

e plates were gently rinsed of non-  
e then examined by inverted phase  
ts scored on the basis of the number  
per 150 X microscopic field.

SULTS

posttransplant nephrectomy showed  
donor kidney cells, but also against  
-A antigens. For example, patient 8  
ed by a graft (HL-A2, 10;12, W17)  
A2, 11;5, 12), (HL-A1, 2;8, 18),  
IL-A 9, 10; W5, W15); but not to  
or (HL-A 11, W32;W5, X). This  
was consistent with the specificity of  
his skin reactions to purified HL-A

while in the midst of a rejection epi-  
ria. The degree of specific reactivity  
ients posttransplant nephrectomy or,  
he reactions of peripheral leukocytes  
ive depletion of cells directed against  
example, patient 2 (HL-A2, 28,17,  
ining (HL-A2, 28;14, 27) was un-  
d toward targets bearing (HL-A1,  
the phenotypes (HL-A 2, W32; 8,  
). Similarly patient 4 (HL-A 9, 11;  
with (HL-A 2, 11;W5, W15) de-  
10;W5, W15) and (HL-A1, 30;14,  
11;W5, W15), (HL-A 2, W32; 8,

dom intervals during the first month  
reacted toward donor cells in vitro,  
nce of clinical rejection for 60 days.  
actions toward donor targets at four  
clinical evidence of rejection, based  
ta, and nuclide scanning. Patient 1  
d from donor with (HL-A 3, 9;7, 8)  
n tested at 25 days post transplant;  
s reacted to donor cells and to targets  
, but not to those bearing (HL-A 2,  
5, W15). Five days later clinical signs  
(HL-A 2, 28;17, 18) engrafted with  
o (HL-A 1, 30;14, X), (HL-A 2,  
5, W15) but not (HL-A 11, X;W5,

W15) four days prior to the onset of a rejection episode. All of the patients who displayed positive reactions underwent transplant rejection. On the other hand, rejection was never observed within six days of a negative reaction.

DISCUSSION

The results reported here have compelling implications for the immunodiagnosis of transplant rejection. The test may distinguish patients with circulating immunoreactive cells prior to clinical evidence of rejection. This method reflects modifications of the techniques reported earlier by Govaerts, by Wolf et al, and by Quadracci et al, as noted earlier (1). The advantages of the present method, which are reflected in its enhanced sensitivity in the detection of cellular immunity, include (a) the small number of requisite target cells, (b) the relatively short incubation period, (c) its simplicity and flexibility, and (d) its apparent dependence on antigen recognition rather than on cellular destruction. Further experience with the method will ascertain whether its immunodiagnostic efficiency warrants intensified immunosuppressive treatment for rejection solely on this basis and without any clinical evidence of graft destruction.

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MIXED LYMPHOCYTE CULTURE AND GRAFT REJECTION

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HL-A TYPING has proved to be a poor predictor of kidney compatibility (1). It has been claimed that genes determining mixed lymphocyte culture (MLC) are apart from those of HL-A (2). Considering

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cellular processes in the induction phase of rejection mechanism, MLC would seem to be a logical tool for donor selection.

#### METHODS

MLC was studied in 42 patients with kidney and 9 patients with liver transplantation. Kidney recipients were divided into primary related (19 patients), primary unrelated (14 patients) and secondary or multiple unrelated transplants (9 patients). None of the first two groups, but all of the last group were under immunosuppression at the time of MLC. Follow-up studies are for one to nine months after transplantation, excluding no patients. Rejection was diagnosed pathologically and by positive findings on two consecutive days of three clinical laboratory tests (blood urea nitrogen, creatinine clearance, and urine sodium concentration for kidney; serum bilirubin, transaminases, and alkaline phosphatase for liver). MLC was performed by Bach's method (3) with modifications. Stimulation index (SI) of MLC was defined by the ratio between the reaction of recipient cells to mitomycin-C-treated donor cells and that to mitomycin-C-treated recipient cells. A SI lower than 10 was considered compatible; those with SI higher than 10 were designated incompatible.

#### RESULTS AND CONCLUSIONS

The results (Table 1) indicated a positive although imperfect correlation between one-way MLC and the clinical course after primary kidney transplantation, either related or unrelated. A good MLC match was much more common than good HL-A matching. Similar findings have been reported by other authors (4,5), although they have used two-way MLC. Except for the double haplotype identical sibling cases, there was no correlation between HL-A and MLC. Even among these sibling cases there were two patients who rejected kidneys despite an identical HL-A and MLC. This finding and the report of Seigler and associates (6) suggests the possibility that minor incompatibilities may have been responsible. Immunosuppressive therapy apparently affected the MLC results, and the potential ability of the recipient to reject the graft was not adequately expressed by the MLC (Table 1). With liver transplantation, there has not yet been a correlation between outcome and MLC.

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Table 1—MLC and Graft Rejection

| MLC-SI | CASES WITH REJECTION | GRAFTS LOST | PATIENTS DEAD* | RANGE OF MLC-SI                 |              | GRAFTS LOST | PATIENTS DEAD* | RANGE OF MLC-SI |
|--------|----------------------|-------------|----------------|---------------------------------|--------------|-------------|----------------|-----------------|
|        |                      |             |                | NO REJECTION                    | NO REJECTION |             |                |                 |
| >10    | 7                    | 1           | 0              | Related Primary Kidney Grafts   |              | 0           | 0              | 0.6 ~ 0.72      |
| <10    | 2                    | 2           | 2              | 11.0 ~ 69.4                     | 0            | 0           | 0              |                 |
|        |                      |             |                | 0.6, 0.7                        | 10           | 0           | 0              |                 |
| >10    | 5                    | 0           | 0              | Unrelated Primary Kidney Grafts |              | 0           | 0              |                 |
|        |                      |             |                | 13.5 ~ 146.6                    | 0            | 0           | 0              |                 |

e of rejection mechanism, MLC for selection.

s  
 kidney and 9 patients with liver e divided into primary related (patients) and secondary or mul-. None of the first two groups, immunosuppression at the time of nine months after transplanta- was diagnosed pathologically tive days of three clinical lab- reatinine clearance, and urine n bilirubin, transaminases, and as performed by Bach's method dex (SI) of MLC was defined recipient cells to mitomycin-C- cin-C-treated recipient cells. A tible; those with SI higher than

CONCLUSIONS

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Table 1—MLC and Graft Rejection

| MLC-SI                                        | CASES WITH REJECTION | GRAFTS LOST | PATIENTS DEAD* | RANGE OF MLC-SI | CASES WITH   |           | GRAFTS LOST | PATIENTS DEAD* | RANGE OF MLC-SI |
|-----------------------------------------------|----------------------|-------------|----------------|-----------------|--------------|-----------|-------------|----------------|-----------------|
|                                               |                      |             |                |                 | NO REJECTION | REJECTION |             |                |                 |
| Related Primary Kidney Grafts                 |                      |             |                |                 |              |           |             |                |                 |
| >10                                           | 7                    | 1           | 0              | 11.0 ~ 69.4     | 0            | 0         | 0           | 0              | 0.6 ~ 0.72      |
| <10                                           | 2                    | 2           | 2              | 0.6, 0.7        | 10           | 0         | 0           | 0              |                 |
| Unrelated Primary Kidney Grafts               |                      |             |                |                 |              |           |             |                |                 |
| >10                                           | 5                    | 0           | 0              | 13.5 ~ 46.6     | 0            | 0         | 0           | 0              | 0.9 ~ 5.8       |
| <10                                           | 1                    | 0           | 0              | 2.2             | 8            | 1         | 1           | 1              |                 |
| Unrelated Secondary or Multiple Kidney Grafts |                      |             |                |                 |              |           |             |                |                 |
| >10                                           | 1                    | 0           | 0              | 22.2            | 0            | 0         | 0           | 0              | 2.1 ~ 3.3       |
| <10                                           | 4                    | 3           | 3              | 0.7 ~ 4.1       | 4            | 0         | 0           | 0              |                 |
| Liver Transplant                              |                      |             |                |                 |              |           |             |                |                 |
| >10                                           | 1                    | 0           | 0              | 39.9            | 3            | 3         | 3           | 3              | 19.4 ~ 39.8     |
| <10                                           | 3                    | 1           | 1              | 2.5 ~ 3.2       | 2            | 1         | 1           | 1              | 0.7, 2.6        |

\* Patients who died are listed in this column and, in addition, their kidneys are also listed in the grafts lost column. Note that all but one of the lost grafts were because of death.

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### RECOVERY FROM HEPATORENAL SYNDROME AFTER SUCCESSFUL ORTHOTOPIC LIVER TRANSPLANTATION

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INASMUCH AS THE KIDNEY failure of the hepatorenal syndrome (1) is believed to be secondary to hepatic dysfunction, replacement of the diseased liver should improve renal function. This objective was realized in three patients with the hepatorenal syndrome treated by orthotopic liver transplantation.

#### CASE MATERIAL

The patients, who were 34, 42, and 44 yr old, suffered from cirrhosis. They had massive ascites and edema and two of them were in stage III or IV coma. All had had normal renal function documented within a few weeks of transplantation, but progressive renal failure had then supervened with azotemia and oliguria. Two patients had a preoperative urine sodium concentration of less than 1 mEq/liter, while in case 3 it was 40 mEq/liter. The degree of combined renal and hepatic failure can be seen in Table 1.

#### RESULTS

Hepatic function in all three patients steadily improved after liver replacement (Table 1), but the course of recovery of kidney function varied. In cases 1 and 3 the characteristic urine findings, including

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Table 1—Renal and Hepatic Function in Three Patients With Hepatorenal Syndrome and Orthotopic Liver Transplantation

| URINE VOLUME<br>(ml/day) | Ccr*<br>(ml/min) | URINE Na<br>(mEq/L) | TOTAL BILIRUBIN<br>(mg/100 ml) | PROTHROMBIN TIME<br>(%) |
|--------------------------|------------------|---------------------|--------------------------------|-------------------------|
|--------------------------|------------------|---------------------|--------------------------------|-------------------------|