“Science, Ethics & Governance”
Who Risks? Who Benefits?
Who Decides?

Thu July 8 @ 7:00 PM

Dr. Elizabeth ‘Betsy’ McGregor
Fellow, Centre for Public Leadership, Kennedy School of Government, Harvard
Deputy Director, IGH, Canadian Institutes of Health Research

Using children’s art work from across Canada, and a highly contentious technology – the transplantation of pigs’ organs into humans – Betsy will facilitate a high-impact interactive negotiation simulation that she developed at Harvard to illustrate some of the complexities that confront us all in regulating front-running life science technologies. If you benefit, but I risk – then who adjudicates? And if the globe is involved – what happens to “informed consent” as we know it? Who makes the choices on technologies with international, intergenerational impacts? All are welcome to an engaging evening. Bring a neighbour; bring the family. Explore how communities can contribute to public policy!

The genie is out of the bottle. We cannot place it back, but we can give it some rules!

Betsy McGregor is a Fellow at the Centre for Public Leadership, Kennedy School at Harvard, and Assistant Director, Institute for Gender and Health, at our Canadian Institutes of Health Research. Betsy recently ran for nomination in the local selection of candidates for the Liberal Party in RNP. Distinguished in 1998 as ‘Head of Public Service’ in Canada, for valuing people and for her commitment to ‘Youth Leadership’, Betsy was seconded to Harvard Medical School where she coordinated for two years, a ‘Global Working Group’ of theologians, scientists, researchers, ethicists, and activists examining issues of citizen engagement and governance in tough choices involving technologies and ethics.

Refreshments will be served – ALL WELCOME!

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Bennett/Mackenzie Room
J. L. Gray Centre
(Entry via rear entrance)
A Pig May Someday Save Your Life

Biotech: Scientists are racing to turn oinkers into organ donors. The effort could bring huge benefits, but it carries huge risks. By Geoffrey Cowley

At first it felt like a cold or a mild flu, nothing to stay in bed for. But 17-year-old Robert Pennington knew something more was wrong a few weeks later, when the whites of his eyes turned yellow. He visited a local clinic in Garland, Texas, where a doctor took one look at his coffee-colored urine and suggested he see a specialist. Robert never got to make an appointment. Within hours, he was so weak that his grandparents checked him into Presbyterian Hospital. His condition worsened steadily for three days, and on the fourth he moved to Baylor University Medical Center, where he promptly fell into a coma. The diagnosis: fulminant hepatic failure. The boy’s liver was dying.

Without an organ transplant, he would survive only hours, and the odds of finding a viable liver that soon were slim. So his grandparents (who are also his guardians) consented to a radical experiment. Under the direction of Dr. Marlon Levy, surgeons excised the liver of a genetically altered pig named Sweetie Pie and placed it next to Robert in a saline bath. Then, after inserting tubes into vessels in the boy’s neck and groin, they began cycling his blood through the pig’s organ. “We could tell right away that it was working,” his grandmother recalls. “The blood leaving Robert’s body was grayish, but it looked normal as it went back in.” The liver was still going strong six-and-a-half hours later, when the Baylor team obtained a human donor organ and implanted it. “I was amazed when I heard what had happened,” Pennington says. He’s turning 20 years old this month, and hoping to start an Internet business.

The technology that saved Pennington’s life could very well revolutionize medicine in the coming century. Researchers on both sides of the Atlantic are now racing to breed pigs whose cells, tissues and organs could be transplanted permanently into humans, without being destroyed by the immune system. Xenotransplantation, the transfer of organs between members of different species, may someday rescue thousands of the people who now die each year waiting for accident victims to give up hearts, lungs or livers. The procedure could also generate big revenues for surgeons and biotech companies—$6 billion a year by 2010, according to some estimates. But where proponents see boundless opportunity, critics see a catastrophe in the making. They fear the new practice could unleash new plagues, by transferring obscure pig pathogens into the human population. And they argue that no effort to save an individual justifies such risks.

Physicians have tried for centuries to rejuvenate ailing patients with animal organs. As you’d expect, they’ve fared best when borrowing from closely related species, such as baboons or chimpanzees. Humans have survived for up to 71 days on baboon livers, and for as long as nine months on kidneys taken from chimpanzees. But neither of these animals shows much promise as an organ supplier. Baboon organs are too small to sustain people for long periods. Chimps are too scarce, and too nearly human, to be routinely slaughtered for spare parts. And any primate can harbor deadly infectious agents. As Harvard microbiologist Ronald Desrosiers explains, “The closer one gets to humans in the evolutionary scale, the greater the risk of transmission.” Considering that the human AIDS viruses originated in chimpanzees and monkeys, even enthusiasts now agree that we’ll have to tap our more distant relatives for “donations.”

That’s where pigs come in. They resemble people in weight and physiology. They’re also plentiful and easy to breed and maintain. And as nonprimates, they provoke fewer ethical and safety-related concerns than chimps or baboons. Animal-rights activists oppose using any mammal as an organ factory—“The fact is, we should not live by the...”
Why pigs? Worldwide, only a third of the 180,000 people awaiting human-donor organs will get them

suffering of fellow creatures,” says Wendy Higgins of the British Union for the Abolition of Vivisection. But given that we already slaughter tens of millions of pigs for food each year, the prospect of killing tens of thousands more for medical purposes isn’t likely to spawn much popular outrage.

Physicians are already using various pig components—heart valves, clotting factors, islet cells, even brain cells—to treat human maladies. Moving whole organs from pigs into people is vastly more complicated. But researchers at Imutan of Cambridge, England, and Nextran of Princeton, N.J., are making headway. And despite all the controversy, health agencies seem content to let them proceed with caution. The U.S. Food and Drug Administration has authorized a number of experiments like the one that saved Pennington, and the British government has set up a regulatory authority to handle xenotransplantation issues. With luck, says Imutan chief operating officer Corinne Savill, the first attempt at a permanent heart or kidney transplant could occur within five years.

The technical obstacles are daunting. As Drs. David Cooper and Robert Lanza observe in their forthcoming book, “Xeno,” success will require “overcoming one of the human body’s oldest and strongest survival mechanisms.” Unless it’s blocked by antirejection drugs, the immune system will destroy even a reasonably compatible human donor organ within weeks. Its reaction to pig organs is far more violent. Pigs’ blood vessels are covered with galactose, or “Gal,” a sugar molecule that also happens to decorate many of the parasites and bacteria we encounter from day to day. We spend our lives generating antibodies to Gal—and when those antibodies encounter pig tissue, they know just what to do. They bind to Gal molecules, prompting the body to release an assortment of toxic proteins known collectively as “complement.” Our own tissues can neutralize these proteins before they cause damage. But human complement can turn an unarmed pig organ to mush within minutes.

No antirejection drug can stop this “hyperacute” reaction, but researchers at Nextran and Imutan have found a clever way around it. Their trick is to outfit pigs with the same “complement regulatory proteins” we use to shield our own tissues. By injecting a small assortment of human genes into one- and two-cell pig embryos, the scientists can occasionally produce an animal that makes these protective proteins naturally. These designer pigs still carry the Gal sugars that set off the complement cascade in humans. But because their tissues stand up to complement, they can survive brief exposure to our blood. With the advent of such pigs, says Dr. Christopher McGregor of the Mayo Clinic, “hyperacute rejection has disappeared off the radar screen” as an obstacle to xenotransplantation. For someone like Pennington, who needs an organ to sustain him for a day or two, that’s significant.

Unfortunately, hyperacute rejection is just the first of many obstacles to permanent transplantation. It’s followed within days or weeks by “acute” rejection, during which the recipient’s antibodies attack the foreign organ directly, destroying the cells that line its blood vessels. No one has yet succeeded at stalling that event in animal studies, but researchers are pursuing several approaches.

In one technique, the recipient’s blood is withdrawn and passed through a machine that separates blood cells from plasma, the watery fluid that carries antibodies and other noncellular constituents. The plasma is then mixed with synthetic Gal sugars that act as decoys, attracting anti-pig antibodies and pulling them out of circulation. When the treated plasma is returned to the body, it remains pig-tolerant until the depleted antibodies regenerate. Researchers have also tried injecting fake Gal directly into the bloodstream. Using these tricks and others, they can now keep pig hearts working for several weeks in baboons. “If we can get survival into the three- to six-month range,” says Nextran vice president John Logan, “we’ll be ready to think about human clinical trials.”

And ready to argue endlessly about the risk of spreading contagion from pigs to people. Nextran is taking elaborate precautions to keep its pigs free of known pathogens. Their water is disinfected, their air cleansed by filters, their feed composed solely of pasteurized plant products. Anyone entering the pigs’ compound has to scrub and dress for surgery. The animals are monitored for any sign of disease, and they’re screened regularly for more than 30 infectious agents, ranging from influenza to anthrax. As Logan points out, that’s more than you can say for any human organ donor.

Pigs, however, harbor some viruses that hygiene can’t elimin-
The War on Disease Goes Miniature

The future of medicine is vast—and it's also amazingly small. One day in the next century, thanks to the burgeoning field of nanotechnology, you could walk out of the doctor's office with a prescription for cancer detectors so tiny you can't see them. In this Lilliputian world, units are measured in nanometers—10,000 times smaller than the diameter of a single human hair. The idea is that if we can build new drugs and devices molecule by molecule, the way the tissues and organs in our own bodies are formed, we can make them much more targeted and effective.

One of the hottest areas of nanoresearch is better drug delivery. Scientists are now working on a miniaturized sensor for diabetics that mimics the glucose-detection system in a healthy body. The device, possibly implanted under the skin, would monitor blood-sugar levels, then release insulin as needed. And researchers at MIT recently made a prototype for an entire mini-pharmacy: a microchip (implanted or swallowed) with as many as 1,000 tiny reservoirs—each the size of a pinprick—that can hold 20 nanoliters of anything from painkillers to antibiotics. MIT's Robert Langer says the chip, now the size of a dime, can be made even smaller. And he plans to make it "smart" by adding a sensor that will know when to release a drug and what the dose should be.

Going small could also mean killing off cancer cells early, before they grow into life-threatening tumors. At the University of Michigan, Dr. James R. Baker Jr. is designing a kind of smart bomb that would target cancer cells by reading their chemical "signatures" and be small enough (about 20 nanometers) to get inside an individual cell and blast it away. Be patient: work on the device has just begun, and preliminary testing in humans won't start for at least five years.

Nanomedicine isn't just about getting rid of the bad—it's about enhancing the good. Imagine artificial red blood cells containing tiny nanopumps that would compress oxygen, allowing each cell to carry more than 200 times as much as its human counterpart. Are you at high risk of having a coronary? Doctors would inject you with an army of nanocells. Even if your heart shut down during an attack, you'd continue to be nourished with lifesaving oxygen.

Don't call your doctor for a nanoprescription just yet. Nanopump cells are only on the drawing board, and many other drugs and devices are more than a decade away. There are also plenty of unknowns. What, exactly, will nanoparticles be made of? And will the body accept them? But scientists are working hard to turn all this sci-fi into medical reality. One day, the smaller the medicine cabinet, the more powerful it may turn out to be.

Nanomedicine: Drugs and cancer tests, cell by cell. By Claudia Kalb

With Anne Underwood in New York and Ginanne Brownell in London

JANUARY 1, 2000 NEWSWEEK 89
Xenotransplantation continues to present daunting scientific hurdles but there is now a genuine prospect for clinical application. There are also significant and unknown risks. We call for a moratorium on all human xenotransplantation and offer a strategy for balancing the ethical, medical, scientific and societal demands of xenotransplantation prior to human clinical trials.

**Uncertainty in xenotransplantation: Individual benefit versus collective risk**

Clinical xenotransplantation, the transplantation of cells, tissues or organs from non-humans to humans, crosses a species barrier that has evolved over millions of years. In doing so, it promises a great benefit to some patients, but it creates the possibility of new disease entering the human population. The ethical issues posed by this dramatic tradeoff of individual benefit against societal risk is the subject of this paper. These ethical issues demand an approach different from that usually taken in the evaluation of new medical technologies. We advocate a process of education in which public discussion and iterative evaluations are used to define the ethical concerns, the potential risks and the benefits of clinical xenotransplantation at the societal level.

Clinical interest in xenotransplantation is prompted by the shortage of human donor organs for allotransplantation. Successful xenotransplantation would provide unlimited numbers of organs, making transplantation available to a greater number of patients. We focus on xenografts from pigs throughout, noting that grafts from evolutionarily more proximate species, such as non-human primates, likely pose even greater risks of infection.

The problems of rejection of a porcine organ by a primate are formidable. However, advances made in the past decade have allowed us to overcome some aspects of these problems and develop promising therapeutic approaches to others, making it conceivable that transplantation of porcine organs to humans will become a clinical reality.

Porcine cells are already being transplanted into the brain of patients with neurological diseases and the Food and Drug Administration has tentatively approved “bridge transplant” protocols to perfuse the blood of patients with liver failure through porcine lives.

Four ethical considerations guide our thinking. First, a risk to the public requires a public mechanism for determining the acceptability of, and method of consent to, the risk. Second, since the risk to the public is not a “one time only” event, its assessment and regulation must be iterative. Third, the standard model of individual informed consent to medical interventions must be modified, since risks involve third parties, requiring that patients and close contacts be carefully monitored. Fourth, the possibility that a new infectious agent with altered pathogenicity will arise within the xenograft recipient may represent a danger to the pig population. Because of these four considerations, xenotransplantation requires a novel process of evaluation at the national level with novel institutional guidelines, responsibilities and resources.

Although a number of lengthy reports have been published dealing with xenotransplantation, no organized method has been developed that addresses how to deal with the assessment and decision-making regarding this infectious risk to the public. A recent report of the U.S. National Research Council outlines an approach to assess and manage such risk-laden situations through an iterative process of analysis and deliberation involving public officials, scientists, and interested and affected parties. We propose such an approach for xenotransplantation.

The Food and Drug Administration (FDA) has already established a broadly constituted advisory committee, including both expert scientists and lay representatives to examine xenotransplantation. However, due to the unique aspects of public risk associated with xenotransplantation, initial discussions must be focused on the ethical issues. It is essential that the larger public interest, reflected in the ethical considerations we note above, be adequately aired and developed prior to developing a regulatory framework driven by technical considerations, and prior to making a commitment to proceed. A publicly constituted national advisory committee would be one vehicle to accomplish this type of broad public discussion.

Such a national committee should be comprised of individuals who are open-minded, sensible and broadly concerned citizens from many walks of life, thus representing a range of philosophical backgrounds and disciplines. Ethicists must be actively involved. Physicians and scientists familiar with technical aspects of the problem should also be included. As part of their own educational process, the committee would invite experts in relevant disciplines to answer questions and give advice. These should include, but not be limited to, those involved in the science of xenotransplantation, epidemiology, ethical aspects of the problem, animal welfare and rights, the medical profession, commercial efforts in transplantation, as well as the law and economics. Transplant recipients should be consulted. It will be important for the committee to have input from experts from the U.S. Food and Drug Administration and the Centers for Disease Control and Prevention.

Education of the members of the national committee is only a preliminary to their participating in decision-making about the future of xenotransplantation. The fundamental aim is to develop a consensus about the risks posed by present clinical trials, whether these efforts in xenotransplantation should be abandoned or expanded and if so, under what conditions. These efforts in the United States must be coordinated internationally with similar efforts, such as those of the Interim Regulatory Authority in the United Kingdom, in countries and with organizations that are likely to become involved in xenotransplantation. Whatever safeguards are needed to avoid infectious spread to the population must be adhered to in all countries concerned.
There are some historical precedents to deal with concerns about risks to the public of infection from novel procedures, such as agents produced by genetic engineering. The Asilomar proposals set standards dealing with recombinant DNA research. The fact that worst-case scenarios that underlay that caution did not materialize is no reason to suspend caution in this case.

**Xenosis**

The term xenosis was coined to describe the transfer of infections by transplantation of xenogeneic tissues or organs. Xenosis, or xenoozoonosis, potentially poses unique epidemiological hazards due to the efficiency of transmission of pathogens, particularly viruses, with viable, cellular grafts. Transplantation in general enhances the risk of infection for a variety of reasons: (i) the graft itself serves as a nidus or “culture plate” from which organisms can spread in the human host, avoiding the need for a vector to achieve disease transmission; (ii) migration of cells from the graft throughout the host may carry cell-associated infection, and (iii) administration of immunosuppressants leads to a diminished host response to infection, allowing infection to proceed in the absence of the usual manifestations of inflammation, often causing a delay in diagnosis.

The risks associated with xenotransplantation may be greater than those of allotransplantation for a variety of reasons (see box). Whereas any type of organism can become a pathogen in the immunocompromised human host, viruses transferred with viable cellular grafts have been a major source of concern with both allotransplantation and xenotransplantation. Recent molecular data suggest that there is a family of closely related porcine endogenous retroviruses (PERV), some of which appear to be infective for human cells in vitro. In vitro infection is not always predictive of in vivo infectivity and does not predict the ability of an agent to cause disease in the host. However, the possibility that a porcine retrovirus might be xenotropic, might have altered biological behavior in the human hosts, or might recombine with genetic material from the host (either in vivo or from exogenous infection) raises the specter of a new disease entity developing. Such pathogens might spread undetected to the general population.

The level of risk for such infections to the recipient and the likelihood that such infection will spread to others is unknown.

**A three-tiered approach to policy development and decisions**

The potential that xenotransplantation could introduce new infectious diseases into the population is the inverse of immunization. Immunization is intended to protect the population at the risk of having occasional individuals experience adverse reactions to the immunization. Xenotransplantation, on the other hand, offers potential benefit to the individual while putting the population at risk. Because the risk is societal and not merely individual, the decision whether to undertake the procedure involves more than ensuring the ability of the surgeon and the transplant team, the capacity of the institution, and the willingness of the patient. Where the risks are collective, the public must not only be educated about the risk but must also be involved in decision-making. The first level of decision-making must therefore occur at the level of social policy; the second at the level of the institutions performing the xenografts; and the third at the level of individual patients and physicians, affecting especially the processes of informed consent and of medical confidentiality.

**Risks associated with xenotransplantation**

- The level of immune suppression and/or rejection may be greater in xenograft recipients enhancing the activation of latent pathogens, including viruses.
- Organisms carried by the graft may not be known human pathogens and/or may include “xenotropic” organisms, that is organisms that are not pathogens in the native host species but cause disease in other species, in this case the human recipient.
- Microbiologic assays may not exist for some organisms derived from non-human species.
- Novel, animal-derived organisms may cause novel and thus unrecognized clinical syndromes.
- Genetic modification of the donor animals (one xenotransplantation strategy) or treatment of the recipient with, for example, tolerance induction or antibody removal, may alter the host’s susceptibility to organisms.

**Societal level**

Our focus on the risk of infection that can spread to the general population, while the most urgent ethical problem in xenotransplantation, should not diminish concerns about ethical issues related to the use of organs in humans from genetically-manipulated donor animals, and the risk to pigs of infection, among others. All the major reports on xenotransplantation released to date have recommended comprehensive monitoring and surveillance of xenograft recipients because of the risk of xenosis. The legal and ethical problems associated with imposing such surveillance on recipients, and perhaps their sexual partners, for what will likely be many years or for life, as well as details about the nature and frequency of monitoring, require further discussion. It is not inconceivable that patients manifesting signs of a possible xenosis after transplantation would have to be quarantined. The maintenance of patient confidentiality, as in all areas of medicine, remains paramount and further complicates the need for adequate monitoring of recipients.

Neither the degree of risk nor the capacity of the medical community to deal with xenosis are known. Hence, perception of uncertain risk becomes key. In general, perceptions of the public about risk are quite different from those of experts. Public views are affected by the degree to which risk is familiar or mysterious, controllable or uncontrollable, and whether it evokes feelings of dread or suggests the potential for catastrophe. While news reports of breakthroughs in the use of animal tissue are appearing frequently, many in the lay community still fear the idea of organ farming and regard the exchange of body parts between animals and humans as macabre and the stuff of horror films. Fears and values play a key role in the way humans view risk.

Experts tend to focus more directly on the degree of likelihood that mortality may result from the practice in question. With respect to the risk of transmission of infection from an animal donor to a human recipient, there are essentially no data which could be used accurately to assess the level of such risk. The range of uncertainty is large, with the possibility of devastating cross-species infection looming in the background.

Because of this uncertainty and because risk can mean very different things to different constituencies, the framing of statements about risk is particularly important. First, the
life-saving potential and enormous impact on the practice of medicine that successful xenotransplantation would have needs to be made clear. Second, the public must be informed of any risk that could arise from xenotransplantation, whether or not the extent of that risk and the degree to which that risk is controllable can be precisely defined. Finally, it would be helpful for the public to have a better understanding of the process by which decisions are made in situations of uncertainty.

The problem cannot be dismissed by talking about education as if the experts have to eliminate ignorance and persuade the public; the public has its own concerns, rooted in quite diverse moral beliefs. There is a needed deliberative task: how do we coalesce the different ethical and factual considerations that merit consideration? A public deliberative process is key with the ultimate control over risk management vested in the public. Decisions as to how xenotransplantation will proceed, and how risk will be handled at different stages of technological development, must emerge from such societal deliberations.

At the outset, there are two alternative, default positions. Either something has to happen to allow moving forward, or something has to happen to prevent moving forward. If the decision is to proceed, then the generally accepted policy in situations of uncertainty is to begin a limited series of experiments proceeding only to the point where risk reaches a certain pre-defined level. The committee would therefore serve to define the milestones for subsequent re-evaluations at each stage of the process.

Because it is impossible for all of the necessary evidence about risk to be available before xenotransplants begin to be performed, an appropriate approach might be to have a controlled initial trial involving a limited number of human recipients, and have those patients followed for a specified period of time. This approach has the advantage of allowing the refinement of regulatory and institutional mechanisms for evaluation of approaches to microbiological testing and other factors. This first phase would ideally last for as long as there is any risk of infectious transmission, which would mean waiting for some number of years. The length of this observation period is one appropriate issue for the committee to discuss and resolve. Society would then be presented with outcomes which could be used to revise the initial risk assessment, allowing reassessment of the safety and advantage of further experimentation. It may then be necessary to modify or extend the monitoring system in order to justify proceeding to the next phase of testing. Such a stepwise approach could be repeated and would require specifying in advance the points of reassessment with the assurance of regulatory controls as the process unfolds.

There will be great pressure on the committee to yield to the reality of “identified victims” who will die without an organ transplant. The central challenge to the committee will be to sustain in balance the uncertain societal risks against the palpable risks to individuals dying of organ failure.

In addition, the national committee must concern itself with at least two other problem areas: the financial commitments that must be made to allow monitoring for a period long enough to cover possible late-occurring xenosis, and the use of transgenic animals (in this case transgenic donor animals) and risks to the pig population of infections arising from xenotransplantation.

The cost of monitoring patients and others for signs of infection would likely be very expensive and must be addressed prior to starting xenotransplantation. There must be discussion with national funding agencies, insurance companies, pharmaceutical and biotechnology companies interested in xenotransplantation, and other health care financing institutions regarding a commitment to meet the required costs of the monitoring procedures for whatever period is deemed necessary.

Xenotransplantation has stimulated renewed interest in the use of animals in research. The use of pigs as a donor species has generally been viewed as reasonable. Some additional concerns have emerged as herds of swine are developed for possible use in xenotransplantation. First, pigs that are quarantined for the purpose of minimizing disease transmission must be assured of appropriate social interactions, which are important for general health and development. Second, xenotransplantation presents the possibility that an infectious organism that did not previously exist might arise in humans that would be devastating to pigs. Transmission to a human recipient of a porcine retrovirus that did not cause disease in pigs could result in modification of the nucleic acid sequences of the virus via recombination or mutation. Such a novel viral strain could cause disease in swine with devastating consequences for pig animal husbandry.

The report of a national advisory committee will provide guidelines for decisions that must be made at the institutional and patient-doctor levels. A supra-institutional public authority will need to be responsible for the regulation and management of xenotransplantation. In that role, the authority would define the conditions under which an institution would be authorized to proceed, and would fix the nature of the commitment that the patient and relevant contacts must make before xenotransplantation can take place. Regulations would likely be aimed at offering a uniform measure of protection to patients, to society and to animals.

As such, decisions at the institutional and individual levels should be guided by the deliberations at the societal level and should not be undertaken before the societal process has taken place. Because the societal discussions are likely to take some time, it is critical that these be started as soon as possible to avoid the unnecessary withholding of therapies from patients in need. Despite the fact that lives of patients needing transplantation may be lost with delay, we believe that the risks are sufficient to warrant refraining from human xenotransplantation until public deliberations on the ethical issues have occurred. Research in xenotransplantation should be strongly encouraged, including studies to define the potential risks of inter-species transplantation.
Institutional policy
At the level of the hospital or research center, institutions must be responsible for establishing and enforcing standards for quality of care, management of risk, monitoring of patients and their contacts, and evaluation of the effectiveness of the procedure in accordance with public guidelines and regulations. Institutions should avoid a situation in which individuals proceed with xenotransplantation in advance of adequate safeguards and should curtail clinical trials until societal guidelines are available.

Patient-Physician Interactions: Consent and Confidentiality.
A new approach to informed consent as it relates to xenotransplantation is called for. A patient’s agreement to participate in xenotransplantation must be premised on perceptions of both individual risk, as is the case with any experimental or extreme procedure, and the risk of new disease to family, friends, close contacts, and society at large. Because of the need for monitoring for signs of infection, the patient and others will have to commit to participate in such monitoring for a period of time that is considered to be longer than the potential time it might take for an infection to become manifest. Patients would not only have to agree to the risks attendant to a transplant procedure, but also to a contract binding the patient and others to carry out future obligations, including the participant’s possible quarantine, as well as modification of the guarantees of confidentiality and surrender of the right to “drop out” of the study. Whether such a contract could be enforced is an issue that the national committee will need to debate. In theory, xenotransplantation might not be allowed unless the patient and family members and sexual partners agree to some onerous conditions for monitoring. For instance, should there be a requirement that the some persons be informed of the fact that the patient is a xenotransplant recipient. Thus, the xenotransplant patient undertakes a social obligation to submit to close monitoring and frequent follow-up, even if this means relinquishing certain freedoms in order to gain the potential benefits of participation.

Concluding comment
We offer a strategy for handling the ethical issues related to xenotransplantation based on the optimistic perspective that xenotransplantation could become a clinically useful procedure, and our strong support of the science being performed. We propose a moratorium on xenotransplantation including those procedures that could be practiced at any time, such as using a pig organ as a temporary “bridge” until an allogeneic organ is found, or as support for patients with hepatic failure. We have a feeling of urgency for a national review to be undertaken given the need of patients who might benefit from xenotransplantation, the impact on the field of the already-arrayed commercial interests, and the present and impending use of xenotransplantation procedures that could cause spread of disease. Past experience with problems involving uncertain public risks that are hard to quantify has shown that individuals and groups with various interests and concerns will have to work together in an interactive manner if appropriate decisions are to be made, and effective and responsible policy is to be generated.

The history of medical innovation has shown us unwilling to resist tangible individual benefit even in the face of unknown risks. It is incumbent upon us now to prepare for the moment when the decision to begin organ xenotransplantation will be well-nigh irresistible.

Acknowledgments
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144

NATURE MEDICINE • VOLUME 4 • NUMBER 2 • FEBRUARY 1999
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<td>COURT SYSTEM</td>
<td>LOCAL: e.g. student's council, school boards, Mayor &amp; city council, Aboriginal Councils</td>
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<td>➢ There are <strong>2 branches</strong> to the Canadian Court System, civil law and criminal law.</td>
<td>PROVINCIAL: Legislative Assembly: each area represented by a Member of Provincial Parliament (MPP or MLA). Certain issues are dealt with only at the Provincial level, like education, but the legislative process here is similar to that of the House of Commons.</td>
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<td>➢ Civil law is anything that is not criminal. If it is, for example, me suing you, or if it is regarding rights, it is civil.</td>
<td>FEDERAL: Canada has a democratic bicameral system, comprised of the House of Commons and the Senate.</td>
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<td>➢ Criminal law has an accusation; a crime of wrong doing, for example drunk driving or murder.</td>
<td>➢ The Prime Minister is the head of the Government and is elected as a Member of Parliament then voted in as the party leader at a party convention. The PM chooses a Cabinet from the elected MPs in his/her party.</td>
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<td>➢ The <strong>Provincial legal system</strong> deals only with criminal law. Decisions at this level can be appealed. The provincial court has a trial division and an appeal division. There is also a provincial Supreme Court.</td>
<td>➢ The Government is usually the party with the most seats after an election (there are 301 seats). Sometimes there will be a minority government, however, if the opposition parties together hold more seats than the government, and they can rule against the government and overthrow them. This would be cause for another election.</td>
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<td>➢ There is also the <strong>Supreme Court of Canada</strong>, which is the final court of appeal for both the Federal Court of Appeal and the Provincial Courts.</td>
<td>➢ The Senate is made up of 102 appointed Senators. Most represent specific parties but some are appointed as independents, and they each represent their own province. Bills can be initiated here as well as in the House of Commons.</td>
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<td>IMPORTANT EXAMPLE: 'The Harvard Oncomouse': Harvard was developing transgenic mice that were specialized to always have cancer. These mice could be used for research on cancer in humans. The company came to Canada looking for patent protection in 1986 but they were rejected at the Federal Court level, including their appeal in 1998, on the basis that it is wrong to patent a mammal. If they were to try again, the judge ruled that they would have to go through parliament, as it was parliament who set the legislation for patenting mammals. This example demonstrates the effectiveness of the judicial channel to set policy through the rendering of legal opinion at the national level. (However, in August, 2000, The Federal Court of Appeal ruled that the oncomouse could be patented...)</td>
<td>EXAMPLE: many Canadians have made positive differences in their communities and all over the world by pressuring their Members of Parliament to bring up certain issues in the House of Commons. MPs (and Senators) can put forth &quot;Private Member's Bills&quot; which are issues of their own concern or of concern to the people of their constituency. They can also address these issues in House of Commons Committees (e.g. Health Committee- see the enclosed case study). They are made up of MPs representing all the different parties.</td>
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<tr>
<td>THE INTERNATIONAL COURT OF JUSTICE</td>
<td><strong>INT'L ASSOCIATIONS OF PARLIAMENTS</strong></td>
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<tr>
<td>The Hague, Netherlands</td>
<td>Some examples of Associations:</td>
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<tr>
<td>The principal judicial organ of the UN has two jobs:</td>
<td>➢ INTERPARLIAMENTARY UNION</td>
</tr>
<tr>
<td>➢ to settle legal disputes submitted by States and</td>
<td>Known for:</td>
</tr>
<tr>
<td>➢ to give advisory opinions to international agencies</td>
<td>• representative democracy</td>
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<td></td>
<td>• international peace and security</td>
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<td>• sustainable development</td>
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<td>• human rights/humanitarian law</td>
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<td>• women in politics</td>
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<td>• education, science and culture</td>
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<td>MORE INFO @: <a href="http://www.ipu.org/iss-e/issues.htm">www.ipu.org/iss-e/issues.htm</a></td>
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<td></td>
<td>ASSEMBLY OF WESTERN EUROPEAN UNIONS</td>
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<td>Made up mainly of 6 committees that focus on political, parliamentary, defense, and technological issues. Heads of the states involved or their Ministers can be invited as guest speakers or can ask to make a presentation before the assembly or before one of the committees.</td>
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<tr>
<td></td>
<td>MORE INFO @: <a href="http://www.weui/assembly">www.weui/assembly</a></td>
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<td></td>
<td>COMMONWEALTH PARLIAMENTARY ASSOCIATION</td>
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<td>Processes up to 300 inquiries per year. They basically provide information and are a reference service to parliamentarians of associated countries, and others interested in parliamentary institutions.</td>
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<td></td>
<td>MORE INFO @: <a href="http://www.comparlhq.org.uk/frames.htm">www.comparlhq.org.uk/frames.htm</a></td>
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<tr>
<td>EXAMPLE: try searching for information on the Court's opinion of nuclear power.</td>
<td>EXAMPLE: try searching the net for one!</td>
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<tr>
<td>NATIVEAL DEPARTMENTS</td>
<td>NON-GOVERNMENTAL ORGANIZATIONS (NGOs)</td>
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<td>The Bureaucracy is the non-elected part of government; the large hierarchical workforce arranged under the Cabinet Ministers chosen by the Prime Minister. Some of the more relevant federal departments to our study are:</td>
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<tr>
<td>Health Canada: <a href="http://www.hc-sc.gc.ca">www.hc-sc.gc.ca</a></td>
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<td>Agriculture Canada: <a href="http://www.agcanada.com">www.agcanada.com</a></td>
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<td>Environment Canada: <a href="http://www.ec.gc.ca">www.ec.gc.ca</a></td>
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<td>Industry Canada: <a href="http://www.ic.gc.ca">www.ic.gc.ca</a></td>
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<tr>
<td>MORE INFO @: <a href="http://www.canada.gc.ca">www.canada.gc.ca</a></td>
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<td>EXAMPLE: Health Canada was a partial sponsor of a national forum on xenotransplantation in 1998. They published a very informative report titled: “National Forum on Xenotransplantation: Clinical, Ethical and Regulatory Issues,” a copy of which is included in this kit.</td>
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<td>EXAMPLE: Industry Canada has a very good website that details a lot of the biotechnological advances that are occurring. It contains a special section on ethics: <a href="http://www.strategis.ic.gc.ca/SSG/tc00006e.html">www.strategis.ic.gc.ca/SSG/tc00006e.html</a></td>
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<tr>
<td>AGENCIES WHO OPERATE SEPARATELY FROM GOVERNMENT (Civil Society)</td>
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<td>Each stakeholder involved has agencies by which it can be represented.</td>
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<td>INDUSTRY NGOs: In Canada the umbrella organization representing biotechnology companies is BiotechCanada (<a href="http://www.biotech.ca">www.biotech.ca</a>). In the US the similar company is called BIO (<a href="http://www.bio.org">www.bio.org</a>).</td>
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<td>PATIENT NGOs: there are many foundations made up of doctors, patients, family members and supporters for different diseases and help fundraise for research money and lobby governments, for example the Kidney Foundation of Canada (<a href="http://www.kidney.ca">www.kidney.ca</a>), the Canadian Diabetes Association (<a href="http://www.diabetes.ca">www.diabetes.ca</a>) and The Parkinsons Foundation of Canada (<a href="http://www.parkinson.ca">www.parkinson.ca</a>).</td>
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<tr>
<td>PROFESSIONAL ASSOCIATION NGOs: Professional groups such as medical doctors (Canadian Medical Association: <a href="http://www.cma.ca">www.cma.ca</a>) and lawyers (Canadian Bar Association: <a href="http://www.cba.org">www.cba.org</a>) that represent their members and take positions on issues. e.g</td>
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<td>ANIMAL WELFARE NGOs: research and represent the perspective of animals in the research and production of products for the marketplace. For example, the Animal Protection Institute: <a href="http://www.api4animals.org">www.api4animals.org</a></td>
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<td>INDIVIDUAL NGOs: Recently, in our research, we came across an interesting scientist named Richard Hayes who spoke to us regarding his new NGO “Exploratory Initiative on the New Human Genetic Technologies.” Although no website is set up at this date, there is an interview with him included in the kit.</td>
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<tr>
<td>UNITED NATIONS</td>
<td>INTERNATIONAL NON-GOVERNMENTAL ORGANIZATIONS (INGOs)</td>
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<td>The UN has, under its large wings, many agencies and organizations that are all over the world and are involved in many different things. Some relevant to this project are:</td>
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<td>World Health Organization (WHO) who is advised by the World Health Assembly (WHA), a group of Health Ministers from all over the world who meet every 6 months</td>
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<td>United Nations Educational, Scientific and Cultural Organizations (UNESCO)</td>
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<td>Food and Agriculture Organization (FAO)</td>
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<td>International Foundation for Agriculture and Development (IFAD)- a subsection of the FAO</td>
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<td>IMPORTANT EXAMPLE: UNESCO put together the “Universal Declaration of Human Rights” in 1945. There is a good article about this at <a href="http://www.unesco.org/opi/1948-98/art19-ve.htm">www.unesco.org/opi/1948-98/art19-ve.htm</a> In 1995 they revamped the declaration to add the human genome. See the attached poster titled “Universal Declaration on the Human Genome and Human Rights.”</td>
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<td>MORE INFO @: <a href="http://www.un.org">www.un.org</a></td>
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<td>Also many links to other international associations through the Canadian Department of International Affairs: <a href="http://www.dfaitmaeci.gc.ca/foreigngnp/menu-e.asp">http://www.dfaitmaeci.gc.ca/foreigngnp/menu-e.asp</a></td>
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<td>NGOs are set up with certain goals in mind, and they work hard at expressing their beliefs to the public and to government organizations. Some groups you might not have realized were NGOs are:</td>
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<tr>
<td>Amnesty International: <a href="http://www.amnesty.org">www.amnesty.org</a></td>
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<td>Sierra Club: <a href="http://www.sierracclub.org">www.sierracclub.org</a></td>
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<td>Greenpeace: <a href="http://www.greenpeace.org">www.greenpeace.org</a></td>
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<tr>
<td>Save the Children: <a href="http://www.savethechildren.org">www.savethechildren.org</a></td>
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<td>Canadian Wildlife Federation: <a href="http://www.cwf-tcf.org">www.cwf-tcf.org</a></td>
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<td>You can easily become involved in an organization that supports your beliefs, or simply learn about these different groups and what they represent by looking up their websites.</td>
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<tr>
<td>More information on NGOs and INGOs in general can be found at the ‘NGO Café’: <a href="http://www.geic.or.jp/geic-ngocafe.html">http://www.geic.or.jp/geic-ngocafe.html</a></td>
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</tbody>
</table>
HOT LINKS

Listed below are some of the references we have used in our research and in preparation of the different tools included in the educational module.

BioteCanada
www.biotech.ca
Bio
www.bio.org
Industry Canada: Bio-Industries: Xenotransplantation Overview
http://strategis.ic.gc.ca/SSG/te00027e.html
(List of links at http://strategis.ic.gc.ca/SSG/te00057e.html#xeno)
The Science of Xeno- Novartis
National Centre for Biotechnological Education
www.ncbe.reading.ac.uk
Public Perception Issues in Biotechnology (great links!)
http://fbox.vt.edu:10021/cals/cses/chagedor/
Xenotransplantation- The International Debate- OECD (good links)
www.oecd.org/dstisiti/s_t/biotech/xenosite/country.htm
Canadian Bioethical Society
www.bioethics.ca
National Bioethics Advisory Commission (USA)
http://bioethics.gov
The Council for Responsible Genetics
www.gene-watch.org
Roslin Institute
http://www.ri.bbsrc.ac.uk
Ethics, Science and Governance: The Xenotransplantation Case (Our website!)
(GOOD LINK DATABASE)
www.xenoproject.org
The Wellcome Trust
www.wellcome.ac.uk/info
Health Canada: Proposed Canadian Standard for Xenotransplantation
http://www.hc-sc.gc.ca/hpfb-dgpsa/bgtsdpbtg/xeno_fact_e.html
Report of (WHO) Consultation on Xenotransplantation
WHO Electronic Discussion Group on International Xenotransplantation Policy Considerations
http://www.who.int/emc/diseases/zoo/meetings/xenodg.html
Organ Donation Links

John Martin: A Photjoournalist Chronicles his Journey Through Kidney Failure
http://www.johnfmartin.net/diagnosis/index.htm

Don Killen: Kidney Transplant Experience
http://web2.airmail.net/dkillen/pages/transplant-long.html

Janelle London: "From Dialysis to a 2,840 Mile Bike Ride: the Biggest Physical Challenge of my Life"
http://www.transweb.org/people/recips/experienc/london/index.htm

Peter Langley: Kidney Failure: A personal journal
http://www.yankeetown.org/plangley/1.html

Monet Thompson: Receiving Charlie's Kidney
http://members.aol.com/monetthom/my_trans.htm

Lisa Forbes: An Australian Kidney Transplant Recipient's Story
http://www.transweb.org/people/recips/experienc/forbes.html

Mary Steenland: A Donor Mother's Story
http://web.idirect.com/~more/donors_stories_1f.html

Martha Stauffer: The Best Gift: My Dad's Kidney Transplant
http://userwww.service.emory.edu/~curt/feb2694.html

Rene Rogers: In Memoriam
http://www.transweb.org/people/recips/memoriam/no_longer/rene_rogers/rene.html

Peter Keller: Rebuilding Me Somewhere Else (story of a kidney donor)
http://www.transweb.org/people/recips/experienc/rebuilding_me.html

Dale Griffey: A tribute
http://www.transweb.org/people/donors/memorials/dale_griffey/griffey.htm

Miriam Newbery: In Memory of My Heart Donor
http://www.transweb.org/people/donors/memorials/memorial/donors/newby_donor_poe.html

Tissot Family: Kidney Transplant Stories
http://www.tissotfamily.com/kidney.html

Kelley Horrigan: "I Love Her With All Our Kidney" (living donor)
http://www.transweb.org/people/live_don/experienc/horrigan.htm

Michelle: Donating a Kidney: A Love Story
http://www.transweb.org/people/live_don/experienc/kickboxing.htm

Lisa Wedemeyer: A Bone Marrow Donor
http://www.transweb.org/people/live_don/experienc/wdmvr_ls.htm

Shannon Breshears: Story of a wonderful friendship between two young women leading to a kidney donation.
http://www.geocities.com/s_breshears
RECIFE, Brazil - When Alberty José da Silva heard he could make money, lots of money, by selling his kidney, it seemed to him the opportunity of a lifetime. For a desperately ill 48-year-old woman in Brooklyn whose doctors had told her to get a kidney any way she could, it was.

At 38, Mr. da Silva, one of 23 children of a prostitute, lives in a slum near the airport here, in a flimsy two-room shack he shares with a sister and nine other people.

"As a child, I can remember seven of us sharing a single egg, or living for day after day on just a bit of manioc meal with salt," Mr. da Silva said in an interview.

He recalled his mother as a woman who "sold her flesh" to survive. Last year he decided that he would, too. Now, a long scar across his side marks the place where a kidney and a rib were removed in exchange for $6,000, paid by middlemen in an international organ trafficking ring.

Among poor men like Mr. da Silva and others who have migrated to slums here from Brazil's parched northeastern backlands, word of the market to sell their organs spread quickly.

Some who had done so were already buying houses, businesses, cars and refrigerators.

The sums being offered seemed a fortune. The minimum wage here is barely $80 a month, and work is hard to find. Many men struggle to exist on odd jobs that pay barely a dollar a day. Initially, the organ brokers paid as much as $10,000 for a kidney - more than a decade's wages.

Donors and recipients were not related, in contrast to the usual preference for legal and medical reasons. In fact, they did not even know each other. But they were linked by a trafficking ring that the authorities now say exploited two very different sets of needs - for money and for life itself - at opposite ends of a tangled chain thousands of miles long.

Tracing the journey of Mr. da Silva's kidney through that chain, which spanned four continents and ended in a one-bedroom apartment in Brooklyn, reveals the inner workings of a network that human rights groups say is by no means unique. Rather, they say, it is representative of a global black market for organs, including livers, kidneys and lungs, that touches dozens of countries and generates many millions of dollars a year.

In Alberty da Silva's case, the authorities here say, the organ's odyssey began with two middlemen based in this gritty port city of 1.5 million people: Gedalya Tauber, a former Israeli police officer, and his partner, Ivan Bonifacio da Silva, a retired Brazilian military police officer.

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The pair, since jailed on organ trafficking charges, not
only handed out cash payments, the authorities say, but also arranged for the medical exams to weed out unqualified donors. They then obtained passports and airline tickets for the donors to travel to South Africa, where the transplants took place. Both countries have laws against commercial trade in organs.

"Six grand is a lot of money, especially when you don't have any," Mr. da Silva said when asked why he had given up his kidney. "No one here warned us that what we were doing was illegal."

Get a Kidney, or Expect to Die

The American woman who received Mr. da Silva's kidney initially worried that what she was doing might be illegal. She described herself as deeply religious and concerned with the ethics of transplants.

But during an interview in April she also recalled the long years of suffering that made her take the risk of seeking an organ on the international market. The decision to go abroad for a kidney, she said at her third-floor walk-up apartment in Brooklyn, was not an easy one, but necessary nonetheless.

"I had been on dialysis for 15 years and on two transplant lists for 7," said the woman, who asked not to be identified by name, for fear of losing support payments vital to maintaining the health of her transplanted organ. "Nothing was happening, and my health was getting worse and worse." Finally, she said, "my doctors told me to get a kidney any way I could," or expect to die.

She took their warning seriously. The years of dialysis had left her with worsening heart and lung problems. She also suffered from severe osteoporosis. "I had seen four other ladies that I knew pass away" while they waited for kidney donors, she said.

More than 3,300 Americans died last year awaiting kidney transplants, and the Brooklyn woman was among 85,000 people on waiting lists in the United States, 60,000 of them in need of kidneys. The average wait can be five years, says the United Network for Organ Sharing, a nonprofit transplant information clearinghouse in Richmond, Va.

It is illegal in the United States to pay a donor for an organ. But Nancy Schepers-Hughes of Organs Watch, a human rights group in Berkeley, Calif., that has long tracked the illegal organ trade and denounced abuses, says irregularities still occur.

"It is a common practice of many larger clinics to advertise on the Internet for transplant tourists, so we're up to our necks in it," Dr. Schepers-Hughes said. Transplant doctors, she says, have developed a "don't ask, don't tell" policy.
The World Health Organization issued guidelines in 1991 to avoid the coercion or exploitation of organ donors. They were endorsed by 192 countries, including the United States, Brazil and South Africa. But the guidelines are not binding, and the recommendations have been widely ignored. At least one country, Iran, has a legally regulated system to trade organs.

As medical science advances and health care increasingly becomes a marketplace transaction, a fierce debate about commercializing transplants has emerged.

On one side, said Alexander M. Capron, the director of the ethics department of the World Health Organization, are "transplant surgeons who believe that a good way to remedy the shortage of organs would be to offer payments," and bioethicists and philosophers who see organ trade as an extension of the principle of autonomy.

But an opposing group, Mr. Capron said, "fears that the line between selling organs and actually selling people is a rather fine one" and that, as in sex trafficking, the marketplace is one in which coercion and exploitation may be unavoidable.

In the case of the Brooklyn woman, her husband had relatives in Israel who had heard of a syndicate that brokered transplants, and reached out to them. The woman and her husband said that relatives and the brokers reassured them that an operation abroad would be perfectly legal.

"I felt helpless, because she was going to die," said the woman's husband, who is in such fragile health himself that he receives disability payments. "Helping her get that kidney was the best thing that I have ever done for anyone in my entire life."

'Mr. Big' or 'the Wrong Guy'?

The syndicate that organized the American woman's transplant, the authorities say, also arranged kidney transfers for at least 100 Israelis. It was led, they say, by a 52-year-old organ broker in Israel, Ilan Peri.

"He's Mr. Big, the one who started the whole thing," Johan Wessels, a forensic investigator in South Africa who works for the Department of Health in KwaZulu-Natal Province and has had access to hospital records there, said in Durban.

Mr. Peri works out of a Tel Aviv suburb through a company called TechCom. He faces charges of tax evasion in Israel, accused of improperly declaring nearly $4 million said to have been earned as an organ broker and is also under investigation in connection with inflating the invoices that he did submit to Israeli health care programs.
When reached by telephone in Tel Aviv and asked to comment on the charges, Mr. Peri said: "I have never been involved in kidney transplants. You are talking to the wrong guy." He eventually hung up the telephone, but not before amending his statement. "I'm not involved in that anymore, so I can't help you," he said.

To those who monitor organ trafficking, it was no surprise that Israel should emerge as the focal point of a syndicate. Organ donation rates in Israel are among the lowest in the developed world, about one-third the rate in Western Europe, in large part because of what Health Ministry officials and doctors describe as a widespread impression that Jewish religious law prohibits transplants as a "desecration of the body."

In reality, religious law is far more nuanced. But influential Orthodox rabbis have been reluctant to make public statements that would encourage either live donors or the harvesting of organs from the deceased.

Israelis needing transplants have suffered as a result. More than 1,000 people in a nation of about 6 million are on Israel's waiting list for organs, more than half of them for kidneys. The list grows by more than 20 percent each year, health officials say. In an average year, more than 80 people die waiting, proportionally a slightly higher rate than in the United States.

To meet Israeli's growing demand for organs, middlemen calling themselves brokers, from prominent doctors to a former spokesman for a health maintenance organization, have rushed into the market to set prices for a scarce product that can reach $150,000 for a kidney. Some advertise openly in Israeli newspapers and on radio stations, soliciting recipients and donors.

"As of today, there is no law in Israel that forbids trafficking in human organs," Meir Broder, a legal adviser to the Health Ministry, explained in an interview in Jerusalem. "There is no criminal aspect at all."

A bill drafted by the Health Ministry that would make trafficking illegal and forbid organ donations for money awaits action in the Parliament. But medical specialists say it faces strong opposition and may not pass.

For now, allowing the brokers to operate with few restrictions in effect benefits the state by exporting Israel's organ shortage overseas. The patients who do go abroad "save the country a lot of money," explained Dr. Michael Friedlaender, a kidney specialist at Hadassah Hospital in Jerusalem, "not only in terms of what doesn't have to be spent on dialysis, but also by opening places for other people who are on the list."

For operations in Israel, the Ministry of Health relies on elaborate procedures to ensure that donors and recipients
act for "altruistic" motives and do not exchange money. But another ministry directive also allows Israelis who go abroad for transplants to be reimbursed as much as $80,000.

Much of the remaining costs can often be obtained from insurance plans, though Israeli health maintenance organizations are supposed to ask for proof when donors and recipients say they are related in "voluntary" operations.

Israeli doctors say those requirements are often ignored, and the government says it has no obligation to monitor operations done abroad. "In the end, a country can only be responsible for what happens within its own borders," said Mr. Broder, the Ministry of Health lawyer.

In the mid-1990's, many of the Israeli organ brokers took their patients to Turkey, flying in teams of Israeli surgeons and relying on donors from Moldova, Romania and Russia. But after some patients died and Dr. Schepers-Hughes of Organs Watch and the Turkish and European news media raised ethical questions, the brokers were forced to search for new locations.

For both the medical expertise available and its low costs, South Africa emerged as a logical alternative.

The South African Connection

It was there, in South Africa, the authorities say, that Mr. Peri's ring brought together Mr. da Silva and the woman who ultimately received his kidney.

After long negotiations in Israel, which she said were conducted by relatives of her husband, the Brooklyn woman flew to South Africa for a transplant. Because of her unusual circumstances, it cost her just over $60,000, which other kidney recipients who dealt with Mr. Peri said was less than half the price the syndicate usually charged.

Even so, that amount was 10 times the payment Mr. da Silva received, though organ recipients in Israel said Mr. Peri routinely told them that the Brazilian donors were being paid $25,000.

While money initially motivated Mr. da Silva to sell his kidney, he said he also came to be moved by the chance to help a stranger. The change, he said, occurred after he, too, arrived in South Africa, his first trip out of Brazil, in what he saw as an adventure that would allow him to see lions, giraffes and elephants.

Instead, after 10 hours of flying last August, Mr. da Silva found himself in Durban, a resort city of 1.4 million on the Indian Ocean, where he was shuttled to a safe house. Later, at St. Augustine's Hospital, he met the American woman and learned of her long ordeal.
"It's hard for me to imagine how a person might feel when a relative is about to die, so I don't blame anybody for trying anything to get a new kidney," Mr. da Silva said.

He said he also made friends with hospital orderlies and a nurse called Mama Tchuka. Mr. da Silva said hospital employees joked openly about the illegal nature of the transplants and the fact that he and the woman receiving his kidney were of different ethnic backgrounds and could not even speak each other's language.

"It was only when I got to South Africa and was told to sign a document saying that the recipient of my kidney was my cousin that I realized that something was wrong," Mr. da Silva said. "But by then it was too late to turn back."

In interviews, Mr. da Silva and several other of the Brazilian men who donated organs said they were treated well in South Africa. But investigators say the donors did not get the same quality of care as the Israelis who received their organs.

The Israelis, for example, like the American woman, were lodged in beachfront hotels before the operation and, afterward, kept under intense observation and given detailed records to be handed over to their doctors back home. The donors, by contrast, were monitored "for a maximum of three days," Mr. Wessels, the South African investigator, said. Some of that time, they were not even in the hospital, but at the safe house the syndicate rented.

"Then they were put on a plane without much further ado," he said.

Based on a detailed study of confiscated records, South African authorities say the kidney transfer between Mr. da Silva and the Brooklyn woman was one of more than 100 suspect transplants performed in less than two years at St. Augustine's.

Today, the director of the kidney transplant unit there, Lindy Dickson, and another employee, Melanie Azor, are among seven people arrested and charged with acting on behalf of the illegal organ ring. Government officials say more indictments are on the way. "Not all the invitation cards have been sent out yet," Barent Groen, the chief government prosecutor in the case, said in an interview in Durban.

Also arrested was Shushan Meir, an Israeli-born South African who authorities said acted as a middleman for Mr. Peri, the Israeli broker.

"He visited transplant clinics in Durban, Johannesburg and Cape Town," Mr. Wessels said of Mr. Peri, "and correspondence shows that he was in touch with the doctors
and the transplant clinic staff here. The impression I get is that he was making sure his investment was running smoothly."

At a court hearing, Mr. Meir said that beyond the 100 or so transplants done in Durban, he had organized "probably about 35" more in Johannesburg. But South African investigators estimate that the actual number is probably closer to 200, divided among hospitals in Johannesburg and Cape Town.

All the hospitals under investigation belong to the same private health care chain, Netcare, which on its Web site boasts of "aiming to uphold South Africa's reputation as 'the transplant capital of the world.' " Since the mid-1990's, the company has been buying up facilities like St. Augustine's, originally a Catholic missionary hospital, and demanding a strong bottom-line performance.

Netcare's chief executive officer, Michael Sacks, declined a request for an interview. Through a press spokeswoman, Martina Nicholson, Netcare has denied conscious involvement in any wrongdoing.

"We do not know of anything untoward having taken place at all," Ms. Nicholson said. "We still firmly believe that there has been no transgression at any of our hospitals or by any of our staff members."

With operatives of Mr. Peri's syndicate now jailed in Brazil and South Africa, and Mr. Peri under pressure in Israel, his ring has apparently been smashed. But the transplant waiting list in Israel continues to grow, and recent reports from kidney specialists say Israeli organ brokers have appeared in China, among other places.

"This is obviously a well-oiled syndicate that knows how to move from one country to another," R. W. Green-Thompson, superintendent general of the KwaZulu-Natal provincial department of health, said in an interview in Durban. "I'm sure that this problem will pop up again in another country soon. The only question is which one."

Unexpected Consequences

These days, Mr. da Silva works 44 hours a week as a security guard, but still earns less than $175 a month, money that is the sole support for the 10 other people he lives with. Even that income was jeopardized when he and other kidney donors were arrested and briefly jailed early this year on suspicion of violating Brazilian laws against trading in human organs.

He and more than a score of other donors still faced criminal charges here.

In the 18 months that ended last November, when the authorities shut down the ring, so many residents from the slums of Recife had volunteered that the middlemen had
begun offering just $3,000 for a healthy kidney.

All told, the police in Brazil estimate that about 100 men, nearly all poor or unemployed, ages 20 to 40, agreed to sell kidneys. Though some would eventually be rejected for having an unusual blood type, frail health or signs of drug use, more than 60 men are believed to have gone to South Africa.

Recife and its slums had become so lucrative a source for organs, in fact, that Brazilian investigators believe that by late 2003, Israeli brokers, in an effort to swell their earnings further, were considering moving their operations to hospitals here and in other nearby cities.

With poverty offering up an unquenchable pool of volunteers, the local authorities say the ring had also begun inquiring about buying other vital organs from poor residents, including lungs, livers and corneas.

"Even after all of this fuss, I'd do it again," said Orley de Santana, a 26-year-old laborer, who went to South Africa but was unable to sell his kidney for $6,000 before the police broke up the ring. "In order not to have to steal or kill, I thought it better to sell my kidney."

Among the men who did give up a kidney, some say they have experienced health problems that no one warned them about.

"For me, the complications began almost immediately," said José Carlos da Conceição da Silva, 24, a day laborer who hauls produce. He said he required a second operation in South Africa on a lung three days after his kidney was removed. Since returning to Brazil his health has worsened, he said.

"I'm tired all the time and can't lift heavy weights, which I have to be able to do if people are going to hire me," he said. "My blood pressure goes up and down, and I feel pain and numbness where the scar from the operation is."

Worse still, after his flight back to Brazil, Mr. da Silva, who is not related to Alberty da Silva, said he was robbed of nearly all of the $6,000 he was paid for his kidney when he went to São Paulo during a layover on his flight home. "I begged and pleaded for them not to take the money, telling them that I had sold my kidney abroad and showing them the scar," he recalled, near tears.

Another donor, Rogerio Bezerra da Silva, not related to the others, also lost his kidney and his cash, which South African authorities confiscated after the ring was exposed late last year, and is now the object of mockery in his slum neighborhood.

On occasion, Alberty da Silva says, he shows pictures of his trip to South Africa to the neighborhood children. During the interview, he showed them to a reporter, too,
including some of him in Durban with the woman who received
his kidney. He also displayed a letter she later wrote,
thanking him for "the gift of life."

The American woman continues to correspond with him and,
though hardly wealthy herself, says she intends to send
cash gifts each Christmas and on his birthday.

"They never want you to see the donor," she said of the
traffickers. "But I kept insisting that we meet because I
know that he is now part of my being. I have a piece of him
inside of me, so who wouldn’t want that bond?"

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Our Father, who has set a restlessness in our hearts and made us all seekers after that which we can never fully find, forbid us to be satisfied with what we make of life. Draw us from base content and set our eyes on far-off goals. Keep us at tasks too hard for us that we may be driven to Thee for strength. Deliver us from fretfulness and self-pitying; make us sure of the good we cannot see and of the hidden good in the world. Open our eyes to simple beauty all around us and our hearts to the loneliness men hide from us because we do not try to understand them. Save us from ourselves and show us a vision of a world made new.

Eleanor Roosevelt's nightly prayer, from Mother R.,
by Elliott Roosevelt and James Brough

Eleanor Roosevelt's Wartime Prayer

Dear Lord,

Lest I continue
My complacent way,
Help me to remember that somewhere,
Somehow out there
A person died for me today.
As long as there be war,
I then must
Ask and answer
Am I worth dying for? Amen.