Hypersensitivity Reactions

Immunology Unit
Department of Pathology
College of Medicine
King Saud University

Reference

Kuby Immunology 7th Edition

2013

Chapter 15 Pages 485-510

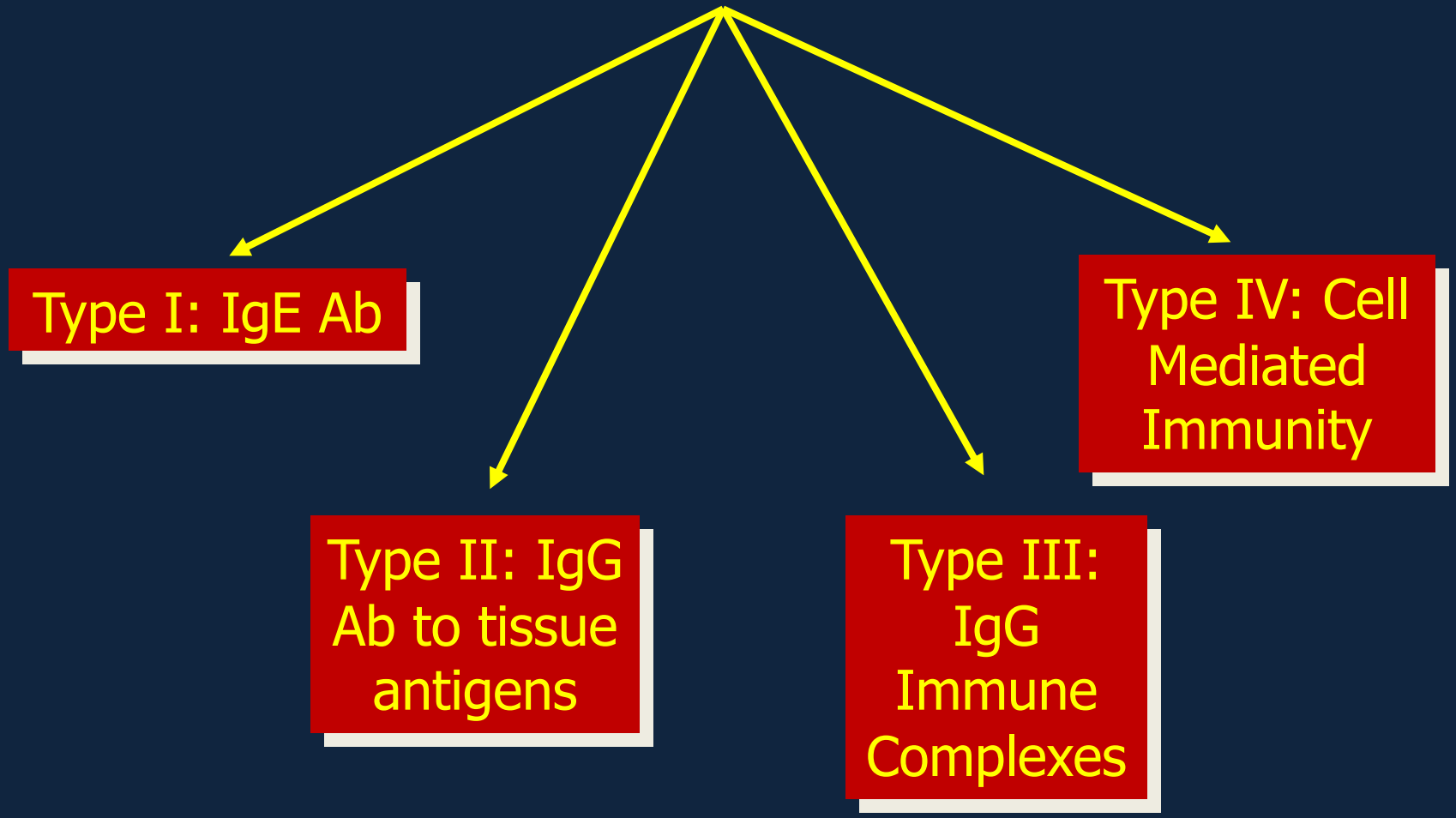
Objectives

- To know that hypersensitivity reactions are over and excessive immune responses that can be harmful to body in four different ways
- To be familiar with inflammatory processes in Type I hypersensitivity reaction that mediates allergic inflammation
- To recognize that Type II hypersensitivity deals with immune responses against antigens that are integral part of cell membrane and are usually associated with autoimmune disorders
- To know that Type III hypersensitivity reactions are mediated by immune complexes and cause vasculitis
- To describe Type IV hypersensitivity is a purely cell mediated immune response associated with chronic inflammation

What is hypersensitivity?

- **Protective immunity**: desirable reaction
- **Hypersensitivity**: undesirable reaction
- Undesirable responses can be mediated by
  - ***Antibody binding*** to antigens (Types I-III)
  - ***Cell mediated reaction*** to chemicals or proteins (Type IV)

Gel and Coombs Classification



Type I: Immediate Hypersensitivity

- Most people will not react to these allergens but some individuals "***atopic***" respond by producing large amounts of IgE in response to those otherwise harmless substances

- Non-allergic individuals respond to these allergens by producing IgG antibodies

Type I Hypersensitivity

- Also termed as:

  Immediate Hypersensitivity

  Allergic reactions

  Anaphylactic reactions are severe and rapidly progressing systemic forms which can be quickly life threatening

(Occurs within minutes to hours)

Features

- Antibody type: IgE

- Cellular components:

  Mast cells, basophiles & eosinophils

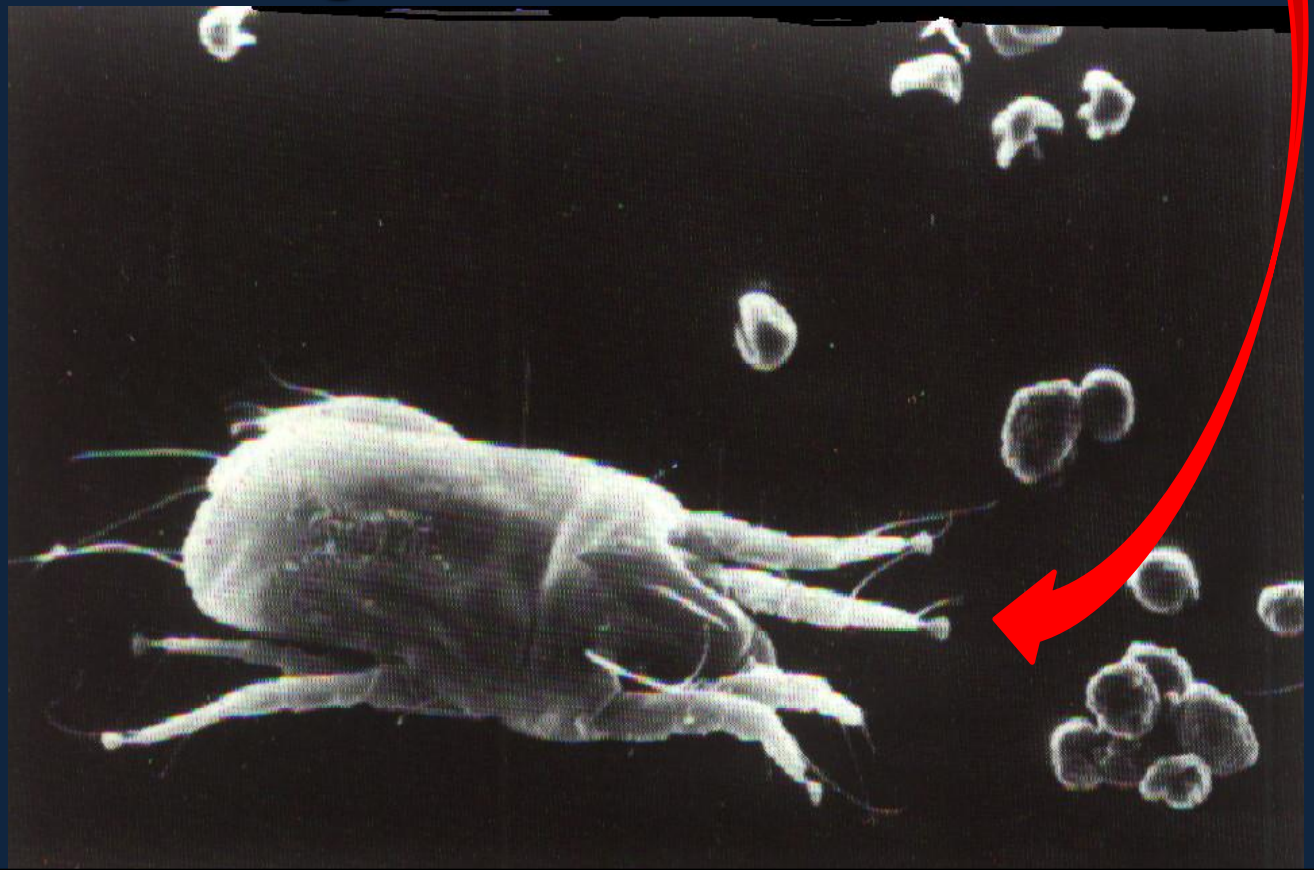
- Antigens:

  Also known as allergens

  (antigens with low molecular weight & highly soluble)

Allergens

- Some of the allergens involved in type I hypersensitivity are: pollens, dust mite allergens, animal dander, nuts, shellfish, various drugs etc

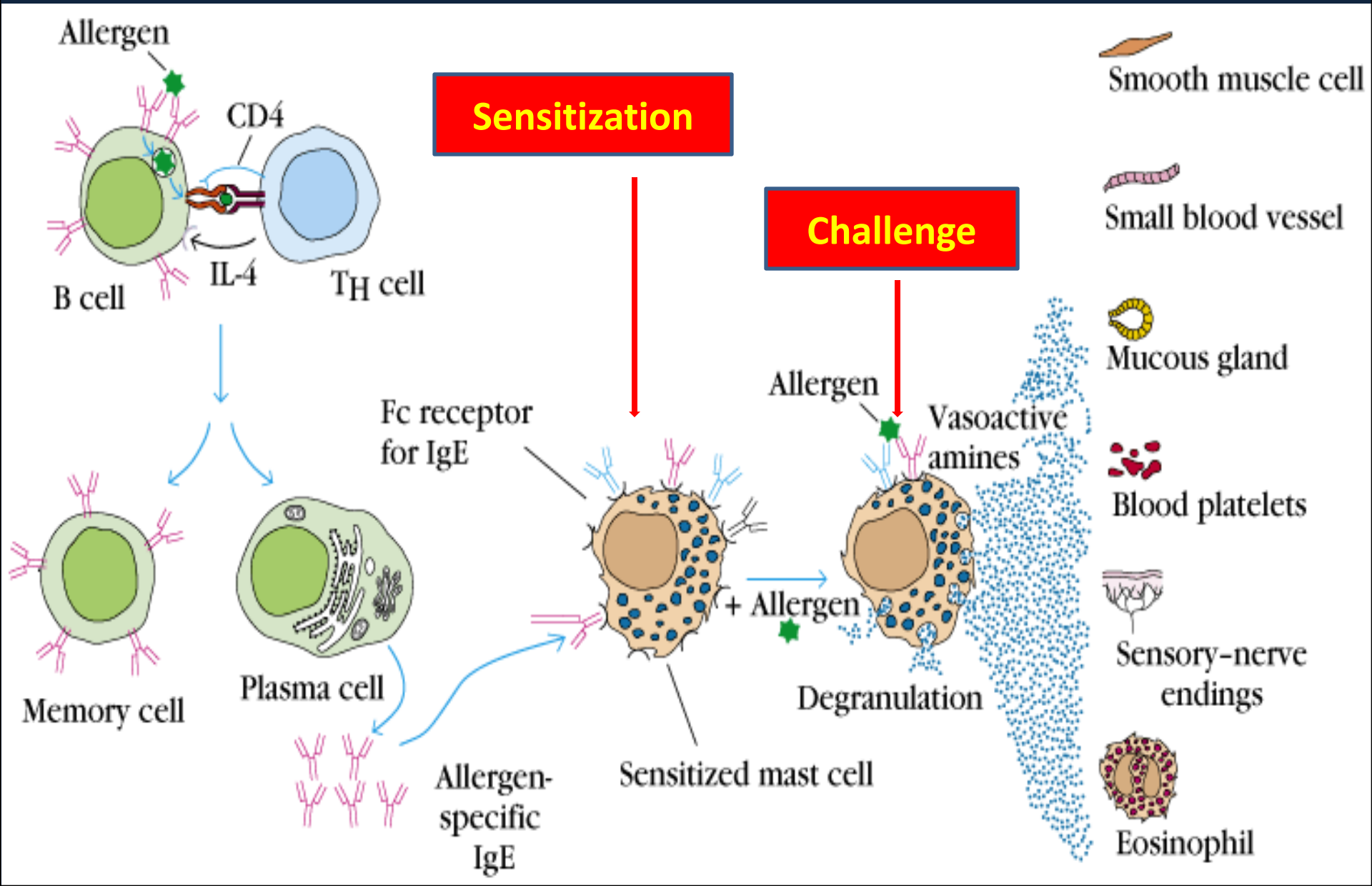


Type I reactions occur in two phases

- **Sensitization phase**
  First contact with allergens

- **Challenge phase**
  Subsequent contact with allergens

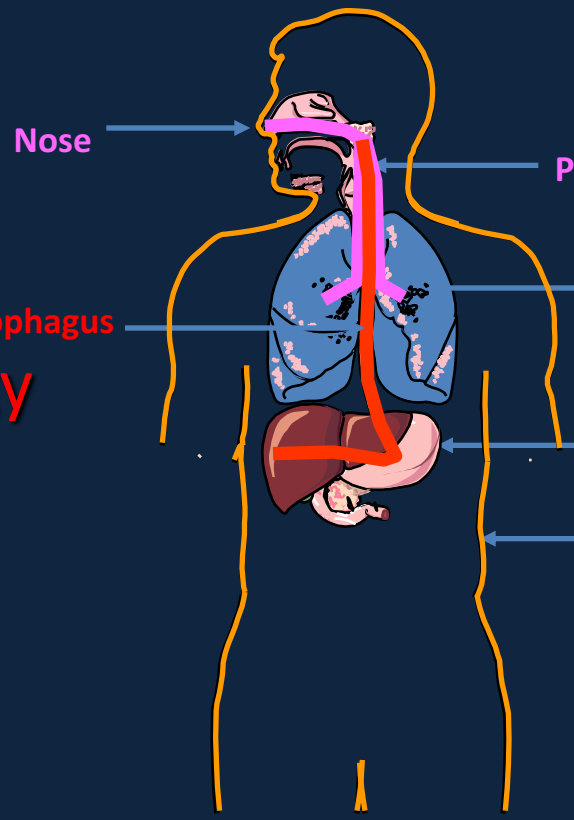
Type I Hypersensitivity (Immediate)



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-α	Systemic anaphylaxis; increased expression of CAMs on venular endothelial cells
IL-2, IL-3, IL-4, IL-5, IL-6, TGF-β, and GM-CSF	Various effects (see Table 12-1)

Allergy is a systemic disorder

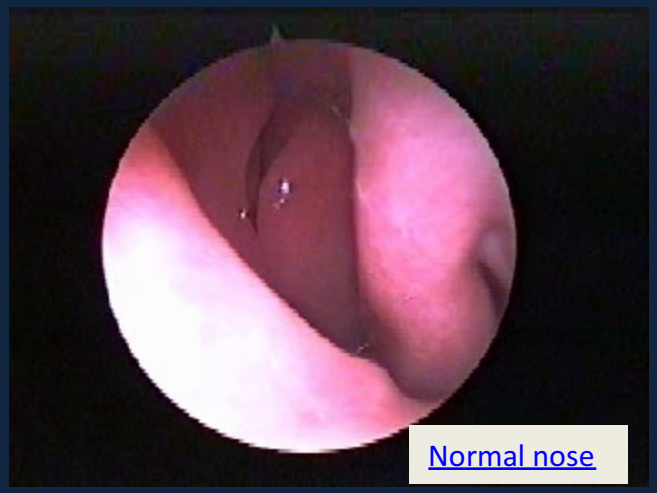


Allergic rhinitis
Asthma

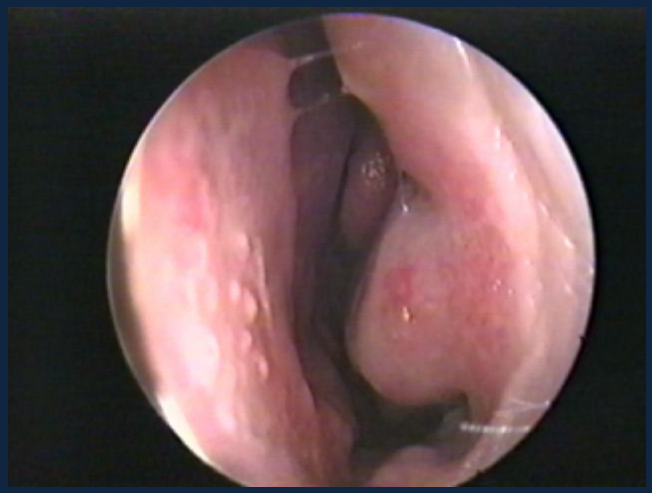
Food allergy

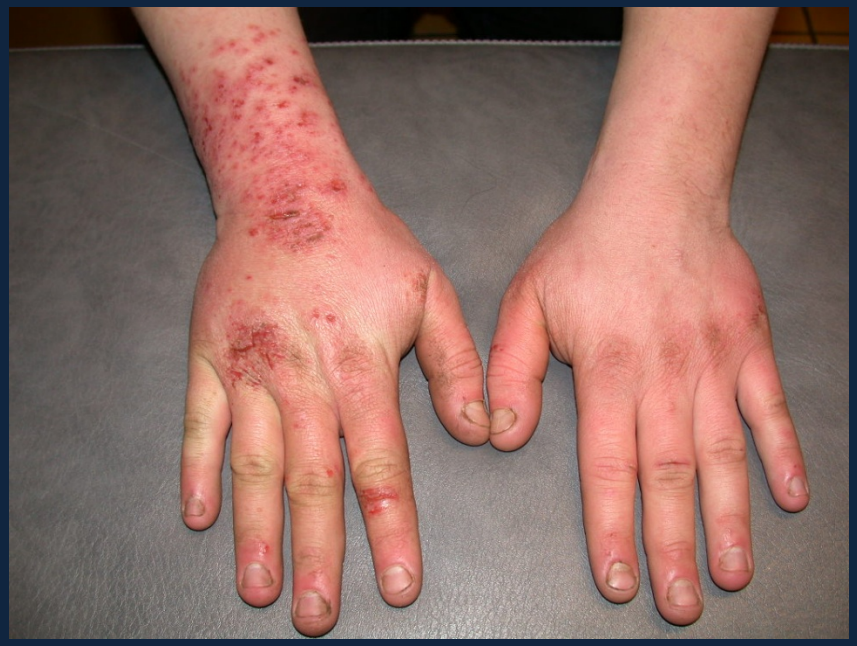
Eczema
Urticaria
Allergic dermatitis

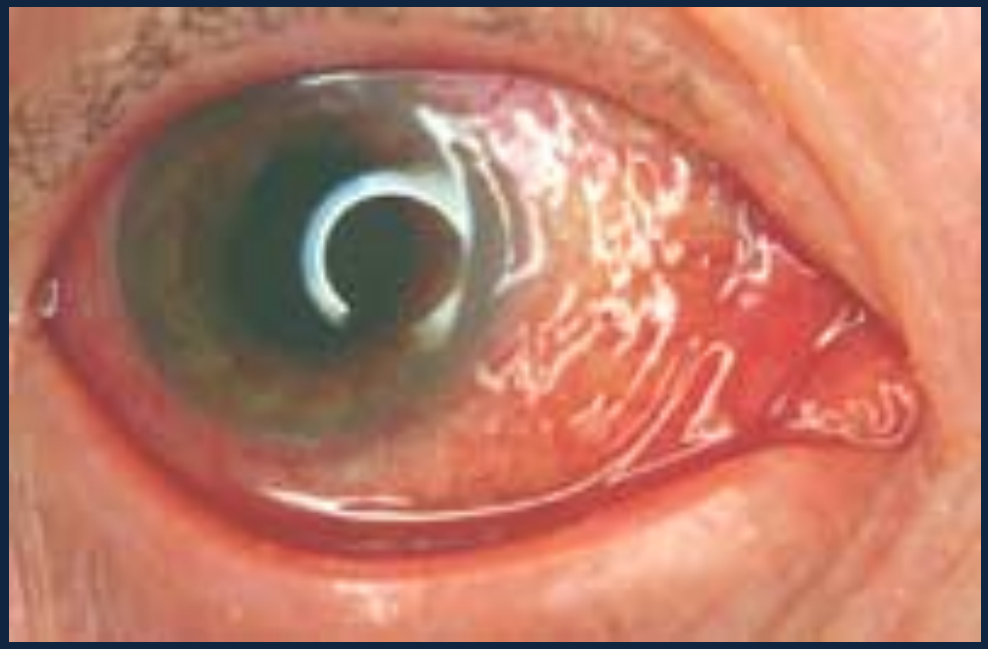
Allergy: Rhinitis, Eczema & Conjunctivitis



Normal nose







* Injected allergens:

Hymenoptera (bees, wasps, ants) sting venom enters the blood stream

→ Systemic inflammation

→ Anaphylactic shock
(life - threatening)

❖ Anaphylactoid reactions:-

Are non - IgE mediated
may result from contrast media or local anesthetics

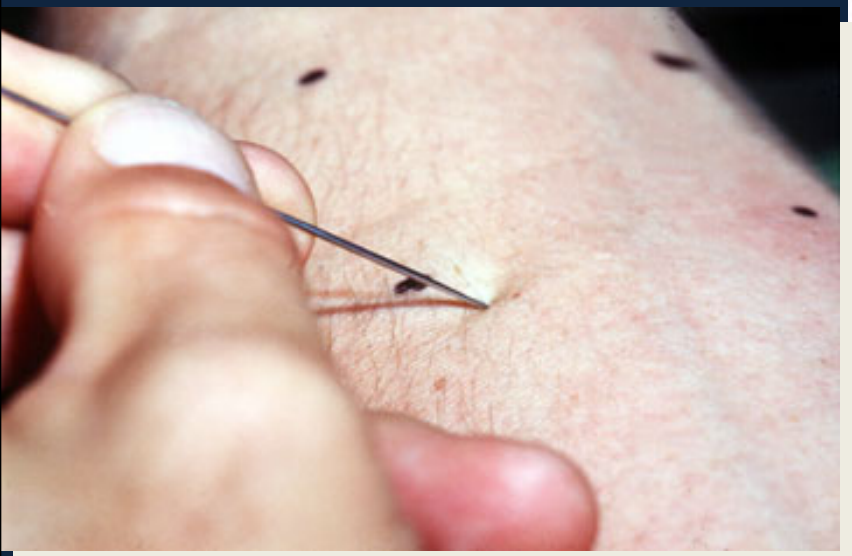
Diagnosis of Allergy

Skin Prick test

1. Skin prick test (SPT)

2. Specific IgE measurement (RAST)

3. Elimination / Provocation test (Food allergy)



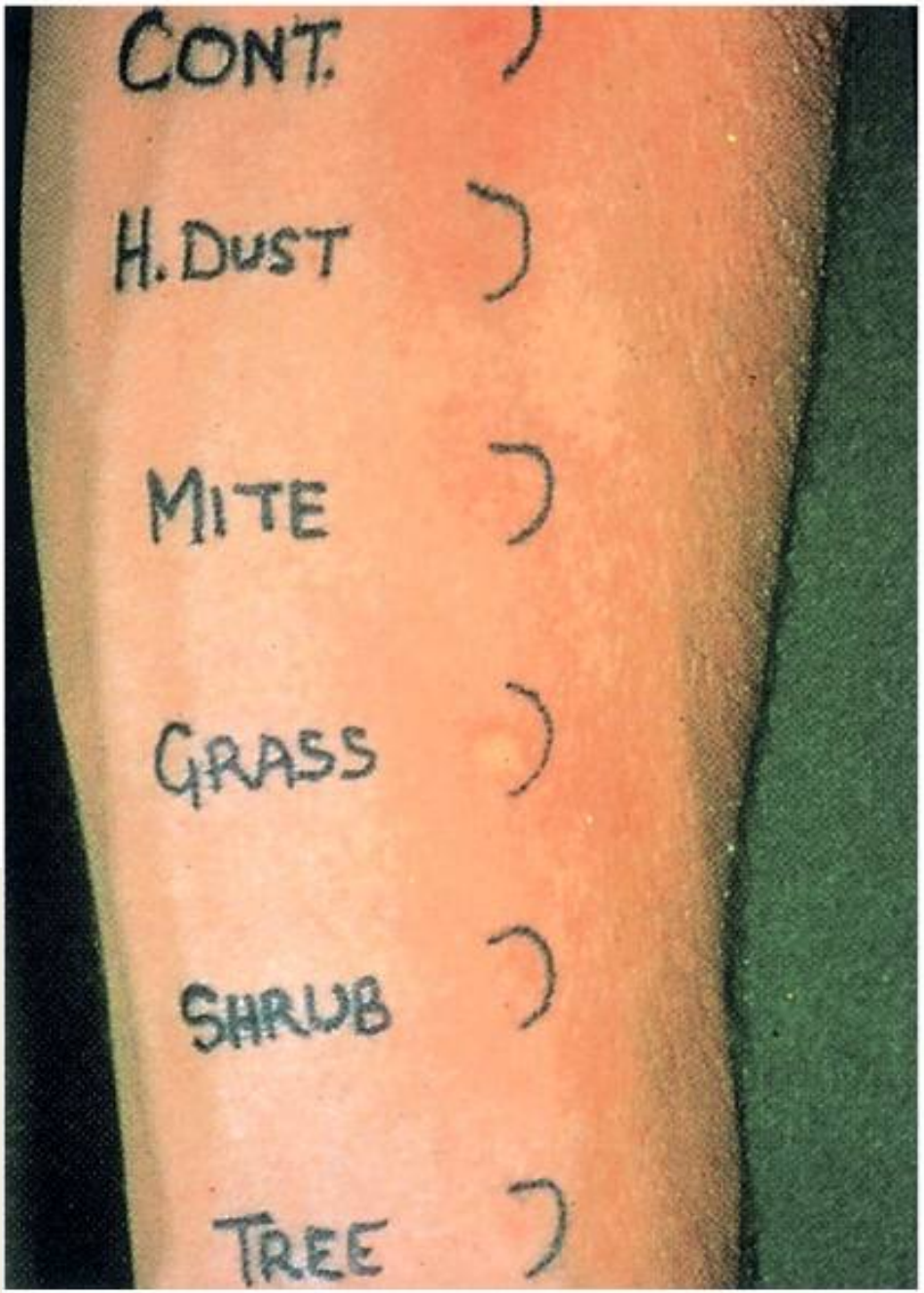


Figure 15-10
Kuby IMMUNOLOGY, Sixth Edition

Type II Hypersensitivity Reactions

- Features:-

- IgG (or IgM)

- Antigens: bound to cell membranes

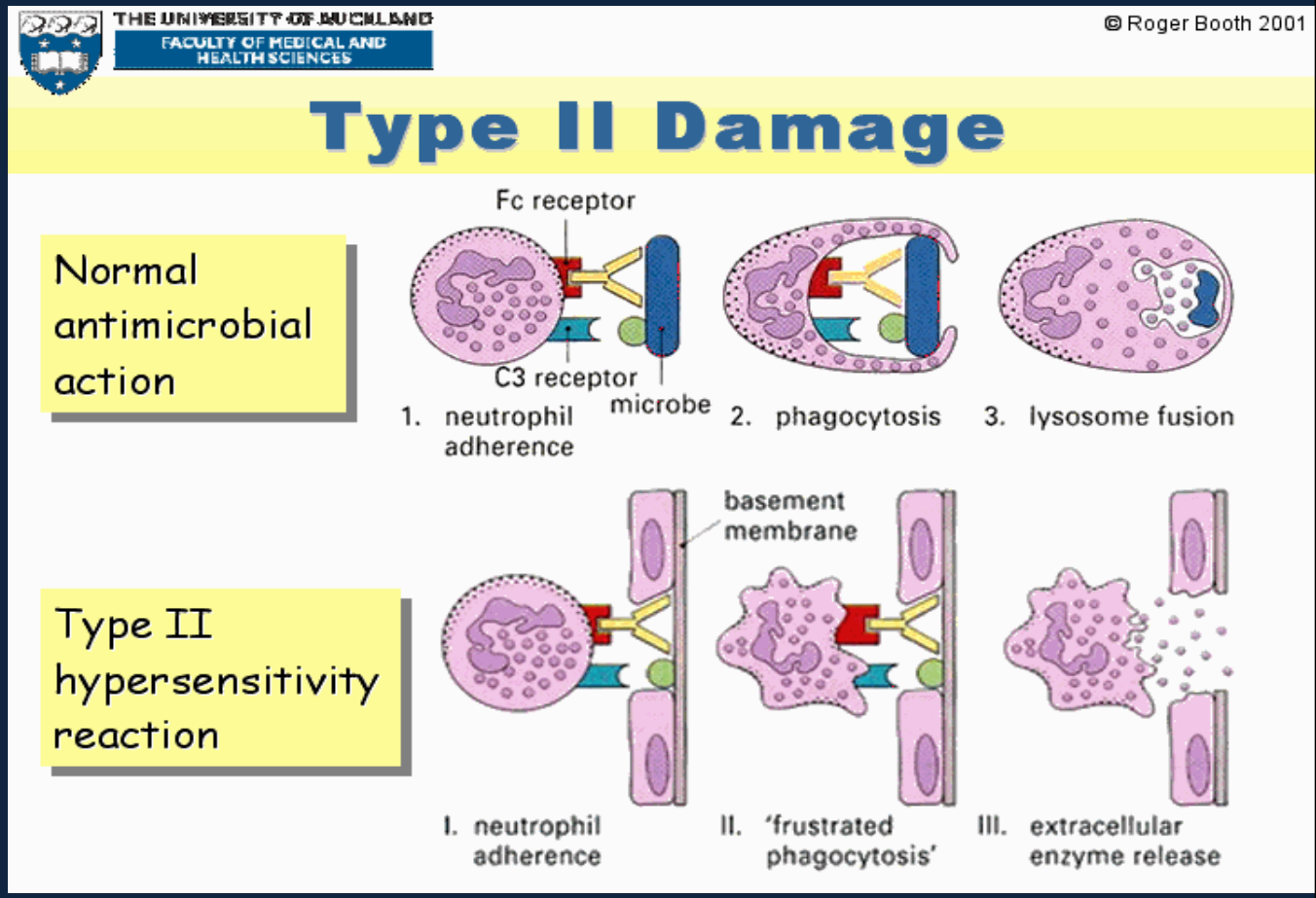
(Self antigens)

- Exogenous antigens

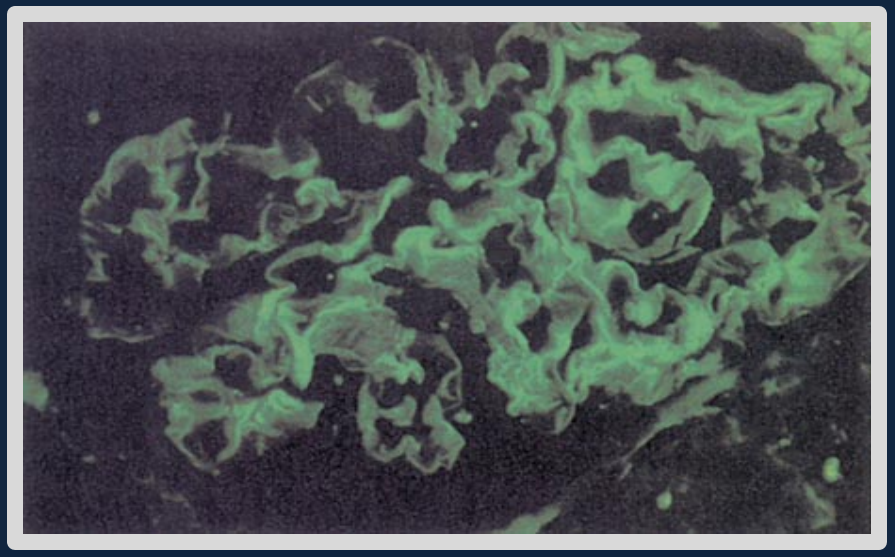
(microbial)

- Complement activation

(Invariable)



Clinical examples:



Glomerulonephritis (anti-glomerular basement membrane)

Mis-matched blood transfusion

Diagnosis

- Detection of antibodies and antigens by Immunofluoresence in tissue biopsy specimens e.g. kidney, skin etc.

Type III: Immune complex hypersensitivity

- When an antigen reacts with an antibody the product they form is called an immune complex which is capable of inducing an inflammatory response

- Immune complexes are deposited in tissues like kidneys (nephritis), joints (arthritis) or blood vessels (vasculitis)

Type III Hypersensitivity (immune–complex mediated)

- Features

Antibody (IgG/ or IgM) + Antigen (soluble)

↓

- Immune – Complex formation

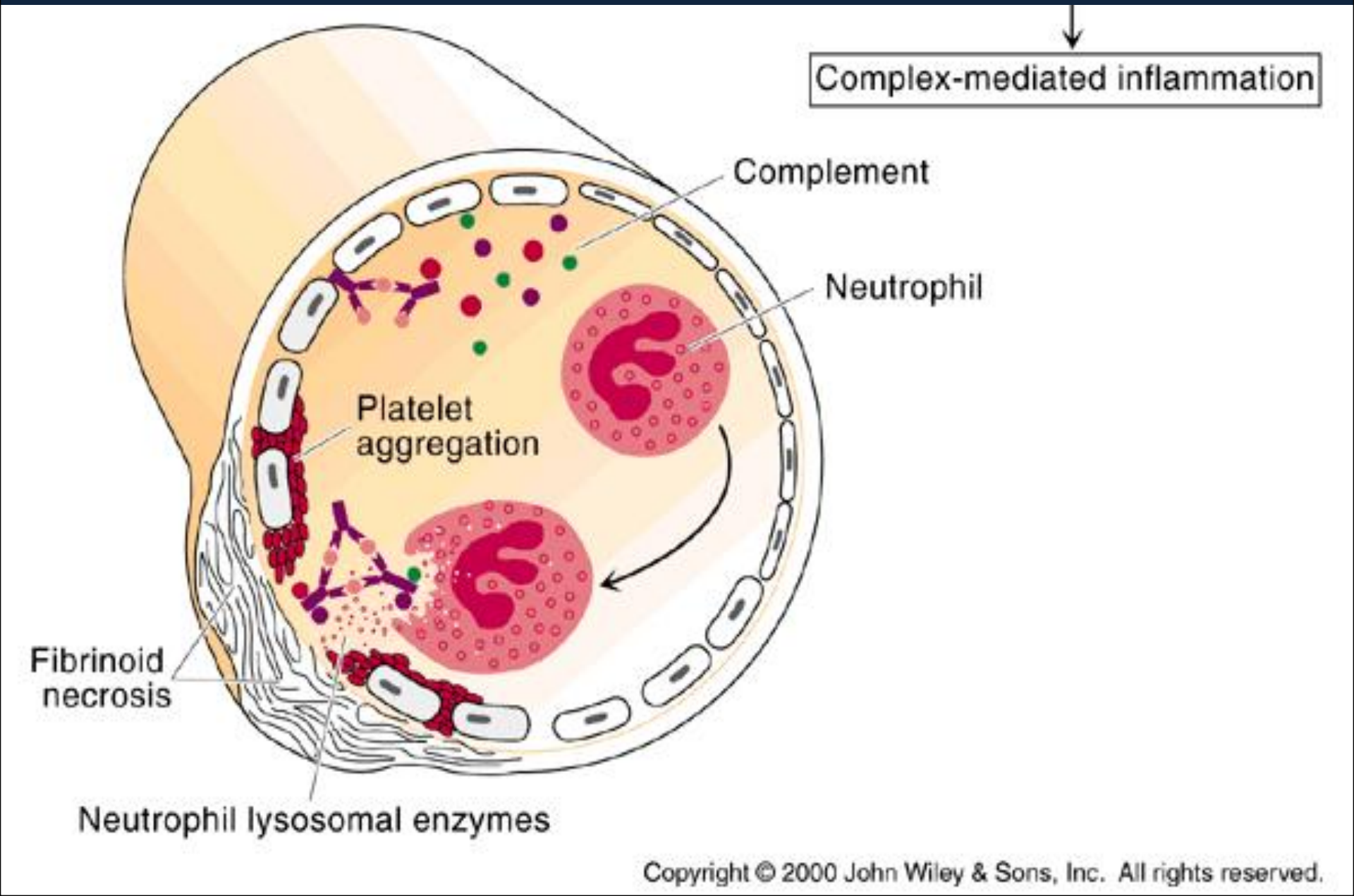
↓

- Complement activation

↓

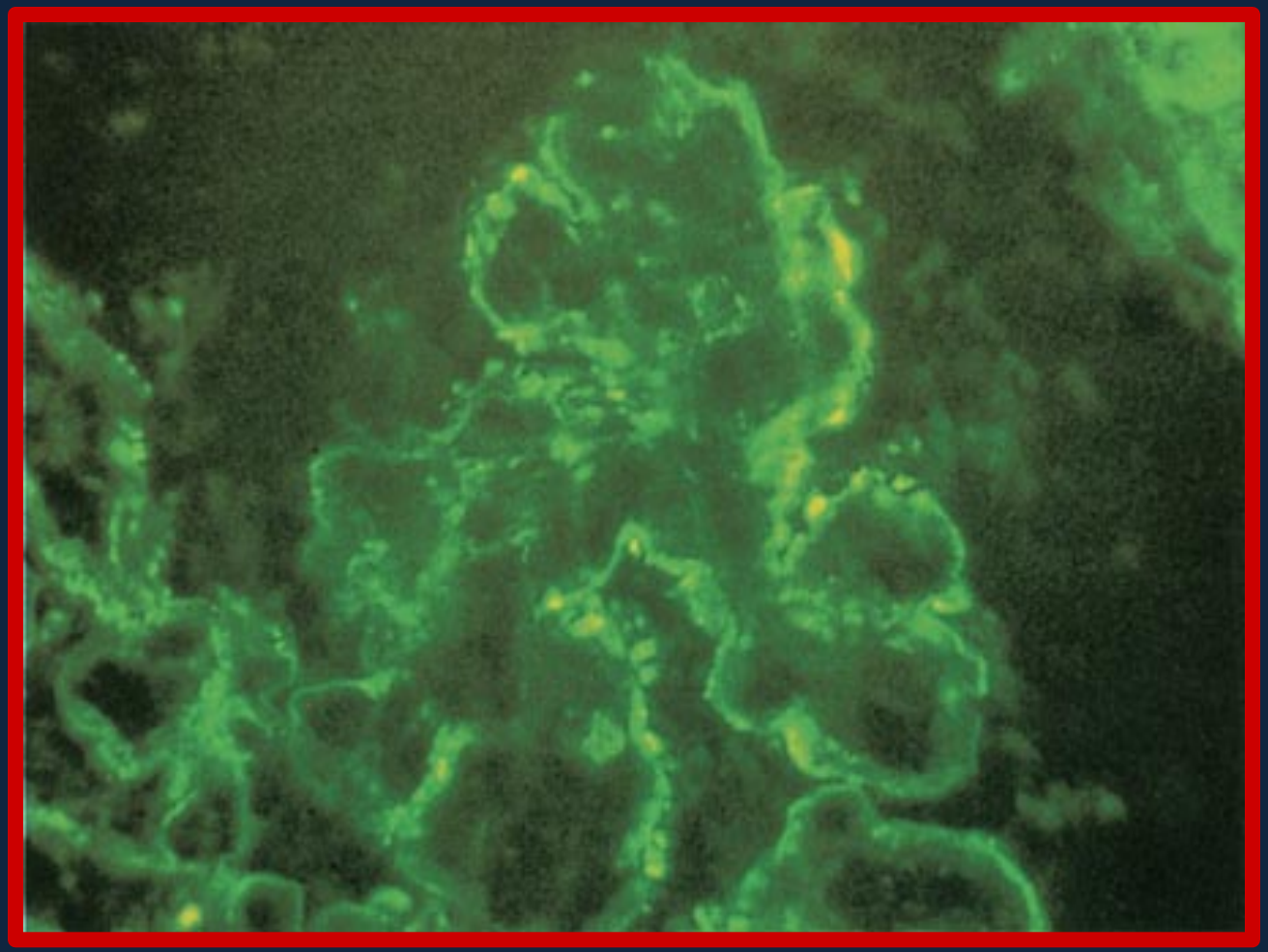
- Attraction of inflammatory cells

Type III Reactions



Type III Hypers. Reactions
Clinical examples:

Glomerulonephritis: Rheumatoid arthritis, SLE



Diagnosis of Type III Hypers. Reactions

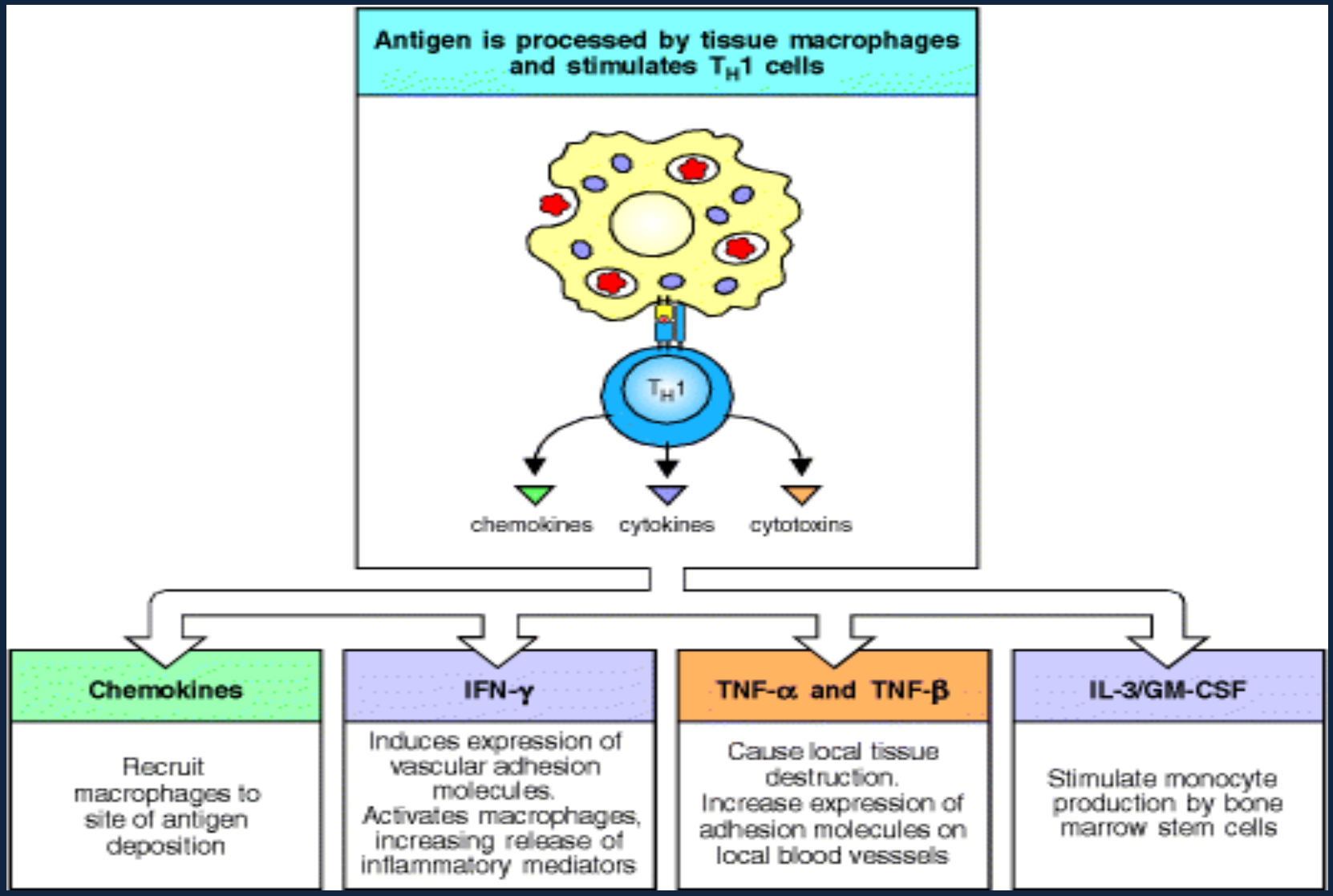
Demonstration of specific immune complexes in the blood or tissues by:

Immunofluoresence

Type IV hypersensitivity reactions (Delayed Hypersensitivity)

- Features
- Cell mediated immune response
  - Antigen dependent T cell (CD4 generally and CD8 occasionally) activation via MHC Class I or II
- Activated macrophages
- Delayed onset (2-4 days)
- Abnormal cellular response
  - (Granuloma formation)

Mediators released by T_{DTH} cells

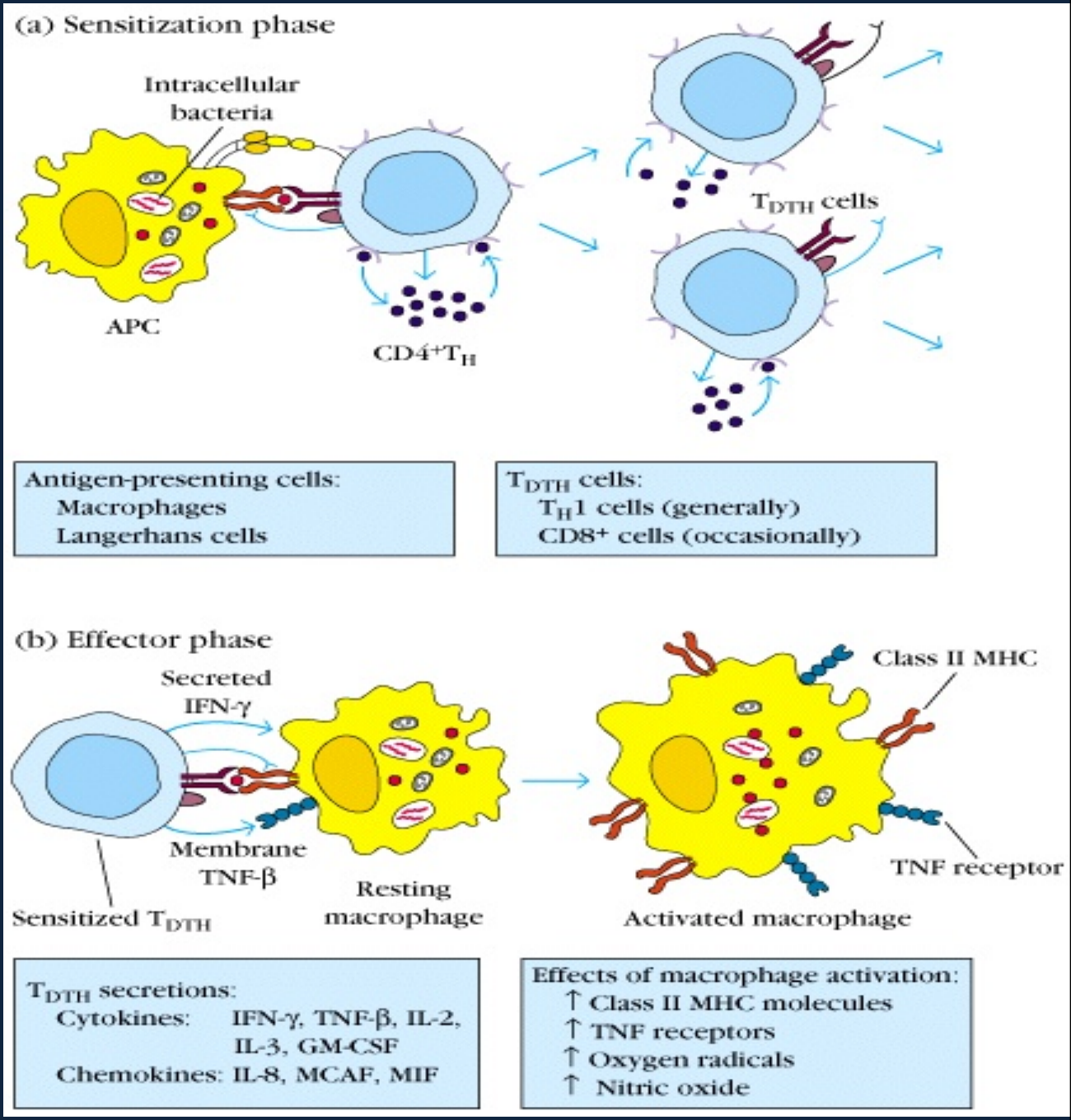


Development of DTH Response

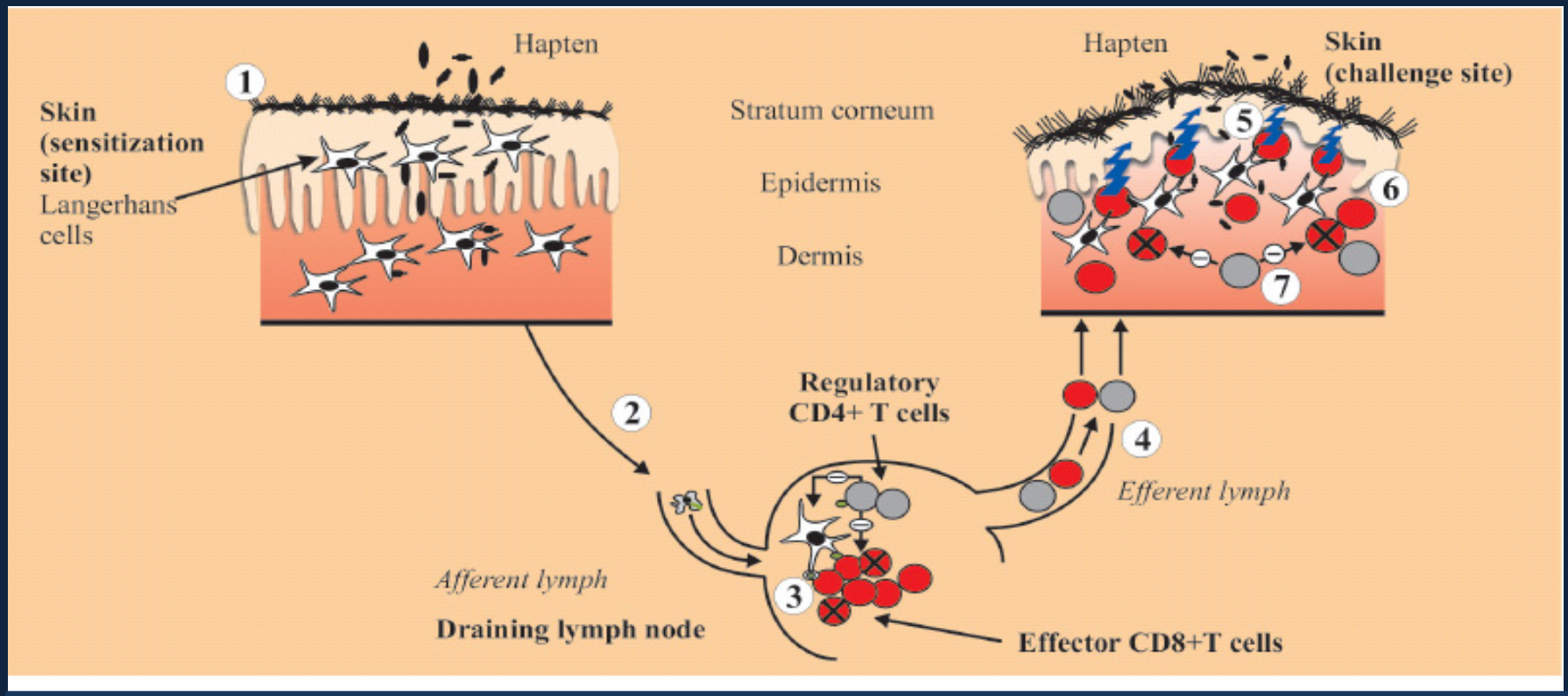
Sensitization phase:
1-2 week period

Effector phase:
24-72 hours

Effector cells (activated macs) act non-specifically

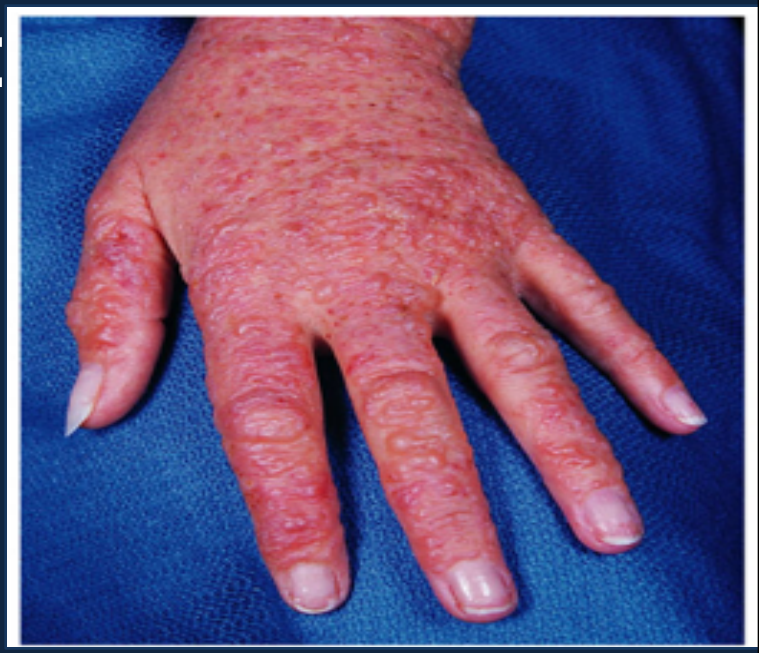


Pathophysiology of Contact dermatitis.

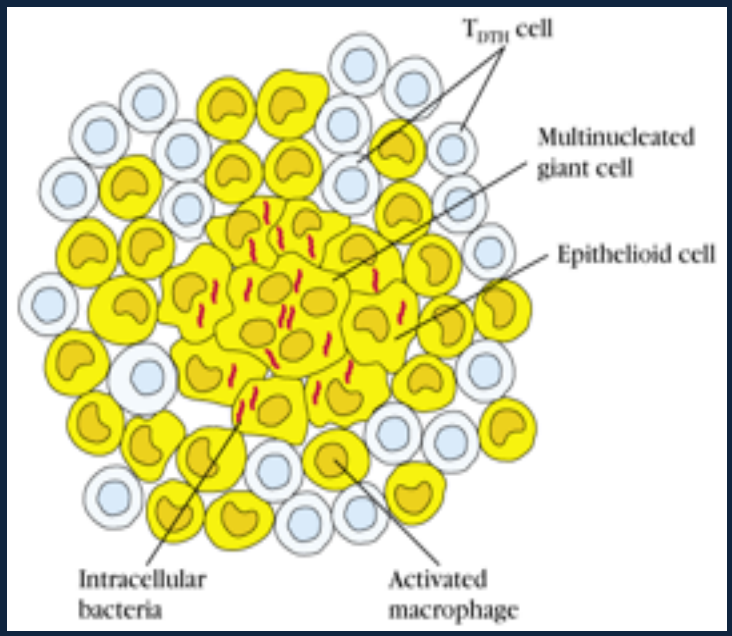


Type IV clinical examples:

Contact dermatitis



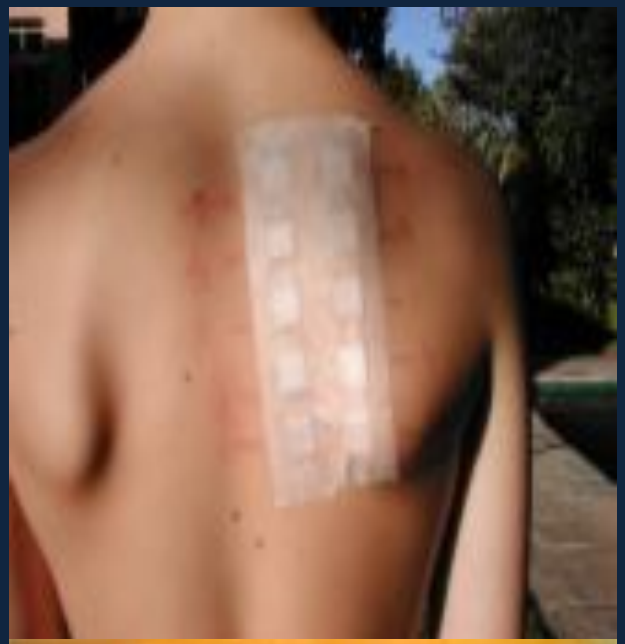
TB granuloma
(persistent antigen)

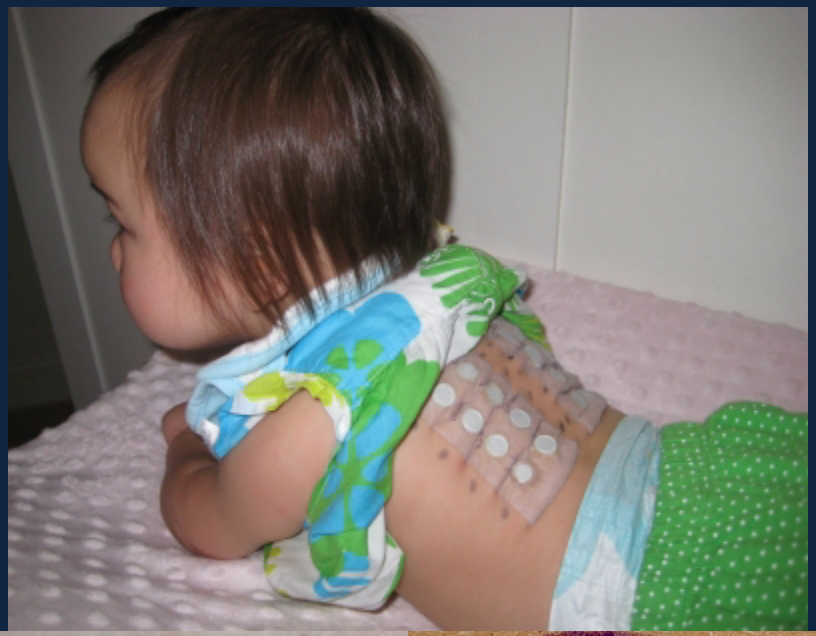


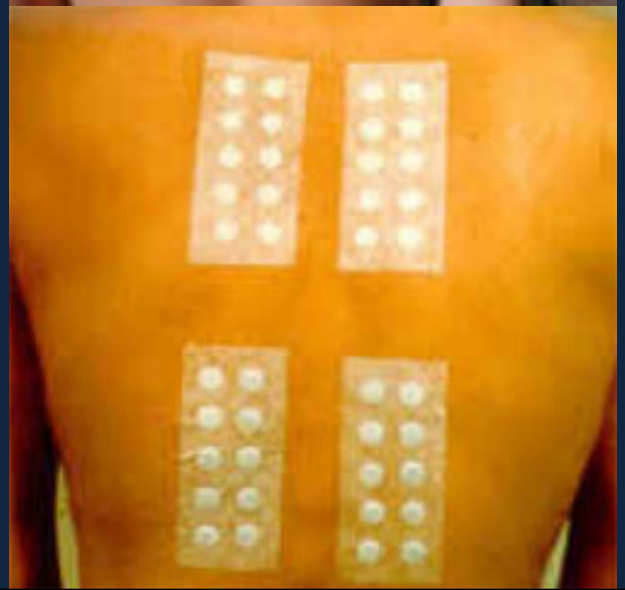
Diagnosis (Type IV)

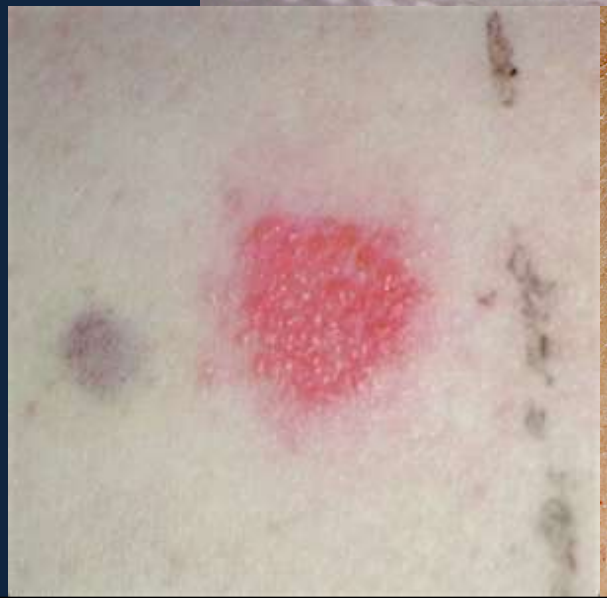
1. Delayed skin test (Mantoux test)
2. Patch test (Contact dermatitis)
3. Lymphocyte transformation test

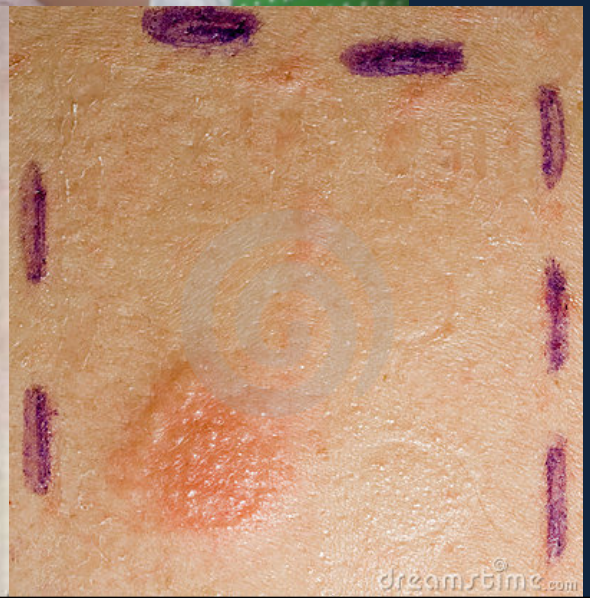
Skin Patch Test











Take Home Message

- 1. Type I (IgE), II (IgG) and III (IgG) hypersensitivity reactions are mediated by *antibodies* whereas Type IV hypersensitivity reaction is a *cell* mediated immune response.

- 2. Hypersensitivity reactions are *undesirable, excessive*, and *aberrant* immune responses associated with disorders such as allergy, autoimmunity and chronic inflammation.