

2002 Presidential Address to the American Society of Transplant Surgeons
“Transplantation; Looking Back to the Future”

Friends and Colleagues:

I stand before you feeling tremendous pride in our organization, and the honor to serve as your President this past year has been one of the highlights of my professional career.

Like you, I have listened, usually politely, to many addresses given by outgoing Presidents over the years. They are usually interesting, and some have been inspiring. Some have been educational, some have been tedious, some have been boring, and some have been quite controversial.

Until a year ago, I thought little about how my predecessors arrived at their subject. As you know, there are no rules, the topic is open ended, and obviously there is no prospective peer review.

However, there is a form of peer review that comes immediately at the conclusion; ...at least for a few minutes during the inevitable post delivery critique, and believe me...it is that daunting thought which has occupied a substantial amount of my time, at least recently.

Now that it is my turn to stand before you, I have also learned, THANKFULLY, that few of you will remember a word of what I say...

...except those of you who are also afforded the great honor to serve as President... You will remind yourself when you read each prior address, as you struggle to identify a worthy subject when your turn comes.... and that it will!!

For a couple of reasons, I will spend a few minutes describing some personal reflections on my path to this day...

First, for the young in the audience, perhaps this may encourage one of you to select a career that will be as exciting and rewarding for you as mine for me

... and

Second, it allows me an opportunity to publicly thank some of the people who have been especially important to me during this journey.

Some of you have heard me describe my introduction to the ASTS, and our remarkable field of transplantation... I held a part time job during medical school, working as a perfusion technician in our 5th President, Fred Merkel's lab. As many of you know, Fred has been widely acknowledged for his important role in the founding of our Society. This was during the middle 1970's, clinical transplantation held tremendous promise with growing success in renal transplantation. However, results with liver and cardiac transplantation were more problematic. There were only 2 active liver programs, one at Colorado under the leadership of our first President, Dr. Thomas Starzl, and the other in Cambridge led by Sir Roy Calne. Similarly, Dr. Norman Shumway led the only active cardiac transplant program at Stanford. Never-the-less, the science was exciting, and the future for this evolving academic field was obviously bright in the eyes of an eager medical student, seeking an academic career in Surgery.

ASTS- The Early Years:

I was also privileged to attend the initial 2 scientific meetings in Chicago... I ran the slide projector!! I recall excitement, I remember the animated discussion and, I was particularly moved by the vigorous debate. It was during those sessions that my interest in this field was solidified. ... and I suppose this also allows me a pretty solid claim that I have worked my way through the ranks.

My introduction to transplantation was important, but my surgical training at the University of Michigan, under our 6th President, Jerry Turcotte, then Chairman of our Department of Surgery, provided me with the background, skills, and perhaps most importantly, the mindset to focus my career. Jerry, am indebted to you and the Michigan Faculty for providing me the chance to join the rich Coller Surgical Heritage. You have been an important mentor, role model, and friend.

My Michigan teachers were many, and I am grateful to each, but in addition to Jerry, I want to mention 2 individuals who have been especially important to me. Dr. Darrell “Skip” Campbell, Jr. with whom I served on the ASTS Council a few years ago, was my first chief resident. Skip, since that first night on call at the County, you have been an advisor, mentor, colleague and most of all a fabulous friend. This is a photo given to me as a gift when I left Ann Arbor in 1984. The setting was a party thrown by Don Dafoe who you know as an outstanding transplant surgeon and Chairman of Surgery at the Jefferson Medical College in Philadelphia.

The other individual, Dr. John Niederhuber, an outstanding immunologist and surgical oncologist, then on the Michigan faculty, and presently at the University of Wisconsin, was for me the consummate surgeon scientist. John ignited my enthusiasm for Immunology research, and he taught me that high quality clinical surgeons can with determination, engage in meaningful scientific research. John also introduced me to Frank Fitch who was soon to become my Immunology mentor.

This was during the late 1970’s, a truly exciting time in cellular immunology. Although the structure and function of immunoglobulin genes had recently been identified, the elusive “T” cell counterpart was a hot topic, and several controversial theories were still in play. The Niederhuber lab was quite active, working in the area of MHC immunogenetics, and John was advising me about options for my upcoming postdoctoral research fellowship. He called one day to urge me to attend a seminar to be delivered by Frank Fitch of The University of Chicago. The topic was “T cell Cloning,” then a newly described, powerful technology whereby monoclonal lines, deriving from a single cell, each sharing identical properties, could be propagated for the study of T cell behavior. Frank’s lab was specifically interested in alloreactive, cytolytic T cells, a subject of obvious relevance to an aspiring transplant surgeon. Frank allowed me to join his lab, and I was extremely fortunate to work during the peak of the enthusiasm over this new technology. My years at The University of Chicago were truly exciting. I learned about alloimmunity, T cell cloning, flow cytometry, and most importantly about hypothesis driven research. While at The U of C, I was also fortunate to establish what has become a deeply

valued, enduring professional friendship with Frank Stuart, our 20th President. Frank, I thank you for your advice, your guidance, your many important contributions to our field, and also for your friendship over the years.

My other mentor, Dr. Barry Kahan, the 16th ASTS President, allowed me the opportunity to begin my academic career with his group at the University of Texas in Houston. I don't believe Barry is here today, but suffice it to say that I am deeply grateful for his mentorship, advice and loyal support over the years.

There are many, many others who I have not specifically mentioned, but each of you have been extremely important to my career. I am sure you know who you are... certainly I do. ...please accept my heartfelt thanks, and my apologies that I did not mention each of you by name...

ASTS; 2001-2002

This year began with high hopes for scientific, educational, and perhaps even political progress for our field and for our organization. My tenure began as an outstanding 2nd successful joint ASTS/ AST annual meeting concluded. We heard Secretary of Health Thompson deliver a refreshing and powerful message of support for our field, as he challenged us to focus our energies with him on the goal of improving organ donation.

Relations between our organizations, the AST and the ASTS were strong, largely the result of efforts from each organizations' leaders during the past couple of years, seeking to emphasize our common goals and our common vision. We also enjoyed the successful launch of our journal, The American Journal of Transplantation, under the able leadership of Editor, Phil Halloran, and his able editorial staff. Ron Busuttil, Jack Lake, Nancy Ascher, and Mo Sayegh deserve special thanks for their important efforts in this regard. ...and you the ASTS and AST members deserve a hearty pat on the back for your hard work and dedication. You are the heart and soul of our field, and our outstanding organizations.

Attack on our nation:

Our agenda was set this year, after an active summer of planning, during our 3rd annual ASTS Strategic Planning retreat on September 9th in New York City at the Waldorf Astoria. The officers, Council and Committee Chairs enthusiastically gathered for a day of reflection, discussion and planning for the coming year. The mood was upbeat, and the discussion was lively, as an ambitious agenda for the year was established.

No one could imagine that, only 2 days later, on a bright, sunny morning, life was going to change horrifically and dramatically for each and every one of us. I expect that each of you remember exactly where you were and what you were doing on September 11, 2001. I was finishing a case in the operating room when the 1st plane hit the World Trade Center. I was walking to visit with waiting family members when, as I walked through the OR lounge, I glanced at the crowd, then up to the television as the 2nd Tower burst into flames. Then, a short time later, the Pentagon, right here in Washington D.C. was struck as well. As most of you know, Yale-New Haven Hospital is only about a 90 minute drive from Manhattan. Consequently, an emergency meeting was convened, as many of us were alerted that we would likely be called upon to help with the care of New York City victims. Although it was not certain whether we would travel to New York, or alternatively that victims would be triaged to New Haven, preparations were underway. However, time passed, but nobody came. We now know that survivors were few in number, but death and destruction was great. These events shocked and for a time paralyzed our nation, and they have occupied our thoughts and actions ever since.

I suppose too, it follows, that my remarks today have been shaped by reaction to those events. I would like to think that the aftermath of September 11th might serve as a wake up call, not only to the realities of danger that these terrorist actions pose, but perhaps also to the danger of our Societies complacency regarding many aspects of our modern lives.

Collapsing Infrastructure During a Time of Plenty:

Sunday, we heard Francis Collins deliver an eloquent address outlining, the potential for translating results from the human genome project to meaningful clinical benefit in the very near future. We are now positioned to answer many among the most challenging questions facing human biology and medicine. Also, recent and continuing growth in the NIH budget, as well as private sector funding for research promises to offer continued opportunities for scientific and technologic progress.

It is also significant that forward thinking people at the NIH and JDF have provided considerable resources to the Immune Tolerance Network. This exciting initiative under Jeff Bluestone's direction, will hopefully emerge from its early growing pains to provide a meaningful platform for progress in our collective quest to achieve clinical tolerance after transplantation.

Just look around; I think you will agree that the science, basic and clinical, in our field, transplantation, is alive, well, and the best is being reported here this week!

Dr. Thomas Starzl, during his inaugural ASTS Presidential Address, referred to the 1962 T.S. Kuhn treatise, *The Structure of Scientific Revolutions*.

Kuhn stated, "...a great advance (in science) necessitates the overthrow of an established dogma, and when that occurs the advance itself becomes the new dogma to which advocates flock. It is natural for those disciplines to become protectors instead of improvers of the status quo, guardians of the past instead of seekers of the future..."

Dr. Starzl issued this warning to the ASTS as a fledgling organization; perhaps we should consider those words today. We have entered a period where scientific discovery has placed us in the position effect major changes in the way we practice medicine, and for that matter in the way we live. However,

it is important to recognize that our ability to effectively translate the considerable promise to actual clinical care has proved challenging. Certainly, our partnership with colleagues from the Pharmaceutical Industry has delivered substantial progress in our field of transplantation. However unfortunately, a recent Time magazine (April 22, 2002) cover page and lead article provided a shockingly negative view of the complex realities and potential pitfalls of the clinical research process. Risk cannot be eliminated from clinical investigation; it is proper for us to debate the manner in which our society elects to share that risk. Certainly, it includes full disclosure, the principles of informed consent, as well as proper safeguards and results monitoring. The dialogue should involve all of the stake holders, including scientists, clinicians, ethicists, lawyers, as well as other interested members of our community. However, unless we are content to accept medical practice in general, and transplantation in particular as it exists today, and I do not believe we as Americans are, clinical investigation must move forward. We are the stewards of this enterprise, and we must accept the responsibility to engage in what will hopefully become a constructive albeit, I expect at times, contentious dialogue.

Beveridge in his 1980 monograph, *The Seeds of Discovery*, observed that major discoveries often occur when individuals working on problems from varied perspectives, come together to identify new dogma shifting paradigms. An interesting approach, but how might we get there?

Most in transplantation work in academic, University – *owned or affiliated* Medical Centers, where certain forces, mostly economic have threatened our ability to remain at the forefront of progress. I doubt anyone here has been successfully protected from the considerable negative influences of our present health care delivery environment. Our hospitals and our practices must participate in the intense competition for shrinking health care dollars, and unfortunately the playing field is not level. As a group, our patients tend to be more seriously ill, often with substantial, serious co- morbidities; and because an important part of our mission includes educating medical students, house staff and fellows, we tend to be somewhat less efficient. Additionally, we increasingly find ourselves responsible for

solving financial implications associated with increasingly more complicated, under- or un- funded mandates levied by payors and/ or our governmental institutions under the “mantra” of accountability. Consequently, at a time when we should be directing our efforts toward improving our translational research infrastructure, we have become distracted. Those of us who focus on clinical problems (surgical and non- surgical) are pulled farther away from the laboratory, and those who are engaged in hypothesis testing research have increasingly less contact with their clinically oriented colleagues.

“Why Johnny Can’t Operate” was the cover caption of an issue of the New Republic last fall, and it accompanied an article written by past Editor of the New England Journal of Medicine, Dr. Arnold Relman, entitled “The Collapse of Medical Education in America.” I believe it sounds another type of alarm! Although my remarks today are not focused specifically on our educational system, even the most dedicated among our colleagues has undoubtedly felt an erosion in enthusiasm as the struggle to limit work hours, maintain clinical experience at a level that will maintain the outstanding level of care we, as members of American Society, have grown to expect, has become increasingly more challenging. Time and work intensive fields such as transplantation seem particularly vulnerable, as concern rises that new graduates are seeking less demanding career pathways. What has changed since those enthusiastic early years?

Back to the Future:

Perhaps a brief look back may help us understand, or at least may provide us perspective from which we might move forward. In his Presidential address to the ASTS, Starzl offered his view that

“...we (the ASTS) exist mainly for the development and exchange of accurate information and informed opinion...”
 “... that we should work with those in health planning who seek our advice, “
 “... that we should work to establish how and how many transplant surgeons should be trained,
 “... and we should develop standards of professional care...”

Modified to include the important progress we have enjoyed through collaborations with our AST colleagues, I trust you agree that these words have important relevance to our discussions today!

I also remember the late Dr. Fred Belzer, our 2nd president, from those early ASTS meetings. He would eagerly rise to the microphone, usually after a well presented paper, to aggressively, albeit in the spirit of good debate, to challenge a particular hypothesis. Arguably, it was those spirited challenges to the dogma of the time, which provided one of the most important ingredients, creating the atmosphere conducive to the eventual successes in clinical transplantation we continue to enjoy today.

During his Presidential Address, Belzer too offered his vision for the ASTS:

... or perhaps any society...

He admonished us:

1. To stimulate progress
2. To make known the progress through scientific exchange and publication
3. To stimulate young physicians to enter the field and make contributions to it
4. To provide leadership in securing financially sound and optimal patient care

Don't those 4 simple statements continue to ring true today??

He continued...

5. To stimulate young physicians to enter our field
6. To work with our colleagues in the medical (he said nephrology) disciplines
7. To support those who have the same basic goals as do we
8. To reduce post transplant mortality
9. To eliminate the effects of steroids
10. To work to increase the number of donor organs, the lifeblood of our field
11. To encourage senior members to reach out to junior colleagues as mentors and as friends

Still relevant today? I think so!

And so it went, as Najarian established the principles for training programs in transplantation, laying the foundation that became so permissive of our growth and maturation. A succession of progressively better annual scientific meetings followed, where the most up to date information on transplant science, basic and clinical, was presented. Our field, transplantation, grew as results became increasingly more acceptable.

Things really began to change, when after an inauspicious beginning, cyclosporine was successfully introduced into clinical transplant practice, setting the stage was for transplantation to move from a

promising, largely experimental therapy to assume its place today as the first line treatment for irreversible organ system failure.

I spoke about the early years of the ASTS, and my personal attachments to this pioneering organization. However, it is important to acknowledge there were shortcomings as well. As I reflect on those exciting early years, recognition of the seminal contributions by many, physicians and scientists who with dedication, foresight, perseverance, and tremendous talent, were also instrumental in this remarkable story of an interesting scientific curiosity growing to become mainstream clinical reality should not be overlooked.

I am referring to a long list of people, only some of whom I will name as examples: In no specific order, they include names like Burnet, Damashek, Schwartz, Merrill, Medawar, Bach, Terasaki, Hitchings, Kohler, Milstein, Gutman, Carpenter, Strom, Benacerraf, Lacy, Dausset, Snell, Fitch, Sachs, Stiller, Borel, Kerman, Milford, Sayegh, Rubin, Southard, Zinkernagel, Strober, Bluestone, Miller, Gonwa, Norman, Helderman, Lake, Halloran, Turka, Lucey, Harmon and the list goes on and on.

... and PLEASE, if I didn't mention your name or your favorite physician or scientist, I am sorry... it was not meant as a slight, the list was by no means inclusive, the real numbers are very large...

To be sure, it took a bold group of determined, focused, and courageous surgeons to drive our field from the laboratory to the operating room, and recall this was often over the loud objections of many... ..and I am proud to count myself among their progeny, but I again emphasize this did not happen in a void...

... beyond all else, it is essential for everyone to understand that WE ARE IN THIS TOGETHER, we always were, and it is clear to me that we always will be...

Collectively, we are the stewards of a very important enterprise, our field of transplantation.

As we seek solutions, our organizations, the AST and ASTS must provide leadership, and I believe we have made important progress, addressing many of the challenges facing our field. Beyond our annual joint meeting, the American Transplant Congress, and the success of our journal, The American

Journal of Transplantation, we have worked effectively together. We have opened the dialogue that will lead to solutions for several of the vexing problems facing our field including organ donation, living and cadaver; financial incentives; generic pharmaceuticals; the growing waiting list, and more. We must continue this journey together, with determination and the resolve to accept the challenges. Assuming we do so, I am convinced that in time, we will develop the tools to successfully provide transplant therapy to those in need, with increasing efficacy, in a well tolerated and timely manner.

Please don't forget that WE are the surgeons, physicians, scientists, transplant coordinators (nurses, PA's, technicians), OPO leaders, and the dedicated labs. We are the leaders in our hospitals, medical schools, and graduate schools. On behalf of our patients- recipients, live donors and donor families we must accept our responsibility to sustain progress toward our goal of providing this remarkable therapy for all who are in need.

A New Organizational Construct:

Our current organizational constructs seem inadequate, and I am convinced we must seek alternatives. Available resources seem insufficient to meet the growing demand. We must work through a confusing morass of poorly understood, seemingly underfunded, and inadequately administered mandates, and we must recognize that we are in the midst of change. It seems appropriate to consider whether the traditional administrative and organizational constructs that have worked in the past should continue.

By example, I will describe an approach we are working to establish in transplantation at Yale, my institution. Together with my valued collaborator, colleague and friend, Dr. Jordan Pober this vision began to take shape during the latter months of 1999 and early 2000. The goal was to encourage the considerable expertise within our faculty, to self- identify as stake holders in transplantation, and to establish a programmatic structure that would encourage their contributions and support.

Toward that goal, we proposed to establish a new Interdepartmental research program in Vascular Biology and Transplantation, (VBT) directed by Dr. Pober. The VBT will act as an umbrella program for collaborative research projects, supporting basic, pre- clinical, and together with its clinical counterpart the Interdisciplinary Program in Clinical Transplantation (PCT), facilitate application of research discoveries to the bedside – yes, true translational research! Presently, approximately 20 investigators from many Yale departments including, Surgery, Medicine, Pathology, Dermatology, Pharmacology, and Immunobiology have elected to participate in the VBT. The VBT seeks to foster new research in vascular biology, and apply the results to clinical transplantation and related fields. The program will also train scientists in these disciplines.

During this process, I have led an effort to similarly re- organize our clinical efforts. The Interdisciplinary Program in Clinical Transplantation (IPCT) will serve as an umbrella organization for clinical transplantation at Yale. As with the VBT, it is the goal of the IPCT to facilitate opportunities for the various stakeholders from different departments and interests to participate meaningfully in programmatic growth. The IPCT seeks to expand clinical volume, facilitate clinical and translational research and training in organ transplantation, by consolidating renal, pancreas and liver transplant efforts into cohesive, comprehensive and focused organ specific programs. The IPCT will provide complete transplant and support services for patients suffering irreversible organ failure, emphasizing new strategies for improving care through results oriented analysis, clinical research, and translation of basic discoveries. The IPCT will also provide an environment to foster training in clinical and transplant science. As most of you know, Dr. Fadi Lakkis recently joined us as co- Director of the PCT; additional recruitments are actively underway.

It is our shared vision that these parallel and inter- digitating programs will attract and support outstanding faculty. Interactions will facilitate basic and clinical research, as well as outstanding clinical care and training in transplantation. The goal of these programs is to establish a model for advancing outstanding patient care through translating relevant discoveries into clinical practice.

Our 3rd ASTS President, Dr. Thomas Marchioro suggested,

“... our destiny is to increase the store of knowledge... “

“... if we are found wanting, others will take our place and we shall be consigned to the dustbin of history”

“... progress has been achieved by unremitting hard work, countless experiments, dashed hopes, and above all the courage to fail...”

Marchioro challenged us accept our job, to educate ourselves, our colleagues, our students, our patients, our society, the public, and the government.

He reminded us of the need to...

“muster once again the qualities of heart and mind that were necessary to prove that organ transplantation was possible...”

... and he quoted Teddy Roosevelt,

“It is not the critic who counts, not the man who points out how the strong man stumbled, or where the doer of deeds could have done them better. The credit belongs to the man who is actually in the arena, who’s face is mared by dust and sweat and blood; who strives valiantly; who errs and comes short again and again; who knows the great enthusiasms, the great devotions; who spends himself in a worthy cause; who, at the best, knows in the end the triumph of high achievement, and who at the worst, if he fails, at least he fails while daring greatly, so that his place shall never be with those timid souls who know neither victory nor defeat.”

Before closing, I wish to acknowledge and thank my colleagues at Yale for putting up with my quirks and idiosyncracies, and to thank you for accepting my time away from Yale this past year with equanimity. However, more importantly thank you for your individual and collective dedication to our mission of outstanding clinical care, new knowledge generation through research, and education of our future colleagues. First, to my partners in our Section of Organ Transplantation and Immunology, Giacomo Basadonna and Amy Friedman. Although this thank you seems inadequate, I hope you know how much you are appreciated. Also, our coordinators, inpatient and outpatient nursing staff, as well as our clinical and laboratory research teams; two of our ever growing crew are here today, Jennifer Nikolich and Noelle Sowers... Thanks. Thanks also to Dr. Lisa Geiselhart, who supervises the outstanding technical staff in our histocompatibility and immune evaluation laboratory, and who is also a deeply appreciated and valued research collaborator. I am also fortunate to work with an outstanding

group of medical colleagues including Peggy Bia, Rich Formica, David Rothstein, Alan Kliger, Tom Eisen, Doug Smith, and far from least the most recent tremendous addition to our team, Fadi Lakkis.

I am also delighted that members of my family have joined us today.

...to my parents, Elaine and Jerry, without your guidance, patience, and probably most of all perseverance, it is not likely that I would ever have been afforded this opportunity!

... and to my wife, Kathy, who many of you know also, because of her outstanding efforts with our clinical research program... what can I say? You are always there for advice, guidance, support, and frequently a little (or sometimes perhaps a lot of) reality testing.

... to my children, David and Beth who have also joined us. You too have made many sacrifices, as I have tried to balance my work with your needs. You have been patient and understanding, and I appreciate that very much. I am also very proud of both of you!

... and Beth, thanks for sharing your graduation week with me!!

Finally, I want to again re-iterate how special the ASTS has been for me. I hope you can understand what an honor it has been for me to serve as your President this past year.

Thank you.

Respectfully submitted,
Marc I. Lorber, M.D.
President, American Society of Transplant Surgeons
April 30, 2002