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A HETEROPHILE SYSTEM IN HUMAN RENAL TRANSPLANTATION

I. DISTRIBUTION OF ANTIGENS AND REACTIVITY OF THE ANTIBODIES[1, 2]

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SUMMARY

This paper presents basic data concerning a heterophile system shown in previous studies to be related to human renal transplantation. Patients with either acute infections from some gram-negative bacteria or acute renal allograft rejections developed substantially higher titers of human antirat erythrocyte antibody than is common in normal people. The heterophile antibodies produced as a consequence of either infection or acute renal allograft rejection reacted with antigens present on rat erythrocytes but not on sheep erythrocytes. Absorption and neutralization studies confirmed the presence of antigens in or on human kidneys, various gram-negative bacteria, and rat erythrocytes which will react in this heterophile system. The antigens are similar but are not serologically identical to the common antigen (CA) of Enterobacteriaceae. Some patients in chronic renal failure were shown to be immunized to the heterophile antigens, presumably from previous infection.

Reactions of antisera with antigens from biologically diverse species are known as heterophile reactions. They are probably best explained by the random recurrence in nature of antigenic determinants sufficiently similar in configuration for antibodies produced against one to cross react with others. Such cross reactions were described as early as 1899 (*16*). Perhaps the most thoroughly studied heterophile system is that discovered by Forssman (*6*), although several others are known (*3*). Antigens of a heterophile system are frequently found scattered seemingly at random among mammals, bacteria, birds, fish, and perhaps plants (*3*). They may be species-specific in one species and allospecific in another, i.e., they may be present in all members of one species and in only some members of another (*3*). Persons who do not carry antigens of a particular heterophile system are frequently immunized "naturally" through random exposure (*3*). Such persons have in their serum "naturally occurring" antibodies and are thus sensitized.

Heterophile systems related to transplantation were suggested by the observation that antiserum against transplantation antigens of A strain mice cross reacted with polysaccharides from *Diplococcus pneumoniae* type 14 and *Shigella shigae* (*2*). It was later found that immunization of several mammalian species with some gram-positive organisms produced hypersensitivity to skin allografts (*4, 12, 13*). In patients bearing kidney allografts, Iwasaki et al. observed antisheep red blood cell heterophile antibodies but these did not appear related to rejection (*7*). Subsequently, others found hemagglutinins active against sheep, guinea pig, and rat erythrocytes present in serum from patients after renal or skin transplantation, in titers substantially

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