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A HETEROPHILE SYSTEM IN HUMAN RENAL TRANSPLANTATION

IV. NATURAL IMMUNITY AND ITS GENETIC IMPLICATIONS [1]

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SUMMARY

Natural heterophile immunity was studied in 949 individuals including 41 recipients and donors of renal transplants and 141 families. The prevalence and strength of the natural immunity was at its maximum during the first two decades of life and declined thereafter. The population could be divided into three groups: one with natural immunity to heterophile transplantation antigens (HT-A), one with a heterophile immunity which was not (anti-HT-A) (i.e., anti-HX-A), and one group which had no heterophile immunity. Transplantation among these groups yielded results which along with family studies and mathematical considerations suggest that the HT-A system is controlled by a single genetic locus comprised of one dominant and one recessive allele.

In previous publications we described a group of heterophile antibodies and antigens which appeared to be involved in human renal transplantation. The data published indicated that the heterophile transplantation antigens (HT-A) were present in some human kidneys but not all, were carried by some Gram-negative bacteria, and were on rat erythrocytes. Antibodies against these antigens were present naturally in some people. Accelerated allograft rejection frequently followed transplantation in such patients. Other patients who experience acute rejection produced the appropriate antibodies in association with rejection.

In an earlier study, about 75% of human sera were found to agglutinate rat erythrocytes. Most reacted with heterophile antigens common to sheep and rat erythrocytes which did not seem to function as compatibility antigens. These we called heterophile X antigens (HX-A). The particular heterophile antibody of interest reacted with antigens (i.e., HT-A) on rat erythrocytes but not on sheep erythrocytes (*1–3*). Thus, we refer to the antirat hemagglutinating activity of human sera as heterophile activity. When such sera are absorbed with sheep erythrocytes and tested against rat erythrocytes, some sera retain agglutinating activity and some do not. We refer to the activity that was removed as anti-HX-A and the activity retained as anti-HT-A (*3*).

The HT antigens were obtained from human kidneys in an emulsion using a method conventionally used to obtain common antigen from Enterobacteriaceae. This material would neutralize the antirat agglutinins of appropriate sera, but it was not immunogenic in a number of species nor has it been possible to obtain serological reactions with it in a number of systems (unpublished observations). Furthermore, preparation of the active material requires such large quantities of renal tissue that its clinical use is impractical.

The failure to obtain direct serological reactions with material obtained from human tissue hampers studies which might determine the number of antigens involved or might lead to pretransplantation prediction of compatibility.

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