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ISSN:2394-2371
CODEN (USA):IJPTIL

UNDERSTANDING AUTOIMMUNE DISEASE: AN UPDATE REVIEW

Shashi Pratab Singh[1]*, Pranay Wal[1], Ankita Wal[1], Vikas Srivastava[2], Ratnakar Tiwari[2], Radha Dutt Sharma[2]

Pranveer Singh Institute of Technology, Kanpur- 209305, U.P., India
Indian Institute of Toxicology Research, CSIR, Lucknow-226001, U.P., India

ABSTRACT

Autoimmune diseases are pathological conditions identified by abnormal autoimmune responses and characterized by auto-antibodies and T-cell responses to self-molecules by immune system reactivity. Some other common autoimmune disorders include rheumatoid arthritis, systemic lupus erythematosus (lupus), and vasculitis. Human autoimmune diseases (AD) occur frequently (affecting in aggregate more than 5% of the population worldwide), and impose a significant burden of morbidity and mortality on the human population. AD are defined as diseases in which immune responses to specific self-antigens contribute to the ongoing tissue damage that occurs in that disease. ADs may be either tissue-specific (e.g., thyroid, β-cells of the pancreas), where unique tissue-specific antigens are targeted, or may be more systemic, in which multiple tissues are affected, and a variety of apparently ubiquitously expressed autoantigens are targeted. Women account for about 75% of the estimated 23.5 million people in America afflicted by autoimmune diseases, and autoimmune diseases constitute some of the leading causes of death and disability in women below 65 years of age. The development of autoimmune diseases depends on a combination of genetic and environmental factors. Most autoimmune diseases are thought to be polygenic, involving more than one gene. For clinicians, autoimmune diseases appear to be either systemic (e.g. systemic lupus erythematosus) or organ-specific (e.g. Type 1 diabetes mellitus). This classification, although clinically useful, does not necessarily correspond to a difference in causation. A more useful division distinguishes between diseases in which there is a general alteration in the selection, regulation or death of T cells or B cells and those in which an aberrant response to a particular antigen, self or foreign, causes autoimmunity. Antigens are taken up by antigen presenting cells (APC) such as dendritic cells (DC) and processed into peptides which are loaded onto MHC molecules for presentation to T cells via clonotypic T cell receptors (TCR).

Keywords: - Autoimmune diseases, T-cell, B cells, Auto-antibodies, Autoantigens.

INTRODUCTION

Autoimmune disease is a condition which is triggered by the immune system initiating an attack on self-molecules due to the deterioration of immunologic tolerance to auto-reactive immune cells.[1] Smith and Germolec state that "autoimmune disorders affect approximately 3% of the North American and European

***Corresponding Author:**
Shashi Pratab Singh, Research Scholar
Pranveer Singh Institute of Technology,
Kanpur- 209305, U.P., India
E.Mail: shashipratapsingh111@gmail.com
Article Published: July-Sept 2016

populations, >75% of those affected being women." The initiation of attacks against the body's self-molecules in autoimmune diseases, in most cases is unknown, but a number of studies suggest that they are strongly associated with factors such as genetics, infections and /or environment.[1] An immune system is a highly regulated biological mechanism that identifies and reacts to antigens from various foreign substances found in an organism's body and reacts to these possible pathological threats by producing certain types of lymphocytes such as white blood cells and antibodies that have the ability to destroy or neutralize various germs, poisons and other foreign agents.[2] Typically, the immune system is able to distinguish the foreign agents from the organism's own healthy cells and tissues. Autoimmunity, on the other hand, describes a diseased condition in which an organism fails to recognize its own cells and tissues, thereby enabling the immune system to trigger a response against its own components.[2]

Autoimmune diseases are pathological conditions identified by abnormal autoimmune responses and characterized by auto-antibodies and T-cell responses to self-molecules by immune system reactivity.[3] Autoimmune diseases occur when there is interruption of the usual control process, thereby allowing the system to malfunction and attack healthy cells and tissues.[4] A common example of autoimmune disease is Type I Diabetes, which affects nearly a million people in the United States. It is a condition in which the pancreas does not produce enough insulin to control sugar blood levels due to the autoimmune destruction of the insulin-producing pancreatic cells.[5] Some other common autoimmune disorders include rheumatoid arthritis, systemic lupus erythematosus (lupus), and vasculitis.[4]

The Immune System and Autoimmunity

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 mechanism are involved in the protection of the body against infectious agent but they can also damage host organism called as autoimmunity.[6] 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.[7]

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).[8] Yet, despite Rose's discovery, over a decade passed before autoimmunity became a commonly accepted precept; the damage was done. The time it took the scientific community to fully accept the growing reality of autoimmunity has delayed the translation of its findings into medical knowledge, with grave implications in current epidemiological diagnosis of autoimmune diseases demonstrated to be a possible factor in reducing incidence of cancer through versatile CD8+ T cells, which kill target self-cells by releasing cytokines capable of increasing the susceptibility of target cells to cytotoxicity, or by secreting chemokines that attract other immune cells to the site of autoimmunity.[9]

Autoimmune Diseases

Human autoimmune diseases (AD) occur frequently (affecting in aggregate more than 5% of the population worldwide), and impose a significant burden of morbidity and mortality on the human population.[10] AD are defined as diseases in which immune responses to specific self-antigens contribute to the ongoing tissue damage that occurs in that disease. ADs may be either tissue-specific (e.g., thyroid, β-cells of the pancreas), where unique tissue-specific antigens are targeted, or may be more systemic, in which multiple tissues are affected, and a variety of apparently ubiquitously expressed autoantigens are targeted.[11] The etiology of autoimmune diseases has been difficult to elucidate. Several factors are thought to contribute to the development of immune response to self, including genetics and environment.[12-14]

Several common autoimmune diseases, such as rheumatoid arthritis, systemic lupus erythematosus and multiple sclerosis, are genetically linked to distinct human major histocompatibility complex (MHC) class II molecules and other immune modulators. Furthermore, autoimmunity often clusters families, indicating the potential for a broad-spectrum genetic defect in immunological tolerance mechanisms. However, the genetic factors leading to the development of immune responses against specific antigens in a tissue and/or organ-specific manner remain largely unknown. Among the environmental factors, infections have been implicated in the onset and/or promotion of autoimmunity.[15]

Classification of Autoimmune Diseases

For clinicians, autoimmune diseases appear to be either systemic (e.g. systemic lupus erythematosus) or organ-specific (e.g. Type 1 diabetes mellitus). This classification, although clinically useful, does not necessarily correspond to a difference in causation. A more useful division distinguishes between diseases in which there is a general alteration in the selection, regulation or death of T cells or B cells and those in which an aberrant response to a particular antigen, self or foreign, causes autoimmunity. An example of a general defect is the absence of the Fas protein or its receptor- proteins involved in cell death- and a representative antigen specific disorder is the demyelination syndrome that follows enteric infection Campylobacterjejuni. This classification is useful in deciding on therapy, which may differ according to the pathogenic mechanism. Alterations that lower the threshold for the survival and activation of autoreactive B cells often cause the production of multiple autoantibodies, as in the case of the antinuclear and anti-DNA antibodies in systemic lupus erythematosu.[16-19] Low levels of these autoantibodies are the rule in all people. Genetic alterations with .global effects on the function of regulatory T cells or cytokine production often leads to inflammatory bowel disease.[20,21] There are more than eighty identified autoimmune diseases.[22]

ADs traditionally have been categorized as organ specific or systemic or both (Table 1). The organ-specific ADs may represent examples of normal immune responses that produce disease because they are “misdirected” against a self-antigen or organ. By contrast, in systemic ADs, multiple organs are targets for immune attack, and chronic activation of innate and adaptive immune cells is usually present. SLE is considered to be the prototypic systemic AD. However, it should be noted that the categorization of an AD as organ-specific or systemic is based primarily on clinical observations rather than the expression pattern of the self antigen that appears to be targeted in the attack.[30] Table1&Figure1.

Women and Autoimmune Diseases

Approximately one-third of the risk of developing an autoimmune disease can be attributed to heritable factors, especially gender. Women account for about 75% of the estimated 23.5 million people in America afflicted by autoimmune diseases, and autoimmune diseases constitute some of the leading causes of death and disability in women below 65 years of age.[23,24] In several instances, such as rheumatoid arthritis, multiple sclerosis, and myocarditis, the autoimmune disease can be induced experimentally by administering self-antigen in the presence of adjuvant (collagen, myelin basic protein, and cardiac myosin, respectively).[25]An important unifying theme

in autoimmune diseases is a high prevalence in women. (Figure- 2)[26,27]

Conservative estimates indicate that 6.7 million or 78.8% of the persons with autoimmune diseases are women.[26] While the relationship between sex and prevalence of autoimmune disorders remains unclear, researchers have noted that women have higher levels of antibodies and mount larger inflammatory responses than men when their immune systems are triggered, possibly increasing the risk of autoimmunity.[23,24] Autoimmune diseases tend to fluctuate in accordance with hormonal changes, such as during pregnancy, menstrual cycle, menopause, aging and usage of birth control pills.[23] Autoimmune diseases fluctuate by racial lines as well, since two gene variants were found that are related to an increased risk of lupus among African American women.[28]TABLE-2[29].

Genetic Risk Factors

The development of autoimmune diseases depends on a combination of genetic and environmental factors. Most autoimmune diseases are thought to be polygenic, involving more than one gene. There is familial clustering, and the rate of concordance for autoimmune disease is higher in monozygotic twins than in dizygotic twins.[31-33] A few autoimmune diseases, such as autoimmune lymphoproliferative syndrome and the syndrome of autoimmune polyglandular endocrinopathy with candidiasis and ectodermal dysplasia (APECED), are due to mutations in single gene. Even in these conditions, other genes modify the severity of disease and not all who possess the mutant gene manifest the disease. Most autoimmune diseases are multigenic, with multiple susceptibility genes working in concert to produce the phenotype. In general, the polymorphisms also occur in normal people and are compatible with normal immune function. Only when present with other susceptibility genes do they contribute to autoimmunity.[34,35] Some of these genes confer a much higher level of risk than others; for e.g. the major histocompatibility complex makes an important contribution to disease susceptibility. Most autoimmune diseases are linked to a particular class I or II HLA molecules[36]

Environmental Factors

Environmental factors may have various roles in promoting, causing or modifying autoimmune diseases. If, and when specific environmental factors contribute to autoimmune diseases, they may well determine the onset of illness, the nature of initial manifestations, or be a determining factor on whether an autoimmune disease contained within an individual might occur at all.[37]

Besides genetic factors, pathological and environmental factors play a role in initiating or exacerbating certain autoimmune disorders. For example, the product of a human gene that confers susceptibility to Crohn's disease recognizes components of certain bacteria, and viral infections have long been suspected as triggers of Type 1 Diabetes. Conversely, other research suggests that the numbers of regulatory T cells that normally hold potentially destructive immune responses in check are reduced by viral infections . Exposure to various synthetic chemicals and metals in the initiation of autoimmune disease may also increase susceptibility to autoimmune disorders. Generally, metals inhibit immune cell proliferation and activation; mercury, gold, and silver, for example, can induce lymphocyte proliferation and subsequent autoimmunity. A broad range of synthetic chemicals, including hormone supplementation, hormone blockers, pesticides, insecticides, fungicides, and food and herbal products, may elicit estrogenic or anti-estrogenic activity.[38]

Autoimmune Disease: Pathogenesis

Multiple arms of the immune system may be involved in autoimmune pathology. Antigens are taken up by antigen presenting cells (APC) such as dendritic cells (DC) and processed into peptides which are loaded onto MHC molecules for presentation to T cells via clonotypic T cell receptors (TCR). Cytolytic T cells (Tc, activated by MHC class I on APC) can directly lyse a target, while T helper cells (Th, activated by MHC class II) release cytokines that can have direct effects or can activate macrophages, monocytes and B cells. B cells themselves have surface receptors that can bind surface antigens. Upon receiving signals from Th cells, B cells secrete antibodies specific for the antigens. Antibody may bind its specific target alone or may bind to and activate macrophages simultaneously via the Fc receptor. Multiple mechanisms have been described to explain how pathogens might induce activation and critical expansion of autoreactive T cells and start autoimmune disease.[39-44]

A microbial antigen can include an epitope that is structurally similar to an autoantigen epitope, providing the basic element of the mechanism referred to as molecular mimicry.[45-50]

Another mechanism would imply that the inflammatory setting and the paracrine secretion of T cell growth factors induce the expansion of activated autoreactive T cells, whose small number was previously insufficient to drive an autoimmune disease. Such a mechanism is referred to as bystander activation.[51] Pathogen-induced tissue inflammation may result in local activation of APC and enhanced processing/presentation of self-antigens that causes T cell priming, followed by T cell

activation and expansion of additional specificities (epitope spreading) [52,53]. Activation of resting autoreactive T cells may be achieved by viral and bacterial superantigens that bind a variety of MHC class II molecules and activate large numbers of T cells, irrespective of their specificity.[54]

Pathogen responses and autoimmunity

The ability of the host to defend against invading pathogens is to a large extent mediated by a group of germline-encoded receptors known as pattern-recognition receptors (PRR). These molecules include Toll-like receptors (TLR), nucleotide-binding and oligomerization domain (NOD)-like receptors (NLR), (RIG-I)-like helicases and a subset of C-type lectin receptors, which together recognize a large number of molecular patterns present in bacteria, viruses and fungi.[55]

Molecular mimicry

Antigen recognition by the TCR allows T-cell activation by different peptides bound to one or even several MHC molecules [56]. The pathogen may carry elements that are similar enough in amino acid sequence or structure to self-antigen, so T cells that are activated in response to the pathogen are also cross-reactive to self and lead to direct damage and further activation of other arms of the immune system. Similarly, antibodies reflecting B-cell receptor specificity were found to recognize both microbial and self-antigens, this hypothesis is know as molecular mimicry.[57]

It is now generally accepted that a single T cell can respond to various distinct peptides, and that different peptide/MHC complexes can lead to cross-reactivity by the same TCR as long as the complexes have similar charge distribution and overall shape.[58-60]

Animal models in which molecular mimicry can trigger autoimmune disease are abundant. These include: Theiler's murine encephalomyelitis virus (TMEV)-induced demyelinating disease (TMEV-IDD), a model of human multiple sclerosis in which intracerebral TMEV infection of mice leads to an autoimmune demyelinating disorder 30-40 days after infection.[53] Mechanism by which pathogens may cause autoimmunity. a) Molecular mimicry describes the activation of crossreactive T cells that recognize both the pathogen-derived epitopes and the self-derived epitopes. Pathogen-derived epitops are taken up by APC and presented to T cells. Activation of T cells results in the direct lysis of self-tissue or release of cytokines and chemokines that activate macrophages, which mediate self-tissue damage, and provide help to pathogen-specific B cells. The subsequent release of self-tissue antigens and their uptake by APC perpetuates the autoimmune disease. b) Bystander activation is the nonspecific activation

of self-reactive T cells. Activation of pathogen-specific T cells leads to inflammation that damages self-tissue in an antigen non-specific manner, and triggers activation of self-reactive T cells. c) Epitope spreading involves a persistent pathogen infection that causes damage to self-tissue. This results in the release of self-peptides, which are engulfed by APC and presented to self-reactive T cells. Continual damage and release of self-peptides results in the spread of the self-reactive immune response to multiple self-epitopes.

FIGURE-3[61]

Treatments for Autoimmune Diseases

Since cures are currently unavailable for most autoimmune disorders, patients often face a lifetime of debilitating symptoms, loss of organ and tissue function, and high medical costs.[62] For many autoimmune disorders, the goals of treatments are to reduce chronic symptoms and lower the level of immune system activity while maintaining the immune system's ability to fight foreign contaminants. Treatments vary widely and depend on the specific disease and the symptoms. For example, those afflicted with Type I Diabetes must replenish their insulin levels, usually through injections. In autoimmune diseases like Type I Diabetes, patients may need supplements to provide a hormone or vitamin that the body is lacking. If the autoimmune disorder either directly or indirectly affects the blood or the circulatory system, such as autoimmune hemolytic anemia (AIHA), lupus, and antiphospholipidal antibody syndrome (AAS), patients may require blood transfusions. In autoimmune disorders that affect the bones, joints, or muscle, such as multiple sclerosis (MS) and rheumatoid arthritis, patients often require assistance to maintain mobility or medication to suppress pain and reduce inflammation in affected areas.[63]

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Table 1(A): 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
Thyroid	Hashimoto's thyroiditis	Thyroid cell antigens (e.g., thyroglobulin)	Autoantibodies
	Graves' disease	Thyroid-stimulating hormone receptor	Autoantibodies /T cells
Muscle	Myasthenia gravis	Acetylcholine receptors	Autoantibodies /T cells
Pancreatic islets	Type 1 diabetes	Beta cell antigens (glutamic acid decarboxylase, insulin)	Autoantibodies /T cells
Hepatocytes	Autoimmune hepatitis	Hepatocyte antigens (cytochrome P450 2D6)	Autoantibodies
Bile duct cells	Primary biliary cirrhosis	Intrahepatic bile duct (pyruvate dehydrogenase complex protein)	Autoantibodies
Heart	Rheumatic heart disease	Myocardial antigens	Autoantibodies
Kidney/lungs	Goodpasture's syndrome	Basement membrane antigens (type IV collagen α3 chain)	Autoantibodies

Table 1(B): Systemic Autoimmune Diseases

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

Table 2 Types of Autoimmune Diseases & Their Symptoms

Disease	Symtoms
Alopecia areata (Al-uh-PEE-shuh AR-ee-AYT-uh) The immune system attacks hair follicles (the structures from which hair grows). It usually does not threaten health, but it can greatly affect the way a person looks.	Patchy hair loss on the scalp, face, or other areas of your body
Autoimmune hepatitis The immune system attacks and destroys the liver cells. This can lead to scarring and hard-ening of the liver, and possibly liver failure	Fatigue, Enlarged liver, Yellowing of the skin or whites of eyes, Itchy skin, Joint pain, Stomach pain or upset
Antiphospholipid (an-teye-FOSS-foh-lip-ihd) antibody syndrome (aPL) A disease that causes problems in the	Blood clots in veins or arteries, Multiple miscarriages, Lacy, net-like red rash on the wrists

inner lining of blood vessels resulting in blood clots in arteries or veins.	and Knees
Celiac disease: A disease in which people can't tolerate gluten, a substance found in wheat, rye, and barley, and also some medicines. When people with celiac disease eat foods or use products that have gluten, the immune system responds by damaging the lining of the small intestines	Abdominal bloating and pain, Diarrhea or constipation., Weight loss or weight gain, Fatigue, Missed menstrual periods, Itchy skin rash, Infertility or miscarriages
Diabetes type 1 A disease in which your immune system attacks the cells that make insulin, a hormone needed to control blood sugar levels. As a result, your body cannot make insulin. Without insulin, too much sugar stays in your blood. Too high blood sugar can hurt the eyes, kidneys, nerves, and gums and teeth. But the most serious problem caused by diabetes is heart disease.	Being very thirsty, Urinating often, Feeling very hungry or tired, Losing weight without trying, Having sores that heal slowly, Dry, itchy skin, Losing the feeling in your feet or having tingling in your feet, Having blurry eyesight
Graves' disease (overactive thyroid) A disease that causes the thyroid to make too much thyroid hormone.	Insomnia, Irritability, Weight loss, Heat sensitivity, Sweating, Fine brittle hair, Muscle weakness, Light menstrual periods, Bulging eyes, Shaky hands, Sometimes there are no symptoms
Guillain-Barre (GEE-yahn bah-RAY) syndrome The immune system attacks the nerves that connect your brain and spinal cord with the rest of your body. Damage to the nerves makes it hard for them to transmit signals. As a result, the muscles have trouble responding to the brain	Weakness or tingling feeling in the legs that might spread to the upper body, Paralysis in severe cases Symptoms often progress relatively quickly, over a period of days or weeks, and often occur on both sides of the body.
Hashimoto's (hah-shee-MOH-tohz) disease (underactive thyroid) A disease that causes the thyroid to not make enough thyroid hormone	Fatigue, Weakness, Weight gain, Sensitivity to cold, Muscle aches and stiff joints, Facial swelling, Constipation
Hemolytic anemia (HEE-moh-lit-ihk uh-NEE-mee-uh) The immune system destroys the red blood cells. Yet the body can't make new red blood cells fast enough to meet the body's needs. As a result, your body does not get the oxygen it needs to function well, and your heart must work harder to move oxygen-rich blood throughout the body.	Fatigue, Shortness of breath, Dizziness, Headache, Cold hands or feet, Paleness, Yellowish skin or whites of eyes, Heart problems, including heart failure
Idiopathic thrombocytopenic purpura (id-ee-oh-PATH-ihk throm-boh-seye-toh-PEE-nik PUR-pur-uh) (ITP) A disease in which the immune system destroys blood platelets, which are needed for blood to clot.	Very heavy menstrual period, Tiny purple or red dots on the skin that might look like a rash, Easy bruising, Nosebleed or bleeding in the mouth
Inflammatory bowel disease (IBD) A disease that causes chronic inflammation of the digestive tract. Crohn's (krohnz) disease and ulcerative colitis (UHL-sur-uh-tiv koh-LEYE-tuhss) are the most common forms of IBD	Abdominal pain, Diarrhea, which may be bloody, Some people also have: • Rectal bleeding • Fever • Weight loss • Fatigue • Mouth ulcers (in Crohn's disease) • Painful or difficult bowel movements (in ulcerative colitis)
Inflammatory myopathies (meye-OP-uh-theez) A group of diseases that involve muscle inflammation and muscle weakness. Polymyositis (pol-ee-meye-uh-SYT-uhss) and dermatomyositis (dur-muh-toh-meye-uh-SYT-uhss) are 2 types more common in women than men.	• Slow but progressive muscle weakness beginning in the muscles closest to the trunk of the body. Polymyositis affects muscles involved with making movement on both sides of the body. With dermato-myositis, a skin rash comes before or at the same time as muscle weakness. May also have:• Fatigue after walking or standing • Tripping or falling • Difficulty swallowing or breathing
Multiple sclerosis (MUHL-tip-uhl sklur-OH-suhss) (MS)	• Weakness and trouble with coordination, balance, speaking, and walking

A disease in which the immune system attacks the protective coating around the nerves. The damage affects the brain and spinal cord.	• Paralysis • Tremors • Numbness and tingling feeling in arms, legs, hands, and feet • Symptoms vary because the location and extent of each attack vary
Myasthenia gravis (meye-uhss-THEEN-ee-uh GRAV-uhss) (MG) A disease in which the immune system attacks the nerves and muscles throughout the body	Double vision, trouble keeping a steady gaze, and drooping eye, Trouble swallowing, with frequent gagging or choking • Weakness or paralysis • Muscles that work better after rest • Drooping head • Trouble climbing stairs or lifting things • Trouble talking
Primary biliary cirrhosis (BIL-ee-air-ee sur-ROH-suhss) The immune system slowly destroys the liver's bile ducts. Bile is a substance made in the liver. It travels through the bile ducts to help with digestion. When the ducts are destroyed, the bile builds up in the liver and hurts it. The damage causes the liver to harden and scar, and eventually stop working.	Fatigue • Itchy skin • Dry eyes and mouth • Yellowing of skin and whites of eyes
Psoriasis (suh-REYE-uh-suhss) A disease that causes new skin cells that grow deep in your skin to rise too fast and pile up on the skin surface.	Thick red patches, covered with scales, usually appearing on the head, elbows, and knees • Itching and pain, which can make it hard to sleep, walk, and care for yourself May have:• A form of arthritis that often affects the joints and the ends of the fingers and toes. Back pain can occur if the spine is involved
Rheumatoid arthritis (ROO-muh-toid ar-THREYE-tuhss) A disease in which the immune system attacks the lining of the joints throughout the body	Painful, stiff, swollen, and deformed joints • Reduced movement and function May also have: • Fatigue • Fever • Weight loss • Eye inflammation • Lung disease • Lumps of tissue under the skin, often the elbows • Anemia

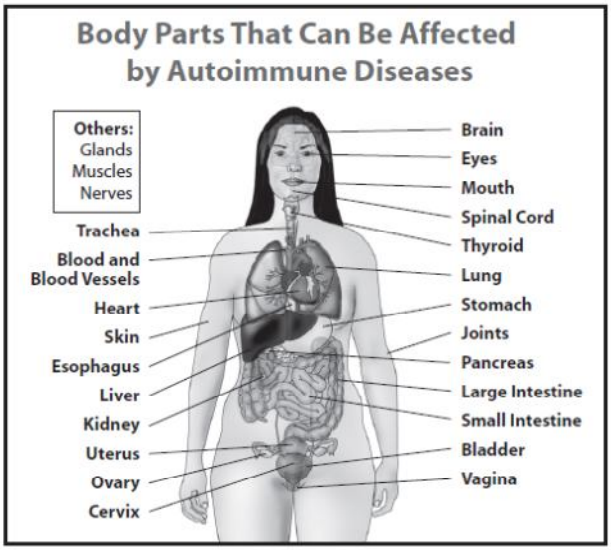

Figure 1: Possible body part affected with Autoimmune disease

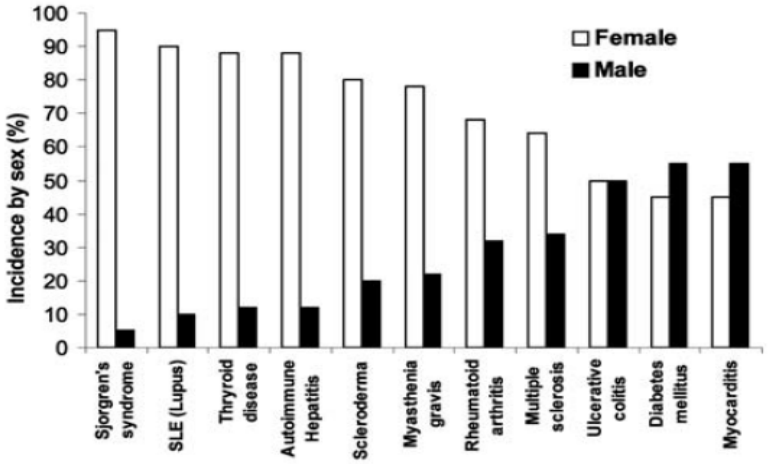

Figure 2: Autoimmune diseases comparison in Male and Female

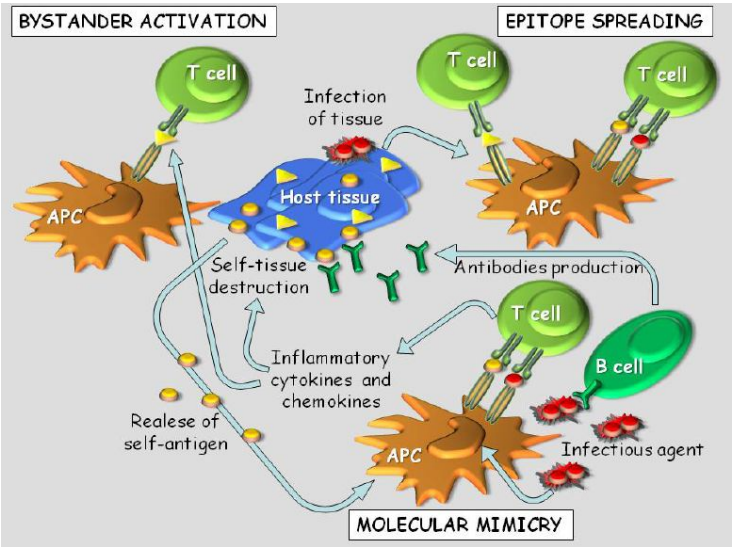

Figure 3: Autoimmune diseases Pathophysiology