Transplantation: A Maturing Surgical Discipline

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The art of modern transplantation can be dated from the technical contributions of Alexis Carrel in the early 1900s or from the initial effort of Dr. Lawler in Chicago, who transplanted a kidney into a human in 1950. The science of transplantation, on the other hand, can be dated from the pioneering work of Drs. Medawar, Brent, Hume, Hamburger, and Starzl in England, Boston, Paris, and Denver in the 1940s and early 1950s. Since that time, renal, cardiac, and bone marrow transplants have become accepted treatment for selected patients with end-stage organ failure. Although these modalities of treatment are now accepted by the scientific medical community, the practice of transplantation surgery is still—even in the mid-1990s—in the early stages of being incorporated into our traditional systems of medical education, organization, and quality assurance. The 1950s and 1960s gave birth to our science; the 1970s have been our adolescence; and the 1980s taught us to prosper and reproduce. ASTS now finds itself in a unique position. We should accept the mantle of responsibility to provide leadership not only for scientific advancement, but also for the maturation and full incorporation of transplantation surgery into American medicine.

First, a few words about the status and future of our science, especially as it relates to histocompatibility testing and immunosuppression. While the HLA system of major histocompatibility antigens was being defined by Dausset, Terasaki, Van Rood, Cepellini, and many others, a logical goal of many transplant centers and histocompatibility laboratories was to seek the bast matches between donor and recipient. This endeavor has an obvious solid experimental basis and rationale. Unfortunately, the goal has not proved to be practical and its pursuit is perhaps illusionary when dealing with an outbred population. At times, our typing results do help us select a two-haplotype match rather than a one-haplotype match familial donor, but more often we do not have that choice and feel fortunate to have available a willing related volunteer of at least a two-antigen match. With cadaver transplantation, the probabilities of find-

ing a well-matched donor are so slim and the logistics and practicalities so complicated that only a small fraction of cadaver transplants in the U.S. are between HLA-compatible donors and recipients. Some have even proposed that we abandon tissue typing for cadaver transplants. Our federal government even recently suggested that, since there is no definite proof that tissue typing benefits cadaver transplantation, Medicare should stop reimbursing for such testing. I am convinced that those who would dismiss tissue typing as irrelevant in cadaver transplantation are both premature and perhaps misdirected in their goals. Rather than continue to seek ever more compatible matches, I would recommend more investigative effort in histocompatibility testing in these areas:

1. Develop histocompatibility tests to rule our donor-recipient combinations in which we know the results will be poor. Certainly a positive crossmatch is one test that already contraindicates transplantation. A mixed lymphocyte culture with a high index of any stimulation also appears promising to rule our poor donor-recipient combinations with related transplants.
2. Identify those antigens to which an individual recipient is unable to mount an active immune response. Matching for nonstimulating antigens seems more logistically feasible than continuing to seek matches on the basis of identical antigens.
3. Recognize the enhanced significance of antigenic matching as immunosuppression improves. If immunosuppression were perfect, then rejection would not be a problem even in the face of great antigenic disparity. On the other hand, when the match is perfect such as with identical twins, no immunosuppression is needed. It is only when we are in the intermediate area of this interdependent continuum that the effect of tissue typing becomes apparent. Thus, as our immunosuppression becomes more effective, rejection will be prevented in a greater proportion of the antigenic disparities encountered and the significance of selecting for better matches may be unmasked.
4. Finally, tissue typing will be of obvious importance to identify the profile of antigens in a particular recipient or donor when our science advances to the point where we can engineer tolerance or enhancement for specific antigens in a given donor-recipient pair.

I would submit, then, that the science of histocompatibility testing remains promising and that its clinical applications are in their infancy.

A few words about a second scientific problem, that is, the status of our art of immunosuppression. Many continue to use the same two agents introduced in the early 1960s, that is, azathioprine and steroids, to prevent or reverse rejection. There is no convincing evidence that the addition of other drugs, the use of radiotherapy, or a course of antilymphocyte globulin has improved the overall or long-term results of renal transplantation. Programs using only the simplest of immunosuppressive regimens report equally good results as those using a more complicated regimen, including adjunctive operations such as splenectomy and recipient nephrectomy. Differences in results between programs are just as readily explained by differences in

selection, differences in population pools, or perhaps by differences in experience and administrative organization.

I believe the only immunosuppressive adjunct for which there is convincing evidence of benefit is the use of pretransplant multiple blood transfusions. Unfortunately, even here we do not understand the mechanism of action. The time has come that we as a scientific community insist that any studies of new immunosuppressants or adjuncts to immunosuppression be both prospective and randomized. The argument that having a concomitant, control series in which the experimental treatment is withheld is unethical simply does not hold up under close inspection when we are talking about potential improvements of the 20% to 30% range.

What is the role of ASTS in all of this? Certainly we can continue to encourage investigation and provide a forum for presentation of outstanding scientific contributions. Our Scientific Studies Committee, chaired by Richard Simmons, has already taken the lead in encouraging and organizing cooperative randomized studies. This effort is expanding and, in my experience, is a unique undertaking of American scientific surgical organizations.

ASTS is also rapidly assuming another and equally important role in the field of transplantation. We are one of the few organizations—perhaps the only representative organization—to which American surgery, the educational community, the government, and others can turn for advice and counsel on issues related to transplant surgery. This role will and should occupy much of our time during the forthcoming years. We do have some unresolved problems and we do have some tasks we need to complete if transplantation is to pass through and assume its proper place in the American surgical community: (1) Many medical students and residents are never exposed to the principles of transplantation; there are probably too few well-qualified candidates entering the field today. (2) The outcomes of transplantation vary widely from center to center and cannot be fully explained simply by differences in patient selection. Programs with poor results and high mortalities reflect badly on our entire discipline, and the public is no longer content with superficial explanations for these differences. (3) The so-called waste rates of cadaver kidneys also vary too widely. Rates as low as 5% and as high as 35% have been reported, with no adequate explanation for the differences. Transplantation has not had adequate input or representation within the National Institutes of Health (NIH) or within the Social Security Administration. NIH research monies allocated for transplantation are small. Many regard the federal guidelines as they relate to reimbursement and network governance as actually discouraging the clinical application of this discipline.

So much for the problems. Many tasks need to be completed. Work has already begun on many of them, especially through the Advisory Committee on Issues chaired by president-elect Jim Cerilli. We need to define the essentials of what should constitute adequate training and education of transplant surgeons. We owe, to the public as well as our medical colleagues, some mechanism to identify individuals who are qualified to engage in transplant surgery. If we follow the traditional norms, there should be a certifying mechanism for transplant surgeons either under one of the existing boards or as a separate board. We need to develop standards to serve as guide-

lines for quality assurance to help hospitals and others evaluate transplant and organ procurement programs. If we complete these tasks, many of our problems will be solved and a system will have evolved that is appropriate for the proper maturation of a professional discipline such as transplantation.

I can think of no better organized or more representative group to deal with these problems than ASTS. Certainly we will and should remain primarily a scientific organization, but we should also accept the responsibility and mantle of leadership to maintain the quality of transplantation surgery and to assure that transplantation is incorporated into the mainstream of American medicine.

It has been my very special privilege to serve on your Council and for this past year as your president, working on these tasks with you. Yes, it has also been my very special pleasure and good fortune to be assisted by such able fellow officers and Council members. It has also been my special blessing to have the support of my family and my wife, Claire, who is with me today. Thank you all for the privilege of serving as your president during the past year.