**Autoimmune Diseases**

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

Tolerance is the state of specific immunological unresponsiveness .

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| **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 marrow  by:  1. Excessive cross-linking of B-cells receptors for antigens (clonal anergy/ignorance).  2. Inadequate co-stimulatory signals  3. Role of T-reg cells and their cytokines  4. 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 |

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| 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**

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| **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

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| 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.

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| 4. Complement levels may be decreased in particular C3 and C4.  5. Immune complexes may be detected in serum  6. HLA typing  7. General laboratory tests .  **Management of autoimmune diseases**  **relieve symptoms, preserve organ function, and target disease mechanisms.**  1. Anti-inflammatory drugs  2. Immunosuppressive agents  3. Biological agents  4. Plasmapheresis  5. Some patients may need supplements to replace a hormone or vitamin that the body is lacking  6. 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 |