L2 Autoimmune diseases

Objectives:

- To know that the inflammatory processes in autoimmune 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.

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Motivation quote:

Live as if you were to die tomorrow. Learn as if you were to live forever."

- Gandhi

Red = Important Notes turquoise blue = Further Explanation gray = Additional Notes Green = Example

Navy: boys notes Purple: girls notes

For any questions or suggestions don't hesitate to contact us on Immunology434@gmail.com ☺

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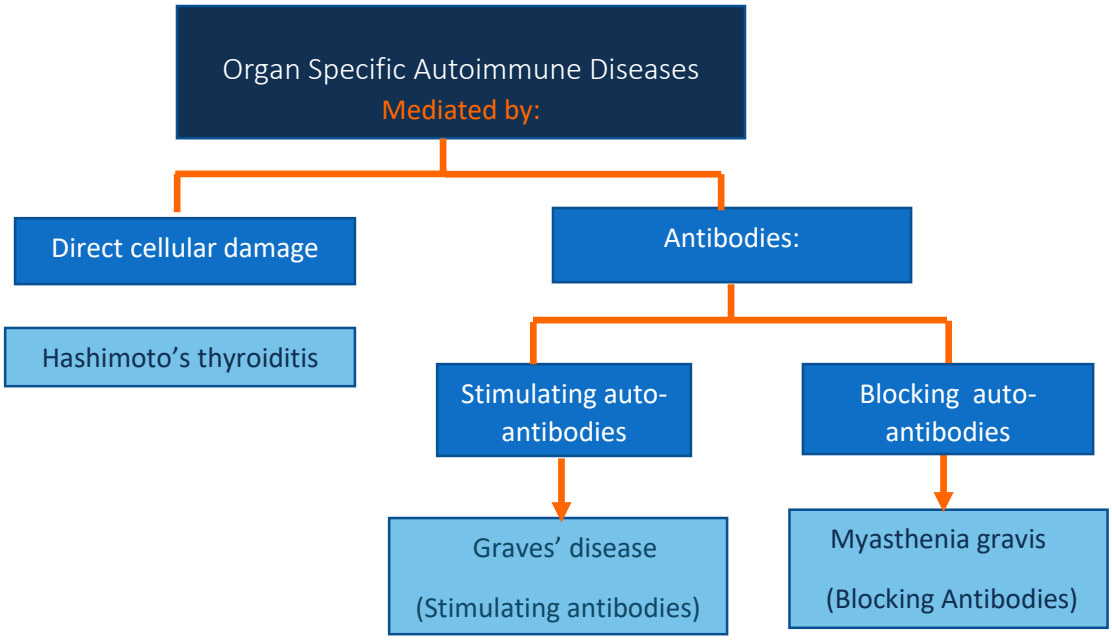
Disease processes and tissue damage are due to Type II Type III and Type IV hypersensitivity reactions



1-Organ Specific Autoimmune diseases:

7:30 minutes but worth checking

1-Graves' disease (Thyrotoxicosis)

The pituitary gland Produce thyroid-stimulating hormones (TSH) which regulate thyroid hormones.

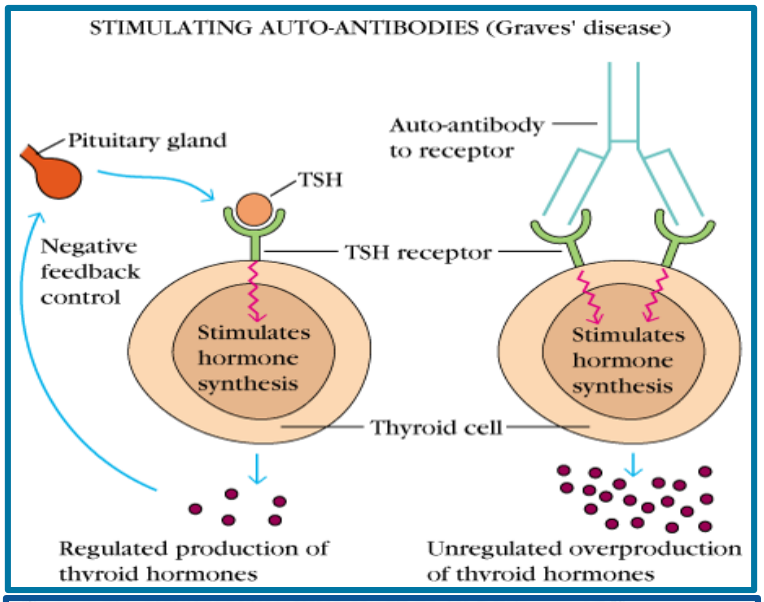
The binding of TSH to thyroid cells stimulates receptor stimulates thyroid gland to synthesize the two thyroid hormones: thyroxine and triiodothyronine

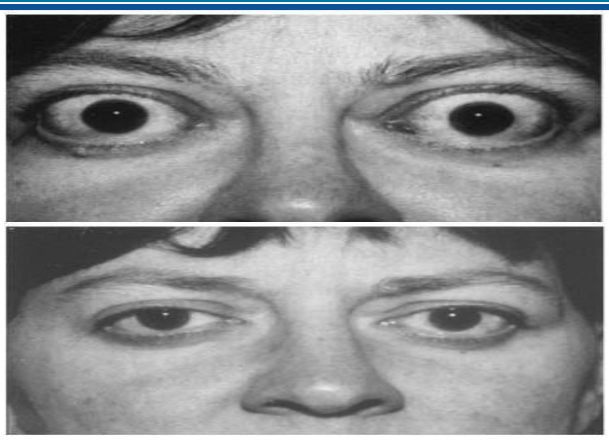
A person with Graves' disease makes auto-antibodies to the receptor for TSH. (Mimicing the TSH)

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

In normal person the negative feedback control the stimulation of TSH but in Graves ' disease the regulation don't give results because the production of thyroid hormones is from the binding of the autoantibody NOT TSH of pituitary gland.

Graves' disease is the most common cause of hyperthyroidism
IgG thyroid-stimulating antibody can cross the placenta and cause transient neonatal hyperthyroidism.
Graves' disease is associated with exophthalmos (protruding eyes) resulting from T cells infiltrating the orbit of the eye. Blood tests show that her thyroid gland is overactive, and she has autoantibodies to thyroid peroxidase and the thyroid-stimulating hormone receptor





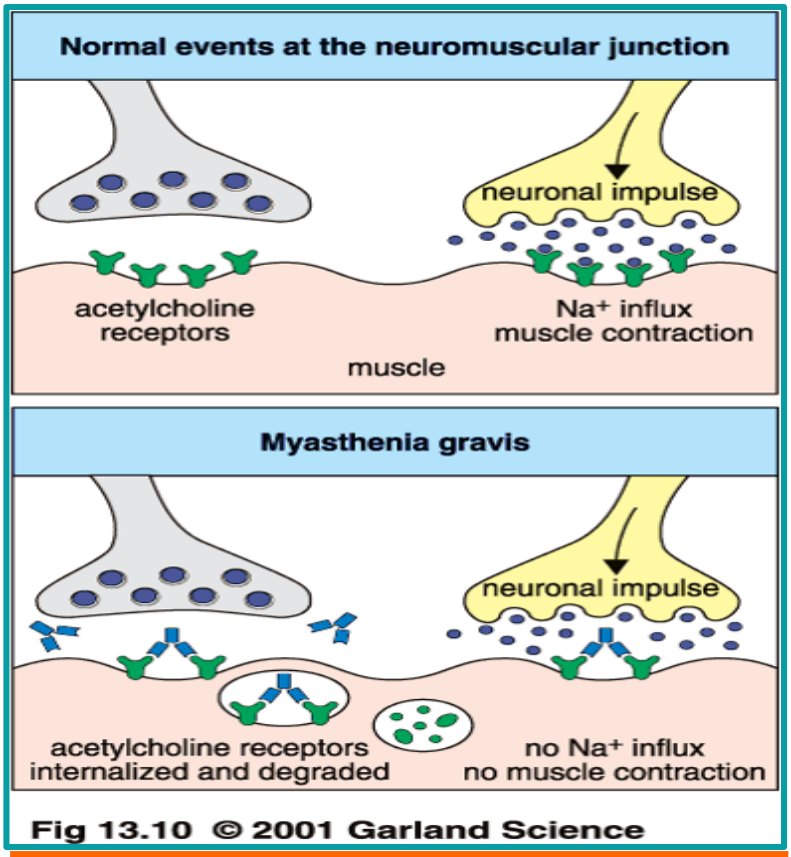


Figure 1A : is of a woman with Graves' disease

Figure 1B : is of a normal woman.

2-Myasthenia Gravis:

9:35 minutes but great for final studying and USMLE Step 1

It's a non-Systemic Autoimmune Immune diseases

Clinically characterized by weakness and fatigability on sustained effort

AntiACH Antibodies directed against acetylcholine receptor (AChR). The binding of the IgG AntiACH Antibodies to postsynaptic AChR at the nicotinic neuromuscular junction (NMJ) block them resulting in a competition between the ach molecules with prolonged effort the muscle weakness and fatigue is felt. No Action potential because the ACH Receptors are blocked meaning No sodium influx or less going inside the muscle (depending on how many receptors are blocked) therefore the action is less or non in the muscle causing weakness.

There is reduction in the number of functional AChR receptors by increasing complement mediated degradation of receptors.

This forms an immune complex which is destroyed by the complement system, leading to decreased number of ACH receptors. As a result, muscles are weakened and are unable to maintain its strength.

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5:46 MINTUES! And great for knowing the systemic symptoms and treatment.

2) Systemic Autoimmune diseases.

3-Systemic lupus erythematosis (SLE)

is the most common autoimmune disorder

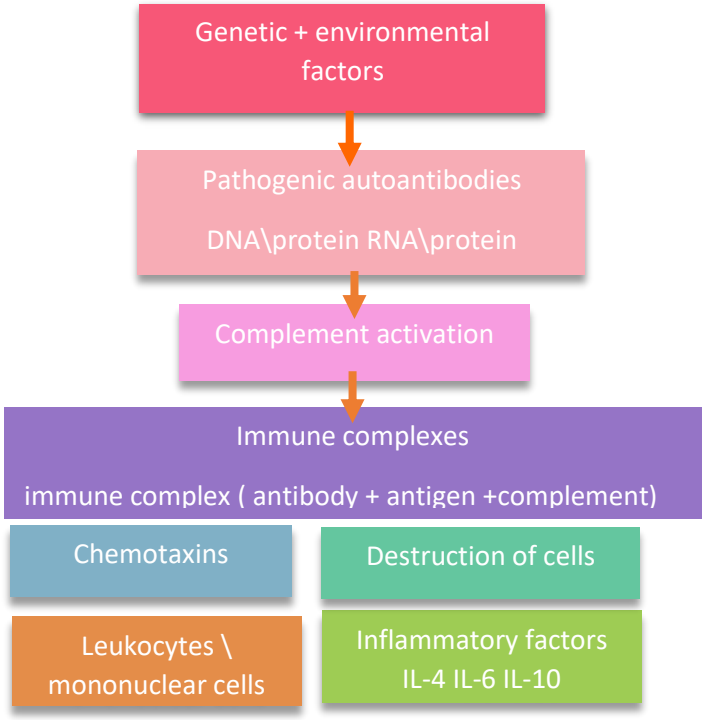
-Usually effect young woman's 20's years old

-Its Type III Hypersensitivity mediated

-The characteristic "butterfly rash"

-Is made worse by exposure to sunlight

-Lupus is a potentially fatal autoimmune disease.



The doctors of both female and male didn't focus on the systemic symptoms of SLE.

Dermatological:
- ✓ Malar rash
- ✓ Discoid lesions
- ✓ Hair loss
- ✓ Oral ulcer
- ✓ Raynauds's
- ✓ Nailfold, erthema
- ✓ Livedo on hands/legs
- ✓ Bullous rash on legs
- ✓ Dermatitis on fingers

CNS:
- ✓ Cognitive defects, anxiety, depression, psychosis, seizures and neuropathies, cerebral punctate vasculitis

Hematological
- ✓ Anemia of chronic disease
- ✓ Asymptomatic leukopenia
- ✓ Thrombocytopenia
- ✓ Lymphadenopathy

Symptoms

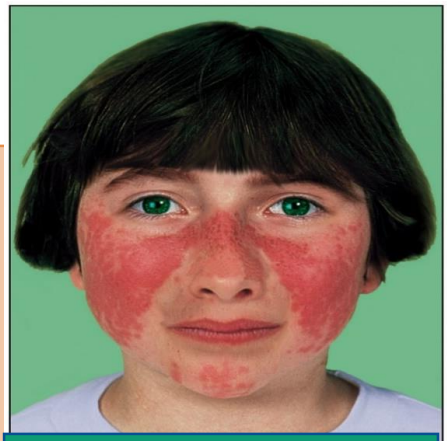
Cardiovascular:
- ✓ Pericarditis
- ✓ Verrucous endocarditis, emboli
- ✓ CAD from steroids

Pulmonary:
- Dyspnea and restrictive LFTs
- Pleurisy, pleural effusion, pneumonitis, interstitial lung disease and pulmonary hypertension

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

GIT:
- ✓ Gastritis, peptic ulcer due to NSAID or corticosteroids
- ✓ Pancreatitis, peritonitis and colitis due to SLE vasculitis
- ✓ Lupoid hepatitis
- ✓ Hepatosplenomegaly

Renal;
- ✓ Glomerulonephritis


Butterfly rash

Autoantibodies:

Antibodies that are found in SLE are :

- Ds DNA: associate with nephritis.
- Histones : associate with drug induced SLE

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

Other investigations

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

4- Rheumatoid Arthritis:

is an autoimmune disease in which the normal immune response is directed against an individual's own tissue Including the:

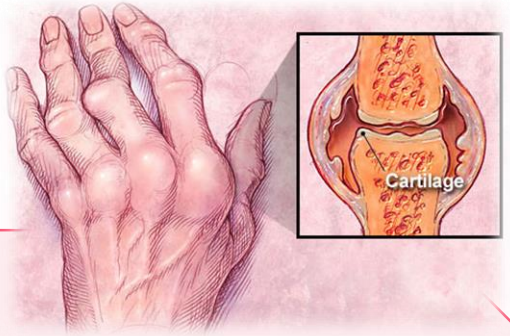
- Joints • Tendons • Bones

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.

5:27 MINTUES! Its 3D and it include everything you need to know about RA.



Pathogenesis

(Type III hypersensitivity reaction also type IV)

In rheumatoid arthritis, many individuals produce a group of autoantibodies known as rheumatoid factor.

These antibodies react with determinants in the FC region of IgG.

Such autoantibodies 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 metalloproteinases; which are known to cause joint destruction.

- Endothelium upregulates adhesion molecules, attracting neutrophils to the synovium.
- Neutrophils are activated to produce metalloproteinases, which digest synovial matrix proteins

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.

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 and cause atrophy in surrounding muscles also causes deformity of the effected joints.

Treatment and Prognosis

Medications

- NSAIDS (Non-steroidal anti-inflammatory drugs)
- Disease-modifying drugs (eg, gold, hydroxychloroquine, sulfasalazine, penicillamine)

- Antimalarial (Blocks antigen presentation) fact: it used also in leukemia
- Immunosuppressive therapy: (Corticosteroids - Methotrexate)
- Surgery • Physical therapy.

Summary

-Effects and tissue damage of autoimmune diseases are due to type II, III, and IV hypersensitivity reactions

1] Organ specific autoimmune diseases.

-Either stimulatory (activating) or blocking (inhibiting) auto antibodies.

A) Graves' Disease.

Auto Antibodies bind to Thyroid Stimulating Hormone (TSH) receptor, and mimics its function (Stimulating the production of Thyroxin).

B) Myasthenia Gravis.

-Characterized by muscle weakness and fatigue

-IgG antibodies bind to Acetylcholine(ACH) receptors, forming an immune complex which is destroyed by the complement system.

- The result is a decreased number of ACH receptors.

2] Systemic Autoimmune diseases.

Systemic Lupus Erythematosis (SLE)

- ANA complexes are destroyed by the complement system, releasing lots of substances that cause other symptoms.
- **Tests for SLE**: ANA test, determined by **immunofluorescence** or **ELISA** tests.
- **Treatment**: 1) NSAIDS 2) Antimalarials 3) Immunosuppressive agents .

Rheumatoid Arthritis.

- IgM antibodies bind to IgG antibodies, forming the rheumatoid factor which is deposited in joints. Macrophages engulf these complexes and release TNF and cytokines and enzymes leading to→ joint destruction.
- **Treatment:**
  1) NSAIDS 2) Disease-Modifying drugs
  3) Immunosuppressive drugs 4) Surgery and physical therapy.

MCQS:

1_ rheumatoid arthritis is an autoimmune disease :

A-T B-F

3-The inflammatory process in auto immune diseases are mediated by anaphylactic hypersensitivity:

A-True b- False

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

7- Which of the following is potentially fatal:

a-Graves b-SLE

c-Myasthenia gravis d-RA

9- What type of hypersensitivity is involved with RA?

a-Type I b-Type II c-Type III d-Type IV

11-RA affect central joints and may cause destruction of both cartilage and bone :

a- true

b- false

2_ cause joint destruction because after TNF induced secretion :

A-synovial membrane

B- cortecosteriod

C- metalloproteinases

4- in myasthenia gravis which of the following antibodies interacts with the post synaptic AChR:

a-IgG b-IgM c- IgA d- IgE

6- The butterfly rash worsened by sun exposure is a characteristic of :

a-Graves b-SLE

c-Myasthenia gravis d-RA

8- Prevalence and incidence of RA is 3 times greater in:

a-Woman than men b-Child than adult

c-Men than women d-Adult than child

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

Answers:

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