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Discussion

DR. ARNOLD G. DIETHELM (Birmingham, Alabama): I was grateful to have the opportunity to review the manuscript prior to the meeting. Dr. D'Alessandro and Dr. Belzer and colleagues have addressed an important and frustrating part of organ transplantation, and that is the organ shortage.

The manuscript is an excellent review of their results and similar to those that we have published from our own institution. They, as well as ourselves, have attempted to modify the problem of organ shortage by using living donors. In fact, they use living unrelated donors. And those results, as you have seen today, are excellent.

There are several important reasons to pursue the living donor, but the risk to the donor is ever-present. The reasons are prompt early function by the graft, which I think in turn provides better long-term graft survival, and, very importantly, the elective date of the transplant. The elective date of the transplant implies that one can preempt dialysis, perform transplantation prior to end-stage renal disease, and avoid a prolonged morbidity that occurs with chronic dialysis. I think that part of the excellent results obtained from the living unrelated donor is the opportunity to start either FK-506 or cyclosporine early in the post-transplant course and avoid nephrotoxicity.

Until the use of xenografts become a practical reality, transplant surgeons will continue to search for organs. Some of them will be living unrelated donors, some will be related donors, some will be distant relatives, and some will be what is called a marginal donor. What is marginal to one surgeon may not be marginal to another.

Now, a final comment about the problem of organ shortage. It is not unique in our country. It is unique the world over. It is really not a scientific problem. And I do not believe it is one of culture. I think it is one of education. And times are improving, but very, very slowly.

Some progress has been achieved, and certainly the Wisconsin group is one of the leaders in terms of organ procurement per million people. But until we have either the xenograft or some other major solution to the organ shortage, we will continue to look for the marginal donor, the living unrelated donor, and close relatives.

The excellent results presented today must be taken in con-

cert with the risk that always involves the living donor. We have done a thousand living donors, somewhat more. We have not had a mortality. But we may have one tomorrow. We may have two next week. And some day, it will happen. I believe it is important that the transplant surgeon never take for granted the generosity of the living donor.

DR. THOMAS E. STARZL (Pittsburgh, Pennsylvania): Thank you for this marvelous paper, which is the distillation of the very well-invested professional life of Fred Belzer, whose contributions have been almost too vast to justify very much discussion. I saw Joe Murray here today. One can only imagine the warm feeling that he must have in realizing where those anxious days and agonizing minutes he spent 35 years ago have led.

I really only have one comment, and one question. The comment concerns the living volunteer donor. I am looking forward to the study of the donors, which Dr. D'Alessandro told me privately was impending. The risks surrounding the operation are small, but the question of risk during the rest of their lives has never been resolved. We had a large experience with living donors more than a third of a century ago at the University of Colorado. The first 64 were tracked down in 1988 and 1989, more than a quarter of a century later (Transplant Proc 1990; 22:2361–2365). Two disquieting suicides had occurred for which no one had a satisfactory explanation, and a third donor had just entered dialysis. We assiduously follow the recipients, but usually not the donors, in whom the lifetime liability of nephrectomy, if any, remains to be defined.

My question concerns a present-day problem about which Dr. Gill Diethelm has written extensively—questioning the justice of HLA matching as a determinant of organ allocation. The results presented by Dr. D'Alessandro showed a significant advantage with the use of perfectly matched donors, which already was evident within 5 years. These were almost all sibling donors. Except for these cases, there was no advantage out to 8 years with various lesser degrees of matching. This was particularly striking in the equivalent results using half matched (three of six antigens, usually parents) donors *versus* completely mismatched, nonrelated donors. The implication, of course, is that except when there is a perfect HLA conformity, matching does not count.

If matching does not count except when it is perfect, a social injustice has been institutionalized by using lesser degrees of matching to determine who receives the organs as a national policy. The impact is most adverse on the minorities, as Diethelm's group have pointed out (Gaston et al. JAMA 1993; 270: 1352–1356).

These niggling comments are not criticisms, but expressions of admiration. My main reason for coming up here is to pay tribute to our companion and colleague, who was too ill to come today. Fred Belzer has always been a gentleman and a scholar. Some might debate which is the more important. Personally, I will take the gentleman over the scholar, but of course scholarship was what underwrote the Gold Medal that was officially bestowed on Fred Belzer this morning. Because Fred was not present, the ceremony was largely for the benefit of the society members.

I was in Wisconsin, in Madison, a little more than a month ago, just before President Sheldon's visit there. I learned as Eric Belzer told us this morning, that this recognition was the greatest thrill of Fred Belzer's life. It seems to me that the way it was given provided one of the golden moments in the history of this great surgical society. I can only commend our leadership for having gone to Fred's home, so far from theirs, to present the medal in person.

DR. JOHN S. NAJARIAN (Minneapolis, Minnesota): I also rise, as did Tom Starzl, to honor our colleague Folkert Belzer for his well-deserved award for scientific merit in the field of transplantation. In particular, his contribution to the development of organ preservation has been seminal.

This paper is another illustration of the kind of work that Fred has accomplished at Madison. He has developed a department and a transplant unit second to none. He started with practically nothing and built his center into one of the most productive, one of the busiest, and one of the most scholarly in the world. Many advances have been added to our transplantation armamentarium as a result of Fred's work, as clearly shown, once again, in today's paper.

I had the pleasure of having Fred as a student and colleague at the University of California in San Francisco when Bert Dunphy recruited him to that institution. At that time, Bert felt transplantation was an area in which Fred could contribute. As Fred and I spent time in the lab together, it became apparent that his major talents could be best directed toward organ preservation.

The effort he expended in developing preservation was a giant step forward in organ transplantation—the primary contribution that resulted in his award.

This paper today emphasizes living donor transplantation, which our transplant group at Minnesota has advocated for the past 28 years. But it was the Wisconsin group that, 13 years ago, recommended using living unrelated donors as well. Today you can see the wonderful fruits of that labor.

This paper also underlines that nondiabetic recipients do better than diabetic recipients. It also emphasizes that living related donors work better than cadaver donors. As Gil Diethelm has admonished, we as transplant surgeons must have a special covenant with living donors because of their very precious gift. At Minnesota, we have now done well over 2000 living related kidney transplants without a single fatality or major complication. I hope that record continues, but it could end, even tomorrow, as Gil warned.

This paper also indicates that HLA-identical donors work better than haploidentical donors and that there is no difference between haploidentical and those mismatched to the recipient. And yes, it is true that typing does not seem to affect recipient survival if the donor was less than an ideal match—whether an HLA-identical or a six-antigen match cadaver donor.

Why did the living unrelated recipients described in this paper do as well as the living related haploidentical recipients? Compared with HLA-matched cadaver donor grafts, the unrelated living donor grafts fared much better.

The reason for this finding puzzled us, so we examined our own clinical experience with cadaver kidney donors (presented last year at the American Society of Transplant Surgeons meeting).

We found that if the cadaver kidney functions immediately, it does much better than if post-transplant function is delayed. With early good-quality function and a fall in the serum creatinine below 3 mg percent within the first 3 days, long-term graft survival was excellent, compared with grafts with delayed function. What this really says to us is that a good-quality kidney is far better and far more important than any graft that is less than a perfect tissue match.

One final question: This paper showed improved results in diabetic recipient survival from the precyclosporine era to the postcyclosporine era—but not in graft survival. What are your thoughts on this finding?

DR. ANTHONY M. D'ALESSANDRO (Closing Discussion): I would like to thank Dr. Diethelm, Dr. Starzl, and Dr. Najarian for their kind remarks, particularly in reference to Dr. Belzer.

As regards Dr. Najarian's comment, and Dr. Diethelm's, on living unrelated transplants, we agree that a good functioning kidney early on is extremely important. That has been shown by Dr. Najarian, as well as in some of Dr. Terasaki's data, that a kidney that functions immediately has a better long-term survival.

We have discussed the importance of excellent immediate function and donor-specific transfusions, and have decided to eliminate donor-specific transfusions in living unrelated and mismatched renal transplants. Our belief is that it is primarily the excellent immediate function that is the most important in the post-transplant period.

I would also like to echo the discussants' comments on the risk to the living donor. Due to the nature of these procedures, every living related transplant and donor nephrectomy at the University of Wisconsin is done by a staff transplant surgeon and staff urologist.

I would like to respond to Dr. Starzl's comment on the very important long-term study of donors. We have a wonderful opportunity with this many donors to truly study more than just the immediate postoperative problems. I know Dr. Najarian has done a study of long-term donors and has found no risk to long-term renal function. But Dr. Starzl does point out that things happen to donors that may or may not be related to the procedure. Perhaps I can come back at a future time and present this donor study.

Also, an important fact that came out of this study is that unless you have a perfect match, matching is not important. This is especially important when allocation systems are being directed by such matching. We have found in our cadaveric transplant recipients that if we match one or two of the DR loci we can achieve survival similar to our haplo-identical survivals.

I believe, as do others, that if there were enough cadaveric kidneys, many of us would certainly choose them over related transplants. Unfortunately, recent history has shown that we will not be able to bridge this gap unless there are major breakthroughs in preventing graft loss or in xenografting.