Twenty-five whole-organ recipients treated from 1981 through September 1988 were HIV carriers. Eleven were infected before transplantation, although this was not known until later in 8 recipients. The other 14 were infected perioperatively. Ten of the 25 recipients were infants or children. The organs transplanted were the liver (n = 15), and the heart or kidney (n = 5, of which 5, and 4/5 of the liver, heart, and kidney recipients, respectively. The best results were in the pediatric group (70% survival) in which only 1 of 10 patients died of AIDS. In contrast, AIDS caused the death of 5 of 15 adult recipients and was the leading cause of death. Transplantation plus immunosuppression appeared to shorten the AIDS-free time in HIV+ patients as compared to nontransplant hemophiliac and transfusion control groups. Accrual of HIV+ transplant recipients has slowed markedly since the systematic screening of donors, recipients, and blood products was begun in 1985.

Human immunodeficiency virus has been a subject of concern in transplantation (1,2) since the infection became a known clinical entity. It was anticipated that transplant patients would be at high risk of HIV infection because of their exposure to blood, blood components, and other sources of HIV infection. However, the extent of the problem was not known until demographic studies were performed by Dummer et al. (3) who examined the stored and current sera of 1043 patients treated with organ transplantation at the University of Pittsburgh from 1981 to 1986. They found that 1.7% of the recipients were either HIV+ at the time of transplantation or seroconverted soon after. Pediatric patients had an unusually high risk (2.3%). Similar disquieting statistics have been reported from single centers (4,5) and from multiinstitutional collaborations (6-8).

Although this was not the intention, a clinical experiment was created by the presence of this pool of HIV+ transplant recipients, many of whom now have lived for years under posttransplant immunosuppression. The records of these patients were studied with particular emphasis to their clinical course, long-term survival, and current status.

MATERIALS AND METHODS

Transplantation patients. Of 3023 transplant recipients treated at the University of Pittsburgh between January 1, 1981 and September 5, 1988, 25 were found to be HIV+ and are included in this report. Eighteen of these patients were found to be positive in a look-back epidemiologic study performed at our center (3). The other 7 have been diagnosed since this study was completed. Two of the 17 male patients had a history of sexual contact with other men.

Two groups of HIV+ transplant recipients were identified: those who were HIV+ at the time of transplantation (prevalent group) and those who seroconverted to HIV after transplantation (seroconverter group). HIV+ patients were those whose sera were positive for antibody to HIV-1 by enzyme immunoassay (LAV-EIA; Genetic Systems, Seattle, WA) and confirmed by Western blot (Immunoblot; Biorad, Richmond, CA). The serologic findings in all HIV+ patients have been confirmed with multiple testing. Universal HIV testing of all blood and tissue donors has been implemented in Pittsburgh since March 1985. Screening for HIV of recipients as a condition for candidacy has been routine since the summer of 1985.

Patients were defined as having AIDS if they met the Centers for Disease Control (CDC) criteria for AIDS (9). All AIDS defining complications were attributed to HIV alone even though these same infections occur frequently after transplantation without AIDS (10). All patients received CsA and prednisone as maintenance immunosuppression. Polyclonal antilymphocyte globulin (Stanford ALG) was used for kidney recipients. Monoclonal OKT3 was used for kidney and liver recipients after November 1984 (11). Azathioprine was given to 13 of the 25 patients. Bactrim and Acyclovir prophylaxis has been used since mid-1985, but only 2 new HIV+ patients were accrued subsequently.

Information regarding the type of immunosuppressive therapy received, the incidence and type of rejection, other complications, long-term survival and current condition, graft function, social status, and general health was also collected. Graft failure in the case of kidney recipients was defined by the need to return to dialysis. In the case of liver and heart transplant recipients, all surviving patients had normal graft function, obviating the need for further categorization of transplant results.

Control groups. Two HIV+ control groups of age-matched nonimmunosuppressed patients with known seroconversion dates were obtained. The first control group consisted of 28 hemophiliac patients cared for (12) at the Hemophilia Center of Western Pennsylvania. The second consisted of 42 patients collected at the CDC who were known to have been accidentally infected by a blood transfusion (13).

* Presented at the 15th Annual Meeting of the American Society of Transplant Surgeons, May 31-June 2, 1989, Chicago, IL.
* This work was supported by research Project Grant No. DK-29961 from the National Institutes of Health, Bethesda, MD.
* Address reprint requests to Andreas G. Tzakis, M.D., Department of Surgery, University Health Center of Pittsburgh, University of Pittsburgh, 3601 Fifth Avenue, SC Falk Clinic, Pittsburgh, PA 15213.
* The Department of Surgery, University Health Center of Pittsburgh.
* The Hemophilia Center of Western Pennsylvania, Pittsburgh, PA.
* The Centers for Disease Control, Atlanta, GA.
We also compared the survival of our HIV+ transplant recipients to that of 1303 consecutive liver recipients treated between January 1, 1980 and September 5, 1988 (14).

Statistical methods. Seroconversion dates for the transfusion and transplantation HIV seroconverter groups were taken as the day of transfusion or transplantation. Seroconversion dates for the hemophiliac group were estimated as the midpoint between last negative and first positive serum samples. All follow-ups were to March 1, 1989. Patients who did not develop AIDS but died, contributed AIDS-free time until their death. Similarly, patients who eventually developed lethal AIDS complications contributed variable amounts of AIDS-free time before the onset of these complications.

Statistical analysis utilized BMDP Statistical Software to generate Kaplan-Meier product-time estimations for both survival and AIDS-free time. The Breslow generalized Wilcoxon test was used for inferences of statistical significance.

RESULTS

Of the 25 HIV+ transplant recipients, 11 were prevalent, and 14 were seroconverters. Seventeen were male, and 8 were female. Three patients underwent transplantation despite their known HIV+ status. Their treatment reflected an institutional policy of not allowing HIV+ status as a sole factor to rule out organ-transplant candidacy.

Survival

Of the 25 patients, 13 (52%) are alive (Tables 1 and 2). Survival is the same in males (53%) as in females (50%).

Survival by organ. Seven (47%) of the 15 liver recipients are alive as well as 4 (80%) of 5 kidney recipients, and 2 (40%) of 5 heart recipients. Mean follow-up in the liver survivors is 4.5±2.1 SD years (range, 0.7–6.6). Mean follow-up in the kidney survivors is 3.4±2.2 SD years (range, 1.0–5.0). The 2 heart recipients have lived for 6.6 and 2.2 years. Because the majority of the HIV+ transplant patients were liver transplant recipients, the survival of the HIV+ patients was compared to the overall liver transplant (n = 1303) survival in our CsA experience of 1980–1988 (Fig. 1). Survival was practically identical at 1 year. Subsequent survival at 2, 4, and 5 years was lower in the HIV+ group although it never reached statistical significance. Five-year survival was 63% in the reference population compared to 53% in the HIV+ group.

Prevalent HIV+ versus seroconverters. The survival was not different in the seroconverter and prevalent transplantation groups (Fig. 2) at any point up to and including 5 years after transplantation (P = 0.69).

The 11 patients who were HIV+ at the time of transplantation (7 livers, 3 kidneys, 1 heart) are listed individually in Table 1. Six (54%) of these patients are alive after a mean 3.3±2.3 (SD) years (range, 0.7–5.7). All 5 of the deaths were of liver recipients, and 3 of them were AIDS related (Table 1).

Seven (50%) of the 14 patients who seroconverted to HIV+ after transplantation are alive (Table 2) after 4.8±1.8 (SD) years (range, 2.1–6.5) including 5 of 8 liver recipients, 1 of 2 kidney recipients, and 1 of 4 heart recipients. One of the surviving liver recipients received a graft from an HIV+ donor and seroconverted between 30 and 80 days after transplantation (15). This patient is alive 2.6 years after transplantation. Ten months ago, he developed a rectal carcinoma that was considered a complication of his preexisting ulcerative colitis. He was treated with total proctocolectomy and is well. Of the 7 deaths, 3 were AIDS related with 1 example each among the liver, kidney, and heart recipients (Table 2).

Pediatric versus adult. The 10 children had a mean age of 7.8±6.2 (SD) years at the time of liver (n = 7), kidney (n = 2), and heart transplantation (n = 1). Seven (70%) are alive after 4.7±1.8 (SD) years (range, 2.1–6.5). Three pediatric liver recipients died, 1 at 5 months from a ruptured hepatic-artery aneurysm, another at 9 months from a preexisting nervous system disorder. The third death at 3.5 years from a systemic CMV infection was attributed to AIDS. One of the pediatric renal recipients was returned to dialysis when the kidney was rejected after 8 months, but the patient is otherwise well (Table 1).

The results were worse in the adults, mean age of 43±9.2 (SD) years of whom only 6 (40%) are alive 3.5±2.4 SD years after transplantation (range, 0.7–6.6). The mortality was organ related: with 1 (25%) death after 4 kidney transplantsations, 3 (75%) of 4 after heart transplantation, and 5 (63%) of 8 after liver transplantation. Five of these deaths were from AIDS (Tables 1 and 2).

Correlations of rejection and immunosuppression. Treatment was started with CsA and prednisone in 12 patients of whom 5 are still alive. Rejection was diagnosed in 8 of them. Azathioprine was also used from the outset in the other 13, and 8

<table>
<thead>
<tr>
<th>Patient</th>
<th>Organ*</th>
<th>Age (years)</th>
<th>Current status</th>
<th>Survival time (SD) years</th>
<th>No. transplants</th>
<th>Cause of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>H</td>
<td>15</td>
<td>Alive</td>
<td>26 months</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>2a</td>
<td>L</td>
<td>48</td>
<td>Alive</td>
<td>8 months</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>3a</td>
<td>K</td>
<td>29</td>
<td>Alive</td>
<td>5 years</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>4a</td>
<td>K</td>
<td>16</td>
<td>Alive</td>
<td>5 years, 5 months</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>5a</td>
<td>K</td>
<td>64</td>
<td>Alive</td>
<td>1 year</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>6a</td>
<td>L</td>
<td>15</td>
<td>Dead</td>
<td>3 years, 6 months</td>
<td>1</td>
<td>CMV</td>
</tr>
<tr>
<td>7a</td>
<td>L</td>
<td>48</td>
<td>Dead</td>
<td>4 months</td>
<td>1</td>
<td>PCP</td>
</tr>
<tr>
<td>8a</td>
<td>L</td>
<td>0.5</td>
<td>Dead</td>
<td>9 months</td>
<td>2</td>
<td>Preexisting CNS disease*</td>
</tr>
<tr>
<td>9a</td>
<td>L</td>
<td>32</td>
<td>Dead</td>
<td>18 months</td>
<td>1</td>
<td>Immunoblastic sarcoma</td>
</tr>
<tr>
<td>10a</td>
<td>L</td>
<td>42</td>
<td>Dead</td>
<td>6 months</td>
<td>2</td>
<td>Colchicine toxicity</td>
</tr>
<tr>
<td>11a</td>
<td>L</td>
<td>3</td>
<td>Alive</td>
<td>5 years, 8 months</td>
<td>3</td>
<td>—</td>
</tr>
</tbody>
</table>

* Abbreviations: L, liver; H, heart; K, kidney.
* Time from first transplant.
* Currently on dialysis, kidney graft lost to acute rejection 8 months after transplant.
* PCP: Pneumocystis carinii.
* CNS: central nervous system.
TABLE 2. Transplant recipients who seroconverted after transplantation

<table>
<thead>
<tr>
<th>Patient</th>
<th>Organ</th>
<th>Age (years)</th>
<th>Current status</th>
<th>Survival time*</th>
<th>No. transplants</th>
<th>Cause of death*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1b</td>
<td>K</td>
<td>38</td>
<td>Dead</td>
<td>5 months</td>
<td>1</td>
<td>Generalized TB</td>
</tr>
<tr>
<td>2b</td>
<td>K</td>
<td>13</td>
<td>Alive</td>
<td>25 months</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>3b</td>
<td>L</td>
<td>46</td>
<td>Dead</td>
<td>4 months</td>
<td>2</td>
<td>HAT</td>
</tr>
<tr>
<td>4b</td>
<td>L</td>
<td>6</td>
<td>Alive</td>
<td>6 years, 6 months</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>5b</td>
<td>L</td>
<td>44</td>
<td>Dead</td>
<td>5 years, 1 month</td>
<td>1</td>
<td>Pneumonitis of unknown cause</td>
</tr>
<tr>
<td>6b</td>
<td>L</td>
<td>5</td>
<td>Alive</td>
<td>5 years, 4 months</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>7b</td>
<td>L</td>
<td>3</td>
<td>Alive</td>
<td>5 years, 8 months</td>
<td>3</td>
<td>—</td>
</tr>
<tr>
<td>8b</td>
<td>L</td>
<td>2</td>
<td>Dead</td>
<td>5 months</td>
<td>2</td>
<td>HA aneurysm</td>
</tr>
<tr>
<td>9b</td>
<td>L</td>
<td>32</td>
<td>Alive</td>
<td>5 years, 2 months</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>10b</td>
<td>H</td>
<td>42</td>
<td>Dead</td>
<td>15 months</td>
<td>1</td>
<td>PCP + List + TOX</td>
</tr>
<tr>
<td>11b</td>
<td>H</td>
<td>53</td>
<td>Dead</td>
<td>4 months</td>
<td>1</td>
<td>Heart failure</td>
</tr>
<tr>
<td>12b</td>
<td>H</td>
<td>34</td>
<td>Alive</td>
<td>6 years, 7 months</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>13b</td>
<td>H</td>
<td>47</td>
<td>Dead</td>
<td>5 months</td>
<td>1</td>
<td>Heart failure</td>
</tr>
<tr>
<td>14b</td>
<td>L</td>
<td>47</td>
<td>Alive</td>
<td>2 years, 7 months</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

* Time from first transplant.

** Abbreviations: TB, tuberculosis; HAT, hepatic artery thrombosis; HA, hepatic artery; PCP, Pneumocystis carinii; List, listeria monocytogenes meningitis; TOX, Toxoplasma gondii.

* Received a liver allograft from an HIV+ donor and seroconverted after transplantation (15, see text).

---

survived. Rejection was diagnosed in 9 of these recipients. Of the 17 patients who developed rejection in the foregoing 2 groups, 10 (59%) died. Six (55%) of 11 patients given OKT3 or ALG died. Only 2 (25%) of 8 who did not develop rejection have died.

Six liver recipients underwent retransplantation: 4 for hepatic artery thrombosis, 1 for uncontrollable acute rejection, and 1 for chronic rejection. Two of these patients are still alive and well 5.7 years later. One renal recipient is well 1.8 years after a second transplant.

** AIDS-related morbidity and mortality.** Six (24%) of the 25 HIV+ transplant recipients (1 heart, 1 kidney, 4 livers) died of AIDS after 5 months to more than 5 years (Tables 1 and 2). Cause of death included Pneumocystis Carinii pneumonia (2 cases), in 1 case coexisting with Listeria monocytogenes and Toxoplasma gondii meningitis, generalized tuberculosis (1 case), systemic cytomegalovirus (1 case), pneumonitis of unknown etiology (1 case), and immunoblastic sarcoma (1 case).

One heart (patient 1a, Table 1) and 2 liver recipients (patients 4b and 9b, Table 2) have been living with AIDS for 8, 21, and 6 months, respectively. Two have interstitial pneumonitis, and the other has oral and esophageal candidiasis and recurrent CMV infections. Posttransplantation follow-ups are 2.2, 6.5, and 5.2 years. Patient 4b has had immunosuppression stopped for 18 months. Patients 1a and 9b have had immunosuppression drastically reduced. All 3 patients have normal graft function.

The AIDS-free time after transplantation was not significantly different in the prevalent versus the HIV seroconverters (Fig. 3). For this reason, the 2 transplant subgroups were combined for comparison with the 2 nontransplant control groups (Fig. 4).

The AIDS-free times of the transplant recipients were poorer than in the blood-transfusion and hemophiliac control groups in that the transplant patients had more-frequent early development of AIDS. Four of 25 transplant recipients developed AIDS within the first 15 months, compared to 0 and 1 example in the 2 control groups (P = 0.04, Fisher's exact test). However, beyond 15 months, the slope of the curves was similar in all 3
liver patients. The difference was not
transplant recipients who remain
transfusion recipients.

AIDS patients are working full time or at school. Three more live at
currently hospitalized with recurrent hepatitis
apparently have a higher rate of
to the virus in blood components, transplanted tissues, unsterile
population (3-8). Patients with vital organ failure are exposed
home but are not able to work.

organ failure should be excluded from transplant candidacy if
their positive
were described almost immediately (1,
mainly due to the paucity of scientific data about subsequent
rehabilitation. Nine of the 13 surviving
patients who have no evidence of
prospect of benefitting from transplantation.

discussed the consequent morbidity and high mortality rates
(7). However, the single institutional series of Dummer et al.
(3) and multicenter studies (6) have shown that early AIDS
death may not be the inevitable or even the usual outcome
after transplantation under immunosuppression.

Almost certainly, the presence of HIV antibodies would have
precluded candidacy if the diagnosis in the cases cited above
from the literature and most of those reported herein had been
in advance. In retrospect, the majority have benefited
from transplantation, although the follow-up is limited to a few
years. Children have been particularly hardy in that only 1 in
10 has died of what was defined as an AIDS-related complica-
and death may not be the inevitable or even the usual outcome
after transplantation under immunosuppression.

With these findings, it was not surprising that the 5-year
survival rate after transplantation of HIV* recipients was 11%
lower than in the HIV- liver patients. The difference was not
statistically significant because of the small HIV* sample, but
there was evidence that the immunosuppression due to HIV*
status and immunosuppression for transplantation could be
more dangerous than either factor alone during the first post-
operative year. During this time, manifestations of AIDS in
organ recipients (all organs) developed at an accelerated rate
compared to HIV* patients in the 2 control groups. After 15
months, this extra risk was no longer apparent.

As risk factors with high predictive value for subsequent
AIDS are delineated (19-25), we should be able to better define
which of the HIV* transplant candidates have a reasonable
prospect of benefitting from transplantation. It already is
obvious that transplantation is medically contraindicated in pa-
ents who have AIDS or signs and symptoms of impending
AIDS.

How to apply this information in future case selection may
depend more on philosophic persuasions than scientific ones
since no form of treatment can provide perpetual life. In HIV*
patients who have no evidence of AIDS, transplantation can
prolong meaningful life in the majority of patients but less
reliably and less safely than in HIV* recipients. It is self-
evident that the same statement could be made about virtually
every other major medical or surgical therapy available today.
Such therapies are not withheld from HIV* patients because
of a predictably lower efficiency or because of high cost (26-
28). The rationing of transplantation services to exclude
asymptomatic HIV* patients from candidacy for such reasons
or even because of a potential shortage of organs would be a
departure from past practices that will have to be carefully
considered and decided upon by each individual center.

Acknowledgments. The authors are indebted to Lawrence Kingsley,
Ph.D., for his invaluable help in analyzing the data.

REFERENCES

immunodeficiency virus in the Pittsburgh transplant population:
358 TRANSPLANTATION


Received 16 June 1989.
Accepted 3 August 1989.