315

e plates were gently rinsed of non-
e then examined by inverted phase
ts scored on the basis of the number
per 150 × 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*)
1 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
) (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.

REFERENCES

1. Kahan BD, Reisfeld RA: Transplantation Antigens. Academic Press, 1972, pp 507
2. Kahan BD, Mittal KK, Reisfeld RA, et al: Surgery (in press)

MIXED LYMPHOCYTE CULTURE AND GRAFT REJECTION

NOBORU KASHIWAGI, MD, JACQUES CORMAN, MD,
SHUNZABURO IWATSUKI, MD, MAKOTO ISHIKAWA, MD,
JEAN MARC FIALA, MD, TORBEN S. JOHANSEN, MD,
DELIA BETHELL, MS, AND
THOMAS E. STARZL, MD, PHD, FACS

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

From the Department of Surgery, University of Colorado Medical Center and the Denver VA Hospital. Supported by research grants from the Veterans Administration and by National Institutes of Health grants AI-AM-08898, AM-07772, RR-00051 and RR-00069.

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.

REFERENCES

1. Halgrimson CG, Rapaport FT, Terasaki PI, et al: Net histocompatibility ratios (NHR) for clinical transplantation. Transplant Proc 3:140–148, 1971

2. Yunis EJ, Seigler RL, et al: HL-A typing, mixed leukocyte reactivity, and skin graft survival in a family with a combinant at the HL-1 chromosomal region. Transplantation 15:435–440, 1973

3. Bach FH, Voynow NK: One-way stimulation in mixed leukocyte cultures. Science 153:545–547, 1966

Table 1—MLC and Graft Rejection

MLC-SI	CASES WITH REJECTION	GRAFTS LOST	PATIENTS DEAD*	RANGE OF MLC-SI	CASES WITH NO REJECTION	GRAFTS LOST	PATIENTS DEAD*	RANGE OF MLC-SI
Related Primary Kidney Grafts								
>10	7	1	0	11.0 ~ 69.4	0	0	0	
<10	2	2	2	0.6, 0.7	10	0	0	0.6 ~ 0.72
Unrelated Primary Kidney Grafts								
>10	5	0	0	13.5 ~ 46.6	9	0	0	0.6 ~ 0.72

e of rejection mechanism, MLC
ıor selection.

S

kidney and 9 patients with liver
e divided into primary related
ıatients) and secondary or mul-
. None of the first two groups,
munosuppression at the time of
nine months after transplanta-
was diagnosed pathologically
utive 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
ecipient cells to mitomycin-C-
cin-C-treated recipient cells. A
ıtible; those with SI higher than

CLUSIONS

sitive although imperfect corre-
linical course after primary kid-
ınrelated. A good MLC match
L-A matching. Similar findings
4,5), although they have used
aplotype identical sibling cases,
ı and MLC. Even among these
ho rejected kidneys despite an
ş and the report of Seigler and
ıat minor incompatibilities may
ive therapy apparently affected
ity of the recipient to reject the
y the MLC (Table 1). With
ıeen a correlation between out-

ES

ci PI, et al: Net histocompatibility
ransplant Proc 3:140–148, 1971
ng, mixed leukocyte reactivity, and
nant at the HL-1 chromosomal re-

lation in mixed leukocyte cultures.

Table 1—MLC and Graft Rejection

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

4. Bach JF, Debray-Sachs M, et al: Correlation between mixed lymphocyte culture performed before renal transplantation and kidney function. Clin Exp Immunol 6:821–827, 1970
5. Cochrum KC, Perkins HA, Payne RO, et al: The correlation of MLC with graft survival. Transplant Proc 5:391–396, 1973
6. Seigler HF, Gunnells JC, Robinson RR, et al: Renal transplantation between HL-A identical donor-recipient pairs. J Clin Invest 15:3200–3215, 1972

RECOVERY FROM HEPATORENAL SYNDROME AFTER SUCCESSFUL ORTHOTOPIC LIVER TRANSPLANTATION

SHUNZABURO IWATSUKI, MD, JACQUES CORMAN, MD, MORDECAI POPOVTZER, MD, MAKOTO ISHIKAWA, MD, AND THOMAS E. STARZL, MD, PHD, FACS

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

From the Departments of Surgery and Medicine, University of Colorado Medical Center and the Denver VA Hospital. Supported by the Veterans Administration, National Institutes of Health grants AI-AM-08898 and AM-07772, and Division of Research Resources grants RR-00051 and RR-00069.

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

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