Exotoxins produced by certain strains of *Staphylococcus aureus* are recognized as etiologic agents of toxic shock syndrome and staphylococcal food poisoning. More recently, these toxins, the staphylococcal enterotoxins and toxic shock syndrome toxin, have been shown to have extraordinary properties as T cell antigens (1). Like other antigens, T cell stimulation by these toxins is dependent upon presentation by MHC molecules. In contrast to conventional antigens, however, they do not require presentation by a "self" MHC molecule; allogeneic antigen-presenting cells are equally effective. The essential requirement is that cells presenting the toxins express MHC class II molecules, as these molecules specifically bind the toxins. Additionally, the staphylococcal toxins are not "processed" within antigen-presenting cells to oligopeptides that are displayed to T cells within the class II antigen-binding groove. Instead, the intact protein binds outside the groove and interacts directly with T cell receptors for antigen. Finally, and most importantly, the staphylococcal toxins bind to a site on the Vβ segment of the T cell receptor heterodimer that is distinct from the complex site for binding of self MHC and foreign peptide antigen. Because the toxins do not bind to a site constituted by the full array of Vβ, Dβ, Jβ, Vα, and Jα gene products, the frequency of T cells responding to these molecules exceeds that of conventional peptide antigens by several orders of magnitude. Hence their name, superantigens.

Recent discovery of superantigens has led to recognition of their production by a broad range of pathogens (1, 2). Unsurprisingly, the homologous erythrogenic exotoxins of streptococci also act as superantigens. However, they are also produced by organisms as diverse as *Mycoplasma* and mouse mammary tumor viruses. This phylogenetic diversity has supported efforts to implicate superantigens in the pathogenesis of a variety of "immunological" diseases of unknown etiology. Particularly interesting data, suggesting tell-tale Vβ-specific T cell stimulation, have been presented in studies of patients with rheumatoid arthritis and Kawasaki disease (2).

In this context a paper in *The Journal* by Takei et al. (3) is especially provocative. In studies carried out entirely in vitro these authors demonstrate that commercial preparations of IgG for intravenous administration (IVIgG) contain high titers of antibodies to eight staphylococcal toxin superantigens. Moreover, these antibodies inhibited T cell responses in an apparently toxin-specific manner. The data thus pose the interesting question whether the presence of antibodies to microbial superantigens in IVIgG relates in any disease to its therapeutic efficacy.

The rationale for use of IVIgG in the array of immunological diseases other than antibody deficiency disorders has been perplexing. Nevertheless, data from multiple trials suggest its effectiveness in treatment of such diseases as acute and chronic autoimmune thrombocytopenic purpura, myasthenia gravis, chronic inflammatory demyelinating polyneuropathy, and Kawasaki disease (4). In none of these diseases has the mechanism of effect been convincingly demonstrated. However, the data of Takei et al. (3) support a hypothesis of toxic superantigen-specific neutralization applicable at least to its efficacy in treatment of Kawasaki disease.

Kawasaki disease in children shares many clinical features with toxic shock syndrome in adults (2). Symptoms may be dramatically alleviated and the incidence of the most serious complication of the disease, the development of coronary artery aneurysms, is reduced by treatment with IVIgG and aspirin (4). Not only does Kawasaki disease share with toxic shock syndrome clinical features and skewing of T cell receptor Vβ representation in peripheral blood (2), but effectiveness of IVIgG has been previously suggested to reflect neutralization of an unknown bacterial toxin (5) and IVIgG suppresses evidence of B cell and T cell activation in vivo that is characteristic of the disease (6).

If the antisuperantigen hypothesis is correct, it should be specifically applicable to diseases in which pathogenesis involves active microbial production of the toxins. In contrast, chronic autoimmune diseases such as rheumatoid arthritis, in which a postulated etiologic role of a superantigen may be a distant initiating event, would seem less likely to demonstrate efficacy by this mechanism.

Although the present data establish only the presence of superantigen antibodies with in vitro neutralizing activity in IVIgG, they pose important additional questions. Most obviously these include the possibility of usefulness of IVIgG in treatment of patients in which the pathogenetic importance of superantigen production is quite certain, such as toxic shock syndrome (7). Supertherapy for acute superantigen-induced diseases? Time, and further study, will tell.

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