

Auto Immunity

Autoimmune Diseases

Auto Immunity

- Auto or Self antigens

- Antigens present in ones own cells
- Altered by the action of bacteria, viruses, chemicals or drugs as a non-self

- Auto antibody

- Altered cell (Auto Ag) - elicits the productions of Antibody

- Auto Immunity (misnomer, alternative= auto allergy)

- Immune response of auto Ab against self Ag
- Humoral or cell mediated immune response against the constitute's of the body's own tissues.
- There are more than 80 different kinds of diseases caused by autoimmunity.

Autoimmune Diseases

- *Autoimmune diseases is a group of disorders in which tissue injury is caused by humoral (by **auto-antibodies**) or cell mediated immune response (by **auto-reactive T cells**) to self antigens.*
- Normally, the immune system **does not attack the self**. However, there is a large group of **autoimmune** diseases in which the immune system does attack self-cells
- The attack can be directed either against a very specific tissue or to a large no. of tissues
- Once started, autoimmune diseases are hard to stop

Causes of Autoimmune Diseases

1. Sequestered or Hidden antigens

- Ag in the secluded places - are not accessible to the immune system.
- E.g. Lens Ag, Sperm Ag & Thyroglubulin.

2. Neo antigens

- Altered or Modified Antigens – by physical (irradiation), chemical (drugs) or microbial agents (intracellular viruses)

3. Cessation of Tolerance

- It may result when tolerance to the self-Ag is abrogated.

Causes of Autoimmune Diseases

4. Cross reacting Antigens

- A foreign Ag which resembles self a 2nd Ag
- Many species share organ specific Ags.
- E.g. Ag of Human brain & Ag of sheep brain, Streptococcal M protein & Heart muscles, Nephritogenic strains of Streptococci Ags &
- Renal glomeruli shares similar epitopes.

5. Loss of Immunoregulation

- Loss of Self tolerance - caused by over activity or lowered activity of T and B- cells

Classification of Autoimmune Diseases

- Broadly classified into 3 groups
 1. Haemolytic autoimmune diseases
 2. Localised & 3. Systemic autoimmune diseases

1. Haemolytic autoimmune diseases

- Clinical disorder due to destructions of blood components. Auto Ab are formed against one's own RBCs, Platelets or Leucocytes.
- E.g. Haemolytic anaemia, Leucopenia, Thrombocytopenia, etc.

Classification of Autoimmune Diseases

2. Localised autoimmune diseases or Organ specific autoimmune diseases

- A particular organ is affected due to auto Abs.
- For example:
 - **Thyroiditis** (attacks the thyroid)
 - **Multiple sclerosis** (attacks myelin coating of nerve axons)
 - **Myasthenia gravis** (attacks nerve-muscle junction)
 - **Juvenile diabetes** or Type I DM (attacks insulin-producing cells)

Classification of Autoimmune Diseases

3. Systemic autoimmune diseases or Non-organ specific autoimmune diseases

- Immune complexes accumulate in many tissues and cause inflammation and damage.
- Affects many organs or the whole body
- For example:
 - **Systemic Lupus Erythematosus** (anti-nuclear Ab.): Harms kidneys, heart, brain, lungs, skin...
 - **Rheumatoid Arthritis** (anti-IgG antibodies): Joints, hearts, lungs, nervous system...
 - **Rheumatic fever**: cross-reaction between antibodies to streptococcus and auto-antibodies.

Autoimmune Diseases

The image features a dark background with abstract, flowing blue and orange lines that create a sense of movement and depth. A small blue dot is visible near the bottom left, connected by thin lines to the larger shapes. The overall aesthetic is modern and artistic.

Autoimmune Haemolytic anemia

- Lysis of RBC is due to the production of autoantibodies against the RBC-antigens.
- RBC half life= 21 days, Ha.anaemia<7days
- Caused by –2^o to infections or Drug therapy [Penicillin, Anti-hypertensive agent like methyldopa results in destruction of RBCs]
- Antibody mediated autoimmune diseases
- 2 classes of autoantibodies involved are
 - IgM or Cold Agglutins- active at 4^o C but not at 37^oC.
 - IgG or Warm Agglutins - active at 37^o C but not at 4^oC.

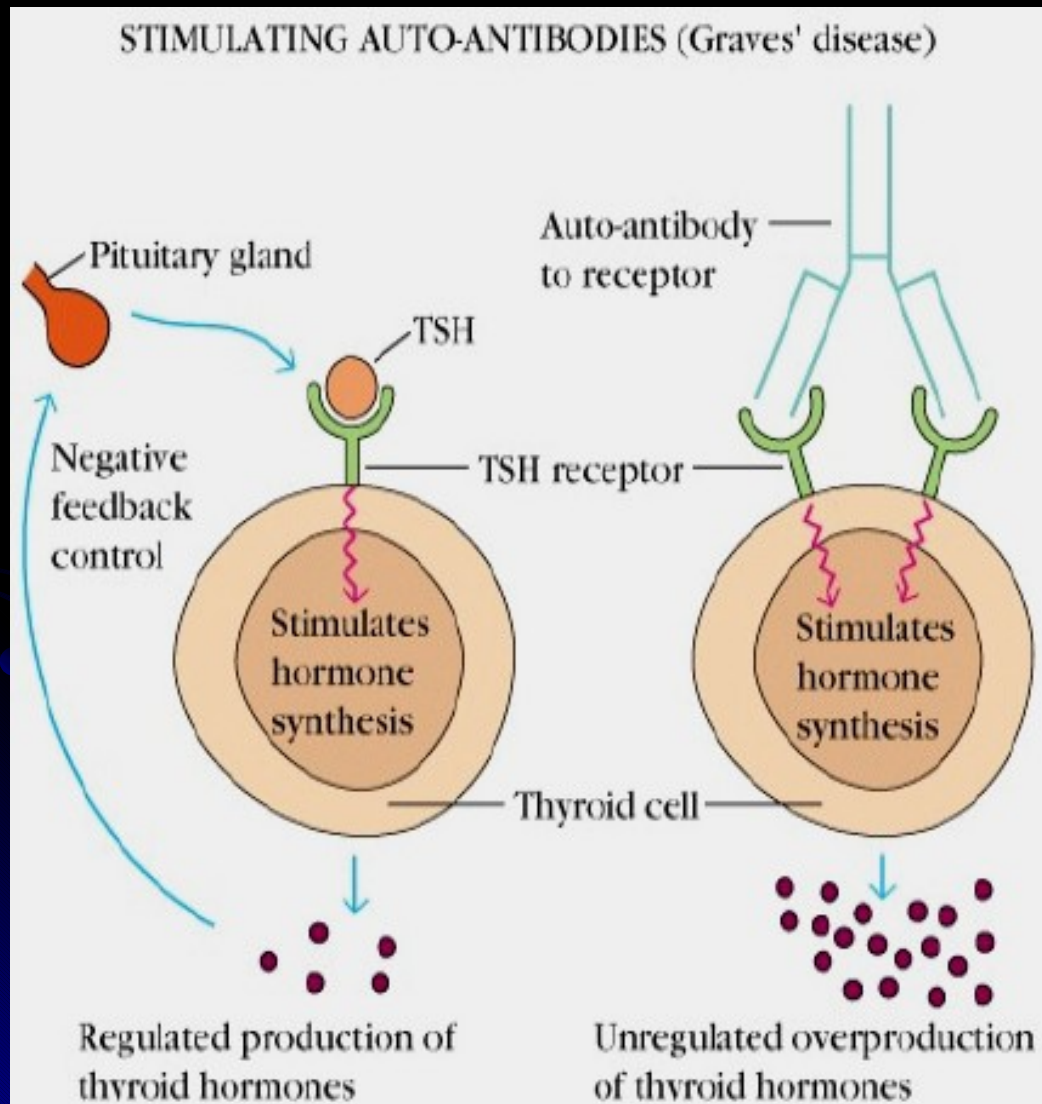
Thrombocytopenia

- Characterized by low platelet count due to the production of antiplatelet Ab. (IgG type)

Mechanism:

- An interaction of Ab with bound drug or new Ag. causes intravascular agglutination of platelets & can be eliminated by phagocytic cells.
- Antibody mediated autoimmune diseases.

Graves' disease (anti-thyroid stimulating hormone; anti-TSH)



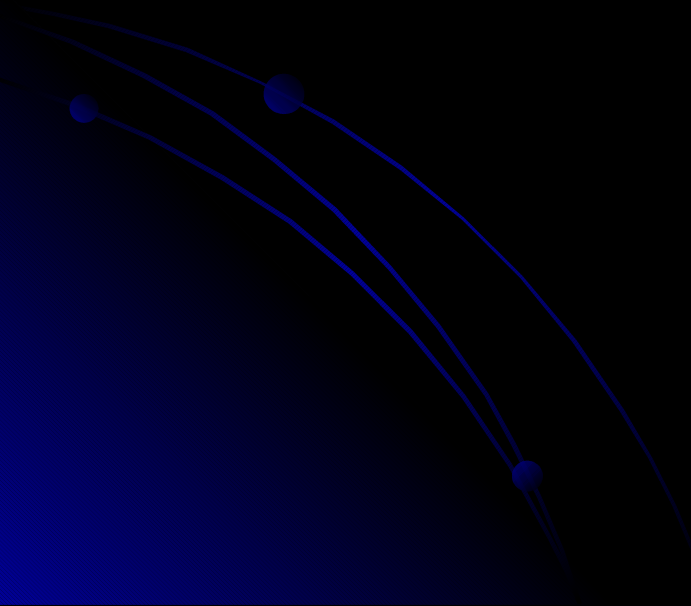
In Graves' disease, the antibodies do not destroy the thyroid but act as if they are TSH (i.e., they bind and activate the TSH receptor)

Thyrotoxicosis or Grave's disease

- The Ab (IgG type) is directed against the receptor for thyroid stimulatory hormone (TSH)
 - This Ab is called as Long acting thyroid (LATS) stimulator or thyroid stimulating Ab (TSab).
 - Primary causes: Stimulation of Thyroid gland to secrete more TH (Hyperthyroidism) resulting in Exophthalmus , bulging eyes & Goitre.
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Addison's disease

- It is due to adrenocortical damage & hence insufficient secretion of adrenal hormones.
- Tissue damage is caused by auto Ab against zona glomerulosa cells of adrenal cortex.



Myasthenia Gravis

- It is caused by auto antibody against muscle antigen & acetylcholine receptor antigen.
- Characterized by ↑muscular weakness that make one fatigue. Speaking, eating & walking become tired some.
- Eventually death from respiratory failure
- Acetylcholine cannot be produced, thus nerve impulse cannot be transmitted from the nerves to the muscles. Hence the neuromuscular junction is severely affected.

Systemic Lupus Erythematosus (SLE)

- It is a skin disease due to the production of antinuclear factor (ANF) or antinuclear auto Ab
- ANF reacts with the breakdown products of nuclei in the normal wear & tear of cells & form immune complexes which cause the tissue damage.
- In these patients, LE cell (a mature neutrophil) appears in blood & bone marrow
 - Function – Phagocytosis in the presence of ANF.

Malar Rash (SLE)

Figure 11.10



Characteristics of SLE

- Appearance of blood red spots over the bridge of nose & cheeks. The lesions take the shape of a butterfly.
- Connective tissues of the skin, kidney, heart. Skin & blood vessels are severely damaged resulting in joint pain, fever & anaemia.
- Glomerulonephritis due to deposition of immune complex in the glomerulus region.
- It is a systemic disease affecting the whole body

Rheumatoid Arthritis

- It is a chronic systemic disease of the joints
- Caused by the auto Antibody of IgM type, called as rheumatoid factors.

Characteristics:

- The synovial fluid of these patients contain increased no. of T-cells & macrophages.
- Marked by inflammatory changes in the synovial membrane & by atrophy of bones.
- In later stage, deformity & ankylosis develops.

Rheumatoid Arthritis

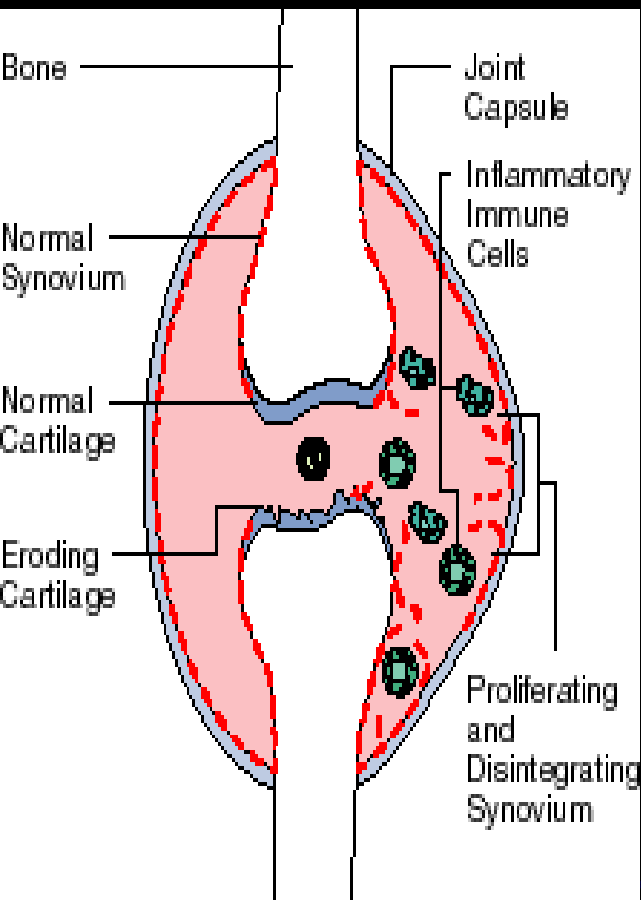
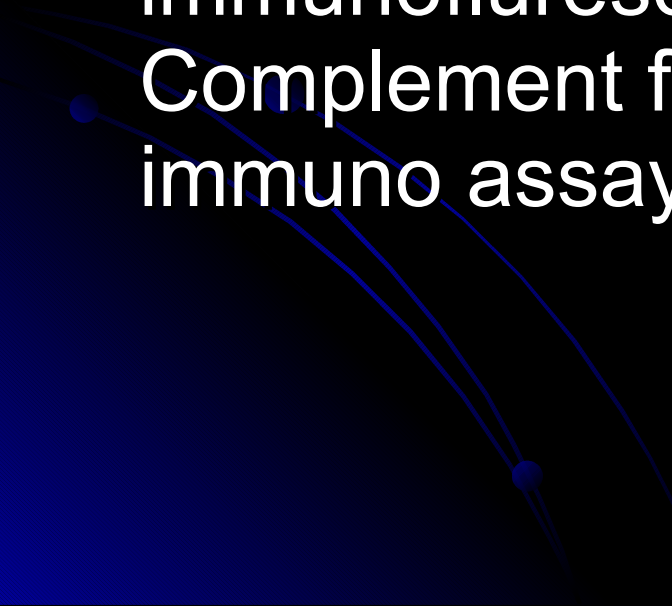


Figure 43.2

Hashimoto's thyroiditis

- Atrophy of thyroid gland, which results in hypothyroidism & destruction of thyroid fun.
- Characterised by Goitre, enlarged thyroid gland, deficiency of TH (Thyroxin)
- Characterized by Type IV hypersensitive rxns.
- Caused by auto Ab of IgG & IgM type against the constituents of thyroid gland (Thyroid epithelial cells, colloid & nuclear components)
- It is a T-cell associated auto immune disease

Diagnosis of Auto immune disease

- Diagnosed by clinical symptoms.
 - Confirmed by detecting the auto Ab in the serum of the patients.
 - Autoantibodies are demonstrated by immunofluorescent Ab test, haemagglutination, Complement fixation, immunodiffusion, Radio immuno assay, etc.
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Treatment

- Some autoimmune diseases are treated with medications that alleviate specific symptoms.
- Haemolytic anaemia: Treated with Vit B₁₂
- Throtoxicosis: Treated with antithyroid drugs.
- Myasthenia Gravis: Treated with Choline esterase inhibitors
- Rheumatoid Arthritis: Anti-inflammatory drugs
- Lupus Erythematosus: Treated with immunosuppressive or antimetabolic drugs such as Corticosteroid, Cyclophosphamide and azathioprine.

Summary

- Autoimmune diseases and conditions exist when the body produces abnormal cells, which attack the body, itself
- Most autoimmune diseases strike women more often than men
- The causes of autoimmune diseases are not known but some autoimmune diseases seem to run in families
- Strike any part of the body, symptoms vary widely and diagnosis and treatment are often difficult
- Medical science is striving to design therapies that prevent autoimmune diseases