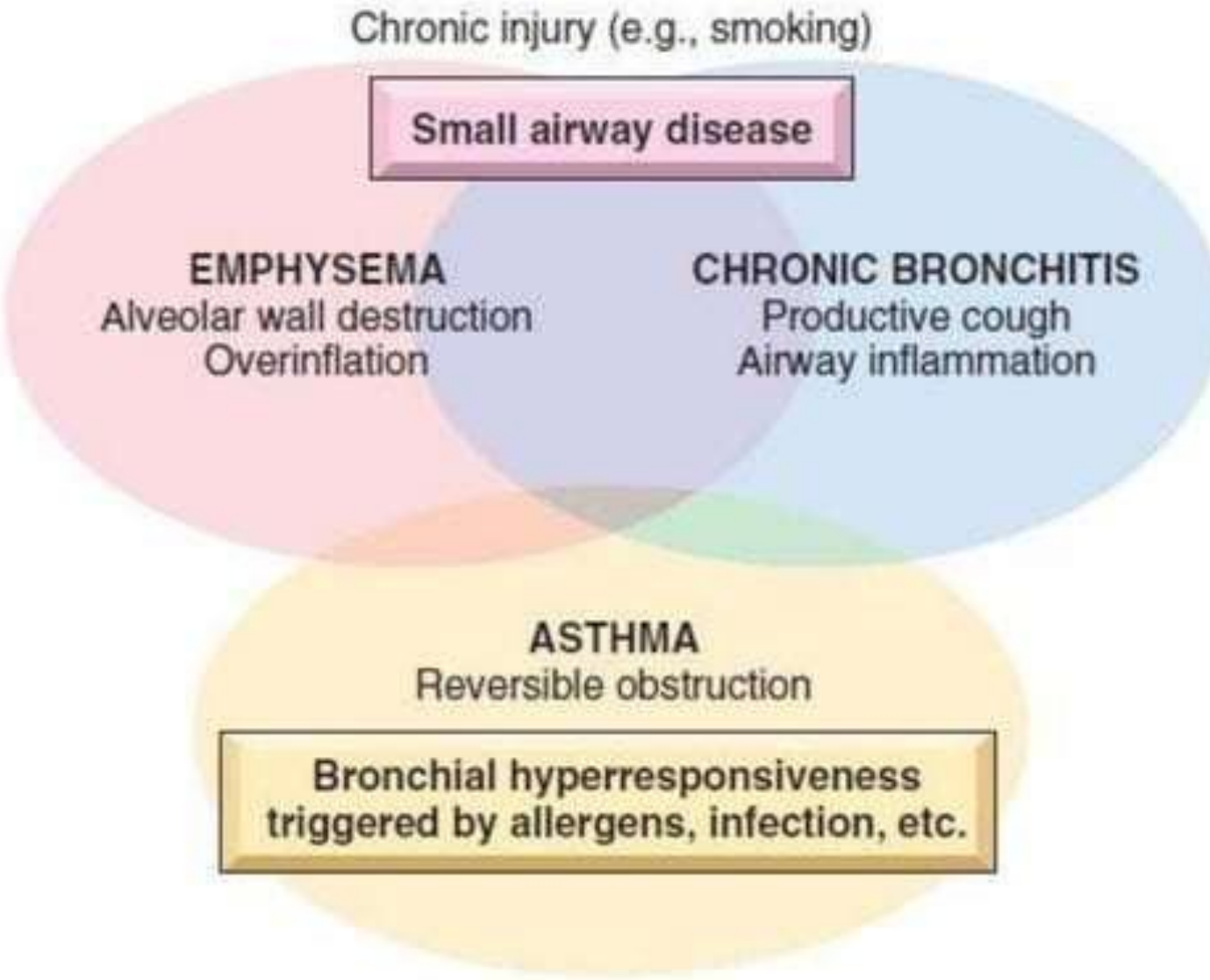
A lung disease characterized by chronic obstruction of lung airflow that interferes with normal breathing and is not fully reversible

-Air flow obstruction
(emphysema, bronchiectasis)

-Thickening of walls

-Deposition at the lumen
(chronic bronchitis)

-Fibrosis


Chronic injury (e.g., smoking)
Small airway disease
EMPHYSEMA
Alveolar wall destruction
Overinflation
CHRONIC BRONCHITIS
Productive cough
Airway inflammation
ASTHMA
Reversible obstruction
Bronchial hyperresponsiveness
triggered by allergens, infection, etc.

EMPHYSEMA

Definition of emphysema

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

Etiology of emphysema

- Tobacco smoke
- Marijuana smoke
- Air pollution
- Manufacturing fumes
- α_1-antitrypsin deficiency

Types of emphysema

1) Centriacinar (centrilobar) emphysema
2) Panacinar (panlobar) emphysema
3) Distal acinar (paraseptal) emphysema
4) Irregular emphysema

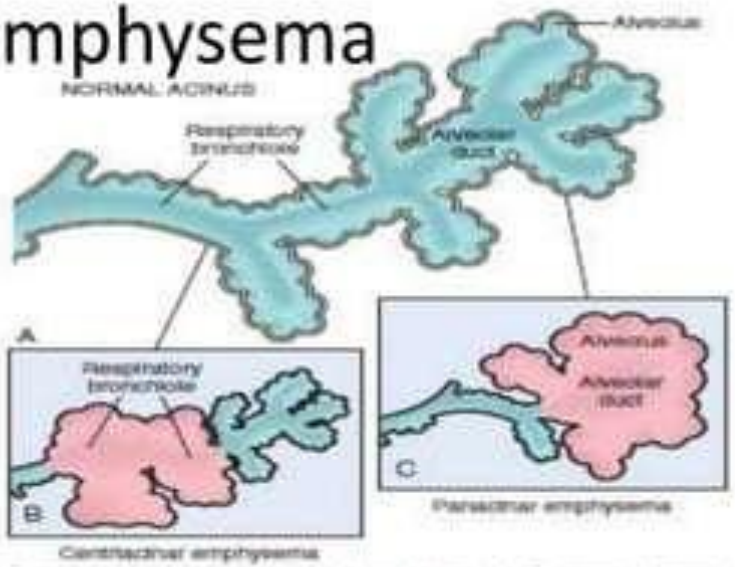


Figure 12-4 Major patterns of emphysema. A, Diagram of normal structure of the acinus, the fundamental unit of the lung. B, Centriacinar emphysema with dilation that initially affects the respiratory bronchioles. C, Panacinar emphysema with initial dilation of all the peripheral structures (i.e., the alveolus and alveolar duct); the disease later extends to affect the respiratory bronchioles.

Centriacinar (centrilobar) emphysema

- Most common; >20%
- ***Central or proximal parts of the acini, formed by respiratory bronchioles, are affected, while distal alveoli are spared***
- Severe type affects the distal alveoli as well
- Seen in cigarette smokers

Panacinar (panlobar) emphysema

- Lower lung zone
- ***Acini are uniformly enlarged, from the level of the respiratory bronchiole to the terminal blind alveoli***
- Usually seen in α_1-antitrypsin deficiency

Distal acinar (paraseptal) emphysema

- ***The proximal portion of the acinus is normal but the distal part is primarily involved***
- Unknown cause → spontaneous pneumothorax in young adults
- Characteristic finding: **multiple**, **contiguous**, **enlarged air spaces** ranging in diameter from <0.5 mm to >2.0 cm
- Sometimes forming cystic structures that, with progressive enlargement, are referred to as *bullae*

Irregular emphysema

- ***Acinus is irregularly involved, is almost invariably associated with scarring***
- Clinically asymptomatic

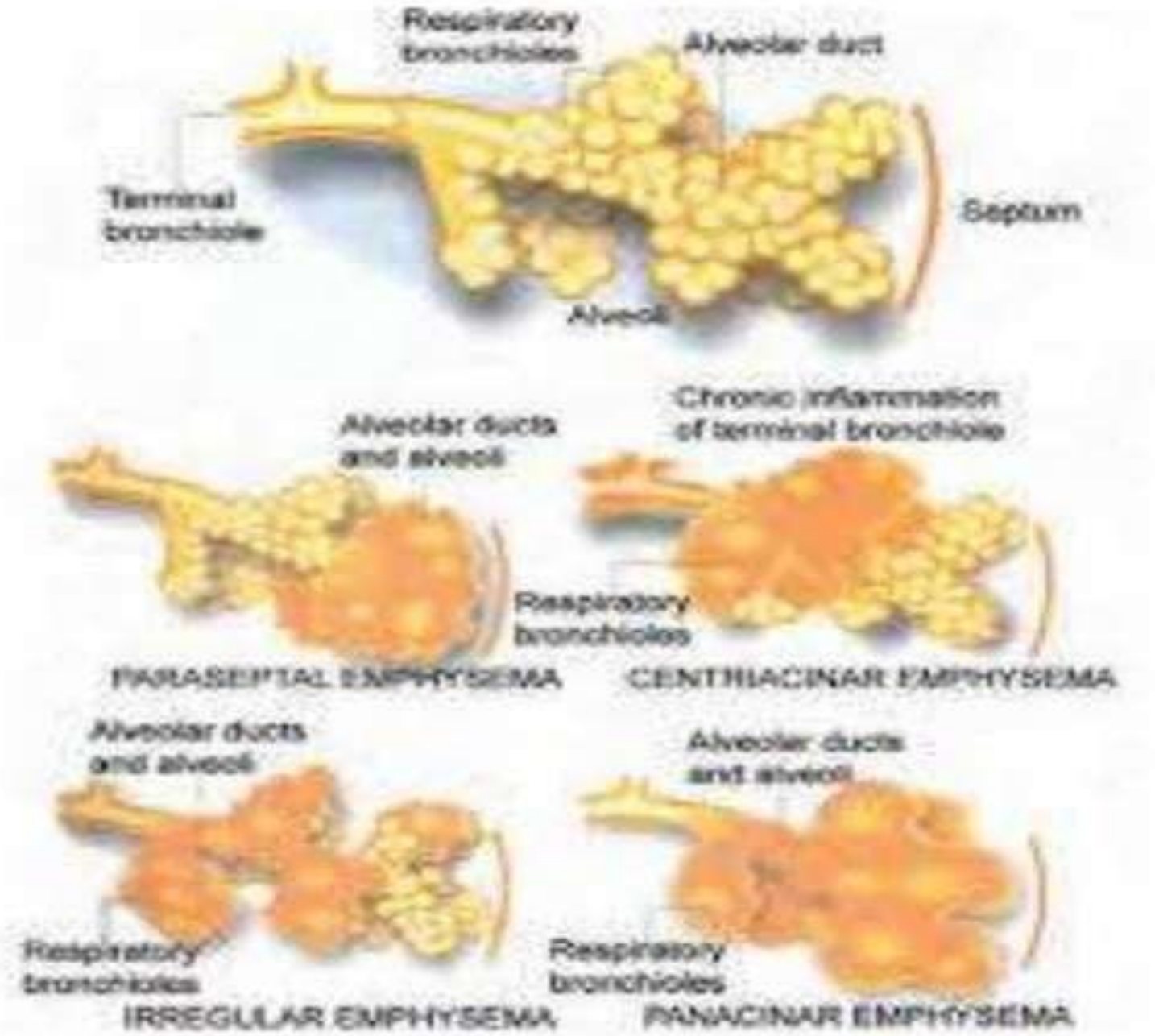
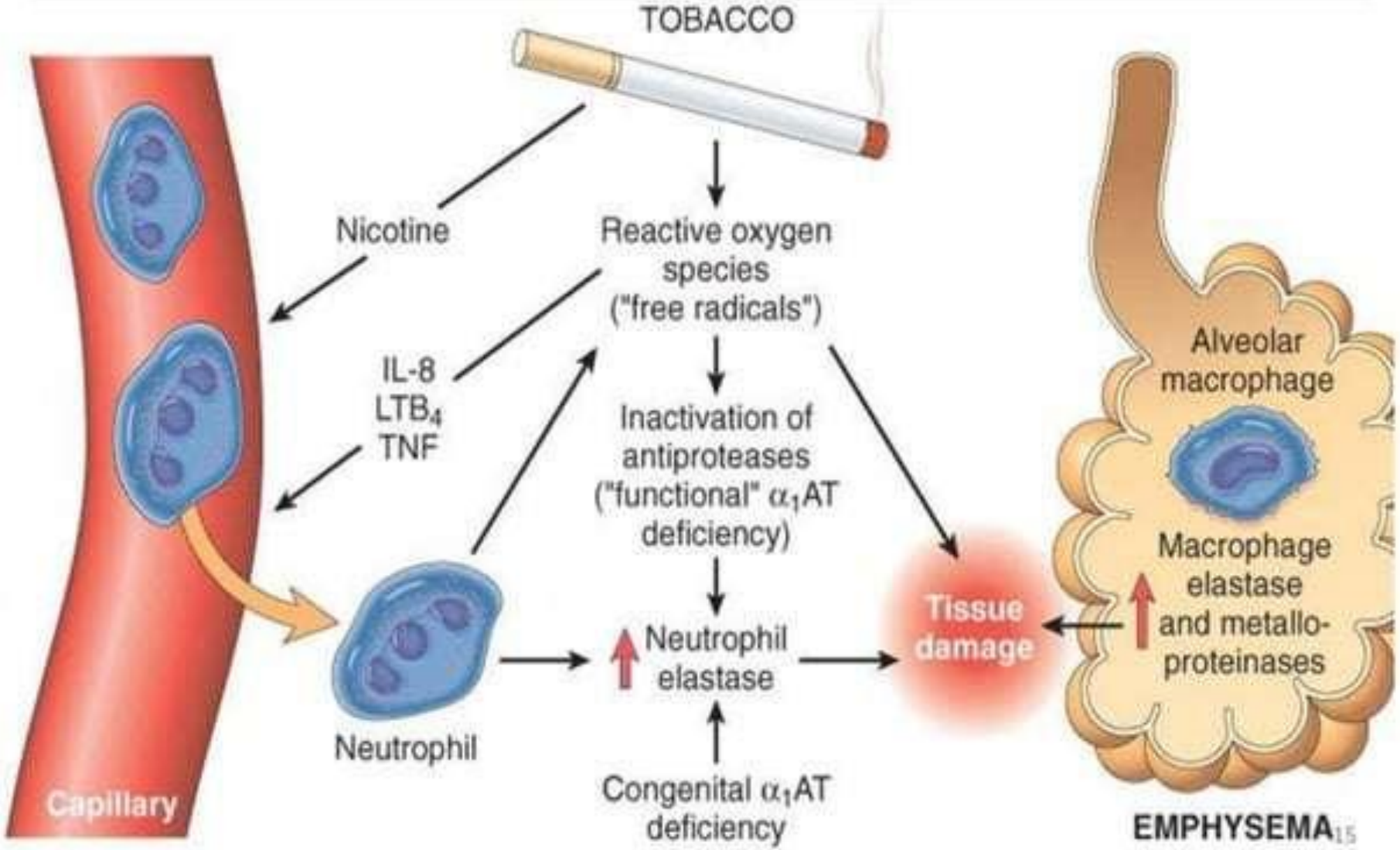


Fig. 4.30: Types of emphysema

Pathogenesis of emphysema



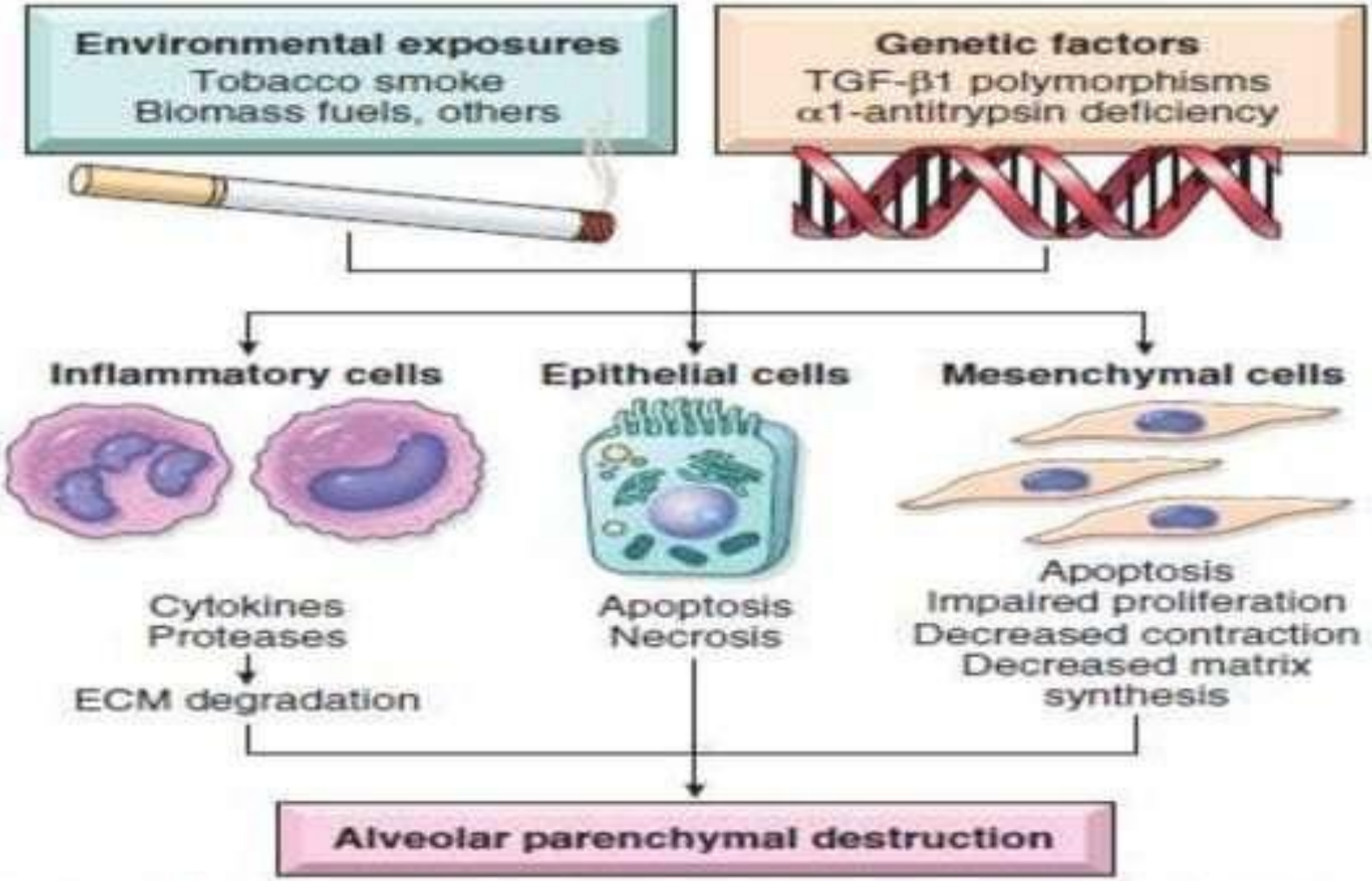


Figure 12–7 Loss of cellular homeostasis in emphysema pathogenesis. Exposure to inhaled toxins (such as cigarette smoke) leads to epithelial cell death, inflammation, and extracellular matrix proteolysis. In susceptible persons, mesenchymal cell survival and reparative functions are impaired by direct effects of inhaled toxic substances and inflammatory mediators and by the loss of the peri- and extracellular matrix. The result is loss of structural cells of the alveolar wall and the associated matrix components.

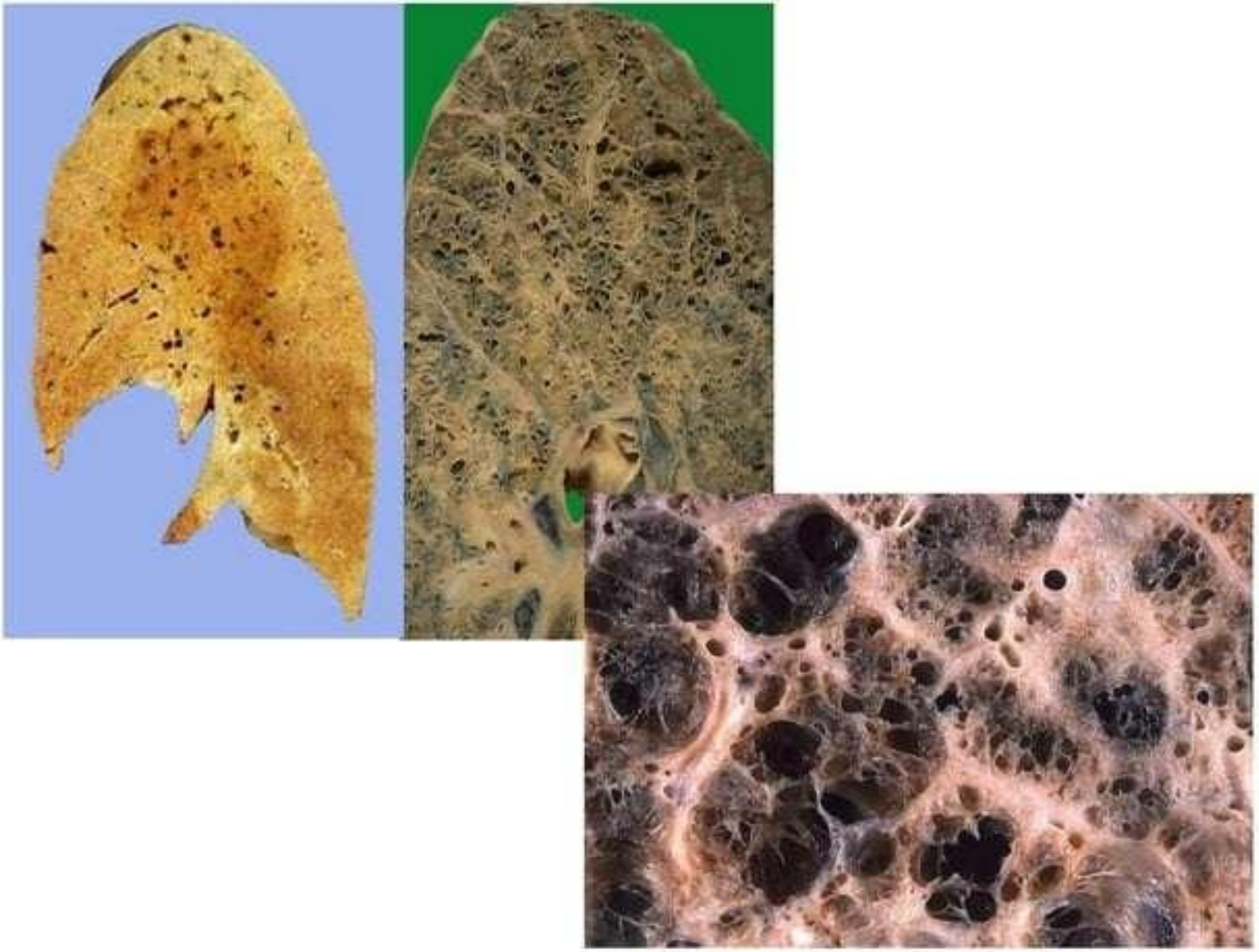
Morphology of emphysema

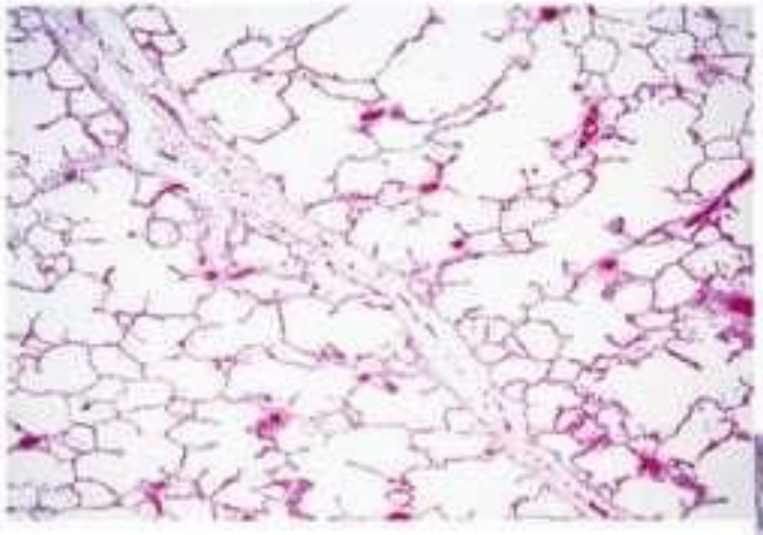
Gross

- **Panacinar emphysema:** pale, voluminous lungs that often obscure the heart when the anterior chest wall is removed at autopsy
- **Centriacinar emphysema:** The lungs are a deeper pink than in panacinar emphysema and less voluminous, unless the disease is well advanced and usually upper two thirds of the lungs are more severely affected than the lower lungs.

Microscopic

- **Destruction** of **alveolar walls without fibrosis**, leading to **enlarged air spaces**
- the **number** of **alveolar capillaries** is **diminished**.
- Terminal and respiratory bronchioles may be deformed because of the loss of septa that help tether these structures in the parenchyma.





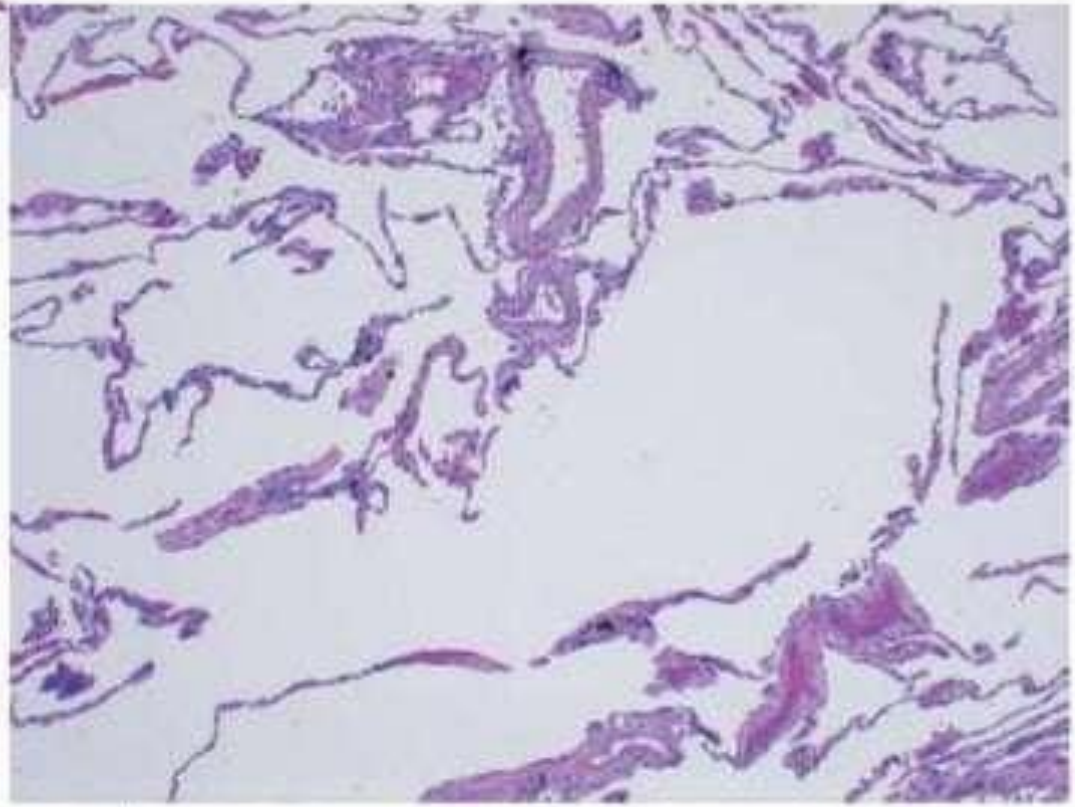


Figure 12–8 Pulmonary emphysema. There is marked enlargement of air spaces, with destruction of alveolar septa but without fibrosis. Note presence of black anthracotic pigment.

Clinical features of emphysema

- Dyspnea
- FEV1 to FVC is reduced
- Barrel chested
- Prolonged expiration, sitting forward in a hunched-over position, attempting to squeeze the air out of the lungs with each expiratory effort.
- Dyspnea and hyperventilation ("pink puffers")
- Secondary pulmonary hypertension develops gradually

Complication of emphysema

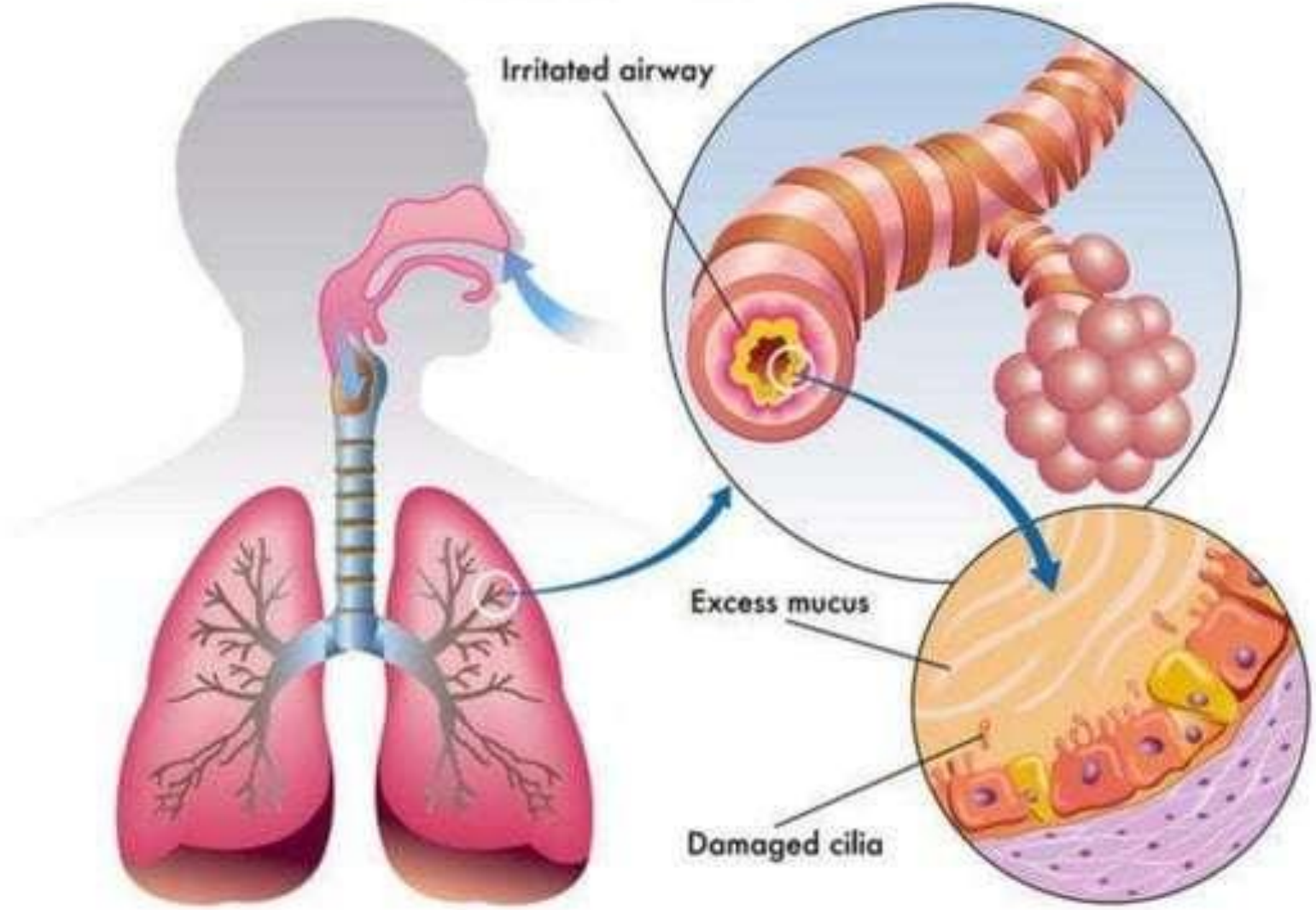
- Pulmonary failure with respiratory acidosis,
- Hypoxia
- Coma
- Right-sided heart failure (cor pulmonale)

Conditions related to emphysema

- Compensatory emphysema
- Obstructive overinflation
- Bullous emphysema
- Mediastinal (interstitial) emphysema

CHRONIC BRONCHITIS

Chronic Bronchitis



Chronic Bronchitis

- 40- to 65-year-old (20-25% are suffering)
- Heavy smoker & pollutants
- Diagnose: ***presence of a persistent productive cough for at least 3 consecutive months in at least 2 consecutive years***
- Early stage: mucoid sputum (w/o obstruction)
- Later stage: intermittent bronchospasm & wheezing

Pathogenesis of chronic bronchitis

1. Irritants
2. Hypertrophy of mucous glands in trachea & main bronchi
3. Hypersecretion of mucus (begin in large airways)
4. Marked increase in mucin-secreting goblet cells
5. Small airway disease & coexist
6. Secondary microbial infection

Morphology of chronic bronchitis

Gross

- Mucosal lining of the **larger airways** usually is **hyperemic and swollen by edema fluid**
- Covered by a layer of **mucinous** or **mucopurulent secretions**
- **Smaller bronchi** and **bronchioles** also may be filled with similar **secretions**

Microscopic

- Trachea and larger bronchi is **enlargement of the mucus-secreting glands**
- **Increase in size** is assessed by the ratio of the thickness of the submucosal gland layer to that of the bronchial wall (the **Reid index**—normally 0.4)
- Inflammatory cells, largely mononuclear but sometimes admixed with neutrophils
- **Goblet cells metaplasia, mucous plugging, inflammation, and fibrosis**
- Severe cases, there may be complete obliteration of the lumen as a consequence of fibrosis (bronchiolitis obliterans). It is the submucosal fibrosis that leads to luminal narrowing and airway obstruction.

$$RI = \frac{gland}{wall}$$

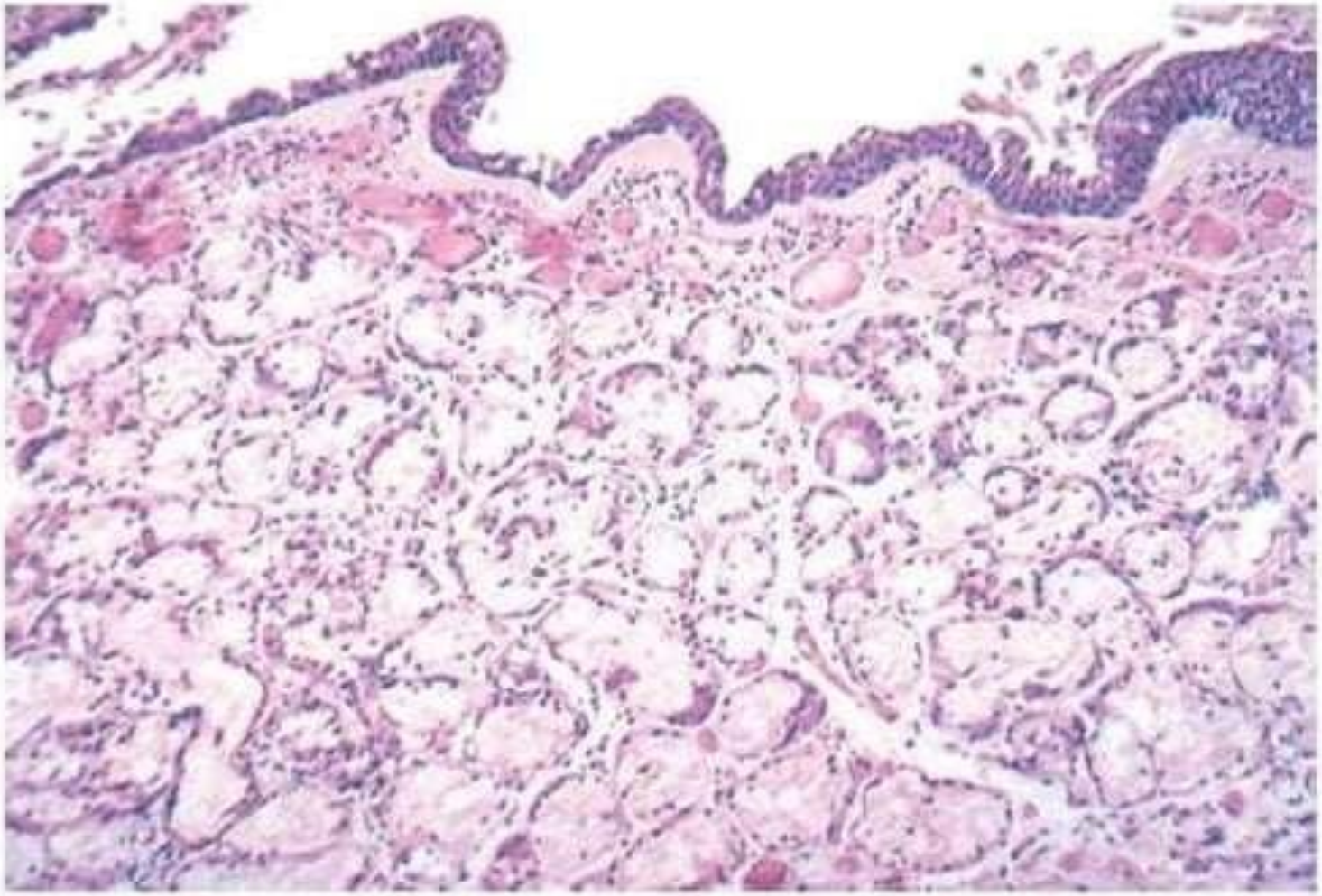


Figure 12–10 Chronic bronchitis. The lumen of the bronchus is *above*. Note the marked thickening of the mucous gland layer (approximately twice-normal) and squamous metaplasia of lung epithelium.

(From the Teaching Collection of the Department of Pathology, University of Texas, Southwestern Medical School, Dallas, Texas.)

Clinical features of chronic bronchitis

- Prominent cough
- Sputum may persist indefinitely without ventilatory dysfunction
- Hypercapnia, hypoxemia, and (in severe cases) cyanosis
- “blue bloaters”

Complication of chronic bronchitis

- Pulmonary hypertension
- Cardiac failure
- Recurrent infections
- Respiratory failure

CHRONIC BRONCHITIS

CLINICAL DIAGNOSIS: DAILY PRODUCTIVE COUGH FOR THREE MONTHS OR MORE, IN AT LEAST TWO CONSECUTIVE YEARS

OVERWEIGHT AND CYANOTIC

ELEVATED HEMOGLOBIN

PERIPHERAL EDEMA

RHONCHI AND WHEEZING

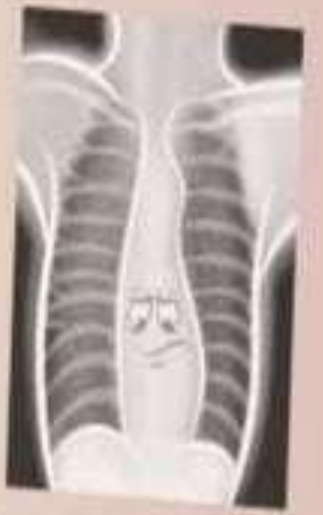
EMPHYSEMA

PATHOLOGIC DIAGNOSIS: PERMANENT ENLARGEMENT AND DESTRUCTION OF AIRSPACES DISTAL TO THE TERMINAL BRONCHIOLE

OLDER AND THIN

SEVERE DYSPNEA

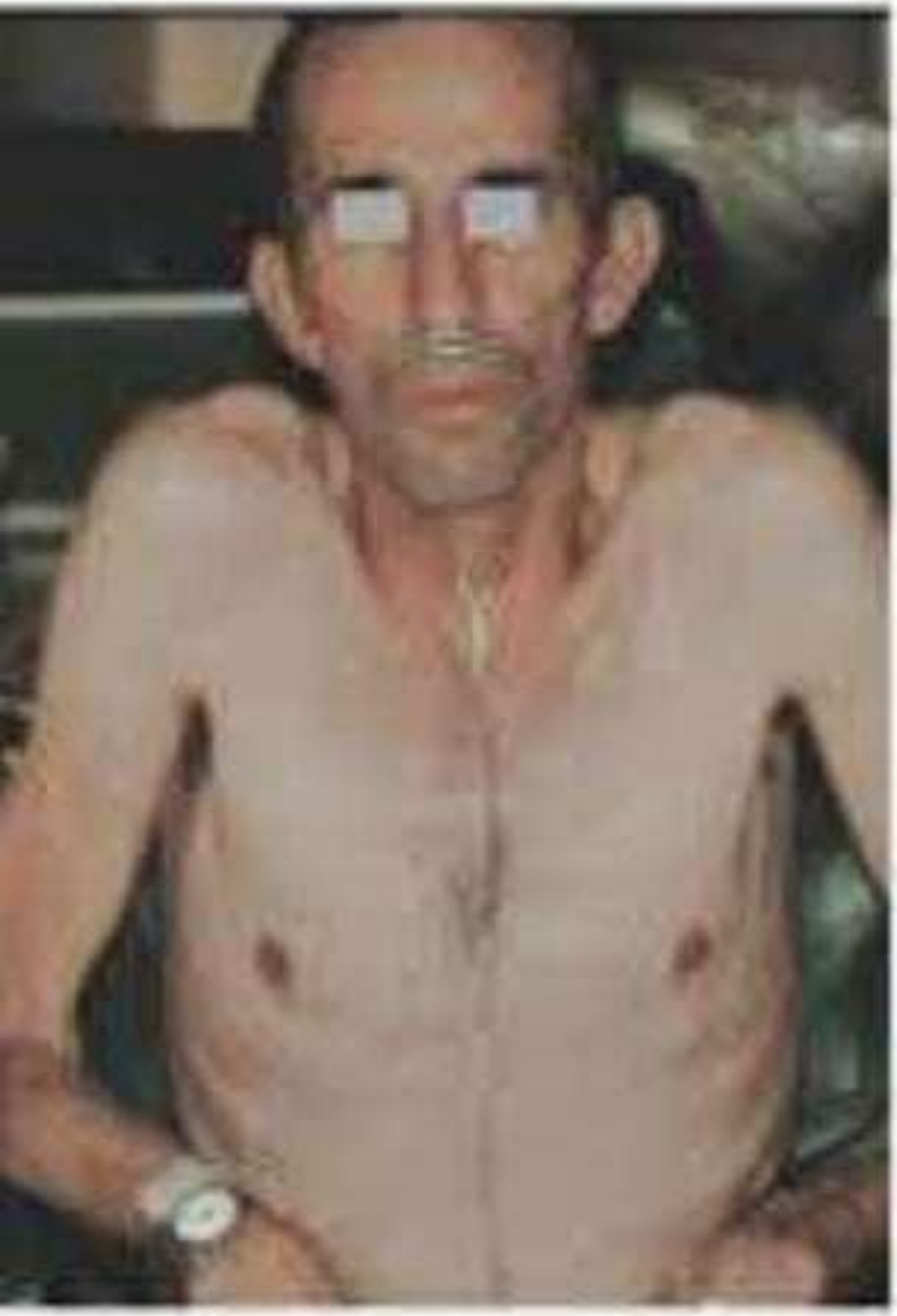
QUIET CHEST

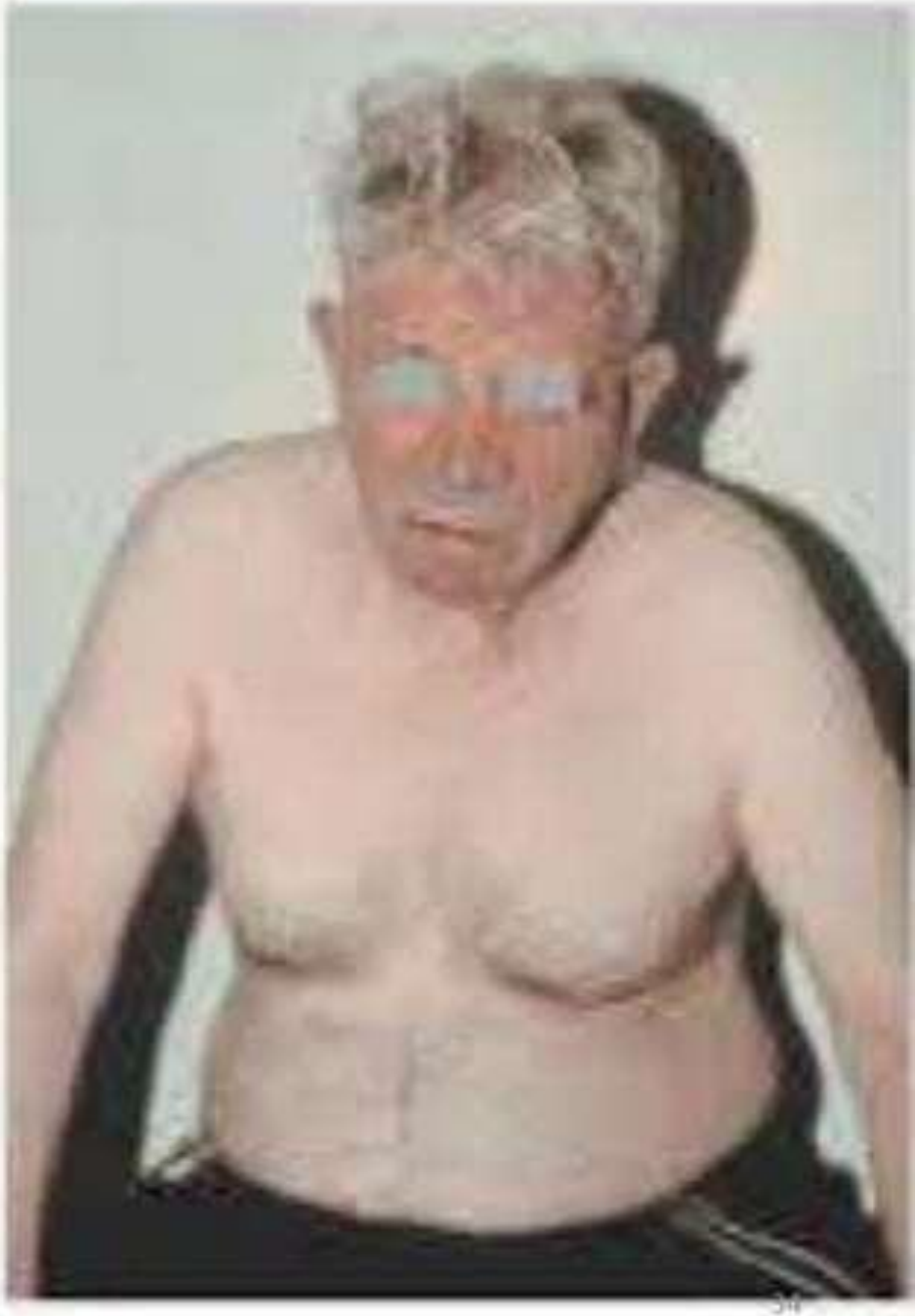


X-RAY: HYPERINFLATION WITH FLATTENED DIAPHRAGMS

Table 11. Clinical Presentation of Chronic Bronchitis and Emphysema

	Symptoms	Signs	Complications
Bronchitis **Blue bloater**	• chronic productive cough • purulent sputum, hemoptysis • mild dyspnea initially	• cyanotic (secondary to hypoxemia and hypercapnia) • peripheral edema from RVF (cor pulmonale) • crackles, wheezes • prolonged expiration if obstructive • frequently obese	• secondary polycythemia due to hypoxemia • pulmonary HTN due to reactive vasoconstriction from hypoxemia • cor pulmonale from chronic pulmonary HTN
Emphysema **Pink puffer**	• dyspnea (+/– exertion) • minimal cough • increased minute ventilation • tachypnea	• pink skin • pursed-lip breathing • accessory muscle use • cachectic appearance due to anorexia + increased work of breathing • hyperinflation/barrel chest, hyperresonant percussion • decreased breath sounds, diaphragmatic excursion	• pneumothorax due to formation of bullae • weight loss due to work of breathing • weight loss due to more work of breathing than bronchitis patients





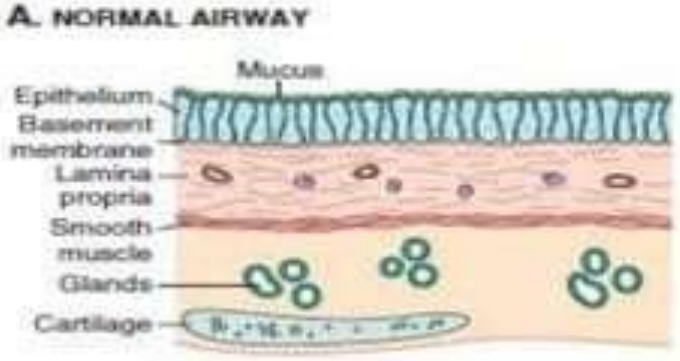
ASTHMA

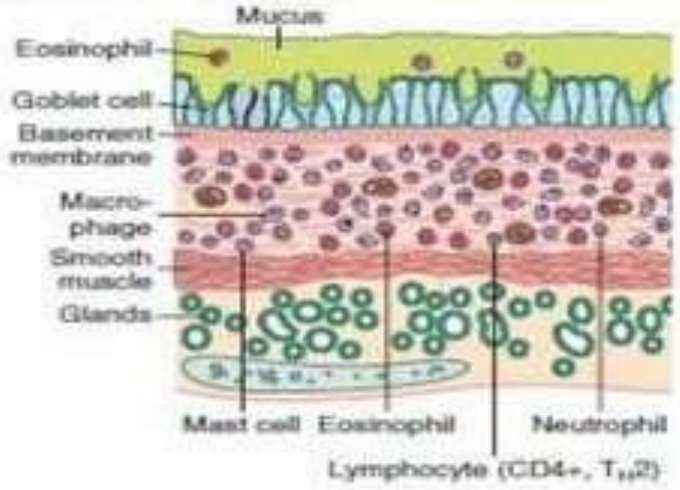
Asthma

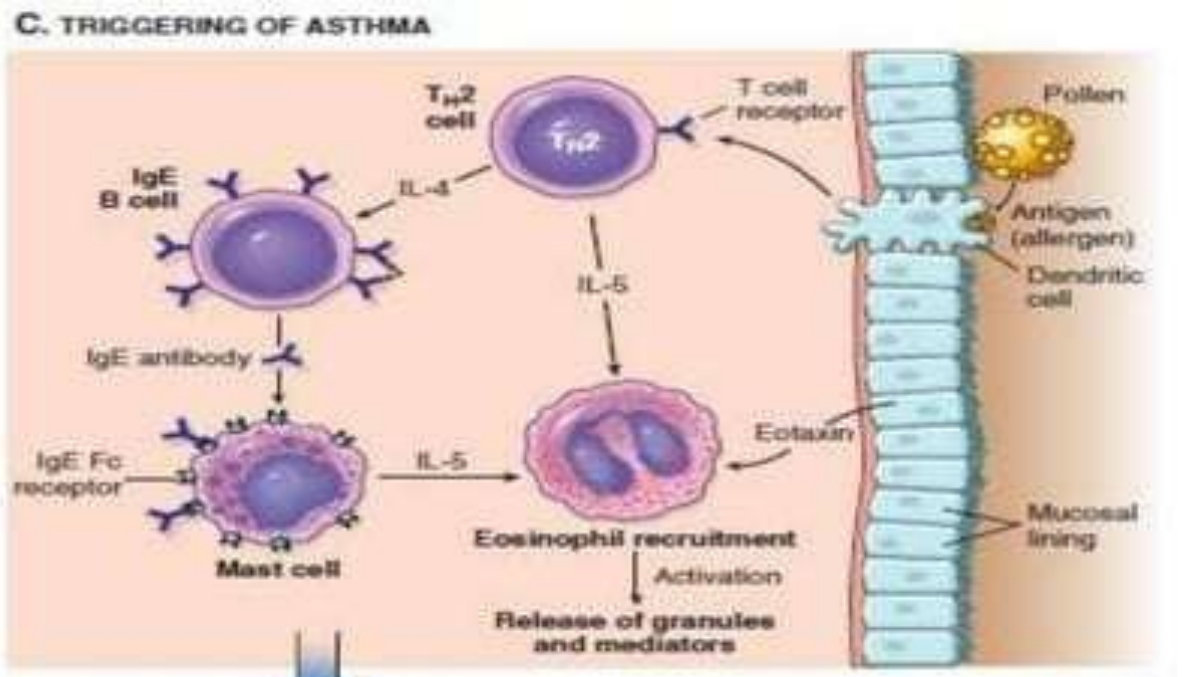
- A chronic inflammatory disorder of the airways
- Recurrent episodes of wheezing, breathlessness, chest tightness, and cough, particularly at night and/or early in the morning
- The hallmarks of the disease are ***intermittent and reversible airway obstruction, chronic bronchial inflammation with eosinophils, bronchial smooth muscle cell hypertrophy and hyperreactivity, and increased mucus secretion***
- Stimuli that trigger attacks in patients would have little or no effect in persons with normal airway

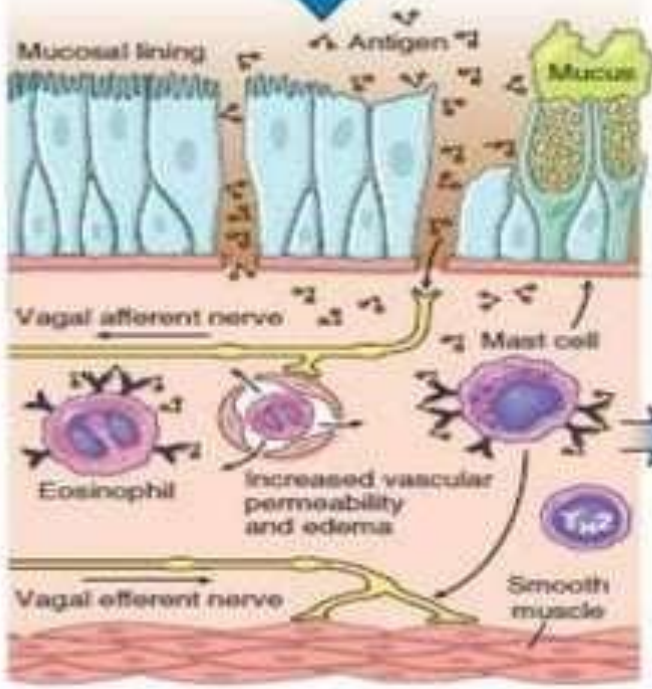
- Eosinophils, mast cells, macrophages, lymphocytes, neutrophils, and epithelial cells. Of note, there has significant increase in the incidence of asthma
- "hygiene hypothesis"
- *Classification:-*
  - ***Atopic asthma*** -***Drug induced asthma***
  - ***Nonatopic asthma*** -***Occupational asthma***
- Bronchospasm can be triggered by diverse mechanisms
- Environmental exposure to irritants (e.g., smoke, fumes), cold air, stress, and exercise.

Pathogenesis of asthma

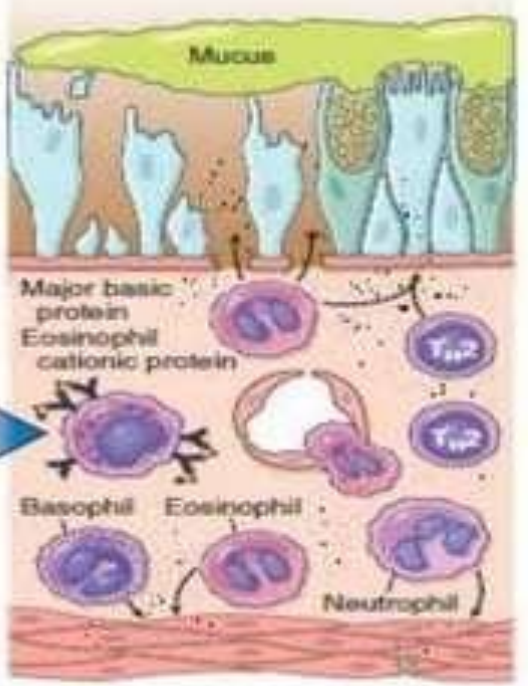








D. IMMEDIATE PHASE (MINUTES)



E. LATE PHASE (HOURS)

Atopic Asthma

- Most **common**
- Usually beginning in childhood, classic example of ***type I IgE–mediated HS***
- *A **positive family** **history***; asthmatic attacks, rhinitis, urticaria, or eczema
- Triggered by **environmental** antigens; Dusts, pollen, animal dander, and foods
- **Infections** can also be a trigger
- A **skin test**; immediate wheal-and flare reaction
- Diagnosis based on serum **radioallergosorbent tests** (RASTs) that identify the presence of IgE specific for a panel of allergens.

Non-Atopic Asthma

- **No** evidence of **allergen sensitization**
- Skin test; usually **negative**
- A positive family history of asthma is less common
- Respiratory infections due to **viruses** and inhaled air **pollutants** are common triggers
- *It is thought that **virus-induced inflammation** of the respiratory mucosa **lowers** the **threshold** of the **subepithelial vagal receptors** to **irritants***
- Humoral and cellular mediators of airway obstruction are common to both atopic and nonatopic variants of asthma
- So they are treated in a similar way

Drug-Induced Asthma

- ***Aspirin***
- Patients with **aspirin sensitivity** present with **recurrent rhinitis** and **nasal polyps**, **urticaria**, and **bronchospasm**
- Precise mechanism remains unknown
- But it is presumed that aspirin inhibits the **cyclooxygenase**-1 pathway of arachidonic acid metabolism without affecting the lipoxygenase route
- Thereby **shifting** the **balance** of **production** toward **leukotrienes** that cause bronchial **spasm**

Occupational Asthma

- Stimulated by fumes (epoxy resins plastics), organic and chemical dusts (wood, cotton, platinum), gases (toluene), and other chemicals
- Asthma attacks usually develop after repeated exposure to the inciting antigen

Morphology of asthma

Gross

- Lungs are **overdistended** because of **overinflation**
- Small areas of **atelectasis**
- **Occlusion** of **bronchi** and **bronchioles** by **thick, tenacious mucous plugs**

Microscopic

- Mucous plugs contain **whorls** of shed epithelium **(Curschmann spirals)**
- **Numerous eosinophils and Charcot-Leyden crystals** (collections of crystalloids made up of eosinophil proteins)
- **"airway remodeling"** include
  - **Thickening** of **airway wall**
  - **Sub-basement membrane fibrosis** (Fig. 12–12)
  - Increased **vascularity** in submucosa
  - An **increase** in **size** of the **submucosal glands** and **goblet cell metaplasia** of the airway epithelium
  - **Hypertrophy** and/or **hyperplasia** of the **bronchial muscle**

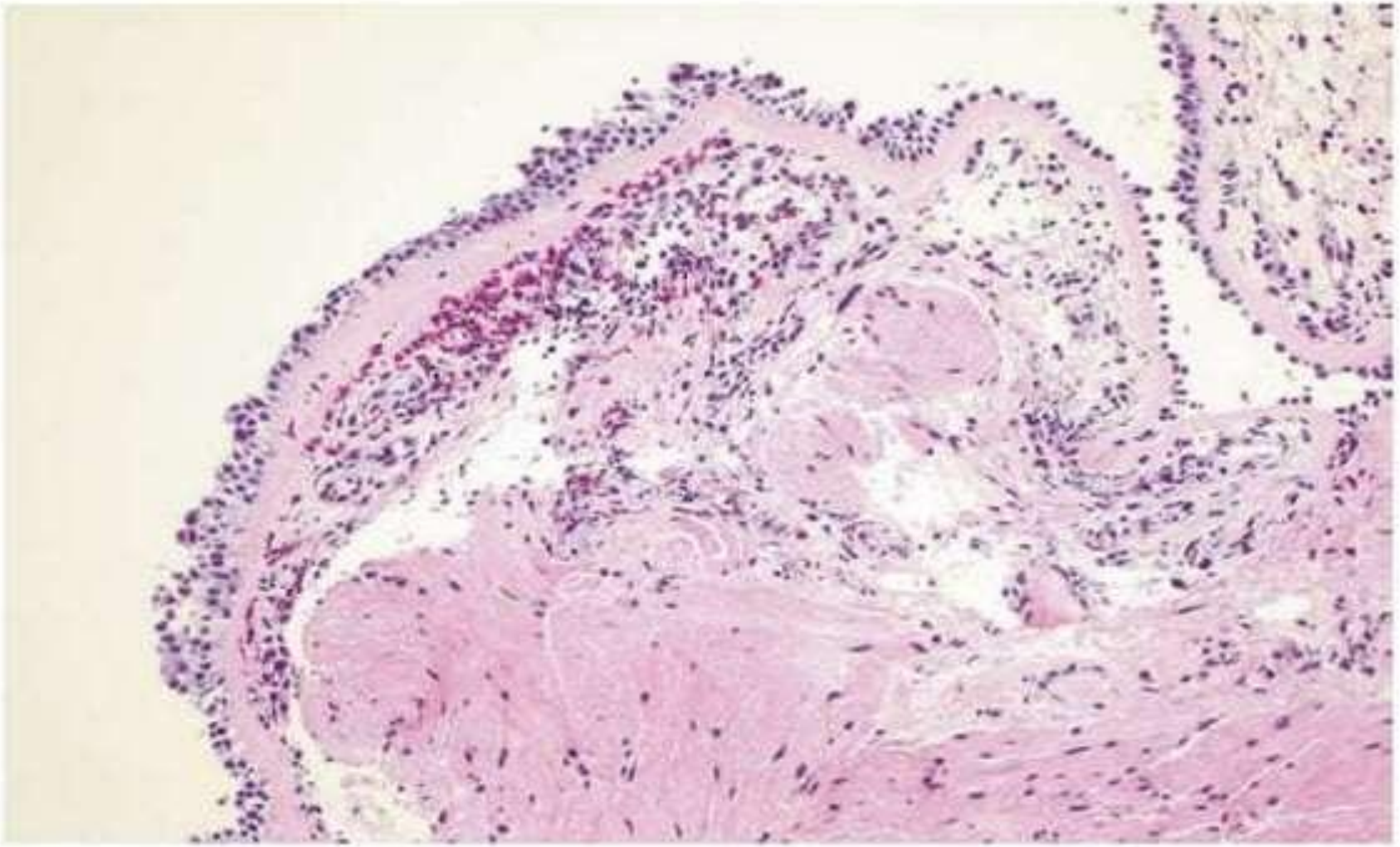


Figure 12–12 Bronchial biopsy specimen from an asthmatic patient showing sub-basement membrane fibrosis, eosinophilic inflammation, and smooth muscle hyperplasia.

Clinical features of asthma

- **Severe dyspnea** with **wheezing**; the chief difficulty lies in expiration
- Progressive **hyperinflation** of the lungs
- Attacks last from 1 to several hours and subside either
- **Spontaneously** or with therapy, usually **bronchodilators** and **corticosteroids**
- Intervals between attacks are characteristically free from overt respiratory difficulties, but persistent, subtle deficits can be detected by **spirometry**
- Occasionally a severe paroxysm occurs that does not respond to therapy and persists for days and even weeks (***status asthmaticus***)
- **Hypercapnia, acidosis,severe hypoxia** may be fatal

BRONCHIECTASIS

Bronchiectasis

Bronchiectasis is the permanent dilation of bronchi and bronchioles caused by destruction of the muscle and the supporting elastic tissue, resulting from or associated with chronic necrotizing infections

- Secondary to persisting infection or obstruction caused by a variety of conditions
- Characteristic symptom: cough & expectoration of copious amounts of foul purulent sputum
- Diagnosis: patient history + radiographic bronchial dilation

Etiology of bronchiectasis

- Bronchial obstruction
- Congenital or hereditary conditions:-
  - ❑In cystic fibrosis
  - ❑In immunodeficiency state
  - ❑Kartagener syndrome
- Necrotizing or suppurative pneumonia

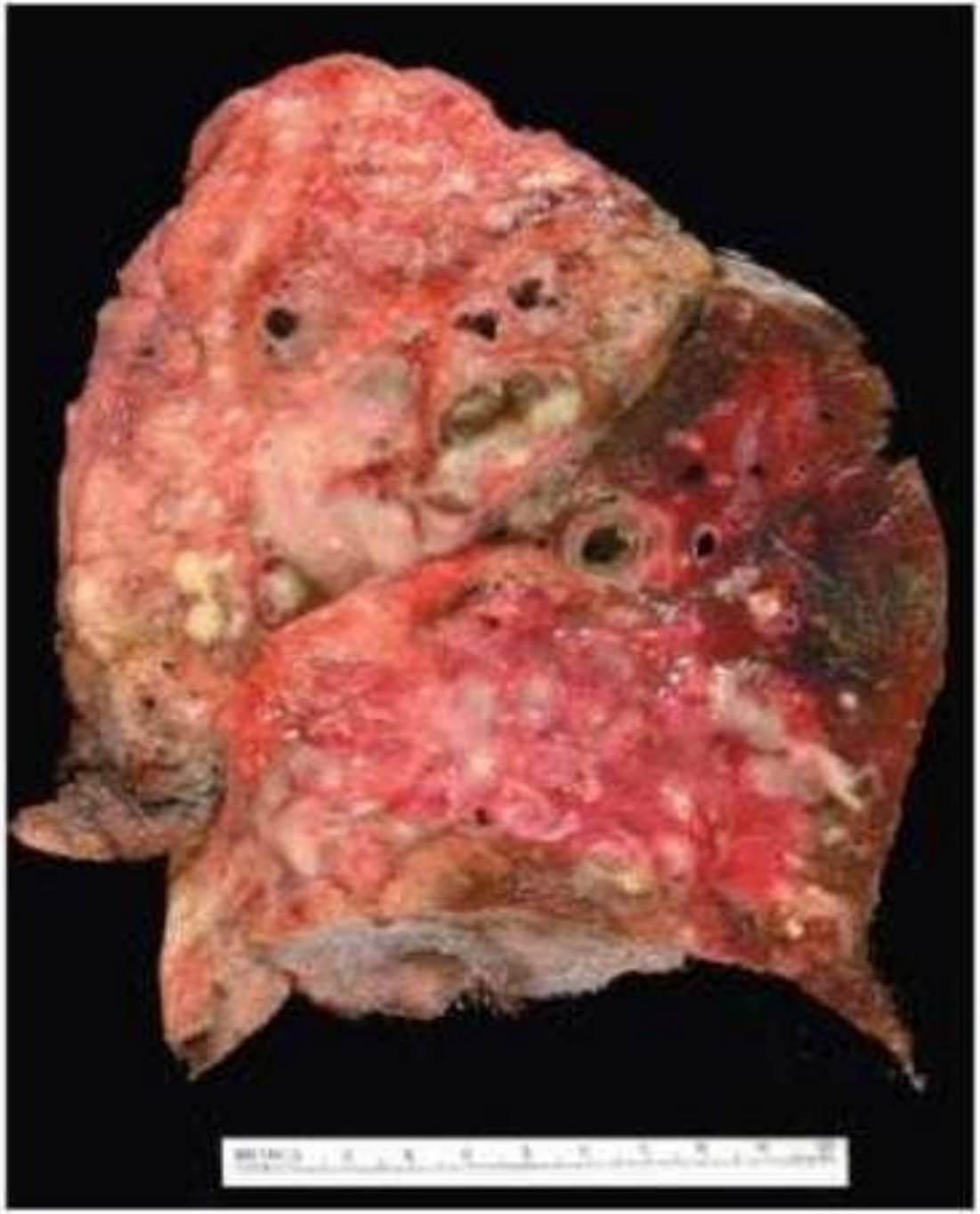
Pathogenesis

- Two processes are crucial
  - **Obstruction**
  - **Chronic persistent infection**
- Either of these may come first
- Usually affects the **lower lobes bilaterally**

Morphology

Gross

- Most severe involvement is more distal bronchi and bronchioles
- Airways are **dilated to as much as 4x their usual**
- Bronchioles can be seen on the pleural surfaces



Microscopic

- Vary with the activity and chronicity of the disease
- In the usual case, a **mixed flora can be cultured from the involved** bronchi
- **Hyperplasia** of epithelium → **metaplasia** of epithelium into squamous cell
- Full-blown active case:-
  - an **intense acute and chronic inflammatory exudate within the walls of the bronchi and bronchioles**
  - **Desquamation** of lining epithelium cause extensive areas of ulceration

- **Healing**: lining epithelium may regenerate completely
- **Healing in chronic case**: Fibrosis of the bronchial and bronchiolar walls and peribronchiolar fibrosis
- In some instances, **necrosis** destroys the bronchial or bronchiolar walls → formation of an **abscess cavity** within which a **fungus ball** may develop

Clinical features of bronchiectasis

- Severe, persistent cough with expectoration of mucopurulent, sometimes fetid sputum
- Sputum; flecks of blood, frank hemoptysis
- Symptoms are episodic, precipitated by upper respiratory tract infections or new pathogenic agents
- Clubbing
- Hypoxemia, hypercapnia, pulmonary hypertension and cor pulmonale (rare)

Complication of bronchiectasis

- Metastatic brain abscesses
- Reactive amyloidosis

Conclusion

Points discussed:-

- Emphysema
- Chronic bronchitis
- Asthma
- Bronchiectasis

References

- Robbins Pathology 9th edition
- Internet


Thank
You!