2.1.7

Type II Hypersensitivity

Watch the video Type II Hypersensitivity-Mechanisms

Type II hypersensitivities are tissue specific, meaning that the antibodies are generally specific to one type of tissue or organ. Earlier in the chapter we talked about the maturation of T-cells and B-cells and how our body will destroy those cells that are self-reactive. Sometimes this selection process doesn't work perfectly and cells that are self-reactive result in an autoimmune disease. In type II hypersensitivity, self-reactive B-cells produce antibodies that attach to antigens on cells or tissue components and cause inflammation and damage. Additionally, some drugs can act as haptens that bind to cell proteins and allow antibodies to bind to the drug/normal cell protein complex. Antibodies can then trigger mechanisms that result in destruction that can induce neutropenia, hemolytic anemia or thrombocytopenia.

In type II hypersensitivities there are three main mechanisms that antibodies use that lead to cell or tissue destruction or dysfunction. They are:

1. Antibody and complement activation lead to cellular destruction.

2. Antibodies and complement activate inflammation.

3. Antibodies can bind tissue components and cells leading to disruption of normal physiologic processes.

1. Antibody and complement activation lead to cellular destruction

Antibodies can activate the classical complement system. C3b that results from this activation can bind to cells and make them "attractive" to phagocytosis by white blood cells. This is called opsonization. C3b opsonization can lead to cellular destruction. Antibodies triggering the complement system also activates the MAC complex. As you recall, this forms on the membrane of a cell as the C5b through C9 fragments of the complement proteins are activated. This allows fluids and molecules to flow freely in and out of the cell and causes the cell to lyse and burst.

Antibodies themselves can also bind to cell membrane bound antigens and provide opsonization as white blood cells bind the Fc portion of the antibody and are triggered to perform phagocytosis. Natural killer cells will also bind the Fc portion of an antibody and be triggered to release chemicals that can lyse the cell membrane that the antibodies are attached to. As you have previously learned, when antibodies attract leukocytes (white blood cells) to perform phagocytosis or release toxic chemicals it is called antibody dependent cell mediated cytotoxicity (ADCC). An example of this is found in mismatched blood transfusions. Antibodies will attach to antigens on the non-matching red blood cells and trigger phagocytosis of these red blood cells by macrophages in the spleen. Other examples of ADCC include Immune thrombocytopenia (ITP), autoimmune hemolytic anemia (AIHA), hemolytic disease of the newborn, and autoimmune neutropenia.

2. Antibody and complement activate inflammation

Sometimes antibodies can bind antigens in the connective tissue matrix of tissues. This can trigger the complement system but does not cause cell lysis because the antigens are in the matrix rather than on specific cell membranes. The antibodies in the matrix will still trigger the complement cascade, however, and this results in chemotaxis of leukocytes

as well as degranulation of local mast cells. The recruited leukocytes will release enzymes and reactive oxygen species in the matrix and the histamine will contribute to edema. Over time, this inflammatory response will damage the tissue. An example of antibodies causing this type of inflammation is Goodpasture's disease which involves autoimmune antibody destruction of basement membrane tissue of the glomeruli of the kidney.

3. Antibodies can bind tissue/cells and disrupt cellular processes

An antibody can disrupt cellular processes when it binds to a cellular antigen and interrupts the way the cell functions. For example, the autoimmune disease Myasthenia Gravis is caused when antibodies against the acetylcholine receptors on muscle cells bind the receptor and block the binding of acetylcholine. This results in the muscles not receiving stimulation and causes them to weaken over time. Graves' disease is another autoimmune disease caused by antibody mediated cellular dysfunction. It involves antibodies targeting thyroid stimulating hormone (TSH) receptors in a way that the receptors are actually activated and thyroid function increases. In this case the type II hypersensitivity response causes hyperthyroidism.