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# Transplant innovation and ethical challenges: What have we learned?

## A collection of perspectives and panel discussion

## We have come far, but selecting organ recipients remains an ethical minefield

**By Denton A. Cooley, MD**

Only 40 years ago, on December 3, 1967, the world was electrified by news of the first cardiac transplantation, performed in Cape Town, South Africa, by the renowned Dr. Christiaan Barnard.

We have progressed considerably since that time, but not all issues have been settled. After several attempts by Dr. Norman Shumway and by Dr. Adrian Kantrowitz in this country, we in Houston performed the first successful cardiac transplantation in the United States in April 1968. Initially we were impressed with the results, and we embarked upon a very active cardiac transplant program, performing as many as had been done in total around the world. But after we had done some 15 or 20 cardiac transplants, the discouraging news began to emerge that the patients were not surviving long: our longest survived for only 2 years.

As a result, our group in Houston, like others, declared a moratorium on cardiac transplantation. The only group that continued throughout this era was at Stanford University under Shumway, who had some success with immunosuppressive drugs. In the early 1980s, a new immunosuppressant, cyclosporine, appeared that was used for kidney transplantation, which reinvigorated us and others to use this drug for cardiac transplantation. Since then, under the direction of my colleague, Dr. Bud Frazier, we have performed more than 1,000 cardiac transplantations at the Texas Heart Institute.

From the beginning, we were called upon to identify appropriate donors and suitable recipients. Although we rely on certain objective factors, such as age, weight, body size, gender, and blood type, many other issues must also be considered. Fortunately, the modern concept of brain death has now been accepted not only by the public and ethicists, but also by the legal community; in contrast, at one time it was considered homicidal to remove a beating heart. I credit Christiaan Barnard with having the courage to remove a beating heart from a 26-year-old donor who had suffered irreversible brain damage. Many of us had wanted to get into the transplant program, but we could not identify a donor.

The following case illustrates some of the other ethical complexities that we continue to struggle with today.

### CASE STUDY: A 17-YEAR-OLD WITH HEART FAILURE AND A DESTRUCTIVE LIFESTYLE

Several years ago, a 17-year-old Latin American boy came to our clinic in heart failure. He was very disarming, but when we looked into his background we found that he had dropped out of high school after 1

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year and was living with a girlfriend who was 2 months pregnant by him and already had a 2-year-old child. The patient's cardiomyopathy was related to cocaine and alcohol abuse. Nevertheless, his stepfather was eligible for Texas Medicaid, and he was accepted for cardiac transplantation.

After the transplantation, he abided by the immunosuppressive drug regimen while he was under our care. Then he moved to Fort Wayne, Indiana, where Indiana Medicaid would not honor his Texas Medicaid coverage. So our hospital had to send him his immunosuppressive drugs, which he used rather sporadically.

While in Indiana, he was incarcerated for assault and battery on his girlfriend. He began to have heart failure but did not qualify to have the biopsies required for proper study of rejection of his heart. He returned to our clinic and was scheduled for catheterization the next day when he went into acute cardiac failure. He had emergency late-night implantation of a percutaneous ventricular assist device, which required catheterizing the left atrium by perforating the interatrial septum, taking the oxygenated blood out of the left atrium, and pumping it back into the aorta with a centrifugal pump. His heart began to recover, and the device was removed after 72 hours.

At this point he needed another transplantation. Our medical review board considered his eligibility and turned him down, citing that others on our waiting list were more deserving of a transplant and that retransplantation has a poorer success rate than initial transplantation.

### EACH CASE POSES PROBLEMS, BUT A RECORD OF SUCCESS EMERGES

Although this patient could be viewed as a sort of sociopath, he nevertheless is a young man who is incapacitated and in need of heroic measures. His case illustrates the kind of nonmedical problems that face those of us who are actively involved in cardiac transplantation. It can be very difficult to find solutions to the myriad social, economic, legal, and ethical issues.

We perform about 50 transplants a year in our institution, and every one of them has some issue. Nevertheless, we just honored 25 patients who have survived more than 20 years with cardiac transplantation.

## Despite the odds, the transplant field has progressed rapidly

**By John J. Fung, MD, PhD**

Dr. Pauline Chen's clinical vignette [see previous article in this supplement] unfortunately still typifies small bowel transplantation. One would not expect to hear that kind of story today for a kidney or liver transplant, but in the early 1970s it was typical.

### 'WHY WOULD ANY YOUNG PHYSICIAN WANT TO GET INVOLVED IN THIS?'

Dr. Cooley's comments about the moratorium on cardiac transplantation brought back memories for me, particularly from when I was studying liver transplantation in the 1970s. There was almost uniform mortality in transplants performed in the late 1960s and early '70s. One wonders why any young physician would have wanted to get involved in transplantation at that time. I was a fellow training with Dr. Thomas Starzl at the University of Pittsburgh and remember him saying, "Just make it work, then let everybody else figure out why." I think that typifies the surgical mentality.

> **If we had proceeded in a very stepwise manner, we probably would not be even a tenth as far along in the transplant field as we are now.**
>
> ***—Dr. John Fung***

We perform transplantations because we know that the alternative is prolonged morbidity and death. Knowing that we can provide a touch of hope is why we move forward in this field.

The technology of transplantation has developed through aggressive scientific developments in the laboratory. It is fascinating that all this has developed in only 50 years. If we had proceeded in a very stepwise manner, we probably would not be even a tenth as far along in the field as we are now.

Heart, lung, liver, and kidney transplantation are now all pretty routine. Intestinal transplantation is in the developing phase. The Cleveland Clinic is currently involved in facial transplantation, which has some different ethical issues related to identity.

Everything in transplantation relates to ethics, from issues about using marginal donor grafts or using beating-heart donors when someone has not been declared brain dead, to issues in patient selec-

tion, which often depends on social, economic (ie, insurance coverage), and psychosocial factors such as substance abuse and nonadherence issues.

### ETHICAL INSIGHTS FROM TRANSPLANTS IN HIV-POSITIVE PATIENTS

An ethical area of particular interest to me that the Cleveland Clinic has also been involved with is transplanting patients who are HIV-positive. This has always been an enigma: why would we want to transplant an HIV-positive patient? Before the advent of antiviral therapies for HIV in the mid-1990s, mortality rates were very high, with patients suffering miserable deaths from Kaposi sarcoma, the JC virus leukoencephalopathies, and other debilitating opportunistic infections.

When I first arrived at the University of Pittsburgh as a fellow, Dr. Starzl was telling us about this mystery virus disease; when they retrospectively analyzed specimens from organ recipients and donors, they realized that HIV was being transmitted to patients from donors as well as from blood transfusions. The exposure to health care providers was also substantial: an average of 20 to 30 units of blood was used for a liver transplant.

Patients who were HIV-positive were excluded from transplants even through the mid-1990s. I remember evaluating standard listing criteria for transplant recipients at a conference and hearing transplant surgeons say that HIV is an absolute contraindication to transplant. I said, "Wait a minute, this is 1997; you cannot say that. Given that attitude, patients with HIV will never be transplanted." The *New England Journal of Medicine* had just published a major paper about the extent of survival in patients being treated with highly active antiretroviral therapy.

So we then started a prospective study of transplantation in HIV-positive patients, and long-term follow-up has shown that these patients can do very well. Interestingly, transplantation offers a new approach to treating HIV-positive patients, in terms of immune reconstitution and the ability of immunosuppressive agents to restore immune competency by preventing the T-cell apoptosis initiated by HIV infection.

## A continued need for evidence-based guidance

**By James B. Young, MD**

Speaking as the lone internist on this panel, and also as a clinical trialist and evidence-based clinical practitioner, the greatest ethical challenge I see for transplantation is how to move the field forward in terms of garnering evidence that can help us treat patients and keep them alive. Nobody will deny that heart transplantation is life-saving therapy: my patients with end-stage ischemic cardiomyopathy can be dramatically transformed by a heart transplant after being near death. The questions now are how best to gain the data to guide the next round of innovations in transplant medicine and how to know when the time is right to attempt those innovations.

**Heart transplant is a bit of a boutique science, so questions arise about how to evaluate it with the rigor of regulatory authority.**
***—Dr. James Young***

### A HISTORICAL GLANCE AT HEART TRANSPLANTATION

Dr. Sharon Hunt, who was one of the first heart transplant cardiologists and worked with Dr. Norman Shumway, almost singlehandedly moved the field of cardiac transplantation forward. She recently chronicled its history,[1] and this sort of historical review yields a couple of insights. First, fewer heart transplants are being done in the United States in this decade than in the 1990s,[2] in large part because other effective interventions for heart failure have been developed. However, the number of heart transplants is in fact on the rise again.[2] Second, survival rates in heart transplant have improved substantially in recent years compared with earlier eras, as documented by registry data from the International Society for Heart and Lung Transplantation.[3]

Among other things, we have learned how to improve the operation, better choose and preserve hearts, and better match hearts to recipients. We now can use hearts from older donors and allow older patients to undergo transplantation. One of the keys to the better survival rates is a dramatic change in the use of medications. Cyclosporine allowed for successful heart transplantation in the 1980s, and we have since seen the advent of agents such as tacrolimus, rapamycin, and mycophenolate mofetil. We rely less on the early immunosuppres-

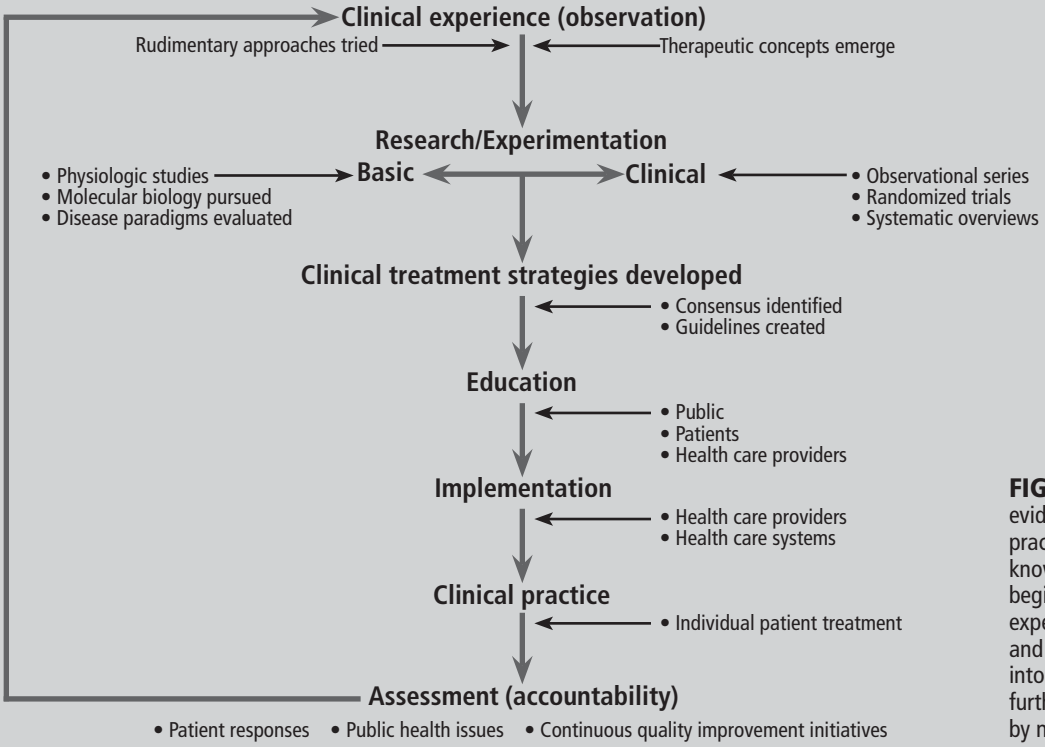


**FIGURE 1.** Flow chart of evidence-based medical practice. The drive for new knowledge is circuitous, beginning with clinical experience and observation and ultimately feeding back into clinical practice and further research prompted by new experience.

sants, such as prednisone and azathioprine.

Despite these successes from a survival standpoint, problems still need to be addressed. For instance, at 5 years, virtually every patient following a heart transplant develops hypertension and dyslipidemia, 1 in 3 has renal dysfunction (some requiring dialysis or transplant), 1 in 3 has diabetes, and some develop a strange allograft arteriopathy.[3]

## THE CHALLENGE OF EVALUATING A BOUTIQUE SCIENCE

Heart transplantation is a bit of a boutique science. Although relatively few heart transplants are performed compared with liver or kidney transplants, heart transplantation is a dramatic operation limited by many ethical challenges surrounding organ donor supply and utilization.

As for any boutique science, questions arise about how to evaluate it with the rigor of regulatory authority—from both the Food and Drug Administration (FDA) perspective and the institutional review board (IRB) perspective—without large clinical trials. Suppose that Dr. Cooley wants to make a minor modification in his immunosuppressive protocol because of an observation of a high incidence of renal failure at the 5-year point; does that ethically demand a large randomized clinical trial?

How can we design clinical trials to help determine which direction to take in immunosuppression intensification or utilization protocols? Other challenges include evaluating outcomes (such as coronary artery vasculopathy) from databases, and then figuring out good and bad practices. For example, databases show us that a donor history of diabetes increases the recipient's long-term risk of developing coronary artery vasculopathy.[3] Receiving a heart from a male donor also increases risk.[3] Better understanding the panoply of adverse events and what leads to better outcomes will give us a sense of how to proceed and can drive the design of clinical trials.

## OTHER ETHICAL CHALLENGES

From an ethical standpoint, how do we change practice? We have data on outcomes at 5, 10, and even 20 years. The half-life of a heart transplanted today is 12.5 years, whereas it used to be about 7 years.[3] Although it is clear that we have made progress, it is a challenge to determine exactly how to make subtle changes in practice, such as addressing polypharmacy post-transplant.

Developing schemes that enable major innova-

tion, particularly through coordination among medical and surgical teams, is another challenge. For example, we are working with preservation techniques that use a beating heart for transplantation. From solid evidence based on animal models, we believe this preparation can allow preservation of a heart for up to 12 hours. To some, that may beg a number of questions: Why do we need to do a clinical trial in humans? Why does the FDA need to regulate us? Why do we even need to answer to an IRB? Why not just make the change to alleviate the problem of donor organ supply?

My perspective is that I believe in evidence-based medicine and in clinical trials. I believe we should try to ethically move the field forward by taking a clinical experience or an observation and moving it through all the necessary elements of evaluation and treatment strategy development **(Figure 1)** to drive knowledge. I believe this applies to post-heart transplant patients as much as it does to patients with conditions such as heart failure or ischemic heart disease.

## What does—and does not—spur innovation?

**By Thomas E. Starzl, MD, PhD**

### LESSONS FROM THE CODMAN ANALYSIS OF FAILURES

Dr. Ernest Codman was a Harvard Medical School professor in the early 20th century who tried to introduce a system of analyzing failures at Massachusetts General Hospital and other Harvard-affiliated hospitals. As a result, he was metaphorically ridden out of town on a rail.

Codman recommended that complications and failures be classified as one of the following:

- An error in diagnosis
- An error in judgment
- An error in technique (if a surgical or a medical problem)
- An error in management.

Only one escape hatch existed that did not indict the surgical or medical team as culpable: the disease. At the time, nothing could be done for many diseases, including cancer, heart disease, renal failure, and bowel insufficiency.

This is a type of analysis that can be brought to a mortality and morbidity conference and will not accept a lot of alibis; it forces the group to always look at what could have been done to prevent a complication or death. Some practitioners always want to blame some factor other than themselves: sometimes the patient, by being deemed noncompliant, is even held responsible for his or her own complication or death.

I think the Codman analysis of failures is a good starting point for discussing innovations, especially since true breakthroughs come in those cases where the failure falls into the category of being caused by the disease itself, not by a medical or surgical error. And that is surely where transplantation falls.

### PROGRESS DOES NOT ALWAYS REQUIRE FULL UNDERSTANDING

Transplantation was first successfully performed in the context of breaking through the donor-recipient genetic barrier on January 6, 1959, when Joseph Murray and his team at the the Brigham Hospital performed a kidney transplant using the patient's fraternal twin as a donor. This event was reproduced in Paris by Jean Hamburger and his team on June 14, 1959, and then on three or four other occasions in the next several years in patients who received sublethal total body irradiation. This was at a time when no pharmacological immunosuppression was available, so no follow-up treatment was offered.

Astoundingly, the first case—the fraternal twin—lived for more than 20 years, and the French case for 25 years, without ever being treated with immunosuppression. They were inexplicably tolerant. When immunosuppressive drugs were developed and survival rates improved, the questions around these early cases were never answered: Why did those transplantations work? What were the mechanisms of engraftment? What was the relationship of engraftment to tolerance? Without answering those questions, there was no way to make other big leaps in improvement of what was already proved in principle—that is, the feasibility of actually doing this kind of treatment. Improvements in patient and graft survival were dependent almost entirely on better drugs.

### RANDOMIZED TRIALS HAVE A DUBIOUS RECORD IN TRANSPLANTATION

I know this will offend just about everyone here, but I have no confidence in evidence-based therapy if we are talking about randomized trials. None of the

great advances in transplantation has had anything to do with randomized trials. In my opinion, randomized trials in transplantation have done nothing but confuse the issue and have very nearly made it impossible for the better immunosuppressants to be brought on board. Cyclosporine offered a tremendous step forward, but the randomized trials, carried out mostly in Europe, did not reveal much difference in outcome from treatment with azathioprine, at least as assessed by patient and graft survival. The same thing occurred when tacrolimus emerged; randomized multicenter trials actually delayed the widespread use of this superior drug for at least half a dozen years.

## IN THE BIG PICTURE, MONEY IS HOBBLING INNOVATION

Earlier it was debated whether money drives everything. I do not believe that money drives everything in medicine in Europe, and it certainly has little to do with driving improvements in Asia. But money does drive everything in the United States, although the real question is whether it has to be that way.

**Randomized trials in transplantation have done nothing but confuse the issue and have very nearly made it impossible for the better immunosuppressants to be brought on board.**
***—Dr. Thomas Starzl***

I believe that innovation is somehow built within our genome. Many of the great advances in transplantation, the elucidation of principles, and the relatively recent discovery of the mechanisms of alloengraftment were achieved without grant support. The researchers involved could not have asked for National Institutes of Health funding because their ideas were so far out of the box that they probably would have been rejected or stolen.

I wonder to what extent the vast amount of money available for research is actually a disincentive for genuine advancements. Part of the problem is that the power of allocation is put in the hands of anonymous peer-review committees. That system generates droves of people to pursue money allocated to a certain area to learn more and more about less and less, in the vague hope that acquiring enough details will result in a realistic concept. Sometimes the picture simply becomes more confused.

Another problem is that we have produced far more scientists than jobs, so that funding becomes the first priority because it is the only means of employment. In earlier days, what drove people more often was that they were confronted with a child who was dying and the central question was, "How can I treat this patient?" They did laboratory research on their own to produce evidence that a new innovative idea could work. I believe that if you have experiments that show that you can keep a heart beating on a preservation device for 12 hours, and you can put it in a dog and it works well, that is the evidence you need to proceed. How are you going to do a randomized trial—hang on to an organ and let it beat for 12 hours just so it conforms with some protocol? That is nonsense.

There was a period when clinical journals—*Surgery of Gynecology and Obstetrics*, *Annals of Surgery*, *Annals of Internal Medicine*, *New England Journal of Medicine*, and others—published front-running discoveries. That ended about 25 years ago when it became more important to learn about details. The journals then became superfluous, and for another reason as well: money drove the wheel more and more. Hospital and program administrators expected the publications to be advertisements, and the minute that articles started promoting something rather than reporting facts, they lost value. Today the impact factors of the surgical journals are at about 2 or 3, meaning that their articles are cited infrequently and have little real influence on the practice of medicine.

How did we reach this point where money drives everything? I think the page was turned in the very early 1990s, and it had to do with how medical practice is governed, especially in academic hospitals. Half of the health care in this country is now provided by hospitals that are associated with medical schools. Those hospitals and basic research laboratories are where our young people will assimilate their ideals. If that climate is not right, then we are raising the wrong kind of doctors.

Earlier researchers looked at a problem and thought, "Here's a question that has to do with this patient before my eyes, and I must find some way to solve it. Let's go to the laboratory." Today there is a real danger that they are thinking, "I need to advance my career, so let's see how I can get some money. A little research will be a stepping stone to my professional development." Our discussion of medical and surgical ethics today should take place within this framework.

## Panel discussion

**Moderated by Mark Siegler, MD**

### WERE FINANCES A DRIVER OF EARLY TRANSPLANT INNOVATION?

**Dr. Mark Siegler:** It is clear that there are more ethical and less ethical ways to introduce innovations. I am reminded of an article in *JAMA* by Francis Moore in the late 1980s in which he warned that one of the things to look at for any new innovation was the ethical climate of the institution.[4] He cautioned us to be very aware of the driving force behind an innovation. Is it to improve patient care? To save lives that otherwise would be lost? Or is it primarily for the self-aggrandizement of an investigator or the financial goals of an institution?

I also remember the chapter in Dr. Starzl's book *The Puzzle People*[5] about the anguish involved in introducing liver transplantation. It seems that financial considerations were not the driver of major steps forward in introducing liver transplantation, in Dr. Starzl's case, or heart transplantation, in Dr. Cooley's case. Would you comment?

**Those of us privileged to spend our entire career in academic settings, with institutions to represent and protect us, have an obligation to become innovators.**
*—Dr. Denton Cooley*

**Dr. Thomas Starzl:** Actually, not only were we not driven by economic gain, we expected financial penalty for focusing on transplantation. If ever there was a field that developed against the grain, that was costly to people who worked in it, whose engagement meant that for most of their career they would work for substandard income compared with their peers—even those peers in academic medicine, let alone those in private practice—it would be transplantation.

It was not until 1973, when the end-stage renal disease (ESRD) program began under Medicare, that cash for transplantation started to become available. The real cash streams did not start until the middle to late 1980s when nonrenal organs became the cash cows. To be fair, no new technology can be assimilated into the health care system unless it at least pays for itself. But you can go beyond that and create baronial kingdoms, and I think that is where you can go wrong.

**Dr. Denton Cooley:** I would add that those of us privileged to spend our entire career in academic settings have an opportunity that others may not have. A lot of brilliant people in private practice are capable of doing many things but do not have an institution to represent and protect them. I have also always felt that those of us in these positions have an obligation to become innovators. Surgeons who merely see how many appendectomies or cholecystectomies they can perform are being very derelict of their responsibility to the institution.

### MEASURING SUCCESS IN HEART TRANSPLANTATION

**Dr. Siegler:** Dr. Cooley, what is the current success rate for heart transplants?

**Dr. Cooley:** Nationwide, around 90% of recipients survive 12 months. Of those, maybe half are still alive 5 years later. Of course, we do not know what the future will hold. It is interesting that the first sign of rejection seems to be coronary occlusive disease. It is a different type of coronary occlusive disease than is seen in atherosclerosis: it is diffuse, involving the entire extent of the coronary circulation, and is not really amenable to coronary bypass or other interventional procedures.

**Dr. Siegler:** We are now at about the 40th anniversary of the first human heart transplants, an extraordinary and historic innovation. Dr. Cooley, do you think the timing was right in 1968 when you did the first heart transplant in the United States? In retrospect, would you have done the first transplant sooner or maybe even a couple of years later?

**Dr. Cooley:** You can argue it both ways. Should we have waited for further developments? At the time, heart transplantation seemed to work fairly well in animals, but we never really know until it reaches the clinical level. It was probably as opportune a time as any. We knew something about organ rejection at the time, and we had immunosuppressive drugs, although they were not as effective as they are today. The news electrified the world. I think we were pretty well prepared for this spectacular event.

**Dr. Siegler:** When would have been the optimal time to do a clinical trial in order to achieve evidence-based medicine in heart transplantation? Would it have been during the big breakthroughs of Shumway, Barnard, and Cooley, or now, when we have the general strategy and can find out how we can do better?

**Dr. James Young:** I would not have done a randomized trial at that time. The patients who were getting transplanted then were nearly dead; all other management was futile. In 1970, *Life* magazine listed the 102 heart transplants that had been done around the world up to that point, and maybe only 2 or 3 of the patients were still alive. That prompted the moratorium that Dr. Cooley referred to.

As ethical clinicians, we are supposed to do our best to make our patients feel better and make them live longer. Sometimes you have to do something radical. On that basis, one can argue that we should not transplant "the walking wounded," that instead we should save organs for patients who are truly terminal without some sort of ventricular replacement therapy. But today we are getting away from transplanting only dying patients, so we need randomized trials to find out how we are doing in transplanting outpatients. That is the setting in which trials are now needed.

## THE ETHICS OF 'LETTING GO'

**Question from audience:** Dr. Chen's story [see previous article] raised the issue of the ethics of "letting go" of one's patient. I wonder if in transplantation, especially when innovative procedures are involved, a commitment to the procedure itself might sometimes conflict with the need to let go of the patient.

**Dr. John Fung:** In the United States, we measure efficacy and benefits in different ways than people do in other parts of the world. Here, for a child with a biliary atresia—the most common reason for liver transplantation—we expend hundreds of thousands of dollars for a liver transplant, which is usually able to save the child's life. But in China, a severely ill child is viewed as a medical and economic liability and will be allowed to die so the family can have another child.

It is also not only the ethics of letting go. We all deal with letting go, not just in transplant medicine. It is also the ethics of actually getting a patient into the system. In the case of transplanting a newborn, as in Dr. Chen's narrative, should they even have embarked on that?

**Dr. Pauline Chen:** For me, the story illustrates the remarkable connection and profound attachment between a surgeon and his or her patient. The fact that three patients are really involved in transplantation—the donor, the recipient, and the patient still on the waiting list because the organ went to the recipient instead—also motivates the team with a sense of obligation to the two unseen patients.

If there is a lesson about the ethics of letting go, I think it is that we often fail to talk about these issues among ourselves. Perhaps if we had discussed end-of-life care or palliative care in Max's case, we might have had more insight into the pressures we felt in considering the lives of three separate people. And those discussions might have—or might not have—changed the situation.

**Dr. Starzl:** I agree completely with the preceding comments. All kinds of motivations might cause a surgeon to cling too long—the ones that were mentioned as well as some ignoble ones, such as vanity, in terms of looking at one's survival numbers.

> **For my vintage of transplant surgeons, death and failure are rarities and are truly a sort of enemy, whereas prior generations of surgeons are wiser and perhaps have a better sense of when it is time to stop intervening.**
>
> *—Dr. Pauline Chen*

I would also like to take a much larger view. Some years ago in Colorado, the governor at the time, Richard Lamm, thought that intensive care units (ICUs) were harmful—that they were economically draining, did not serve society, and prolonged suffering. My position, which was really the opposite, was that maybe he was right in his philosophy but transplantation had, in a sense, changed all that. Transplantation took desperate people who were in the ICU, with no chance of coming out, and dramatically returned them to wonderful health.

As procedures get better, this scenario happens more and more often. I agree that there is a time when you realize that no intervention will work and you should stop treatment. That is a bitter pill. But it is very hard to define when that moment occurs.

**Dr. Chen:** There also may be somewhat of a generational difference in approach.

Most surgeons will fully acknowledge that they stand on the shoulders of giants, and that holds particularly true in a field like transplantation. When I was training in liver transplantation, for example, 80% to 90% of the patients could fully expect to survive 5 years. For my vintage of surgeons, then, death and failure were rarities and they were truly a sort of enemy, whereas surgeons like Dr. Starzl and Dr. Cooley have seen so much more and are far more used to all the variations of outcomes. Because of that breadth of experience that you have, I think you are wiser than

my generation of surgeons, for whom death often has to be ablated at all costs. I think it follows, then, that you would also have a better sense of when to stop.

**Dr. Starzl:** There is a generational change—there is no doubt about it.

## IS TRANSPLANT ETHICAL WHEN A LIFE IS NOT AT STAKE?

**Question from audience:** What are the ethical implications of non-lifesaving transplants, specifically of the hand and face?

**Dr. Young:** I have been on many peer-review committees charged with looking at this issue. Although the ethics can be very troubling, I have resolved important questions in my mind by examining them through the context of human suffering. Our mission as physicians and caregivers is to relieve suffering, which can take the form of pain, a shortened lifespan, or even a debilitating disfigurement of the face or a severe limitation, such as after traumatic amputation. Looking at the issue this way, I am less troubled than I was initially, when I viewed these kinds of transplantations as simply altering physical appearance or extending ability.

**Dr. Starzl:** The next big movement in transplantation is going to be in composite tissue allotransplantation—that is, transplantation of the face, limbs, etc. Mechanisms of alloengraftment have recently been uncovered such that it is now possible to formulate protocols that use either very light immunosuppression (avoiding the 20% or 25% rate of renal failure at 5 years that we heard about from Dr. Young) or no immunosuppression at all.[6] Without the heavy burden of immunosuppression, this type of transplantation can become worthwhile. Putting a new hand or face on someone is astounding: it changes the morphology of the brain, which can be observed with functional magnetic resonance imaging. It changes the soul, if that is what you want to think of when talking about the brain. I think it will be very important.

**Thomas Jefferson wrote, 'We should never return to earlier times when all scientific progress was proscribed as innovation.' His insight is still modern and relevant today.**

***—Dr. Mark Siegler***

**Dr. Siegler:** This extraordinary panel has not only discussed events from 50 years ago; each of the panelists spoke of a future that is rich in promise and innovation—and in ethical issues. It reminds me of a remarkable letter written in 1794 by Thomas Jefferson to John Adams, which says, "We should never return to earlier times when all scientific progress was proscribed as innovation." More than 200 years later, Jefferson's insight remains modern and relevant.

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