# DISEASE OF THE RESPIRATORY SYSTEM

# Pathology of lung diseases

- Very important in clinical medicine.
- Primary lung infection.
- Complication of cigarette smoking and air pollution.
- Malignancy.
- Others.

# BRONCHIACTASIS

# Bronchiactasis

- Chronic necrotizing infection of the bronchi and bronchioles leading to or associated with abnormal dilatation of these airways.
- Bronchial dilatation should be permanent.

# Conditions associated with Bronchiactasis

1. Bronchial obstruction

   Localized:

   - tumor, foreign bodies or mucous impaction

   Generalized:

   - bronchial asthma
   - chronic bronchitis

2. Congenital or hereditary conditions:
   - Congenital bronchiactasis
   - Cystic fibrosis.
   - Intralobar sequestration of the lung.
   - Immunodeficiency status.
   - Immotile cilia and kartagner syndrome.
3. Necrotizing pneumonia.

   Caused by TB, staphylococci or mixed infection.

# Bronchiactasis

## Etiology and pathogenesis

- Obstruction and infection.

  Bronchial obstruction (athelectasis of airway distal to obstruction) – bronchial wall inflammation.

- These changes become irreversible:

  1. If obstruction persist.
  2. If there is added infection.

# Kartagener Syndrome

- Inherited as autosomal recessive trait.
- Patient develop bronchiactasis, sinusitis and situs invertus.
- Defect in ciliary motility due to absent or irregular dynein arms.
- Lack of ciliary activity interferers with bronchial clearance.
- Males have infertility.

# Morphology of Bronchiactasis

- Usually affects lower lobes bilaterally (vertical airways).
- Dilated airways up to four times of normal, reaching the pleura.
- Tube-like enlargement (cylindroid) or fusiform (saccular).
- Acute and chronic inflammation, extensive ulceration of lining epithelium with fibrosis.

# Bronchiactasis

## Clinical Course:

- Severe persistent cough with sputum (Mucopurulent, fetid sputum) sometime with blood.
- Clubbing of fingers.
- If severe, obstructive pulmonary function develop.
- Rare complications: metastatic brain abscess and amyloidosis.

# Chronic Obstructive Pulmonary Disease (COPD)

- A group of conditions that share a major symptom – dyspnea.
- Chronic or recurrent obstruction to airflow within the lung.
- The incidence of COPD has increased dramatically in the past few decades.
- Include chronic bronchitis, bronchieactasis, asthma and emphysema.
- Emphysema and chronic bronchitis often co-exist.

# Chronic Bronchitis

- Common among cigarette smokers and urban dwellers.
- The diagnosis of chronic bronchitis is made on clinical grounds.
- Persistent productive cough for at least 3 consecutive months in at least 2 consecutive years.
- Can occur in several forms:
  1. Simple chronic bronchitis.
  2. Chronic mucopurulent bronchitis.
  3. Chronic asthmatic bronchitis.
  4. Chronic obstructive bronchitis.

# Chronic bronchitis (contd)

## Pathogenesis

- Hypersecretion of mucus that starts in the large airways.
- Causative factor are cigarette smoking and pollutants.

## Morphology

- Enlargement of the mucus-secreting glands, increased number of goblet cells, loss of ciliated epithelial cells, squamous metaplasia, dysplastic changes and bronchogenic carcinoma.
- Inflammation, fibrosis and resultant narrowing of bronchioles.
- Coexistent emphysema.

## Clinical Course

- Prominent cough and the production of sputum.
- COPD with hypercapnia, hypoxemia and cyanosis.
- Cardiac failure.

# Obstructive and Restrictive Pulmonary Diseases

Diffuse pulmonary diseases are divided into:

1] Obstructive disease: characterized by an increase in resistance to airflow owing to partial or complete obstruction at any level from trachae to respiratory bronchioles.

- Pulmonary function test: limitation of maximal airflow rate during forced expiration (FEVI).

2] Restrictive disease: characterized by reduced expansion of lung parenchyma with decreased total lung capacity while the expiratory flow rate is near normal.

Occur 1. Chest wall disorder.

2. Acute or chronic, intestinal and infiltrative diseases, e.g. ARDS and pneumoconiosis.

# Chronic obstructive pulmonary diseases

## Bronchial asthma

- Chronic relapsing inflammatory disorder characterized by hyperactive airways leading to episodic, reversible bronchoconstriction owing to increased responsiveness of the tracheobronchial free to various stimuli.
- It has been divided into two basic types:
  1. Extrinsic asthma.
  2. Intrinsic asthma.
- Clinical features: attacks of dyspnea, cough and wheezing.

# CLASSIFICATION OF ASTHMA

## Extrinsic Asthma

- Initiated by type 1 hypersensivity reaction induced by exposure to extrinsic antigen.
- Subtypes include:
  a. atopic (allergic) asthma.
  b. occupational asthma.
  c. allergic bronchopulmonary aspergillosis.
- Develop early in life

## Intrinsic Asthma

•Initiated by diverse, non-immune mechanisms, including ingestion of aspirin, pulmonary infections, cold, inhaled irritant, stress and exercise.

•No personal or family history of allergic reaction.

•Develop later in life.

# Extrinsic Asthma

- Atopic (allergic) asthma is the most common form
- Other allergic manifestation
- Other family member is also affected
- Serum IgE and eosinophil are increased
- immune related, $T_H2$ subset of CD4+ T cells

# Pathogenesis of Bronchial Asthma

EXAGGERATED BROCHOCONTRICTION

- Two components:
  1. Chronic airway inflammation.
  2. Bronchial hyperresponsiveness.
- The mechanisms have been best studied in atopic asthma.

# Pathogenesis of Extrinsic Asthma

- Begins in childhood.
- Triggered by environmental antigens, e.g. dusts, pollen, animal dander or food.
- Positive family history of atopy.
- Preceded by allergic rhinitis, urticaria, eczema.
- Skin test with antigen result in an immediate wheel and flare reaction.

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# Pathogenesis of Atopic Asthma

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- Positive family history of atopy.
- Preceded by allergic rhinitis, urticaria, eczema.
- Skin test with antigen result in an immediate wheel and flare reaction.

# Pathogenesis of Atopic Asthma (contd)

- A classic example of type 1 IgE-mediated hypersensitivity reaction.
- In the airway – initial sensitization to antigen (allergen) with stimulation of Th2-type T cells and production of cytokines (IL-4, IL-5).
- Cytokines promote:
  1. IgE production by B cell.
  2. Growth of mast cells.
  3. Growth and activation of eosinophils.

# Pathogenesis of Atopic Asthma (contd)

- IgE-mediated reaction to inhaled allergens elicits acute response (within minutes) and a late phase reaction (after 4-8 hours).

# Pathogenesis of Bronchial Asthma (contd)

- Mediator preduced during acute-phase respnse are from mast cells, including chemotactic factors and cytokines.
- In the late phase reaction, mediators are preduced by:
  1. Inflammatory cells. e.g. major basic protein of eosinophils.
  2. Endothelium.
  3. Airway epithelial cells e.g. eotaxin.
- Important mediator includes:

  A. Bronchoconstrictor – 1. Leukotriens C4, D4 & E4.
  2. Acetylcholine.

  B. Others – histamine, postaglandin D2 and PAF

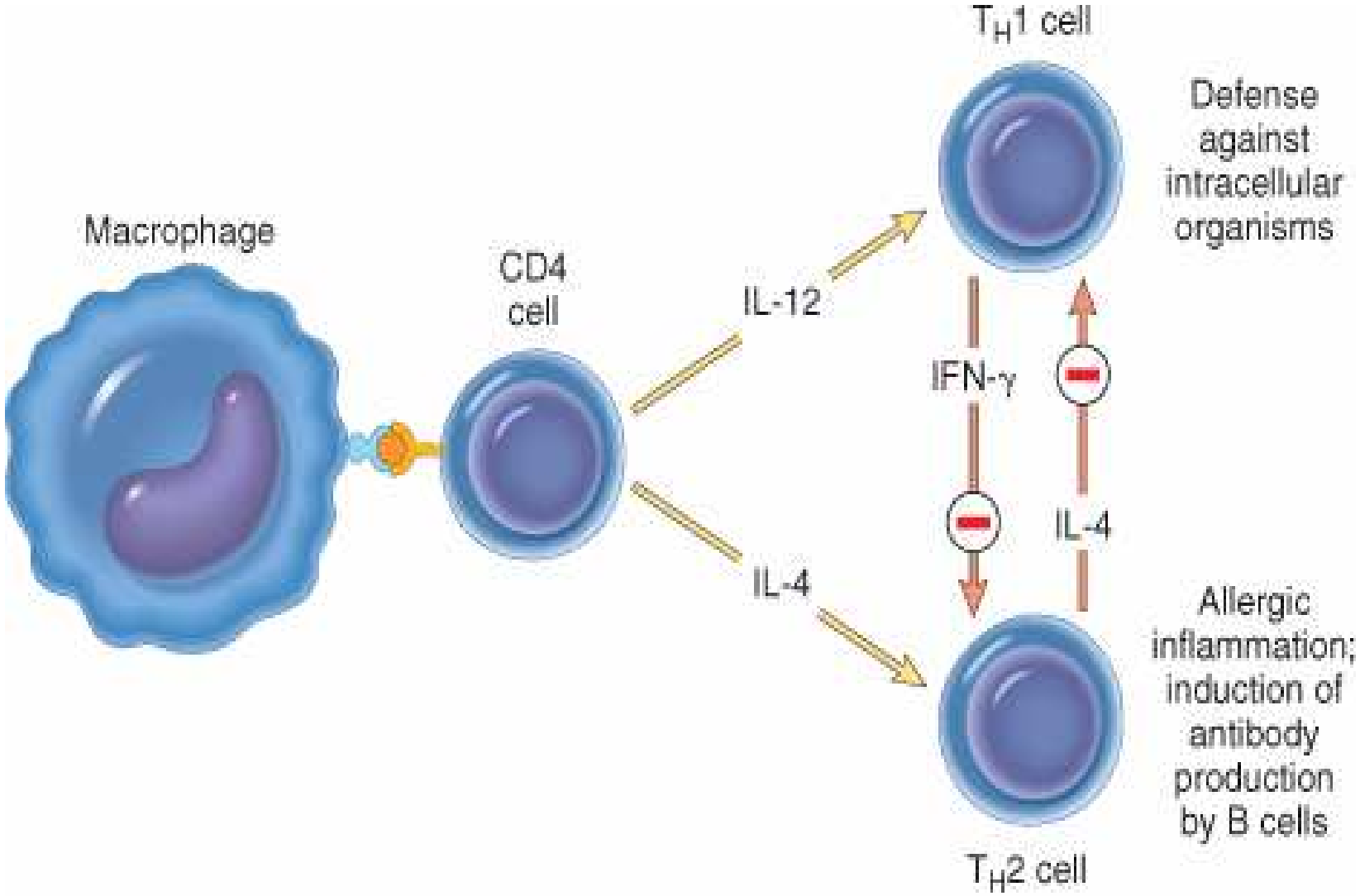
  C. Cytokines (IL-1, TNF, IL-6).

# Non-Atopic Asthma

- Triggered by respiratory tract infection including viruses and inhaled air pollutants e.g. sulfur dioxide, ozone.
- Positive family history is uncommon.
- Serum IgE – normal.
- No other associated allergies.
- Skin test – negative.
- Hyperirritability of bronchial tree.
- Subtypes:
  1. Drug-induced asthma.
  2. Occupational asthma.

# Morphology of Asthma

- Grossly: - lung overdistended (over inflammation)
  - occlusion of bronchi and bronchioles by thick mucous.
- Histologic finding: mucous contain Curschmann spirals, eosinophil and Charcot-Leyden crystals.
- Thick BM.
- Edema and inflammatory infiltrate in bronchial wall.
- Submucosal glands increased.
- Hypertrophy of the bronchial wall muscle.



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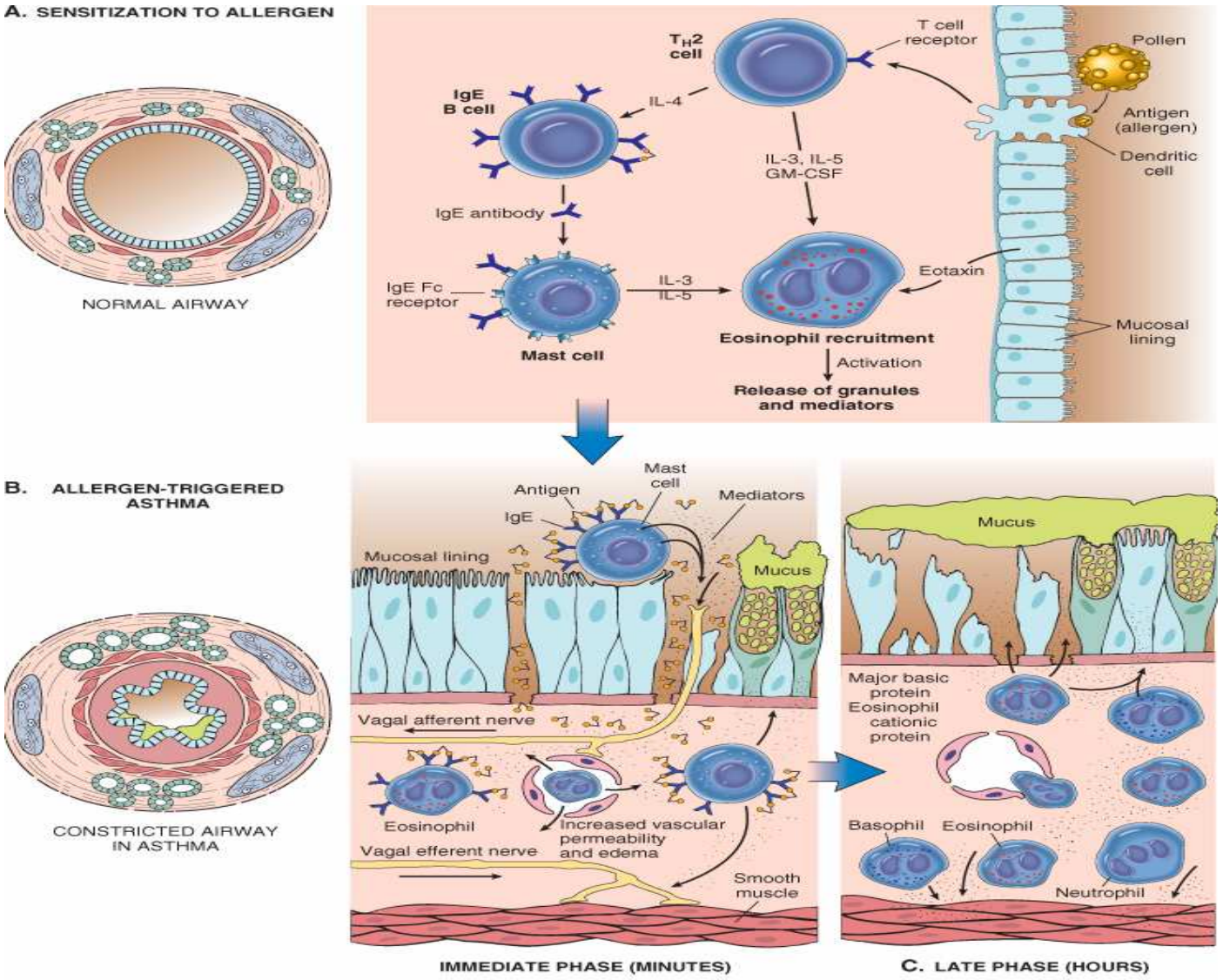


- IgE-mediated reaction to inhaled allergens elicits acute response (within minutes) and a late phase reaction (after 4-8 hours)
- Mediators induce bronchospasm, vascular permeability & mucous production.

# Pathogenesis of Atopic Asthma

- Mediator produced during acute-phase response are :
  - Leukotrienes C4, D4 & E4
  - Prostaglandins D2, E2, F2
  - Histamine
  - Platelet-activating factor
  - Mast cell tryptase.
- In the late phase reaction, recruitment of leukocytes mediated by product of mast cells including:

1. Eosinophil and neutophil chemotactic factors
2. IL-4 & IL-5 and induceTH2 subset ofCD4+ T cells
3. Platelet-activating factor
4. Tumor necrosis factor.

- Other cell types are involved: activated epithelial cells, macrophages and smooth muscle (eotaxin)

# Pathogenesis of Atopic Asthma

Late phase reaction:

- The arrival of leukocytes at the site of mast cell degranultion lead to:
  1. Release of more mediators to activate more mast cells
  2. Cause epithelial cell damage .

  Eosinophils produce major basic protein, eosinophilic cationic protein and eosinophil peroxidase. These amplify and sustains injury without additional antigen.

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# Clinical Coarse

- Classic asthmatic attack – dyspnea, cough.
- Status asthmaticus – severe cyanosis and death.
- May progress to emphysema.
- Superimposed bacterial infection may occur.