

Topic: Type II and Type III Hypersensitivity reactions

SOS In Microbiology

M.Sc 2nd Semester

Paper code: 202 (Immunology)

Unit 4

Antibody-Mediated Cytotoxic (Type II) Hypersensitivity

- Type II hypersensitive reactions involve antibody-mediated
- destruction of cells. Antibody can activate the complement
- system, creating pores in the membrane of a foreign cell (see
- Figure 13-5), or it can mediate cell destruction by
- antibody-dependent cell-mediated cytotoxicity (ADCC).
- In this process,
- cytotoxic cells with Fc receptors bind to the Fc region of
- antibodies on target cells and promote killing of the cells (see
- Figure 14-12). Antibody bound to a foreign cell also can serve
- as an opsonin, enabling phagocytic cells with Fc or C3b
- receptors
- to bind and phagocytose the antibody-coated cell

1. Transfusion Reactions

- A large number of proteins and glycoprotein on the membrane of red blood cells are called blood group antigen. In addition antibodies are also found in blood for these epitopes except from which are showing on our blood cells (Blood group A, antibody against B epitop).
- An individual possessing one form of blood group antigen can recognize other antigen (present in transfused blood) as foreign and elicit immune response.
- In some cases, the antibodies have already been induced by natural exposure to similar antigenic determinants on a variety of microorganisms present in the normal flora of the gut. This is the case with the ABO blood-group antigens.

- Antibodies to the A, B, and O antigens, called isohemagglutinins (usually of IgM class). A
- An individual with blood type A, for example, recognizes B-like epitopes on intestinal microorganisms and produces isohemagglutinins to the B-like epitopes.
- If a type A individual is transfused with blood containing type B cells, a transfusion reaction occurs in which the anti-B isohemagglutinins bind to the B blood cells and mediate their destruction by means of complement-mediated lysis.
- Antibodies to other blood-group antigens may result from repeated blood transfusions because minor allelic differences in these antigens can stimulate antibody production (usually of the IgG).
- The clinical manifestations- Massive intravascular hemolysis of the transfused red blood cells by antibody plus complement.
may be either

1. **Immediate (associated with ABO blood-group incompatibilities)**- which lead to complement mediated lysis by IgM.
 - Within hours, causes hemoglobinuria and high levels of bilirubin which is toxic.
 - Typical symptoms include fever, chills, nausea, clotting within blood vessels, pain in the lower back, and hemoglobin in the urine.
2. **Delayed**- Who have received repeated transfusions of ABO-compatible blood that is incompatible for other blood group antigens.
 - The reactions develop between 2 and 6 days after transfusion. The transfused blood induces clonal selection and production of IgG against a variety of blood-group membrane antigens, most commonly Rh, Kidd, Kell, and Duffy.
 - The predominant isotype involved in these reactions is IgG, which is less effective than IgM in activating complement.

2. Hemolytic Disease of the Newborn

- Hemolytic disease of the newborn develops when maternal IgG antibodies specific for fetal blood-group antigens cross the placenta and destroy fetal red blood cells.
- The consequences of such transfer can be minor, serious, or lethal.
- Severe hemolytic disease of the newborn, called **erythroblastosis fetalis**, most commonly develops when an Rh⁺ fetus expresses an Rh antigen on its blood cells that the Rh⁻ mother does not express.

3. Drug-Induced Hemolytic Anemia

- Certain antibiotics (e.g., penicillin, cephalosporin, and streptomycin) can adsorb nonspecifically to proteins on RBC membranes and form a complex similar to a hapten-carrier complex.
- In some patients, when drug is absorbed it binds to RBC, such drug-protein complexes induce formation of antibodies and induce complement mediated lysis and thus progressive anemia.
- When the drug is withdrawn, the hemolytic anemia disappears.
- Penicillin is notable in that it can induce all four types of hypersensitivity with various clinical manifestations.

Immune Complex–Mediated (Type III) Hypersensitivity

- The reaction of antibody with antigen generates immune, this complex facilitates the clearance of antigen by phagocytic cells.
- In some cases, however, large amounts of immune complexes can lead to tissue-damaging type III hypersensitive reactions.
- The magnitude of the reaction depends on the quantity of immune complexes as well as their distribution within the body.

Localised reaction- When the complexes are deposited in tissue very near the site of antigen entry.

Generalised reaction- When the complexes are formed in the blood, a reaction can develop wherever the complexes are deposited frequently on blood-vessel walls, in the synovial membrane of joints, on the glomerular basement membrane of the kidney, and on the choroid plexus of the brain.

The deposition of these complexes initiates a reaction that results in the recruitment of neutrophils to the site. The tissue there is injured as a consequence of granular release from the neutrophil.

- Type III hypersensitive reactions develop when immune complexes activate the complement system's. they cause localized mast-cell degranulation and consequent increase in local vascular permeability.
- Larger immune complexes are deposited on the basement membrane of blood vessel walls or kidney glomeruli, whereas smaller complexes may pass through the basement membrane and be deposited in the subepithelium.
- The type of lesion that results depends on the site of deposition of the complexes.

- Much of the tissue damage in type III reactions stems from release of lytic enzymes by neutrophils.

1. Type III Reactions Can Be Localized (Arthus reaction)—

- Injection of an antigen intradermally or subcutaneously into an animal that has high levels of circulating antibody specific for that antigen-----leads to formation of localized immune complexes, which mediate an acute Arthus reaction within 4–8 h.
- Microscopic examination of the tissue reveals neutrophils adhering to the vascular endothelium and then migrating into the tissues at the site of immune complex deposition.
- As the reaction develops, localized tissue and vascular damage results in an accumulation of fluid (edema) and red blood cells (erythema) at the site.
- The severity of the reaction can vary from mild swelling and redness to tissue necrosis.

2. Type III Reactions Can Also Be Generalized

- When large amounts of antigen enter the bloodstream and bind to antibody, circulating immune complexes can form.
- If antigen is in excess, small complexes form; because these are not easily cleared by the phagocytic cells, they can cause tissue-damaging type III reactions at various sites.

When antitoxins containing foreign serum (horse antitetanus or antidiphtheria serum) is administered



The recipient of a foreign antiserum develops antibodies specific for the foreign serum proteins



These antibodies then form circulating immune complexes with the foreign serum antigens.



Typically, within days or weeks after exposure to foreign serum antigens, an individual begins to manifest a combination of symptoms that are called **serum sickness**.

- **Symptoms-** These symptoms include fever, weakness, generalized vasculitis (rashes) with edema and erythema, lymphadenopathy, arthritis, and sometimes glomerulonephritis.
- Formation of circulating immune complexes contributes to the pathogenesis of a number of conditions other than serum sickness like-
- *Autoimmune Diseases* (Systemic lupus erythematosus, Rheumatoid arthritis
- Goodpasture's syndrome)
- *Drug Reactions*-Allergies to penicillin and sulfonamides
- *Infectious Diseases*-Poststreptococcal glomerulonephritis, Meningitis Hepatitis Mononucleosis, Malaria, Trypanosomiasis