



MEDICINE
KING SAUD UNIVERSITY

Foundation Block

Lecture Five

Hypersensitivity

IMMUNOLOGY

4 3 6 ' s T E A M W O R K

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

- **Important.**
- Extra notes.
- **Females notes**
- **Males notes.**

What is hypersensitivity?

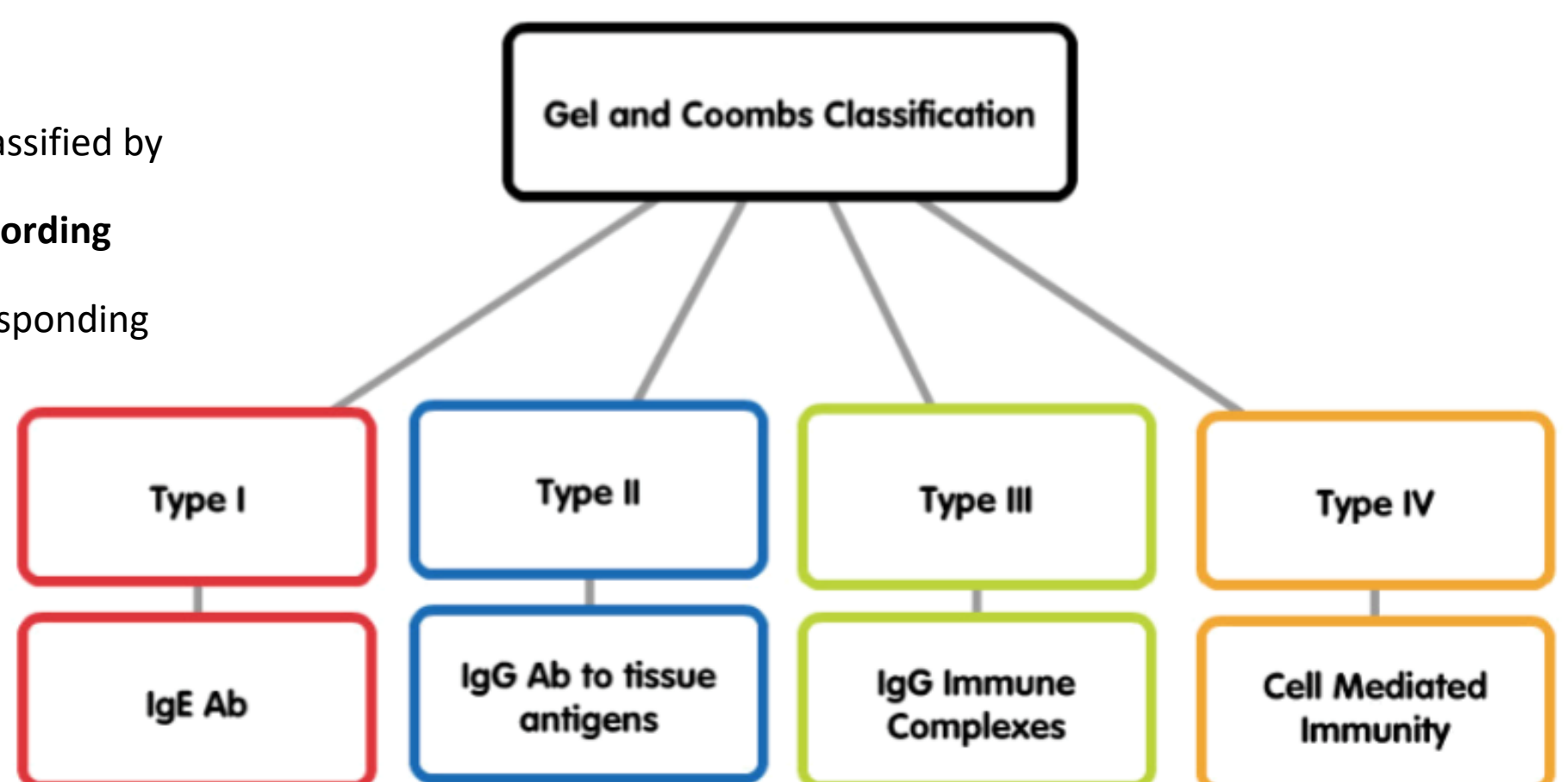
Protective immunity: desirable reaction.

Hypersensitivity: **undesirable** damaging reaction produced by excessive immune reactions.

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

Types of hypersensitivity:

4 Types of hypersensitivity responses are classified by GEL AND COOMBS (names of scientists) according to the responding **mechanisms**, NOT the responding antigens:



*From 433 team

Type I:

1- Also termed as:

- **Immediate Hypersensitivity.**
- Allergic reactions. (e.g. asthma and eczema)
- Anaphylactic reactions: **severe** and **rapidly progressing** systemic forms which can be quickly **life threatening**. (causes vasodilation and hypovolemia which causes heart stop then death)

2- 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.

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

4- **Features:**

- **Antibody type:** IgE
- **Cellular components:** Mast cells, basophiles & eosinophils
- **Antigens:** Also known as **allergens** (antigens with low molecular weight & highly soluble).

5- **(Occurs within minutes to hours).**

Allergens:

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



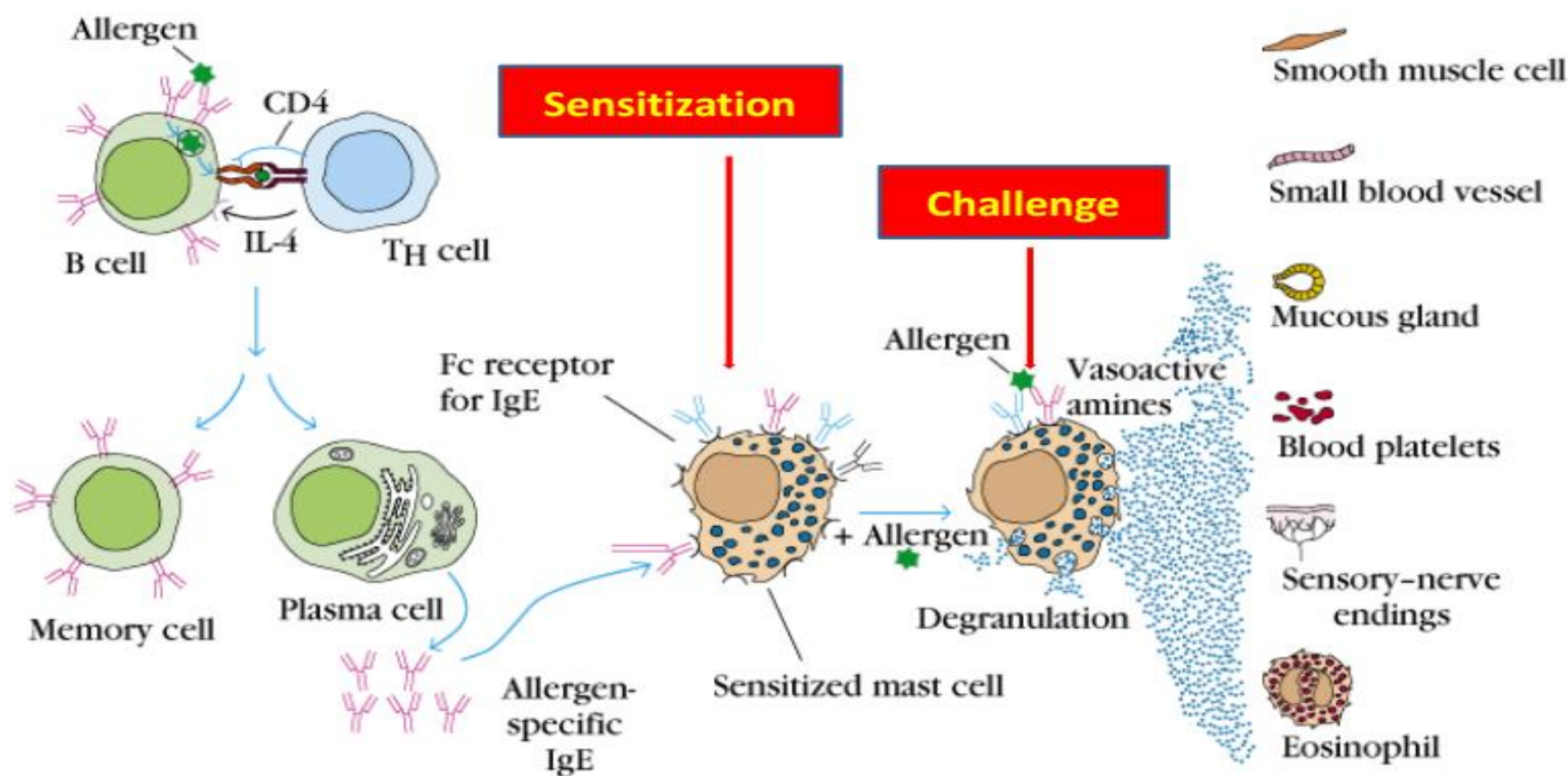
Type I reactions occur in **two** phases

1- Sensitization

2- Challenge

First contact with allergens

Subsequent contact with allergens



Sensitization phase:

Antigen presenting cell (APC) takes the antigen, processes it, degrades it, then presents it with association of class II MHC.

T Helper 2 comes in contact with the B Cell and turns it into a Plasma Cell or a Memory Cell. Plasma Cells then produce IgE antibodies specific for that type of allergen. Then, the IgE antibody attaches to a Mast Cell which has receptors for this antibody. Mast Cells are said to be synthesized when they are bound to an antibody.

Challenge phase:

Occurs when we have a subsequent encounter with the similar antigen it will bind to the Ig(Antigen) and lead to degranulation of the mast cells making it produce a large amount of its mediators which cause what we see in allergic patient (sneezing, muscle contraction, mucus production,..etc) (subsequent contact with allergens)

Primary and Secondary Mediators

Mediator

Effects

PRIMARY

Histamine, heparin

Serotonin

Eosinophil chemotactic factor (ECF-A)

Neutrophil chemotactic factor (NCF-A)

Proteases

Increased vascular permeability; smooth-muscle contraction

Increased vascular permeability; smooth-muscle contraction

Eosinophil chemotaxis

Neutrophil chemotaxis

Bronchial mucus secretion; degradation of blood-vessel basement membrane; generation of complement split products

SECONDARY

Platelet-activating factor

Leukotrienes (slow reactive substance of anaphylaxis, SRS-A)

Prostaglandins

Bradykinin

Cytokines

IL-1 and TNF- α

IL-2, IL-3, IL-4, IL-5, IL-6, TGF- β , and GM-CSF

Platelet aggregation and degranulation; contraction of pulmonary smooth muscles

Increased vascular permeability; contraction of pulmonary smooth muscles

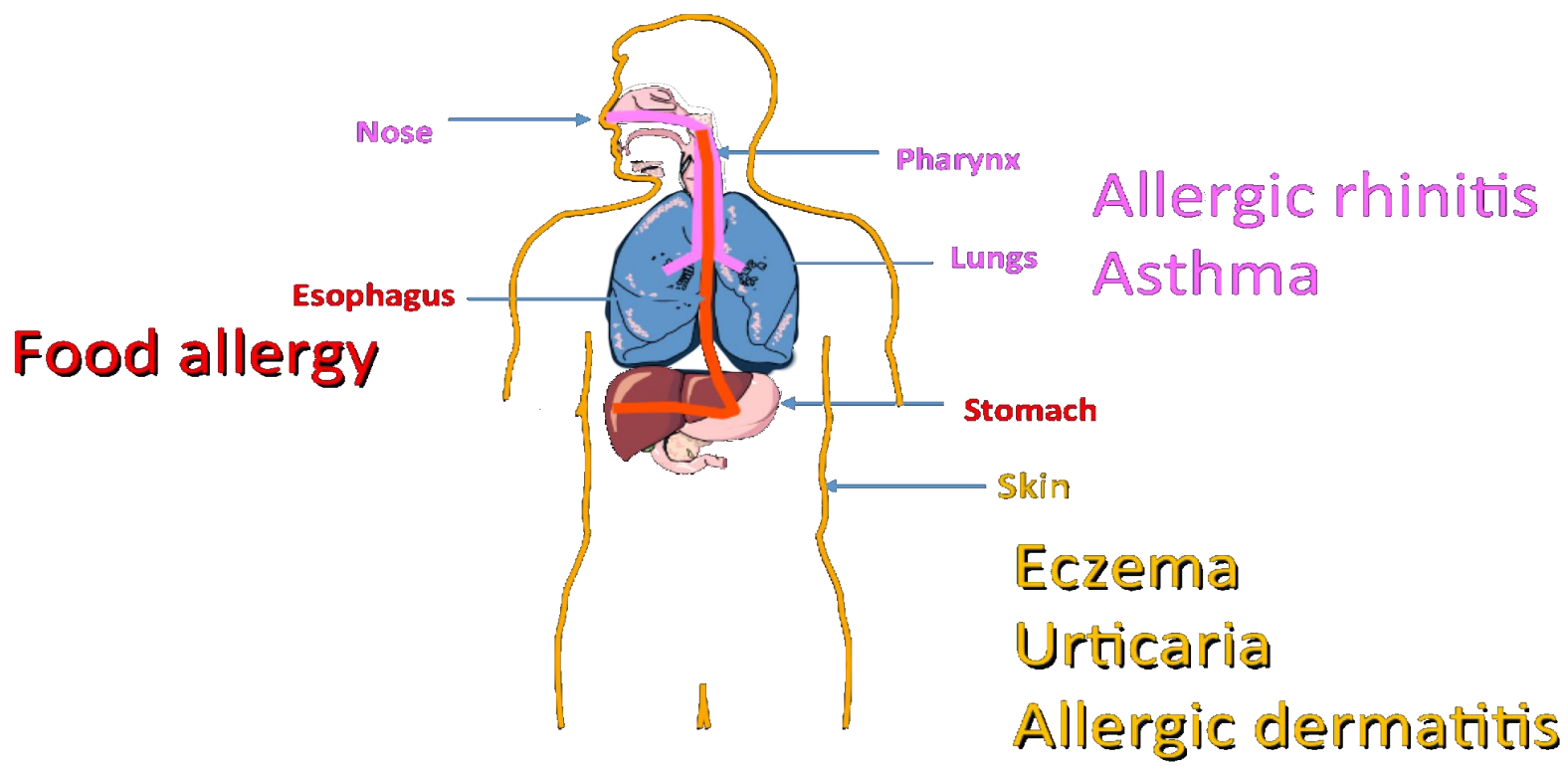
Vasodilation; contraction of pulmonary smooth muscles; platelet aggregation

Increased vascular permeability; smooth-muscle contraction

Systemic anaphylaxis; increased expression of CAMs on venular endothelial cells

Various effects (see Table 12-1)

Allergy is a systemic disorder



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 (SPT)	Specific IgE measurement (RAST)	Elimination / Provocation test (Food allergy)
<p>sterile needle</p> <p>positive test: area becomes red and swollen</p> <p>suspected allergen</p> <p>a number of suspected allergens are tested on the arm at the same time</p>	<p>Team435:</p> <p>radioallergosorbent test (RAST) is a blood test used to determine the substances a subject is allergic to.</p>	<p>Team435:</p> <p>أكثر طريقة تأخذ وقت: يستبعد الطبيب أنواع مختلفة من الطعام الذي قد يسبب الحساسية للشخص، ثم يراقب الطبيب نتائج المريض على مدى أسابيع إلى أن يحدث حساسية فيعرف الطبيب ماذا أكل وما سبب الحساسية</p>

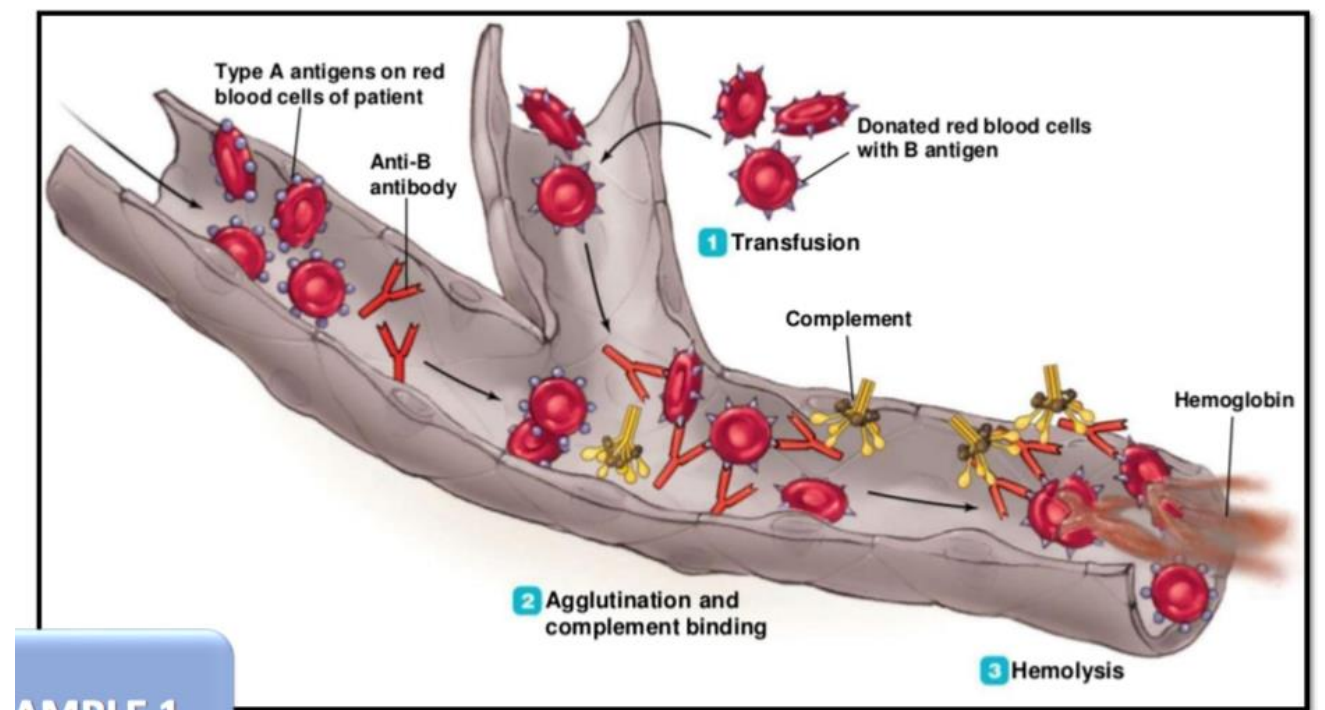
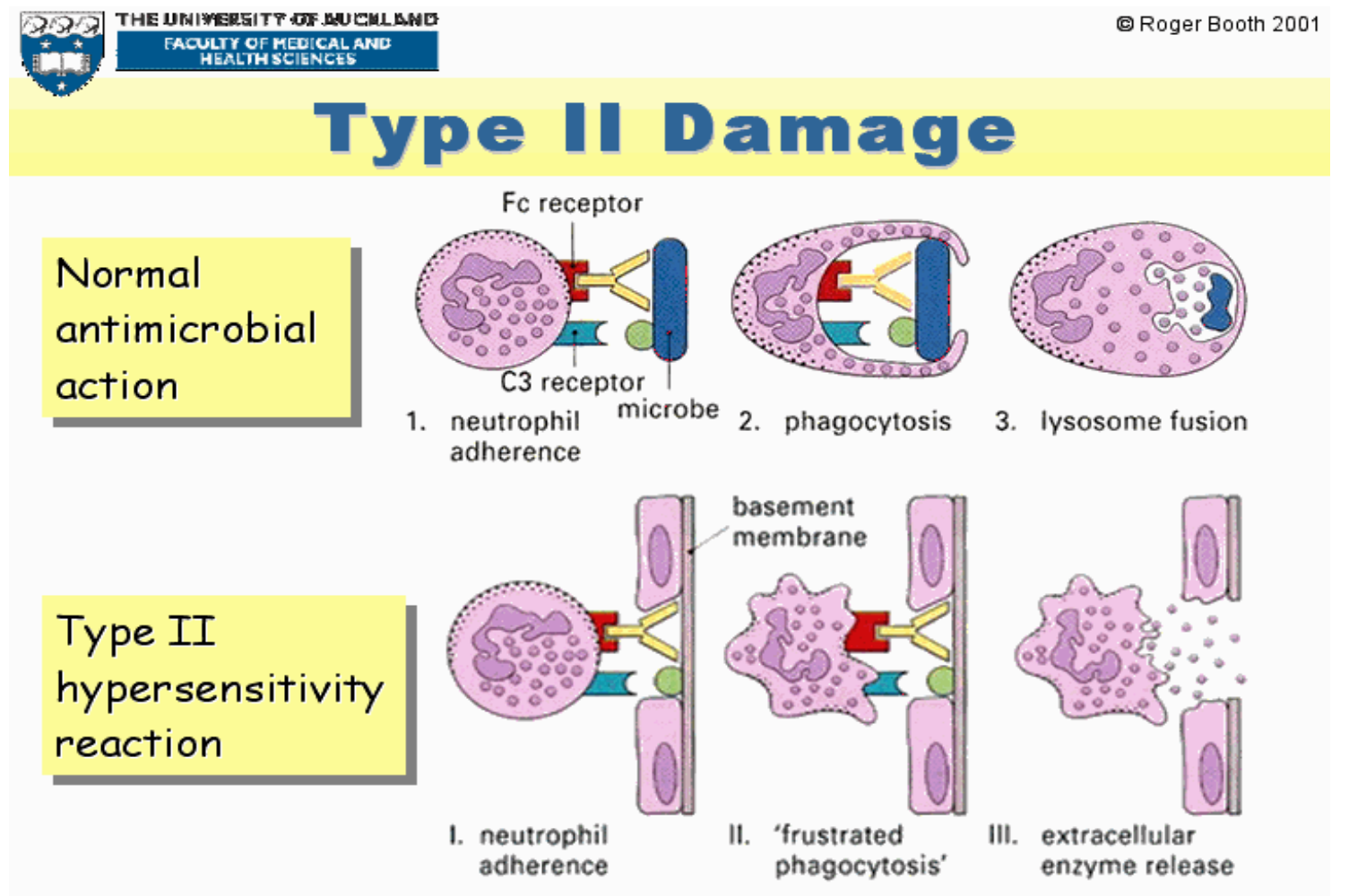
Type II Hypersensitivity Reactions:

Features:

- **IgG** (or **IgM**)
- Antigen:
 1. bound to cell membranes (**Self antigens**)
 2. 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 etc.

Type III: (component of cells)

- When an antigen reacts with an antibody the product they form is called an **immune complex** (**antigen** (here it's soluble) + **antibody** (IgG) + **complement** (C3a, 4a and 5a) = **immune complex** = **inflammatory response**) which is capable of inducing an inflammatory response.
- Immune complexes are (**found in the zones of filtration**) deposited in tissues like kidneys (nephritis), joints (arthritis) or blood vessels (vasculitis).

Features and Mechanism:

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



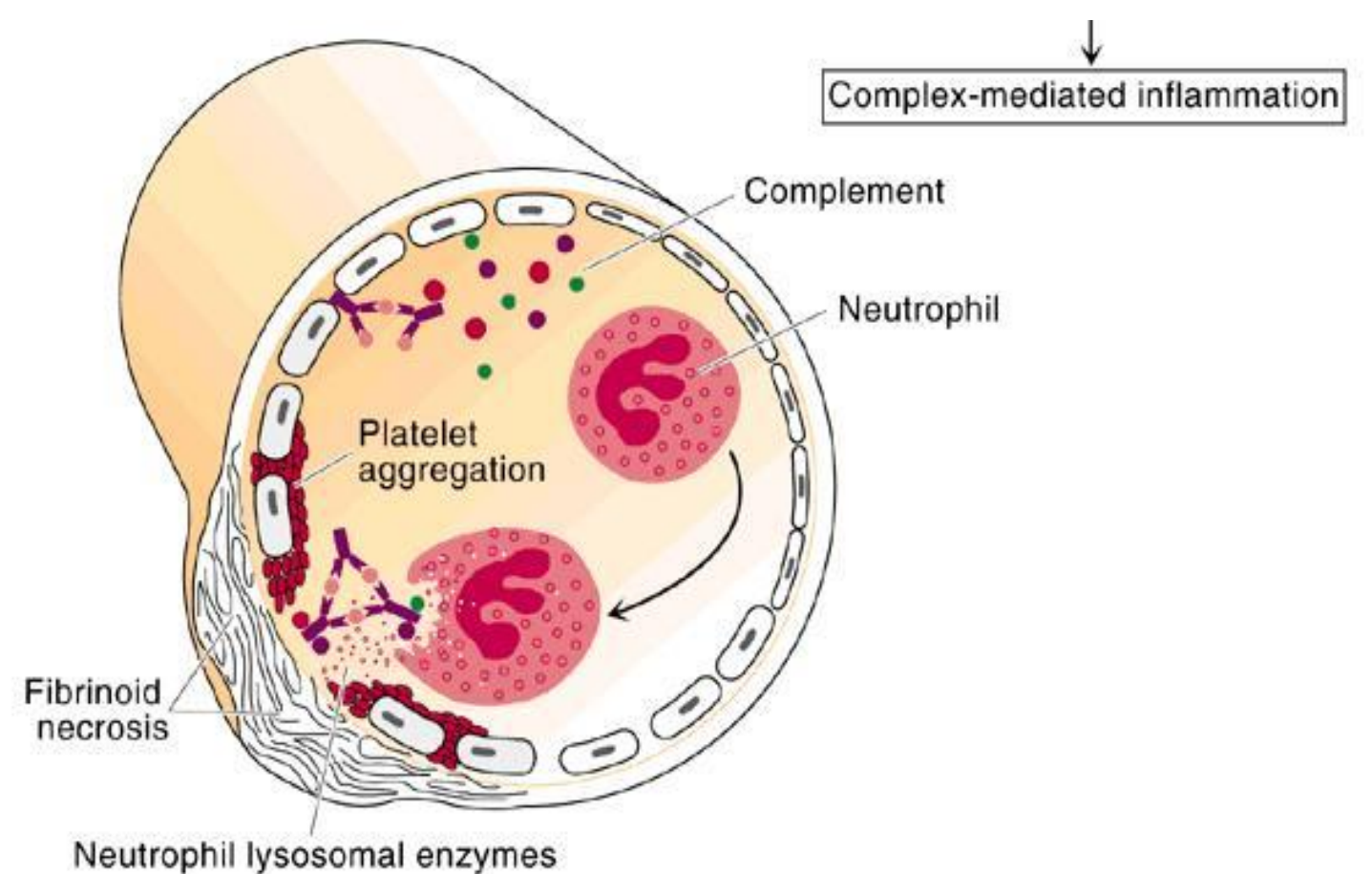
Immune - Complex formation



Complement activation



Attraction of inflammatory cells



Clinical examples:

- Glomerulonephritis: Rheumatoid arthritis, SLE (systemic lupus erythematosus)

Diagnosis:

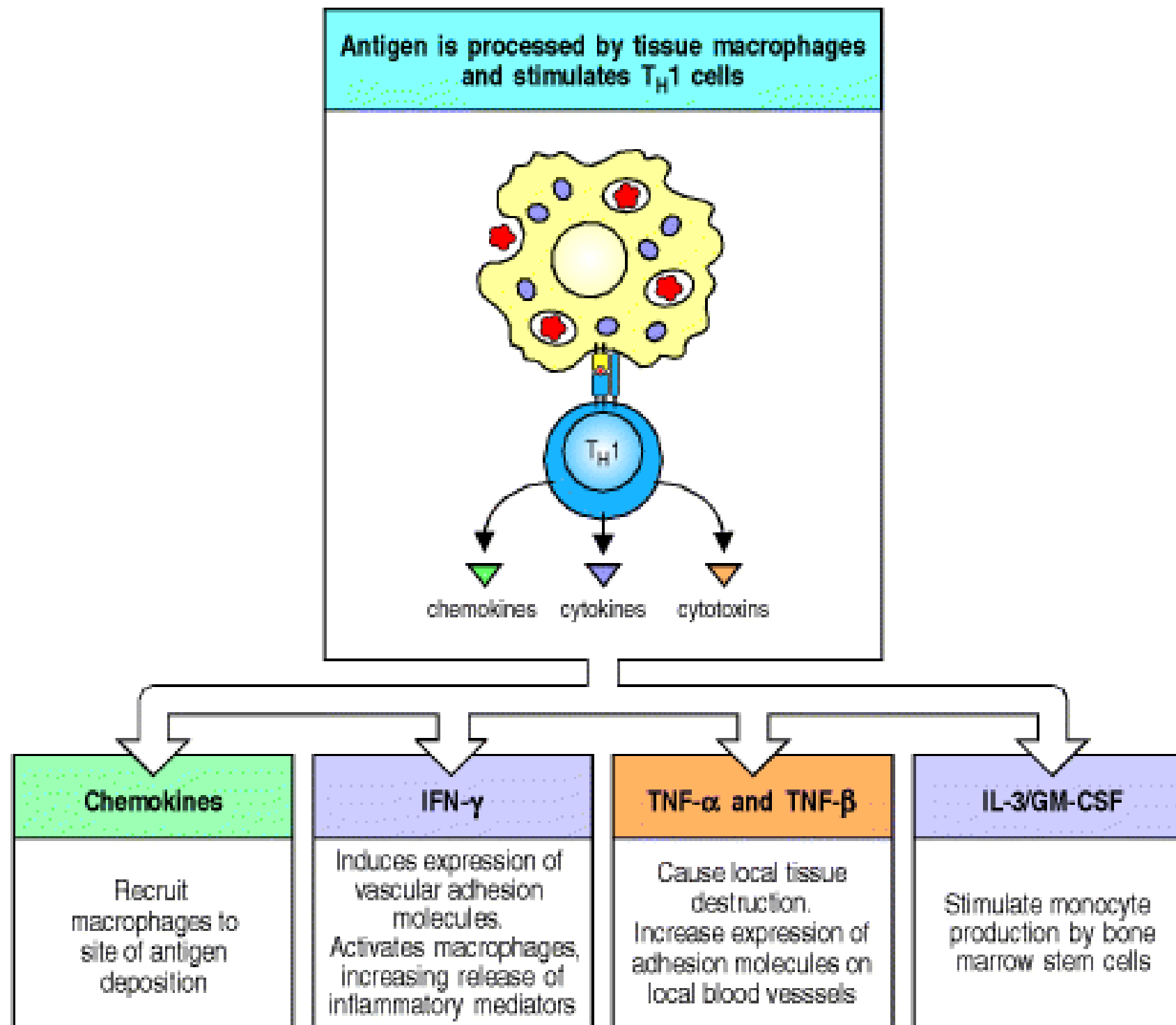
Demonstration of specific immune complexes in the blood or tissues by: **Immunofluorescence**

Type IV hypersensitivity reactions:

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:

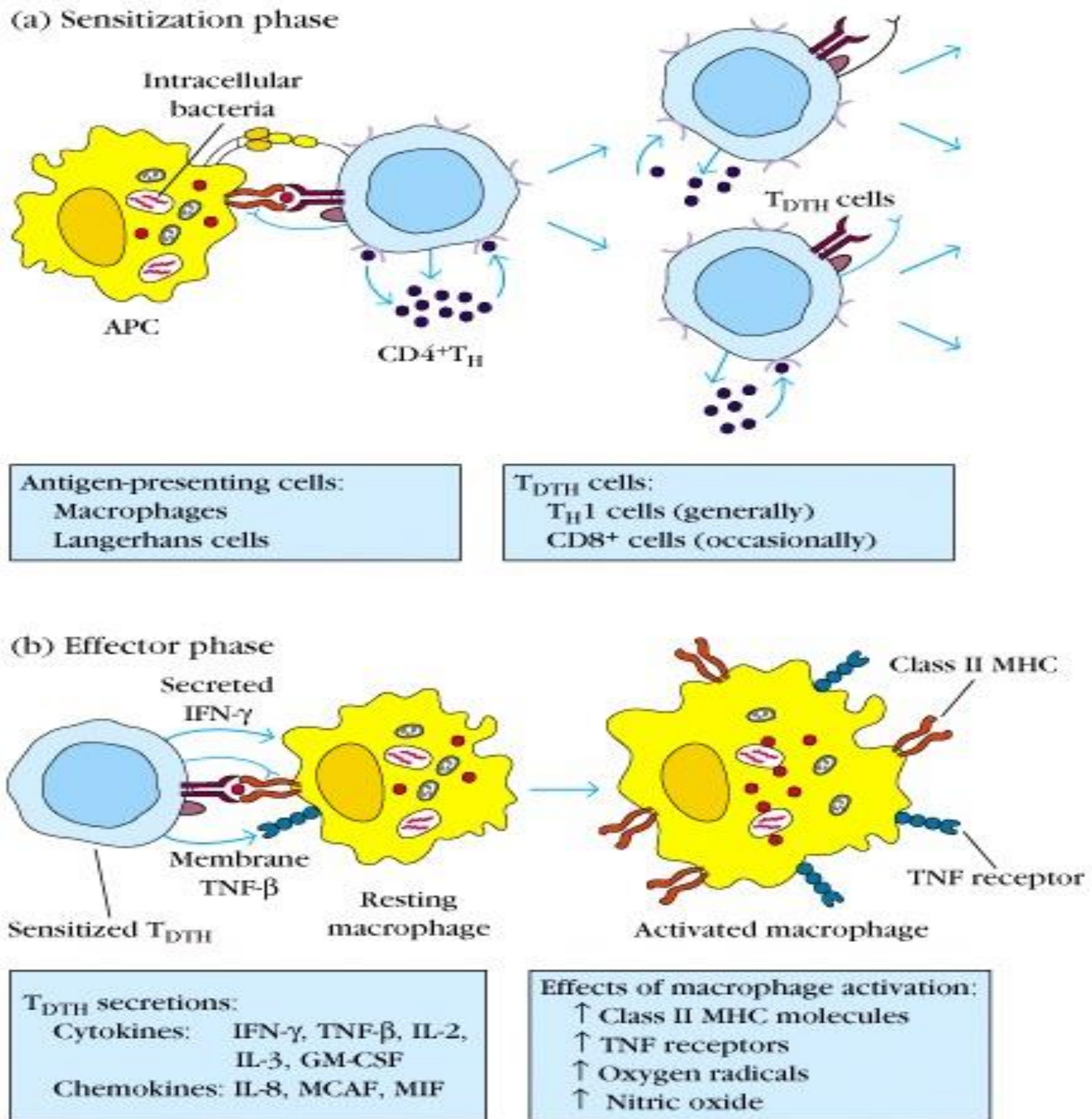


Development of DTH (delayed type hypersensitivity) Response:

1- Sensitization phase: 1-2 week period

2- Effector phase: 24-72 hours

Effector cells (activated macs [The membrane attack complex]) act non-specifically

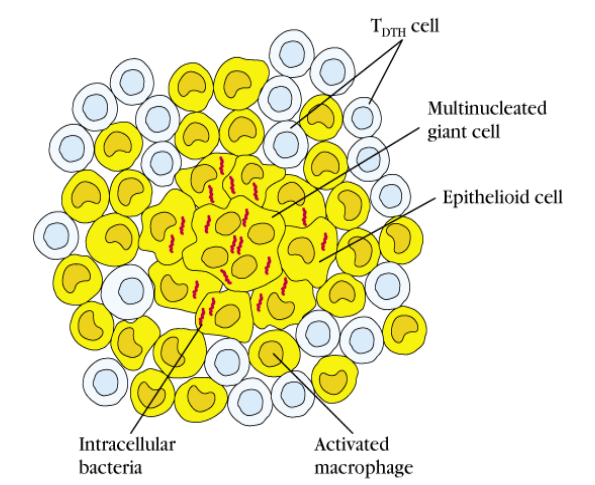
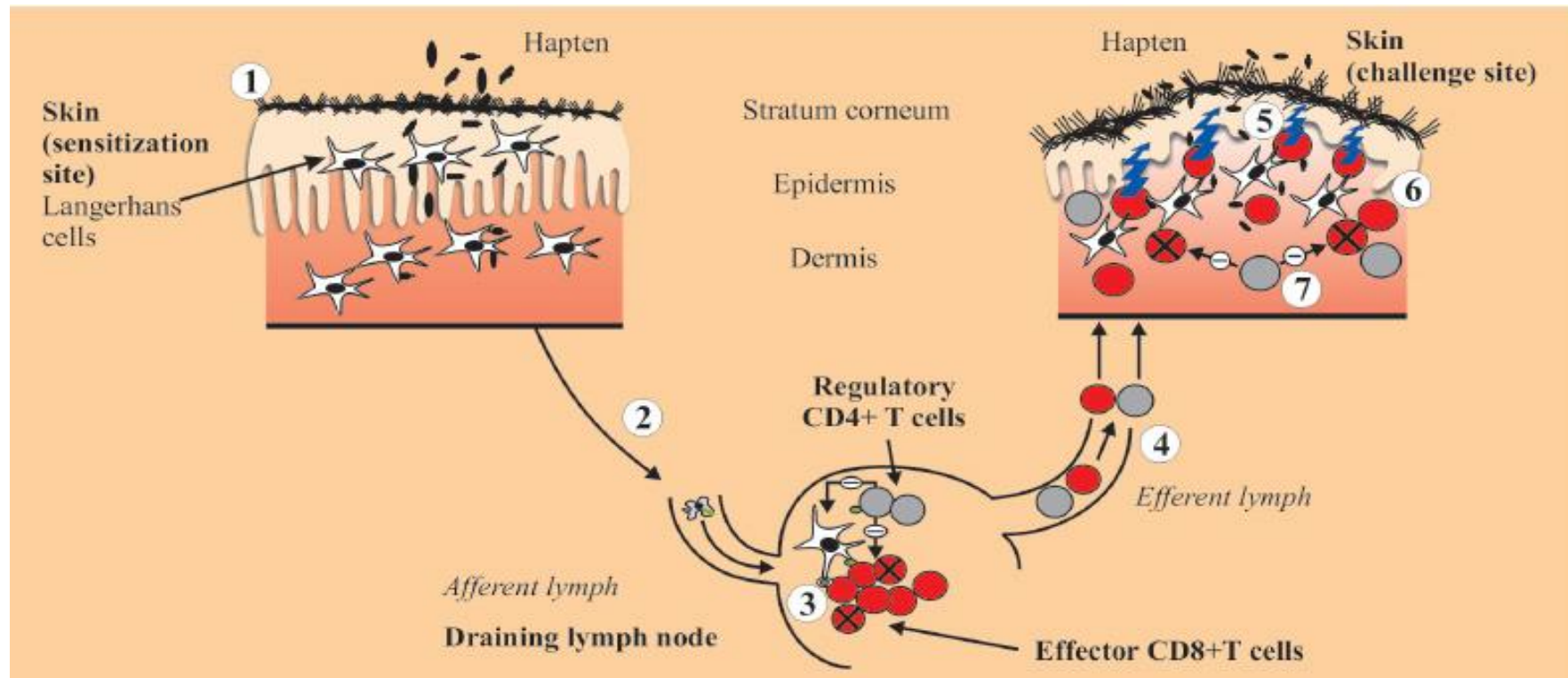


Clinical examples:

1. Contact dermatitis: (e.g. necklace)

Pathophysiology of contact dermatitis:

(Hapten doesn't induce immune reaction by itself because it's very tiny, it has to combine with epidermis protein to be allergen)



2. TB granuloma (persistent antigen)

Diagnosis:

1. Delayed skin test (Mantoux test)
2. Patch test (Contact dermatitis) (48-72h)
3. Lymphocyte transformation test



Take Home Messages

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

Useful Videos:

- Type1 Hypersensitivity Videos Animations:

<https://www.youtube.com/watch?v=IGDXNHMwcVs>

<https://www.youtube.com/watch?v=y3bOgdvV-M&feature%20?>

- Type 1 Hypersensitivity ANAPHYLAXIS :

<https://www.youtube.com/watch?v=9Qmzt94rRAw&index=4&list=LLhph2500UDsKDIf2o-pH0A>

- Explanation for Type 1 Hypersensitivity (has additional information but very helpful to understand):

https://www.youtube.com/watch?v=2tmw9x2Ot_Q&index=3&list=LLhph2500UDsKDIf2o-pH0A

- Type II hypersensitivity:

<https://m.youtube.com/watch?v=kLaUz58CBMc>

- Explanation for Type 3 Hypersensitivity (has additional information but very helpful to understand):

https://www.youtube.com/watch?v=SyxzU2Sl_Yw&index=2&list=LLhph2500UDsKDIf2o-pH0A

- Type 4 Hypersensitivity Animation :

<https://www.youtube.com/watch?v=9v4CBctjQHk&index=1&list=LLhph2500UDsKDIf2o-pH0A>

MCQs:

1- Anaphylactic reactions occur in which type of hypersensitivity ?

- a) type I b) type II c) type III d) type IV

2- Rheumatoid arthritis is a Clinical example of which type of hypersensitivity ?

- a) type I b) type II c) type III d) type IV

3- type III hypersensitivity is also known as ?

- a) Immediate Hypersensitivity b) Cell Mediated Immunity
c) Immunofluorescence d) Immune complex

4- which one of the following is a Feature of Type IV hypersensitivity ?

- a) Complement activation b) require Mast cells
c) Antibody type IgE d) Delayed onset

5- Atopic individuals respond to the allergens by producing ?

- a) IgG b) IgE c) IgA d) IgM

6- Which of the following is secondary Mediator of Allergic reactions ?

- a) histamine b) heparin c) proteases d) bradykinin

7- Diagnosis of Type IV hypersensitivity by which of the following ?

- a) Skin prick test (SPT) b) Elimination - Provocation test
c) Skin patch test d) Detection of Ab & Ag by Immunofluorescence

8- which of the following Allergies affect the Skin ?

- a) Urticaria b) Asthma c) Allergic rhinitis d) none of above

9- Granuloma formation occur in which type of hypersensitivity ?

- a) type I b) type II c) type III d) type IV

10- Mis-matched blood transfusion is a Clinical example of which type_of hypersensitivity?

- a) type I b) type II c) type III d) type IV

- 1-A
2-C
3-D
4-D
5-B
6-D
7-C
8-A
9-D
10-B

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