

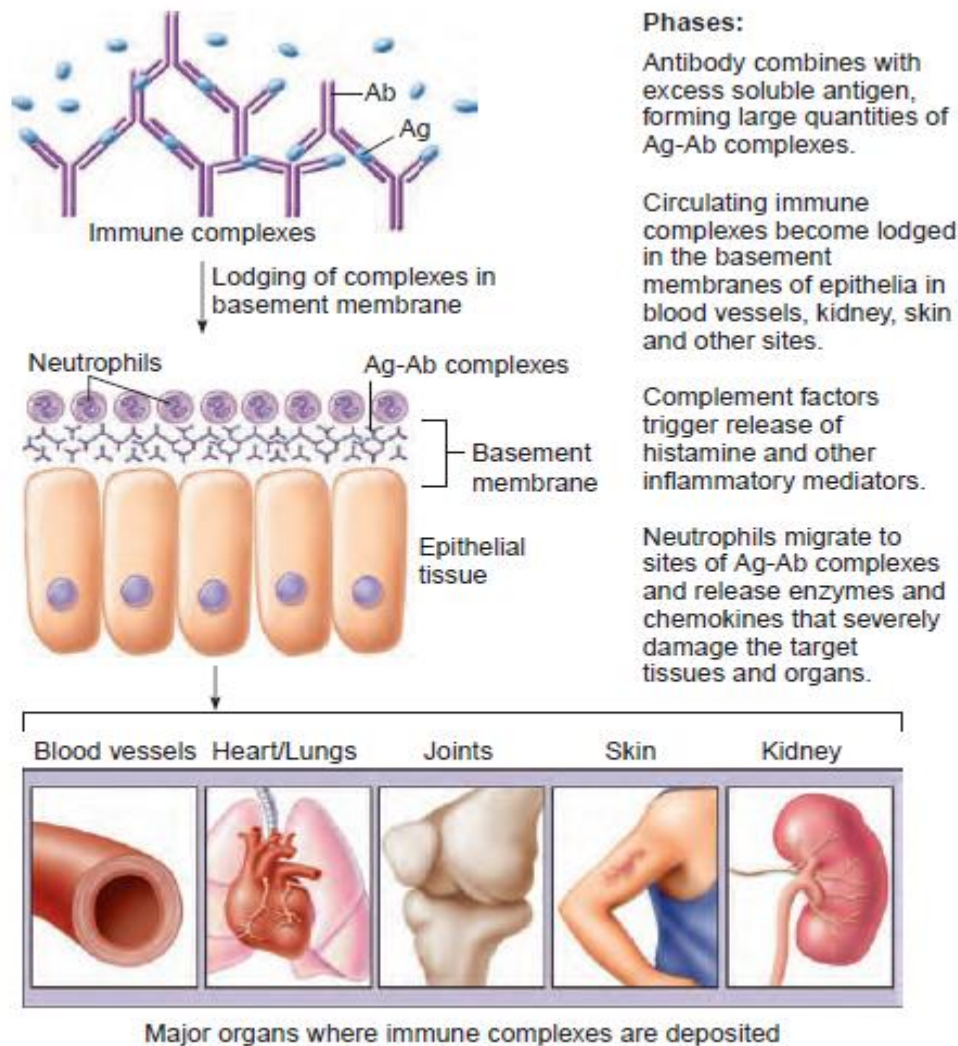
**Type III (Immune Complex) Reactions**

Type III hypersensitivity involves the reaction of soluble antigen with antibody and the deposition of the resulting complexes in basement membranes of epithelial tissue. It is similar to type II, because it involves the production of IgG and IgM antibodies after repeated exposure to antigens and the activation of complement.

Type III differs from type II because its antigens are not attached to the surface of a cell. The interaction of these antigens with antibodies produces free-floating complexes that can be deposited in the tissues, causing an immune complex reaction or disease. This category includes therapy-related disorders (serum sickness and the Arthus reaction) and a number of autoimmune diseases (such as glomerulonephritis and lupus erythematosus).

**Mechanisms of Immune Complex Diseases**

After initial exposure to a profuse amount of antigen, the immune system produces large quantities of antibodies that circulate in the fluid compartments. When this antigen enters the system a second time, it reacts with the antibodies to form antigen-antibody complexes. These complexes summon various inflammatory components such as complement and neutrophils, which would ordinarily eliminate Ab-Ag complexes as part of the normal immune response. In an immune complex disease, however, these complexes are so abundant that they deposit in the basement membranes of epithelial tissues and become inaccessible. In response to these events, neutrophils release lysosomal granules that digest tissues and cause a destructive inflammatory condition. The symptoms of type III hypersensitivities are due in great measure to this pathologic state.



### Types of Immune Complex Disease

During the early tests of immunotherapy using animals, hypersensitivity reactions to serum and vaccines were common. In addition to anaphylaxis, two syndromes, the Arthus reaction and serum sickness, were identified. These syndromes are associated with certain types of passive immunization (especially with animal serum). Serum sickness and the Arthus reaction are like anaphylaxis in requiring sensitization and preformed antibodies. Characteristics that set them apart from anaphylaxis are (1) they depend upon IgG, IgM, or IgA (precipitating antibodies) rather than IgE; (2) they require large doses of antigen (not a minuscule dose as in anaphylaxis); and (3) their symptoms are delayed (a few hours to days). The Arthus reaction and serum sickness differ from

each other in some important ways. The Arthus reaction is a localized dermal injury due to inflamed blood vessels in the vicinity of any injected antigen. Serum sickness is a systemic injury initiated by antigen antibody complexes that circulate in the blood and settle into membranes at various sites.

### **The Arthus Reaction**

The Arthus reaction is usually an acute response to a second injection of vaccines (boosters) or drugs at the same site as the first injection. In a few hours, the area becomes red, hot to the touch, swollen, and very painful. These symptoms are mainly due to the destruction of tissues in and around the blood vessels and the release of histamine from mast cells and basophils. Although the reaction is usually self-limiting and rapidly cleared, intravascular blood clotting can occasionally cause necrosis and loss of tissue.

### **Serum Sickness**

Serum sickness was named for a condition that appeared in soldiers after repeated injections of horse serum to treat tetanus. It can also be caused by injections of animal hormones and drugs. The immune complexes enter the circulation; are carried throughout the body; and are eventually deposited in blood vessels of the kidney, heart, skin, and joints. The condition can become chronic, causing symptoms such as enlarged lymph nodes, rashes, painful joints, swelling, fever, and renal dysfunction.

Homework

- 1- Contrast type II and type III hypersensitivities with respect to type of antigen, antibody, and manifestations of disease.
- 2- Explain what occurs in immune complex disease and give examples.