Newer Treatment Strategies for Autoimmune Diseases

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In contemporary parlance, autoimmune disease has been used as a designation for a variety of chronic inflammatory disorders that are characterized by the presence of autoantibodies. This rubric has been applied to diseases whose etiologies are not infectious, neoplastic or degenerative in nature. The autoantibody profile may simply include a positive antinuclear antibody (ANA) test or it may be further defined by autoantibodies with specific identifiable autoantigens. By this description, autoimmune disease encompasses a wide variety of disorders manifesting as chronic inflammation confined to a tissue or organ or as a systemic inflammatory disease. Although, this nosology may serve to define syndromes that may be amenable to specific anti-inflammatory or immunosuppressive treatments, it has not served to advance our understanding of the etiology of these diseases, nor does it imply that the autoantibodies themselves directly participate in the pathogenesis of the disease. While these diseases may be "immunologically-mediated", there is often very little evidence that these autoantibodies actually are involved in the disease pathogenesis.

A stricter definition of autoimmune disease would include the stipulation, that not only should autoantibodies be present, but that there is evidence to support the notion that they actually participate in the etiopathogenesis of the disorder. This definition adds a more rational framework for understanding autoimmune disease. It also allows for a better characterizing of the immunopathogenesis of these syndromes and can more readily allow for immunotherapy directed at specific pathways ("targeted therapies").

In this issue of the *Rhode Island Medical Journal,* we review four inflammatory syndromes traditionally considered to be autoimmune in nature. By the above definition, two of these (SLE, pemphigus) would be viewed as autoantibody-mediated but the other two (cytopenias, CIDP) both likely fit the criteria even though the demonstration of specific autoantibodies in these disorders has been elusive. Other immunologically-mediated diseases (rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease, myasthenia gravis, and autoimmune thyroid and liver disease) should also be viewed as autoimmune in nature. There have been significant developments in immunomodulatory therapy as reviewed in the introductory article by Lefebvre and McAuliffe. There is convincing evidence that the diseases listed in this review article are characterized by antigen-driven T-Cell activation and subsequent pro-inflammatory cytokine generation. However, effective strategies to abrogate T-cell activation and block resultant cytokines or cytokine receptors have outpaced the ability to identify specific triggering antigens or subsequent autoantibodies that are pathogenic. Nonetheless, the advent of such sophisticated targeted therapies will undoubtedly improve management and outcomes for immunologically-mediated diseases, some, but not all, of which should be considered auto-immune in nature.

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