RENAL HOMOTRANSPLANTATION IN IDENTICAL TWINS*

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with comments by

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This is a report of the successful kidney transplantation from one identical twin to another with good renal function persisting after 9 months.

Previous attempts at renal homotransplantation both clinically and experimentally had been unsuccessful, with the one exception between di-zygotic bovine twins in which a kidney transplant has survived and functioned for over a year. Success in that instance presumably resulted from the production of an acquired mutual tolerance to each other’s tissues by the mingling of fraternal protein in the common placental circulation.1 In all other instances, failure of the transplanted kidney occurs by what appears to be an immune, or “antigen-antibody-like,” reaction between donor tissue and recipient. The microscopic pattern of the rejected kidney indicates that the homograft itself is actively reacting against the recipient to a greater degree than had been suspected by earlier investigators.2,3

Transplantation of kidneys in dogs rarely maintain function for more than 10 to 14 days in spite of vigorous attempts to alter the rejection response.4,5,6 Although human renal homotransplants have functioned for a longer period of time, I for as long as 51/2 months, permanent survival has not occurred and the clinical and microscopic pattern of rejection is similar to that in the experimental animal.7

There are, however, several experimental observations which made success between identical twins seem likely and justified the removal of a normal kidney from a healthy donor. (1) Immunologic and genetic similarity apparently accounts for the permanent survival of skin homografts between identical twins.8 (2) When skin or kidney homografts are carried out between antigenically dissimilar individuals the early function and the histological picture of rejection of each appear similar.9 (3) Skin and kidney homografts possess a common antigen which can sensitize a recipient to a subsequent homograft of either tissue from the same donor.10 This further suggests that skin and kidney grafts might behave similarly. (4) We had established to our own satisfaction that renal autografts had normal function indefinitely in animals. This observation is important because pre-supposing initial success of the transplant between antigenically similar (identical) twins, a second problem to be weighed was the permanency of such function.

Lacking reported instances of adequate functional studies in long term renal autografts we observed in our own experiments that permanently successful function of a single life-sustaining renal autograft resulted from the use of a recipient site which allows direct implantation of the ureter into the bladder, which...
has a normal thermal environment, and which permits gravity drainage from the renal pelvis to the bladder.

This laboratory technique proved adaptable for use in man provided that the left kidney is placed into the right iliac area, or the right kidney into the left iliac fossa, thus reversing the normal anteroposterior relationship of the artery, vein and ureter.

The natural site for the homograft, the renal fossa, has 2 disadvantages. First it requires simultaneous nephrectomy thus increasing the magnitude of the operation. Secondly, it necessitates an uretero-ureteral anastomosis with the possibility of subsequent stricture formation, because the length of transplanted ureter vascularized via the renal pedicle is too short to reach the bladder.

The upper thigh, the site of the 13 previous homotransplants, was not used because it requires a skin ureterostomy, with the possibility of subsequent ascending infection. In addition it creates a problem in the collection of urine.

The selected site retroperitoneally within the pelvis utilizing the iliac vessels allows implantation of the short ureteral segment directly into the bladder and places the kidney on its natural thermal environment. Furthermore gravity drainage of the renal pelvis and the ureter approaches normal physiological conditions.

**History and Physical Examination.** Richard H., a 24 year old white single male, was apparently well until August 1953, when he noticed some puffiness about the eyes and on a routine physical examination elevation of blood pressure was noted. Several months’ study at another hospital revealed an elevated blood pressure and a persistent 2 to 3+ proteinuria, a fixed specific gravity of the urine at 1.010, with red cell casts. PSP excretion was less than 1 per cent in 2 hours and an intravenous pyelogram revealed no dye excretion on either side. In the following months he became chronically ill. The blood pressure was 180/120, with hypertensive retinal changes. The blood urea nitrogen was 185 mg. per cent. He required maintenance on intravenous infusions and became increasingly drowsy, disoriented, and irritable and had several generalized convulsions. Since the patient had a twin brother, Ronald, it was suggested, and irritable and had several generalized convulsions. Since the patient had a twin brother, Ronald, it was suggested by Dr. David C. Miller of the Public Health Service that the possibility of homotransplantation of a kidney should be considered. For the investigation of this possibility he was transferred to the Peter Bent Brigham Hospital on October 26, 1954.

On admission, the patient appeared thin, pale, drowsy and extremely disoriented and restless. On the fourth hospital day the patient was treated with the artificial kidney for a 4 hours’ period. Good chemical response was obtained and 36 hours later the patient was rational and cooperative and able to eat. On the fifteenth hospital day full thickness skin grafts, 2 1/2 by 2 1/2 cm. were transferred between the twins. A control autograft was placed proximally and the homograft was placed 1 cm. distally, allowing a bridge of normal tissue to intervene between the 2 grafts. The following day the patient was discharged feeling relatively well. On December 13, 1954 he was re-admitted to the Peter Bent Brigham Hospital because of marked increase in the signs and symptoms of his congestive failure. His blood pressure was 220/146, there was 3+ pitting edema of the lower legs up to the knees, bilateral basilar rales, and the liver edge was tender and 4 cm. below the right costal margin. A chest film showed marked cardiac enlargement with evidence of fluid at the right base. On December 16 the skin grafts were biopsied; grossly and microscopically the homograft was indistinguishable from the control autograft. Because of this evidence of tissue compatibility and other ancillary observations that the twins were mono-zygotic, on December 23 a normal
Dr. Merrill and Dr. Dammin had their labs at the Brigham. But we all were at home in each other’s labs and shared laboratory facilities and personnel regularly. As work progressed and situations changed, we adapted our individual protocols, often in midstream, to optimize our resources. We held joint lab rounds several times each week, as well as daily clinical rounds. We had lots of fun. My surgical fellows on occasion also worked in the quadrangle labs of Drs. Cliff Barger, Bernie Davis, and Guido Majno.

Persons around the world often ask why and how did the Brigham succeed first in organ transplantation. At that time just after World War II, there were other players in the field: two excellent groups in Paris and others in London, Edinburgh, and Chicago. In my opinion, the reason we succeeded was because we had strong, firm, and generous leadership at the top, Dr. George W. Thorn, Chief of Medicine, and Dr. Francis D. Moore, Chief of Surgery. We had available a functioning “artificial kidney” to treat end-stage renal disease and prepare patients for surgery. As a result, we became a large-scale referral center for all sorts of renal problems under the care of Dr. John Merrill.

I came to the Peter Bent Brigham Hospital for fellowship training in large measure because of the promise of transplantation. The timing was extraordinary, as 1962 was the year that azathioprine, as monotherapy, had achieved some success in producing functioning renal grafts. I was designated as the “transplant fellow” and entered into the routine of rounds with Joseph Murray and John Merrill, dutifully reported the details of my daily urinalyses, and became familiar with the history and philosophies of the field. I had read the 1956 identical twin phenomenon. It was a seminal time for me, as I came to realize that there was very little known about allotransplantation. John Merrill, encouraged by the chairman of medicine, George Thorn, had made renal transplantation possible because of the development of dialysis support. In the 1960s, each procedure still required fresh vascular cutdowns, and the practicality of chronic maintenance dialysis was only a dream. Joseph Murray, with the support and encouragement of Francis D. Moore, chairman of surgery, had been working in the surgical research laboratory since 1951, perfecting the technique of intra-abdominal placement of a transplanted kidney. The hospital had a clear mission to move this new field into the clinic.

My recollections of those days as a fellow are many, but the first things that come to mind are the extraordinary team-
blood pressure ranged from 125/70 to 146/82 and his blood chemistries are normal.

**DISCUSSION**

The removal of the 2 damaged kidneys was accomplished for 4 reasons: The evidence from intravenous pyelography that the renal homograft was functioning well, the possibility of infection of the graft from the 2 remaining diseased kidneys, the experimental evidence suggesting that a non-functioning or infected kidney may ultimately interfere with the normal function of the normal kidney particularly with regard to its role in renal hypertension, and the data indicating almost total lack of function in the 2 diseased organs.

The survival of the renal homograft for this period of time with continuing good function indicates the complete lack of a rejection response by the host and demonstrates that renal transplantation is a technically feasible procedure. The implications of the dramatic response of the malignant hypertensive disease to the transplantation of a normal kidney should carry considerable weight in future thinking about the renal mechanism in human hypertension. Why one identical twin and not the other should develop glomerulonephritis, and whether the kidney of the unaffected twin transplanted into the diseased recipient will be susceptible to further attacks, are questions still to be answered.

**REFERENCES**