**Autoimmune Diseases**

the failure of self-tolerance; and is a specific immunological reaction against self-structures

Tolerance is the state of specific immunological unresponsiveness .

|  |  |  |
| --- | --- | --- |
| **C. Phagocytic Cells Tolerance**Antigens or immune complexes which cannot be cleared up from the body result in tolerance. | **B. Peripheral tolerance**deal with escaped self-reactive B- and T- cells after leaving the bone marrowby:1. Excessive cross-linking of B-cells receptors for antigens (clonal anergy/ignorance).2. Inadequate co-stimulatory signals3. Role of T-reg cells and their cytokines4. Idiotype-Anti-idiotype network | **A. Central tolerance**Clones of B- and T-cells reactive to self-antigens are deleted in the bone marrow and the thymus respectively by a process called negative selection |

|  |  |
| --- | --- |
| Tolerogenic antigens lead to apoptosis or a state of anergy of lymphocyte response. | Immunogenic antigens lead to the stimulation and proliferation of lymphocytes |

**Promotion or break of tolerance**

1. High doses of antigens leading to excessive cross-linking of B-cell antigen receptors.

2. Failure of clearance of the antigen or immune complexes

3. Low levels of co-stimulatory signals

4. Intravenous or oral administration of the antigens.

5. Sequestered antigens

6. Molecular mimicry (cross-reactivity),

7. Infective agents may provide excessive T-cell stimulation, tissue destruction and antigenic modification .

8. Superantigens that activate numerous T-cell clones.

9. Age and gender

10. Life style (smoking )

11. Complement deficiencies

**Classification of autoimmune diseases**

|  |  |
| --- | --- |
| **Systemic autoimmune diseases**- SLE- Systemic sclerosis- Mixed connective tissue disease | **Organ-specific autoimmune diseases**- Insulin-dependent DM (type-I)- Rheumatoid arthritis- Grave's disease- Goodpasture's syndrome- Myasthenia gravis |

**Aetiology of Autoimmune Diseases**

I. Release of sequestrated antigens

II. Infectious microbes may produce peptide antigens that are similar to self antigens, this is called “molecular mimicry”

Example one: Antibodies formed against M protein of Streptococcus pyogenes cross react with cardiac myosin leading to rheumatic fever.

Example two: Rubella and diabetes type I

 III. Alteration of self antigens or appearance of new antigens under effects

IV. defects in immune regulatory mechanisms.

V. T-Cell Bypass

VI. Genetic predisposition

 1. There is a familial incidence of autoimmune diseases. Certain diseases run in families

 2. There is a concordance rate of susceptibility to development of diseases

 3. Most of autoimmune diseases appear to be associated with certain HLA antigens/ genes

 4. Females are more prone to develop autoimmune diseases than males

**Mechanisms of Tissue Damage in Autoimmune Diseases**

Can be due to any type of hypersensitivity except type 1

|  |  |  |
| --- | --- | --- |
| 3. DHS (type IV) by T cells as in ulcerative colitis, coeliac disease | 2. Immune complex deposition (type III) in blood vessel walls, skin, joints, glomeruli | 1. Cytotoxic reactions (type II) as occurs in autoimmune haemolytic anaemias , |

**Symptoms of autoimmune diseases**

Symptoms that often occur with autoimmune diseases include fatigue, malaise, and fever. When symptoms get worse, it is called a flare-up. Most autoimmune diseases are [chronic](http://www.nlm.nih.gov/medlineplus/ency/article/002312.htm), but many can be controlled with treatment.

|  |  |
| --- | --- |
| 4. Complement levels may be decreased in particular C3 and C4.5. Immune complexes may be detected in serum6. HLA typing7. General laboratory tests .**Management of autoimmune diseases****relieve symptoms, preserve organ function, and target disease mechanisms.**1. Anti-inflammatory drugs2. Immunosuppressive agents3. Biological agents4. Plasmapheresis5. Some patients may need supplements to replace a hormone or vitamin that the body is lacking6. Surgery sometimes is required to correct or preserve functions | **Laboratory Diagnosis of Autoimmune Diseases**  1. Autoantibodies  2. Total immunoglobulin concentration may be increased 3. Cryoglobulins are antibodies directed against other immunoglobulins that form immune complexes which precipitate in cold.  - Type I: Monoclonal IgM paraprotein with no particular specificity, e.g. lymphoproliferative diseases ,normal complement level - Type II: Monoclonal IgM against IgG constant region, e.g. hepatitis C or B; decreased C4- Type II: Polyclonal IgM or IgG against IgG constant region, e.g. hepatitis C or B, SLE decreased C4 |