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STUDIES OF HOMOGRAFT SEX AND OF GAMMA GLOBULIN PHENOTYPES AFTER ORTHOTOPIC HOMOTRANSPLANTATION OF THE HUMAN LIVER

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IT HAS BEEN ESTABLISHED that several serum proteins synthesized exclusively by the liver convert in the recipient to the phenotype specificity of the original donor following orthotopic liver transplantation (1, 2, 3). In this study the gamma G globulins (IgG) which are normally thought to be nonhepatic in origin were examined in 10 human recipients of replacement livers. When it was unexpectedly found that the Gm types of the donor were transmitted to the recipient, histopathologic studies of the livers were carried out to determine their source.

METHODS

Phenotypes Gm [1, 2, and 12] were identified with the hemagglutination-inhibition test of Martensson (4). The only modification (5) was preliminary heating of the patient sera for 10 min. at 63° C. to inactivate rheumatoid factors (anti-IgG antibodies) which were present in 6 of the 10 recipients before transplantation and in all 10 afterwards.

Lymphoid tissue transplanted with the human hepatic homografts was examined postoperatively in 12 patients. In addition nine liver homografts from male donors were analyzed by the technique of Barr (6) 12 hr. to 400 days after they had been placed into female recipients. With this method the nuclei of female cells contain a distinctive chromatin mass. The sex was determined of the graft Kupffer cells and of the hepatic arterial and portal venous endothelial cells (7).

RESULTS

Gm Types: In 5 of the 10 patients the presence or absence of the Gm types [1, 2, and 12] was determined without efforts at quantitation, before transplantation, and on a single occasion from 1 to 25 days later. In every instance all three of the phenotypes were found whether or not these had previously been present in the donor or the recipient. The indiscriminate conversion of the gamma G globulin

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types was thought to be an artefact from multiple blood transfusions during and immediately after operation.

In the other five recipients of six homografts, quantitative studies (Gm titers) were carried out serially for 60 days to almost one year. The new Gm types apparently caused by transfusion, tended to die out within 1 to 2 months, making it possible thereafter to trace the fate of the preexisting Gm profiles of the donors and recipients.

In 3 of the 6 sets of observations the donor did not have one or more of the Gm phenotypes which were in the recipient. In the late follow-ups the previously present Gm types of the recipients remained the same during periods of six months to almost a year; new types were not added.

In the other three patients with serial studies, the situation was the converse in that the donors each had one Gm type not naturally found in the recipient. During follow-ups of 60 to 326 days, these phenotypes could now be detected in the recipient serum in highly significant quantities. In some instances the titer of the new Gm remained constant whereas in others there was a very gradual diminution but never a complete loss of the added Gm type.

Special Pathologic Studies: The sex identification was performed in nine homografts ½, ½, 4, 11, 23, 35, 105, 380, and 400 days after transplantation. At all times the vascular endothelial cells remained male. However, the Kupffer cells became female and therefore of host origin in the three livers with the longest host residence.

In each of the 12 hepatic homografts in which a special search was made for lymphoid tissues, these were found. The lymphoid follicles had prominent germinal centers and many plasma cells in the medulla.

CONCLUSIONS

These observations indicate that new IgG phenotypes may be introduced by hepatic homotransplantation and maintained for long periods thereafter. The new immunoglobulins are apparently not from cell lines differentiating from Kupffer cells since the latter cells eventually become the genotype of the host. It is probable that lymphoid tissue transplanted with the liver is the source of the donor type IgG found in some of the patients long after transplantation.

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