Musculoskeletal Block

Immunology

Lecture 2

Autoimmune Diseases

In this document you will find some main points gathered from the 1st lecture..This document is NOT a replacement for the lecture..If you need additional information go back to the lecture or use a book as a reference so you understand everything correctly.

Hopefully all the information is correct and Hope you find them Useful.

Good Luck to everyone.

430 Immunology Team

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Immunology

Autoimmune Diseases

Some main points you can go through and revise from:

Note:
Autoimmune Diseases are caused by a problem or a breakdown of the tolerance of the immune system.

Note:
-Some autoimmune diseases affect one organ
-Others affect more than one organ (Systemic)

Note:
-Autoimmune diseases can be caused by Auto-reactive T-cells and Auto-reactive antibodies.
-Others are caused by Auto-reactive antibodies only

Table showing examples of organ specific autoimmune diseases and systemic autoimmune diseases

SOME AUTOIMMUNE DISEASES IN HUMANS

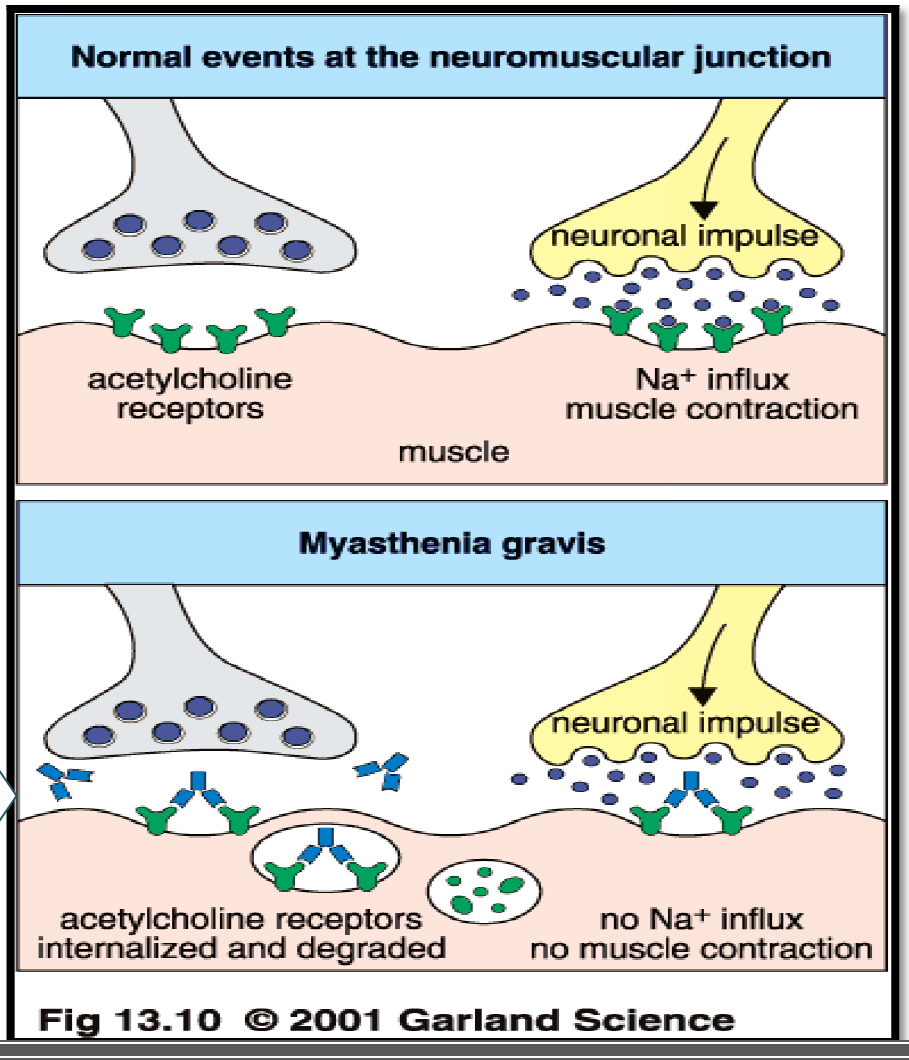
Disease	Self-antigen	Immune response
	Organ-specific autoimmune diseases	
Addison's disease	Adrenal cells	Auto-antibodies
Autoimmune hemolytic anemia	RBC membrane proteins	Auto-antibodies
Goodpasture's syndrome	Renal and lung basement membranes	Auto-antibodies
Graves' disease	Thyroid-stimulating hormone receptor	Auto-antibody (stimulating)
Hashimoto's thyroiditis	Thyroid proteins and cells	T_{DTH} cells, auto-antibodies
Idiopathic thrombocyopenia purpura	Platelet membrane proteins	Auto-antibodies
Insulin-dependent diabetes mellitus	Pancreatic beta cells	T_{DTH} cells, auto-antibodies
Myasthenia gravis	Acetylcholine receptors	Auto-antibody (blocking)
Myocardial infarction	Heart	Auto-antibodies
Pernicious anemia	Gastric parietal cells; intrinsic factor	Auto-antibody
Poststreptococcal glomerulonephritis	Kidney	Antigen-antibody complexes
Spontaneous infertility	Sperm	Auto-antibodies
	Systemic autoimmune disease	
Ankylosing spondylitis	Vertebrae	Immune complexes
Multiple sclerosis	Brain or white matter	T_{DTH} and T_C cells, auto-antibodies
Rheumatoid arthritis	Connective tissue, IgG	Auto-antibodies, immune complexes
Scleroderma	Nuclei, heart, lungs, gastrointestinal tract, kidney	Auto-antibodies
Sjogren's syndrome	Salivary gland, liver, kidney, thryoid	Auto-antibodies
Systemic lupus erythematosus (SLE)	DNA, nuclear protein, RBC and platelet membranes	Auto-antobidies, immune complexes

*Know the Examples of organ-specific and systemic autoimmune diseases

Autoimmune Diseases

1-Myasthenia Gravis

-Patients show weakness and fatigability
-**Antibodies directed against acetylcholine receptors (AChR)**
-Postsynaptic Acetylcholine receptors are blocked by:
* **IgG Antibodies**
-The receptors are then destroyed by complements (complement mediated destruction)
-Therefore the number of AchR (Acetylcholine Receptors) is reduced



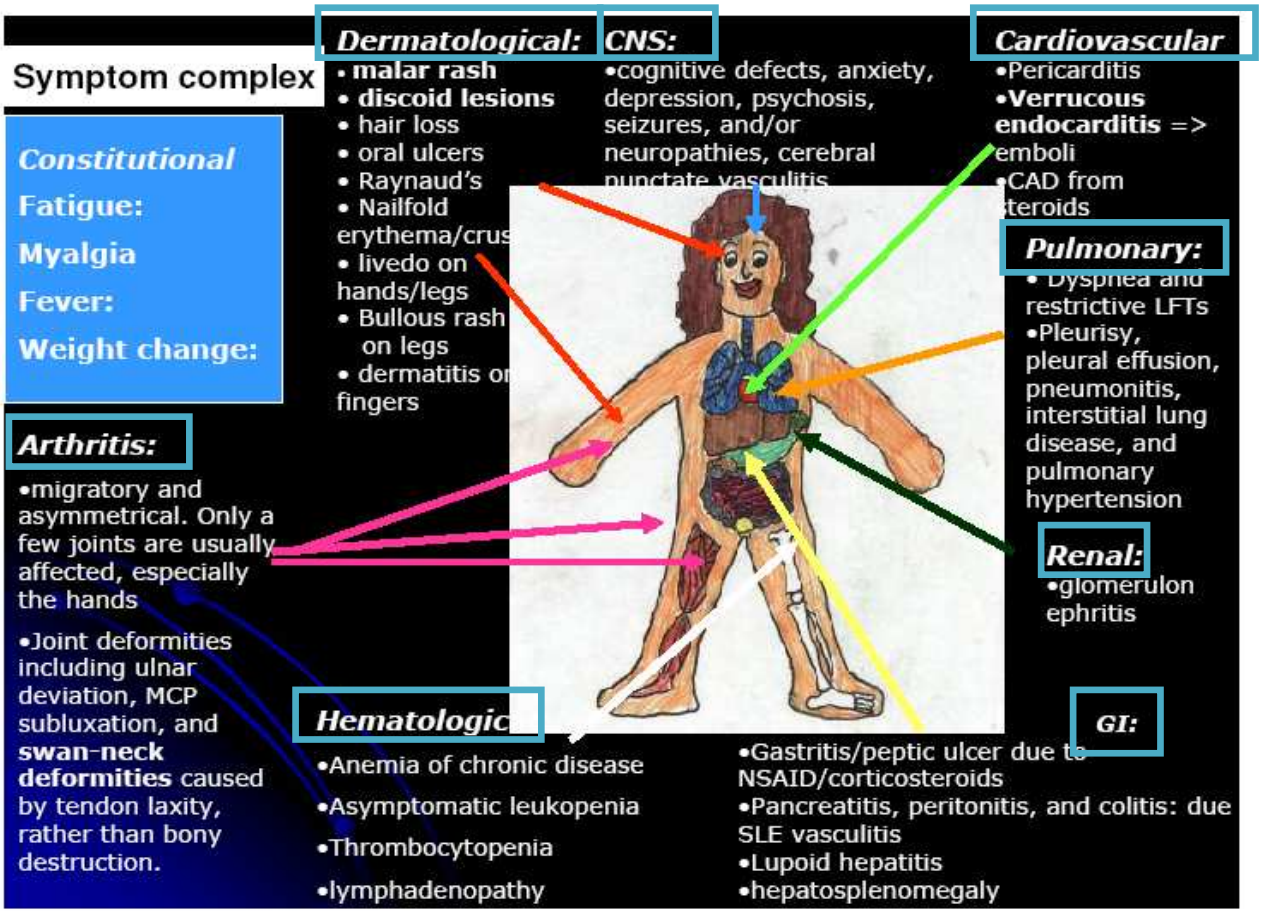
-No Ach receptors = No Ach

-No Ach= Na+ channels will not open (No Na+ influx)

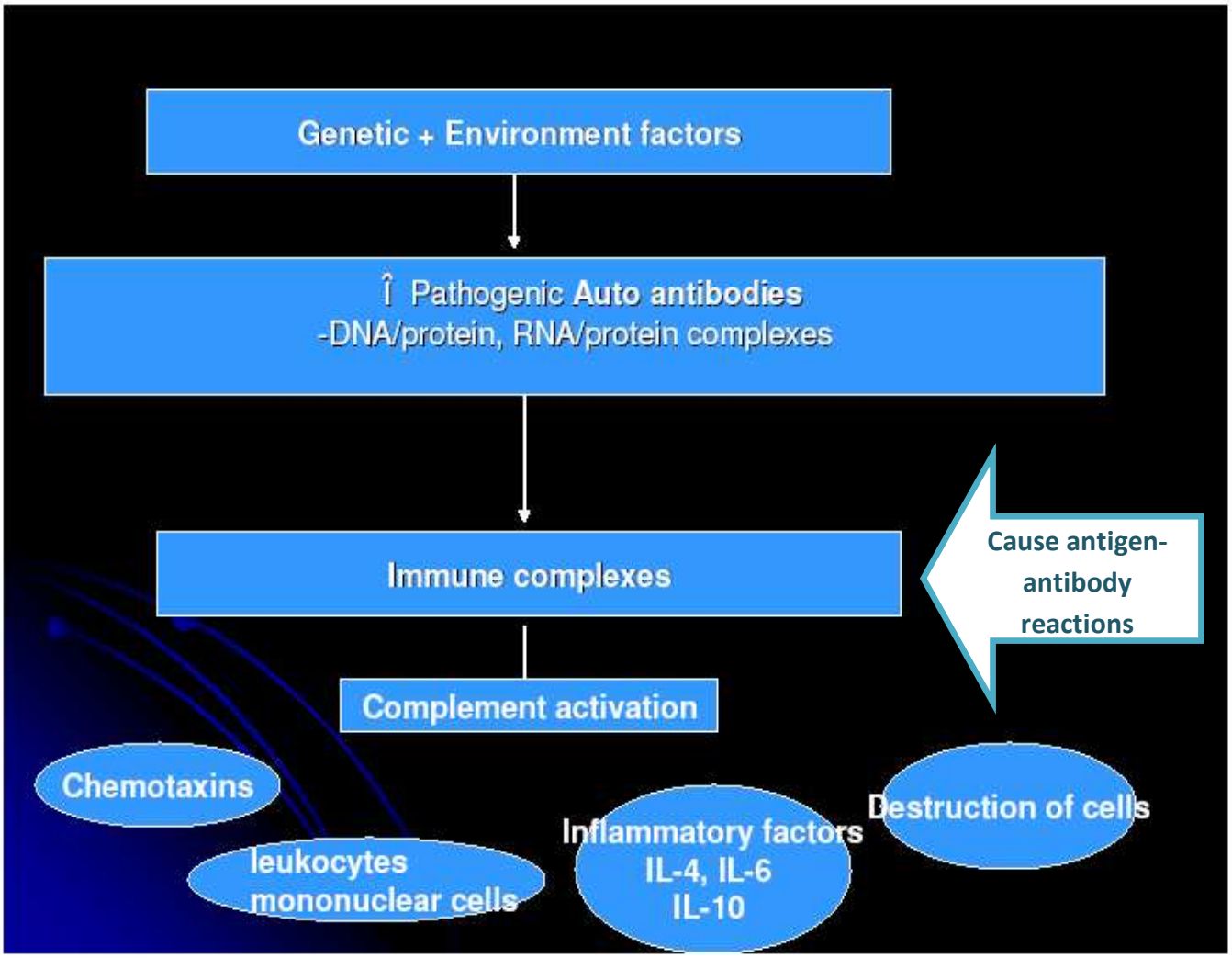
-No Na+ influx = No muscle contraction.

2-Systemic Lupus Erythematosus (SLE)

-**Multi system autoimmune disorder.**
-Characterized by: Butterfly rash → worsens under sunlight.
-SLE is a potentially fatal autoimmune disease.



*Know the systems & organs effected by SLE

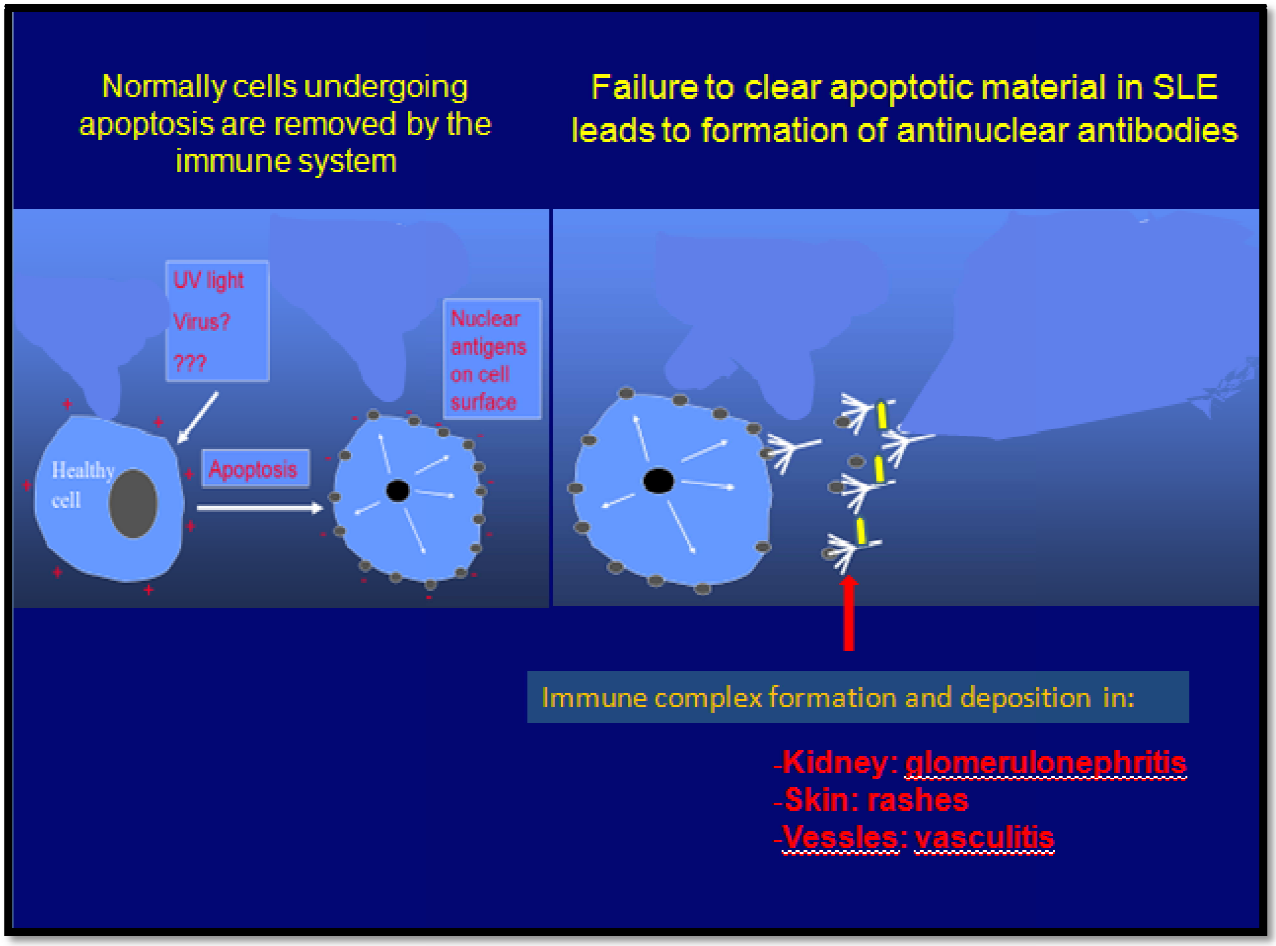

Genetic + Environment factors
↑ Pathogenic Auto antibodies
-DNA/protein, RNA/protein complexes
Immune complexes
Cause antigen-antibody reactions
Complement activation
Chemotaxins
leukocytes mononuclear cells
Inflammatory factors IL-4, IL-6 IL-10
Destruction of cells

-Normally Cells that undergo apoptosis (Programmed cell death) are removed by the immune system.

-Failure to clear apoptotic material (Meaning that the remains of the dead cells are not being cleaned up) → Leads to formation of auto-antibodies

<u>Immune complex formation and deposition occurs in:</u>

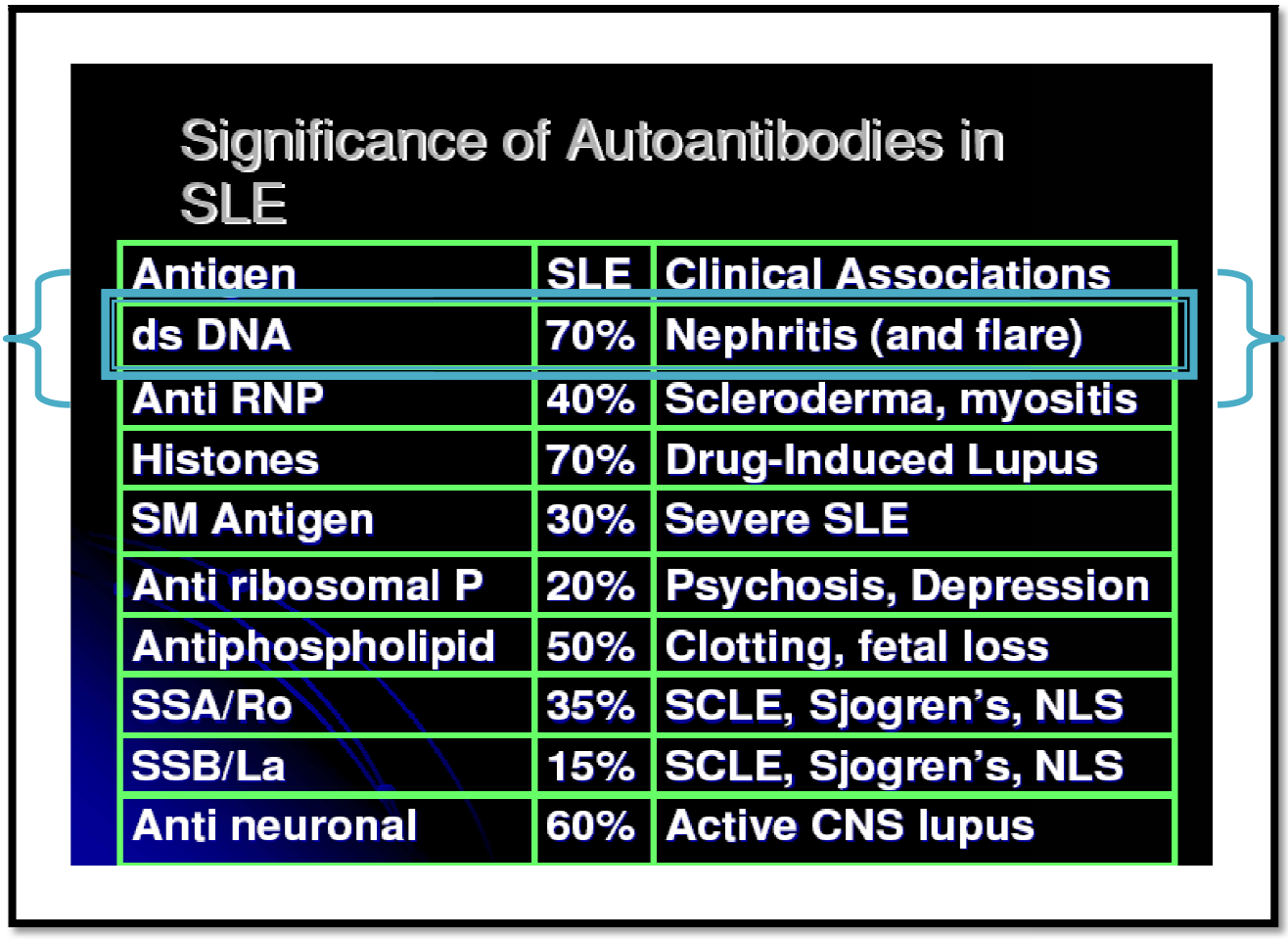
-Kidney: Glomerulonephritis
-Skin: rashes
-Vessels: vasculitis



Auto antibodies

Best screening test for SLE:
The anti-nuclear antibody (ANA) test

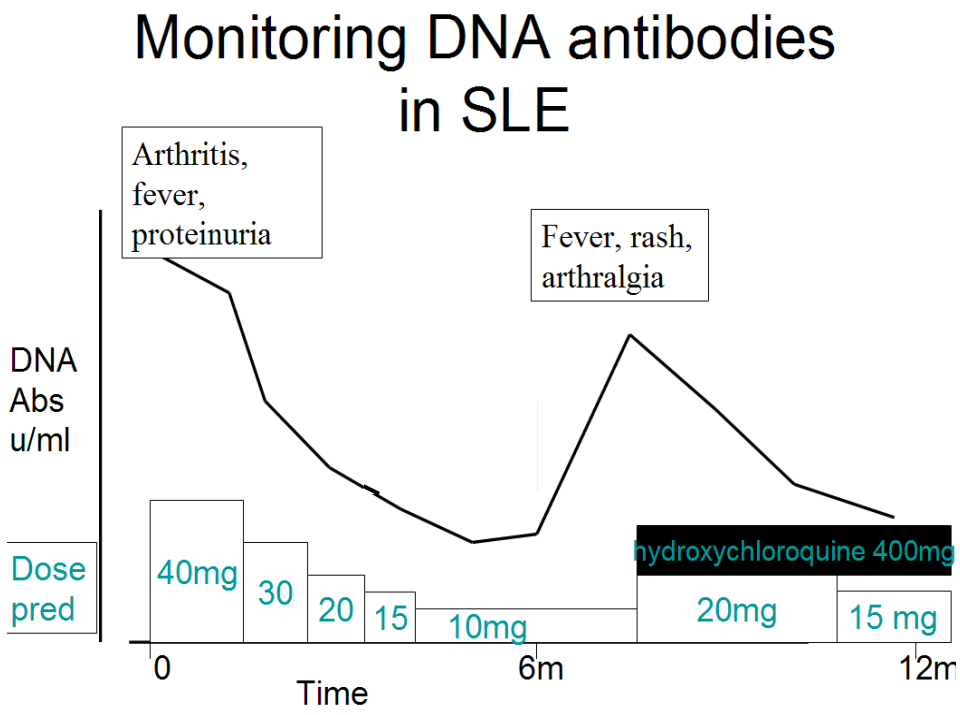
Screening test for SLE and is determined by:
Immunofluoresence or ELISA tests



*Most Important point is highlighted in blue

Disease Activity

-Anti-double-stranded DNA titers
-Complement Levels (CH50, C3, C4) →**the complements will decrease in number = the activation of complement**
-ESR
-CRP
-Complement Split products →**Will increase in level**
-Decreased complement C1q



Monitoring DNA antibodies in SLE using drugs

Treatment

-NSAIDs (Non-steroidal anti-inflammatory drugs)
-Antimalarials (Hydroxychloroquine)
-Immunosuppressive agents

3-Rheumatoid Arthritis

-Autoimmune disease
-Normal immune responses are directed against own tissue (Attacks and destroys own tissues) such as:
-Joints
-Tendons
-Bones
-**The cause** of rheumatoid arthritis is **not known** → Tests show it might be a foreign antigen such as a virus.
-**Effects more women than men**

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Pathogenesis

How the disease happens:

-A group of auto antibodies are produced
- IgM antibody attaches to Fc region of IgG antibody → Forming an IgM-IgG complexes
- IgM(Which attaches to Fc region of IgG) = Rheumatoid Factor
- IgM-IgG complexes are deposited in joints.
- Immune complexes → Start complement system → Results in a Type 3 Hypersensitivity reaction → Causing chronic inflammation of the joints = Rheumatoid arthritis

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Functional Presentation and Disability of RA

(How the disease manifests (shows) and the damage it causes)

- Warmth, pain, and redness, with decreased range of motion of the affected joint.
- Progression of the disease eventually results in fixed deformities.
-Muscle weakness and atrophy develop in many people.

←Rheumatoid Arthritis continued..

Complications of Rheumatoid Arthritis

*Complications include:

-Carpal tunnel syndrome
-Baker's cyst
-Vasculitis
-Subcutaneous nodules
-Peripheral neuropathy
-Cardiac and pulmonary involvement

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Treatment and Prognosis

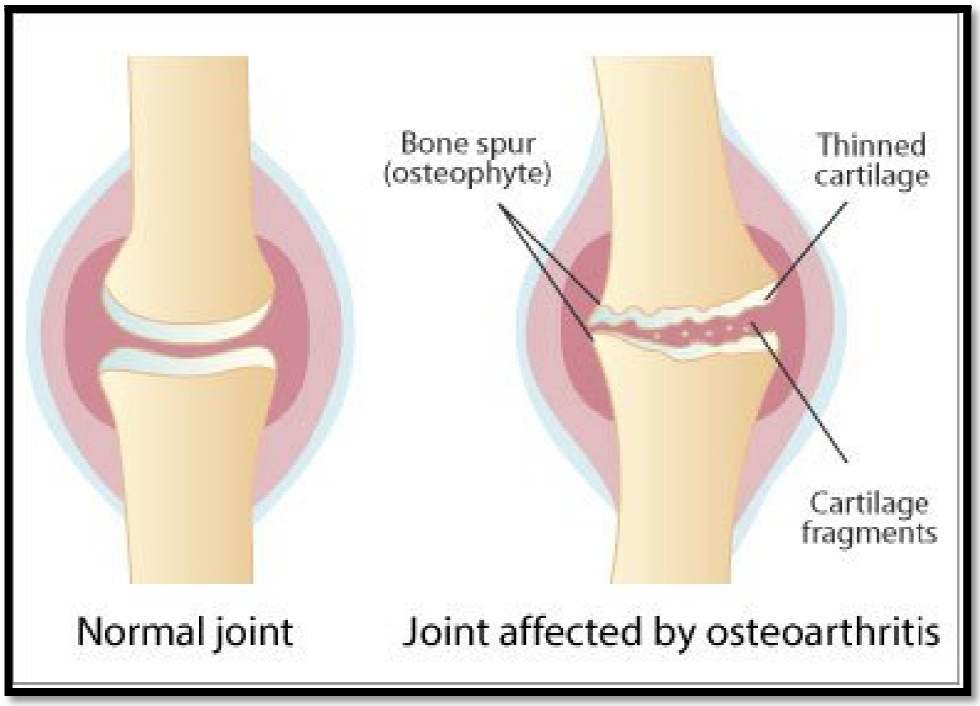
Medications:

-NSAIDS (Non-steroidal anti-inflammatory drugs)
-Disease-modifying drugs (eg, gold, hydroxychloroquine, sulfasalazine, penicillamine)
-Immunosuppressive therapy:
-Corticosteroids
-Surgery
-Physical therapy

4-Osteoarthritis (Degenerative Joint Disease)

*Most common rheumatic disease.

-progressive loss of cartilage.
-reactive changes at the margins of the joint and in the subchondral bone (Changes occur in the cartilage and the bone it covers)
-The final outcome is full-thickness loss of cartilage down to bone (All the cartilage covering the bone is lost)



Comparison between Rheumatoid Arthritis & Osteoarthritis
(Very Important)

Rheumatoid Arthritis	Osteoarthritis
Autoimmune disorder	Degenerative disorder and more common
May begin at any time in life	Usually begins later in life
Usually affects small joints of hands, wrist, feet ankle, spine etc.	Weight bearing joints, knee, hip, lumbosacral
Usually symmetrical joint involvement	Un-symmetrical joint involvement
Chronic inflammation by mononuclear cell infiltration	Wear and tear arthritis may be associated with damage in the past or the over use of joint
Speed of onset is rapid over weeks and months	Slower over years
Joints are swollen, painful and stiff	Joints may be tender but little or no swelling
Fatigue and general feeling of being unwell	Whole body symptoms are not present

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Treatment of Osteoarthritis

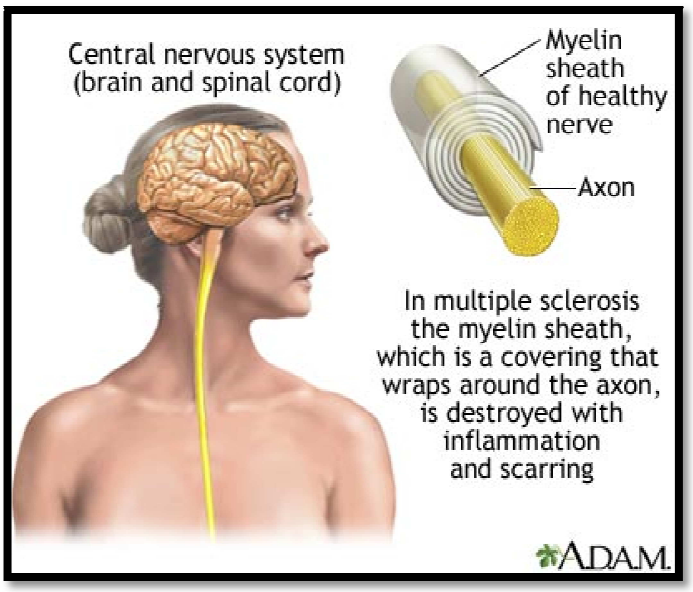
-Medicines: analgesics
-Early physiotherapy/exercises
-The eventual outcome is complete destruction of the joint
-and ultimately surgical intervention is required

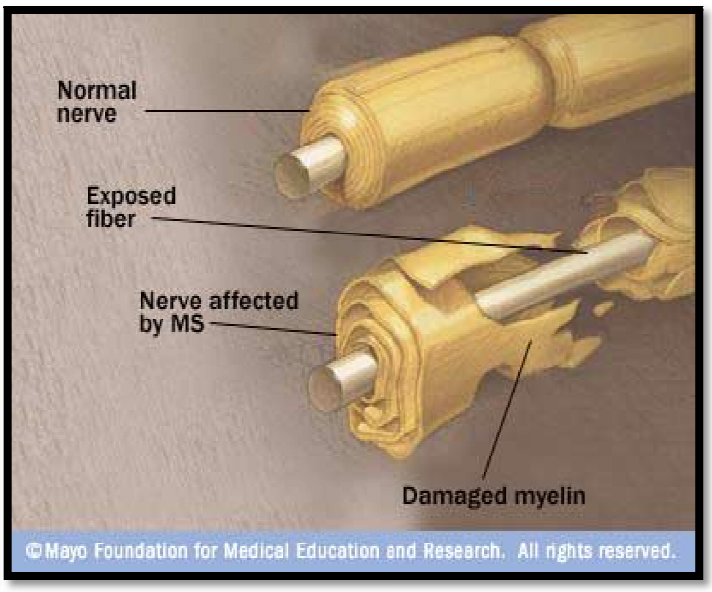
5-Multiple Sclerosis (MS)

-MS is believed to be an autoimmune disease
-Commonly affects between 20 to 50 years old individuals
-Involves central nervous system
-Triggers are unknown, but research is focusing in on:

- **Viruses**
- **Environmental and genetic factors**
- **More common in cooler climate**
- **Women affected more than men**

-Multiple sclerosis affects central nervous tissues
-Auto-reactive **T cells react with myelin sheath of** nerve fibers.
-Demylination → Loss of myelin sheath which surrounds the nerve.**→ interference of nerve conduction & permanent damage nervous tissue.**





← Multiple Sclerosis continued..

SYMPTOMS

Symptoms are unpredictable and vary

-Fatigue – 90%
-Depression – 70%
-Motor involvement – muscle weakness, numbness
-Visual symptoms – blurring, twitching of eyes
-Cerebellar involvement – intention tremor, seizure
-Genitourinary symptoms (Related to the genital and urinary organs or their functions) **→ Constipation, urine frequency**
-Cognitive defects (Cognitive =the process of knowing)
→Short-term memory dysfunction

TREATMENT

***There is No cure for MS**

-Treatment focused on relief of symptoms and slowing progression
-Corticosteroids – most common
- Interferons