



# Atopy & Allergies

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429 immune Team:

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**Allergic diseases** : Human disease caused by immune responses to environmental antigens that lead to immediate reactions in the target tissues & rapid onset of symptoms.

Allergic diseases are classified under Immediate (type I ) hypersensitivity

In clinical practice these reactions are commonly called allergy or atopy

- An atopic person is a person who has the tendency to react to an antigen (allergen) through an immediate ( type I ) hypersensitivity reactions (cause an allergic disease).
- atopy refers to : a genetic predisposition for development of immediate hypersensitivity reactions in certain individuals.

### Characteristics of allergens :

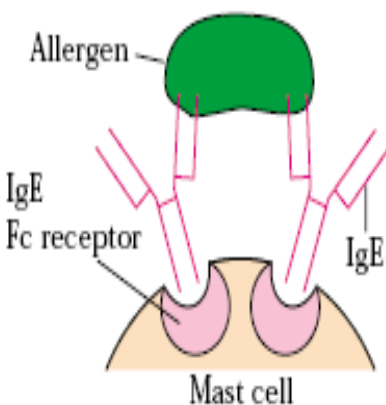
1. proteins in nature or chemicals bound to proteins and some have enzyme activity.
2. low molecular weight.
3. glycosylation (glycoprotein).
4. high solubility in body fluids.

Allergen = antigen


The genes participating in production of allergic response are located at:

- A. chromosome 11q → encodes the b subunit high affinity IgE receptors (Fc receptors)

(a) Allergen crosslinkage of cell-bound IgE



The allergen will cross link two Fab portions from two different IgE. Allergen cross linkage stimulates degranulation of mast cells.

B. chromosome 5q  contain many cytokines genes that will promote (act on ) Th 2 cells to induce an immune response by increasing the production of IgE.

- increase production of cytokines (mostly, eosinophils chemotactic cytokines)



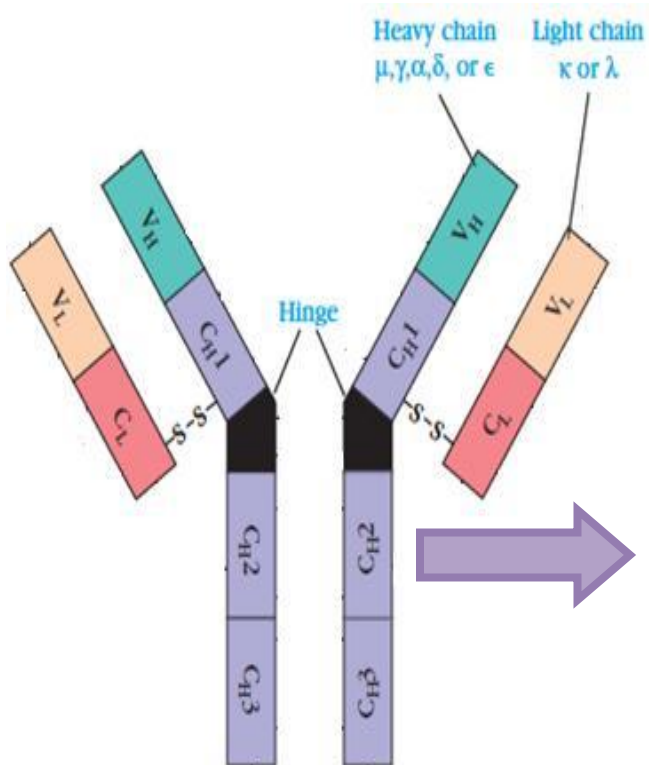
increase numbers of eosinophils in the blood

- The 5q locus contain genes for :

- IL-3 , 4 , 5 , 9 & 13

These cytokines promote TH2 responses by improving :

- ∂ IgE isotype switching in B cells
- ∂ eosinophils survival ((stay longer in the blood stream))
- ∂ mast cell proliferation



As you remember, when we studied immunoglobulin, we took that it has a heavy chain and a light chain.

The heavy chain isotype (isotype = α, δ, ε, γ, μ) determines the class of an antibody (μ: IgM, γ: IgG, δ: IgD, α: IgA, and ε: IgE).

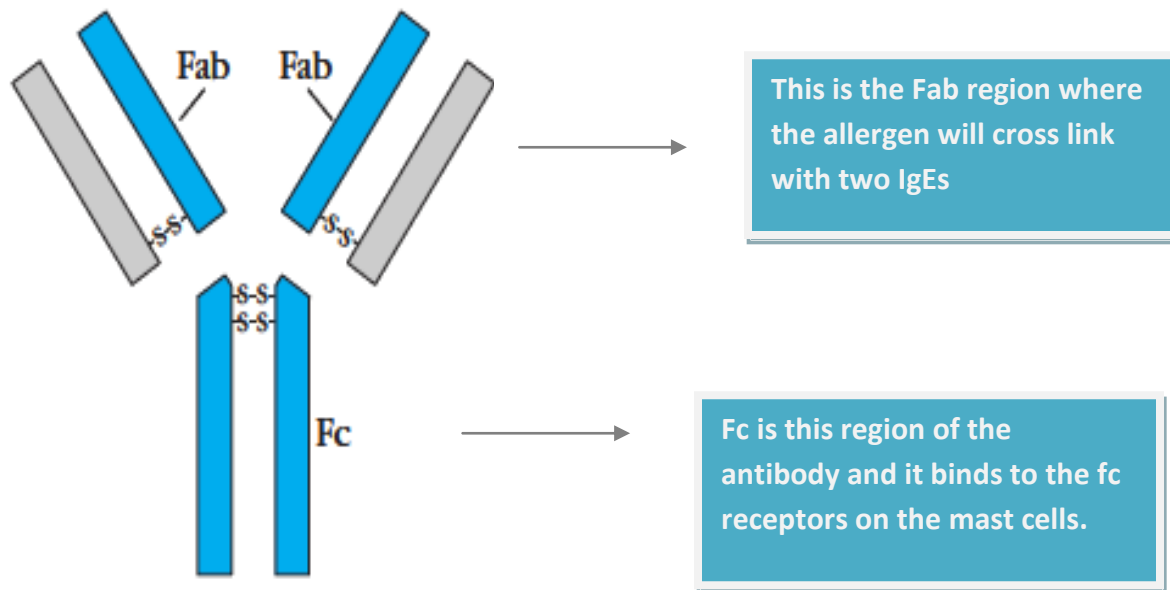
For understanding only but you have to know that IgE is made up of ε domains.

الحين .. بالدم فيه immunoglobulins تدور IgM & IgD  
 اول ما يدخل allergen على الجسم .. ال isotype اللي في ال immunoglobulins سواء كان μ او γ او غيره  
 يتحول الى ε فيصير عندي IgE

This happens because of the effect of cytokines      اللي 5q gene  
 طلوعوا من ال

This is how the **isotype switching** mechanism happens. Mostly, in **atopic patients.**

The cytokine that is responsible for isotype switching is **IL-4**



### Manifestation of allergic diseases requires two steps:

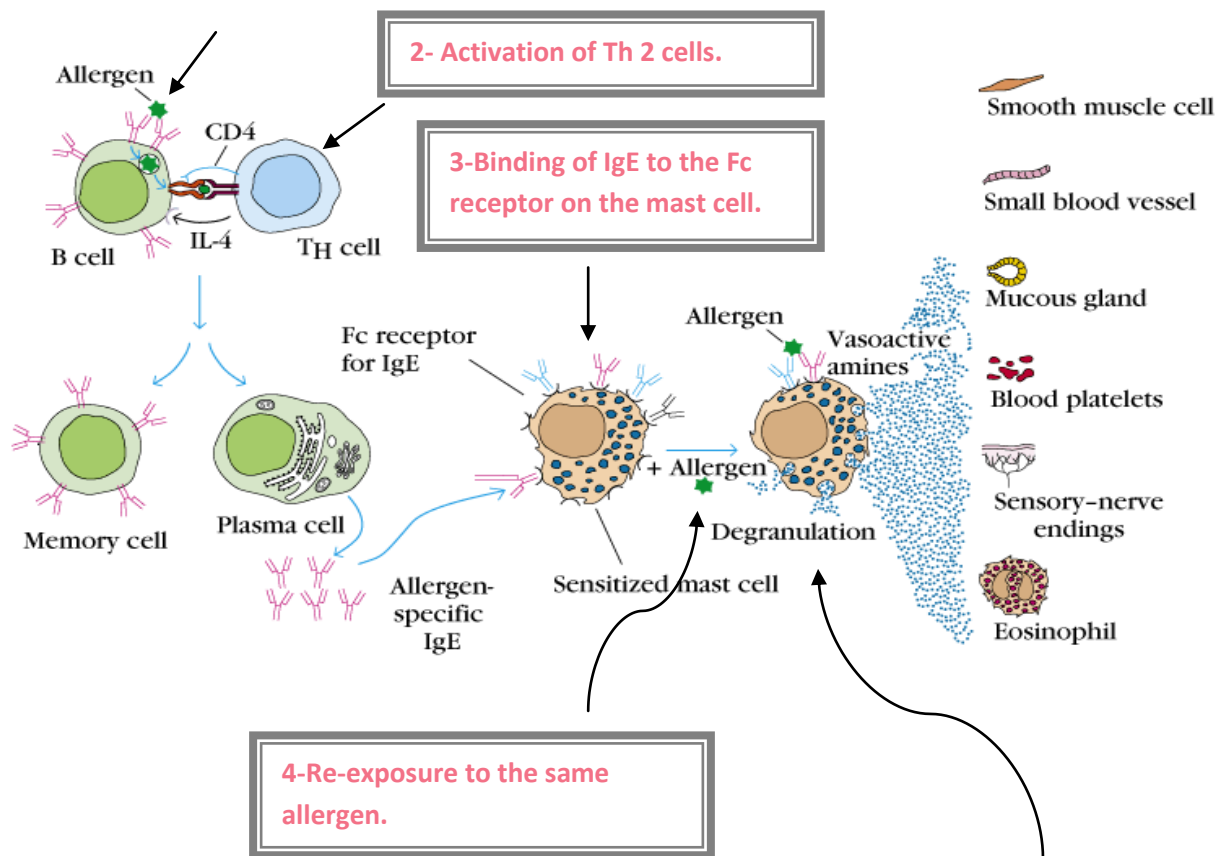
#### firstly , sensitisation phase:

- 1- exposure to the allergen.
- 2-Activation of TH2 cells & stimulation of IgE class switching in B –cells
- 3- Binding of IgE to Fc $\epsilon$  receptor on mast cells.
- **sensitization:** is the attachment of **specific IgE** to Fc $\epsilon$  receptors on the mast cells.

#### secondly , challenge phase:

- 1-Repeated exposure to allergen
- 2-Activation of mast cells (**by cross linking**) which will lead to its degranulation and the release of the mediators.

1-Exposure to the allergen for the first time.



### Common allergens associated with type I hypersensitivity

**Proteins**  
Foreign serum  
Vaccines

**Plant pollens**  
Rye grass  
Ragweed  
Timothy grass  
Birch trees

**Drugs**  
Penicillin  
Sulfonamides  
Local anesthetics  
Salicylates

**Foods**  
Nuts  
Seafood  
Eggs  
Peas, beans  
Milk

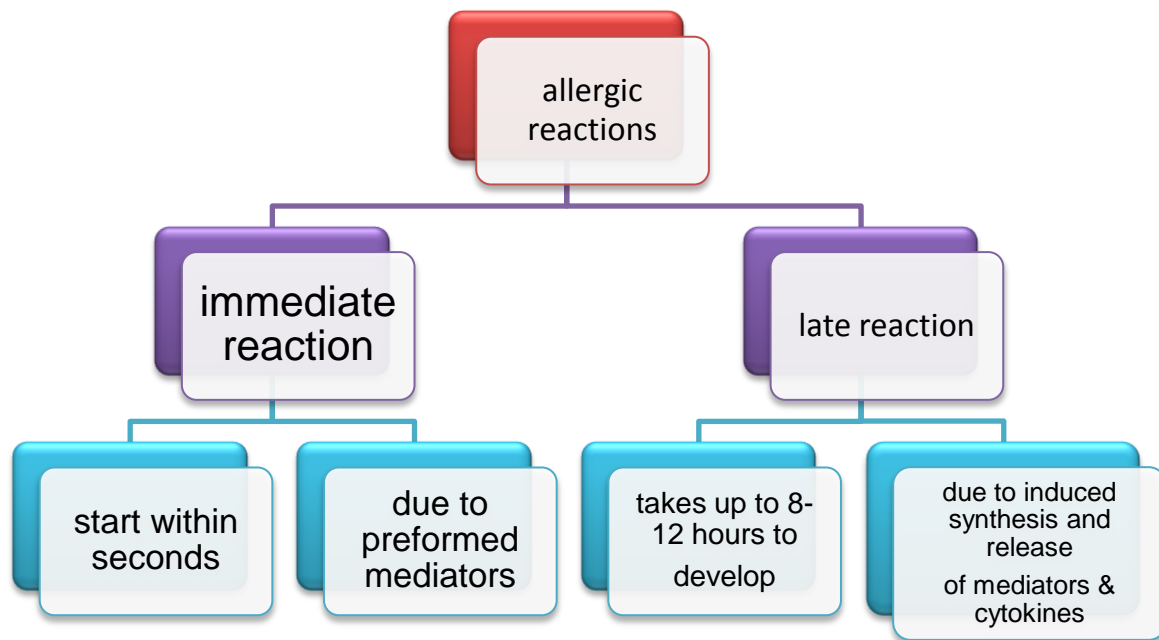
**Insect products**  
Bee venom  
Wasp venom  
Ant venom  
Cockroach calyx  
Dust mites

**Mold spores**  
Animal hair and dander

## Common environmental allergens :

- Fungal spores (aspergillus)
- tree pollens ( mesquite ) in Saudi Arabia
- Ragweed & ragweed pollens
- House dust mite
- Cockroach insects
- Honey-bee
- black( fire ) ant

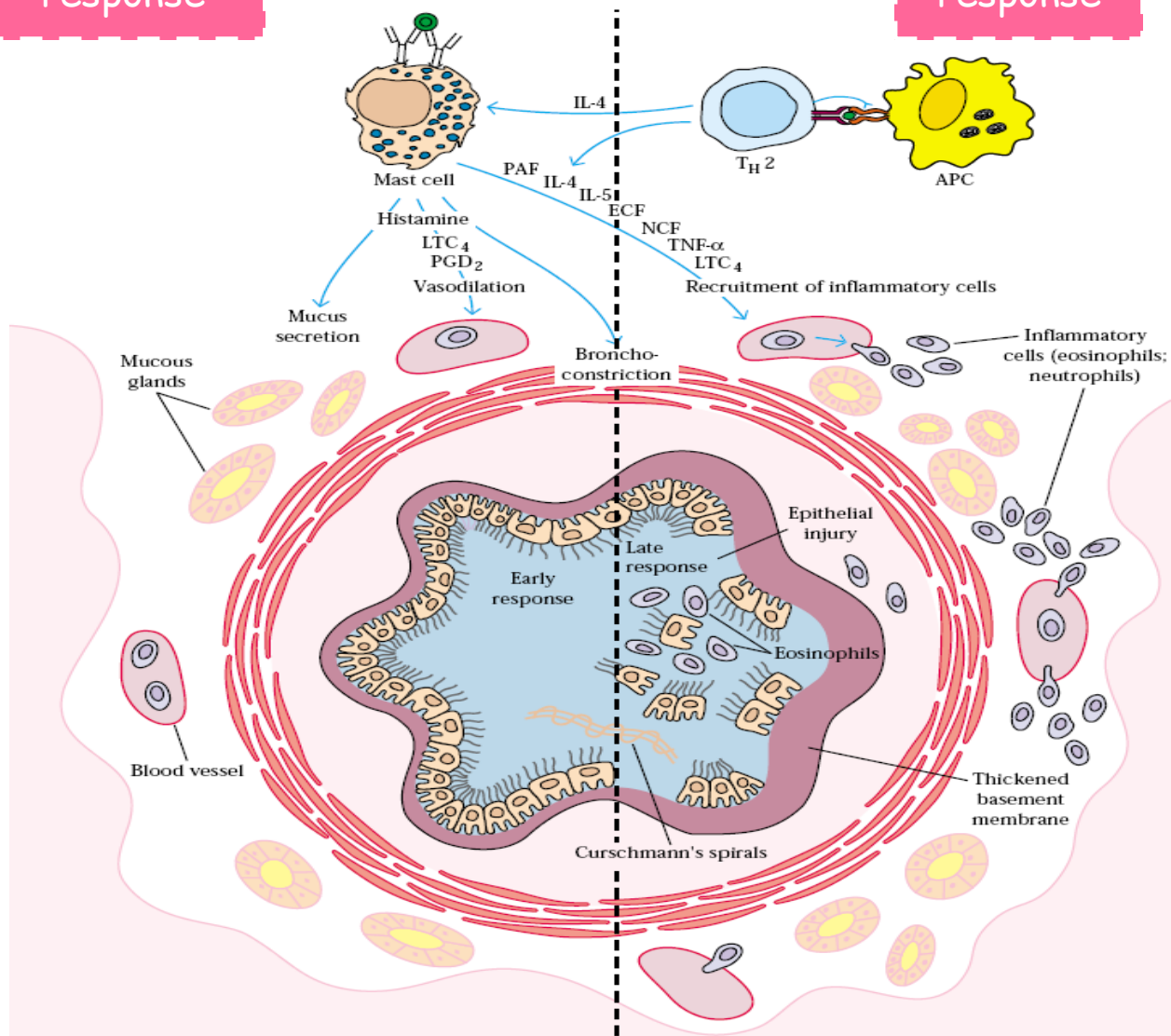
Common causes of anaphylaxis





## Immediate response

## Late response

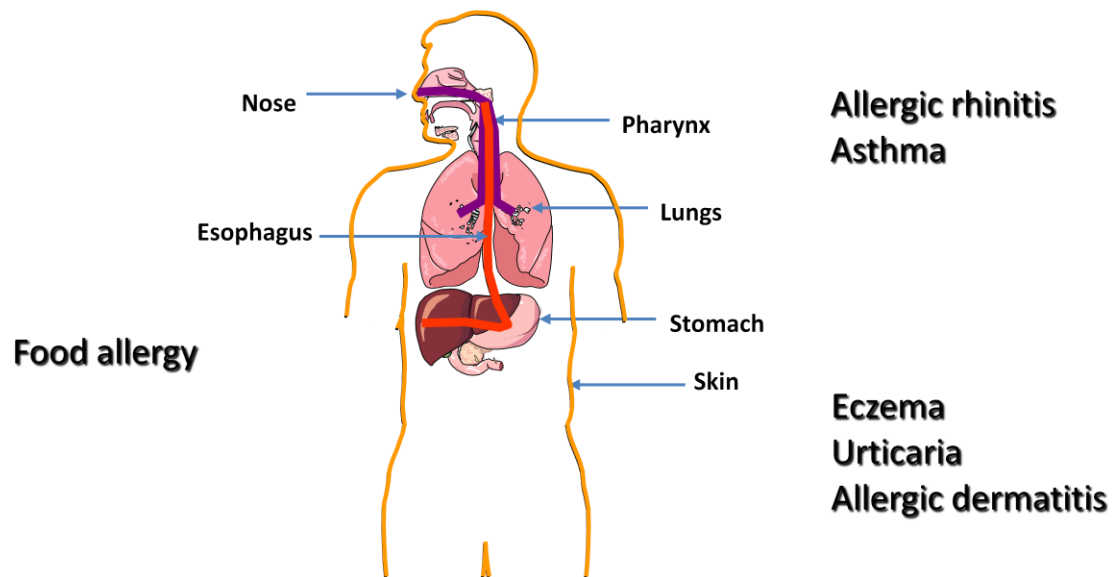


EARLY RESPONSE (minutes)		LATE RESPONSE (hours)	
Histamine	Vasodilation	IL-4, TNF-α, LTC <sub>4</sub>	Increased endothelial cell adhesion
PGD <sub>2</sub>	Bronchoconstriction	PAF, IL-5, ECF	Leukocyte migration
LTC <sub>4</sub>	Mucus secretion	IL-4, IL-5	Leukocyte activation

## Primary and secondary mediators

Mediator	Effects
PRIMARY	
Histamine, heparin	Increased vascular permeability; smooth-muscle contraction
Serotonin	Increased vascular permeability; smooth-muscle contraction
Eosinophil chemotactic factor (ECF-A)	Eosinophil chemotaxis
Neutrophil chemotactic factor (NCF-A)	Neutrophil chemotaxis
Proteases	Bronchial mucus secretion; degradation of blood-vessel basement membrane; generation of complement split products
SECONDARY	
Platelet-activating factor	Platelet aggregation and degranulation; contraction of pulmonary smooth muscles
Leukotrienes (slow reactive substance of anaphylaxis, SRS-A)	Increased vascular permeability; contraction of pulmonary smooth muscles
Prostaglandins	Vasodilation; contraction of pulmonary smooth muscles; platelet aggregation
Bradykinin	Increased vascular permeability; smooth-muscle contraction
Cytokines	
IL-1 and TNF- $\alpha$	Systemic anaphylaxis; increased expression of CAMs on venular endothelial cells
IL-2, IL-3, IL-4, IL-5, IL-6, TGF- $\beta$ , and GM-CSF	Various effects (see Table 12-1)

## Allergy is a systemic Disorder:



- **Allergic disease** is the **5<sup>th</sup> leading chronic disease** among all ages.
- And the **3<sup>rd</sup> chronic disease** among **children under 18 years old**; up to one child in three is affected.

## Clinical presentations:

- 1- Allergic rhinitis
- 2- Allergic asthma
- 3- Skin allergy
- 4- Food allergy
- 5- Systemic anaphylaxis

### 1- Allergic rhinitis :

- **Mechanism:** inhaled allergens activate mucosal mast cells beneath the nasal epithelium this will cause a release of mediators which will lead to the diffusion of secretions across the mucous membranes of the nasal passage.

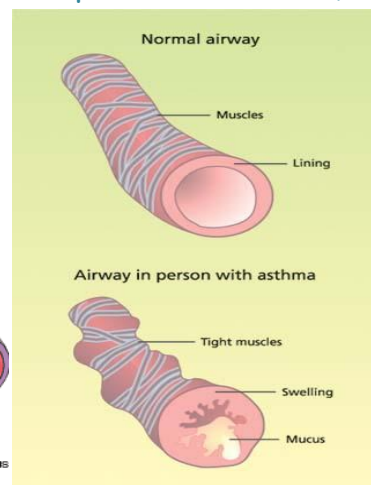
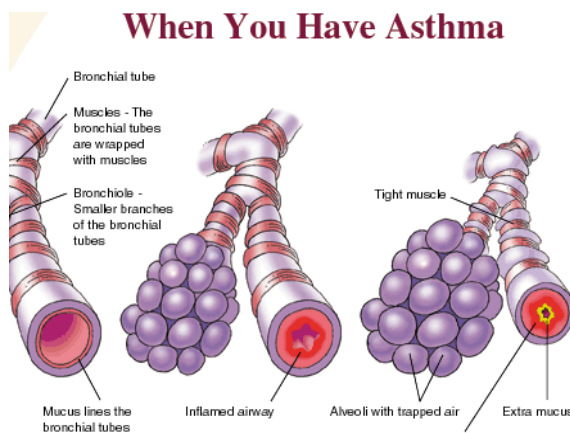


## Characteristics of the immediate reaction in allergic rhinitis:

- 1- intense itching & edema
  - 2- local edema → Blocked nasal passage
  - 3- Nasal discharge (Rich in eosinophils)
  - 4- Irritation of the nose (result of histamine release)
- A similar reaction to airborne (floating in the air) allergens in the conjunctiva of the eye result in: **Allergic conjunctivitis.**

## 2-Allergic asthma:

- **Mechanism:** Inhaled allergens activate sub-mucosal mast cells in the lower airways that will release the mediators then it will lead to a contraction of bronchial smooth muscles.
- Difficulty in breathing.
- Increased secretion of mucus.
- Increased vascular permeability.
- influx of inflammatory cells ( including eosinophils & TH2 cells ).



An important feature of asthma is **chronic inflammation of the airways** which is a result of the influx of inflammatory cells:

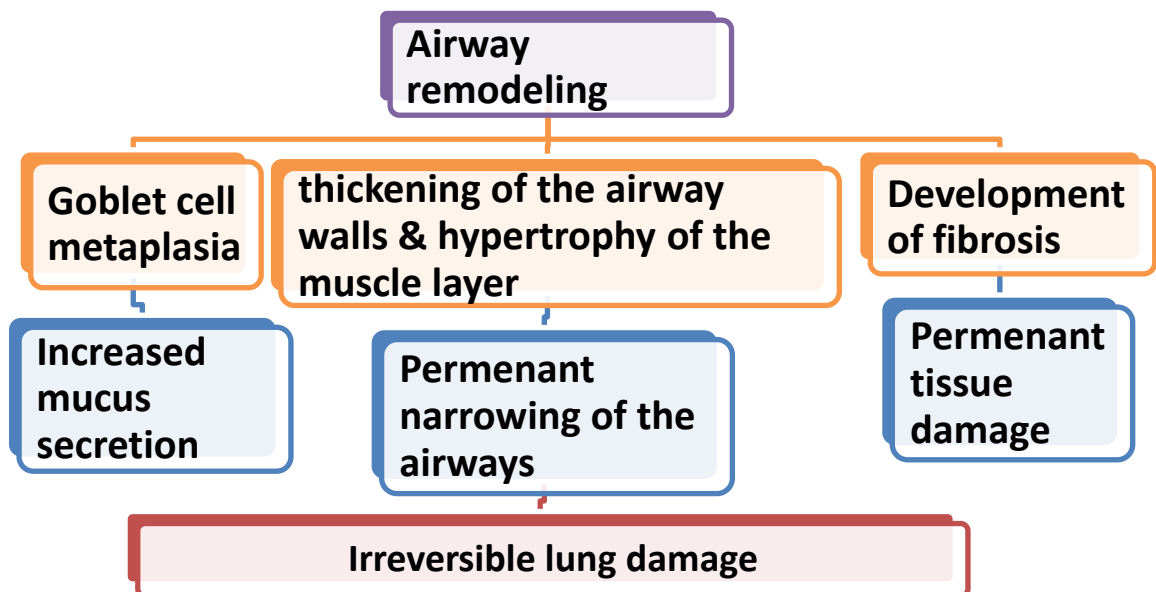
- Th 2 cells secretes IL-9 & IL-13
- Eosinophils ( major basic proteins)
- Neutrophils secretes proteolytic enzymes.
- Lung epithelium cells

## Products of these cells acts on:

- 1- Air smooth muscle cells.
- 2- Lung fibroblasts.
- 3- Mucous glands.

Which will cause  **Airway remodeling**

Airway remodeling could cause an irreversible lung damage by:



- Hyper reactive airways react to non-specific factors:

- 1- Chemical irritants
- 2- Smoke & strong perfumes.
- 3- Sulphur dioxide & air pollutants.
- 4- Viral & bacterial respiratory infections

### 3-Skin allergy

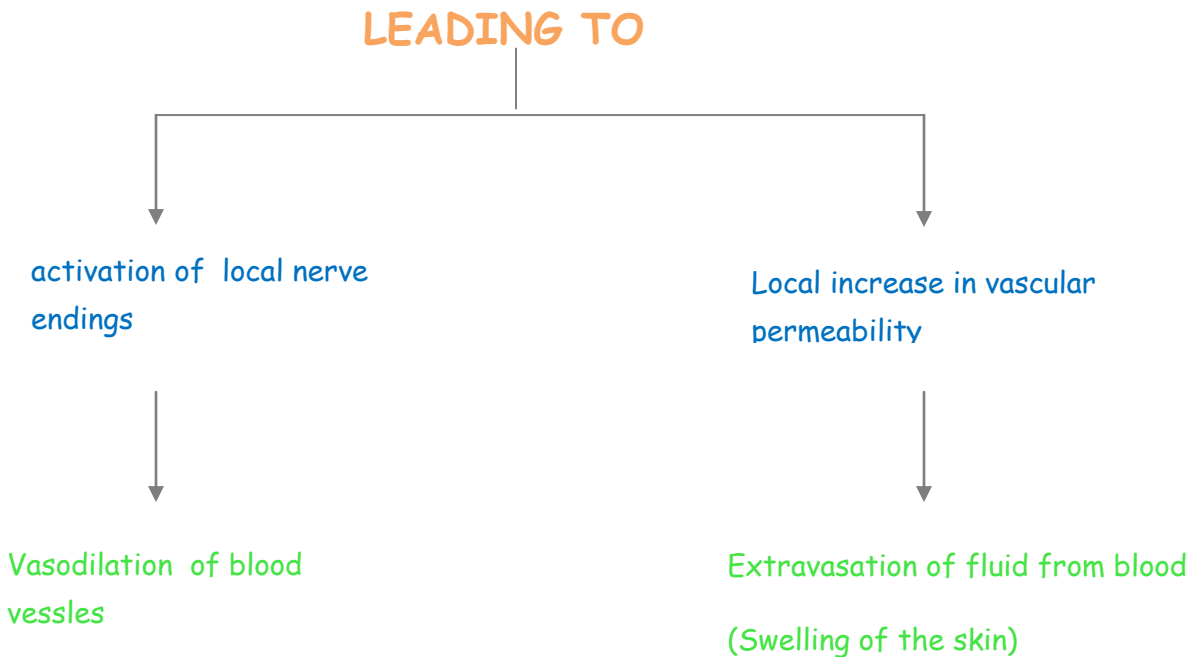
#### Manifest as:

- Acute urticaria
- chronic eczema

#### • Allergens enter the epidermis or dermis by :

1. a stinging insect
2. direct contact
3. through the blood ( ingested food or drug ).

**Mechanism:** Local connective tissue mast cells become activated (after contact with allergens) & release mediators.



This skin lesion is called:

**Wheal-and flare reaction**



## Acute Urticaria:

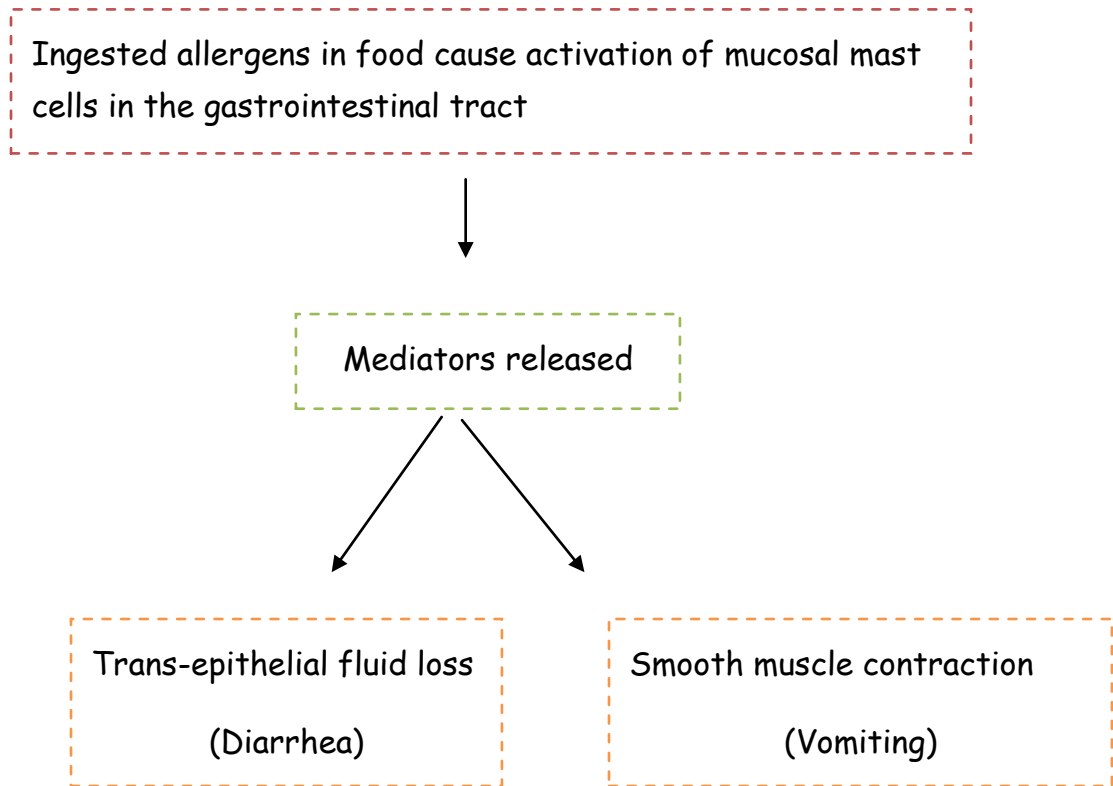
- is a disseminated form of the wheal-and-flare reaction
- sometimes appear when ingested allergens enter the blood stream and reach the skin
- Histamine released by mast cells in the skin causes:  
(Urticaria or hives) large , itchy red swellings of the skin.

- Swelling of the lips and eyes (Angioedema) may be associated with urticaria.

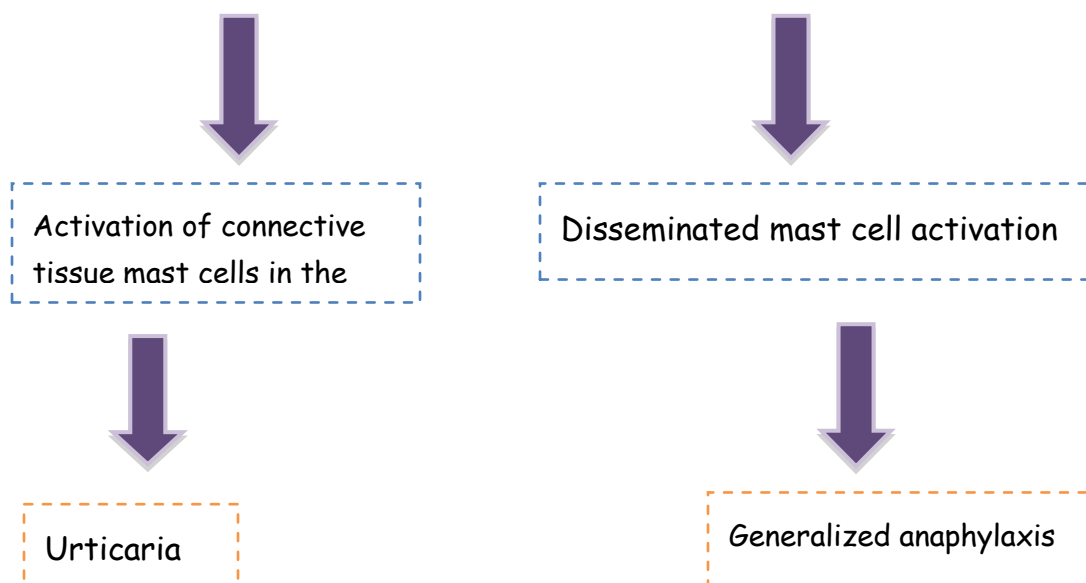


- A significant health problem especially in children.
- food allergens resist digestive enzymes & therefore reach the mucosal surface of the small intestine as an intact molecule.

## Mechanism:

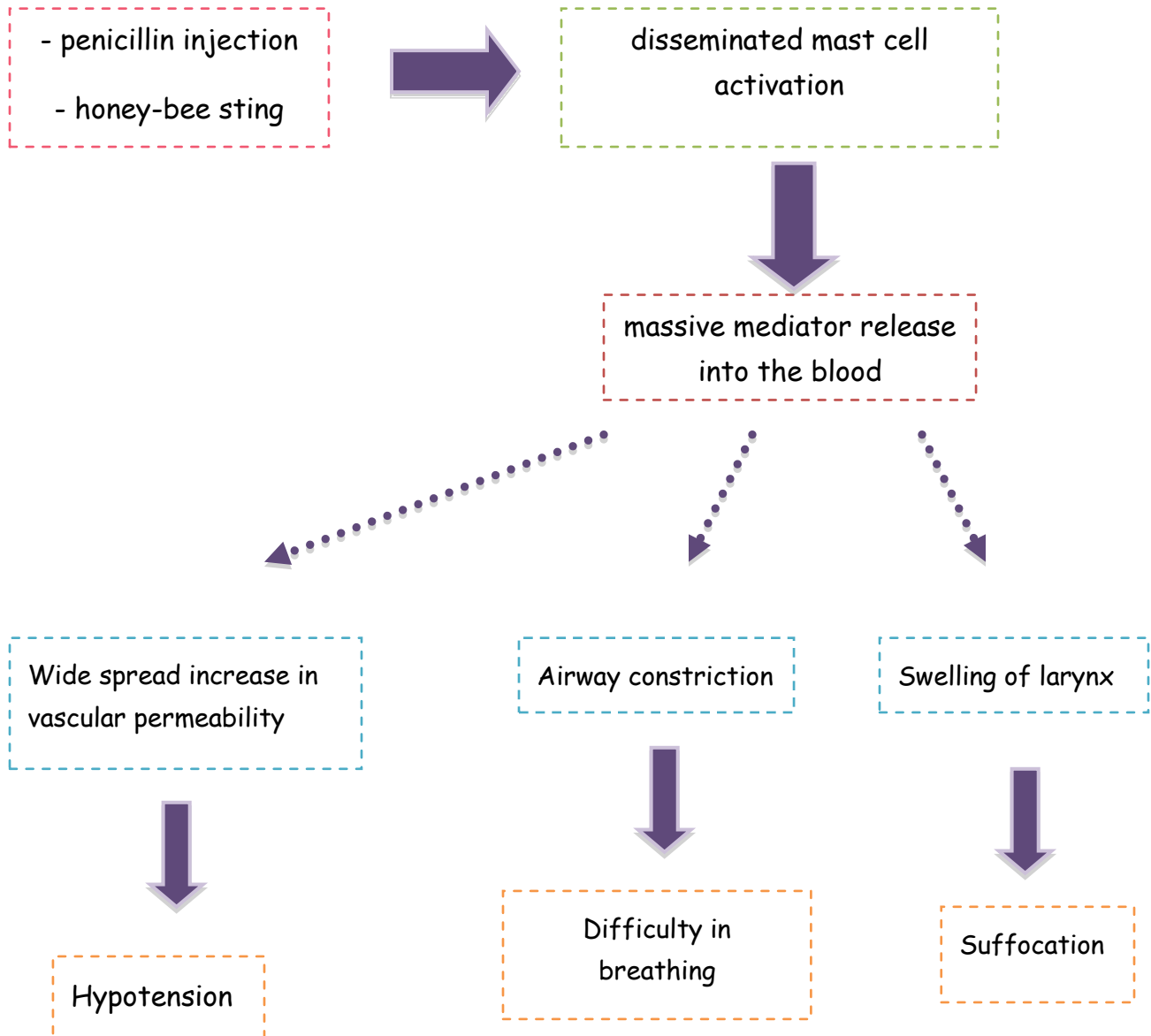


Ingested food allergens may enter the bloodstream  
and cause systemic reactions



## Systemic anaphylaxis (Anaphylactic shock):

- Allergens may be introduced directly into the bloodstream as a result of:



Anaphylactic shock can be rapidly fatal but can be controlled by immediate injection of **epinephrine ( adrenaline )** .

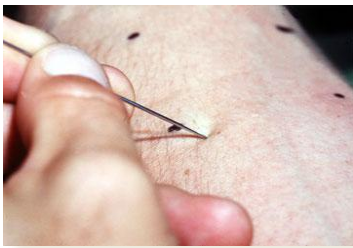
## Diagnosis of allergic diseases :

1-skin prick test (SPT).

2-specific IgE measurement

3-challenge tests

4-elimination-provocation-tests...(foodallergy)



Skin prick test