

## Responding to Organ Failure in HIV-Infected Patients

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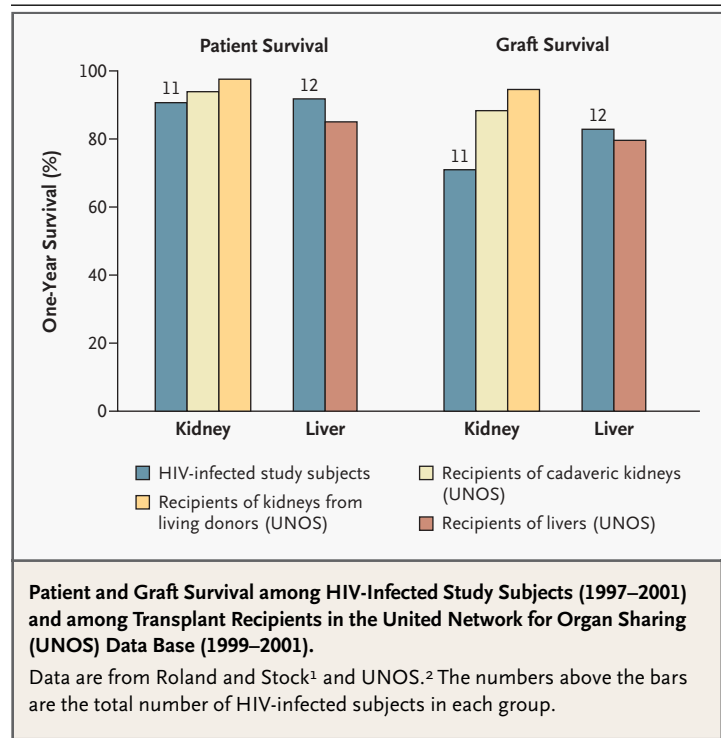
Until recently, patients infected with the human immunodeficiency virus (HIV) who had organ failure were not routinely evaluated for transplantation. The poor prognosis for persons with the acquired immunodeficiency syndrome (AIDS) early in the HIV epidemic led to their exclusion from organ-transplant waiting lists that were overflowing with patients who were expected to live much longer. The few patients with unrecognized HIV infection who received a transplant had a variable course, often characterized by rapid progression of HIV disease. Furthermore, there was an understandable fear of transmission of HIV to health care workers during invasive procedures.

Even as the prognosis for HIV-infected persons improved with the introduction of new therapies in the late 1990s, the reluctance to recommend organ transplantation for this population persisted. There remained uncertainty regarding the durability of the life-sustaining responses to treatments for HIV infection. In addition, therapeutic strategies for HIV that focused on restoring the immune system were seemingly at odds with those in transplantation medicine that aimed at blunting the immune response in an effort to prevent organ rejection. Potential transplantation candidates with HIV infection were thought to have an unacceptably high risk of post-transplantation infectious and neoplastic complications.

This view began to change as a result of advances in both the HIV and transplantation fields. Not only did life expectancy for HIV-infected persons increase, but also the risk of opportunistic infections dramatically decreased. With prolonged survival, more HIV-infected patients faced end-organ disease from coexisting conditions such as hepatitis B or C and HIV nephropathy, which posed a

more serious threat than did HIV disease itself. At the same time, there was a growing understanding that immune activation may contribute to the progression of HIV disease. This knowledge raised the intriguing possibility that the immunosuppression used to prevent rejection might be beneficial for patients with HIV disease that had been successfully controlled by antiretroviral agents.

Outcomes in transplant recipients also improved with better immunosuppression strategies. More effective prophylactic regimens led to a reduction in the rate of opportunistic infections. The criteria for





Dr. Robert Zackin

transplantation were expanded to include a much broader population of patients. The transplantation field has never shied away from patients with complex medical diseases such as hepatitis, diabetes, or collagen vascular disease. Hence, it is not surprising that when the incidence of end-organ disease increased among HIV-infected patients, the response to the question of whether to consider an HIV-infected patient with organ failure for transplantation evolved from “why?” to “why not?”

This issue of the *Journal* contains a remarkable report of a successful heart transplantation in a patient infected with HIV type 1 (HIV-1) (pages 2323–2328). The patient (Dr. Robert Zackin) presented with AIDS as we first knew it — *Pneumocystis carinii* pneumonia, Kaposi’s sarcoma, disseminated *Mycobacterium avium* complex, and cytomegalovirus infection of the gastrointestinal tract. He began receiving anti-HIV therapy, switching regimens as quickly as each new HIV drug became available. He ultimately had an excellent response to treatment, with substantial increases in CD4 cell counts and suppression of HIV-1 in plasma. Unfortunately, a cardiomyopathy, probably resulting from his previous treatment for Kaposi’s sarcoma, worsened, threatening his life. Despite a previous history of severe opportunistic infections, he was accepted on the waiting list for heart transplantation at the Cleveland Clinic. His condition deteri-

orated, necessitating intraaortic balloon counterpulsation for cardiac support while he was awaiting an organ. He survived long enough to receive a heart transplant. He had no opportunistic infections postoperatively. Even his Kaposi’s sarcoma, a potentially serious complication in immunosuppressed transplant recipients, has not recurred. As testimony to his fortitude and determination, he has returned to full-time work and exercises regularly.

The contribution of the extraordinary care provided by an institution and caregivers with expertise in HIV disease and transplantation to the outcome in this exceptional case cannot be underestimated. This case is reported against a background of growing clinical experience with solid-organ transplantation in HIV-infected persons. In a recent study of 45 HIV-infected recipients of kidney or liver transplants, outcomes in the subgroup of 23 patients with at least one year of follow-up were in the range of those reported by the United Network for Organ Sharing for more than 45,000 patients (see graph). In the period after transplantation, there were only two opportunistic complications, CD4+ T-cell counts remained stable, and HIV RNA levels in plasma were suppressed. This group of patients was carefully selected. No patients with a history of opportunistic infections or with a CD4 cell count below 200 per cubic millimeter before kidney transplantation or below 100 per cubic millimeter before liver transplantation were included. In addition, it was expected that, with antiretroviral therapy, HIV suppression after transplantation would be achievable in all of them.

What has been learned from the transplantation experience in HIV-infected patients in this new era? First, patients in whom optimal control of HIV disease has been achieved appear to have a reasonable short-term prognosis that is similar to that for transplant recipients without HIV infection. Second, careful monitoring for interactions between immunosuppressant drugs and anti-HIV medication is required in order to ensure that effective therapy for both HIV and rejection is sustained. Finally, the multidisciplinary team evaluating and caring for these patients must include clinicians with expertise in both HIV disease and transplantation. In response to the need for further definition of the outcomes in HIV-infected transplant recipients, the National Institutes of Health is supporting a multicenter study of 150 kidney transplantations and 125 liver transplantations. Originally, that study was to

include heart transplantations, but its design was revised to focus on those organs for which there is a greater need. It is hoped that funds will become available to add heart transplantation if the preliminary results are positive.

Progress in the clinical management of HIV infection has been influenced not only by investigators and clinicians, but also by patients and their advocates. Revisiting the policy of excluding HIV-infected persons from consideration for solid-organ transplantation has involved collaboration among clinicians, basic and clinical scientists, patients, and activists. The patient described in the current case report is the senior author of the report and an academician. He is also an activist representing the concerns of people with HIV infection with regard to transplantation. Another patient, who is a prominent playwright and AIDS activist, received a liver transplant because of hepatitis B-induced cirrhosis more than a year ago. In the process, he has become acutely aware of the shortage of organs and is a vocal advocate for increasing the number of organs donated in the United States.

This case report of a heart transplant in an HIV-1-infected recipient who is doing well two years after transplantation, in conjunction with preliminary results from current studies of liver and kidney transplantation, provides hope that selected patients with HIV infection and end-organ failure can benefit from solid-organ transplantation. Bringing the worlds of HIV treatment and transplantation together opens up the possibilities of synergy and progress in important scientific arenas, including immunology and pharmacology; in clinical areas such as the management of peritransplantational hepatitis C; and in public policy. Such progress can benefit all patients who now need or might someday need a transplant and the families and friends who love them.

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1. Roland ME, Stock PG. Review of solid organ transplantation in HIV-infected patients. *Transplantation* 2003;75:425-9.
2. UNOS home page. Richmond, Va.: United Network for Organ Sharing. (Accessed May 5, 2003, at <http://www.unos.org>.)

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## The New Medical Malpractice Crisis

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A major medical malpractice crisis is unfolding in the United States today. The American Medical Association has identified 18 states in which physicians and institutional health care providers are having grave difficulties obtaining affordable professional liability insurance. In the past two years, insurance premiums in these states have increased dramatically for physicians in high-risk specialties such as obstetrics, emergency medicine, general surgery, surgical subspecialties, and radiology (see Figure). Another 26 states are on "orange alert," with indicators suggesting a serious and worsening situation. Physicians in West Virginia, New Jersey, Florida, Pennsylvania, Mississippi, Illinois, Texas, and Missouri have held or threatened work stoppages to draw attention to their plight, and several hospitals in the states that have been hit the hardest have temporarily closed or threatened to close emergency room, obstetrical, or other services.

Although alarming to many clinicians and policymakers, today's problems are not new. There have been two other major medical malpractice crises in recent history. The first, in the early to mid-1970s, has generally been described as a crisis of insurance availability. Its distinguishing features were the exit of major malpractice insurers from the market and the inability of many physicians to obtain coverage at any price. This led to the formation in many states of insurance companies owned and operated by physicians ("bedpan mutuals") and state-sponsored joint underwriting associations, many of which still operate today. The second crisis, in the early to mid-1980s, was a crisis of affordability: insurers continued to write policies but charged premiums that many physicians could not afford to pay. Notwithstanding these differences, both previous crises involved a key sequence of events. Physicians in multiple states encountered a sudden spike in mal-