A heterophile system in human renal transplantation. VI. Biologic effect of heterophile (HT-A) and nonheterophile (HL-A) compatibility on allograft survival

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A series of 79 selected renal allografts has been studied to determine the biologic importance of the heterophile (HT-A) locus and the relative effects of HT-A and nonheterophile (HL-A) loci on allograft survival. The results demonstrate that HT-A and HL-A compatibility together yield very good results, whereas HT-A and HL-A incompatibility together yield poor results. HT-A incompatibility with any serologically determined HL-A incompatibilities give a one year allograft survival of 34 percent, and with two or more HL-A incompatibilities the one year survival rate is only 22 percent. Compatibility at one locus with incompatibility at the other yields intermediate results. Thus incompatibilities at both loci seem cumulative. The chief difference in the effect of incompatibility of the two loci is that HT-A incompatibility is decisive early, whereas HL-A effects are seen later. The HT-A system appears to be a major determinant of renal allografts success which needs to be taken into account in compatibility testing.

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FOR SOME YEARS this laboratory has studied a heterophile system pertinent to human renal transplantation, which has been termed the heterophile transplantation antigen (HT-A) system. Evidence has been presented to support the following principles. (1) A number of patients reject renal allografts in association with anti–HT-A immunity even though their lymphocytes are simultaneously incapable of producing a blastogenic response on stimulation by donor lymphocytes, or other antigens, (purified protein derivative, mumps, etc.) to which they were sensitive prior to transplantation and immunosuppressive therapy.[10] (2) The HT-A's are species specific in the rat. They are distinguished from other irrelevant heterophile antigens on the rat erythrocyte by the fact that the irrelevant antigens are common to rat and sheep erythrocytes, whereas the HT-A are not.[7] This observation was confirmed recently by Kano and co-workers.[3] (3) HT-A's are allogeneic in man and are present in some human kidneys.[7] (4) Antigens, either identical or very similar to HT-A's, are present on enterobacteria. These antigens are also very similar, but not serologically identical, to the common antigen of enterobacteriaceae.[5, 12] (5) Infection with enterobacteria in the appropriate individual can stimulate an immune response indistinguishable from that stimulated by renal transplantation.[6] This was confirmed recently by Waller and colleagues.[13] (6) In the absence of infection, variation in the antirat erythrocyte antibody titer is useful in diagnosing acute heterophile rejection.[7, 11] (7) Individuals who, prior to transplantation, have high titers of antirat erythrocyte antibody which contain the anti–HT-A specificity frequently reject renal allografts by complete acceleration acute rejection.[6] (8) The human HT-A system is somewhat analogous to the ABO blood group system. Most people whose tissues do not contain HT-A have a detectable humoral immunity to HT-A produced by natural immunization from enteric flora. Presumably all such people are sensitized but the sensitization in

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