Human Immunodeficiency Virus Infection and Kidney Transplantation in the Era of Highly Active Antiretroviral Therapy and Modern Immunosuppression

KEVIN C. ABBOTT,* S. JOHN SWANSON,† LAWRENCE Y.C. AGODOA,‡ and PAUL L. KIMMEL, MD§

**Nephrology Service, Walter Reed Army Medical Center (WRAMC), Washington, DC, and Uniformed Services University School of the Health Sciences, Bethesda, MD; †Organ Transplant Service, WRAMC, Washington, DC, and National Institutes of Health, Bethesda, MD; ‡NIDDK, National Institutes of Health, Bethesda, MD; and §Division of Kidney Diseases and Hypertension, Department of Medicine, George Washington University Medical Center, Washington, DC.*

Abstract. Before the era of highly active antiretroviral therapy, kidney transplant recipients infected with HIV had increased risk of death compared with HIV-uninfected recipients. More recent single-center reports have indicated improved results, but this has not been assessed in a national population. Therefore, a retrospective cohort study of US adult deceased donor kidney transplant recipients from January 1, 1996, to May 31, 2001 was conducted; patients were followed until October 31, 2001. A total of 27,851 patients had valid recipient HIV serology. Cox regression analysis was used to model adjusted hazard ratios for mortality and graft loss, respectively, adjusted for other factors, including comorbid conditions from Centers for Medicare and Medicaid Studies Form 2728. Factors independently associated with HIV infection were also assessed by logistic regression analysis. Only 12.8% of HIV-infected recipients were black, compared with 27.6% in the entire study cohort. HIV-infected kidney transplant recipients were significantly less likely to be black in logistic regression analysis (adjusted OR, 0.29; 95% CI, 0.08 to 0.99; $P = 0.049$), which was the only factor independently associated with HIV infection. It was found that HIV-infected recipients had improved survival compared with HIV-uninfected recipients, although this was not statistically significant in adjusted analysis (adjusted HR, 0.36; 95% CI, 0.05 to 2.53; $P = 0.31$). Kidney transplantation in HIV-infected patients is plausible and ongoing, but HIV-infected candidates who underwent kidney transplantation in the United States during the course of the study were demographically unrepresentative of HIV-infected candidates generally.

The expected clinical course of HIV infection as it affects organ transplant recipients remains a controversial topic in kidney transplantation (1–5). In the era before highly active antiretroviral therapy (HAART), an analysis of the United States Renal Data System showed that HIV-infected recipients were at increased risk of death and graft loss compared with HIV-uninfected recipients of cadaver kidneys (6). Since the introduction of HAART in 1996, HIV-infected dialysis patients have had dramatically improved survival (7), although management of HIV-infected dialysis patients remains suboptimal, in part as a result of the complexity of medication regimens and the frequent occurrence of hepatitis C virus (HCV) coninfection (8–10). A clinical trial reported 100% survival of HIV-infected kidney transplant recipients at 1 yr (11). However, whether these results represent national experience has not been determined. To better study whether recipient HIV serologic status remains important in graft and patient survival in modern clinical transplantation, a retrospective cohort study analyzing the 2002 United States Kidney Data System (USRDS) data assessed those factors associated with HIV-infected recipients while controlling for variables previously established to affect outcomes.

Materials and Methods

Data Sources and Study Sample

The data set and analytical techniques have previously been described (12). In summary, the USRDS standard analysis file provided the primary data, including information at the time of transplantation. Follow-up information included dates and causes of graft loss, dates and causes of death, approximate dates of allograft rejection, and follow-up serum creatinine levels. Files were merged with the main file by using unique patient identifying codes to obtain follow-up data. The file was also merged with standard analysis file patient data to obtain dates and causes of death. HAART therapy, as well as therapy with sirolimus and tacrolimus, was not widely used in clinical practice until 1996. Therefore, analysis was limited to adult patients who

Received November 12, 2003. Accepted March 31, 2004.

The opinions are solely those of the authors and do not represent an endorsement by the Department of Defense or the National Institutes of Health. This is a government work. There are no restrictions on its use.

Correspondence to Dr. Kevin C. Abbott, Nephrology Service, Walter Reed Army Medical Center, Washington, DC 20307-5001. Phone: 202-782-6462/6463/6288; Fax: 202-782-0185; E-mail: kevin.abbott@na.amedd.army.mil

1046-6673/1506-1633
Journal of the American Society of Nephrology

DOI: 10.1097/01.ASN.0000127987.19470.3A

underwent deceased donor kidney transplantation from January 1, 1996, to May 31, 2001. Information about medications was limited to immunosuppressive medications. Only one transplant for a given patient during the study period (which could have been a repeat kidney transplant or a multiorgan kidney transplant) was included in analysis. Only cases with specified HIV data for both donor and recipient were included. HIV serology (from the variable "HIVC-SRN") was not independently confirmed. Because donor hepatitis C serology has recently been identified as an independent predictor of survival in this cohort (13), and because HIV and HCV infection may coexist, analysis was also limited to patients with valid recipient and donor HCV status. Similarly, the cause of end stage kidney disease could not be independently confirmed. Comorbidity data, including selected laboratory data, from the time patients presented to dialysis was also available from the Centers for Medicare and Medicaid Studies Form 2728. Because these data were not available for all patients, these variables were used in separate models. Patients were followed through October 31, 2001.

Analytic Variables and Outcome Measures

Factors Associated with HIV-Infected Recipients. This analysis used stepwise logistic regression (forward likelihood ratio method) of factors considered to be clinically significant, such as history of access complications, as well as demographic and other factors related to patient survival, including donor and recipient age, gender, race, duration of dialysis before transplantation, body mass index, receipt of previous transplant, recipient sensitization, cold ischemic time, HLA mismatch, and use of immunosuppressive medications.

Patient and Graft Survival. Survival time was defined as the time between the date of transplantation and death, the most recent follow-up date, or the end of the study period. Graft failure was defined as return to dialysis after transplantation and did not include death with a functioning graft. Variables entered into the model were those previously associated with patient and graft survival after transplantation, and included the transplantation center. Medication use was determined as induction therapy (at discharge from the initial transplantation hospitalization, primarily for antibody induction therapy) and maintenance therapy. Maintenance therapy was determined at follow-up visits at 6, 12, and 24 mo. To allow for changes in medication use, any use of medication at the specified visits was considered maintenance therapy. This resulted in overlap of medications. Therefore, models were also performed excluding medication overlap. Analyses were also performed excluding patients who received multiple organ transplants.

Covariates whose Kaplan-Meier plots violated the assumption of proportional hazard over time were assessed by yearly intervals after transplantation, as described in other similar studies (14). Because of the small number of HCV-infected patients, models were performed with covariates limited to HIV status, age, race, gender, year of transplantation, peak plasma renin activity percentage, and duration of renal replacement therapy because these were the only factors significantly associated with HIV infection in unadjusted analysis. Files were converted from SAS to SPSS by DBMS Copy 7.0 (Conceptual Software, Houston, TX). SPSS version 11.5.0 (SPSS, Chicago, IL) was used for primary analysis.

Results

From January 1, 1996, to May 31, 2001, there were 46,078 adult recipients of deceased donor kidney transplants meeting study criteria in the United States. Patients with unspecified HIV or HCV status were excluded. Thus, of the original 47,078 recipients, 2914 (6.3%) had no data regarding their donor hepatitis C status; they and an additional 6387 (13.9%) lacking data for recipient HCV status were excluded (with some overlap between the two groups), leaving 36,956 patients for study in multivariable analysis. Notably, recipients with missing HIV data (their own or their donor) did not differ statistically from patients for whom these data were known. Among study patients, 9125 (24.6%) were missing valid information on HIV recipient status and were excluded from further analysis. Of the study population, 47 patients (0.2%) were listed as HIV positive. Of these, further confirmatory information was not reliably available. None of the HIV-infected recipients were coded as lost to follow-up after the date of kidney transplantation *versus* 63 (0.2%) of HIV-uninfected recipients.

Among continuous variables (Table 1), elevated patient sen-

Table 1. Characteristics of study population (continuous variables)[a]

Factor	*n*, Missing (%)	Study Cohort	HIV-Infected Recipients
Age, yr			
recipient, mean (SD)	27,851 (0)	47.2 ± 12.6	48.2 ± 10.6
donor, mean (SD)	25,243 (9.4)	35.3 ± 17.1	33.0 ± 16.6
Recipient BMI, kg/m^2, mean (SD)[b]	24,364 (12.5)	26.3 ± 21.5	26.6 ± 4.8
Cold ischemic time, h, mean (SD)	25,903 (7.0)	19.4 ± 8.4	21.3 ± 8.3[b]
Peak PRA%, mean (SD)	26,594 (4.5)	14.0 ± 26.0	16.4 ± 28.0[c]
HLA Mismatches (0 to 6)		3.3 ± 1.80	3.3 ± 1.7
Years of RRT	25,790 (7.4)	3.80 ± 3.90	4.8 ± 5.0[c]
Values from Medical Evidence Form 2728			
hematocrit (%)	16,345 (41.3)	28.6 ± 5.8	29.2 ± 6.7
albumin (gm/dl)	14,014 (49.7)	3.5 ± 0.7	3.5 ± 0.6

[a] Analysis limited to patients with valid HIV serologies, as well as valid recipient and donor hepatitis C serologies. RRT, kidney replacement therapy before kidney transplant.
[b] $P < 0.05$ by *t* test *versus* non-HIV-infected patients.
[c] $P < 0.05$ by Mann-Whitney test *versus* non-HIV-infected patients.

sitization, longer cold ischemic time, and increased duration of dialysis before transplantation were associated with HIV-infected recipients. In general, HIV-infected recipients were younger with remarkably preserved hematocrit and albumin levels at presentation to end-stage kidney disease. In categorical variables (Table 2), only recipient black race (which was much less common among HIV-infected recipients than among the entire study population) and use of Zenapax (Daclizumab) immunosuppression were significantly associated with HIV-infected recipient status. Only two HIV-infected recipients were not either black or white (one each Asian and Native American). The numbers of HIV-infected patients by year of

Table 2. Analysis of associations with recipient HIV seropositivity by variable, adult cadaveric kidney transplant recipients between January 1, 1996 and May 31, 2001[a]

	All Cadaveric Kidney Transplant Recipients *n* (%)	HIV-Infected Recipients
n	27,851	47 (0.2)
Mean follow-up, yr	2.99 ± 1.59	2.62 ± 1.32
Graft loss	1898 (6.8)	1 (2.1)
Death	3569 (12.8)	2 (4.3)
Variable, *n*		
recipient hepatitis C-positive	8875 (6.8)	3 (6.4)
recipient male (*versus* female)	16,890 (60.6)	30 (63.8)
recipient African-American (*versus* all other races)	7684 (27.6)	6 (12.8)[b]
dialysis in the first week posttransplant (Y/N)	6349 (23.0)	9 (19.1)
rejection in the first year posttransplant, diagnosis and treatment (Y/N)	5217 (18.8)	8 (17.0)
Cause of kidney disease		
diabetes	7833 (31.8)	13 (30.2)
GN	4306 (15.5)	4 (8.5%)
repeat transplant (*versus* primary)	3084 (11.2)	9 (19.0)
Primary insurance		
private or self-pay	8874 (31.9)	16 (34)
Medicare	17,121 (61.7)	29 (61.7)
Medicaid	1225 (4.4)	1 (2.1)
other government	354 (1.3)	1 (2.1)
Maintenance medications[c]		
cyclosporine	16,974 (67.4)	30 (68.2)
tacrolimus	10,776 (42.8)	19 (43.2)
mycophenolate	19,732 (78.4)	38 (86.4)
azathioprine	6014 (23.9)	7 (15.9)
induction antibody use	13,436 (48.3)	22 (46.8)
Medicare claims		
Access related complications		
ACS		
CHF		
Comorbidities from Medical Evidence Form 2728[d]		
illicit drug use	89 (0.5)	0
ischemic heart disease	1758 (7.4)	4 (13.8)
congestive heart failure	2493 (10.5)	1 (3.4)
peripheral vascular disease	1108 (4.5)	3 (19.3)
smoking	976 (5.5)	1 (3.4)
alcohol use	145 (0.8)	0

[a] Results given as % (*n*) or mean ± standard deviation. SD, standard deviation; ESRD, end-stage kidney disease; PRA, panel reactive antibody. Only demographic factors and factors significantly associated with HIV in univariate analysis were included in the logistic regression model.

[b] $P < 0.05$ by chi-square test *versus* non-HIV-infected patients.

[c] Percentages do not total to 100 due to missing values and overlap.

[d] The information from this form was available only for patients who started dialysis on or after April 1, 1995, or for 23,405 (63.3%) of the study population.

transplantation and by race are shown in Figure 1, which shows an increase in the proportion of HIV-infected recipients who are black since 2000, although this difference was not statistically significant. Illicit drug use and alcohol use, as well as repeat transplantation, were not associated with HIV infection. Cardiac comorbid conditions, with the exception of ischemic heart disease, were less common in HIV-infected recipients, but not significantly so. Graft failure/repeat transplantation as a cause of graft loss was significantly associated with HIV infection, but the original cause of kidney disease was not specified for those patients. Neither focal segmental glomerulosclerosis nor HIV-associated nephropathy (HIVAN) was listed as a cause of kidney disease for any of the HIV-infected patients.

In logistic regression analysis, only African American race remained independently associated with HIV-infected status (adjusted OR, 0.29; 95% CI, 0.08 to 0.99; $P = 0.049$). For validation, data were also obtained for the total cohort of 46,078 deceased donor kidney transplant recipients regardless of HCV status. In this cohort, 54 recipients were coded as HIV infected, of whom 14.8% were black in comparison to 27.5% of non–HIV-infected recipients ($P = 0.04$, χ^2 test).

Patient and Graft Survival

Figure 2 shows a Kaplan-Meier plot of patient survival stratified by HIV status. HIV-infected patients had more than 95% survival past 3 yr beyond kidney transplantation; only two HIV-infected patients (4.3%) died, compared with 3569 (12.8%) of HIV-uninfected patients during the study period. The corresponding figures for graft loss are listed in Table 2 (2.3% for HIV infected and 6.8% for HIV uninfected). In Cox regression analysis adjusted for donor and recipient age, race, gender, duration of dialysis before transplantation, donor and recipient HCV status, use of mycophenolate immunosuppression, delayed graft function, and body mass index, HIV was not independently associated with improved patient survival, although the risk of death for HIV-infected recipients was lower than for HIV-negative recipients (adjusted HR, 0.36; 95% CI, 0.05 to 2.53; $P = 0.31$).

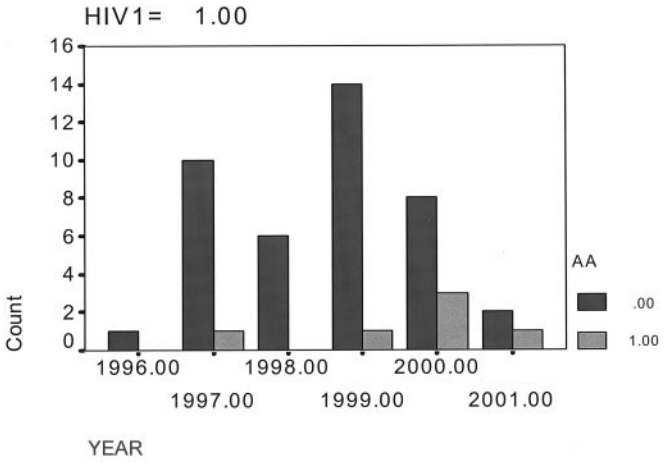

Figure 1. Number of HIV-infected patients who received deceased donor kidney transplants in the United States, according to United Network for Organ Sharing/United States Kidney Data System reports, from 1996 to June 2001. As shown, the proportion of HIV-infected recipients who were black was quite low, although this trend appeared to change starting in 2000. Only three HIV-infected patients were transplanted from January to June 2001, precluding further interpretation. The lighter shaded bars (right) represent black HIV-infected patients; the darker bars (left) represent white HIV-infected patients.

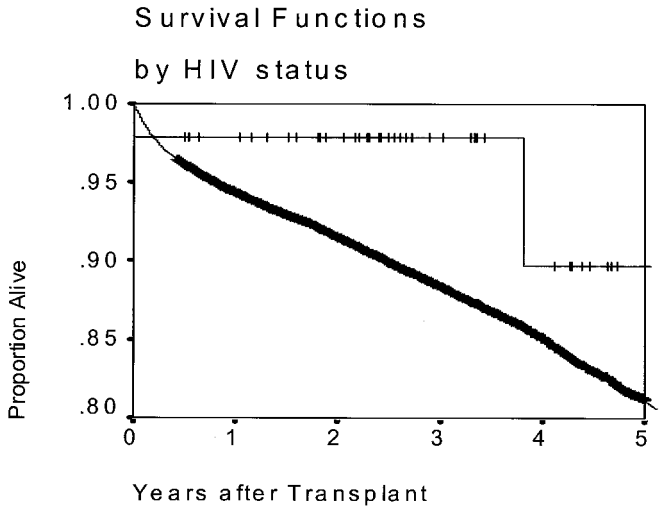

Figure 2. Kaplan-Meier plot of patient survival after deceased donor kidney transplantation, stratified by patients with HIV infection (HIV+) *versus* no HIV infection (HIV−). Survival of HIV-infected patients was not different compared with uninfected patients ($P = 0.15$, log-rank test).

Discussion

Similar to results of recent clinical trials, post–kidney transplantation outcomes for HIV-infected recipients in the United States were quite good (11). In our previous USRDS analysis of deceased donor kidney recipients during the pre-HAART era, we found that HIV-infected recipients had 3-yr patient survival of 83% compared with 88% in uninfected patients (6). Although this finding was independently significant in adjusted analysis, it was more modest than expected and not nearly as adverse as the effect of HIVAN on survival in chronic dialysis patients in the pre-HAART era (15), which has also improved in recent years (7). Although survival for HIV-infected patients was no different than for HIV-uninfected patients in the study, we suspect selection bias may have resulted in patients who were substantially healthier than their HIV-uninfected counterparts. Transplantation centers looking for early successes may have been more restrictive in selecting HIV-infected candidates for kidney transplantation than recommended in a recent review (16). This is suggested by the extraordinarily low proportion of black HIV-infected recipients in the study presented here, as well as the fact that none of the HIV-infected patients had focal segmental glomerulosclerosis or HIVAN as a cause of end-stage renal disease, the most common causes of nephropathy in this population (5), or evidence of HCV seropositivity. Two recent studies reported that over 80% of HIV-infected patients on maintenance dialysis were black, and over

60% were also HCV infected (8,9); further, over 45% who underwent biopsy had a diagnosis of HIVAN. In addition, with few exceptions, HIV-infected patients had evidence of better general health than their HIV-uninfected counterparts, although few differences were statistically significant because of small numbers.

This is in contrast to findings of significantly lower hematocrit and serum albumin levels among HIV-infected patients in our previous USRDS study (15). Given these potential biases and the much smaller proportion of HIV-infected patients undergoing kidney transplantation than undergoing maintenance dialysis (4,11), no broad conclusions about improved posttransplantation survival for HIV-infected recipients in the modern era should be drawn on the basis of the study presented here. However, it does appear that HIV-infected patients can enjoy successful posttransplantation outcomes. Perhaps even more important than this finding is that use of kidney transplantation for HIV-infected candidates in the United States appears to be highly restrictive and unrepresentative of the HIV-infected population generally. These characteristics stand in contrast to HCV-infected kidney transplant recipients, whose demographic characteristics are quite similar to HCV-infected patients on dialysis and in the general population (17). Therefore, potential barriers to transplantation for HIV-infected candidates should be investigated.

Beyond the possible selection bias above, other factors make the remarkable posttransplantation survival of HIV-infected recipients plausible as well. The course of HIV-infected recipients after kidney transplantation may benefit from many serendipitous effects of commonly used immunosuppressive agents. For example, sirolimus inhibits HIV replication at the transcriptional level (18), and more recently, sirolimus has been reported to cause downregulation of CCR5 and accumulation of anti-HIV β-chemokines (19). Curiously, although there have been a few exceptions (20), mycophenolate has consistently been associated with increased risk of cytomegalovirus infection after kidney transplantation (21–24). Mycophenolate, which has inhibitory effects on HIV (25), is synergistic with many antiretroviral agents (26,27) and is being used for multidrug-resistant cases of HIV (28,29). Even certain calcineurin inhibitors such as cyclosporine and its analogs have anti-HIV activity (30,31). In contrast, no such beneficial findings have been reported for tacrolimus, and the HIV inhibitory activity may be independent of FKBP (32). In addition, we are not aware of any reports showing a beneficial effect of azathioprine on HIV infection. On the basis of the evidence above, it might make the most sense to design regimens excluding azathioprine and tacrolimus for HIV-infected patients, particularly given recent registry results indicating that use of sustained release cyclosporine (Neoral) is associated with equivalent graft survival to tacrolimus (33).

HAART therapy interacts with most immunosuppressive therapy above, requiring careful monitoring and dose adjustment (34,35). Several studies have now documented that HAART therapy is underused in chronic dialysis patients (8–10). Whether the same is true for transplant recipients is unknown, and such information could not be obtained from the USRDS database. However, it is likely the benefits of HAART therapy outweigh the disadvantages. Recommendations for use of HAART in dialysis patients are available (1,36); recommendations regarding the use of HAART after kidney transplantation has been more individualized (11) pending recommendations (37).

Limitations of the study presented here include our inability to determine use of HAART therapy or to determine the clinical stage and other manifestations of disease in HIV-infected patients. The main concern is the possibility that the renal transplant recipients listed in the database represent false positives. Unfortunately, as a result of the limitations of the database, this cannot be cross-verified. For example, information on the Medical Evidence Form (for all variables) was missing in 38% of HIV-positive recipients. Because information on HIV status is missing for more than 80% of dialysis patients in Form 2728 generally, an even higher percentage of HIV-positive recipients did not have information on HIV status from Form 2728 in the study presented here (89%), and no HIV-positive recipients were indicated as positive (which would indicate HIV status at the time of presenting to dialysis). The mean duration of dialysis before transplantation for the HIV-positive patients was 4.5 yr for white HIV-positive recipients and 6.2 yr for black HIV-positive recipients, so many could have become positive after starting dialysis. Use of Medicare claims data would likely be even more limited because of fears of uninsurability as a result of reporting to Medicare, as well as requiring that the database be limited to patients with evidence of Medicare as primary payer at the time of transplantation, which would further decrease sample size, although false positives would be unlikely. In the absence of data on the time of wait-listing the study cannot examine the effect that differential wait list times may have on the observed racial differences in achieved transplantation rates. However, because of the long wait before transplantation, it is highly unlikely patients would be reported to the United Network for Organ Sharing as HIV positive without verification. Because of the research agreement of the USRDS, we were prohibited from contacting individual centers or patients regarding their status.

Information on the use of other agents that have shown benefit in HIVAN, such as angiotensin converting enzyme inhibitors (38,39), was also not available. We were unable to confirm the diagnosis or stage of HIV infection. HIV-infected patients indicated in the USRDS database do not appear to be representative of most HIV-infected patients with chronic kidney disease, and thus results are most likely not generalizable. Nevertheless, description of the clinical practice patterns of kidney transplantation for HIV-infected patients is useful to look at trends and perhaps to determine whether transplantation is being used equitably for HIV-infected transplant candidates.

In summary, this analysis of the USRDS transplant population indicates that kidney transplantation in HIV-infected recipients is plausible and ongoing. The proper use of immunosuppression and HAART therapy awaits the results of properly designed prospective clinical trials. The unrepresentative clinical characteristics of the HIV-infected patients in this study

suggest extreme caution on the part of transplantation centers will be necessary to assure good early outcomes for this practice. It is expected that the number of HIV-infected patients undergoing renal transplantation will increase substantially after the performance of multicenter collaborative clinical trials. The finding of white patients being overrepresented is consistent with non-HIVAN patients receiving transplants, *i.e.*, those with diabetic nephropathy or another disease who became coinfected with HIV during the course of treatment, as outlined by Glassock *et al.* (40) early in the course of the epidemic. Undoubtedly, data in the future will show much more diffusion of transplantation to African Americans with HIVAN. However, given the success in this and previous studies, it may be time to apply kidney transplantation more widely to HIV-infected candidates.

References

1. Rao TK: Human immunodeficiency virus infection in end-stage kidney disease patients. *Semin Dial* 16: 233–244, 2003
2. Kuo PC, Stock PG: Transplantation in the HIV-infected patient. *Am J Transplant* 1: 13–17, 2001
3. Gow PJ, Pillay D, Mutimer D: Solid organ transplantation in patients with HIV infection. *Transplantation* 72: 177–181, 2001
4. Halpern SD, Ubel PA, Caplan AL: Solid-organ transplantation in HIV-infected patients. *N Engl J Med* 347: 284–287, 2002
5. Kimmel PL, Barisoni L, Kopp JB: Pathogenesis and treatment of HIV-associated kidney diseases: Lessons from clinical and animal studies, molecular pathologic correlations, and genetic investigations. *Ann Intern Med* 139: 214–226, 2003
6. Swanson SJ, Kirk AD, Ko CW, Jones CA, Agodoa LY, Abbott KC: Impact of HIV seropositivity on graft and patient survival after cadaveric kidney transplantation in the United States in the pre highly active antiretroviral therapy (HAART) era: An historical cohort analysis of the United States Kidney Data System. *Transpl Infect Dis* 4: 144–147, 2002
7. Ahuja TS, Grady J, Khan S: Changing trends in the survival of dialysis patients with human immunodeficiency virus in the United States. *J Am Soc Nephrol* 13: 1889–1893, 2002
8. Rodriguez RA, Mendelson M, O'Hare AM, Hsu LC, Schoenfeld P: Determinants of survival among HIV-infected chronic dialysis patients. *J Am Soc Nephrol* 14: 1307–1313, 2003
9. Szczech LA, Kalayjian R, Rodriguez R, Gupta S, Coladonato J, Winston J: Adult AIDS Clinical Trial Group Kidney Complications Committee: The clinical characteristics and antiretroviral dosing patterns of HIV-infected patients receiving dialysis. *Kidney Int* 63: 2295–2301, 2003
10. Abbott KC, Trespalacios FC, Agodoa LY, Ahuja TS: HIVAN and medication use in chronic dialysis patients in the United States: Analysis of the USRDS DMMS Wave 2 study [Electronic publication]. *BMC Nephrol* 4:5, 2003
11. Stock PG, Roland ME, Carlson L, Freise CE, Roberts JP, Hirose R, Terrault NA, Frassetto LA, Palefsky JM, Tomlanovich SJ, Ascher NL: Kidney and liver transplantation in human immunodeficiency virus-infected patients: A pilot safety and efficacy study. *Transplantation* 76: 370–375, 2003
12. Swanson SJ, Hypolite I, Oliver JD, Kirk AD, Ko CW, Agodoa LY, Peters TG, Abbott KC: Effect of donor factors on early graft survival in adult cadaveric kidney transplantation. *Am J Transplant* 2: 68–75, 2002
13. Abbott KC, Bucci JR, Matsumoto CS, Swanson SJ, Agodoa LY, Holtzmuller KC, Cruess DF, Peters TG: Hepatitis C and kidney transplantation in the era of modern immunosuppression. *J Am Soc Nephrol* 14: 2908–2918, 2003
14. Mange KC, Joffe MM, Feldman HI: Effect of the use or nonuse of long-term dialysis on the subsequent survival of kidney transplants from living donors. *N Engl J Med* 344: 726–731, 2001
15. Abbott KC, Hypolite I, Welch PG, Agodoa LY: Human immunodeficiency virus/acquired immunodeficiency syndrome–associated nephropathy at end-stage kidney disease in the United States: Patient characteristics and survival in the pre highly active antiretroviral therapy era. *J Nephrol* 14: 377–383, 2001
16. Roland ME, Lo B, Braff J, Stock PG: Key clinical, ethical, and policy issues in the evaluation of the safety and effectiveness of solid organ transplantation in HIV-infected patients. *Arch Intern Med* 163: 1773–1778, 2003
17. Abbott KC, Bucci JR, Matsumoto CS, Swanson SJ, Agodoa LY, Holtzmuller KC, Cruess DF, Peters TG: Hepatitis C and kidney transplantation in the era of modern immunosuppression. *J Am Soc Nephrol* 14: 2908–2918, 2003
18. Roy J, Paquette JS, Fortin JF, Tremblay MJ: The immunosuppressant rapamycin represses human immunodeficiency virus type 1 replication. *Antimicrob Agents Chemother* 46: 3447–3455, 2002
19. Heredia A, Amoroso A, Davis C, Le N, Reardon E, Dominique JK, Klingebiel E, Gallo RC, Redfield RR: Rapamycin causes down-regulation of CCR5 and accumulation of anti-HIV beta-chemokines: An approach to suppress R5 strains of HIV-1. *Proc Natl Acad Sci U S A* 100: 10411–10416, 2003
20. Giral M, Nguyen JM, Daguin P, Hourmant M, Cantarovich D, Dantal J, Blancho G, Josien R, Ancelet D, Soulillou JP: Mycophenolate mofetil does not modify the incidence of cytomegalovirus (CMV) disease after kidney transplantation but prevents CMV-induced chronic graft dysfunction. *J Am Soc Nephrol* 12: 1758–1763, 2001
21. Abbott KC, Hypolite IO, Viola R, Poropatich RK, Hshieh P, Cruess D, Hawkes CA, Agodoa LY: Hospitalizations for cytomegalovirus disease after kidney transplantation in the United States. *Ann Epidemiol* 12: 402–409, 2002
22. Schnitzler MA, Lowell JA, Hardinger KL, Boxerman SB, Bailey TC, Brennan DC: The association of cytomegalovirus seropairing with outcomes and costs following cadaveric kidney transplantation prior to the introduction of oral ganciclovir CMV prophylaxis. *Am J Transplant* 3: 445–451, 2003
23. Zmonarski SC, Boratynska M, Madziarska K, Klinger M, Kusztel M, Patrzalek D, Szyber P: Mycophenolate mofetil severely depresses antibody response to CMV infection in early posttransplant period. *Transplant Proc* 35: 2205–2206, 2003
24. Grinyo JM, Gil-Vernet S, Cruzado JM, Caldes A, Riera L, Seron D, Rama I, Torras J: Calcineurin inhibitor-free immunosuppression based on antithymocyte globulin and mycophenolate mofetil in cadaveric kidney transplantation: Results after 5 years. *Transpl Int* 16:820–827, 2003
25. Chapuis AG, Paolo Rizzardi G, D'Agostino C, Attinger A, Knabenhans C, Fleury S, Acha-Orbea H, Pantaleo G: Effects of mycophenolic acid on human immunodeficiency virus infection in vitro and in vivo. *Nat Med* 6: 762–768, 2000
26. Margolis DM, Kewn S, Coull JJ, Ylisastigui L, Turner D, Wise H, Hossain MM, Lanier ER, Shaw LM, Back D: The addition of mycophenolate mofetil to antiretroviral therapy including abacavir is associated with depletion of intracellular

deoxyguanosine triphosphate and a decrease in plasma HIV-1 RNA. *J Acquir Immune Defic Syndr* 31: 45–49, 2002
27. Hossain MM, Coull JJ, Drusano GL, Margolis DM: Dose proportional inhibition of HIV-1 replication by mycophenolic acid and synergistic inhibition in combination with abacavir, didanosine, and tenofovir. *Antivir Res* 55: 41–52, 2002
28. Press N, Kimel G, Harris M, Yip B, Craib KJ, Montaner JS: Case series assessing the safety of mycophenolate as part of multidrug rescue treatment regimens. *HIV Clin Trials* 3: 17–20, 2002
29. Coull JJ, Turner D, Melby T, Betts MR, Lanier R, Margolis DM: A pilot study of the use of mycophenolate mofetil as a component of therapy for multidrug-resistant HIV-1 infection. *J Acquir Immune Defic Syndr* 26: 423–434, 2001
30. Billich A, Hammerschmid F, Peichl P, Wenger R, Zenke G, Quesniaux V, Rosenwirth B: Mode of action of SDZ NIM 811, a nonimmunosuppressive cyclosporin A analog with activity against human immunodeficiency virus (HIV) type 1: Interference with HIV protein-cyclophilin A interactions. *J Virol* 69: 2451–2461, 1995
31. Franke EK, Luban J: Inhibition of HIV-1 replication by cyclosporine A or related compounds correlates with the ability to disrupt the Gag–cyclophilin A interaction. *Virology* 222: 279–282, 1996
32. Minder D, Boni J, Schupbach J, Gehring H: Immunophilins and HIV-1 infection. *Arch Virol* 147: 1531–1542, 2002
33. Kaplan B, Schold JD, Meier-Kriesche HU: Long-term graft survival with neoral and tacrolimus: A paired kidney analysis. *J Am Soc Nephrol* 14: 2980–2984, 2003
34. Jain AK, Venkataramanan R, Shapiro R, Scantlebury VP, Potdar S, Bonham CA, Ragni M, Fung JJ: The interaction between antiretroviral agents and tacrolimus in liver and kidney transplant patients. *Liver Transpl* 8: 841–845, 2002
35. Jain AK, Venkataramanan R, Fridell JA, Gadomski M, Shaw LM, Ragni M, Korecka M, Fung J: Nelfinavir, a protease inhibitor, increases sirolimus levels in a liver transplantation patient: A case report. *Liver Transpl* 8: 838–840, 2002
36. Izzedine H, Launay-Vacher V, Baumelou A, Deray G: An appraisal of antiretroviral drugs in hemodialysis. *Kidney Int* 60: 821–830, 2001
37. Izzedine H, Launay-Vacher V, Baumelou A, Deray G: Antiretroviral and immunosuppressive drug-drug interactions: An update. *Kidney Int* 2004, in press.
38. Kimmel PL, Mishkin GJ, Umana WO: Captopril and kidney survival in patients with human immunodeficiency virus nephropathy. *Am J Kidney Dis* 28: 202–208, 1996
39. Wei A, Burns GC, Williams BA, Mohammed NB, Visintainer P, Sivak SL: Long-term kidney survival in HIV-associated nephropathy with angiotensin-converting enzyme inhibition. *Kidney Int* 64: 1462–1471, 2003
40. Glassock RJ, Cohen AH, Danovitch G, Parsa KP: Human immunodeficiency virus (HIV) infection and the kidney. *Ann Intern Med* 112: 35–49, 1990 [Erratum in *Ann Intern Med* 112: 476, 1990]