



Organ Transplantation in HIV

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kidney disease or HIV-related harm to the kidneys (*called HIV-associated nephrotoxicity or HIVAN*).

Anti-HIV therapies that are processed through the liver or kidney can also, in some cases, worsen these conditions and there have been some instances where the damage to the organ has been wholly caused by the side effects of therapies to treat HIV. For people with very advanced liver disease, liver transplantation is often the only option. People with kidney disease have slightly greater options, including dialysis, which involves being hooked up periodically to a machine to circulate and cleanse the blood. It is critical to assess the effectiveness of organ transplantation in people with HIV in order to determine if it prolongs life, improves quality of life and if so then costs should be covered by third-party payers (insurance, Medicaid/MediCal, etc.). The answers to these questions are not obvious since the kind of surgery associated with organ transplants can be very hard on anyone, let alone people suffering from HIV infection.

Background

Historically HIV has been a contraindication for organ transplantation, meaning that if a person were living with HIV they were not considered a candidate to receive an organ. Transplant surgeons were often unwilling to perform the surgery and third-party payers were not willing to pay the costs for the required supportive long-term care, as they considered the transplants unproven and “experimental” in HIV-positive people. A number of years ago AIDS activists, including activists from Survive AIDS in San Francisco and Project Inform, got involved with this issue. With the support and leadership of two researchers at the University of California San Francisco, HIV specialist Michelle Roland and transplant surgeon Peter Stock, a local pilot project has blossomed into a national project providing important information to move this field forward.

As people with HIV are living longer due to advances in HIV medicines, there is a rise in death rates from conditions not historically associated with HIV. This includes an increase in risks and rates of both liver and kidney failure, often caused by hepatitis B or C, and underlying

The Study

Dr. Roland presented an overview of findings from 53 people undergoing kidney or liver transplantation in the setting of potent anti-HIV therapy. To be eligible people must have:

- no prior history of opportunistic infections,
- a CD4+ cell count greater than 200 for kidney transplant candidates and greater than 100 for liver transplant candidates, and
- a viral load below 50 copies/ml for kidney transplant candidates and *either* a viral load below 50 copies/ml for liver transplant candidates or if the person is unable to tolerate anti-HIV therapies due to their liver condition, a protocol HIV specialist must determine that after transplantation the individual will be able to construct an effective anti-HIV regimen that will result in maximal viral suppression.

Of the 53 patients reported on at the conference, 45 fit the above eligibility criteria and 8 did not. The reason it's important to include the information on the 8 ineligible people is it helps to determine whether or not the eligibility criteria is appropriate, or if it is perhaps too rigid.

The Results

Focusing first on the 45 eligible study participants, 26 received kidneys and 19 received livers. There were six deaths among eligible volunteers receiving transplants, two among those receiving kidney and four among liver transplant recipients. For the most part deaths were happening at similar rates and were due to the same causes that would typically be seen among HIV-negative transplant recipients, such as recurrent HCV disease or post-operative pancreatitis.

In one instance, death was deemed to be caused by a person stopping their anti-HIV medication without consulting the study team. When a person undergoes organ transplantation, they are given immune-suppressive therapy for the rest of their life in order to prevent their





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body from rejecting the new organ. Anti-HIV therapies have notable interactions with these anti-rejection medications. A great deal of care is taken in monitoring levels of anti-rejection medications and adjusting doses as needed. When the individual stopped anti-HIV medication abruptly, their blood levels of the anti-rejection medication fell dramatically and they died due to a serious organ rejection event. The important lesson here is that when a person receives an organ transplant, they have less flexibility in implementing choices around anti-HIV therapy. Moreover, adherence to medications has even more critical and potentially life-threatening consequences. Implementing a decision to discontinue the use of anti-HIV therapy, for example, must be done in careful consultation with the transplant team so that dose adjustments for anti-rejection drugs can be made and carefully monitored. Even the simple act of switching anti-HIV drugs can alter blood levels of anti-rejection drugs and must be done with a higher degree of care.

For the most part, liver and kidney transplantation had little to no effect on either viral load or CD4+ cell counts. CD4+ cell counts among kidney transplant recipients were about 441 pre-transplant and about 436 post-transplant. CD4+ cell counts were about 280 pre-transplant for liver recipients and about 218 afterwards. Viral loads were basically undetectable in both groups pre-transplant and remained so afterwards. In terms of the short-term safety issues, this is all good news. The median follow up on the entire group is about 314 days, so almost 1 year (with some people having been followed only 3 days but others having been followed for close to 1,700 days—nearly five years).

When comparing the outcomes of the transplant recipients to the larger population of people receiving kidney and liver transplants, survival outcomes thus far appear to be very similar after one year. Some scientists have worried that a higher rate of organ rejection would be seen among people with HIV compared to transplant recipients in the general population. So far, this has not occurred. Among the kidney transplant recipients there was a 38% rejection rate and among liver patients the rate was 21%. Rates of patient survival appear to be similar among the study observations and survival rates observed in the UNOS registry (a registry of outcomes for transplantation in the general population).

Among the eight ineligible subjects who also received transplants, two have died of severe neurologic condition associated with HIV infection called progressive multifocal leukoencephalopathy (PML). There is currently no way to know whether this was in any way related to the transplants. The reasons folks were deemed ineligible included: one was undiagnosed with HIV at the time of transplantation, a few kidney transplant recipients had viral load above the requisite 50

copies/ml, low CD4+ cell counts and altered mental status (which is also disallowed by the protocol). Of note, those with detectable viral load prior to study entry are currently doing fine as are those with CD4+ cell counts lower than the required threshold. The deaths occurred in the individual with altered mental status and the individual who was not known to be HIV-positive at the time of transplantation.

Where do we go from here?

NIH funding is pending for the formal national multi-center study. Results to date are quite encouraging and may already be enough to begin dialog with third-party payers around reimbursement policies. In the meantime, the study is enrolling and providing an option for people with HIV who are or may be in need of kidney or liver transplantation. It is critical that the community push for this study to be expanded to include other organ transplantation approaches, such as heart transplants, as well. While there may be openness by investigators to include such approaches in the study, there remain barriers to overcome. For more details about these study results, and for a list of transplant sites participating in the multi-center study, call the Project Inform hotline. Moreover, your help is needed in political action to insure that organs are available to all those who need them.

The Bottom Line

- Initial information on kidney and liver transplantation in people with HIV in the current era of potent therapy looks very encouraging.
- Though data remain preliminary and on only a small number of people, survival rates after one year of transplant look similar between people with HIV and the general transplant recipient population.
- The study will continue and likely expand with anticipated government funds, and eligibility criteria around prior history of opportunistic infections have already relaxed. In the longer-term eligibility criteria around viral load is hoped to loosen as well.
- Of course wherever possible, preventing and managing conditions that lead to organ damage is preferable to organ transplantation and this should be discussed with a provider—this might include hepatitis B vaccination, implementing HCV prevention/risk reduction or considering HCV treatment.

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We Must Have Presumed Consent

By Larry Kramer

More and more people with HIV and/or hepatitis are going to need organ transplants, particularly liver transplants. As more of us all over the world discover we are carrying one or more of these viruses, even if we are being treated for them—or particularly if we are being treated for them—the more likely it becomes that one of our organs is going to cease working effectively. And the longer we are being treated, the longer we live and the more that chance grows.

With all the new drugs for HIV and viral hepatitis, it is now safe, ok, kosher to transplant “coinfecteds.” The New England Journal of Medicine has even written approvingly of such transplants. Insurance companies can no longer simply refuse to pay for these expensive procedures on the grounds that they are “experimental.” Too many of them have been done successfully.

Right now there are hundreds of thousands of people in this country waiting for organs. Most of them will die before they get them. Many will die after they have been put on a waiting list. Why is this? Because not enough people in America donate their organs to be used after they die. It is as simple and as complicated at that. There are more than five people waiting for every organ made available by donation.

In many countries this extreme shortage does not exist. That is because these countries (including Austria, Belgium, Denmark, Finland, France, Italy, Norway, Singapore and Spain) have what is called a Presumed Consent organ collection system. That means that every person is deemed to be an organ donor unless s/he specifically opts out. When an accident occurs to a person who has not opted out, and brain death is declared, organs can be taken immediately without the time-wasting rigmarole America requires for “approval.” An organ only has a few hours to get from one body to the next. In America, you sign the back of your driver’s license if you are willing to be a donor, and even then most centers still require permission from a family member, which, believe it or not, may not be given.

I have been trying, since my transplant, to find a way of changing America’s organ donor system to one of Presumed Consent. Well, you would have thought that Presumed Consent was akin to the biggest blasphemy known to civilization. Opponents from the right, the conservatives, the orthodox, you name it, including the ACLU (did you know that the organs of dead people have rights?) have screamed in opposition. These opponents do not care that Spain, a very Catholic country, has the most successful organ procurement system in the world.

And no one I can find knows how the system can be legally changed. Who does it? Congress, by passing a law? HHS, by issuing an edict? State-by-state or community-by-community, by putting it on a local ballot? As Robert Bazell, the chief medical correspondent for NBC Nightly News, warned me when I embarked upon this new activist journey, “Larry, you will find that it is like punching air.”

One person who can help change this system more than anyone else is Senator Bill Frist (R-TN). He is a transplant surgeon himself. He knows the hideous horrors of watching people desperate for organs die. But he is a politician with Presidential ambitions, so he is not exactly willing to be Mr. Flag Waver for organ transplants. He has prepared a bill, with Sen. Christopher Dodd (D-CT), to investigate Presumed Consent. But this bill has no hope of getting passed, which is not so bad because it is such a wishy-washy piece of legislation that we are better off without it. It is an all-talk no-action kind of bill.

Frist needs to be reminded that going out further on this issue is not only the morally right thing to do, but also will ultimately help him win voter support. Despite what people think, voters like candidates who take moral, life-saving positions. And all the people who need organs have lots of relatives and friends.

AIDS activists have been here before. It is the beginning of a new crisis and no one of any importance wants to pay it an iota of attention. In the coming years, the number of people around waiting for new organs is going to rise to the millions from the several hundred thousand currently in need. Once again I find myself screaming out loud about a huge and coming catastrophe and no one is listening.

I would like to close words from Dr. John Fung, who saved my life: “Patients are dying and the public still does not understand that saying no to donation means someone will die. No one wants to be so blunt. No one wants to raise the American conscience to make people feel that it is their human obligation to pass along their body to the living when they die. This is a systematic deficiency in American culture, the idea that you are out only for yourself and have little or no obligation to society as a whole.”

Tell Senator Bill Frist: America must have presumed consent for organ donation! Email him and tell everyone you know to email him or call his office: Bill_Frist@frist.senate.gov or 202-224-3344.