Autoimmunity and Autoimmune Diseases

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Autoimmunity

- **The process of mounting an immune response against a normal body component.**
- **Autoantigen:** A normal body component that acts as an antigen.
- **Autoantibodies:** Antibodies directed against epitopes on normal body tissues.
- **Autoimmune Disease**: Disease caused by an immune attack against an individual's own tissues.

Induction of Autoimmunity

Autoimmunity can be induced by the followings:

1-EXPOSURE OF HIDDEN ANTIGENS

A- Antigens Hidden in cells or Tissues.

Example: The testicular tissues after damage.

Antibodies formed after heart attack

B-Antigens Generated by Molecular Changes

1-Rheumatoid factors (RFs) are autoantibodies directed against other immunoglobulins.

2-Immunoconglutinins (IK) are autoantibodies directed against the complement components C2, C4 and C3.

Induction of Autoimmunity

2-Molecular Mimicry

In which epitopes are shared between the infectious agents and normal body tissues.

Example: Trypanisoma cruzi contains agents that cross-react with mammalian neurons and cardiac muscle.

***M protein of group A Streptococcus cross-react with cardiac myosin.**

Induction of Autoimmunity

3- Alteration in Antigen Processing: Production of autoantibodies because of an alteration in responding to self antigens.

Example: Thyrotoicosis, Diabetes.

4-Failure of Regulatory Control:

Example: injection of mice with rat RBCs.

Myasthenia gravis (autoantibodies to neuromuscular junction) is sometimes associated with Thymoma.

Induction of Autoimmunity

5-Viruses:

Example: mice infected with certain reoviruses develop an autoimmune diabetes mellitus.

6-Genetic Basis: In which autoimmunity may be a result of defective thymic selection.

(If a self peptide bind poorly to an MHC molecules, it may not trigger negative selection and self-reactive T cells may then escape into the body).

Induction of Autoimmunity

7-Drugs:

Examples: Sedormed to platelets and penicillin to red cells.

8-Polyclonal activation: Many microbial products like endotoxins, DNA, etc, can stimulate B cells, including-reactive ones. The EB virus infects B cells themselves and makes them proliferative continuously.

MECHANISMS OF TISSUE DAMAGE IN AUTOIMMUNITY

1-Type I hypersensitivity:

Milk allergy in cattle

2-Type II hypersensitivity:

RBCs hemolysis (hemolytic cytotoxicity)

-Autoimmune hemolytic anemia

-Thrombpcytopnia

-Autoantibodies to thyroid stimulating hormons

-Autoantibodies to β-adrenoceptors cause severe asthma.

MECHANISMS OF--------

3-Type III hypersensitivity:

example: Systemic lupus erythematosus (SLE): autoantibodies against DNA and RNA and the resulting complexes deposit in widespread throughout the vascular system.

4-Type IV hypersensitivity:

Examples: **Insulin-dependent diabetes mellitus.**

The damage caused by Tc cells.

ORGAN-SPECIFIC AUTOIMMUNE DISEASES

1-Autoimmune Endocrine Diseases

a-Lymphocytic Thyroiditis.

b-Hyperthyroidism in older cats.

c-Lymphocytic Parathyriditis

d-Insulin-dependent diabetes mellitus

e-Autoimmune Adrenalitis in dogs

Organ-specific-----

2-Autoimmune Neurological Diseases

a-Equine polyneuritis

b-Canine polyneuritis (coonhound paralysis).

it is an acute polyneuritis that affects dogs following a bite or scratch from a raccoon.

3-Autoimmune Eye Diseases.

a-Equine Recurrent Uveitis

The most common cause of blindness in horses.

b-Vogt-Koyanagi-Harada Syndrome

Humans and dogs

Uveitis, poliosis(whitening of hair) and vitiligo

Organ-specific-----

4-Autoimmune Reproductive Diseases.

a-Damaged testicular tissues

b-Absorption of sperms through vagina, uterus, fallopian tubes.

c-Antibodies to sex hormones.

5-Autoimmune Skin Diseases

a-Pemphigus foliaceus superfecially and mild

b-Pemphigus vulgaris , deeper and very severe.

c-Pemphigus vegetans rare and mild

d-Pemphigus erythematosus: mild form of pemphigus foliaceus.

Organ-specific----

Bullous Pemphigoid: is a rare disease of skin basement membrane, multiple bullae develop around mucocutaneous junction and axillae.

Alopecia Areata: is an autoimmune disease directed against cells in hair follicles. Multiple round spots of hair loss in the absence obvious inflammation.

Organ-specific------

6-BLOOD

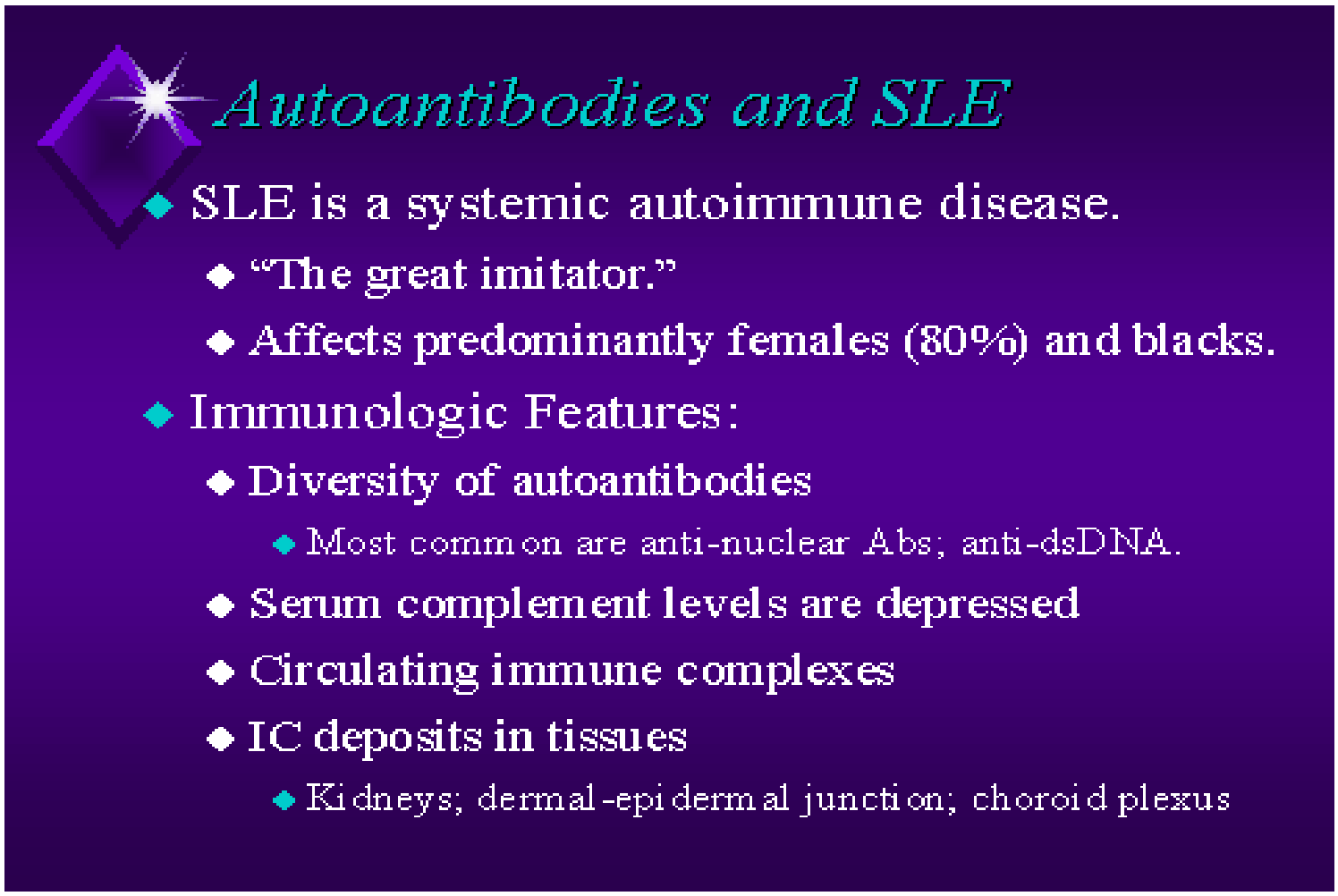
a-Autoimmune Hemolytic Anemia

b-Autoimmune Thrombocytopenia

7-AUTOIMMUNE MUSCLE DISEASES

a-Myasthenia gravis:- **It is the disease of skeletal muscles, characterized by abnormal fatigue and weakness after relatively mild exercise. Autoantibodies are formed against post synaptic acetylecholine receptors.**

Systemic lupus erythematosis (SLE)



Affected Organs

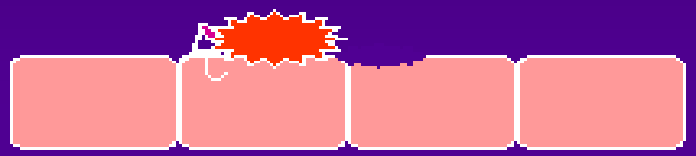
Organ Systems Involved in SLE

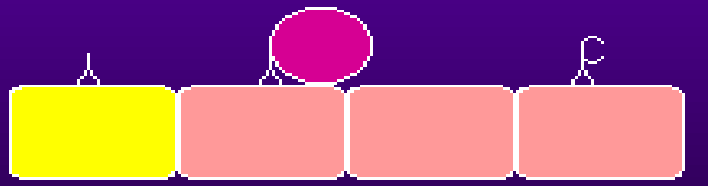
- Many organ systems can be involved:
  - Joints and muscles - arthritis
  - Skin - erythematous rash
  - Kidneys - glomerulonephritis
  - Lungs - pneumonitis
  - Heart - myocarditis (rare)
  - Eyes - retinal vasculitis; corneal ulceration (Sjogren's s.)
  - Gastrointestinal system - GI ulceration (uncommon)
  - Vascular system - small vessel vasculitis (common)
  - Central nervous system - neurologic and psychiatric

Mechanisms

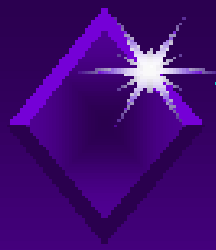
Pathogenic Mechanisms

- Immune complex mediated
  - Deposition in tissues
  - Inflammatory response
- Autoantibody mediated
  - Complement activation
  - Cell mediated (e.g., NK)
  - Functional
    - receptor stimulation or blockade.





Antibodies involved



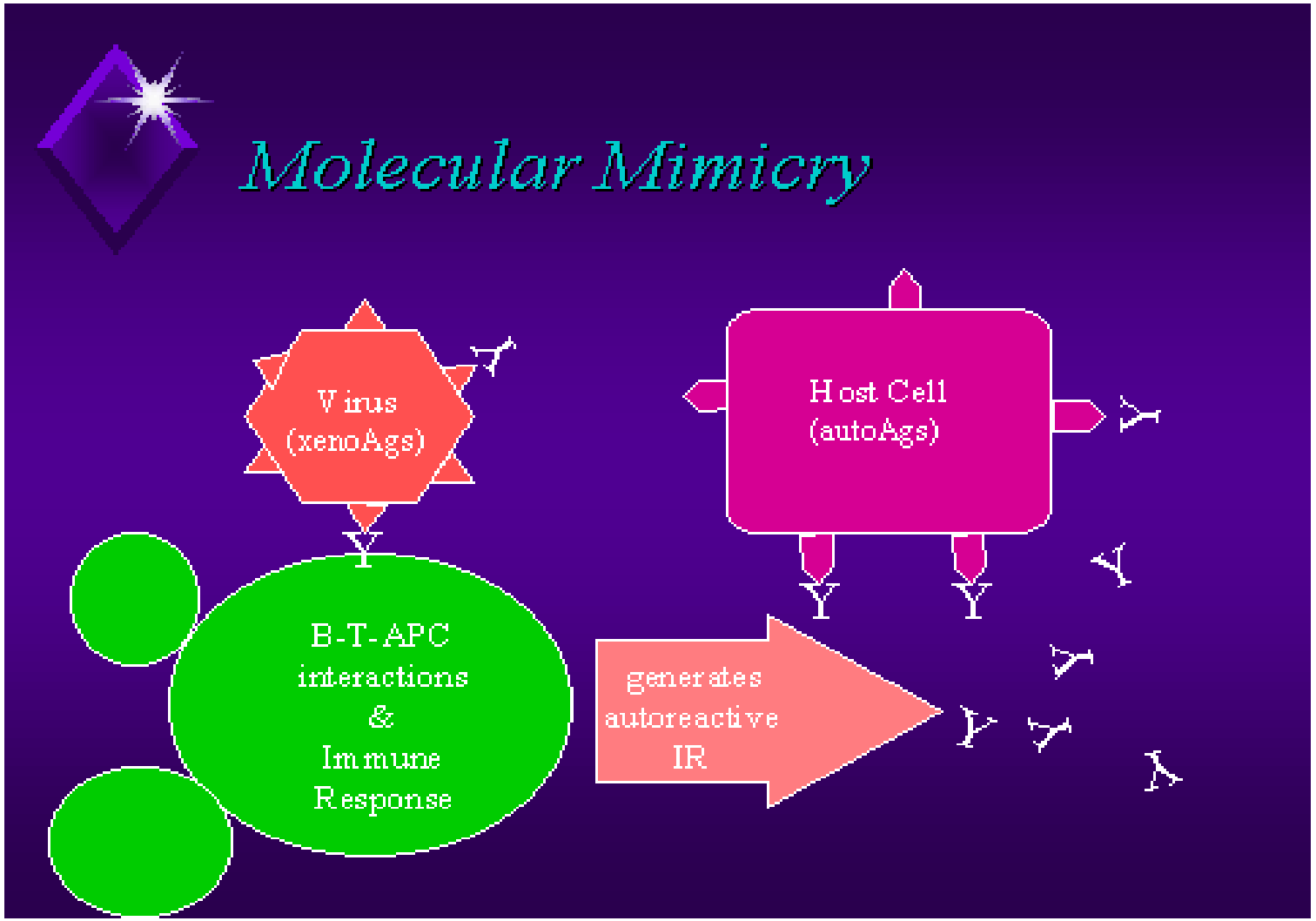
Autoantibodies in SLE

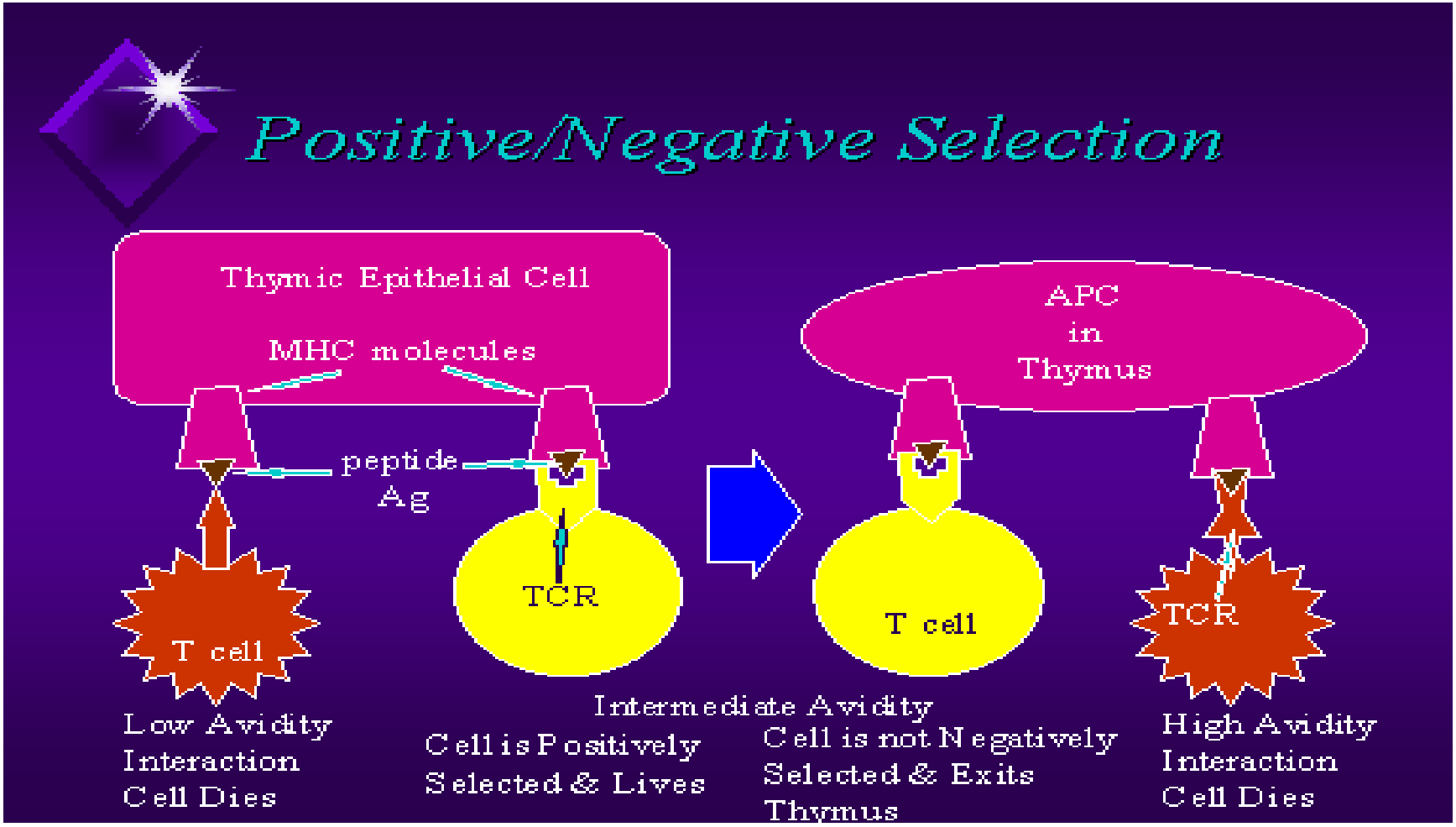
- Anti-Nuclear Antibodies
  - ss & dsDNA
  - ss & ds RNA
  - Deoxyribonucleoprotein (DNA histones)
  - Ribonucleoprotein
  - Sm (a nuclear glycoprotein)
- Anti-Cytoplasmic Antibodies
  - Ribosomes (P proteins)
  - Mitochondria
  - Lysosomes
  - Ro (glycoprotein associated with RNAse)
  - La (RNA-protein)

Antibodies inv-----

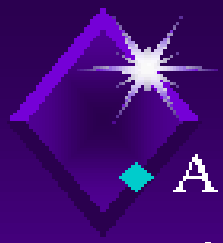
Autoantibodies in SLE (cont'd)

- Anti-Cellular Antibodies
  - Lymphocytes
  - Neutrophils
  - Erythrocytes
  - Platelets
  - Thyroid
  - Neurons
- Others
  - Rheumatoid factors (Fc Ig)
  - C1q
  - Heat shock proteins (hsp 90 & 70)


Molecular Mimicry
Virus
(xenoAgs)
Host Cell
(autoAgs)
B-T-APC
interactions
&
Immune
Response
generates
autoreactive
IR


Positive/Negative Selection
Thymic Epithelial Cell
MHC molecules
peptide
Ag
TCR
T cell
APC
in
Thymus
T cell
TCR
Low Avidity
Interaction
Cell Dies
Intermediate Avidity
Cell is Positively
Selected & Lives
Cell is not Negatively
Selected & Exits
Thymus
High Avidity
Interaction
Cell Dies

Finally-----



Contributing Factors

- Autoimmunity is multifactorial:
  - Immunological
    - cytokines
  - Genetic
    - MHC
  - Neural/Hormonal
    - corticosteroids
    - sex hormones
  - Environmental
    - Microbial
    - Pollutants and chemicals (e.g., cigarette smoke)

- Multiple sclerosis

- Myasthenia gravis
- (acetylcholine receptor
- autoantibodies)
-
- Autoimmune neuropathies
- Autoimmune uveitis
-
-

Finally -------

- Autoimmune hepatitis
- Autoimmune hemolytic anemia
- Autoimmune thrombocytopenia
- Antiphospholipid antibody

Vitiligo

Pemphigus vulgaris

Dermatitis herpetiformis

Psoriasis skin

Systemic Lupus Erythematosus

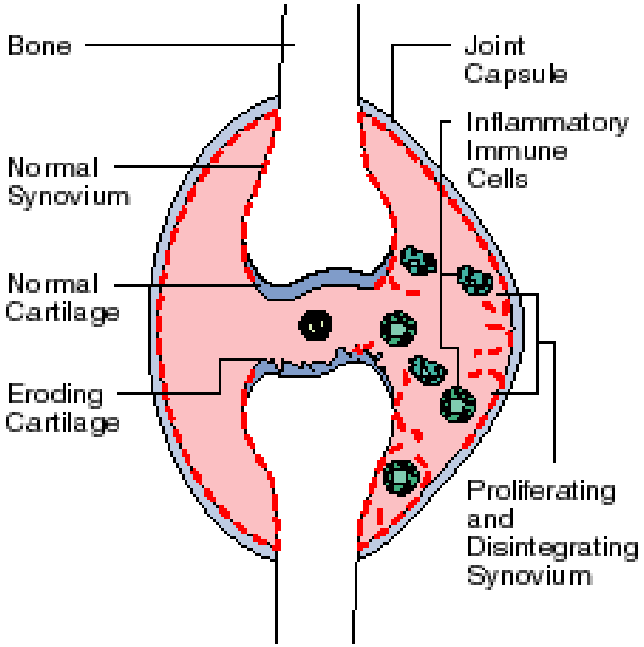
SLE *is the most commonly known autoimmune disorder.*

This characteristic "butterfly" rash is made worse by exposure to sunlight.

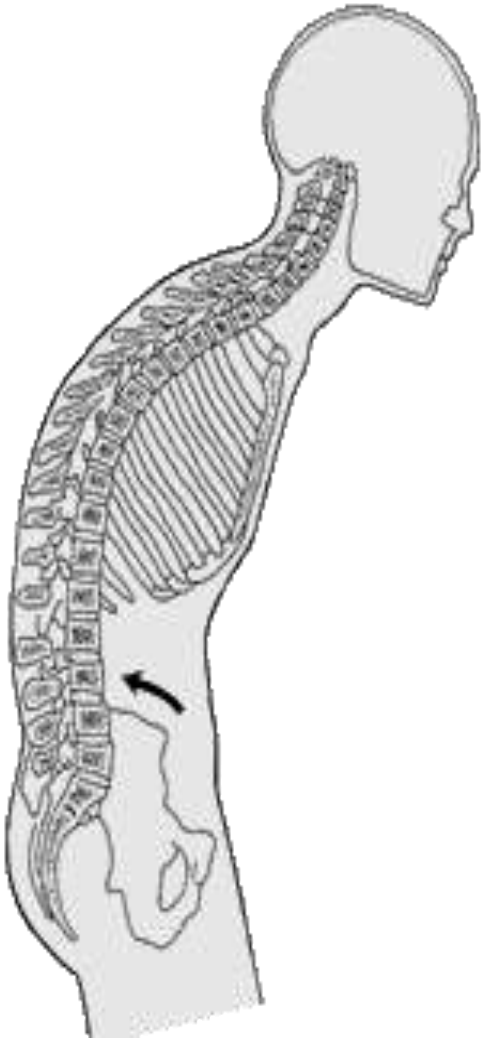
Lupus is a potentially fatal autoimmune disease that strikes 1 in 2,000 Americans and 10 times as many women as men.

Rheumatoid arthritis (RA) affects peripheral joints and may cause destruction of both cartilage and bone. The disease affects mainly individuals carrying the **DR4** variant of MHC genes.

This fact can lead to better prognoses and in aiding efforts to change immune reactions that involve the DR4 variant while leaving other reactions intact.



Ankylosing spondylitis



(Bechterew's Disease), a joint inflammation mainly affecting the spine, occurs only in individuals carrying a certain variant of MHC molecule (HLA-B27). Much evidence suggests that molecules derived from microorganisms interact with the B27 molecule in causing the destructive immune reactions

Treatment

- What are some of the treatments for autoimmune diseases?
- Diminishing of the activity of the immune system

This necessitates a delicate balance, controlling the disorder while maintaining the body's ability to fight disease in general.

Drugs most commonly used are corticosteroid drugs.

- Cyclosporin A (CsA) inhibits a signal transmission pathway in T lymphocyte cells.

1- Metabolic control:

a. Graves' disease: antithyroid drugs, surgical, radiation

b. Hashimoto's thyroiditis: Thyroxin.

c. Pernicious anemia: vitamin B12.

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c. Pernicious anemia: vitamin B12.

d. IDDM: insulin

2- Antiinfalamtory and cytotxic drugs:

Nonsteroidal antiinflamatory (NSAID)

Corticosteroids

Cytotoxic drugs: Cyclophosphamide, Azothioprine, Cyclosporin

3- Thymectmy:

Myasthenia gravis after anticholinesterase

4- Plasmapheresis or Plasma exchange:

GBS, SLE, Goodpasture's

5-Spleenectomy:

Hemolytic anemia, ITP

6- Intravenous Gammaglobulin therapy

GBS, Dermatomyositis

7- Cytokines and inhibitors: anti-TNF1 DDM: insulin

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