

2007 Presidential Address
American Society of Transplant Surgeons
American Transplant Congress

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Clinical Transplantation - Some of Today's Challenges

It is a tremendous honor to be standing here today as the 33rd President of the American Society of Transplant Surgeons. Since its inception, the ASTS has been an important part of my life. In fact, a few years ago, Rob Corry reminded me that I had presented the first paper at the first meeting of the ASTS. I remember that presentation – it was one of the few times that I gave a slide presentation while reading from notes; and I got lost between the slides and the notes. I have rarely used notes since – but am doing so today, so I hope that the same thing does not happen.

In the last few months, I have thought a great deal about what I would say today. I read previous presidential addresses. Some reflected on the society – what it had accomplished and its ongoing mission; others addressed topics outside of transplantation. I struggled to come up with my own theme (of course, wanting to leave an indelible mark on the future). But reality soon hit. The best I could do was provide a personal perspective and highlight what I see as some critical challenges for the future.

As a junior surgery resident over 3 decades ago, 3 of the things that attracted me to transplantation, and which still remain relevant today, were:

- First, our long-term commitment to the recipient and the recipient's family;
- Second, the fact that, although transplantation was and is clearly a surgical subspecialty, it needs multidisciplinary knowledge and effort; and
- Third, our field's tremendous enthusiasm for asking new questions to benefit future recipients (obvious not only at my own institution but also at those early ASTS meetings).

Back in the mid 1970s, the principal focus of clinical research in our field was to minimize acute rejection, minimize graft loss to acute rejection, minimize early infection,

and improve short-term recipient and graft survival. But today, I believe that the preeminent clinical challenges are different. To me, they are:

- a) To improve long-term recipient and graft survival;
- b) To minimize post transplant morbidity; and
- c) To eliminate the organ shortage.

I want to spend some time discussing each of these 3 challenges and then focus on the ASTS response. I will end with what I see as new challenges for the individual transplant surgeon.

Our first challenge is to improve long-term recipient and graft survival.

Although the first successful kidney transplant was in 1954, it was not until the late 1960s and early 1970s that a large number of recipients were alive and well with successful allografts. In 1963, Joseph Murray (who would win the Nobel Prize for his work in transplantation) and others established a kidney transplant registry to collect information on cases from around the world. Their initial report was from a conference put together to review all accumulated cases (1,2). The proceedings were published in *Transplantation*; Dr. Murray gave the opening remarks, stating: "This conference was organized to collect and evaluate data on all kidney transplants done so that we can share experiences... We have on hand all pertinent facts on practically every known kidney transplant performed prior to July 1, 1963." At that time, 244 kidney transplants had been done worldwide; 92 of the recipients were still alive. At the conference, the discussion was on a case-by-case basis.

The 5th report of the kidney transplant registry, published in 1967, was the first to present cumulative data on the percentages of patient and graft survival (3). That report included information on 1,187 transplants from 63 institutions in 19 countries. Interestingly, many of the problems that still plague our recipients - such as an increased rate of posttransplant malignancy, infection, and cardiovascular disease - were noted in those early reports from the mid and late 1960s.

The 9th report in 1972 represents my introduction to transplantation (4). For recipients with a sibling donor, the 1-year patient survival rate was 84%; the 1-year graft

survival rate, 76%. For recipients with a deceased donor, the 1-year patient survival rate was 67%; the 1-year graft survival rate, 54%.

Contrast the data from this 9th registry report with today's data from the SRTR. I want to thank Bob Merion and the SRTR group for providing me with the following data. For living donor kidney transplant recipients in the United States, the 1-year patient survival rate is now 98%; the 1-year graft survival rate, 95%. For deceased donor kidney transplant recipients, the 1-year patient survival rate is 95%; the 1-year graft survival rate, 90%. We have made considerable progress in preventing and treating both acute rejection and CMV infection. Similarly, the 3-year outcome for today's recipients far exceeds the expected 2-year outcome for those transplanted before 1972.

In addition, the 1-year outcome has continued to improve for recipients of other solid-organ transplants. Table 1 shows the 1-year recipient and graft survival rates for liver, heart, lung, pancreas, and intestine transplants.

But what about the long-term outcome? By 5 years posttransplant, there is a significant falloff in both patient and graft survival for all recipients (Table 2).

By 10 years, the survival is abysmal, worse than that for patients with certain malignancies. Compare the data, as shown in Table 3, with what we hope the outcome is for our patients – i.e., 100% long-term survival. Even when we look at death-censored graft survival for kidney transplant recipients, the 10-year results are disappointing. We still have a lot of work to do.

Our second challenge is to minimize posttransplant morbidity.

In addition to the dismal long-term patient and graft survival rates, as you are all aware, a myriad of other posttransplant problems also affect our recipients' general health and quality of life. These problems include infectious diseases, posttransplant diabetes, malignancy, cardiovascular disease, and drug-specific side effects. For solid-organ donors, we need to be concerned about the surgical and long-term consequences of nephrectomy or of liver or lung lobectomy. New drug development, refinement of recipient protocols, and clinical research must also focus on minimizing posttransplant morbidity.

Our third challenge is to eliminate the organ shortage.

As I stated earlier, much work is needed to improve transplant results. Nonetheless, the outcome for a transplant recipient is clearly far superior to the outcome with alternative therapies. As of April 26, 2007, a total of 96,260 candidates were on the waiting list for a deceased donor transplant in the United States – over 70,000 on the kidney waiting list alone. In the last 4 decades, despite ongoing attempts to increase organ donation, demand has increased more rapidly than supply. More recently, progress has been made with paired donation, desensitization, nondirected donation, and the Breakthrough Collaborative – and these efforts all need to be encouraged. Still, the kidney waiting list has continued to grow.

A consequence of this growing list, without a commensurate growth in the supply, is that candidates for a kidney transplant are waiting longer; and mortality on the waiting list is increasing. In 2001, 6.3% of candidates on the list died each year; by 2005, this death rate had increased to over 8%. It is critical to realize that those dying on the waiting list were acceptable transplant candidates when listed. At our institution, we studied waiting list deaths over a 2-year period. We found that, of those dying while waiting, the mean age was 55; 70% were waiting for a first transplant; and 70% had a 0% PRA level (5).

Looking ahead, UNOS has set goals for organ recovery by 2013 - after implementation of all the new initiatives. Yet, using their own data, even if the UNOS goals were able to be achieved for kidney donors, the number of available kidneys each year would still be far short of the number of new transplant candidates listed each year. Sheehy and others previously noted, “Even in an ideal world in which all brain-dead potential donors became actual donors and the demand for organs remained constant rather than increasing, the supply of organscould not meet the needs of all the patients on waiting lists (6).

Unless we make dramatic changes in our policies and in our practice, the waiting list will only continue to grow, and our transplant candidates will wait longer. If waiting

longer were the only issue, perhaps I would not be so concerned. But the long wait on dialysis has significant adverse consequences: patient survival and quality of life are far worse on dialysis than after a successful transplant; and the outcome of a transplant is increasingly worse for every year spent on pretransplant dialysis.

It is time for innovation, not fine-tuning! My suggestion is that we advocate for a regulated system of living donor kidney compensation. Richard Fine, in his AST presidential address last year, presented many of the compelling ethical arguments for such a system. Today, I want to make 4 points:

- First, because a transplant is cost-effective as compared with dialysis, a regulated system of compensation could be cost-neutral to the health care system. Schnitzler has shown that a living unrelated donor transplant saves the health care system about \$95,000 (and that figure does not account for the priceless value of improved quality of life). Thus a minimum of \$95,000 per transplant would be available for administrative costs and compensation for the donor – without any additional costs to our health care system.
- Second, by a regulated system, I mean one that entails:
 - a) A fixed payment by the government or insurance companies to the donor;
 - b) Allocation by the OPO using a predetermined algorithm (like the one currently used for deceased donor allocation) so that all candidates on the waiting list have a chance
 - c) Thorough evaluation of the donor;
 - d) Informed consent and safeguards;
 - e) Long-term health care and follow-up; and
 - f) No sales permitted outside the system.

The compensation to the donor could include term life insurance, lifetime health insurance, reimbursement of expenses, college tuition, a tax break, a direct payment, or any other of a menu of options.

It is essential to differentiate the regulated system that I am proposing from unregulated systems currently in existence. In an unregulated or free market, system, the donor and the recipient find each other (sometimes with brokers involved) and negotiate a price. Many problems mar such unregulated systems, including the lack of protection and the

lack of follow-up for both the paid donor and the recipient; moreover, only recipients who can afford to will be able to participate. We have already seen unregulated systems fail elsewhere. In stark contrast, in a regulated system, the price would be fixed, the donor and the recipient would be protected, and everyone on the waiting list would have an opportunity to be transplanted.

- Third, a regulated system would not be difficult to implement. We could use the infrastructure already in place for deceased donor evaluation and allocation -- in the United States, the OPOs. In brief:
 - a) National criteria would be developed for acceptance or rejection;
 - b) Potential donors would call the OPO for a screening interview (if they are accepted, a medical and psychological evaluation would be done and then reviewed by an OPO panel consisting of a surgeon, physician, transplant coordinator, social worker, and donor advocate);
 - c) If the donor is accepted, the computer algorithm for allocation would be run (similar to our current practice for deceased donors) and the kidney would be offered to the center with the top-ranked transplant candidate;
 - d) All bills (for donor evaluation, the operation, and follow-up) would be sent to the OPO, which would handle all financial tasks, all donor payment, and all long-term donor follow-up;
 - e) The OPO would charge a fee to the recipient's transplant center (to be paid by the recipient's insurance);
 - f) The opportunity to be a paid donor would be available only to citizens and legal residents (so that long-term health care and follow-up could be provided).

- The fourth point regarding a regulated system of compensation is this: as a transplant community, we need to remember that we already accept donation. Any argument against compensation must separate sales from donation. I do not have time to detail each specific argument or counterargument here. For those of you who are interested, a number of excellent articles are in the literature (7-10). I only want to note that I realize this is a complex ethical question. However, not implementing a policy of compensation has major negative consequences – condemning many transplant candidates to suffer and

die on dialysis. We can make a difference in their lives by increasing the number of available organs.

Given today's 3 challenges - improving long-term recipient and graft survival, minimizing posttransplant morbidity, and eliminating the organ shortage - what is the American Society of Transplant Surgeons doing? In fact, the ASTS is addressing the very concerns that I have raised today. Our annual meeting, the American Transplant Congress (ATC), held in conjunction with the AST, has become the most prominent annual meeting in transplantation for disseminating and discussing new information on enhancing outcome. Special thanks go to the organizing committee and to Pam Ballinger and her staff, for, again this year, helping us put on a superb meeting.

Our journal, the *American Journal of Transplantation*, again done in conjunction with the AST, has become the most highly cited transplant journal in the world.

In January of this year, the ASTS held its 7th annual winter meeting. The theme, "Solving the Organ Shortage Crisis," specifically addressed one of the major challenges that I have put before you. We had record attendance. Next year's winter meeting addresses another important topic – "Transplanting the high-risk patient." I encourage all of you to attend.

Of note, the ASTS has taken a substantive step, in the form of a video, toward enhancing the process of obtaining truly informed consent from donors. Aimed at potential kidney donors, the video will be available to all transplant programs in the country. It concisely details the risks to the donor. The video is being previewed at the ASTS booth – I encourage each of you to see it and to determine how you can use it for your own program. At my home institution, the University of Minnesota, we have used a similar video and have found it extremely useful. We send the video to prospective donors before their first clinic visit; they can then come to the clinic armed with their questions.

What else is the ASTS doing? In association with the University of Michigan, we applied for and were awarded a grant from HRSA to provide travel expenses and subsistence costs for living donors, thus removing some of the financial disincentives

from donation -- again addressing one of our 3 major challenges. In addition, a National Donor Assistance Center will be established at the ASTS national office to study the impact of reimbursement on donation rates.

The ASTS has established a database of transplant centers interested in doing clinical trials – again, an effort to improve long-term outcome. At the end of last year, a request for information was sent to all kidney transplant centers regarding the structure of their program and their interest in clinical trials. This database information will be available to individuals or companies that are setting up multicenter trials; our hope is that this database will facilitate initiation of clinical research. A similar request for information will soon be sent to all liver transplant centers.

One of our most exciting new initiatives is the development of a formal curriculum for transplant fellows. With a formal curriculum, we can ensure that fellows in all ASTS training programs will be provided with a similar core of information. It may be possible that this curriculum could also be used by ASTS members to meet their American Board of Surgery Maintenance of Competency requirements.

We are all excited about passage of the Norwood Paired Donation legislation. The ASTS, along with many of our partners, advocated strongly for passage of this bill. Other patient care areas where we can hopefully make a difference include payment for long-term coverage for immunosuppressive drugs, a tax credit for living donor expenses, a gift of life Congressional medal, and funding for the Organ Donation Act. Perhaps one of the most notable aspects of the passage of the Norwood legislation was that the Congressional Budget Office – for the first time – clearly documented that a transplant was cost-saving, long-term, as compared with dialysis. This step has huge implications as we develop other initiatives.

Development of new initiatives is only useful if we can disseminate the information to our membership. To that end, we have a new user-friendly website and an updated look to our bulletin, *The Chimera*. The website contains up-to-date information on all of our activities. Importantly, for ASTS members, information is available on physician reimbursement and educational meetings; a job board is also kept current. We have begun sending intermittent emails to all of you describing our efforts in

support of our membership. I do not have time today to describe each initiative, but encourage you to go the website and explore.

So far, I have discussed 3 prime challenges for the field of transplantation and how the ASTS is trying to meet them. I now want to separately discuss several challenges facing both current and future transplant surgeons. Progress in our field will not come from doing the same things over again; progress will come from basic, translational, and clinical research. But, it seems to me that 3 intersecting issues, in particular, are impeding our ability to meet the current challenges: limited NIH funding, changes in medical economics, and the 80-hour workweek. As a result, surgeons nowadays are driven toward spending more of their time on clinical care and less time on research.

Limited NIH funding minimizes the dollars available for research; changes in medical economics, and within departments of surgery, encourage surgeons to maximize their time in the operating room; and given the 80-hour workweek, we must focus on teaching housestaff to be outstanding clinical surgeons – and there is little time left for encouragement of research.

My fear is that we are moving toward a future where surgeons spend the lion's share of their time in the operating room and leave the "challenges" to our colleagues in other areas. My challenge to you is to resist this trend. Transplantation as a specialty could not exist without surgery; the recipients and their donors are our patients. I am not minimizing the significance of our multidisciplinary interactions, but surgical research – basic, translational, and clinical – has led to some of the seminal advances in our field. Surgeons have the best perspective on the integration of pre-, peri-, and postoperative care.

As I stated at the beginning, one of the most fascinating attractions to me of transplantation is the long-term commitment to the recipient, which necessitates integrating all facets of patient care. The decisions that we make affect not only patient and graft survival but also the incidence of infection, of malignancy, and of other long-term morbidities.

For every one of our recipients, we should be asking “what can I do better?” To me, that means “what studies can we do to learn what we can do better?” My challenge to you is to continue the investigative enthusiasm that launched our field in the first place. This may mean running a research lab. It may also mean being part of a multidisciplinary team focusing on improving transplant outcome – whatever the opportunity; I encourage you to be involved, in some way, in studies that advance our knowledge and thus our patient care.

In closing, I would like to say thank you to a few people. I have been extremely fortunate this year to work with an exceptional executive council and committee chairs. The ASTS and I sincerely appreciate your hard work, commitment, and enthusiasm – my hope is that your ongoing enthusiasm will continue to keep our society vibrant. Katrina Crist, our executive director and her staff - Kim Gifford, Joyce Williams, and Chantay Parks - work tirelessly for our society, and I thank them. I have already mentioned Pam Ballinger and her group from Association Headquarters. They have been responsible for our annual meeting for longer than I (and probably she) care to remember. Again, this year the organization has been fantastic and we thank them.

My enthusiasm for transplantation was generated by my mentors – John Najarian, Dick Simmons, Carl Kjellstrand, and this year’s Pioneer Award winner, David Sutherland. Rough around the edges, I was shaped by Ian Tellis in New York. Although each of them has a different style, they each taught me the importance of the individual patient; I thank each of them for the knowledge they have imparted and for their friendship over the years. My enthusiasm for transplantation has been maintained by our transplant fellows at the University of Minnesota, whose dedication and questioning challenge each of us.

I would also like to thank our own transplant team at the University of Minnesota – all of the physicians, nurses, coordinators, researchers, and my assistant, Stephanie Daily. Through their efforts, we are able to care for our donors and recipients, and to carry out the studies that I think are indispensable for improving outcome for future patients. And, I would especially like to thank the transplant candidates who give us the privilege of taking care of them.

Those who know me well know that I have a much better half. She challenges me, and provides guidance, support, and reality-testing. She is the source of my greatest happiness. Sandy, thank you for being my best friend.

I want to reiterate how special the ASTS has been for me. It has been a privilege to serve you. Finally, as a proud Canadian, let me be the first to welcome you to the ATC in Toronto, in 2008 – the first time that our annual meeting will be held in Canada. A year from now, I hope we will see new strides toward improving long-term recipient and graft survival, minimizing post transplant morbidity, and eliminating the organ shortage.

Thank you.

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Table 1. 1-year survival – 1st Transplant (2003-2004) (SRTR)

	<u>Recipient</u>	<u>Graft</u>
Liver-DD	87%	84%
Liver-LD	91%	84%
Heart	88%	88%
Lung	85%	84%
Pancreas SPK	95%	85%
Pancreas PAK	96%	80%
Intestine	88%	81%

Table 2. 5-Year Survival – 1st Transplant (1999-2004) (SRTR)

	<u>Recipient</u>	<u>Graft</u>
Kidney-DD	81%	68%
Kidney-LD	90%	81%
Liver-DD	73%	69%
Liver-LD	77%	69%
Heart	74%	73%
Lung	52%	50%
Pancreas-SPK	86%	71%
Pancreas-PAK	84%	59%
Intestine	50%	41%

Table 3. 10-Year Survival – 1st Transplant (1994-2004) (SRTR)

	Recipient	Graft
Kidney-DD	61%	41%
Kidney-LD	76%	57%
Liver-DD	59%	55%
Liver-LD	76%	67%
Heart	53%	51%
Lung	26%	24%
Pancreas-SPK	70%	54%
Pancreas-PAK	61%	28%
Intestine	41%	29%

