Autoimmune Diseaes

Immunology Unit
Department of Pathology
College of Medicine, KSU

بسم الله

هذه النقاط المهمه الي اخذتها من

الدكتور للاسف ما قدرت اخذ منه كل

شي

وحاولت اختصرها وانشاء الله تفيدكم

النوتات والنقاط

تحياتي

Team immune

ملاحظه المهم بالاحمر

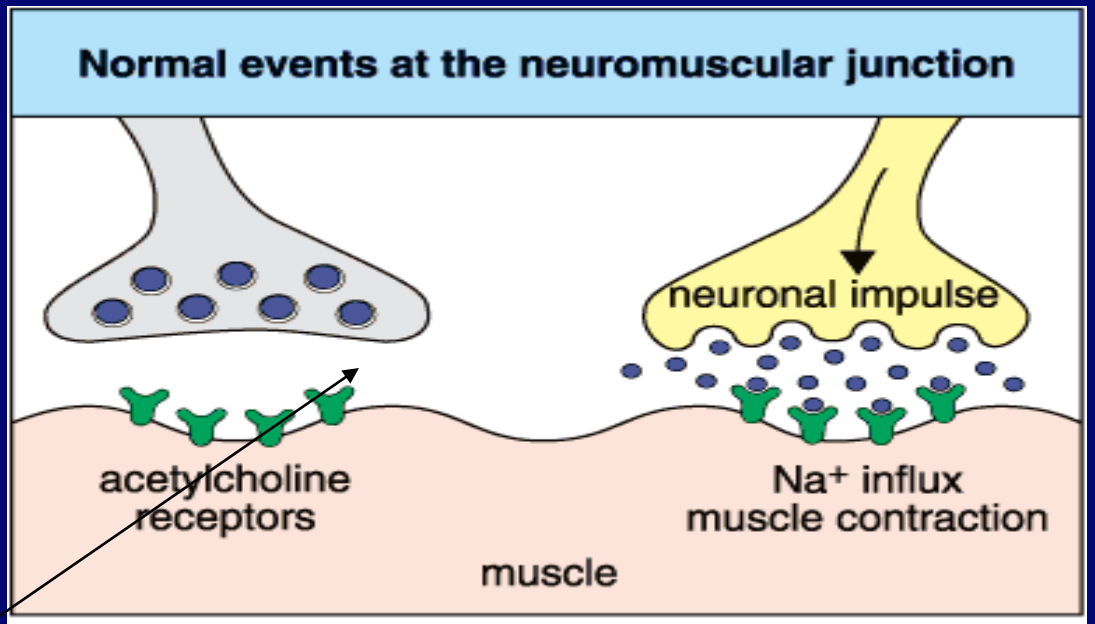
SOME AUTOIMMUNE DISEASES IN HUMANS

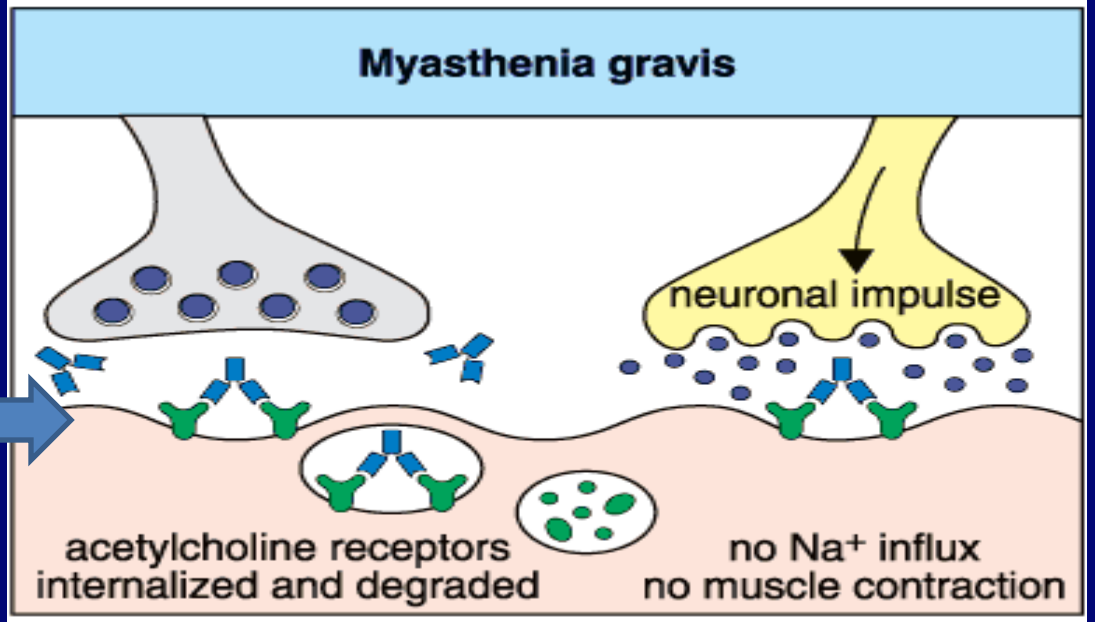
Disease	Self-antigen	Immune response
Organ-specific autoimmune diseases		
Addison's disease	Adrenal cells	Auto-antibodies
Autoimmune hemolytic anemia	RBC membrane proteins	Auto-antibodies
Goodpasture's syndrome	Renal and lung basement membranes	Auto-antibodies
Graves' disease	Thyroid-stimulating hormone 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 glands, liver, kidney, thryoid	Auto-antibodies
Systemic lupus erythematosus (SLE)	DNA, nuclear protein, RBC and platelet membranes	Auto-antobidies, immune complexes

Myasthenia Gravis

- Clinically characterised by **weakness and fatigability** on sustained effort
- Antibodies directed against acetylcholine receptor (AChR)
- IgG interact with the postsynaptic AChR at the neuromuscular junction (NMJ)
- This reduces the number of functional AChR receptors by complement mediated destruction of receptors

Myasthenia gravis





Motor end-plates of muscles

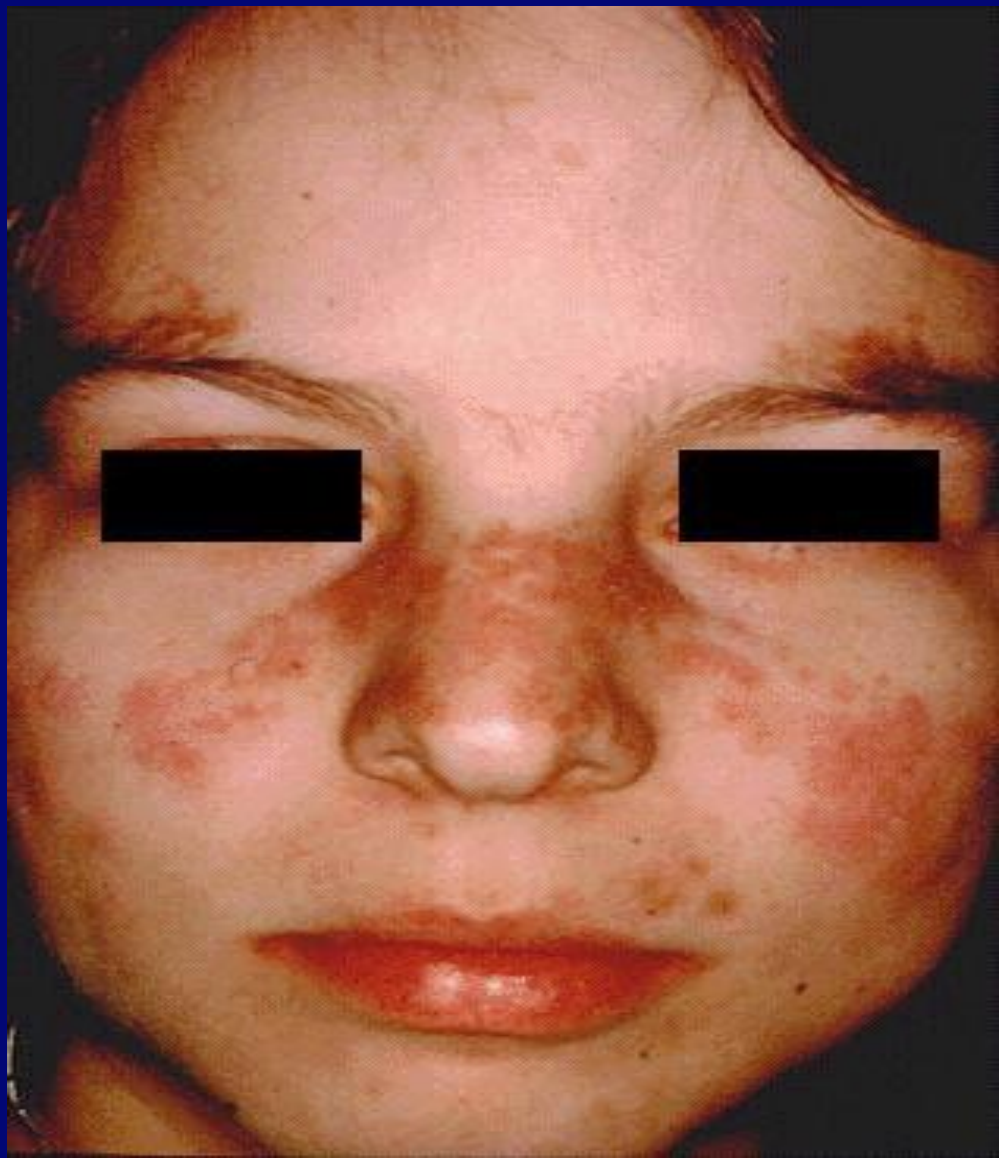
The impulse can't go to the receptors for hat no contraction

Systemic Lupus Erythematosus (SLE)

Systemic lupus erythematosis is multi-system autoimmune disorder.

Characterized by "butterfly rash" made worse by exposure to sunlight.

Lupus is a potentially fatal autoimmune disease



Symptom complex

Constitutional

Fatigue:

Myalgia

Fever:

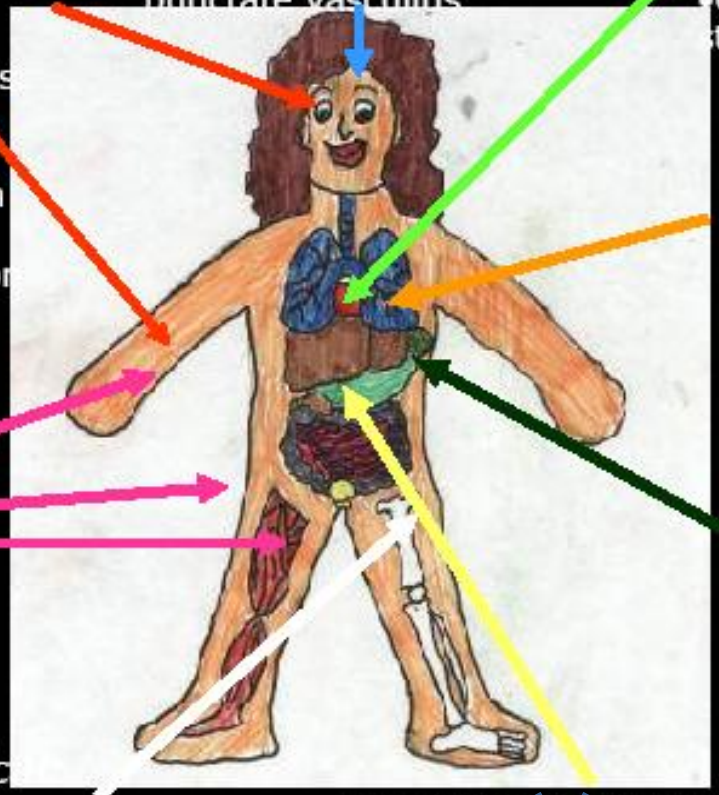
Weight change:

Dermatological:

- **malar rash**
- **discoid lesions**
- hair loss
- oral ulcers
- Raynaud's
- N[illegible]d
- eryt[illegible]ma/crus
- li[illegible]on hands/legs
- Bullous rash on legs
- dermatitis or fingers

CNS:

•cognitive defects, anxiety, depressio[illegible]sychosis, seizures, [illegible]/or neuropat[illegible] cerebral punctate vasculitis



Cardiovascular

•Pericarditis

•**Ve[illegible]ous end[illegible]rditis** => emb[illegible]

•CA[illegible]m steroids

Pulmonary:

• Dyspnea and restrictive LFTs

•Ple[illegible]is pleu[illegible]effusion, pneu[illegible]nitis, inte[illegible]l lung disease, and pulmonary hypertension

Renal:

•glomerulon ephritis

Arthritis:

•migratory and asymmetrical. Only a few joints are usually aff[illegible]te[illegible] especially the [illegible]ds

•Jo[illegible]eformities including ulnar deviation, MCP subluxation, and **swan-neck deformities** caused by tendon laxity, rather than bony destruction.

Hematologic

•Anemia of chronic disease

•Asympt[illegible]tic leukopenia

•Thromb[illegible]topenia

•lymphadenopathy

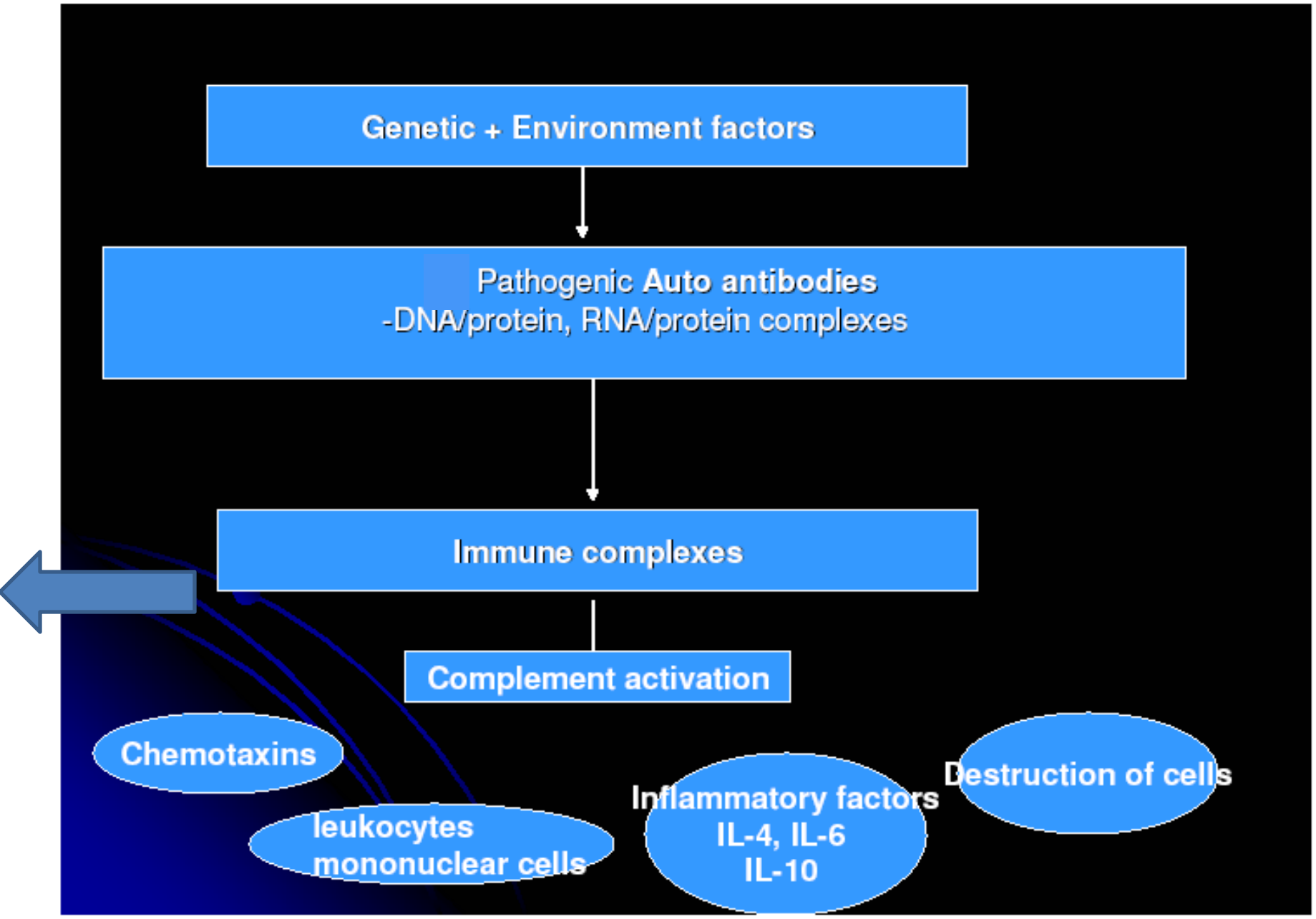
GI:

•Gastritis/[illegible]p[illegible] ulcer due to NSAID/cort[illegible]steroids

•Pancreatiti[illegible]eritonitis, and colitis: due SLE vascul[illegible]s

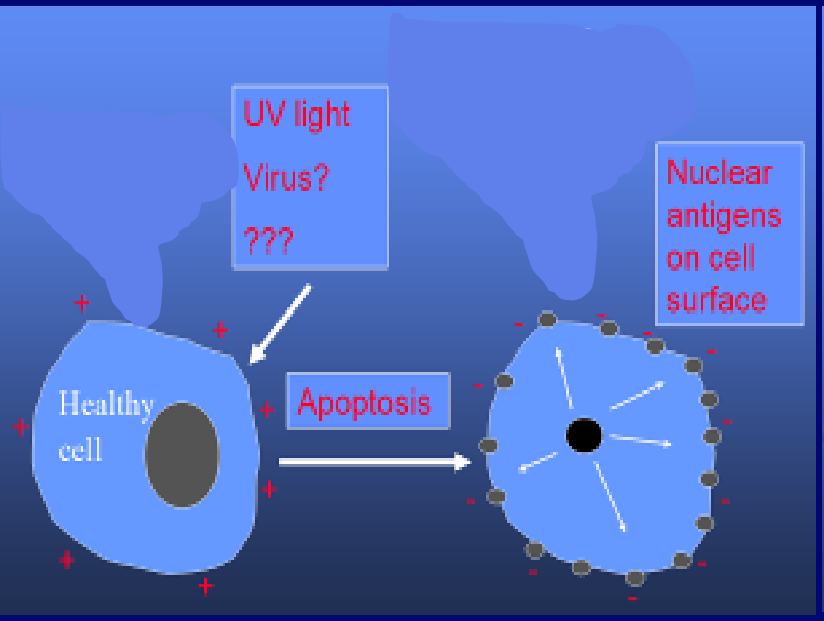
•Lupoid hepatitis

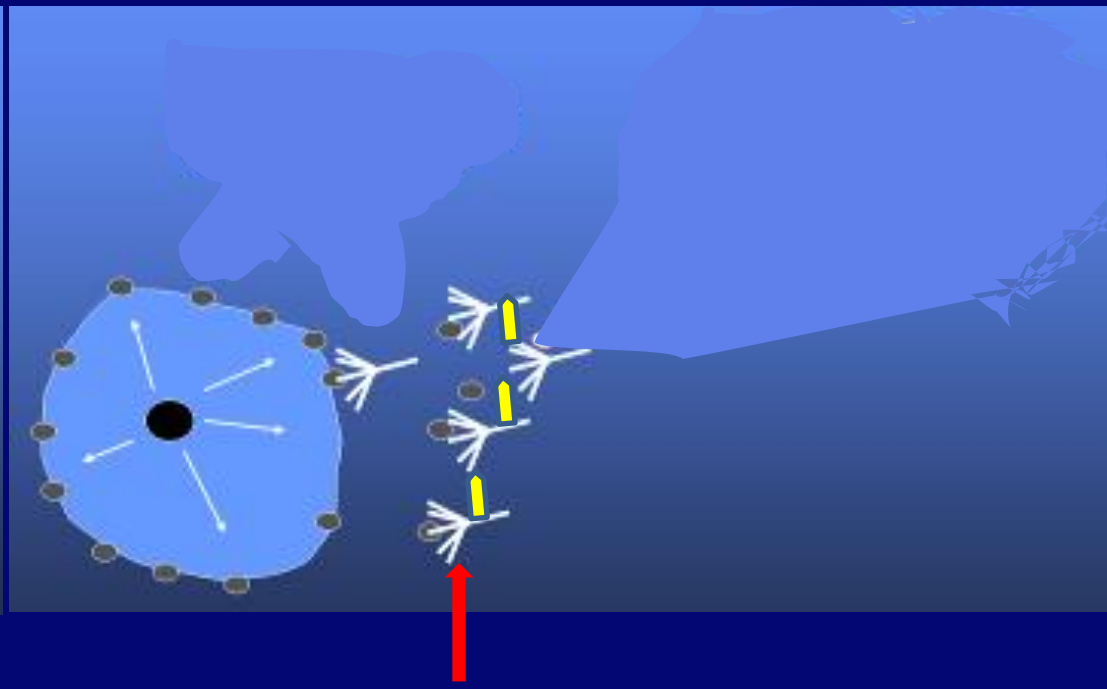
•hepatosplenomegaly


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

Normally cells undergoing apoptosis are removed by the immune system

Failure to clear apoptotic material in SLE leads to formation of antinuclear antibodies



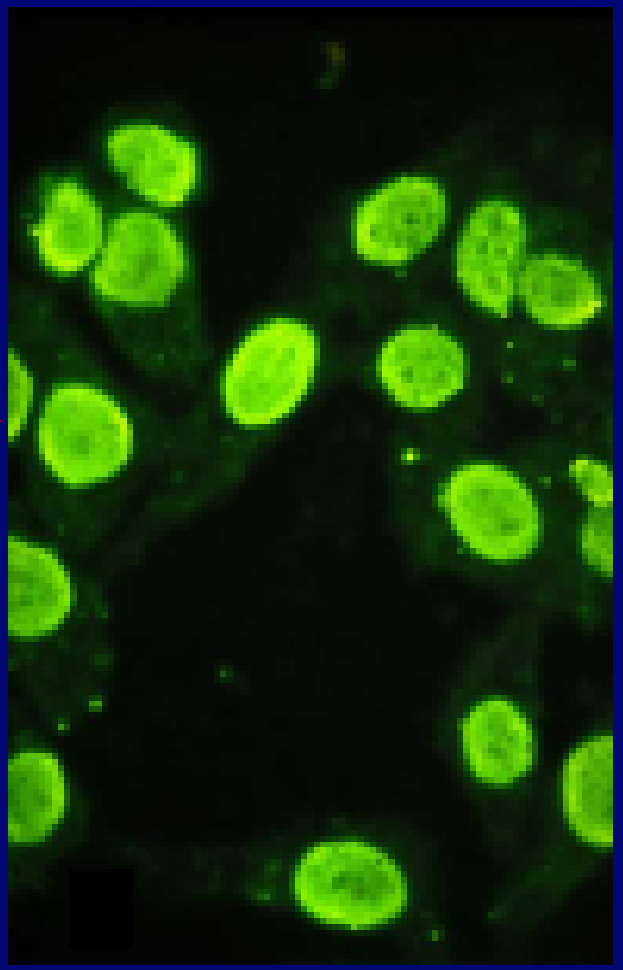


Immune complex formation and deposition in:

-Kidney: glomerulonephritis
-Skin: rashes
-Vessles: vasculitis

Auto antibodies

- 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

Significance of Autoantibodies in SLE

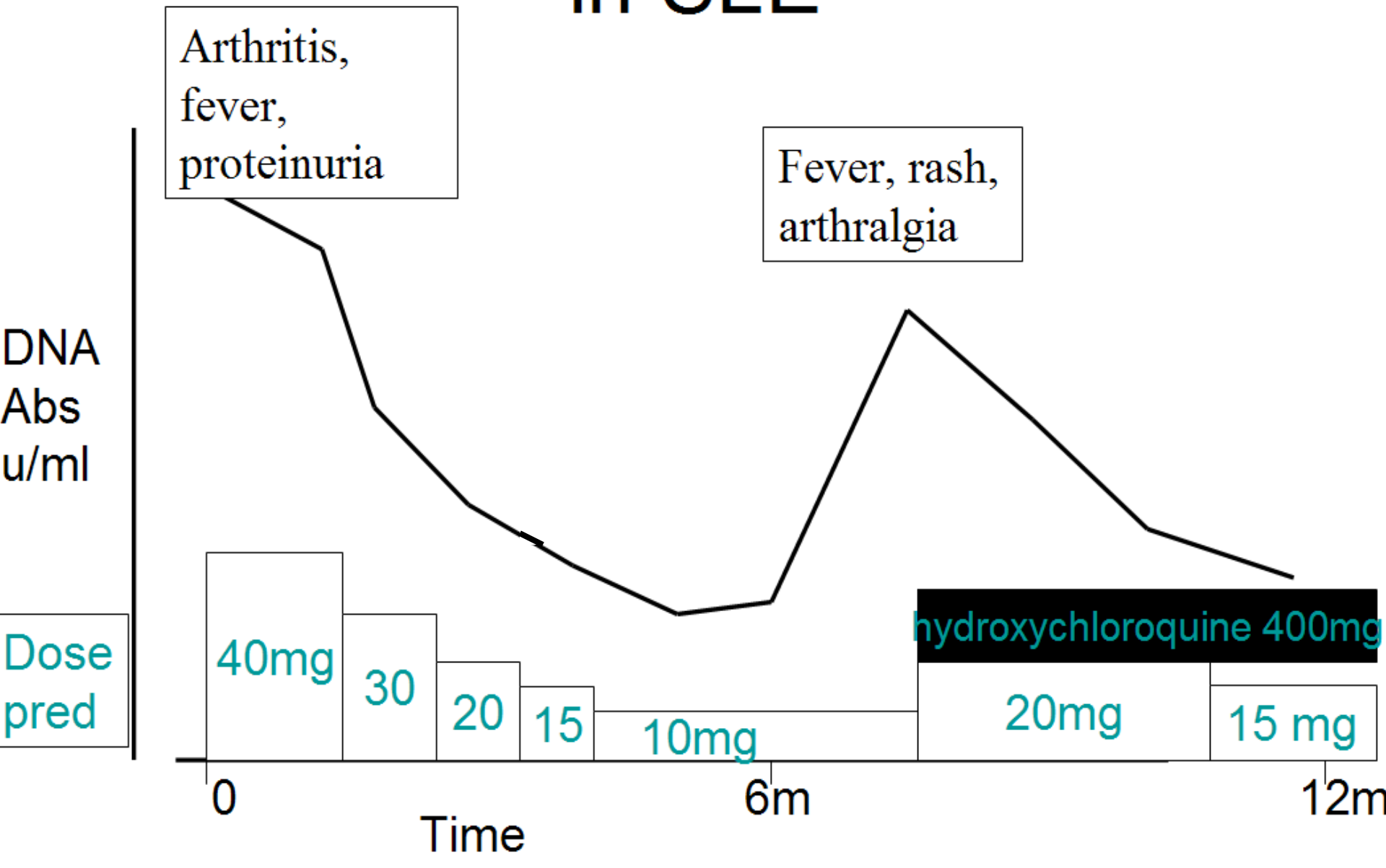
Antigen	SLE	Clinical Associations
ds DNA	70%	Nephritis (and flare)
Anti RNP	40%	Scleroderma, myositis
Histones	70%	Drug-Induced Lupus
SM Antigen	30%	Severe SLE
Anti ribosomal	20%	Psychosis, Depression
Antiphospholipid	50%	Clotting, fetal loss
SSA/Ro	35%	SCLE, Sjogren's, NLS
SSB/La	15%	SCLE, Sjogren's, NLS
Anti neuronal	60%	Active CNS lupus

Disease Activity

- Anti-double-stranded DNA titers
- Complement Levels (CH50, C3, C4)
- ESR
- CRP
- Complement Split products
- Decreased complement C1q

Will increase in level

Monitoring DNA antibodies in SLE



Treatment

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

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, and 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

Pathogenesis

In rheumatoid arthritis, many individuals produce a group of auto-antibodies known as rheumatoid factor

These antibodies react with determinants in the F_C region of IgG

The classic rheumatoid factor is an IgM antibody with this kind of reactivity.

Pathogenesis

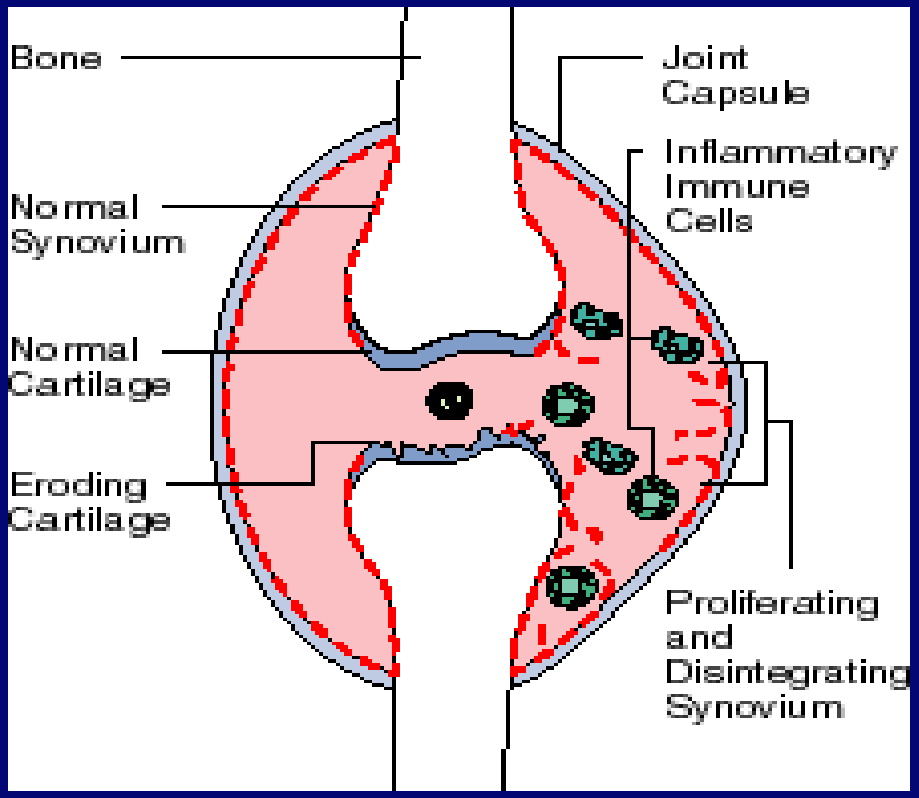
Such auto-antibodies bind to normal circulating IgG, forming IgM-IgG complexes which may be deposited in joints.

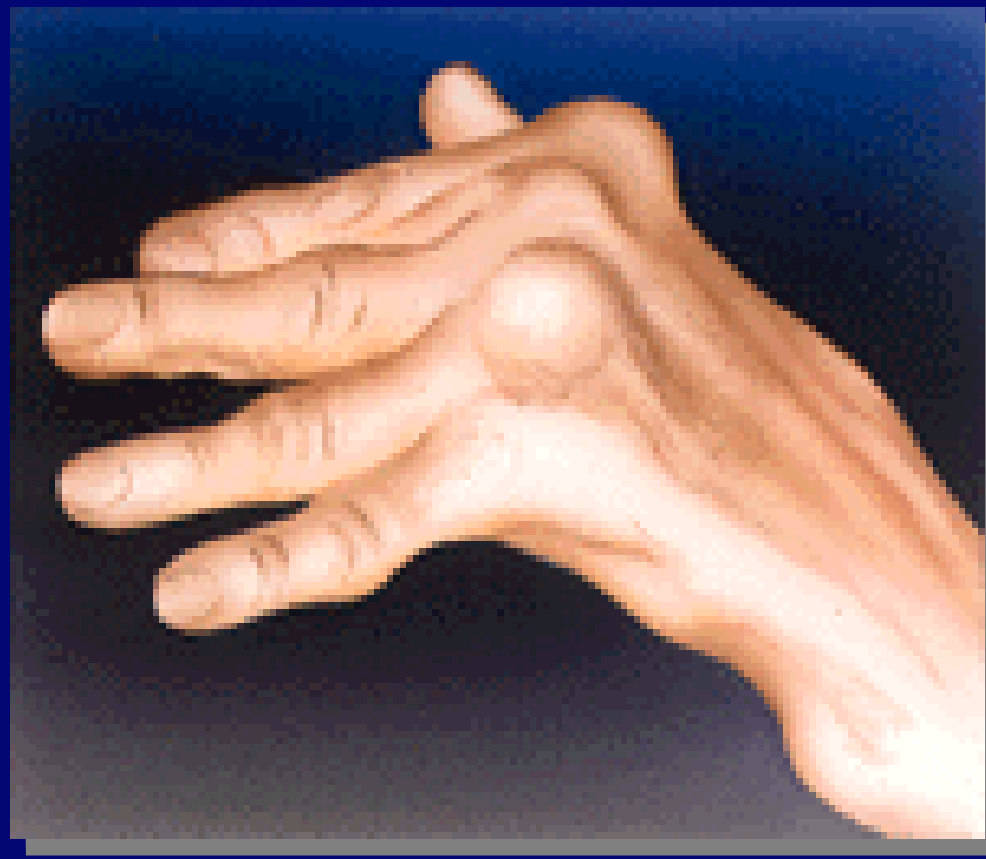
These immune complexes can activate the complement cascade, resulting in a type III hypersensitive reaction; leading to chronic inflammation of the joints.

Functional Presentation and Disability of RA

- In the initial stages of each joint involvement, there is 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

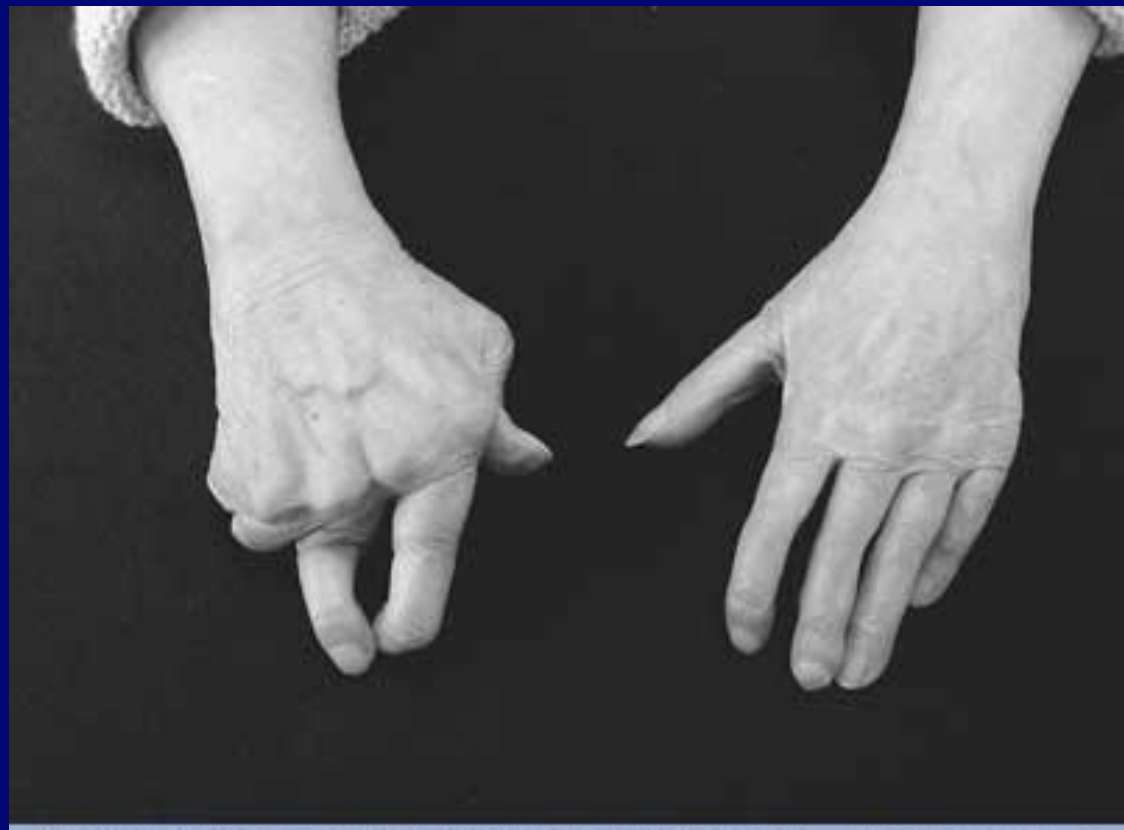




Rheumatoid Arthritis

- **Description**
  - Morning stiffness
  - Arthritis of 3 or more joints
  - Arthritis of hand joints
  - Symmetrical arthritis
  - Rheumatoid nodules
  - Serum rheumatoid factor
  - Radiographic changes

- A person shall be said to have rheumatoid arthritis if he or she has satisfied any of 7 criteria, with criteria 1-4 present for at least 6 weeks



Complications of Rheumatoid Arthritis

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

Treatment and Prognosis

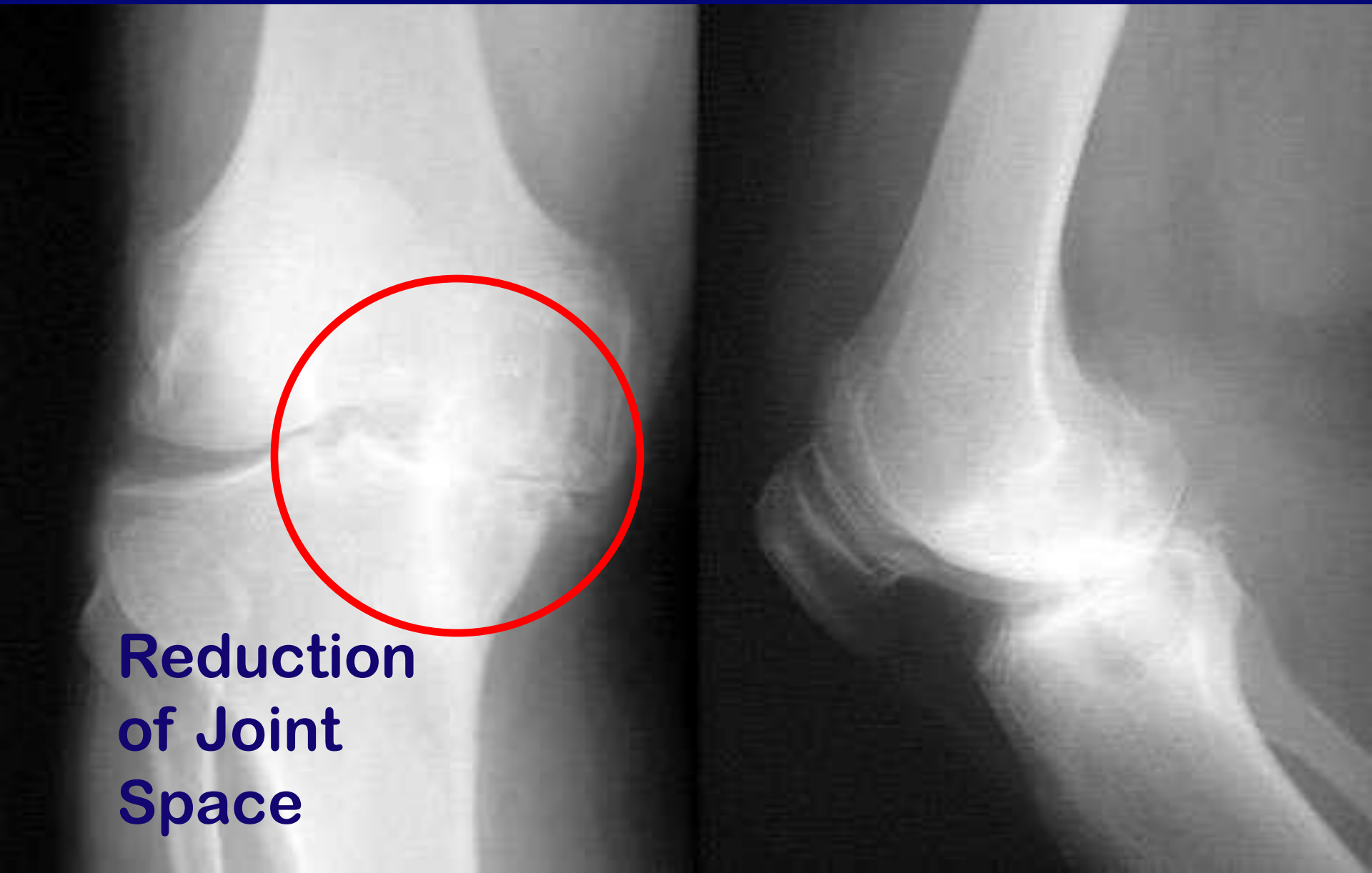
Medications

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

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
  - The final outcome is full-thickness loss of cartilage down to bone

Osteoarthritis: radiological findings



Very important

Comparison

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

Treatment of Osteoarthritis

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

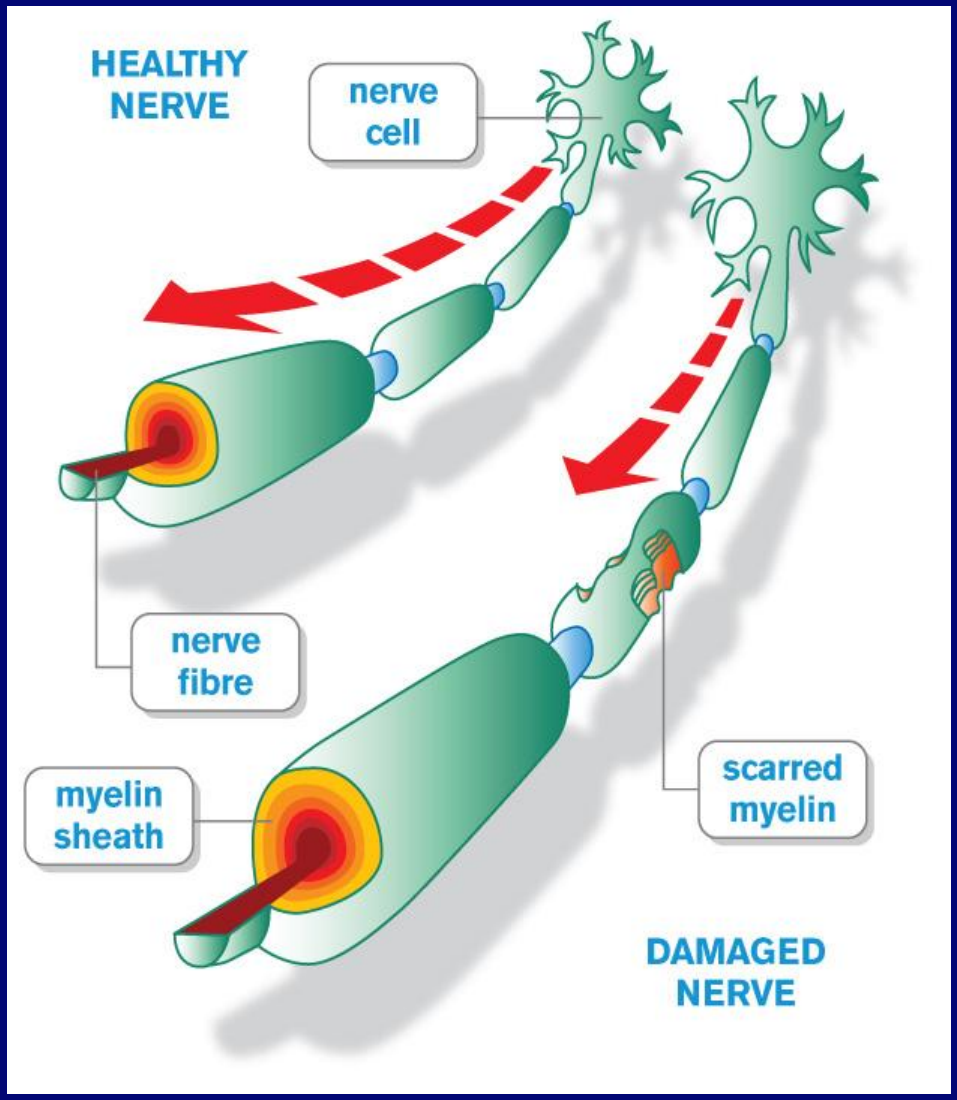
Multiple Sclerosis (MS)

- 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 of nerve fibers occurs resulting in interference of nerve conduction and permanent damage to the nervous tissue



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 – constipation, urine frequency
- Cognitive defects – short-term memory dysfunction

TREATMENT

- No cure for MS
- Treatment focused on relief of symptoms and slowing progression
- Corticosteroids – most common
- Interferons

Thank you