Disorders Associated with the Immune System

Hypersensitivity

The term hypersensitivity refers to an antigenic response beyond that which is considered normal; the term allergy is more familiar and is essentially synonymous. Hypersensitivity responses occur in individuals who have been sensitized by previous exposure to an antigen, which in this context is sometimes called an allergen. When an individual who was previously sensitized is exposed to that antigen again, his or her immune system reacts to it in a damaging manner. The four principal types of hypersensitivity reactions, are :

1- Type I anaphylactic.

2- Type II cytotoxic

3- Type III immune complex, and

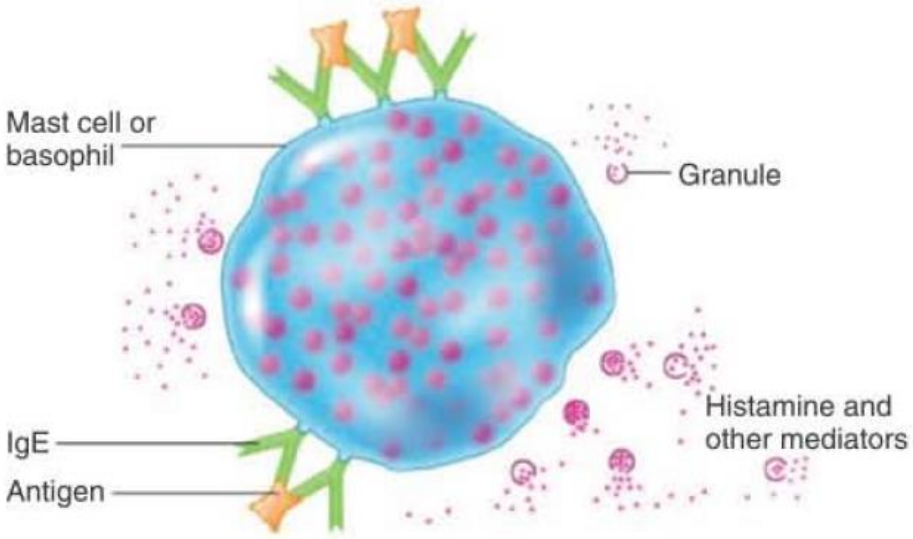
4-Type IV cell-mediated (or delayed -type) reactions.

Type I (Anaphylactic) Reactions

Type I, or anaphylactic, reactions often occur within 2 to 30 minutes after a person sensitized to an antigen is reexposed to that antigen. Anaphylaxis means "the 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 fewer 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 can attach to one of these specific receptor sites on such a cell, leaving two antigen-binding sites free. Of course, the attached IgE monomers will not all be specific for the same antigen. But when an antigen such as plant pollen encounters two adjacent antibodies of the same appropriate specificity, it can bind to one antigen-binding site on each antibody, bridging the space between them. This bridge triggers the mast cell or basophil to undergo degranulation, which releases the granules inside these cells and also the mediators they contain. These mediators cause the unpleasant and damaging effects of an allergic reaction . The best-known mediator is **histamine**. The release of histamine increases the permeability and distension of blood capillaries, resulting in edema (swelling) and erythema (redness). Other effects include increased mucus secretion (a runny nose, for example) and smooth muscle contraction, which in the respiratory bronchi results in breathing difficulty.



(a) IgE antibodies, produced in response to an antigen, coat mast cells and basophils. When an antigen bridges the gap between two adjacent antibody molecules of the same specificity, the cell undergoes degranulation and releases histamine and other mediators.

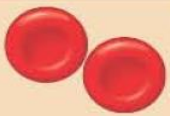
Other mediators include **leukotrienes** of various types and **prostaglandins**. Collectively, all these mediators serve as chemotactic agents that, in a few hours, attract neutrophils and eosinophils to the site of the degranulated cell. They then activate various factors that cause inflammatory symptoms, such as distension of the capillaries, swelling, increased secretion of mucus, and involuntary contractions of smooth muscles.

Type II (Cytotoxic) Reactions

Type II (cytotoxic) reactions generally involve the activation of complement by the combination of IgG or IgM antibodies with an antigenic 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.

A person's ABO blood type depends on the presence or absence of carbohydrate antigens located on the cell membranes of red blood cells (RBCs). Cells of blood type O lack both A and B antigens. The table below shows that the plasma of individuals with a given blood type, such as A, have antibodies against the alternative blood type, anti-B antibody. These antibodies are presumed to arise in response to microorganism and ingested foodstuffs that have antigenic determinants very similar to blood group antigens. Individuals with type AB cells have plasma with no antibodies to either A or B antigens. Type O individuals have antibodies against both A and B antigens.

Blood Group	Erythrocyte or Red Blood Cell Antigens	Illustration	Plasma Antibodies	Blood That Can Be Received
AB	A and B		Neither anti-A nor anti-B antibodies	A, B, AB, O
B	B		Anti-A	B, O
A	A		Anti-B	A, O
O	Neither A nor B		Anti-A and Anti-B	O

The Rh Blood Group System

The roughly 85% of the population whose cells possess this antigen are called Rh +; those lacking this RBC antigen (about 15%) are Rh - . Antibodies that react with the Rh antigen do not occur naturally in the serum of Rh - individuals, but exposure to this antigen can sensitize their immune systems to produce anti-Rh antibodies.

Blood Transfusions and Rh Incompatibility If blood from an Rh + donor is given to an Rh - recipient, the donor's RBCs stimulate the production of anti-Rh ant ibodies in the recipient. If the recipient then receives Rh + RBCs in a subsequent transfusion, a rapid, serious hemolytic reaction will develop.

Hemolytic Disease of the Newbom Blood transfusions are 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 +

Drug-Induced Cytotoxic Reactions

Blood platelets (thrombocytes) are minute cell-like bodies that are destroyed by drug-induced cytotoxic reactions in the disease called thrombocytopenic purpura. The drug molecules are usually hapten because they are too small to be antigenic by themselves; but, in the situation illustrated in Figure 19.5, a platelet has become coated with molecules of a drug and the combination is antigenic. Both antibody and complement are needed for lysis of the platelet. Because platelets are necessary for blood dotting, their loss results in hemorrhages that appear on the skin as purple spots (purpura).

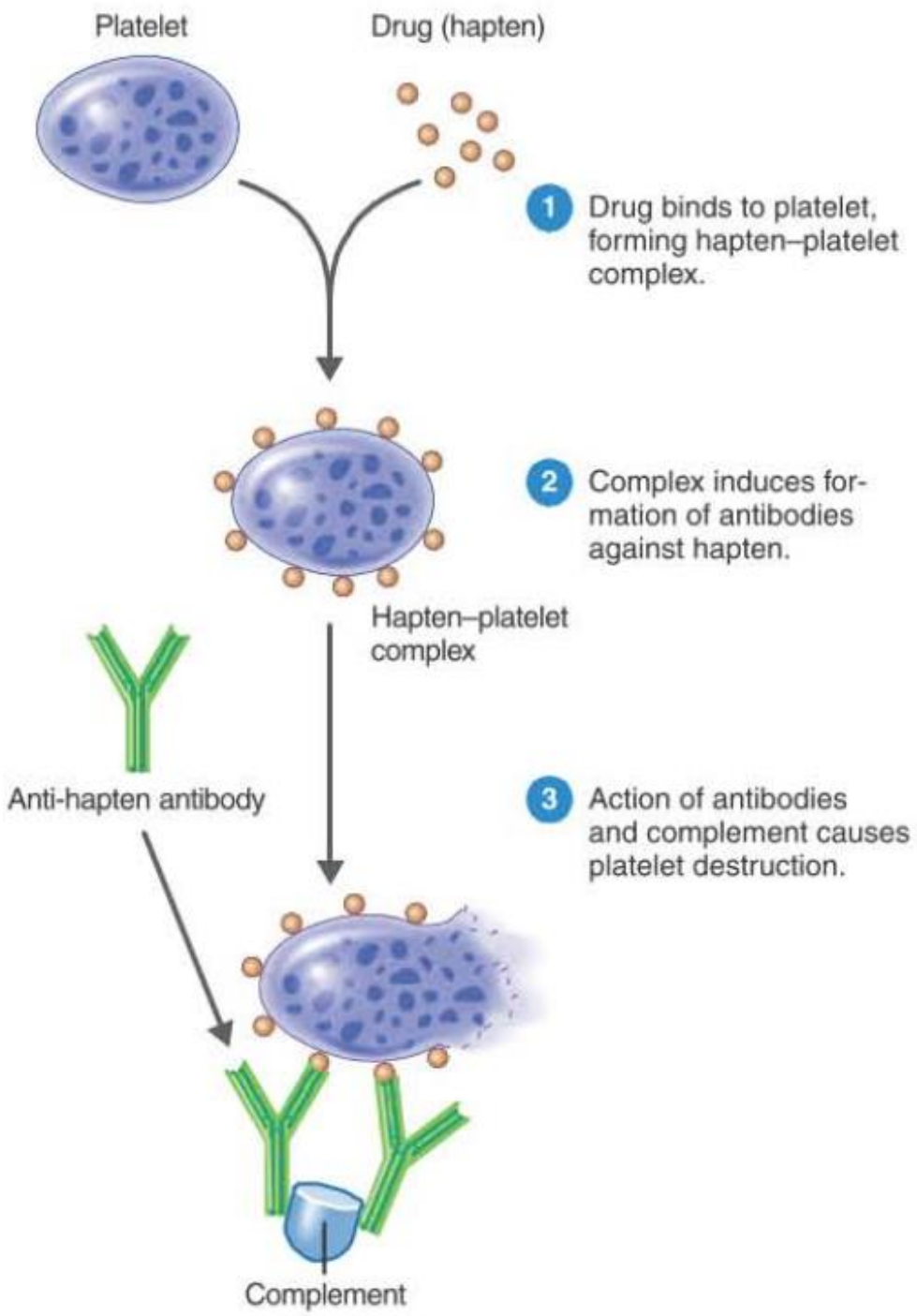


Figure 19.5 Drug-induced thrombocytopenic purpura.
Molecules of a drug such as quinine accumulate on the surface of a platelet and stimulate an immune response that destroys the platelet.