

\* AUTOIMMUNITY : is a misdirected immune response that occurs when, the immune system goes faulty and attacks own healthy cells & tissues. This is often due to failure of Self Tolerance.

### Immunological Tolerance / Tolerance.

Refers to Reduction or Complete inhibition of 'Ability' of host to mount specific immune response to an Antigen.

Specific immunological non-reactivity / unresponsiveness to an antigen

\* SELF-TOLERANCE :- specifically means lack of immune response to one's own (self) tissues or self-cellular antigens.

### PATHOGENESIS / MECHANISM of Autoimmune Diseases

Autoimmune Disease are those that occur due to breakdown of one or more mechanisms of Self-Tolerance, resulting in an immunological attack on own tissue, resulting in damage of structure & function of tissues / organs.

Various mechanism involved are as below:-

#### ① FAILURE OF Activation-induced Cell Death :-

Persistent activation of T-cells, usually leads to their apoptosis (death) finally. Defects in this pathway, allow persistence & prolif<sup>n</sup> of Autoreactive T-cells leading to autoimmune diseases.

#### ② BREAKDOWN of T-cell ANERGY :-

Normally, auto-reactive cells that ESCAPE Central deletion, become ANERGIC (non-functional) when they come in contact of Self-Antigens, as these lack Co-stimulatory signals. Such Anergy is broken, if normal cells (due to some

infection/genetic defect) are induced to express co-stimulatory molecules (which normally they do not express)

### (3) Molecular mimicry (Resemblance) :-

structural or functional or immunological similarity shared between macromolecules found on (i) Infectious Antigens and those on (ii) Host Tissues.

### (4) FAILURE of T-cell mediated Suppression :-

### (5) Bypass of B-cell Requirement for T-cell help :-

Antibody response to self-antigens occur when self-reactive B-cells receive help from T-cells.

In normal conditions, such helper-T-cells undergo DELETION or ANERGY, to keep & maintain Tolerance to Self-tissues.

When, requirement of Tolerant T-cell is BYPASSED or SUBSTITUTED for B-cell activity, it leads to formation of AUTOANTIBODIES

### (6) POLYCLONAL LYMPHOCYTE ACTIVATION :-

Several microorganisms & their Toxins cause Polyclonal activation of B-cells, leading to Auto-Antibody Prod<sup>n</sup>.

### (7) Release of SEQUESTERED ANTIGEN :-

During development of Tolerance, few self-antigens stay completely hidden or sequestered, so tolerance does not develop for them.

In later life, due to severe injury/inflammation, such self tissue antigens may be introduced back to immune system, leading to Autoimmune Disease.

Eg:- Spermatozoa & Ocular Antigen fall in this category.

## (8) Exposure to CRYPTIC (hidden) self-Epitopes.

instead of self-antigens on tissues, few epitopes over the protein antigen remain hidden

During T-cell selection & maturation, they are not exposed to such cryptic epitopes of self-antigens. If these hidden epitopes are exposed in later life, it leads to Autoimmune diseases.

### Examples of AUTOIMMUNE DISEASES :-

#### (I) Autoimmune Diseases of Single Organs :-

##### (1) Autoimmune Endocrine Disease :-

✓ Autoimmune THYROIDITIS - in Dogs, chicken.  
Auto antibodies develop against Thyroglobulin & Thyroid colloid antigen.

##### (2) Autoimmune Neurological Disease :-

Autoimmune POLYNEURITIS in Horses / Dogs

Degenerative Myelopathy in Dogs

##### (3) Autoimmune Skin Diseases

✓ Pemphigus vulgaris - charac. by dev<sup>t</sup> of bullae/blisters around moco-cutaneous junctions of nose, lips, eyes, anus & prepuce.

Autoantibodies against intracellular cement of skin layers.

##### (4) Autoimmune Hemolytic Anemia (AIHA) - in Dogs & Cats,

- auto antibodies to antigens on RBCs → cause destruction.

##### (5) Autoimmune Thrombocytopenia (AITP) → in Horse & Dogs.

Affected animals show many petechiae on skin, Gums & Conjunctiva with Epistaxis & Melena could also be seen.

##### (6) Autoimmune MUSCLE DISEASE :-

✓ "MYASTHENIA GRAVIS" (MG) in Dogs & Cats - is a disease of skeletal muscles characterized by Abnormal Fatigue & weakness even on very mild exercise. Due to Auto antibodies against Acetylcholine receptor proteins, deficiency of Acetylcholine receptor takes place. So, MG result from failure of

Transmission of Nerve Impulses across motor-end plate of striated muscles, due to deficiency of Acetylcholine Receptors.

## (II) SYSTEMIC AUTO IMMUNE DISEASES :-

in such, multiple organs are involved.

### ① Systemic Lupus Erythematosus (SLE) :-

is a generalized autoimmune disorder seen in humans, HORSES & DOGS.

Charac. feature of SLE is development of Auto antibodies against Antigens in Cell Nucleus (Anti-Nuclear Antibodies),

\* Immune Complexes may get deposited in glomeruli causing Membranous Glomerulonephritis  
DOGS also in Arteriolar walls, → causing local fibrinoid Necrosis  
also in Synovia → provoking Arthritis

In Horse (Equine Lupus) - disease mainly occur as Generalized SKIN Disease, involving Alopecia, Dermal ulceration & crust formation.

### ② Sjogren's Syndrome :- in Dogs

due to autoimmune attack on Salivary & Lacrimal Glands leading to Conjunctival Dryness & Kerato-conjunctivitis Sicca and Mouth dryness (XEROSTOMIA)

### ③ Rheumatoid Arthritis : autoimmune Erosive Polyarthritis common in Dogs.