BHARATHIDASAN UNIVERSITY

Tiruchirappalli – 620 024,
Tamil Nadu, India

Programme: M.Sc., Biotechnology (Marine)

Course Title : Immunology

Course Code : 21 CC7

Unit : V

Hypersensitivity

Dr. K. ANBARASU
Professor
Department of Marine Biotechnology

Hypersensitivity

- **Hypersensitivity (Immunological reaction)** refers to undesirable immune reactions produced by the normal immune system.

- **Hypersensitivity reactions**: When an immune response result in exaggerated or in appropriate reactions harmful to the host the term hypersensitivity or allergy used.

- **Hypersensitivity reactions:** four types; based on the mechanisms involved and time taken for the reaction, a particular clinical condition (disease) may involve more than one type of reaction.

Classification of Hypersensitivity

- -Type I
- -Type II
- -Type III
- -Type IV

Type I, II and III → Antibody Mediated

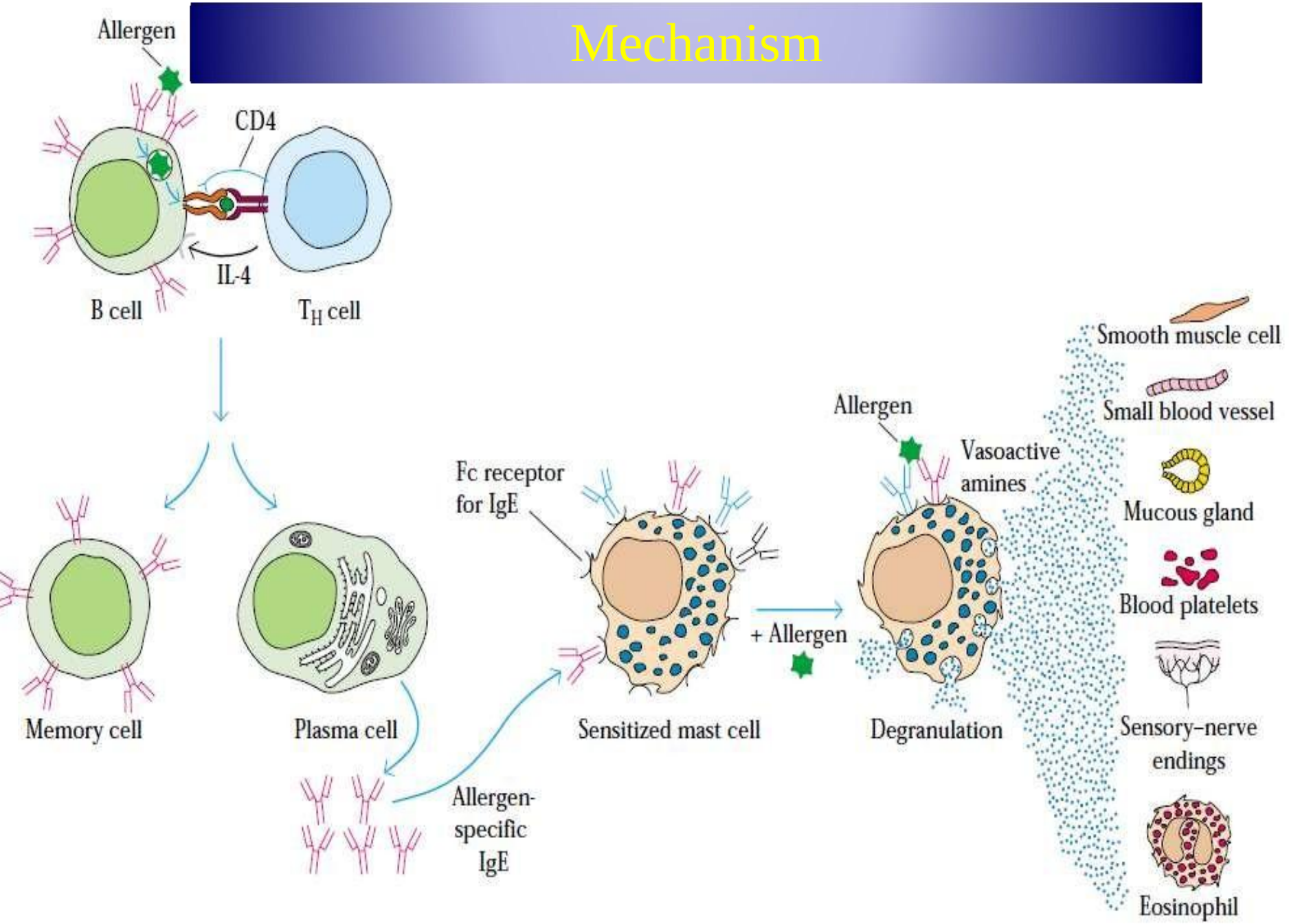
Type IV → Cell Mediated

Type I (Immediate) Hypersensitivity

- Commonly called allergy
- Mediated by IgE antibodies produced by plasma cells in response to stimulation of Th2 cells by an **antigens.**
- The antigens that stimulate it are called allergens

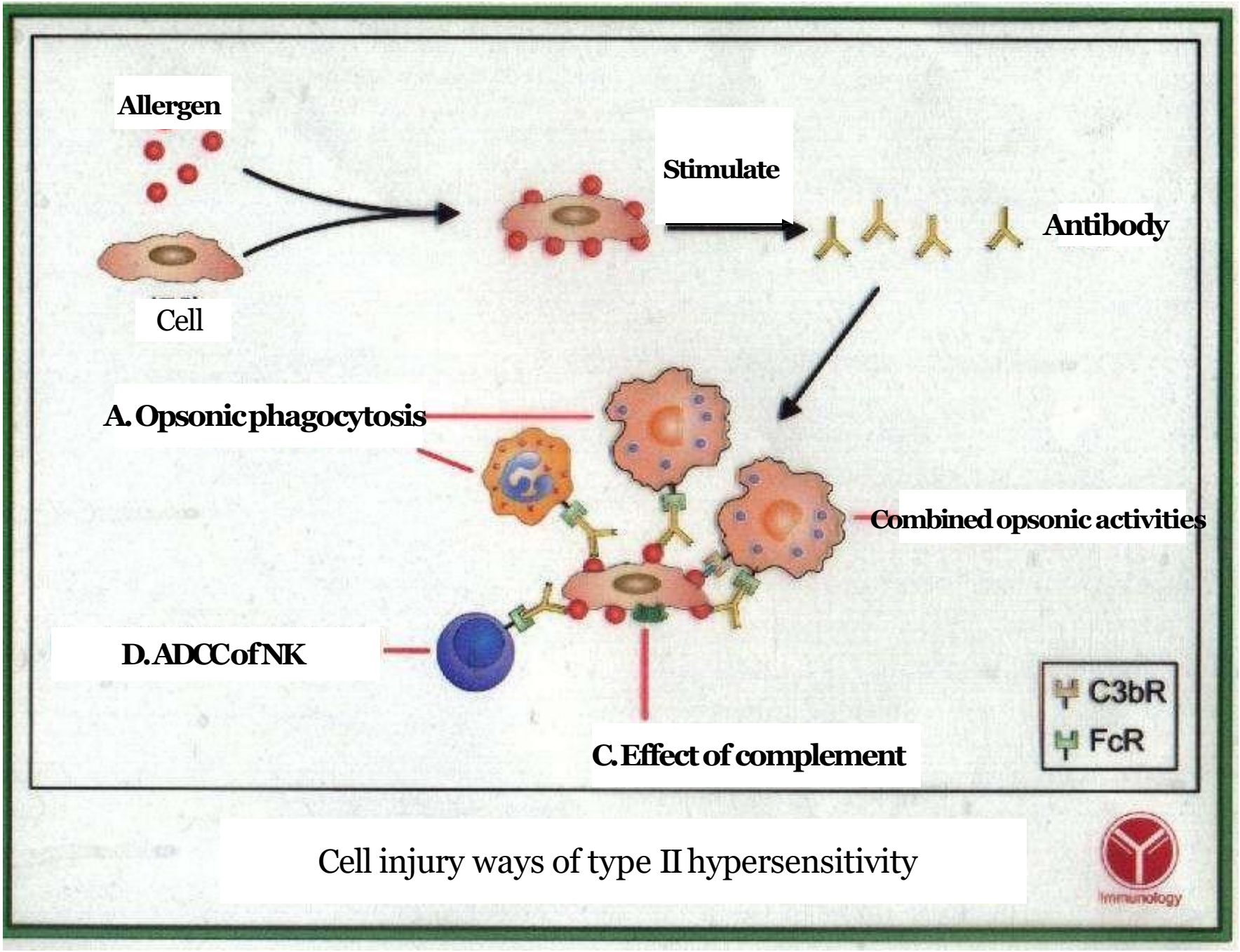
  (i.e. House dust, Pollens, Cosmetics, Insects, Clothing and Drug)
- Exposure may be ingested, inhalation, injection or direct contact.
- Type I hypersensitivity reactions can be systemic (e.g., systemic anaphylaxis) or localized to a specific target tissue or organ (e.g., allergic rhinitis, asthma).

Mechanism

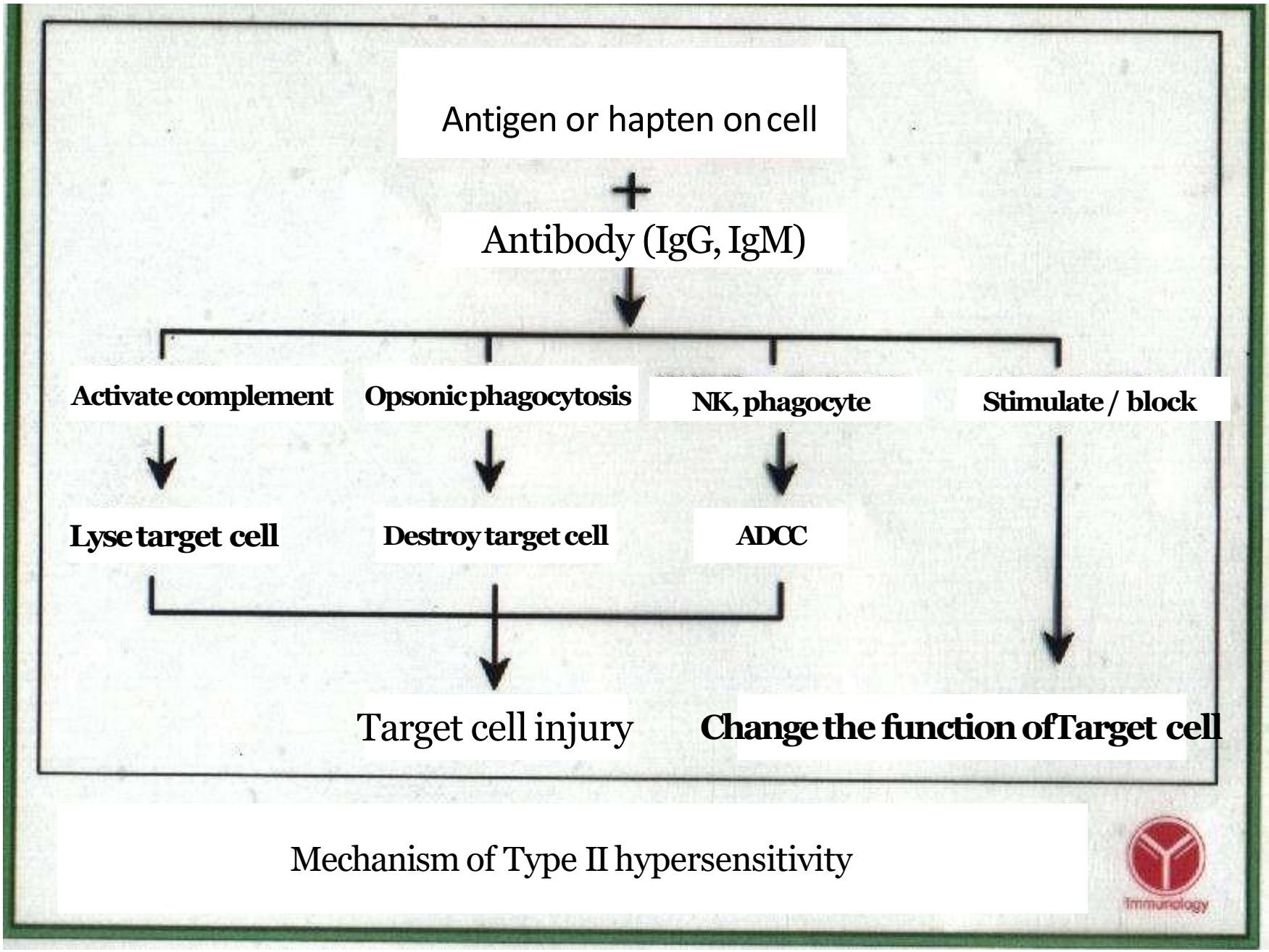

Allergen
CD4
IL-4
B cell
T_H cell
Memory cell
Plasma cell
Allergen-specific IgE
Fc receptor for IgE
Sensitized mast cell
+ Allergen
Allergen
Vasoactive amines
Degranulation
Smooth muscle cell
Small blood vessel
Mucous gland
Blood platelets
Sensory–nerve endings
Eosinophil

Type II (Cytotoxic) Hypersensitivity

- Cytotoxic
- Type II hypersensitivity involves IgG or IgM antibody-mediated
- IgM or IgG immunoglobulin react with cell-surface antigens to activate the complements system and produce direct damage of the cell surface.
- Transfusion reactions and hemolytic disease of the newborn are examples of type II hypersensitivity.



Cell injury ways of type II hypersensitivity



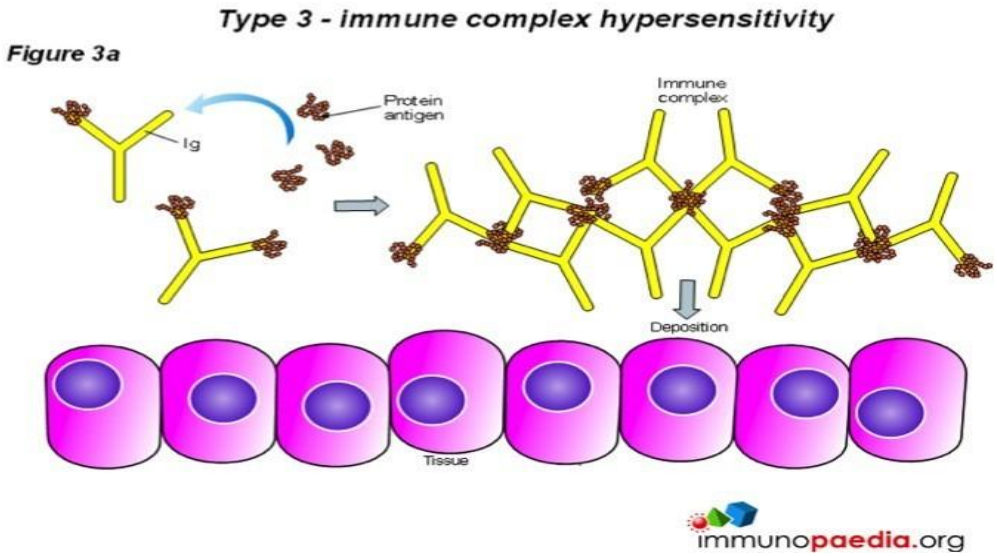
Mechanism of Type II hypersensitivity

Immunology

Diseases

- TRANSFUSION SYNDROME
- ERYTHROBLASTOSIS FOETALIS
- DRUG INDUCED AUTO HEMOLYTIC ANEMIA

Hypersensitivity Type III



Type III (ICM) Hypersensitivity

Type III (Immune Complex–Mediated) Hypersensitivity

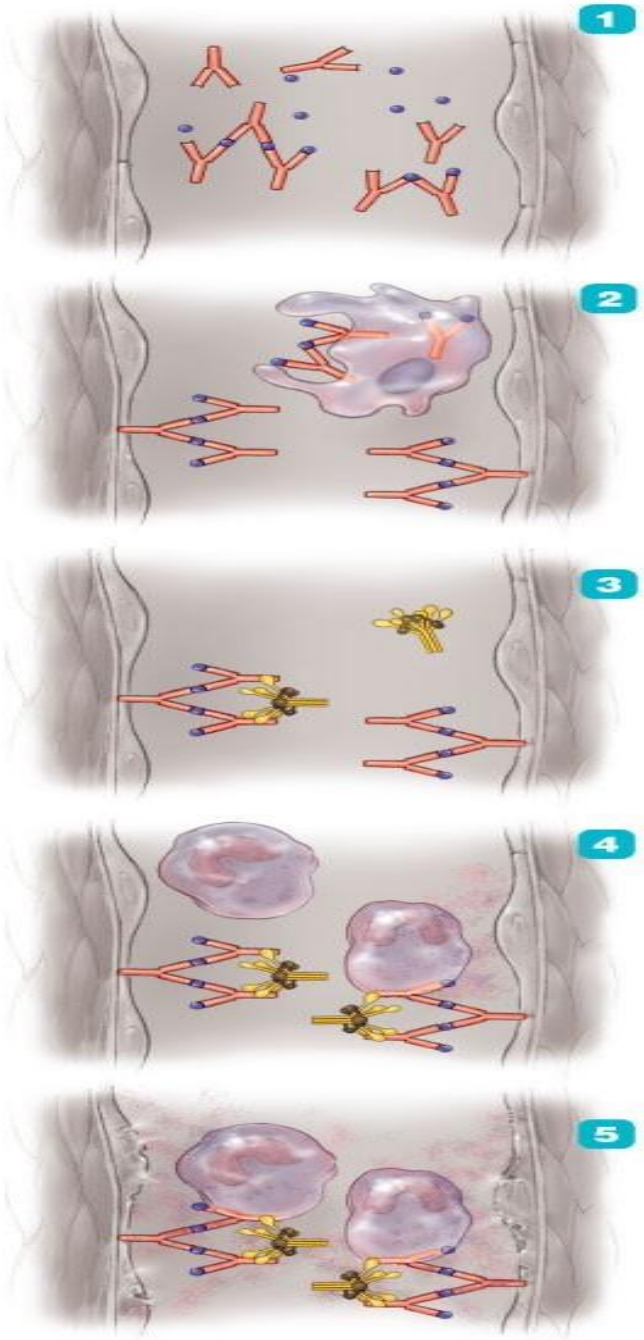
- Type III hypersensitivity is also known as immune complex hypersensitivity.
- The reaction may take 3 - 10 hours after exposure to the antigen (as in Arthus reaction).
- The reaction may be general (*e.g.*, serum sickness) or may involve individual organs including or other organs.
- Antigens causing immune complex mediated injury are:
  - Exogenous
  - Endogenous

Type III (ICM) Hypersensitivity

Mechanism of Type III Hypersensitivity

- Antigens combines with antibody within circulation and form immune complex
- Wherever in the body they deposited
- They activate compliment system
- Polymorphonuclear cells are attracted to the site
- Result in inflammation and tissue injury

The mechanism of type III (immune-complex mediated) hypersensitivity-overview



Antigens combine with antibodies to form antigen-antibody complexes.

Antigen

Antibody (IgG)

Antigen-antibody complex

Phagocytes remove most of the complexes, but some lodge in the walls of blood vessels.

There the complexes activate complement.

Inactive complement Active complement

Antigen-antibody complexes and activated complement attract and activate neutrophils, which release inflammatory chemicals.

Neutrophil

Inflammatory chemicals

Inflammatory chemicals damage underlying blood vessel wall.

Type III (ICM) Hypersensitivity

Hypersensitivity Type III Reactions

Local Reactions

- **Arthus Reaction:**
  - It is named for Dr. Arthus.
  - Inflammation caused by the deposition of immune complexes at a localized site.
  - Clinical Manifestation is :
    Hypersensitivity Pneumonitis

Systemic Reactions

- **Serum Sickness:**
  - Systemic inflammatory response to deposited immune complexes at many areas of body.
  - Few days to 2 weeks after injection of foreign serum or drug it results in :
    Fever, Urticaria, Artheralgia, Eosinophila, Spleenomegally, and Lymph adenopathy

Immune Complex Diseases

Type III (ICM) Hypersensitivity

Immune Complex Diseases:

- Hypersensitivity Pneumonitis
- Glomerulonephritis
- Rheumatoid Arthritis
- Systemic Lupus Erythematosus

Type III (ICM) Hypersensitivity

Hypersensitivity pneumonitis

- Inhalation of antigens into lungs stimulates antibody production
- Subsequent inhalation of the same antigen results in formation of immune complexes
  - Activates complement

Type III (ICM) Hypersensitivity

Glomerulonephritis

- Immune complexes in the blood are deposited in glomeruli
- Damage to the glomerular cells impedes blood filtration
- Kidney failure and, ultimately, death result

Type III (ICM) Hypersensitivity

Rheumatoid arthritis

- Immune complexes deposited in the joint
  - Results in release of inflammatory chemicals
  - The joints begin to break down and become distorted
- Trigger not well understood
- Treated with anti-inflammatory drugs

The crippling distortion of joints characteristic of rheumatoid arthritis

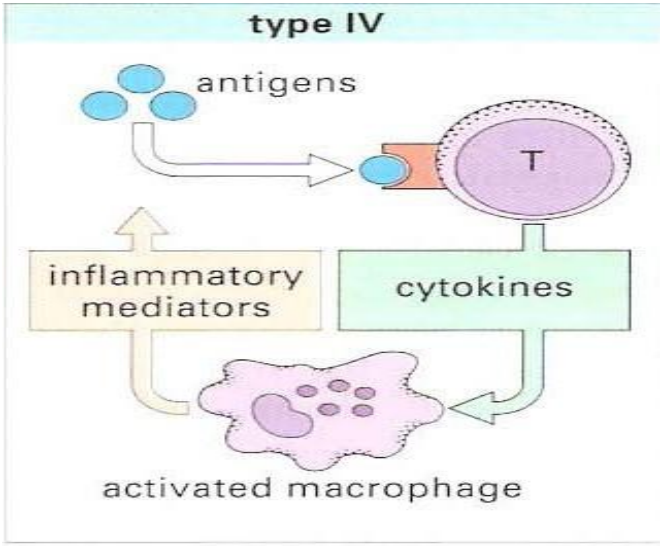
Type III (ICM) Hypersensitivity

Systemic lupus erythematosus

- Autoantibodies against DNA result in immune complex formation
- Many other autoantibodies can also occur
  - Against red blood cells, platelets, lymphocytes, muscle cells
- Trigger unknown
- Immunosuppressive drugs reduce autoantibody formation
- Glucocorticoids reduce inflammation

The characteristic facial rash of systemic lupus erythematosus

Hypersensitivity Type IV



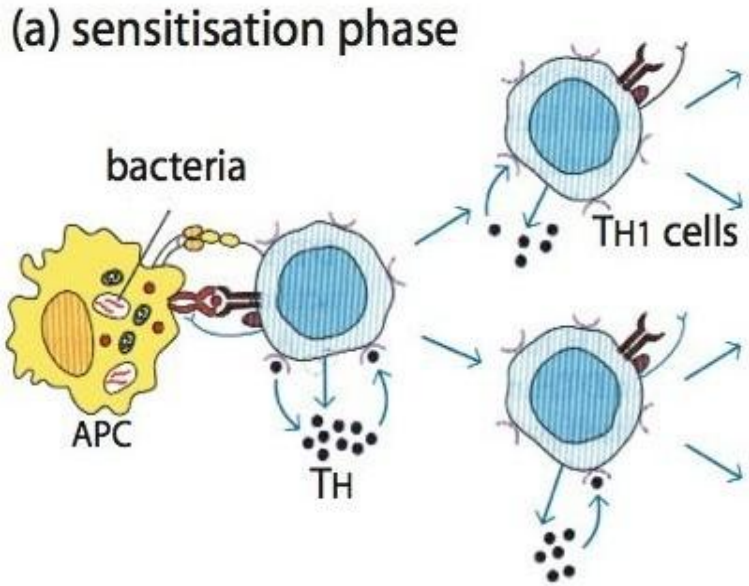
Type IV (Cell Mediated) Hypersensitivity

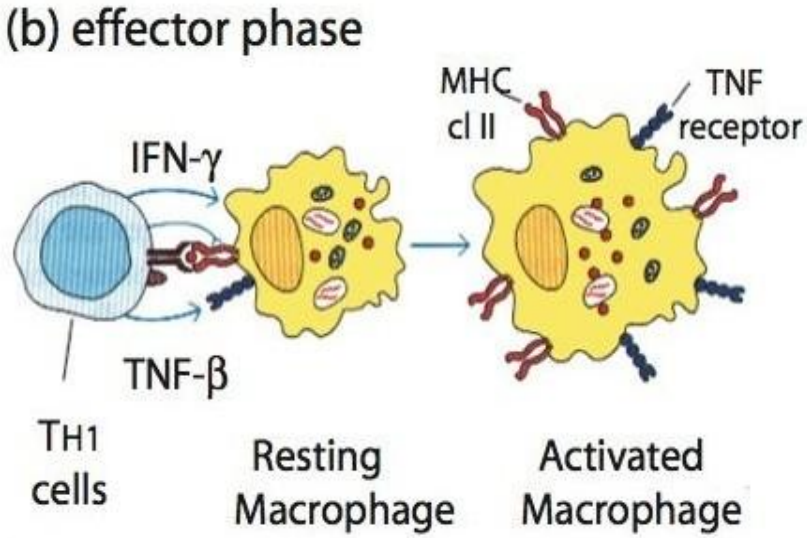
Type IV (Delayed or Cell-Mediated) Hypersensitivity

- Delayed hypersensitivity is a function of **T Lymphocytes, not antibody**.
- It starts hours (or Days) after contact with the antigen and often lasts for days.
- It can be transferred by immunologically committed (Sensitized) T cells, not by serum.
- Principal pattern of immunologic response to variety of intra cellular microbiologic agents
    - *Mycobacterium tuberculosis*
    - Viruses
    - Fungi
    - Parasites

Type IV (Cell Mediated) Hypersensitivity

Pathogenesis of type IV hypersensitivity





APCs: Macrophages

DTH Cells: TH1

TH1 products: IFN-γ, TNF-β, IL-2, IL-3, IL-8, MCAF, MIF

Macrophage activation: MHC cl II, TNF receptor, oxygen radicals, nitric oxide

Goldsy RA et al. Immunology 5th Ed, 2003, p 384

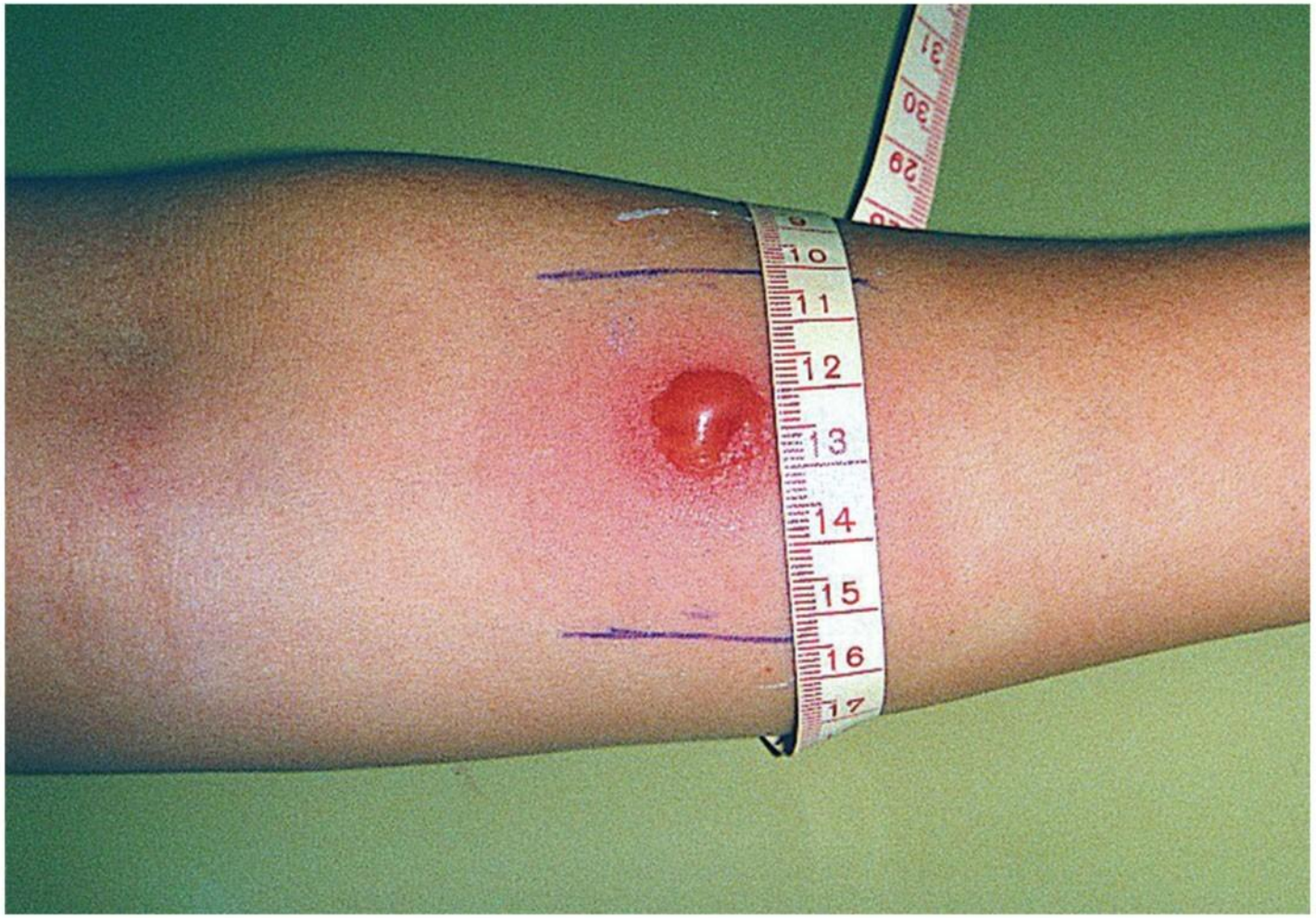
Clinically Important Delayed Hypersensitivity Reactions

Type IV (Cell Mediated) Hypersensitivity

The tuberculin response

- An injection of tuberculin beneath the skin causes reaction in individual exposed to tuberculosis or tuberculosis vaccine
- Used to diagnose contact with antigens of *tuberculosis*
    - No response when individual not infected or vaccinated
    - Red, hard swelling develops in individuals previously infected or immunized

A positive tuberculin test



Type IV (Cell Mediated) Hypersensitivity

Allergic contact dermatitis

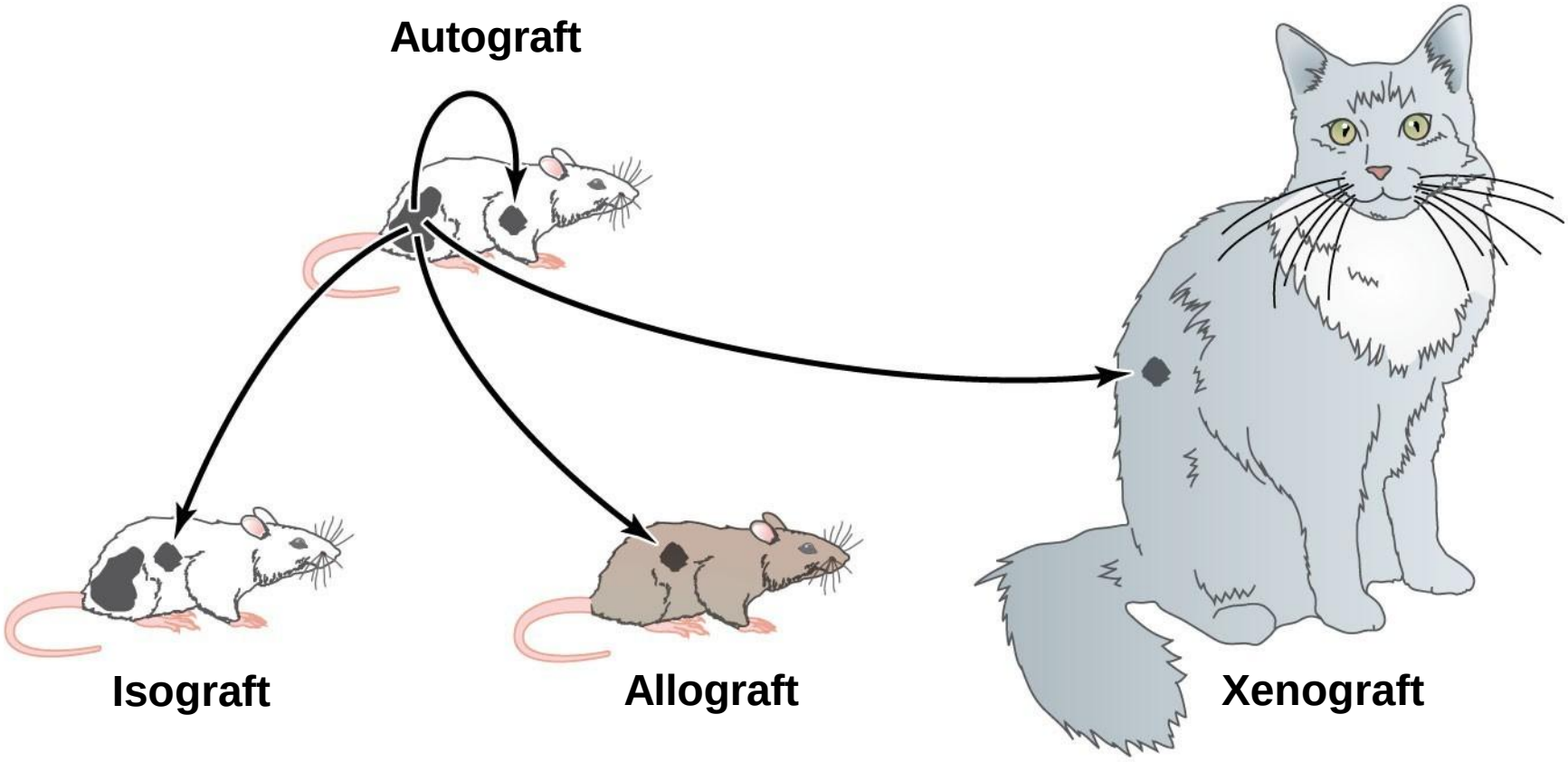
- Cell-mediated immune response
- Results in an intensely irritating skin rash
- Triggered by chemically modified skin proteins that the body regards as foreign
- Acellular, fluid-filled blisters develop in severe cases
- Can be treated with glucocorticoids

Allergic contact dermatitis

Type IV (Cell Mediated) Hypersensitivity

Graft rejection

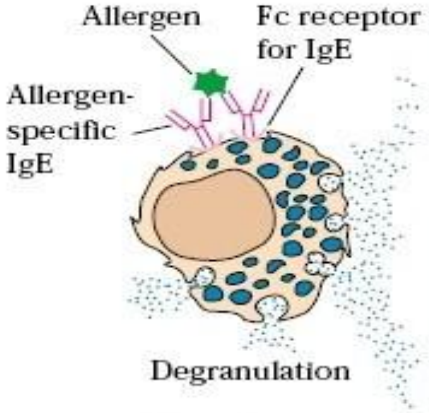
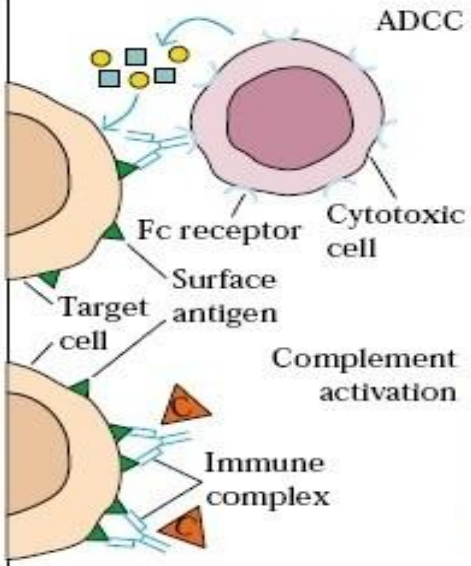
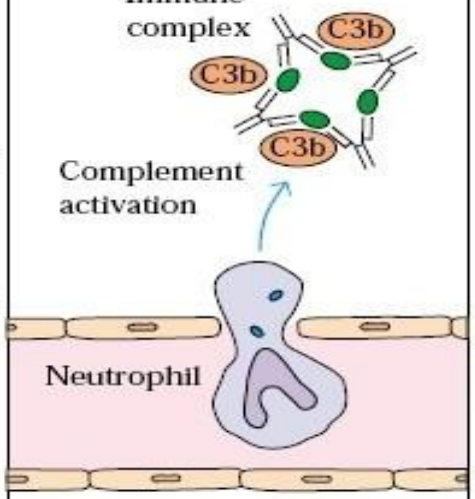
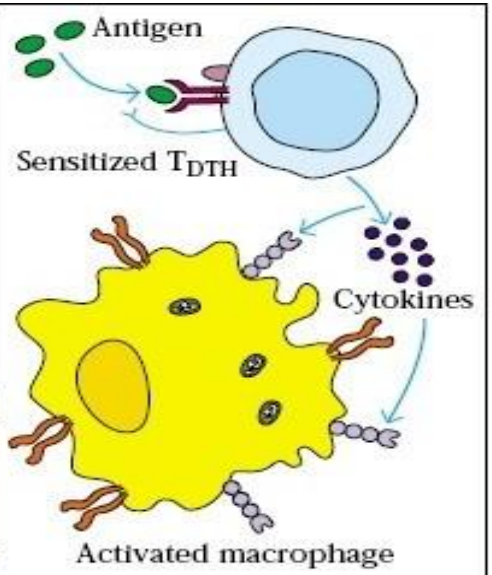
- Rejection of tissues or organs that have been transplanted
- Grafts perceived as foreign by a recipient undergo rejection
- Immune response against foreign MHC on graft cells
- Rejection depends on degree to which the graft is foreign to the recipient
- Based on the type of graft



Genetically identical sibling or clone

Genetically different member of same species

Hypersensitivity Reactions Conclusion:

 Type I	 Type II	 Type III	 Type IV
IgE-Mediated Hypersensitivity	IgG-Mediated Cytotoxic Hypersensitivity	Immune Complex-Mediated Hypersensitivity	Cell-Mediated Hypersensitivity
Ag induces crosslinking of IgE bound to mast cells and basophils with release of vasoactive mediators	Ab directed against cell surface antigens meditates cell destruction via complement activation or ADCC	Ag-Ab complexes deposited in various tissues induce complement activation and an ensuing inflammatory response mediated by massive infiltration of neutrophils	Sensitized T_H1 cells release cytokines that activate macrophages or T_C cells which mediate direct cellular damage
Typical manifestations include systemic anaphylaxis and localized anaphylaxis such as hay fever, asthma, hives, food allergies, and eczema	Typical manifestations include blood transfusion reactions, erythroblastosis fetalis, and autoimmune hemolytic anemia	Typical manifestations include localized Arthus reaction and generalized reactions such as serum sickness, necrotizing vasculitis, glomerulnephritis, rheumatoid arthritis, and systemic lupus erythematosus	Typical manifestations include contact dermatitis, tubercular lesions and graft rejection