

## Desert Storm Syndrome and Immunization

The latest report<sup>1</sup> about the search for causes of the "Desert Storm syndrome" must be very disappointing, not only for the 20 000 victims, but also for medical scientists. Four years after the end of the Gulf War, information still derives from the arbitrary collection of very restricted data from small cohorts of veterans. Is this a question of medical concepts? Are the symptoms of the Desert Storm syndrome or "Gulf War disease" indeed so unique and unpredictable<sup>1,2</sup> that it is not possible to develop reasonable concepts for investigation?

Together with the predominant chronic fatigue syndrome, joint pain, and rash, there have been reports of increased polyspecific antibody concentrations against viruses such as Epstein-Barr virus, cytomegalovirus, and arbovirus, as well as symptoms that resemble those of immunologic disorders.

What can be a consistent explanation of these disseminated symptoms of obviously chronic disease other than changes in immune responses? Is it contrary to previous experience that immunizations in adults can produce side effects? With up to nine immunizations in a few days in 700 000 troops, we calculate the incidence of chronic side effects to be 0.3% per antigen. This percentage may be similar to that of the complications seen in travelers who are immunized before a visit to high-risk countries. Unfortunately, to our knowledge, such data are not available to date.

From the viewpoint of the immunologic network theory,<sup>3</sup> the symptoms mentioned are those that might be expected. Classic immunologic theory holds that each infection or immunization in an organism leads to the selection of a specific antibody-producing B-cell clone, but what is not taken into consideration by the clonal selection theory is that immunization or infection also changes the individual's network of interacting components: antibodies with anti-idiotypic antibodies and accidentally cross-reacting autoantibodies. As seen in Guillain-Barré radiculitis,<sup>4</sup> the increased concentrations of antibodies and autoantibodies to noncausative antigens cover a large spectrum of speci-

fities (eg, antiganglioside, antiviral, and antibacterial antibodies) with an individual pattern. Similarly, in the classic course of streptococcal pneumonia, these individual polyspecific immune responses have been found with temporarily increasing concentrations of IgG class antibodies, eg, against nonpersistent viruses such as rubella or mumps, and with increasing autoantibody concentrations such as anti-double-stranded DNA (S. Heitmann and H.R., unpublished findings, 1995). Uninvolved antibodies and autoantibodies are modulated in their concentrations by any changes in the network. It is the concentration, together with the affinity of the autoantibodies, that determines the regulatory efficiency of the network,<sup>3,5</sup> an irreversible change in which might lead to a pathologic state of the immune system.

It is possibly the restricted view of the sophisticated mechanisms of B-cell-T-cell-cytokine-receptor interactions that prevents many immunologists from seeing the clinically relevant, emergent properties<sup>3</sup> of the whole immune system, such as tolerance, memory, and autoimmunity. For all traditional investigations on this subject, the crucial problem is that the necessarily individual response patterns vary from patient to patient.

Before progress can be made in alleviating the suffering of the Gulf War veterans, cooperative immunologic investigations involving a suitably large spectrum<sup>3</sup> of antibodies and autoantibodies together with cellular components must be funded and organized.

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