

## **Autoimmunity :**

Autoantibodies are a normal phenomenon, IgM of low affinity and multiple specificities ( do not depend on foreign antigen for production ). No pathological action, function may be :

- a)- eliminate degraded autoantigens.
- b)- Cross react with foreign antigens ( head start, innate immunity).
- c)- bind environmental epitopes that may cross react with autoantigens thus protecting against autoimmunity.

These antibodies may not have a function at all and represent antibodies released from anergic (self reactive) B cells when they die. They are produced by CD5 +ve B cells.

In autoimmune disease the antibodies are IgG and are involved in the production of pathology.

Spectrum of autoimmune disease :

Organ specific ----- Centre ----- Systemic A.I. disease.

Hashimoto's disease            Iry biliary cirrhosis            S.L.E.

Patients are more prone to cancer (organ) or lymphoreticular.

## **Background of autoimmunity :**

### 1)- Genetic :

Family aggregation of disease, 50% concordance in identical twins, more than in dizygotic twins 5%, and more than siblings with identical HLA haplotypes, which indicates that there is more to it than HLA genes ( or HLA linkage ). For example C1 and C2 and C4 deficiencies predispose to auto-immune disease.

In animals there are breeds that are genetically prone to disease e.g. NZ BW mice and SLE.

### 2)- Sex :

Females : SLE, worsens during pregnancy, effect of oestrogen (promotes antibody production).

Males : ankylosing spondylitis ( which is believed to be autoimmune ).

Some like IDDM affect men and women equally.

### 3)- Environment :

The lack of 100% concordance in identical twins indicates the presence of other factors.

Diet (RA), sunshine (SLE), Goodpasture (solvents).

Microbes : Rh fever, very slow growing mycobacteria, unidentified viruses.

Reactive arthritis associated with Chlamydiae and Salmonella infections.

The inflammatory process may induce the presentation of self antigens in an immunogenic form.

The autoimmune process is driven by antigen, IgM switches to IgG with somatic mutation and high affinity production.

The auto-immune response is identical to adaptive immunity, cells and antibodies are involved, and the same mechanisms as in infection are involved and result in the tissue damage e.g. complement, neutrophils, macrophages, lymphocytes etc.

## **Mechanisms of autoimmunity :**

- 1)- Modification of autoantigen :  
Drug hapten, somatic mutation, adjuvant presence.
- 2)- Polyclonal activation of B cells : LPS, EBV.  
of T cells : Superantigens.
- 3)- Molecular mimicry :
- 4)- Sequestration of antigen : Sperm and lens. *EAR*
- 5)- Loss of suppression : thymectomy 2-4 days after birth in mice results in AI disease, AI disease more common in old (tired immune system).  
The AIRE gene in medullary thymic epithelial cells.
- 6)- Idiotypic networks :  
Virus interacts with receptor X, anti-virus is image of receptor, anti-idiotypic interacts with receptor X.
- 7)- Aberrant expression of MHC II molecules on non-APC in tissues may induce autoimmunity. ( gamma interferon ).  
There is no need for a second signal if large amounts of cytokines were produced during a prolonged infection, probably because the naive T cells become primed by this excessive cytokine production.
- 8)- Left handedness has been associated with some AI disease !

Examples of auto-immune diseases :  
Organ and system diseases.

- Pernicious anaemia : anti-parietal cell antibody, anti intrinsic factor antibodies.  
Rheumatoid arthritis : rheumatoid factor Igm anti-IgG antibody, cell mediated autoimmunity.  
Diabetes mellitus : anti-insulin antibodies, cell mediated, anti islet antibodies.  
Hashimoto s thyroiditis : anti-thyroglobulin antibodies, anti-microsomal (peroxidase) antibodies.  
Graves disease : anti TSH receptor antibodies, anti-peroxidase antibodies.  
Multiple sclerosis : cell mediated TH17, anti myelin antibodies.  
SLE : assortment of antibodies.  
Myasthenia gravis : anti-acetylcholine receptor antibodies.

DISEASE ASSOCIATION WITH MHC MOLECULES