



## Autoimmunity

Lecture 17

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## Learning objectives

After reading this lecture you should be able to:

- Describe the mechanisms of autoimmunity.
- Classify autoimmune diseases.
- List autoimmune diseases.

## Introduction

- the immune system have the capacity to distinguish self from nonself antigens.
- Normally, a person is tolerized to self-antigens during the development of the immune system as a fetus and later in life by other mechanisms (e.g. oral tolerization).
- Paul Ehrlich realized that the immune system could go away and can attack on self-antigens.
- Autoimmunity is a condition in which structural or functional damage is produced by the action of immunologically competent cells or antibodies against the normal components of the body.
- Autoimmunity is due to production of autoantibodies and autoreactive T cells.
- In normal individual, immune system mechanisms of self-tolerance normally protect an individual from potentially self-reactive lymphocytes, if there are failures will develop autoimmune disease.
- Autoimmunity represents the end result of the break- down of immune tolerance.

## **Autoimmunity and immune tolerance**





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#### **Peripheral tolerance**





Peripheral tolerance: deletion or anergy of lymphocytes that recognize self antigens in peripheral tissues

Figure 16-1b Kuby IMMUNOLOGY, Sixth Edition © 2007 W. H. Freeman and Company

## Features of diseases of autoimmune origin

- 1. An elevated level of immunoglobulins.
- Demonstrable autoantibodies.
- 3. Deposition of immunoglobulins or their derivatives at sites of election, such as renal glomeruli.
  - Accumulation of lymphocytes and plasma cells at the sites of lesion.
- 5. Benefit from corticosteroids or other immunosuppressive therapy.
- 6. The occurrence of more than one type of autoimmune lesion in an individual.
- 7. A genetic predisposition towards autoimmunity.
- 8. Incidence higher among females.
- 9. Chronicity: Usually nonreversible.

## **Mechanisms of induction autoimmunity**

- 1. somatic mutation of Forbidden clones
- 2. Neoantigens or altered antigens by physical, chemical or biological influences
- 3. Molecular mimicry: antigenic determinants of some microbes are identical normal host cell components, Molecular mimicry by cross-reactive microbial antigens can stimulate autoreactive B and T cells.
- 4. **Polyclonal B cell activation**: certain stimuli nonspecial turn on multiple B clones
- 5. Activity of helper and suppressor T cells: Enhanced helper T cell and decreased suppressor T cells functions have been suggested as causes of autoimmunity.
- 6. Sequestered antigens: Lens Antigen of the Eye, Sperm Antigens, Heart Muscle Antigens
- 7. Genetic factor

## **Classification of autoimmune diseases**

- Based on the site of involvement and nature of lesions, autoimmune diseases may be classified as:
- A. Localized (or organ-specific)
- B. Systemic (or nonorgan-specific)
- Other classification:
- 1. Haemocytolytic autoimmune diseases
- 2. Organ-specific or localized autoimmune diseases
- 3. Nonorgan-specific or systemic autoimmune diseases
- 4. Transitory diseases

#### Localized (or organ-specific) Autoimmune Diseases

- 1. Autoimmune Diseases of the Thyroid Gland
- Hashimoto's Thyroiditis (Lymphadenoid Goiter): the autoantibodies interferes with iodine uptake and leads to decreased production of thyroid hormone (hypothyroidism).
- Thyrotoxicosis (Grave's Disease): IgG antibodies against specific domains of the thyroid stimulating hormone (TSH) lead to produce increased amounts of thyroid hormones and becomes greatly enlarged.
  - 2. Addison's Disease: lymphocytic infiltration of the adrenal glands and the presence of circulating antibodies directed against the cells of the zona glomerulosa.
- Autoimmune Diseases of the Eye: Phacoanaphylaxis, Sympathetic Ophthalmia
- 4. Pernicious Anemia: autoantibodies block intrinsic factor which facilitate absorption vitamin B12 from the small intestine lead to immature red blood cells

#### Localized (or organ-specific) Autoimmune Diseases

#### Disease

Hashimoto's thyroiditis Graves' disease Goodpasture's syndrome

Autoimmune hemolytic anemia Addison's disease

Idiopathic thrombocytopenia purpura Insulin-dependent diabetes mellitus Myasthenia gravis Myocardial infarction

Pernicious anemia Poststreptococcal glomerulonephritis Myasthenia gravis Spontaneous infertility

Organ-specific autoimmune diseases Self-antigen Immune response Thyroid proteins and cell Thyroid-stimulating hormone receptor Renal and lung basement membranes RBC membrane proteins Adrenal cells Platelet membrane proteins Pancreatic beta cells Heart

Gastric parietal cells; intrinsic factor

Acetylcholine receptors

Kidney

Sperm

Autoantibodies Autoantibodies Autoantibodies Autoantibodies

Autoantibodies Autoantibodies T<sub>DTH</sub> autoantibodies

Autoantibodies Autoantibodies Antigen-antibody complexes Autoantibodies (blocking) Autoantibodies

### Systemic (Nonorgan-Specific) Autoimmune Diseases

- In systemic autoimmune diseases, Tissue damage is wide- spread, both from cell-mediated immune responses and from direct cellular damage caused by autoantibodies or by accumulation of immune complexes.
- 1. Systemic Lupus Erythematosus (SLE): typically appears in women between 20 and 40 years of age. SLE results from tissue damage caused by pathogenic subsets of autoantibodies and immune complexes.
- 2. Rheumatoid Arthritis: Rheumatoid arthritis is a common autoimmune disorder, most often affecting women from 40 to 60 years old. The major symptom is chronic inflammation of the synovial membranes of joints. RF is detected by agglutination tests using, as antigens, particles coated with globulins.
- 4. Sjögren's Syndrome: Sjögren's syndrome is a clinicopathologic entity cha- racterized by dry eyes and dry mouth resulting from immunologically-mediated destruction of the lacrimal and salivary glands.

#### Systemic (Nonorgan-Specific) Autoimmune Diseases

Disease

Systemic lupus erythematosus (SLE)

Multiple sclerosis Rheumatoid arthritis Scleroderma

Sjögren's syndrome Ankylosing spondylitis

#### Systemic autoimmune diseases

Self-antigen

#### Immune response

DNA, nuclear protein, RBC and platelet Autoantibodies, immune complexes membranes

Brain or white matter

Connective tissue, IgG Autoantibodies, im Nuclei, heart, lungs, gastrointestinal Autoantibodies tract, kidney

Salivary gland, liver, kidney, thyroid Vertebrae Th1 cells and Tc cells, autoantibodies Autoantibodies, immune complexes Autoantibodies

Autoantibodies

Immune complexes

# Thank you