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Virus-induced autoimmunity through molecular mimicry

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The fundamental cause of many chronic debilitating diseases is not known. However, host responses to self could play an important role in many of these instances. Mi-croorganisms and/or viruses in coalition with host immune responses are often as-sociated with occurrences of disease. Viruses have been implicated with the initiation of autoimmunity; however, direct cause and effect evidence is often hard to derive. Immunologic cross-reactions or molecular mimicry, that is, shared determinants between a microorganism and self epitopes, could account for the breaking of tolerance and the initiation of antiself responses, leading to autoimmunity. Advances in current methodology have allowed us to explore the immunologic cross-reactions and deter-mine what epitopes are important in the induction of disease.

The first suggestive evidence that viruses could share common determinants with their hosts came from experiments showing an association between infection and the incidence of autoantibodies in patients with infectious active hepatitis. Ajdukiewicz et al. reported the presence of anti-smooth muscle antibodies. Later Toh et al. extended these observations to include infectious hepatitis, chicken pox, measles, and mumps viruses. They found reactivity to intermediate filament proteins. Over half the sera from infected individuals reacted with intermediate filament proteins. Only 6% of control sera were positive. Similar antibodies were also found in patients with infectious mononucleosis. However, in many instances it was not clear if these antibodies reacted with virus and self, or if the antibodies arose through polyclonal B-cell activation, or both.

Reaction to other intracytoplasmic proteins has been described by Sotelo et al They found autoantibodies against axonal neurofilaments in patients with subacute spongiform encephalopathies such as Kuru and Jakob-Creutzfeldt disease. These sera were tested in in vitro central nervous system cultures. Almost two thirds of patients with Jakob-Creutzfeldt disease and approximately one third of patients with Kuru had autoantibodies. These findings were the first evidence of an immune reaction occurring in relation to either of these encephalopathic diseases.

In mouse studies of vaccinia virus infection, Steck et al. demonstrated that in-oculation of mice with a neurotropic strain resulted in the production of antibodies. that reacted with myelin and oligodendrocytes. No antibodies were found to bind to neurons or thymocytes. Mice injected with a dermotropic strain of vaccinia did not produce autoantibodies to central nervous system elements. The antimyelin and the antioligodendrocyte antibodies could therefore not be removed by absorption using

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