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Will Any Organ Do?

By GRETCHEN REYNOLDS

Last summer at one hospital in Dallas, four people died from rabies, an unheard-of level of incidence of this rare disease. As it turned out, each patient was infected by an organ or tissue -- a kidney, a liver, an artery -- that he or she received in a transplant several weeks earlier. Their shared donor, William Beed Jr., a young brain-dead man, had rabies, caught apparently through a bite from a rabid bat, something the surgeons never suspected. They all thought he had suffered a fatal crack-cocaine overdose, which can produce symptoms similar to those of rabies. "We had an explanation for his condition," says Dr. Goran Klintmalm, a surgeon who oversees transplantation at Baylor University Medical Center, where the transplants occurred. "He'd recently smoked crack cocaine. He'd hemorrhaged around the brain. He'd died. That was all we needed to know."

Since the rabies deaths, recriminations have flown, procedural reviews have begun and sorrow and regret have dogged the families of the organ recipients. But the outbreak also exposed a controversy that until then was roiling only the rarefied world of transplant specialists. The issue, although freighted with monetary and bio-ethical complexities, can be boiled down to one deceptively simple question. Should transplant surgeons be using organs from nearly anyone?

Organ transplanting has become, in fundamental ways, a victim of its own success. Not long ago, transplant surgery was a dodgy, last-ditch response to end-stage kidney failure. But with the advent of better antirejection drugs and surgical techniques, transplantation has become the treatment of choice for a growing range of conditions, including chronic kidney failure, end-stage lung or liver disease and some congestive heart failure. Kidneys are implanted routinely, as are increasing numbers of livers, hearts and pancreases.

Fifteen years ago, about 20,000 people in the United States were on waiting lists for organs. Today, about 88,000 are. The number of donors has not come close to keeping pace. There were about 15,000 transplants completed with organs from cadavers in 1993 and about 20,000 last year. Patients used to wait weeks for an organ. Now they wait years. On average, 18 people on organ waiting lists die every day.

Doctors, patients and politicians concerned about transplantation have responded with proposals for increasing donations. In 2002, the American Medical Association voted to endorse pilot projects to give families financial incentives, like cash payments to help cover the costs of funerals, for donating their deceased loved ones' organs. The next year, Congress held hearings on the topic. Representative James Greenwood, Republican of Pennsylvania, introduced a bill that would have authorized demonstration projects to determine whether offering financial

incentives to families of brain-dead patients would increase donation rates. There was a public outcry against "buying" organs and the bill died. (A few states offer tax incentives to families who donate relatives' organs.)

Increasingly desperate people in need of transplants have turned to highway billboards and Internet sites to solicit donors. Donations from living people have helped. Today the number of living kidney donors is greater than the number of dead donors. But living donations of other organs are rare because they can be dangerous or are impossible.

All of which has led transplant specialists to quietly begin to relax the standards of who can donate. As a result, according to surgeons I spoke with and reports in medical journals, the transplanting of what doctors refer to as "marginal" or "extended criteria" organs, organs that once would have been considered unusable, has increased considerably in the last several years. The definition of a marginal organ differs from transplant center to transplant center and also from one type of organ to another. This makes it difficult to quantify the increase in the use of these organs. But the expansion is undeniable and has become a much-discussed issue in the field, a topic of ethics papers, surgical conferences and soul-searching on the part of many of the surgeons involved.

Fifteen years ago, William Beed Jr. would not have qualified as an organ donor. When he died in May 2004, he was 20, unemployed and had been living with his mother and sister in a bat-infested apartment building in Texarkana, Ark. Throughout his life, Beed had been in and out of trouble, his mother acknowledged when I spoke to her recently. Marijuana and cocaine were found in his urine at the time of his death, according to a report in *The New England Journal of Medicine*.

Beed's drug use alone would have disqualified him as a donor. (It still would keep him from giving blood.) "What people have to understand is that donors now, except for the 75-year-olds who die of intracranial bleeds, are not part of the church choir," Klintmalm told me when I met with him in Dallas earlier this year. "The ones who die are the ones you don't want your daughter or your son to socialize with. They drink. They drive too fast. They use crack cocaine. They get caught up in drive-bys."

The donor pool was different in the early days of transplantation. Beginning in the 60's and through the 80's, a majority of donors were head-trauma victims, people who had been involved in car accidents, botched suicides or tumbles off horses or ladders. These donors were almost all young, between 15 and 45. (In the 80's, few transplant surgeons would take a 50-year-old organ.) They were of average weight, with no history of diabetes, cancer, infectious disease, imprisonment, high blood pressure, cigarette-smoking habits, tattoos (which have been associated with blood-borne illnesses) or unsafe sexual behaviors. The chosen organs, said Klintmalm, who has been in practice for about 25 years, "were pristine."

It was easy to adhere to those standards at first. "We didn't perceive any shortage of organs back

in the day," says Dr. Nicholas Tilney, the Francis D. Moore professor of surgery at Harvard Medical School and one of the nation's premier kidney-transplant surgeons. "If a patient had to wait a few weeks for a kidney, that seemed long. We never foresaw the kind of situation we have today."

Conditions began to change in the 90's. Seat-belt use was more common by then, and fewer Americans were dying of head injuries, depriving transplantation of its most reliable sources of pristine organs. At the same time, the demand for transplants was growing. Surgeons had little choice but to start looking to alternative sources for organs.

On April 28, 2004, William Beed Jr. complained to his mother that he was feeling sick. "He couldn't swallow," his mother, Judy, a practical nurse, recalled when I spoke with her earlier this year. They decided he should go to an emergency room, she said, and the doctors there examined him and sent him home with medication, saying he was dehydrated. By that evening, he was drooling, throwing up, shaking and still having difficulty swallowing. His fever was rising. He started vomiting blood. His father drove him to another E.R.

Diagnosis is often a matter of context. Because of doctor-patient confidentiality rules, doctors involved with this case would not talk about it on the record, but a few did say that had Beed not had cocaine in his blood, the E.R. doctors might have investigated his symptoms more aggressively instead of assuming he had overdosed. (Because no autopsy was done, doctors have not been able to establish whether the rabies or the drugs actually killed him.)

Soon after, Beed fell into a coma and was put on a ventilator. After a few days, his mother said, the doctors told her and her family that their son was brain-dead. Transplant surgeons use organs from brain-dead patients because they still have a heartbeat, and if the patients are placed on a ventilator, their organs continue to get oxygen. Without oxygen, the organs degrade within minutes.

According to Judy Beed, a transplant coordinator approached her and asked whether she would be willing to donate her son's organs. She agreed, and in the middle of the night on May 4, the parents of Joshua Hightower received a phone call offering them William Beed's kidney.

Joshua Hightower, who lived in Gilmer, Tex., had had kidney problems since he was 2. They had grown progressively worse over the years. "When he was 16, things got really bad," said his mother, Jennifer Hightower, a special education assistant in the public schools, when I met with her in February. "He was pale and droopy. He weighed 112 pounds. He was sleeping all the time." His teachers at Gilmer High School walked him up and down the halls between classes to help him stay awake. A doctor urged his parents to get him on the waiting list for a kidney. In the meantime, Joshua began daily dialysis at home. The process, which purified his blood of toxins, required that he be home every evening by 10. Once there, he was tethered to the dialysis machine for between 9 and 16 hours. When the Hightowers received the call from the hospital, they jumped at the opportunity.

It is impossible to know now when the first less-than-pristine organ was retrieved and transplanted. But over the course of the 90's, according to surgeons I spoke with, many barriers fell. Age was almost certainly the first to go. Instead of accepting donors 45 and younger, some transplant centers began, gradually, to take those who were 48, 49, 50 and then up from there. "I wrote a paper for The Journal of the American Medical Association back in 1989," Dr. Lewis Teperman, director of transplantation at New York University Medical Center, told me when I talked to him earlier in the spring. "It was looking at the outcomes of using older donors. By older donors, we meant someone over 60. That was considered really, really old." Recently, N.Y.U. transplanted a liver from a deceased 80-year-old. A couple of years ago, a Canadian hospital used a 93-year-old liver from a deceased donor.

Almost imperceptibly, most of the other traditional prohibitions evaporated. Surgeons started accepting lungs from people who had smoked, sometimes for decades. They accepted hearts and kidneys from those who had had high blood pressure or had been obese. They took organs from alcoholics and drug users. (Because cocaine is flushed from the body relatively quickly, it is considered one of the least problematic drugs in donors.) Infectious disease was no longer an automatic disqualifier, either. Most surgeons would have once discarded organs from someone with hepatitis C, for instance, since it destroys the liver. But the virus, often spread by injected drug use, is now so common in urban areas that few transplant surgeons will immediately turn down an organ infected with it. Ideally the surgeons implant these infected organs into patients who already harbor hepatitis C. But lately there have been cases in which doctors, as a last resort, have transplanted infected livers into patients who don't have hepatitis C. There is little published data yet about the long-term outcomes for these patients.

The expansion into "marginal" or "extended criteria" organs has not been systematic. One transplant surgeon will use a marginal organ from, say, a morbidly obese donor or a drug user. His patient survives. Then he will repeat it again and again. At the next big transplant conference, he will talk to his colleagues about his success, and they will go back to their own transplant centers and accept, for the first time, an obese donor or a crack-cocaine user. "You sometimes have to experiment," Klintmalm says.

Klintmalm and other surgeons I spoke with who work in urban areas say that marginal organs are well on their way to being the majority of organs they transplant. Klintmalm, though, takes issue with the very definition of marginal. "Older organs should not be called 'marginal,'" Klintmalm maintains, referring to donors over age 55. "They're standard for us." But two years ago, when the United Network for Organ Sharing (UNOS), the private organization that oversees organ transplantation in the United States, published its first definition of extended-criteria organs, age was prominent. The UNOS classification, which applies only to kidneys, defines a marginal kidney as one that comes from a deceased person over 60 or one over 50 with two of three characteristics: stroke, hypertension or abnormal kidney function. The definition does not mention smoking, diabetes, hepatitis, alcoholism, obesity or drug use.

No government agency sets standards for what makes an organ acceptable. The Department of

Health and Human Services contracts with UNOS to handle the day-to-day logistics of the transplant system (getting organs to the next person on the list and so on). But the government's main concerns in policing transplants are that donors and recipients be matched for blood type and that organs be distributed primarily based on medical need, not the wealth, race or celebrity of the recipients. So decisions about whether organs are usable are made on the spot by individual surgeons.

To date, not many peer-reviewed studies have been published that examine the long-term outcomes of using marginal organs. The research that has been done mostly looks at kidneys.

Recent studies of older kidneys (usually defined as over 50), for instance, have shown that they can function almost as well as younger ones. They don't work for as long, however. In a report presented by UNOS, which adjusted for the health of the recipient, among other things, about a third of extended-criteria kidneys failed within three years. (About 20 percent of non-extended-criteria organs also failed within three years.) Transplantation, even under the best of circumstances, still involves risk. In assessing marginal organs, it is difficult to know whether a bad outcome -- the recipient's death or the organ's failure -- was caused by the organ, the surgery or the fragile health of the recipient.

Except for age-related research, few large-scale studies have yet investigated the effects of other extended-criteria kidneys. Do kidneys from diabetics, the obese, alcoholics, smokers or drug users generally work over the long term? Surgeons and scientists can't say for sure.

There is even less information about imperfect livers, hearts or lungs. Surgeons do know that livers, for some reason, don't age at the same rate as their original owners. Sixty- or 70-year-old livers can be in fine shape. Hearts and lungs aren't as durable and are more likely to fail as they get older. But surgeons are using them. A 2003 report by the UNOS-administered Organ Procurement and Transplantation Network stated: "The need to more aggressively utilize available organs for the candidate population as a whole competes with the expectation of each individual."

And this is, ultimately, the crux of the matter. The marginality of any given organ is relative. It depends on how sick the waiting recipient is. There is a kind of mad, desperate arithmetic that goes into calculating whether to use a marginal organ and when. "We're all trying to quantify the risks," Lewis Teperman, the N.Y.U. transplant director, says. "If we know that there's a 0.7 increase in relative risk of an extended-criteria organ failing, which is about what we've seen in kidneys so far, you take that number, look at your patient's chances for survival, which might be 90 percent with a perfect organ and 80 percent with an extended-criteria one and. . . ." He trails off. "It sounds very clinical when I put it like that, which isn't what I want." He starts again. "It's easy enough to come up with these kinds of calculations. But it's difficult for any of us to apply them in practice, when we're dealing with very sick people's lives."

Dr. Marlon Levy, a liver-transplant surgeon in Fort Worth and the medical director for the

Southwest Transplant Alliance, the group that unwittingly collected and distributed the rabid organs last year, told me: "You have this immensely complex weighing of benefits and risks in each of these cases. Is the recipient sick enough to justify using any organ, even a really marginal one, to try and save his life and give him a few more years? Or say you have a slightly healthier patient, and you think he's doing well enough to pass on a marginal organ and wait for a better one. Then, suddenly, he develops complications and dies before another organ becomes available. Were these decisions wrong?"

It is extremely difficult to predict outcomes. "The best thought-out decision doesn't work out all the time," Teperman says. "I have put in extended-criteria organs that worked perfectly, and the person walked out the door a week later. Other times, a patient has gotten an extended-criteria organ and remained hospitalized for months. I've also waited, thinking a better organ would come along, and the patient has died in the meantime."

To some extent, surgeons' hands are tied. In general, the current system requires that the most desperately ill patient must get the next organ that comes in, whether it is the best organ for that patient or not. "Things would work best if we could put the most extended-criteria organs into the less critically ill patients and the healthiest organs into the sickest patients," Teperman says.

The calculus may be even more complex from the patient's perspective. Dr. Grant Campbell, an epidemiologist with the Centers for Disease Control and Prevention, had a liver transplant in 1990. At that time, he was chronically ill and knowingly accepted an organ infected with cytomegalovirus, a common and usually mild disease but one that can be serious in immunosuppressed transplant patients. Fortunately, he didn't become sick.

Even the most rational attempts to weigh the risks and benefits of marginal organs tend to fall apart in the face of truly boundless human despair. "We would have taken any lungs," said Harry Littlejohn, 59, of Lewisville, Tex., whose 28-year-old daughter, Carmen, died in 2001 of cystic fibrosis. She had been No. 1 on the state waiting list for new lungs for eight weeks by then. None became available. "We would have done anything to save her," he said, "anything. But there was nothing we could do."

Joshua Hightower turned 18 on May 10, 2004, in the transplant recovery ward at Baylor University Medical Center. Photos from around that time show him propped up in bed, looking wan, but smiling.

Joshua had been added to the lengthy transplant waiting list the year before. The doctors said they could not estimate how long the wait would be, Jennifer Hightower, his mother, told me.

After the Hightowers received the call from the hospital, his mother recalled, she had wondered about the donor. Anonymity has been crucial to the workings of the organ-transplant system. Donation is supposed to be a blind act of altruism. Donor families aren't told at the time who will receive the organs, and recipients generally are told only the age and sex of the donor.

"You don't want people coming in and saying, 'I'll only donate to Italians.' Or 'I only want them to go to someone in the Ku Klux Klan,'" says Sheldon Zink, director of the program for transplant policy and ethics at the University of Pennsylvania. You also don't want recipients turning down organs because of their own biases.

But how much should a surgeon tell a patient who is about to receive a compromised organ? Should he explain that the new kidney comes from a retiree, a drug user or an alcoholic, a chain smoker or a member of a motorcycle gang? Does he have to tell a patient that the organ he is about to receive is considered marginal?

"I wish we had been told more," Jennifer Hightower says. Her son, she went on to say, would have declined the kidney had they known more about Beed's background and his death. Joshua, she says, was not so sick that he couldn't wait. "I would have made him pass on it."

Her attitude worries Zink, the ethicist. "I would question anyone's motivation in refusing an organ from a drug user," she told me. "They aren't responding to clinical information, because the available clinical data" -- the anecdotal reports from doctors -- "indicates that organs from crack-cocaine users are fine, in general. So they must be responding to preconceptions about that person's lifestyle. That's only one small step from declining an organ because the donor is black or Hispanic."

At the moment, no formal national medical standards dictate what transplant surgeons should tell their patients about organs other than kidneys or what they can withhold. Each doctor makes that decision based on how he feels about the ethics of the situation.

"I believe in erring on the side of telling the patient as much as possible," Teperman says. "We have a lengthy consent form here at N.Y.U., and it goes into the use of marginal organs. We ask patients if they will accept one. You don't want to be calling someone at 2 a.m. and saying: 'You can take this organ we just got in that may not be very good or you can wait and maybe die. What do you want to do?' That's an unrealistic burden to put on a patient. We try to have the conversation early on, when patients are a little more clearheaded. That's not always an easy conversation to have. Some patients would rather not think about it. They'd rather the doctor just make the decision for them."

Some surgeons insist on making decisions about marginal organs unilaterally. "There are transplant surgeons who think they absolutely know best," Zink says. "They don't bother asking the patient if he wants a marginal organ because they don't want the patient having a choice. They make it for him."

When Zink recently asked surgeons at a major transplant conference how many of them always tell their patients if they are about to implant a marginal organ, "about half said they tell the patient," Zink told me. "Half said they don't."

Some surgeons withhold information because they are concerned about litigation (better to say nothing than to say that an organ might be compromised, have your judgment proved right and be sued for it). Others are prodded by compassion. "There are doctors out there who think that a patient will recover better if he isn't worrying about the quality of the organ inside of him," Zink says.

Wry pragmatism also plays a role. "At some large urban transplant centers, virtually all organs nowadays are extended-criteria organs," Zink points out. Why discuss the option of accepting or declining an imperfect organ? If a patient says he doesn't want one, he'll most likely never get an organ at all. "I've had doctors tell me they don't even tell their patients that they're about to get an organ that might be infected with hepatitis C because so many of the donated organs may have it," Zink says.

On Friday, May 28, 24 days after his transplant, Joshua Hightower, who had been released from the hospital, graduated from high school. He clutched his diploma, climbed up into the stands and threw up, Jennifer Hightower said. He didn't stop vomiting all through the celebrations that followed. The next day, he was stumbling, and by the evening, he was having convulsions. Spit dribbled down his face. Doctors at the nearest emergency room hurriedly transferred him to the E.R. at Baylor.

Upstairs in the transplant wing, around the same time, three other patients who had received donations from William Beed Jr. lay dying, each with convulsions, delirium or pain. Within two weeks, all but Joshua were dead. Rabies was confirmed as the cause of death a few weeks later.

There is no formal system that tracks the short-term fate of individual organs from a particular donor. Surgeons report raw data about deaths and severe surgical complications to UNOS. Had all of the people who received an organ from William Beed Jr. not come back to the same hospital and died, one after another, their rabies may not have come to light.

In May, three people died who had received organs from the same donor in New England. As it turned out, the donor had passed along lymphocytic choriomeningitis virus, a rare illness transmitted to humans from rodents like hamsters. Two of the recipients, after getting ill, went to the same hospital, which helped doctors there determine that the transplant was the cause.

"I doubt very much that this is the only time" that rabies has killed transplant patients, says Charles Rupprecht, the C.D.C.'s rabies expert about the Beed case. "And I doubt that it will be the last." In February, doctors in Germany announced that four patients there had been infected with rabies after receiving organs from a rabid young woman who had died, they had thought, of a heart attack associated with an overdose of cocaine and Ecstasy.

"Rabies is a sentinel disease," argues Dr. Matthew Kuehnert, the assistant director for blood safety at the C.D.C., who has studied outbreaks of disease in transplant recipients. "It tells us we should be paying attention, that something needs to change."

What, though? "We cannot start testing every donor for rabies or any of the other once-in-a-lifetime diseases that might crop up," Klintmalm says. "We don't have time. It would cost too much. You might as well shut down every transplant center. If another case came in today exactly like that one, a young man who used crack cocaine and died, I would not demand more explanation. Why? We'll never get the risk of transplants down to zero. It's stupid to pretend we can. That young man appeared to be a perfect donor. I wish we had more like him."

The broader question is what, if anything, should change in transplantation as marginal organs become everyday organs? "We at the C.D.C. wish that there were more formal disease surveillance and follow-up of transplant patients," Kuehnert said. "We simply don't know the risks of using certain types of donors at this point." The C.D.C. has no authority to require such follow-up and study, though. Only other regulatory agencies within the Department of Health and Human Services or state agencies can set such mandates.

In June 2004, the New York State Department of Health became the first regulatory agency in the country to start formally looking into the growing use of marginal organs and to formulate recommendations about what patients should be told and what kinds of organs should be allowed. Its report is due soon.

In the meantime, the United Network for Organ Sharing has created a designation for patients who say they will accept a marginal kidney. At the end of February, 42 percent of the adults waiting for a kidney in the United States said they would take a marginal organ.

A year ago, while Joshua Hightower lay unconscious but alive, the doctors decided to surgically remove his transplanted kidney. But by then, rabies (not yet identified as the culprit) was everywhere in him. His condition worsened. On June 18, a Friday, doctors tested for brain activity. They found none and declared him brain dead. Stung with grief, Jennifer Hightower and the rest of her family sat with the boy through a wrenching weekend while he remained on a ventilator. On that Monday, his parents agreed to end life support. That afternoon, with his family watching, doctors turned off the ventilator. His mother held him as his heart stopped.

It will not be a simple matter in the years ahead to decide how best to save lives with transplants. At some point this year, the number of people on transplant waiting lists in the United States will very likely top 100,000. Unless there is an enormous effort, probably from the federal government, to increase organ donation, the shortage will only grow. "All these kids we see with diabetes," Nicholas Tilney says, "so many of them will need a new kidney in a few years. Where are those organs going to come from?"

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