

Alteration in immune responses

Hypersensitivity and Autoimmune disorders

Hypersensitivity

It means tissue damage due to reaction between immune system and endogenous or exogenous antigen.

Types of Hypersensitivity

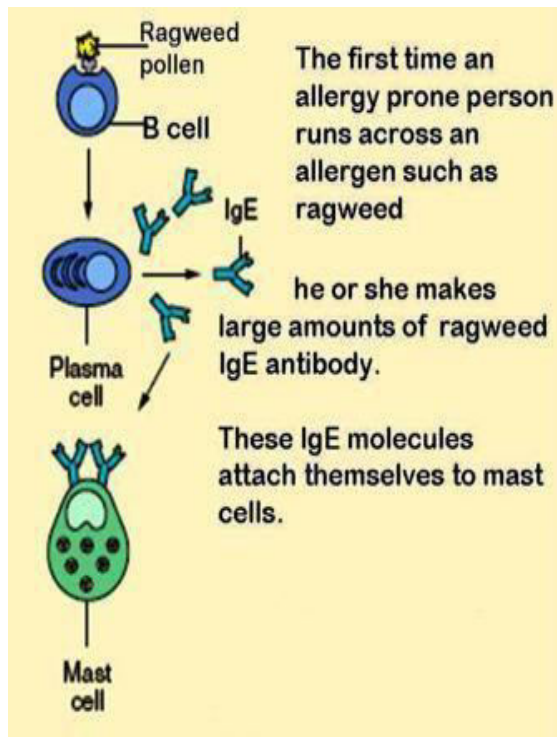
- Type I = Anaphylaxis
- Type II = Cytotoxic antibodies reaction.
- Type III = Arthus reaction (locally) or Serum Sickness Systemic.
- Type IV = Delayed hypersensitivity.

Hypersensitivity type I = Anaphylaxis = Immediate Hypersensitivity

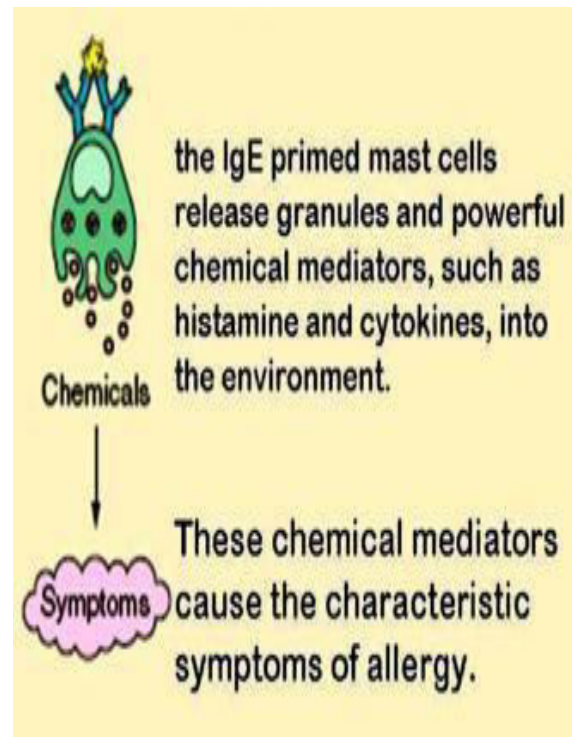
Occurs in people, genetically has ability to produce high level of immunoglobulin type IgE.

- ◆ Most IgE molecules are bound to the surface of mast cells and blood basophils.
- ◆ Mast cells in many respects are similar to basophils. Their cytoplasm is filled secretory granules. These granules contain chemical mediators such as histamine and proteoglycan.
- ◆ Histamine is a potent vasodilator, increase permeability of blood vessels, bronchial contraction and enhance inflammation.
- ◆ Mast cells present in connective tissues of all the body, specially in the skin, respiratory tract, and intestine.
- ◆ The commonest manifestations of atopy are hay fever and extrinsic asthma

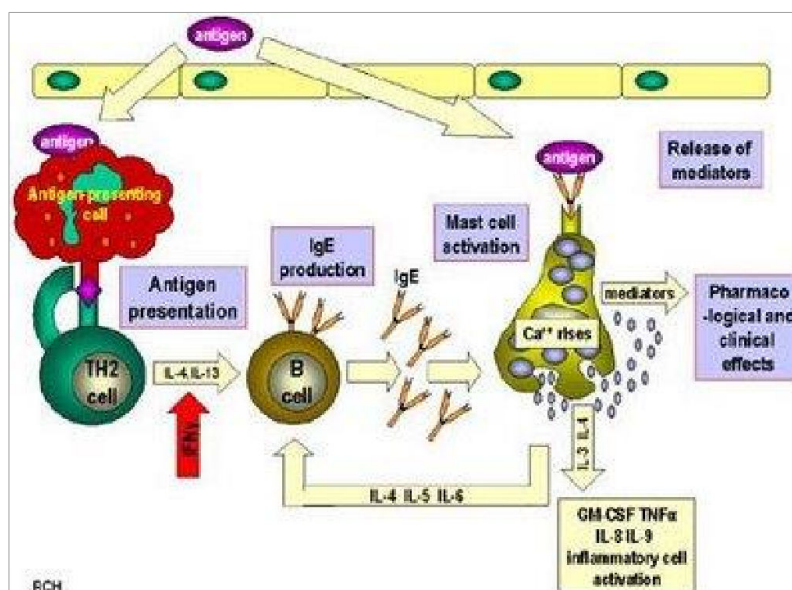
First exposure to the allergen



Second exposure to same allergen



Type I = Anaphylaxis

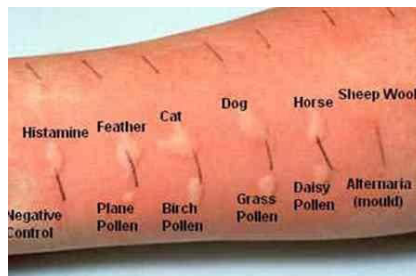


Hay Fever

- ◆ Hay fever is initiated by hypersensitivity to a large group of allergen (plant pollen, fungi, animal allergens, and dust mites).
- ◆ In hay fever there is acute inflammation of the nasal and conjunctival mucous membrane with sneezing, itching and watery discharge from the eyes and nose.
- ◆ Severe attacks may be accompanied by systemic malaise, fatigue. Sinus obstruction may cause headache.

Diagnosis

1. History of the patient.
2. Physical examination.
3. Microscopic identification of nasal eosinophilia.
4. Skin test to identify the causative allergen.



Skin Allergy Test

Treatment

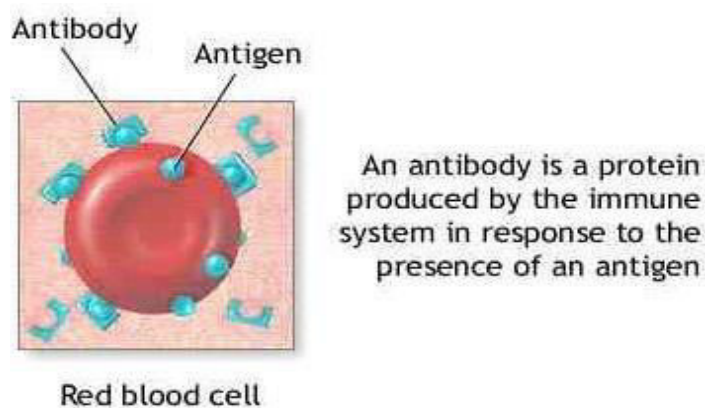
- ◆ It is symptomatic in most cases, and includes use of oral antihistamines and decongestion.
- ◆ Used intranasal drugs which act by prevent mast cell from degranulation.
- ◆ A program of desensitization may be used when symptoms are particularly bothersome.
- ◆ Desensitization involves frequent (usually weekly) injection of the offending antigens (Ag) the antigens which are given in increase doses, stimulate production of high levels of IgG act as blocking antibodies by combining with the Ag before it can combine with the cell bound IgE antibodies.

Type II Hypersensitivity = Cytotoxic Antibody Reaction

◆ This type of hypersensitivity is caused by antibodies that react with antigen present on cell surfaces.

◆ Examples on this type of hypersensitivity are:

1. Autoimmune hemolytic anemia
2. Incompatible blood transfusion
3. Drug hypersensitivity like “penicillin hypersensitivity”.



Drug Hypersensitivity

◆ Some drugs or their metabolites are capable to binding to the surface of red cells (like penicillin), leukocytes, or platelets and acting as haptens.

◆ Antibody develops and binds to the hapten on the cell surface, and cell injury and destruction.

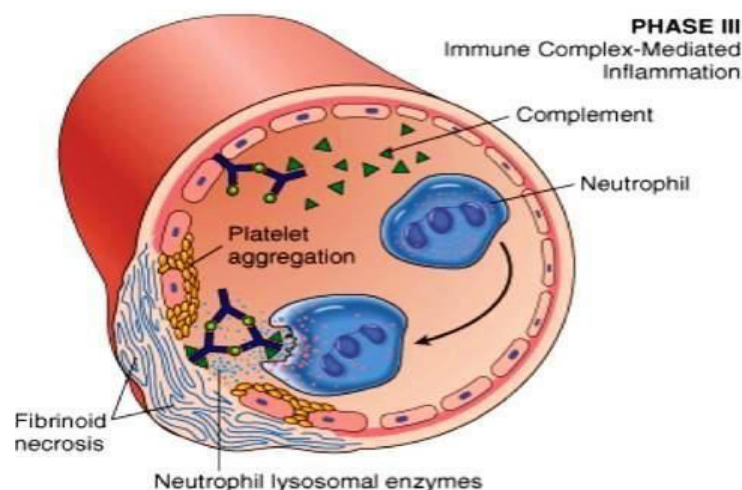
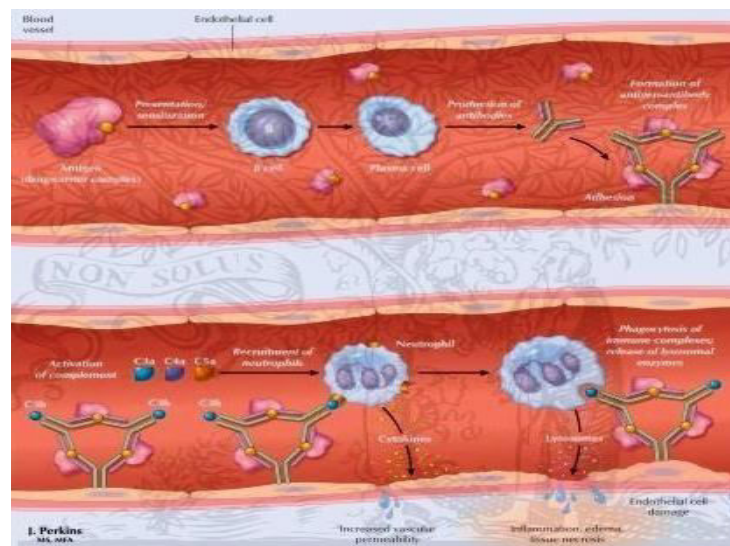
◆ After heavy dosage, high titer of IgG antibody develop in some patients and this brings about the destruction of sensitized red cells.

◆ Hapten: is a small molecule which has no ability to provoke immune response but when bind with other molecules it becomes large and then it can enhance immune response.



Type III Hypersensitivity= Immune Complex Mediated Hypersensitivity

- ◆ It occurs when antigen- antibody complexes deposit in the basement membrane of blood vessels and provoke inflammation in the site of deposition.
 - ◆ It may be localized or systemic.
 - ◆ Localized type (in particular organ like kidney) is called **Arthus reaction**.
 - ◆ Systemic type is called **serum sickness**.
1. Immune complex formation.
 2. Immune complex deposition and activate complement which leads to attract neutrophils.
 3. Mediate inflammation and tissue injury.



Systemic Lupus Erythematosus (SLE)

- ◆ SLE is a multisystem disease of autoimmune origin, characterized by presence of **auto-antibodies against nuclear components, i.e. antinuclear antibodies**.
- ◆ That leads to chronic inflammatory injury and damage of multiple organ system “ **skin, joints, kidney, serosal surfaces and brain**”.
- ◆ Clinically, SLE is episodic in nature and its course characterized by flare and remission.

Etiology and pathogenesis

- ◆ The cause remains unknown, but there is defect in the self tolerance mechanisms.
- ◆ Both genetic and environmental factors play a role in the pathogenesis of SLE.
- ◆ Environmental factors include:
 1. Exposure to UV.
 2. Sex hormones; during the reproductive years, the frequency of SLE is 10 times greater in women than in men.
- ◆ 1. Drugs

Clinical Features

- ◆ Fever, fatigue, weakness, and weight loss, occur early and may recur.
- ◆ Skin erythematous rash may appear in face “butterfly”, neck extremities, or trunk.
- ◆ Chest pain, pleurisy.
- ◆ Carditis, involving myocardium, endocardium, or pericardium.
- ◆ Renal disorders.
- ◆ Neuronal disorders include; depression, convulsions,



The young woman has a malar rash (the so-called "butterfly" rash because of the shape across the cheeks). Such a rash suggests lupus. Discoid lupus erythematosus (DLE) involves mainly just the skin and is, therefore, relatively benign compared to systemic lupus erythematosus (SLE). In either case, sunlight exposure accentuates this erythematous rash. A small number (5 to 10%) of DLE patients go on to develop SLE (usually the DLE patients with a positive ANA).

Type IV Hypersensitivity= Delayed Type Hypersensitivity

- ◆ In this type the cytotoxic lymphocyte (CD8) kills the antigen bearing target cells.
- ◆ Tissue destruction by CD8 may be an important component of many of many T cell mediated diseases such as type I diabetes.
- ◆ Tuberculin test.

Autoimmune Diseases

- ◆ Immune reaction against self-antigens is called autoimmunity.
- ◆ Autoimmunity results from self tolerance.
- ◆ Self tolerance refers to lack of responsiveness to an individual's own antigens.
- ◆ Autoimmunity arises from combination of the inheritance of susceptibility genes, which may contribute to the breakdown of self tolerance, and environmental triggers, such as infections, and tissue damage, which promote the activation of self reactive lymphocytes.