Pathology Of Bronchial Asthma

COLOR INDEX:

MAIN TEXT (BLACK)

FEMALE SLIDES (PINK)

MALE SLIDES (BLUE)

IMPORTANT (RED)

DR'S NOTE (GREEN)

EXTRA INFO (GREY)

Editing file:

Objectives

- To understand the definition of bronchial asthma
- Understand asthma as an episodic, reversible bronchoconstriction caused by increased responsiveness of the tracheobronchial tree to various stimuli.
- Know that asthma is divided into two basic types: extrinsic or atopic allergic and intrinsic asthma.
- To know the morphological changes (gross and microscopic) seen in the bronchial asthma
- To understand the pathogenesis of bronchial asthma
- Bronchial asthma as a part of obstructive pulmonary disease group
- To know the clinical presentation and the prognosis of bronchial asthma

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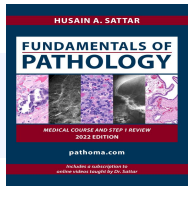

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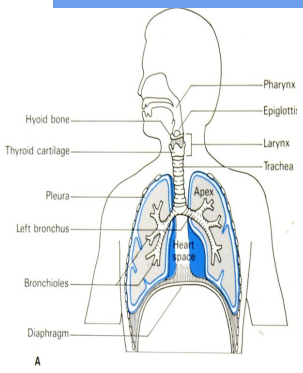
Introduction

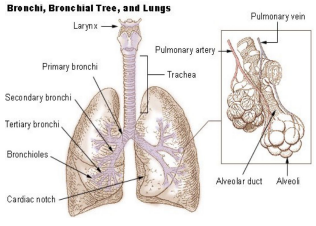
Male slide

Right lung divided into upper middle and lower lobes supplied by 3 bronchi.

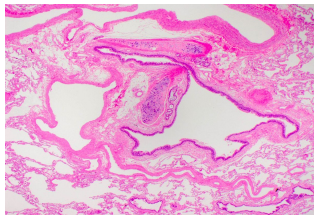


Left lung divided into upper and lower lobes, supplied by 2 bronchi.

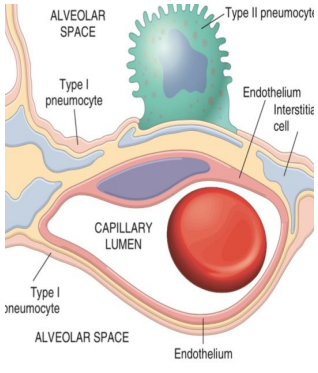
Bronchi branch → termed bronchioles (distinguished from bronchi by the lack of cartilage and submucosal glands within their walls).



Terminal bronchioles → acinai; are the functional units of the lungs and they form the site of gaseous exchange and lined by pneumocytes.

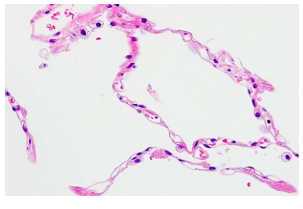


Pulmonary acini are composed of respiratory bronchioles that proceed into alveolar ducts.



Immediately branch into alveolar sacs, the blind ends of the respiratory passages.

Bronchovascular bundle: bronchiole + blood vessels.



The alveolar walls (or alveolar septa) consist of the following components:
1.The capillary endothelium and basement membrane. 2.The pulmonary interstitium
3.Alveolar epithelium.

Obstructive lung diseases

Characterized by limitation of airflow, usually resulting from an increase in resistance caused by partial or complete obstruction at any level

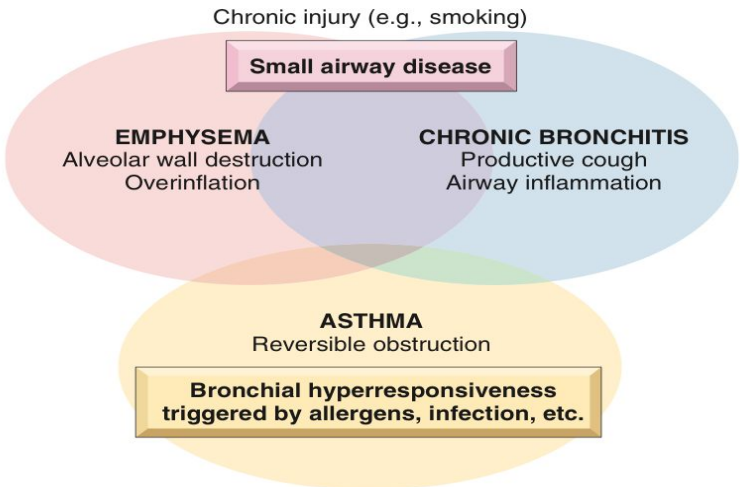
The spectrum of chronic obstructive pulmonary disease (COPD)

- Chronic bronchitis
- Emphysema
- Bronchiectasis
- Bronchial asthma

It should be noted:

- emphysema is defined on the basis of morphologic and radiologic features
- whereas chronic bronchitis is defined on the basis of clinical features.

Emphysema and chronic bronchitis often are grouped together under the rubric of chronic obstructive pulmonary disease (COPD).



Bronchial Asthma

helpful video

helpful video osmosis

Definition

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 morning.

Hallmarks of asthma are:

1. Intermittent,reversible airway obstruction.
2. Chronic bronchial inflammation with eosinophils
3. Bronchial smooth muscle cell hypertrophy and hyperreactivity
4. Increased mucus secretion

Etiology and pathogenesis (of atopic asthma):

Asthma is a complex disease with contribution of:

- Genetic predisposition to type I hypersensitivity (atopy)
- Acute and chronic airway inflammation (Especially viral)
- Bronchial hyperresponsiveness to variety of stimuli (smoke,fumes,cold air,stress, and exercise)

Classification of bronchial asthma:

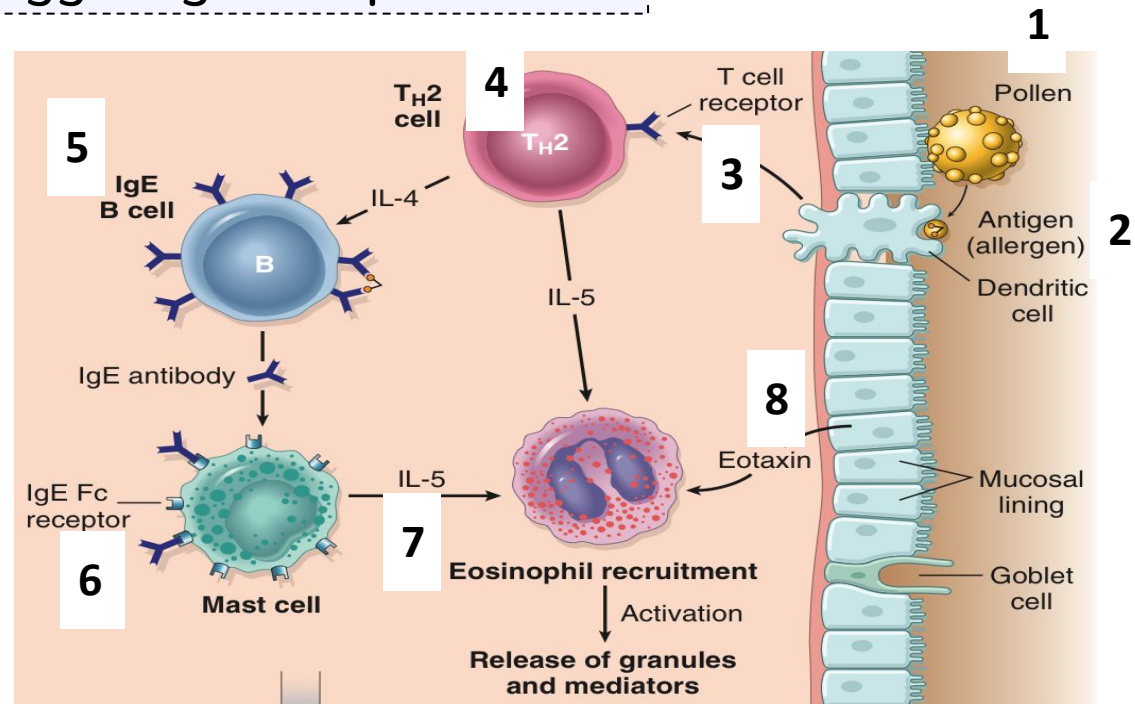
Classification	Characteristics
Atopic asthma	Triggered by immunologically mediated hypersensitivity reaction Type I against foreign substances or allergens, in 70% of cases
Non-atopic asthma	Do not have evidence of allergen sensitization. Respiratory and inhaled air pollutants are common triggers.
Drug-Induced asthma	Attack of asthma related to intake of some drugs ex; aspirin Patients with aspirin sensitivity present with recurrent rhinitis, nasal polyps, urticaria, and bronchospasm
Occupational asthma	Asthma related to long term exposure to certain occupational hazard. ex: wood, cotton, platinum, etc.

Atopic asthma

- Atopic asthma is associated with excessive reaction of T-helper 2 cells to environmental antigens.
- T-helper 2 cells secrete:
  - IL-4 and IL-3 → stimulates the production of IgE by B lymphocytes
  - IL-5 → activates eosinophils
  - IL-13 → stimulates mucous production
- IgE is responsible for mast cell degranulation and the release of 1ry and secondary mediators leading to an early and late phase of the reaction.
- Childhood.
- Positive family Hx -History- of allergy.
- Attacks may be triggered by allergens in dust, pollen, animal dander, or food, or by infections.
- The onset of asthmatic attacks is often preceded by allergic rhinitis, urticaria, or eczema.
- A skin test with the offending antigen results in an immediate wheal-and-flare reaction.

Pathogenesis (of atopic asthma)

1)Triggering of atopic asthma



Explanation:

1. Antigen enters the body
2. Antigen is recognised by APC e.g. Dendritic cells, macrophages
3. APC (dendritic cell) take the antigen and present it to TH2 cell
4. Th 2 will secrete IL-3 & IL-4 (they will activate B cell to release IgE) Also Th2 will release IL-5
5. IL -4 will activate B cell to release IgE
6. FC portion of IgE-Ab attaches to mast cell receptor and stimulate the release of cytokines such as histamine and will secrete eotaxin IL-5, which helps in the activation of eosinophils
7. Eosinophils will release granules and eosinophils mediators toxic to epithelial cells..
8. Injured bronchial mucosal lining cells will secrete eotaxin which helps in the. Eosinophils recruitment.

2) Early Phase (minutets)

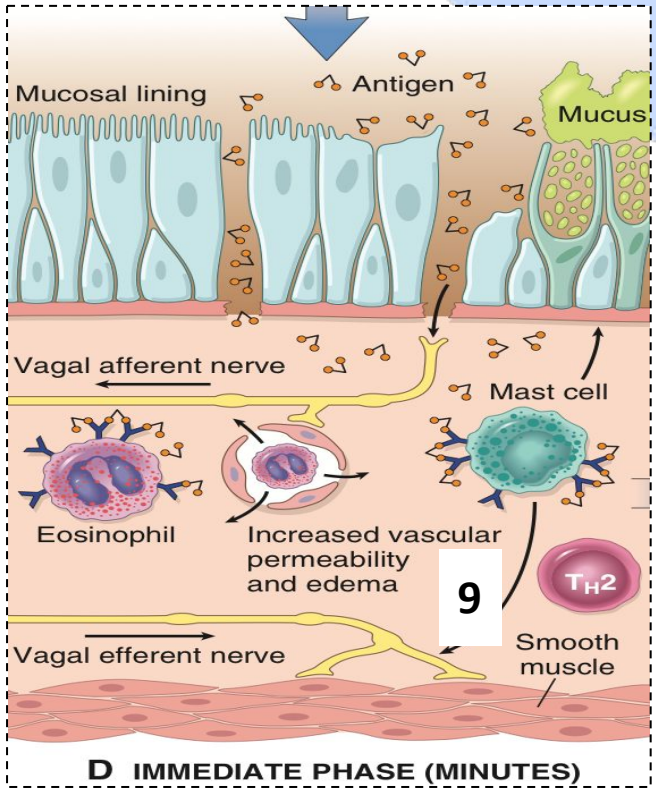
Dominated by:

1- bronchoconstriction: is triggered by mediators released from mast cells:

- Histamine
- Prostaglandin D2
- Leukotrienes LTC4, D4, and E4

2- increased mucus production

3- vasodilation

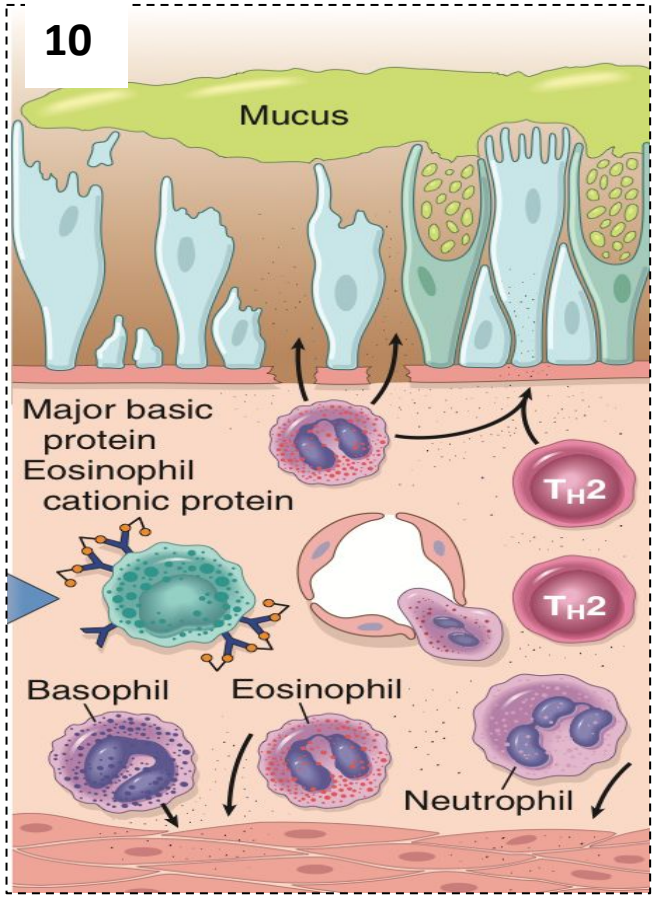


D IMMEDIATE PHASE (MINUTES)

9 Mast cell activates the vagal afferent nerve (then Bronchoconstriction and muscle hypertrophy happen)

3) Late Phase (hrs)

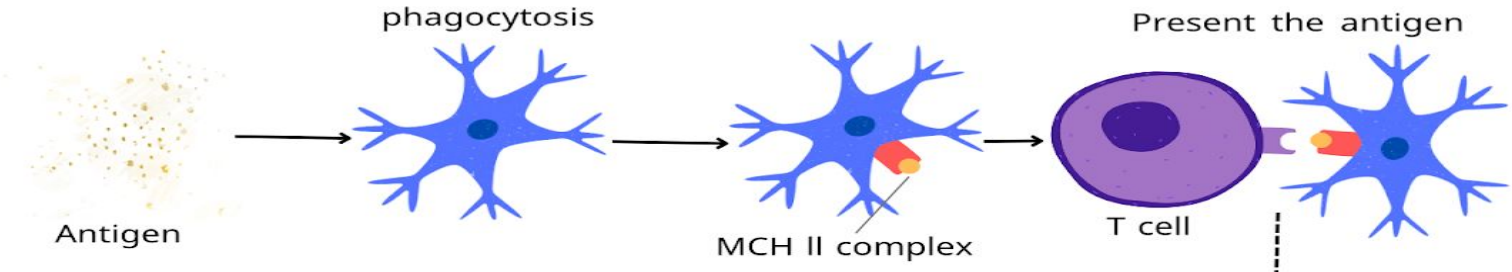
- Inflammatory in nature
- Inflammatory mediators stimulate epithelial cells to produce chemokines:
  - 1- Eotaxin: promote the recruitment of TH2 cells
  - 2- eosinophils: amplifying an inflammatory reaction that is initiated by resident immune cells.



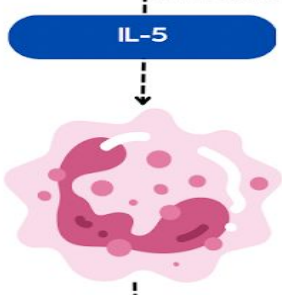
10 Increase in the mucus due to the recruitment of inflammatory cells & Smooth muscle hyperplasia

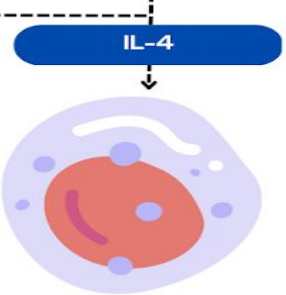
Summary

EXTRA

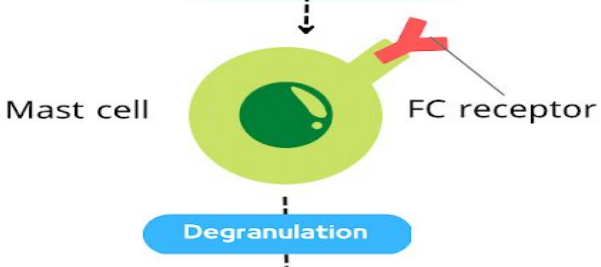


T-helper 2 cells secrete:
1. IL-4 and IL-3 → stimulates the production of IgE by B lymphocytes
2. IL-5 → activates eosinophils
3. IL-13 → stimulates mucus production
4. IL-9 : Damages the bronchial epithelium directly





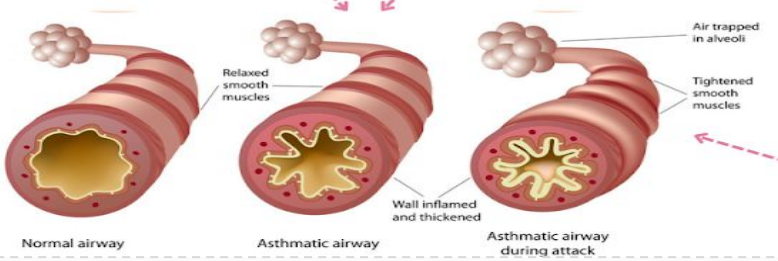
Release



Toxic mediators to epithelial cells

Granules

Release



Histamine

Other cytokines Like IL-5 which will activate Eosinophils

Early phase :
1- bronchoconstriction: is triggered by mediators released from mast cells
2- increased mucus production
3- vasodilation
Late phase :
Inflammatory mediators stimulate epithelial cells to produce chemokines

Made by : Lama Alotaibi

non-atopic asthma

Non-Atopic asthma

- No evidence of allergen sensitization and is triggered by non-immune stimuli such as psychological disturbance, stress
- Skin tests are negative
- In 30% of patients
- Positive family history is less common
- Precipitated by Viral infection and Inhaled air pollutants associated with chronic eosinophilic infiltrate (that lead to similar reaction to atopic one).

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

	Atopic Asthma	Non-atopic asthma
Underlying abnormality	Immune reaction (atopic) Atopic asthma is associated with excessive reaction of Th2 cells stimulated by environmental antigens	Abnormal autonomic regulation of airway No evidence of allergen sensitization and is triggered by non-immune stimuli such as psychological disturbance,stress or exercise
Triggers & Factors	Allergens in dust, pollen, animal dander, food, or by infections. -The onset of asthmatic attacks is often preceded by allergic rhinitis, urticaria, or eczema. - Common in childhood.	Precipitated by viral infection and inhaled air pollutants associated with chronic eosinophilic infiltrate.
Onset	Childhood	Adulthood
Distribution	60%	40%
Allergens	Recognized	None identified
Family history	Present (Positive family Hx of allergy)	Absent (No family Hx)
Skin Test	Positive (immediate wheal-and-flare reaction)	Negative
Predisposition to form IgE antibodies	Present	Absent
Natural progression	Improves	Worsens
Eosinophilia	Sputum and blood	Sputum
Drug hypersensitivity	Absent	Present

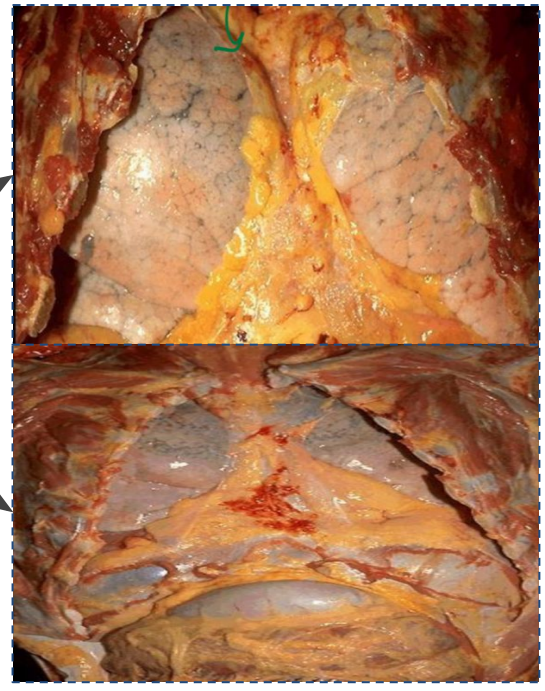
Very important summary

Morphology of Asthma

Gross Morphology

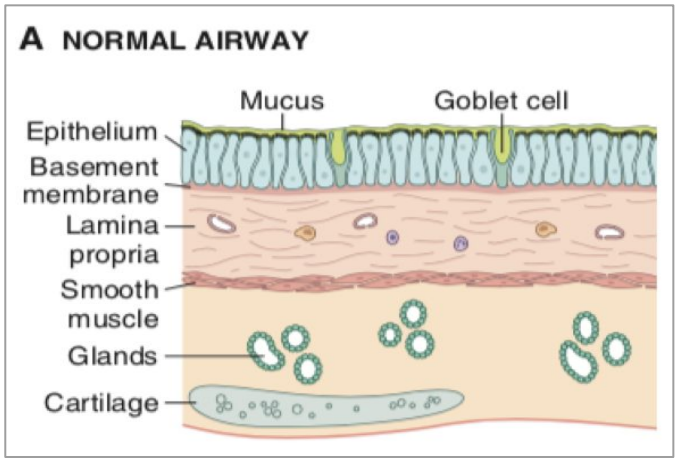
- Presence of congested (reddish) mucosa and mucoid secretions.
- Occlusion of bronchi and bronchioles by thick tenacious mucus plugs (condensed mucus balls).

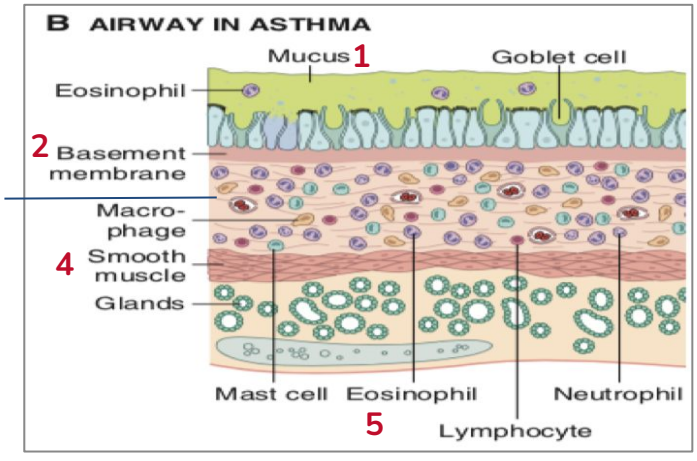
- Overdistention (hyper-inflated) of lungs due to over inflation.
- Small areas of atelectasis. (Lung collapse)



Morphology of Asthma

Microscopic Morphology





1- mucus over secretion

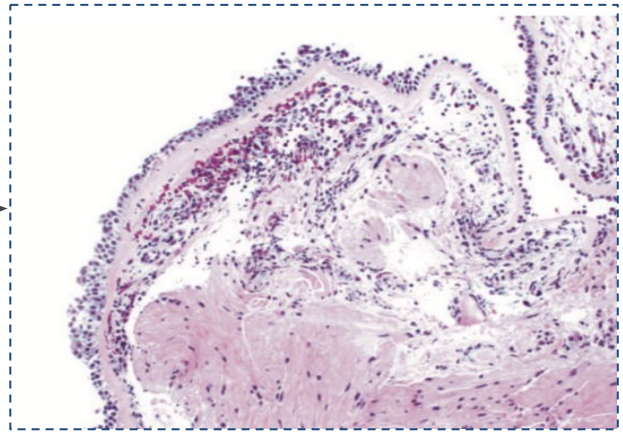
2- thickening of basement membrane

3- More inflam. cells in lamina propria

4- Hypertrophy of smooth muscle

5- Predominant Eosinophil

Eosinophils are key inflammatory cells found in almost all subtypes of Asthma, and its products (such as major basic protein) are responsible for Airway Damage.



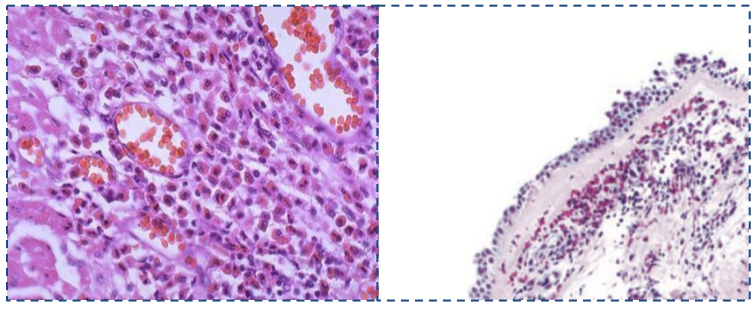
Morphology of Asthma

Microscopic Morphology

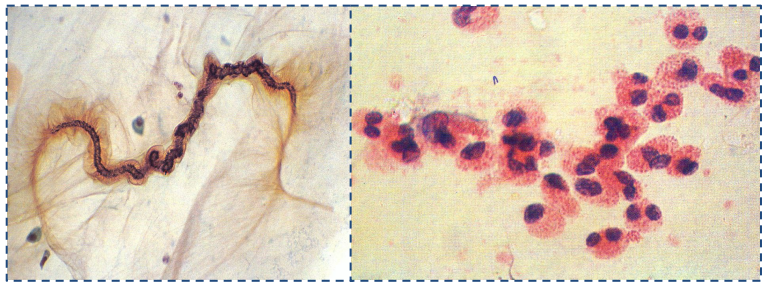
Airway remodelling:

1. Thickening of airway wall
2. Sub-basement membrane fibrosis
3. Increased submucosal vascularity
4. An increase in size of the submucosal glands and goblet cell
5. Metaplasia of the airway epithelium
6. Hypertrophy and/or hyperplasia of the bronchial muscle

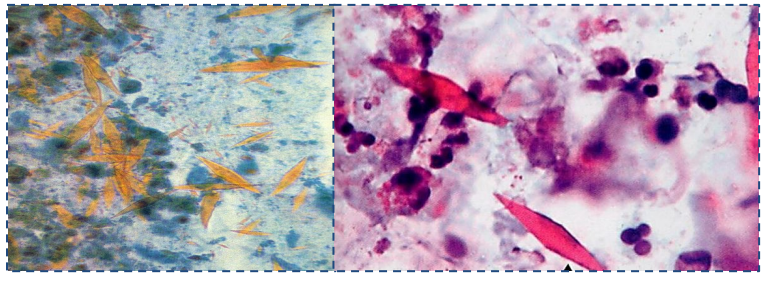
Inflammation of bronchial wall (eosinophils (5-50%), mast cells, lymphocytes, plasma cells)



LEFT: Mucous plugs containing whorls of shed epithelium (Curschmann spirals).
RIGHT: Eosinophils from a case of Bronchial Asthma.



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



Clinical Features of Asthma

click here

Asthma

01 Severe dyspnea (shortness of breath) & wheezing due to bronchoconstriction

02 mucus plugging, which leads to trapping of air in distal airspaces

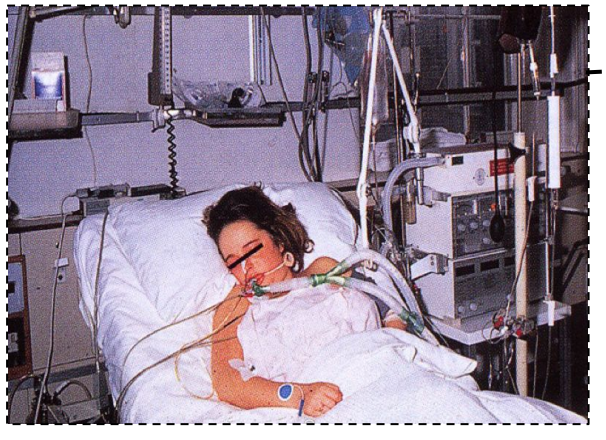
03 progressive hyperinflation of the lung

04 Attacks last from 1 to several hours and subside either spontaneously or with therapy
And may be followed by Nocturnal cough (night cough).

05 Intervals between attacks are characteristically free from overt respiratory difficulties
(so between the attacks the patient becomes normal and doesn't experience any respiratory difficulties)

Complications of Asthma

1. Superimposed infection i.e., pneumonia
2. Chronic bronchitis (inflammation of bronchial wall) i.e. Asthmatic bronchitis: chronic bronchitis with superimposed asthma
3. Emphysema, (destruction of alveolar septal & trapping of air & fusion of alveolar space) pneumothorax (Presence of air in the pleural space) and pneumomediastinum (نيومو-ميديا-ستاينم) (Presence of air in mediastinum) (rare complications)
4. Bronchiectasis (irreversible damage, permanent Dilation of the bronchial wall)
5. Status asthmaticus This patient presented as a medical emergency with acute severe breathlessness and diagnosed as a case of status asthmaticus (Overinflated lungs because of severe obstruction and air trapping) which required immediate intensive care including intermittent positive-pressure ventilation
6. Respiratory failure which requiring intubation
7. Hypercapnia, acidosis, and severe hypoxia. In some cases, cor pulmonale and heart failure develop



Prognosis of Asthma

Male slide

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)

Bronchiectasis 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.(Rare) (associated with non-atopic asthma)

Treatment of Asthma

1- Control of factors contributing to Asthma severity

2- Medications:

- Anti-inflammatory drugs, particularly glucocorticoids
- Bronchodilators such as beta-adrenergic drugs
- Leukotriene inhibitors

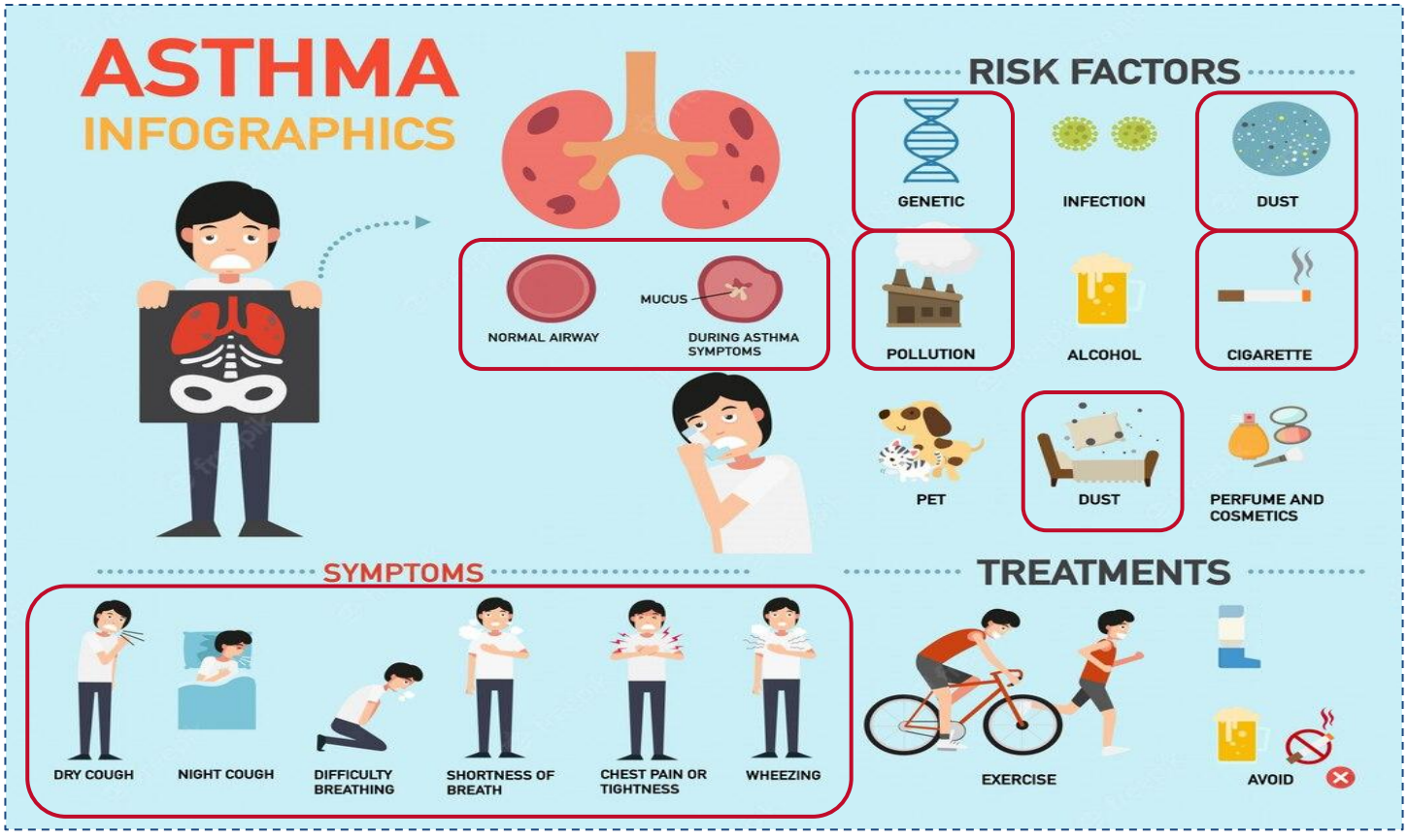
Infographic & Summary

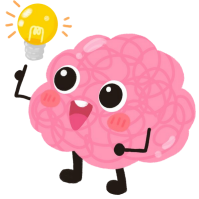
Asthma is characterized by reversible bronchoconstriction caused by airway hyper responsiveness to a variety of stimuli.

Atopic asthma most often is caused by a TH2 and IgE-mediated immunologic reaction to environmental allergens and is characterized by early-phase(immediate) and late-phase reactions. The TH2 cytokines IL-4, IL-5, and IL-13 are important mediators. Non-TH2 inflammation also has roles in atopic asthma that are being defined. Triggers for nonatopic asthma are less clear but include viral infections and inhaled air pollutants, which also can trigger atopic asthma.

Eosinophils are key inflammatory cells found in almost all subtypes of asthma; eosinophil products (such as major basic protein) are responsible for airway damage.

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





KEYWORDS

Obstructive lung disease	Characterized by limitation of airflow, usually resulting from an increase in resistance caused by partial or complete obstruction at any level
Bronchial Asthma	Asthma is a chronic inflammatory disorder of the airways that causes recurrent episodes of wheezing,breathlessness, chest tightness, and cough
Atopic (Extrinsic) Asthma	Triggered by immunologically mediated hypersensitivity reaction Type I against foreign (extrinsic) substances or allergens, in 70% of cases
Non-Atopic (intrinsic) Asthma	Do not have evidence of allergen sensitization (thus intrinsic). Respiratory and inhaled air pollutants are common triggers.
Early phase of Asthmatic attack	Dominated by: bronchoconstriction triggered by mediators released from mast cells, which are: Histamine, Prostaglandin D2, Leukotrienes LTC4, D4, and E4. Also increased mucus production and vasodilation.
Late phase of Asthmatic attack	Inflammatory in nature, Inflammatory mediators stimulate epithelial cells to produce chemokines: Eotaxin to promote the recruitment of TH2 cells. And eosinophils, amplifying an inflammatory reaction that is initiated by resident immune cells.
Eosinophils	Key inflammatory cells found in almost all subtypes of Asthma, and its products (such as major basic protein) are responsible for Airway Damage.
Airway remodelling	structural changes that occur in both large and small airways relevant to miscellaneous diseases including Asthma.
Status Asthmaticus	Overinflated lungs with severe obstruction and air trapping
Atelectasis	Lung collapse

Answers:
1-A 2-B 3-D 4-D 5-C
6-A 7-A 8-B

MCQ

1- Which one of the following induce acute asthma attack ?			
A) Physical exercise	B) Oxygen Therapy	C) Sudden weight loss	D) Severe burns
2- Which ONE of the following cell types triggers inflammation of allergic asthma?			
A) Eosinophils	B) Mast cells	C) Natural Killer cells	D) Neutrophils
3- A 24 year old male started working as a lumberjack five years ago without any problems but recently got diagnosed with asthma what kind of asthma does he have?			
A) Atopic Asthma	B) Non-atopic Asthma	C) Drug-induced Asthma	D) Occupational Asthma
4- What stimulates mucus production?			
A) IL-3	B) IL-4	C) IL-5	D) IL-13
5- In which of the following conditions Charcot-Leyden Crystals are seen in the sputum?			
A) Acute Bronchitis	B) Bronchiectasis	C) Severe bronchial asthma	D) Panacinar emphysema
6- Which ONE of the following is produced by active Th2 in bronchial asthma ?			
A) IL-4	B) TNF-a	C) FGF	D) IF-gamma
7- The severe form of bronchial asthma			
A) Status asthmaticus	B) Hypercapnia	C) Pneumonia	D) Hypoxia
8- Do not have evidence of allergen sensitization. Respiratory and inhaled air pollutants are common triggers			
A) Atopic Asthma	B) Non-Atopic Asthma	C) Drug-induced Asthma	D) Occupational asthma

Answers:
1-C 2-D 3-D 4-A

Cases

1- A 47 years old worker had a lung cancer after repeated exposure to Asbestos which is a naturally occurring fibrous silicate mineral he would probably experienced what type of asthma before having the cancer?			
A) Extrinsic Asthma	B) Intrinsic Asthma	C) Occupational Asthma	D) Drug-induced Asthma
2- A 32 years old woman developed asthma after having aspirin for her headache , her type of asthma is :			
A) Extrinsic Asthma	B) Intrinsic Asthma	C) Occupational Asthma	D) Drug-induced Asthma
3- A 15-year-old girl with an FEV1/FVC ratio of = 56 % which of the diseases she would be less likely to have :			
A) Asthma	B) Emphysema	C) Chronic Bronchitis	D) Interstitial pulmonary fibrosis
4- A 5 years old patient with severe dyspnea and Inability to speak in full sentences examination showed Respiratory rate over 25 breaths per minute his septum sample showed Numerous eosinophils and Charcot-Leyden crystals , he would probably have:			
A) Asthma	B) Emphysema	C) Chronic Bronchitis	D) Sickle cell disease

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