Asthma and Bronchiectasis

MEDEMIA ACADEMY

Asthma

- Chronic inflammatory disorder of the airways.
- Causes recurrent episodes of wheezing(due to bronchospasm), Dyspnea, chest tightness and cough particularly at night and/or early in the morning(due to lowest level of steroid).
- **its hallmarks are, usually found at biopsy :**
  - Intermittent and reversible(opposite to bronchiectasis)airway obstruction (bronchospasm).
  - Chronic bronchial inflammation with eosinophils(unlike chronic bronchitis).
  - Bronchial smooth muscle cell hypertrophy and hyper- reactivity(remodeling).
  - increased mucus secretion(lesser amount in compare of chronic bronchitis).

Major factors & Triggers

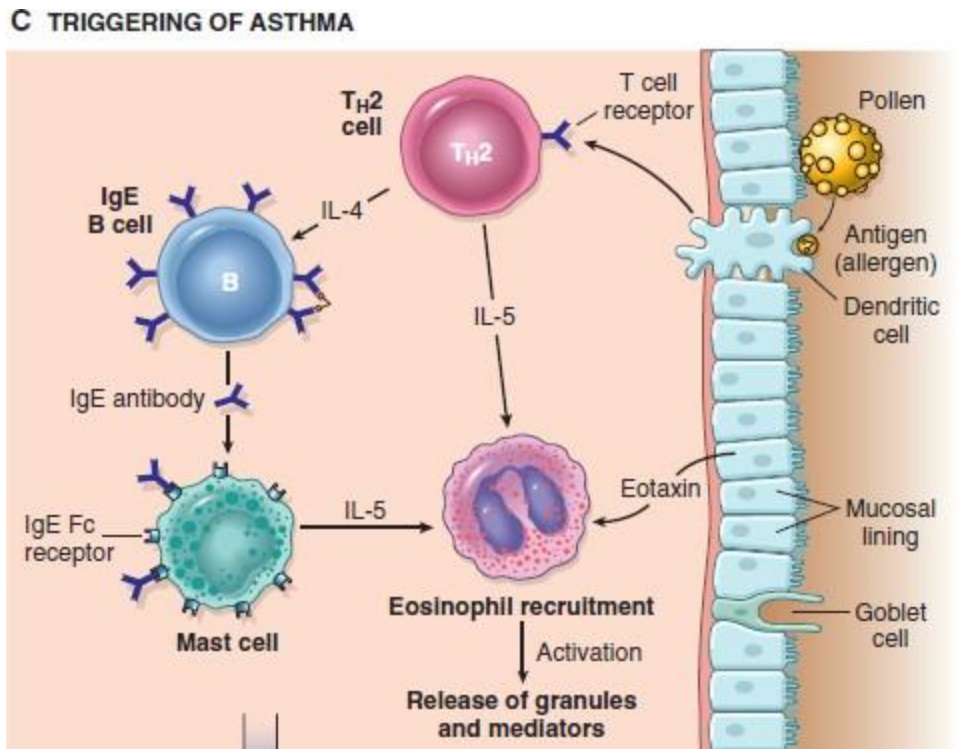
❖Major factors

- Genetic predisposition to type I hypersensitivity(atopy),which is igE mediated as in Rhinosinusitis and urticaria(atopic Triad with asthma).
- Acute(when there is signs and symptoms)and chronic airway inflammation.
- Bronchial hyperresponsiveness to a variety of stimuli

❖Triggers

- Respiratory infections (especially viral),URTI
- Airborne irritants (smoke, fumes)
- Cold air
- Stress
- Exercise
- Drugs

Pathogenesis



Pathophysiology

A. Initial Phase: Sensitization

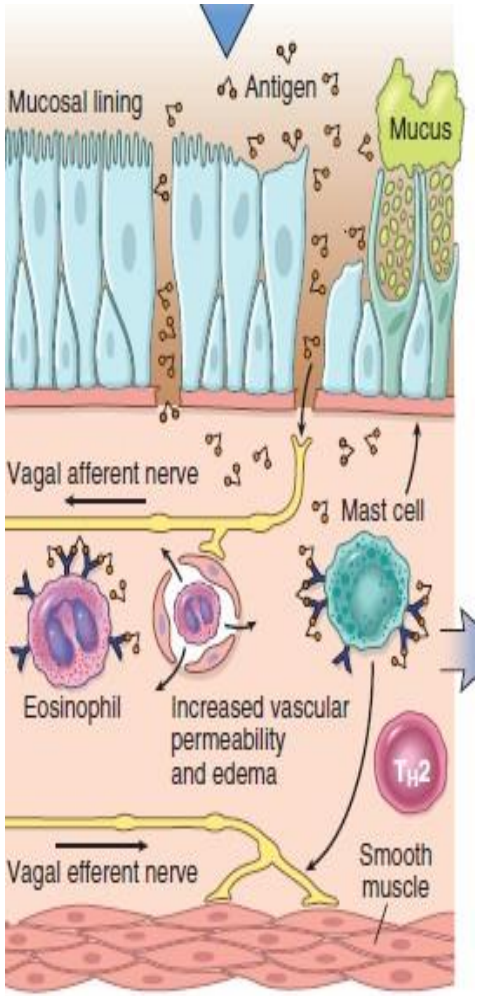
- An antigen is taken up by dendritic cells(APC), leading to the production of IgE by the cytokines that produced.
- IgE binds to Fc receptors on mast cells.

❖Exposure to Antigen

- Excessive Activation of type 2 helper T cells (TH2).
- Cytokine Production:
  - IL-4 and IL-13: Stimulate IgE production.
  - IL-5: Activates eosinophils by secretion of Eotaxin(secreted from epithelium).
  - IL-13: Also stimulates mucus production.

B. Early-Phase Reaction (Immediate Reaction) on re-exposure to Ag

- Triggered by Ag-induced cross-linking of IgE on mast cells.
- Mast cells release preformed mediators that directly and via neuronal reflexes induce:
  - Bronchoconstriction(bronchospasm) (due to action of vagal nerve).
  - Increased Mucus Production.
  - Vasodilation(Increased vascular permeability).
  - Recruitment of leukocytes.

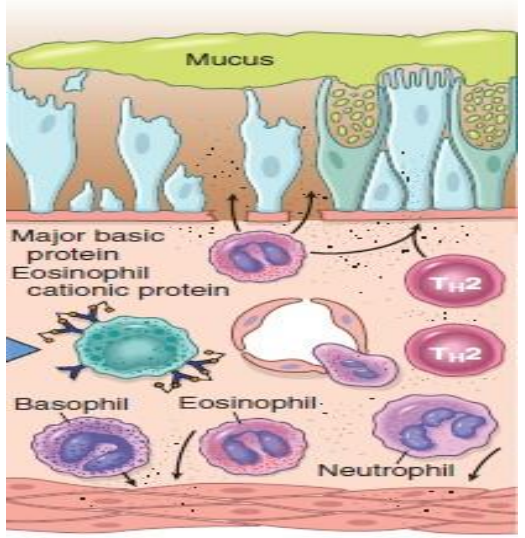


D IMMEDIATE PHASE (MINUTES)

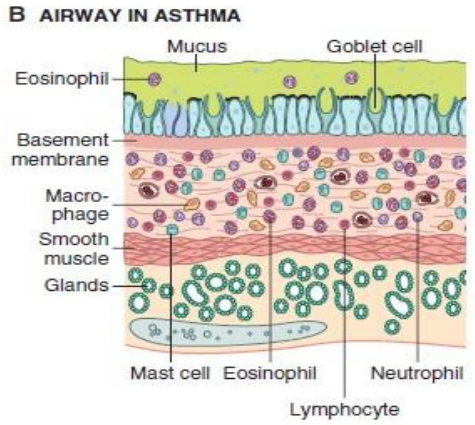
Pathophysiology Cont.

C. Late-Phase Reaction (Inflammatory)

- Prolonged activation of initial pathophysiological response (early phase) results in the cellular destruction.
- Inflammatory Mediators stimulate epithelial cells to produce:
  - Chemokines (eotaxin)
  - Recruit TH2 cells, eosinophils, and other leukocytes, amplifying inflammation.
- Recruited Leukocytes to site of reaction(neutrophils, eosinophils, basophils, lymphocytes, monocytes) release mediators, initiating late-phase asthma.
- Eosinophils release major basic protein and eosinophil cationic protein, damaging the epithelium.



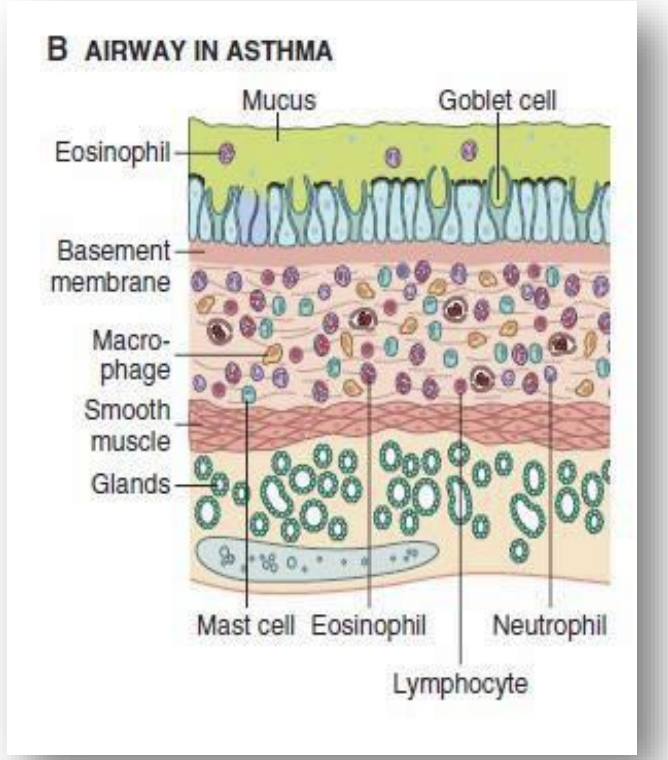
E LATE PHASE (HOURS)

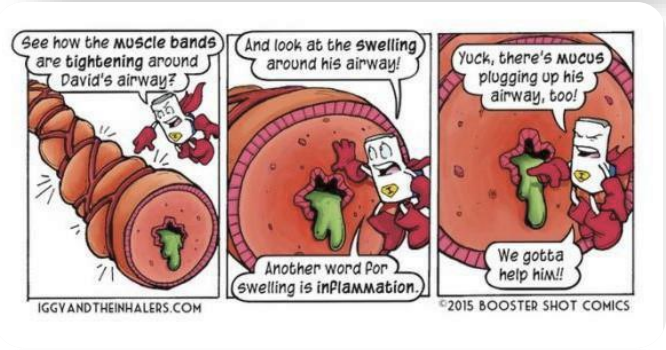


Pathophysiology Cont.

D. Structural Changes (Airway Remodeling)

- Due to recurrent pouts of inflammation, results in structural changes in bronchial wall (airway remodeling) includes :
  - Hypertrophy and hyperplasia of bronchial smooth muscle, due to intense chronic inflammation.
  - Hypertrophy of mucus glands and accumulation in brachial lumen.
  - Hypertrophy of submucosa glands.
  - Increased vascularity.
  - Deposition of subepithelial collagen(fibrosis), thickened basement membrane.





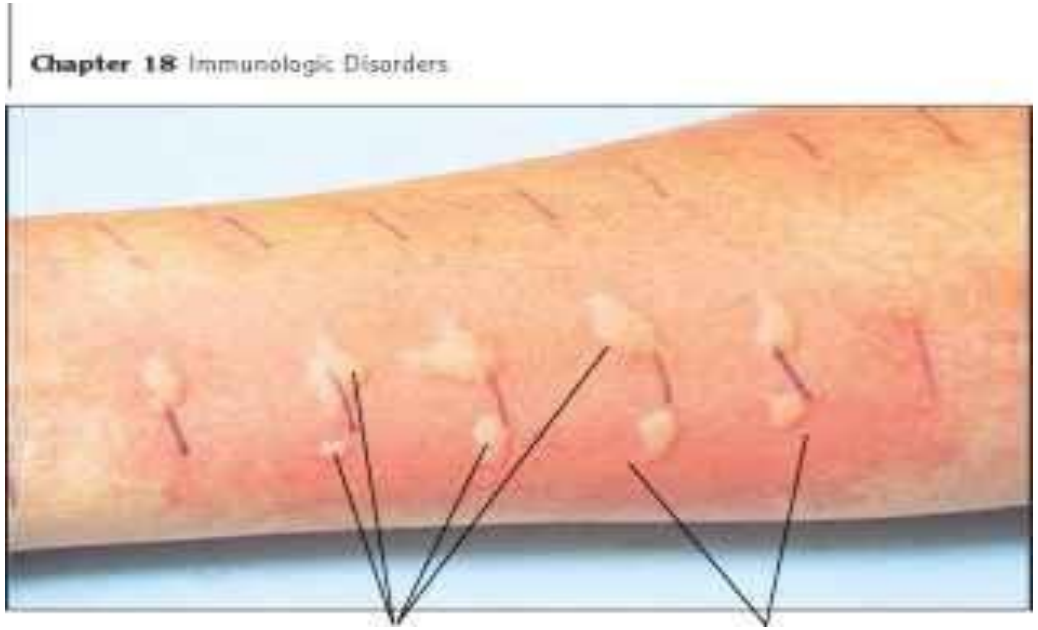
Types of asthma

1. Atopic asthma :

- The most common.
- Classic example of type I IgE–mediated hypersensitivity reaction.
- beginning in childhood.
- Positive family history of atopy and/or asthma attacks are preceded by allergic rhinitis, urticaria, or eczema.
- Attacks are triggered by allergens in dust, pollen, animal dander, or food, or by infections.
- Exposure to the antigen excessive activation of type 2 helper cells and Cytokines production :
  - IL-4
  - IL-5
  - IL-13
- IgE coats submucosal mast cells release of Mast cell–derived mediators produce two waves of reaction:
  - early (immediate) phase of reaction
  - late phase of reaction

Diagnosis

- **Clinical history**
- **Skin test with the antigen:**
  - Immediate wheal-and-flare reaction.
- **Serum radioallergosorbent tests (RASTs) :**
  - Detects allergen specific IgE in the blood.
- Confirm diagnosis of asthma with PFTs(post bronchodilator test).

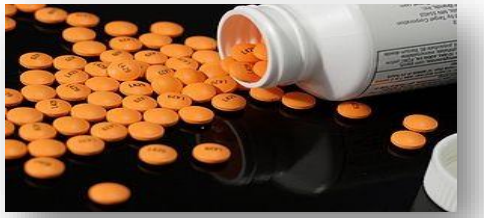


Types of asthma Cont.

2. Non-atopic asthma :

- No evidence of allergen sensitization.
- Negative skin test.
- A positive family history of asthma is less common.
- Triggered by:
  - viral respiratory infections (rhinovirus, parainfluenza virus).
  - inhaled air pollutants (sulfur dioxide, ozone, nitrogen dioxide).

Types of asthma Cont.



3. Drug induced asthma:

❖Eg: Aspirin(NASID) induced asthma .

❖The precise pathogenesis is unknown, involve some abnormality in prostaglandin metabolism from inhibition of cyclooxygenase by asprin.

- Inhibition of COX-1→ ↓ PGE2 (normally has an anti-inflammatory effect and decreases production of proinflammatory leukotrienes→ ↑ leukotrienes and inflammation → submucosal edema→ airway obstruction.

❖ Present with recurrent rhinitis ,nasal polyps , urticaria, and bronchospasm.

❖Characterized by the Samter triad:

- Bronchial asthma and/or chronic rhinosinusitis with polyposis

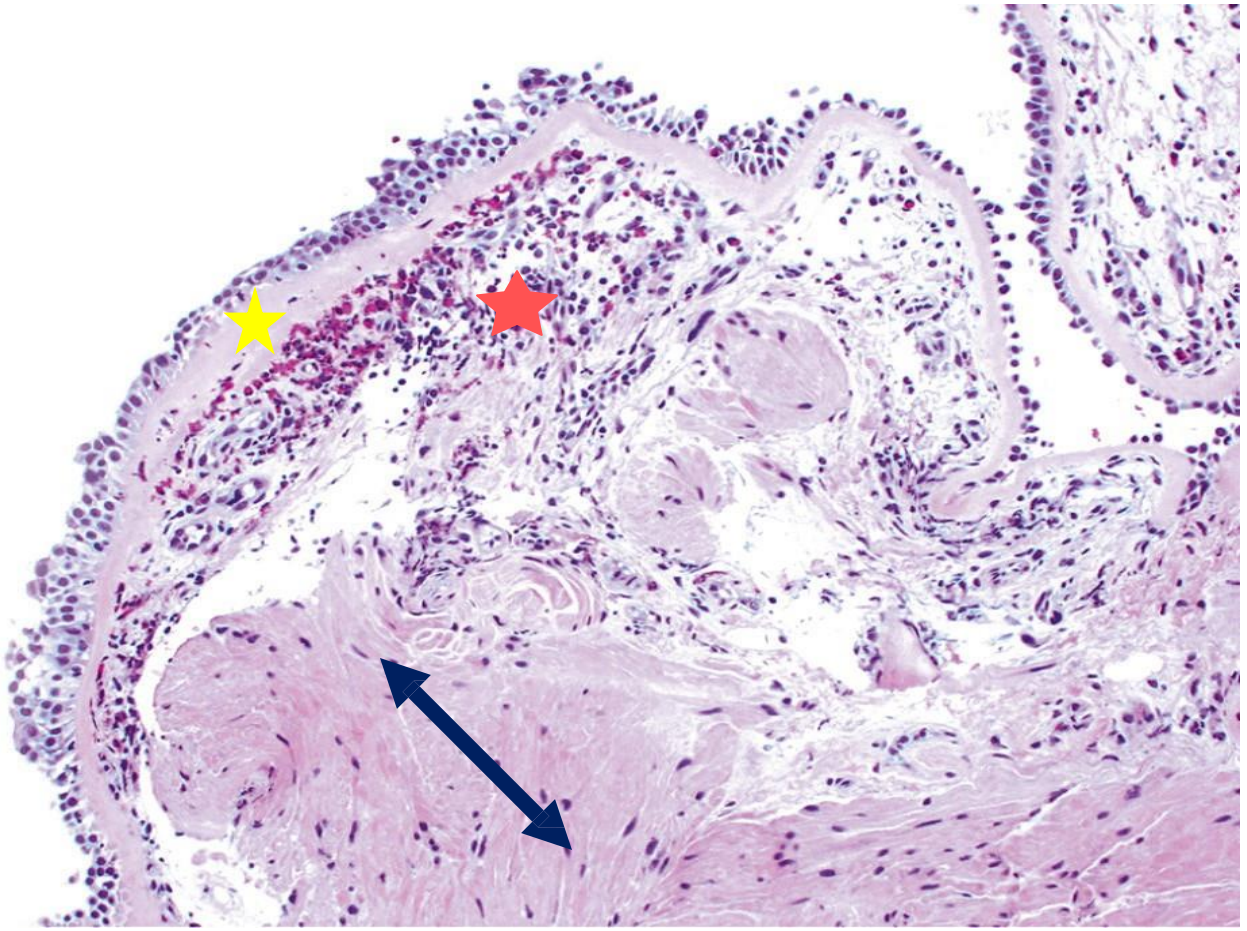
Types of asthma cont.

4. Occupational asthma :

- ❖ 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 antigen.

Morphology

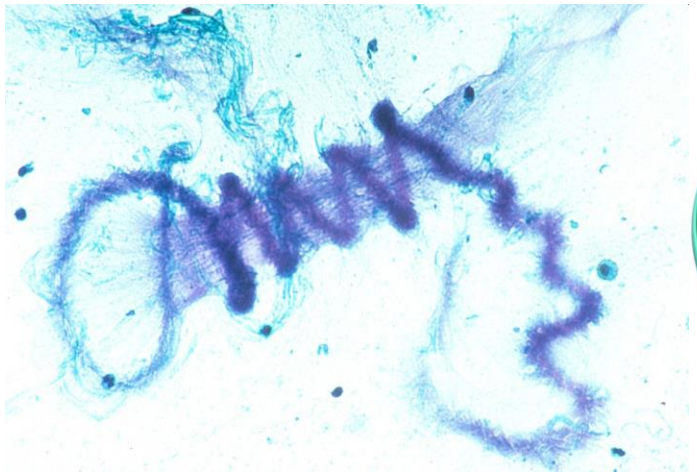
- Bronchial biopsy specimen from an asthmatic patient showing:
  - sub basement membrane fibrosis reflected in Yellow star.
  - Eosinophilic inflammation reflected in Red star.
  - Smooth muscle hyperplasia reflected in the Arrow.



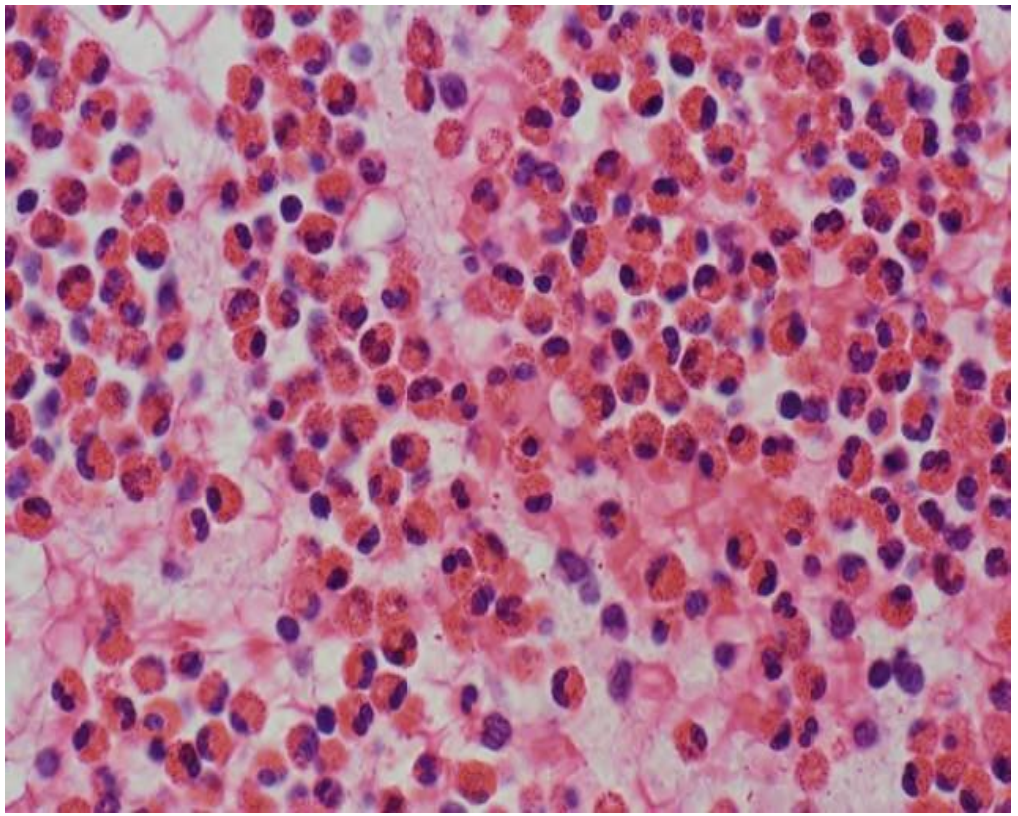
Morphology Cont.

❖**Curschman Spirals in sputum:**

❖Occlusion of bronchi and bronchioles by thick mucous plugs that contain whorls of shed epithelium called Curschmann spirals

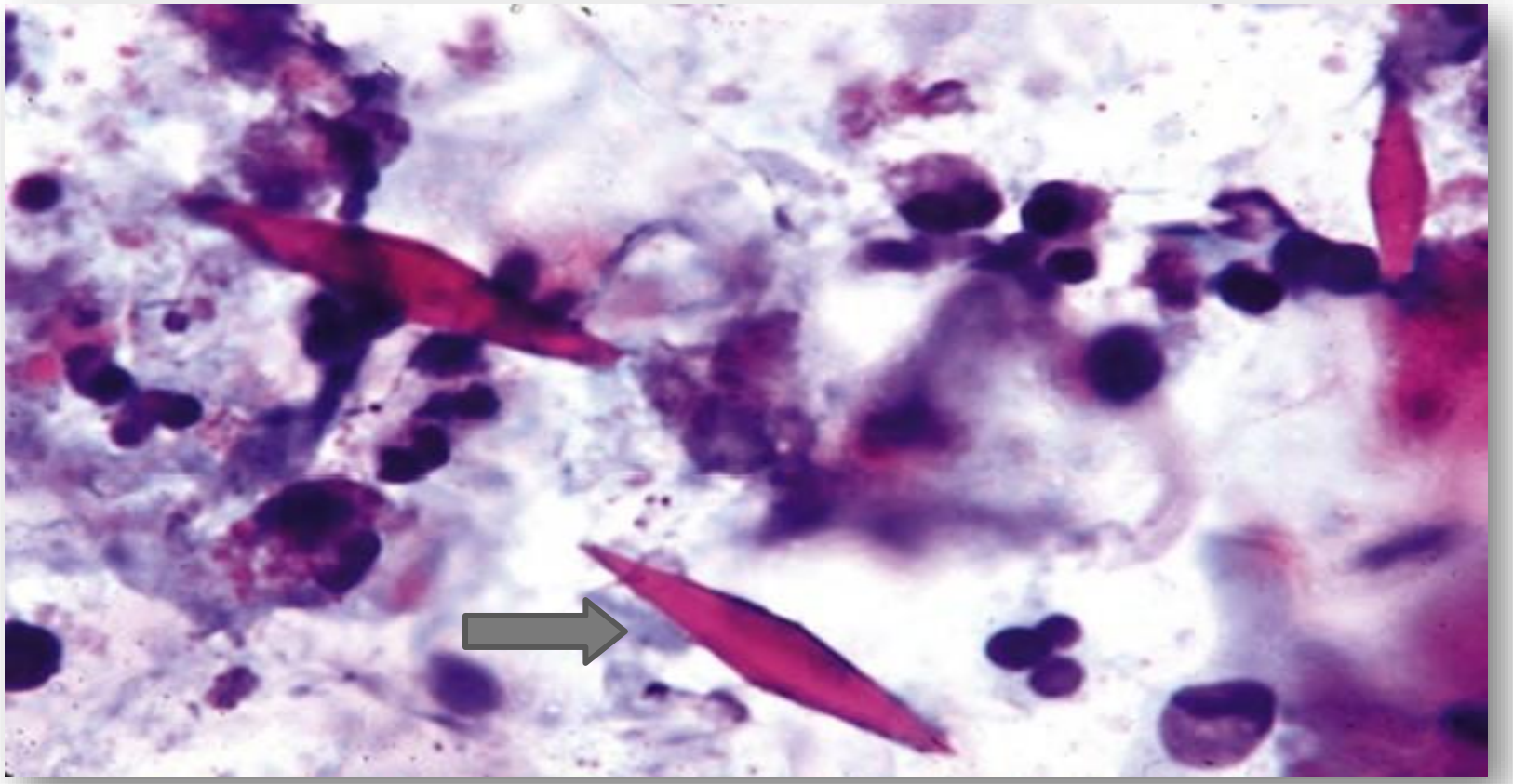


❖**Eosinophils:**



Morphology Cont.

- Charcot-Leyden crystals (destroyed Eosinophils): crystalloids made up of the eosinophil protein galectin-10.

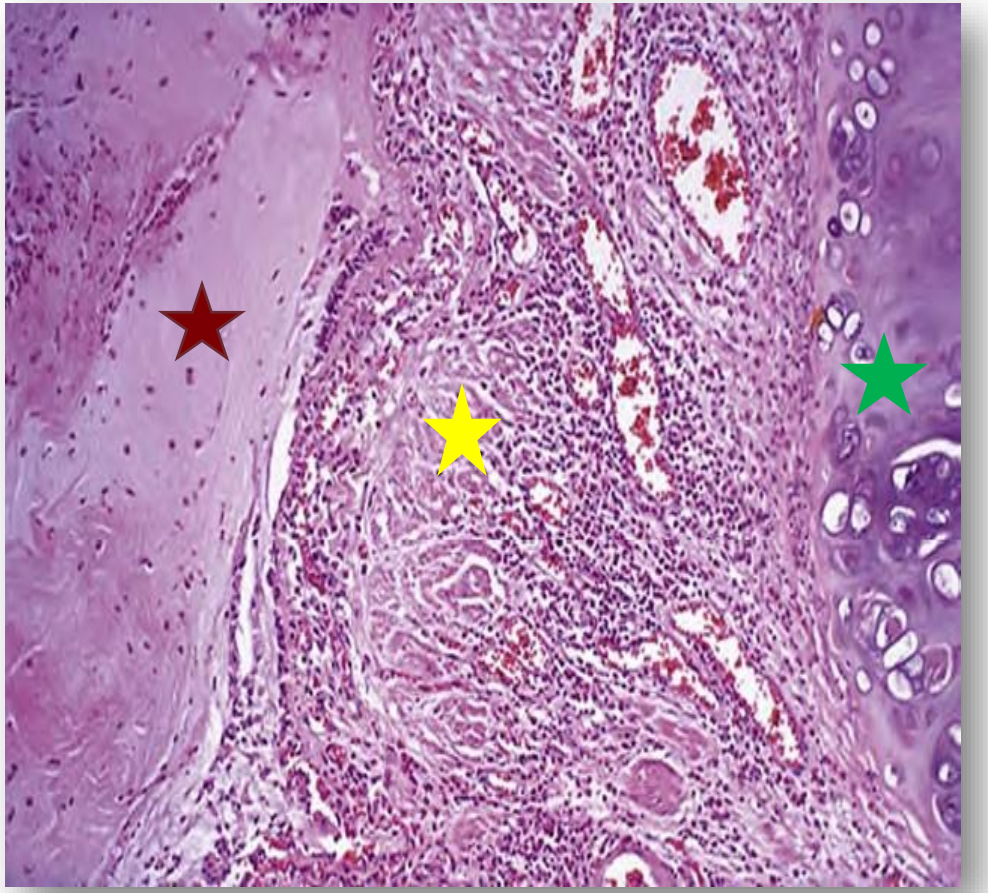


Morphology Cont.

- **Airway remodeling, including:**
  - Thickening of airway wall
  - Sub-basement membrane fibrosis
  - Increased submucosal vascularity
  - An increase in size of the submucosal glands and goblet cell metaplasia of the airway epithelium.
  - Hypertrophy and/or hyperplasia of the bronchial muscle.
  - In fatal cases distension of lungs.

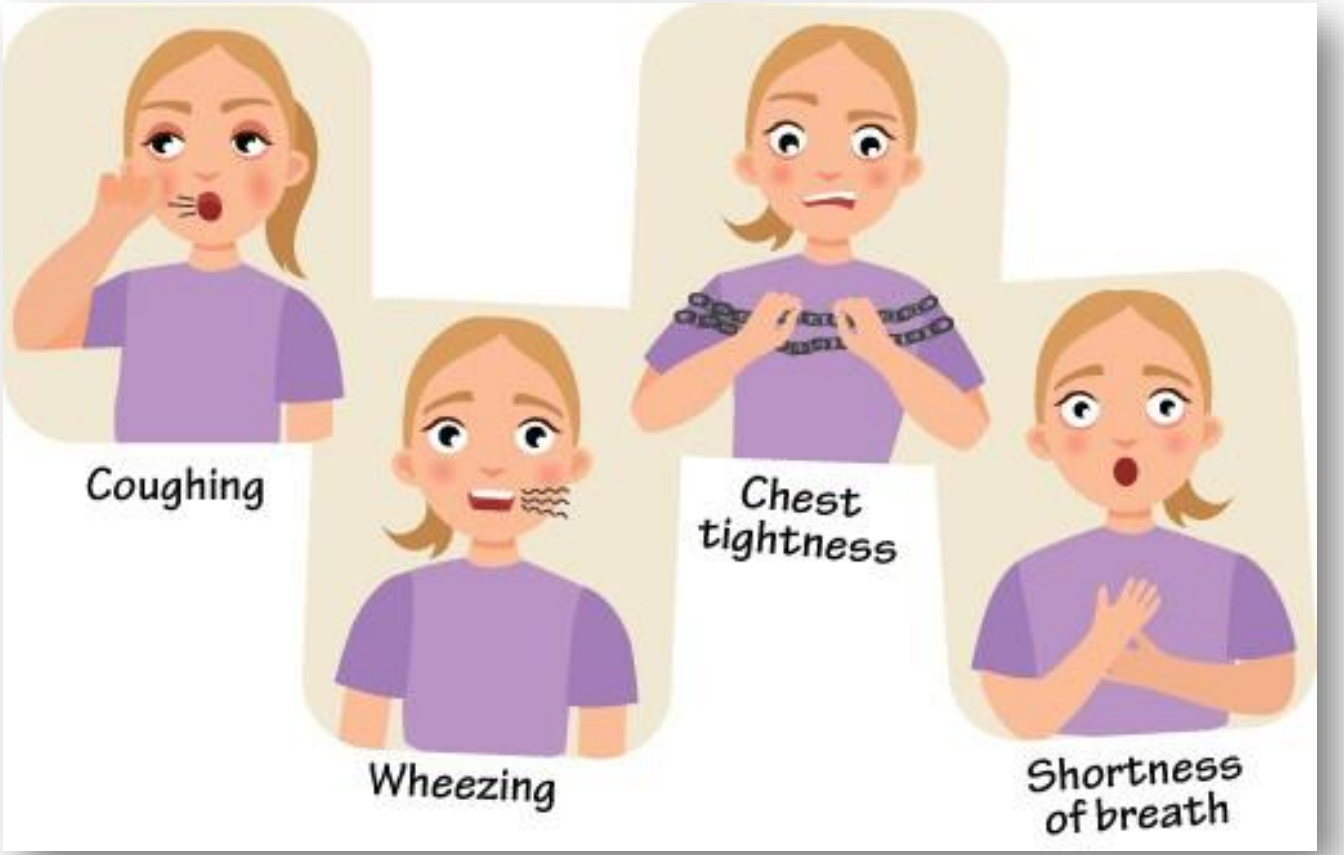
Morphology Cont.

- Main Bronchus section(cartilage exists):
  - Red star refer to smooth muscle hypertrophy.
  - Yellow star refer to Eosinophils.
  - Green star refer to cartilage.



Clinical features

- Sounds of Wheeze in link below :
  - https://www.youtube.com/watch?v=7oTfvJff7go

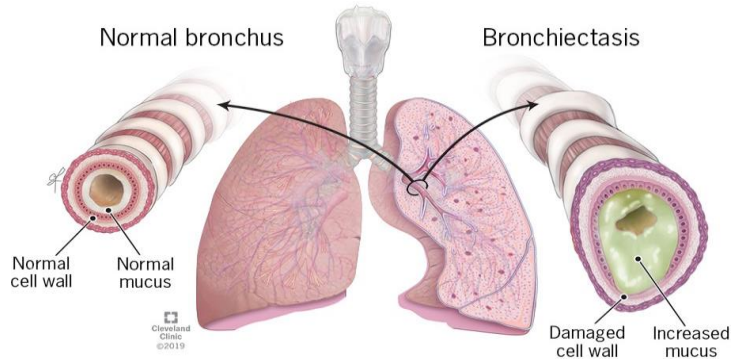


Status asthmaticus:

- status asthmaticus is a severe paroxysm that does not respond to therapy and persists for days or weeks, needs hospital admission.
- The associated hypercapnia, acidosis, and severe hypoxia may be fatal.
- Clinical feature :
  - Tachypnea
  - Tachycardia
  - Pulsus paradoxus
  - Hypoxemia (SpO2 < 90% on ambient air, possible cyanosis)
  - Silent chest
- Standard therapies include:
  - Anti-inflammatory drugs(glucocorticoids) usually given in Intravenous route opposite in mild or moderate asthma (oral route or only Bronchodilators).
  - Bronchodilators (beta-adrenergic drugs),we avoid using BB with asthma patients.
- Leukotriene inhibitors as (Montelukast).

Bronchiectasis

- **Definition:** Permanent dilation of bronchi and bronchioles caused by destruction of smooth muscle and the supporting elastic tissue.
- Typically results from or is associated with chronic necrotizing infections.
- It is not a primary disorder, as it always occurs secondary to persistent infection or obstruction.
- **Clinical feature**: cough and expectoration of copious(infected)amounts of purulent sputum(foul swelling).



Bronchiectasis Cont.

- **Diagnosis:** appropriate history and radiographic demonstration of bronchial dilation.
- Findings on imaging Bronchial dilation
  - Cylindrical or tubular (most common) : tram track sign and signet ring sign
  - Saccular or cystic (most severe form)
- Thickened bronchial walls, mucus plugging, honeycombing (suggests late-stage bronchiectasis)

Etiology

- **The conditions that most commonly predispose to bronchiectasis include:**
- **Bronchial obstruction:**
  - By tumors, foreign bodies, and impaction of mucus OR as a complication of atopic asthma and chronic bronchitis.
- **Necrotizing, or suppurative, pneumonia:**
  - Particularly with virulent organisms such as Staphylococcus aureus or Klebsiella spp.

Etiology Cont.

❖ **Congenital or hereditary conditions:**

A. Cystic fibrosis:

- caused by defective chloride channels due to genetic mutations, Early signs include meconium ileus, poor growth, and malabsorption issues. As the disease progresses, patients may suffer from chronic respiratory infections, pancreatitis, and infertility, thickened mucus in the lungs leads to lung damage and recurring infections and damaging to cilia ,diagnosis is usually confirmed with a sweat chloride test and genetic testing.
- widespread severe bronchiectasis
- Due to obstruction caused by abnormally viscid mucus (stagnated mucus).
- secondary infections.

Etiology Cont.

B. Immunodeficiency states:

- Due to recurrent bacterial infections
- localized or diffuse

C. Primary ciliary dyskinesia (immotile cilia syndrome):

- rare autosomal recessive disorder results in abnormalities of cilia
- persistent infections.
- bronchiectasis + sterility(impaired cilia function in sperm) in males

Pathogenesis

❖Two intertwined processes contribute to bronchiectasis(vicious cycle results in damaging to smooth muscles and elastic layer):

A. Obstruction:

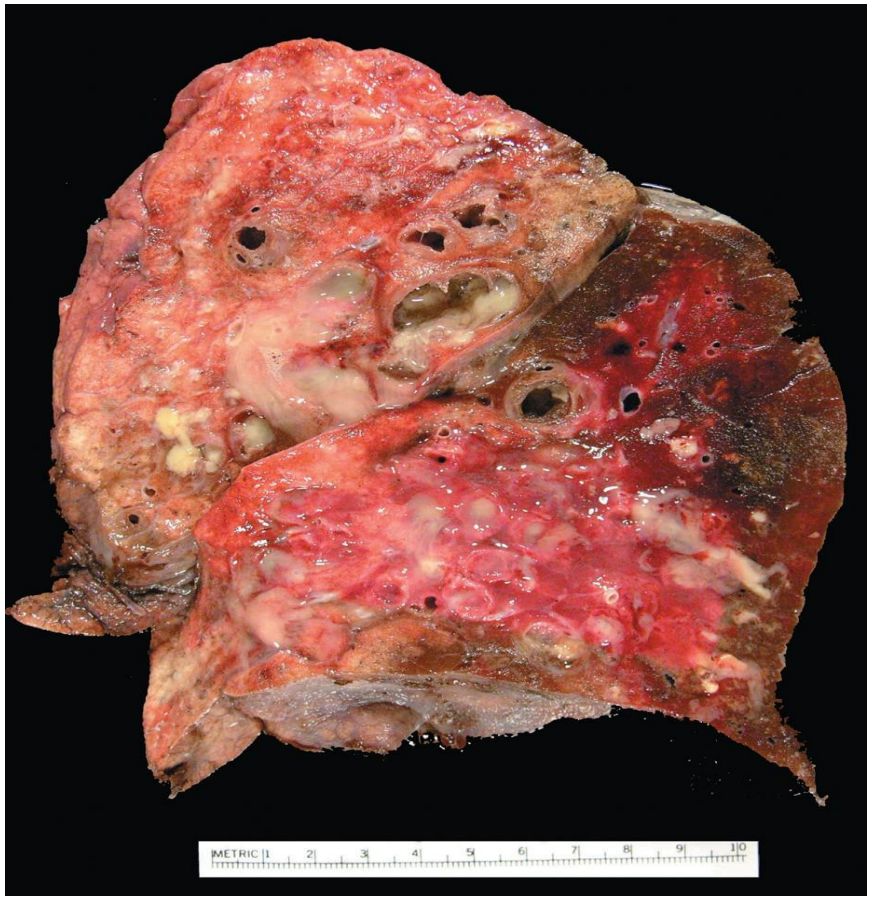
- Obstruction will impairs clearance of secretions results in superimposed infection then inflammatory damage to the bronchial wall and the accumulating exudate then airways distention end in irreversible dilation.

B. Chronic infection:

- Persistent necrotizing infection in the bronchi or bronchioles results in poor clearance of secretions, obstruction, and inflammation with peribronchial fibrosis and traction on the bronchi ends in irreversible dilation.

Morphology ,Macroscopic appearance

- Lower lobes bilaterally.
- most severe involvement in distal bronchi and bronchioles.
- The airways may be dilated to as much as four times their usual diameter
- **As appears in the picture :** Markedly dilated bronci filled with purulent mucus.

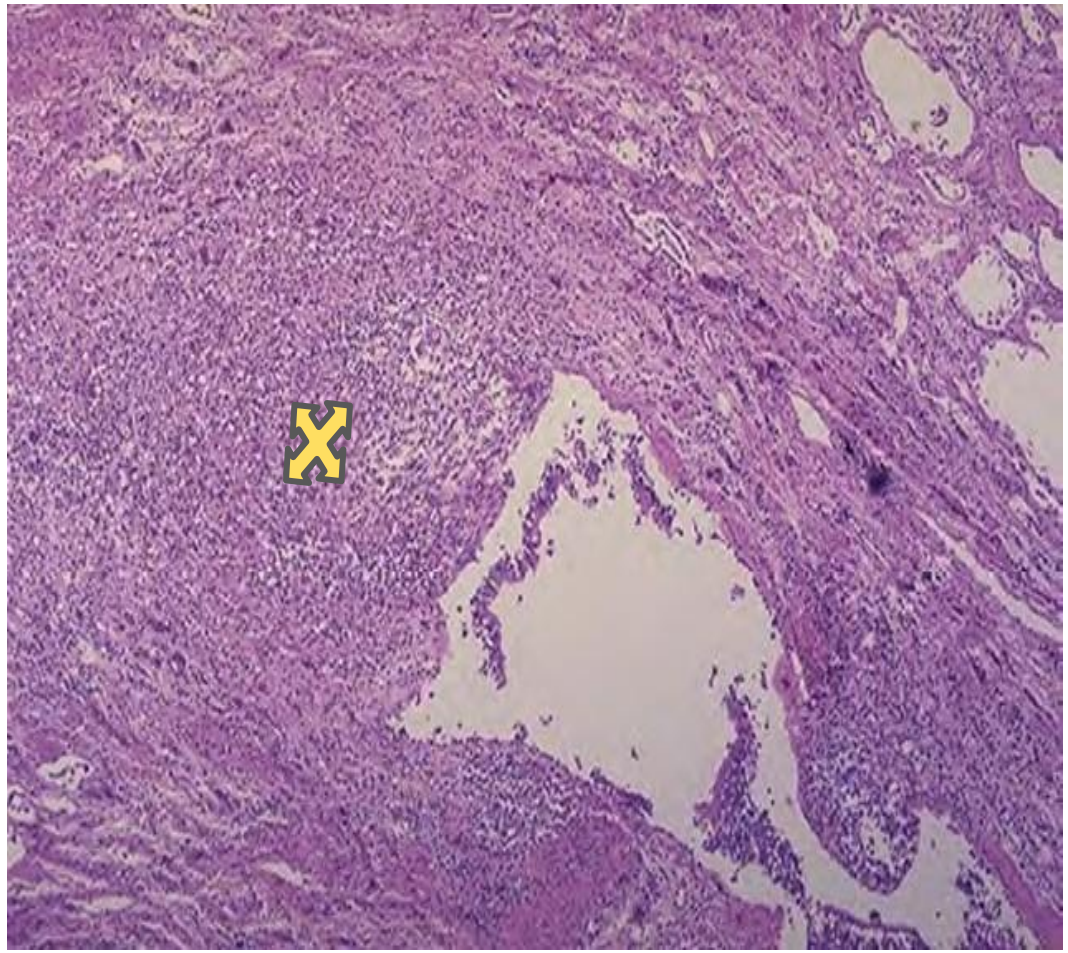


Morphology ,Macroscopic appearance Cont.

- **In full-blown active cases:**
  - intense acute and chronic inflammatory exudate within the walls of the bronchi and bronchioles and desquamation of lining epithelium and extensive ulceration.
  - mixed flora are cultured from the sputum.
- **When healing occurs:**
  - The lining epithelium may regenerate completely abnormal dilation and scarring(opposite in emphysema which there is no or minimum fibrosis expect in distal acinar emphysema).
  - Fibrosis of bronchial and bronchiolar walls.
  - Peribronchiolar fibrosis.
  - Abscess formation in some cases.

Cross Section

- Picture finding : Bronchiectasis, microscopic dilated bronchus in which the mucosa and bronchial wall are not seen(or very thin) clearly because of the necrotizing inflammation (the cross mark, which is mainly neutrophils due to pus formation) with tissue destruction, and abscess formation which is sheets of neutrophils.



Clinical features

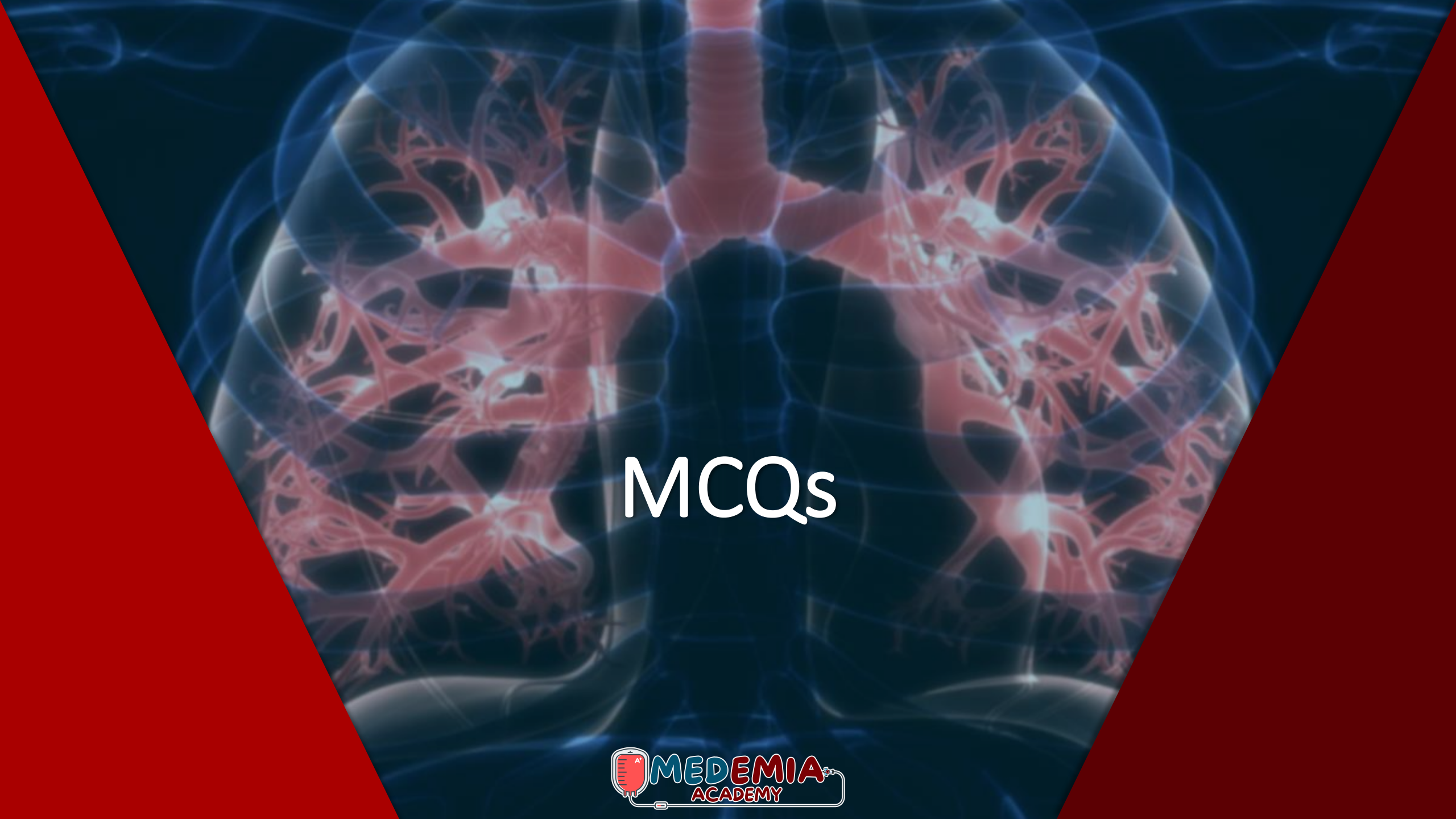
- Severe, persistent cough with mucopurulent sputum.
- Other symptoms: dyspnea, rhinosinusitis, and hemoptysis.
  - Episodic
  - precipitated by URTI.
  - Severe widespread bronchiectasis : significant obstructive ventilator defects, hypoxemia, hypercapnia, pulmonary hypertension, and cor pulmonale, and may results in Amyloidosis.

Summary

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.


MCQs
MEDEMIA
ACADEMY

Case

- A 45-year-old gentleman smoked two packs of cigarettes per day for 20 yrs. For the past 4 years, he has had a chronic cough with copious mucoid expectoration. During the past year, he has had multiple respiratory tract infections. He has also developed difficulty breathing, tightness of the chest, and audible wheezing. His breathing difficulty is relieved by inhalation of a β-adrenergic agonist and disappears after the chest infection has resolved. Which of the following pathologic conditions is most likely responsible for his clinical condition?
  a. α1-Antitrypsin deficiency with panlobular emphysema
  b. Centrilobular emphysema with cor pulmonale
  c. Chronic asthmatic bronchitis
  d. Cystic fibrosis with bronchiectasis

MCQs

1. **One of the following sentences is CORRECT about Bronchiectasis?**
   a. Characterized by permanent enlargement of the air spaces distal to the terminal bronchioles.
   b. Characteristic symptoms is dry. non productive cough.
   c. Obstruction and chronic infections are two intertwined processes contribute to its development.
   d. It is always associated with history of smoking.
   e. Diagnosis defined by persistent productive cough for at least 3 consecutive months in at least 2 consecutive years.

MCQs Cont.

2. **One of the following in INCORRECT about Bronchiectasis?**
   a. Primary ciliary dyskinesia is a rare disorder associated with bronchiectasis and sterility in males.
   b. Both obstruction and chronic infection contribute to bronchiectasis.
   c. Airways are dilated up to four times their usual diameter mostly in the upper lobes.
   d. Severe suppurative Staphylococcus aureus infection is associated with bronchiectasis.
   e. Bronchiectasis mainly is a permanent dilation of bronchi and bronchioles.
3. **Severe widespread bronchiectasis complicated EXCEPT?**
   a. Hypocapnia
   b. Amyloidosis
   c. Cor pulmonale
   d. Pulmonary hypertension

MCQs Cont.

4. **Which causes honeycomb appearance?**
   - a. Bronchiectasis
5. **Asthma before age 12 is considered:**
   - a. Genetic
6. **In a young asthmatic patient with arterial hypoxia during acute severe attack?**
   - a. low arterial Pco2 would be expected and if high, would be cause for concern
   - b. The arterial Pco2 would be expected to be high
   - c. 21% oxygen is the appropriate inspired gas.
   - d. Pulsus paradoxus cannot be detected
   - e. A low arterial Pco2 would be expected but if high, would not be an important problem

MCQs Cont.

7. **Which of the following cytokines produced by T-helper cell 2 in asthmatic attack activates eosinophils?**
   a. IL-13
   b. IL-5
   c. IL-2
   d. IL-4
   e. IL-6
8. **Which of the following does not belong to symptomatic bronchial asthma?**
   a. Chest pain
   b. Wheeze
   c. Cough
   d. Expectoration
   e. Dyspnea

MCQs Cont.

9. **Not concerned with modern increases in asthma:**
   - **a. Decrease in family size**(As archive answered, BUT **it's Incorrect!** >
   - ➢ Decrease in family size has actually been linked to an increase in asthma in modern times. This is due to the "hygiene hypothesis," which suggests that children in smaller families are less exposed to germs and infections early in life, which can lead to weaker immune system development and higher asthma rates.

MCQs Cont.

10. One isn't a clinical marker of acute severe asthma?

- a. Dizziness and confusion As archive answered, BUT **it's Incorrect!**)
- In fact, dizziness and confusion can be signs of severe or life-threatening asthma because they may indicate reduced oxygen levels (hypoxia), which happens when airflow is extremely restricted. These symptoms are more associated with a critical stage of asthma.

MCQs Cont.

11. **Regarding Asthma one statement is correct?**
    - a. Exposure to bacterial endotoxin in early childhood increases asthma.
    - b. Use of antibiotics in early life has been linked to the decrease of asthma.
    - c. It is more common in the young than the old.
    - d. Increased cleanliness leading decreases in asthma.
    - e. Increased family size leading to increases asthma.
12. **What is the form of lung disease that mostly complicates aspirin use?**
    - a. Chronic pneumonitis.
    - b. Acute bronchospasm.
    - c. Pulmonary fibrosis.
    - d. Alveolitis.
    - e. Acute pneumonitis.

MCQs Cont.

13. One of the following is not among the hallmark of Asthma?

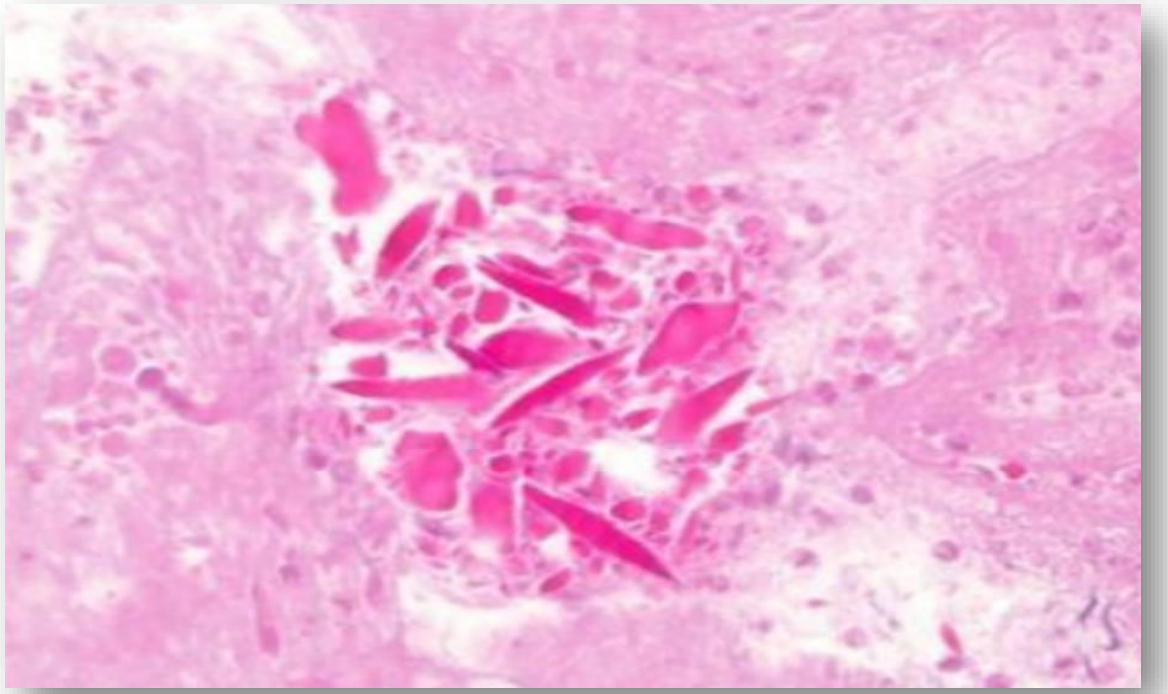
- a. Increased mucus secretion.
- b. Permanent enlargement of the air spaces distal to the terminal bronchioles.
- c. Bronchial smooth muscle cell hypertrophy and hyperreactivity.
- d. Intermittent, reversible airway obstruction.
- e. Chronic bronchial inflammation with eosinophils.

14. Regarding Asthma all the following statements are correct EXCEPT?

- a. It is two times greater in boys than girls
- b. It's worldwide prevalence rate is 1 -18%.
- c. More than 80% of its mortality occurred in low and middle income countries
- d. Adult males have a higher rate than females
- e. It is more common in the young age than the old age

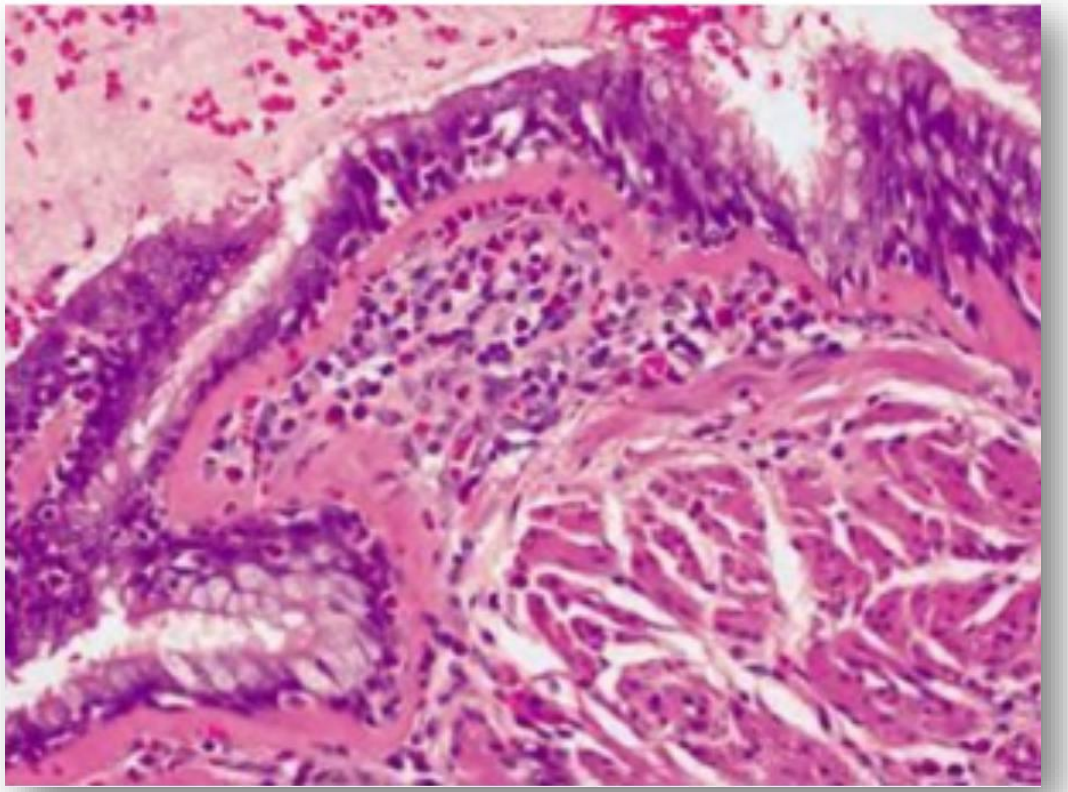
Lab

1. **Which of the following inflammatory cells is mainly responsible for the production of these structures?**
   a. Macrophages
   b. Eosinophils
   c. Basophils
   d. Lymphocytes
   e. Neutrophils



Lab Cont.

2. **The attached photo is most likely representing the late chronic changes of which of the following diseases?**
   a. Chronic bronchitis
   b. Tuberculosis
   c. Asthma
   d. Bronchiectasis
   e. Panacinar emphysema



Answers MCQs and Labs

❖**Case Answer:**

1. **C**

❖**MCQs Answers:**

1. C
2. C
3. A
4. A
5. A
6. B
7. B
8. D
9. A
10. A
11. C
12. B
13. B
14. D

❖**Labs Answers:**

1. B
2. C