

Bronchial Asthma

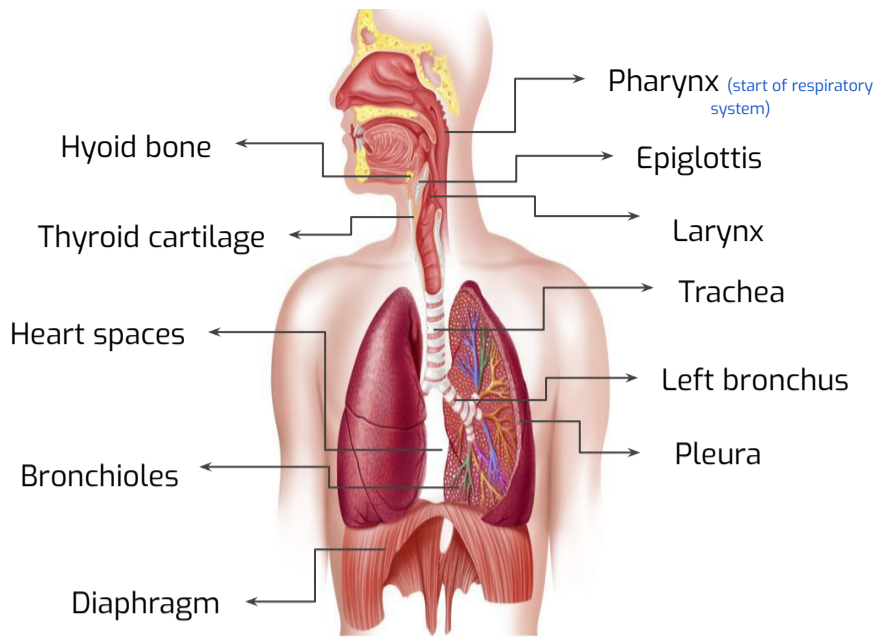
Objectives:

- 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.

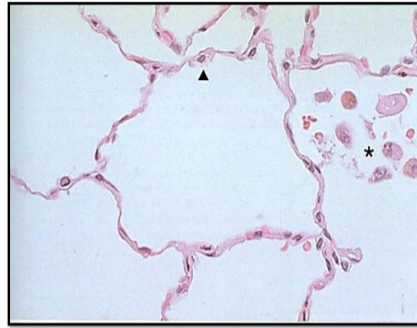
Rikabi's content

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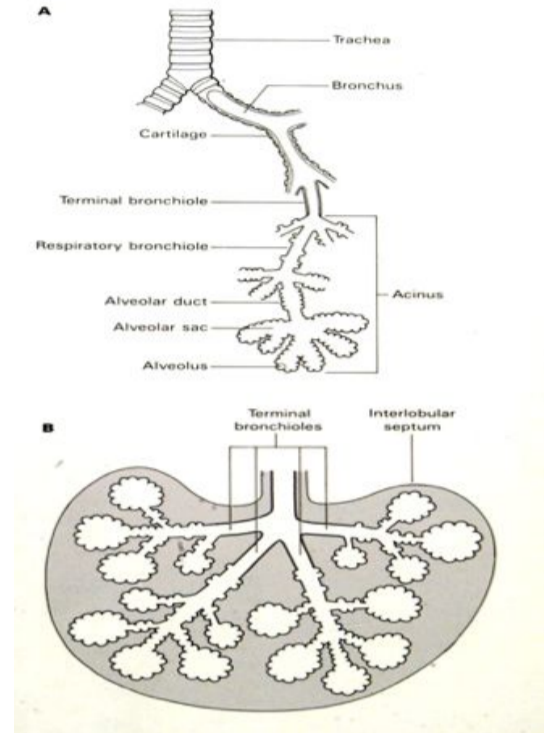
please review the histology and anatomy



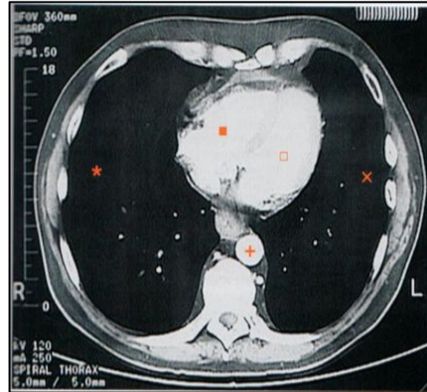
Normal lung



The wall of alveoli contains type 1 pneumocyte (flat cells, not capable to regenerate) and type 2 pneumocyte (secrete surfactant which keep the tension inside the alveoli, capable to regenerate)



Respiratory System



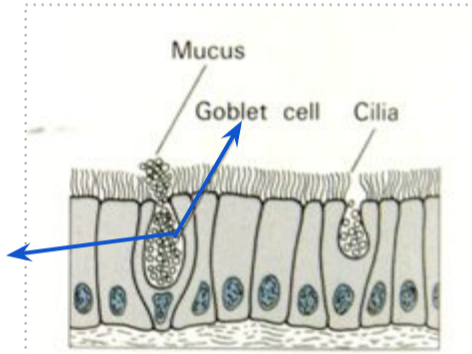
CT scan

The lower respiratory tract

Respiratory Epithelium

Ciliated columnar epithelium

mucus secreting cell and between them there are neuroendocrine cells and clara cells (in the terminal bronchioles, most common cells of tumors)



General complaints of patients:
 1- Dyspnea: difficulty in breathing (not necessarily shortness of breath)
 2- Cough: productive (obstructive) and dry (restrictive)

Tumors

there are general symptoms of neoplasia (mentioned in foundation block) and there are specific respiratory tract symptoms that will be mentioned in later lectures

hereditary

- Immotile ciliary syndrome (primary ciliary dyskinesia)
 - Cystic fibrosis

infections

like pneumonia, TB (can be classified as a stand alone respiratory disease), etc...

chronic obstructive pulmonary disease (COPD)

Difficulty exhaling all the air

shortness of breath

types of COPD:

asthma

It's not like the other COPD because it's reversible

chronic bronchitis

Permanent damage

bronchiectasis

Permanent damage

emphysema

Permanent damage

Results

Damage to the lungs

Narrowing of the airways inside the lungs

Symptomes

Dyspnea (difficulty in breathing)

Productive cough

Hemoptysis

chronic restrictive pulmonary disease (CRPD)

The lung capacity is reduce

Inability to expand the lung.

Results

Fibrosis

Honeycomb (end stage diffuse interstitial pulmonary fibrosis)

Symptomes

Dyspnea (difficulty in breathing)

Dry cough

Reducing the chest volume

Diseases of the Respiratory System

Bronchial asthma

Definition

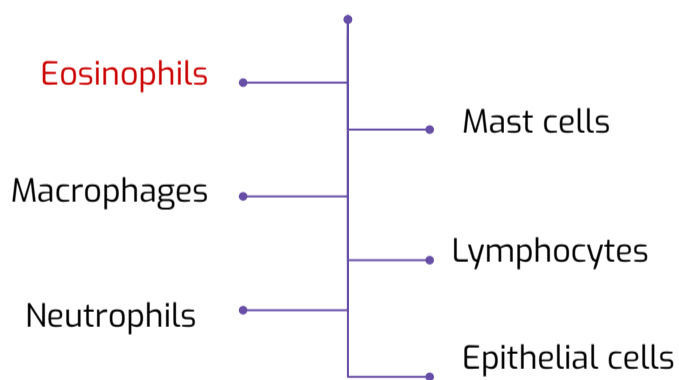
Chronic inflammatory disorder of the **airways** (chronic obstructive airway "bronchus and terminal bronchioles" disease) that causes recurrent episodes of **wheezing*** (the sound of breathing in people who have asthma), **breathlessness (dyspnea)**, chest tightness, and cough, particularly at night and/or early in the morning. (patient comes because of the wheezing and dyspnea)

Bronchial asthma is an **episodic** (تمر بفترات اشتداد), **reversible** bronchoconstriction caused by increased responsiveness of the tracheobronchial tree to various stimuli

* People who have asthma they have:
 - Spasm in bronchial wall and increase the contraction of smooth muscle fibers in bronchial wall
 - The lumen of bronchi is narrowed.
 So when the air flow in narrow track will cause **wheezing.**

The hallmarks of asthma are:

Many cells play a role in the inflammatory response:



1 - Intermittent
 - Reversible airway obstruction

2 - Chronic bronchial inflammation with eosinophils

3 - Bronchial smooth muscle cell hypertrophy
 - Hyperreactivity

4 - Increase mucus secretion

Major factors contributing to the development of asthma

Genetic factor

-Genetic predisposition to type I hypersensitivity (atopy)
 -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.
 -Most important contributors are the long arms of chromosome 5 and 22

Airway inflammation factor

Acute and chronic airway inflammation

Bronchial hyperresponsiveness factor

Bronchial hyperresponsiveness to a variety of stimuli

Epidemiology

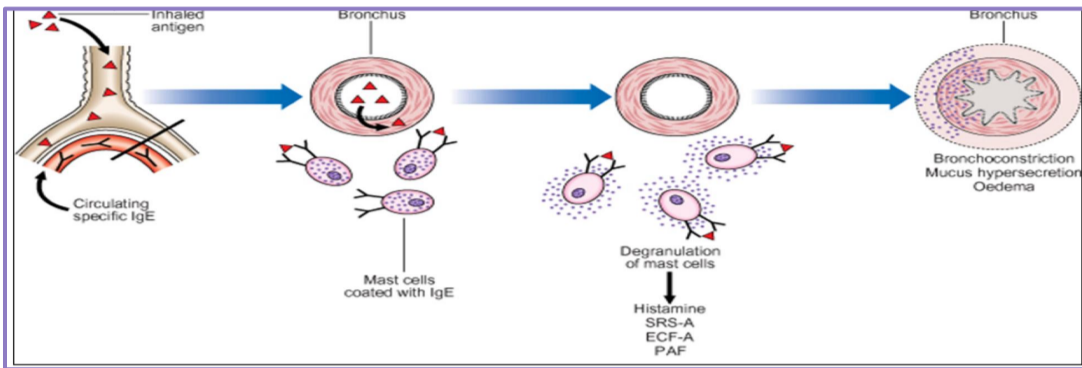
Asthma has increased in incidence significantly in the Western world over the past 4 decades.

Hygiene hypothesis

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

Type of asthma	Atopic (Extrinsic) asthma	Nonatopic (Intrinsic) asthma	Drug-Induced asthma	Occupational asthma
Definition	Bronchospasm is induced by inhaled antigens due to type one hypersensitivity reaction cause production of IgE	A disease in which the bronchial hyperreactivity is induced by non-immune mechanisms	people who have sensitivities to certain drugs that can precipitate an asthma attack	refers to new onset asthma or the recurrence of previously quiescent asthma directly caused by exposure to an agent at workplace
Asthma onset	Childhood	Adult		
Causative factor (asthma triggers)	<p>-The onset of asthmatic attacks is often preceded by allergic rhinitis, urticaria, or eczema = previous history of allergic condition</p> <p>Extrinsic factor : environmental antigens Allergens in dust, pollen, animal dander, or food, or by infections especially viral infection</p>	<p>Triggered by non-immune stimuli such as :</p> <ul style="list-style-type: none"> - Intrinsic factor : cold temperature, exercise, psychology stress - Drugs e.g. Aspirin and beta blockers -Respiratory infections due to viruses (e.g., rhinovirus, parainfluenza virus) -Inhaled air pollutants (e.g., sulfur dioxide, ozone, nitrogen dioxide) <p>These lower the threshold of the subepithelial vagal receptors to irritants</p>	Several pharmacologic agents provoke asthma, aspirin being the most striking example.	triggered by fumes (epoxy resins, plastics), organic and chemical dusts (wood, cotton, platinum), gases (toluene), and other chemicals
Family history	Positive family Hx of allergy	(Usually negative) positive family history of asthma is less common		
Skin test	Positive A skin test with the offending antigen results in an immediate wheal-and-flare (redness - swelling) reaction	Usually Negative , No Hx of allergy		
Result	<p>Allergic conjunctivitis, allergic rhinitis, eczema.</p> <p>عموماً عندهم جميع الأمراض التحسسية</p>		<p>-Patients with aspirin sensitivity present with recurrent rhinitis, nasal polyps, urticaria, and bronchospasm</p> <p>-The precise pathogenesis is unknown but is likely to involve some abnormality in prostaglandin metabolism stemming from inhibition of cyclooxygenase by aspirin</p>	-Asthma attacks usually develop after repeated exposure to the inciting antigen(s)
	- They Cause airway inflammation , edema , mucous plugging			
Treatment	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			

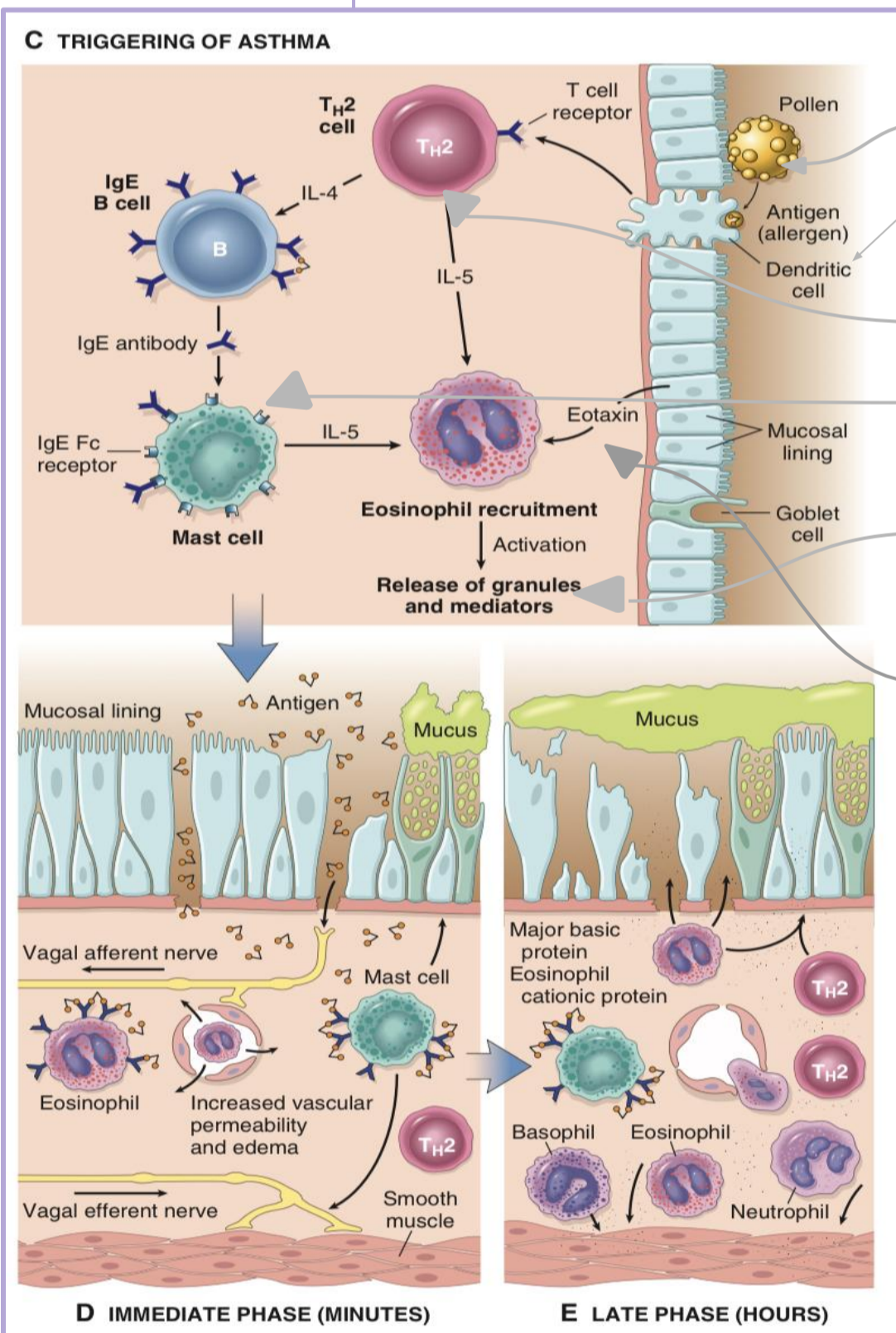
Pathogenesis of allergic asthma



The antigens could be:

Pollen dust, virus, animal fur, sand bacteria, certain smells, Storm, certain particles, exercise, certain drugs, perfume.

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



1. Antigen enters the body

2. Recognized by the dendritic cell or any other APC

3. Activate naive T cell to become activated TH cell (CD4) called **TH2 cell** then releases of cytokines such as **IL-13** and **IL-4** that **activate B-cell to produce IgE**

4. IgE bind to Ag and set on mast cell and stimulate the mast cell to release cytokines such as histamine, serotonin and IL-5, PAF, mediators

5. IL-5 attract **eosinophils** (found in the septum, wall of bronchi, mucus) will release the granules and mediators which are toxic to epithelial cells (causing mucosal damage, edema, spasm of the small muscles fibers)

6. Damage of the bronchial wall by eotaxin (produced by bronchial epithelial cells and further stimulate the eosinophils), galectin 10, major basic protein "e.g cationic protein" (produced by eosinophils cause damage to mucosa and stimulate secretion of mucus and stimulate more eosinophils), also **IL-13 increase secretion of mucus**

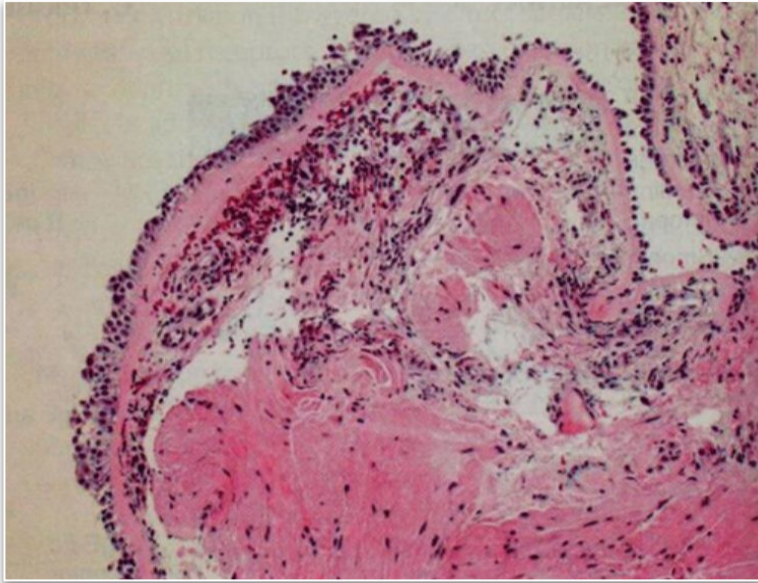
also those antigens stimulate branches of vagus nerve (C10) that help in spasm of bronchi.

(E) 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

(D) On re-exposure to antigen (Ag), 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 induced bronchospasm, **increased vascular permeability**, mucus production, and recruitment of leukocytes.

The final results are bronchospasms, bronchial damage accumulations mucus and eosinophils.

Morphological changes Of BA

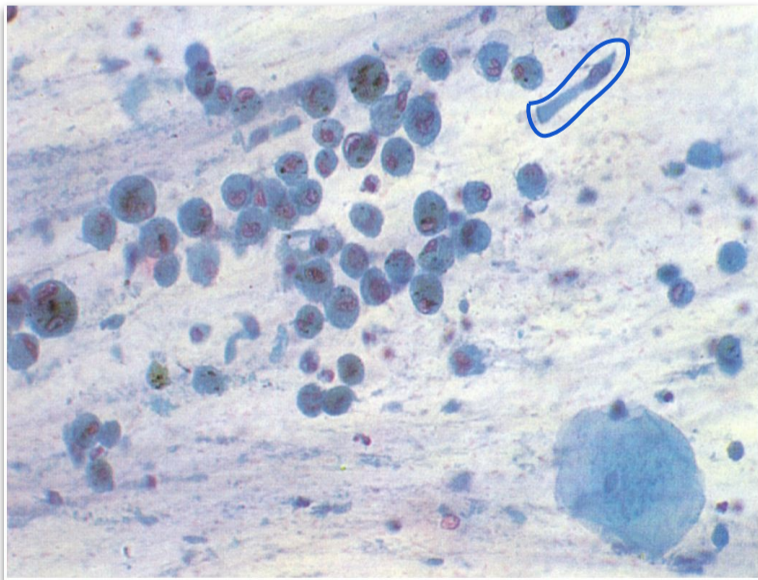


Bronchial biopsy specimen from an asthmatic patient showing thickened sub-basement membrane fibrosis, eosinophilic inflammation and smooth muscle hyperplasia



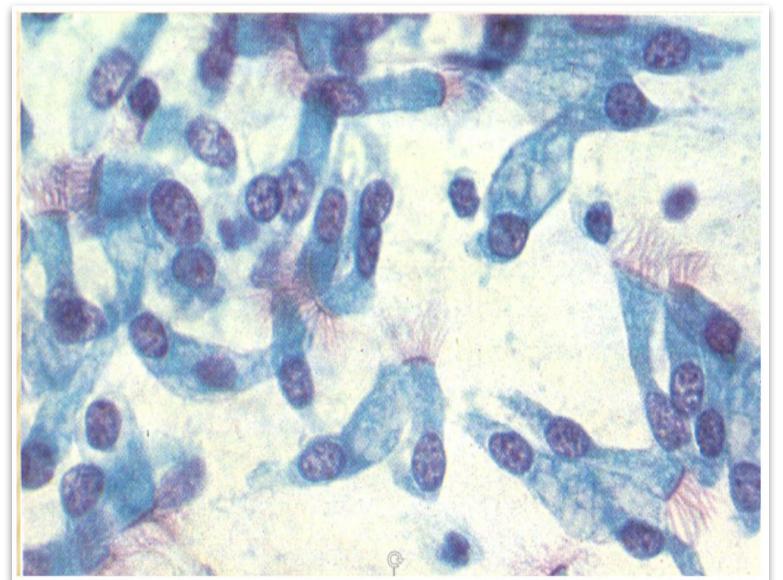
Bronchitis in an asthmatic patient. Note the presence of congested mucosa and mucous secretions.

ciliated columnar epithelium



Composition of satisfactory specimen: Sputum (very rich in eosinophils due to IL-5)
Alveolar (anthracotic) macrophages: granules rich in Co2
ciliated columnar epithelium

If it's Silva it's not good sputum for examination



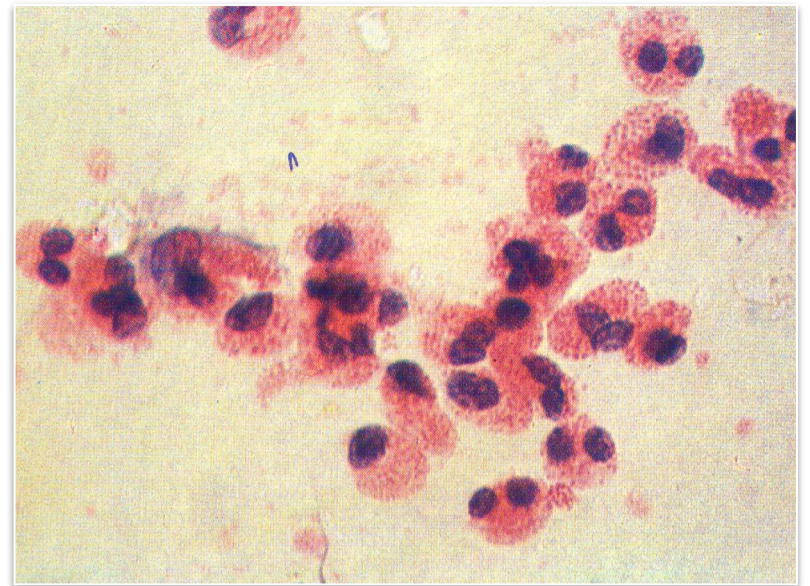
Ciliated columnar cells

Morphological changes Of BA



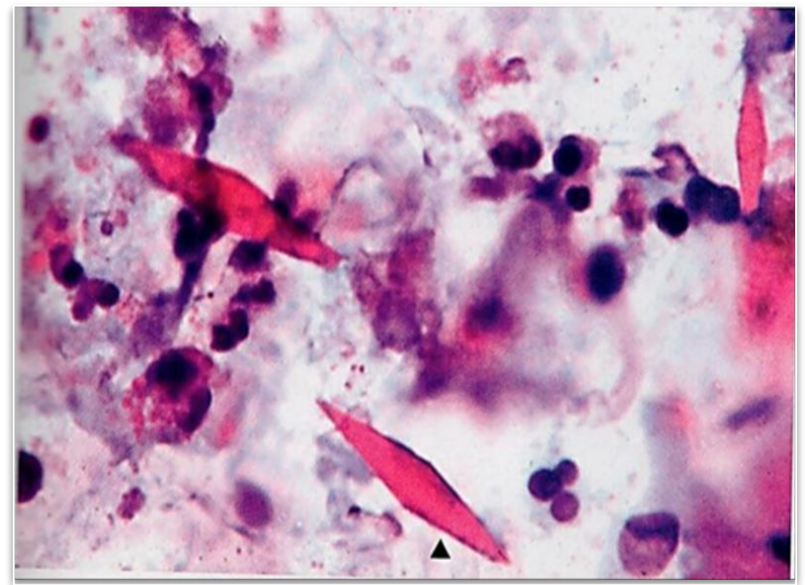
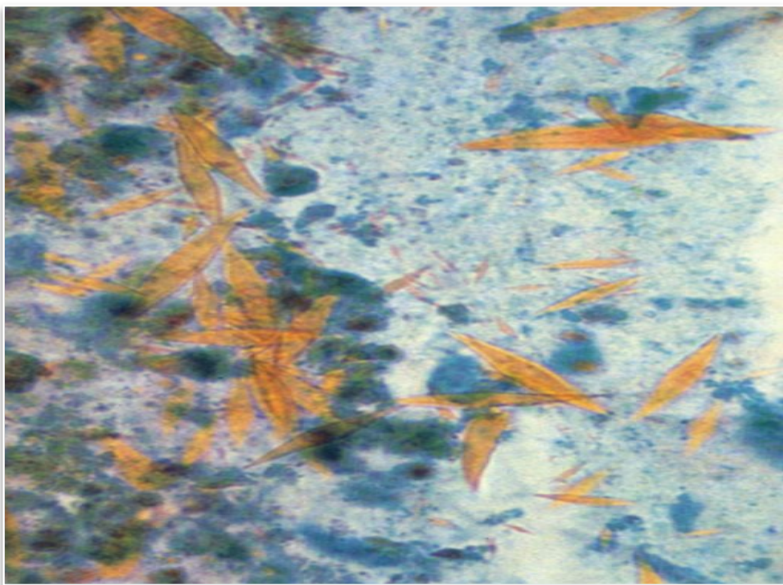
Curschmann's spiral: Sputum

The spiral is condensed (تكتف) mucus which is formed from IL - 13 (IL-13 stimulate the bronchial tree and the goblet cells to secrete mucus to cause mucus plugs (سدادة))



Eosinophils From A case of Bronchial Asthma

Eosinophils has granules (major basic proteins, galectin 10, cationic proteins that lead to damaging the bronchial tree, increase mucus production, destroy columnar epithelium under the influence of of IL-5)



Bronchial Asthma, Microscopic: Charcot - Leyden Crystals

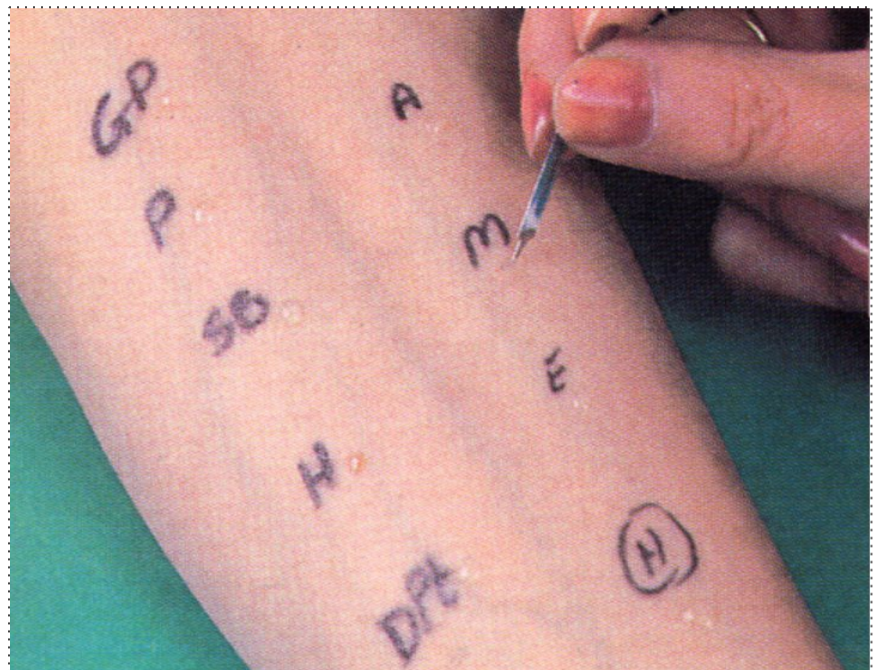
- The crystals are formed by proteins of eosinophils.
- we can see them in the nasal secretion or sputum of patient with allergic reactions (e.g. rhinitis, bronchial asthma), fungal infections (e.g. aspergillus), parasitic infections.

Skin prick testing in a patient with asthma

A skin prick test is used to check immediate allergic reaction as much as 40 different substances at once (e.g. protein from the dust, pollen, mold, pet dander, dust mites and foods) It's used to identify allergy.

It uses needles that barely penetrates the surface of the skin, it doesn't cause bleeding.

In adults, the test is usually done on the forearm. Children may be tested on the upper back.



IgE mediated type I hypersensitivity reaction to inhaled allergens

we can also use the RAS test for the patient to look for a specific subtype of IgE (check immunology foundation hypersensitivity lecture)

Diagnosing the patient with asthma by spirometry

It's respiratory function test.
we measure two volumes:

- FEV1 (forced expiratory volume in one second):
it reduced in asthma due to mucus plug,
accumulation of eosinophils, smooth muscle
spasm of bronchial wall.

- FVC (Forced vital capacity):
either normal or increase
(لأن المريض ما يقدر يطلع الهواء بسبب انسداد الـ
bronchial tree)



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.

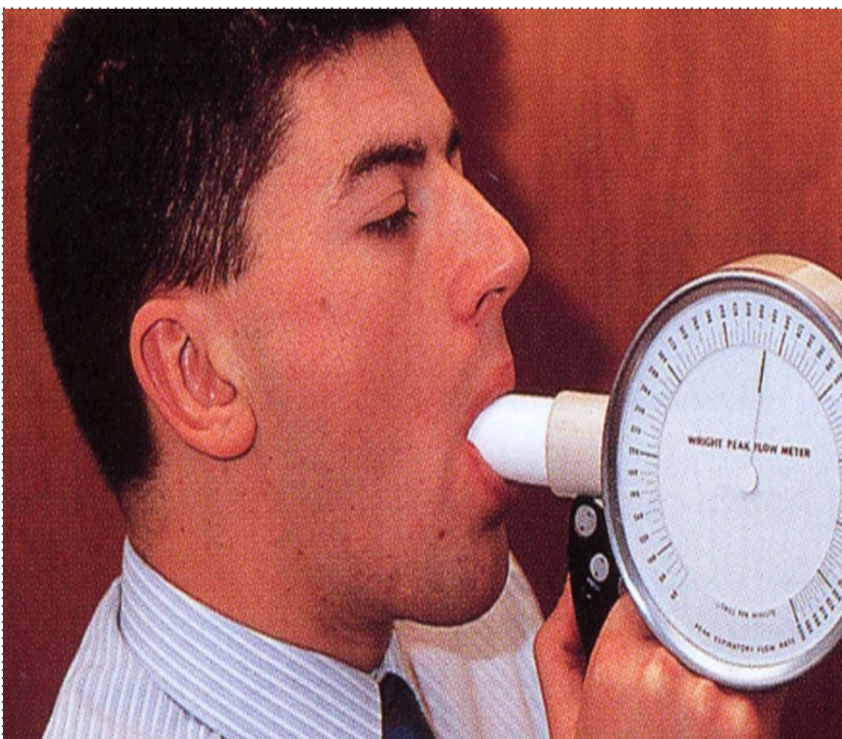
Nocturnal cough (cough at the night)

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**

Clinical course

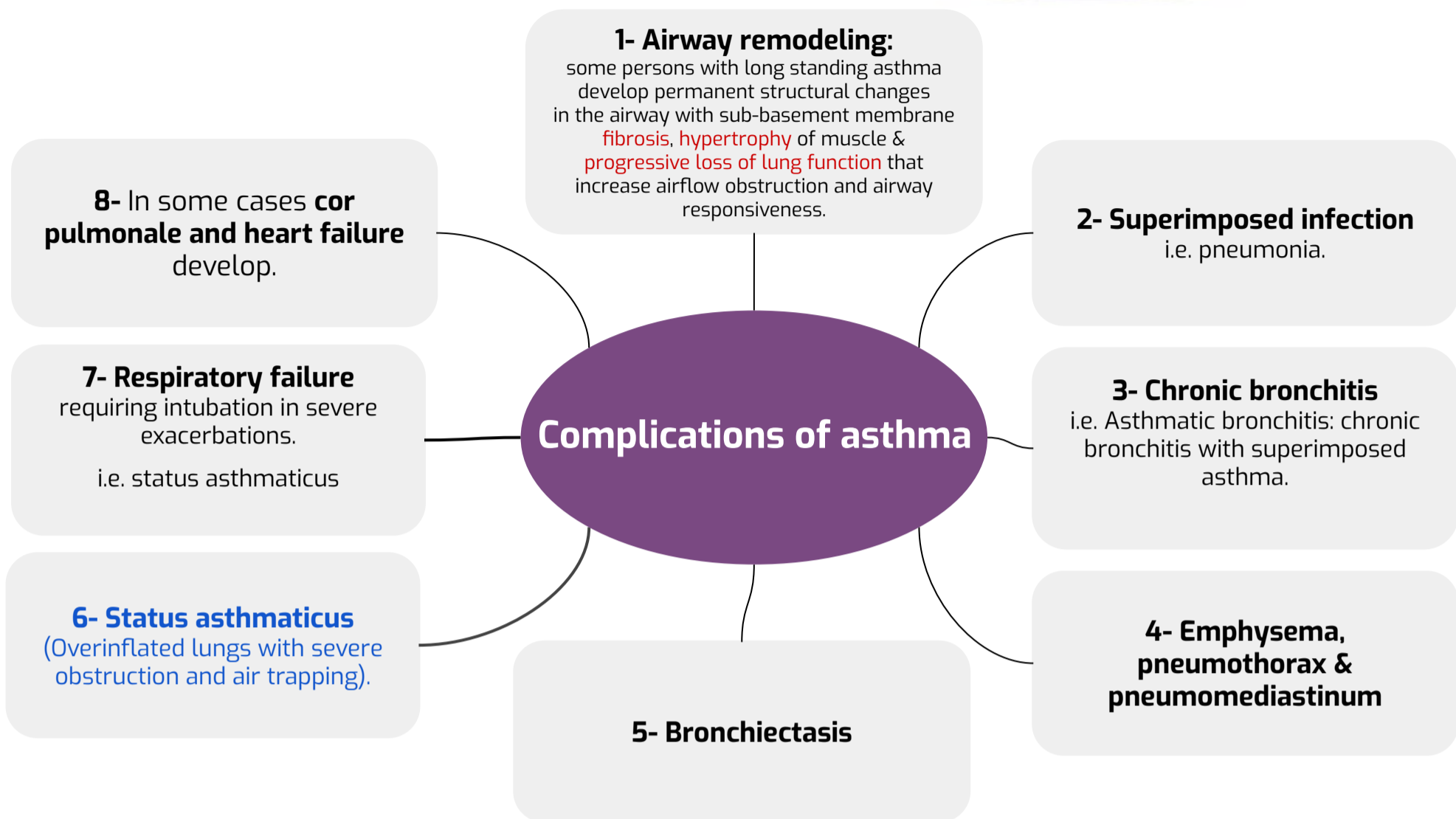
The range of presentation in asthma. This patient was found incidentally to have a degree of reversible airways obstruction during a **routine medical examination**.



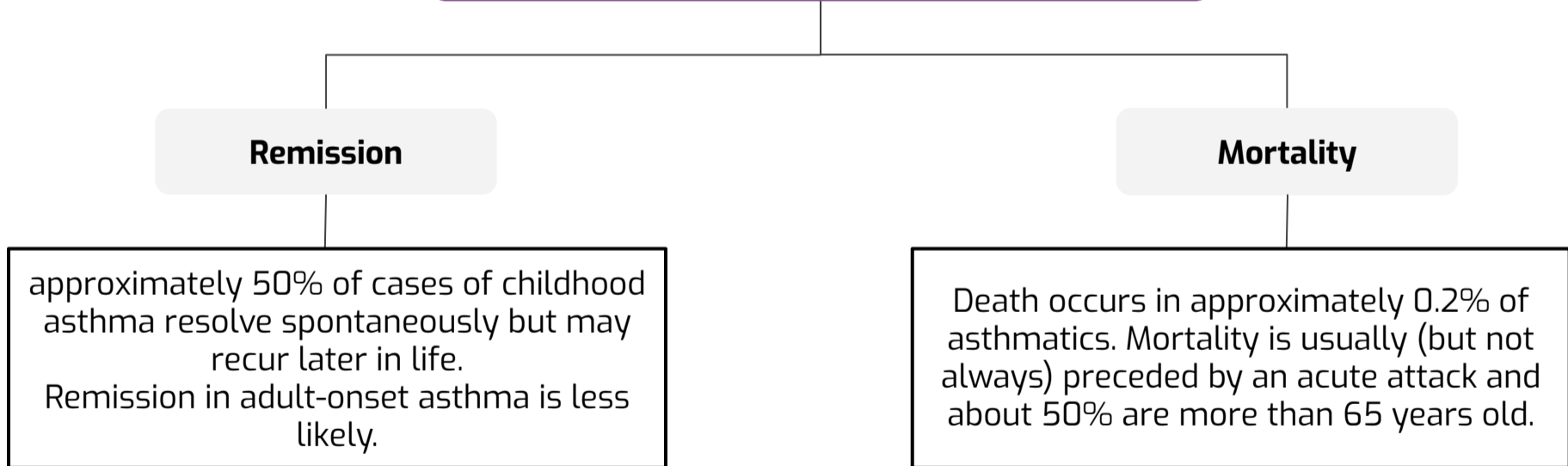
Status asthmaticus

This patient presented as **an acute medical emergency, irreversible** with acute severe breathlessness and diagnosed as a case of status asthmaticus (Overinflated lungs because of severe obstruction and air trapping) which **persist for days and required intensive care** including intermittent positive-pressure ventilation. Use oxygen therapy (because the patient has hypoxemia, hypercapnia (increase CO₂ in the arterial blood))





Prognosis



Prevention:

01

Control of factors contributing to asthma severity

- Exposure to irritants or allergens has been shown to increase asthma symptoms and cause exacerbations.

02

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.

Summary

[click here for Rikabi's lone lecture notes](#)

Asthma

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 and eosinophils

Thickened BM

Mucus plug & Curschmann spirals & Charcot-Leyden crystals.

Remodeling with sub-basement membrane fibrosis and hypertrophy of muscle layer

Pathogenesis

The antigens enter the bronchial tree and stimulate the production of IgE (has light chain and heavy chain) then those immunoglobulins E set on the mast cell (because it has receptors for the immunoglobulin on its cytoplasmic membrane) leading to degranulate and release histamine & platelet-activating factor that cause increase vascular permeability, induce edema, induce contraction of the bronchial tree, mucus hypersecretion..

Complication

Superimposed infection

Chronic bronchitis

Pulmonary emphysema

Cor pulmonale

Status asthmaticus (Overinflated lungs with severe obstruction and air trapping)

Quiz

1- what is the hallmark of asthma?

a- chronic bronchial inflammation	b-bronchial smooth muscle cell hypertrophy	c- increase mucus secretion	d- all of them
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2- Which type of asthma have positive skin test ?

a- Atopic (Extrinsic) asthma	b- Nonatopic (Intrinsic) asthma	c- Drug-Induced asthma	d- Occupational asthma
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3-A child with a peanut allergy has also recently been diagnosed with asthma. The healthcare provider instructs the parents on ways to prevent the child coming in contact with peanuts. This is because the child is at increased risk for which of these problems?

a- Anaphylaxis and respiratory failure	b-vomiting,diarrhea	c- headache,seizures	d- painful rash
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4- The products of Eosinophils are inducing by:

a- IL-4	b- IL-5	c- IL-13	d- IL- 15
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5-A condition in which overinflated lungs with severe obstruction & air trapping.

a- bronchiectasis	b- Status asthmaticus	c- Emphysema	d- chronic bronchitis
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6-A patient experiencing an acute asthma exacerbation arrives at the urgent care clinic. Which of these assessment findings require immediate action by the healthcare provider?

a- Inaudible breath sounds and an ineffective cough	b- tachycardia	C- prolonged expiration	d- All of them
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7-When providing discharge teaching to a patient who is newly diagnosed with asthma, which of these points should the healthcare provider emphasize?

A-Eliminate or reduce exposure to known asthma triggers."	B- when you by the attack take your prophylactic drug	C-take corticosteroid drug	D-take NAISD daily
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SAQ

1-D
2-A
3-A
4-B
5-B
6-A
7-A

1- Name the cells that play a role in the inflammatory response?

Eosinophils, mast cells, macrophages, lymphocytes, neutrophils, epithelial cells

(important)

2- What is the main difference between atopic and nonatopic asthma ?

Atopic asthma : preceded by allergic rhinitis, urticaria, or eczema = previous history of allergic condition
Non-atopic : Triggered by non-immune stimuli

3- What is the main Morphological changes of BA ?

- 1/ Accumulation of mucus in the bronchial lumen
- 2/ Hypertrophy of submucosal glands, and increased submucosal vascularity
- 3/ Thickening of airway wall
- 4/ Hyperplasia of smooth muscle cells

4- A 10 years old boy came to the emergency department complaining from difficulty in breathing & severe cough accompanied by sputum especially at night . He remember that he played with a kitty 2 days ago.The blood test shows high level of IgE & Eosinophil count.

What type of bronchial asthma does he have?

special thanks for

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