THE ERA OF THE CHIMERA

My dear colleagues,

When Hans Sollinger called my Chicago hotel room at 7 AM Wednesday two years ago, it was with the unexpected and frightening news that I was designated President-Elect of the ASTS. Unexpected, because I never considered myself as part of the ASTS establishment, and frightening because what immediately came to mind was the question of what in the world I would say in a Presidential address two years hence.

Having heard all of the addresses from David Sutherland's charming flight of ideas about grafts in the plant kingdom, to the erudite and fascinating insights into our history by Clyde Barker, and by Hans, with Clyde's wonderfully close relationship with Bill Billingham, and Hans' scholarly history of Ray Owen's Freemartin calf chimerism work at the University of Wisconsin in the mid-1940's. Then, going all the way back to the address of our first and most famous President, Tom Starzl, similar to Washington's farewell address to his Continental Army in 1783. Washington later had something to say about avoiding entangling foreign alliances, foreshadowing what is to follow in this talk. Tom's presidential address was delivered in the ballroom of the Drake Hotel, a place perhaps now somewhat analogous in our own Society's history to Washington's choice of New York City's old Fraunces Tavern.

So, I became part of our Society's establishment in a rush, with only a survey course of ASTS 101, hastily presented by Ron Ferguson last year and, for virtually two years, the question of what this address should be about has become increasingly terrifying. So, here it is.

It is entitled "The Era of the Chimera", and despite the obvious, that I am the least politically adroit person in this room, please resign yourselves to the fact that, seriously, with the real honor and the duty of having been given the stewardship of ASTS this year, this is, and must be, a strong, if not pungent, political address that is not necessarily politically correct but is absolutely required in this place and this time.

What is a Chimera? -- a mythical xenograft, each component of which functions as an integral part of the whole wondrous creature. Is our future unification with our non-surgical colleagues to be as seemingly impossible to create as the storied chimera and, as illusive as Norm Shumway has suggested of xenografts, when he has said, "The future of transplantation is in xenografts and always will be"?

We now face, most unnecessarily, most redundantly, and most irritatingly the presence of two Societies -- the ASTS, and the AST, that John Neylan, their President this past year, proudly proclaimed last December 21st:

"The designation of the American Society of Transplantation more suitably characterizes the diversity of our growing membership and underscores the collaborative interdisciplinary roles that physicians, surgeons, and scientists perform to advance the science and clinical application of transplantation medicine. The largest professional organization in North America that focuses on transplantation medicine and immunology."

We now have two organizations representing to the public, the Federal government, the pharmaceutical corporations, and the NIH, among many others -- redundantly and confusingly -- clinical organ transplantation in America. We should not deny the existence of a group that we all know that we need in transplantation. As physicians, even when they were the ASTP, they were not only our referring doctors, but as transplantation became more successful and we had more patients out there, someone had to follow the details of their long-term care. Now, most of us in our own centers work productively, effectively and collegially with our non-surgical colleagues. We help each other. The rank and file of both societies, of which I hope soon to become again. But what can we do now to correct this confusing picture? To wake up from what has become a political nightmare that only affects us individually because it has affected us collectively.

It has become patently obvious that despite the crazy circumstances that I was thrust into, this should be my subject. At the outset I must make the point, that although this is a presidential address, I express the views of none but myself. No political dogmas, no policies, no consensus positions -- consensus that I have otherwise been religiously strict in adhering to in all other aspects of this presidency year until now. I have had an overly generous share of input from members of the ASTS, expressing deep concern -- insecurity about the present, and frank despair about the future, purely in response to the proclamation of this new organization. The murmurings have also come from other officialdoms outside both organizations, with raised eyebrows as to who is leading what. You all recognize that I am not Abe Lincoln; but, at the outset I must clearly declare that such an entity divided will not stand. It must be crystal clear that this situation will not weather the test of time in this most public and political era of organ transplantation in America. There must be a single society of transplant surgeons, physicians, and scientists that speaks with a single voice on issues critical to the future of organ transplantation in America. How could I, who even at the outset of this, our twenty-fifth anniversary year, considered myself the wrong person at the wrong time, do what was best in this confusing time for our society and for our patients? In my view, we were at a real crossroads in our history.

What can we, even now, do -- you as my respected colleagues, the membership of ASTS and I, soon quite cheerfully to be an immediate past-president -- to gather the scattered pieces and create a functioning chimera? I will describe two elementary components to the cure, one medical and the other surgical, that in my personal view, need to be accomplished together to be successful.

But first, in order for us to clearly and confidently face the future of a new millennium in organ transplantation, we have to understand our heritage -- where we have been in the ASTS. We have to know where we are. We have to understand the present, and, although none of us is a prophet, we can then, at least, have a sense of confidence of how we must function and plan for the future as best as we can make it -- a bright and certain future in our field for all of us: surgeons, physicians, and scientists. And make no mistake, this is our responsibility.

What is the history of the ASTS? And, what is the history of the dissidents, now called the AST, a.k.a. ASTP -- who, with a clever, if simple, strategy have come to outnumber us by proselytizing to include some of us? More importantly, what is really happening and what should and has to happen? First, are we not and have we not been part of the problem? Or, as Pogo Possum said, "We have met the enemy and they is us". Before we get into this analogy -- the history of the <u>AST</u> and our ASTS contribution to their growth, let's clarify the issues; let's have a reality check about ourselves.

I hope to be forgiven by our former and future leaders for sinking into the next highly partisan down-and-dirty political segment of this address. As Mario Puzo said, "It's really not personal; it's business". And so, I will paraphrase a former governor of Texas, Ann Richards, mocking the Reagan cabinet during the Iran contra scandal in her keynote speech at the Democratic National Convention in 1988 ("Where was George?").

What has been our past in organ transplantation? It has been surgeon driven and surgeon-funded, and it was the surgeons and their patients with whom they developed an unbelievable bond of trust, who paid the price so that we could all reap the rewards — The American Transplant Surgeons and their patients. Let us divide our earlier history into twelve year intervals until the present era, Joseph Murray, David Hume, Francis Moore, Tom Starzl, Keith Reemtsma, Jim Hardy — a great dawning of clinical transplantation (1954—1966). They created the methods. They created the tools, the technology, and the therapy. It was plain old hard work and stick-to-it-iveness. Azathioprine, steroids, cadaver organ transplantation, brain death (1954—1966). Where was the AST?

1966 - 1978: Tom Starzl, Tony Monaco, Paul Russell, John Najarian, and Richard Simmons, Norman Shumway, Oscar Salvatierra, Fred Belzer, and their patients -- polyclonal anti-lymphocyte globulin, transplantation in the diabetics, liver transplantation, heart transplantation, donor-specific blood transfusions, organ preservation. Where was the AST?

1978 - 1990: Monoclonal antibodies, cyclosporine, pancreas transplantation, UNOS. Ben Cosimi, Tom Starzl, Nicholas Tilney, Barry Kahan, Ronald Ferguson, David Sutherland, Hans Sollinger, Robert Corry, John MacDonald and their patients. The ASTS developed the original organ retrieval teams and began to organize them into a donor organ procurement and transplant network. They created NOTA and pushed it through to law in the United States Congress. 1978-1990: Where was the AST?

1990 & onwards: What is the real present in organ transplantation in the United States? It is still surgeon-driven, and surgeon-funded. Surgeons and their patients take the lead and pay the price. FK-506, mycophenolate, rapamycin, humanized monoclonals, stem cell and bone marrow infusion, chimerism, chronic rejection. Hans Sollinger, Ron Ferguson, Bob Kirkman, Barry Kahan, Tom Starzl, Nick Tilney, John Fung and their patients. 1990 - to date: Where is the AST?

Now, and into the new millennium -- increasing organ donation and availability, and increasing the efficacy of really doing it operationally -- improving organ retrieval and its technology. Split livers, xenografts, tolerance protocols, multiviscerals, anti-sense, molecular tolerance, anti-CD40 and its ligands, other anti-costimulatory pathways, anti-idiotype therapy, islet transplants. Barry Kahan, Mark Hardy, Ron Busuttil, John Fung, Andy Tzakis, David Sachs, Hugh Auchincloss, Chris Larsen, Stuart Knechtle, Alan Kirk, David Harlan, Avi Shaked, Dick Thistlethwaite, Camillo Ricordi. 2000 and beyond: "Where will the AST be?" Our future lies in being surgeon-driven and it's the surgeons and their patients who pay the price, and it is the surgeons, our surgeons of the ASTS, that our patients look to for leadership and for the salvage and renewal of their lives by organ transplantation. Where will the AST be? Lord Raglan said it best to his Brigadier in the Crimean War, "Charge, I am right behind you!"

So, we have a sick entity.

However, before proposing a cure, let's get to the disease pathogenesis.

The dissidents -- where did they come from? Lest we get to feeling too good about ourselves! Does the reality check really end here? How did the AST begin?

It began when we began to feel too elite. Did we really do it alone? Were we really that fantastic? What about 1954 - 1966 -- George Thorn, John Merrill, Peter Medawar, JFAP Miller, Gus Nossal, McFarlan Burnet, Hitchings, Schwartz, Scribner, Kolff, Damashek, Thomas, Good, Terasaki. Permanent hemodialysis, the pharmacological basis of immunosuppression, bone marrow transplantation, the new immunology and the thymus gland, tissue typing, the artificial heart, acquired immunological tolerance. Where was the ASTS when they did their seminal work? Where were we except to take advantage of it?

1966 - 1978: Fritz Bach, Ron Gutman, Bernie Carpenter, Ceasar Milstein, Barruj Benacerraf, Paul Lacy, Jean Dausset, George Snell. Enhancement, passenger cells, hybridomas, genetic control of the immune response, autoimmune pathogenesis and diabetes, the mixed lymphocyte reaction.

Where were we when this work was done, except to use it? Where was our society policy except to exclude them?

1978 - 1990: What about Calvin Stiller, Jean Borel, Tony Allison, Jim Southard, Rolf Zinkernagel, Henry Balfour, Sam Strober. Immunological monitoring, calcineurin inhibitors, other potent anti-metabolic pathways, better organ preservation, histocompatibility and the natural control of the immune response, anti-CMV therapy. Where were we, the ASTS, except to jump on a science express train? Where were we, except to ride their coattails?

1990 - today: What about Jeff Bluestone, Les Miller, Tom Gonwa, Jack Lake, Phil Halloran, Mo Sayegh, and John Neylan. Where were we when they asked, "What about our science?" Where are we when they ask, "What about our accomplishments?"

Who takes long-term responsibility for the created chaos of our overly broad brushstrokes, tempering them with medicinal doses of reality? Who conceives and introduces new basic science that we feed on?

We, the ASTS, thought ourselves an elitist club back then in the Drake Hotel, that the others could not join, and what went around came around, because they became the dissidents who made things easier, but who also recognized good science, even if it were produced by surgeons, and produced much of it themselves, so that to paraphrase Groucho Marx: "Any country club that would accept me for a member, I wouldn't join." Any science that was exclusively selected by the ASTS for presentation, was not necessarily worth joining in, and some very good material began to come out of ASTP meetings, presented by surgeons, seduced by the beautiful voices of sea sirens of the ASTP.

Were we, as some of us think of ourselves, the elitist keepers of the true faith, going to emasculate ourselves by our own scalpels? This is what we were faced with at the opening of the ASTS year. If we withdrew into our exclusivity, we could not fight the right battles that so impact on society -- when we were encased in a thick isolationist shell. The principles of the OPTN rule, organ donation initiatives, the First Family Pledge, the National Organ Transplant Act renewal, reimbursement for life-long immunosuppression, and when and how to institute xenografts, to name a few examples.

The last segment of this talk discusses what, to me, has become increasingly obvious over the past twelve months. There are only two take-home lessons that I would implore

the membership to focus on -- two components to the cure that the ASTS must embark on to arrive at a single, complete, functioning chimera in the next millennium.

The following is a significant part of the Mission Statement of ASTS developed after our society this year by a vote of 240 to 12 decided to include qualified scientists and physicians in its regular membership:

"The American Society of Transplant Surgeons is the leadership organization of the surgeons, physicians and scientists who have pioneered and continue to advance the frontiers of life-sustaining organ transplantation. Our society has taken the field from experimental trials to highly developed treatment modalities that increasingly offer a growing number of men, women, and children a new chance at an ever longer and healthier life.

ASTS members have the responsibility for directing transplantation surgery, medicine and research programs at America's major medical centers."

Sound familiar? Would not the AST create the same statement? Why did we as a council suggest to the ASTS membership to become more catholic in its make-up? Was there not another society doing exactly the same thing for the past 10 years? Were we not copycats, reinventing the wheel? Not quite! Let me explain why.

The cure to fixing this chimera -- Part I has actually just been described. It is medicinal and nutritional. Mind ourselves, strengthen and nourish our ASTS. "Strengthen our society" should certainly be an over-riding principal of your president and council. It is really an age old credo. The exclusivity of our ASTS needed to be abolished. That this should have happened more than 15 years ago did not make it any less certain this year, and by a bylaws change, our society was strengthened to recognize respected colleagues doing equally important work with us, not just those, dare I say it, with somewhat less pretentious qualifications. What this really means is that ASTS, with the inclusion of a broader crosssection of expertise, but only of those who have demonstrated a true career commitment to the field, has positioned itself to maintain its leadership and yet to have the counsel of those of our non-surgical colleagues, whose advice we all deal with on a day-to-day basis. And, in that quality, there still lies the difference between us which we must emphasize so that the two societies can come together in an effective and mutually respectful way to act with one governing voice on issues critical to transplantation in America -- whenever that day comes. By the way, there is nothing wrong with still calling our own organization a surgical one despite its new more varied but qualified make-up. That is what transplantation biology and pre- and post-op medical care is all about. It is how to make organ and tissue transplantation, nothing if not a surgical challenge, more successful.

This finally brings us to the cure Part II. It took me a long time to get there during the course of this year, but in a deliberate, if not agonizing, decision, it became enlighteningly obvious. It is my strong personal belief that the quickest and most effective way of forming a single society is for ASTS members to relinquish their membership in the AST. To be clear and simple, to resign from the AST — those of us (myself included) who have been there, and I have resigned. The AST, G-d bless them, I personally believe that I had to leave them as they were represented by their leadership this year, in the hope of joining with them when we can work together again.

What was sad this year and caused our inability to reach accord with our AST counterparts was the assumption by their power structure and even by some of us that our

ASTS was folding and would by crumbling rot become the fertilizer for growth of this new and vigorous AST, which as I already quoted their President's words, is the, "Largest professional organization in North America that focuses on transplantation medicine and immunology". I found that the reports of our demise had been greatly exaggerated. We have during the last three years that Avi Shaked and his team have been Program chairman and committee, increased our scientific abstract submissions to our yearly meeting from 270 in 1996 to 592 in 1999. Not too bad for a society of some 700 members. I fervently hope that we will reach a closer working relationship with them, with their new governance.

However, the AST leadership perception this past year was if we as surgeons were already part of them, why not just have the others in the ASTS come in to roost as well?

Let's look at the reality once more. These were the two proposed principles as a starting point of negotiation that were sent to the a.k.a.-ASTP by our ASTS council in the hope of eventually bringing us together in a mutually respectful process: Please note the timing and the reactions --

ASTS Proposed Statement of Principles on Process for a mutually respectful Creation of a

Single Society
(November 1, 1998)

The ASTS and ASTP agree that the interests of transplant surgeons as well as transplant physicians and scientists will be given equal weight in a new society, with the two groups holding equal or APPROPRIATE representation on the Council and all committees, and representatives of each group alternating in the presidency and other offices, for the first decade after formation of the society.

The ASTS and ASTP agree that as of November 1, 1998, in anticipation of combining in a new society, neither society will undertake any major new program or activity, including change of societal name -- or incur any major new contractual obligation -- that would become an inherited obligation of the new society without the concurrence of the other society. This includes launching a new transplantation journal.

Received by John Neylan, President ASTP, by fax November 2, 1998. AST name change initiative: letter -- to ASTP members, November 3, 1998 -- the very next day.

The surgeons of our ASTS would have been most gratified had these two principles continued to be discussed, and some kind of compromise reached. That very statement went with our fax. We would still be happy with some type of equal representation in a totally new society, since names can be changed and it is what is behind the name that is important. Can equal stature in a new society be accepted, even now, by our non-surgeon colleagues? I ask, can you accept equitably the voice of surgeons and non-surgeons in this new entity? Why have you not answered us since November of 1998? Our fax is still running. As Mrs. Goldberg asked, Mr. Anthony, the Answer Man, on the radio in the 1940's, "Mr. Anthony, my husband left the house 20 years ago in the middle of supper without saying a word to me before I served the chicken soup. Should I still keep it warm for him?"

The rest of my message is devoid of humor, and is as direct as I can make it. I must again say that this is a personal view and that I have made it a point of honor to impose it on no one, either within or outside of the ASTS establishment. Please, make no make mistake. This issue, the future of transplantation in America is our responsibility, yours and mine. We have committed our professional careers and our joint lifelong efforts to it. It has always required a team approach. We are not dealing with personalities here. There are no exclusive solos for what I am proposing. Otherwise, we are left with a cacophony of total chaos. What I have attempted to describe so far, and will in this last segment try to clarify to you, are not the voices of single individuals, not of John Neylan or Josh Miller, not of Jack Lake or Ron Busuttil, not of Mo Sayegh or Nancy Ascher, but the conclusions and the philosophy that has taken the 25 years of our existence and of theirs, the leadership of our non-surgical colleagues last year, that reached this critical point in time, and it seemed to me that critical, and that we had to act while we had the opportunity.

Here is the reality. >90% of all transplant programs in the United States are directed by surgeons in 1999, with a similar amount of clinical and applied basic science research directed by transplant surgeons, many of whom are the leaders of your ASTS.

Here it seemed to me was the AST leadership perception: But if the surgeons are already part of us, why do we have to merge with them? Have we not already formed a single new society, the AST?

Here is the reality. It is the surgeons that do the transplants for end-stage organ failure. This cannot be accomplished by giving more dig(oxin) or less dig(oxin), more dialysis or less dialysis, more interferon or less interferon, more insulin or less insulin, more oxygen or less oxygen. This is what will always separate organ transplantation from any other clinical arena in which medical specialists and scientific specialists relate to surgeons. It is not a question of the alternative medical treatment. Organ transplantation cannot be done by hypnosis and the direction of immunosuppressive protocols is still an integral part of transplantation surgery.

Here is the plain, obvious fact that may not have been emphasized enough. With a single meeting planned from the year 2000 and onwards made up of surgical and non-surgical program committee members with ASTS and AST in equal representation (this single program committee is already in action by the way), and with a single blinded abstract form, there is only one science that will be presented -- no dissident groups, no Pharisees, no Sadducees. No redundancy, just good science. We, the ASTS, have demonstrated that we are prepared to abolish our exclusivity and to join with our non-surgical colleagues. We removed the requirement of surgical training from our bylaws. We even voted in another ballot to face a new future with our non-surgical colleagues in a totally new Society.

Here it seemed to me was the AST leadership perception: But if they are sending in abstracts as AST members, why does there even have to be ASTS contributions to the combined meeting? Maybe they just ought to have an evening surgical club meeting for, "technical discussions."

It is as plain as day that we must continue to work cooperatively and productively with our non-ASTS colleagues on joint policy and new transplant science, to avoid a wasteful duplication of effort and confusing external perceptions in this period of confusion, and for all of the reasons that the recounting of our joint history in the last part of this 20th century has brought to mind. But it is just as plain that this cooperation must be mutually respectful and, above all, not undermined by our own schizophrenia.

Here might be an AST leadership perception: Why in the world should non-surgeon physicians and scientists join the ASTS when you say you are leaving us?

But here is the reality. Many of you non-surgeons were always part of the ASTS and we were just too slow to recognize it. You were and are our non-physician scientists and our physicians, as we are your transplant surgeons. We wish above all to join with you to lead transplantation into the 21st century. We wish to be equal partners and to share this responsibility together, and not to become lost like a thin prophetic voice in a whirlwind of humanity, your membership. This would be a disaster for organ and tissue transplantation in America. To lose this, our ASTS voice, in the vastness of some numbers game is to lose the heart and soul and (please give us credit) at least half the brains of our work together. We are not in a recruiting war. We are just trying to do what is right.

To those of you in our ASTS who have the <u>false</u> perception that this talk and these actions are too little and too late, let me again emphasize the reality to you. You are still the leaders in our field, you are still in charge, because no one else can do it. No one else has the commitment and the confidence and trust of our patients and the American public. It is up to us as to whether this prescription for a cure will work. It was always up to us.

And, I therefore express to you now my personal view, if surgeons were going to continue to be in this leadership and if the explosive progress in organ transplantation is to carry on in the future as it has in the past and continues in the present in America, this is the obvious path that I had to choose. I must for the last time emphasize that this conclusion is a personal one that has neither been endorsed nor denied by the ASTS Council since I have made it a point that this should not be policy, but personal. As your president this past year, I think I am entitled to this last hurrah. To me, it is an objective decision arrived at by years of personal observation of events and the conclusions that one can draw from them.

My personal prescription for Part II of the Cure was therefore, surgical. It is an explant of myself from the AST, an excision of what might have been inaccurately perceived by me earlier as a working remnant of our crumbling former glory. I had to square my actions with my conscience in the hope that I could emerge together with the non-surgeon physicians and scientists in whatever organization we all choose to call ourselves, in an equal partnership in this totally new creature of the new millennium. This is not machiavellian, nor is there any innuendo. To me, this is just simple logic. To me this is as plain and as clear as a sunny day in May in Chicago.

The AST -- G-d bless them; I had to leave them for their own good, so that I could eventually join with them for the universal good in The New Era of the Chimera. Transplant Surgeons, Physicians, and Scientists of America.

Respectfully submitted, Joshua Miller, M.D. ASTS Presidential Address - May 21, 1999