IMMUNOLOGY

AUTOIMMUNITY

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AUTOIMMUNE DISORDERS

Introduction

- Under normal circumstances immune system will not destroy self antigens.
- Inappropriate response of the immune system against self-components termed **auto immunity**

- A number of mechanism exist to protect an individual from potentially self reactive lymphocytes, these are given the general term **Tolerance**(a state of unresponsiveness by an antigen)
- 1**. central tolerance** –deletes T or B cell clones before the cell are allowed to mature with receptors to recognize self antigen. It mainly occur in primary lymphoid organs.
- 2. **Peripheral tolerance** describes the mechanisms that take place outside of primary lymphoid tissues to prevent lymphocytes from initiating potentially dangerous immune responses against the body's own tissues, or against other harmless materials.
- Despite this layered system of regulation , self reactive clones of T cells or B cells are occasionally activated generating humoral or cell mediated response of immune system against self component is termed **autoimmunity .**

Autoimmune *Response*

- Antibody directed against “self”, termed auto-antibody
- Considered abnormal but usually does not result in disease.
- May occur in healthy individuals.

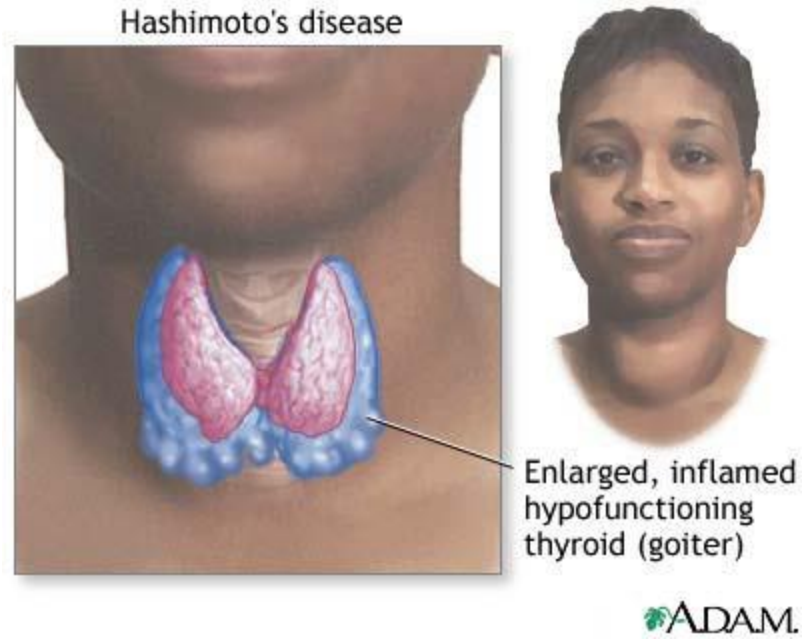
Classification of Autoimmune Diseases

- Systemic- the auto-immunity is directed against an **antigen** that is present at many different sites and can include involvement of several organs
- Organ specific - Organ specific means the auto-immunity is directed against a component of one particular type of organ.

Organ specific autoimmune diseases

Hashimoto's(Chronic) thyroiditis:-

- Prevalent in middle aged women.
- In affected patient autoantibodies and CD4-TH1 are produced specific for thyroid gland antigens . These cells secrete cytokines which induce bioactive inflammatory cells such as macrophages, monocytes etc which causes destruction of thyroid cell resulting thyroiditis.
- The inflammatory response induce goiter (visible enlargement of thyroid) which is evident of physiological response to hypothyroidism.
- Auto antibodies are generated against autoantigen protein like thyroglobulin & thyroid peroxidase which are both concerned with uptake of iodine. The so formed antibodies that leads to decreased production of thyroid hormones and compliment protein which destroy thyroid cells.


Hashimoto's disease
Enlarged, inflamed hypofunctioning thyroid (goiter)
A.D.A.M.

Good pasture syndrome

- Disease of lungs and kidney which affect all age group.
- Auto antibodies specific for certain basement membrane antigen bind to basement membrane of kidney-glomeruli, and alveoli of lung.
- Subsequent compliment activation leads to direct cellular damage and an ensuing inflammatory response mediated by a build up of complement split product.

Insulin dependent diabetes mellitus (type 1)

- Caused by immunological destruction of the pancreas.(insulin producing bete cells of islets of langerhans)
- It leads to decreased production of insulin and consequently increased level of blood glucose.
- First CTLs migrate into islets &began to attack Beta cells along with local cytokine production (IFN-r, TNF-alfa,IL1).
- Auto antibody production can also be a contributing factor in IDDM ,by facilitating either antibody mediated complement lysis or antibody dependent cell mediated cytotoxicity leads to beta cell destruction.
- The destruction of cells results in serious metabolic problems include ketoacidosis, increased urine production ; in later stages characterized by atherosclerotic vascular lesion, renal failure and blindness.If untreated leads to death.
- Treatment –daily administration of insulin,transplantation of purified islets.

Autoimmune anemia

- 1.Pernicious anemia:
- Autoantibodies to intrinsic factor-a membrane intestinal protein on gastric parietal cells
- This factor facilitates uptake of vitamin B12 from the small intestine
- Binding of auto antibodies to intrinsic factor blocks the absorption of vit B12.
- Absence of sufficient amount of vit B12 which is necessary for the hematopoiesis, the no. of functional mature RBC decreases below normal with accompanying weakness, loss of appetite, fatigue.

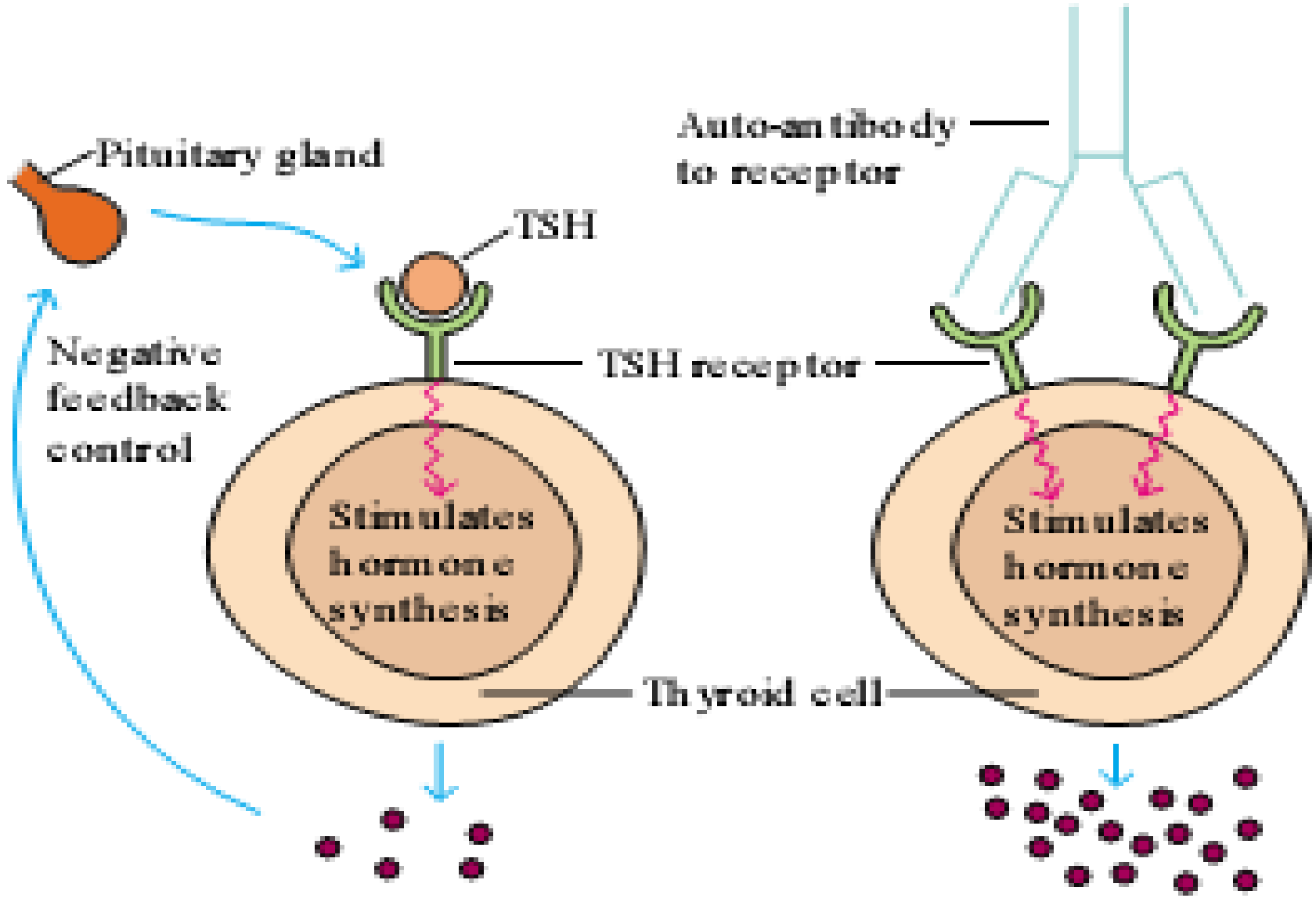
2.Autoimmune haemolytic anaemia- An individual with this disease produces autoantibodies against a variety of red blood cell antigens. These antibodies react with self RBC, destroying or removing red blood cells .

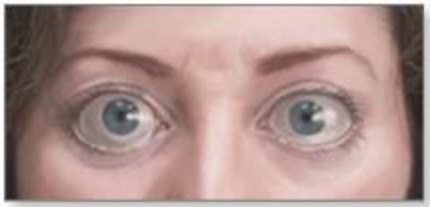
3.Drug induced haemolytic anaemia- certain drugs like penicillin or alfa methyldopa interact with RBC antigen. These antigen recognized as foreign &body generate autoantibodies leading to haemolytic anaemia.

Graves disease

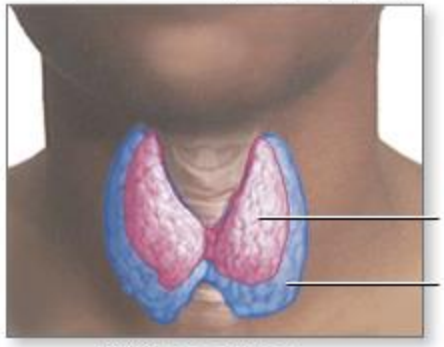
- The production of thyroid hormones is carefully regulated by thyroid-stimulating hormone (TSH), which is produced by the pituitary gland.
- Binding of TSH to a receptor on thyroid cells activates adenylate cyclase and stimulates the synthesis of two thyroid hormones, thyroxine and triiodothyronine.
- A patient with Graves' disease produces auto-antibodies that bind the receptor for TSH and mimic the normal action of TSH, activating adenylate cyclase and resulting in production of the thyroid hormones.
- Unlike TSH, however, the autoantibodies are not regulated, and consequently they overstimulate the thyroid. For this reason these auto-antibodies are called long-acting thyroid-stimulating (LATS) antibodies

STIMULATING AUTO-ANTIBODIES (Graves' disease)





Exophthalmos (bulging eyes)



Diffuse goiter

Graves' disease is a common cause of hyperthyroidism, an over-production of thyroid hormone, which causes enlargement of the thyroid and other symptoms such as exophthalmos, heat intolerance and anxiety

Graves' Disease

TSH receptor antibodies
(usually stimulatory)

Initiation of
autoimmune response

TSH receptor

Thyroid gland

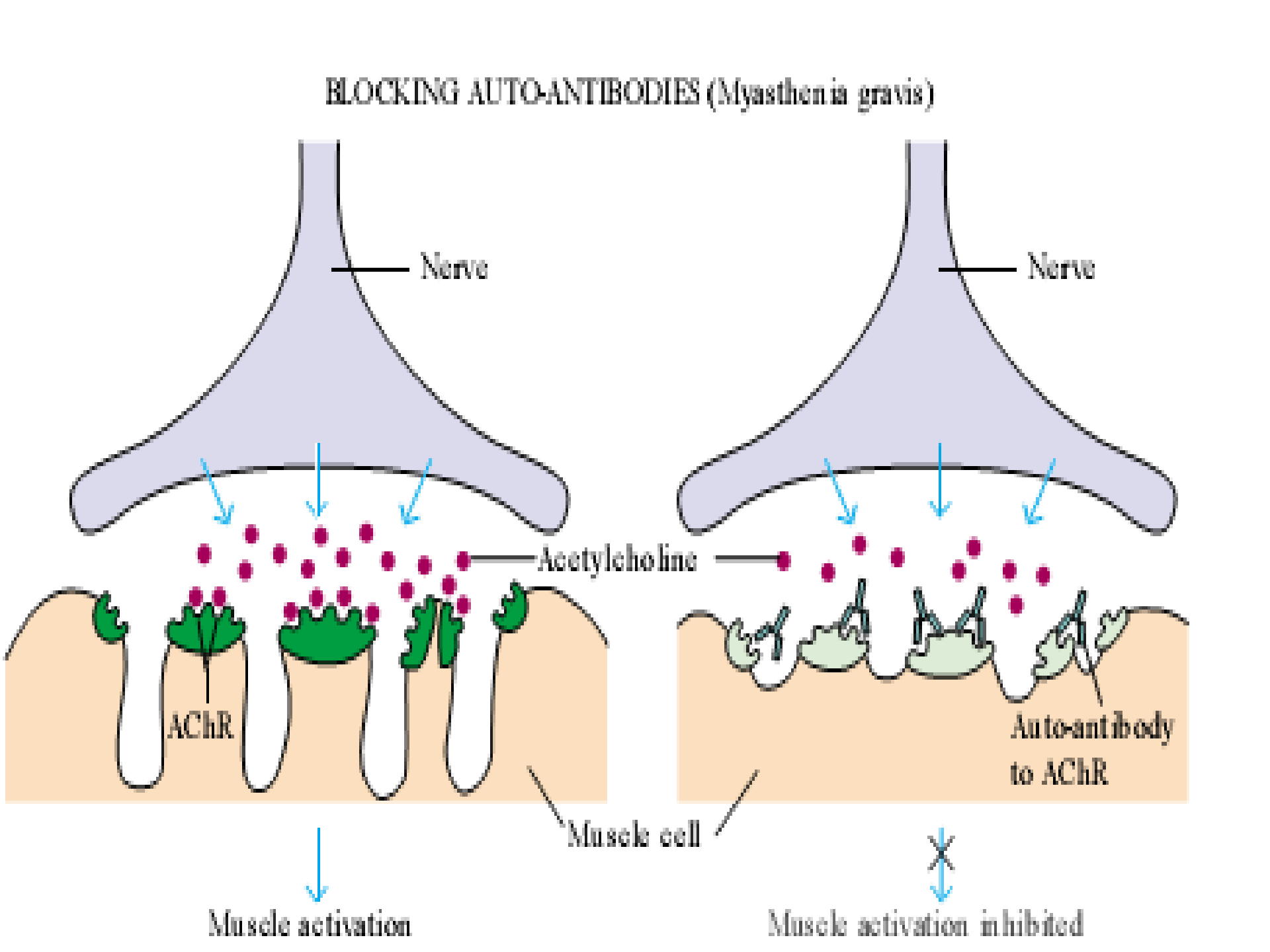
Goitre

Excess
thyroid
hormone

Graves' goitre

Myasthenia gravis

- It is chronic autoimmune disease resulting from faulty neuromuscular transmission.
- Patients with this disease generate autoantibodies against acetylcholine receptor.
- The result is a progressive weakening of the skeletal muscle .
- Ultimately the antibodies cause the destruction of the cells bearing the receptors.
- The early signs of this disease include drooping eye lids and inability to retract the corners of the mouth.


BLOCKING AUTO-ANTIBODIES (Myasthenia gravis)
Nerve
Nerve
Acetylcholine
AChR
Auto-antibody to AChR
Muscle cell
Muscle activation
Muscle activation inhibited

Systemic autoimmune diseases.

Systemic lupus erythematous(SLE)

Typically in women between 20 and 40 year of age.

It is characterized by fever, weakness, arthritis, skin rashes , kidney dysfunction.

Affected person may produce autoantibodies to a vast array of tissue antigens, such as DNA, histones, RBC, platelets, leukocytes, and clotting factors.

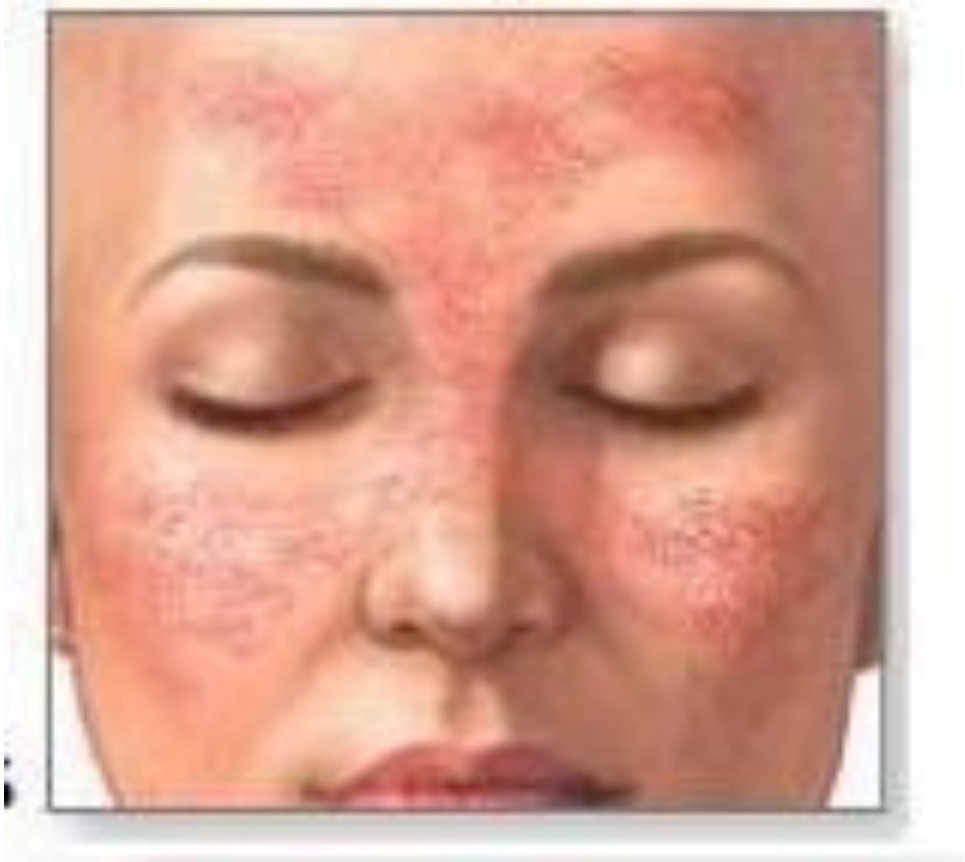
Autoantibodies specific for RBC and platelets can lead to complement mediated lysis resulting in hemolytic anaemia & thrombocytopenia respectively.

When immune complexes of autoantibodies with various nuclear antigen are deposited along the walls of small blood vessels , a type 3 hypersensitivity reaction develops.

Generate membrane attack complexes and complement split products that damage walls of blood vessels resulting in vasculitis and glomerulonephritis.

Excessive complement activation in patients with severe SLE produce elevated serum levels of complement products C3a,C5a as a result number of neutrophils and its aggregation declines that leads to tissue damage.

Butterfly rash



Multiple sclerosis

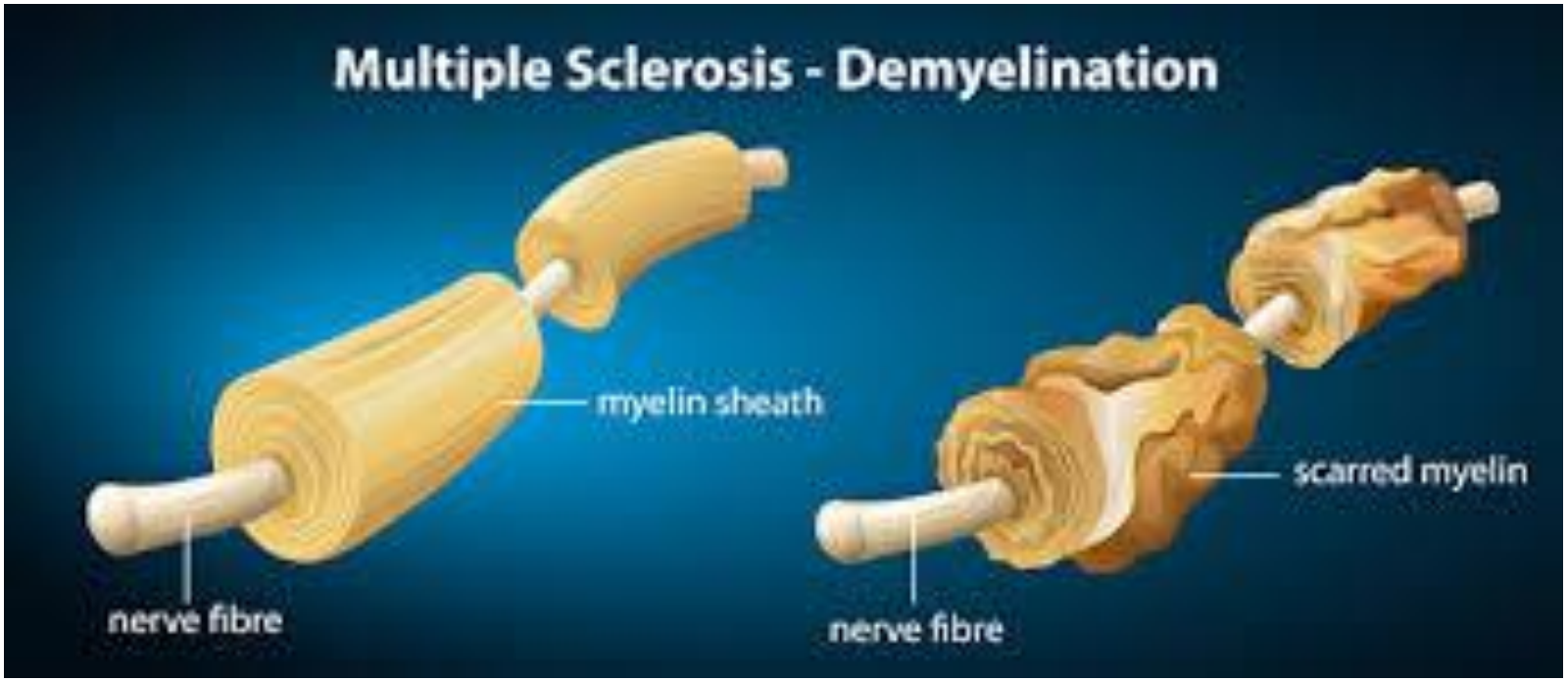
It affects CNS.

Symptoms include motor weakness leading to numbness of limbs or paralysis, ataxia (uncontrolled movement of limbs) , impaired vision, urinary bladder dysfunction and mental aberration.

Usually people b/w age of 20 & 40 are affected.

Most patients show auto reactive T lymphocyte cells in the spinal fluid that infiltrate the brain tissue and cause characteristic sclerotic lesions . These lesion along the myelin sheath lead to numerous mental abberations.

The infection by certain virus tend to predispose an individual to multiple sclerosis.


Multiple Sclerosis - Demyelination
myelin sheath
nerve fibre
scarred myelin
nerve fibre

Rheumatoid arthritis

- Affecting women b/w age of 40-60.
- Symptoms-chronic inflammation of the joints, cardiovascular and respiratory systems are also frequently affected.
- These patients produce a group of auto antibodies called rheumatoid factor that are reactive with determinants in Fc region of IgG.
- The classic rheumatoid factor is an IgM antibody that bind to normal circulating IgG forming a IgG-IgM complex that are deposited in the joints which leads to chronic inflammation of joints.

THANK YOU..