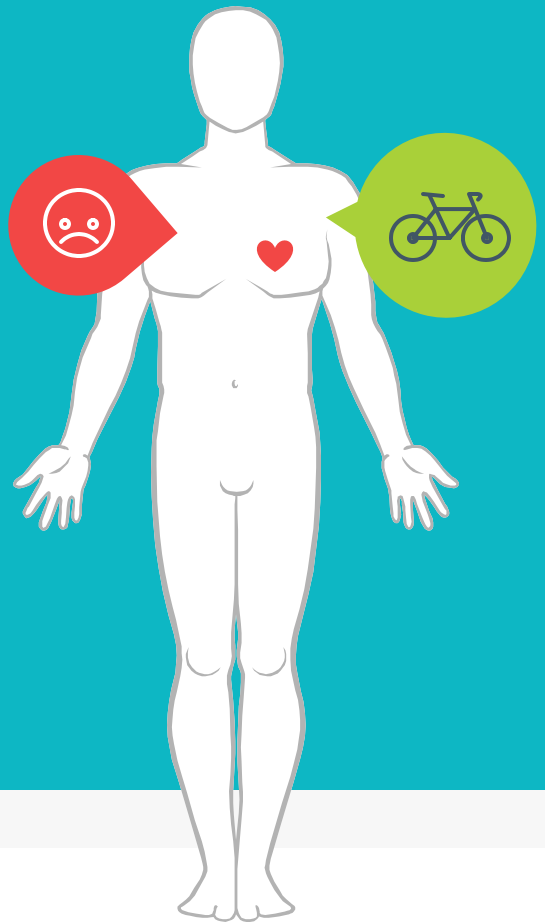
Respiratory System Pathology: Obstructive Lung Disease II



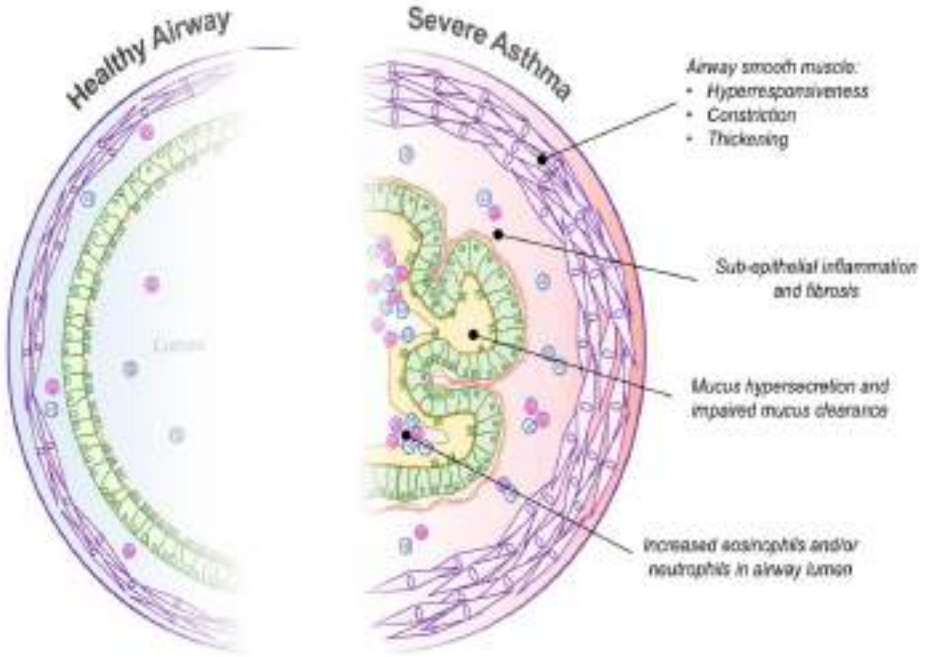
Ghadeer Hayel, M.D.
Assistant Professor of Pathology
Consultant Hematopathologist
10/16/2025

3. Asthma

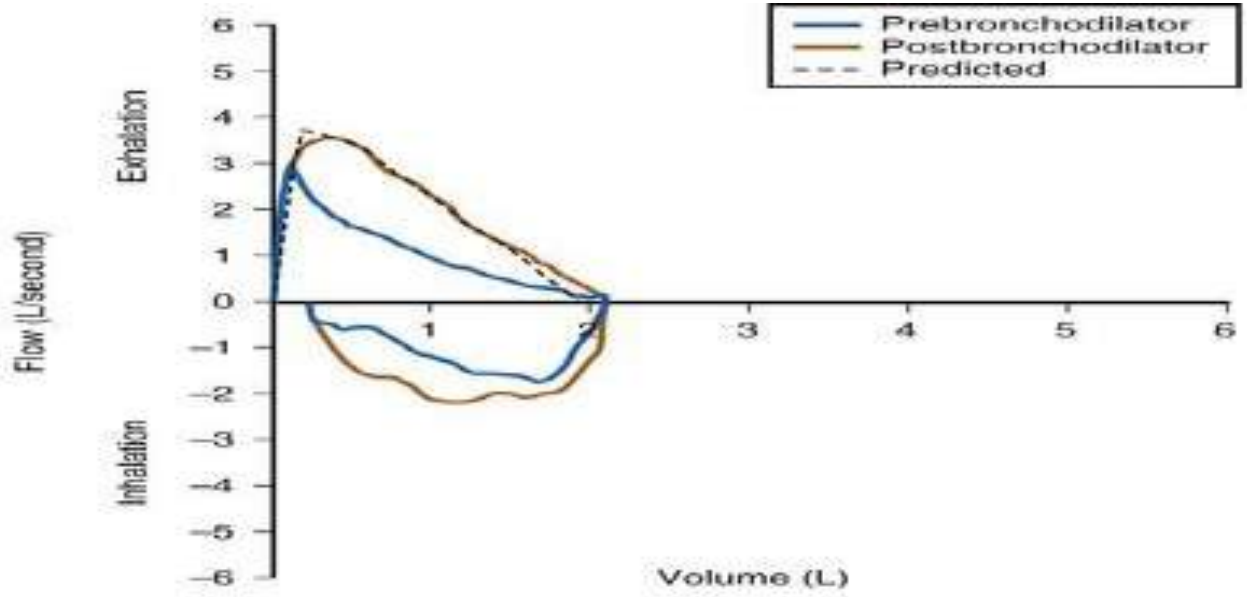
Asthma is a chronic inflammatory disorder of the airways that causes recurrent episodes of wheezing, breathlessness, chest tightness, and cough, particularly at night and/or early in the morning

The hallmarks of asthma

- Intermittent, reversible airway obstruction.
- Chronic bronchial inflammation with eosinophils.
- Bronchial smooth muscle cell hypertrophy & hyperreactivity.
- Increased mucus secretion.



Asthma - PFT

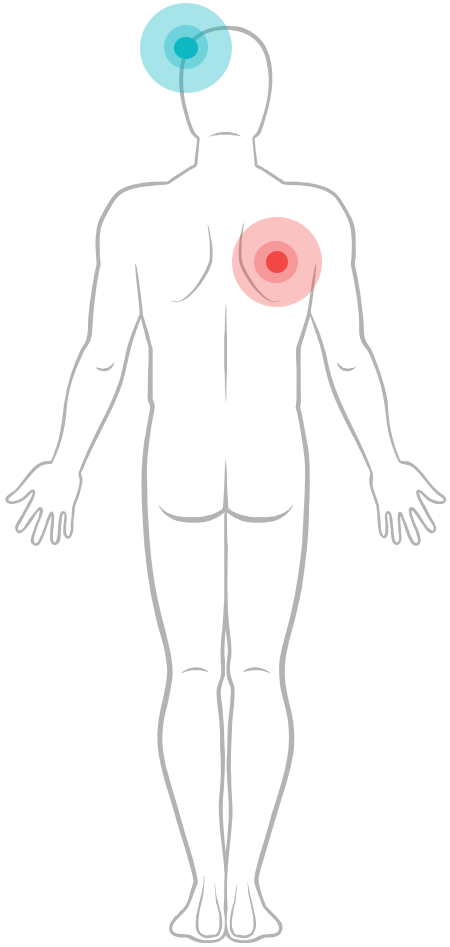


Spirometry Parameter	Units	Predicted Value	Observed Pre	Observed Percent Pred	Observed Post	Observed Percent Pred	Percent Change
FVC	Liter	1.94	2.15	111	2.14	110	0
FEV_1	Liter	1.71	1.30	76	1.82	106	40
FEV_1/FVC	Percent	90	60	67	85	94	42

Asthma main categories:

Atopic

- Most common
- Evidence of allergen sensitization.
- Usually begins in childhood.
- +ve family history.
- IgE-mediated (type I) hypersensitivity reaction.
- triggered by environmental allergens, eg. dusts, pollens.
- Ass/w allergic rhinitis, urticaria, or eczema.



Asthma main categories:

Non-Atopic

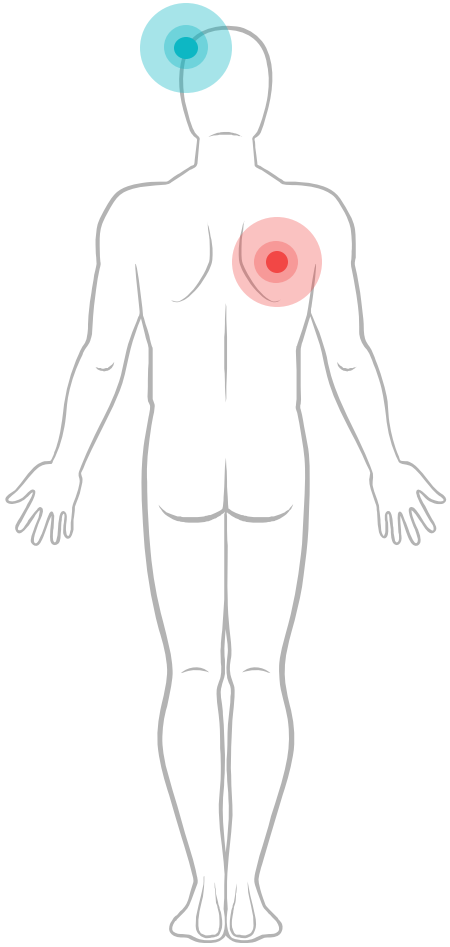
- No evidence of allergen sensitization.
- Triggers: Viral Respiratory infections & inhaled air pollutants
- Less common family Hx.

Drug-Induced

Several pharmacologic agents provoke asthma. Aspirin is the most striking e.g.

Occupational

Triggered by fumes, organic & chemical dusts (wood, cotton, platinum), gases, & other chemicals



Asthma – Pathogenesis

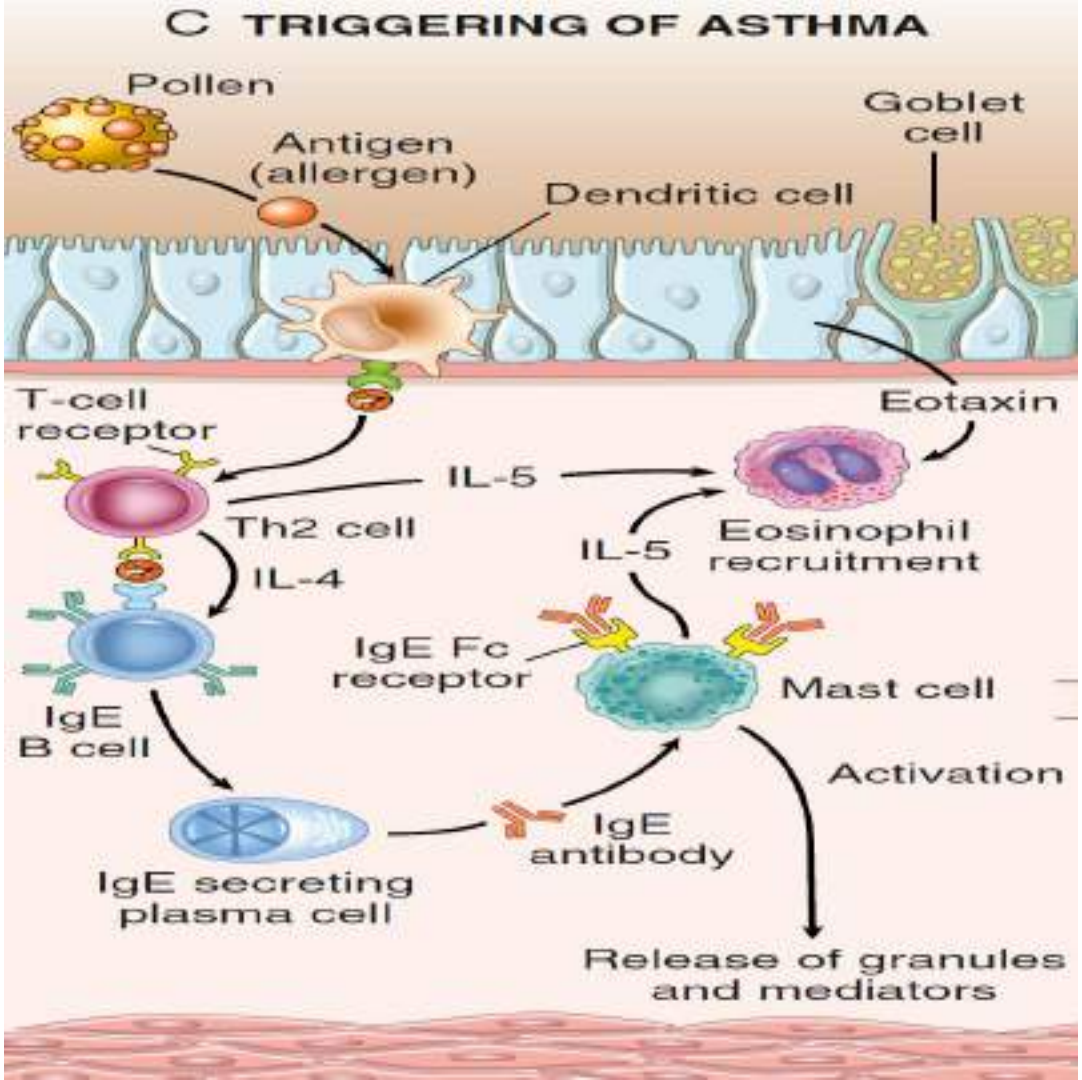
T_H2 Responses, IgE & Inflammation:

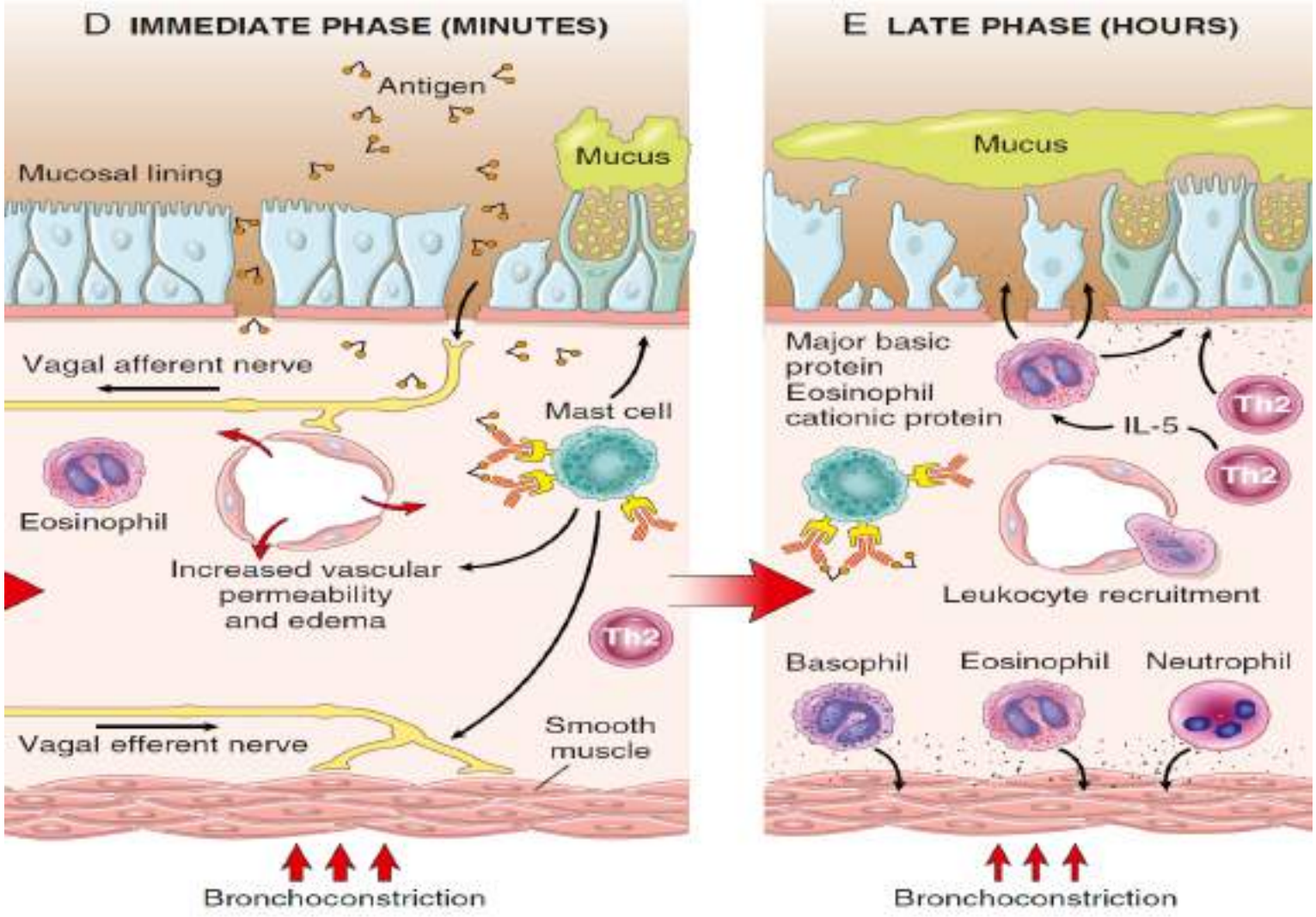
- A fundamental abnormality in asthma is an exaggerated *T_H2* response to normally harmless environmental antigens (in genetically predisposed individuals.).
- *T_H2* cells secrete **cytokines** →promote inflammation & stimulate B cells to produce IgE & other antibodies:
  IL-4: stimulates IgE production
  IL-13: stimulates mucus secretion & promotes IgE production by B cells.
  IL-5: activates eosinophils.

Asthma – Pathogenesis

IgE coats submucosal mast cells → on exposure to allergen release their granule contents (cytokines & mediators) → two reaction:

- Early (immediate) phase reaction: dominated by (bronchoconstriction, ↑mucus production, & vasodilation) Bronchoconstriction is triggered by mediators (histamine, prostaglandin D2, & leukotrienes C4, D4, & E4) & also by reflex neural pathways.
- Late-phase reaction: Inflammatory in nature; mediators stimulate epithelial to produce chemokines → recruitment of TH2 cells, eosinophils & other leukocytes → amplifying the inflammatory reaction.


C TRIGGERING OF ASTHMA
Pollen
Antigen (allergen)
Dendritic cell
Goblet cell
T-cell receptor
Eotaxin
IL-5
Th2 cell
IL-5
Eosinophil recruitment
IL-4
IgE Fc receptor
Mast cell
IgE B cell
Activation
IgE antibody
IgE secreting plasma cell
Release of granules and mediators

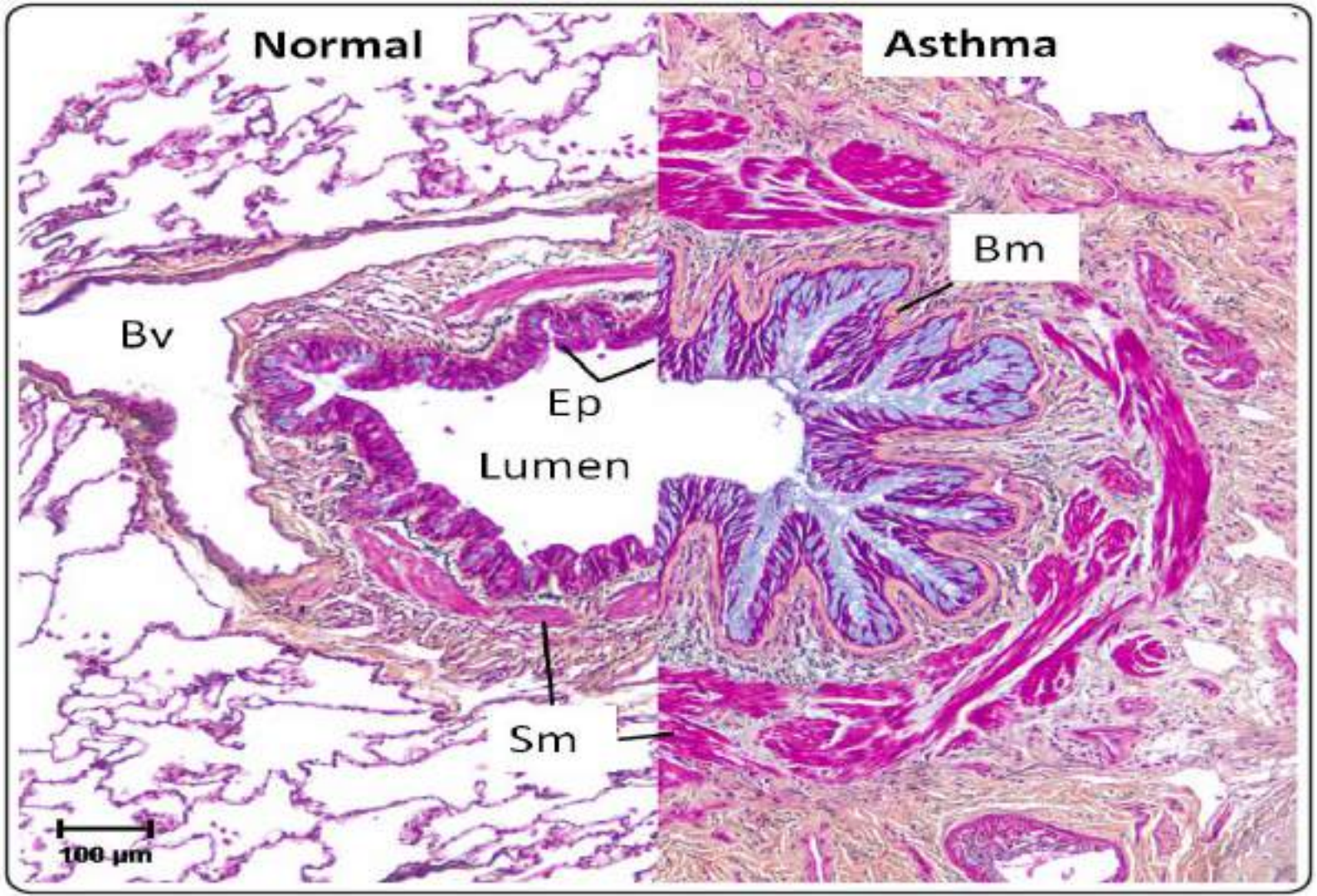

D IMMEDIATE PHASE (MINUTES)
Antigen
Mucosal lining
Mucus
Vagal afferent nerve
Mast cell
Eosinophil
Increased vascular permeability and edema
Th2
Vagal efferent nerve
Smooth muscle
Bronchoconstriction
E LATE PHASE (HOURS)
Mucus
Major basic protein
Eosinophil cationic protein
IL-5
Th2
Th2
Leukocyte recruitment
Basophil
Eosinophil
Neutrophil
Bronchoconstriction

Asthma – Pathogenesis

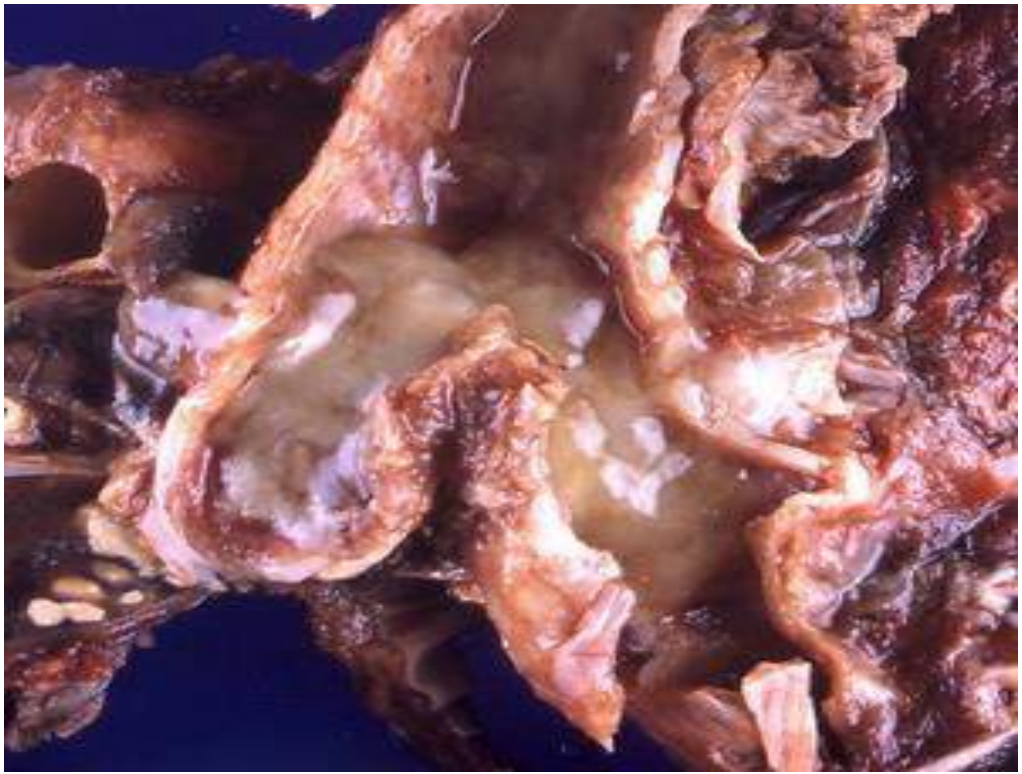
Airway remodeling:

Repeated bouts of inflammation → structural changes in the bronchial wall called airway remodeling:

- Thickening of airway wall
- Subbasement membrane fibrosis (deposition collagen)
- Increased vascularity
- ↑ in size of submucosal glands & number of goblet cells
- Hypertrophy and/or hyperplasia of bronchial wall muscle

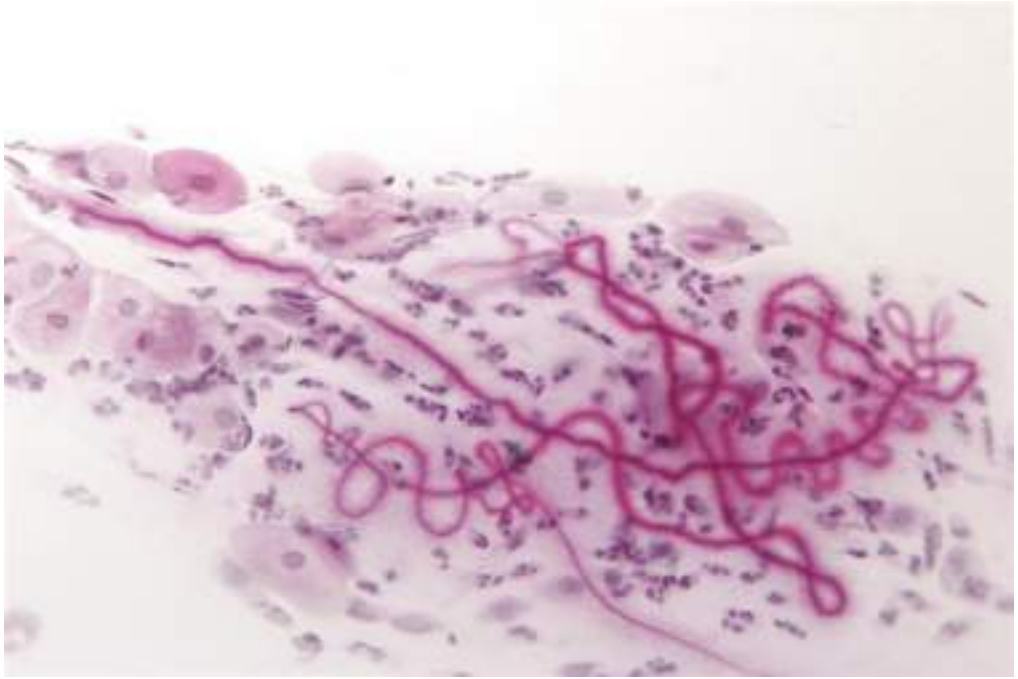

Normal
Asthma
Bm
Bv
Ep
Lumen
Sm
100 µm

Asthma – Morphology



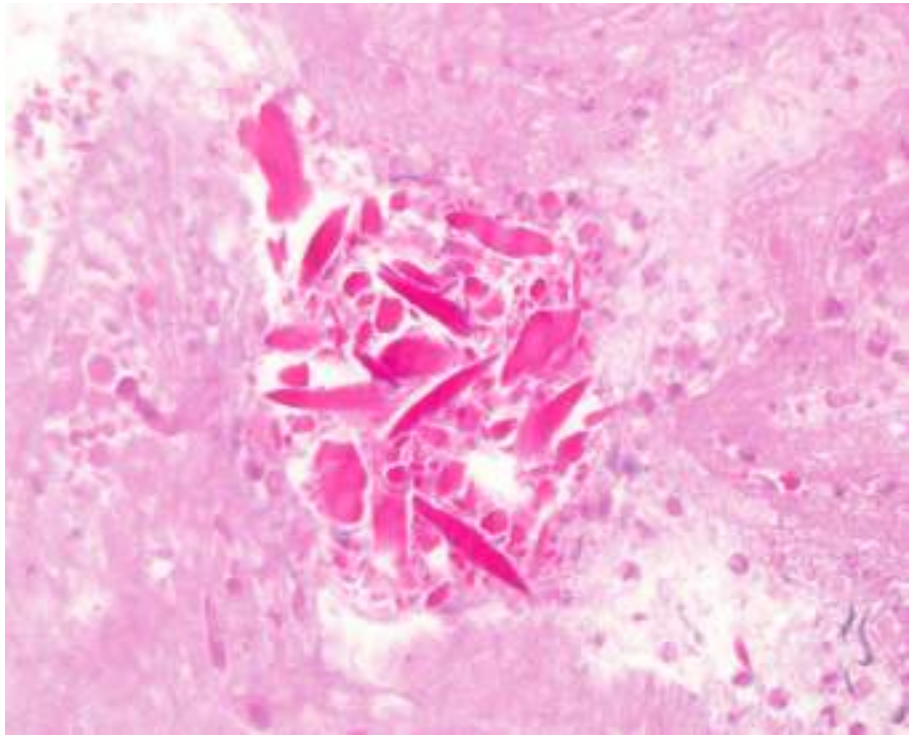
The most striking finding is occlusion of bronchi and bronchioles by thick, **tenacious mucous plugs**

Asthma – Morphology



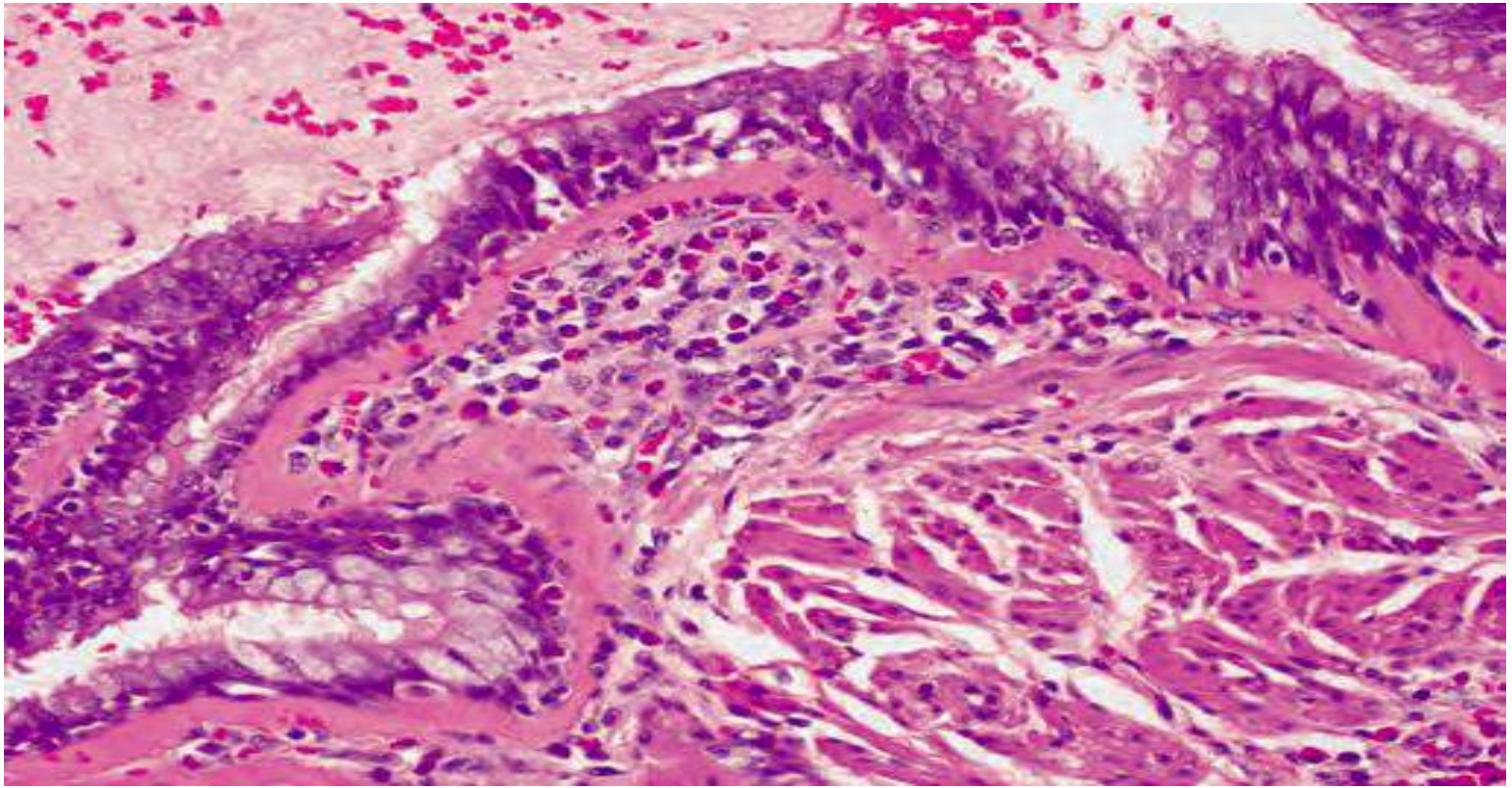
Curschmann Spirals → result from extrusion of mucus plugs from subepithelial mucous gland ducts

Asthma – Morphology



Numerous eosinophils and **Charcot-Leyden crystals** (crystalloids made up of the eosinophil protein galectin-10)

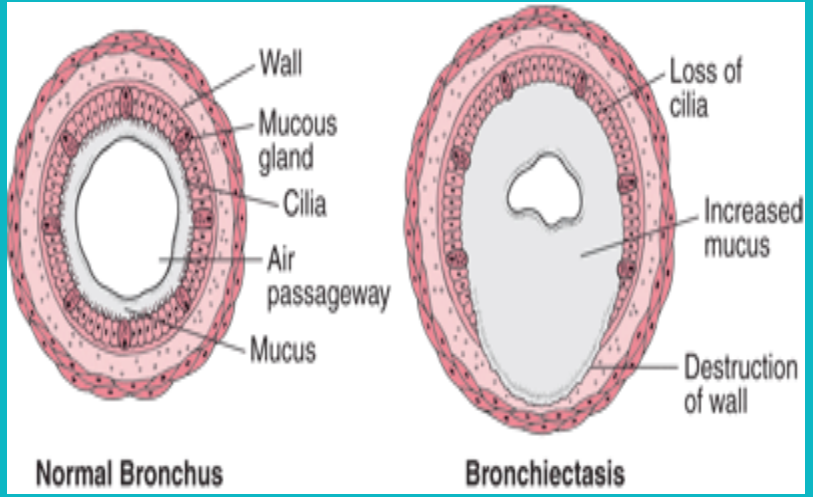
Asthma – Morphology



Asthma – Clinical features

- **Classic asthmatic attack:** chest tightness, dyspnea, wheezing, & coughing (with or w/out sputum) due to bronchoconstriction & mucus plugging → trapping of air in distal airspaces & progressive hyperinflation of lungs.
- Intervals between attacks are characteristically free from overt respiratory difficulties. (early disease)
- Occasionally a severe paroxysm occurs that does not respond to therapy and persists for days and even weeks *(status asthmaticus) a*ss/w hypercapnia, acidosis, and severe hypoxia → may be fatal.

4. Bronchiectasis



The permanent dilation of bronchi & bronchioles caused by destruction of smooth muscle & the supporting elastic tissue; it typically results from or is associated with chronic necrotizing infections

Bronchiectasis

- Not a primary disorder → always occurs secondary to **persistent infection or obstruction** caused by a variety of conditions.
- **Characteristic symptom complex:** cough & expectoration of copious amounts of purulent sputum.
- **Diagnosis**: appropriate history & radiographic demonstration of bronchial dilation.

Conditions predispose to Bronchiectasis

- Bronchial obstruction: caused by tumors, foreign bodies, & impaction of mucus. (localized to the obstructed lung segment).
- Congenital or hereditary conditions:

1. Cystic fibrosis: widespread severe bronchiectasis results from obstruction caused by abnormally viscid mucus and secondary infections.
2. Immunodeficiency states: develops because of recurrent bacterial infections.

Conditions predispose to Bronchiectasis

3. Primary ciliary dyskinesia: (immotile cilia syndrome): Rare AR disorder ass/w bronchiectasis & sterility in males. Caused by inherited abnormalities of cilia → impair mucociliary clearance of the airways → persistent infections.

- Necrotizing, or suppurative, pneumonia: particularly with virulent organisms such as *Staphylococcus aureus or Klebsiella spp.*, predispose affected patients to development of bronchiectasis.

Bronchiectasis – Pathogenesis

- **Two intertwined processes contribute to bronchiectasis: obstruction and chronic infection.** Either may be the initiator:
- E.g., obstruction by a foreign body impairs clearance of secretions → a favorable substrate for superimposed infection → inflammatory damage to bronchial wall & accumulating exudate distend the airways → irreversible dilation.
- E.g., Persistent necrotizing infection in bronchi or bronchioles → poor clearance of secretions, obstruction, & inflammation with peribronchial fibrosis and traction on the bronchi, culminating again in full-blown bronchiectasis

Bronchiectasis – Morphology

Usually affects lower lobes, particularly those that are most vertical (gravitational).

The airways dilated up to four times their usual diameter → seen on gross examination almost out to the pleural surface (**normally** cannot be followed by eye beyond a point 2 to 3 cm from the pleura)

Bronchiectasis – Morphology

- The histological changes vary with the severity and duration of the disease.
- In an active full-blown disease: an intense acute & chronic inflammatory exudates within the wall of the bronchi & bronchioles seen & desquamation of lining epithelium cause extensive ulceration .
- In severe cases abnormal dilatation occurs due to necrosis & fibrosis of muscle coat with associated peribronchial fibrosis .
- In severe cases lung abscesses may develop .

Bronchiectasis – Clinical features

- **Symptoms**: severe, persistent cough ass/w expectoration of mucopurulent sputum.
- Other symptoms: dyspnea, rhinosinusitis, and hemoptysis. (precipitated by upper respiratory tract infections).
- Severe, widespread bronchiectasis → significant obstructive ventilatory defects → hypoxemia, hypercapnia, pulmonary hypertension & cor pulmonale.
- Current treatment outcomes improved → severe complications of bronchiectasis (brain abscess, amyloidosis & cor pulmonale) occur less frequently now than in the past.

Questions?
Thanx!

'Things get bad for all of us, almost continually, and what we do under the constant stress reveals who/what we are.'

”