

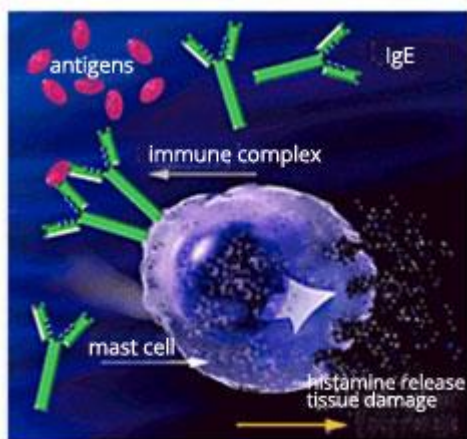
# Hypersensitivity Reactions

## Types of Hypersensitivity Reactions

The response of the host to the presence of foreign substances can trigger four types of hypersensitivity reactions:

- I. Immediate
- II. Cytotoxic
- III. Immune complex
- IV. Cell-mediated

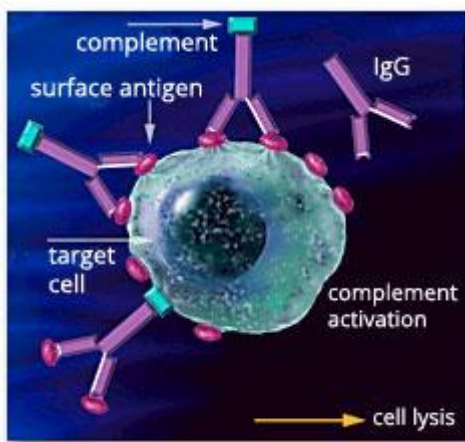
### Type I: Immediate Hypersensitivity (Anaphylactic Reaction)



The reaction may involve skin (urticaria and eczema), eyes (conjunctivitis), nasopharynx (rhinorrhea, rhinitis), bronchopulmonary tissues (asthma) and gastrointestinal tract (gastroenteritis). The reaction is the result of an antigen cross-linking with membrane-bound IgE antibody of a mast cell or basophil. Histamine, serotonin, bradykinin, and lipid mediators (e.g., platelet activating factor, prostaglandins, and leukotrienes) are released during the anaphylactic reaction. These released substances have the potential to cause tissue damage.

The precise mechanism as to why some individuals are more prone to type-I hypersensitivity is not clear. However, it has been shown that such individuals preferentially produce more of TH2 cells that secrete IL-4, IL-5 and IL-13 which in turn favor IgE class switch. IgE has very high affinity for its receptor (Fcε; CD23) on mast cells and basophils.

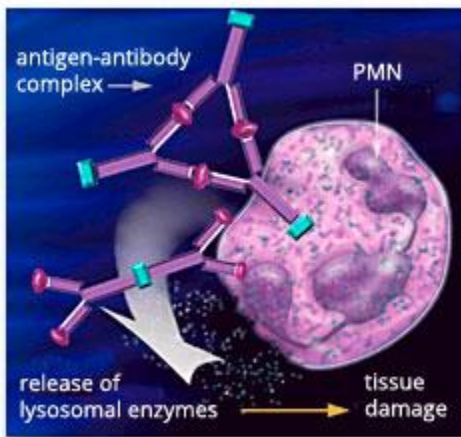
## Type II: Cytotoxic Reaction (Antibody-dependent)



In a cytotoxic reaction, the antibody reacts directly with the antigen that is bound to the cell membrane to induce cell lysis through complement activation. These antigens may be intrinsic or “self” as in autoimmune reactions or extrinsic or “non-self.” Cytotoxic reactions are mediated by IgG, IgM and complement. Phagocytes and K cells may also play a role.

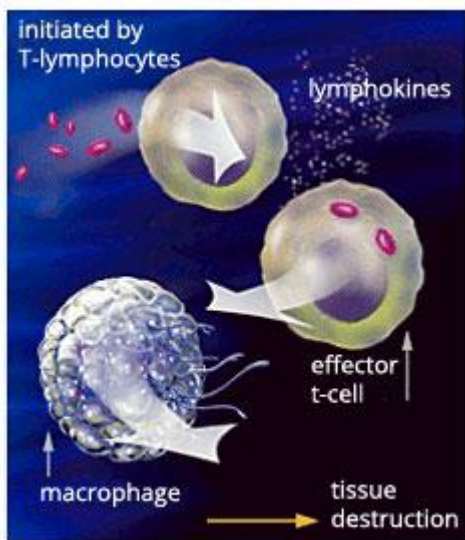
Examples of cytotoxic reaction are the Rh incompatibility of a newborn, blood transfusion reactions, and autoimmune diseases like Pemphigus Vulgaris, Bullous Pemphigoid, autoimmune hemolytic anemia and Goodpasture's syndrome to name a few.

## Type III: Immune Complex Reaction



IgG and IgM bind antigen, forming antigen-antibody (immune) complexes. These activate complement, which results in PMN chemotaxis and activation. PMNs then release tissue damaging enzymes. Tissue damage present in autoimmune diseases (e.g., systemic lupus erythematosus), and chronic infectious diseases (e.g., leprosy) can be attributed, in part, to immune complex reactions. . The reaction may be general (e.g., serum sickness) or may involve individual organs including skin (e.g., systemic lupus erythematosus, Arthus reaction), kidneys (e.g., lupus nephritis), lungs (e.g., aspergillosis), blood vessels (e.g., polyarteritis), joints (e.g., rheumatoid arthritis) or other organs. This reaction may be the pathogenic mechanism of diseases caused by many microorganisms.

## Type IV: Cell-Mediated (Delayed Hypersensitivity)



Cell-mediated reactions are initiated by T-lymphocytes and mediated by effector T-cells and macrophages. This response involves the interaction of antigens with the surface of lymphocytes. Sensitized lymphocytes can produce cytokines (Major lymphokines involved in delayed hypersensitivity reaction include monocyte chemotactic factor, interleukin-2, interferon-gamma, TNF alpha/beta, etc), which are biologically active substances that affect the functions of other cells. This type of reaction takes 48-72 hours, or longer, after contact with the antigen to fully develop. Many chronic infectious diseases, including tuberculosis and fungal infections, exhibit delayed hypersensitivity.

Evidence suggests that hypersensitivity reactions, particularly Type III and IV, may be involved in the pathogenesis of periodontal disease.

**Table - Comparison of Different Types of hypersensitivity**

Characteristics	Type-I (anaphylactic)	Type-II (cytotoxic)	Type-III (immune complex)	Type-IV (delayed type)
Antibody	IgE	IgG, IgM	IgG, IgM	None
Antigen	Exogenous	Cell surface	Soluble	Tissues and organs
Response time	15-30 minutes	Minutes-hours	3-8 hours	48-72 hours
Appearance	Weal and flare	Lysis and necrosis	Erythema and edema, necrosis	Erythema and induration
Histology	Basophils and eosinophil	Antibody and complement	Complement and neutrophils	Monocytes and lymphocytes
Transferred with	Antibody	Antibody	Antibody	T-cells
Examples	Allergic asthma, hay fever	Erythroblastosis fetalis  Goodpasture's		