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Use of Living Donors for Renal Homotransplantation

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The use of volunteer living donors to provide kidneys for renal homotransplantation has many medical, social, and legal implications. The infliction of major operative trauma upon healthy well-motivated donors cannot be dismissed lightly since the chance for ultimate viability of the homograft in its new environment is highly speculative. In the long run, justification for continued use of volunteer donors depends upon the demonstration that the donor operation carries a negligible risk and that the benefit for the recipient patients is substantial and predictable.

In this communication, data will be analyzed concerning the risk involved to the donor, based upon experience with 40 patients. In addition, a detailed account of the donor operation will be provided. In the existing literature on renal transplantation, this phase of technical care has never been fully described, although it is evident that both the operative risk and the quality of the homograft obtained are dependent upon the details of nephrectomy.

Case Material

Forty living donors were used for the treatment of the first 37 cases of renal transplantation, including two identical twins. Their ages ranged from 18 to 53 (Table 1).

Selection of Living Donors.—Priority is given to those volunteers having genetic relationship to the patient (Table 1). Of the 40 donors, 27 were either parents or siblings. The other 13 were not genetically related to the recipient. In the last group, there were three wives, nine convicts, and one volunteer who responded to a public appeal (Table 1).

A mass of experimental evidence can be cited in support of the position that homografts are tolerated better and for a longer period of time if the donor and recipient subjects are closely related. In humans a similar but less incontrovertible tendency has been noted.[1] In our experience, the incidence of success has been greatest with mother-to-offspring donations, next with siblings, and lowest with donations from unrelated volunteers.

In discussing kidney donations with those who wish to volunteer, an objective account is given concerning the risk to themselves and the chances of salvaging the recipient patient. The sacrifice of the donor is so great that he must not commit himself to participation without realizing that there is a significant chance of early transplant failure. Furthermore, he must understand that the results in late stages of homotransplantation are not known with any degree of certainty.

When possible, the major blood groups in the donor and recipient patients are matched. When this is not feasible, donations are accepted from patients with different blood types, provided they conform to the general scheme of tissue transfer in which O is the universal donor and AB+ is universal recipient.[2]

The potential donor is given a thorough general medical examination. Unsuspected pathologic findings of importance are sometimes uncovered. One 39-year-old lady was found to have a large serous cystadenoma of the ovary (Fig 1). Another patient

TABLE 1.—*Donor Age and Relation to Recipient*

Age	0-19	20-29	30-39	40-49	49+	
Father		0	0	1	0	1
Mother	0	0	5	3	0	8
Brother	1	7	3	2	1	14
Sister	0	0	2	2	0	4
Wife	0	0	2	1	0	3
Husband	0	0	0	0	0	0
Convict	0	6	3	0	0	9
Volunteer	0	0	0	1	0	1
Total	1	13	15	10	1	40

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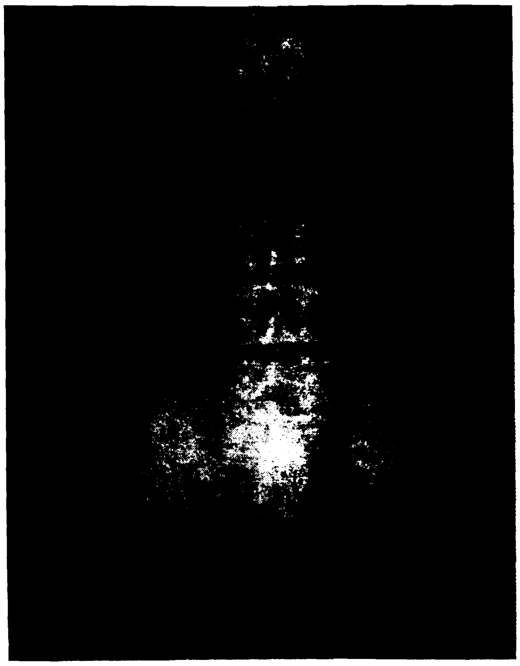

Fig 1.—Abdominal roentgenogram of a prospective renal donor. There is a large, soft tissue mass rising from the pelvis and occupying a considerable portion of the abdominal cavity. This mass was unsuspected by the patient and the abdominal fullness had been attributed to obesity.

was found to have a coin lesion of the right lower lobe which was removed by pulmonary wedge resection and found to be a histoplasmoma. The latter patient subsequently underwent donor nephrectomy.

General determinations of renal function are obtained with blood urea nitrogen (BUN), creatinine clearance (CCr), multiple urine cultures, and intravenous pyelogram. If all other tests are normal, retrograde aortography is performed.

The aortogram is of the utmost importance in determining which kidney is to be used. Inasmuch as the rapidity with which transplantation can be carried out appears to have an important influence on both immediate and long range prognosis,[3] aortographic evaluation of the donor assumes a special significance. The use of donor organs which have two or more arteries inevitably leads to prolongation of the time necessary for completion of the vascular anastomoses. Ischemic periods of 85, 71, 61, and 41 minutes were required for revascularization of four kidneys in our experience which had double arteries. In these four cases, early function was sluggish or absent. It has, therefore, become our policy not to consider donors with multiple blood vessels, no matter how favorable the genetic relationship of the donor to the recipient, with the sole exception of identical twins. An idea of the importance of aortography in selecting the side for nephrectomy can be obtained from the fact that in the 36 remaining patients who provided a kidney with a single renal artery, the contralateral organ which was not removed had two or more sources of supply (Fig 2) in 11 cases. Thus, the aortogram has been for us the single most useful determinant in deciding which kidney is to be excised.

Aside from allowing selection of the kidney which can be transplanted with the greatest facility, aortography has on occasion afforded protection to the donor patient as well. In two cases, long renal arteries were detected which appeared to have significant segmental occlusive disease. Both pa-

Fig 2.—Preoperative retrograde aortogram demonstrating two renal arteries to the right kidney and a single vessel on the left side. In this instance, the left kidney was used for homotransplantation. Exposure is at 1.25 seconds.

Fig 3.—Retrograde aortogram demonstrating a ptotic right kidney supplied by an elongated renal artery which has intimal roughening. The right kidney was selected for homotransplantation and at operation the irregularity of the vessel seen on aortography was thought to be atherosclerosis. Exposure at 0.75 seconds.

tients were young women with moderately ptotic right kidneys (Fig 3). Excision of the more commonly used donor left kidneys would have left them with a predictably high future morbidity. If any equivocal abnormality is detected in either of the donor kidneys, the less perfect organ is used for the transplant. The first consideration of safety is always given to the donor.

A previous anatomic analysis by Ross and his associates[4] concerning the random usability of kidneys for homografting is an interesting one in light of the present experience. For various reasons, these authors concluded that the left kidney was anatomically satisfactory in only 33% of the cases and that the right kidney would be suitable for transplantation only in 3% of cases. In practical experience, however, we have found that all kidneys, no matter what their side of origin, could be inserted without difficulty. In the present series, 22 left kidneys were placed in the right iliac fossa, and 16 right kidneys in the left iliac fossa. In two unusual cases, adult right kidneys were transplanted to the right paravertebral gutter of children.[5]

The Operation

Homograft Cooling.—The amount of ischemia imposed on the homograft is related to the quality of its subsequent function.[3] To mitigate the harmful effects of

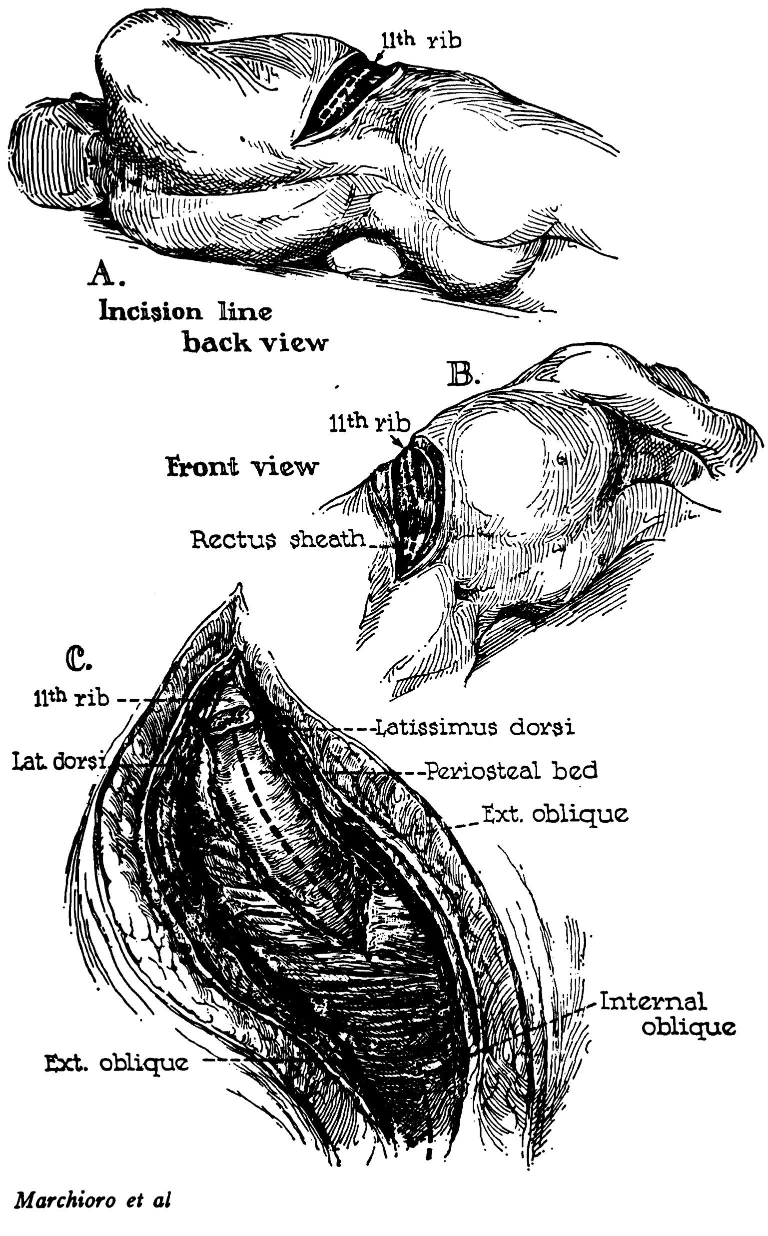

Fig 4.—*A*, incision overlying the eleventh rib seen from behind. *B*, incision seen from the front. *C*, the tip of the 11th rib has been excised exposing the periosteal bed. The internal oblique muscle is being cut.

ischemia, homograft cooling is provided in one of two ways. For donors whose major blood group matches that of the recipient, total body hypothermia to 30 C (86.0 F) is employed. Systemic heparinization with 2.0 mg/kg is provided five minutes before removal of the organ. Heparin neutralization is accomplished with an equal dose of hexadimethrine bromide (Polybrene) or protamine sulfate given in 100 ml of 5% dextrose in water over a 15-minute period, beginning as soon as the renal vessels have been occluded. Thirty-one donors were treated in this way.

The second method of homograft cooling is used when the donor and recipient differ in their major blood types. Donor nephrectomy is performed at normal body temperature and systemic heparin is not used. As soon as the renal vessels have been transected, infusion of the kidney with a solution of lactated Ringer's solution cooled to 15 C (59.0 F) and containing 1.0 gm procaine chloride and 50 mg heparin per liter is begun. Ordinarily, passage of 250-300 ml serves to cool the organ adequately and wash out all residual blood. This procedure, which was first described by Kiser and his associates,[6] has been

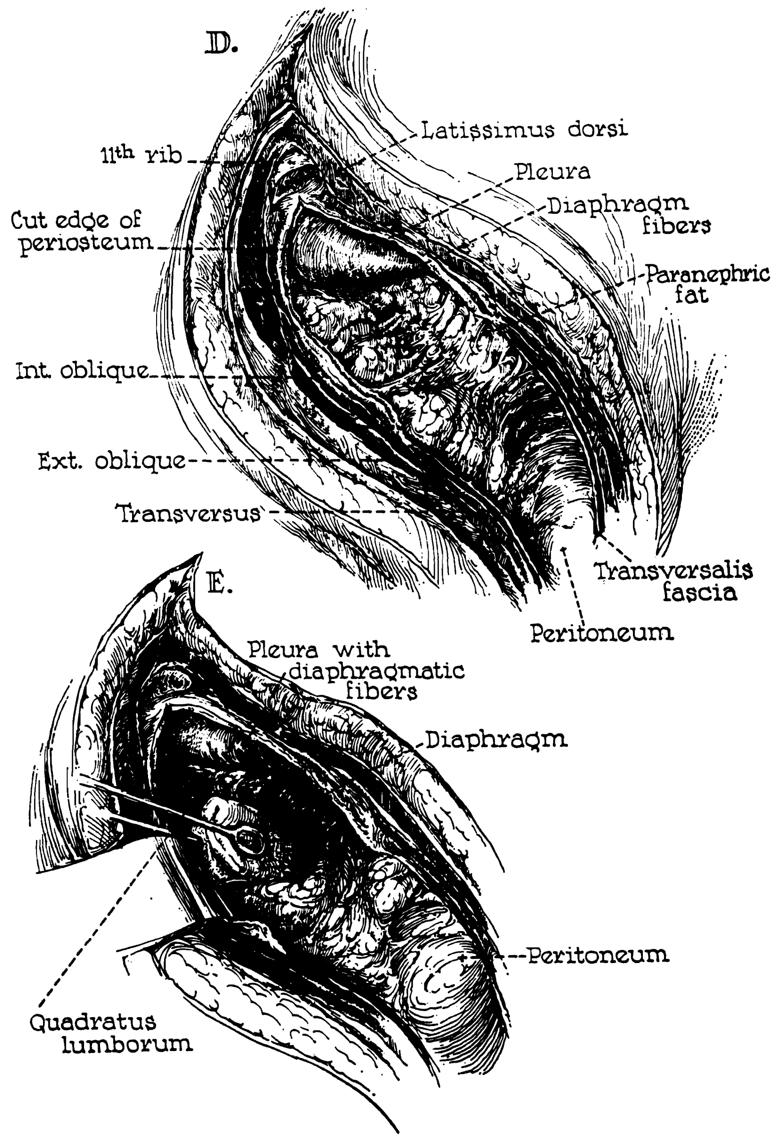

Fig 5.—*D*, the musculature of the abdominal wall has been incised, exposing the paranephric space. A small lappet of pleura is seen in the upper end of the wound underlying the periosteal bed. *E*, the paranephric fat is being dissected free from its attachments. The kidney and its covering investments are swept anteriorly off the psoas and quadratus lumborum muscles.

carried out in nine of the 40 cases and has taken an average of 6.5 minutes to accomplish.

Right Nephrectomy.—Right nephrectomy is performed if transplantation is planned to the left iliac fossa of the recipient. The patient is positioned laterally (Fig 4). An oblique incision is made over the eleventh rib (Fig 4*B*). The incision is deepened to the level of the retroperitoneal and subperiosteal space after excision of the anterior portion of the 11th rib (Fig 4*C*). In the posterior end of the wound, pleura is almost always seen protruding beneath the upper portion of the residual rib stump (Fig 5*D* and *E*).

A vertical incision is made in the paranephric fat and the underlying Gerota's fascia is exposed (Fig 6*F*) and opened. The perirenal fat is then detached from the renal capsule to which it is attached by numerous areolar bands containing fine blood vessels. These vessels must be ligated or electrocoagulated (Fig 6*F*).

The kidney is then mobilized fully, usually freeing the upper pole first in order to allow inferior retraction of the specimen into the wound (Fig 6*G*). In carrying out this step, caution is exercised not to divide an anomalous polar branch of the artery, a danger which is largely avoided if preopera-

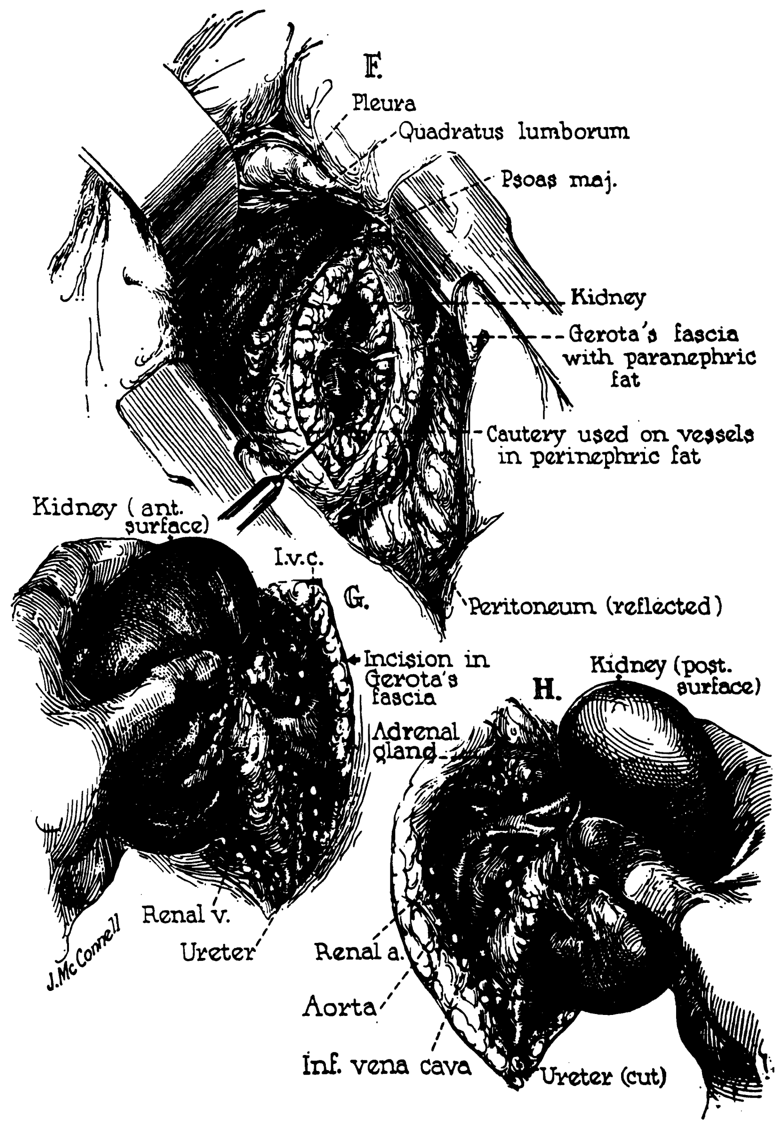

Fig 6.—*F*, Geörta's fascia has been incised longitudinally, and the perinephric fat is separated from the renal capsule by sharp dissection with the electrocautery. *G*, the proximal portion of the right renal vein is identified at its junction with the inferior vena cava. The fatty and areolar tissue lying between the renal vein and artery inferiorly and the adrenal gland superiorly is ligated in continuity and divided. Similarly, the tissue lying between the ureteropelvic junction laterally and the inferior vena cava medially is ligated and divided. *H*, the kidney is rotated anteromedially and the renal artery identified at its origin from the aorta. The remaining areolar tissue connecting the ureter to the posterior body wall is ligated in continuity and divided. The ureter is ligated as far inferiorly as possible and divided proximal to the ligature. The kidney is now ready for removal.

tive aortograms have been obtained with which such aberrant vessels can be detected in advance. After completing mobilization of the convexity of the kidney, attention is directed to identification and dissection of the proximal renal vein. On the right side, junction of this vessel with the inferior vena cava is seen almost immediately and is cleared of all areolar tissue for approximately 1 cm (Fig 6*G*). Next, the groove between the renal vein and the more superiorly located adrenal gland is separated, ligating and dividing in continuity the bridges of tissue between these structures (Fig 6*G*). After this, the groove between the inferior vena cava and the ureteropelvic junction is separated with a similar technique (Fig 6*H*).

Finally, the kidney is rotated anteriorly (Fig 6*H*) and the renal artery is identified as far proximally as possible, usually at the point where it passes beneath the inferior vena cava (Fig 6*H*). The proximal portion of the artery is skeletonized. The right kidney is now completely free except for its vascular and ureteral connections. If the recipient room is nearly ready for receipt of the kidney, the ureter is divided as far inferiorly as possible with a single ligature of

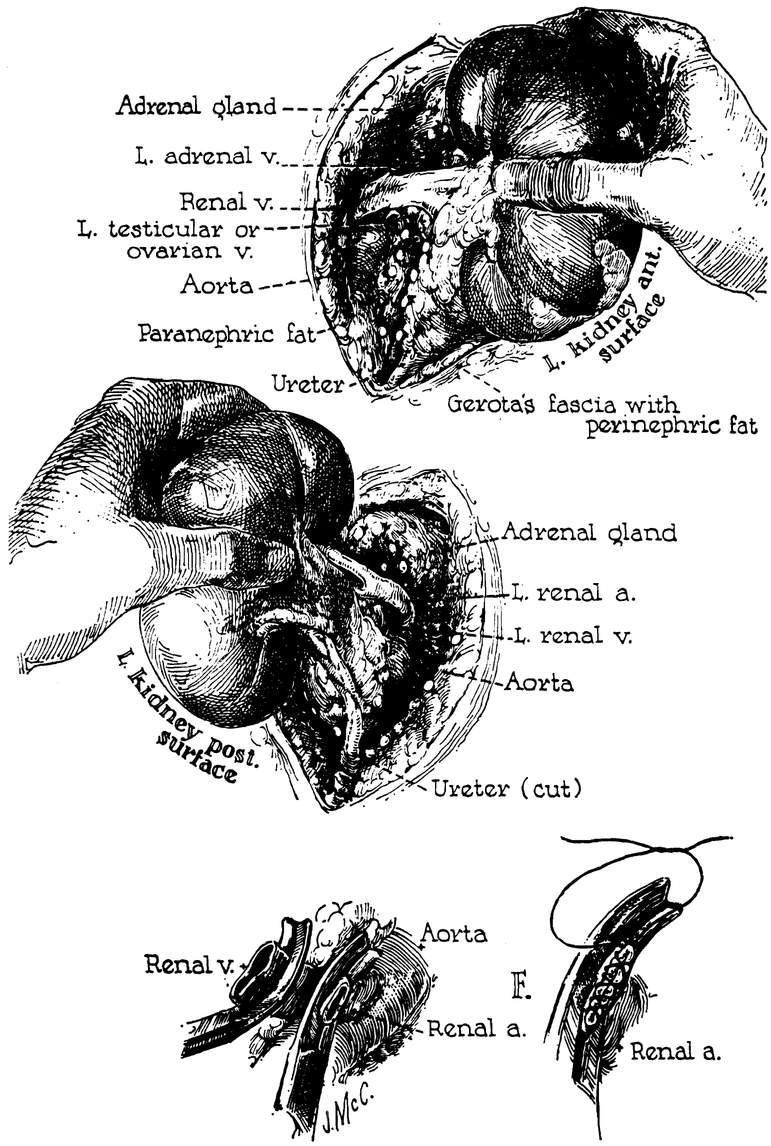

Fig 7.—Left nephrectomy showing differences in hilar anatomy and dissection compared to the right side. *Top,* renal vein passes over aorta to vena cava which is hidden. Note that an adrenal and testicular (or ovarian) vein must be ligated. *Middle,* renal artery origin is easily seen in the central part of the field in contrast to the right. *Bottom,* method of closure of stumps of renal vessels employed on both sides.

2-0 silk, taking pains to preserve adequate length. A few residual areolar connections of the ureter to the posterior body wall are now ligated and divided. Upon signal from the recipient room that all is ready, the final steps preparatory to removal of the kidney are carried out. If the donor patient is under total body hypothermia, heparin is administered intravenously, or if the kidney is to receive hypothermic infusion, the necessary equipment is checked. For the actual final removal, right-angle Pott's clamps are used to grasp the artery and vein individually (Fig 7). For transection of the artery, a single clean cut is made, leaving a cuff of 2 or 3 mm for closure of the stump (Fig 7). Division of the vein is best accomplished by making a small incision in the inferior border of the vessel distal to the vascular clamp. By compressing the vein between the index finger and the thumb, the incision can be kept bloodless and the anterior and posterior walls of the vein incised separately. For those donors who have received systemic heparin, a neutralizing dose of protamine sulfate is started at once.

The vessel stumps are closed with continuous 5-0 vascular silk which is reinforced with a second layer (Fig 7). The wound is extensively irrigated and all of the fat or debris is removed. Occasionally, a pneumothorax is encountered due to a rent in the pleura at the upper angle of the wound. Such pleural defects are closed with interrupted figure-of-eight silk sutures. Prior to closure of such a defect, a No. 20 French catheter is passed into the pleural space to evacuate the air. The wound is closed in layers using interrupted silk technique throughout. Drainage is not used.

Left Nephrectomy.—Left nephrectomy is performed if the transplantation is planned to the recipient right iliac fossa. The general technique in all the steps of exposure are comparable. There are important differences, however, in the dissection in and around the hilum of the kidney, which should be thoroughly appreciated (Fig 7).

As on the right side, the renal vein is the most anterior structure. Its junction with the inferior vena cava cannot, however, be easily seen since this is deeply located within the wou[illegible] to the right of the aorta. In addition, the [illegible]t renal vein regularly admits the testicular or ovarian and the adrenal veins within the field of dissection, and these vessels must be sacrificed (Fig 7).

The dissection necessary for the renal artery also differs. In contrast to the situation on the right side, the junction with the aorta is easily visualized (Fig 7). Dissection of the groove separating the aorta from the ureteropelvic junction (Fig 7) and the left renal vein from the left adrenal gland (Fig 7) is performed with a technique similar to that used on the other side. It is especially important in opening the space between the adrenal gland and the left renal artery that any small branches be accurately identified. A small adrenal artery is frequently encountered in this location which must be ligated, but it is easy in this field of dissection to injure a small branch of the superior pole of the kidney which also takes origin from the segment of the main renal artery. Inadvertent ligation of such a vessel has resulted in a small superior polar infarct in two cases. The subsequent steps on the left side are the same as those on the right (Fig 7).

Venous Anomalies

In ten of the 40 patients, significant variations in venous anatomy were found at operation (Table 2). Four patients had a large lumbar vein joining the left renal vein, close to where the renal vein crossed the aorta, requiring simple ligation. Three patients had a double renal vein, two on the left and one on the right (Table 2). In two instances there were three renal veins, both on the right

TABLE 2.—*Venous Anomalies*

Left lumbar entering renal vein		4
Double renal veins		3
Right	1	
Left (one retroaortic)	2	
Triple renal veins		2
Right	2	
Left	0	
Left ureteral vein replacing testicular		1

TABLE 3.—*Complications*

Wound infection	2
Pneumothorax	2
Atelectasis	1
Transient peroneal nerve palsy	1

side. In view of Smith's previous anatomic study of human kidneys in which rich venous interconnections were demonstrated under such circumstances,[7] all but the largest vessel were ligated. There were no harmful sequelae. The final anomaly encountered was replacement of the left testicular vein by a large ureteral vein.

Complications

Two pneumothoraces, one bout of atelectasis, two superficial wound infections, and one transient peroneal nerve palsy occurred (Table 3), for a complication rate of 15%. All patients were discharged within seven days of operation except one with a superficial wound infection, who remained 14 days. No vocational disability has occurred. There were no deaths or life-threatening complications.

Postoperative Renal Function

Follow-up studies of renal function extend from one month to one year. With statistical analysis, the average differences in pre- and postoperative blood urea nitrogen and serum creatinine were not significant, no abnormal values having been detected. Postoperative creatinine clearance studies performed within the first month show an average decrease of 21.6 ml/min. Follow-up is incomplete at this time due to the fact that many donors live a long distance from this center and are reluctant to return, either to us or to their family physician, for further special examination. Continued observation is necessary before final conclusions regarding residual renal function can be drawn. Up to one year, however, no significant impairment has been observed.

Simultaneous determinations of blood urea nitrogen and creatinine clearance have been performed in three different donor-recipient pairs, 90, 146, and 217 days after transplantation. Creatinine clearances were 98.4 and 86 ml/min, 70.5 and 73.3 ml/min, and 89.8 and 91.8 ml/min for donor and recipient, respectively. Blood urea nitrogen values were also in close agreement. It is of considerable practical importance that once adaptation has occurred in the recipient, compensatory hypertrophy is comparable in the transplanted and nontransplanted organs.

Comment

The donor operation must satisfy two requirements. It must be safe for the patient sacrificing the kidney. In addition, it must guarantee delivery of a minimally traumatized organ, inasmuch as one of the single most important factors in the ultimate outcome of the transplant procedure is the quality of the tissue which is transferred.[3] The procedure described has appeared to satisfy these objectives. Thirty-seven of the 38 recipients have received homografts that underwent immediate diuresis, although in three of these, a first transplantation had failed. No life-threatening complications were observed in the donors.

A special note should be made concerning the surgical exposure employed, as it relates to the full needs of donor nephrectomy. In contrast to many extirpative renal operations, complete vision is needed for each step. Sharp dissection is required in many areas that are ordinarily mobilized by blunt means. Because of the long vessel segments required and the consequent necessity to free them to their origins, perfect exposure is mandatory near the aorta and inferior vena cava. Finally, the ureteric and pelvic blood supply can be preserved with certainty only under ideal operating conditions. The generous incision which is used allows exposure for such meticulous dissection, thereby providing protection not only for the patient, but for the specimen as well.

The use of cooling in protecting renal tissue from the effects of ischemic injury is of undoubted value.[6,8,9] The question of the best and safest methods to achieve organ hypothermia is, however, not yet settled. In this series, intra-arterial infusion of cold solution has been used only for those cases in which the major donor blood groups were different from those of the recipient. There are several disadvantages to the use of this method. First, three to ten minutes of additional ischemia are imposed by the use of this technique, since this is the time investment necessary for adequate perfusion. Secondly, there is a risk of inflicting damage upon the renal artery at the time of insertion of the perfusing tip. Finally, the exact effect upon ultimate renal function of instilling cold electrolyte solutions is not precisely known, although no harmful sequelae have been seen in our experience.

There are, however, two important advantages of the infusion method. The kidney can readily be cooled to a much lower temperature than with the use of donor total body hypothermia. More importantly, the slight theoretical risks of donor heparinization and total body cooling are thereby avoided. Should intra-arterial hypothermic perfusion prove to be completely innocuous to the homograft, it will become the preferable technique for all cases.

Comment on this topic would be incomplete without consideration of the future of cadaveric as opposed to living volunteer donors as a source of organs. During the past few years, it has become increasingly evident that a major, if not the single most important, deterrent to the successful employment of cadaveric homografts is the ischemic injury imposed during the agonal and postmortem periods. One of the most important consequences of the use of living donors has been clarification of many previously unanswered questions concerning the behavior of human renal homografts. An increasingly lucid understanding of the problems which are to be expected has resulted, and a number of at least partially satisfactory solutions have evolved. It is to be hoped that this information can ultimately be transferred back to the more difficult problems involved with use of cadaveric organs in which postoperative therapy must usually be provided in the absence of good homograft function. With the use of living donors, empiric regimens can first be outlined which are not so dependent upon function of the renal homograft for formulation of day-to-day therapy. In this way, the present employment of living volunteer donors will contribute to the eventual solution of the cadaveric homograft problem.

In the future, it is inevitable that cadavers will be used with increasing frequency as a source for renal homografts, particularly when better immunosuppressive regimens have been developed. The concept of obtaining needed organs without the necessity of placing living donors in jeopardy is so attractive as to be irresistible in the long view. In order to utilize effectively cadaveric sources, considerable developmental work will be necessary, in both the social and the scientific spheres. An increased understanding and willingness by the public and by physicians to cooperate in the procurement of permission to promptly remove postmortem tissue will be necessary. In addition, more effective ways of processing and preserving autopsy specimens will have to be devised. For the last purpose, a recently described method for hypothermic postmortem perfusion may prove to be of value.[10]

Justification for the use of living donors depends partially upon the demonstration that a substantial success rate can be attained in treating the recipient. Within the limitations of relatively brief follow-ups in the present series, maternal and sibling donations appear to meet this criterion.[11] In contrast, the failure rate is very high when genetically unrelated living donors are used, especially if the recipient is beyond 35 years of age.[11] In the latter category of recipient patient, strong justification is present for the use of only cadaveric organs, since some hope for survival could still be offered without the useless sacrifice in such cases of a large number of living donor kidneys.

Summary

The procedure is described which is followed at the University of Colorado Medical Center for the selection and evaluation of living donors for renal homotransplantation.

Priority is given to volunteers who have a close genetic relationship to the recipient. The aortogram is the single most useful test for determining which kidney to be used. If either organ has a single artery, it can be employed for homografting without fear of encountering anatomic difficulties at the time of its subsequent insertion into the recipient. Twenty-two left and 18 right kidneys have been excised.

The donor operation has been a safe one. The only complications have been two pneumothoraces, one atelectasis, one transient peroneal nerve palsy, and two subcutaneous wound infections. Renal hyperplasia of the remaining kidney apparently occurs promptly since the creatinine clearance returns to or toward normal within a few weeks after operation. Interestingly, the same phenomenon is also observed in the homograft in those recipients who have a successful result.

The steps in the donor operation are described for both right and left sides. Wide exposure, block removal of the specimen, and meticulous technique are required—both to protect the donor from surgical accidents and to insure a homograft of high quality. Homograft cooling is provided either by total body hypothermia of the donor or by a method in which intra-arterial infusion of a chilled electrolyte solution is used.

The relative future roles of living and cadaveric donors are discussed. The results with parental or sibling donations have been good enough to justify further employment of these sources. In cases in which a genetically unrelated donor must be used, a sounder policy may be to seek cadaveric organs, especially if the recipient falls in an older age group.

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