جامعة الملك سعود
King Saud University

MED438
KING SAUD UNIVERSITY

Autoimmune Diseases

Color code:
Important in red
Extra in blue

Immunology
MED438

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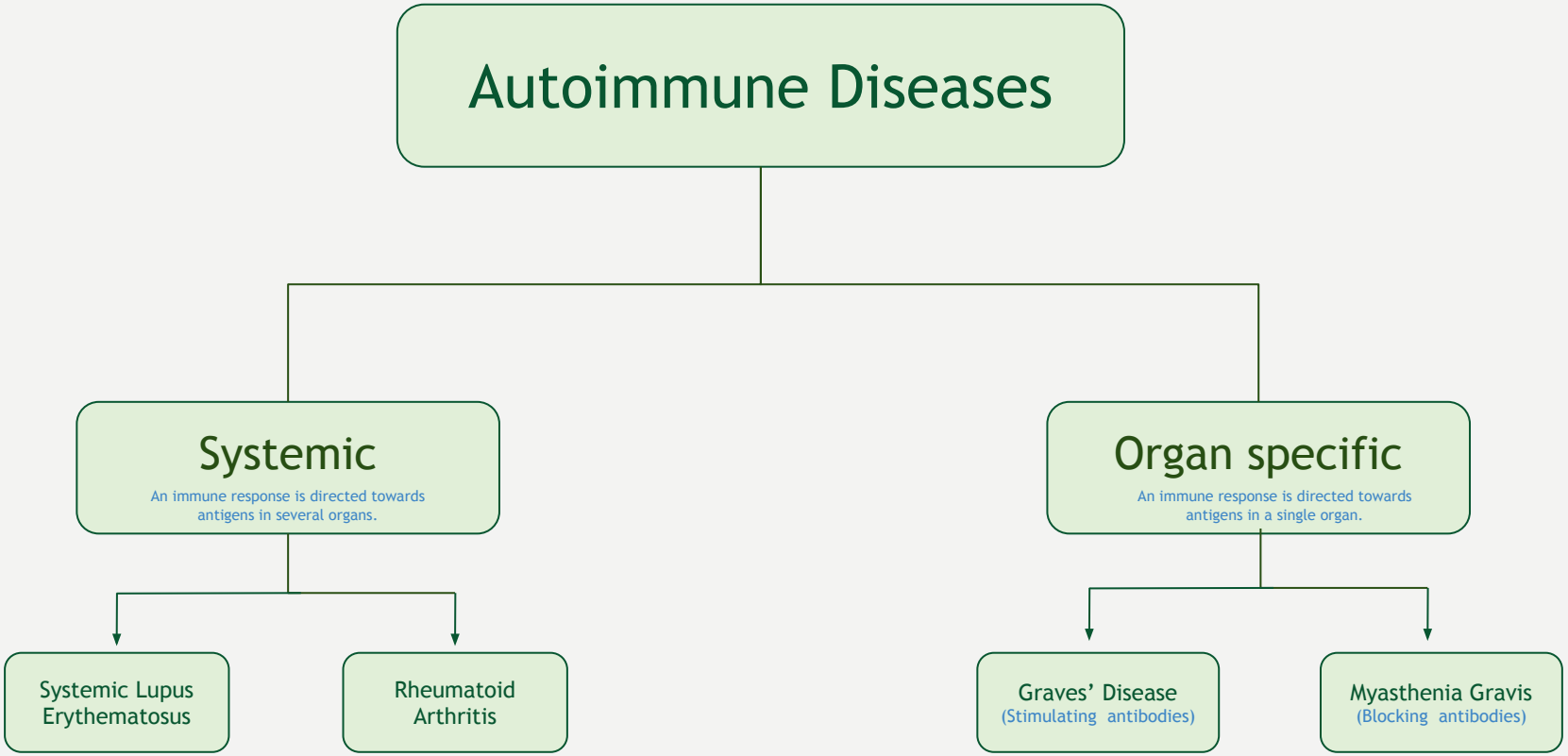
Editing file

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.



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

Some Autoimmune Diseases in Humans

ONLY know basic disease names (whether they're organ specific or systemic)

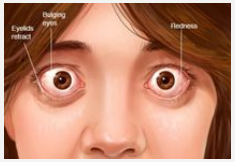
Disease	Self-antigen	Immune response
ORGAN-SPECIFIC AUTOIMMUNE DISEASES		
Addison's disease	Adrenal cells	Auto-antibodies
Autoimmune hemolytic anemia	RBC membrane proteins	Auto-antibodies
Goodpasture's syndrome	Renal and lung basement membranes	Auto-antibodies
Graves' disease	Thyroid-stimulating hormone 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 DISEASES		
Ankylosing sponkylitis	Vertebrae	Immune complexes
Multiple sclerosis	Brain or white matter	T_H1 cells and T_C cells, auto-antibodies
Rheumatoid arthritis	Connective tissue, IgG	Auto-antibodies, immune complexes
Systemic Lupus Erythematosus	DNA, RBC, Nuclear Protein, and platelet membranes	Auto-antibodies, immune complexes
Sjogren's syndrome	Salivary gland, liver, kidney, thyroid	Auto-antibodies

Not that important but scleroderma is here as well

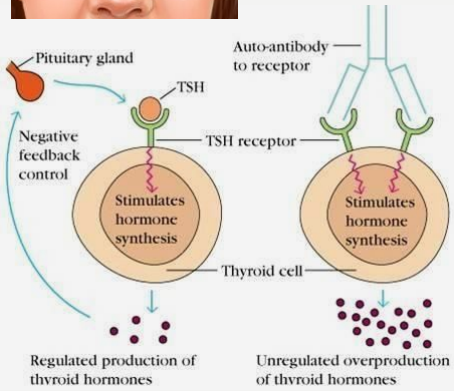
Organ specific autoimmune diseases

Graves' diseases

Normal event	Thyroid stimulating hormones (TSH) binds to thyroid cells' receptors and stimulate the synthesis of two thyroid hormones: Thyroxine and Triiodothyronine (regulated by negative feedback control)
Pathophysiology	(Stimulating antibodies) Production of stimulating autoantibodies that mimic the action of TSH causing hyperthyroidism (overstimulation of the thyroid gland). Side effects: tremors, weight loss, heat intolerance. And it could lead to amputation. Hypothyroidism has the OPPOSITE side effects

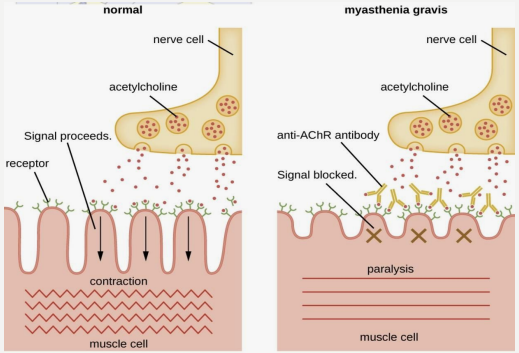


Exopthalmos: Bulging eyes/visible sclera



Myasthenia gravis

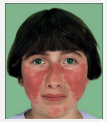
Normal event	An action potential arrives at NMJ, ACh is released and then binds to receptors and opens Na ion channels, leading to muscle contraction.
Pathophysiology	(Blocking Antibodies) Antibody (IgG) directed against (ACh) receptor by interacting with postsynaptic AChR at the nicotinic NMJ. Reduction in the number of functional AChR by increasing degradation (complement mediated) of receptor. Side effects: weakness, fatigability, and bilateral ptosis



Systemic Autoimmune Diseases

Systemic Lupus Erythematosus (SLE)

(type III hypersensitivity)

Definition	Systemic autoimmune disease where the body attacks its own tissues.
complications	Mostly affects joints (arthritis), blood vessels (vasculitis), kidneys (glomerular nephritis). Affects patients with sun-sensitive butterfly rash. 
Prevalence & incidence	Women are 90% more prevalent to the disease.
Treatment	• NSAIDs • Antimalarials like hydroxychloroquine. (block antigen presentation) • Immunosuppressive agents (chronic cases)
SLE tests	• Antinuclear antibodies test (immunofluorescence) (most sensitive) • Complement protein levels. (CH50 + decrease in C3 and C4) • Anti-ds DNA titers (70% in SLE, causing nephritic flare) (specific and used when ANA is +) • SM Antigen (most specific, also used when ANA is +)

Constitutional Symptoms of SLE: Fatigue, myalgia, fever, and weight change.

Pathophysiology of SLE

↓

Genetic + environmental factors

↓

Pathogenic autoantibodies -DNA/RNA protein complexes (antinuclear antibodies)

↓

Immune complexes

↓

Complement activation

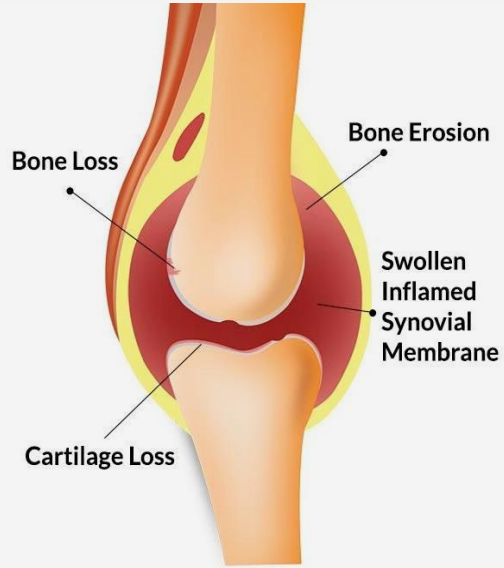
IL-4, IL-6, and IL-10 released

Systemic Autoimmune Diseases

Rheumatoid Arthritis

(Type III hypersensitivity)

Definition	Systemic autoimmune disease that results in the destruction and inflammation of joints (synovium), tendons, and bones.
Systemic complication	CVS and respiratory complications that may lead to early death.
Prevalence & incidence	Women more than men by 2-3 times.
Cause	Unknown but triggered by genotype and environmental factors.
Genetic factors	HLA-DR B1 locus alleles are susceptible. due to a common amino acid motif (QKRAA) in the shared epitope region



Rheumatoid Arthritis

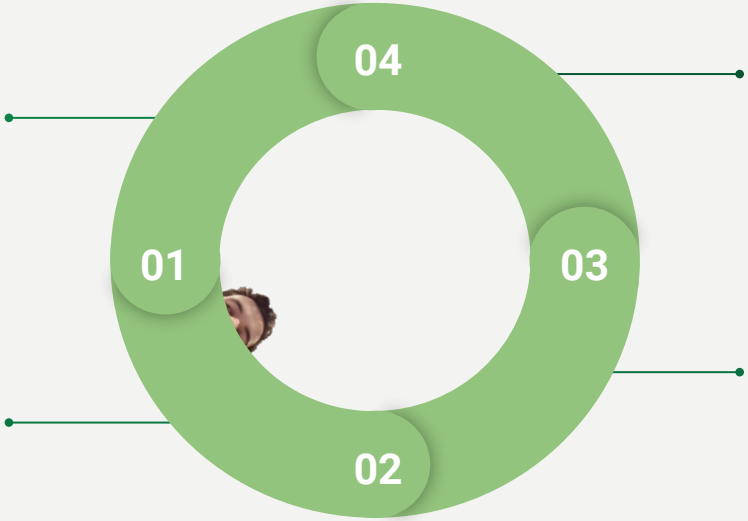
Pathogenesis of RA:

Pathogenesis:

Arginine will be replaced by citrulline and form citrullinated proteins that will trigger the immune system as foreign bodies.

T cell Activation:

The immune system will activate T cells due to the unknown antigen, and this will lead to the inflammation and attraction of inflammatory cells



Inflammatory cells Activation:

- **inflammatory cells** will produce TNF-α and IL-1 which will induce the secretion of metalloproteinases leading to the destruction of the joints (by degrading collagen type II).

-**Synovial macrophages** will engulf the immune complexes and release TNF and IL-1 (due to IgM-IgG complexes)

B cells Activation:

The immune system will also activate B cells to secrete two main antibodies.

1. **Anti-citrullinated proteins antibodies:** They attack the citrullinated proteins.

2. **Rheumatoid Factor (IgM):** attaches to Fc region of normal circulating IgG and forms IgM-IgG complex that will be deposited in joints.

Diagnosis	- Anti-citrullinated proteins (ACP)/ ACCP specific markers - Rheumatoid Factor
Treatment	- NSAIDS - DMARDs (Hydroxychloroquine, penicillamine, gold...etc) - Surgery - Immunosuppression (corticosteroids, methotrexates)

Yeah they actually used gold injections to treat RA. Look up “gold therapy” A very famous person does it too btw. Don’t believe us? Click the syringe 

Take home messages

- The spectrum of autoimmune diseases is wide, ranging from 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.

Quiz:

1. Which of the following is the disease associated with stimulating antibodies?

a) Myasthenia Gravis
b) SLE
c) Graves'
d) Rheumatoid Arthritis

2. Which of the following is a side effect of hypothyroidism?

a) Heat intolerance
b) Weight gain
c) Blue skin
d) Palpitations

3. Which antibody is directed against AchR in MG?

a) IgM
b) IgD
c) IgG
d) None of the above

4. Which of the following DMARDS treats SLE in addition to RA?

a) Penicillamine
b) Tocilizumab
c) Methotrexate
d) Hydroxychloroquine

5. Which of the following is replaced by citrulline in RA?

a) Citrullinated proteins
b) Proline
c) Arginine
d) DMARDs

6. Which of the following is the reason why MSK is difficult?

a) Anatomy
b) The study of the human bodily structure
c) Bones
d) Muscles
e) Your life

1.C 2.B 3.C 4.D 5.C 6.E

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