LECTURE 2

AUTOIMMUNE DISEASES

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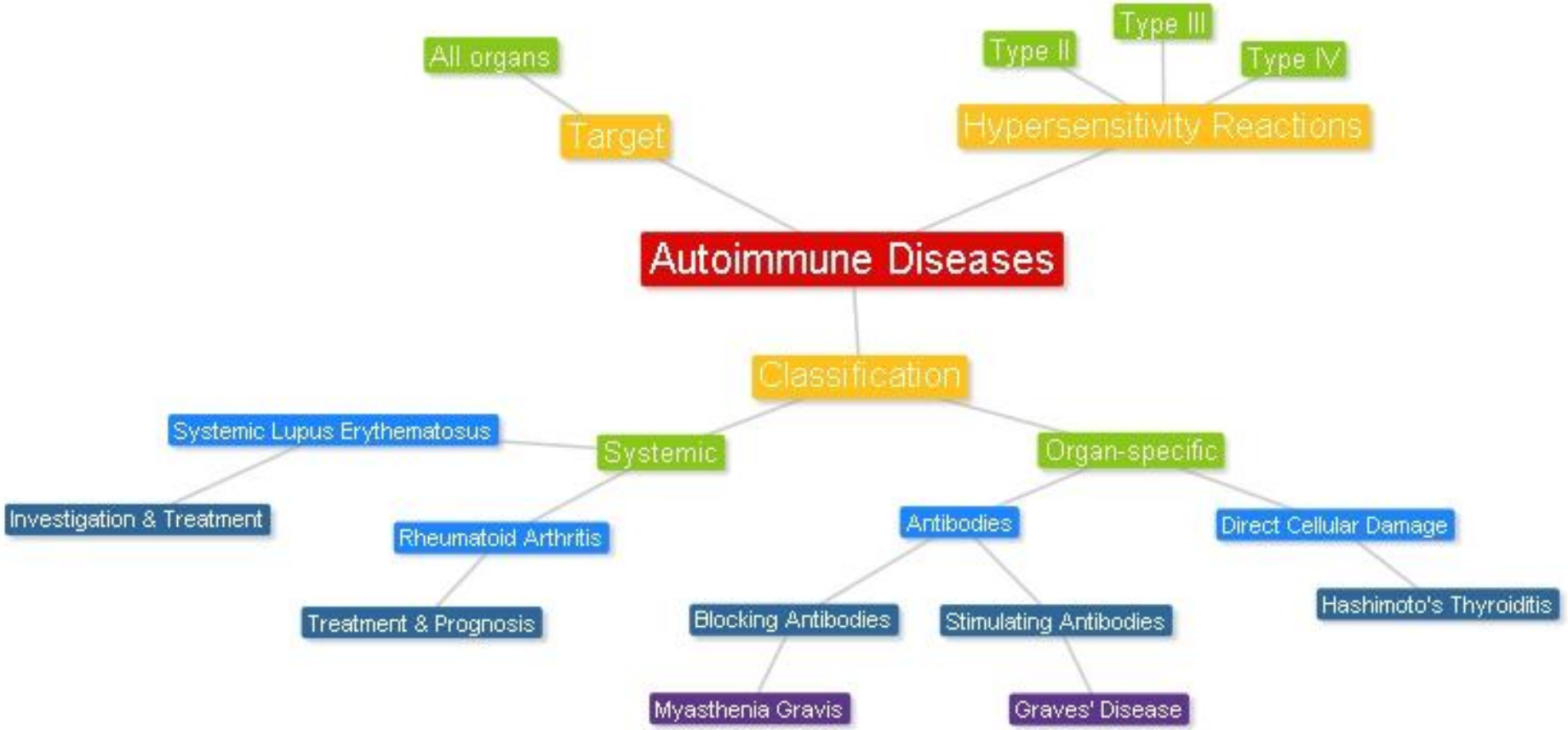
OBJECTIVES

To know that:

- The inflammatory processes in auto immune diseases are mediated by hypersensitivity reactions (type II, III and IV).
- Autoimmune diseases can be either organ specific or may be generalized involving many organs or tissues.
- The manifestations of autoimmune diseases depend upon the organ and the degree of damage inflicted on the target tissues.


All organs
Target
Type III
Type II
Type IV
Hypersensitivity Reactions
Autoimmune Diseases
Classification
Systemic Lupus Erythematosus
Systemic
Organ-specific
Investigation & Treatment
Rheumatoid Arthritis
Antibodies
Direct Cellular Damage
Treatment & Prognosis
Blocking Antibodies
Stimulating Antibodies
Hashimoto's Thyroiditis
Myasthenia Gravis
Graves' Disease

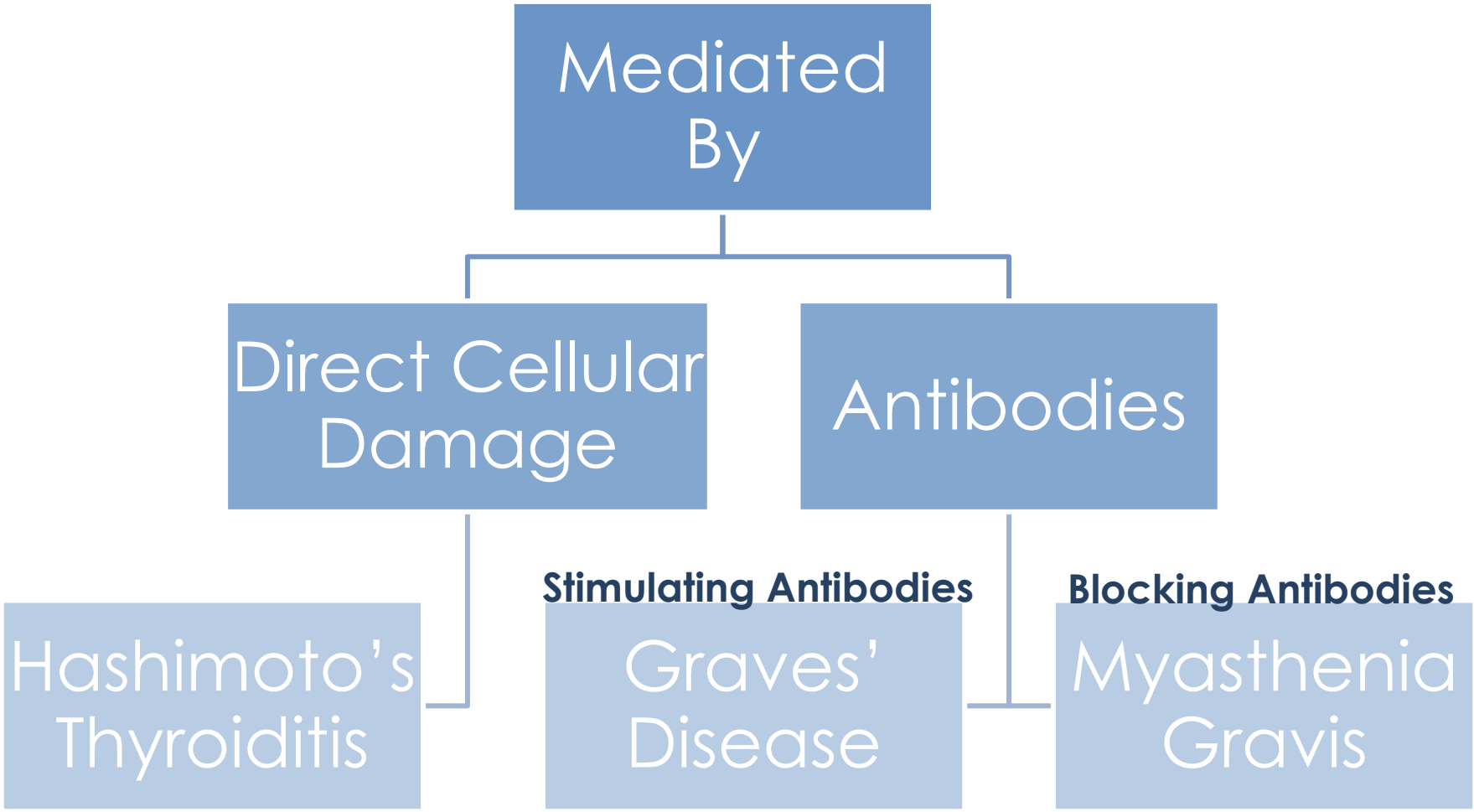
- **Disease processes and tissue damage are due to hypersensitivity reactions:**
  - **Type II** (IgG Ab to tissue antigens)
  - **Type III** (IgG Immune Complexes)
  - **Type IV** (Cell Mediated Immunity)
- **Autoimmunity can affect ANY organ or organ system in the human body.**
- **Can be classified into** *organ specific & systemic diseases.*

Note: Some diseases can be both organ specific and systemic.

CLASSIFICATION

Organ-specific autoimmune diseases	Systemic autoimmune diseases
Type I diabetes mellitus	Rheumatoid arthritis
Goodpasture's syndrome	Scleroderma
Multiple sclerosis	Systemic lupus erythematosus Primary Sjögren's syndrome Polymyositis
Graves' disease Hashimoto's thyroiditis Autoimmune pernicious anemia Autoimmune Addison's disease Vitiligo Myasthenia gravis	

ORGAN-SPECIFIC DISEASES

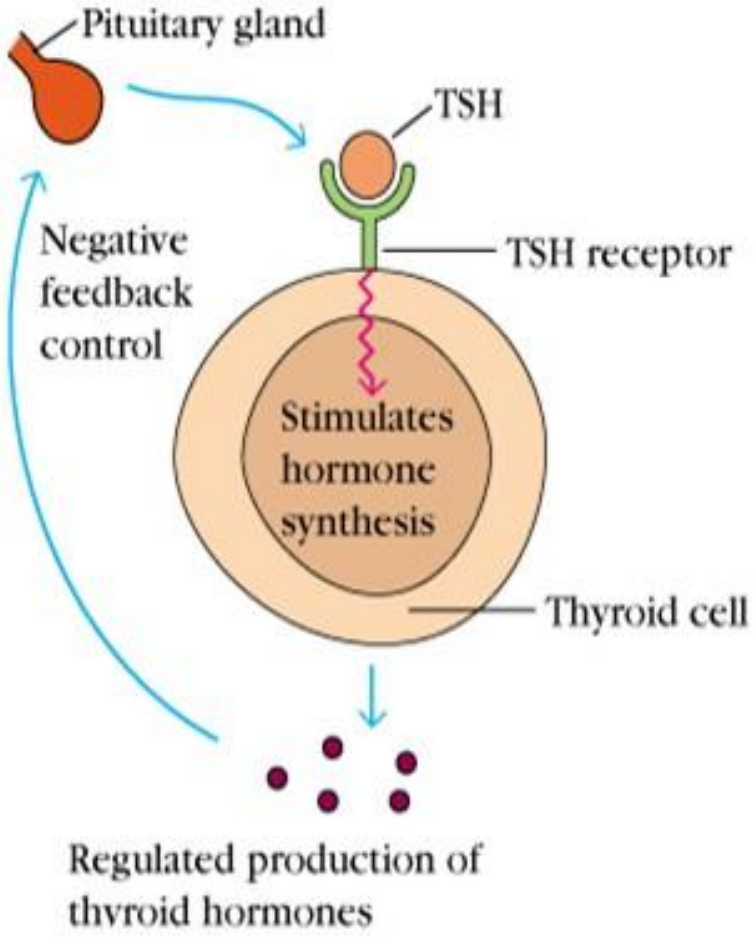


GRAVES' DISEASE (THYROTOXICOSIS)

WHAT NORMALLY HAPPENS:

- Production of thyroid hormones is regulated by *thyroid-stimulating hormones* (TSH).

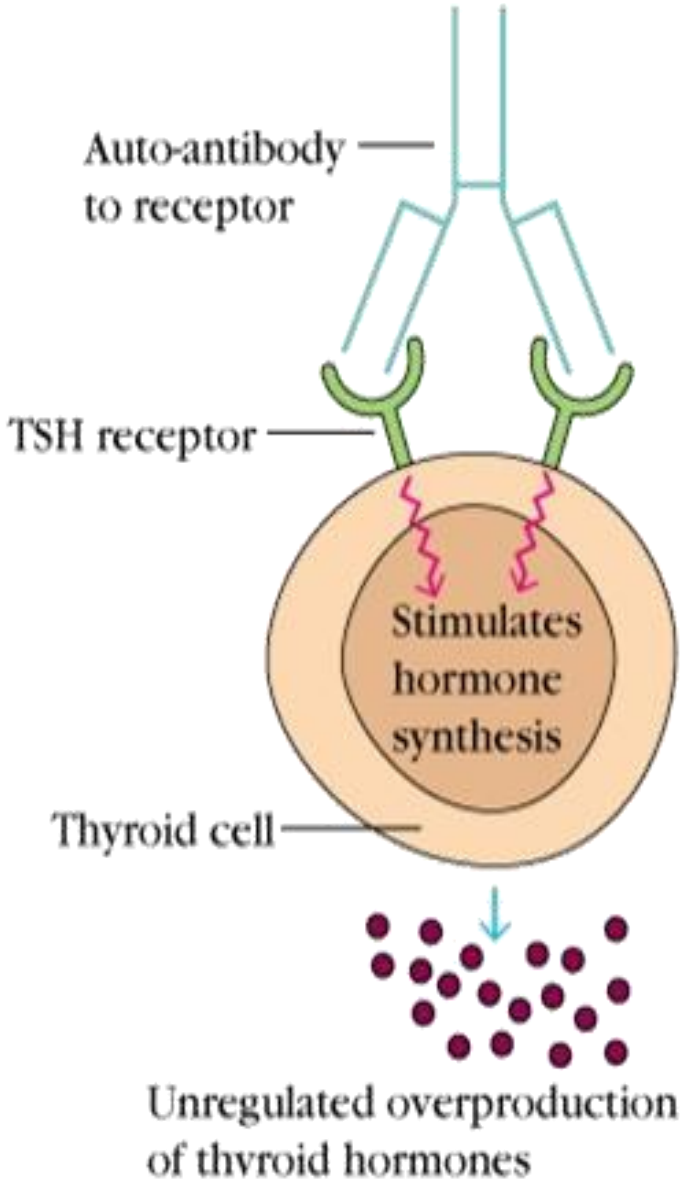
- The binding of TSH to a receptor on thyroid cells stimulates the synthesis of two thyroid hormones: *thyroxine* and *triiodothyronine*



WHAT HAPPENS IN GRAVES' DISEASE:

- A person with Graves' Disease makes *auto-antibodies* to the receptor for TSH.

- Binding of these auto-antibodies to the receptor mimics the normal action of TSH leading to over-stimulation of the thyroid gland.

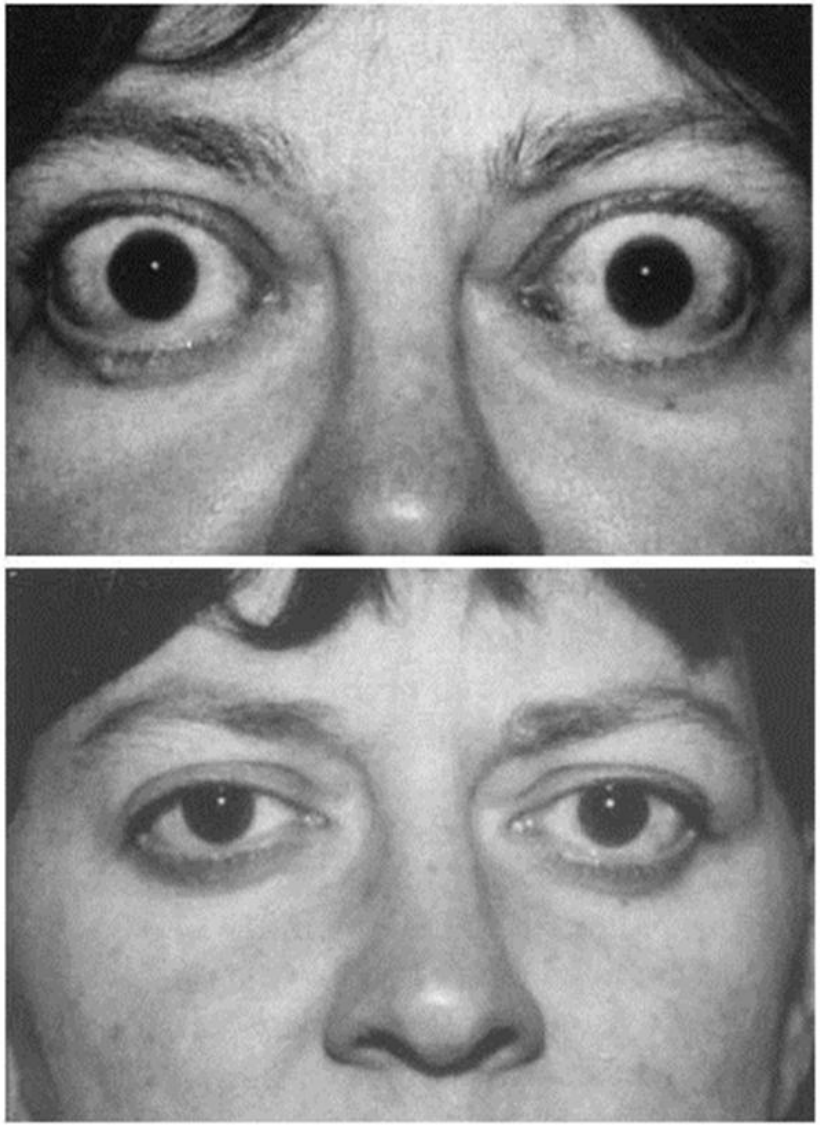


SYMPTOMS

- **Hand tremors**
- **Weight loss**
- **Bulging eyes**
- **Trouble sleeping**
- **Hyperthyroidisms**

Note: Most people with Graves' disease have symptoms of an overactive thyroid.

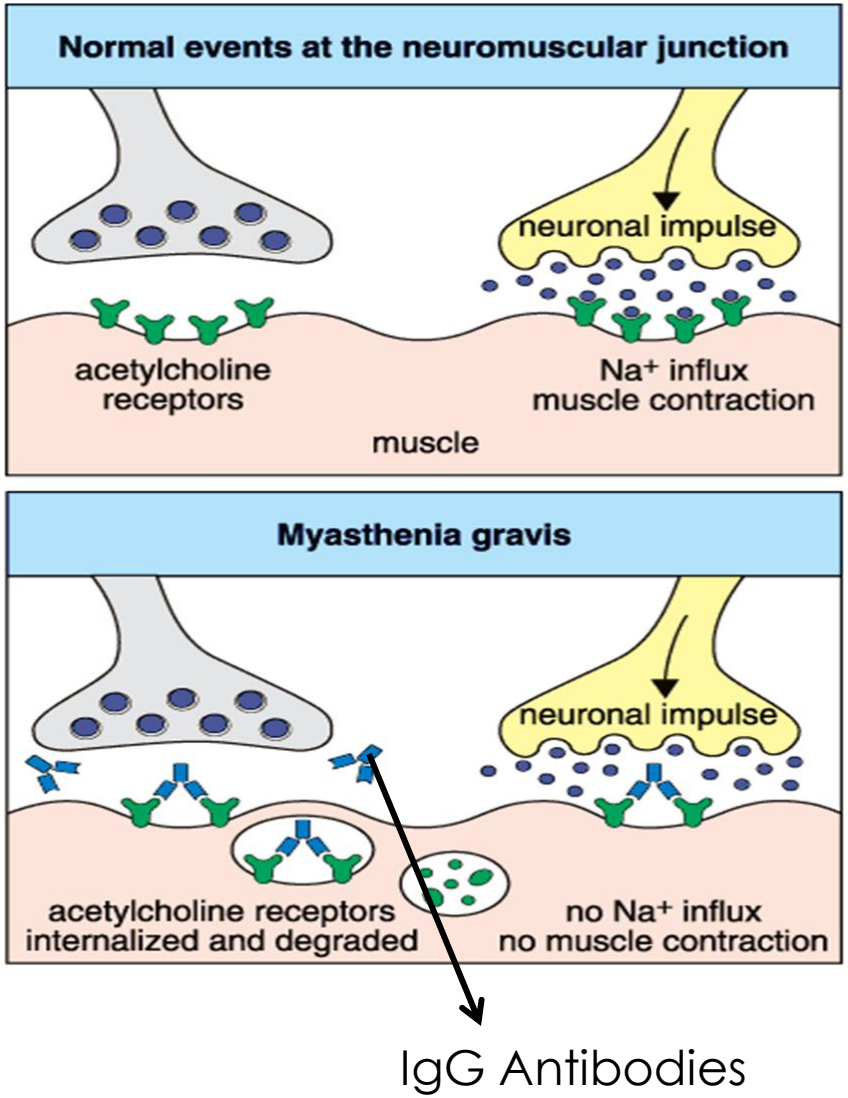
Note: It is more common in women.



MYASTHENIA GRAVIS

WHAT HAPPENS IN MYASTHENIA GRAVIS:

- Antibodies directed against acetylcholine receptor (AchR).
- IgG Ab interact with the postsynaptic AChR at the nicotinic neuromuscular junction (NMJ).
- There is reduction in the number of functional AChR receptors by increasing complement mediated degradation of receptors.

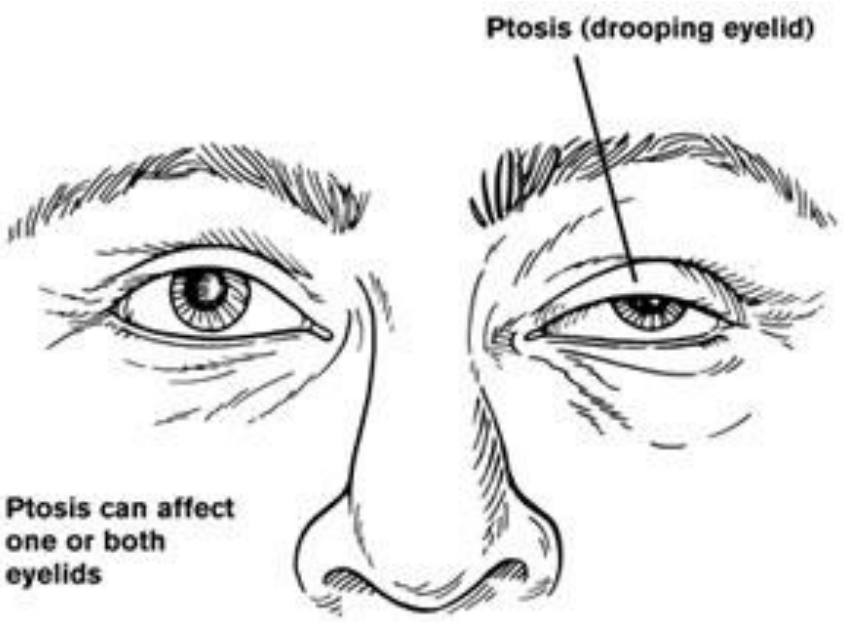


SYMPTOMS

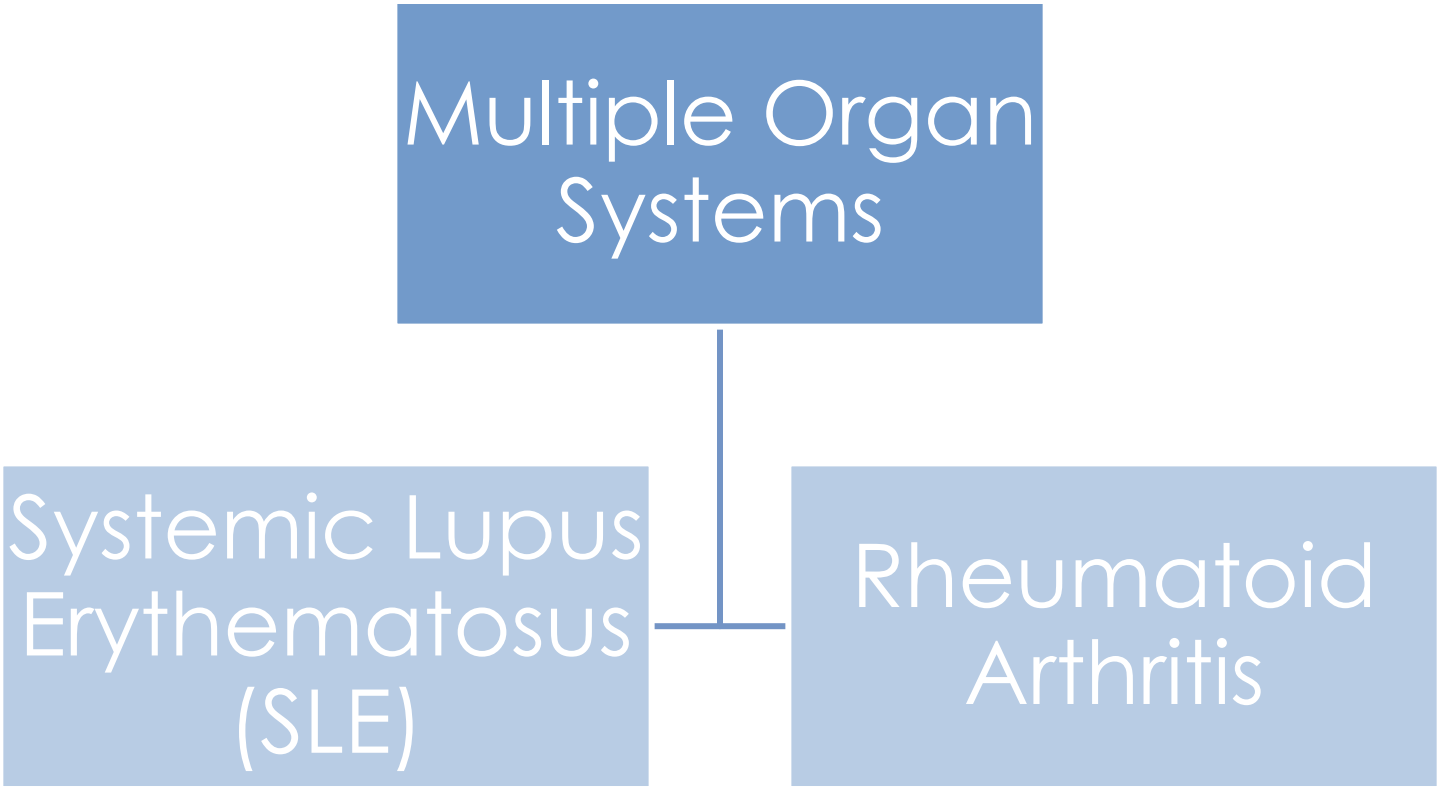
- **Weakness**
- **Fatigability with effort**
- **Drooping eyelids**

Note: It is a disease that affects the nervous system.

Treatment : Plasmapheresis

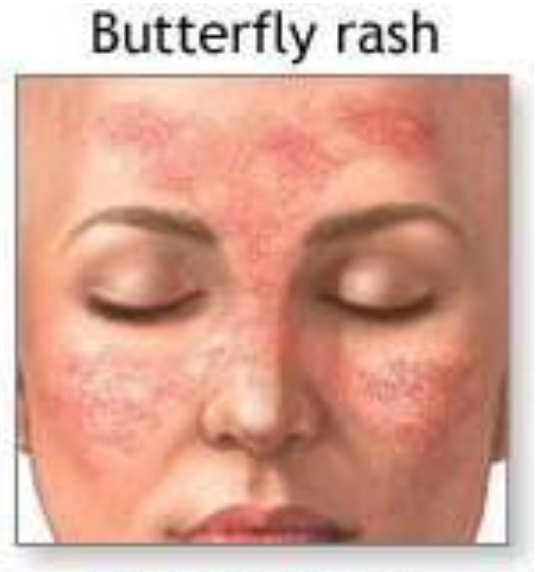


SYSTEMIC DISEASES



SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

- **Systemic Lupus Erythematosus is the most common autoimmune disorder.**
- **The characteristic "butterfly rash" is made worse by exposure to sunlight.**
- **It can affect any organ in the human body.**
- **Lupus is a potentially fatal autoimmune disease.**



Note: It is a true multi-system disease, it can affect any part of the body. It is unpredictable.

- **DNA/RNA + Protien complexes**
- **Chemotaxins**
- **Leukocytes, mononuclear cells**
- **Inflammatory factors** (IL-4, IL-6, IL-10)
- **Destruction of cells**

Note: If the cell is destroyed, ribosomes will come out. These cells are what out immune system reacts to. If the damage continues, patient will eventually die.

Note: Think of SLE in case of any weird formation in the body.

INVESTIGATIONS

- **Autoantibodies**
  - The anti-nuclear antibody (ANA) test is the best screening test for SLE and is determined by immunofluorescence or ELISA tests.
  - The ANA is positive in significant titer (usually **1:160** or higher) in virtually all patients with SLE.
- **Anti-double-stranded DNA titers**

Antigen	SLE	Clinical Associations
ds DNA	70%	Nephritis (and flare)

- **Complement Levels (CH50, C3, C4)**
- **ESR (erythrocyte sedimentation rate)**
- **CRP (C-reactive protein)**
- **Complement Split products**
- **Decreased complement C1q** (The 1st complement of classical pathway, it is decreased because is being used)

TREATMENT

- **NSAIDs (Non-steroidal anti-inflammatory drugs)**
- **Antimalarial (Hydroxychloroquine)** (it is also anti-rheumatoid)
- **Immunosuppressive agents**

Note: There is no cure for SLE. The goal of treatment is to control symptoms.

RHEUMATOID ARTHRITIS

- Rheumatoid arthritis is an autoimmune disease in which the normal immune response is directed against an individual's own tissue, including the :

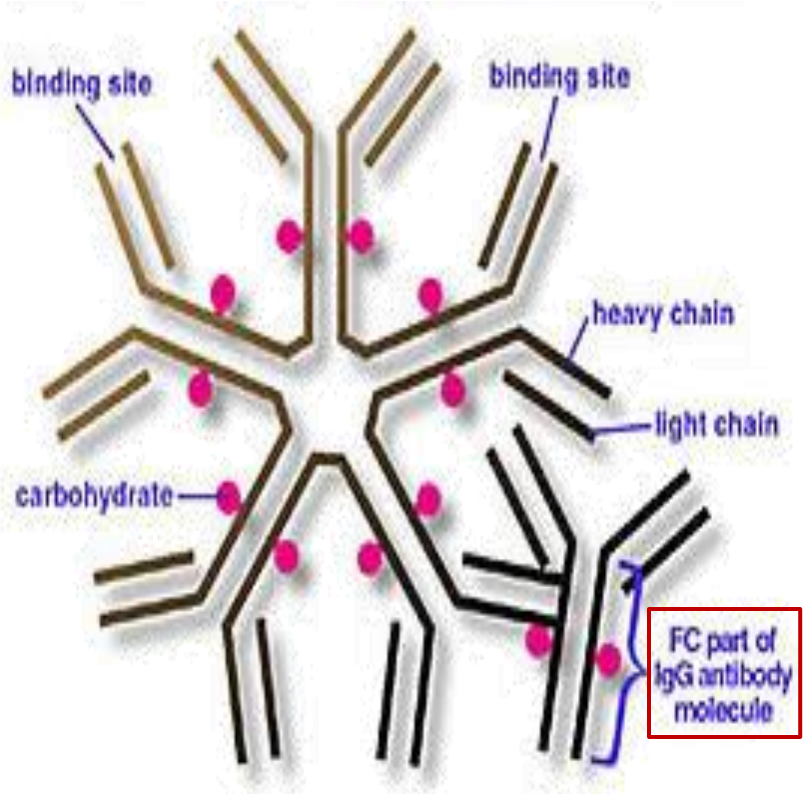
  Joints, Tendons, Bones

- Resulting in inflammation and destruction of these tissues.
- The cause of rheumatoid arthritis is not known.
- Investigating possibilities of a foreign antigen, such as a virus.
- Both prevalence and incidence are 2-3 times greater in women than in men.

Note: The main difference between rheumatoid and osteoarthritis is that osteoarthritis is a degenerative disease.

RHEUMATOID FACTOR

- In rheumatoid arthritis, many individuals produce a group of auto-antibodies known as rheumatoid factor.
- These antibodies react with determinants in the FC region of IgG (Self-antigen is IgG)
- The classic rheumatoid factor is an IgM antibody with this kind of reactivity.



Type III Hypersensitivity Reaction				
Such auto-antibodies bind to normal circulating IgG, **forming IgM-IgG complexes** which may be deposited in joints	This leads to **activation of synovial macrophages**	The macrophages engulf the immune complexes and then **release TNF and other pro-inflammatory cytokines** e.g., IL-1	TNF induces the **secretion of metalloproteinase**; which are known to **cause joint destruction**	**T cell activation** due to unknown antigens also contributes to the inflammation in RA

- Rheumatoid arthritis (RA) affects peripheral joints and may cause destruction of both cartilage and bone. e.g., interphalangeal joints

TREATMENT AND PROGNOSIS

- **Medications**
  - NSAIDS (Non-steroidal anti-inflammatory drugs)
  - DMARD (Disease-modifying anti-rheumatoid drugs) e.g., Oral gold, Hydroxychloroquine, Sulfasalazine, Penicillamine
- **Immunosuppressive therapy**
  - Corticosteroids
  - Methotrexate
- **Surgery**
- **Physical therapy**

REMEMBER

- Autoimmune disorders is a single organ involvement to a systemic disease.
- The disease process is usually prolonged and is generally associated with significant morbidity and mortality.
- The mainstay of the treatment is to maintain immunosuppression.

MCQS

1. **Which of the following is a non-organ-specific (systemic) autoimmune disease:**

   A. Myasthenia gravis.
   B. Systemic Lupus Erythematosus (SLE).
   C. Hashimoto's thyroiditis.
   D. Insulin-dependent diabetes mellitus.

2. **Which of the following method is used to test the presence anti-nuclear antibodies:**

   A. Gene rearrangement studies
   B. Anti-double-stranded DNA titers
   C. Analysis of urine for protein
   D. ELISA test

3. **In rheumatoid arthritis auto-antibodies bind to which immunoglobulin:**

   A. IgE
   B. IgM
   C. IgG
   D. IgA

1-B, 2-D, 3-C