



Pathogenesis of Autoimmune Diseases: A Short Review

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ABSTRACT

Autoimmunity is characterized by the reaction of cells (auto reactive T-lymphocytes) or products (autoantibodies) of the immune system against the organism's own antigens (autoantigen). It may be part of the physiological immune response (natural autoimmunity) or pathologically induced, which may eventually lead to development of clinical abnormalities (autoimmune disease). Different mechanisms are involved in the induction and progression of autoimmunity. These include genetic or acquired defects in immune tolerance or immune regulatory pathways, molecular mimicry to viral or bacterial protein, an impaired clearance of apoptotic cell material. A number of diseases have been identified in which there is Autoimmunity, due to copious production of autoantibodies and autoreactive cells. The aim of the present article is to review on the pathogenesis of autoimmune diseases.

Keywords: Autoimmunity, Immunity, Immunoglobulins, Tolerance.

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INTRODUCTION

Immunology is the science that deals with body's response to antigenic challenge (Latin Immunitas, freedom from). The term 'immunity' traditionally refers to the resistance exhibited by host toward injury caused by microorganisms and their products. Immunity is of different types it can be innate (native) or acquired (adaptive) immunity. Immunity is a very broad scientific discipline involving concept of recognition, specificity and memory. Immunological mechanism are involved in the protection of the body against infectious agent but they can also damage host

organism called as autoimmunity.¹ Autoimmunity is the mechanism where an organism fails to recognize its own constituent parts (down to the submolecular levels) as 'self', which results in an immune response against its own cells and tissues. Any disease that results from such an aberrant immune response is termed an autoimmune disease.²

Autoimmunity is characterized by the reaction of cells (auto reactive T-lymphocytes) or products (autoantibodies) of the immune system against the organism's own antigens (autoantigen). It may be part of the physiological immune response (natural autoimmunity) or pathologically induced, which may eventually lead to development of clinical abnormalities (autoimmune disease).³ According to the clinical manifestation, autoimmune diseases may be classified as systemic (e.g. SLE) or as organ specific (e.g. Graves diseases). Different mechanisms, which are not mutually exclusive, may be involved in the induction and progression of pathologically autoimmunity these include genetic or acquired defects in immune tolerance or immune regulatory pathways, molecular mimicry to viral or bacterial protein, an impaired clearance of apoptotic cell material.⁴ The aim of this article is to provide a framework about pathogenesis autoimmune diseases.

Association of Autoimmunity with Disease

Disease of autoimmune origin usually exhibit the following features:¹

- An elevated level of immunoglobulins
- Demonstrable autoantibodies
- Accumulation of lymphocytes and plasma cells at the sites of lesion.
- Benefit from corticosteroid or other immunosuppressive therapy.
- The occurrence of more than one type of autoimmune lesion in an individual.
- A genetic predisposition toward autoimmunity
- Higher incidence among females
- Chronicity, usually nonreversible.

Classification of Autoimmune Diseases

The Autoimmune diseases are classified based on site of involvement and nature of lesion as hemocytolytic, localized (or organ specific) and systemic (or nonorgan specific).⁵

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Hemocytolytic Autoimmune Diseases

- Autoimmune hemolytic anemias
- Autoimmune thrombocytopenia
- Autoimmune leukopenia.

Localized (Organ Specific) Autoimmune Diseases

Autoimmune diseases of the thyroid gland:

- Hashimoto's disease (Lymphadenoid goiter)
- Thyrotoxicosis (Graves disease)
 - Addison's disease
 - Autoimmune orchitis
 - Myasthenia gravis
 - Autoimmune diseases of the eye
 - Pernicious anemia
 - Autoimmune disease of nervous the system
 - Autoimmune disease of the skin.

Systemic (Nonorgan Specific) Autoimmune Diseases

- Systemic lupus erythematosus
- Rheumatoid arthritis
- Polyarteritis nodosa
- Sjogren's syndrome.

Mechanisms of Autoimmune Diseases

Cells or tissues may undergo antigenic alteration as a result of physical, chemical, or biological influences, such altered or neoantigens may elicit an immune response. Neoantigens can arise in a variety of ways. Physical agents such as irradiation may cause antigenic alteration. Several chemicals, including drugs may combine with cells and tissues and alter their antigenic nature. The various mechanisms of autoimmune diseases is listed are as follows:

1. *By pass of helper T-cell tolerance:* Tolerance of CD4+ helper T cell is critical to the prevention of autoimmunity. Therefore, tolerance may be broken if the helper T cells is bypassed or substituted.⁶
2. *Emergence of sequestered antigen:* The induction of tolerance requires interaction between the antigen and the immune system. Thus any self-antigen that is completely sequestered during development is likely to be viewed as foreign if introduced into circulation, and an immune response will develop. Spermatozoa, myelin basic protein and lens crystallin fall into this category of antigens.⁷
3. *Imbalance of suppressor helper T-cell function:* A loss of suppressor T cell function will contribute to autoimmunity and conversely, excessive T-cell help may drive B cells to extremely high levels of autoantibody production.⁶

4. *Microbial agents in autoimmunity:* A variety of microbes, including bacteria, mycoplasmas and viruses have been implicated in triggering autoimmunity. Microbes may trigger autoimmune reactions in several ways. First, viral antigens and autoantigens may become associated to form immunogenic units and bypass T-cell tolerance. Second, some viruses (EBV) are nonspecific, polyclonal B-cell mitogens and may thus induce formation of autoantibodies. Third, viral infection may result in loss of suppressor T-cell function.⁷
5. *Molecular mimicry:* Several infectious agents cross react with human tissues and their haptenic determinants. The infecting microorganisms may trigger an antibody response by presenting the cross reacting haptenic determinants in association with their own carrier to which helper T cell are not tolerant. The antibody so formed may then damage the tissue that shares cross reacting determinants.⁶
6. *Polyclonal lymphocyte activation:* Several microorganisms and their products are capable of causing polyclonal (i.e. antigen nonspecific) activation of B cells. The best investigated among these is bacterial lipopolysaccharide (endotoxin), which can induce mouse lymphocyte to form anti-DNA, antithymocyte and anti-red cell antibodies *in vitro*.⁷

ENVIRONMENTAL TRIGGERS IN AUTOIMMUNE DISEASE

Autoimmune disorders may result from multiple interactions of genes and environmental factors. Even if inherit a genetic predisposition, the autoimmune disease will not occur unless there is an environmental trigger. There are several suspects in the search for triggers such as viruses, bacteria, diet, toxins, radiation, metal, estrogen, chronic infections, etc. Genetics accounts for about half of the risk of developing an autoimmune disease. The other half is the agent in the environment which triggers the process. In an individual with a susceptible genotype, exposure to environmental factors can act to initiate an autoimmune process.⁸

GENETIC FACTORS IN AUTOIMMUNITY

The different genes can increase susceptibility to autoimmune diseases. Established genetic risk factors include genes encoding histocompatibility molecules, complement proteins, immunoglobulins, peptide transporter proteins, and genes controlling the production of sex hormones. Each factor may independently enhance the immunogenicity of autoantigens, either by increasing their processing and presentation of B lymphocytes and macrophages or by increasing the chance for recognition by autoreactive T and B lymphocytes.⁹



NUTRITION AND AUTOIMMUNITY

Nutritional deficiencies can alter the immune response. Example, protein–energy malnutrition is widespread in developing countries and results in the functional impairment of T-cells, phagocytic cells and secretory immunoglobulin A antibody response, as well as reduced levels of several complement components. Other impairments of immune function have been reported for moderate deficiencies of trace minerals (such as zinc) and vitamins (particularly A and D).¹⁰

APOPTOSIS AND AUTOIMMUNITY

Apoptosis Greek word means ‘falling of leaves from trees and defined scientifically as programmed cell death. Apoptosis is essential to regulate and maintain tissue growth and maintain homeostasis. Dying cells undergo morphological modifications including chromatin condensation, nuclear fragmentation and generation of apoptotic bodies. Furthermore, they express so called ‘eat-me’ signals on the cell surface that allow macrophage recognition and phagocytosis. Clearance of apoptotic cells is fundamentally important, since otherwise apoptotic cells tend to become secondary necrotic, release intracellular contents, and provoke inflammation and autoimmunity. Within the immune system alone, it has been estimated that more than 109 cells undergo apoptosis daily and these are cleared rapidly by neighboring tissue cells or professional phagocytes, normally without inciting an inflammatory reaction. Indeed, the most significant difference between phagocytosis of pathogens and the uptake of apoptotic cells has been traditionally considered the immune response. A proinflammatory reaction is often induced after phagocytosis whereas the secretion of anti-inflammatory cytokines follows the engulfment of apoptotic cells.¹¹

It is found that autoantigens are found within apoptotic bodies and that apoptotic cells are critical in the presentation of antigens, activation of innate immunity and regulation of macrophage cytokine secretion.

THE CONSEQUENCES OF APOPTOSIS IN AUTOIMMUNE DISEASES

Three different processes involving apoptotic cells have been demonstrated to be related to the development of autoimmunity: (1) apoptosis is the mode of cell killing

by immune processes, e.g. cytotoxic T lymphocyte; it can make autoantigens available for self-perpetuating disease. (2) Apoptosis in excess can be a source of autoimmunogenic fragments. (3) Genetic faults in apoptosis pathways, prototypically Fas/FasL, can interfere with deletion of lymphocytes and facilitate autoimmunity; a typical example of this is the autoimmune Lymphoproliferative syndrome.¹¹

CONCLUSION

Autoimmunity is the mechanism where an organism fails to recognize its own constituent parts (down to the sub-molecular levels) as ‘self’, which results in an immune response against its own cells and tissues. Any disease that results from such an aberrant immune response is termed an autoimmune disease. Autoimmune diseases generally have varied systemic manifestations. The disease process may affect any organ system in the body and create physical, psychological, social and economical disability in the patient. This is an attempt to review the available literature on pathogenesis of autoimmune diseases.

REFERENCES

1. Ananthanarayanan R, Jayaram CK. Paniker’s text book of microbiology, 7th ed. 70-79.
2. De Lisa Fair-weather. Autoimmune disease mechanisms. Encyclopedia of life sciences 2007;p. 1-6.
3. Kasper, Braunwald, Sanci, Houser, Longo, Jameson. Harrison’s principles of internal medicine. 16th ed. McGraw Hill Medical 2003;2:471-477.
4. Environmental health criteria 236 principals and assessing methods of autoimmunity associated with exposure to chemicals. World Health Organization p. 1-70.
5. Dennis R, Gonagle MC, Mcdermott MF. A proposed classification of immunological diseases research in translation PLOS Medicine 2006 Aug 3(8):1243-1248.
6. Kumar, Abbas, Robbins F, Cotran. Pathologic basis of disease, 5th ed, Aster Saunders Elsevier, Philadelphia, USA: 120-136.
7. Kumar, Abbas, Robbins F, Cotran. Pathologic basis of disease, 7th ed, Aster Saunders. Elsevier, Philadelphia USA: 171-189.
8. Carson DA. Genetic factors in the etiology and pathogenesis of autoimmunity. The FASEB Journal 1992 July;6: 2800-2805.
9. Davidson A. Autoimmune diseases. N Eng Med 2001;340-345.
10. Selmi C, Tsuneyama K. Nutrition, geoeidemiology, and autoimmunity. Autoimmunity reviews 9;2010: A267-A270.
11. Lleo T, Selmi C, Invernizzi P, Podda M, Gershwin ME. The consequences of apoptosis in autoimmunity. Journal of Autoimmunity 2008;31:257-262.