

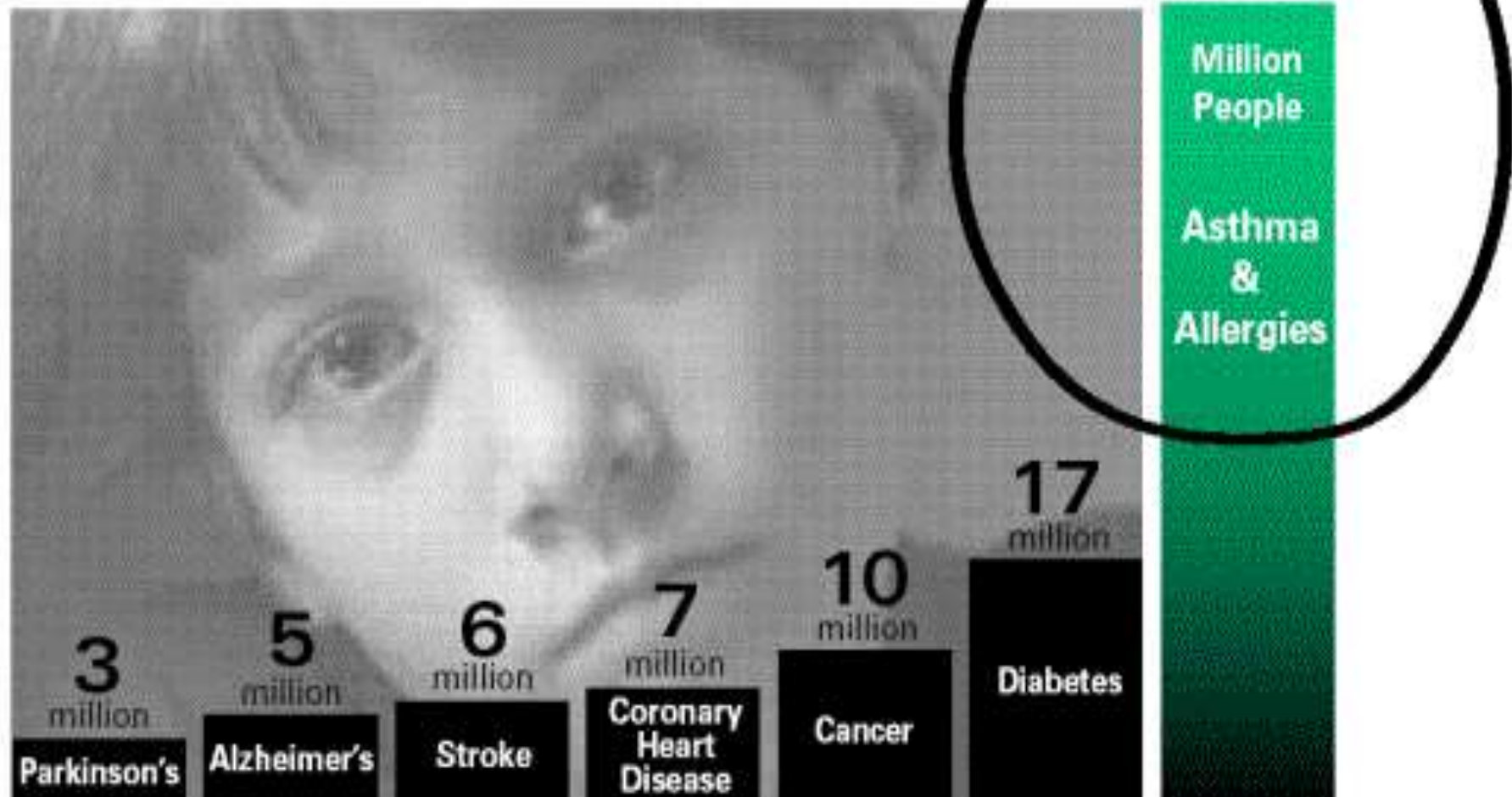
بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ



**COMMON  
PEDIATRIC  
ALLERGIES**

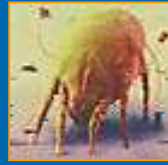
**HYPERSENSITIVITY**

Asthma and allergies  
strike 1 out of 4 Americans



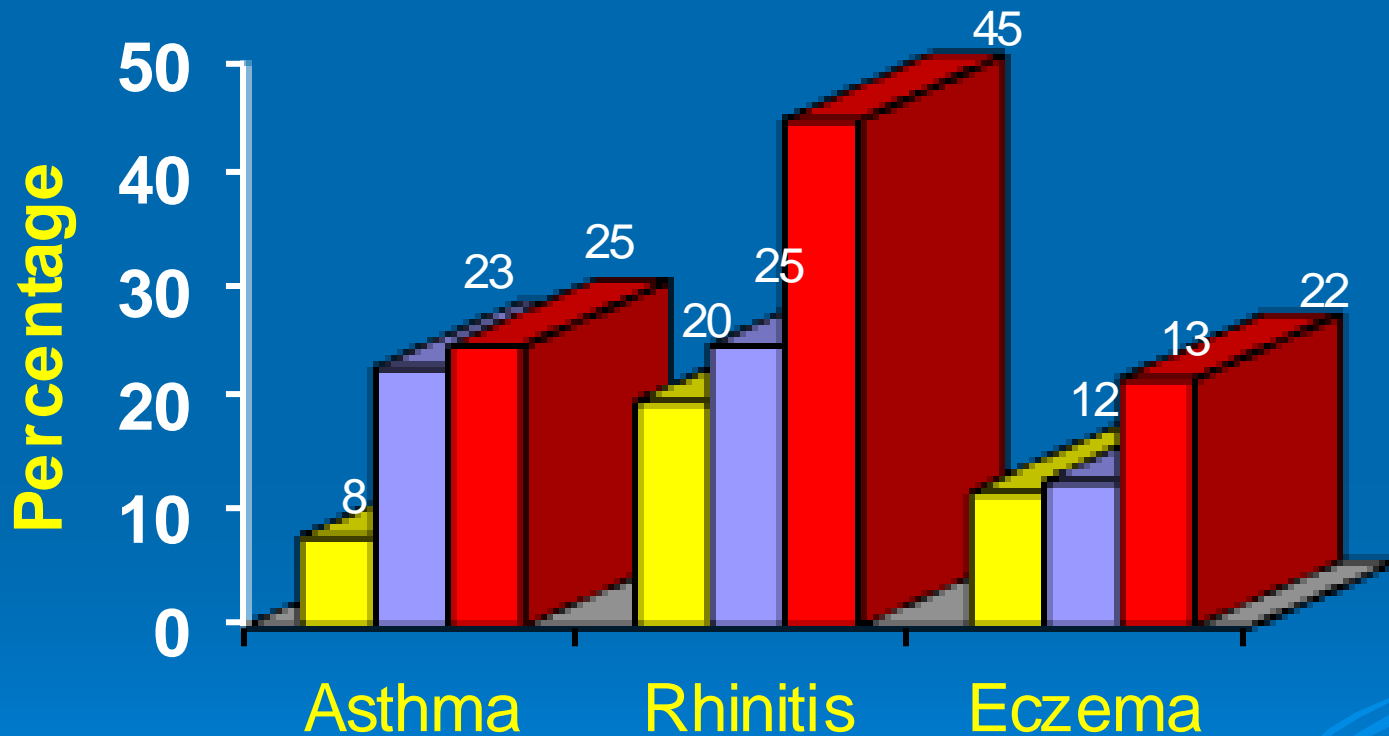
# PREVALENCE OF ATOPY AND ASTHMA IN PRIMARY SCHOOL CHILDREN IN AUSTRALIA

<b>Asthma diagnosed</b>	<b>31.0%</b>
<b>Hay Fever</b>	<b>38.4%</b>
<b>Eczema</b>	<b>24.8%</b>



- Allergic disease is the 5th leading chronic disease among all ages
- 3rd common chronic disease among children under 18 years old; up to one child in three is affected
- Trends indicate that by 2015, half of all Europeans may be suffering from an allergy

# Prevalence of Asthma, Rhinitis and Eczema in Saudi Arabia



1986: n=2123, 1995: n=1008, 2001:n=1014

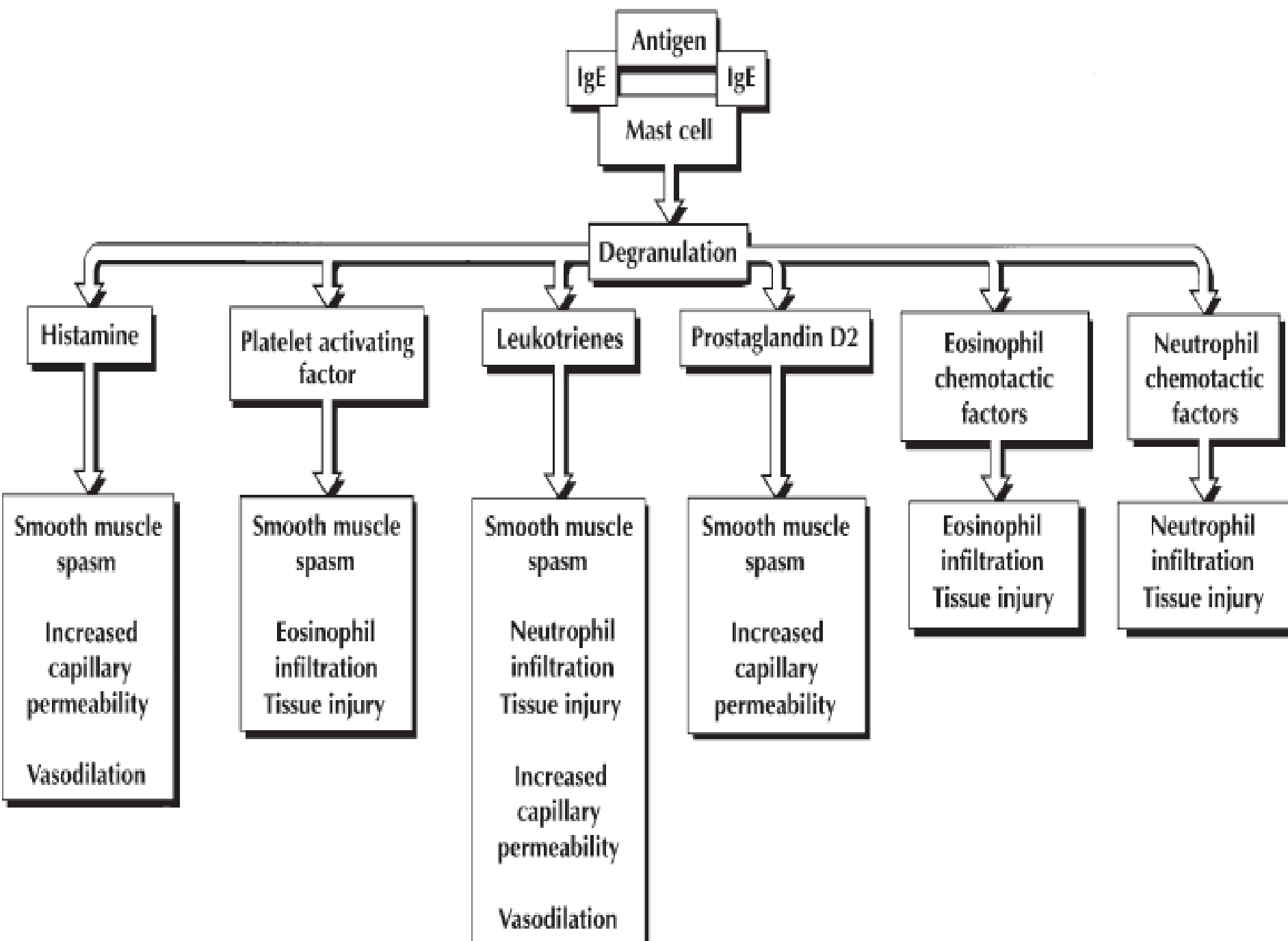
**Middle Bar indicates Physicians' diagnosed Asthma**

**Red Bar indicates highly suspected asthma**

## Type I.

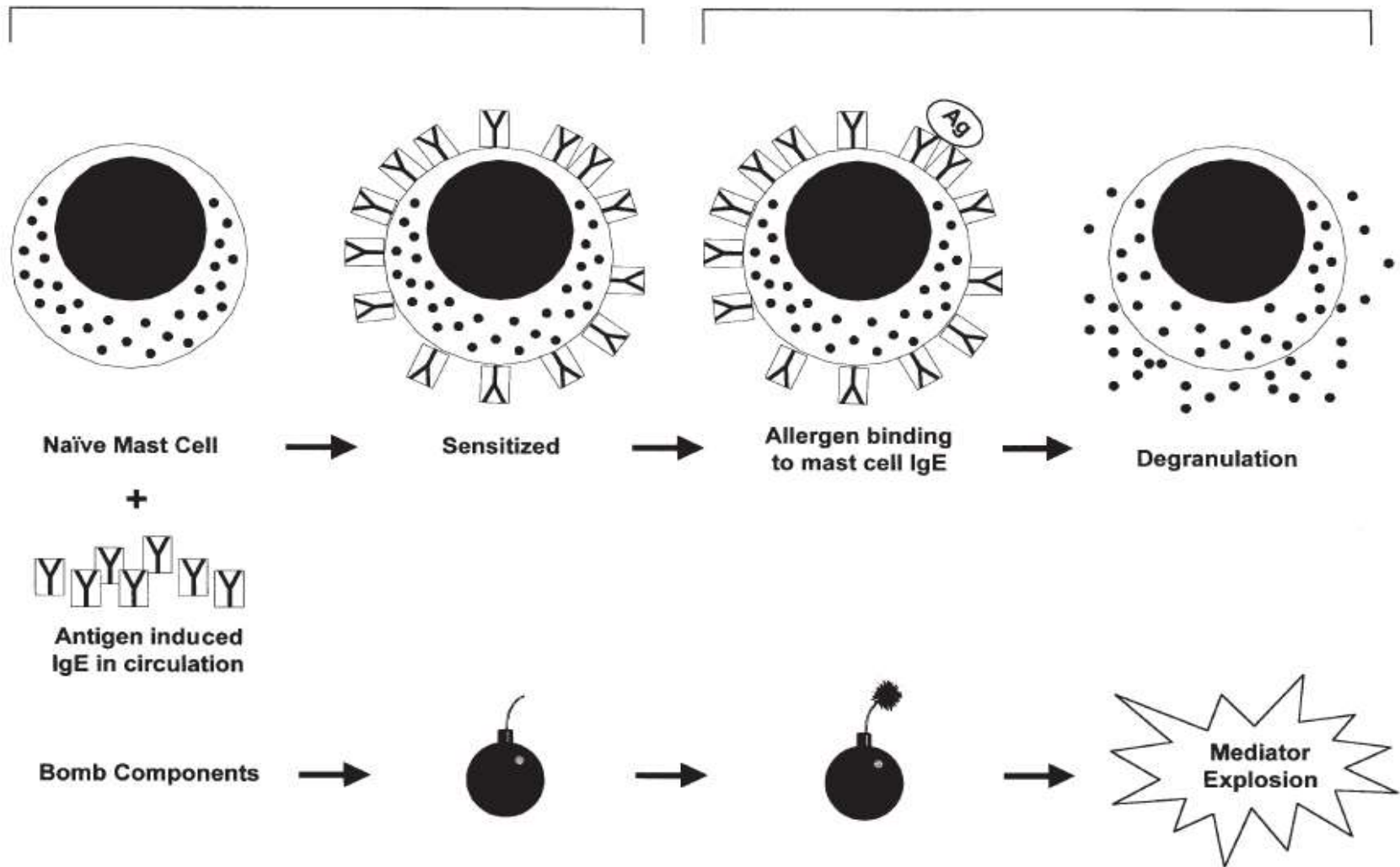
Acute: immediate; allergic; anaphylactic (e.g. hay fever). Production of IgE to specific antigens, often pollens or animal proteins, known as allergens. IgE binds to receptors on mast cells and basophils; further contact with the allergen cross links this IgE and the cell degranulates, releasing mediators which cause vascular permeability, mucus secretion, bronchial constriction. Tested for by immediate skin test.



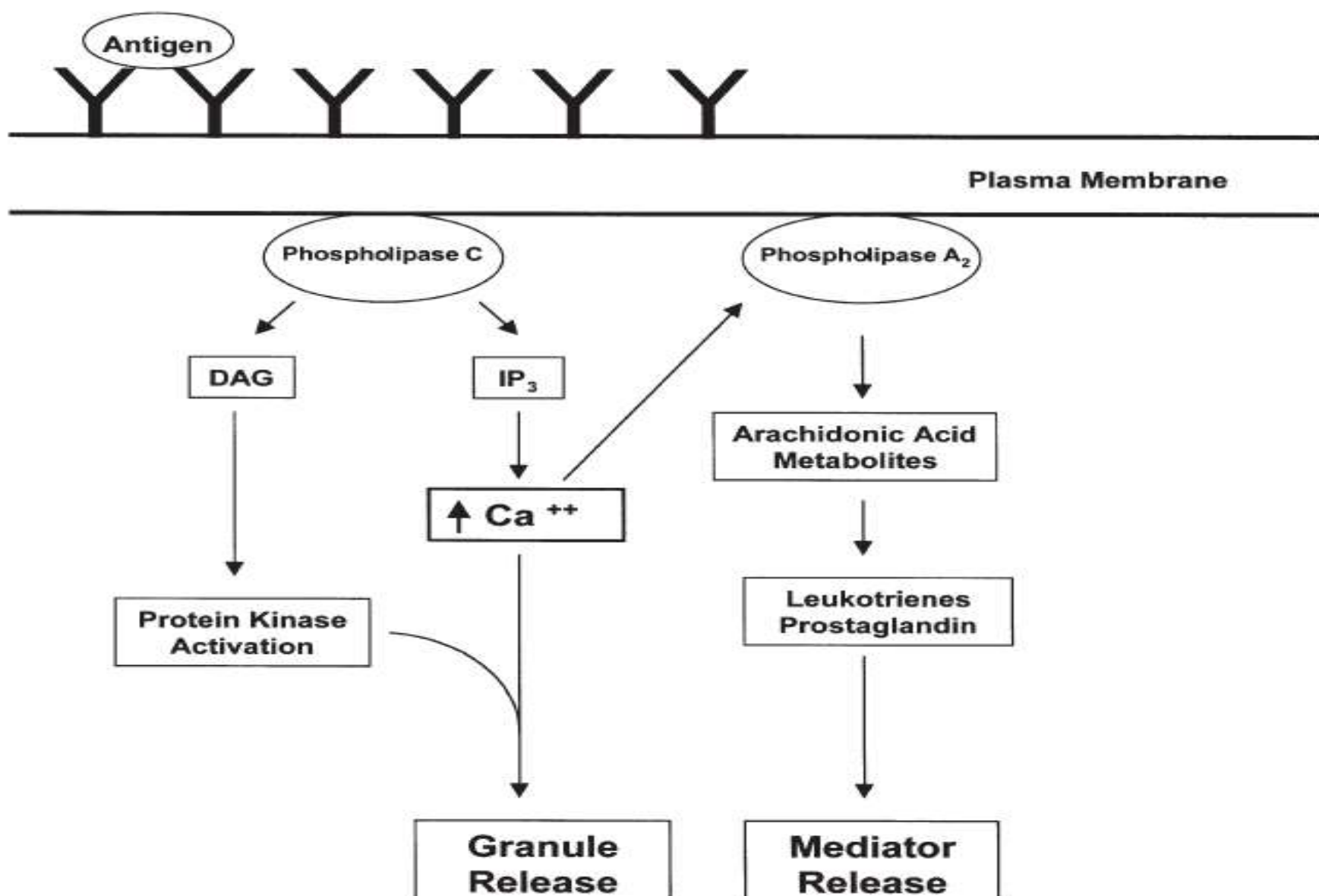


## Step 1: Sensitization

## Step 2: Allergic Reaction



**■**. Allergic sensitization and degranulation. The process of sensitization and degranulation in mast cells is analogous to the construction and detonation of a bomb. Initial binding of specific IgE to the naïve mast cell surface “primes” the cell for activity, in effect building the bomb. Subsequent binding of allergen to the mast cell is akin to lighting the fuse of the bomb. Intracellular biochemical events lead to the ultimate “explosion”—a cellular degranulation leading to mediator release.



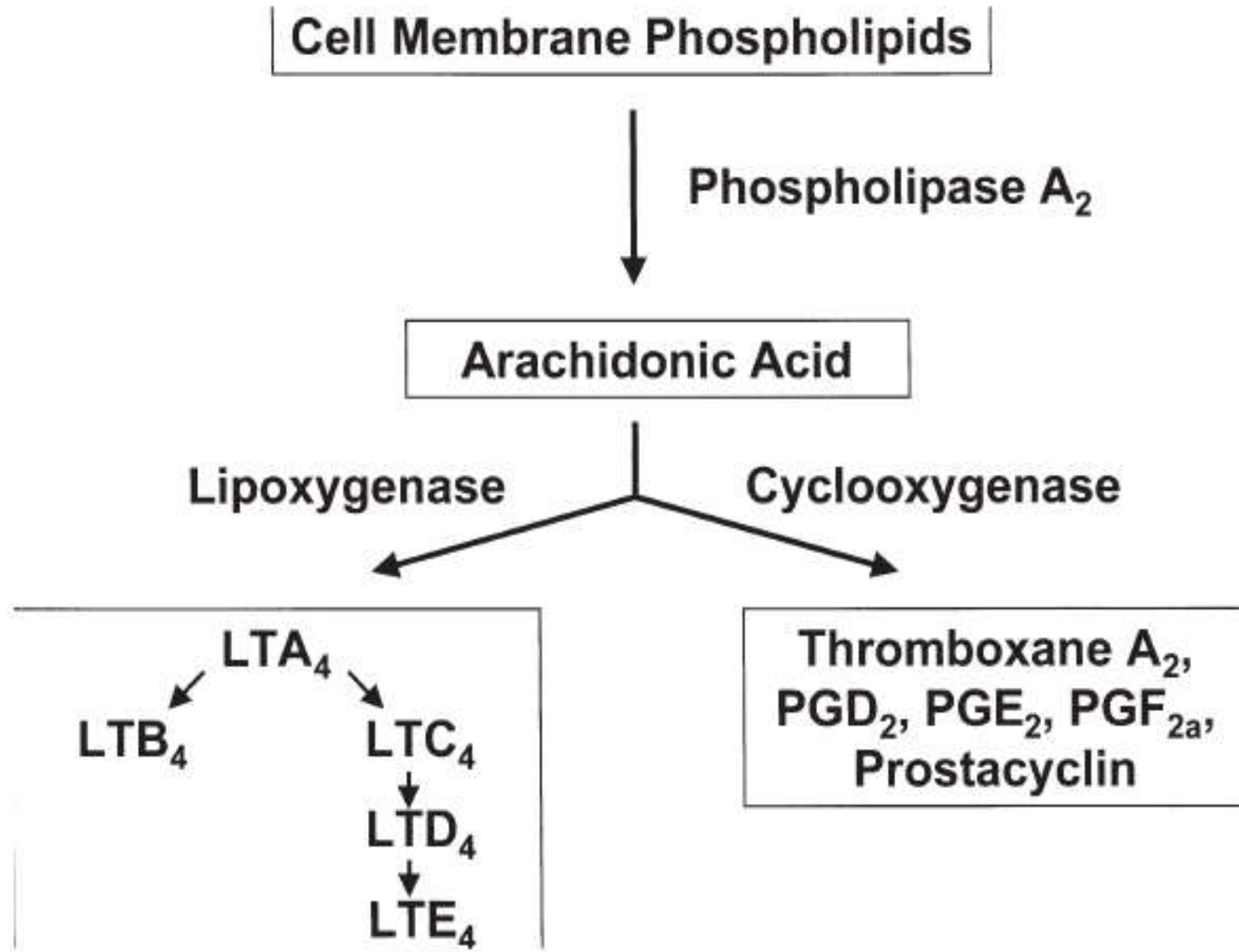
**Mast cell activation: biochemical reactions.** Following IgE crosslinking by antigen, a series of protein kinase reactions culminate in the activation of phospholipase C, releasing diacylglycerol (DAG) and inositol triphosphate (IP<sub>3</sub>) from the plasma membrane. The IP<sub>3</sub> releases calcium stored in the endoplasmic reticulum, which, along with DAG-stimulated kinases, leads to granule release. The intracellular calcium also activates phospholipase A<sub>2</sub>, which generates arachidonic acid metabolites, leading to the release of leukotrienes and prostaglandins, which are mediators of inflammation.

## MEDIATORS OF ALLERGIC REACTIONS

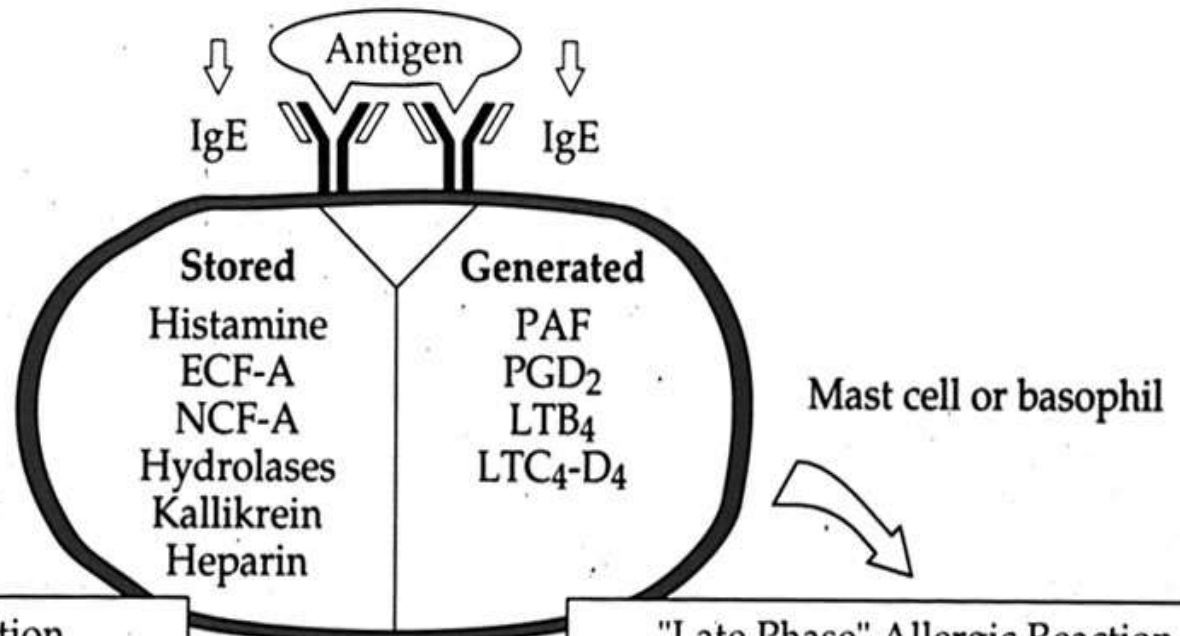
Molecules released from activated mast cells and basophils account for many allergic symptoms. This list includes a sampling of those chemicals and some of their effects, which can be redundant.

	CHEMICAL	ACTIVITY	SYMPTOMS
MEDIATORS FROM GRANULES	Histamine	Constricts bronchial airways	Wheezing; difficulty breathing
		Dilates blood vessels	Local redness at sites of allergen delivery; widespread dilation can contribute to potentially lethal hypotension (shock)
		Increases permeability of small blood vessels	Swelling of local tissue; if widespread, increased permeability can contribute to shock
		Stimulates nerve endings	Itching and pain in skin
		Stimulates secretion of mucus in airways	Congestion of airways
	Platelet-activating factor	Constricts bronchial airways	<i>Same as for histamine</i>
		Dilates blood vessels	<i>Same as for histamine</i>
LIPID MEDIATORS	Leukotrienes	Constricts bronchial airways	<i>Same as for histamine</i>
		Increase permeability of small blood vessels	<i>Same as for histamine</i>
	Prostaglandin D	Constricts bronchial airways	<i>Same as for histamine</i>

1. Mast cell mediators and their effects. (Adapted from Lichtenstein L. Allergy and the immune system. Sci Am 1993;369:117-124, with permission.)



Arachidonic acid metabolic pathways. Arachidonic acid, released as a result of phospholipase activity on the cellular membrane, is broken down by two distinct biochemical pathways: The lipoyxygenase pathway results in formation of the leukotrienes (LT), whereas the cyclooxygenase pathway generates prostaglandins, thromboxanes, and the prostacyclin (PGI<sub>2</sub>).



**"Classic" Allergic Reaction  
(Immediate Hypersensitivity)**

↓ Minutes

Smooth Muscle Contraction  
Vascular Leakage  
Flush  
Hypotension  
Mucous Secretion  
Pruritus

Key:  
ECF-A: eosinophil chemotactic factor of anaphylaxis  
NCF-A: neutrophil chemotactic factor of anaphylaxis  
PAF: platelet activating factor  
PGD<sub>2</sub>: prostaglandin D<sub>2</sub>  
LTB<sub>4</sub>: leukotriene B<sub>4</sub>  
LTC<sub>4</sub>-D<sub>4</sub>: leukotriene C<sub>4</sub>-D<sub>4</sub>

**"Late Phase" Allergic Reaction**

↓ Hours (2-8)

Infiltration with Eosinophils and Neutrophils  
Fibrin Deposition

↓ Days (1-2)

Infiltration with Mononuclear Cells (Macrophages, Fibroblasts)  
Tissue Destruction

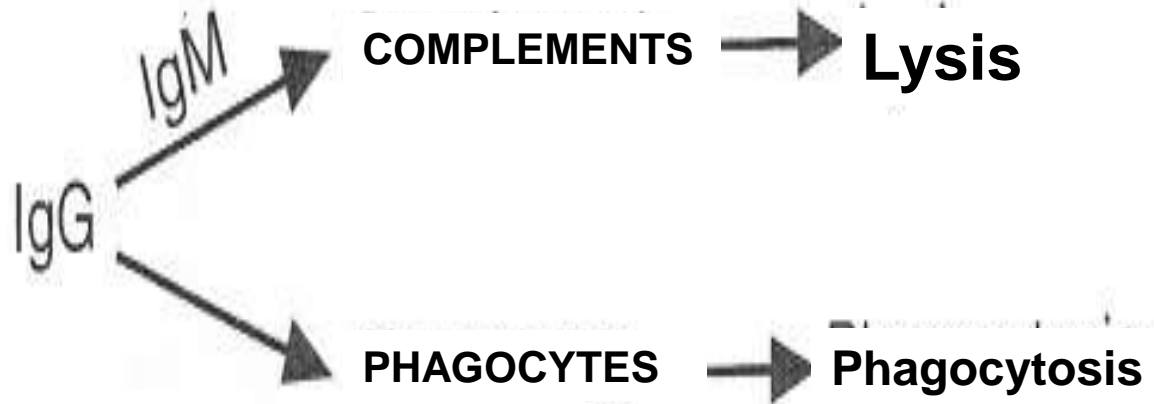
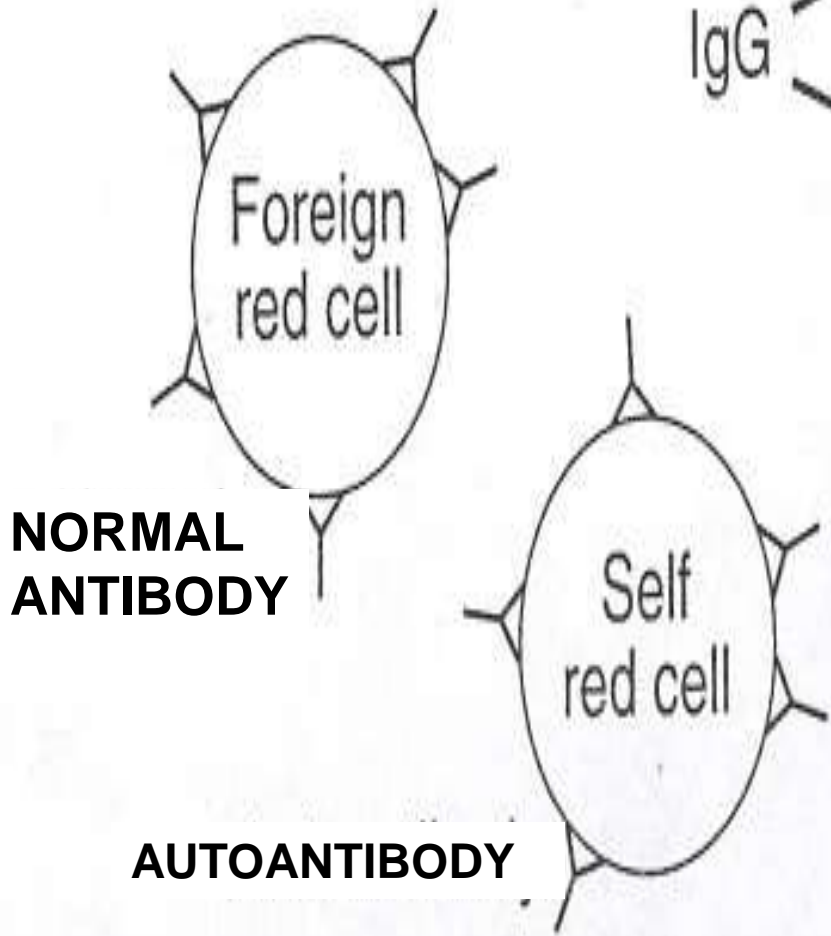


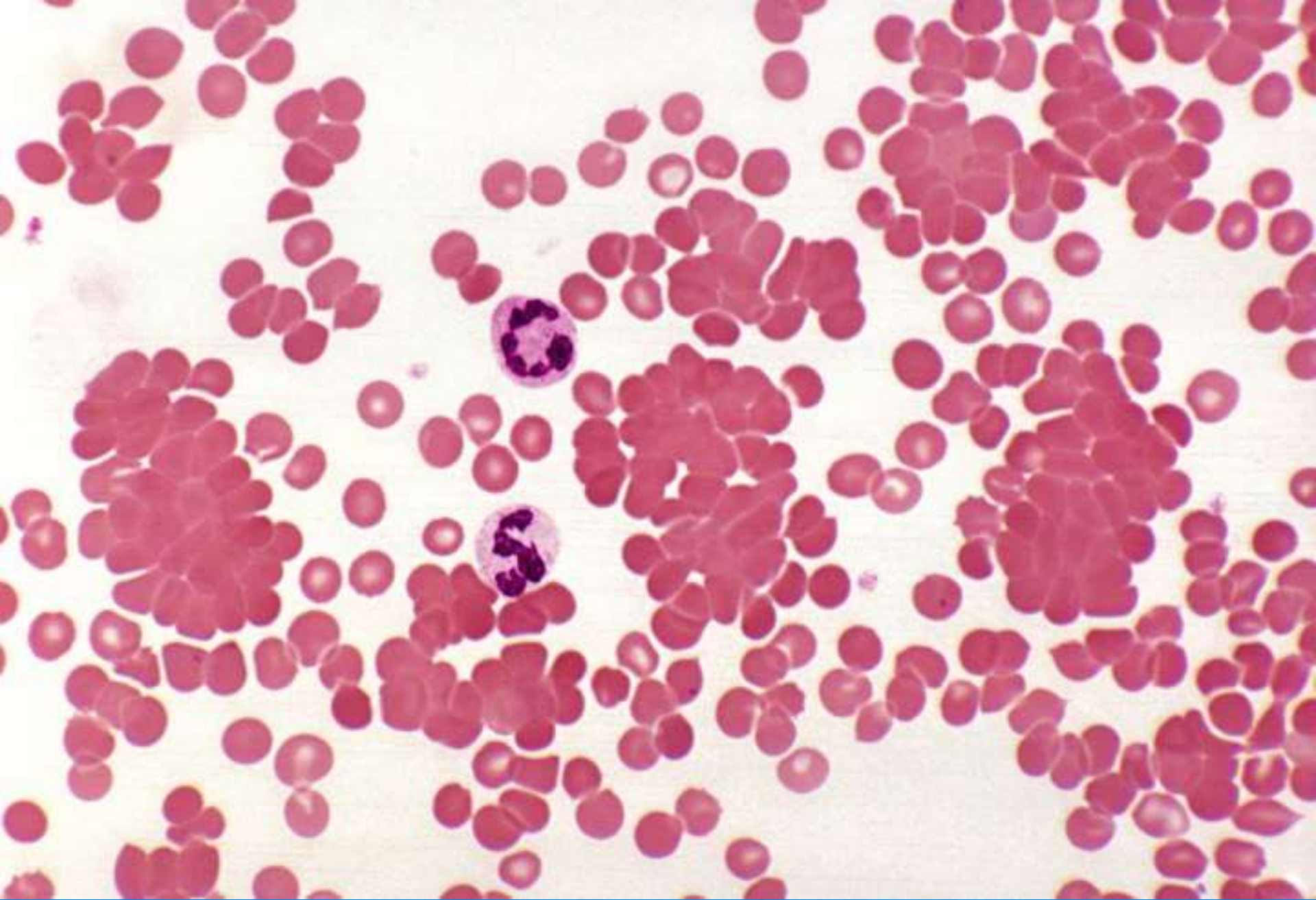
## Type II

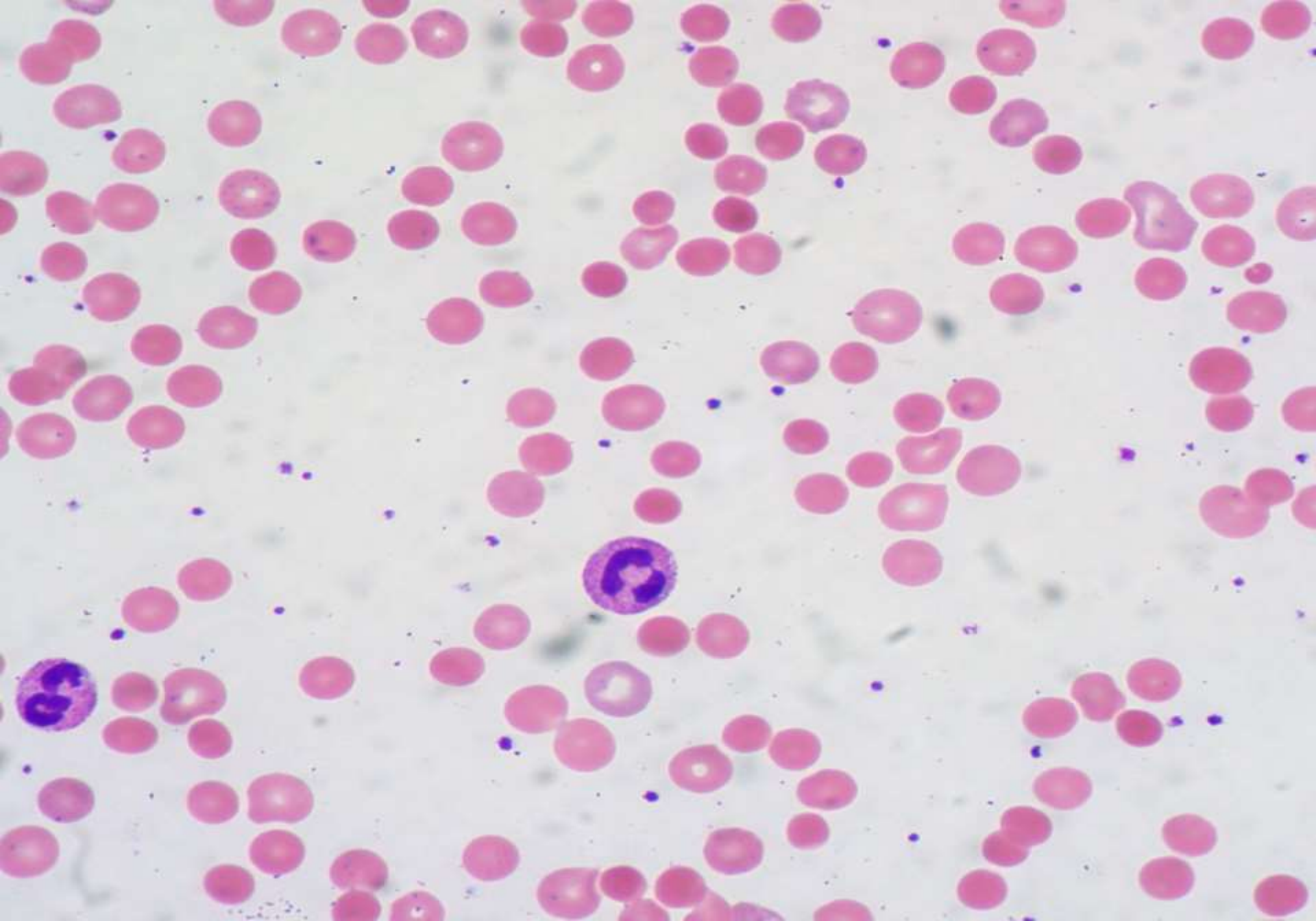
Cytotoxic: (e.g. autoimmune haemolytic anaemia). Production of IgM or IgG to body components. These may be non-self material whose elimination is not desired, such as transfused blood, bone marrow, etc, or self material to which the T or B lymphocytes have lost tolerance, leading to a state of autoimmunity.









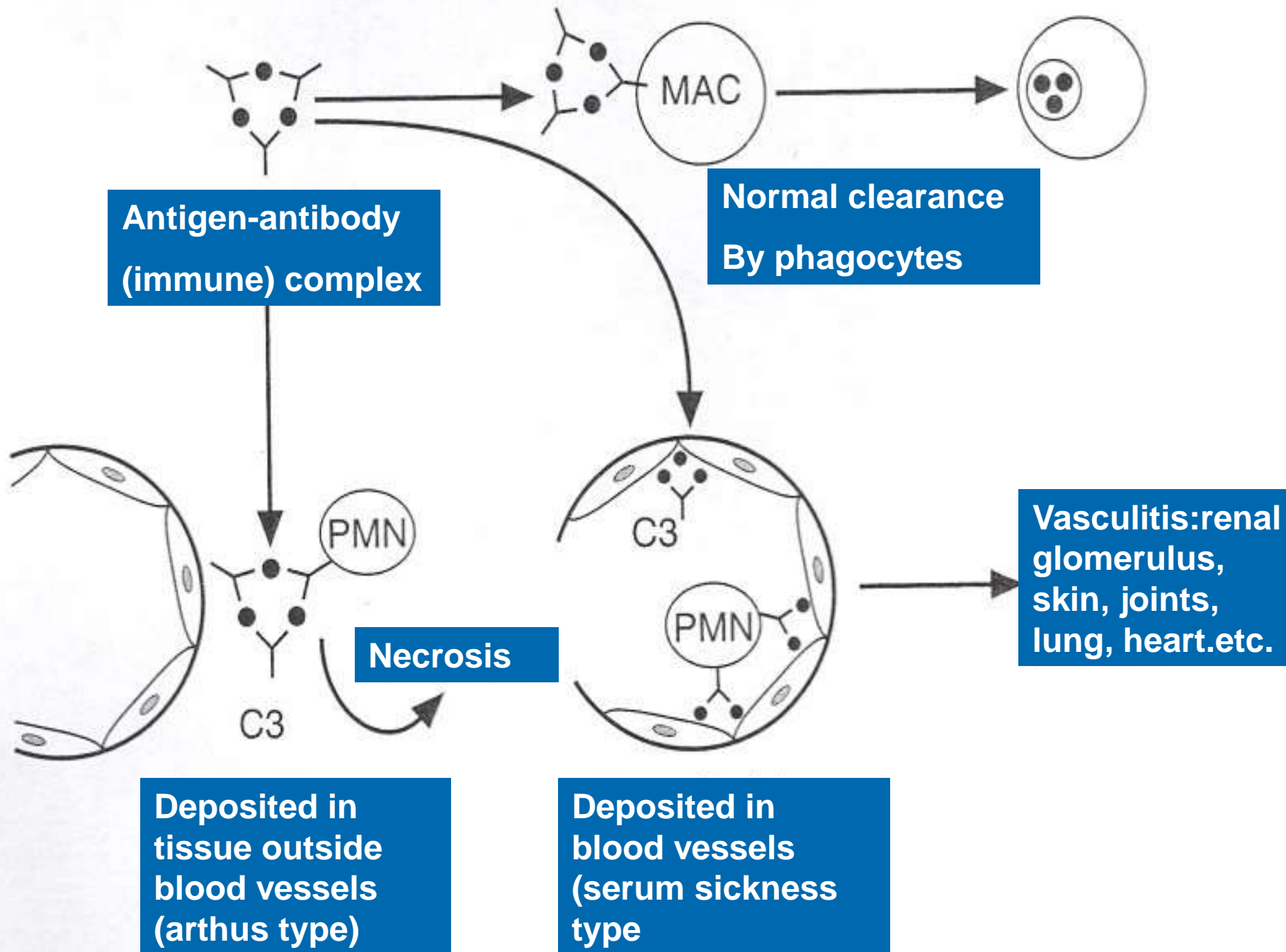


## Type III

Immune complex-mediated (e.g. serum sickness).

Here the problem is that some times the complex of antigen and antibody, instead of being removed by phagocytic cells, remains in the tissues or the circulation. Phagocytic cells and complement will now be activated and may cause severe damage in the vicinity. This is particularly serious when the complexes are stuck to the walls of vital blood vessels such as the renal glomeruli. Two classical examples are serum sickness (following repeated intravenous injections of animal serum) and the arthus reaction (necrosis following sub-cutaneous injection) but neither of these is seen much nowadays.





**Antigen-antibody  
(immune) complex**

**Normal clearance  
By phagocytes**

**Vasculitis: renal  
glomerulus,  
skin, joints,  
lung, heart.etc.**

**Necrosis**

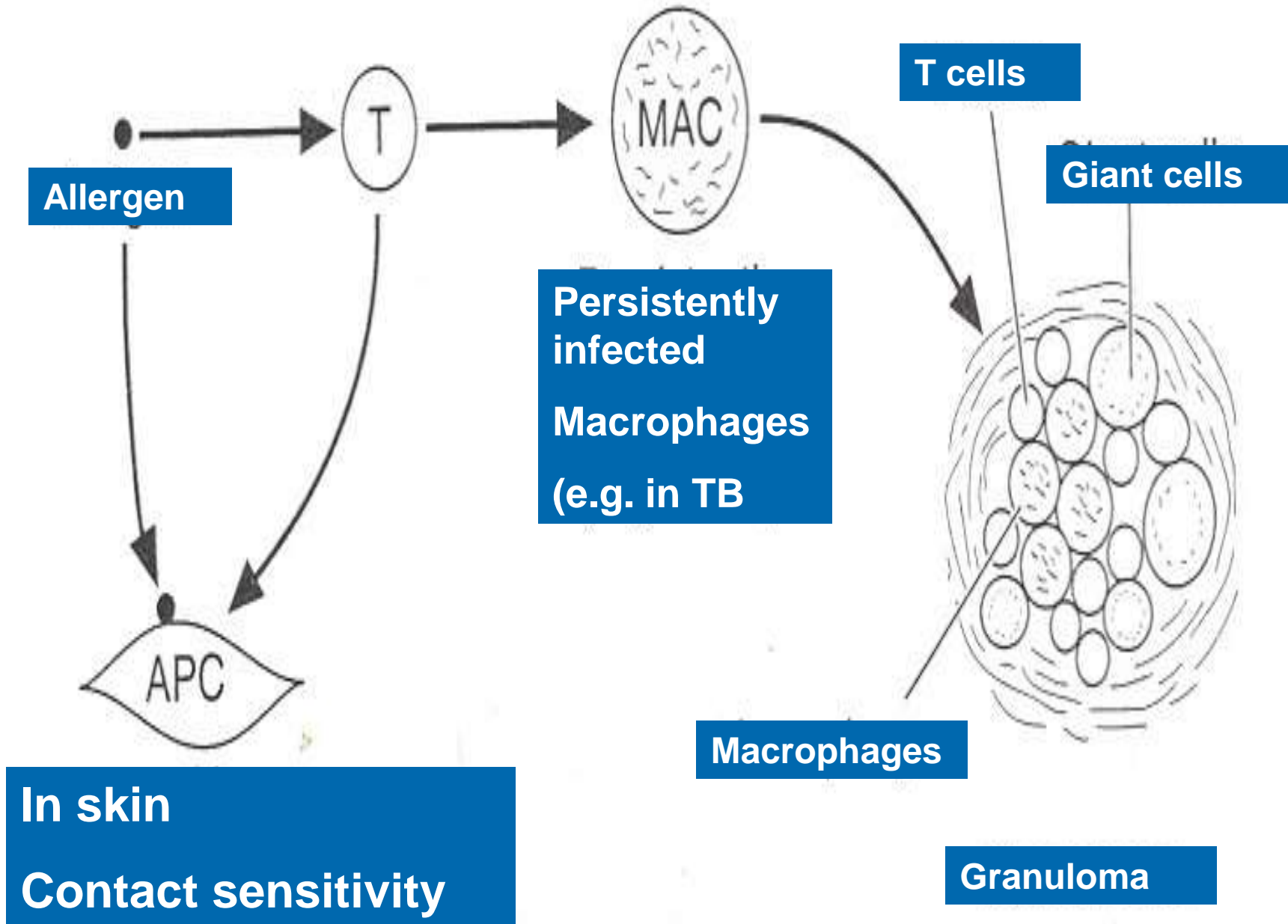
**Deposited in  
tissue outside  
blood vessels  
(arthus type)**

**Deposited in  
blood vessels  
(serum sickness  
type)**

## Type IV

Cell-mediated; delayed-type; tuberculin type: (e.g. TB granuloma). The activation of macrophages as a result of prolonged T cell responses is often accompanied, in solid organs, by granuloma formation. When the responsible antigen enters via the skin, as in contact sensitivity, an eczematous rash with oedema develops at the site. Can be tested for by delayed skin test.





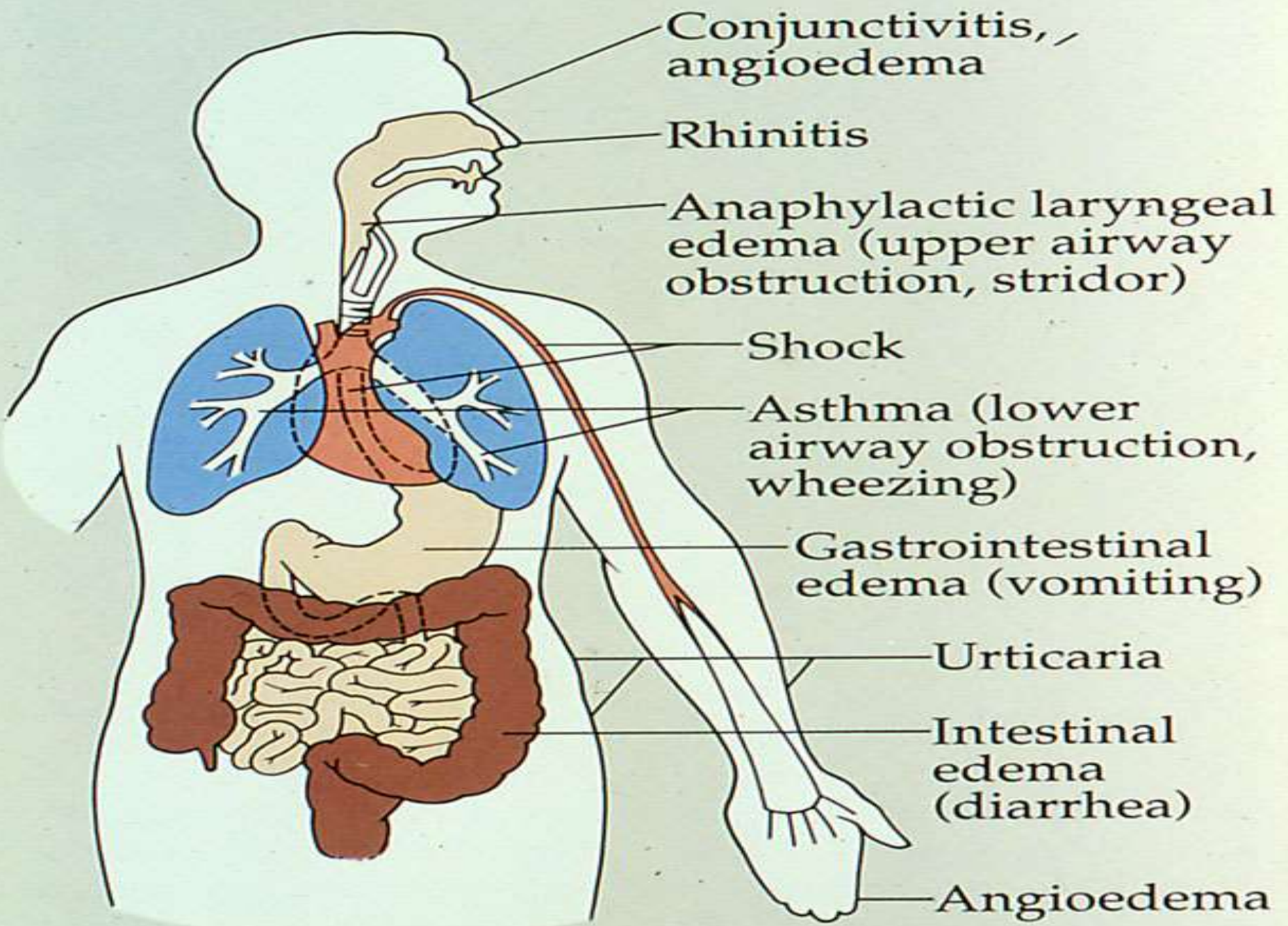


# Relative Distribution of the Two Predominant Human Mast Cell Phenotypes in Immunologically Relevant Tissues and Cell Population

*Organ % MCT Cells %MCTC Cells (Tryptase & Chymase)*

- ✓ Skin 5 --- 95
- ✓ Intestinal mucosa 80 --- 20
- ✓ Intestinal submucosa 30 --- 70
- ✓ Alveolar wall 95 --- 5
- ✓ Bronchial subepithelium 40 --- 60
- ✓ Dispersed lung mast cells 90 --- 10
- ✓ Tonsils 40 --- 60
- ✓ Nasal mucosa 65 --- 35

Adapted from Holgate and Church, Allergy. London: Gower Medical Publishing



Conjunctivitis, /  
angioedema

Rhinitis

Anaphylactic laryngeal  
edema (upper airway  
obstruction, stridor)

Shock

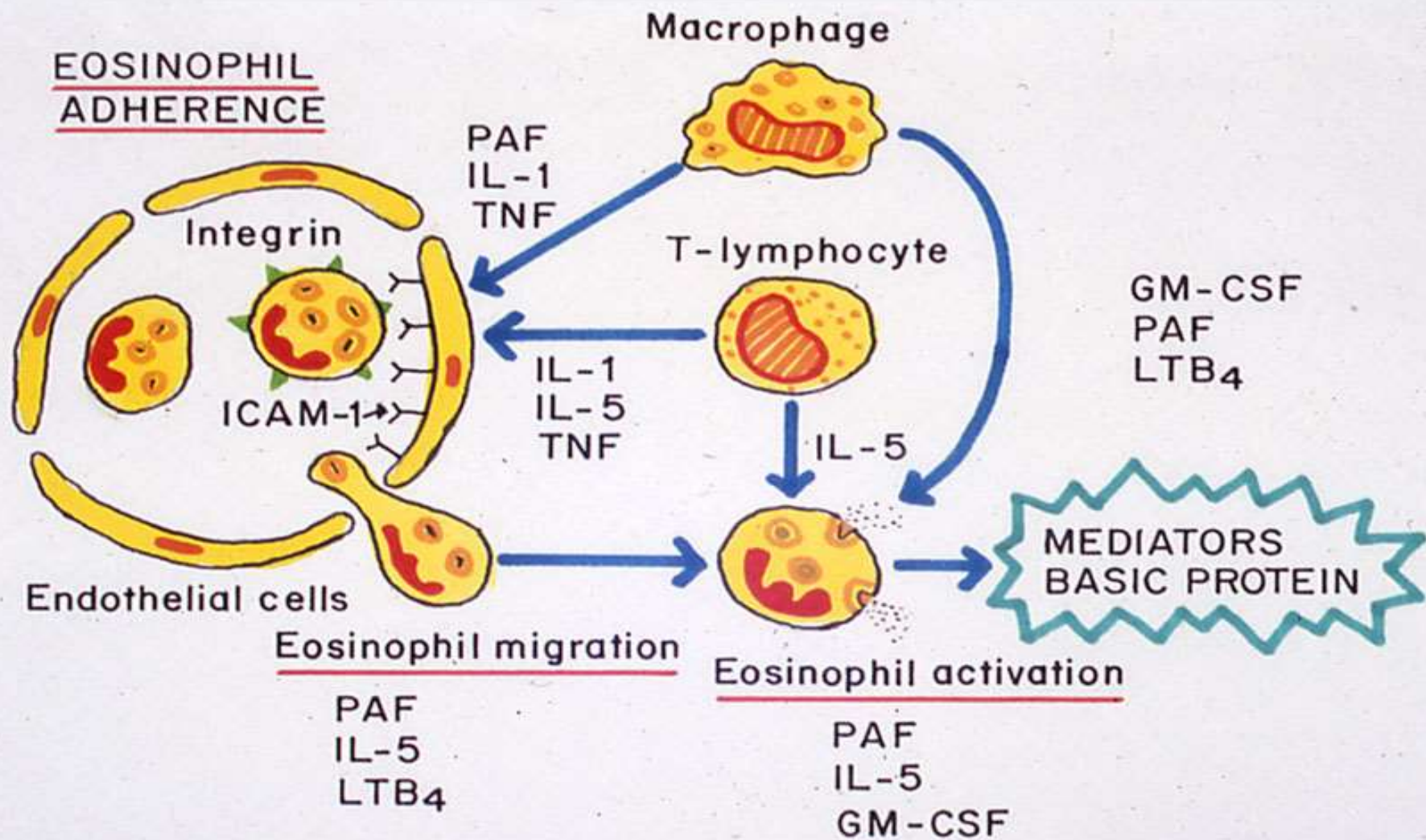
Asthma (lower  
airway obstruction,  
wheezing)

Gastrointestinal  
edema (vomiting)

Urticaria

Intestinal  
edema  
(diarrhea)

Angioedema



**Mechanisms of eosinophilic inflammation.** Eosinophils firstly adhere to endothelial cells in the bronchial circulation, then migrate into the tissue where they survive and are activated to release mediators and granule products. Each step is directed by specific agents which may be released from macrophages and T-lymphocytes.



**BERMUDA**



**RYE**





**ATRIPLEX (RUGHL)**





Amaranthus SP

سندار ، عرف الديك ، قَطِيفَة



Amaranthus SP

سندار عرف الديك ، قَطِيفَة



**Amaranthus Viridis (Orf Al-Deek, Cendar)**



**Salsola SPP. (Herm)**



**Chenopodium Album (Etra)**



**PROSOPIS**







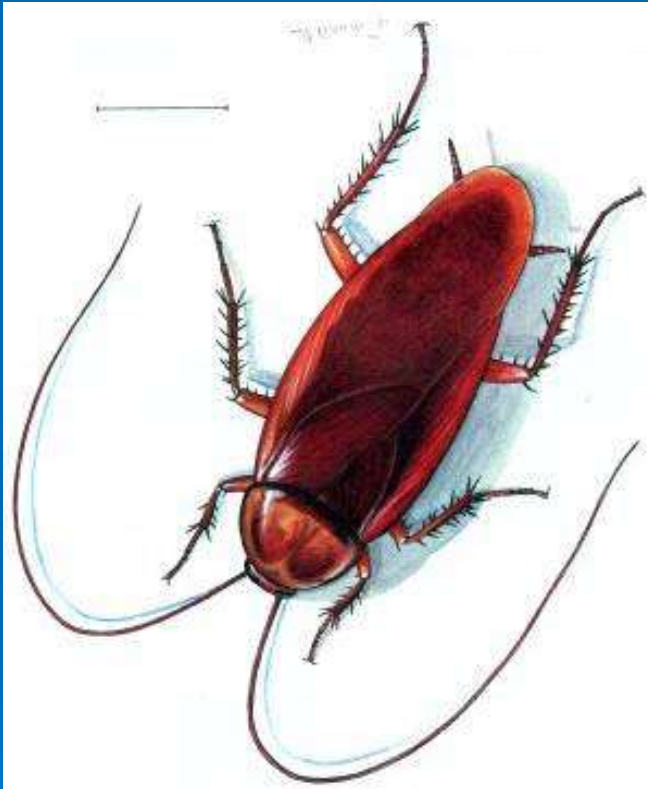
**Cat**



**DOGS**



# COCKROACH



**AMERICAN COCKROACH**

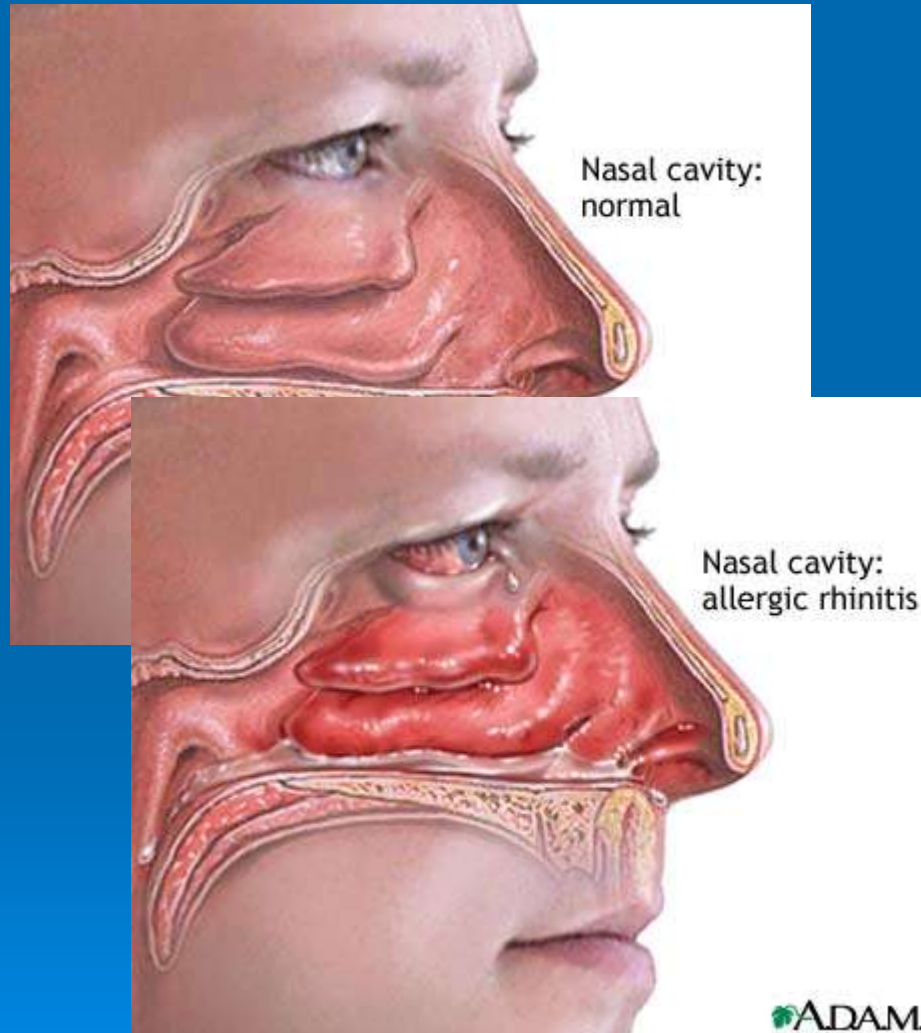


**DUSTMITE**

**ALLERGIC  
RHINITIS**

*The history is the most important element in the evaluation of allergy. Key features of the history are:*

- ✓ *Worsening of symptoms on exposure to aeroallergens*
- ✓ *Seasonal variation in symptoms related to pollination of trees, grasses, and weeds*
- ✓ *A family history of atopic disease*
- ✓ *An environmental history assessing exposure to indoor and outdoor allergens and the presence of associated allergic conditions*



- Rhinorrhoea
- Nasal blockage
- Postnasal drip
- Itchiness
- Sneezing
- Associated health effects

**!! IgE mediated**

# Diagnosis of Allergic Rhinitis

1. History & symptoms of recurrent or persistent rhinitis and/or associated health effects
2. Signs of atopy and recurrent or persistent rhinitis
3. Demonstration of IgE allergy
4. Exclusion of other causes of rhinitis

# Family history

- Because allergic rhinitis has a significant genetic component, a positive family history for atopy makes the diagnosis more likely.
- A greater risk of allergic rhinitis exists if both parents are atopic than if one parent is atopic.
- However, the cause of allergic rhinitis appears to be multifactorial, and a person with no family history of allergic rhinitis can develop allergic rhinitis.



# Diagnosis of Allergic Rhinitis

## 2. Signs of atopy and recurrent or persistent rhinitis









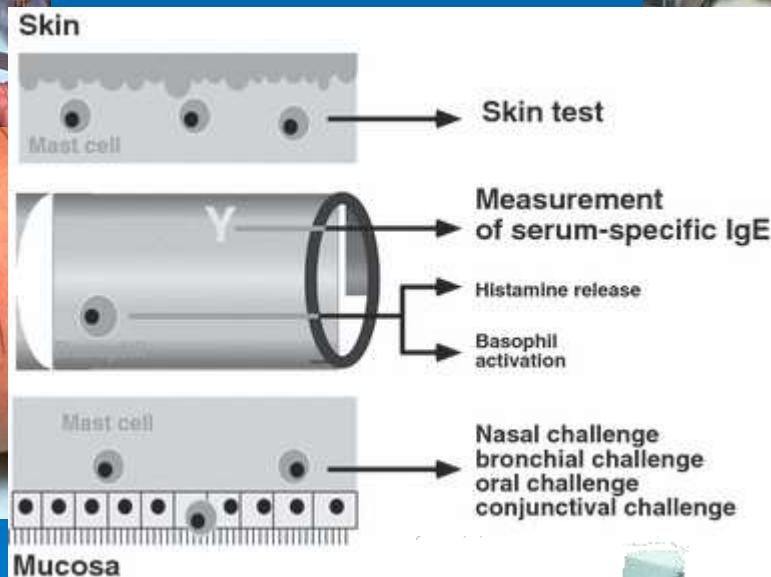
# Health Effects of Allergic Rhinitis

- Social inconvenience
- Sleep disturbances/obstruction
- Learning difficulties
- Impaired maxillary growth
- Dental problems
- Infection: nose and sinuses
- Co-morbidities: conjunctivitis, asthma, rhinosinusitis, otitis media

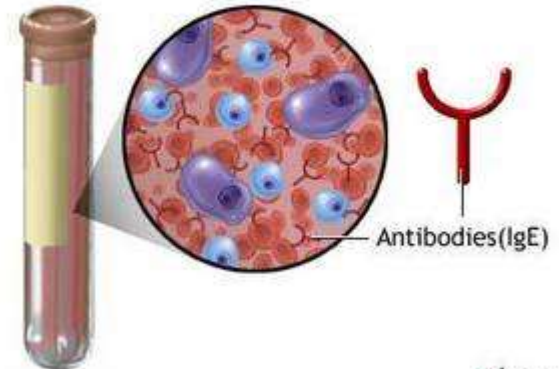


# Diagnosis of Allergic Rhinitis

## 3. Demonstration of IgE allergy



The blood test measures the levels of allergy antibody, or IgE, produced when your blood is mixed with a series of allergens in a laboratory



ADAM.



# WORKUP OF PATIENTS WITH ALLERGIC RHINITIS

- PERIPHERAL BLOOD EOSINOPHILIA  $>400/\mu\text{l}$  IS COMMON BUT 50% OF PTS. HAVE NO EOSINOPHILIA ON ANY ONE OCCASION.
- NASAL EOSINOPHILS --> WRIGHTS STAIN  $>15/100$  cells SIGNIFICANT

# WORKUP OF PATIENTS WITH ALLERGIC RHINITIS CONT.


- BLOOD EOSINOPHILS 250-400 cell/mm<sup>3</sup>
- NASAL EOSINOPHILS >15/100 cells
- SPT
- NASAL PROVOCATION TEST
- RHINOMETRY
- IgE
- RAST



# SKIN PRICK TEST (SPT)

- POSITIVE RESULT WHEN WHEAL >3mm MORE THAN CONTROL
- 80% OF +VE SKIN TEST GIVE +VE RAST
- AND 50% GIVE +VE CHALLENGE
- PANEL OF TEST ANTIGENS APPROPRIATE TO THE LOCALITY AND SEASON AND HISTORY SHOULD BE USED.

*The most important ancillary test to confirm the diagnosis of allergy is the skin test, which is the gold standard in this regard. The skin test results must be interpreted in light of the history to determine the importance of a positive test.*

The background of the slide is a solid blue color. In the lower half, there are several decorative elements consisting of concentric circles, resembling ripples in water, rendered in a lighter shade of blue. These circles are scattered across the bottom, with one prominent set on the right side and others towards the center and left.

## ***Recording and Scoring Skin-Test Results***

*Skin-test reactions to allergens are normally evaluated 15-20 min after the tests have been placed, when the reactions are typically maximal. The best method to record the results of skin tests is to measure the greatest diameter of the wheal and flare in millimeters and record these results for all tests and for the positive and negative controls. After measurement, the result of a test can be easily recorded as, for example, 5/21, meaning that the wheal was 5 mm in greatest diameter and the flare was 21 mm in diameter. Any epicutaneous test that produces a wheal at least 3 mm larger than the wheal of the negative control with a larger surrounding flare is normally considered positive for the presence of allergen-specific IgE.*

**ALLERGENIC  
DERMATITIS  
AND  
ATOPIC ECZEMA**













Atopic Eczema



© 2010 Logical Images, Inc.

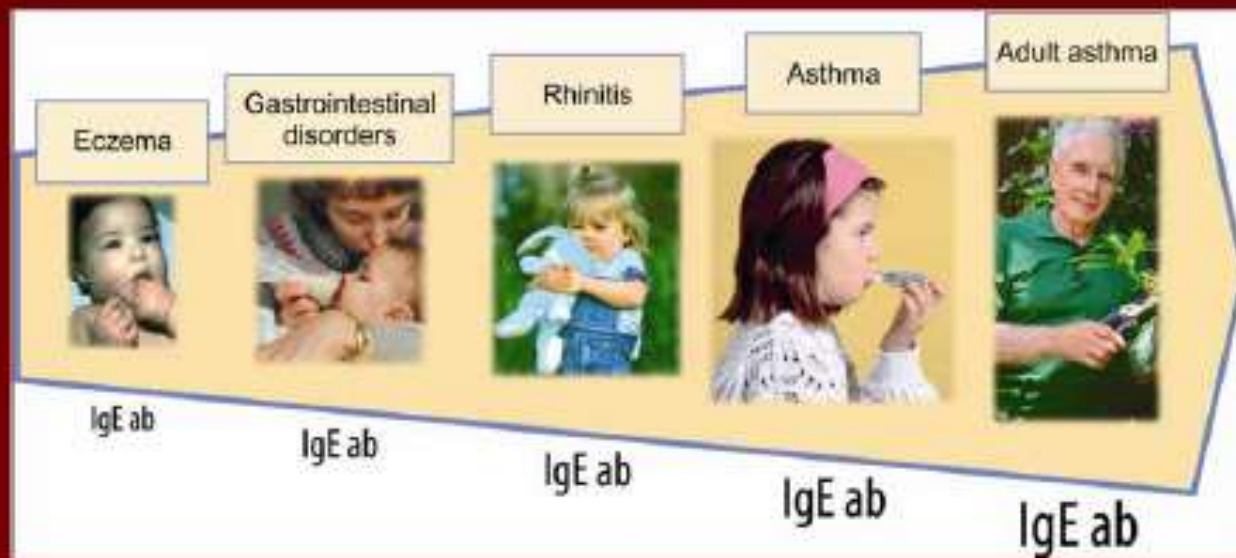


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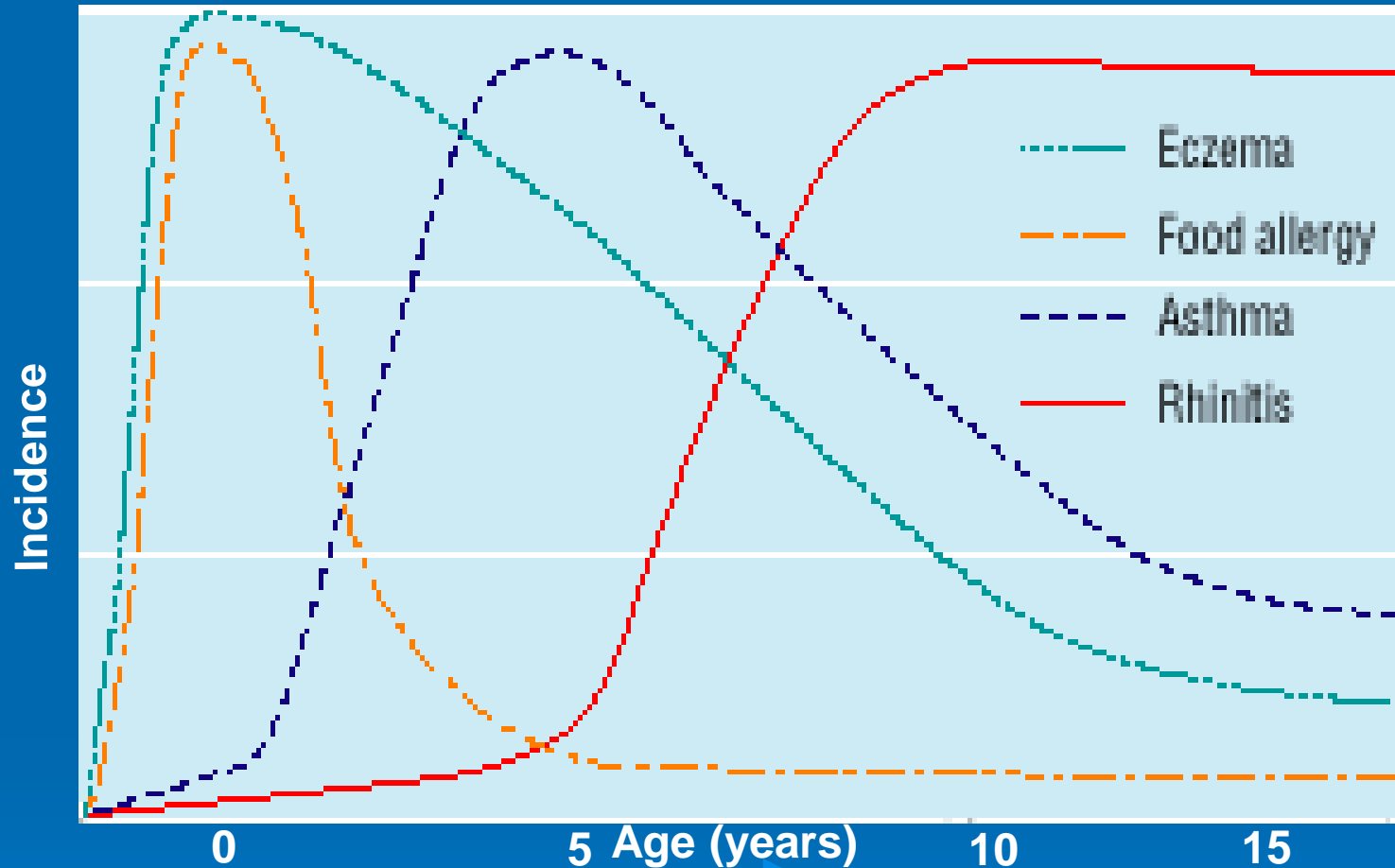




# Allergy symptoms and progression



# THE “ATOPIC MARCH”



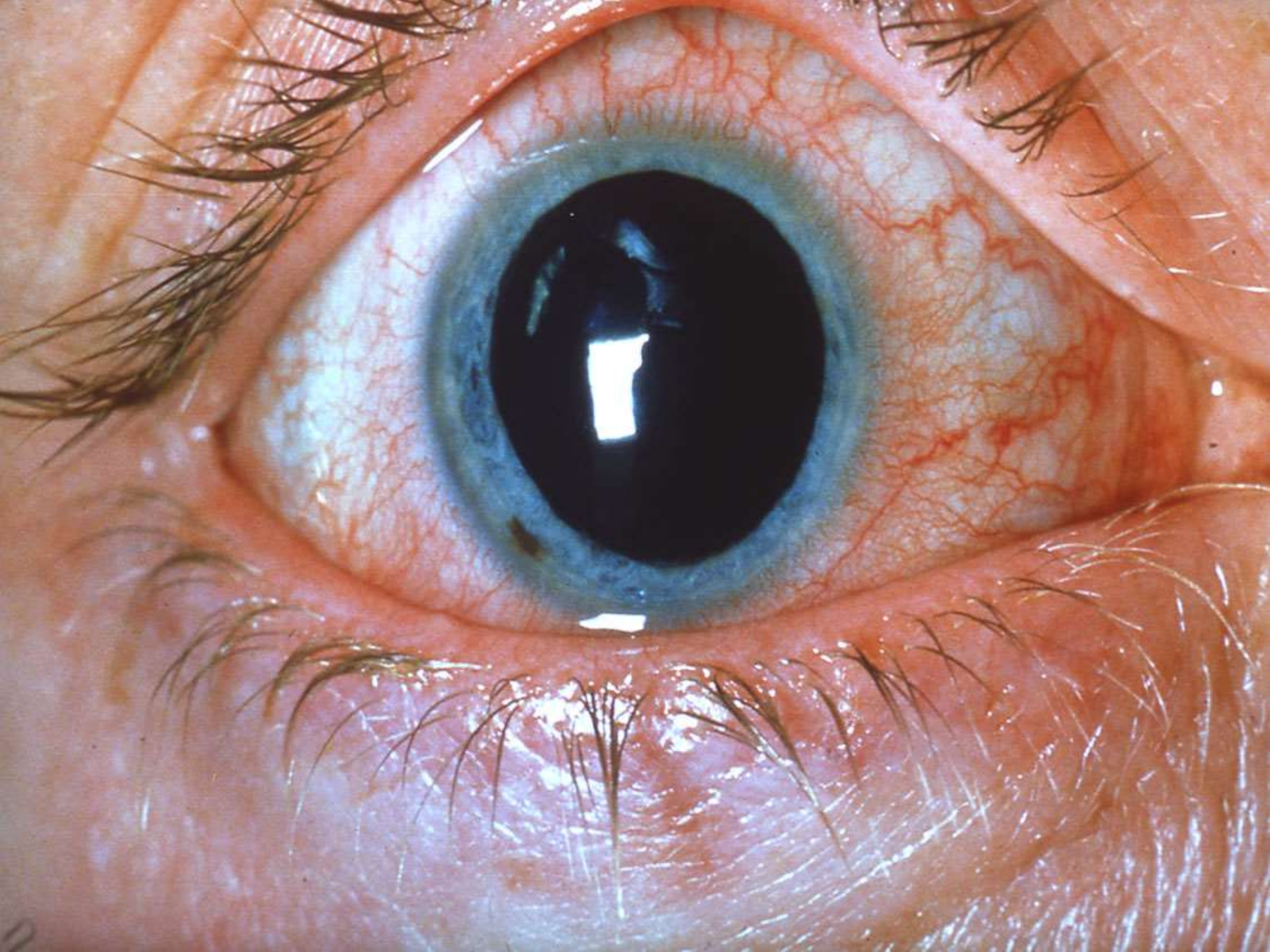
*IgE levels in blood*

→ *AD is in most cases the first manifestation of the atopic disposition*

Modified from Barnetson & Rogers. *BMJ* 2002, 324:1376–9

**ALLERGIC  
CONJUNCTIVITIS**





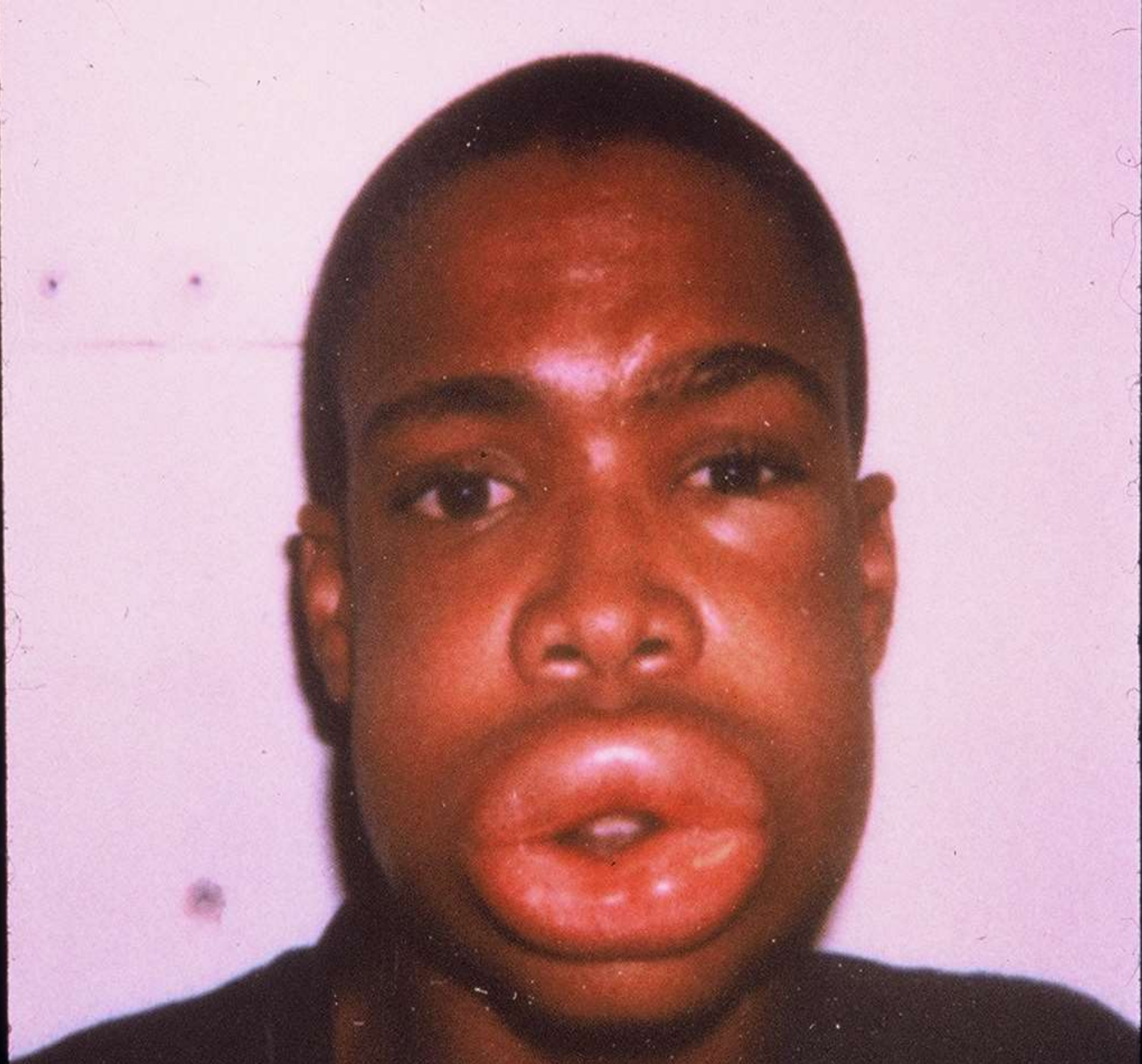




**URTICARIA  
AND  
ANGIOEDEMA**











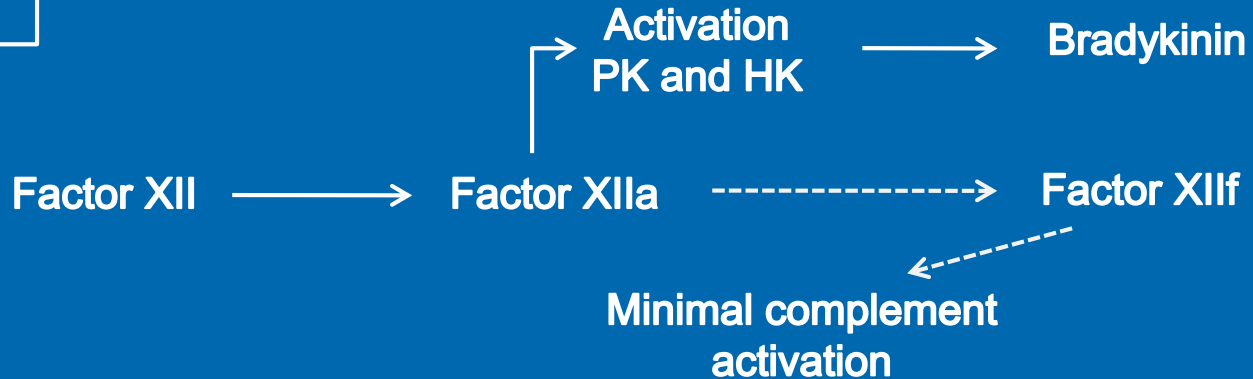


# Types of Urticaria/Angioedema

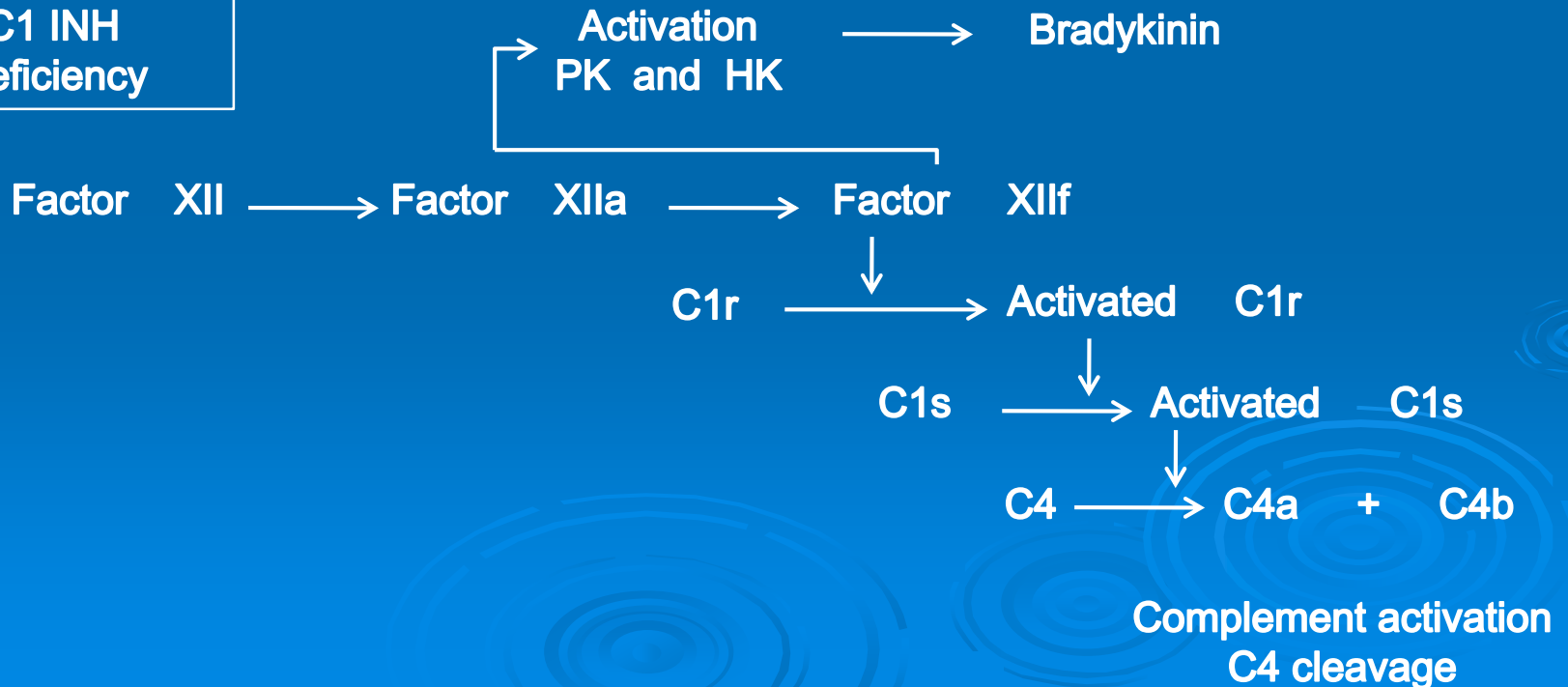
- Acute urticaria/angioedema – lasts less than 8 weeks
- Chronic urticaria/angioedema – lasts more than 8 weeks
  - Idiopathic , autoimmune
  - Urticarial vasculitis
- C1 inhibitor deficiency angioedema

# Activation of Normal vs. C 1 Inhibitor-Deficient Plasma

Normal



C1 INH  
Deficiency



# C1 Inhibitor Functions

- Inhibits C1r and C1s of the complement system
- Inhibits activated factor XIIa and kallikrein
- An inhibitor of factor XIa and plasmin
- Inhibits activation of C1

# Causes of Acute Urticaria (Specific)

- **Drugs**
- **Foods**
- **Infection**
- **Inhalants**
- **Bites and Stings**
- **Contact Urticaria**

# Causes of Chronic Urticaria (Immunologic)

- Autoimmune

- Idiopathic

- Urticarial Vasculitis

# Clues Suggesting Urticarial Vasculitis

- ◆ Persistence of individual lesions longer than 24-48 hours
- ◆ Foci of purpura in wheals
- ◆ Residual “bruising” at sites of lesions
- ◆ Associated constitutional symptoms
- ◆ Elevated ESR, positive ANA, abnormal urinalysis

# Treatment

- Avoidance of identified causative agents when feasible
- Psychological support
- Epinephrine for acute episodes unless contraindicated
- H1 type antihistamines; potent agents may be required
  - Consider a less sedating newer generation drug
- If inadequate, try adding an H2 antagonist or ephedrine, and/or a leukotriene antagonist
- Alternate day corticosteroids



# Major Features of Hereditary Angioedema

- Onset generally in youth
- Autosomal dominant inheritance
- Abdominal pain common
- Laryngeal edema relatively common
- Urticaria and pruritus absent
- C1 inhibitor deficiency

# Laboratory Tests for C1 Inhibitor Deficiency

- C4 low; C4d/C4 ratio always elevated
- C1 inhibitor protein low in about 85% of cases
- C1 inhibitor only functionally deficient in about 15%
- C1q antigen low in acquired deficiency
- Abnormal C1 inhibitor mobility (lower molecular weight) on SDS gel electrophoresis

# Treatment of Hereditary Angioedema

- Patient education very important; test family
- No regular medication needed in many cases
- Prophylactic stanozolol or danazol
- Epsilon aminocaproic acid (EACA) an option
- Fresh frozen plasma before emergency surgery
- Symptomatic treatment during attacks

**FOOD**

**ALLERGY**

# Adverse Reactions to Food

---

IgE-Mediated  Non-IgE Mediated

➤ Oral Allergy Syndrome

➤ Anaphylaxis

➤ Urticaria

- Eosinophilic esophagitis
- Eosinophilic gastritis
- Eosinophilic gastroenteritis
- Atopic dermatitis

- Protein-Induced Enterocolitis
- Protein-Induced Enteropathy
- Eosinophilic proctitis
- Dermatitis herpetiformis

# Frequently allergenic foods

## ○ Most common food allergies in young children:

- Milk (casein, whey)
- Eggs
- Wheat (gluten)
- Soy
- Peanuts
- Tree nuts
- Shellfish

## ○ Most common food allergies in older children & adults

- Fish
- Shellfish
- Peanuts



# Food Allergy vs Food Intolerance

- Reactions to food consist of a variety of reactions to food or food additive ingestion
- Usually not allergenic and caused by food intolerance
  - Symptom-inducing food properties
  - Metabolic disorders
  - Bacterial food contamination



# Oral Allergy Syndrome (OAS)



- OAS refers to clinical symptoms in the mucosa of the mouth and throat that:
- Result from direct contact with a food allergen
- In an individual who also exhibits allergy to inhaled allergens.
- Usually pollens (pollinosis) are the primary allergens
- Pollens usually trigger rhinitis or asthma in these subjects



# Oral Allergy Syndrome

## Allergens

- Pollens and foods that cause OAS are usually botanically unrelated
- Several types of plant proteins with specific functions have been identified as being responsible for OAS:
  - Profilins
  - Pathogenesis-related proteins
  - Hevamines

# Oral Allergy Syndrome

## Cross-Reactivity

- Occurs most frequently in persons allergic to birch and alder pollens
- Also occurs with allergy to:
  - Ragweed pollen
  - Mugwort pollen
  - Grass pollens

# Oral Allergy Syndrome

## Associated foods

- Foods most frequently associated with OAS are mainly fruits, a few vegetables, and nuts
- The foods cause symptoms in the oral cavity and local tissues immediately on contact:
  - Swelling
  - Throat tightening
  - Tingling
  - Itching
  - “Blistering”

# Oral Allergy Syndrome

## Cross-reacting allergens

- Birch pollen (also: mugwort, and grass pollens) with:
  - Apple
  - Stone Fruits (Apricot, Peach, Nectarine, Plum, Cherry)
  - Kiwi Fruit
  - Orange
  - Melon
  - Watermelon
  - Potato
  - Tomato
  - Peanut
  - Hazelnut
  - Carrot
  - Celery
  - Fennel

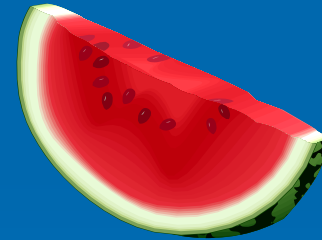
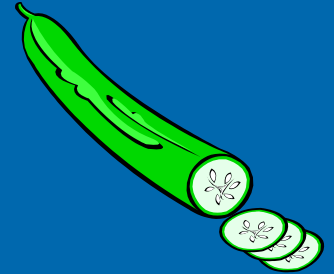
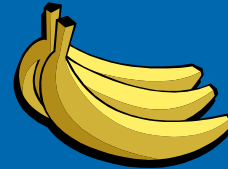


# Oral Allergy Syndrome

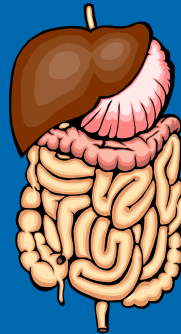
## Cross-reacting allergens

### ➤ Ragweed pollen with:

- Banana
- Cantaloupe
- Honeydew
- Watermelon
- Other Melons
- Zucchini (Courgette)
- Cucumber

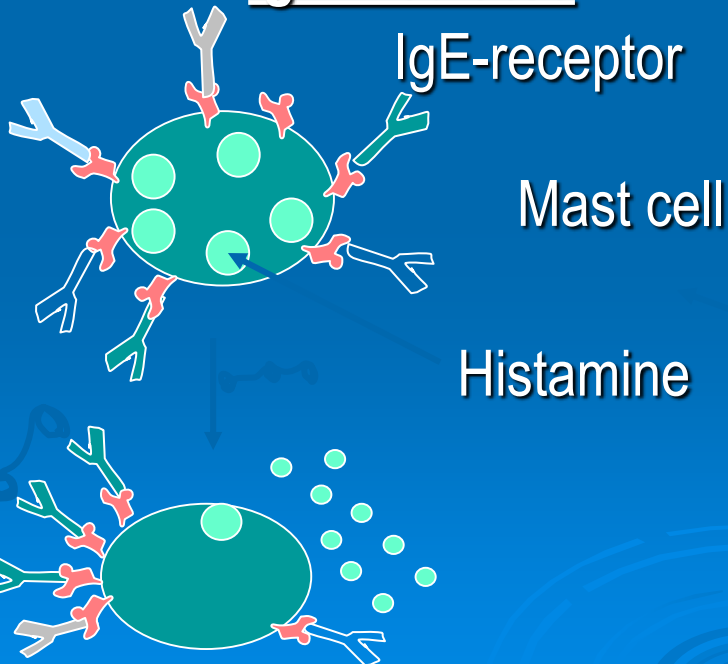


# Pathophysiology: Immune Mechanisms

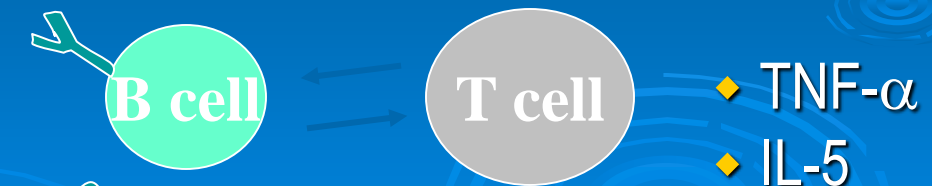


- ◆ Protein digestion
- ◆ Antigen processing
- ◆ Some Ag enters blood

## IgE-Mediated



## Non-IgE Mediated



# Food Allergy Prevalence in Specific Disorders

Disorder	Food Allergy Prevalence
Anaphylaxis	35-55%
Oral allergy syndrome	25-75% in pollen allergic
Atopic dermatitis	37% in children (rare in adults)
Urticaria	20% in acute (rare in chronic)
Asthma	5-6% in asthmatic or food allergic children
Chronic rhinitis	Rare

# Prevalence of Clinical Cross Reactivity Among Food “Families”

Food Allergy	Prevalence of Allergy to > 1 Food in Family
Fish	30% -100%
Tree Nut	15% - 40%
Grain	25%
Legume	5%
Any	11%



THANK YOU!





# ALLERGY

- 17% of population are suffering from one or more allergic disease (NIH).
- 10-25% in (KSA) are suffering from one or more allergic disorder.

➤ Allergy is a specific, acquired change in host reactivity mediated by an immunologic mechanism and causing an untoward physiologic response.

- IgE antibodies, like IgA antibodies, are synthesized by plasma cells located predominantly under mucosal surfaces and particularly in the respiratory and gastrointestinal tracts. IgE-forming plasma cells arise following antigen-stimulated differentiation of B cells or their precursors.

➤ The terms antigen and allergen are often used interchangeably, but not all antigens are good allergens and vice versa. For example, tetanus and diphtheria toxoids are highly antigenic but are only rarely responsible for allergic reactions. On the other hand, ragweed pollen protein, one of the most potent allergens, is not a particularly potent antigen by immunologic criteria.

- Mast cells play the central role in immediate hypersensitivity responses.
- Mast cells and basophils are involved not only in IgE-mediated reactions (e.g. allergic respiratory diseases) but also in other chronic inflammatory disorders, for example, inflammatory bowel disease, rheumatoid arthritis, and parasitic infections.

# Interpretation of Laboratory Tests

- Positive prick test or RAST
  - Indicates presence of IgE antibody NOT clinical reactivity (~50% false positive)
- Negative prick test or RAST
  - Essentially excludes IgE antibody (>95%)
- ID skin test with food
  - Risk of systemic reaction & not predictive
  - Contraindicated
- Unproven/experimental tests (useless)
  - Provocation/neutralization, cytotoxic tests, applied kinesiology, hair analysis, IgG4

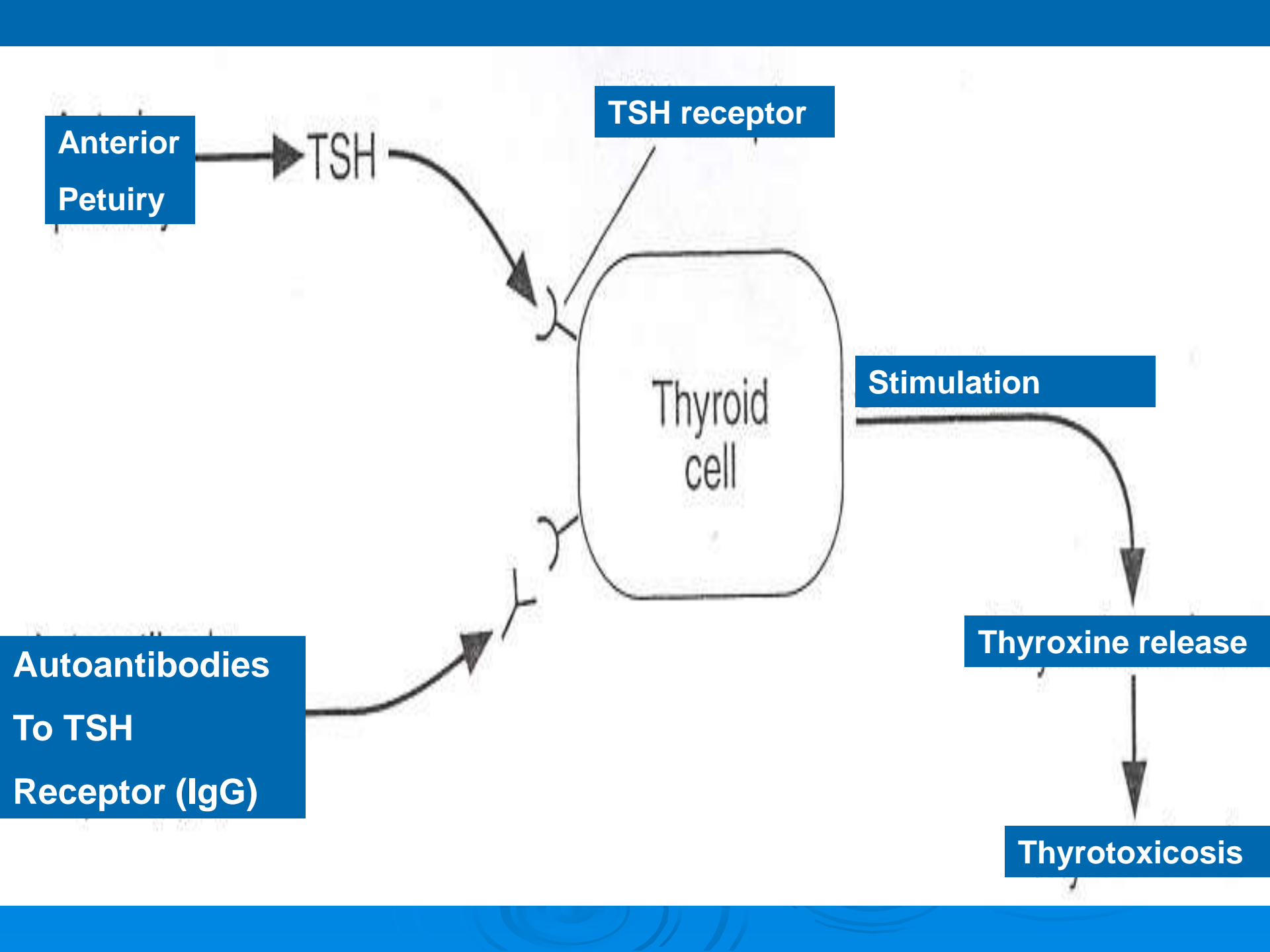


# Type V

Stimulatory (a new category )  
(e.g. Graves' diseases).

Autoantibodies against certain hormone receptors can mimic the hormone and stimulate the cell, e.g.. Anti-TSH receptors on thyroid cells in thyrotoxicosis.

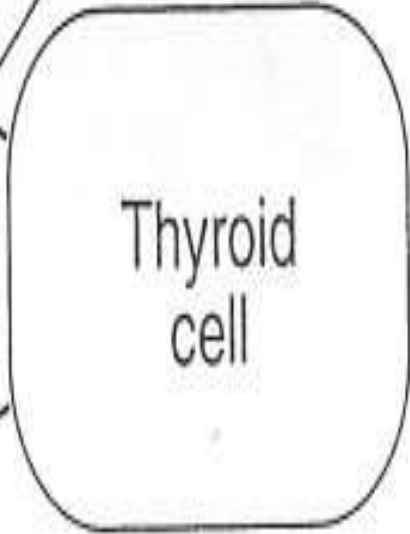




Anterior Pituitary

TSH

TSH receptor



Stimulation

Thyroxine release

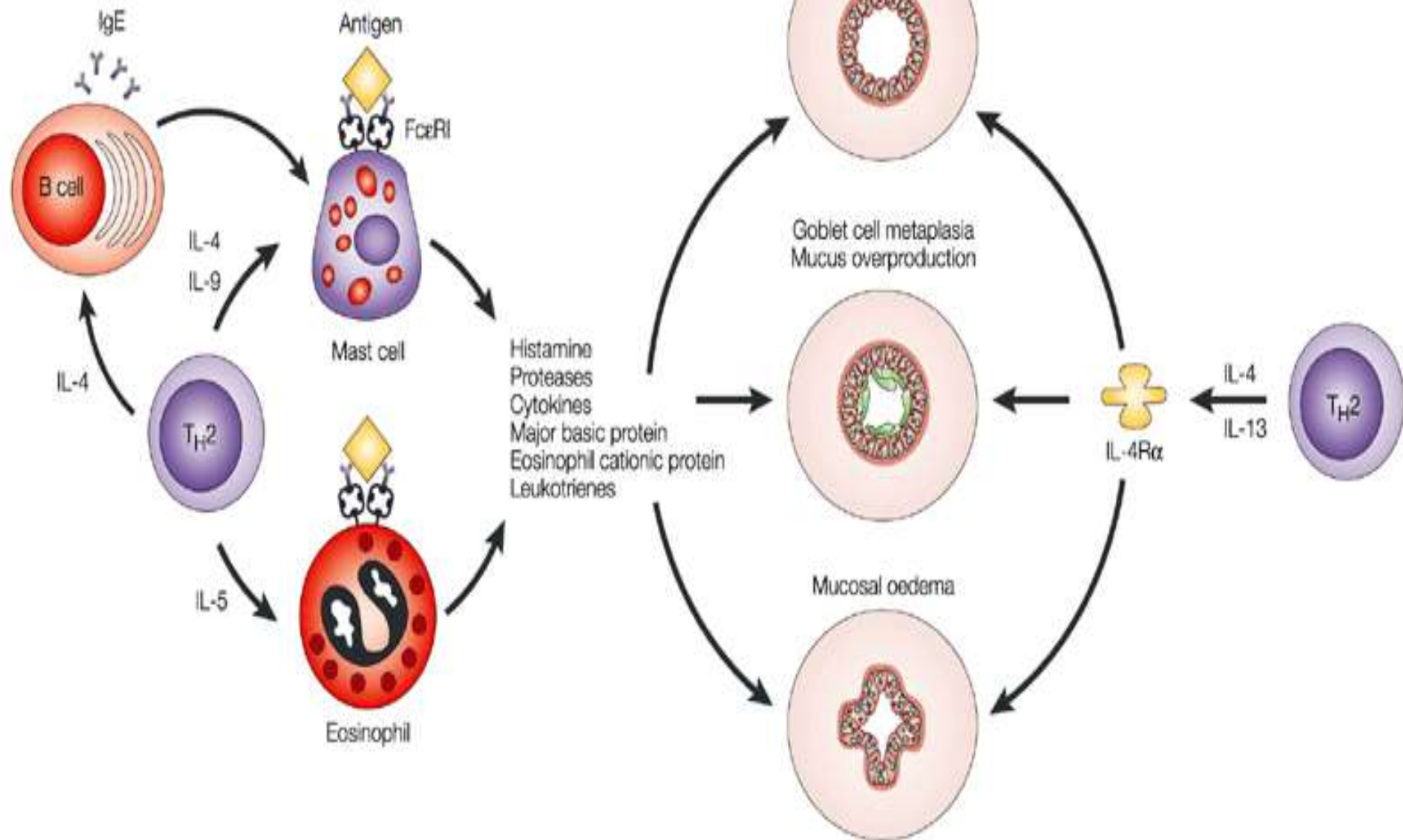
Thyrotoxicosis

Autoantibodies To TSH Receptor (IgG)

### Type I hypersensitivity

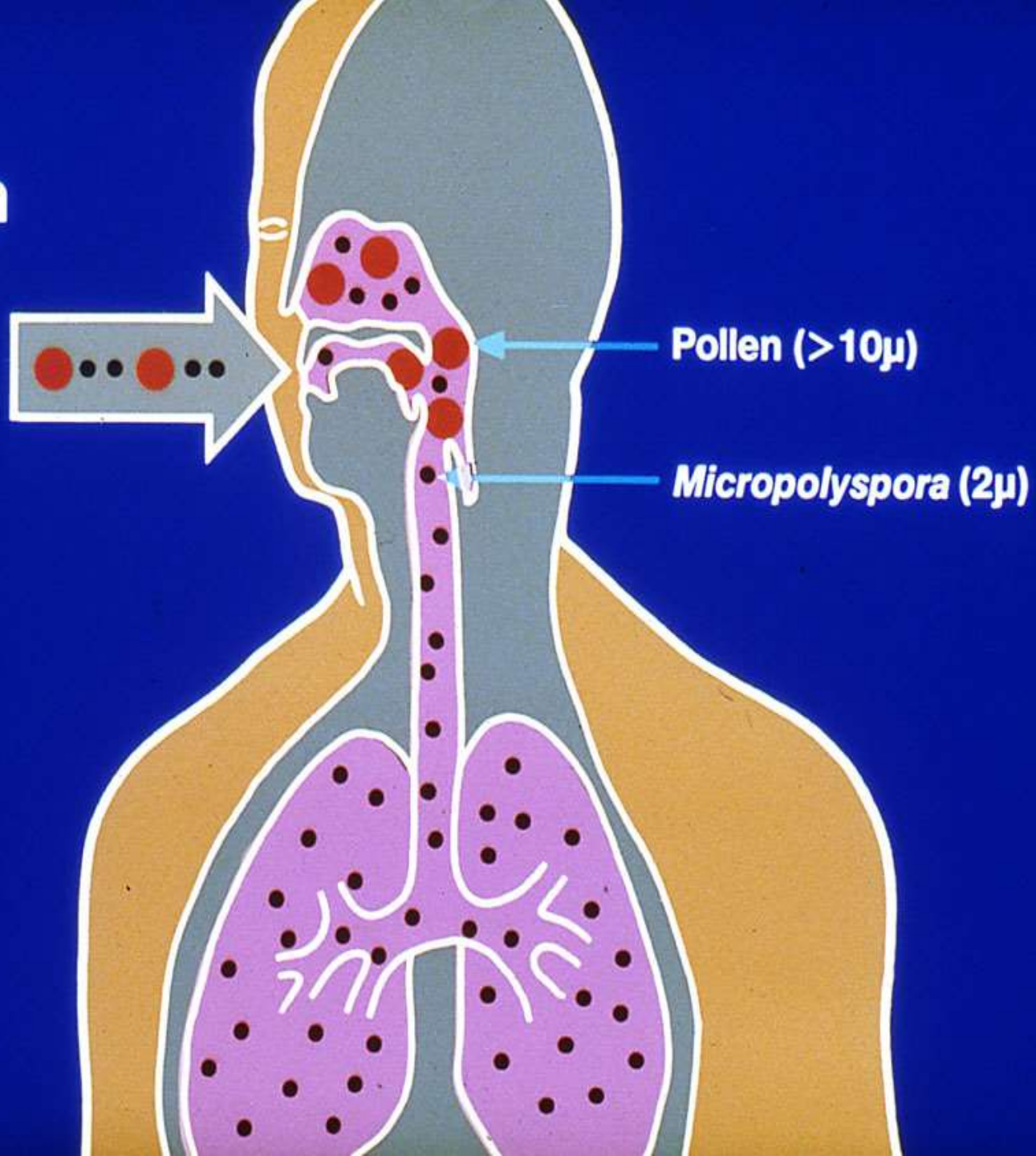
### Airway hyper-responsiveness

### Type IV hypersensitivity



➤ Molecules smaller than 10,000 d would be unable to bridge the gap between adjacent immunoglobulin E (IgE) antibody molecules on the surface of mast cells, a requirement for release of the mediators of the allergic reaction. Molecules larger than 70,000 d would not easily pass through mucosal surfaces to reach IgE-forming plasma cells.

# Pollen deposition



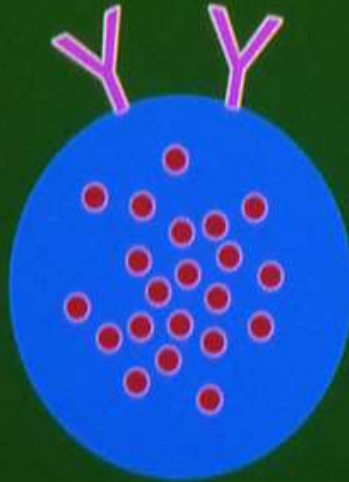
# Mechanism of the allergic reaction

1



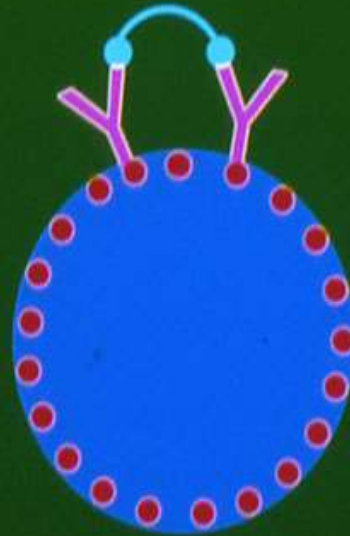
IgE produced  
by plasma  
cells

2



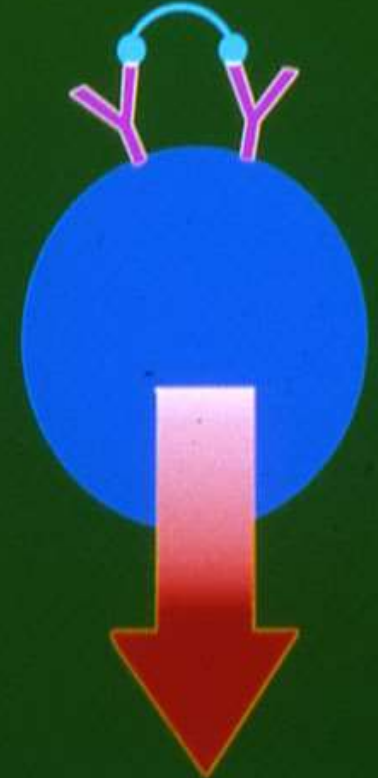
IgE binds to surface  
receptors on mast  
cells and basophils

3



Pollen antigen binds  
to IgE and cross-links  
receptors

4



Histamine is  
released from cell  
receptors