A Heterophile System in Human Renal Transplantation
III. The HT-A Specificities

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IN our first study of this heterophile system we found acute and irreversible renal allograft rejection to be consistently accompanied by an eightfold or greater rise in the recipient's serum titer of human anti-rat hemagglutinins. These changes in titer occurred even though, at the same time, recipient's lymphocytes were unable to undergo blastogenic transformation when exposed to the allograft donor's lymphocytes or to other antigens to which they had been sensitive preoperatively.[1] These data were presented as evidence that humoral immunity was involved in acute renal allograft rejection in immunosuppressed human subjects. Moreover, the original publications of Rapaport et al. were confirmed.[2,3]

Other studies indicated that careful observations of the titer of these heterophile antibodies in the post-transplantation period could be helpful as a serologic method of diagnosing acute renal allograft rejections.[4,5]

Evidence has also been presented indicating that the antigens involved were present in at least some human kidneys, some Gram-negative bacteria, and in rat erythrocytes. They were not present on human leukocytes (and therefore not HL-A), nor were they present on sheep erythrocytes. The antigens were very similar to the common antigen of Enterobacteriaceae. Some Gram-negative infections produced an immunity to these heterophile antigens, and thus some patients were found sensitized to them before transplantation. Transplants into presensitized patients frequently failed, usually by accelerated acute rejection, while transplants into nonsensitive recipients usually developed immunity to these antigens, if and when acute rejection occurred. Hyperacute and chronic rejection did not seem related to the system, but acute rejection was much more closely correlated to it than to HL-A incompatibility.[5,6]

In those studies, absorption experiments indicated that the reactive site of concern was on rat erythrocytes but not sheep erythrocytes, although additional antigens shared by rat and sheep erythrocytes also engendered a heterophile response. We originally referred to these two antigen systems as the rat-restricted antigens and the antigens common to both rat and sheep erythrocytes. These terms are bulky and not sufficiently precise. Consequently, the former have been designated heterophile transplantation (HT) and the latter heterophile-X (HX) antigens.

There was a close correlation between the heterophile antirat hemagglutinin titer and the presence of anti-HT activity, i.e., the higher the titer the more likely the serum was to contain anti-HT activity. However, this relationship was not absolute in that some high titered sera contained only anti-HX activity. This suggested that the reverse might also be true, i.e., some low titered sera might contain anti-HT activity. To clarify this question, anti-HT activity has been determined in a larger group of sera and correlated with the clinical outcome of 70 human renal allografts. Thus, data can now be presented relating

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