REVISION SGD # 1

- A 26 years old boy develops rashes all over his body after stung by bee while handling a bee hive to collect honey.
- Which type of hypersensitivity is this?
- Name the antibody involved in this reaction.
- Write down its complete mechanism.
- Enumerate four other examples of this particular hypersensitivity reaction.

Type I
IMMEDIATE HYPERSENSITIVITY

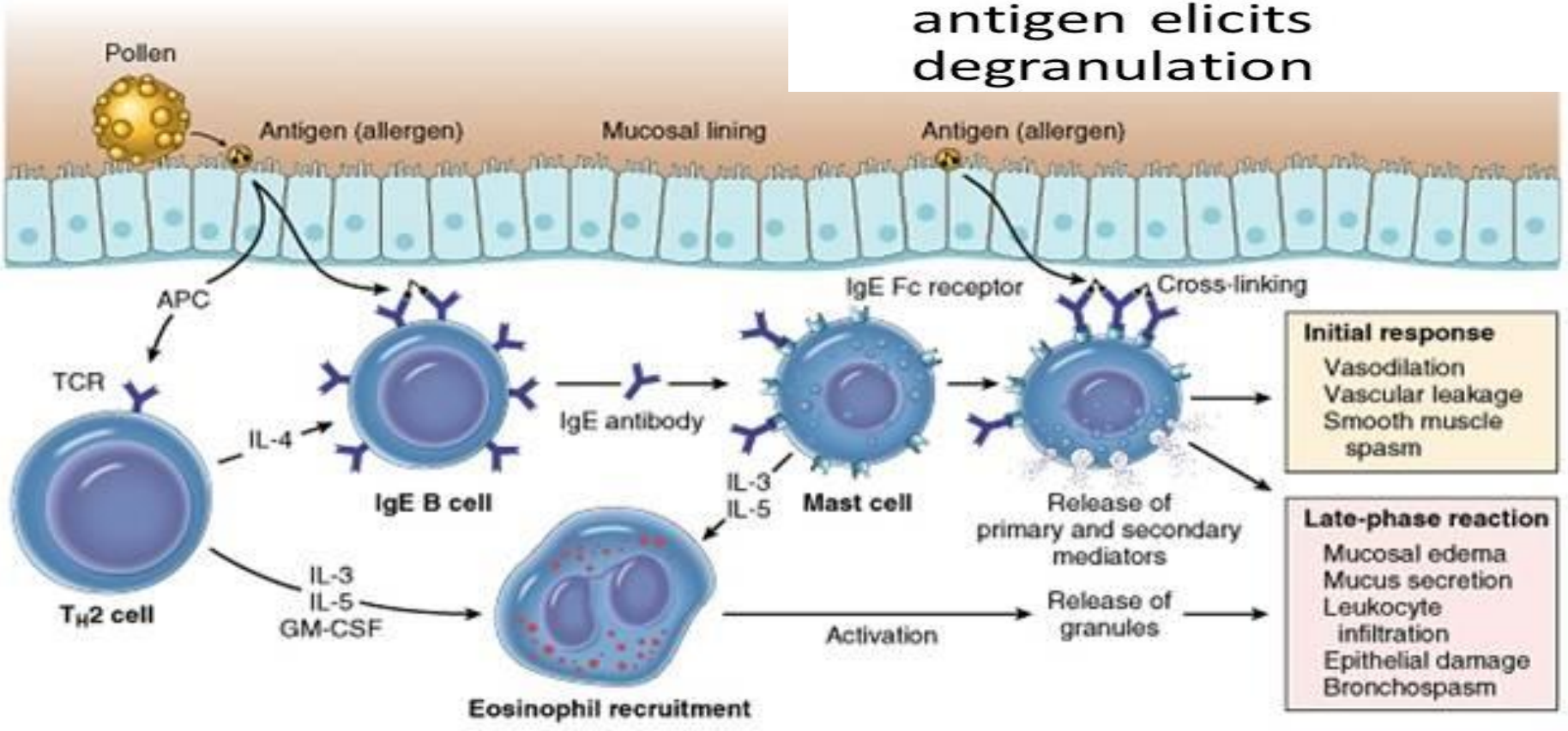
- **"Immediate" means seconds to minutes**
- **"Immediate Allergic Reactions", which may lead to anaphylaxis, shock, edema, dyspnea,death**

  After exposure to allergen there is

  - **1) IMMEDIATE phase: Mast cell degranulation, vasodilatation, vascular leakage, smooth muscle contraction (bronchospasm)**
  - **2) LATE phase: (hours, days): Eosinophils, PMNs, T-Cells**

Mechanisms of allergic response

- "Allergic" reaction
- Involves initial activation of T_H2 cells and production of IgE from B-cells
- IgE binds to mast cells
- Secondary exposure of IgE-coated mast cells to antigen elicits degranulation



Pathogenic mechanisms

First exposure to allergen

Allergen stimulates formation of antibody (Ig E type)

Ig E fixes, by its Fc portion to mast cells and basophiles

Second exposure to the same allergen

It bridges between Ig E molecules fixed to mast cells leading to activation and degranulation of mast cells and release of mediators

Pathogenic mechanisms

* Three classes of mediators derived from mast cells:

1) Preformed mediators stored in granules (histamine)

2) Newly sensitized mediators:

leukotrienes, prostaglandins, platelets activating factor

3) Cytokines produced by activated mast cells, basophils

e.g. TNF, IL3, IL-4, IL-5 IL-13, chemokines

* **These mediators cause: smooth muscle contraction, mucous secretion and bronchial spasm, vasodilatation, vascular permeability and edema**

Atopy

(Local form of type I hypersensitivity)

Exposure to certain allergens that induce production of specific Ig E

There is a strong familial predisposition to atopic allergy which is genetically determined

* Allergens :

Inhalants: dust, mite faeces, pollens, mould spore.

Ingestants: milk, egg, fish, choclate

Contactants: wool, nylon, animal fur

Drugs: penicillin, salicylates, anesthesia

REVISION SGD # 2

- A 28 years old mother gives birth to her first child. The father is homozygous Rh D positive and the mother is homozygous Rh D negative. The baby is born without any complications but the mother is not given anti Rh immunoglobulins following the delivery. 18 months later, she delivers another child who is anemic, slight jaundiced and has an enlarged spleen and liver.
- Which type of hypersensitivity best describes this condition?
- Give the immunological mechanism of this hypersensitivity reaction.
- Give two other examples of this hypersensitivity reaction.

Type II Hypersensitivity

- Antibody-mediated reactions/ Cytotoxic reactions
- Takes hours to days to develop after exposure to Ag
- Antibody can be either IgG or IgM
- An antibody (Ig G or Ig M) reacts with antigen on the cell surface
- This antigen may be part of cell membrane or circulating antigen (or hapten) that attaches to cell membrane e.g., Ag as a part of RBC membrane, or embedded in neutrophil membrane or platelet membrane or glomerular basement membrane
- No free circulating immune complexes formed

Mechanism of Type II Hypersensitivity

Cell lysis results due to :

1) **Complement fixation** to the antigen antibody complex on cell surface. The activated complement will lead to cell lysis

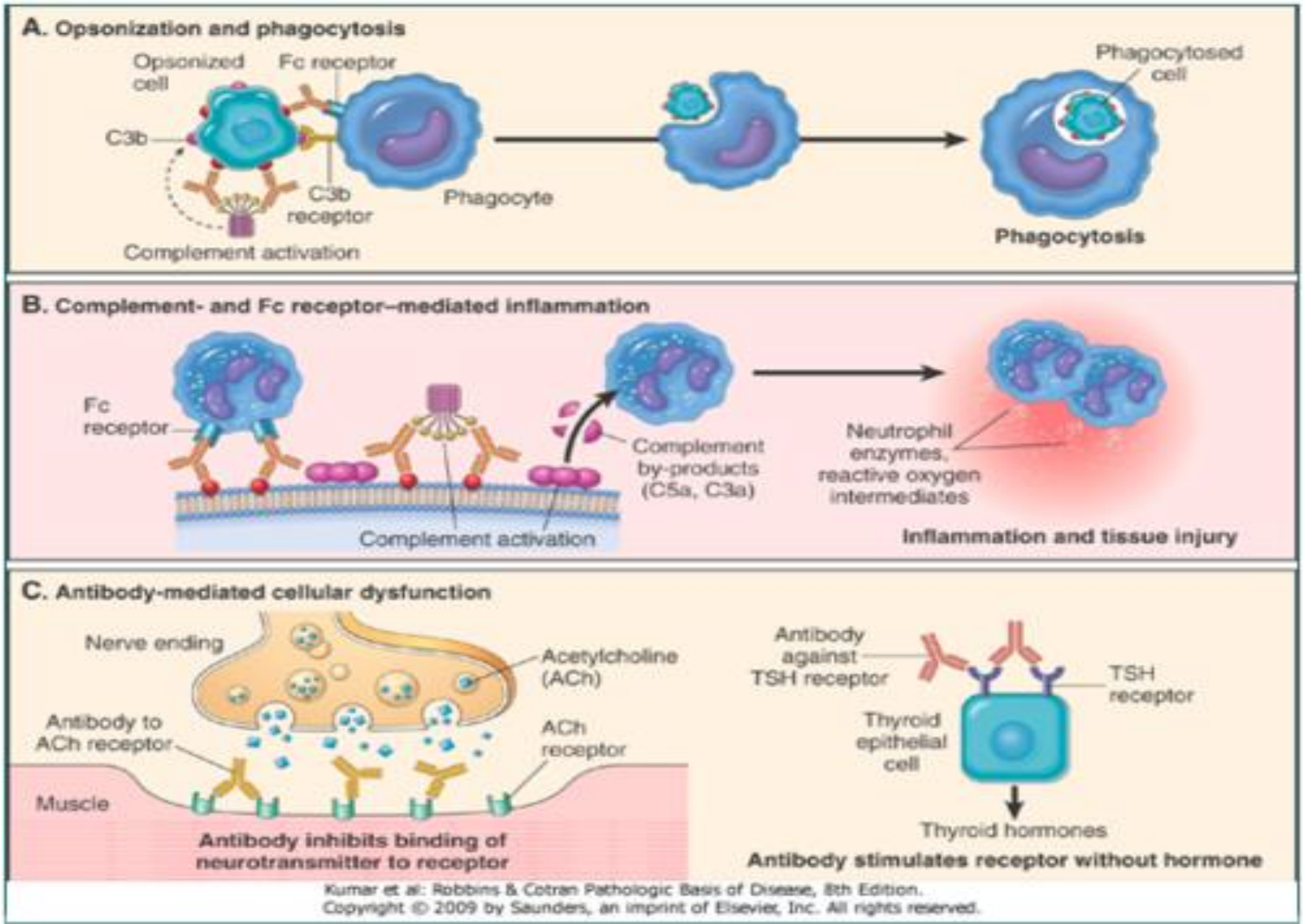
2) **Phagocytosis** is enhanced by the antibody (opsonin) bound to cell antigen leading to opsonization of the target cell

3) **Antibody dependent cellular cytotoxicity (ADCC):**

- Antibody coated cells e.g., tumor cells, graft cells or infected cells can be killed by cells which possess Fc receptors
- The process is different from phagocytosis and independent of complement
- Cells most active in ADCC are:

  NK cells, monocytes, macrophages, neutrophils

Mechanism of Type II Hypersensitivity



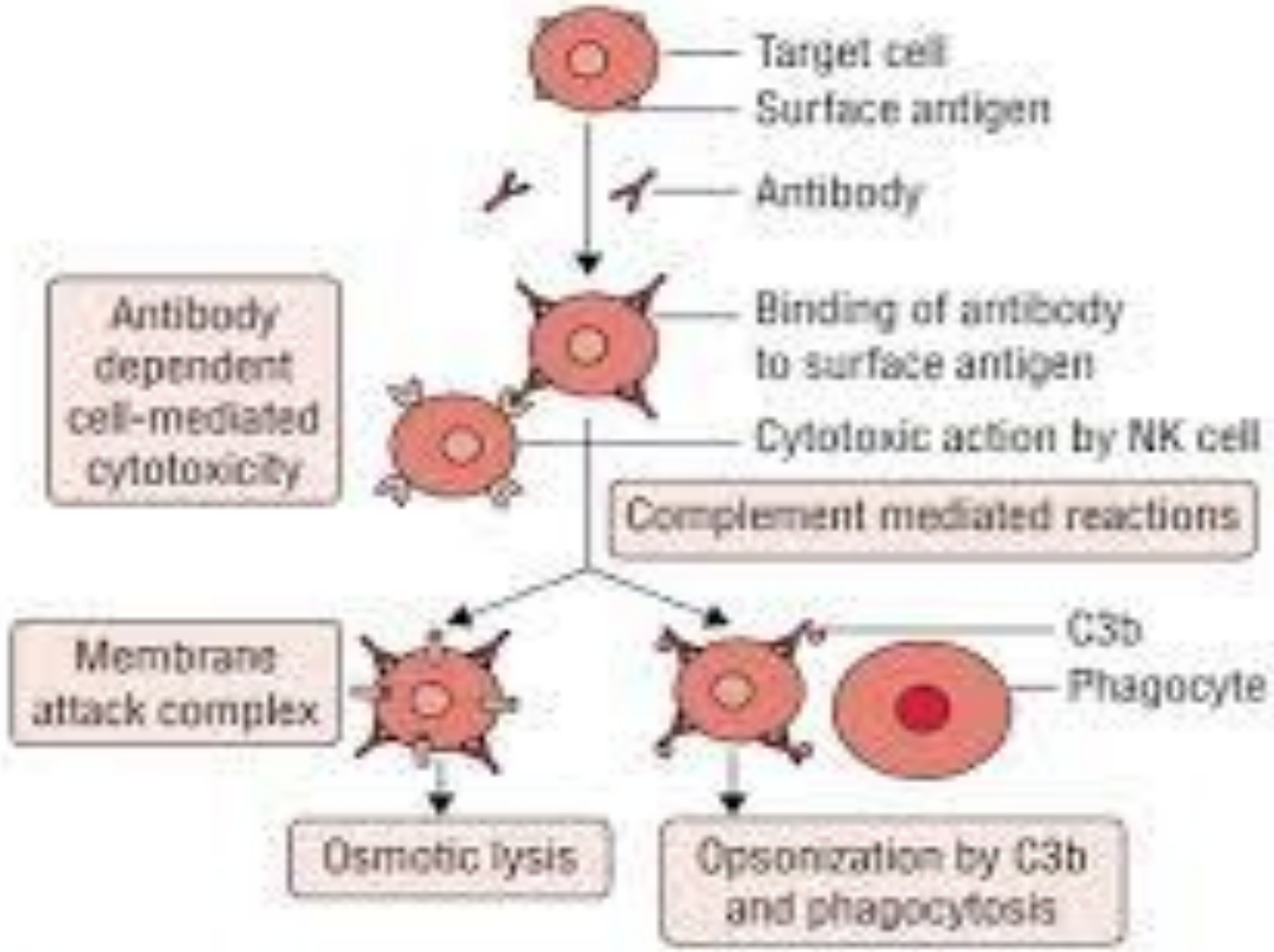


FIG. 19-2. A schematic diagram showing type II hypersensitivity reaction.

Examples of Type II Hypersensitivity

- ABO transfusion reactions
- Rh incompatibility (erythroblastosis fetalis, hemolytic disease of the new born)
- Hemolytic anemia
- Grave's disease
- Goodpasture's syndrome
- Rheumatic fever

REVISION SGD # 3

- Serum sickness is an example of which type of Hypersensitivity?
- Give two more examples of this hypersensitivity reaction.
- Write in detail the immunological mechanism of this hypersensitivity reaction.
- Write a short note on Arthus reaction.

- Type III hypersensitivity reaction

- Examples:
- Systemic lupus erythematosus(SLE)
- Rheumatoid arthritis(RA)
- Post-streptococcal glomerulonephritis
- Serum sickness
- Arthus reaction
- Farmer’s lung

Type III Hypersensitivity

- Immune-complex mediated
- 2-3 weeks after exposure to the Ag
- Occurs when Ag-Ab complexes induce an inflammatory response in tissues
- Ag may be exogenous or endogenous but always free
- Ab is also free and either IgG or IgM
- Free circulating immune complexes are formed either in circulation or tissue fluids

- Normally immune complexes are promptly removed by the reticuloendothelial system

- Occasionally they persist and are deposited in tissues resulting in several disorders:

✓ Joints---Arthritis

✓ Kidneys---Nephritis

✓ Blood vessels---Vasculitis

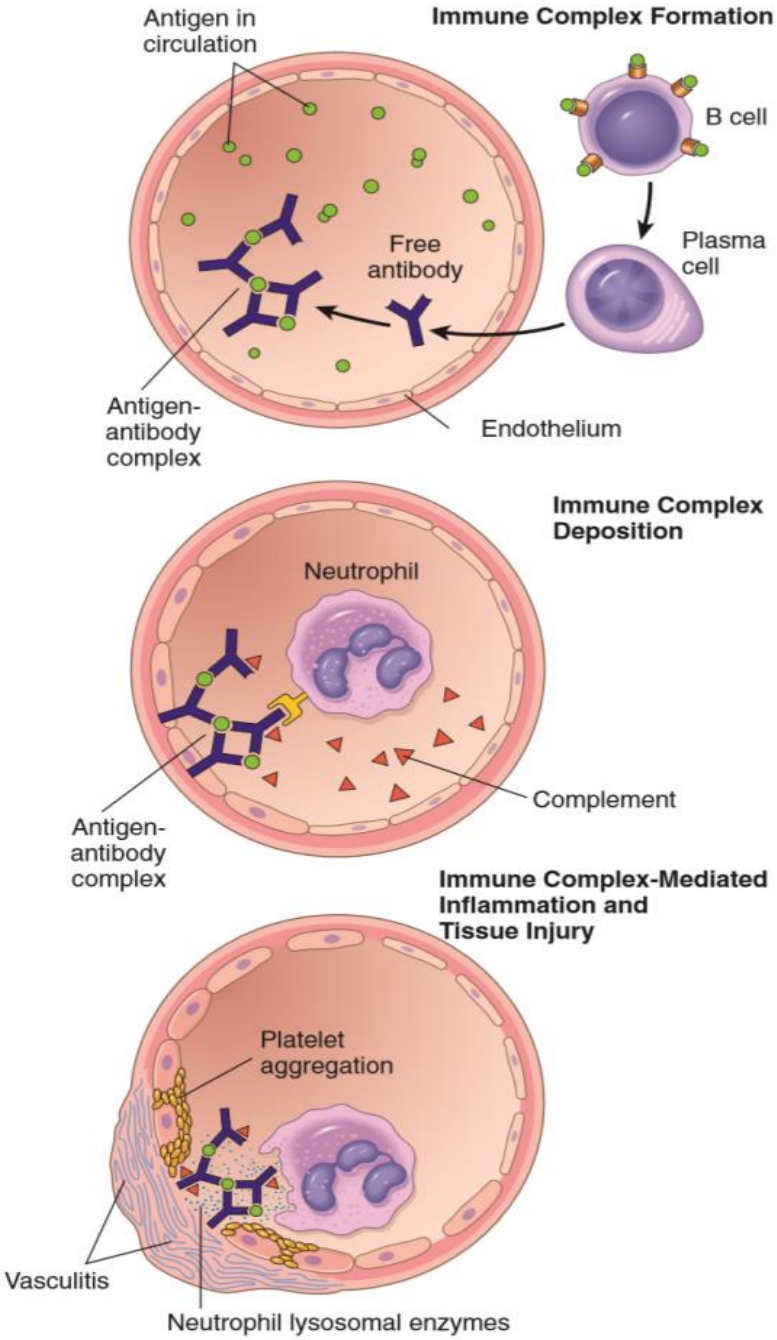
Mechanisms of Type III Hypersensitivity

i. **Activation of complement:**

- Formation of immune complexes in circulation→→→ deposit in various tissues →→→ trigger classical pathway of the complement system

ii. **Fc receptor-mediated recruitment and activation of leukocytes:**

- Polymorphonuclear cells are attracted to the site →→→ inflammation and tissue injury occur



Phases of disease:

1. Formation of Ag-Ab complexes in the circulation
2. Deposition of immune complexes in various tissues
3. Inflammatory reaction and destruction of host tissues

Examples include:

- Systemic lupus erythematosus
- Streptococcal glomerulonephritis
- Polyarteritis nodosa
- Reactive arthritis
- "Serum sickness" (reaction to foreign serum)

- **Arthus Reaction:**
- Inflammation caused by the deposition of immune complexes at a localized site e.g., diabetic patients receiving insulin subcutaneously or when boosters are administered to individuals who already possess high antibody titers to vaccine molecules

- Local reactions in the form of edema, erythema, ulceration and necrosis

- Immune complexes deposited in small blood vessels result in vasculitis, microthrombi formation, vascular occlusion and necrosis

- **Serum Sickness:**
- It is a hypersensitivity vasculitis due to foreign objects
- Systemic inflammatory response to the presence of immune complexes deposited in many areas of the body
- Injection of large doses of foreign serum such as horse serum or certain drugs such as penicillin, diphtheria antitoxin etc
- Antigen is slowly cleared from circulation
- Antibody production starts
- Immune complexes are formed which may circulate or be deposited at various sites
- A few days to 2 weeks after injection of the foreign serum or drug, fever, urticaria, arthralgia, lymphadenopathy, splenomegaly and eosinophilia occurs
- Symptoms improve as the immune system removes the antigen and subside when the antigen is eliminated

REVISION SGD # 4

- A 22 years old male presented to the OPD with history of chronic cough over a period of 3 months, low grade fever, anorexia and weight loss. He was diagnosed as a case of Pulmonary Tuberculosis.
- What type of hypersensitivity reaction is responsible for pulmonary TB?
- Describe the mechanism of this reaction in detail.
- What is the basis for tuberculin test?
- Give four other examples of this hypersensitivity reaction.

Type IV Hypersensitivity

- Cell-mediated Hypersensitivity/ Delayed Hypersensitivity
- Involves T-lymphocytes , not antibodies
- The response is “delayed” i.e. it starts hours or days after contact with the antigen and lasts for weeks.
- It is a principal pattern of immunologic response to intracellular microbiological agents particularly, Mycobacterium tuberculosis, as well as viruses, fungi, protozoa and parasites

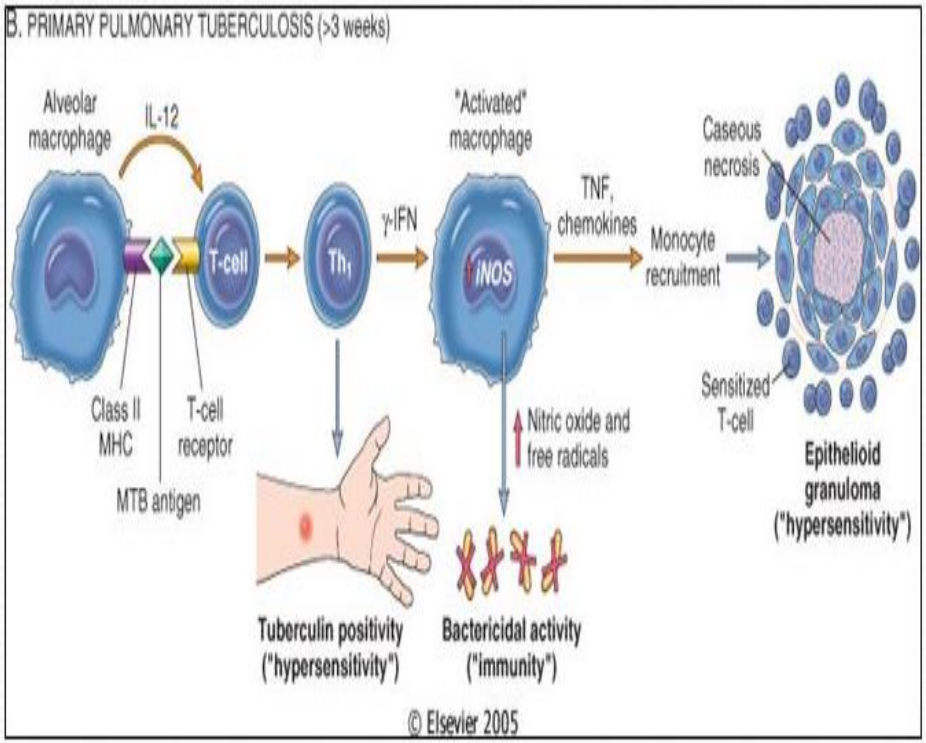
Mechanisms of Type IV Hypersensitivity

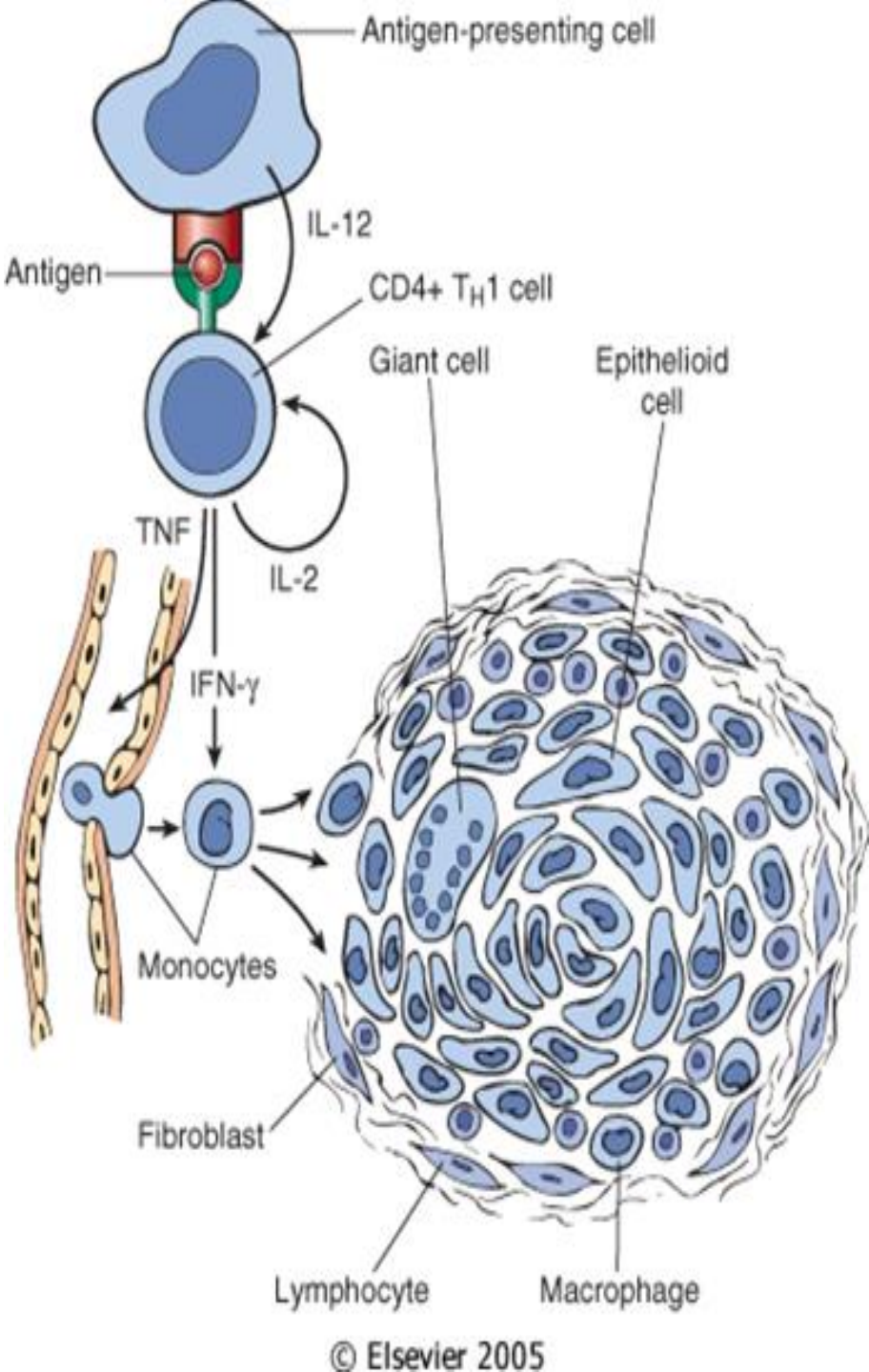
- Mediated by T-cell dependent effector mechanisms
- Involve both CD4 helper T cells and CD8 cytotoxic T cells

CD4 T cell mediated Type IV Reaction

- CD4 T cells cause delayed hypersensitivity through macrophage activation and cytokine mediated inflammation
- The activated Th1 cells release various cytokines which cause accumulation and activation of macrophages, which in turn cause local damage at the target site
- **Examples:** Tuberculin skin test, contact dermatitis, granulomatous inflammation

Granuloma Formation





CD8 T cell mediated Type IV Reaction

- Sensitized CD8 T cells kill antigen bearing target cells
- T-cell mediated cytotoxicity through direct target cell lysis and also cytokine mediated inflammation
- **Examples:** Graft rejection, Virus infections, Tumor immunity

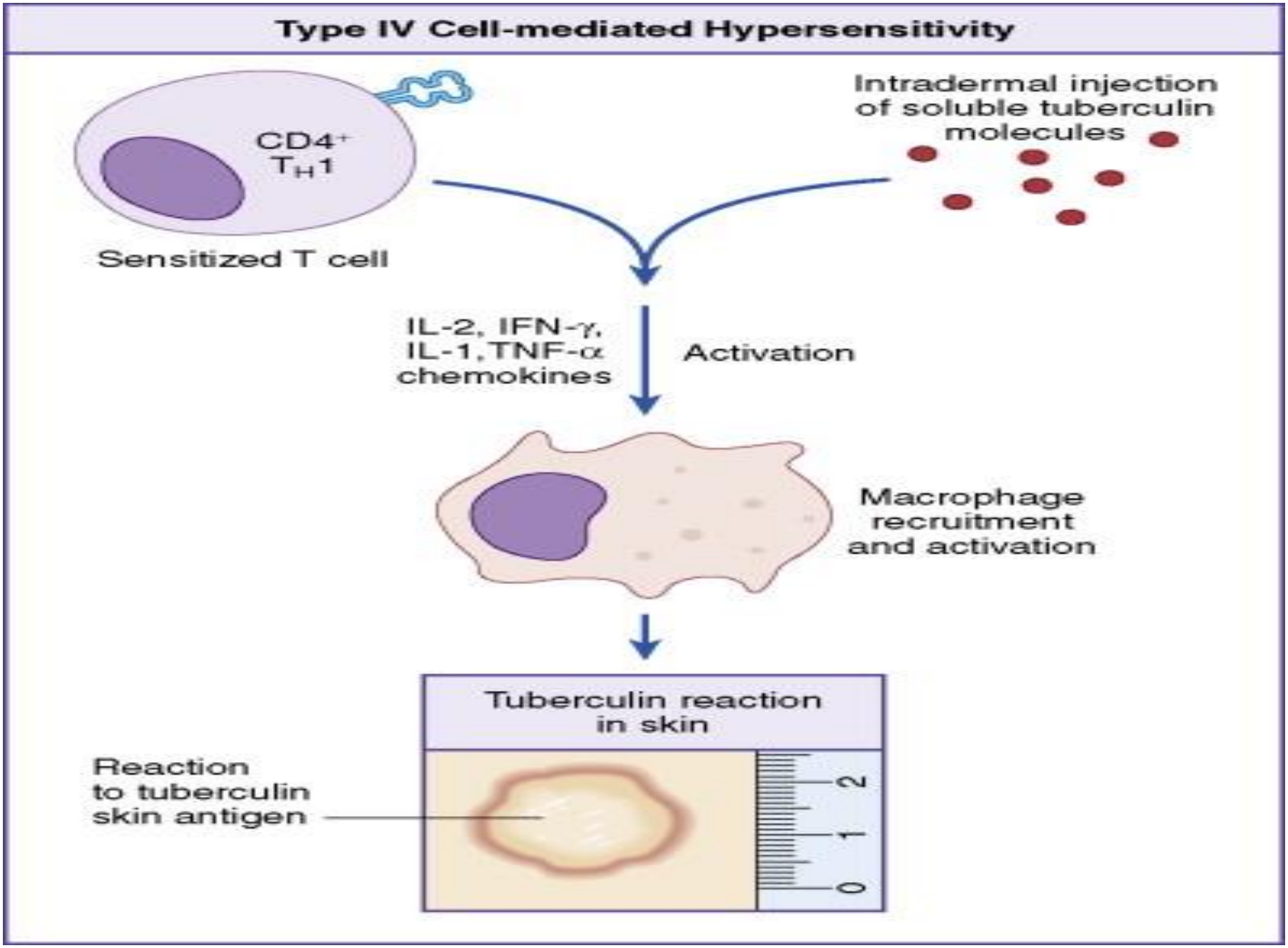
Examples of Type IV Hypersensitivity

- Contact dermatitis
- Poison oak/ivy
- Tuberculin skin test reaction
- Stevens-Johnson syndrome
- Erythema multiforme
- Acute graft reaction
- Graft versus host disease

Tuberculin skin test reaction

- A positive skin test assists in the diagnosis of Tuberculosis and also provides support for chemoprophylaxis or chemotherapy
- When a person previously exposed to M.tuberculosis is injected with a small amount of tuberculin i.e., PPD(purified protein derivative) intradermally, there is little reaction in the first few hours
- Gradually, induration and redness develop and reach a peak in 48 to 72 hrs

- Indurations appear due to accumulation of macrophages and T lymphocytes
- A positive skin test indicates that the person has been infected with the agent but does not confirm the presence of current disease
- If the skin test converts from negative to positive, it suggests recent infection


Type IV Cell-mediated Hypersensitivity
CD4+
TH1
Sensitized T cell
Intradermal injection
of soluble tuberculin
molecules
IL-2, IFN-γ,
IL-1, TNF-α
chemokines
Activation
Macrophage
recruitment
and activation
Tuberculin reaction
in skin
Reaction
to tuberculin
skin antigen
2
1
0