Respiratory system pathology

By

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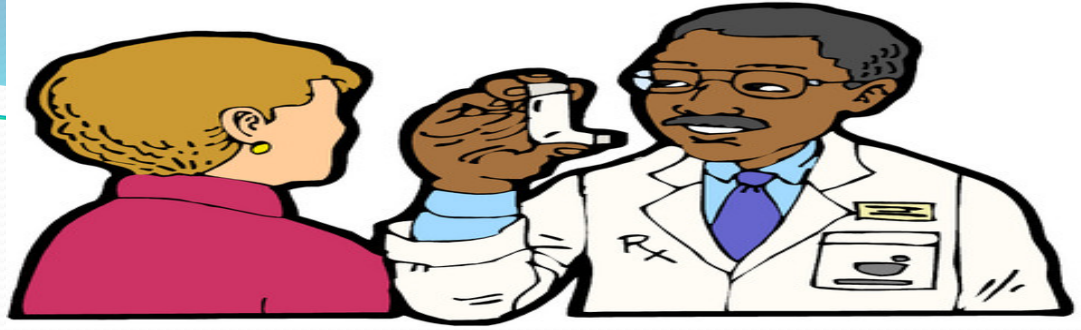
Objectives

Asthma (definition ,pathogenesis and clinical -1 features and morphological features)

Asthma



Asthma is chronic relapsing inflammatory disorder is characterized by paroxysmal reversible bronchospasm (due to smooth muscle hyper- reactivity) when trigger to certain stimuli. Increased mucus production is also a feature.

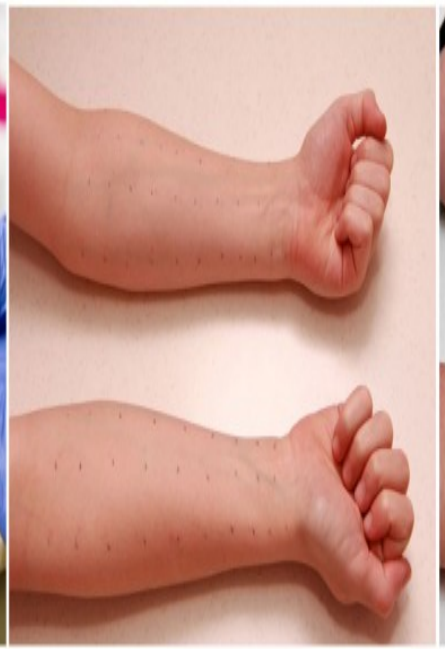
The reversibility of the airway obstruction in asthma is feature that distinguishes it from other forms of obstructive lung diseases .

Asthma classify in to:-

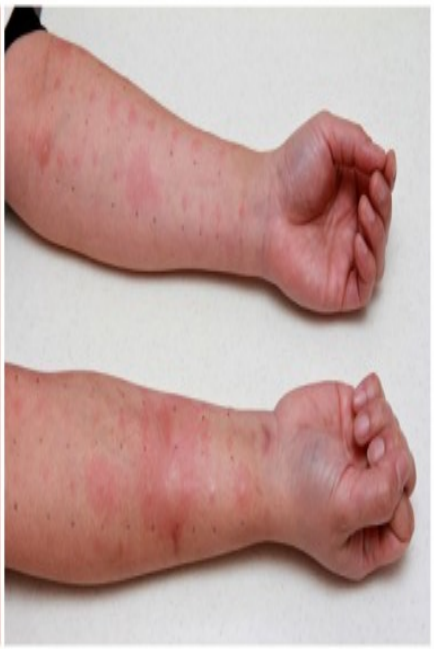
1-Atopic (allergic) asthma is the most common type (two-thirds of the cases) of asthma , the disease is "extrinsic"

It is caused by a classical type I (i.e. IgE) mediated hypersensitivity reaction trigger by environmental antigens (e.g. pollen , certain foods) . Family history of atopy is common . Serum IgE levels are usually elevated . A skin test with the offending antigen results in an immediate wheal and flare reaction .

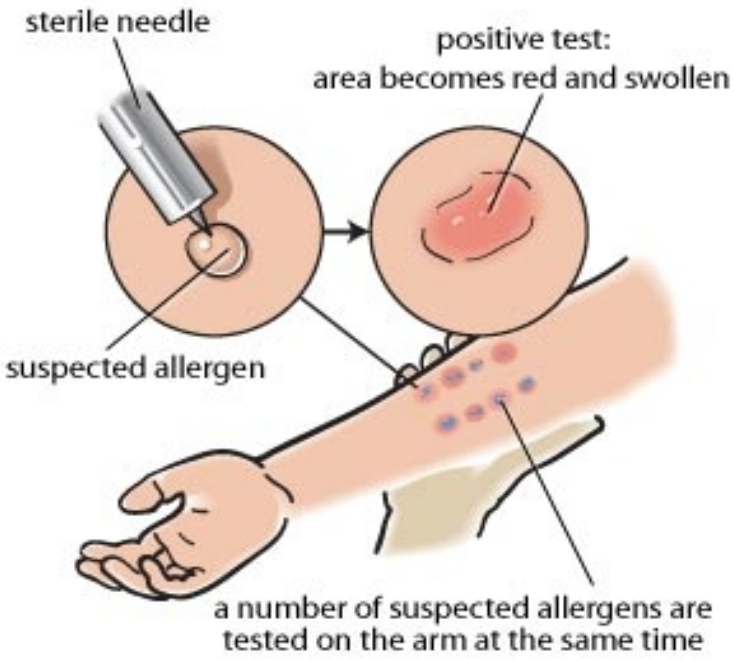
Allergy Skin Testing



Negative Allergy Skin Test



Positive Allergy Skin Test



2-Nonatopic asthma (one-third) , asthma is "intrinsic" and it is triggered by non-immune stimuli .Usually without a family history . Serum IgE levels are normal . A skin test results are usually negative .

Subtype of non atopic asthma :-

A-Such as pulmonary infections, especially viral (rhinovirus, parainfluenza virus) ; psychological stress, cold temperature, exercise and etc.

B-Drug induced –asthma affect about 10% of adults with a diagnosis of asthma like NSAIDs (inhibition of the enzyme cyclooxygenase (COX). e.g, Aspirin ,voltarin , brufen , etc)

C- Occupational asthma is caused by workplace triggers including fumes and dusts .

Pathogenesis

The major etiologic factors of asthma are

1-In the "atopic" form of asthma is associated with an excessive TH2(T- helper cell type -2) reaction and formation of IgE antibodies against environmental antigens , primary leukotriene (interleukins) and secondary cytokine mediator release.

The Role of TH2:-In the airways the inhaled antigens stimulates the TH2 cells and induction to release of their interleukins . Interleukins produced by TH2 cells are responsible for most of the features of asthma;

1. IL-4 stimulates B-cell for IgE production

2. IL-5 activates eosinophil's

3. IL-13 stimulates mucus production.

This stage called sensitization to allergen.

Acute phase

Subsequent exposure of IgE-coated mast cells to the same antigen causes the direct stimulation of subepithelial vagal receptors provokes reflex bronchospasm , mucus secretion and leukocyte recruitment .

histamine release (bronchospasm and edema , due to increased vascular permeability) , These occur within minutes after stimulation thus called acute, or immediate response.

Late phase

Mast cells release the cytokines that cause the influx of other leukocytes, including eosinophil's . These inflammatory cells set the stage for the late-phase reaction, which starts 4 to 8 hours later.

Eosinophil's cells are particularly important in the late phase.

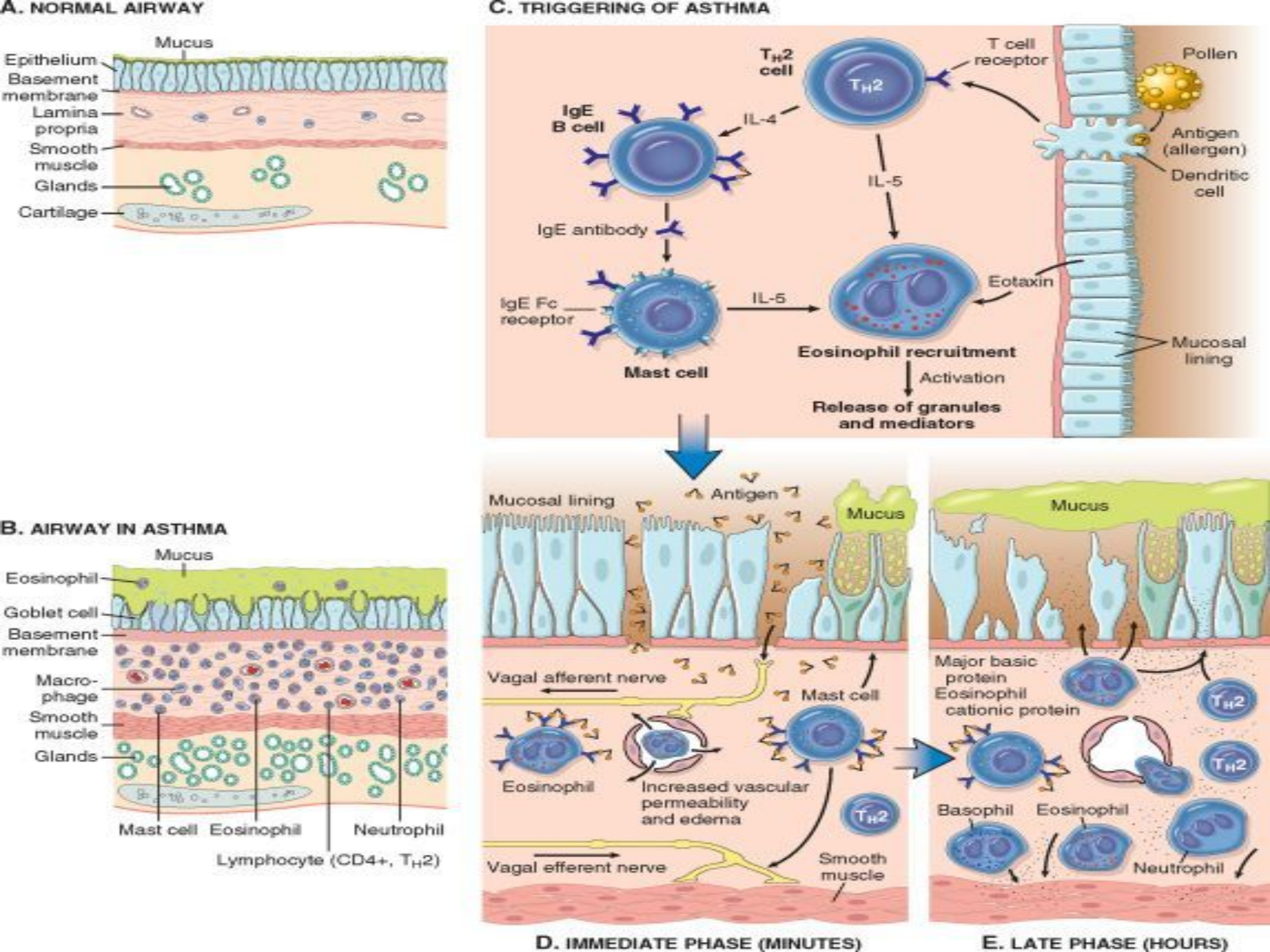
Their effects are mediated by

1. Major basic protein and eosinophil cationic protein, which directly damage airway epithelial cells.

2. Eosinophil peroxidase causes tissue damage through oxidative stress.

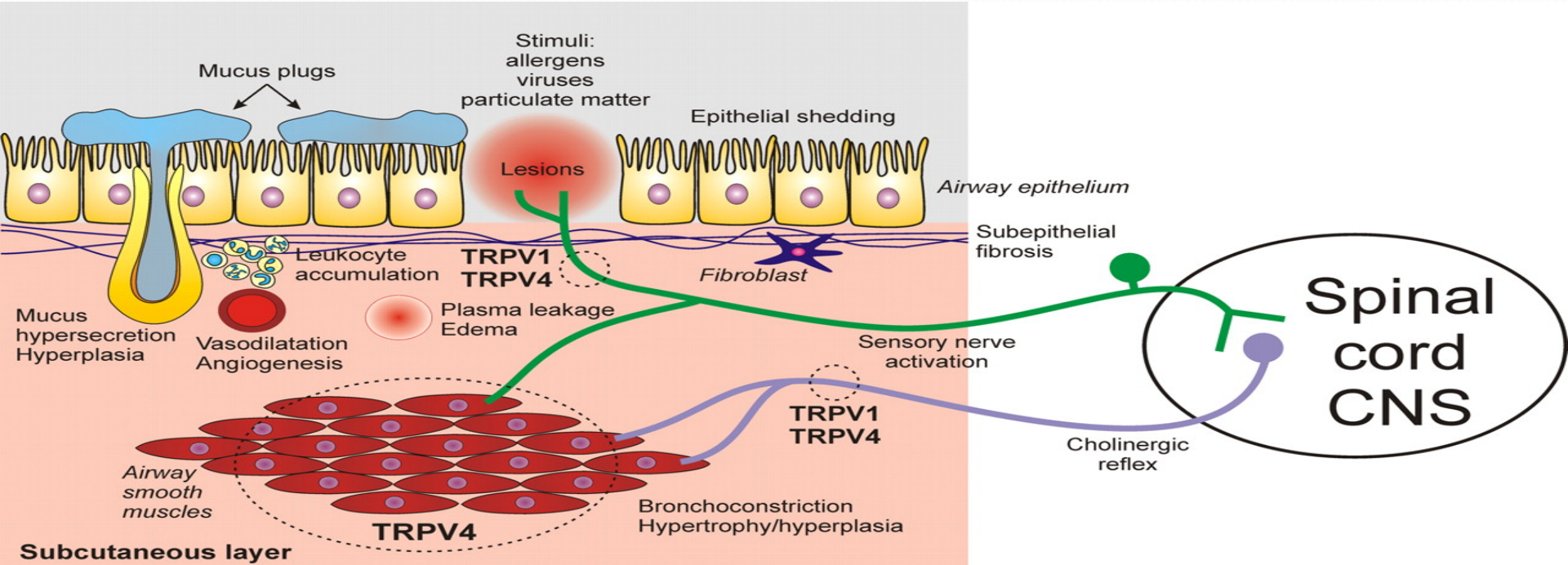
3. Leukotriene C4, which contribute to bronchospasm.

***Late phase is characterized by persistent bronchospasm and edema ,leukocyte infiltration ,epithelial damage and loss**


A. NORMAL AIRWAY
Mucus
Epithelium
Basement membrane
Lamina propria
Smooth muscle
Glands
Cartilage
C. TRIGGERING OF ASTHMA
T_H2 cell
T cell receptor
Pollen
IgE B cell
IL-4
Antigen (allergen)
Dendritic cell
IL-5
IgE antibody
IgE Fc receptor
IL-5
Eotaxin
Mucosal lining
Eosinophil recruitment
Activation
Mast cell
Release of granules and mediators
B. AIRWAY IN ASTHMA
Mucus
Eosinophil
Goblet cell
Basement membrane
Macrophage
Smooth muscle
Glands
Mast cell
Eosinophil
Neutrophil
Lymphocyte (CD4+, T_H2)
Mucosal lining
Antigen
Mucus
Vagal afferent nerve
Mast cell
Eosinophil
Increased vascular permeability and edema
Vagal efferent nerve
Smooth muscle
Mucus
Major basic protein
Eosinophil cationic protein
Basophil
Eosinophil
Neutrophil
D. IMMEDIATE PHASE (MINUTES)
E. LATE PHASE (HOURS)

2-In Non atopic asthma

Airway hyperirritability is attributed to virally or chemically induced inflammation through the direct stimulation of subepithelial vagal receptors provokes reflex bronchospasm,mucus secretion and eosinophils recruitment (Eosinophils are key inflammatory cells found in all subtypes of asthma; eosinophil products such as major basic protein are responsible for airway damage .

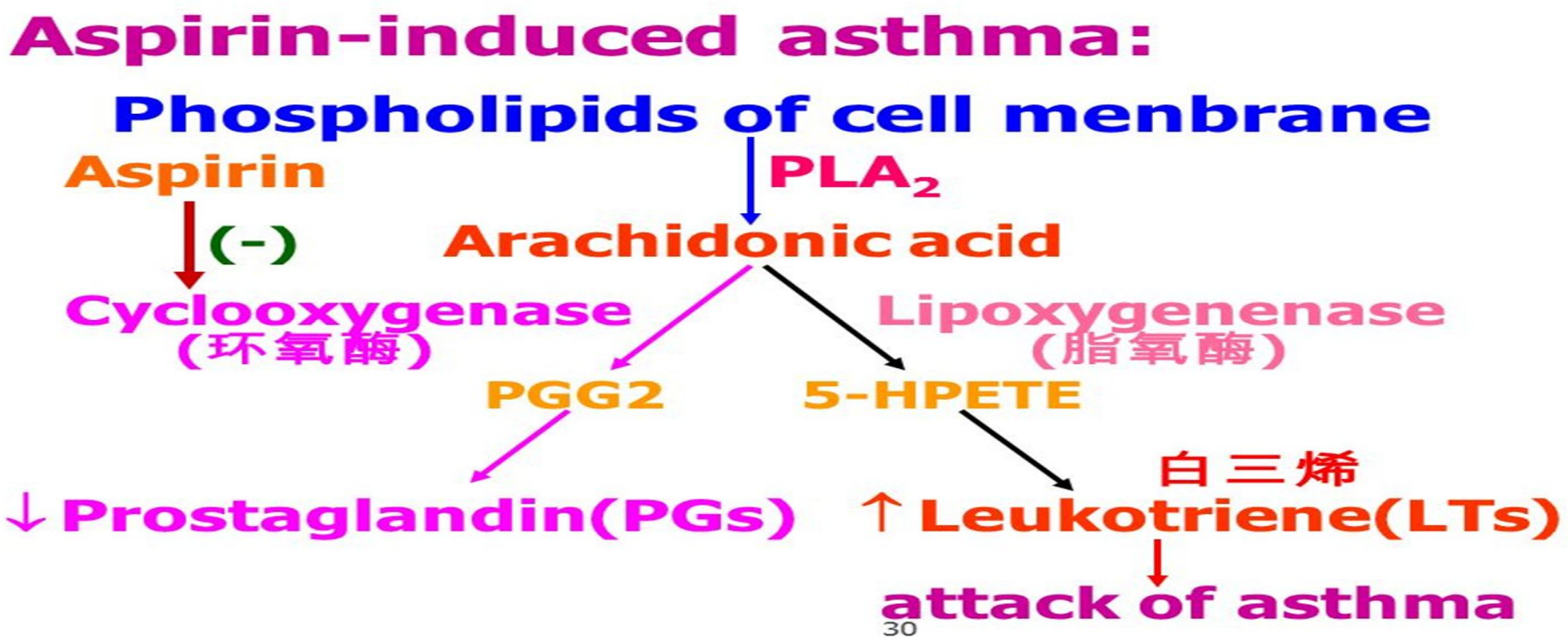


Aspirin induce asthma

Patients with aspirin sensitivity present with recurrent rhinitis and nasal polyps, urticaria and bronchospasm

Aspirin inhibits the cyclooxygenase-1 pathway of arachidonic acid metabolism without affecting the lipoxygenase route .

There by shifting the balance of production toward leukotrienes that cause bronchial spasm .



Exercise-induced asthma

Characterized by bronchoconstriction that .accompanies increased physical activity

Pathogenesis is unknown can be correlated to air, temperature gradient and mucosal irritation

3-Genetic factors for asthma

Asthma is a complex genetic trait in which multiple susceptibility genes interact with environmental factors to . initiate the asthma

-:The strongest genetic associations have been made with

ADAM-33:- (ADAM-33 gene normally responsible for-1 . smooth muscle proliferation)
If mutation occur in ADAM-33 gene (activation the gene) lead to accelerate proliferation of bronchial smooth muscle cells and fibroblasts, thus contributing to bronchial spasm

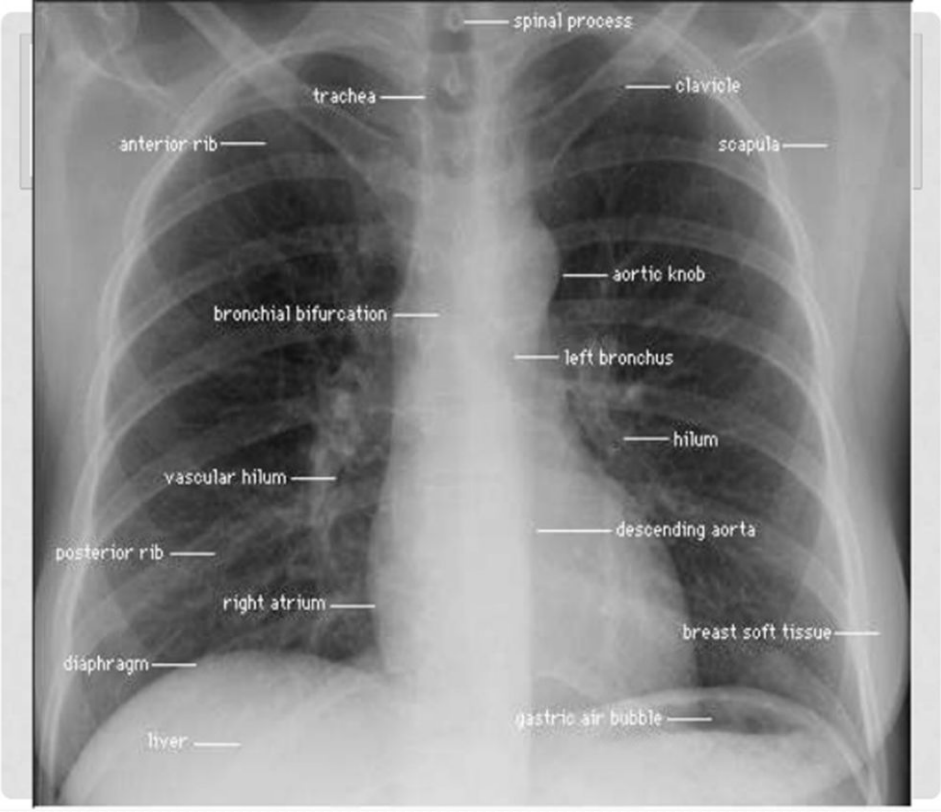
IL-4 receptor gene: -If mutation occur in the gene-2 encoding the IL-4 receptor (activation the receptor) lead to .elevated total serum IgE and then lead to atopic asthma

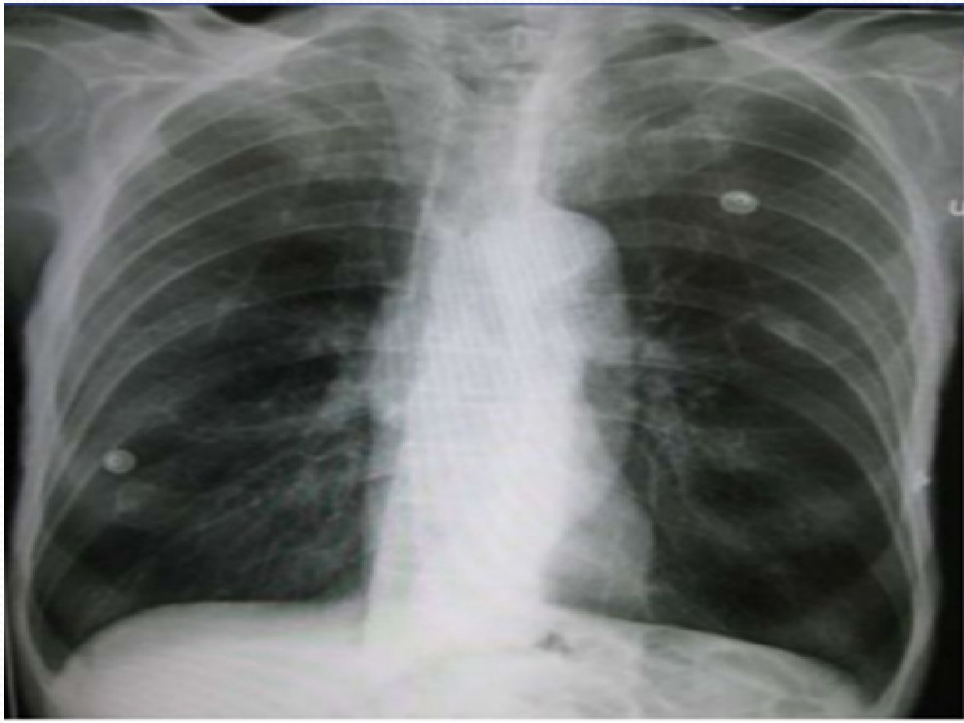
B2 –adrenergic receptor (normally lead to-3 bronchodilator) while in mutation lead to loss its function

Clinical features of asthma

Classic attacks last up to several hours ;symptoms include chest tightness , wheezing , dyspnea , cough .
Problems with expiration cause lung over inflation .
In sever episodes (status asthmaticus) , acute symptoms persist for days to weeks ,and significant airflow obstruction can cause cyanosis and death .

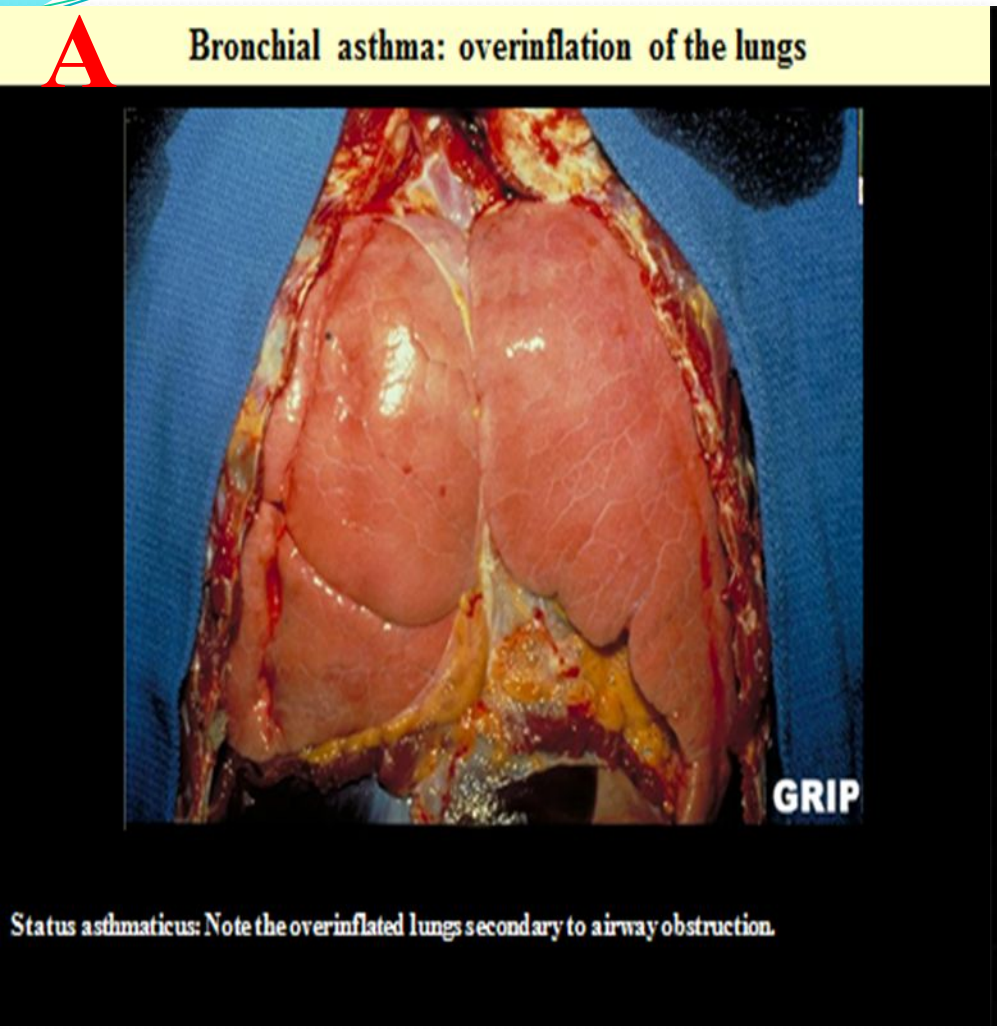
Normal CXR

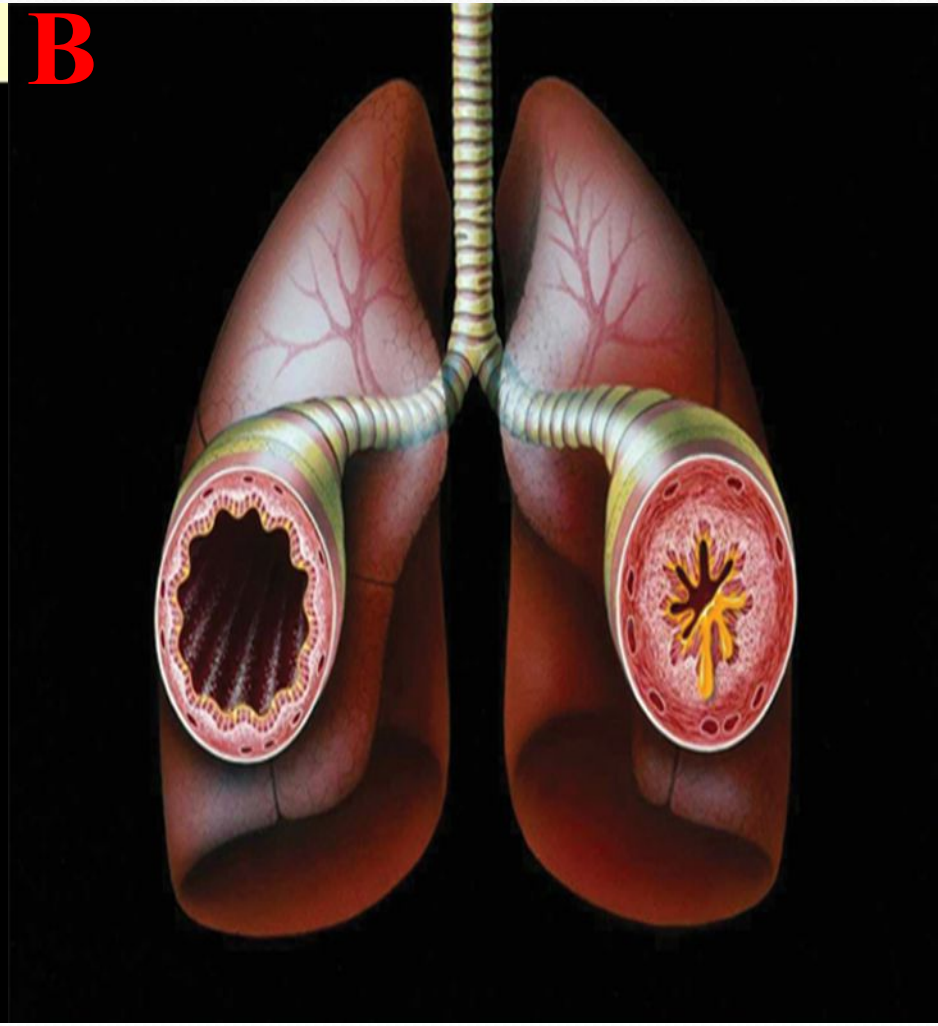




CXR with asthma show hyper-inflation and diaphragmatic flatting

Asthma grossly





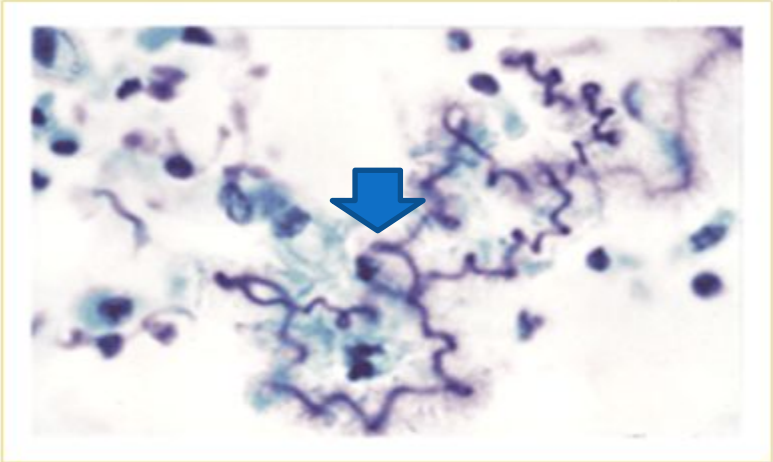
A- Over inflation of both lung

B-There is occlusion of bronchi and bronchioles by thick, tenacious mucous plugs .

Morphology of sputum

Curschmann spirals

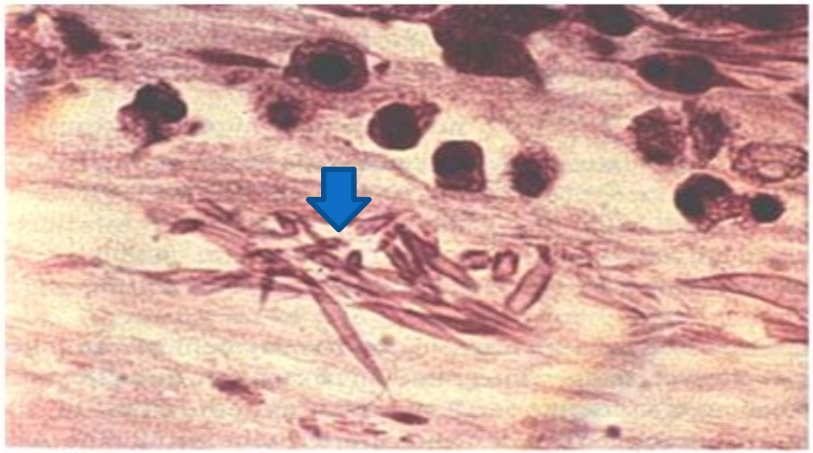
- Coiled, basophilic plugs of mucus formed in the lower airways and found in sputum and tracheal washings



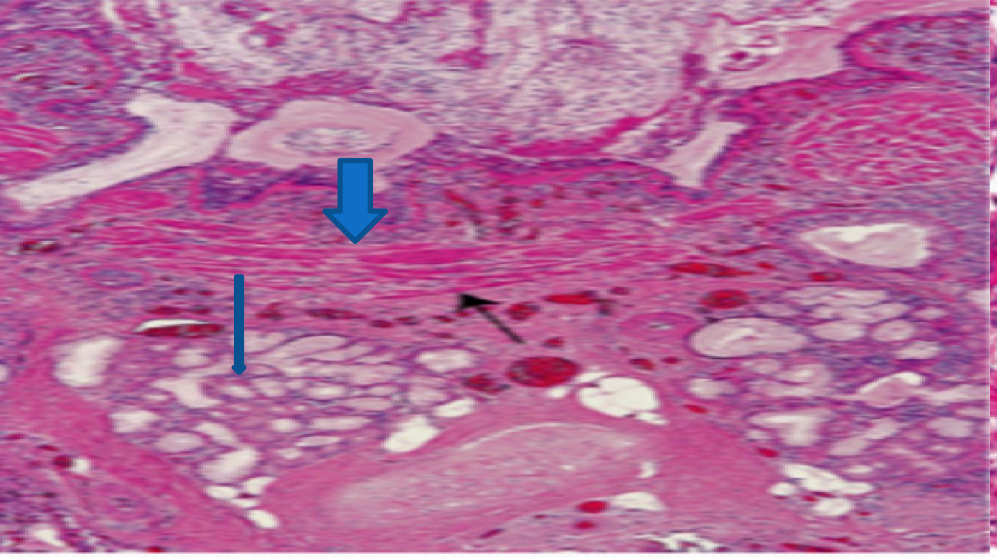
Curved airway epithelium

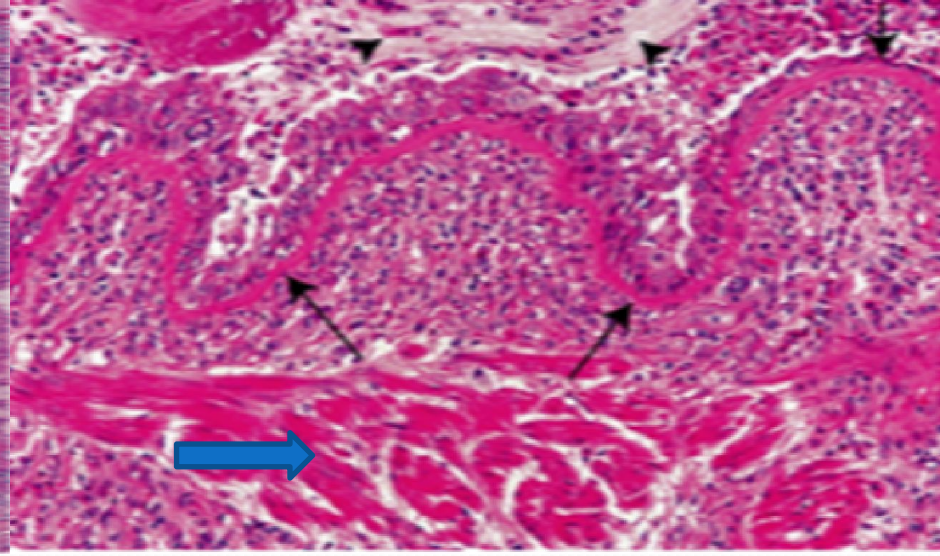
Charcot-Leyden crystals.

- Eosinophilic needle-shaped crystalline structures.



Breakdown of eosinophil's





Microscopic features

1-There is occlusion of bronchi and bronchioles by thick, tenacious mucous plugs, which contain numerous eosinophils.

2-Structural changes of airways include thickening of the basement membrane of the bronchial epithelium(2 black arrows)

3-Edema and an inflammatory infiltrate in the bronchial walls, with a prominence of eosinophils (eosinophils are key of inflammatory cells in all subtypes of asthma) and mast cells.

4- Hypertrophy and hyperplasia of the sub mucosal glands (thin blue arrow) .

5- Hypertrophy of the bronchial muscle (thick blue arrow) .

MANAGEMENT OF ASTHMA

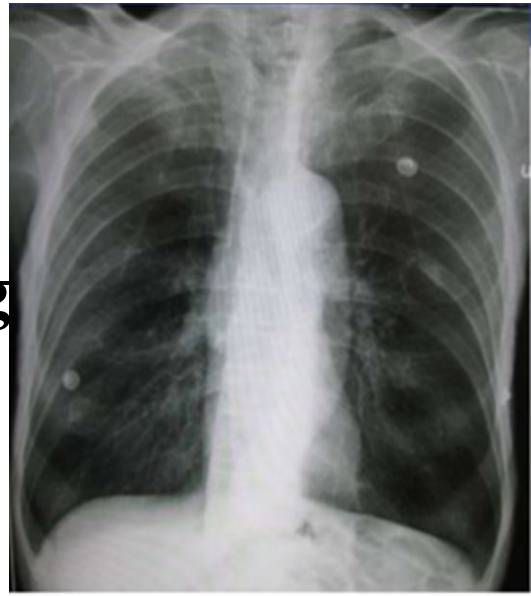
- **A** – Adrenergics (Beta 2 Agonists) (Albuterol) — Bronchodilator
- **S** – Steroids
- **T** – Theophylline — Bronchodilator
- **H** – Hydration (IV)
- **M** – Mask O_2
- **A** – Anticholinergics

THAN YOU

You learn something every day if you pay attention

QUIZ

A 25 y –old men suffered from episodic attach of sever dyspnea with wheezing and cough after ingestion the aspirin drug ,patient with –ve family history to allergen . The CXR showed mild hyperinflation .



1-What are the expected serological finding

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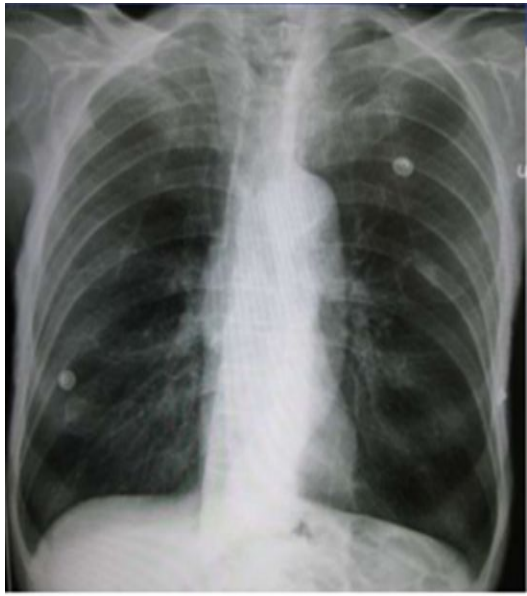

1- pathophysiology of aspirin induce asthma