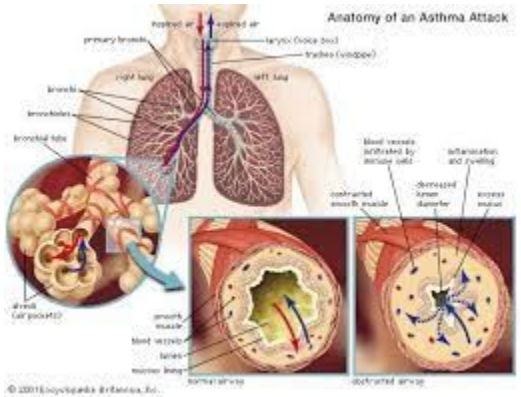
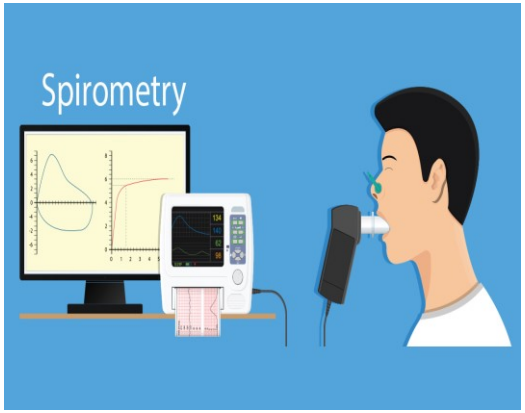
PATHOPHYSIOLOGY OF RESPIRATORY SYSTEM





Course Name: Pathophysiology

Course Code: 0520300

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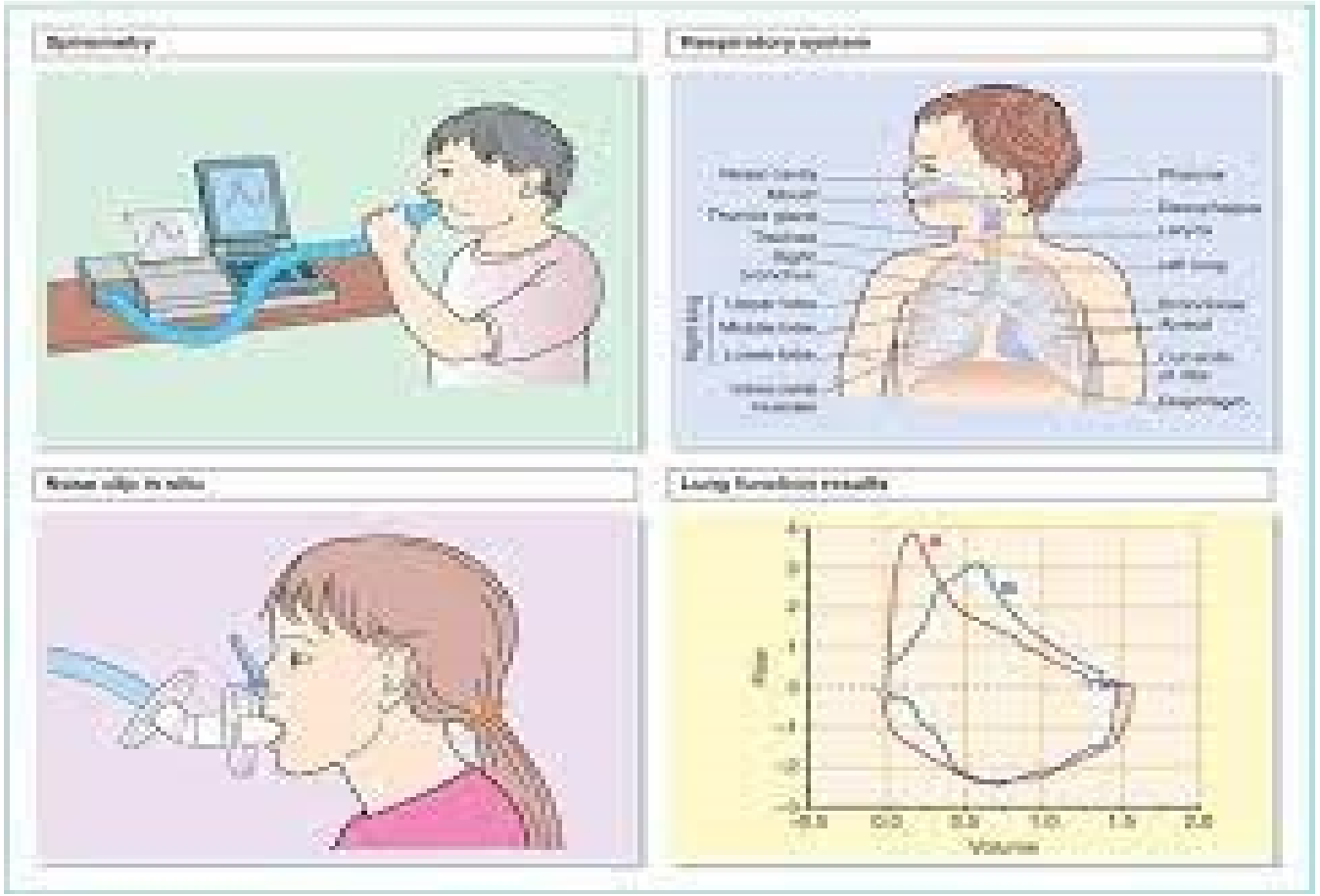
Spirometry


Spirometry
Respiratory system
Nasal cavity
Pharynx
Larynx
Trachea
Left lung
Right lung
Bronchioles
Alveoli
Lobar bronchi
Middle lobe
Lower lobe
Pulmonary artery
Pulmonary vein
Diaphragm
Nasal slip in situ
Lung function results
Volume

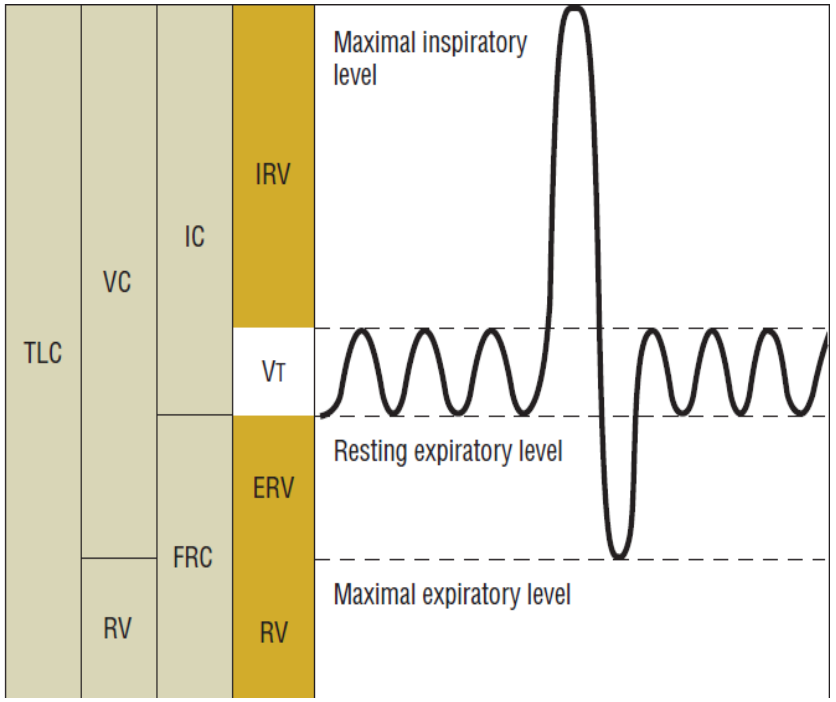
Lung volumes and capacities

- ✓ *Forced vital capacity (*FVC), which represents the total amount of air that can be exhaled, can be expressed as a series of timed volumes.
- ✓ The *forced expiratory volume in the first second of expiration* (FEV1) is the volume of air exhaled during the first second of the FVC maneuver.
- ✓ Although FEV1 is a volume, it conveys information on obstruction because it is measured over a known time interval. FEV1 depends on the volume of air within the lung and the effort during exhalation; therefore, it can be diminished by a decrease in TLC or by a lack of effort.
- ✓ A more sensitive way to measure obstruction is to express FEV1 as a ratio of FVC. This ratio is independent of the patient's size or total lung capacity (TLC); therefore, FEV1/FVC is a specific measure of airway obstruction with or without restriction. Normally, this ratio is $\geq$75%, and any value <70% to 75% suggests obstruction.

Revision/ Lung volumes and capacities

Lung volumes and capacities:

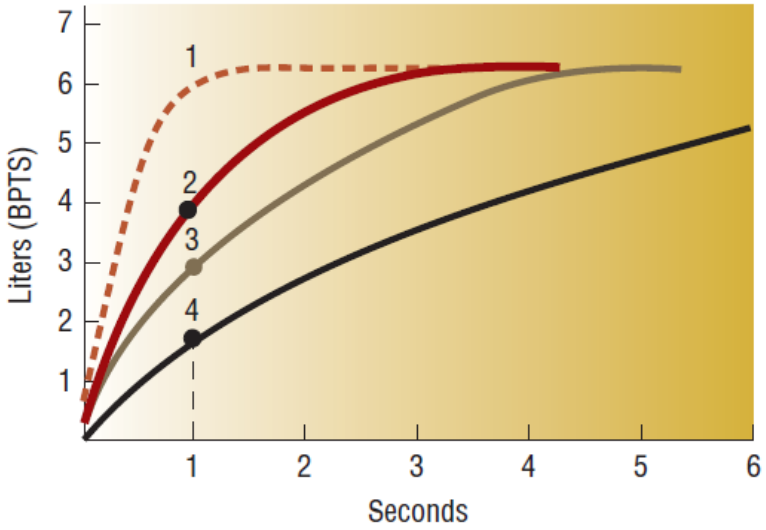
1- ERV, expiratory reserve volume
2- FRC, functional residual capacity
3- IC, inspiratory capacity
4- IRV, inspiratory reserve volume
5- RV, residual volume
6- TLC, total lung capacity
7- VC, vital capacity
8- VT, tidal volume



SPIROMETRY/FLOW–VOLUME LOOP

- Spirometry is the most widely available and useful PFT.
- It takes only 15 to 20 minutes, carries no risks, and provides information about obstructive and restrictive disease.
- Spirometry allows for measurement of all lung volumes and capacities except RV, FRC, and TLC; it also allows assessment of FEV1 and FEF25%–75%.
- Spirometry measurements can be reported in two different formats—standard spirometry (Fig. 27–2) and the flow–volume loop (Fig. 27–3).

FIGURE 27-2. Standard spirometry.

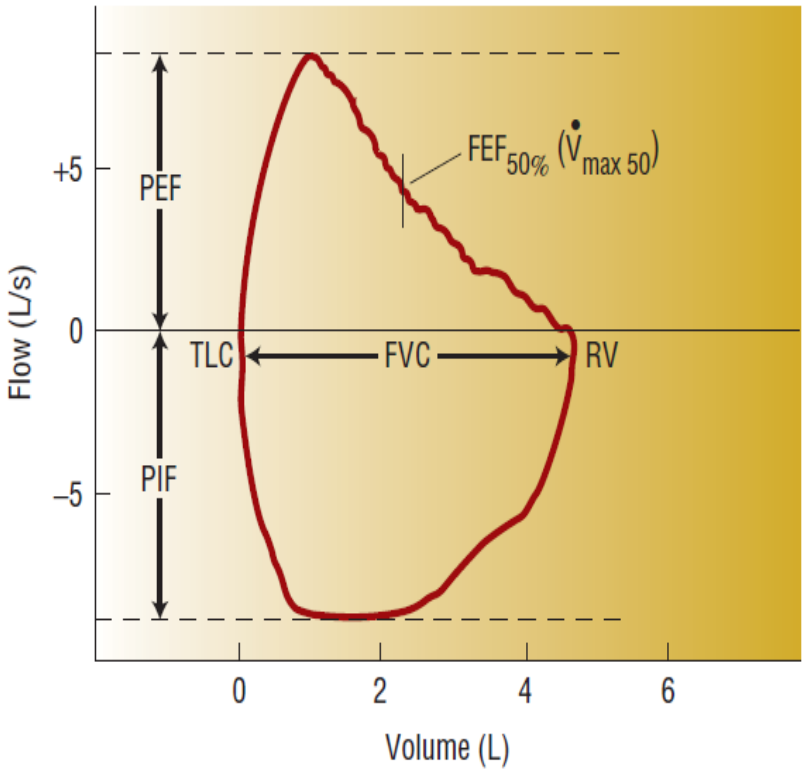


- Curve 1 is for a normal subject with normal FEV1
- Curve 2 is for a patient with mild airways obstruction
- Curve 3 is for a patient with moderate airways obstruction
- Curve 4 is for a patient with severe airways obstruction

→ *(BPTS, body temperature saturated with water vapor.)*

FIGURE 27-3. Normal flow–volume loop.

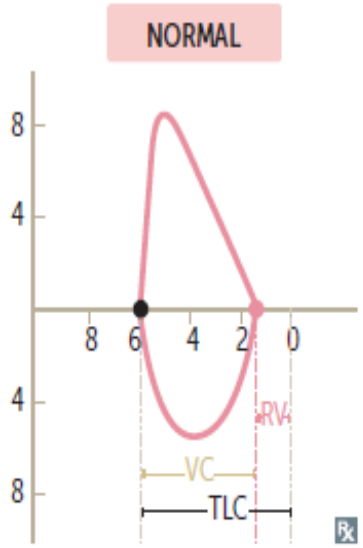
- Flows are measured on the vertical (y) axis, and lung volumes are measured on the horizontal (x) axis.
- Forced vital capacity (FVC) can be read from the tracing as the maximal horizontal deflection.
- Instantaneous flow (V•max) at any point in FVC also can be measured directly.

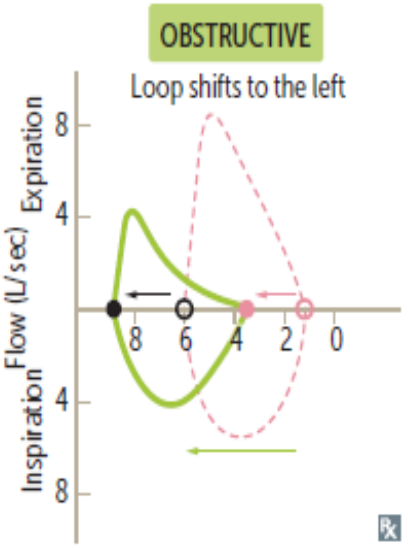


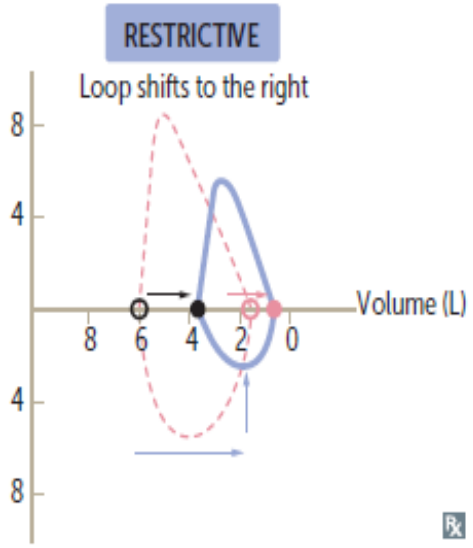
- FEF50%, forced expiratory flow at 50% of forced vital capacity
- PEF, peak expiratory flow
- PIF, peak inspiratory flow
- RV, residual volume
- TLC, total lung capacity

Flow-volume loops

FLOW-VOLUME PARAMETER	Normal	Obstructive lung disease	Restrictive lung disease
RV		↑	↓
FRC		↑	↓
TLC		↑	↓
FEV_1	>80% predicted	↓↓	↓
FVC	>80% predicted	↓	↓
FEV_1/FVC	>70%	↓ FEV_1 decreased more than FVC	Normal or ↑ FEV_1 decreased proportionately to FVC







Common Bronchial and Pulmonary Diseases: lung pathology

A common approach in the study of lung pathology, is to organize lung diseases into those affecting

(1) The airways,

(2) The interstitium,

(3) The pulmonary vascular system.

This division into discrete compartments is deceptively neat. In reality, disease in one compartment is generally accompanied by alterations of morphology and function in another.

OBSTRUCTIVE VERSUS RESTRICTIVE PULMONARY DISEASES

Diffuse pulmonary diseases can be classified in two categories

(1) Obstructive disease (airway disease), characterized by limitation of airflow usually resulting from an increase in resistance caused by partial or complete obstruction at any level→ time

(2) Restrictive disease, characterized by reduced expansion (compliance) of lung parenchyma accompanied by decreased total lung capacity → vol

(Diffuse= involve the pulmonary parenchyma and interfere with gas exchange)

*FIRST: Obstructive Lung (*Airway) Diseases

In their prototypical forms, the four disorders in this group:

1- EMPHYSEMA

2- CHRONIC BRONCHITIS

3- ASTHMA,

4- BRONCHIECTASIS

Chronic Obstructive Pulmonary Disease (COPD)

The diseases have distinct clinical and anatomic characteristics (Table 13.1), but overlaps between emphysema, chronic bronchitis, and asthma are common.

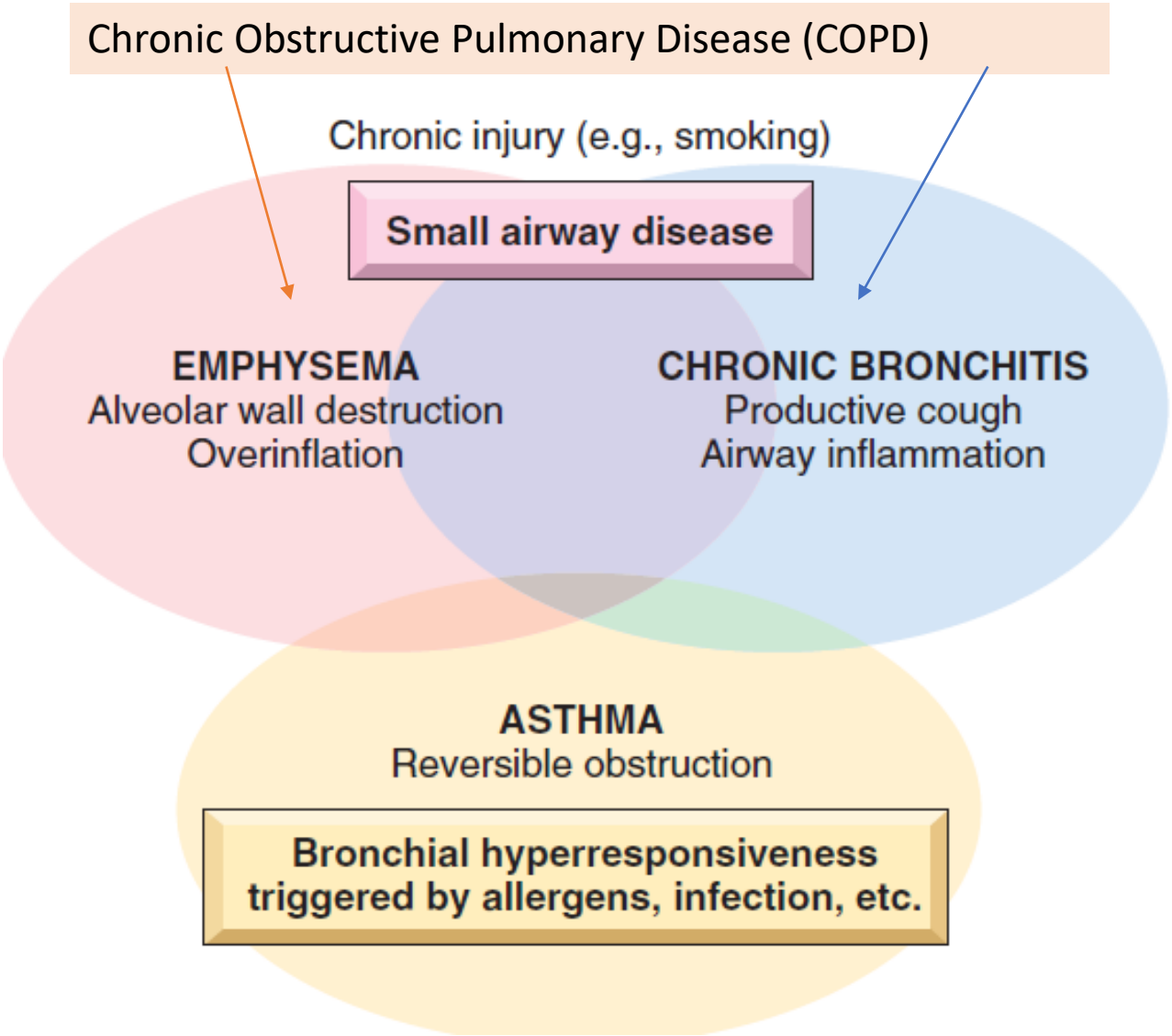
Table 13.1 Disorders Associated With Airflow Obstruction: The Spectrum of Chronic Obstructive Pulmonary Disease

Clinical Entity	Anatomic Site	Major Pathologic Changes	Etiology	Signs/Symptoms
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
Emphysema	Acinus	Air space enlargement, wall destruction	Tobacco smoke	Dyspnea
Small airway disease, bronchiolitis*	Bronchiole	Inflammatory scarring, partial obliteration of bronchioles	Tobacco smoke, air pollutants	Cough, dyspnea

*Can be present in all forms of obstructive lung disease or by itself.

*** Additional branching of bronchioles leads to *terminal bronchioles*; the part of the lung distal to the terminal bronchiole is called an *acinus*.

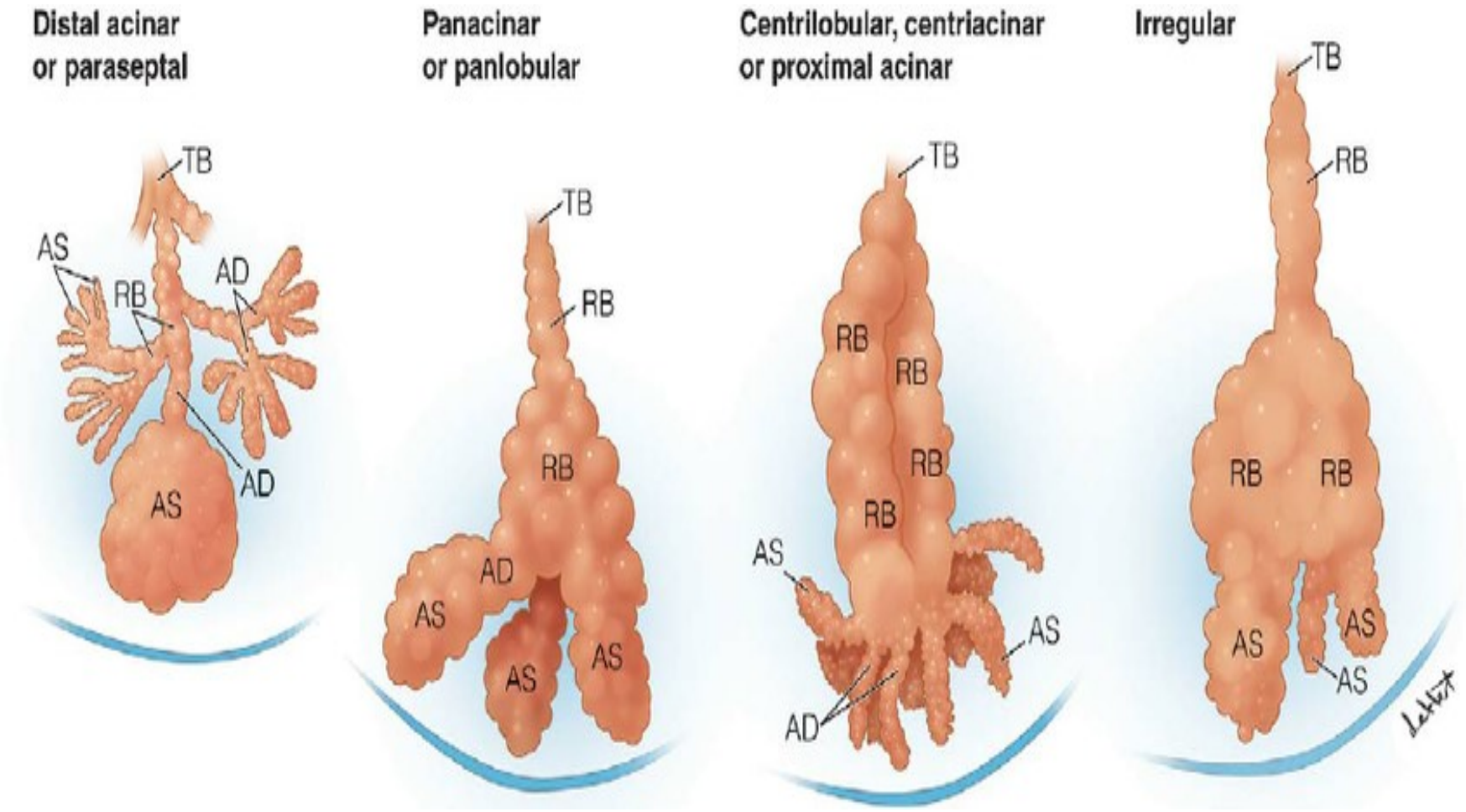
Fig. 13.4 Schematic representation of overlap between chronic obstructive lung diseases.



Obstructive Lung Diseases : 1- Emphysema

Emphysema is a chronic obstructive airway disease characterized by enlargement of air spaces distal to terminal bronchioles.

- Subtypes include centriacinar (most common: smoking-related), panacinar (seen in α1-anti-trypsin deficiency), distal acinar, and irregular.
- Smoking and inhaled pollutants cause ongoing accumulation of inflammatory cells, which are the source of proteases such as elastases that irreversibly damage alveolar walls.
- Patients with uncomplicated emphysema present with increased chest volumes, dyspnea, and relatively normal blood oxygenation at rest (“pink puffers”).
- Most patients with emphysema also have signs and symptoms of concurrent chronic bronchitis, since cigarette smoking is a risk factor for both.



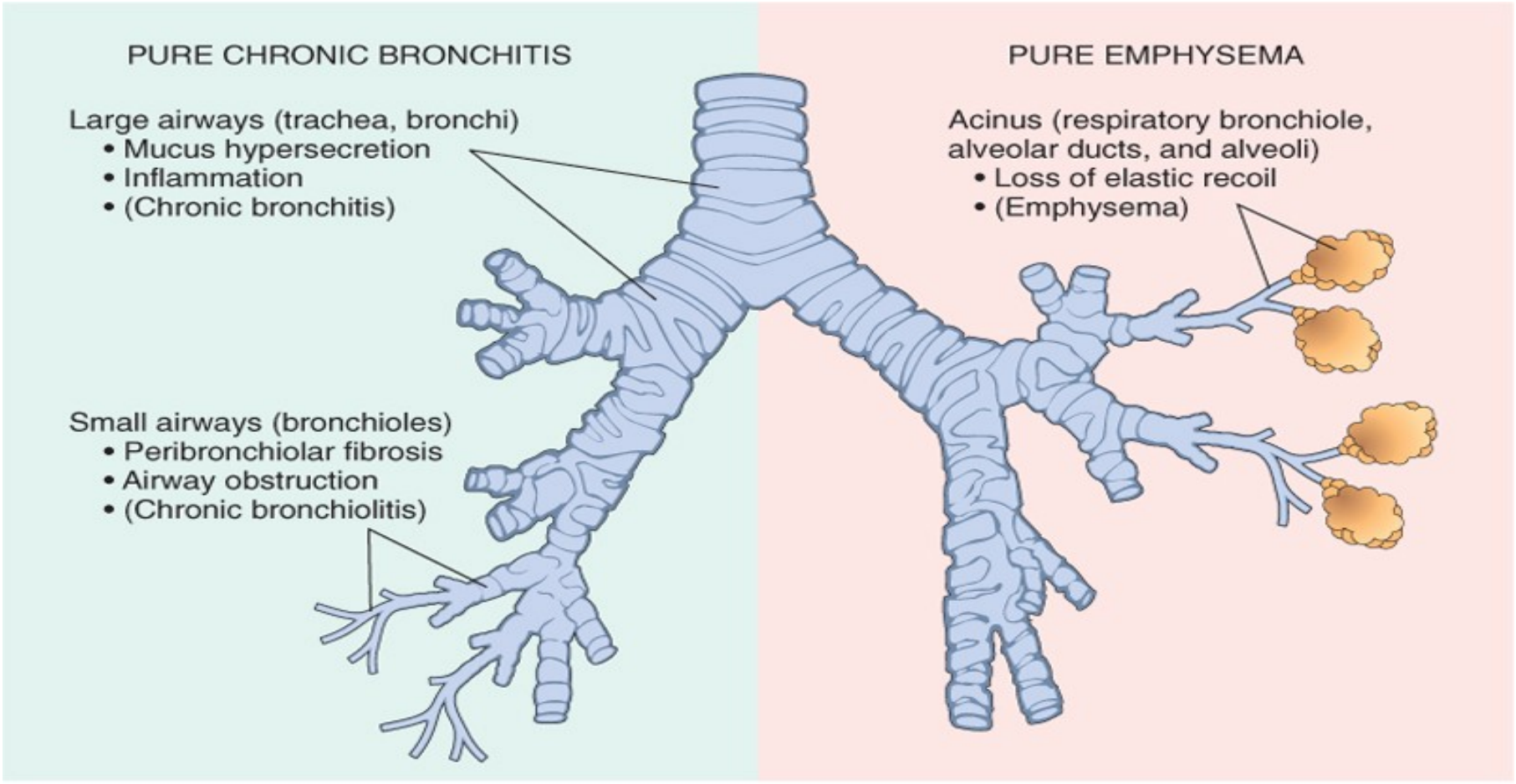
Source: https://www.physio-pedia.com/Emphysema

Obstructive Lung Diseases: 2- Chronic Bronchitis

- Chronic bronchitis is defined as persistent productive cough for at least 3 consecutive months in at least 2 consecutive years→ Blue bloaters
- Cigarette smoking is the most important underlying risk factor; air pollutants also contribute.
- Chronic airway obstruction largely results from small airway disease (chronic bronchiolitis) and coexistent emphysema.
- Histologic examination demonstrates enlargement of mucus- excreting glands, goblet cell metaplasia, and bronchiolar wall fibrosis.

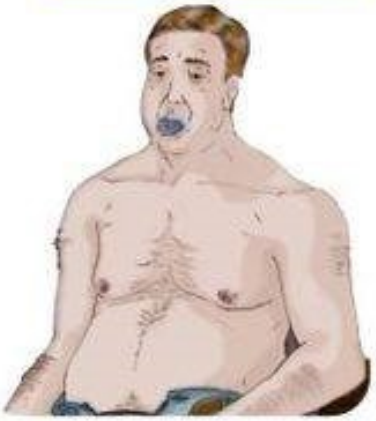
Anatomic distribution of pure chronic bronchitis and pure emphysema.

In chronic bronchitis the small-airway disease (chronic bronchiolitis) results in airflow obstruction, while the large-airway disease is primarily responsible for the mucus hypersecretion.



Blue Bloater

Chronic Bronchitis



Symptoms

- Chronic , productive cough
- Purulent sputum
- Hemoptysis
- Mild dyspnea initially
- Cyanosis (due to hypoxemia)
- Peripheral edema (due to cor pulmonale)
- Crackles, wheezes
- Prolonged expiration
- Obese

Complications

- Secondary polycythemia vera due to hypoxemia
- Pulmonary hypertension due to reactive vasoconstriction from hypoxemia
- Cor pulmonale from chronic pulmonary hypertension

Pink Puffer

Emphysema

Symptoms

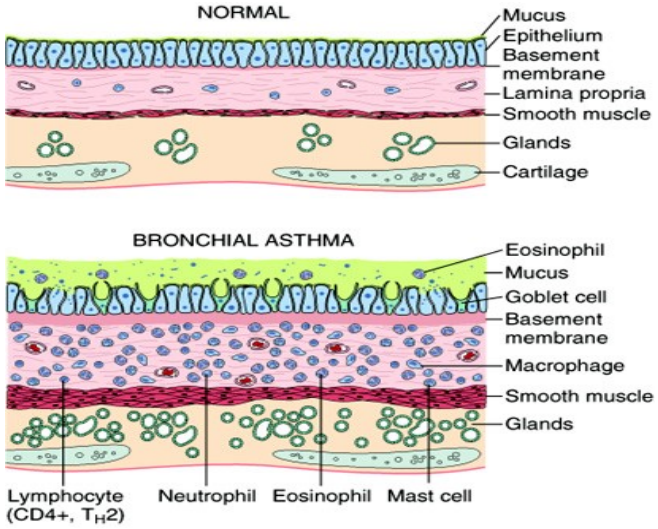
- Dyspnea
- Minimal cough
- Increased minute ventilation
- Pink skin, Pursed-lip breathing
- Accessory muscle use
- Cachexia
- Hyperinflation, barrel chest
- Decreased breath sounds
- Tachypnea

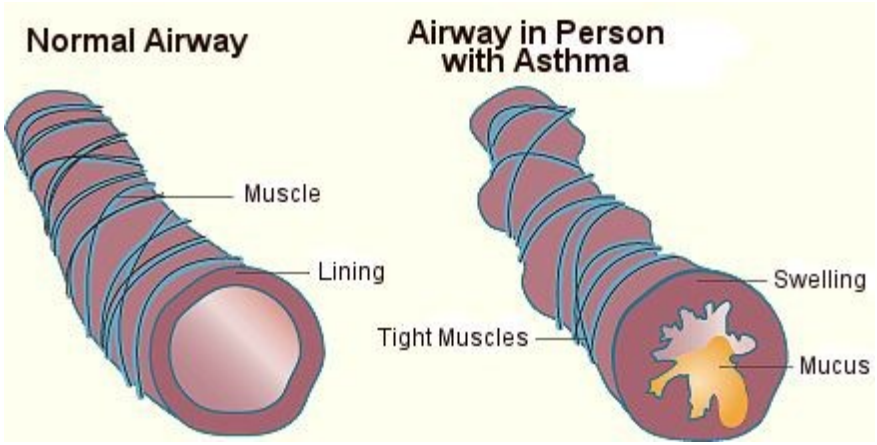
Complications

- Pneumothorax due to bullae
- Weight loss due to work of breathing

Obstructive Lung Diseases : 3- Asthma

- ✓Asthma is a chronic inflammatory disorder of the airways that causes recurrent episodes of wheezing, breathlessness, chest tightness, and cough, particularly at night and/or early in the morning.
- ✓Eosinophils are key inflammatory cells found in almost all subtypes of asthma; eosinophil products (such as major basic protein) are responsible for airway damage.





Obstructive Lung Diseases : 3- Asthma

TYPES OF ASTHMA:

1- ATOPIC ASTHMA

- Most often is caused by a *type 2 helper T cells (*T_H2) and IgE-mediated immunologic reaction to environmental (extrinsic) allergens and is characterized by early-phase (immediate) and late-phase reactions.
- The T_H2 cytokines IL-4, IL-5, and IL-13 are important mediators.
- Non- T_H2 inflammation also has roles in atopic asthma that are being defined.
- **This is the most common type of asthma and is a classic example of type I IgE–mediated hypersensitivity reaction**
- It usually begins in childhood.
- A positive family history of atopy and/or asthma is common, and the onset of asthmatic attacks is often preceded by allergic rhinitis, urticaria, or eczema.
- Attacks may be triggered by allergens in dust, pollen, animal dander, or food, or by infections. A skin test with the offending antigen results in an immediate wheal-and-flare reaction. Atopic asthma also can be diagnosed based on serum radioallergosorbent tests (RASTs) that identify the presence of IgEs that recognize specific allergens.

Obstructive Lung Diseases : 3- Asthma (REMODELLING)

- Airway remodeling (sub-basement membrane thickening and hypertrophy of bronchial glands and smooth muscle) adds an irreversible component to the obstructive disease.

- atopic asthma is characterized by structural changes in the bronchial wall, referred to as *"airway remodeling.“*

- These changes include hypertrophy of bronchial smooth muscle and deposition of subepithelial collagen.

Obstructive Lung Diseases : 3- Asthma

TYPES OF ASTHMA: (continued-1)

2- NONATOPIC ASTHMA

- Triggers for nonatopic asthma are less clear but include aspirin intake, viral infections, stress, exercise and inhaled air pollutants, which also can trigger atopic asthma.
- Intrinsic :initiated by diverse **non-immune** mechanisms
- Patients with nonatopic forms of asthma do not have evidence of allergen sensitization, and skin test results usually are negative. In the asthmatic subjects the bronchial response, manifested as spasm, is much more severe and sustained.
- A positive family history of asthma is less common.
- Respiratory infections due to viruses (e.g., rhinovirus, parainfluenza virus) and inhaled air pollutants (e.g., sulfur dioxide, ozone, nitrogen dioxide) are common triggers.
- It is thought that virus-induced inflammation of the respiratory mucosa lowers the threshold of the subepithelial vagal receptors to irritants. Although the connections are not well understood, the ultimate humoral and cellular mediators of airway obstruction (e.g., eosinophils) are common to both atopic and nonatopic variants of asthma, so they are treated in a similar way.

Obstructive Lung Diseases : 3- Asthma

TYPES OF ASTHMA: (continued-2)

3- DRUG-INDUCED ASTHMA

- Several pharmacologic agents provoke asthma, aspirin being the most striking example.
- Patients with aspirin sensitivity present with recurrent rhinitis, nasal polyps, urticaria, and bronchospasm.
- The precise pathogenesis is unknown but is likely to involve some abnormality in prostaglandin metabolism stemming from inhibition of cyclooxygenase by aspirin.

4- OCCUPATIONAL ASTHMA

- Occupational asthma may be triggered 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(s).

Obstructive Lung Diseases : 3- Asthma
STAGES OF ASTHMA

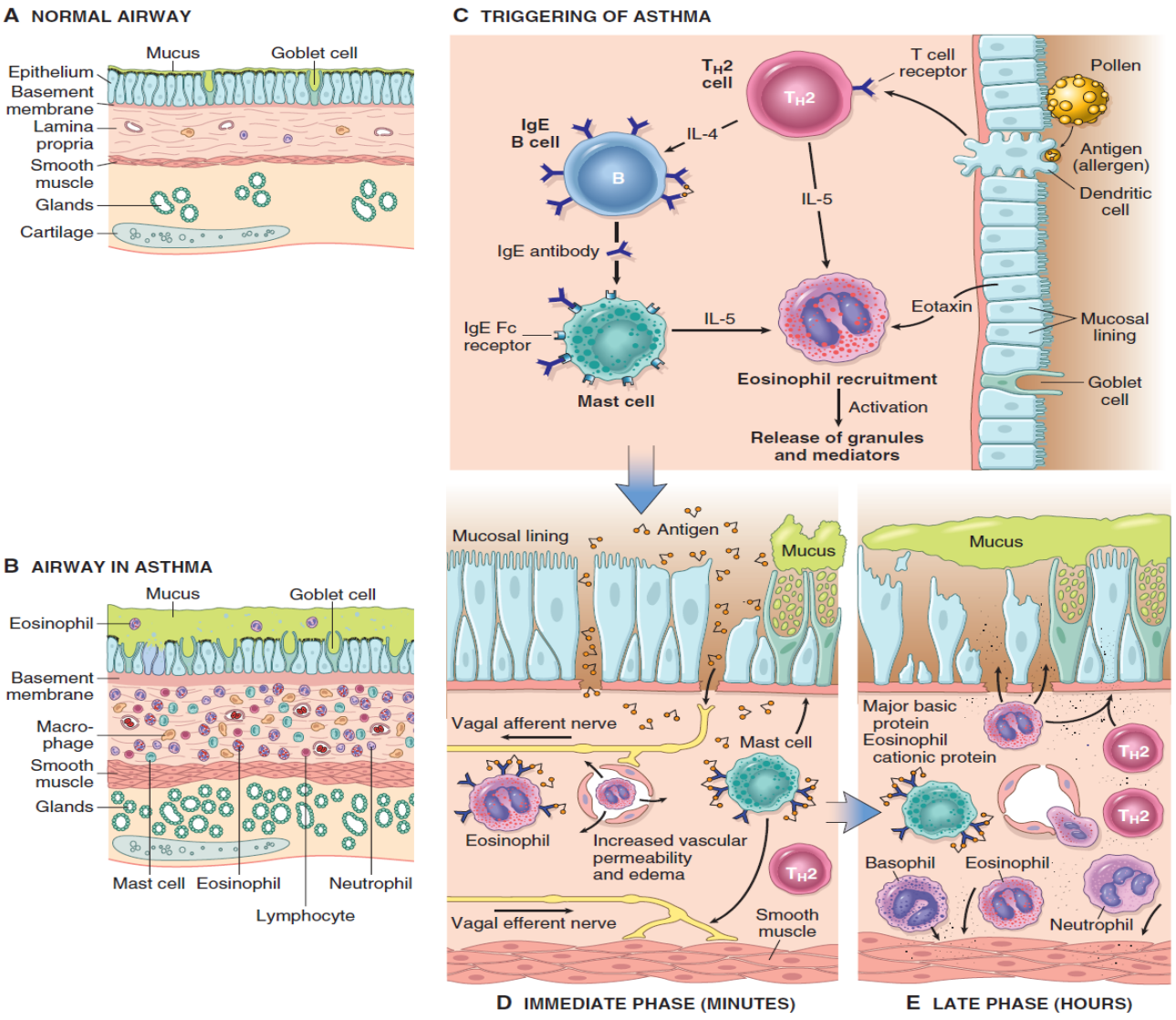
1. *Early Phase of Asthma*

- Occurs rapidly (less than 30 min) after exposure to an asthmatic trigger.
- The early phase of asthma is characterized by marked constriction and spasm of bronchial airways that is accompanied by airway edema and the production of excess mucus. Activation of parasympathetic nervous system may also occur and can exacerbate bronchospasm and further increase mucus production.

2. *Late Phase of Asthma*

- The late phase of asthma can occur several hours after the initial onset of symptoms and manifests mainly as an inflammatory response.
- Infiltration of immune cells such as neutrophils, eosinophils and basophils further enhance the inflammatory response. Cytokines such as tumor necrosis factor (TNF-α) and interleukins (IL-4, -5, and -13) have also been shown to play an important role in the airway inflammation associated with atopic asthma.

Obstructive Lung Diseases : 3- Asthma
STAGES OF ASTHMA



Obstructive Lung Diseases : 3- Asthma

CLASSIFICATION OF ASTHMA

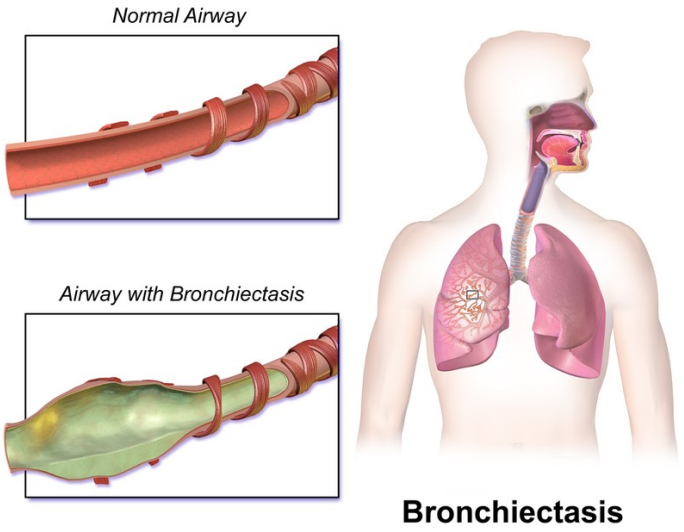
Table 14.9 Clinical Classification of Asthma

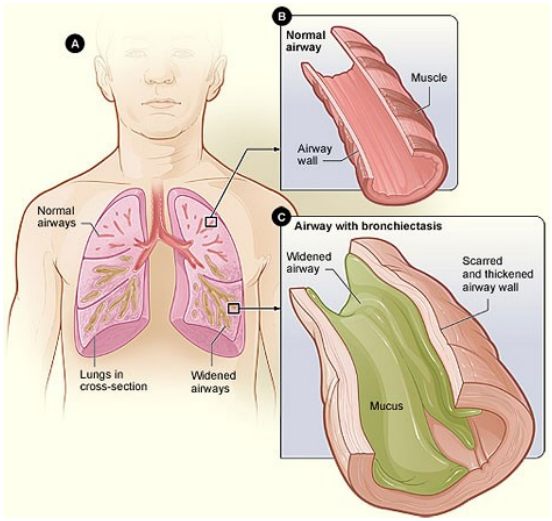
Mild intermittent — Attacks occur 2 times per week or less
Mild persistent — Attacks occur more than 2 times per week
Moderate persistent — Attacks occur daily or almost daily and are severe enough to affect activity
Severe persistent — Attacks are very frequent and persist for a long period of time; attacks severely limit activity

Components of Severity		Classification of Asthma Severity (Youths ≥12 years of age and adults)			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment **Normal FEV_1/FVC:** **8–19 yr 85%** **20 –39 yr 80%** **40 –59 yr 75%** **60 –80 yr 70%**	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3–4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not >1x/day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV_1 between exacerbations • FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 ≥80% predicted • FEV_1/FVC normal	• FEV_1 >60% but <80% predicted • FEV_1/FVC reduced 5%	• FEV_1 <60% predicted • FEV_1/FVC reduced >5%
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year (see note)	≥2/year (see note) →		
		← Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. →			
		Relative annual risk of exacerbations may be related to FEV_1			

Obstructive Lung Diseases: 4- Bronchiectasis

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





SECOND: Restrictive Diseases

- FVC is reduced
- the expiratory flow rate is normal or reduced proportionately.
- Hence, *the ratio of FEV_1 to FVC is near normal.*

- ↓lung volumes (↓ FVC and TLC). PFTs: normal or ↑FV1/FVC ratio. Patient presents with short, shallow breaths.

Types of Restrictive lung diseases

1- Altered respiratory mechanics (extrapulmonary):

- ✓ Respiratory muscle weakness—polio, myasthenia gravis, Guillain-Barre syndrome, ALS
- ✓ Chest wall abnormalities—scoliosis, severe obesity

Types of Restrictive lung diseases (continued)

2- Diffuse parenchymal lung diseases, also called interstitial lung diseases (pulmonary):

- ✓ Pneumoconioses (eg, coal workers' pneumoconiosis, silicosis, asbestosis)
- ✓ Sarcoidosis: bilateral hilar lymphadenopathy, noncaseating granulomas; ↑ACE and Ca2+
- ✓ Idiopathic pulmonary fibrosis
- ✓ Granulomatosis with polyangiitis
- ✓ Pulmonary Langerhans cell histiocytosis (eosinophilic granuloma)
- ✓ Hypersensitivity pneumonitis
- ✓ Drug toxicity (eg, bleomycin, busulfan, amiodarone, methotrexate)
- ✓ Acute respiratory distress syndrome
- ✓ Radiation-induced lung injury—associated with proinflammatory cytokine release (eg, TNF-α, IL-1, IL-6). May be asymptomatic but most common symptoms are dry cough and dyspnea +/– low-grade fever. Acute radiation pneumonitis develops within 3–12 weeks (exudative phase); radiation fibrosis may develop after 6–12 months.