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Chronic Immunosuppression, Australia Antigenemia, and Hepatitis

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MANY early workers in renal transplantation noticed a rather high incidence of hepatic dysfunction in their chronically immunosuppressed kidney recipients, but there were difficulties in determining the etiology of these liver complications. The two leading possibilities were hepatitis of viral etiology and drug toxicity of the agents being administered. With the discovery of the Australia (Au) antigen marker by Blumberg, it became possible to investigate the whole matter more completely, and about 1 yr ago we undertook a formal study to learn the causes of this kind of morbidity. The serologic studies were performed by Torisu and have been published.^{1,2}

From 89 patients who were either admitted to the hospital or visited the clinic for routine follow-up, serum was obtained. In addition, stored serum samples taken from these patients as long as 5 yr previously were available for thawing and retrospective serologic examination. The Au antigen was looked for in these samples with the precipitation methods of detection and by the more sensitive technique of complement fixation. By one or the other methods, there were 23 (26%) of the 89 recipients whose sera contained the Au antigen. In 11 additional patients who had abnormal liver function but who were Au negative, rabbits were inoculated with a

pool of the stored recipient sera. Four of the 11 negative pools raised heterologous anti-Au antibody after 12–24 wk of immunization, indicating that these patients had been Au positive but with trace quantities that were immeasurable with standard detection techniques.

Because of the existence of the stored samples of serum, it was possible to find out, in many instances, precisely when the Au antigenemia developed. Surprisingly, about one-half the patients had already been Au-antigen positive while on pre-transplantation dialysis. Inadvertently, they had been entered into the transplantation program as established serum hepatitis carriers.

The carrier state in the patients with preexisting Au antigenemia, as well as in those who developed the Au antigen after the advent of chronic immunosuppression, usually persisted following transplantation. Thus, none of our patients in whom the Au antigen could be detected by the precipitation methods has ever had disappearance of the antigen, and the same has often been true when only the complement fixation tests were positive. Consequently, the renal transplant population is a potentially dangerous reservoir for the perpetuation of serum hepatitis. The disease can be passed to the health care personnel. Many of our staff members have developed serum hepatitis, and one of our transplant research technicians died of this disease.

In the transplant recipients, there was a very poor correlation between Au antigenemia and the presence of hepatic dysfunction which occurred with almost equal frequency in people who were Au negative. From these latter observations, it may be inferred that hepatitis caused by other

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kinds of viruses may play a role in post-transplantation hepatic disorders or, alternatively, that hepatotoxicity of the immunosuppressive agents themselves is a

significant factor. In some of our Au negative patients, we have switched from azathioprine to cyclophosphamide with reversal of serious liver function abnormalities.

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