Transplantation and HIV: Facing Two Threats to Life
Laurie Carlson, MSN

Thanks to the tremendous progress in antiviral treatment, HIV is now considered a chronic illness, with all the benefits—and challenges—of increased life expectancy and improved quality of life. Among the demands of “living” with a chronic illness that have received the most attention are: adhering to complex treatment regimens and treatment side effects, making decisions about a newly extended future, and negotiating an often rediscovered sexuality. One that has received less attention is confronting the physical consequences of HIV over the long term, perhaps the most frightening of which is organ failure.

Increasingly, people with HIV develop kidney and liver failure—in spite of well-controlled HIV disease. The leading cause of liver failure among people with HIV is co-infection with hepatitis C virus (HCV) or hepatitis B virus (HBV). It is also notable that HCV- and HBV-related liver failure is a leading cause of death among people with HIV.1,2 Liver failure may also occur in response to the toxic effects of HIV antiviral drugs. HIV-associated nephropathy is one of the leading causes of kidney failure in young Black men. It occurs seven to ten times more frequently in men than in women, and 30 percent to 60 percent of people with HIV-associated nephropathy have used injection drugs. Renal lesions in HIV-positive people are also caused by hepatitis C, diabetes, and hypertension.

Although transplantation is considered the treatment of choice for end-stage organ failure, until recently, it was not available to people with HIV. Concerns ranged from reticence about allocating scarce organs to people already facing a shortened life expectancy, to fears that the effects of the immunosuppressive medications necessary to prevent organ rejection might place the health of an already immunosuppressed person at unacceptable risk. Today, with improved HIV treatment, these medical concerns are no longer as compelling. (See “The Medicine of HIV-Related Organ Transplantation,” page 5.)

But in the context of a disease that already presents a huge array of psychosocial challenges—ranging from dealing with stigma to facing death—the transplantation process raises some new concerns for people with HIV. This article discusses these ramifications in the context of two sets of research literature: one on coping with HIV, the other on coping with transplantation. It is also based on personal experience with 12 HIV-positive transplant recipients treated at the University of California San Francisco over the past two years.

Building on HIV-Related Strengths

In many respects, people with HIV seem better equipped than most people to deal with the challenges of being transplant recipients. Living with HIV has helped many individuals develop remarkable coping skills. Many have developed a “survivor spirit” and have learned to manage complex medication and medical regimens. They have confronted their own mortality and dealt with the body changes and side effects that accompany a life-threatening chronic illness. Often, they have strong social support from the HIV community as well as from partners, family, and friends, and frequently, they are active, rather than passive, in their pursuit of care. Transplantation challenges these skills in new ways, but with the help of their providers, people with HIV can capitalize on these strengths and find ways to apply them in this new situation.

Perhaps the biggest challenge facing transplant recipients, including those with HIV, is an unfamiliarity with the pre-transplant process and the realities of the post-transplant experience. While this challenge...
Imagine regaining your health—triumphing, at least for now, over HIV—only to face death from an unexpected quarter: the failure of your liver or kidney. Imagine, after all the uncertainty involved with living with HIV, confronting the uncertainty of whether a donor organ will become available before your body gives out. Imagine mastering the complexity of an HIV medication regimen, the dozen or so pills, the dosing requirements, the side effects, only to add another dozen or so antirejection, antihypertensive, antidepressant pills to the daily ritual.

A growing number of people with HIV are experiencing “solid organ failure.” But the treatment of choice—transplantation—represents a limited resource, and the procedure is extreme and invasive. As significant, living with a transplant, like living with HIV, requires a lifelong commitment.

The connection between AIDS and transplantation received a lot of attention last December when AIDS activist Larry Kramer became one of the few HIV-positive people to receive a new liver. In this issue of FOCUS, colleagues Laurie Carlson and Michelle Roland describe the range of both the psychosocial and medical issues involved in HIV-related organ failure and transplantation. Carlson examines how living with HIV has both advantages and disadvantages when a person with HIV faces organ failure. The primary advantage is the “remarkable coping skills” that HIV instills, including a “survivor spirit” and the ability to manage complex and ongoing medical treatment. Roland discusses the combined research and clinical trials that are unfolding throughout the United States.

Despite the progress of clinical trials, however, this life-saving treatment will always be limited by the scarcity of donor organs. Any policy or legislative actions to increase the number of organs available helps not only people with HIV but everyone facing organ failure. Several options are being considered, including improving public awareness of the option of donating organs, revising the medical criteria for transplantation, as is the case for HIV-positive transplant recipients, but it is often perceived by them and people in the HIV community as such. Many people with HIV do not realize that many of the difficulties of transplantation—the long waiting period, the insufficient supply of organs, the process of allocating organs, the fear of dying or deteriorating prior to transplant—pertain to anyone with organ failure. Instead, people with HIV often ascribe these “standard” difficulties to HIV-positive status. They may also overestimate the benefits of transplantation because people with HIV as a group were excluded from this process for so long.

The Transplantation Process

The transplantation process, as is the process of living with HIV, is fraught with uncertainty. The first step is being evaluated and accepted as a suitable candidate for transplant. This step—defined by physically, emotionally, and financially taxing medical tests—can create performance anxiety for many patients who worry about whether they will pass the evaluation.

Once accepted, transplant candidates confront an invariably long waiting period. Currently 46,000 people are waiting for kidney transplants and 19,000 are waiting for liver transplants. Approximately 30 percent of those waiting for livers and 25 percent of those waiting for kidneys receive transplants each year. During this period, even people facing kidney failure, which can be treated with dialysis, worry that they will die, become too old, or deteriorate to the degree that they will be disqualified when an organ becomes available. Individuals also often feel guilty about the correlation between wishing for an organ and wishing for another’s death.

When the time to transplant approaches, potential recipients face new fears. Those
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Waiting for a kidney from someone who has died worry about missing “the call” when they are out of the house. Most liver recipients waiting for such “cadaver” organs must be hospitalized for weeks to months before the transplant due to their deteriorated medical condition. Those scheduled to receive a living donor transplant are in a better position to plan and prepare for the surgery. But recipients from all groups must undergo a series of procedures in an accelerated time frame once an organ becomes available, which can heighten anxiety.

After transplant surgery, kidney recipients typically stay in the hospital only three to five days and liver recipients stay seven to ten days. Despite pre-operative education, most recipients have a difficult time assimilating transplant-related change—including recovering from surgery and understanding how to maintain the complex regimen of transplant-related drugs—and experience anxiety about being discharged from the hospital so quickly after surgery. Within the first six months, recipients experience heightened concerns about post-operative complications, organ rejection, and loosing their transplant. Many never completely overcome these fears. As is true for many other people recovering from a serious illness, transplant recipients frequently have difficulty relinquishing the role of “patient” and resuming their usual family, social, and work responsibilities. The severity of organ failure and the uncertainty of the transplant process also take a toll on informal caregivers, who may be either so overprotective that they slow the recipient’s recovery or so burnt out from the burden of care that they are unable to provide appropriate support during recovery.

Finally, transplant-related medications have emotionally challenging side effects. Many reduce libido. Some, especially the immunosuppressive agents, produce weight gain and increased hair growth, changes that often have a negative effect on a person’s body image and sense of desirability. These effects can be exacerbated by concerns about the possibility of death or injury during sexual activity.

HIV-Specific Challenges

There are at least three psychosocial challenges regarding transplantation, which are related to the difficulty of managing the two chronic life-threatening conditions of HIV disease and organ failure. Among these challenges are: physical complications that result from accommodating two multi-drug regimens; frustrations that arise from being treated through a pioneering procedure, offered at a limited number of centers where both providers and participants are learning as they go along; and depression and anger over the cosmic injustice of having to handle both HIV and organ failure.

A transplant recipient can expect to take three different immunosuppressive medications and at least four other medications to prevent infection. For a person with HIV, this means adding a minimum of seven medications to his or her current regimen. The encouraging news is that people living with HIV have already mastered complicated, daily regimens. Moreover, they understand the importance of taking their medications as prescribed and the consequences of not doing so. This skill is critically important after transplantation, since the long-term success of the transplanted organ is directly related to taking immunosuppressive medications as directed and for life.

However, all these additional medications, their side effects, and their potential interactions present significant physical and psychological challenges. “Therapeutic optimism,” for example, reminding patients that the number and dosages of medications will decrease over time and that side effects will often improve or disappear at lower doses, helps people with HIV react constructively to these new stresses. It is also helpful to provide information about potential side effects, so that individuals can identify new symptoms as side effects and know how to manage them. Finally, it strengthens an individual’s sense of mastery when he or she successfully integrates the transplant regimen into his or her established HIV regimen.

There are only 14 transplant centers in the United States currently evaluating and transplanting HIV-positive recipients, mostly as participants in a clinical trial. While being part of a pioneering clinical trial is rewarding, it is also stressful: the short- and long-term outcomes of the procedure are unknown, and participants are exquisitely aware that their medical practitioners are learning with them and through them. Although it is empowering to participate in discussions about care, the level of participation in the decision making can be overwhelming. In addition, many participants may need to relocate, at least temporarily, to the area of one of the few transplant centers. This can place enormous financial, emotional, and

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practical burdens on potential recipients and leave them feeling unmoored from their social support networks.

While the surgical procedure itself is standard, the unknowns faced by those with HIV lie in the interaction between immunosuppressive medications and HIV antiviral medications, the impact that immunosuppression has on HIV progression, and the impact that HIV disease might have on the functioning of the new organ. Each of these variables is significant and increases the recipient's uncertainty and stress after transplant. Moreover, no amount of information can prepare a person for the lived experience of handling these uncertainties. The best assistance clinicians can provide is regular contact and easy access, offering ongoing education and communication, and a continuing focus on the recipient's strengths.

Finally, depression, which is commonly experienced by both transplant recipients and people with HIV, has some unique presentations among HIV-positive organ recipients. One form is situational, becoming evident when the recipient has to adjust his or her pre-transplantation expectations to the reality of the post-transplant experience. Many individuals experience serious depression upon discovering that all of their medical or psychosocial problems have not been solved by transplant. Depression may be complicated by feelings of guilt, which may arise among recipients who feel that they have no “right” to be depressed. These individuals may feel that they have received a scarce resource that grants them life at the expense of another (that is, the organ donor and the 60 percent of people on the transplant list who do not receive organs). They may also feel that they are among the few people with HIV to receive a transplant. This self-censorship of depressive feelings exacerbates an enormous psychic burden that can undermine an individual’s recovery and health.

To counteract this response, recipients must be allowed to explore a wide range of reactions to their situation with a caring and knowledgeable health care provider. Health care providers must learn to listen with empathy and without judgment or overzealous counsel: “It is often through the quality of our listening and not the wisdom of our words that we are able to effect the most profound changes in the people around us.” Such opportunities for ongoing, unstructured communication may even eliminate the need for more formal counseling.

**Conclusion**

Dealing with the transplant experience raises significant challenges for anyone and particular difficulties for people with HIV. But it is important to realize that for some people, living with a chronic illness can transform life in positive ways. Surprisingly, this seems to be the case for individuals who face two life-threatening conditions: HIV disease and organ failure. Here, Viktor Frankl’s concepts of self-transcendence and purposeful living seem particularly meaningful. As he and others argue, finding meaning in life is not dependent upon physical health or external circumstance. Nor is the limitation that accompanies illness necessarily caused by the illness itself; rather it may be caused by the meaning a person assigns to the illness.

For some people, living with HIV first and then organ failure fosters personal transformation rather than despair. These individuals have discovered that acceptance of death can lead to more meaningful living and less conformity to social expectation. Although this may appear to be dependent on the personality of the individual, medical and mental health providers should do all that they can to nurture this response.

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**Clearinghouse: HIV and Transplantation**

**References**


People with HIV are experiencing not only the joys of extended life and improved health, but also the challenges of aging and medication toxicity. As a result, they suffer end-stage disease of key organs such as the liver and kidneys for many of the same reasons as people without HIV.

Common causes of kidney failure include not only diabetes and high blood pressure, but also an HIV-specific disease called HIV nephropathy, which is seen most often in African American men. Common causes of liver failure include alcohol use and hepatitis B and hepatitis C. Because of the shared routes of transmission of the hepatitis viruses, people with HIV infection have a higher prevalence of hepatitis B (especially among men who have sex with men) and hepatitis C (especially among people with a history of injection drug use) than the general population. People with HIV are also at risk for a variety of toxic effects on the liver from HIV antiviral agents. This article describes the medical issues related to transplantation, including the reasons people with HIV have been excluded from it, the data on transplantation for people with HIV, and the transplantation process.

Concerns about HIV and Transplantation

While the United Network for Organ Sharing (UNOS)—the organization that maintains the nation’s waiting lists for organ transplants from deceased donors—has not excluded HIV-positive patients from being listed, many insurance companies and transplant centers have, until recently, balked at the idea. In fact, a 1998 study found that of 149 kidney transplant centers that responded to a survey, only about 10 percent would agree to transplant a kidney into an asymptomatic HIV-positive patient who was otherwise a good transplant candidate.1

People with HIV infection have usually been considered ineligible for organ transplantation for two important reasons. First, due to the severe shortage of organs, transplant centers have always made allocation decisions based, in part, on the likelihood of the survival of the organ recipient. Highly active antiretroviral therapy (HAART) has changed the natural history of HIV infection in the developed world,2 invalidating the first objection to transplantation in HIV-positive patients who have relatively intact immune systems.

The second concern is that the immunosuppressive drugs required to prevent organ rejection after transplantation may accelerate HIV-induced immune depletion, causing rapid HIV disease progression. It remains unclear to what extent otherwise successful HIV antiviral treatment will restore immune function and allow transplant recipients to tolerate anti-rejection drugs without compromising their health.

Organ Transplantation in People with HIV

The medical literature provides limited insight into this second and critical question, because published studies occurred prior to the advent of HAART. Although some pre-HAART reports demonstrated poor outcomes for HIV-positive organ recipients, others suggested that some HIV-positive transplant recipients can tolerate transplant-related immunosuppression and demonstrate transplant survival comparable to that of HIV-negative transplant recipients.3-7

The use of HAART in HIV-positive transplant recipients may further improve post-transplant patient and organ (the "graft") survival. Small pilot studies researching this question have been underway for several years at the University of Pittsburgh.
and at the University of California, San Francisco. In 2000, a multi-site study involving 13 transplant centers throughout the United States was initiated. Analyses of this more recent experience, presented at scientific meetings, have been encouraging—although they have followed small numbers of patients over limited periods.

A study presented at the February 2002 Conference on Retroviruses and Opportunistic Infections undertook both a prospective analysis of subjects in the current multi-site study and a retrospective analysis of patients transplanted at one of 20 other centers, who would have met eligibility criteria for the current study had the study been available at the time of their transplants. Eligibility criteria, which reflect successful HIV antiviral treatment, included: no history of opportunistic infection or neoplasm; CD4+ cell counts of greater than 200 for kidney recipients and greater than 100 for liver recipients; and undetectable HIV viral load while on stable antiretroviral therapy (or, for liver recipients unable to tolerate antiviral treatment, prediction of full viral suppression post-transplant based upon a history of successful HIV treatment and, when available, the results of resistance testing).

Twenty-two kidney and 19 liver recipients were eligible for this analysis. Over the median follow-up period of 279 days, three liver recipients and one kidney recipient died. None of these deaths was due to HIV-associated opportunistic complications. Over the 279 days, CD4+ cell counts remained stable, and median viral load at the last follow-up was less than 50 in both groups. The one-year patient and graft survival rates for the 41 HIV-positive transplant recipients was similar to the one-year rates derived from the UNOS database for kidney and liver transplants in uninfected patients: more than 90 percent of HIV-positive patients survived the 279 day follow-up.

The Transplant Process

Eligibility for transplant is determined by a team of physicians, nurses, and social workers who review all potential transplant candidates. Considerations include non-HIV related medical history focusing on cardiovascular status and malignancy history, substance abuse history, availability of social support, and study-specific requirements for CD4+ cell count, viral load, and opportunistic infection history. An organ for transplant may come from the "cadaveric" (deceased) donor waiting list maintained by UNOS or from a living donor. Potential living donors are evaluated by a separate team to ensure that there is no pressure to donate. Living kidney and liver donors are usually biologically or emotionally related family members who donate one of their kidneys or a portion of their liver. While living kidney donation is a standard procedure, living liver donation is relatively new and considered by some to be experimental.

It can take up to five years to get an appropriate organ, during which time many potential recipients die. Kidney candidates are prioritized based on time on the list, liver recipients, based on the severity of liver disease. The technical aspects of both procedures are well established. Liver transplantation, however, is complicated by more elaborate pre-transplant management and the unavailability of options other than transplantation for liver failure.

After a transplant, patients must strictly adhere to a complex medication regimen and follow-up laboratory and medical visits. Medications include HIV antivirals, usually two or three immunosuppressive drugs, and numerous agents to prevent opportunistic infections. Some of these drugs interact with each other. Study patients at some sites must undergo periodic 12- to 24-hour pharmacokinetic monitoring to help define these complex drug interactions. Post-transplant complications can include organ rejection, infection, and metabolic disorders similar to those seen with HIV antiviral treatment.

Conclusion

Transplantation and post-transplant immunosuppression constitute a complex medical condition, necessitating regular monitoring and strict medication adherence. Transplant candidates often underappreciate the fact that they may be trading one set of problems for another. However, transplantation generally improves length and quality of life. The medical management of people with HIV who receive transplants and the impact of transplantation on quality of life is an important area of further study.

Comments and Submissions

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Recent Reports

Criteria for Allocating Organs
Corley MC, Westerberg N, Elswick RK Jr., et al. Rationing organs using psychosocial and lifestyle criteria. Research in Nursing and Health. 1998; 21(4): 327–337. (Virginia Commonwealth University; Medical College of Virginia Hospitals; and U.S. Navy.)

People who are HIV-positive, have used cocaine, or are in prison for a serious crime are more likely than others to be excluded from receiving an organ transplant, according to a survey of “psychosocial and lifestyle criteria” used by transplant coordinators throughout the United States.

Of the 768 organ transplant coordinators who are members of the North American Transplant Coordinators Organization (NATCO), 559 returned surveys. Most respondents were female (94 percent), White (90 percent), and registered nurses (95 percent). Fifty-seven percent of respondents had less than seven years of experience; 59 percent had experience in kidney transplant, the most commonly represented type of transplant. The survey included two indices to measure: criteria for selecting transplant recipients and the nature of participation of coordinators with others in the recipient selection process.

More than 90 percent of the coordinators either “always” or “often” considered patients’ lifestyle characteristics. Twenty-five percent of patients whom coordinators rated as poor candidates based on psychosocial or lifestyle characteristics went on to receive a transplant. Only 4 percent of coordinators explicitly stated that patients were denied a transplant based on lifestyle or psychosocial factors.

Factors listed under the “stigma” section of the criteria index—including having AIDS or being HIV-positive, being a prisoner, and being a cocaine or heroin user—were the most likely to be used to exclude patients from transplant. “Current lifestyle and psychosocial” factors—representing a range of concerns about compliance and psychiatric symptoms—were the second most likely to be used. The “habits” factor—addiction to substances including tobacco, marijuana, and alcohol—and the “recover” factor—psychiatric or substance abuse conditions treated or controlled—were less widely used, but were also deemed as suitable for exclusion. “Cost” factors and “family/socioeconomic” factors comprised the smallest barriers to transplant acceptance.

Effects of Transplantation on Quality of Life

According to a study of liver transplant patients, patients whose pre-transplant optimistic expectations remained unfulfilled after transplantation had a markedly lower quality of life compared to those with less optimistic expectations.

Austrian researchers interviewed 55 patients—32 men and 23 women with a mean age of 52 years—an average of 4.7 years since transplantation. Questions focused on current perceptions of their lives, preoperative expectations, and preoperative information on the consequences of transplantation. Respondents also completed two questionnaires, both based on widely used indices. The first index was a self-assessment of physical, social, emotional, and functional well-being (and was used to compare participants with an external reference group of 594 demographically comparable and healthy subjects), and the second was an assessment of the impact of transplantation on physical and psychosocial activities.

While 60 percent of respondents had expected to be able to lead a “normal life” after transplant, only 40 percent claimed that they met this expectation. Of the remaining 60 percent, 42 percent said they experienced “limitations” and 18 percent said they were not able to lead normal lives. Thirty-one percent cited physical problems such as inability to work, medication side effects, fatigue, or other illnesses as reasons for their negative assessment, while 33 percent cited psychosocial reasons such as distress, occupational handicaps, early retirement, and depression.

The results of the respondents’ self-assessment of transplantation-induced impairments and well-being concurred with the telephone interviews: in nearly all areas, physical abilities and psychosocial abilities of the respondents were well below those of the reference group on which the index is based. The most prominent deficits were in the area of work, recreation/pastimes, alertness behavior, sleep and rest, and social interaction. The

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functional assessment index found a significant correlation between severe complications during inpatient treatment and poorer quality of life after transplantation, suggesting that patients who experience considerable complications should be offered more intensive postoperative care, including additional psychosocial support and more frequent follow-up visits.

The Psychological Distress of Waiting

A German study of individuals awaiting heart transplantation found that increases in depression over the four-month waiting period were most associated with level of depression at the beginning of the period. Participants also experienced a decline in quality of life and a worsening of cardiac symptoms during the waiting period.

Researchers evaluated 42 patients in 1996, administering questionnaires, including a depression scale, a physical, emotional, and social quality of life questionnaire, and a measurement of limitations due to physical symptoms at the beginning and end of a four-month waiting period for organs. Ninety-eight percent of the patients were men, 86 percent were married, and 98 percent had some type of formal education. The sample’s mean age was 56.

Overall, there was a continuous decline in emotional well-being, with the rise of depression levels concurrent with reports of cardiac symptoms, exhaustion, and general distress. Initial level of depression explained 84 percent of the changes in the level of depression during the waiting period, suggesting that early evaluation of depression can be a powerful tool in predicting and treating later depression.

Distress and “Living-Related” Transplantation

Liver transplantation from a living donor results in a relatively high incidence of postoperative psychiatric disorders among transplant recipients, according to a study of donor-recipient pairs living in Tokyo. It also leads to high rates of postoperative paradoxical psychiatric syndrome (disorders that occur despite successful transplantation) for both donors and recipients.

Researchers interviewed 116 pairs of recipients and donors who underwent liver transplantation and 325 pairs who underwent kidney transplantation. These pairs were divided into two sets: adult (over age 20) and pediatric (under age 20). All the donors for both liver and kidney transplantation were adults.

The highest incidence of psychiatric disorders for both kidney and liver transplantation occurred among adult recipients during the three-month period after transplantation, most likely due to postoperative delirium, which occurs more frequently in recipients immediately after living-related transplant. Fifty-four percent of adult liver recipients—compared with 28 percent of kidney recipients—exhibited psychiatric disorders. Even after excluding cases with postoperative delirium, psychiatric disorder rates among liver recipients soared above those for kidney recipients (37 percent versus 20 percent).

Furthermore, 34 percent of adult liver recipients experienced postoperative paradoxical psychiatric syndrome (PPS) compared to 5 percent of adult kidney recipients. The most frequent occurrence of PPS for both donor and recipients occurred when the donor was the adult child of the recipient (50 percent of such cases showed PPS). Among pediatric recipients, the incidence of psychiatric disorders was relatively low (less than 5 percent) for both kidney and liver transplantation.

Next Month

Behavior has a sociological as well as a psychological context, and understanding the role of behaviors, including risky ones, for communicating status within a subpopulation may lead to risk reduction. In the June issue of *FOCUS,* Terry Trussler, EdD, a researcher at the Community-Based Research Centre in Vancouver, discusses the ways in which “frustrated desire”—in terms of social status, anti-gay violence, and personal relationships—may affect risk behavior.

Also in June, Rodrick Wallace, PhD, Research Scientist at the New York State Psychiatric Institute and Technical Director of the Public Interest Scientific Consulting Service, Inc., discusses how societal forces act on marginalized communities—for example, the gay community or communities of color—to substitute destructive behaviors for more affirmative ones as ways of conveying status and self-worth.
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