Hypersensitivity Reactions

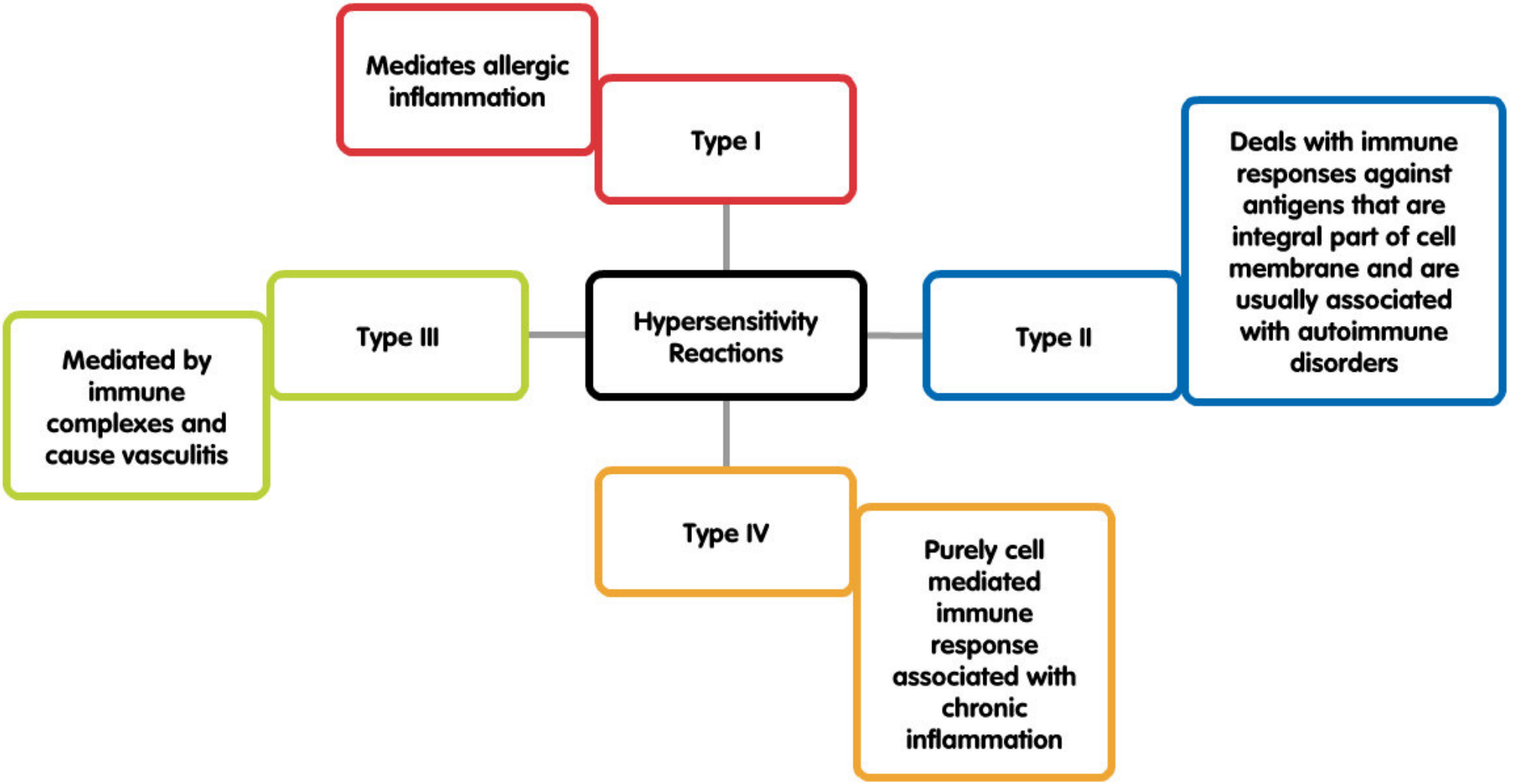
Lecture 5

Objectives

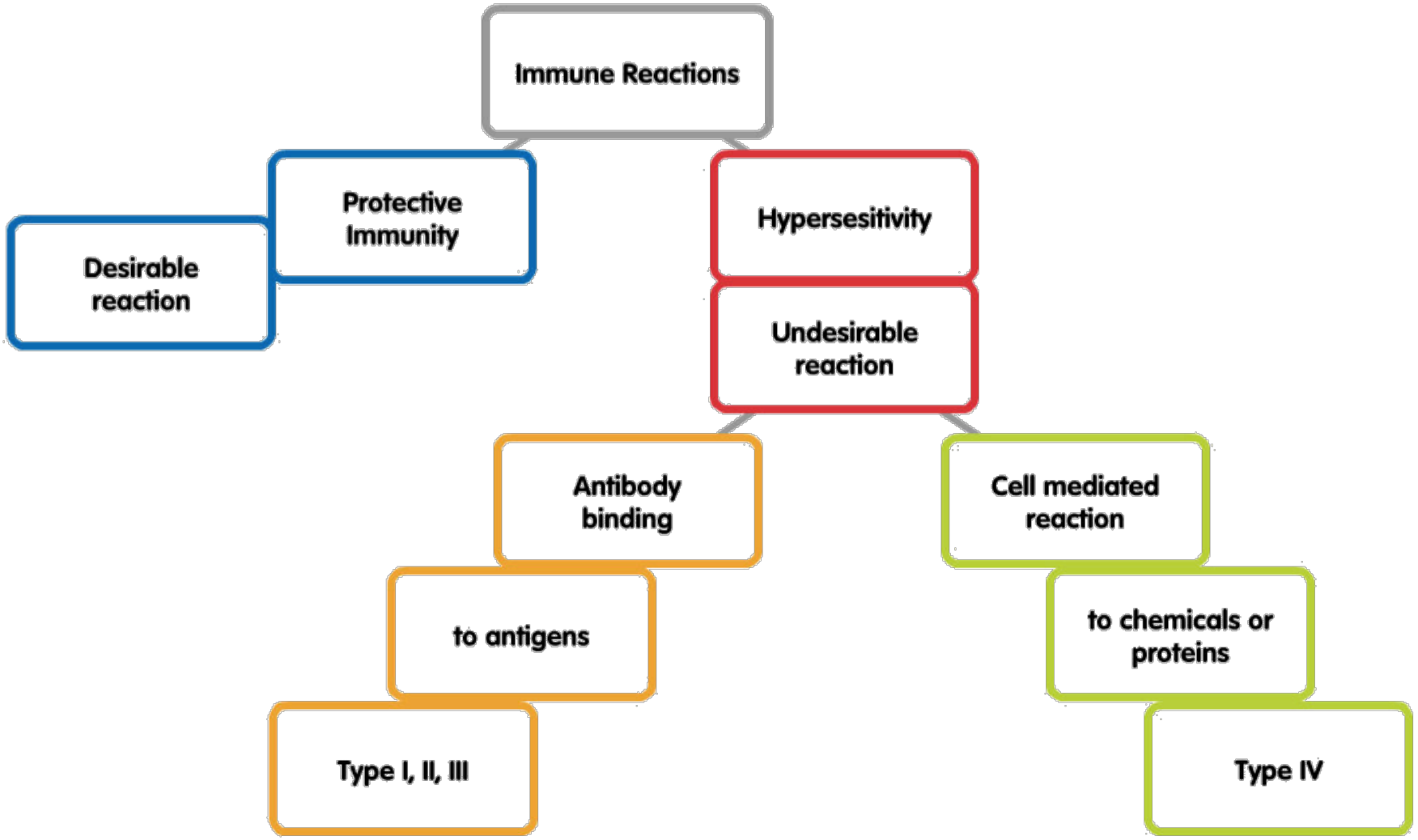
- **Hypersensitivity reactions are over and excessive immune responses that can be harmful to body in four different ways.**
- **Be familiar with all four types.**

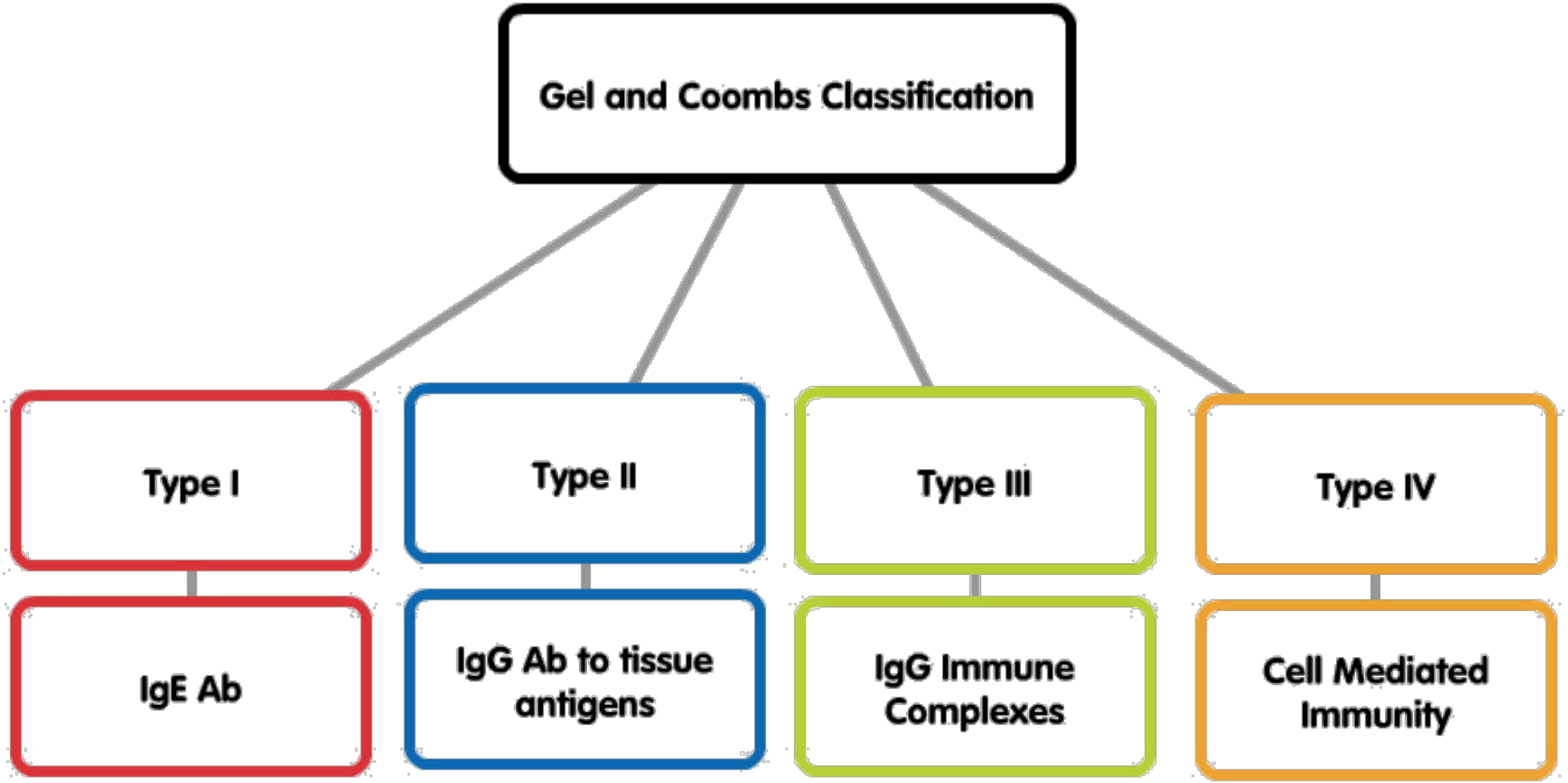
Immuno Hypersensitivity Reactions

http://www.youtube.com/watch?v=E935RDEA5Qg


Hypersensitivity Reactions
Type I
Mediates allergic inflammation
Type II
Deals with immune responses against antigens that are integral part of cell membrane and are usually associated with autoimmune disorders
Type III
Mediated by immune complexes and cause vasculitis
Type IV
Purely cell mediated immune response associated with chronic inflammation

What is Hypersensitivity?




Gel and Coombs Classification
Type I
IgE Ab
Type II
IgG Ab to tissue antigens
Type III
IgG Immune Complexes
Type IV
Cell Mediated Immunity

Type I: Immediate Hypersensitivity

- Most people will not react to these allergens but some individuals "***atopic***" respond by producing large amounts of IgE.
- Non-allergic individuals respond to these allergens by producing IgG antibodies.

Also termed as:

- Immediate hypersensitivity
- Anaphylactic reactions
- Allergic reactions (occurs with mins - hrs)

Features:

- **Antibody type:** IgE
- **Cellular components**: mast cells, basophils, eosinophils.
- **Antigens (Allergens):** antigens with low molecular weight & high solubility.

Antigens:

- Pollens
- Dust mites
- Animal Dander
- Nuts
- Shellfish
- Various drugs

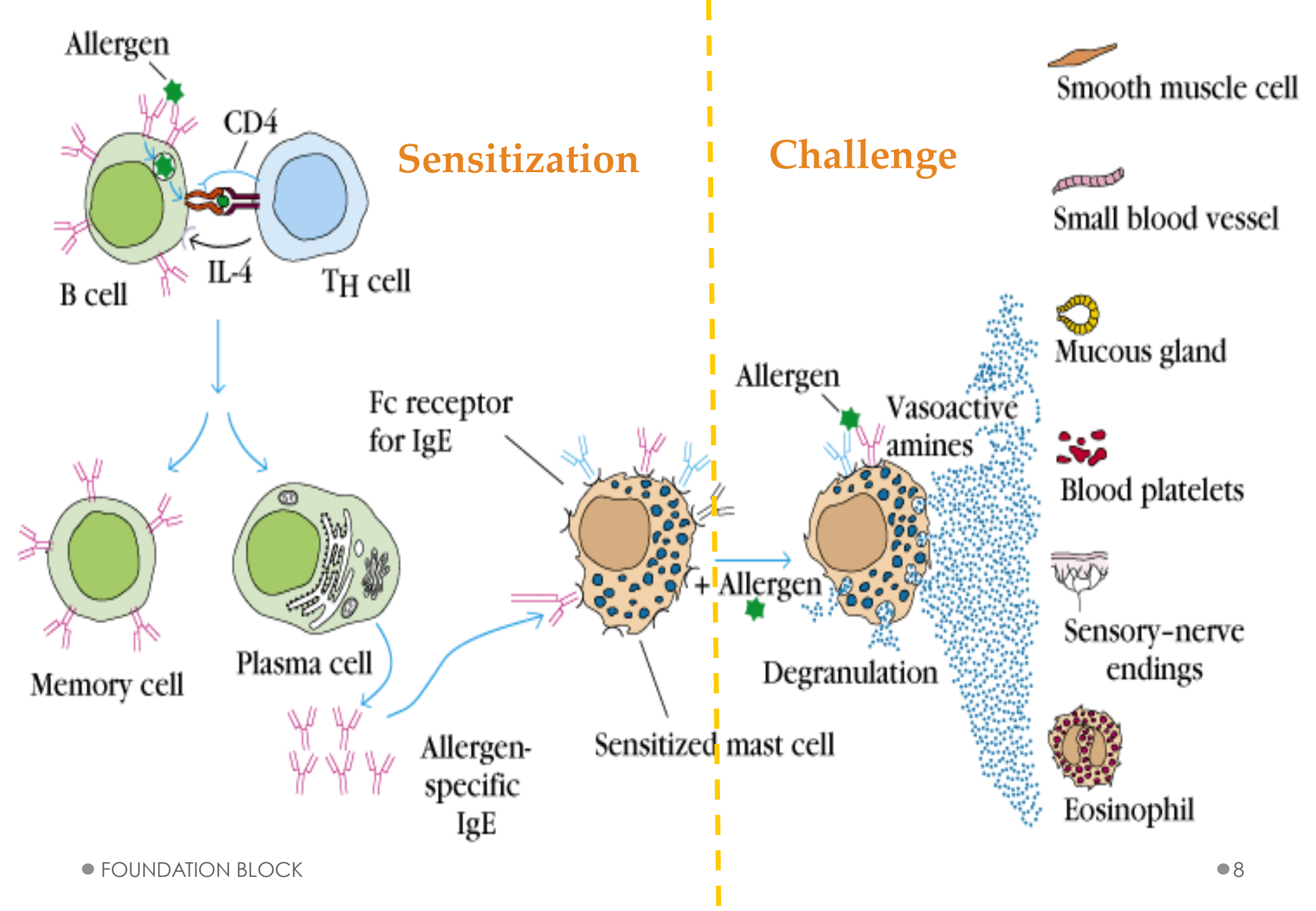
Reactions occur in 2 phases:

1. **Sensitization phase**

   First contact with allergens (antigens).

2. **Challenge phase**

   Subsequent contact with allergens.

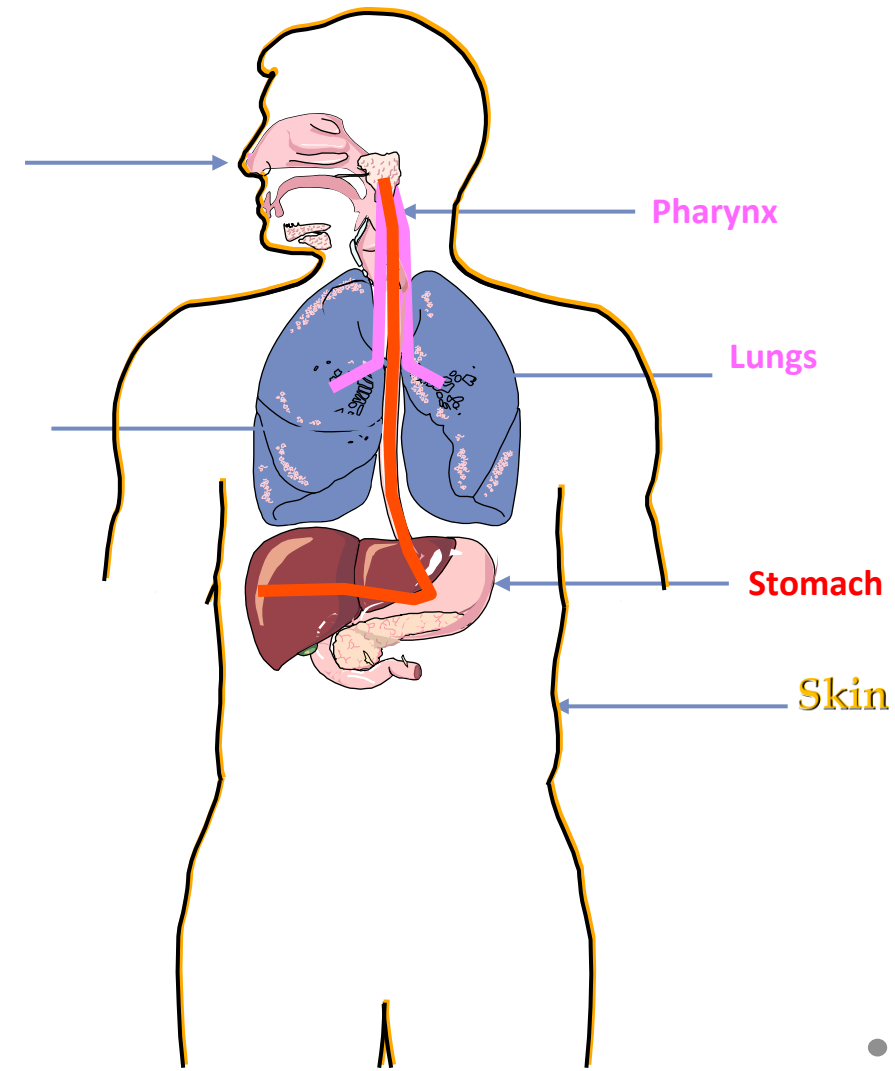

Allergen
CD4
IL-4
B cell
TH cell
Sensitization
Challenge
Smooth muscle cell
Small blood vessel
Mucous gland
Blood platelets
Sensory-nerve endings
Eosinophil
Memory cell
Plasma cell
Fc receptor for IgE
Allergen-specific IgE
Sensitized mast cell
+ Allergen
Allergen
Vasoactive amines
Degranulation

Primary & Secondary Mediators: Important

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:

- **Respiratory System:**
  - Allergic rhinitis
  - Asthma
- **Digestive System:**
  - Food allergy
- **Skin:**
  - Eczema
  - Urticaria
  - Allergic dermatitis



Injected allergens:

Bee sting venom enters the blood stream

- Systemic inflammation
- Anaphylactic shock (life - threatening)

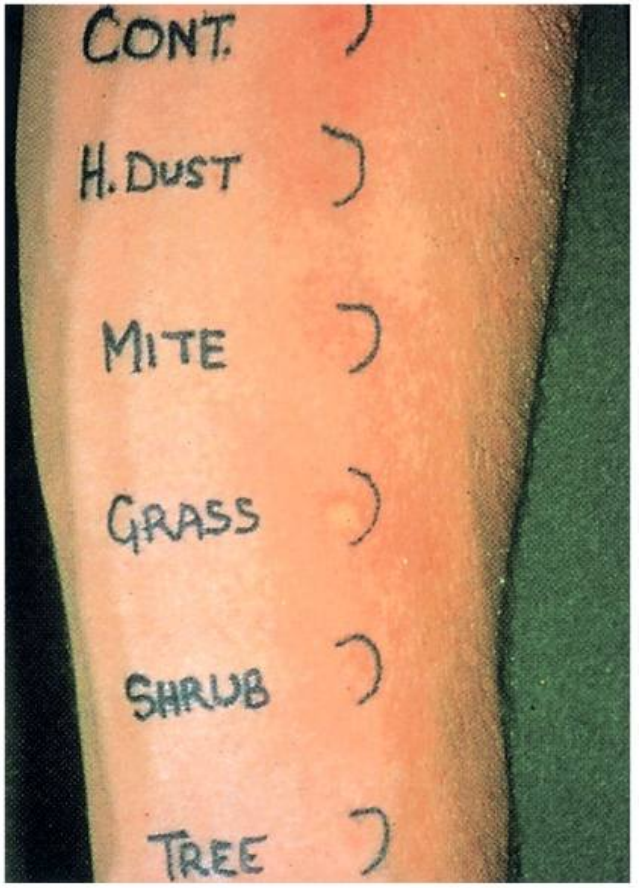


Figure 15-10
Kuby IMMUNOLOGY, Sixth Edition

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)

Type II: Hypersensitivity Reactions

Features:

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

Clinical examples:

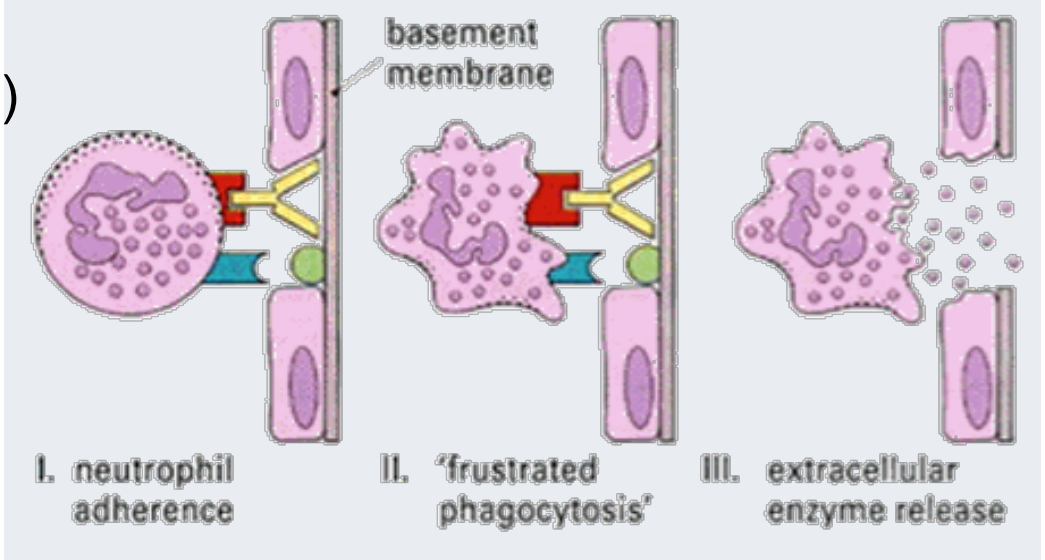
- Glomerulonephritis

(anti-glomerular basement membrane)

- Mis-matched blood transfusion

Diagnosis:

Detection of antibodies and antigens by Immunofluorescence in tissue biopsy specimens **e.g.** kidney, skin.



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).

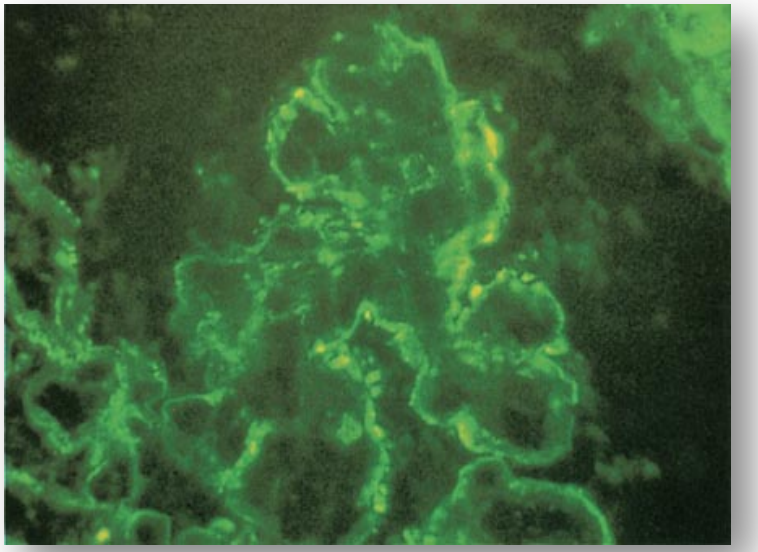
Type III Hypersensitivity (immune–complex mediated):

Type III H/S: Clinical examples

Glomerulonephritis: Rheumatoid arthritis, SLE

Diagnosis

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

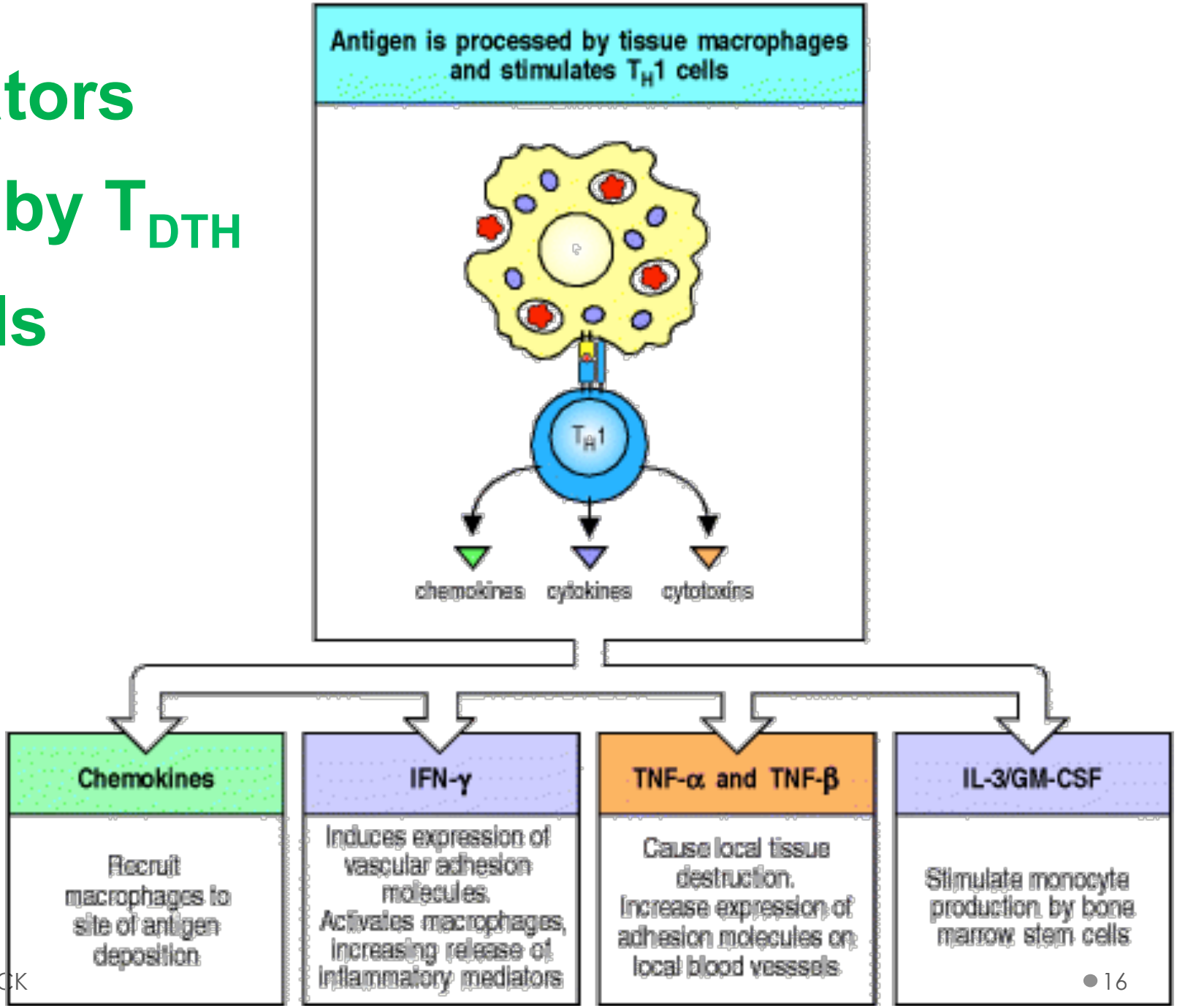


Type IV hypersensitivity reactions (Delayed Hypersensitivity)

Features:

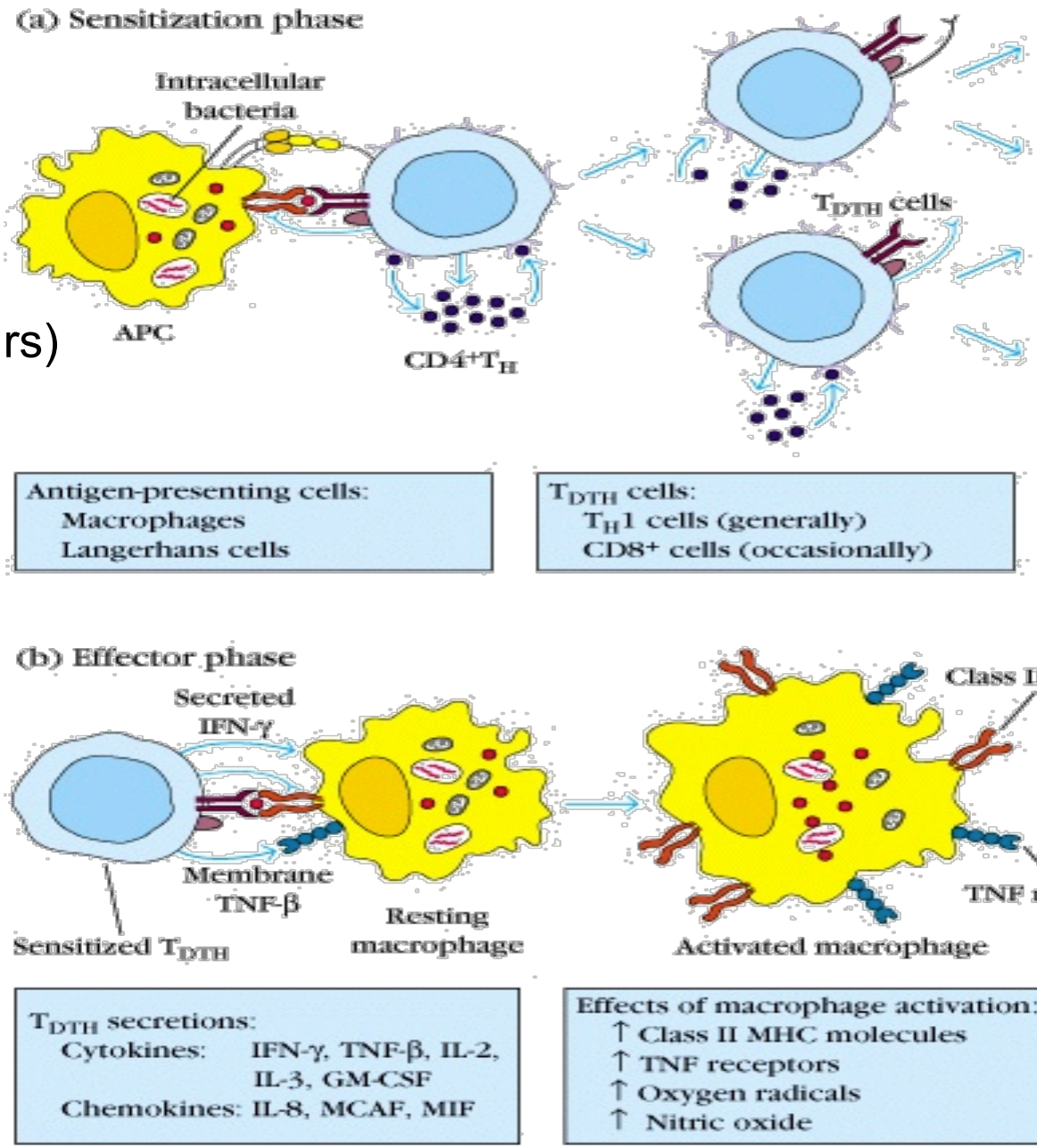
- Cell mediated immune response
- Antigen dependent T cell (CD4 generally and CD8 occasionally) activation via MHC Class I or II
- Activated macrophages
- Delayed onset (2-4 days)
- Abnormal cellular response
- (Granuloma formation)

Mediators released by T_{DTH} cells

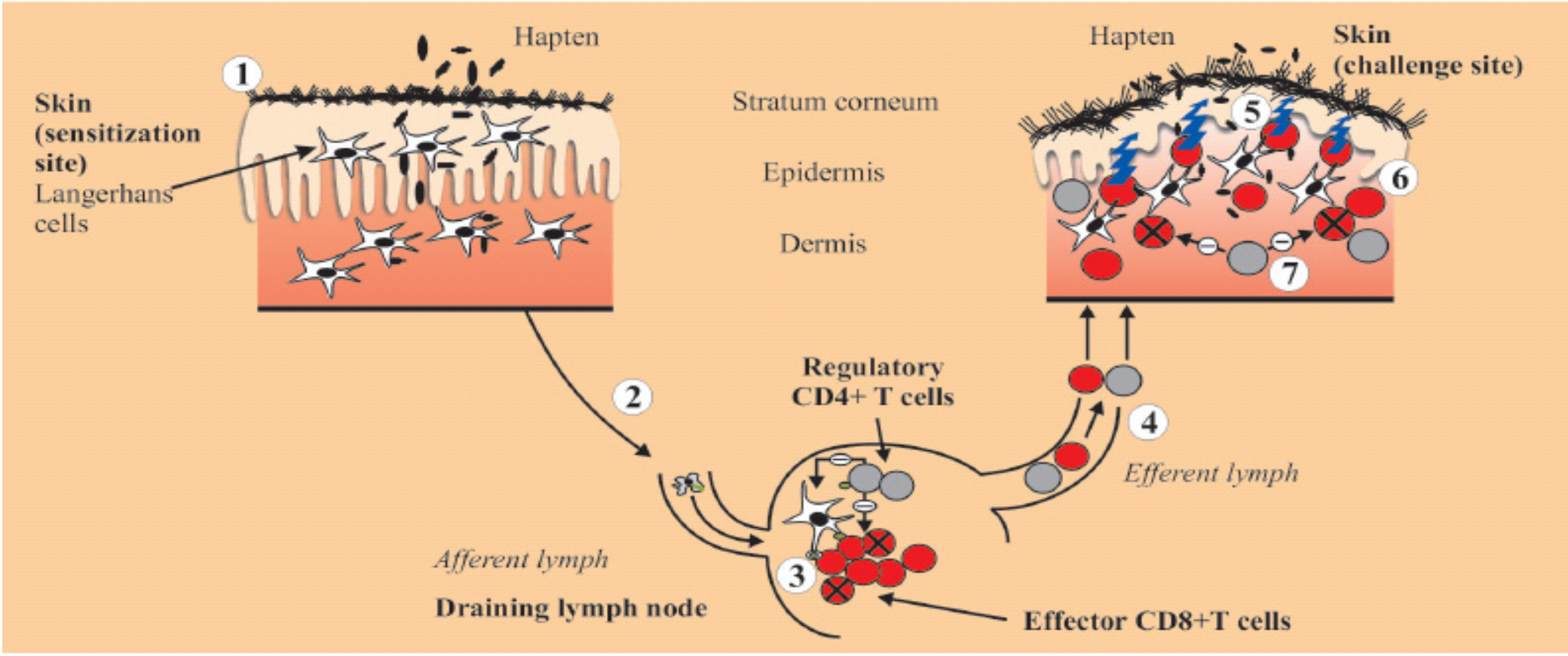


Development of DTH Response:

- Sensitization phase: (1-2 week period)
- Effector phase: (24-72 hours)
- Effector cells
  (activated macs)
  act non-specifically

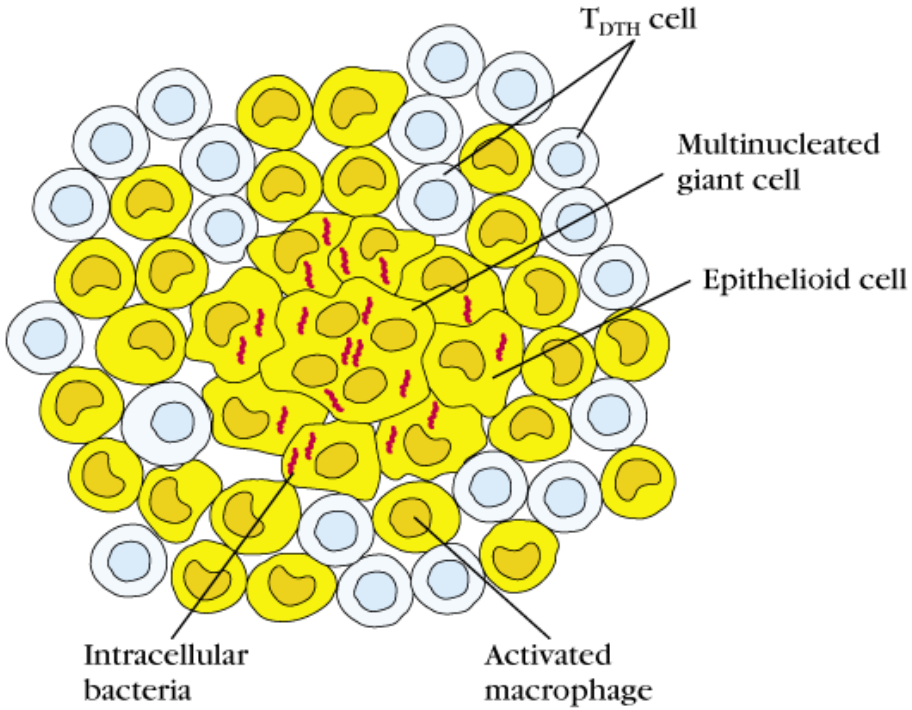


Pathophysiology of allergic contact dermatitis



Type IV clinical examples:

- Allergic contact dermatitis
- TB granuloma (persistent antigen)



Diagnosis (Type IV)

- Delayed skin test (Mantoux test)
- Patch test (Contact dermatitis)
- Lymphocyte transformation test

Allergy Skin Patch Test:

Remember

1. Type I (IgE), II (IgG) and III (IgG) hypersensitivity reactions are mediated by antibodies.
2. Type IV hypersensitivity reaction is a cell mediated immune response.
3. Hypersensitivity reactions are undesirable, excessive, and aberrant immune responses associated with disorders such as allergy, autoimmunity and chronic inflammation.