AUTOIMMUNE DISEASE

Introduction

1. Normal individuals do not produce destructive immune responses to their own tissues due to "immune tolerance.
2. Autoimmune disease
   a. Disorder in which tissue injury is caused by an immunologic reaction of the host to his own tissues.
   b. Precise mechanisms that initiate autoimmune diseases are not known.
   c. Can be classified as systemic or organ specific, frequently have overlap.

Mechanisms involved in autoimmune disease.

1. Forbidden Clone Theory
   a. A clone of changed or altered lymphocytes arises through mutation.
   b. These cells lack foreign surface antigens and are not destroyed by the host.
   c. Because of alteration may recognize host as foreign.
2. Altered Antigen Theory
   a. Surface antigens on host altered by chemical, biological or physical means.
   b. This new antigenic determinant may be recognized as foreign by the host.
3. Sequestered Antigen Theory
   a. Some antigens in the body are hidden from cells of the immune system.
   b. If there is damage to these organs causing exposure of these sequestered antigens an immune reaction may occur

4. Genetic influence

a. It is well recognized that certain immune disorders predominate in females and in families.

b. Determined by family studies.

c. Genetic links have occurred between diseases and HLA antigens

5. Molecular Mimicry

Cross-reacting antibodies are thought to be the cause of heart damage in rheumatic fever, which can sometimes develop after a *Streptococcus* infection. In this case, the antibodies are to streptococcal antigens, but they cross-react with the heart muscle.

Autoimmune diseases can be divided into:

A. Organ specific

The immune response is directed to a target antigen unique to a single organ or gland, so that the manifestations are largely limited to that organ. The cells of the target organs may be damaged directly by humoral or cell-mediated effector mechanisms. Alternatively, the antibodies may over-stimulate or block the normal function of the target organ.

B. Systemic

The response is directed toward a broad range of target antigens and involves a number of organs and tissues.

Tissue damage is widespread, both from cell mediated immune responses and from direct cellular damage caused by auto-antibodies or by accumulation of immune complexes.

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
Scleroderma	Nuclei, heart, lungs, gastrointestinal tract, kidney	Auto-antibodies
Sjogren's syndrome	Salivary gland, liver, kidney, thyroid	Auto-antibodies
Systemic lupus erythematosus (SLE)	DNA, nuclear protein, RBC and platelet membranes	Auto-antibodies, immune complexes

HASHIMOTO'S THYROIDITIS

individual produces auto-antibodies and sensitized TH1 cells specific for thyroid antigens. The DTH response is characterized by an intense infiltration of the thyroid gland by lymphocytes, macrophages, and plasma cells causes a goiter (visible enlargement of the thyroid gland)

Antibodies are formed to a number of thyroid proteins involved in the uptake of iodine. Binding of the auto-antibodies to these proteins interferes with iodine uptake and leads to decreased production of thyroid hormones (hypothyroidism).

Autoimmune anemias

Include pernicious anemia, autoimmune hemolytic anemia, and drug-induced hemolytic anemia.

Pernicious anemia is caused by auto-antibodies to intrinsic factor, a membrane-bound intestinal protein on gastric parietal cells. Intrinsic factor facilitates uptake of vitamin B12 from the small intestine. Binding of the auto-antibody to intrinsic factor blocks absorption of vitamin B12.

The immunodiagnostic test for autoimmune hemolytic anemias generally involves a **Coombs test**

Goodpasture's syndrome

Auto-antibodies specific for certain basement-membrane antigens bind to the basement membranes of the kidney glomeruli and the alveoli of the lungs. Subsequent complement activation leads to direct cellular damage and inflammatory response.

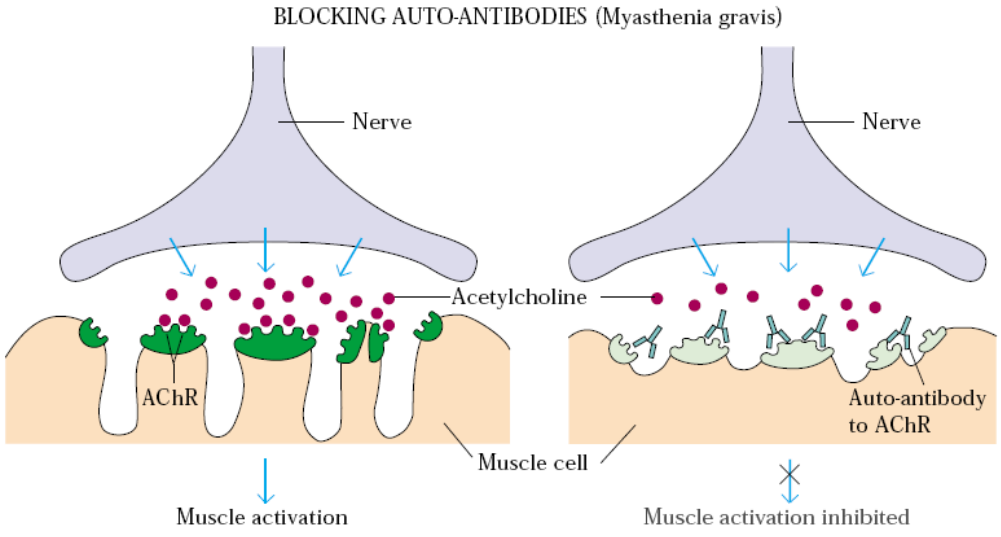
Insulin-dependent diabetes mellitus (IDDM)

Caused by an autoimmune attack on the pancreas. The attack is destroy specialized insulin-producing cells (beta cells) that are located in islets of Langerhans. This results in decrease production of insulin and consequently increased levels of blood glucose.

GRAVES' DISEASE

The production of thyroid hormones is carefully regulated by thyroid-stimulating hormone (TSH), which is produced by the pituitary gland. Binding of TSH to a receptor on thyroid cells stimulates the synthesis of two thyroid hormones. A patient with **Graves' disease** produces auto-antibodies that bind the receptor for TSH and stimulate the production of the thyroid hormones.

Myasthenia gravis



Systemic lupus erythematosus (SLE)

Appears in women between 20 and 40 years of age; the ratio of female to male patients is 10:1. Autoantibodies to a variety of tissue antigens, such as DNA, histones, RBCs, platelets, leukocytes, and clotting factors. Auto-antibody specific for RBCs and platelets, for example, can lead to complement-mediated lysis, resulting in hemolytic anemia and thrombocytopenia, respectively. When immune complexes results from binding of auto-antibodies with various nuclear antigens are deposited along the walls of small blood vessels, a type III hypersensitive reaction develops.

Laboratory diagnosis of SLE

Screening test for antinuclear antibody by ELISA and Indirect immunoflourecent staining.

Multiple sclerosis (MS)

Most people with MS are diagnosed between the ages of 20 and 40. Individuals with this disease produce autoreactive T cells that participate in the formation of inflammatory lesions along the myelin sheath of nerve fibers. The cerebrospinal fluid of patients with active MS contains activated T lymphocytes, which infiltrate the brain tissue and cause characteristic inflammatory lesions, destroying the myelin and leads to numerous neurologic dysfunctions.

Rheumatoid arthritis

Individuals with rheumatoid arthritis produce a group of auto-antibodies called **rheumatoid factors** (mostly IgM) bind to normal circulating IgG, forming IgM-IgG complexes that are deposited in the joints. These immune complexes can activate the complement cascade, resulting in a type III hypersensitive reaction, which leads to chronic inflammation of the joints.

The diagnosis of autoimmune diseases is not straightforward, and requires a history, physical exam, laboratory testing, radiography, and sometimes biopsies.

Blood tests to diagnose an autoimmune disease may include:

- **Auto-antibody tests.** For some autoimmune disorders, there are blood tests that can look for *auto-antibodies* in the blood
- **Inflammation and organ function tests.** Since certain autoimmune disorders can cause organs to function abnormally.