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An Update Review on Autoimmune Disease

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Abstract--- *Autoimmune diseases are the pathological conditions which are identified by the abnormal autoimmune responses and characterized by the reactivity of the immune system by auto-antibodies and T-cell responses to self-molecules. Rheumatoid arthritis, vasculitis and systemic lupus erythematosus (lupus) are some other severe autoimmune disorders. Human autoimmune diseases (AD) frequently occur (in general, affecting higher than 5% of the world's population) and put a major burden on the human population of morbidity and mortality. AD is characterized as diseases in which the immune response to particular self-antigens leads to the ongoing damage to the tissue that occurs in that state. ADs can either be tissue-specific (e.g., thyroid, pancreatic β-cells), aimed at particular tissue-specific antigens, or even more systemic affecting several tissues, and targeting a range of seemingly widely expressed autoantigens. Autoimmune diseases are some of the leading causes of death and injury in females below the age of 65. Autoimmune disease development depends on a combination of the environmental and genetic factors. A more practical distinction distinguishes between disorders in which the proliferation, death or regulation of T or B cells is normally altered and those in that an aberrant reaction to a single antigen, whether self-related or foreign, induces autoimmunity.*

Keywords--- *Autoimmune Diseases, Autoimmunity, Autoantibodies, Autoantigens, B Cells, Pathological Conditions, T-Cell, Tissue-Specific.*

I. INTRODUCTION

Autoimmune disease is a disorder triggered by the immune system, which initiates an attack on self-molecules owing to deterioration of immunological tolerance towards auto-reactive immune cells. The initiation of the attacks on body's self-molecules in autoimmune diseases is unknown in most cases, but several studies indicate that they are significantly associated with the factors such as infections, genetics, and/or environment[1]. An immune system is a strictly regulated biological mechanism which identifies and responds to antigens from different foreign substances found in the body of an organism, and reacts to these potential pathological threats by producing certain types of lymphocytes such as white blood cells and antibodies capable of destroying or neutralizing various poisons, germs and other foreign agents. The immune system typically is able to differentiate the foreign agents from healthy cells and tissues of the organism itself[2]. On the other hand, autoimmunity defines a diseased situation where an organism does not recognize its own cells and tissues, thus allowing the immune system to trigger the response against its own components. Autoimmune diseases are the pathological conditions which are identified by the abnormal autoimmune responses and are described by reactivity of the immune system by auto-antibodies and T-cell responses to self-molecules[3]. Autoimmune diseases arise when the normal control process is disrupted, thereby causing the device to

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fail and invade healthy tissues and cells. Type I diabetes is a common example of autoimmune disease, affecting nearly a millions of people around the globe. It is a situation in which pancreas due to the autoimmune degradation of the insulin-producing pancreatic cells does not produce enough insulin to control the blood sugar levels. Rheumatoid arthritis, vasculitis and systemic lupus erythematosus (lupus) are some other common autoimmune disorders[1], [3].

I.I The Autoimmunity and Immune System

Immunology is the science dealing with the response of the body to antigenic challenge. Traditionally, the term "immunity" refers to the resistance that the host exhibits to microorganisms and their products causing injury. Immunity can be natural (native) or acquired (adaptive) immunity, of different types[4]. Immunity is a very specific scientific discipline that includes principle processes in shielding the body from infectious agents, but it can also affect the host organism through autoimmunity. Autoimmunity is the mechanism in which an organism fails to acknowledge its own constituent parts as "self" (down to the submolecular levels), resulting in an immune response to its tissues and cells[5]. Every disorder arising from such an abnormal immune response is considered an autoimmune disease.

Autoimmunity is described by the immune system's response to cells (auto-reactive T-lymphocytes) or substances (autoantibodies) to its own antigens (autoantigenes). It could be part of physiological immune response (natural autoimmunity) or pathologically mediated, that may probably lead to psychiatric anomalies (autoimmune disease). However, following Rose's finding, more than a decade has elapsed since autoimmunity became a generally accepted precept; the damage has been done[1], [4]. The time it took for the scientific community to completely accept the the reality of autoimmunity has postponed the translation of its discoveries into the medical knowledge, with serious implications in the modern epidemiological treatment of autoimmune diseases proving to be a possible factor in reducing cancer incidence by flexible CD8+ IT cells, which destroy target self-cells by releasing cytokines capable of enhancing target cell susceptibility to cytotoxicity, or by secreting the chemokines that attract certain immune cells to the autoimmune location[3], [5].

I.II Autoimmune Diseases

Human autoimmune diseases (AID) frequently occur (in total, affecting more than the 5% of world's population) and place a substantial burden on human population of mortality and morbidity. AD is defined as diseases where the immune response to specific self-antigens contributes to the ongoing damage to the tissue that occurs in that condition[6]. ADs can either be tissue-specific (e.g., thyroid, pancreatic Iβ-cells), targeted at unique tissue-specific antigens, or more systemic, affecting multiple tissues, and targeting a variety of reportedly commonly expressed autoantigens. The etiology of the autoimmune diseases was challenging to elucidate. Many influences, including genetics and environment, are believed to contribute to the development of an autoimmune response[5], [6].

Many specific autoimmune diseases, e.g. systemic lupus erythematosus, rheumatoid arthritis, and multiple sclerosis, are genetically linked to distinct category II molecules of a major human histocompatibility complex (MHIC) and other immune modulators. In addition, autoimmunity frequently clusters families, indicating the potential for a broad-spectrum genetic defect in mechanisms of immunological tolerance[7]. Nonetheless, the genetic factors which lead to the formation of tissue and/or organ-specific immune responses against specific antigens remain largely unidentified[6].

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Infections have been involved among the environmental factors in the development and/or onset of autoimmunity.

I.III Classification of Autoimmune Diseases

Among physicians, autoimmune diseases tend to be either chronic (like systemic lupus erythematosus) or organ-specific (like type 1 diabetes mellitus). Such distinction, while scientifically useful, may not necessarily represent a disparity in causation[8]. A more practical distinction distinguishes between disorders in which there is a general modification in the proliferation, control or death of T or B cells and those in which an aberrant reaction to a single antigen, self or foreign triggers autoimmunity[6], [8]. An example of a common defect is the lack of Fas protein or its receptor–proteins implicated in cell death–and a common antigen-specific deficiency is demyelination syndrome after Campylobacterjejuni enteric infection. This distinction is helpful when agreeing on treatment, which may vary depending on the pathogenic pathway[2], [5]. Changes that lower the survival threshold and activation of self-reactive B cells also cause multiple autoantibodies to be formed, such as antinuclear and anti-DNA antibodies in systemic lupus erythematosus. In all men, low levels of those autoantibodies are the norm. Genetic alterations in the activity of regulating T cells or cytokine development with global consequences also contribute to inflammatory bowel disease. More than 80 autoimmune diseases have been reported[9].

ADs have historically been defined as organ systemic or specific or both (Table 1)[3]. The organ-specific ADs may be examples of natural immune responses which cause disease since they are “misdirected” against an organ or self-antigen. In comparison, several organs are targets for immune attack in systemic ADs, and typically there is persistent activation of innate and adaptive immune cells[6]. The prototypical structural AID is known to be SILE. It should be remembered, however, that perhaps the classification of an AID as organ-specific or systemic is largely based on medical findings, instead of the self-antigen expression pattern that tends to be targeted in attack. Table 1&2[8]

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Table 1: Organ-Specific Autoimmune Diseases

Organ	Diseases	Self-antigen	Major Autoimmune Mechanism
Adrenal cells	Addison's disease	Cytochrome P-450 antigens	Autoantibodies
Blood cells	Autoimmune hemolytic anemia	Red blood cell membrane proteins	Autoantibodies
Pleatlets	Idiopathic thrombocytopenic purpura	Platelet antigens (GP IIb/IIIa)	Autoantibodies
Stomach	Pernicious anemia	Gastric parietal cell antigens (H+/ATPase, intrinsic factor)	Autoantibodies /T cells
Small bowl	Celiac sprue (gluten enteropathy)	Transglutaminase	Autoantibodies /T cells
Hepatocytes	Autoimmune hepatitis	Hepatocyte antigens (cytochrome P450 2D6)	Autoantibodies
Muscle	Myasthenia gravis	Acetylcholine receptors	Autoantibodies /T cells
Bile duct cells	Primary biliary cirrhosis	Intrahepatic bile duct (pyruvate dehydrogenase complex protein)	Autoantibodies
Heart	Rheumatic heart disease	Myocardial antigens	Autoantibodies
Kidney/lungs	Good pasture's syndrome	Basement membrane antigens (type IV collagen α3 chain)	Autoantibodies

Table 2: Systemic Autoimmune Diseases

Diseases	Self-antigen	Major Autoimmune Mechanism
Ankylosing sponkylitis	Vertebrae	Immune complexes
Rheumatoid arthritis	Connective tissue, IgG	Auto-antibodies, immune complexes
Multiple sclerosis	Brain or white matter	TH1 cells and TC cells, autoantibodies
Systemic lupus erythematosus	DNA, nuclear protein, RBC and platelet membranes	Auto-antibodies, immune complexes
Scleroderma	Nuclei, heart, lungs, gastrointestinal tract, kidney	Auto-antibodies

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I.IV Women and Autoimmune Diseases

About one-third of the likelihood of developing an autoimmune disease may be related to genetic factors, particularly gender. Females account for about 75 per cent of the estimated 25 million people living with autoimmune diseases and autoimmune diseases are some of the major causes and injury in females below the age of 65[10]. In several cases, such as rheumatoid arthritis, multiple sclerosis, and myocarditis, autoimmune disease can be experimentally caused by adjuvant self-antigen administration (myelin base protein, collagen, and cardiac myosin, respectively)[10]. A high prevalence of women is an important theme which unifies autoimmune diseases.

Conservative estimates show that women account for 7 million or 79 per cent of people with autoimmune diseases[7]. Whereas the relationship between gender and the prevalence of autoimmune disorders remains unknown, researchers have observed that when their immune systems are triggered women have higher levels of antibodies and mount greater inflammatory responses than men, potentially increasing the risk of autoimmunity[1], [8], [10]. Autoimmune diseases fluctuate according to hormonal changes like menstrual cycle, pregnancy, menopause, aging, and use of pills for birth control. Autoimmune diseases often fluctuate along racial lines, as two gene variants have been identified that are associated with increased lupus incidence in women.

I.V Genetic Risk Factors

Autoimmune disease development depends on genetic and environmental factors combination. Many autoimmune diseases are considered to be polygenic and involve more than one gene. Familial clustering occurs, and in monozygotic twins the concordance risk for autoimmune disease is greater than in dizygotic twins[2]. Several autoimmune diseases, like autoimmune lymphoproliferative syndrome, and autoimmune polyglandular endocrinopathy syndrome with candidiasis and ectodermal dysplasia, was triggered by single-gene mutations. Even under these circumstances, certain mutations change the nature of the disorder and not everyone who carries the mutant gene experiences the illness[6]. The bulk of autoimmune diseases are multigenic, with multiple genes with resistance acting together to generate the phenotype. The polymorphisms often generally occur in normal people, and are associated with natural immune function[5], [11]. They only contribute to the autoimmunity when present with other susceptibility genes. Some of these genes carry a much higher level of risk than others; so, for example, the great complex of histocompatibility makes a significant contribution to the vulnerability to disease. Many autoimmune diseases are associated with HLA molecules of a particular class I or II[11].

I.VI Environmental Factors

Environmental factors may have different roles for the promotion, causation or modification of autoimmune diseases. If, and when various environmental factors contribute to an autoimmune disease, they may well decide the occurrence of illness, the type of initial symptoms, or be a determinant of whether an autoimmune disease found within a person may arise at all[12].

Pathological and environmental factors play a role in the development or exacerbation of certain autoimmune disorders, in addition to genetic factors. For example, the result of a human gene that gives susceptibility to the “Crohn's disease” identifies components of certain microbes, and as causes of type 1 diabetes, viral infections have long been hypothesized for[13]. Conversely, other research suggests that viral infections reduce the number of

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controlled T cells that normally hold potentially destructive immune responses in place. Exposure to different synthetic chemicals and metals may also improve the vulnerability of autoimmune diseases when inducing autoimmune disease. Metals typically inhibit proliferation and activation of immune cells; for example, mercury, gold, and silver may cause proliferation of lymphocytes, and corresponding autoimmunity[11], [12]. A wide variety of synthetic chemicals may result in estrogenic or antiestrogenic activity, including hormone supplementation, pesticides, hormone blockers, insecticides, fungicides, and foods and herbal products.

I.VII Pathogen responses and autoimmunity

The potential of the host to protect against invasive pathogens is primarily regulated by a group of germline-encoded receptors defined as pattern-recognition receptors (PRIRs). These molecules involve Toll-like receptors (TLIR), (RIIG-I)-like helicases, nucleotide-binding and oligomerization domain (NOID)-like receptors (NILR), and a subset of C-type lectin receptors that together identify a huge number of molecular patterns present in viruses, bacteria and fungi[14].

I.VIII Pathogenesis of Autoimmune Disease

The autoimmune disease may involve multiple arms of immune system. Antigens are absorbed by antigen presenting cells (AIPCs) like dendritic cells (DCs) and converted into peptides that are loaded upon MHC molecules for the presentation to T cells via clonotypic T cell receptors (TCRs). Cytolytic TI cells (Tc, activated on AIPC by MHC class I) can lysis a target directly, whereas T Ihelper cells (Th, activated by MIHC class II) release cytokines that may have immediate effects or trigger monocytes, macrophages, and B cells[15]. B cells itself have surface receptors capable of binding antigens to the surface. B cells secrete antibodies specific to the antigens once they receive signals from Th cells[8], [15]. Antibody can bind its specific target alone, or can simultaneously bind to and activate macrophages via the Fc receptor. Different pathways have been identified to understand how pathogens may cause autoreactive T cell activation and vital expansion and start autoimmune disease[13].

A microbial antigen may include a structurally similar epitope to an autoantigen epitope, which provides the fundamental element of the mechanism called molecular mimicry. Another pathway would suggest that T-cell growth factors in inflammatory environment and paracrine secretion cause the proliferation of activated autoreactive T-cells, whose small number was historically inadequate to trigger an autoimmune disease. The activation of such a system is called bystander activation[12], [14], [15]. Inflammation of the pathogen-induced tissue can result in local activation of APC and increased self-antigens presentation/processing that triggers T-cell priming, followed by the T-cell activation and expansion of the additional particularities (epitope spreading). Activation of autoreactive resting T cells can be achieved by viral and bacterial superantigens, which bind a range of MHC class II molecules and trigger huge numbers of T cells, regardless of their specificity[15].

II. CONCLUSION

Because treatments for most autoimmune disorders are presently unavailable, patients often face a lifetime of exhausting symptoms, loss of tissue and organ function and higher medical costs. For many autoimmune disorders, the aims of the medications are to reduce chronic effects and lower the level of activation of the immune system

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while maintaining the ability of the immune system to combat foreign pathogens. Treatments vary widely and depend on the particular illness and symptoms. For example, those suffering from Type I Diabetes must replenish their insulin levels, normally by injection. In autoimmune diseases such as type I diabetes, patients might need supplementation to provide body lacking hormone or vitamin. Unless the autoimmune disorder affects the blood or circulatory system either directly or indirectly, such as lupus, autoimmune hemolytic anemia (AIHA), and anti-phospholipidal antibody syndrome (AAS), patients might need blood transfusion. For autoimmune disorders involving the limbs, joints, or muscles, such as rheumatoid arthritis and multiple sclerosis (MS) patients often need assistance maintaining movement or treatment to relieve discomfort and reduce inflammation for affected areas.

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