

Diseases of the Respiratory System



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Respiratory block
Pathology
Lec 1
2020

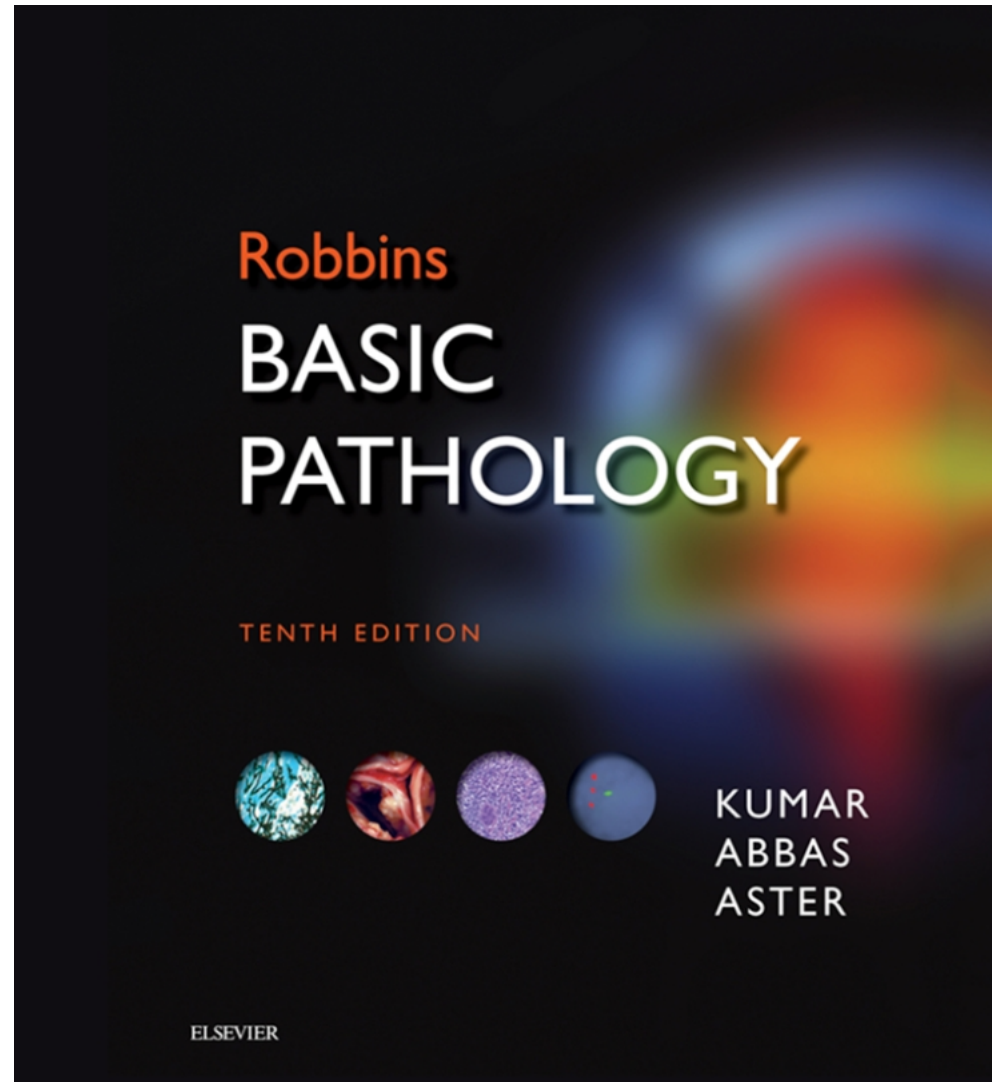
Diseases of the Respiratory System

Lecture 1
2018

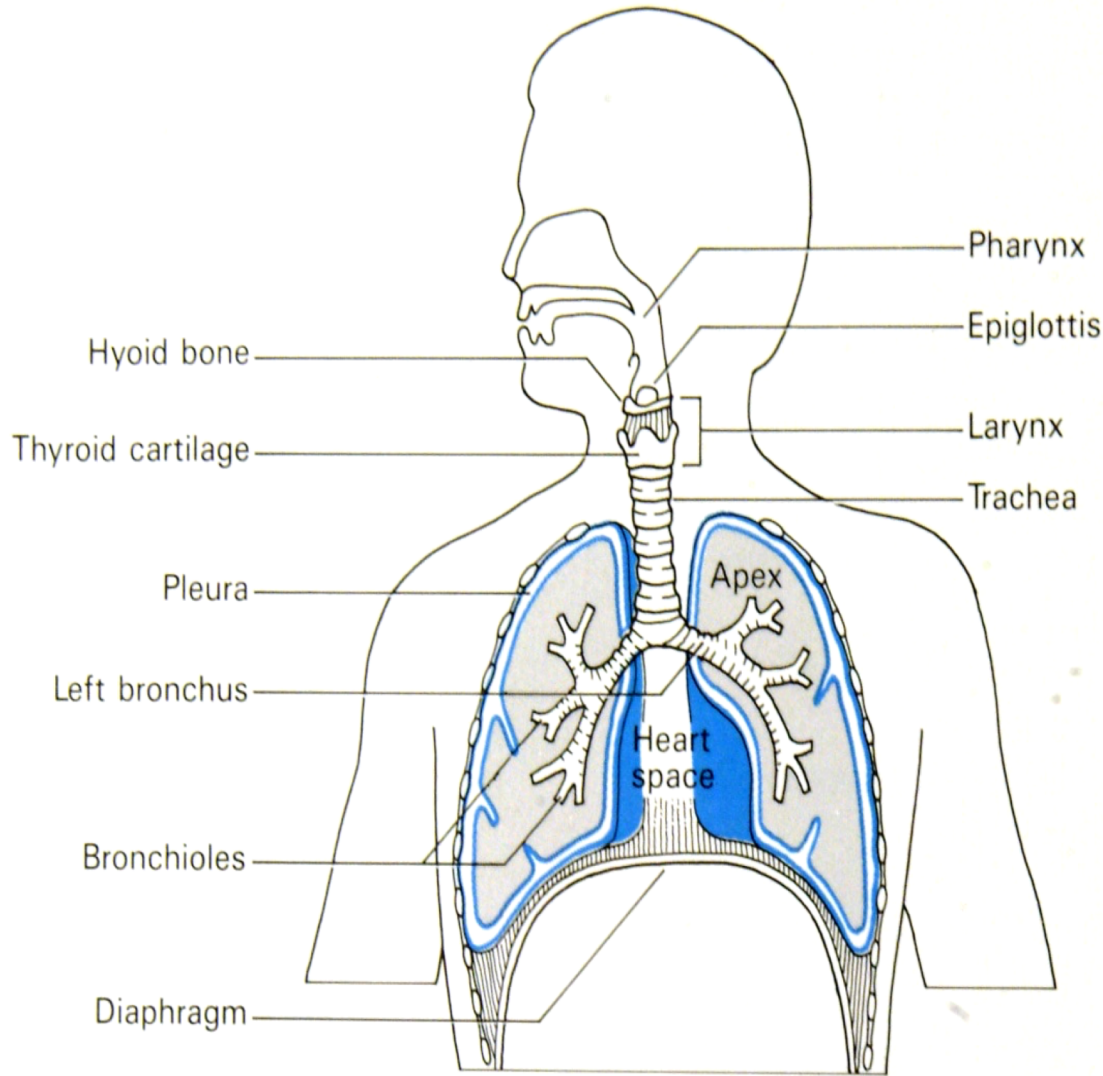
**Review of the normal Anatomy and
Histology of the Respiratory System**

Bronchial asthma

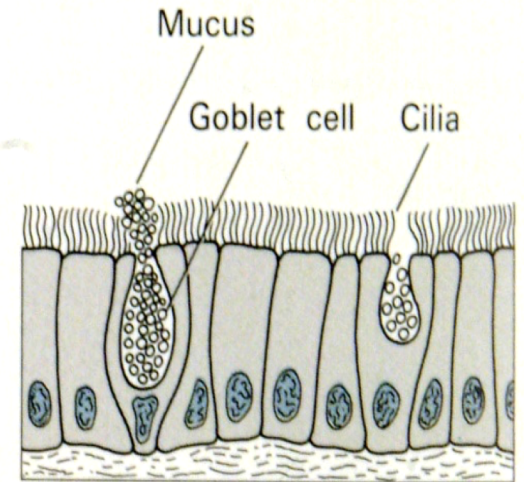
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Diseases of Lung



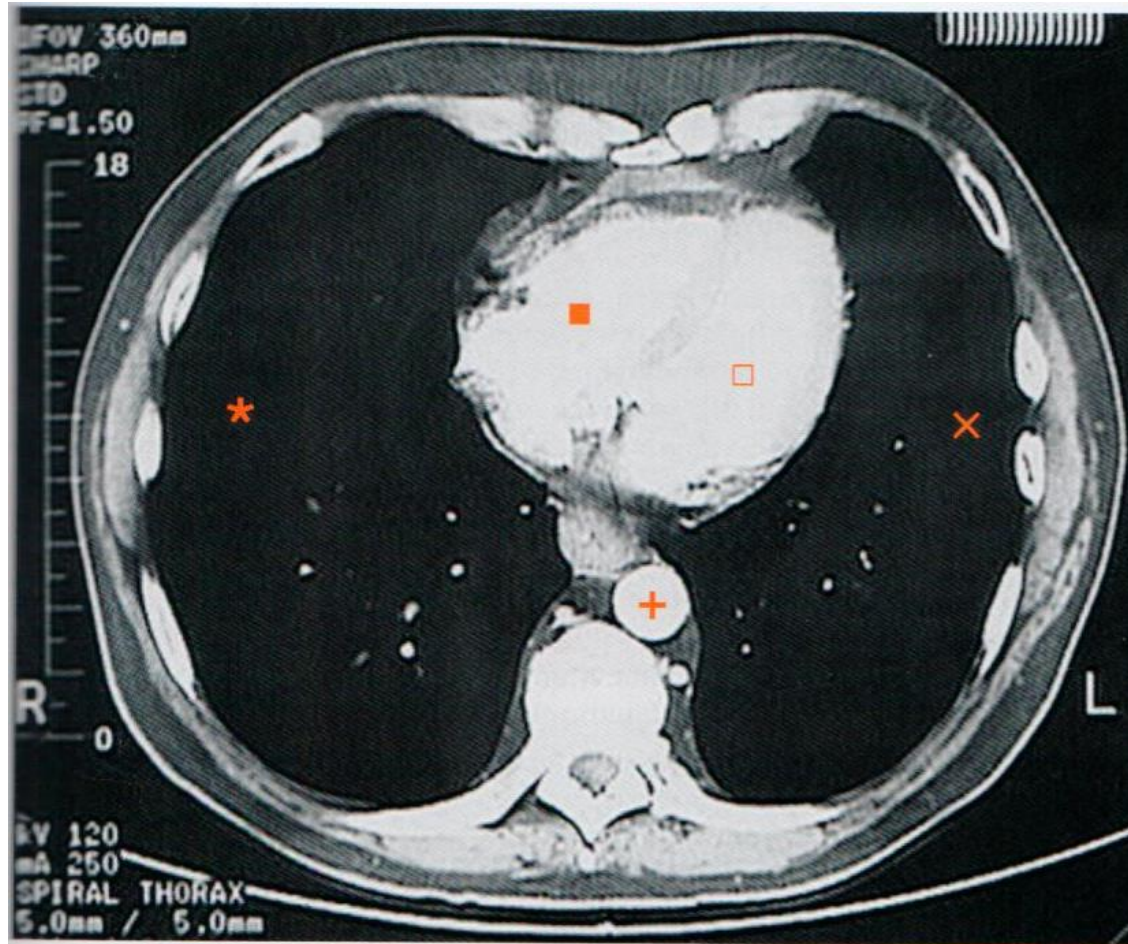
A



B

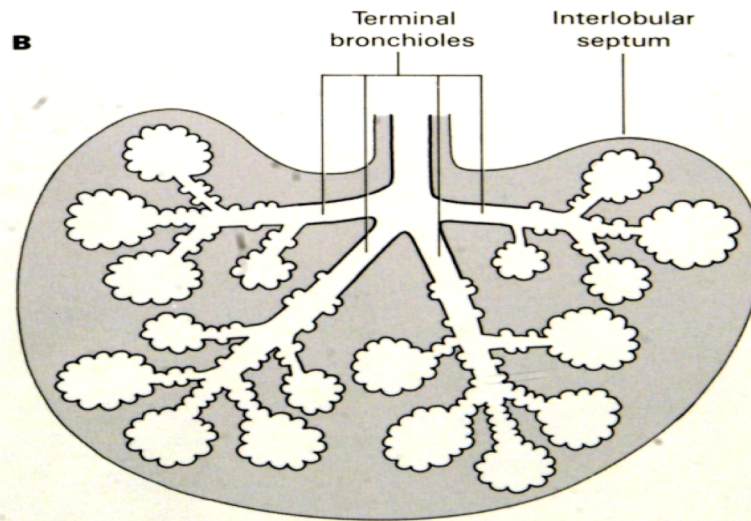
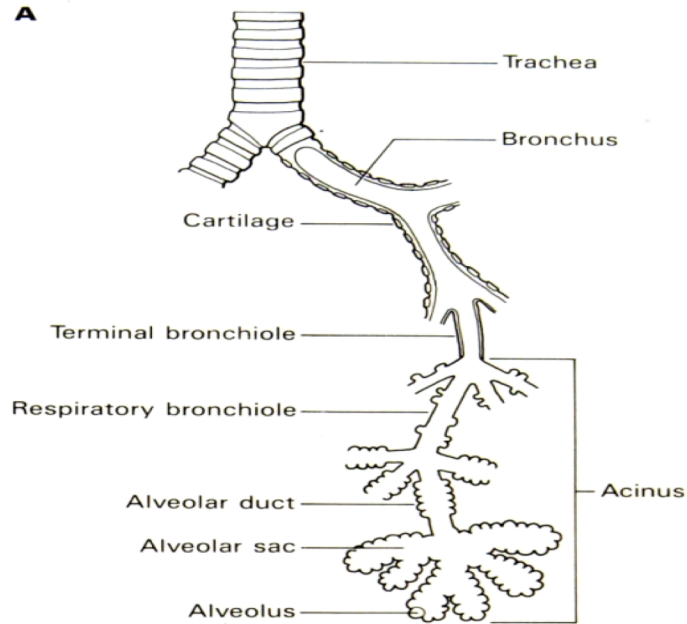
Respiratory epithelium

The respiratory system



Normal lung, CT image

Diseases of Lung



The lower respiratory tract



Normal adult lung

Diseases of the Respiratory System

**Chronic Obstructive Pulmonary Diseases (COPD)
including Bronchial Asthma**

Bronchial asthma

Objectives

BA is an episodic, reversible bronchoconstriction caused by increased responsiveness of the tracheobronchial tree to various stimuli.

- Define bronchial asthma (BA)
- Understand the pathogenesis
- Understanding the morphological changes
- Know the manifestation and clinical course of BA
- List the complications of BA
- Define status asthmaticus
- Know the prognosis and prevention of BA

- 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 are:
 - intermittent, reversible airway obstruction
 - chronic bronchial inflammation with eosinophils
 - bronchial smooth muscle cell hypertrophy and hyperreactivity
 - increased mucus secretion.

- Many cells play a role in the inflammatory response:
 - Eosinophils
 - Mast cells
 - Macrophages
 - Lymphocytes
 - Neutrophils
 - Epithelial cells

Epidemiology:

Asthma has increased in incidence significantly in the Western world over the past 4 decades.

One explanation is: the *hygiene hypothesis*

A lack of exposure to infectious organisms (and possibly nonpathogenic microorganisms as well) in early childhood results in defects in immune tolerance and subsequent hyperreactivity to immune stimuli later in life

Pathogenesis

- **Major factors contributing to the development of asthma include:**
 - Genetic predisposition to type I hypersensitivity (atopy)
 - Acute and chronic airway inflammation
 - Bronchial hyperresponsiveness to a variety of stimuli.

Classification

- **Atopic (Extrinsic) asthma:** (with evidence of allergen sensitization)
 - Type 1 Hypersensitivity reaction, IgE
 - Childhood
 - Viral infection
 - Positive family Hx of allergy
 - 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.

Nonatopic (Intrinsic) asthma:

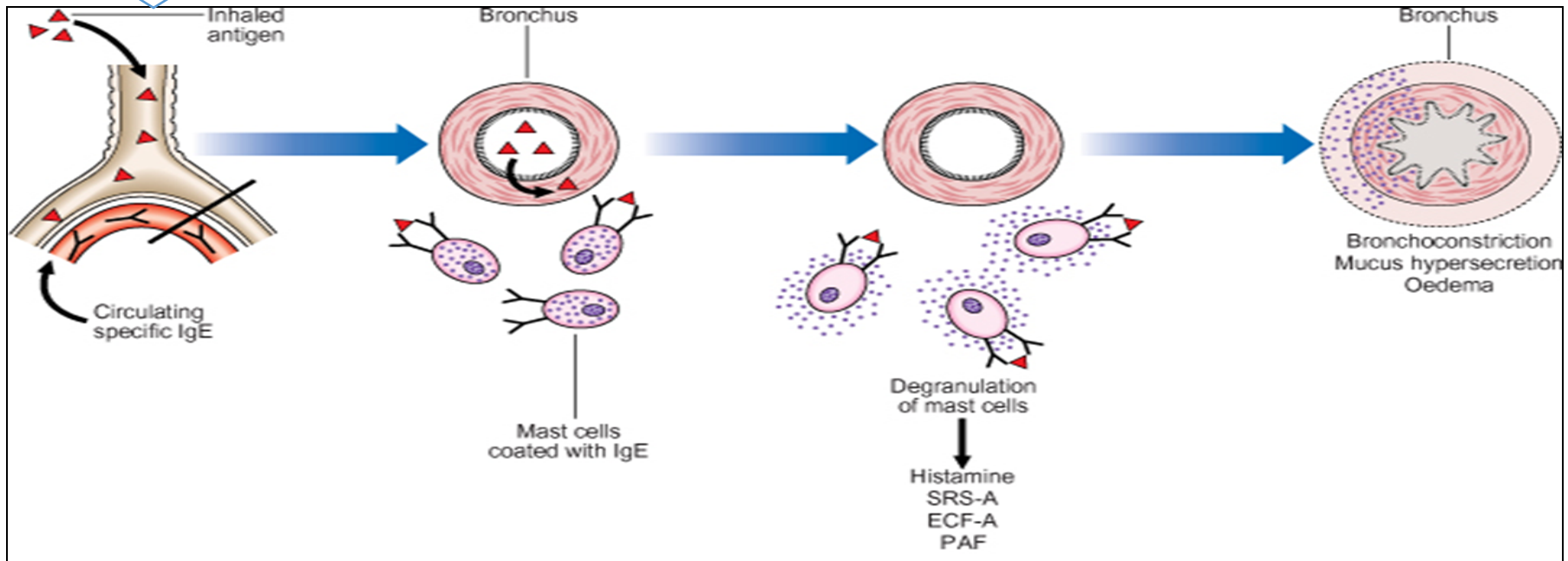
- BA associated with aspirin, exercise, cold, fumes, organic and chemical dusts.
- No Hx of allergy and skin test results usually are negative
- A positive family history of asthma is less common.
- Trigger factors:
 - Respiratory infections due to viruses (e.g., rhinovirus, parainfluenza virus)
 - Inhaled air pollutants (e.g., sulfur dioxide, ozone, nitrogen dioxide)

These lowers the threshold of the subepithelial vagal receptors to irritants

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.

Pathogenesis of allergic asthma

Pollen
dust, virus,
animal fur,
sand
bacteria



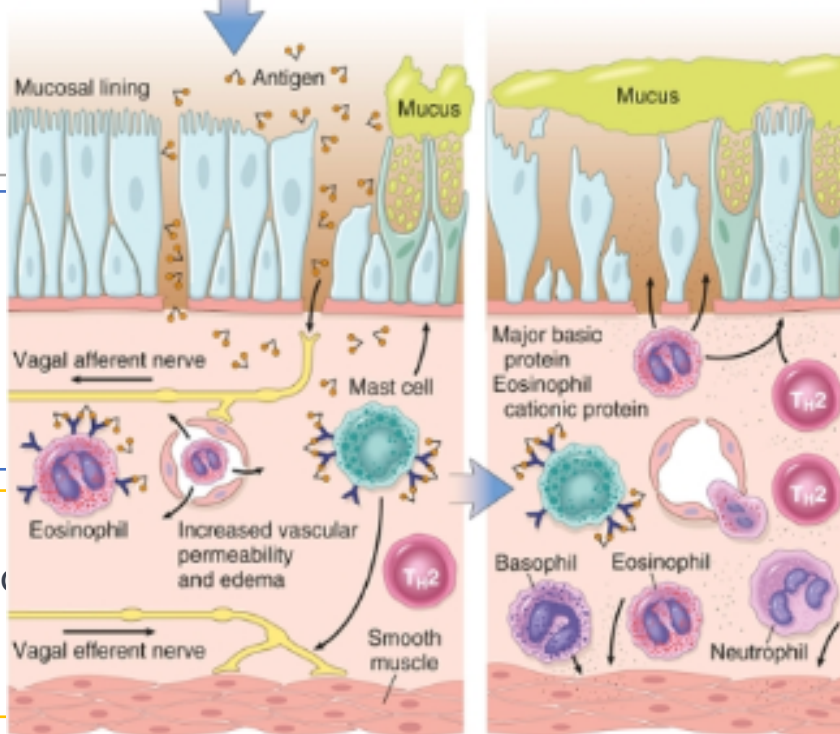
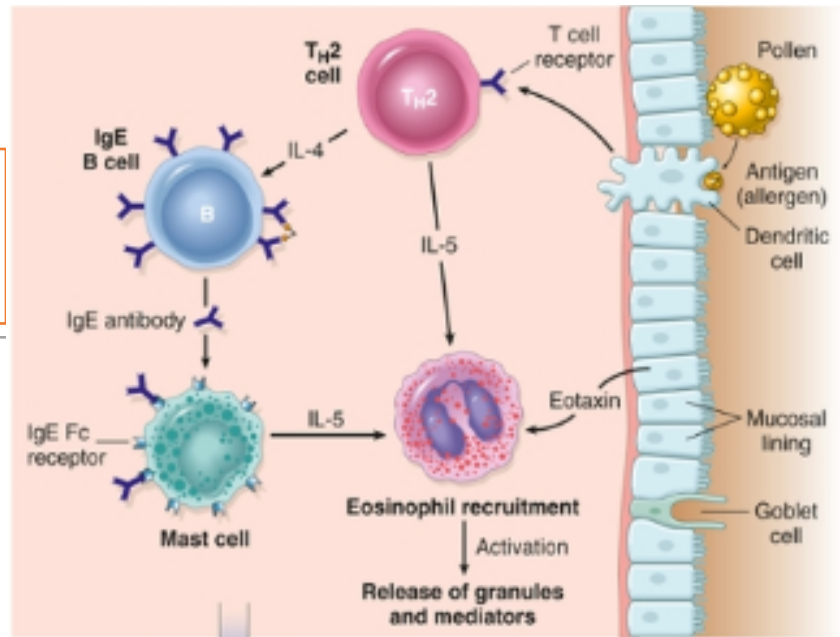
Pathogenesis

Inhaled allergens (antigen) elicit a TH2-dominated response favoring IgE production and eosinophil recruitment.

On reexposure to antigen, the immediate reaction is triggered by Ag-induced cross-linking of IgE bound to Fc receptors on mast cells. These cells release preformed mediators that directly and via neuronal reflexes induce bronchospasm, increased vascular permeability, mucus production, and recruitment of leukocytes.

Leukocytes recruited to the site of reaction (neutrophils, eosinophils, and basophils; lymphocytes and monocytes) release additional mediators that initiate the late phase of asthma.

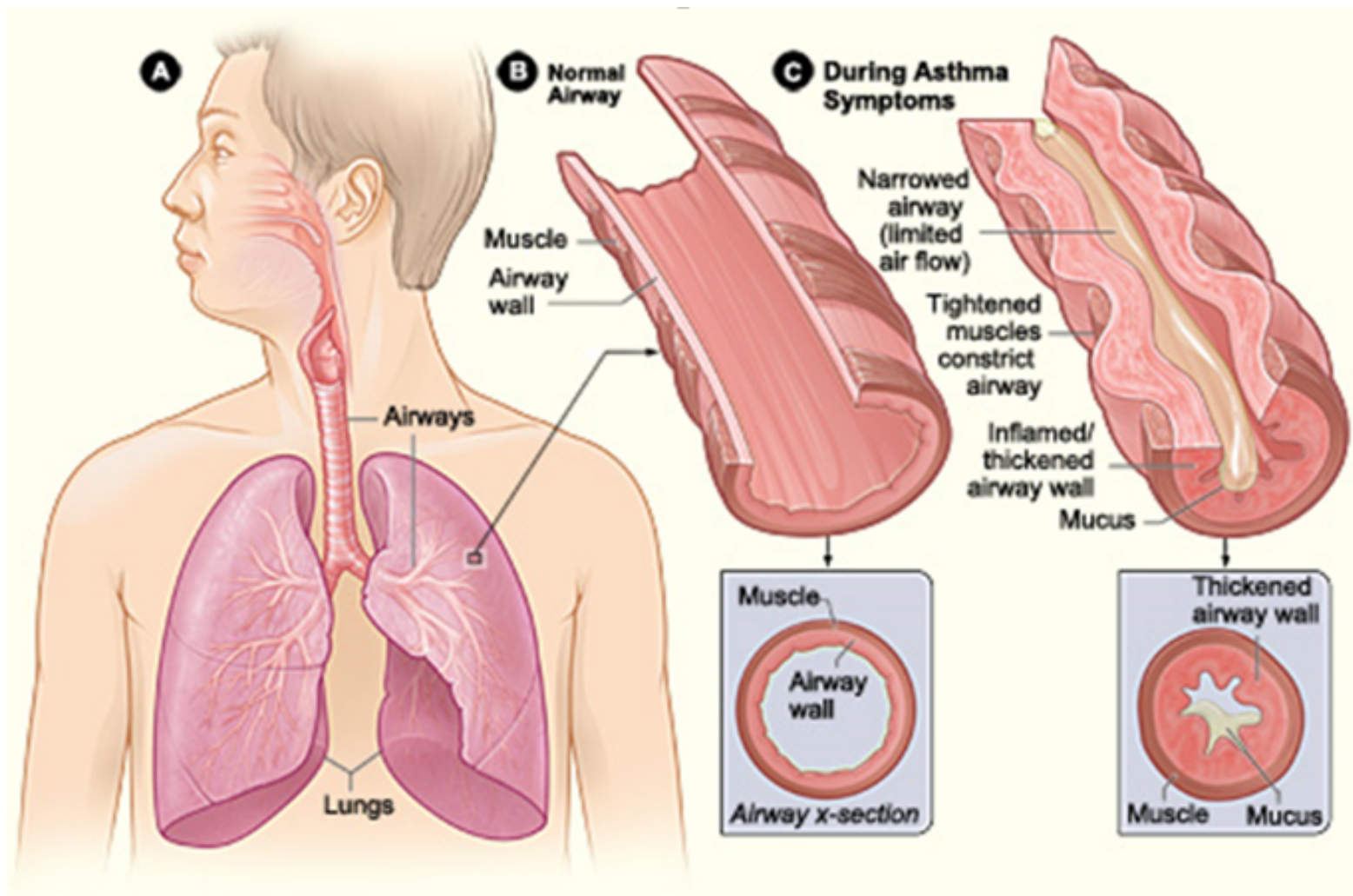
Several factors released from eosinophils (e.g., major basic protein, eosinophil cationic protein) also cause damage to the epithelium.



Pathogenesis: Genetic factor

- Asthma tends to “run” in families, but the role of genetics in asthma is complex.
- The precise contribution of asthma-associated genetic variants to the development of disease remains to be determined.

Morphological changes Of BA

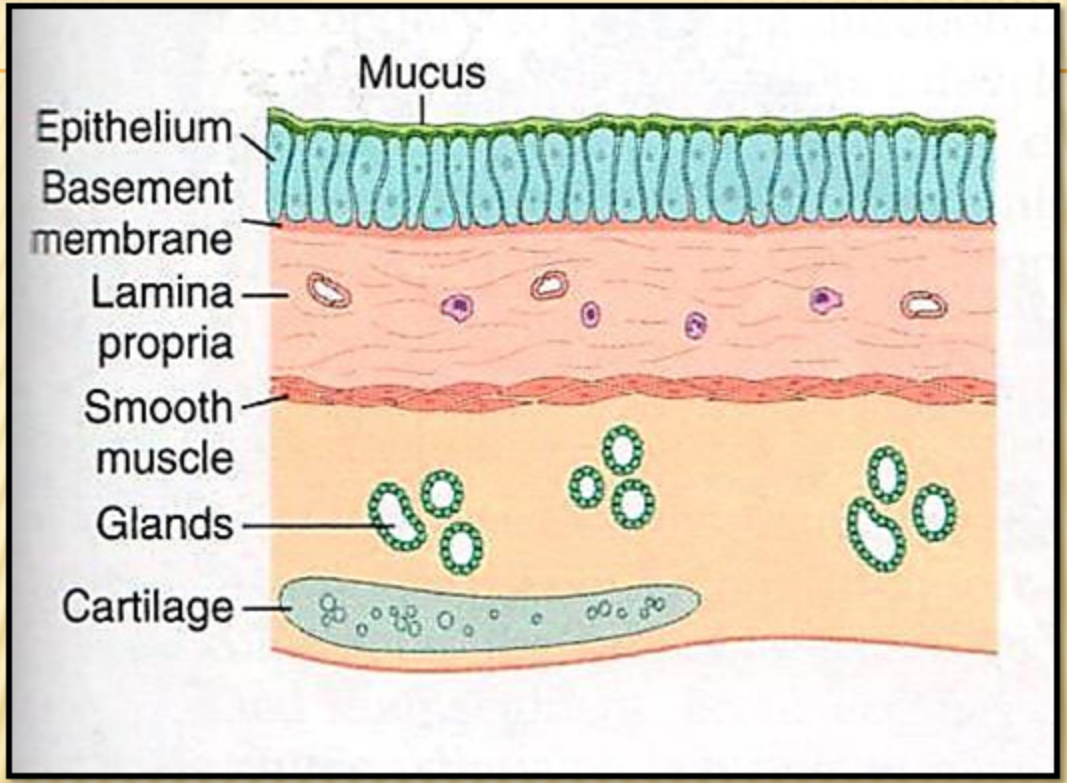


Morphological changes Of BA



Bronchitis in an asthmatic patient. Note the presence of congested mucosa and mucoid secretions.

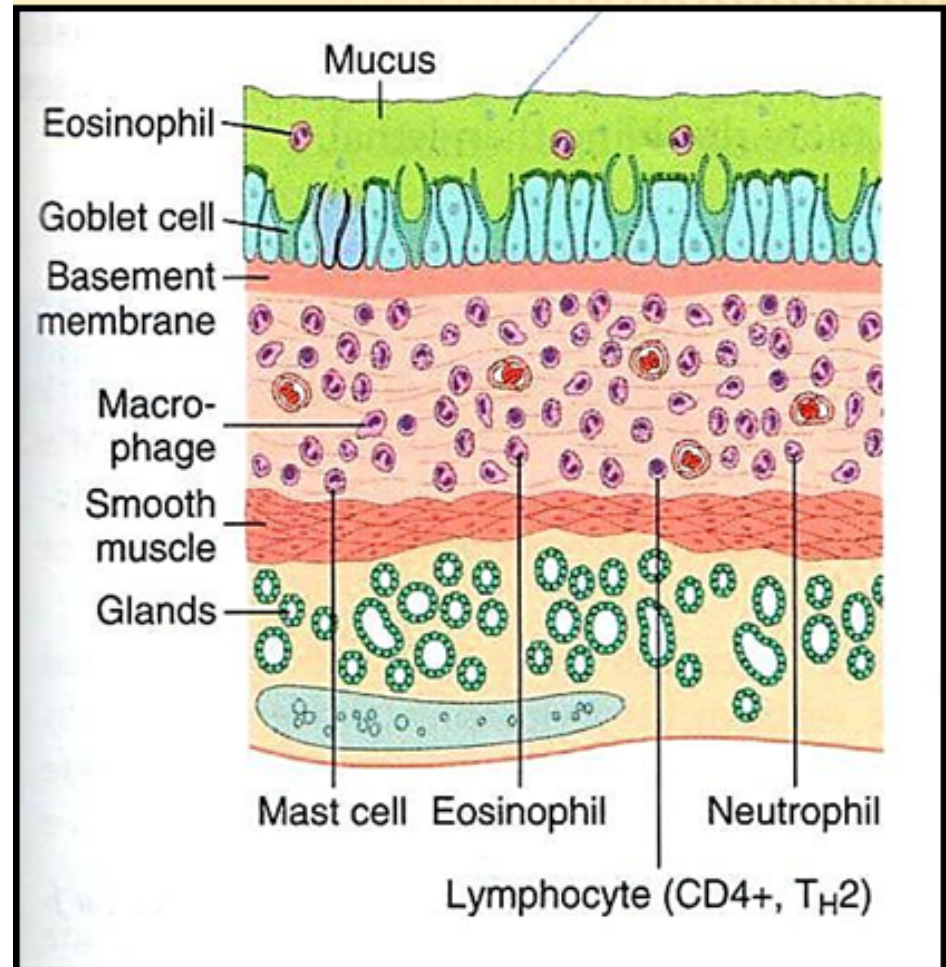
Morphological changes Of BA



Bronchial airway in normal lung

Morphological changes Of BA

- Occlusion of bronchi and bronchioles by thick, tenacious **mucous plugs**
- Mucous contains numerous eosinophils with Curschmann spirals and Charcot-Leyden crystals.



Bronchial airway in asthma patient

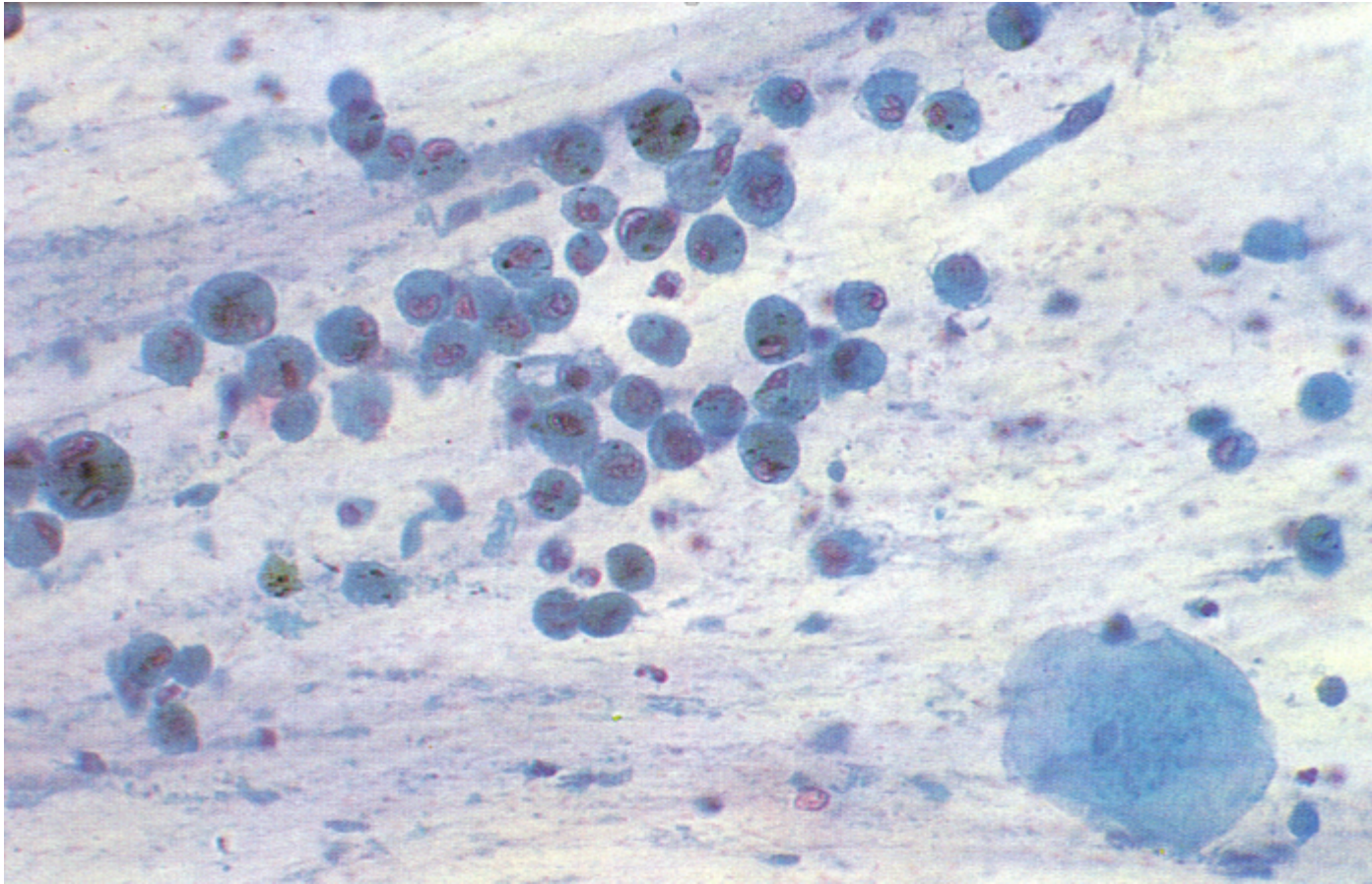
Airway remodeling, include:

- Thick Basement Membrane.
- Sub-basement membrane fibrosis
- Increased submucosal vascularity
- Submucosal glands increased and goblet cell metaplasia of the airway epithelium.
- Hypertrophy of the bronchial wall muscle.



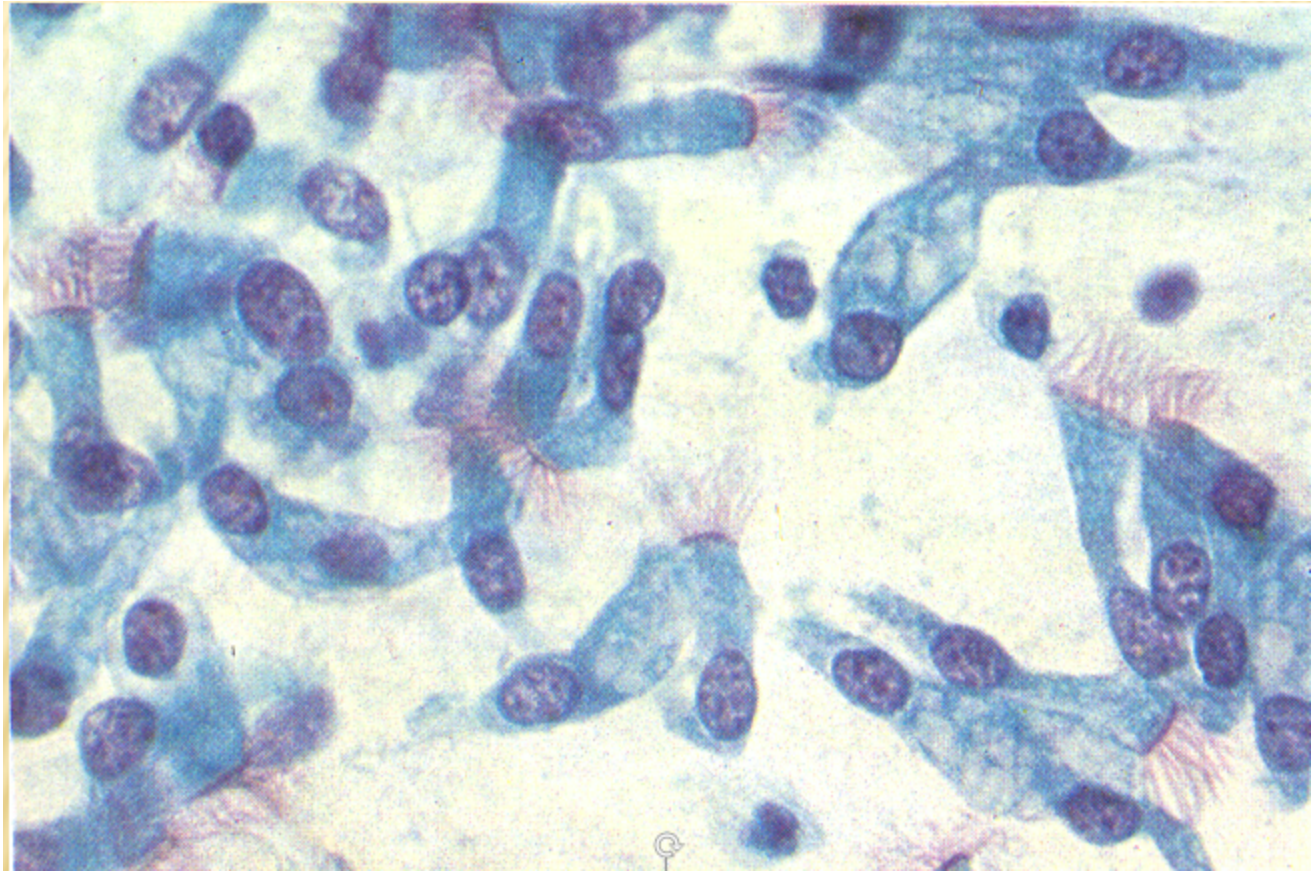
Bronchial biopsy specimen from an asthmatic patient showing sub-basement membrane fibrosis, eosinophilic inflammation and smooth muscle hyperplasia

Morphological changes Of BA



Composition of satisfactory specimen : Sputum

Morphological changes Of BA



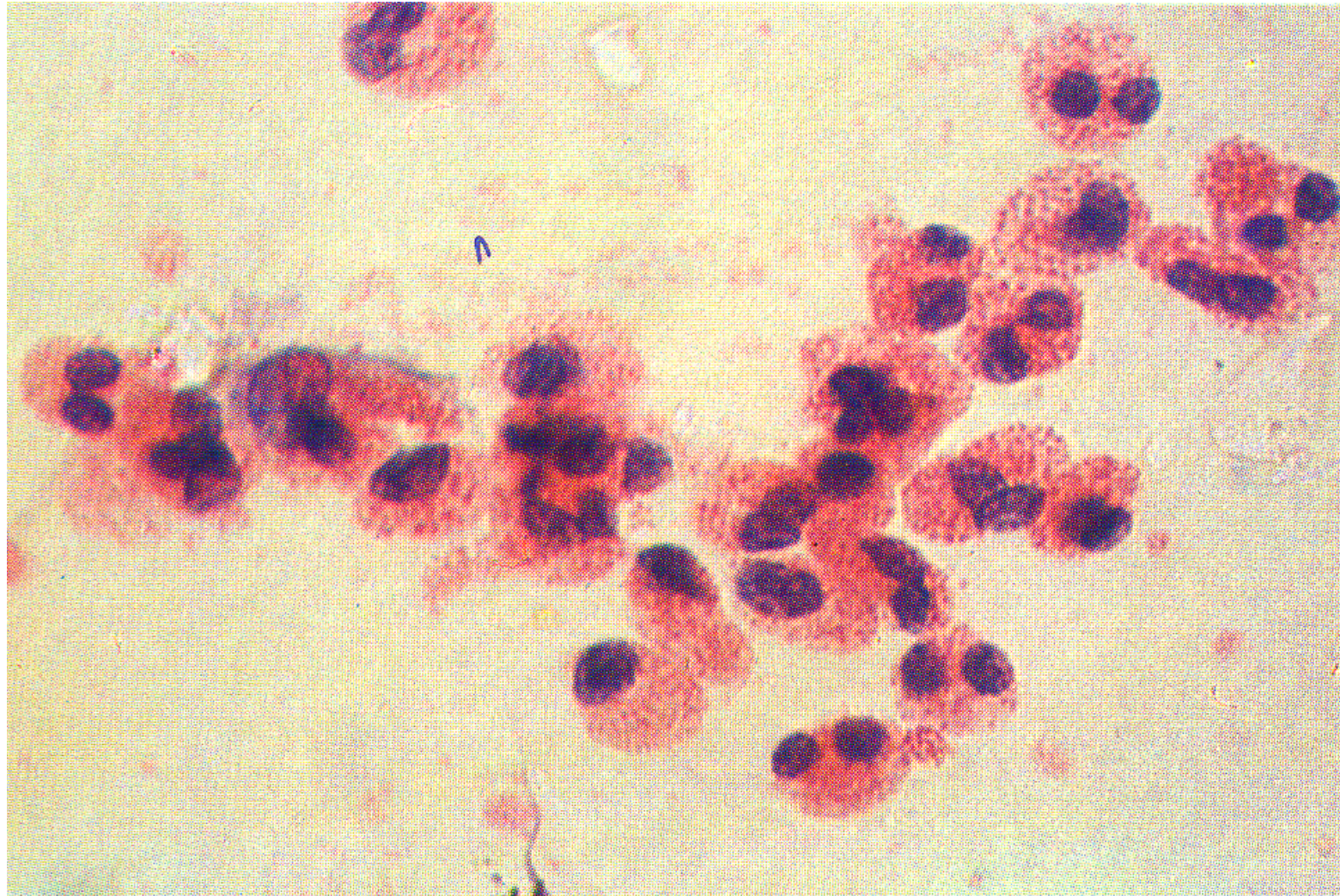
Ciliated columnar cells

Morphological changes Of BA

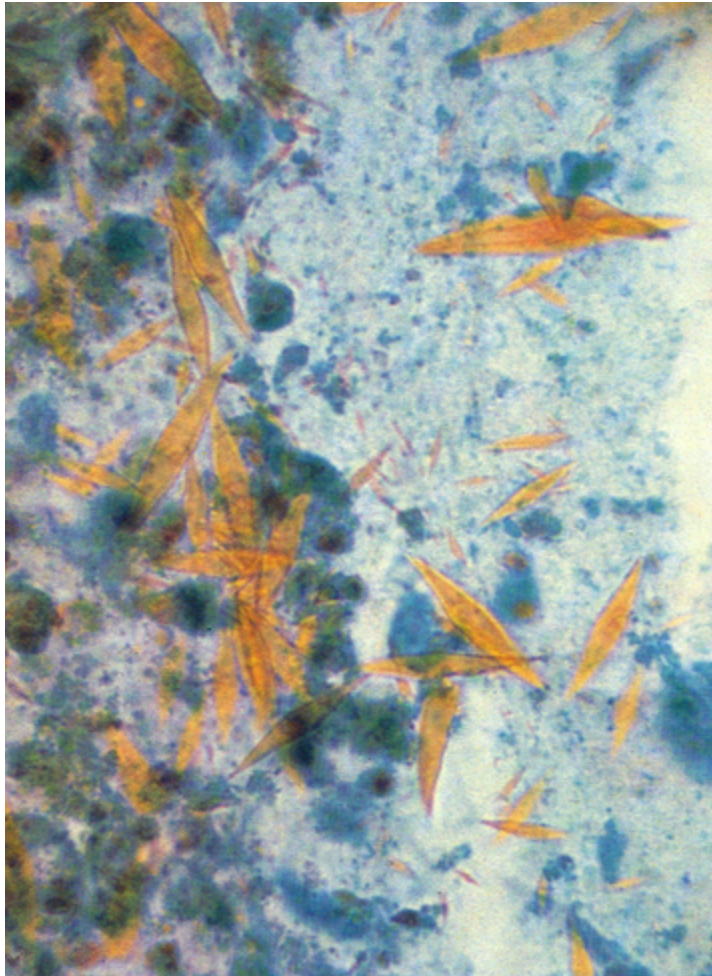


Curschmann's spiral : Sputum

Morphological changes Of BA

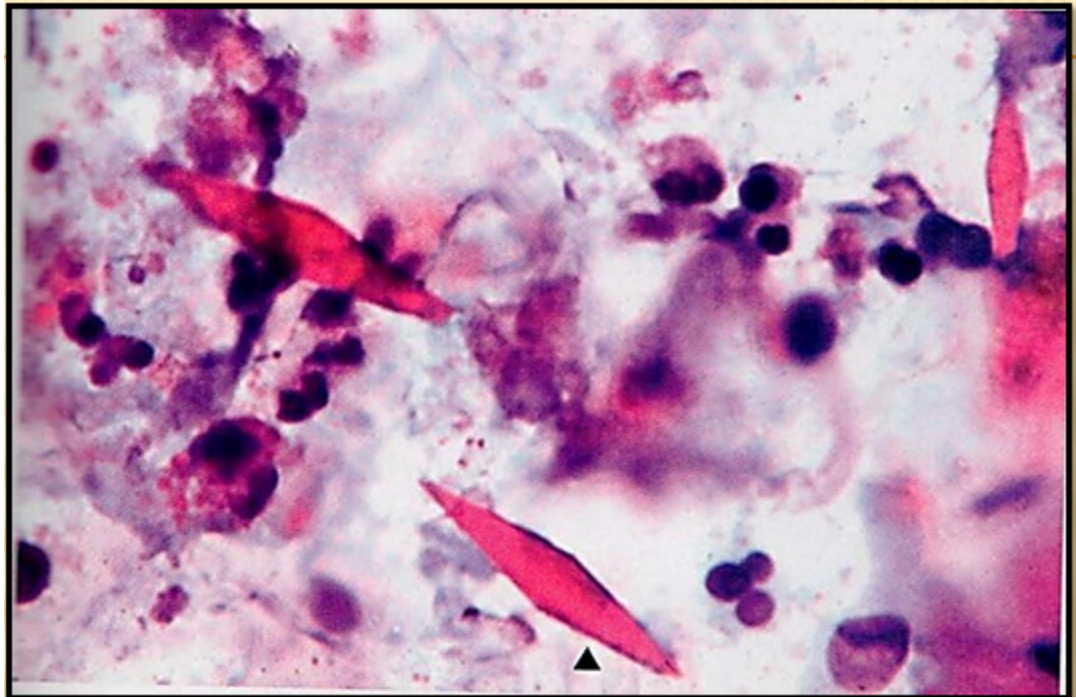


Eosinophils from a case of Bronchial Asthma



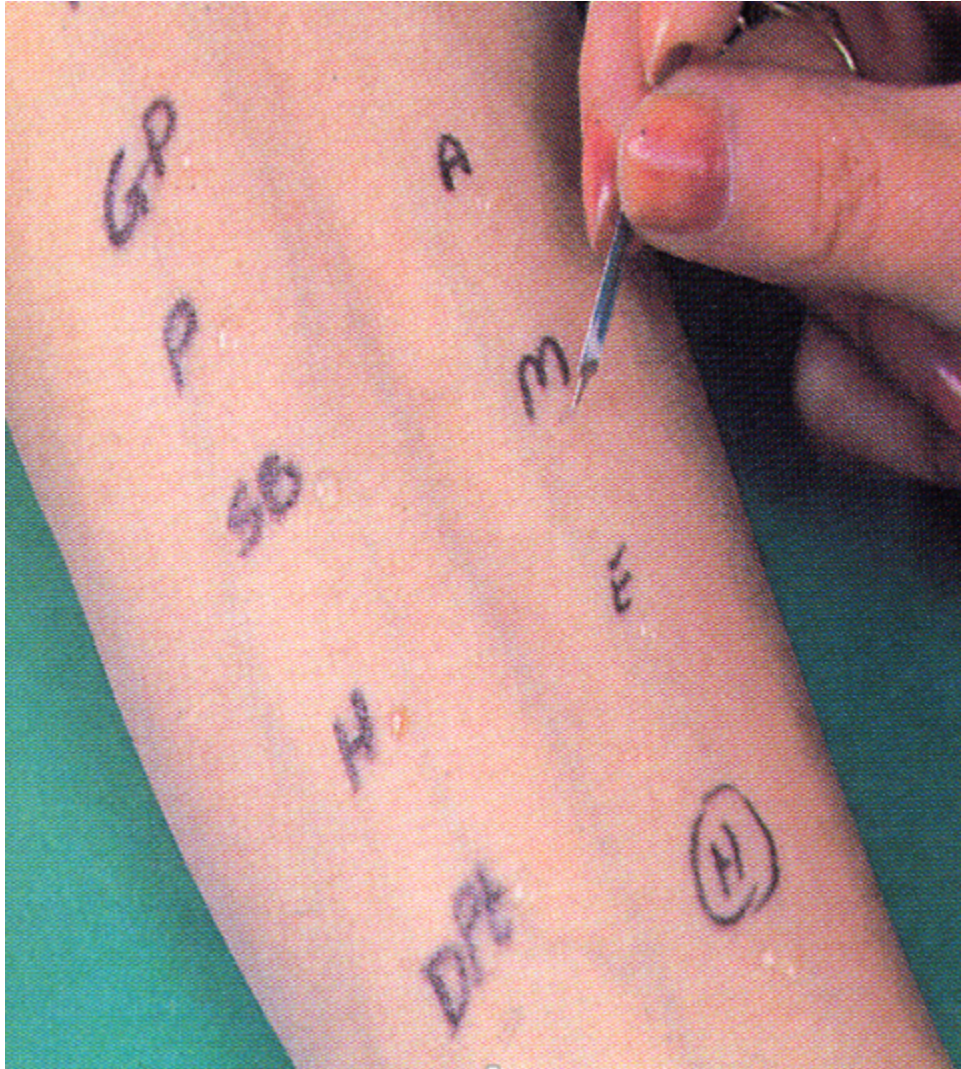
Bronchial asthma :
Charcot – Leyden
Crystals

Morphological changes Of BA



Bronchial Asthma, microscopic

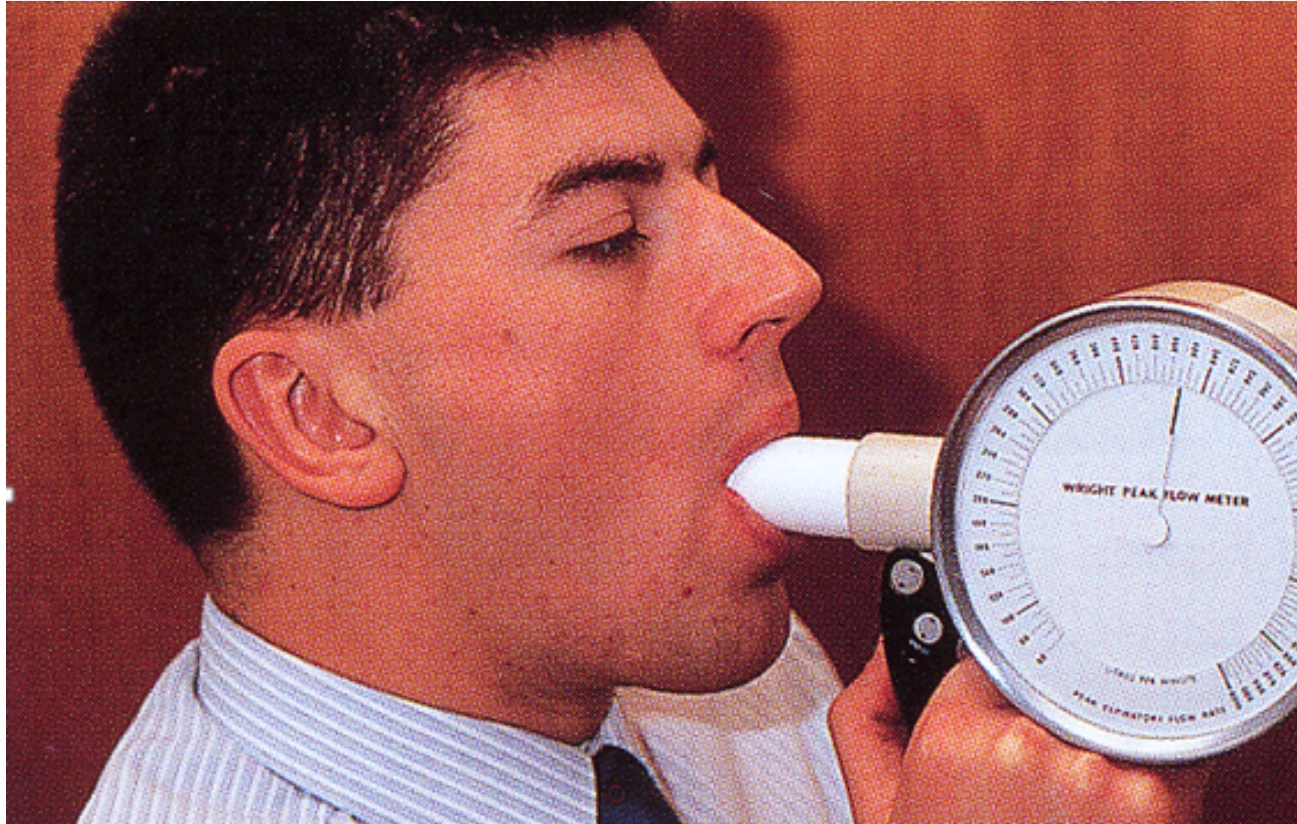
Skin prick testing in a patient with asthma.



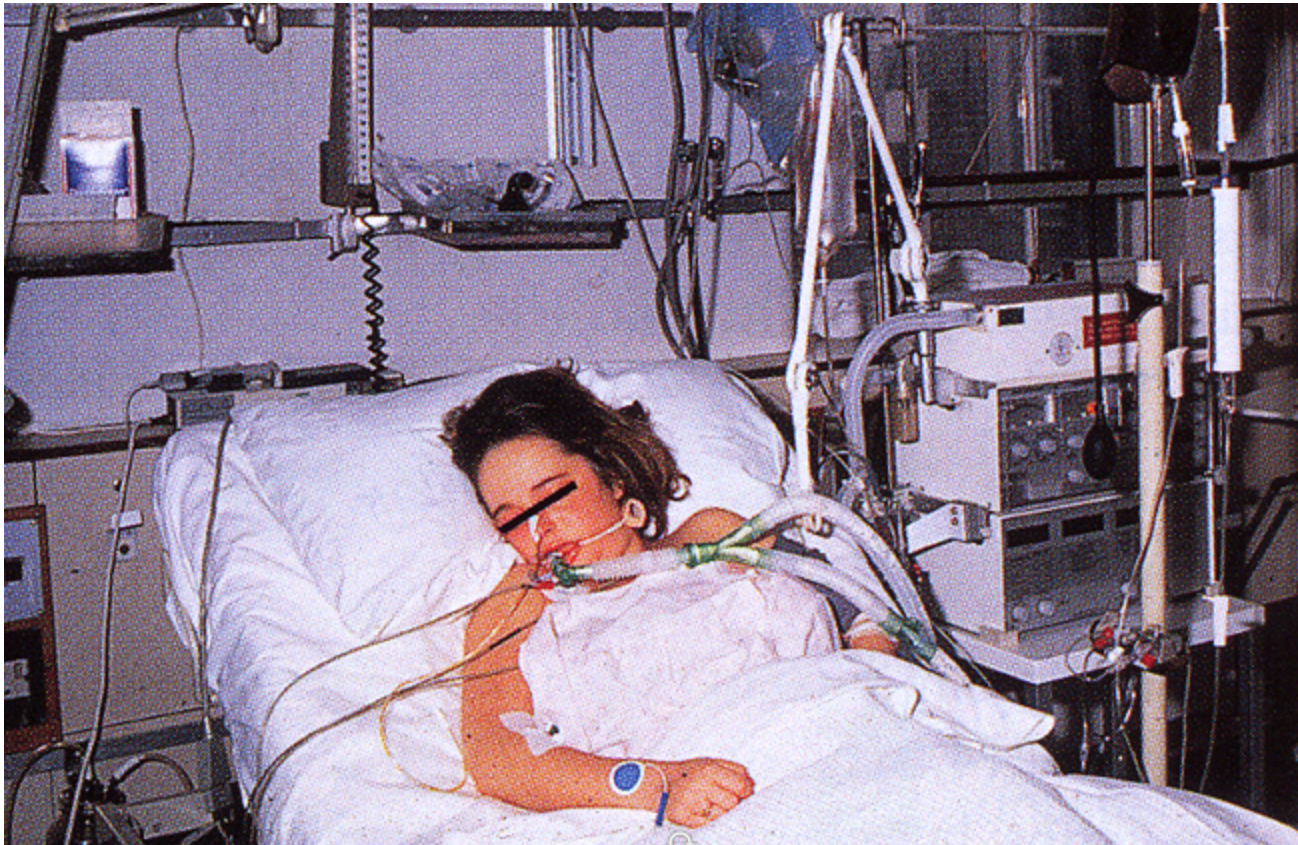
IgE mediated type I
hypersensitivity reaction to
inhaled allergens

CLINICAL Features

- manifestations vary from occasional wheezing to paroxysms of dyspnea and respiratory distress.
- In a classic asthmatic attack there is **dyspnea, cough, difficult expiration, progressive hyperinflation of lung and mucous plug in bronchi**. This may resolve spontaneously or with treatment.
- Nocturnal cough
- Increased anteroposterior diameter, due to air trapping and increase in residual volume
- Status asthmaticus – Overinflated lungs with severe obstruction and air trapping leading to severe cyanosis and persistent dyspnea, may be fatal



The range of presentation in asthma. This patient was found incidentally to have a degree of reversible airways obstruction during a routine medical examination.



This patient presented as a medical emergency with acute severe breathlessness and diagnosed as a case of status asthmaticus (Overinflated lungs because of sever obstruction and air trapping) which required immediate intensive care including intermittent positive-pressure ventilation.

COMPLICATIONS OF ASTHMA

- **Airway remodeling:**
 - some persons with long standing asthma develop permanent structural changes in the airway with *sub*-basement membrane fibrosis, hypertrophy of muscle and progressive loss of lung function that increase airflow obstruction and airway responsiveness.
- **Superimposed infection** i.e. pneumonia
- **Chronic bronchitis**
 - i.e. Asthmatic bronchitis: chronic bronchitis with superimposed asthma
- **Emphysema, pneumothorax and pneumomediastinum**
- **Bronchiectasis**
- **Status asthmaticus (Overinflated lungs with severe obstruction and air trapping)**
- **Respiratory failure**
 - requiring intubation in severe exacerbations i.e. status asthmaticus
- In some cases **cor pulmonale and heart failure** develop.

Prognosis

- Remission- approximately 50% of cases of childhood asthma resolve spontaneously but may recur later in life; remission in adult-onset asthma is less likely.
- Mortality- death occurs in approximately 0.2% of asthmatics. Mortality is usually (but not always) preceded by an acute attack and about 50% are more than 65 years old.

Prevention

- ▣ Control of factors contributing to asthma severity.
 - ▣ Exposure to irritants or allergens has been shown to increase asthma symptoms and cause exacerbations.

- ▣ Skin test
 - ▣ results should be used to assess sensitivity to common indoor allergens.
 - ▣ All patients with asthma should be advised to avoid exposure to allergens to which they are sensitive.

Asthma: Summary

Episodic attacks of bronchoconstriction (reversible)

Types

- **Extrinsic asthma: Type 1 Hypersensitivity reaction, IgE, viral infection, childhood, family Hx of allergy.**
- **Intrinsic asthma: BA associated with, aspirin, exercise, cold induced. No Hx of allergy**

Morphology

- **Hypertrophy of bronchial smooth muscle & hyperplasia of goblet cells e eosinophils, thickened BM**
- **Mucous plug e Curschmann spirals & Charcot-Leyden crystals.**
- **Remodeling with sub-basement membrane fibrosis and hypertrophy of muscle layer**

Complication

- **Superimposed infection**
- **Chronic bronchitis**
- **Pulmonary emphysema**
- **Status asthmaticus (Overinflated lungs with sever obstruction and air trapping)**
- **Cor pulmonale**