**Lecture 10 General pathology Dr. Ali H. Murad**

***Type III, Immune-Complex Disorders:***

They are mediated by the formation of insoluble antigen antibody complexes that activate complement which will generates chemotactic and vasoactive mediators that cause tissue damage by a variety of mechanisms, including alterations in blood flow, increased vascular permeability, and the destructive action of inflammatory cells.

The reaction occurs when the antigen combines with antibody, whether in the circulation (circulating immune complexes) or at extravascular sites where antigen may have been deposited.

Immune complexes formed in the circulation produce damage when they come in contact with the vessel lining or are deposited in tissues, including the renal glomerulus, skin venules, lung, and joint synovium.

There are two general types of antigens that cause immune complex mediated injury:

1- Exogenous antigens such as viral and bacterial proteins.

2- Endogenous antigens such as self-antigens associated with autoimmune disorders.

Type III reactions are responsible for the acute glomerulonephritis that follows a streptococcal infection and the manifestations of autoimmune disorders such as systemic lupus erythematosus (SLE).

Unlike type II reactions, in which the damage is caused by binding of antibody to body cells, the harmful effects of type III reactions are indirect (i.e., secondary to the inflammatory response induced by activated complement).

Acute serum sickness is the type of a systemic immune complex disease. Serum sickness is a syndrome consisting of rash, lymphadenopathy, arthralgias, and occasionally neurologic disorders that appeared 7 or more days after injections of horse antisera for prevention of tetanus. Although this therapy is not used today, the name remains.

The most common causes of this allergic disorder include: antibiotics (especially penicillin), various foods, drugs, and insect venoms. Serum sickness is triggered by the deposition of insoluble antigen-antibody (IgM and IgG) complexes in blood vessels, joints, heart, and kidney tissue.

The deposited complexes activate complement, increase vascular permeability, and recruit phagocytic cells, all of which can promote focal tissue damage and oedema.

The signs and symptoms include:

1-Urticaria.

2- Patchy or generalized rash.

3- Extensive oedema (face, neck, and joints).

4- fever.



***Type IV, Cell-Mediated Hypersensitivity Disorders:***

It is mediated by cells, not antibodies; occur 24 to 72 hours after exposure of a sensitized individual to the offending antigen. They are mediated by helper T lymphocytes that are directly cytotoxic or that secrete inflammatory mediators like cytokines that cause tissue changes. Cytokines will attract T or B lymphocytes as well as monocytes, neutrophils, eosinophils, and basophils. Some of the cytokines promote differentiation and activation of macrophages that function as phagocytic and antigen-presenting cells (APCs).

The best-known type of delayed hypersensitivity response is the reaction to the tuberculin test, in which inactivated tuberculin or purified protein derivative is injected under the skin. In a previously sensitized person, redness and indurations of the area develop within 8 to 12 hours, reaching a peak in 24 to 72 hours. A positive tuberculin test indicates that a person has had sufficient exposure to the *M.tuberculosis* organism to incite a hypersensitivity reaction.

Certain types of antigens induce cell mediated immunity with an especially pronounced macrophage response. This type of delayed hypersensitivity commonly develops in response to particulate antigens that are large, insoluble, and difficult to eliminate. The accumulated macrophages are often transformed into so-called epithelioid cells because they resemble epithelium. A microscopic aggregation of epithelioid cells, which usually are surrounded by a layer of lymphocytes, is called a granuloma. Inflammation that is characterized by type IV hypersensitivity is called granulomatous inflammation.

Direct T-cell–mediated cytotoxicity, will cause necrosis of antigen-bearing cells. It is important in the eradication of virus infected cells, autoimmune diseases such as Hashimoto’s thyroiditis, and host-versus-graft or graft-versus host transplant rejection. Allergic contact dermatitis and hypersensitivity pneumonitis are presented as examples of cell mediated hypersensitivity reactions.

