Antisera, Immunesera , Serotherapy

Preperation containing antibodies introduced into the body of the patients to provide passive immunity. Antisera contain readymade antibodies usually IgG and is mostly used for therapeutic purpose where immediate cure is needed.

It is also used prophylactically.

Preparation

Antisera are prepared by injecting bacteria or viruses or their products into laboratory animals for experimental purpose or in other large animals for commercial purpose. So as to produce immunity which is manifested by formation of antibodies in blood of animals

Antisera may be of following types

1) **Antitoxin Sera**

In Preparing antitoxin sera the antigen used is either specific toxin in sublethal dose or toxiod. Examples Antitetnus sera, antidiptheria sera, antisnake venom sera

2) Antibacterial Sera

Graded dose of bacterial suspension either living or dead are injected in large animals such as horses or other animals. Test bleeding is done to know concentration of antibodies. If titer concentration of antibody is sufficient animal is finally bled and sera is separated and stored.

2) **Antiviral Sera**

Is prepared in host animals against viral infections. Antiserum against Rabies and measeles etc.

Storage.

They should be protected from sunlight. They should be stored below 10 C. preferably 2-4 C.

Action and uses

Use for therapeutic purpose for passive Immunization.

Adverse Reaction

Serum reaction of anaphylactic type may occur in some individuals. They may be treated by administration of adrenaline, antihistaminic drugs and corticosteroids.

Immune system Disorders

Fall into following broad categories:

Immunodeficiency, in which parts of the immune system fail to provide an adequate response example include AIDS, an immunodeficiency characterized by the suppression of CD4+ ("helper") T cells, dendritic cells and macrophages by the Human Immunodeficiency Virus (HIV).

Autoimmunity, in which the immune system attacks its own host's body (examples include systemic lupus erythematosus, rheumatoid arthritis, and myasthenia gravis).

Hypersensitivities (such as in asthma and other allergies) that respond inappropriately to otherwise harmless compounds.

1. **Autoimmune Diseases**

When the action of the immune system is in response to self antigens and causes damage to one's own organs, the result is an autoimmune disease. More than 40 autoimmune diseases have been identified. Although relatively rare, they affect about 5% of the population in the developed world. About 75% of the cases of autoimmune disease selectively affect women. Treatments for

autoimmune diseases are improving as knowledge of the mechanisms controlling immune reactions improves.

Autoimmune diseases occur when there is a loss of self tolerance, the immune system's ability to discriminate self from non self. In the generally accepted model by which T cells become capable of distinguishing self from non self, the cells acquire this ability during their passage through the thymus. In autoimmune diseases, the loss of self-tolerance leads to the production of antibodies or a response by sensitized T cells against a person's own tissue antigens.

Graves' Disease

Is caused by antibodies called long-acting thyroid stimulators. These antibodies attach to receptors on thyroid gland cells that are the normal target cells of the thyroid stimulating hormone produced by the pituitary gland. The result is that the thyroid gland is stimulated to produce increased amounts of thyroid hormones and becomes greatly enlarged.

The most striking signs of the disease are goiter (a disfiguring swelling of the thyroid gland) and markedly bulging, staring eyes.

Myasthenia Gravis

Is a disease in which muscles become progressively weaker. It is caused by antibodies that coat the acetylcholine receptors at the junctions at which nerve impulses reach the muscles. Eventually, the muscles controlling the diaphragm and the rib cage may fail to receive the necessary nerve signals, and respiratory arrest and death result.

Immune complex autoimmune reactions

Rheumatoid arthritis

Is a disease in which immune complexes of IgM, IgG, and complement are deposited in the joints. In fact, immune complexes called *rheumatoid factors* may be formed by IgM binding to

the Fc region of normal IgG. These factors are found in 70% of individuals suffering from rheumatoid arthritis. The chronic inflammation caused by this deposition eventually leads to severe damage to the cartilage and bone of the joint.

Insulin-dependent diabetes mellitus

Insulin-dependent diabetes mellitus is a familiar condition caused by immunological destruction of insulin-secreting cells of the pancreas. T cells are clearly implicated in this disease; animals that are genetically likely to develop diabetes fail to do so when their thymus is removed in infancy.

Hypersensitivity

Type I (Anaphylactic) Reactions

Type I, or anaphylactic, react ions often occur within 2 to 30 minutes after a person sensitized to an antigen is reexposed to that antigen. *Anaphylaxis* means opposite of protected," from the prefix *ana-*, meaning against, and the Greek *phylaxis*, meaning protection. Anaphylaxis is an inclusive term for the reactions caused when certain antigens combine with IgE antibodies.

Anaphylactic responses can be ***systemic reactions,*** which produce shock and breathing difficulties and are sometimes fatal, or ***localized reactions***, which include common allergic conditions such as hay fever, asthma, and hives (slightly raised, often itchy and reddened areas of the skin). The IgE antibodies produced in response to an antigen, such as insect venom or plant pollen, bind to the surfaces of cells such as mast cells and basophils. These two cell types are similar in morphology and in their contribution to allergic reactions. Mast cells are especially prevalent in the connective tissue of the skin and respiratory tract and in surrounding blood vessels. Basophils circulate in the bloodstream, where they constitute less than 1 % of the leukocytes. Both are filled with granules containing a variety of chemicals called *mediators.*

Mast cells and basophils can have as many as 500,000 sites for IgE attachment. The Fc (stem) region of an IgE antibody. Other mediators include leukotrienes of various types and Prostaglandins. These mediators are not preformed and stored in the granules but are synthesized by the antigen-triggered cell. Collectively, all these mediators serve as chemotactic agents that, in a few hours, attract neutrophils and eosinophils to the site of the degranulated cell. They then activate various factors that cause inflammatory symptoms, such as distension of the capillaries, swelling, increased secretion of mucus, and involuntary contractions of smooth muscles Systemic anaphylaxis (or *anaphylactic shock)* can result when an individual sensitized to an antigen is exposed to it again. The release of mediators causes peripheral blood vessels throughout the body to enlarge, resulting in a drop in blood pressure (shock). This reaction can be fatal within a few minutes. There is very little time to act once someone develops systemic anaphylaxis.

Treatment usually involves self-administration with a preloaded syringe of epinephrine, a drug that constricts blood vessels and raises the blood pressure. In the United States, 50 to 60 people die each year from anaphylactic shock caused by insect stings.

Localized Anaphylaxis localized anaphylaxis is usually associated with antigens that are ingested (foods) or inhaled (pollen). The symptoms depend primarily on the route by which the antigen enters the body. In allergies involving the upper respiratory system, such as hay fever, sensitization usually involves mast cells in the mucous membranes of the upper respiratory tract. The airborne antigen might be a common environmental material such as plant pollen, fungal spores, feces of house dust mites, or animal. The typical symptoms are itchy and teary eyes, congested nasal passages, coughing, and sneezing. Antihistamine drugs, which compete for histamine receptor sites, are often used to treat these symptoms. Asthma is an allergic reaction

that mainly affects the lower respiratory system. Symptoms such as wheezing and shortness of breath are caused by the constriction of smooth muscles in the bronchial tubes. Avoiding contact with the sensitizing antigen is the most obvious way to prevent allergic reactions. Unfortunately, avoidance is not always possible. Some individuals experience an allergic reaction after eating an assortment of foods. In such cases, they may not know exactly what antigen they are sensitive to. In some cases, skin tests might be of use in diagnosis. These tests involve inoculating small amounts of the suspected antigen just beneath the epidermis of the skin. Sensitivity to the antigen is indicated by a rapid inflammatory reaction that produces redness, swelling, and itching at the inoculation site. This small affected area is called a *wheal.* Once the responsible antigen has been identified, the person can either try to avoid contact with it or undergo desensitization.

This procedure usually consists of a series of gradually increasing dosages of the antigen carefully injected beneath the skin. The objective is to cause the production of IgG rather than IgE antibodies in the hope that the circulating IgG antibodies will act as *blocking antibodies* to intercept and neutralize the antigens before they can react with cell-bound IgE. Desensitization is not a routinely successful procedure, but it is effective in 65-75% of individuals whose allergies are induced by inhaled antigens and in a reported 97% of people allergic to insect venom.

Type II (Cytotoxic) Reactions

Type II (cytotoxic) reactions generally involve the activation of complement by the combination of IgG or IgM antibodies with an antigen in cell. This activation stimulates complement to lyse the affected cell, which might be either a foreign cell or a host cell that carries a foreign antigenic determinant (such as a drug) on its surface. Additional cellular damage may be caused within 5 to 8 hours by the action of macrophages and other cells that attack antibody-coated cells.

The most familiar cytotoxic hypersensitivity reactions are *transfusion reactions*, in which red blood cells are destroyed as a result of reacting with circulating antibodies. These involve blood group systems that include the ABO and Rh antigens.

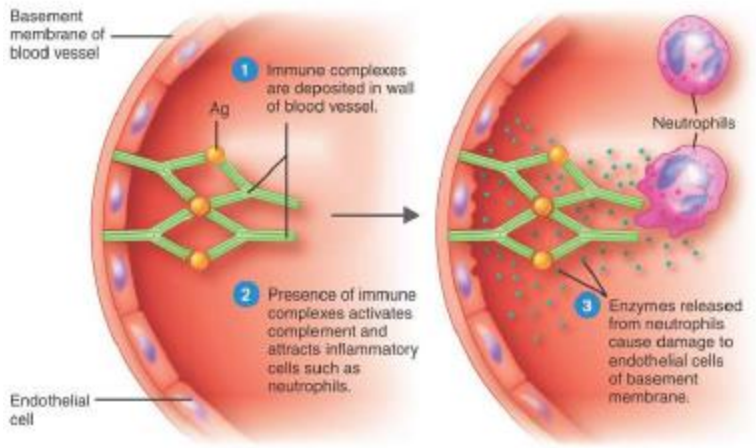
Hemolytic Disease of the Newborn Blood transfusions arc not the only way in which an Rh - person can become sensitized to Rh + blood. When an Rh - woman and an Rh + man produce a child, there is a 50% chance that the child will be Rh + . If the child is Rh +, the Rh - mother can become sensitized to this antigen during birth when the placental membranes tear and the fetal Rh + RBCs enter the maternal circulation, causing the mother's body to produce anti-Rh antibodies of the IgG type. If the fetus in a subsequent pregnancy is Rh +, her anti-Rh antibodies will cross the placenta and destroy the fetal RBCs. The fetal body responds to this immune attack by producing large numbers of immature RBCs called erythroblasts. Thus, the term *erythroblastosis fetalis* was once used to describe what is now called hemolytic disease of the newborn (HDNB). Before the birth of a fetus with this condition, the maternal circulation removes most of the toxic by-products of fetal RBC disintegration. After birth, however, the fetal blood is no longer purified by the mother, and the newborn develops jaundice and severe anemia. HDNB is usually prevented today by passive immunization of the Rh - mother at the time of delivery of any Rh + infant with anti Rh antibodies, which are available commercially (RhoGAM). These anti-Rh antibodies combine with any fetal Rh+ RBCs that have entered the mother's circulation, so it is much less likely that she will become sensitized to the Rh antigen. [f the disease is not prevented, the newborn's Rh + blood, contaminated with maternal antibodies, may have to be replaced by transfusion of uncontaminated blood.

Type III (Immune Complex) Reactions

Type III reactions involve antibodies against soluble antigens circulating in the serum. (In contrast, type II immune reactions are directed against antigens located on cell or tissue surfaces) The antigen-antibody complexes are deposited in organs and cause inflammatory damage.

. The antibodies involved are usually IgG. A significant excess of antibody leads to the formation of complement-fixing complexes that are rapidly removed from the body by phagocytosis. When there is a significant excess of antigen, soluble complexes form that do not fix complement and do not cause inflammation. However, when a certain antigen-antibody ratio exists, usually with a slight excess of antigen, the soluble complexes that form are small and escape phagocytosis.

These complexes circulate in the blood, pass between endothelial cells of the blood vessels, and become trapped in the basement membrane benea th the cells. In this location, they may activate complement and cause a transient inflammatory reaction Glomerulonephritis is an immune complex condition, usually resulting from an infection, that causes inflammatory damage to the kidney glomeruli, which are sites of blood filtration



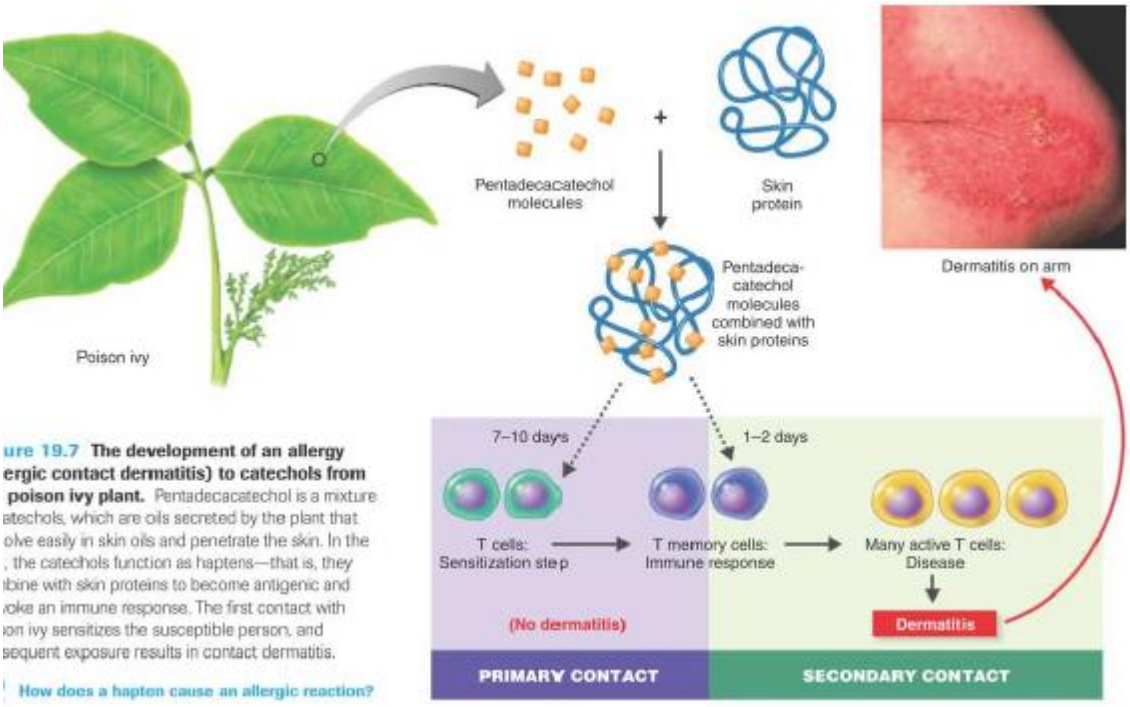
Type IV (Delayed Cell-Mediated) Reactions

Are not apparent for a day or more. A major factor in the delay is the time required for the participating T cells and macrophages to migrate to and accumulate near the foreign antigens.

We have seen that hypersensitivity symptoms are frequently displayed on the skin . One delayed hypersensitivity reaction that involves the skin is the familiar skin test for tuberculosis.

Because *Mycobacterium tuberculosis* is often located within macrophages, this organism can stimulate a delayed cell mediated immune response. As a screening test, protein componen ts of the bacteria are injected into the skin. If the recipient has (or has had) a previous infection by tuberculosis bacteria, an inflammatory reaction to the injection of these antigens will appear on the skin in I to 2 days this interval is typical of delayed hypersensitivity reactions.

Allergic contact dermatitis, another common manifestation of delayed cell -mediated hypersensitivity, is usually caused by haptens that combine with proteins (particularly the amino acid lysine) in the skin of some people to produce an immune response. Reactions to poison ivy (Figure 19.7), cosmetics, and the metals in jewelry (especially nickel) are familiar examples of these allergies



ure 19.7 The development of an allergy ergic contact dermatitis) to catechols from poison ivy plant. Pentadecacatechol is a mixture atechols, which are oils secreted by the plant that olve easily in skin oils and penetrate the skin. In the , the catechols function as haptens—that is, they bine with skin proteins to become antigenic and oke an immune response. The first contact with on ivy sensitizes the susceptible person, and sequent exposure results in contact dermatitis.

How does a hapten cause an allergic reaction?