AUTOIMMUNITY

Introduction — Both B cells of humoral immune responses and T cells of cell mediated immune responses maintain tolerance. In B cells and T cells Sometimes there is a break or loss of Self tolerance. The hosts own protein become epitope and act as Self antigens which induces generation of antibodies called autoantibodies. These autoantibodies damage hosts own tissues. Similarily the activated effector CD8 cells cause cell and tissue damage. This kind of tissue damage by interaction of Self antigens Self autoantibodies is called as autoimmunity. Autoimmunity may also be induced by hidden antigens, development of new epitopes, molecular mimicry, viral induced autoimmunity and genetic factors. In autoimmunity important diseases caused are Hashimoto's disease, thyroiditis, graves disease, rhematoid arthritis multiple sclerosis myasthenia graves Systemic lupus erythematosis Goodpasture's Syndrome and insulin dependent diabetes mellitus.

The Study of Autoimmunity has been divided into following headings —

1) Physiological autoimmunity.
2) Induction of autoimmunity
3) Mechanism of development of autoimmune diseases.
4) Hormonal factors and Autoimmune disease
5) T cell tolerance to gut and autoimmune diseases.
6) Hypersensitivity reactions and tissue damage in autoimmunity, and
7) commonly occurring autoimmune diseases.

2. Physiological Autoimmunity — Blood constitutes important media for the physiological, biochemical and immunological functions of the host. All the immune components and blood components have common origin from hematopoetic stem cells. Antigen antibody interactions occur in blood. The hyper variable regions of immunoglobulins are also known as idiotypes of antibodies (immunoglobulins) can act as epitope and induce the generation of autoantibodies and autoidiotypes. Anti-idiotypes can also provoke productions of anti-idiotypic antibodies. These anti anti idiotypic antibodies play important role in antibody responses.

These autoantibodies also play useful role in removing old and aged erythrocytes. As the erythrocytes (RBC) become old, an anion transporter glycoproteins is cleaved from the membrane proteins called as band 3 and a new epitope is exposed. This band 3 epitope is recognized by naturally occuring autoantibodies. The autoantibody has ion affinity for band 3 proteins epitope but it ~~has~~ has very affinity for complement proteins C3b. The C3b autoantibody complex opsonizes old red blood cells and thus they promote their phagocytoses by macrophages in Spleen.

(2) Induction of Autoimmunity — The precise pathway for the development of autoantibodies or of autoimmunity is not clear, but experimental evidences gives idea to understand induction of autoimmunity in following ways —

(1) Hidden antigens Autoimmunity. In our body there are some parts where immune reactions do not take place. Certain antigens are found in brain cells and testes

where normally circulation lymphocytes does not reach. In case of injury the hidden antigens are released into blood circulation where they are encountered with B cells and from the immune response. The B cells and T cells attain tolerance only when they encounter with such hidden antigens. Similarly in case of myocardial infarction, the autoantibodies are produced against antigens antigens present inside cells like mitochondria of heart muscles.

(III) Development of New Epitopes Induces Autoimmunity.

RBC induces formation of autoantibodies. Two autoantibodies produced in this way consist of immunocoglutinins and rhematoid factors. Immunocoglutinins antibodies formed against epitopes on the activated complement proteins C_2, C_4 and C_3. C_3 are most important as it enhances opsonization.

The rhematoid factors Comprise immunoglobulins against epitopes of other antibodies when antibody binds to C_4 antigen, fab regions are stabilized in such manner that the new epitope is exposed on the F_c portion of antibody. The rhematoid factors are developed in large amount in rhematoid arthritis and SLE disease.

Polyclonal Antibodies may induce autoimmunity —

various viruses and bacteria may induce non specific activation of B cells which may produce polyclonal antibodies, cytomegalovirus Epstein Barr virus, Gram negative bacteria are all known activators of polyclonal antibodies. The B cells reacting to self antigens induce production of autoantibodies.

Mechanisms of Development of Autoimmune disease.

The autoimmune diseases are induced by various factors like viral, genetic, hormonal, loss of tolerance, MHC molecules, environmental factors and loss of tolerance etc.

virus have been associated with autoimmune diseases. In NZB mice continuous infection of C-retrovirus is due to development of antibodies against erythrocytes and DNA. The C-retroviruses and Paramyxovirus cause formation of auto antibodies and SLE disease in Man and dog. The retroviruses induce development of antibodies against Pituitary, Pancreas, glucagon growth hormone and insulin.

Breach of B cell tolerance leads to loss of control of lymphocyte responses this induces autoimmune diseases by antibodies. The autoreactive B cells after encounter with soluble autoantigens become unresponsive due to loss of surface IgM as antibodies

Hormonal factors and Autoimmune diseases.

Certain autoimmune diseases are predominantly more common in females than males per eg - augmented estrogen induced enhanced interferon gamma (IFNγ) which causes disease destruction by accelerating expression of MHC molecules and also inducing activation of macrophages.

T cell Tolerance of Gut and Autoimmune diseases

The gastrointestinal tract has to cope with stress, great variety of foreign antigens moving with food contents electrolytic concentration and enzymatic secretion. The brush border and mucosal membrane has to

discriminate between Pathogens, commensal micro organisms E. Coli and useful food Stuffs. Under these conditions the responses to harmless gut antigens are called immunological tolerance or oral tolerance. The mucosa associated oniner responses induce proliferation of B cell and T cell. B cell on encounter with gut antigens are transferred into plasmocytes which secrete specific antibodies. The CD4 T_H cells produce cytokines which induce inflammatory reactions and cell mediated immunity.

Hypersensitivity Reactions and Tissue Damage Autoimmunity.

It is of 4 types.

Type I - ~~Autoallergy~~ Autoimmune disease is milk allergy found in mammary gland.

Type II - Hemolytic Anaemia, thrombocytopenia and thyroiditis.

Type III - Systemic Lupus erythematosus SLE glomerulonephritis and ~~rheumatoid~~ rheumatoid arthritis.

Type IV mediated by CD4 and CD8 cells All types of tissue damage takes place in this type.

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