Renal Transplantation in the Highly Sensitized Patient: The Role of Thoracic Duct Drainage, Plasmapheresis, and Staph A Immunodepletion

R. Shapiro and T. E. Starzl

Department of Surgery, University Health Center, University of Pittsburgh, and Veterans Administration Medical Center, Pittsburgh, Pennsylvania, U.S.A.

Renal transplantation has had a significant impact on many patients with end-stage renal disease. Unfortunately, there exists a large subgroup of dialysis patients who for immunological reasons cannot be transplanted (1). These patients have become sensitized to most or all HLA antigens from previous transplants, blood transfusions, or multiple pregnancies. They react strongly to all kidneys that become available and can spend years on transplant waiting lists. The example of the waiting list at the University of Pittsburgh illustrates the problem (Table 1). Over one third of the patients on the list have a panel reactive antibody (PRA) level of greater than 80%, and over half have a PRA greater than 40%. Furthermore, when these patients are finally transplanted, their graft survival rate is inferior to that of low PRA patients (2) (Fig. 1). Thus, the problem of the highly sensitized patient represents a significant impediment to progress in renal transplantation.

The present approach to these patients involves waiting for a kidney with a negative crossmatch. Aggressive immunosuppression with cyclosporine, azathioprine, and prednisone and usually with an antilymphocyte preparation can improve results to a 1 year graft survival rate of 75% (2) (Fig. 2). Unfortunately, relatively few patients can be treated in this manner. Only 15% of the patients that are transplanted at the authors' center have a PRA greater than 40%, and this figure is a result of an allocation policy designed to give priority to sensitized patients (3) (Table 2).

A more effective technique of transplanting the sensitized patient must involve some mechanism of lowering the antibody level and maintaining it at a low level. In this regard, there are a few potentially useful techniques. One is thoracic duct drainage (TDD), which has had a long history in renal transplantation and which may have new applications because of recent technical developments. Another is plasmapheresis, which has been somewhat controversial. Finally, there is Staph A immunodepletion, which is currently in an early stage of development but which may become an important tool in the near future. This paper discusses

TABLE 1. *University of Pittsburgh kidney transplantation waiting list, April 1989*

Panel reactive antibody level	<40	40–80	>80
Patients (number)	47 (48%)	15 (16%)	35 (36%)

the development of and the experience with these three techniques and their application to renal transplantation in sensitized patients.

Thoracic Duct Drainage

Experimental studies in the early 1960's demonstrated that chronic TDD led to a diminution of the primary antibody response in rats (4). In a rat skin graft model, pretreatment with TDD was associated with prolongation of graft survival; an interaction with an anti-lymphocyte preparation was also noted (5,6) (Table 3). A similar effect was seen in a canine renal allograft model (7).

The first clinical use of TDD as pretreatment for renal transplantation was reported in 1964 by Franksson, who performed a successful living-related donor kidney transplant from father to son after 3 to 4 days of preoperative TDD (8). Subsequent work by Franksson et al. in Sweden has included over 50 patients

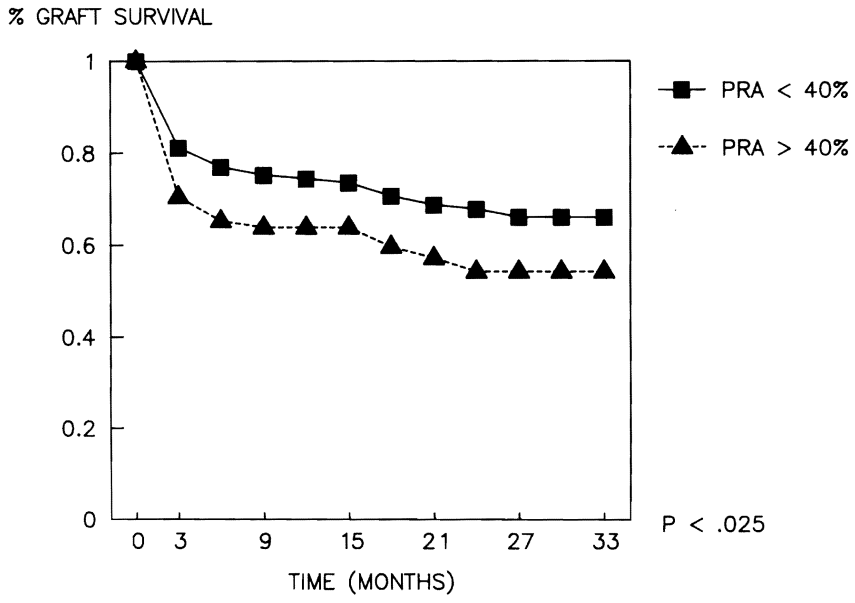

FIG. 1. Kidney transplantation: actuarial graft survival for high and low panel reactive antibody (PRA) patients.

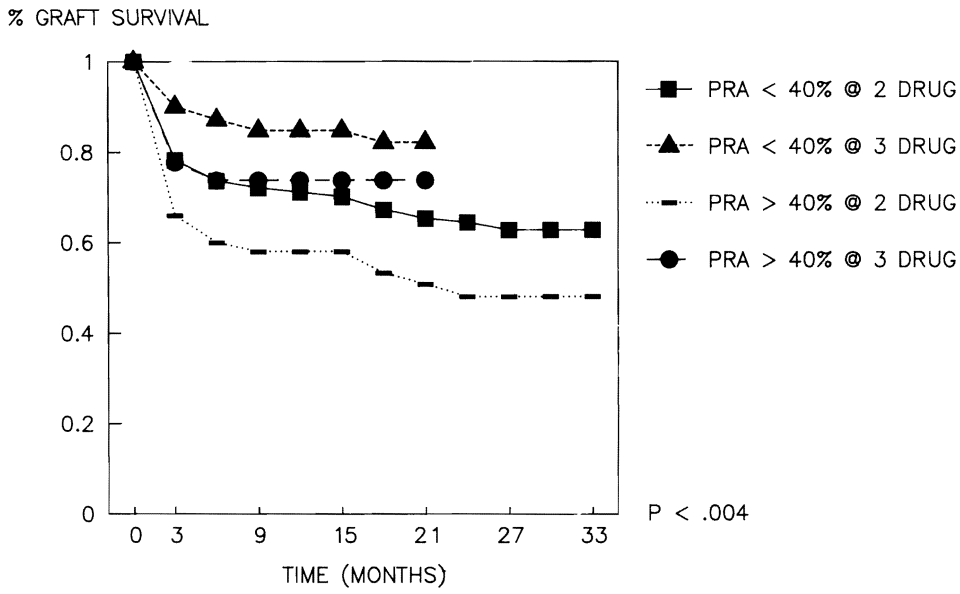

FIG. 2. Kidney transplantation: actuarial graft survival for high and low panel reactive antibody (PRA) patients with 3-drug and 2-drug immunosuppression.

(9,10). Most of the patients had TDD started during the first week after transplantation. Just under half of the patients also underwent thymectomy; some patients received anti-lymphocyte globulin as well. The results in living donor transplants showed no advantage, with excellent graft survival both in patients who had or did not have TDD (Table 4). However, in cadaver transplantation, 1 year graft survival was significantly improved in patients who were treated with TDD. The length of time of TDD also seemed to be important. Graft survival was significantly better in patients who had 30 days or more of TDD com-

TABLE 2. *Equitable allocation of organs—recipient selection factors*

Point system
Waiting time
HLA antigen matching
PRA
Medical urgency
Logistical factors

TABLE 3. *Skin graft survival in rats*

Treatment	Mean graft survival (days)	Fall in lymphocyte count (%)
Control	8	—
Thoracic duct drainage	13	50
Thoracic duct drainage + anti-lymphocyte preparation	35	90

Reprinted by permission from *Nature,* Vol. 200, p.702. Copyright © 1963, Macmillan Magazines Ltd.

TABLE 4. *One year actuarial graft survival*

	TDD + (%)	TDD − (%)
Living-related donor	84	84
Cadaver	72	47
$p < 0.05$		

Reproduced, with permission, from Franksson C, Lungre G, Magnusson G, Ringden O. Drainage of thoracic duct lymph in renal transplant patients. *Transplantation* 1976;21:133–40.

pared to those patients with less than 30 days of treatment (Table 5). The effects of TDD on the immune system included a significant depletion of lymphocytes from both lymph nodes and the peripheral blood although the latter effect was only noted after 2 to 3 weeks. Furthermore, serum immunoglobulin levels were seen to fall as well. Delayed hypersensitivity, as determined by the PPD skin test, also disappeared.

The group at the Peter Bent Brigham Hospital in Boston accumulated expe-

TABLE 5. *Actuarial graft survival*

	1 year (%)	2 years (%)
TDD $\geq$ 30 days	85	85
TDD $\leq$ 30 days	63	50
$p < 0.01$		

Reproduced, with permission, from Franksson C, Lungre G, Magnusson G, Ringden O. Drainage of thoracic duct lymph in renal transplant patients. *Transplantation* 1976;21:133–40.

rience with 22 cases of successful TDD in living-related donor transplants (11–13). Patients were treated with TDD before transplantation for an average of 16 days in the successfully treated group. The investigators found improved long-term patient and graft survival in the treated group (Table 6).

In Texas, the group at Galveston treated 14 patients with TDD prior to cadaveric renal transplantation (14). They also found lymphocyte depletion in lymph nodes as well as in the spleen and the intestine. Delayed hypersensitivity was also diminished although changes in the serum immunoglobulin levels were not apparent. These patients were not treated with additional immunosuppression initially; 8 patients had good long-term graft survival.

The group at Vanderbilt University in Tennessee used TDD for 3 to 4 weeks as a pretreatment for cadaver renal transplantation (15,16). When a battery of immunological tests including skin testing, mixed lymphocyte culture, cell-mediated lympholysis assays, absolute lymphocyte counts, and T-cell rosetting demonstrated a diminution of the immune response, the patients were transplanted with no attempt at HLA matching. Thoracic duct drainage led to significant improvement in 1 year graft survival although there was no difference in patient survival (Table 7).

In Denver, TDD before or after cadaver renal transplantation was performed in 83 patients between April 1978 and December 1979 (17–22). The initial reports were enthusiastic. Problems of prolonged fistula patency and infections

TABLE 6. *Survival rates following living-related renal donor transplants*

	Patient (%)	Graft (%)
TDD	73	73
Attempted TDD	50	50
No TDD	42	27

Reproduced, with permission, from Tilney NL, Atkinson JC, Murray JE. The immunosuppressive effect of thoracic duct drainage in human kidney transplantation. *Ann Intern Med* 1970;72:59–64.

TABLE 7. *One-year actuarial survival after cadaveric renal transplantation*

	Patient (%)	Graft (%)
TDD +	83	76
TDD −	88	48

Reproduced, with permission, from Johnson HK, Niblack GD, Tallent MB, Richie RE. Immunologic preparation for cadaver renal transplant by thoracic duct drainage. *Transplant Proc* 1977;9:1499–1503.

related to TDD were not major issues. Most of the patients were transplanted before the cyclosporine era, and excellent results were noted. Particular emphasis was given to prolonged pretreatment because these patients had the greatest benefit. The investigators' final paper, in which 1 year or more follow-up was available on all 83 patients, represents a good summary of the results. The best outcome was in patients who had 4 or more weeks of pretreatment with TDD: the 1 year graft survival rate was 73%. Patients with less than 4 weeks' pretreatment had a 1-year graft survival rate of 67% although that figure included 2 patients who were expected to lose their grafts, and the expectation was of an approximate graft survival rate of 50%. This latter figure was not substantially different from that of patients who had TDD started at the time of transplantation or those who did not undergo TDD at all (Fig. 3).

Other early reports from around the world showed less impressive results (23–26). With the exception of the experience in Nagoya, Japan, where excellent results have been obtained in living-related transplants (27–30) (Table 8), TDD has been largely abandoned throughout the world. There are several reasons for this. First, the TDD technique is not simple. Technical complications precluded its use in 20 to 50% of the cases even in experienced centers (10,12). Prolonged expensive hospitalization was required, infectious problems and even deaths occurred. Thus, TDD was difficult, complicated, and expensive. Second, in spite of the good immunosuppressive effect of TDD, follow-up with the best immunosuppressive protocols of that era, namely azathioprine, prednisone, and antilymphocyte globulin, was insufficient to prevent late graft loss (22). Finally, the advent of cyclosporine, changing as it did the entire fabric of transplantation, rendered TDD superfluous. With the early results of 80 to 90% 1 year graft survival rates in the pioneering studies of cyclosporine in renal transplantation

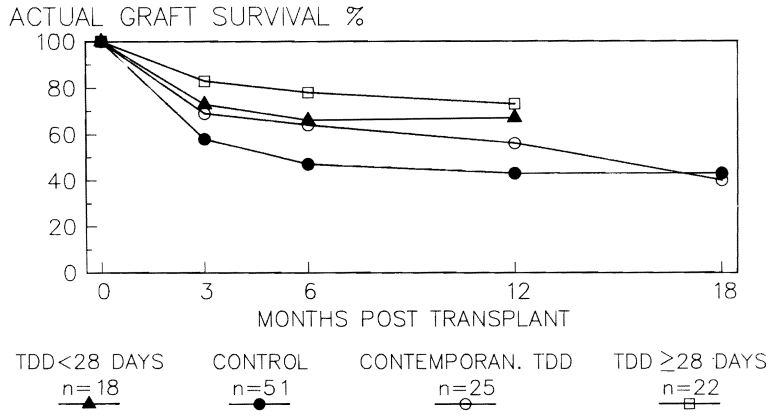

FIG. 3. Effect of thoracic duct drainage (TDD) on graft survival in primary cadaveric kidney transplantation, (Reprinted, with permission, from *Surgery, Gynecology & Obstetrics* 1981;153:377–82).

TABLE 8. *One-year survival rates after living-related donor renal transplantation*

	Patient (%)	Graft (%)
TDD + cyclosporine	87	87
TDD + azathioprine	98	95

Reproduced, with permission, from Ohshima S, Ono Y, Kinukawa T, Matsuura O, Takeuchi N, Hattori R. The long-term results of thoracic duct drainage in living related kidney transplantation. *Transplant Proc* 1989;21:1972–3.

(31) and the improved results in extrarenal transplantation (32), TDD was no longer needed for routine immunosuppression.

The question remains whether there is a subset of patients in the cyclosporine era that would benefit from TDD. The most popular immunosuppressive protocols utilize triple drug or sequential 4 drug regimens and are associated with 88% 1 year graft survival in first transplants. However, the group of sensitized patients remains more problematic. In this regard, the ability of TDD to deplete serum immunoglobulin may be important. Prolonged pretreatment with TDD might reduce the anti-HLA antibody levels to the point that sensitized patients would be able to undergo transplantation. The recent development of a new filter that can be adapted to TDD and utilized in a closed system may well simplify the procedure. At present, an experimental trial of this filter in the laboratory is being planned. If successful, a clinical trial in sensitized patients will be considered.

Plasmapheresis

Plasma exchange has been used in two different contexts in renal transplantation. It has been used to remove anti-HLA antibodies as a pretreatment for transplantation, and it has also been utilized to treat humoral or antibody-mediated rejection.

The pretreatment model has combined antibody reduction by plasmapheresis with immunosuppression to prevent antibody resynthesis. A specific anti-B cell agent, cyclophosphamide, was used in combination with azathioprine and prednisolone. This work was done by Taube and his colleagues in London (33,34). They reported on 5 highly sensitized patients who were successfully transplanted. At least 1 of the patients was treated postoperatively with plasma exchange to combat a humoral rejection. There was 1 episode of severe sepsis leading to death in this group; this fact may have had some role in the abandonment of the trial. However, the technique did seem to be effective.

In contrast, the use of plasma exchange to treat rejection has been less successful. Although some writers have reported successful reversal of rejection (35–37), many have seen no benefit whatsoever and have pronounced it to be useless or worse (38). One of the first reports, by Cardella and his group in

Toronto, describes successful reversal of rejection in 5 of 7 episodes with successful engraftment in 3 of 5 patients (35) (Table 9). Another study, by Naik et al. in England (36), describes favorable responses in 4 of 5 cases of rejection with 2 patients having good long-term graft survival.

A controlled trial of plasmapheresis as a treatment for rejection, comparing plasmapheresis and steroids with steroids alone, showed that there was no benefit to plasma exchange (38) (Table 10). It should be noted that the steroid-only group received an average of 900 mg more intravenous steroid than the plasmapheresis-steroid group (2.1 vs. 1.2 g). Another study from Australia looked at 7 cases of rejection treated with plasmapheresis, with no patients having long-term graft survival (39). Thus, at best, plasmapheresis has been associated with improved graft survival in a minority of cases; at worst, it has demonstrated no benefits.

The disadvantages of plasmapheresis also include its expense and the need for transfusion with fresh frozen plasma. These issues, combined with the questionable benefits, have led to the near abandonment of plasma exchange in renal transplantation. However, there is some very preliminary evidence that there is a role for plasma exchange in the management of liver transplant patients in the

TABLE 9. *Use of plasma exchange to reverse renal transplant rejection*

	Rejection episodes (number)
Reversed	5
Not reversed	2
	Grafts (number)
Functioning	3
Lost	2

Reproduced, with permission, from Cardella CJ, Sutton D, Uldall PR, DeVeber GA. Intensive plasma exchange and renal transplant rejection. *Lancet* 1977;1:264.

TABLE 10. *Use of plasmapheresis and steroids in treatment of renal allograft rejection*

	Plasma exchange + steroids	Steroids only
Graft funtioning	3	6
Graft lost	8	3

Reproduced, with permission, from Kirubakaran MG, Disney APS, Norman J, Pugsley DJ, Mathew TH. Trial of plasmapheresis in the treatment of renal allograft rejection. *Transplantation* 1981;32:164–5.

early postoperative period. This work, which is still in the early stages of evaluation in Pittsburgh, has used plasmapheresis to treat patients with early nonfunctioning grafts (40). It is unclear whether the benefit is in supporting patients with livers that have suffered severe but reversible ischemic damage, or whether there is a component of humoral rejection that is being treated. What is clear is that there are several patients in whom at the very least the need for urgent retransplantation has been avoided by the use of plasma exchange.

Staph A Immunodepletion

A relatively new development that deals directly with the antibody problem utilizes the ability of the *Staphylococcus aureus* protein A to bind the Fc receptor of IgG (41). Although this observation is not new, it has recently become possible to attach protein A to a cyanogenbromide-activated sepharose and to manufacture a column of bound protein A (Immunosorba-Excorim, DuPont). A computer controlled device, the Citem-10, which can control the flow of plasma and other solutions across the Staph A column, has been developed. A source of plasma from a standard plasmapheresis unit is linked in series with the Citem-10, which contains two Staph A columns in parallel. As plasma passes over 1 column, the IgG is adsorbed. Low pH citrate is used to elute the adsorbed antibody as plasma is passed over the other Staph A column. Cycles of adsorption and elution are alternated every 10 min. The immunodepleted plasma is returned with the plasmapheresed red blood cells to the patient; because only the antibody is removed, transfusion of blood products is not necessary. It is possible to deplete serum IgG levels by 75 to 90% with a single treatment of 2 to 3 plasma volumes (42). Thus, Staph A immunodepletion can be used to reduce the level of anti-HLA antibodies in sensitized dialysis patients.

While potentially exciting, the development of this new technology is not by itself the entire solution. Overnight rebound of IgG levels occurs initially, presumably secondary to reequilibration from the interstitium (42). Furthermore, as the antibody levels fall, the immune system compensates by resynthesizing IgG. Thus, Staph A immunodepletion must be combined with effective immunosuppression to maintain a low antibody titer. The most common regimen has utilized cyclophosphamide and steroids.

In Europe, about 30 dialysis patients have been treated with Staph A immunodepletion (43). Five patients have withdrawn from the study, but only 1 was for a treatment-related problem, namely a reaction to citrate. Seventeen patients underwent transplantation; in 14 cases the pre-immunodepletion serum crossmatch was positive. Ten of these 14 transplants were successful.

Taube et al. recently published their experience with their first 10 patients treated with immunodepletion (44,45). One patient withdrew because of an unrelated cause, a myocardial infarction, 1 month after treatment. Seven patients received transplants, and no kidneys were lost to hyperacute rejection although 1 graft was lost to chronic rejection at 1 year and 1 graft never functioned.

In the United States, a multicenter trial of Staph A immunodepletion is being conducted at several university medical centers; currently, no patients have undergone transplantation. While the outcome is still unknown, the development of this new technology promises to be interesting and may have important implications for the large number of sensitized patients on transplant waiting lists.

Conclusion

This paper has focused on solutions to the problem of renal transplantation in highly sensitized patients. The history of TDD has been presented, and its potential application in this patient population has been described. The use of plasma exchange has been discussed, mainly to emphasize its lack of utility in renal transplantation although its application in certain cases of liver transplantation may prove to be lifesaving. Finally, the new technology of Staph A immunodepletion and its clinical application, which is still developmental, has been presented. What is clear is that a solution to the problem of the sensitized patient will require the ability to deal with the high levels of preformed antibodies. One or more of the techniques described here may well be used to solve this difficult clinical and immunological problem.

Acknowledgment

This work was supported by research grants from the Veterans Administration and Project Grant No. DK 29961 from the National Institutes of Health, Bethesda, Maryland, U.S.A.

References

1. Ting A. In: Morris PJ, ed. *Kidney transplantation, principles and practice*. 3rd ed. Philadelphia: W.B. Saunders Company, 1988;183–213.
2. Shapiro R, Tzakis AG, Hakala TR, Lopatin W, Mitchell S, Koneru B, Steiber A, Gordon RD, Starzl TE. Cadaveric renal transplantation at the University of Pittsburgh: a two and one half year experience with the point system. *Clin Transplant* 1988:181–87.
3. Starzl TE, Hakala T, Tzakis A, Gordon R, Stieber A, Makowka L, Klinoski J, Bahnson H. A multifactorial system for equitable selection of cadaveric kidney recipients. *JAMA* 1987;257:3073–5.
4. McGregor DD, Gowans JL. The antibody response of rats depleted of lymphocytes by chronic drainage from the thoracic duct. *J Exp Med* 1963;117:303–20.
5. Woodruff MFA, Anderson NA. Effect of lymphocyte depletion by duct fistula and administration of antilymphocytic serum on the survival of skin homografts in rats. *Nature* 1963;200:702.
6. McGregor DD, Gowans JL. Survival of homografts of skin in rats depleted of lymphocytes by chronic drainage from the thoracic duct. *Lancet* 1964;1:629–32.
7. Singh LM, Vega ER, Makin GS, Howard JM. External thoracic duct fistula and canine renal homograft. *JAMA* 1965;191:1009–11.
8. Franksson C. Letter to the editor. Survival of homografts of skin in rats depleted of lymphocytes by chronic drainage from the thoracic duct. *Lancet* 1964;1:1331–2.
9. Franksson C, Blomstrand R. Drainage of the thoracic lymph duct during homologous kidney transplantation in man. *Scand J Urol Nephrol* 1967;1:123–31.

10. Franksson C, Lungre G, Magnusson G, Ringden O. Drainage of thoracic duct lymph in renal transplant patients. *Transplantation* 1976;21:133–40.
11. Tilney NL, Murray JE. Chronic thoracic duct fistula: operative technic and physiologic effects in man. *Ann Surg* 1968;167:1–8.
12. Murray JE, Wilson RE, Tilney NL, Merrill JP, Cooper WC, Birtch AG, Carpenter CB, Hager EB, Dammin GJ, Harrison JH. Five years' experience in renal transplantation with immunosuppressive drugs: survival, function, complications, and the role of lymphocyte depletion by thoracic duct fistula. *Ann Surg* 1968;168:416–35.
13. Tilney NL, Atkinson JC, Murray JE. The immunosuppressive effect of thoracic duct drainage in human kidney transplantation. *Ann Intern Med* 1970;72:59–64.
14. Sarles HE, Remmers Jr AR, Fish JC, Canales CO, Thomas FD, Tyson KR, Beathard GA, Ritzmann SE. Depletion of lymphocytes for the protection of renal allografts. *Arch Intern Med* 1970;125:443–50.
15. Walker WE, Niblack GD, Richie RE, Johnson HK, Tallent MB. Use of thoracic duct drainage in human renal transplantation. *Surg Forum* 1977;28:316–17.
16. Johnson HK, Niblack GD, Tallent MB, Richie RE. Immunologic preparation for cadaver renal transplant by thoracic duct drainage. *Transplantation Proc* 1977;9:1499–1503.
17. Starzl TE, Koep LJ, Weill III R, Halgrimson CG, Franks JJ. Thoracic duct drainage in organ transplantation: will it permit better immunosuppression? *Transplantation Proc* 1979;11:276–84.
18. Starzl TE, Weill III R, Koep LJ, McCalmon RT, Terasaki PI, Iwaki Y, Schroter GPJ, Franks JJ, Subryan BS, Halgrimson CG. Thoracic duct fistula and renal transplantation. *Ann Surg* 1979;190:474–86.
19. Koep LJ, Weill III R, Starzl TE. The technique of prolonged thoracic duct drainage in transplantation. *Surg Gynecol Obstet* 1980;151:61–4.
20. Starzl TE, Weill III R, Koep LJ, Iwaki Y, Teraski PI, Schroter PJ. Thoracic duct drainage before and after cadaveric kidney transplantation. *Surg Gynecol Obstet* 1979;149:815–21.
21. Starzl TE, Weill III R, Koep LJ. The pretreatment principle in renal transplantation as illustrated by thoracic duct drainage. Presented in part at the Dialysis and Kidney Transplantation 25th Anniversary Celebration, Boston, Massachusetts, September 15, 1979.
22. Starzl TE, Klintmalm GBG, Iwatsuki S, Schroter G, Weill III R. Late follow-up after thoracic duct drainage in cadaveric renal transplantation. *Surg Gynecol Obstet* 1981;153:377–82.
23. Martelli A, Bonomini V. In: Bertelli A, Monaco AP, eds. *Pharmacological treatment in organ and tissue transplantation*. Baltimore: Williams & Wilkins, 1970; 140.
24. Archimbaud JP, Banssillon VG, Bernhardt JP et al. *J Chir (Paris)* 1969;98:211.
25. Sonoda T, Takaha M, Kusunoki T. Prolonged thoracic duct lymph drainage. Application for human renal homotransplantation. *Arch Surg* 1966;93:831–3.
26. Ianhez LE, Verginelli G, Sabbaga E et al. *Rev Bras Pesqui Med Biol* 1974;7:265.
27. Ono Y, Ohshima S, Kinukawa T et al. *Transplant Proc* 1986;19:1985.
28. Ohshima S, Ono Y, Fujita T et al. *J Urol* 1987;138:33 190:474.
29. Ohshima S, Ono Y, Kinukawa T et al. *Transplant Proc* 1988;20:415.
30. Ohshima S, Ono Y, Kinukawa T, Matsuura O, Takeuchi N, Hattori R. The long-term results of thoracic duct drainage in living related kidney transplantation. *Transplantation Proc* 1989;21:1972–3.
31. Starzl TE, Klintmalm GBG, Weil R III, Porter KA, Iwatsuki S, Schroter GPJ, Fer-

nandez-Bueno C, MacHugh N. Cyclosporin A and steroid therapy in sixty-six cadaver kidney recipients. *Surg Gynecol Obstet* 1981;153:486–94.
32. Starzl TE, Klintmalm GBG, Porter KA, Iwatsuki S, Schroter GPJ. Liver transplantation with use of cyclosporin A and prednisone. *N Engl J Med* 1981;305:266–9.
33. Taube DH, Welsh KI, Kennedy LA et al. Successful removal and prevention of re-synthesis of anti-HLA antibody. *Transplantation* 1984;37:254–5.
34. Taube DH, Cameron JS, Ogg CS, Welsh KI et al. Renal transplantation after removal and prevention of resynthesis of HLA antibodies. *Lancet* 1984;1:824–6.
35. Cardella CJ, Sutton D, Uldall PR, DeVeber GA. Intensive plasma exchange and renal-transplant rejection. *Lancet* 1977;1:264.
36. Naik RB, Ashlin R, Wilson C, Smith DS, Lee HA, Slapak M. The role of plasmapheresis in renal transplantation. *Clin Nephrol* 1979;5:245–50.
37. Rifle G, Chalopin JM, Turc JM, Guigner P et al. Plasmapheresis in the treatment of renal allograft rejections. *Transplant Proc* 1979;11:20–6.
38. Kirubakaran MG, Disney APS, Norman J, Pugsley DJ, Mathew TH. Trial of plasmapheresis in the treatment of renal allograft rejection. *Transplantation* 1981;32:164–5.
39. Power D, Nichols A, Muirhead N, MacLeod AM, Engeset J, Catto G et al. Plasma exchange in acute renal allograft rejection: is a controlled trial really necessary? *Transplantation* 1981;32:162–3.
40. Teperman L. Personal communication.
41. Forsgren A, Sjoguist J. "Protein A" from *S. aureus*. *J Immunol* 1966;97:822–7.
42. Shapiro R, Tzakis AG, Scantlebury AG, Makowka L, Watt R, Oks A, Yanaga K, Podesta L, Casavilla A, Wos S, Murray J, Oral A, D'Andrea P, Banner B, Starzl TE. Immunodepletion in xenotransplantation. *J Invest Surg* (in press).
43. Gjorstrup P et al. Presentation given at a conference on immunoadsorption sponsored by E.I. DuPont de Nemours and Company, September 1988.
44. Palmer A, Taube D, Welsh K, Bewick M, Gjorstrup P, Thick M. Removal of anti-HLA antibodies: preliminary clinical experience. *Transplant Proc* 1987;19:3750–1.
45. Palmer A, Taube B, Welsh K, Bewick M, Gjorstrup P, Thick M. Removal of anti-HLA antibodies by extracorporeal immunoadsorption to enable renal transplantation. *Lancet* 1989;1:10–12.