Serum Antibodies in Transplantation*

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APPARENTLY *allograft rejection is an immunologic process involving serum antibodies. Such antibodies have been demonstrated by hemagglutination, cytotoxicity, leukoagglutination, lymphoagglutination, mixed agglutination, and antiglobulin consumption. However, antibodies if detected following allografts by any of these methods are usually in low titer, and their appearance usually lags behind allograft destruction by several days. Mixed agglutination reactions obtained on tissue cultures of donor origin is easily reproduced and is very sensitive. The antiglobulin consumption test is bulky and difficult but has useful features. Not only do serum antibodies occur regularly following allografts but also there are at least two populations of antibodies each probably stimulated by separate antigens. Under some circumstances serum antibodies can injure or destroy grafts, under others they protect them. A serologic method of predicting graft rejection is possible.*

IN THE EARLY 1940's Medawar[1,2] set about to study the process of allografting (homografting) systematically by using full-thickness skin grafts in the rabbit. He and his associates found that such grafts would thrive for a few days but were inevitably attacked and then inexorably destroyed. This destruction was termed rejection and required an average of nine days. This reaction itself came to be called the first set response to distinguish it from the second set response which occurred when a second skin allograft was performed between the same donor and recipient. After this second graft, the whole rejection process was repeated, but in a more vicious and greatly accelerated manner. It was largely this accelerated second set reaction, this sensitization, that led to the conclusion that allograft rejection was an immunologic process.

If allograft rejection were an immunologic process, it seemed logical to assume that there were antibodies involved. A number of experiments were designed to demonstrate serum antibodies stimulated by allografts, but those experiments in general failed. This failure, it is now known, was due to several reasons. Chief among them was the fact that histocompatibility antigens are insoluble, and most standard serologic technics require antigens to be presented for reaction in soluble form. Most studies, therefore, used methods which were inadequate.

Other experiments demonstrated that allograft immunity could not be passively transferred by serum under usual conditions. It was then shown that while serum from a sensitized host would not passively transfer allograft sensitivity, living lymphocytes from the same host would cause accelerated rejection when transferred to a nonsensitized host.[3]

Allograft immunity therefore seemed likely to be an example of delayed hypersensitivity in which the immunity was effected by cells, either without free circulating antibodies or without serum antibodies of importance in rejection. Indeed, this hypothesis has held general sway until the past few years.

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