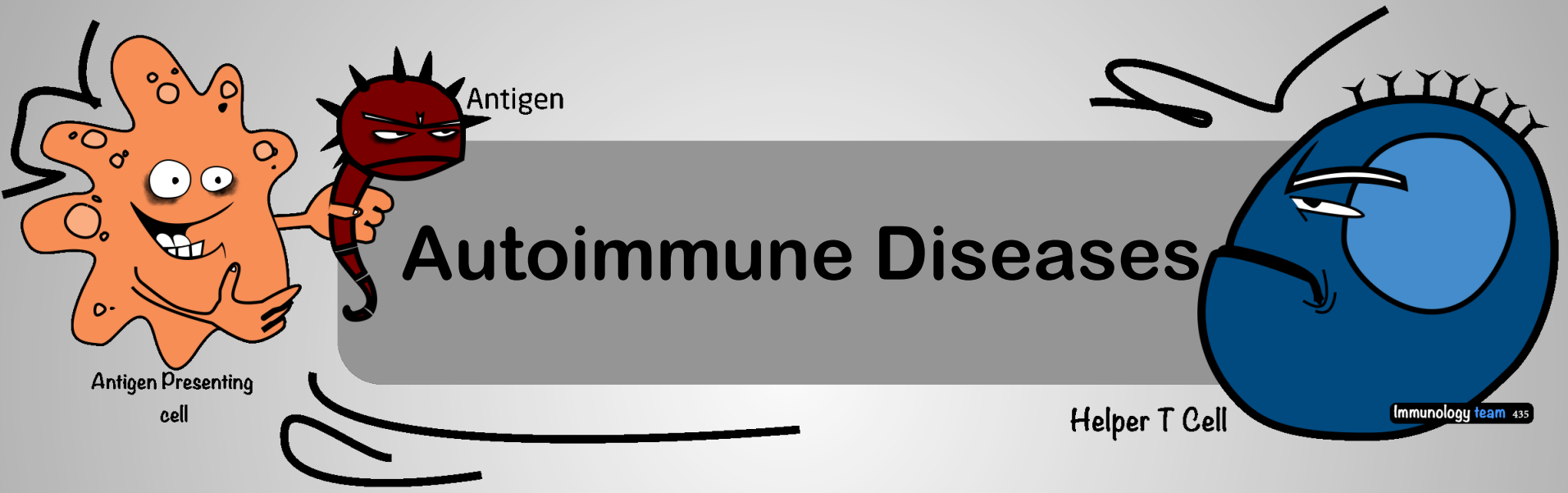


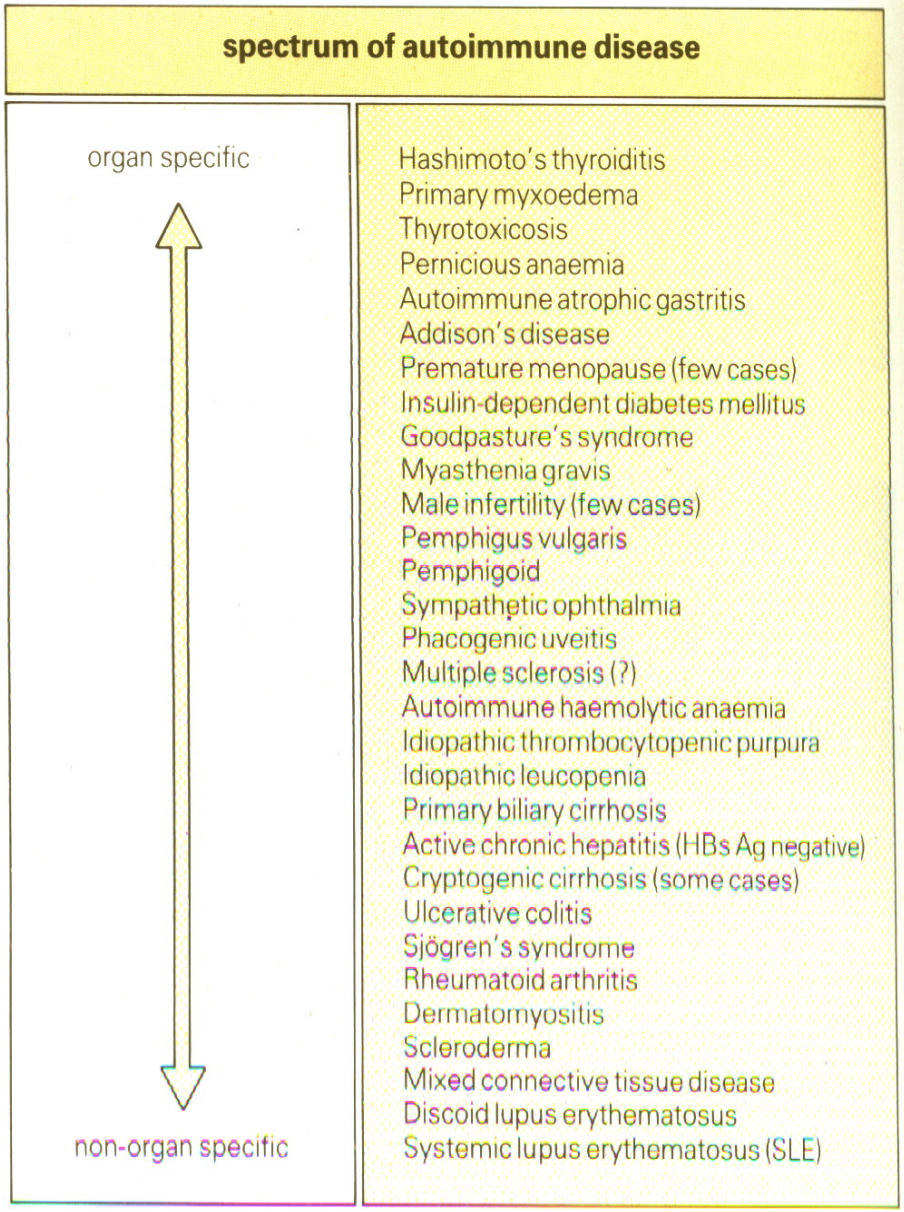
Autoimmune Diseases

Color index

- Important
- Clarification
- Required

Objectives

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



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

Our doctor said that we are not required to memorize the tables .
The point of these tables is for you to know that there are (organ specific) and (non-organ specific) diseases.

Examples of Autoimmune Diseases Affecting Different Systems:

Nervous System:

Multiple sclerosis
Myasthenia gravis
Autoimmune neuropathies such as:
- Guillain-Barré Syndrome (GBS)

Autoimmune uveitis

Blood:

Autoimmune hemolytic anemia
Pernicious anemia
Autoimmune thrombocytopenia

Blood Vessels:

Temporal arteritis
Anti-phospholipid syndrome
Vasculitides such as
Wegener's granulomatosis
Behcet's disease

Skin:

Psoriasis
Dermatitis herpetiformis
Pemphigus vulgaris
Vitiligo

Gastrointestinal System:

Crohn's Disease
Ulcerative colitis
Primary biliary cirrhosis
Autoimmune hepatitis

Endocrine Glands:

Type 1 or immune-mediated diabetes mellitus
Grave's Disease
Hashimoto's thyroiditis
Autoimmune oophoritis and orchitis
Autoimmune disease of the adrenal gland

Multiple Organs, Musculoskeletal System

Rheumatoid arthritis
Systemic lupus erythematosus
Scleroderma
Polymyositis, dermatomyositis
Ankylosing spondylitis
Sjogren's syndrome

- Disease processes and tissue damage are due to Type II, Type III and Type IV hypersensitivity reactions.

Organ Specific Autoimmune Diseases

These diseases are mediated by stimulating or blocking auto-antibodies.

1) Graves' disease (caused by → Stimulating antibodies)

2) Myasthenia gravis (caused by → Blocking Antibodies)

Stimulating (That means that auto-antibodies is simulating the role of the agonist to the receptor leading to abnormal function)

Blocking (that means that the auto-antibodies is preventing the agonist from binding to the receptor and that also will lead to abnormal function)

Graves' Disease (Thyrotoxicosis)

- Production of thyroid hormones is regulated by thyroid-stimulating hormones (TSH). (from the pituitary gland)

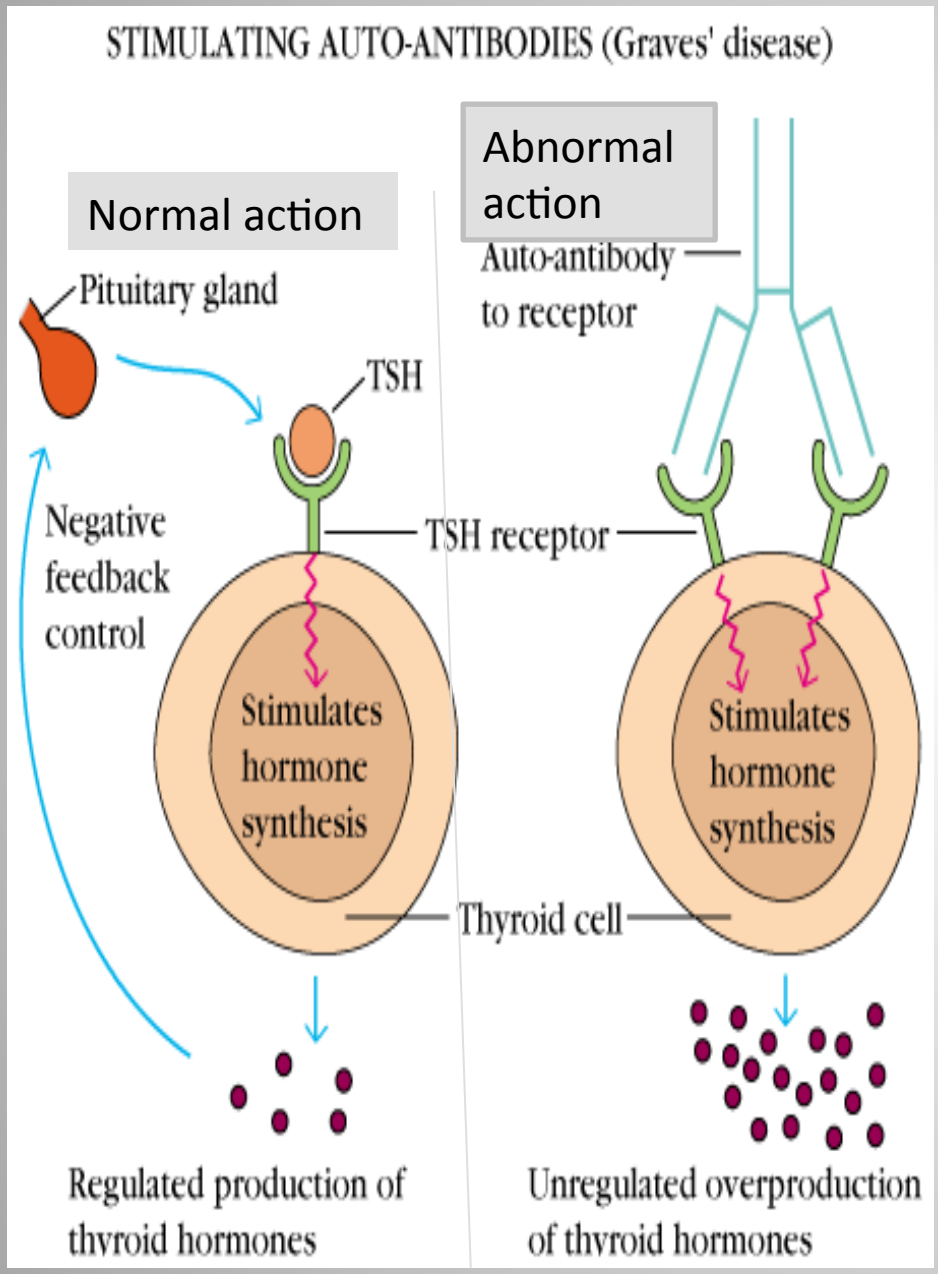
- The binding of TSH to a receptor on the thyroid cells stimulates the synthesis of two thyroid hormones:

1) Thyroxine.
2) Triiodothyronine.

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

(يكوّن اجسام مضادة عملها شبيه بعمل الهرمون لتعمل عمله ويكون الإنتاج مفرط)

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



Protruded eyes of a patient

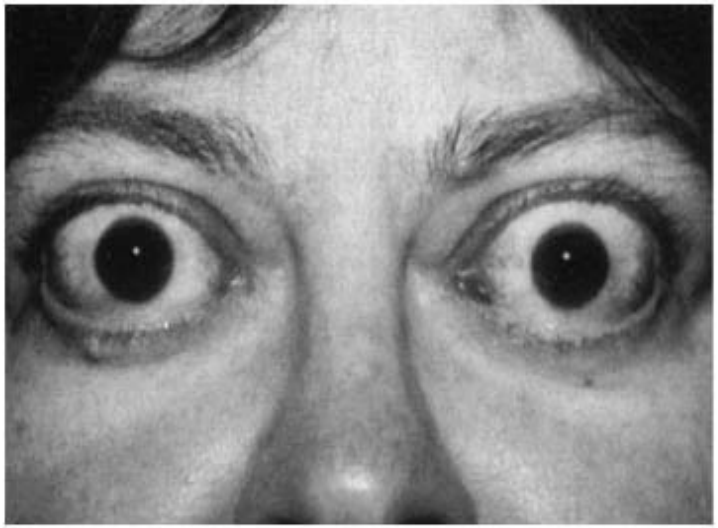


Fig. 1A

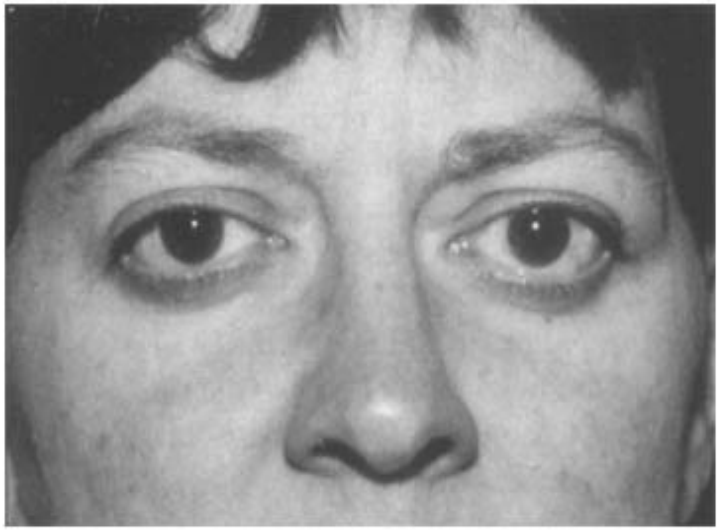


Fig. 1B

Myasthenia Gravis

تعمل الأجسام المضادة كعازف بين الناقل العصبي وبين المستقبل فلا يحدث انقباض للعضلة

- Clinically characterized by weakness and fatigability on sustained effort.
  الشعور بالضعف و الاجهاد مع الجهد المستمر
- 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.

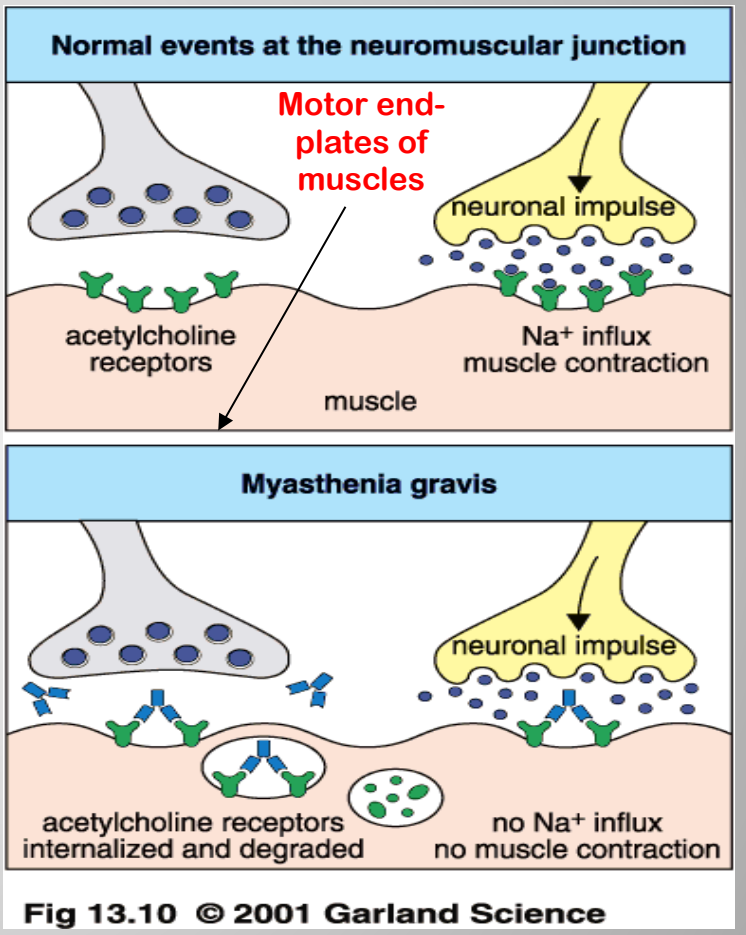


Fig 13.10 © 2001 Garland Science

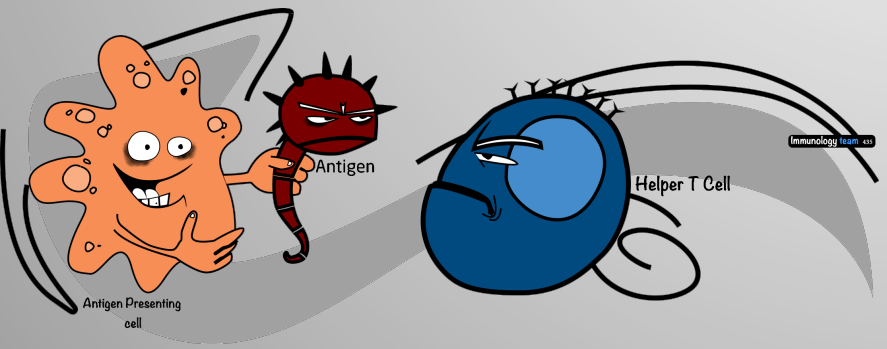
Systemic Autoimmune Immune diseases

1- Systemic lupus erythematosis (SLE) :

- It's the most common the most common autoimmune disorder.
- The characteristic "butterfly rash" is made worse by exposure to sunlight.

  يسبب احمرار او طفح جلدي على شكل اجحنة الفراشة .

- Lupus is a potentially fatal autoimmune disease



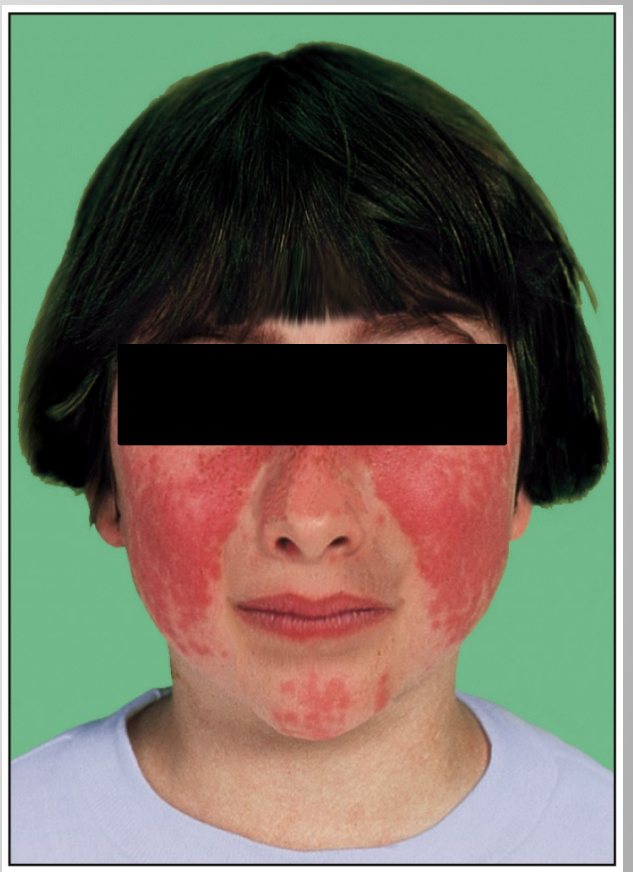


Figure 13.11 The Immune System, 3ed. (© Garland Science 2009)

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

Symptom complex

Constitutional

Fatigue:

Myalgia

Fever:

Weight change:

Dermatological:

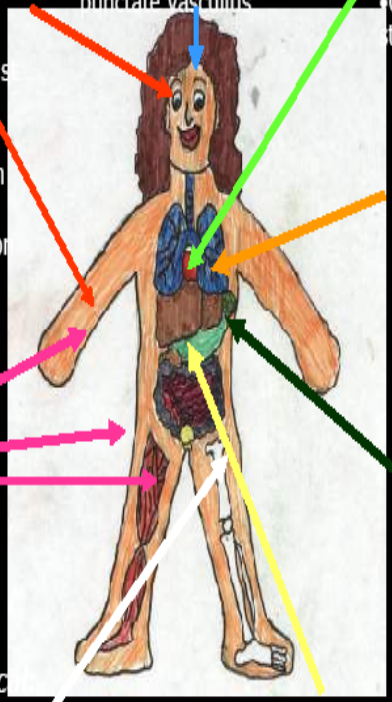
- **malar rash**
- **discoid lesions**
- hair loss
- oral ulcers
- Raynaud's
- Nailfold erythema/crus
- livedo on hands/legs
- Bullous rash on legs
- dermatitis o fingers

CNS:

•cognitive defects, anxiety, depression, psychosis, seizures, and/or neuropathies, cerebral punctate vasculitis

Cardiovascular

•Pericarditis
•**Verrucous endocarditis** => emboli
•CAD from teroids



Pulmonary:

• Dyspnea and restrictive LFTs
•Pleurisy, pleural effusion, pneumonitis, interstitial lung disease, and pulmonary hypertension

Renal:

•glomerulon ephritis

Arthritis:

•migratory and asymmetrical. Only a few joints are usually affected, especially the hands

•Joint deformities including ulnar deviation, MCP subluxation, and **swan-neck deformities** caused by tendon laxity, rather than bony destruction.

Hematologic

•Anemia of chronic disease

•Asymptomatic leukopenia

•Thrombocytopenia

•lymphadenopathy

GI:

•Gastritis/peptic ulcer due to NSAID/corticosteroids
•Pancreatitis, peritonitis, and colitis: due SLE vasculitis
•Lupoid hepatitis
•hepatosplenomegaly

Auto-antibodies

The anti-nuclear antibody (ANA) test is the best screening test for SLE and is determined by immunofluorescence or ELISA (enzyme-linked immunosorbent assay) tests

The ANA is positive in significant titer (usually 1:160 or higher) in virtually all patients with SLE

Titer is a measurement of the amount or concentration of a substance in a solution(ratio)

Other investigations

- Anti-double-stranded DNA titers
- Complement Levels (CH50, C3, C4)
- ESR "not specific, but great for checking the effects of medications"
- CRP (C-reactive protein)
- Complement Split products
- Decreased complement C1q

Treatment

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

2-Rheumatoid Arthritis

Rheumatoid arthritis is an autoimmune disease in which our immune system responds against an individual's own tissue, including the :

-Joints (weight baring joints)

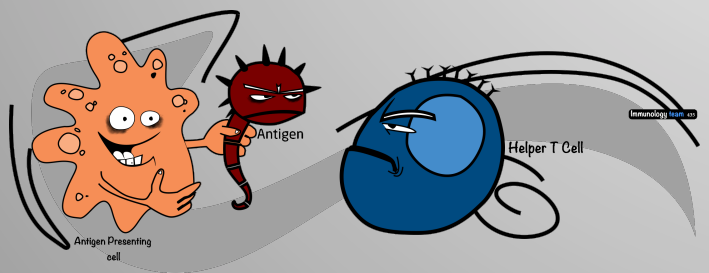
-Tendons

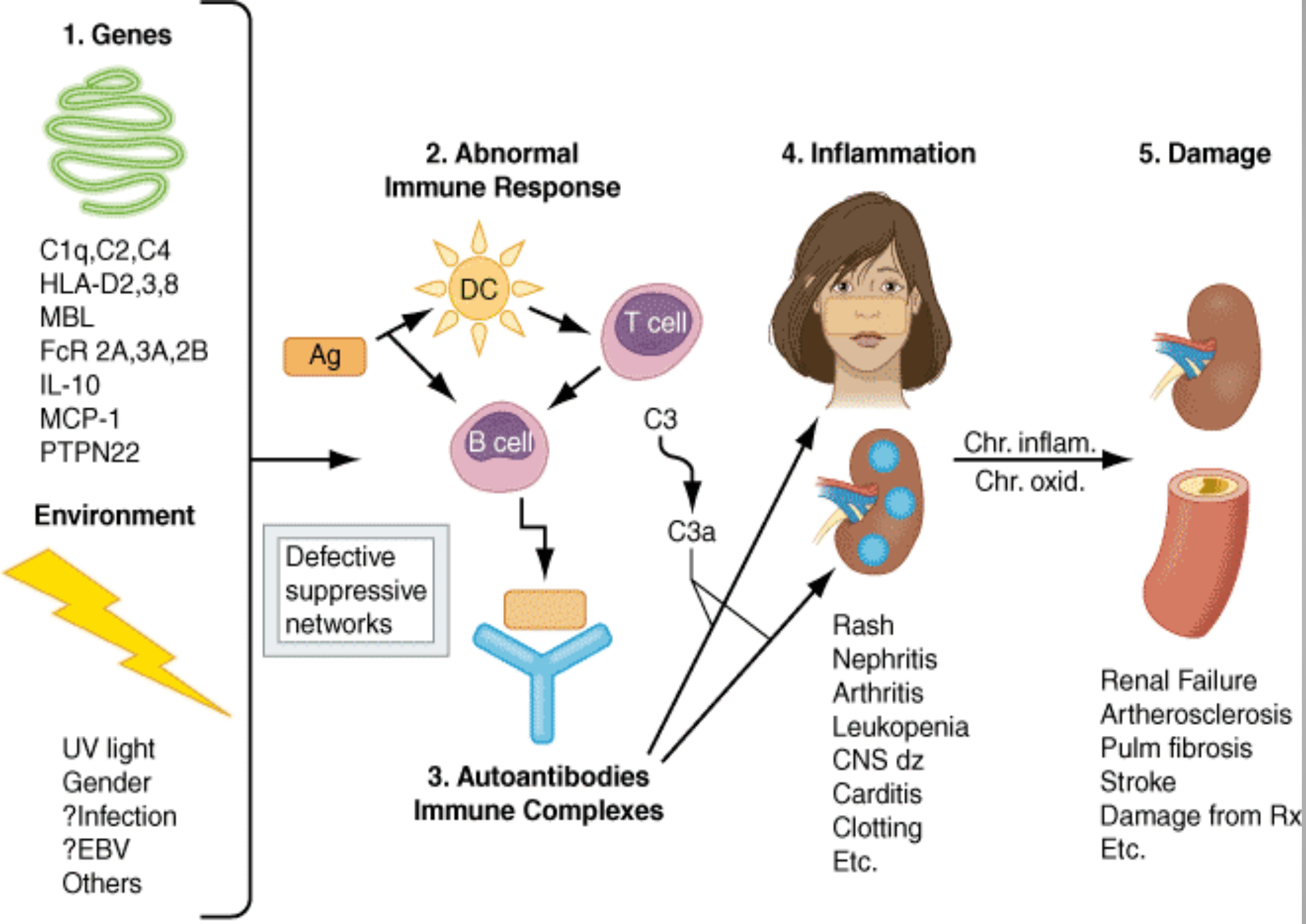
-bones

Which leads not only to an inflammatory response, but also to the destruction of cartilage and some other tissues .

The cause of rheumatoid arthritis is not known (Idiopathic)
Investigating possibilities of a foreign antigen, such as a virus .

prevalence and incidence are 2-3 times greater in women than in men. (Because it is an autoimmune disease)





Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

RA can be categorized as a Type III (immune complex disease)

- Many individuals produce a group of autoantibodies known as rheumatoid factor. It is the result of IgG binding to IgM , which will deposit in the joints. These antibodies react with determinants in the FC region of IgG.

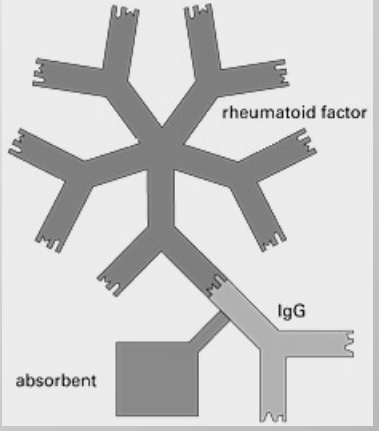
- RA synovial fluid is completely enriched with macrophages, neutrophils, T lymphocytes, and dendritic cells.

- The synovial macrophages engulf the immune complexes and then release TNF and other pro- inflammatory cytokines e.g., IL-1

- TNF induces the secretion of metalloproteinases; which are known to cause degradation of bone, cartilage and dentin.

- T cell activation due to unknown antigens could also contribute to the inflammation in RA

Why is it also type IV? Because of T cells role. The Cytokines secreted by T cells and macrophages in the synovium cause the majority of symptoms in RA, T-cell cytokines stimulate B cells in the synovium to produce rheumatoid factor. Rheumatoid factor may produce immune complexes within the joint, adding to the inflammation.



Treatment

NSAIDS (Non-steroidal anti-inflammatory drugs)

Disease-modifying drugs (eg, gold, hydroxychloroquine, sulfasalazine, penicillamine)

Antimalarial (Blocks antigen presentation) fact: it used also in leukemia

Surgery (in severe cases)

Immunosuppressive therapy: (Corticosteroids - Methotrexate)

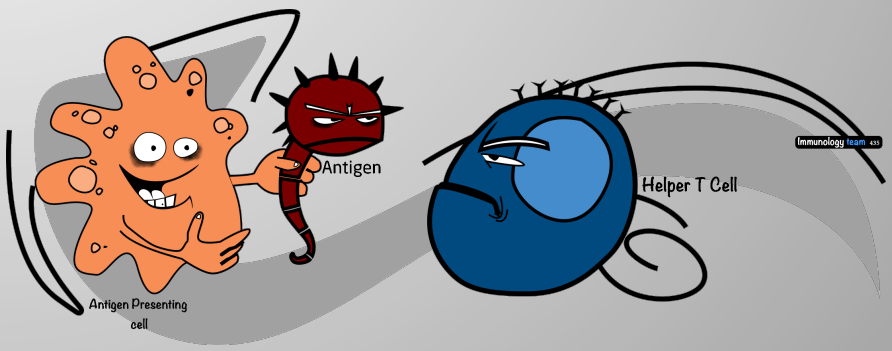
Physical therapy

.

Diagnosis

Anti–citrullinated protein (ACP) antibody

Rheumatoid factor

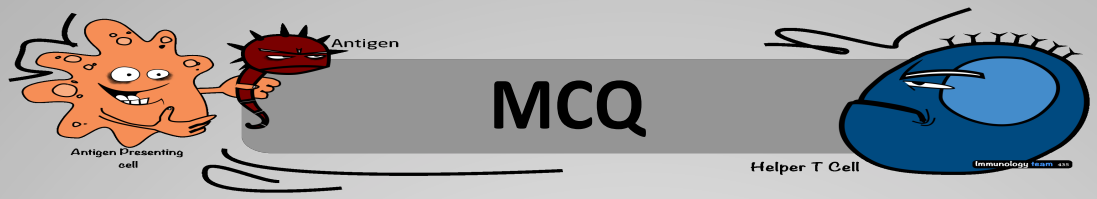


videos for illustration:

Graves' Disease 

Myasthenia Gravis 

SLE 



- 1_ rheumatoid arthritis is an autoimmune disease :
  A-T B-F

- 2_ cause joint destruction because after TNF induced secretion :
  A-synovial membrane
  B- cortecosteriod
  C- metalloproteinases

- 3-The inflammatory process in auto immune diseases are mediated by anaphylactic hypersensitivity:
  A-T B- F

- 4- in myasthenia gravis which of the following antibodies interacts with the post synaptic AChR:
  A-IgG B-IgM C- IgA D- IgE

- 5-regarding myasthenia gravis there is a reduction in the number of AChR due to an increasing ..... Degradation of receptors:

A-Complement mediated B- T cell mediated C-B cell mediated D-None of the above

- 6- The butterfly rash worsened by sun exposure is a characteristic of :
  A-Graves B-SLE C-Myasthenia gravis D-RA

- 7- Which of the following is potentially fatal:
  A-Graves B-SLE C-Myasthenia gravis D-RA

- 8- Prevalence and incidence of RA is 3 times greater in:
  A-Woman than men C-Men than women
  B-Child than adult D-Adult than child

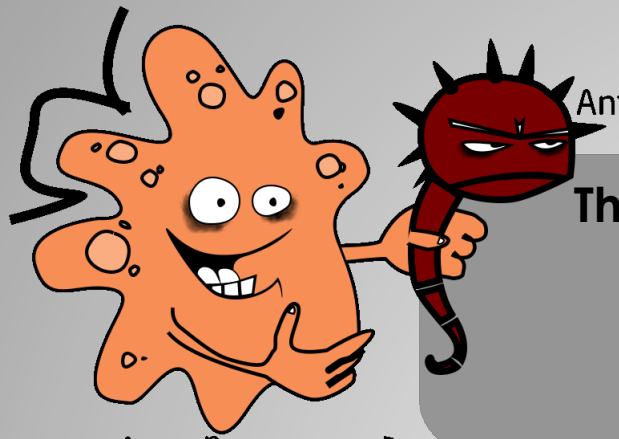
- 9- What type of hypersensitivity is involved with RA?
  A-Type I B-Type II C-Type III D-Type IV

- 10- Which one of the following is true regarding the rheumatoid factor?

A-it forms IgG-IgA complex B- it forms IgM-IgA complex C-it forms IgG-IgE complex D-it forms IgG-IgM complex

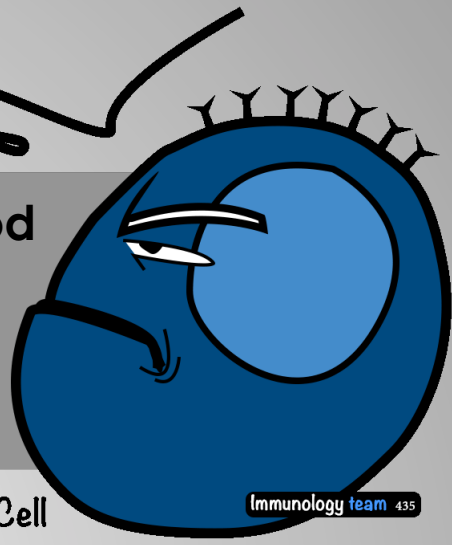
- 11-RA affect central joints and may cause
- destruction of both cartilage and bone :
  a- true
  b- false

1- a
2- c
3- b
4- a
5- a
6- b
7- b
8- a
9- c&d
10- d
11-a



Thank you for checking our work, Good luck. If you have any suggestions or alterations contact us!

Email Immunology435@gmail.com



Special thanks to :
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