

# Hypersensitivity Reactions

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**Reference**  
**Kuby Immunology 7<sup>th</sup> Edition**  
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**Chapter 15 Pages 485-510**

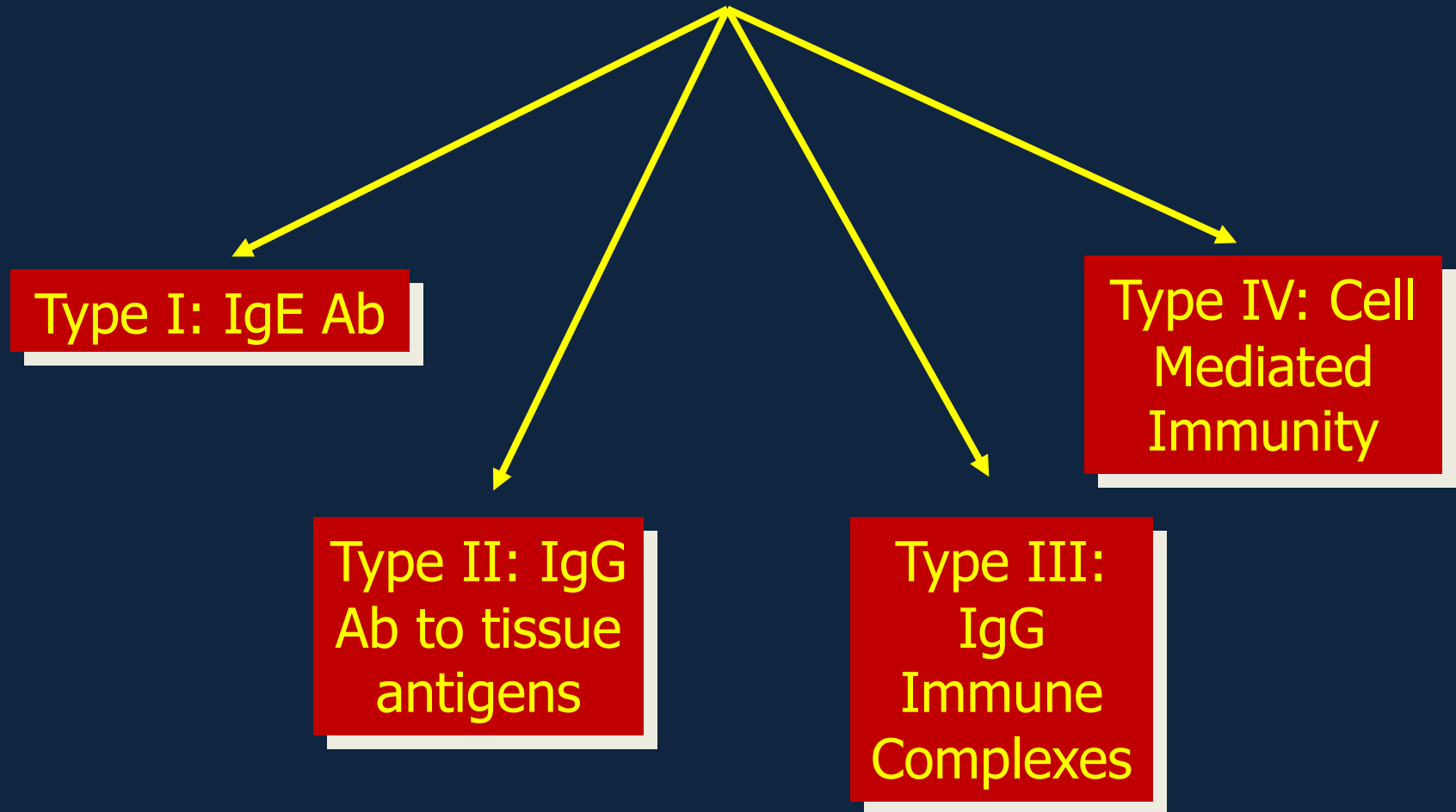
# Objectives

- 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

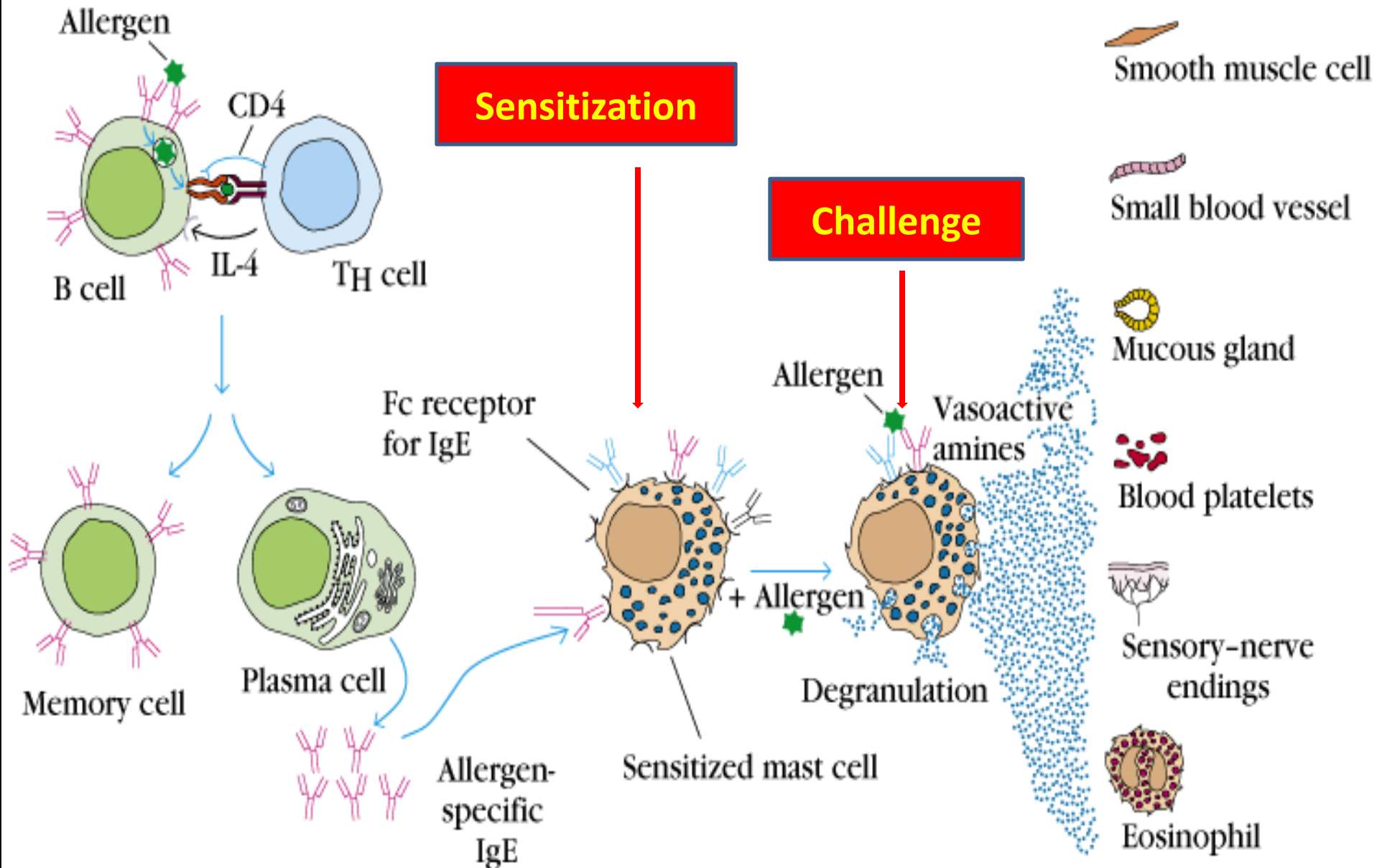
- **Sensitization phase**

First contact with allergens

- **Challenge phase**

Subsequent contact with allergens

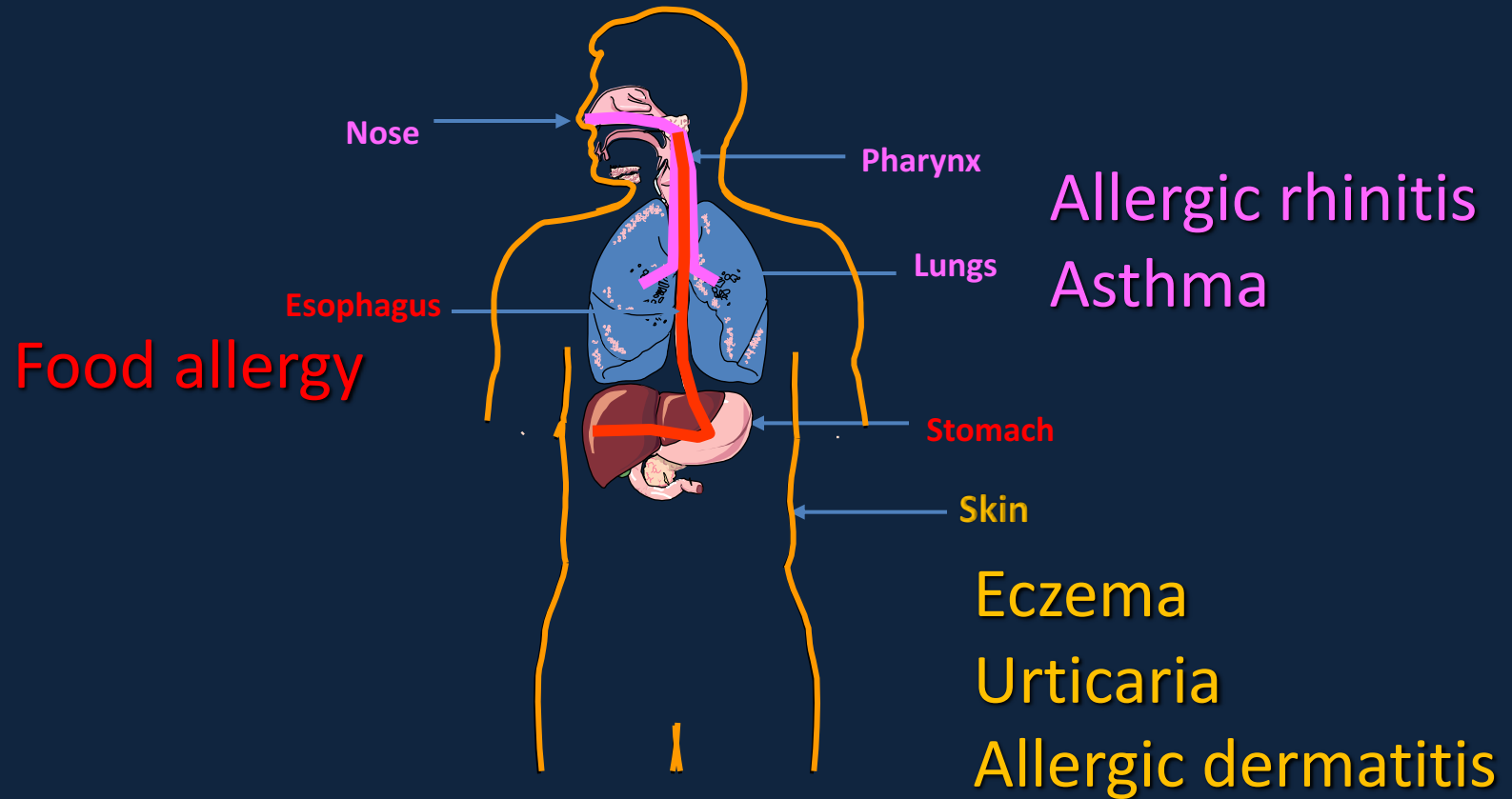
# Type I Hypersensitivity (Immediate)



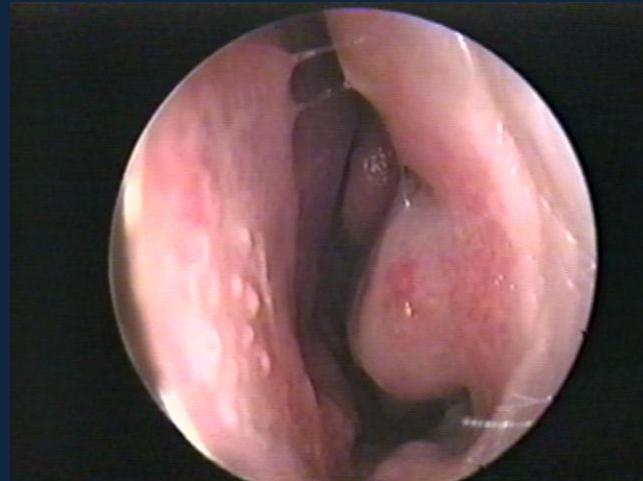
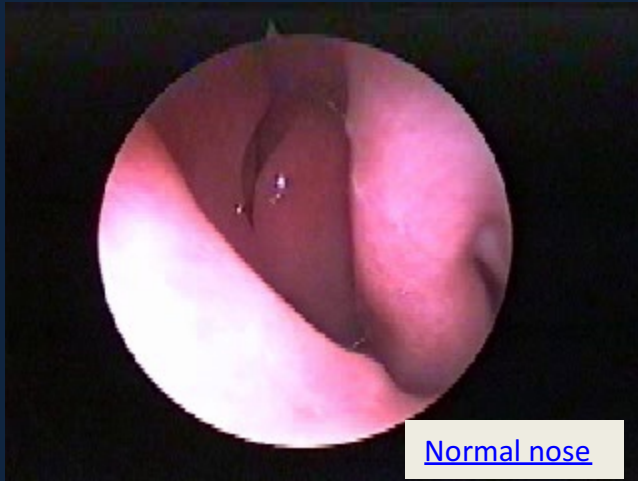
# Primary and Secondary Mediators

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- $\alpha$	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



# Allergy: Rhinitis, Eczema & Conjunctivitis



## \* Injected allergens:

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

→ Systemic inflammation

→ Anaphylactic shock  
(life - threatening)



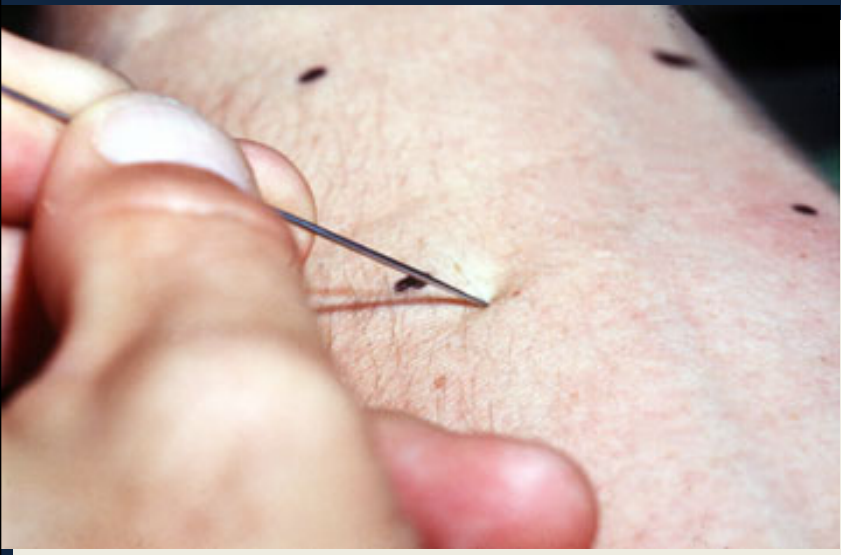
## ❖ Anaphylactoid reactions:-

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*  
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# Type II Hypersensitivity Reactions

- Features:-

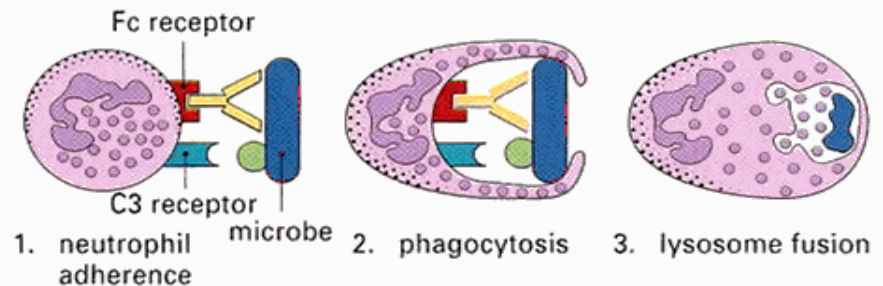
- IgG (or IgM)
  - Antigens: bound to cell membranes
    - (Self antigens)
  - Exogenous antigens (microbial)
- Complement activation (Invariable)



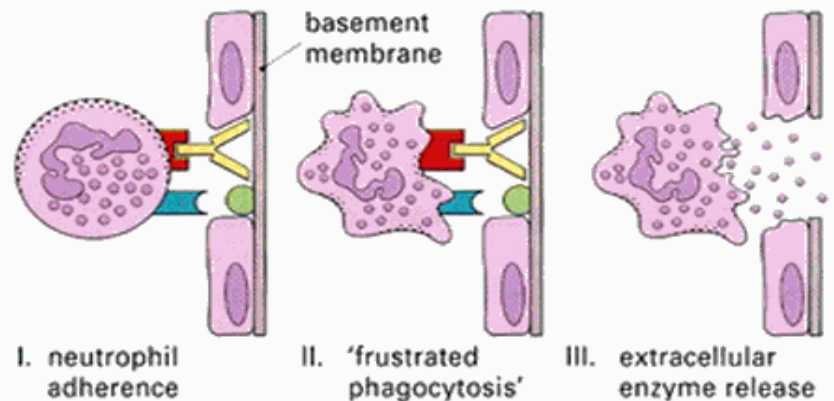
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## Type II Damage

Normal antimicrobial action

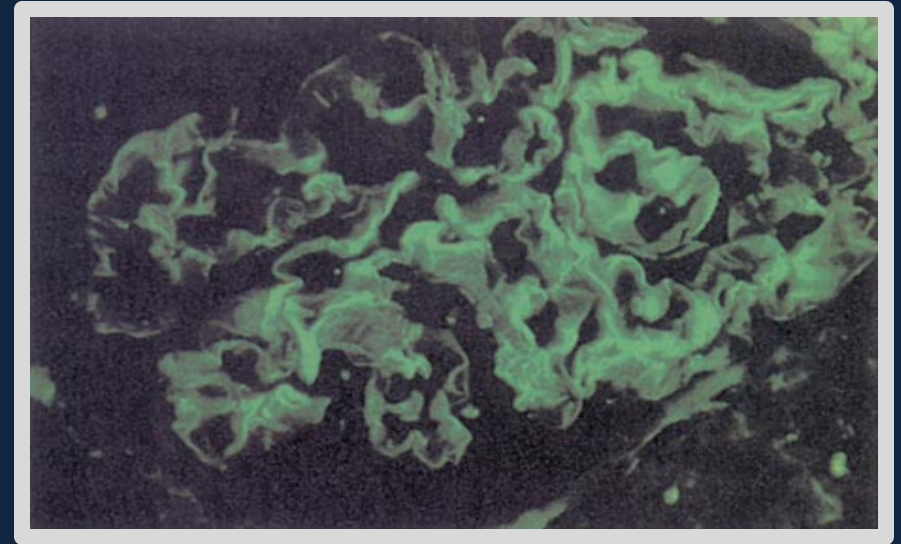


Type II hypersensitivity reaction



## 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

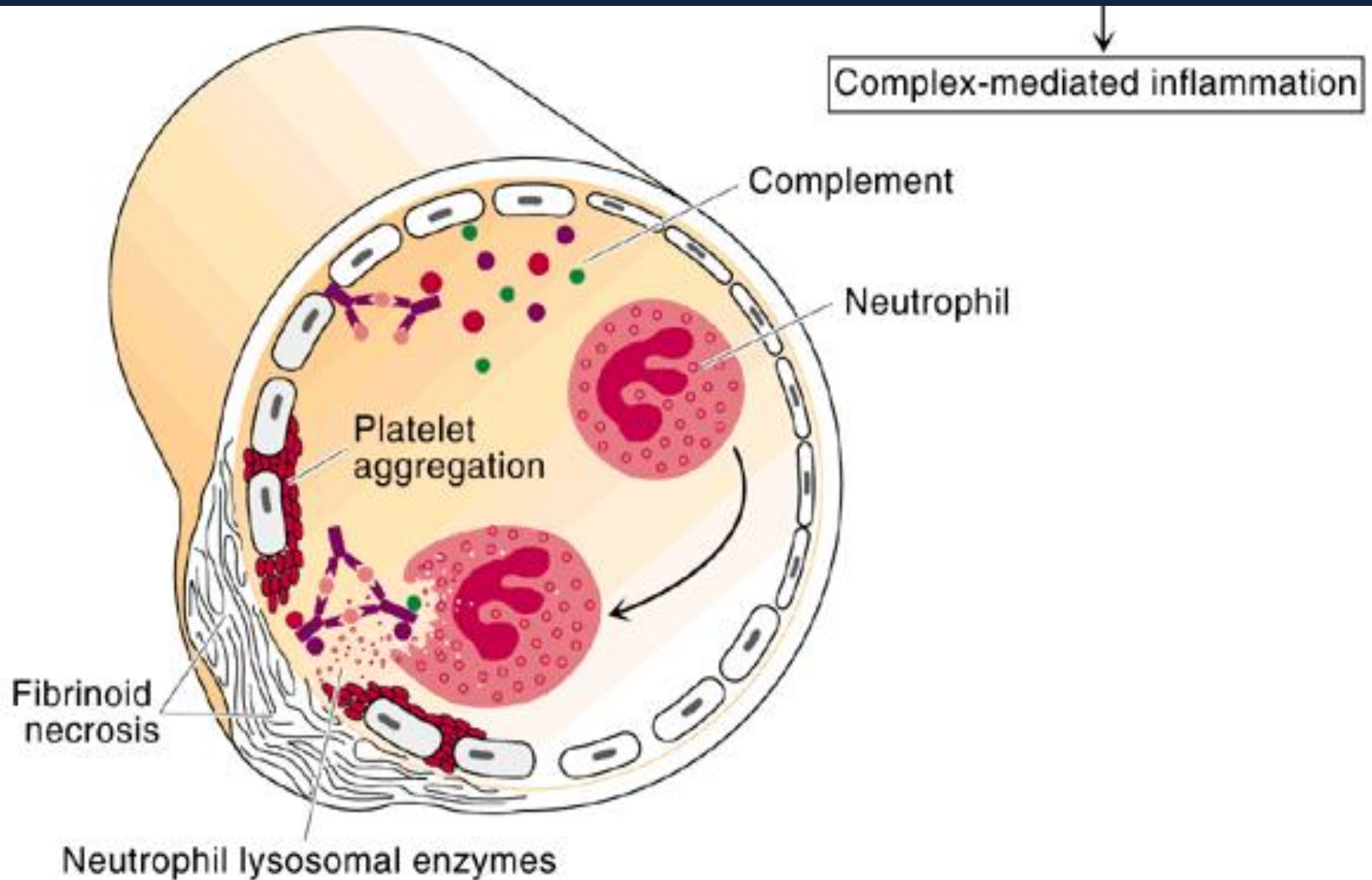


- Complement activation



- Attraction of inflammatory cells

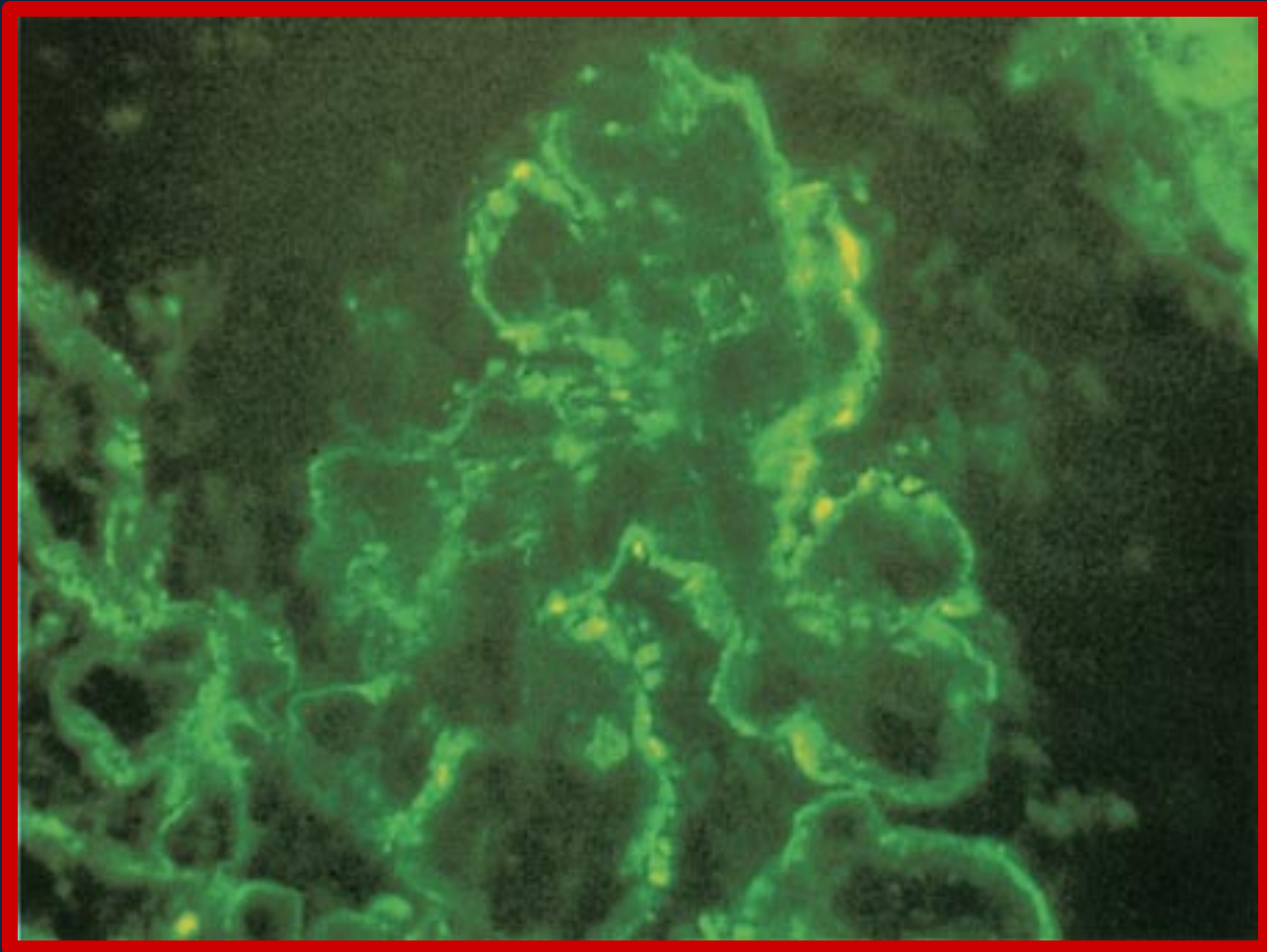
# Type III Reactions



# Type III Hypers. Reactions

Clinical examples:

Glomerulonephritis: Rheumatoid arthritis, SLE



# Diagnosis of Type III Hypers. Reactions

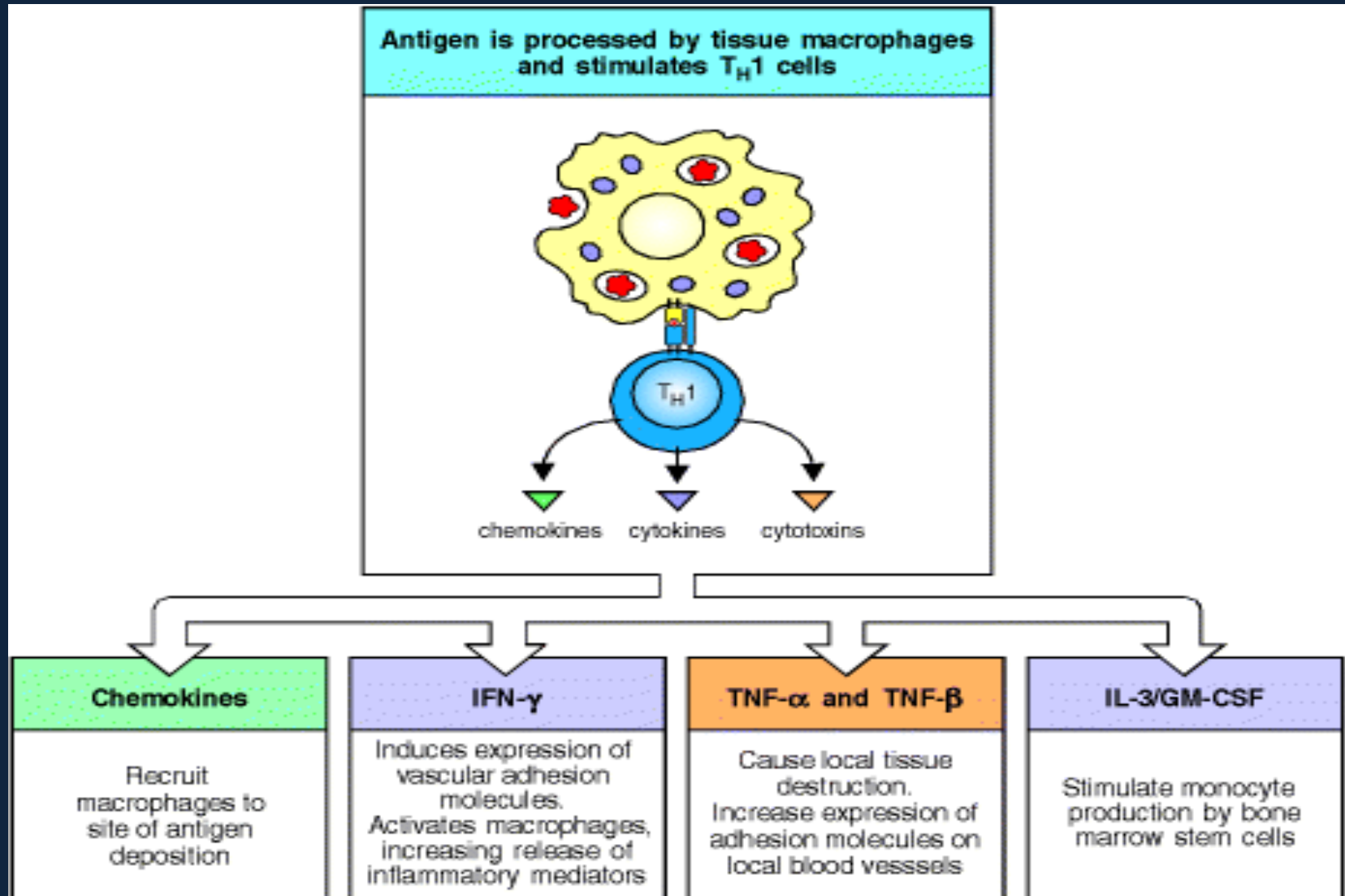
Demonstration of specific immune  
complexes in the blood or tissues by:  
Immunofluoresence



# 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



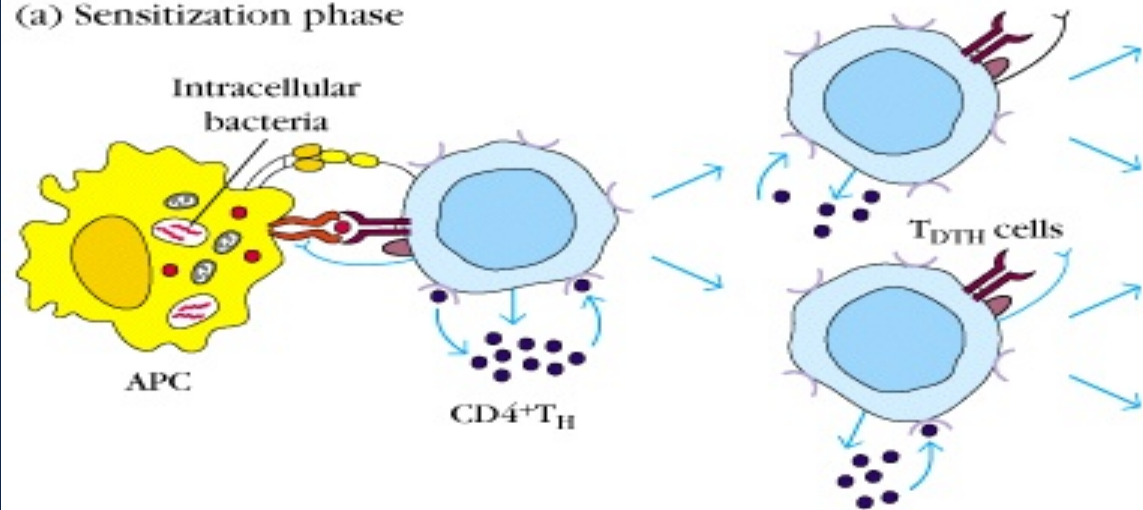
# Development of DTH Response

Sensitization phase:  
1-2 week period

Effector phase:  
24-72 hours

Effector cells  
(activated macs)  
act non-specifically

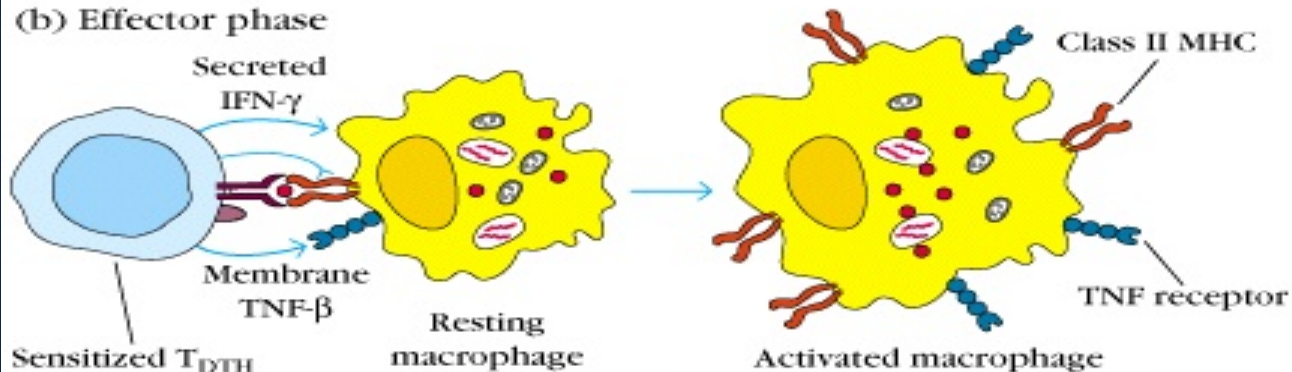
(a) Sensitization phase



Antigen-presenting cells:  
Macrophages  
Langerhans cells

T<sub>DTH</sub> cells:  
T<sub>H</sub>1 cells (generally)  
CD8<sup>+</sup> cells (occasionally)

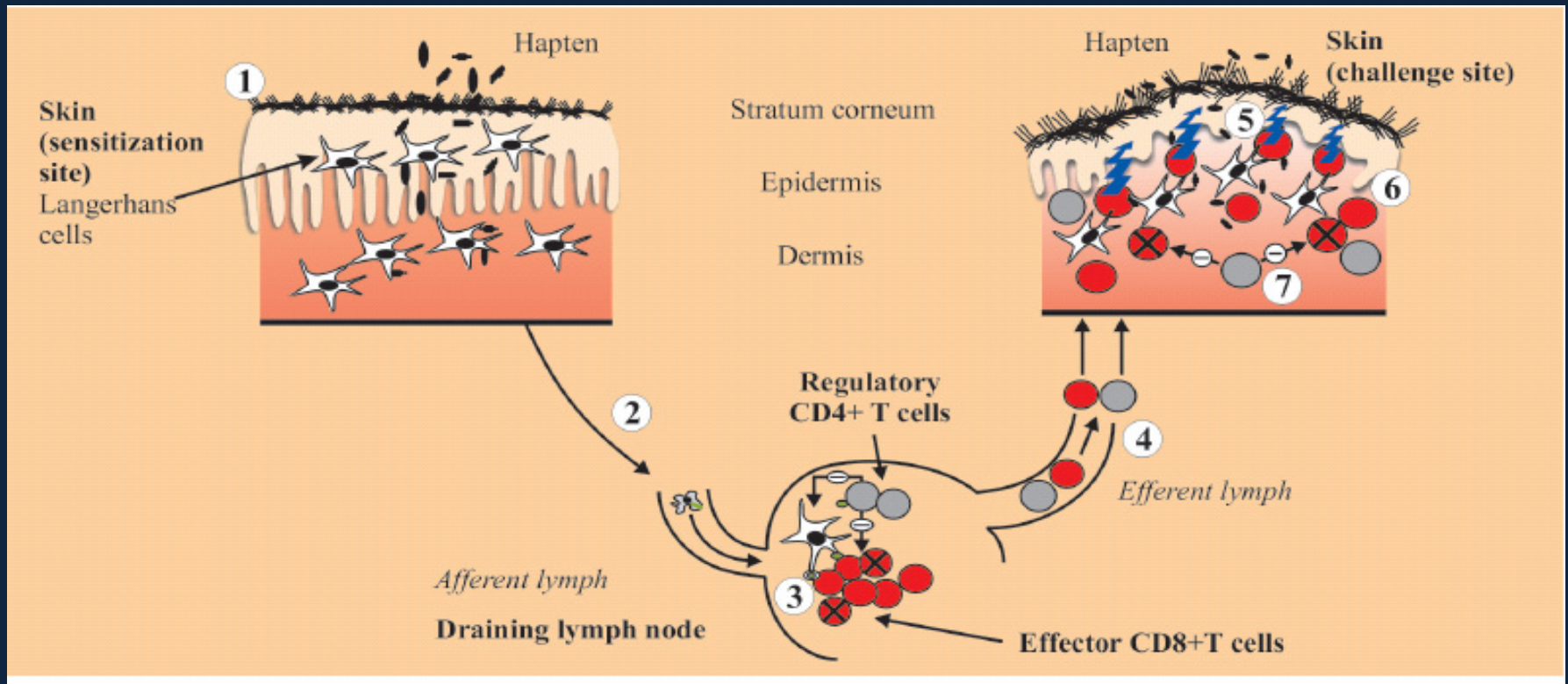
(b) Effector phase



T<sub>DTH</sub> secretions:  
Cytokines: IFN-γ, TNF-β, IL-2,  
IL-3, GM-CSF  
Chemokines: IL-8, MCAF, MIF

Effects of macrophage activation:  
↑ Class II MHC molecules  
↑ TNF receptors  
↑ Oxygen radicals  
↑ Nitric oxide

# Pathophysiology of Contact dermatitis.

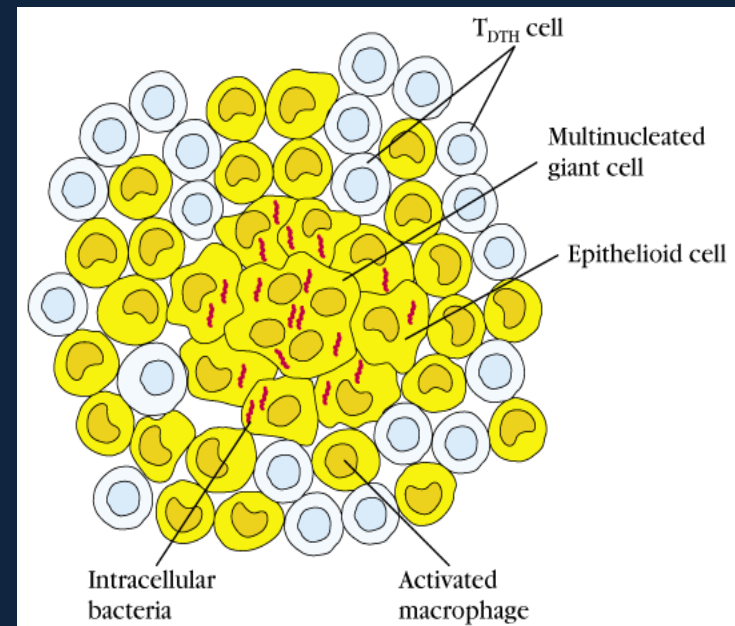


# Type IV clinical examples:

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.