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STUDY OF CURRENT AND EMERGING HUMAN AUTOIMMUNE DISEASES

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Abstract:

Immune system disorders cause abnormally low activity or over activity of the immune system. In cases of immune system over activity, the body attacks and damages its own tissues (autoimmune diseases). Immune deficiency diseases decrease the body's ability to fight invaders, causing vulnerability to infections. Some of the autoimmune disease are as follows rheumatoid arthritis, systemic lupus erythematosus (lupus), inflammatory bowel disease (IBD),multiple sclerosis (MS),Type 1 diabetes mellitus, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy, psoriasis.

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INTRODUCTION:

The diversity in immune system development is to fulfil the primary function of protecting hosts from the infectious agents. There are two major areas in which this pleiotropic immune system leads to pathology first is immune deficiency syndromes in which there is an inability of one or more components of the immune system to respond in a protective pattern to a pathogen, and secondly autoimmune diseases. The failure to distinguish self from nonself is often termed as tolerance and is the basis for autoimmune disease and the focus of this review. Historically, autoimmune diseases were considered to be rare but, through rigorous epidemiological studies, have now been shown to affect 3–5% of the population, with autoimmune thyroid disease and type I diabetes (T1D) being the most common of these conditions. However, more importantly, there are nearly 100 distinct autoimmune diseases, some of which are organ specific such as primary biliary cirrhosis (PBC) and some of which reflect a variety of immunological dysfunction involving multiple organs such as systemic lupus erythematosus (SLE). [1] In the past few years there have been significant advances in diagnosis and disease classification, as well as improvements in prognosis, achieved through both the development of technologies in molecular immunology and evidence-based clinical laboratory testing. Several key concepts should be introduced to understand immune tolerance, including central tolerance, peripheral energy, T regulatory cells (Tregs) and the homeostasis produced by cytokines and chemokines and their receptors. Central tolerance in the thymus and bone marrow plays a key role in shaping immune system homeostasis. In the thymus, developing lymphocytes undergo positive selection in the cortex before maturing and entering the circulation. While a healthy host, lymphocytes with potential reactivity against self-peptides are negatively selected and deleted in the thymic medulla. Importantly, after exiting the thymus, mature T cells are subjected to secondary selection (peripheral tolerance) by which the majority of self-reactive T cells are deleted or rendered anergy. In addition, if immature B cells express surface IgM that recognizes self cell-surface antigens, they are eliminated by a process known as clonal deletion or clonal anergy. Auto reactive B cells can escape deletion by a process known as receptor editing. Mature B cells are also under the control of peripheral tolerance.

The Epidemiology of Autoimmunity:

Autoimmune diseases are generally thought of as being relatively uncommon, but their effects on mortality and morbidity are significant. The overall prevalence of autoimmunity is approximately 3–5% in the general population.[2,3] A huge advances in the diagnosis and the treatment of autoimmune diseases, there is still clearance of data on the aetiological events that lead to clinical pathology.

Incidence and prevalence vary amongst the autoimmune diseases. The geo epidemiology becomes more complex when variations in age, gender, ethnicity and other demographic features are considered. Autoimmune diseases can occur at any age, but different diseases have their own characteristic age of onset. In almost all patients, the prevalence is increased in first-degree relatives and is even higher in monozygotic twins. [4] There is an increased frequency of autoimmune diseases in women, with a female-to-male ratio ranging from 10: 1 to 1: 1 [an exception is Crohn's disease, with a ratio of 1: 1.2]. The sex bias of autoimmunity has attracted enormous attention, but remains unresolved.

The Genetic Basis of Autoimmunity:

The majority of autoimmune diseases are not monogenic, but rather have multiple genetic factors that play a role. Although there have been a variety of early studies showing associations with the major histocompatibility complex (MHC) in human autoimmune diseases, the results have often have failed to lead to associations that have significant predictive strength for the clinician. The major histocompatibility complex is located on the short arm of chromosome 6 and genes encoding molecules involved in antigen presentation and therefore is critical in distinguishing self from nonself. In humans, the gene products of major histocompatibility complex are termed human leucocyte antigens (HLAs). A number of linkage studies have identified genetic variants associated with autoimmune diseases. [5]

The Environmental Influence of Autoimmunity:

The identification of specific environmental factors has critical importance for understanding individual susceptibility, but there are very few agents that clearly have a role and identification of generic risk factors remains unknown. These environmental factors include nutrition, the microbiota, infectious processes and xenobiotic, such as tobacco smoke, pharmaceutical agents, hormones, ultraviolet light, silica solvents, heavy metals, vaccines and collagen/silicone implants [57–59]. Infectious agents have long been the most well studied environmental factors. [6] The best example of a relation between infection and immunity is acute rheumatic fever, which occurs following exposure in genetically susceptible hosts to Streptococcus pyogenes. [7] The

mechanism of autoimmunity in acute rheumatic fever is thought to be 'molecular mimicry' between the bacterial M protein and human lysoganglioside that leads to loss of immunological tolerance and the development of cardiac reactive T cells. [8] The term 'molecular mimicry' was first coined by Damian in 1964, who suggested that selected antigenic determinants of microorganisms could potentially resemble host epitopes and were therefore capable of eliciting an autoimmune response. [9,10] Unlike autoantibodies, relevant (disease-associated) auto reactive T cells [11] act on the target tissue and circulate only at very low precursor levels. In other words, the auto reactive T-cell precursor level in the target tissue is much higher, often more than 100-fold in the target organ, than in the peripheral blood. Auto reactive cytotoxic T lymphocytes (CTL) recognize a target cell by binding the T-cell receptor (TCR) to the appropriate combination of major histocompatibility complex I and auto antigen-derived peptides. Then, a complex of major histocompatibility complex I and auto antigen-derived peptides directly kills target cells through different mechanisms:(i) secretion of cytotoxic granules (perforin and granzyme B) resulting in disintegration of the cell membrane and induced apoptosis; (ii) activation of Fas–Fas ligand, which induces apoptosis; and (iii) release of cytokines (such as TNF-a and interferon-c), leading to tissue injury. [12] The paradigm of Th1/Th2 balance has shifted due to the increasing body of information on other CD4 subsets, including Th17 [13], T regulating cells and T follicular helper cells (Tfh). [14,15]

New Approaches to Therapy:

The new paradigm in the treatment of autoimmune diseases is the use of biological agents that modify specific inflammatory and effector pathways. The agents that block TNF-a were the first drugs approved and since then drugs have been developed not only for the treatment of rheumatoid arthritis, but also for systemic lupus Erythematosus, psoriasis, psoriatic arthritis, inflammatory bowel disease, multiple sclerosis MS and many others. It is clear that the goal for treating patients with autoimmunity is a specific agent that will completely reverse if not cure the disease. At present, this does not exist for any autoimmune disease. By contrast, it is hoped that it would also be possible to modify the host immune system to restore tolerance. Although this is possible in selected mouse models of autoimmunity, it has not proven effective as yet in humans despite many attempts using immunotherapy, including stem cell therapies. However, our understanding of human autoimmune disease has and continues to be developed through a huge number of molecular studies investigating not only genetic factors, but also the role of epigenetics,[16]the environment, infection and the microbiota. In addition, there have been improvements in laboratory testing methods, including standardization of serology and development of new autoantibody tests. Further, improved understanding of geoepidemiology has led to a much better appreciation of what is happening to individual patients during a breach of tolerance. Autoimmunity is a challenge for all clinicians nevertheless, the prognosis for patients with these diseases has dramatically improved in the past decade and we anticipate further improvements in the future.

Autoimmune Lymphproliferative Syndrome (ALPS):

Autoimmune lymphoproliferative syndrome (ALPS) is a rare genetic disorder of the immune system first described by NIH scientists in the mid-1990s that affects both children and adults. In ALPS, unusually high numbers of white blood cells called lymphocytes accumulate in the lymph nodes, liver, and spleen and can lead to enlargement of these organs. ALPS can also cause anemia (low level of red blood cells), thrombocytopenia (low level of platelets), and neutropenia (low level of neutrophils, the most common type of white blood cell in humans). These problems can increase the risk of infection and hemorrhage.

Inflammatory Bowel Diseases (IBDs):

Inflammatory bowel diseases (IBDs), including Crohn's disease and ulcerative colitis, cause inflammation of the digestive system. Crohn's can affect any area from the mouth to the anus and often affects the lower part of the small intestine called the ileum. Ulcerative colitis leads to sores on the large intestine, or colon.

Crohn's Disease:

Crohn's disease is a chronic, or long lasting, disease that causes inflammation and irritation in your digestive tract. The most common symptoms of Crohn's disease are diarrhea, cramping and pain in your abdomen, and weight loss.

Multiple Sclerosis (MS):

Multiple sclerosis (MS) is a nervous system disease that affects the brain and spinal cord. Multiple sclerosis damages the myelin sheath, the material that surrounds and protects nerve cells. This damage slows down or blocks messages between the brain and other body parts, leading to the symptoms of multiple sclerosis.

Psoriasis:
Psoriasis is a chronic (long-lasting) disease in which the immune system works too much, causing patches of skin to become scaly and inflamed. Most often, psoriasis affects the:

- Scalp.
- Elbows.
- Knees.

The symptoms of psoriasis can sometimes go through cycles, flaring for a few weeks or months followed by times when they subside. Psoriasis, may have a higher risk of getting other serious conditions, including:

- Psoriatic arthritis.
- Heart attack or stroke.
- Mental health problems, such as low self-esteem, anxiety, and depression.

Rheumatoid Arthritis (RA):
Rheumatoid arthritis (RA) is a form of autoimmune inflammation that causes pain, swelling, stiffness and loss of function in your joints. Rheumatoid arthritis can affect any joint but is common in the wrists and fingers.

Systemic Lupus Erythematosus:
In lupus, the immune system attacks healthy cells and tissues by mistake. This can damage the joints, skin, blood vessels and organs. There are many kinds of lupus. The most common type, systemic lupus erythematosus, affects many parts of the body. Discoid lupus causes a rash that doesn't go away. Subcutaneous and cutaneous lupus causes sores after being out in the sun. Another type can be caused by medication. Neonatal lupus, which is rare, affects newborns.

Scleroderma:
Scleroderma means “hard skin” and refers to a group of diseases that cause abnormal growth of connective tissue. Connective tissue is the material inside the body that gives tissues their shape and helps keep them strong. In scleroderma, the tissue gets too hard or thick and can cause swelling or pain in the muscles and joints.

Type 1 Diabetes:
Diabetes means a person’s blood glucose, or blood sugar, levels are too high. In type 1 diabetes, the pancreas does not make insulin. Insulin is a hormone that helps glucose get into cells to provide energy. Without insulin, too much glucose stays in the blood. Over time, high blood glucose can lead to serious problems with the heart, eyes, kidneys, nerves, and gums and teeth. Type 1 diabetes happens most often in children and young adults but can appear at any age.

CONCLUSION:

An autoimmune disease is a condition in which your immune system mistakenly attacks your body. The immune system normally guards against germs like bacteria and viruses. When it senses these foreign invaders, it sends out an army of fighter cells to attack them. However the treatment of autoimmune disease are under research and new tools for the prognosis are being in development. The main reason for its occurrence is not well known are not diagnosed by the clinicians however the researches are done.

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