International Encyclopedia of Rehabilitation

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This publication of the Center for International Rehabilitation Research Information and Exchange is supported by funds received from the National Institute on Disability and Rehabilitation Research of the U.S. Department of Education under grant number H133A050008. The opinions contained in this publication are those of the authors and do not necessarily reflect those of CIRRIE or the Department of Education.

Autoimmune Diseases

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The body needs to protect itself to remain normal.

Unlike the earlier stages of evolution, when independent individual cells performed all activities, fewer protective mechanisms were necessary. As cells grouped themselves and developed into extremely complex systems such as human beings, there was increasing requirement for defense against virulent organisms was necessary. The immune system is one of the important ways in which foreign cells are identified and removed. When the immune system is faulty and begins to attack the body's own cells, autoimmunity develops and diseases resulting from this abnormal reaction are called autoimmune diseases.

Autoimmune diseases are common; some studies suggest that in USA between 10 and 50 million persons have an autoimmune disease. One does not know how exactly they are caused, but leads show that one's genetic susceptibility and environmental factors are both involved. As yet one can treat the symptoms of these diseases; they cannot be cured, like many other common inconveniencing though not immediately life-threatening diseases.

To identify the diseases and to find cures, one must understand how they develop in the first place.

When one looks back far into time, life began more than 3.5 billion years ago as single celled organisms. Organisms with many cells (multicellular organisms) formed 600 million years ago when the atmospheric oxygen levels increased. Once begun, they diversified into a variety of forms, leading some to call it the 'evolutionary big bang.' Once complexity began to appear in the cellular arrangement, mechanisms were developed to coordinate the functions of different parts; defense against cells and chemicals coming from outside and which were potentially toxic formed a major component of development (Max et al. 2006).

To overcome this, a system called immunity was conceived which protected at many levels: innate and adaptive; adaptive system identified substances that were foreign to the body, and developed a memory for these intruders so that they could be repelled when they were encountered a second time (Hoffmann et al. 1999).

An abnormality in this smoothly functioning system brings about cells of the immune system to mistakenly identify the body's own cells are being foreign, and to try to attack them, resulting in autoimmune diseases.

The immune system developed over millions of years and has panoply of components to be effective. Thereby, faults can occur at many levels to give rise to autoimmune diseases.

The coordinated reaction against foreign substances takes place at two functional divisions of the immune system: the innate and acquired. Innate immunity is the first line of defense against invading pathogens which comprises of physical barriers such as skin, soluble factors and cells white blood cells which destroy infective agents. These have no inherent memory to remember pathogens that it encountered earlier. These are 'identified by the broad molecular patterns rather than detailed features of specific pathogens' such as pathogen-associated molecular patterns. When cells of innate immune system find such pattern, they secrete circulating chemicals that signal danger to other cells, which often mount an inflammatory response to quell the danger.

Innate immunity operates in concert with the next step of defense, the acquired immune system, which takes longer to get activated, but which is longer lasting and has 'immunological memory', viz remembers pathogens that were encountered earlier.

Abnormal identification of the body's own cells leads to autoimmune disease.

In contrast to innate immunity, which is evolutionarily ancient, the acquired immunity highly specific, involving blood cells called lymphocytes, each of which carries cell receptor for a single antigen protein (Hoffmann et al. 1999). Acquired immunity begins to be effective several days after the foreign protein is presented, and the efficacy persists, called immunological memory. Memory ensures that the next time the protein is encountered, a stronger and more effective immune response is mounted.

One type of lymphocytes called B lymphocytes produce chemicals called antibodies or immunoglobulin Ig which specifically interact with an individual antigen. They act in may ways: by binding the proteins and thus preventing attachment to host cells, by activating another system called complement, which promotes foreign protein destruction. Humoral immunity mediated by B lymphocytes essentially deal with pathogenic organisms that come from outside.

Other foreign cells and proteins which escape B cells are dealt by cell mediated immunity mediated by another type of cells called T lymphocytes. T lymphocytes can express antigen speicific receptor on their surface. However they can identify only those which were previously 'presented' to them.

Once the fact that a cell is infected is transmitted to T lymphocytes by cell surface expression of peptides derived from the infective agent. These peptide fragments are transported to the cell surface and expressed along with other proteins called major histocompatibilty complex. Together, the complex is recognized by T lymphocytes.

Pathogens existing within cells stimulate cytotoxic lymphocytes to destroy the infected cell. Pathogens existing outside cells stimulate a Th-mediated response. Th cells (ie antigen activated CD4+ T lymphocytes) secrete cytokines in delayed type hypersensitivity reaction (Calder 2007).

Communication within and between the innate and acquired immune systems occurs by cell to cell contact involving cell surface proteins and by production of chemical messengers among cells; cytokines are the chief of the latter chemicals and include tumor necrosis factor and the interleukins among many others. Both groups of chemicals mediate the immune response and an inappropriate secretion or overproduction can both be dangerous.

At first it seemed inconceivable that the body would attempt to destroy its own cells and lead to autoimmune disorders. The immune system was meant to destroy foreign substances, but how could it damage its own cells? It soon became apparent that the immune system could be misdirected to considering 'self' as 'non-self', resulting in damage and disease. For this to occur there had to be dysfunction of the immune regulation, which was soon implicated to involve environmental or extraneous factors as well as genetic susceptibility.

There is no single gene or environmental pathogen which consistently leads to autoimmune disease. A constellation of genetic susceptibility and exposure to known and as yet unknown chemicals leads to an autoimmune process, which in turn manifests as autoimmune disease once the body's balancing power (homeostasis) is tipped over.

Genetic basis for autoimmune susceptibility was obtained from many lines of evidence: autoimmune diseases run in families, which share genes as well as environment (Davidson and Diamond 2001). Different members of a family can have a single or many autoimmune diseases such as type 1 diabetes mellitus, Hashimotos thyroiditis, Sjogren disease or rheumatoid artiritis. Secondly, studies in twins showed that pairs who shared the same genetic makeup (monozygous twins) had greater risk of developing autoimmune diseases than sets who did not (ie heterozygous twins). Genetic risk comprises upto half the susceptibility for autoimmune diseases. Women are particularly prone to autoimmune diseases, perhaps due to differential hormonal regulation of the immune system.

The other group of factors are environmental, ie those which are present outside the body: these can be infections (streptococcal infection leading to rheumatic disease), sunlight (slystemic lupus sometimes precipitated by exposure to sunlight), dietary intake (eg iodine, leading to autoimmune thyroiditis). Environmental factors alone are not sufficient to cause autoimmunity in the absence of implicating genetic factors. Conversely genetic predisposition is by itself insufficient to cause disease. A combination of genetic susceptibility along with environmental triggers are both necessary to cause disease (Goodnow 2007).

What these make clear therefore is that autoimmune diseases, produced by a combination of genetic and environmental factors involve a whole spectrum of body tissues, and produce an equally diverse group of diseases. The underlying theme of common pathogenesis leads one autoimmune disease (eg rheumatoid arthritis) to be associated with another (eg type 1 diabetes mellitus). As different physicians (specialists) treat each condition, they must bear in mind the co-occurrence of another autoimmune disease if one occurs; namely, a woman being treated for autoimmune hypothyroidism may have joint involvement due to rheumatoid arthritis or may lose weight following the development of type 1 diabetes mellitus. Overlap may occur in the same invidividual as well among members of the extended family (viz parents, siblings and others).

Are there ways to ensure proper treatment of autoimmune diseases? Certain tips were given to meet this 'difficult challenge' [InFocus vol 10, no 2, June 2002]: Check whether other members in ones family have autoimmune diseases, and if yes, what. As mentioned earlier, chance of an autoimmune disease increases when another family member has one. Keep a list of 'symptoms' that may at first seem unrelated: eg change in weight, joint pains, changes in skin, mental disturbances; when they are all collated a pattern suggestive of autoimmune disease may be evident. Make an effort to go to a physician who is experienced in dealing with autoimmune diseases and to a good medical centre where appropriate evaluation including clinical is performed.

Autoimmune diseases are best managed rather than cured; therefore the patient must partner with the treating physician in management which understandably leads to stress. Unfortunately stress by itself can aggravate autoimmune diseases through cross talk between the brain and the immune response. Trying to lower stress by meditation or other practices can help diminish the adverse effects of autoimmune conditions.

Coping with autoimmune diseases: Considering that most autoimmune diseases are not 'cured', may often result in physical discomfort and the patient must be a partner in treatment, are there coping methods for these conditions? One should understand the nature and course of the disease and carefully follow the treatment prescribed by the physician. Keep an open communication channel with the physician to warn of new conditions that may develop or of adverse effects of treatment. Dietary regulation may be needed in some conditions; ensure that adequate nutrition is not compromised. Consult a physician or clinical psychologist if the stress threatens to overwhelm one's ability to cope. Stress response is not abnormal, but seek help when it threatens to overpower.

So what does the future hold? Research is being conducted to understand the immune system, how it is disturbed, leading to autoimmune diseases. Translational research is also underway to transform what knowledge is already available to identify the diseases early, and to develop cures for the diseases.

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