Anesthetic Aspects of Renal Homotransplantation in Man

With Notes on the Anesthetic Care of the Uremic Patient

Leroy D. Vandam, M.D., J. Hartwell Harrison, M.D., Joseph E. Murray, M.D., John P. Merrill, M.D.

THIS is a report of a procedure wherein anesthesia is required for transplantation of a kidney from a healthy donor to a recipient in the terminal stages of renal failure. At the time of writing 17 such operations had been performed in identical twins, except for one pair whose identity was not quite the same.[1] Though the anesthetic aspects of this epoch-making procedure are least important, it has been a unique problem. Foremost are the ethical implications of anesthetizing a voluntary donor and secondarily the management of the terminal renal patient. Hitherto the only situations in which two patients have been anesthetized simultaneously have been for operation on "Siamese" twins[2] or the procedure of utilizing the lungs of a living person for extracorporeal oxygenation.[3] Undoubtedly problems of this nature will be encountered frequently when the tissue-immune response can be prevented and transplantation of living tissue between individuals is possible.[4]

Background

The reader is referred to Hume[5] for the history of renal transplantation. At the start of this century the kidney was chosen for experimental transplantation because it is a paired organ, survival of an animal is possible with only one kidney, and blood vessel anastomosis can be accomplished successfully. Kidneys were transplanted to the same or another site in the same animal (autografts), to another animal of the same species (homografts), and between different species (heterografts), utilizing various sites, the neck, renal fossa, or inguinal region. In most of these experiments quantitative data on renal function in the transplant are lacking. Autografts survived indefinitely if the site selected and technique were right. The others were quickly rejected by an immune tissue response.

Isolated reports of transplantation of kidneys from cadaver to man appeared in the thirties, none of which survived for long with measurable function. The introduction of the artificial kidney made it possible for the patient with renal insufficiency to survive for a longer time and to approach transplantation in better condition. Following this Hume[5] performed homologous renal transplantation, utilizing human kidneys from a cadaver or those removed at operation for various reasons. The kidney was placed in the thigh with anastomosis to the femoral vessels. It is significant that one of these homologous grafts survived for 180 days and that several patients with advanced uremia were returned temporarily to a normal chemical state before the kidney was ultimately rejected. Ancillary skin homografts and studies in uremia indicated that uremia *per se* prolonged survival and function of the transplant. It was upon this background of homologous transplantation in man and experience with the use of an artificial kidney that an interdisciplinary group at the Peter Bent Brigham Hospital in 1954[6,7] performed the first transplantation between identical twins.

The appearance on the scene of identical twins, one with terminal renal disease, brought up many matters for consideration. Skin grafts had been shown to survive between identical twins[8]: immunologic and genetic identity accounted for this survival. Moreover, it was known that the pattern of rejection in antigenically dissimilar humans was the same histologically for skin and kidneys, thus suggesting that skin and kidneys might behave

Received from the Division of Anesthesia, Departments of Surgery and Medicine, Peter Bent Brigham Hospital and Harvard Medical School, Boston, Massachusetts, and accepted for publication July 26, 1962.

similarly. It had also been established that renal autografts could survive indefinitely with normal function in animals.[9] Lastly, it was obvious that man could live with one kidney when one had been surgically removed or if there were congenital absence of one of these organs. The survival of skin grafts provided sufficient justification for removal of a kidney from a healthy donor and transplantation into a recipient with the expectation that both individuals would survive.

The fact that soon after the first transplant was performed, 15 other pairs of twins were discovered to be in the same predicament revealed interesting statistical facts. The incidence of twinning is approximately one in 90 pregnancies, but only one of three sets is monozygotic, truly identical and monovular.[10] Thus of every 300 live births, one pair of identical twins is born. In a population of 170 million people in the United States there should be between 500,000 and 600,000 potential donor-recipient combinations. Of further interest is the fact that twins do not show the same susceptibility to disease[11]: Addis[12] noted that contraction of renal disease in twins is due to environmental rather than genetic factors. It is not surprising, therefore, that so many pairs of twins with this unique problem became known and that operations on them have since been performed at other institutions in this country and abroad.

The remainder of this report will indicate the specific problems posed by donor and recipient from an anesthetic viewpoint, describe the operative procedure, note the choice of anesthesia, and briefly refer to the postoperative course.

The Donor

Performance of a major operation upon a healthy volunteer caused much concern, for no anesthetic or operation can be guaranteed free of morbidity or mortality. First, is the problem of consent: this can be granted by an adult, but there was no precedent for minors. Most of the cases were in the younger age groups because patients with renal impairment rarely survive to old age. The common disease leading to renal failure in these cases was glomerulonephritis, largely a disease of childhood. Usually parental consent is controlling in regard to medical treatment if it be of potential benefit to the child: but how could removal of a normal kidney be interpreted as beneficial? The issue was settled by a declaratory judgment of the Supreme Judicial Court of Massachusetts in favor of the proposed actions of the hospital medical staff and Board of Trustees.[13] Upon the testimony of a psychiatrist that grave emotional damage might be visited on the healthy twin if his brother should die, and predicating full understanding of the significance of the operation by the donor twin, benefit was seen in the operation.[14]

The donor was investigated in every way to establish the fact of his good health, particularly that disease might not be present in the genitourinary tract. This required the taking of a detailed history, performance of a meticulous physical examination, and the usual laboratory studies. In addition, the genitourinary tract was studied by means of contrast urography, renal clearances, cultures for infection, and performance of the cold pressor test to detect a hypertensive tendency. Psychiatric evaluation was carried out in a few. Not all of the donors were well. One had moderatively severe restrictive pulmonary disease, the result of several operations in childhood for drainage of chronic empyema. Another had a hemorrhagic cystitis, while a third with a tendency to develop sore throat underwent tonsillectomy several weeks after nephrectomy. Still another had a gastric ulcer and several demonstrated positive urine cultures that required treatment.

Both donor and recipient underwent immunologic tests to establish genetic identity. With the exception of one pair of dizygotic twins, all showed identical blood types in the presently-known major and minor groupings. Information that there had been a common placenta was obtained in some from hospital birth records. Physical features were compared including iris color, structure, and pigment pattern. Final proof of genetic similarity was shown by survival of full thickness skin grafts, both autologous and isologous, in the donor and recipient. This procedure was performed under local anesthesia, and at least four weeks, if the health of the recipient permitted, was allowed to elapse to detect the characteristic rejection phenomenon.

It was the plan to give the donor the most nearly perfect anesthetic. This required assignment of a competent anesthetist and giving him rein to choose the anesthetic safest in his hands. Consideration was given to the possibility of transmitting infection by anesthetic apparatus. General anesthesia was thought best even through tracheal intubation might theoretically act as a portal of entry for bacteremia. The electrocardiogram was monitored. The ready availability of several units of cross-matched blood proved wise in view of the fact that the first, and one subsequent donor, experienced hemorrhage. Brisk hemorrhage occurred in the first donor when the entire renal artery was taken and not enough cuff was left in the full length clamp that was used. Digital control of the aorta was successful and a Potts' clamp applied which permitted satisfactory suturing of the defect. Subsequently, atraumatic Potts or Satinsky clamps have been used and an adequate arterial cuff retained to permit suturing of the stump distal to the clamp.[15] In the other instance, bleeding complicated dislodgment of a Satinsky clamp. Thus transfusion with its hazards, though unwanted, was found necessary. We also believe that infusion of excessive quantities of solutions during anesthesia can so overdistend the urinary bladder that postoperative catheterization may be required: in turn, this may lead to urinary tract infection if aseptic precautions are not constantly maintained. This is mentioned because it illustrates one aspect of anesthetic conscience necessary to prevent complications ordinarily not attributed to anesthesia.

The donors fared well but with several postoperative pulmonary and urinary complications. These were minor and easily treated. All left the hospital following the expected normal recovery period.

The Recipient

While it would be informative to present a detailed history of the most seriously ill of the recipients, more may be learned from a composite picture of the patient in terminal renal failure. No matter what the original disease, the terminal picture of renal failure is the same, with impairment of all of the bodily systems involved in homeostasis. The patient in chronic renal failure tolerates and adjusts to biochemical and physiological disturbances that are often fatal in acute renal failure because of the time factor in development. While blood urea nitrogen (BUN) is generally held to be the best indication of failure there are many pitfalls in its interpretation. Once an irreversible level of 50 mg./100 ml. is reached, there is very little renal reserve and the correlation between chemical disturbance and symptoms is poor.

Commonly encountered symptoms in this series of patients may be seen in table 1.

TABLE 1

Common Symptoms and Signs in Renal Failure

Fatigue, Lethargy, Stupor
Shortness of Breath
Peripheral and Pulmonary Edema
Nausea and Vomiting
Chest Pain, Leg Cramps
Bleeding Tendency

Biochemical Disturbances

Anemia
Azotemia
Hyponatremia
Hyperkalemia
Hyperphosphatemia
Calcium Deficiency
Metabolic Acidosis

The origin of these may be evident in the biochemical disturbances likewise listed in the table. In addition to renal disease, all had developed hypertension to the point of encephalopathy and congestive heart failure, frequently with pericarditis, pleuritis, and ascites. These developments alone can explain most of the symptoms. A ready explanation for the nausea and vomiting is not forthcoming. Convulsions may be related to encephalopathy or biochemical disturbance: electroencephalograms showed various abnormalities and postictal patterns.[16] Leg cramps may be associated with severe abnormalities in sodium concentration. A reason for the bleeding tendency has not yet been found in studies of the clotting mechanism.

A word must be said about artificial renal dialysis in the treatment and preparation of these patients for operation. The indications for this procedure in chronic renal failure are not routine.[17] We believe that only when

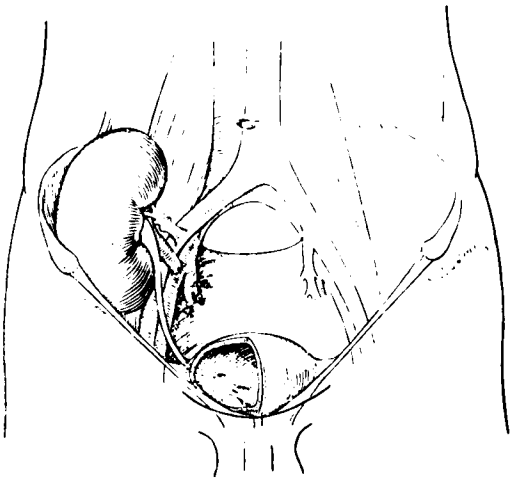

FIG. 1. Schematic diagram of renal homograft *in situ*, showing vascular anastomoses completed and ureter implanted in bladder. Renal artery end-to-end with hypogastric; renal vein end-to-side with common iliac; ureter mucosa-to-mucosa anastomosis with bladder. From Merrill, J. P. *et al.*[7]

there is a major disturbing symptom or a threatening chemical abnormality, irreversible by other means, is this procedure necessary. Dialysis is hazardous in the digitalized patient and in the presence of a bleeding tendency. Enhancement of digitalis toxicity, overloading of the circulation, and the possibility of massive bleeding following heparinization are the deterents to routine dialysis in these patients. At present, peritoneal dialysis seems to hold great promise in the treatment of the uremic patient.

With this background of signs and symptoms, some of the problems in the preparation of the patient and in anesthetic management may be discussed. Potassium intoxication calls for monitoring of the electrocardiogram and observation for progressing neurological disability. Death from cardiac standstill or acute arrhythmia is not uncommon with potassium intoxication, just as progressive weakness is the neurological counterpart.[16] Transfusion of banked blood adds excess potassium to the circulation, while adequate fluid replacement is difficult to judge in congestive heart failure and excesses predispose to pulmonary complications. Nausea and vomiting may continue up to the time of operation, posing the threat of aspiration and requiring use of antiemetic drugs with their attendant adverse effects on the circulation and central nervous system.

Poor circulation in congestive heart failure adds to the difficulty of administering inhalation anesthetics and in the distribution and metabolism of intravenously given medications. When digitalis is administered for treatment of congestive heart failure or arrhythmias in these ill patients, the borderline between therapeutic effect and toxicity is minimal: signs of toxicity or under-digitalization may be readily evoked by stressful anesthetic induction, another reason for monitoring the electrocardiogram. Drowsiness and semicoma make it possible to avoid heavy doses of preanesthetic medication although the shorter acting barbiturates may be given safely in the presence of renal disease.

The uremic patient is a prey to infection, the most common complication leading to a fatal outcome.[18] This is enhanced by the fact that in transplantation between nonidentical twins, total body irradiation or the administration of antimetabolites to eliminate the immune response depletes the bone marrow and deprives the individual of defenses against bacterial invasion.[19] For these reasons, we have kept our kidney recipients under strict reverse precautions preoperatively as well as in the operative and postoperative periods. Anesthetic equipment has been sterilized, the anesthetist gowned and gloved, and intubation of the trachea avoided lest bacteremia be induced.

Anemia must be considered among the therapeutic dilemmas. The hematocrit values in this group of patients averaged about 20 per cent, representing a hemoglobin of less than 7 Gm./100 ml. in most cases. Despite this, operation had to proceed. As noted above, transfusion in these individuals is hazardous, while correction of the anemia is not likely to be achieved easily. There is not only a reduced formation of hemoglobin and red cells in the uremic but in some a greater tendency to destruction of infused red cells when multiple transfusions are given. Each patient seems to settle at a characteristic hemoglobin level which is difficult to alter and to which he seems to make an adequate adjustment.

Finally, it must be evident that many drugs, some of which have been considered contra-

indications to the administration of anesthesia, must be employed in the treatment of these patients. Note has already been made of digitalis and tranquilizers. The administration of adrenal steroids to treat renal disease such as acute glomerulonephritis has obvious implications from the anesthetic standpoint. Contrary to general opinion, we have found that anesthesia can be given safely to individuals who require reserpine up to the time of operation. The safety factor in all instances where preoperative drug therapy poses a problem in safe administration of anesthetics is the knowledge that these drugs have indeed been given: in this way, precautions can be taken should circulatory collapse, the common denominator, ensue. If resperpine has been given the physiological antidotes, epinephrine and norepinephrine, are available; and we attempt to use anesthetics which do not call forth a strong sympathoadrenal response, or do not require the active participation of the sympathoadrenal system for maintenance of homeostasis.

Operation

Since problems of the donor and recipient have been noted, the surgical procedure must be described in detail before choice of anesthesia is discussed. Operation entails simultaneous anesthetization of two individuals in adjacent operating rooms. The left kidney of the donor is exposed with its vascular pedicle and ureter while the transplantation site is prepared in the recipient.[15] The kidney is placed extraperitoneally into the right inguinal region of the recipient so that the normal relationships of blood vessels and ureter are preserved. The renal artery is anastomosed end-to-end to the transected hypogastric artery, the renal vein end-to-side to the iliac vein (fig. 1). The ureter is then implanted into the bladder through a muscular tunnel. Eventually the kidney comes to rest, a bit uncomfortably perhaps, in the concavity of the ilium with some tendency to be pushed forward (fig. 2): however, it is protected in its new position by the overlying abdominal muscles and fascia and does not require fixation sutures. The contents of the peritoneal cavity seem to be sufficient to immobilize the transplant.

Some additional facets of the operation are worthy of comment. Not infrequently accessory renal vessels in the donor kidney must be anastomosed to additional branches of the transected hypogastric artery.[20] The recipient site is prepared with this in mind, and the surgeon performing the transplant joins the operation on the donor in the adjacent operating room to study the vasculature of the donor kidney as it lies *in situ*. A most important aspect of the operation is the maintenance of

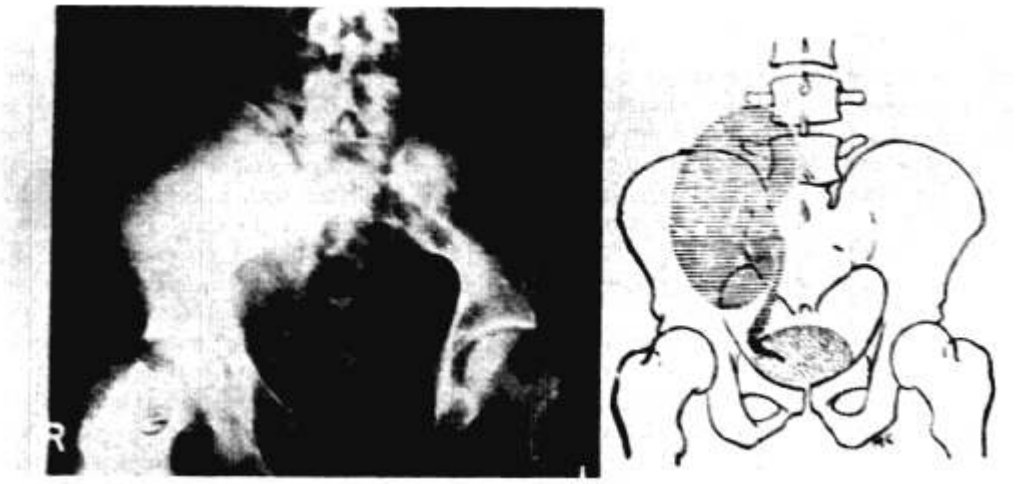

FIG. 2. There is prompt excretion of the opaque medium in good concentration. Renal pelvis shows no extrarenal dilatation, but there is definite dilatation of ureter, attributed to complete denervation of the kidney. No evidence of ureterovesicle obstruction is seen and prompt emptying of ureter into bladder occurs. Bladder is seen to be partially filled on this exposure and more so on subsequent exposures. From Merrill, J. P. *et al.*[7]

communication between the two surgeons in order that the two operations are accurately coordinated at all times. The final dissection of the vascular pedicle is not carried out until the recipient's vessels are ready for the anastomosis to be performed. It is important, we believe, to avoid trapping of blood in the kidney. The artery or arteries to the donor kidney are first clamped and the kidney allowed to empty of blood before the vein is clamped. The vessels are then simultaneously divided and the kidney placed in a specimen pan covered with sterile gauze and delivered to the surgeon operating on the recipient. The period of ischemia, from the time the renal vascular pedicle is clamped until the vascular anastomoses have been completed, even when three or four anastomoses have been required, has averaged less than an hour, the shortest time being about 29 minutes. Despite this period of total ischemia, it is usual to observe clear urine issuing from the ureter soon after completion of anastomosis. This observation is of importance in relation to the general problem of renal ischemia, and the not infrequent development of acute tubular necrosis after ordinary surgical procedures. Experimental perfusion of a donor kidney with heparinized saline during the period of ischemia has seemed to worsen the renal situation; and hypothermia, though presenting theoretical advantages, has not yet been found necessary. Actually the initial function of the transplanted kidney is not unlike that seen in the early recovery phase of acute tubular necrosis. There is an initial copious output of dilute urine, in one instance amounting to 30 liters in the first 24 hours following transplantation. This diuresis poses hazards in the way of fluid and salt depletion that must be carefully corrected: it is well known that death is common in the early diuretic phase of recovery from acute tubular necrosis.

From a practical viewpoint nephrectomy in the donor has usually lasted about two to three hours, the reason being the meticulous dissection of the renal vascular pedicle required while especially avoiding handling of the kidney. The procedure in the recipient has averaged about four hours, partly because of delay in arrival of the donor kidney, time consumed in vessel preparation and anastomosis, and the need to avoid ureteral stenosis and reflux of urine by a careful implantation of the ureter. Finally, closure of the recipient site must be carefully done to avoid pressure on the transplant and interference with the blood supply.

Choice of Anesthesia

Aside from the special points listed above, the choice of anesthesia for the donor is a straightforward one of general anesthesia for nephrectomy. The anesthetics chosen (table 2) may surprise the majority of anesthetists,

TABLE 2. Anesthetic Management in 15 Renal Homotransplants

Donor

Left Nephrectomy—General Anesthesia
Nitrous oxide–oxygen–ether (13)—Thiopental, N_2O, Relaxant (2)

Recipient

1. Transplant—Serial Spinal (13), Single Dose (1) Serial Epidural (1)
2. Subsequent Nephrectomy—Predominantly Single Dose Spinal (Pontocaine, Glucose Epinephrine, or Hypobaric Nupercaine)

since nitrous oxide, oxygen and ether were the choice in the great majority of cases. This anesthetic sequence represents the choice of a competent anesthetist who felt that this was safest in his hands: there is latitude in the method, controllability, opportunity to observe anesthetic signs, and avoidance of prolonged effects of muscle relaxants. Muscle relaxants were subsequently used with safety for anesthetization of the donor once considerable experience had been gained in the overall management of this problem. The trachea was always intubated with a cuffed endotracheal tube to provide a tight seal. In several cases ether was used in the presence of the diathermy, since it is our belief that the choice of anesthesia is of greater importance than the theoretical hazard of an anesthetic explosion. Furthermore, it is believed that the explosion hazard is nonexistent beyond a two-foot radius of the face when a combustible anesthetic is given by inhalation with a tight seal.

The anesthetic course of the donors was largely uneventful except for the instances of bleeding noted above. Other than the usual

complaint of sore throat following intubation, development of minor pulmonary atelectasis in one patient, and the necessity for catheterization of the bladder in still another, there were no postanesthetic complications.

It can likewise be reasoned that the anesthetic requirements for the recipient are simple. Confronted with a lower abdominal extraperitoneal surgical procedure requiring little or no muscular relaxation, continuous spinal anesthesia seemed to be a logical choice (table 2); and we were willing to accept the risk of development of leakage headache for the advantages otherwise provided. The distribution of blood flow to the transplanted kidney seems theoretically to be better during spinal anesthesia. Pressor drugs were not given prophylactically, and development of hypotension was not a problem in spite of the well-known tendency of spinal anesthesia to lower the blood pressure and the prior administration of drugs known to cause hypotension during anesthesia. Indeed, we find it difficult to lower blood pressure in individuals with this humoral type of hypertension just as the physician finds it difficult at times

TABLE 3. Operative Sequences in 15 Renal Homotransplants

Transplant, Bilateral Nephrectomy	7
Transplant, Sequential Nephrectomy	5
Bilateral Nephrectomy, Transplant	1
Nephrectomy, Transplant and Nephrectomy	1
Transplant	1

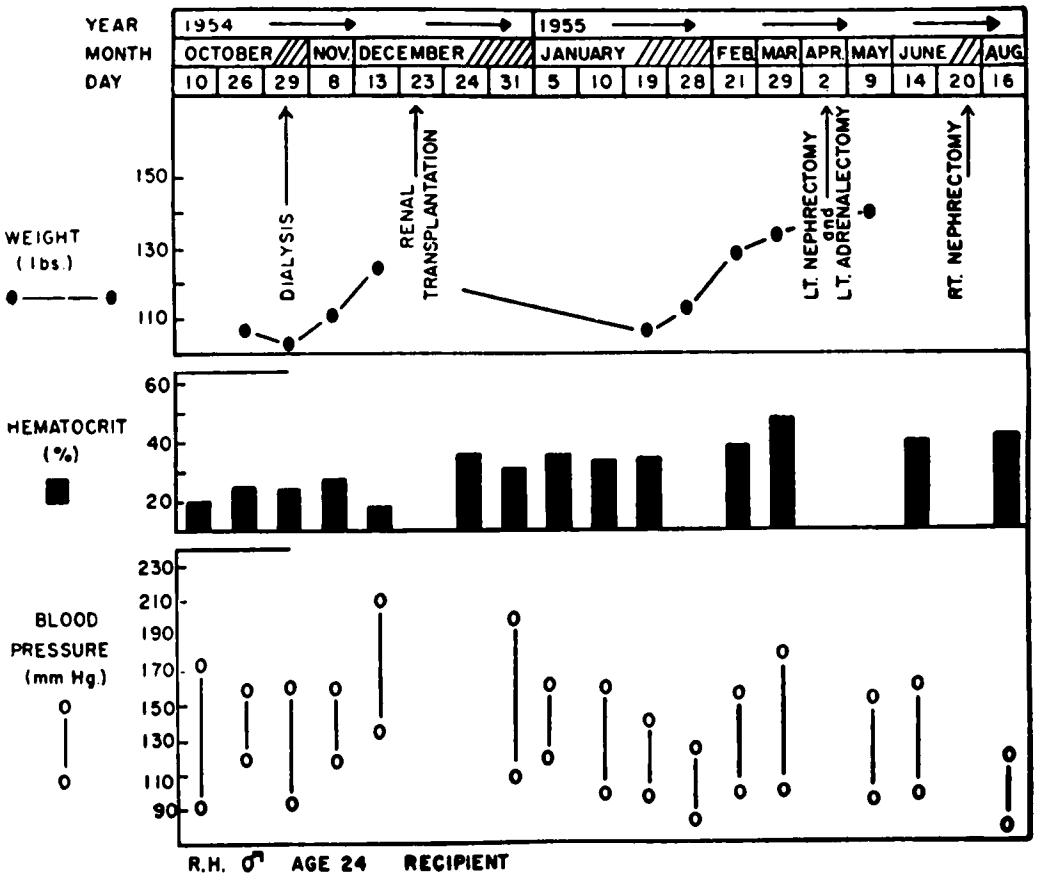

FIG. 3. There is striking decrease in blood pressure immediately after renal transplantation and some tendency for this to rise again with improved levels after left nephrectomy and return to normal values after removal of the second diseased kidney. Increase in hematocrit and gain in weight reflect improvement in general clinical condition. From Merrill, J. P. *et al.*[7]

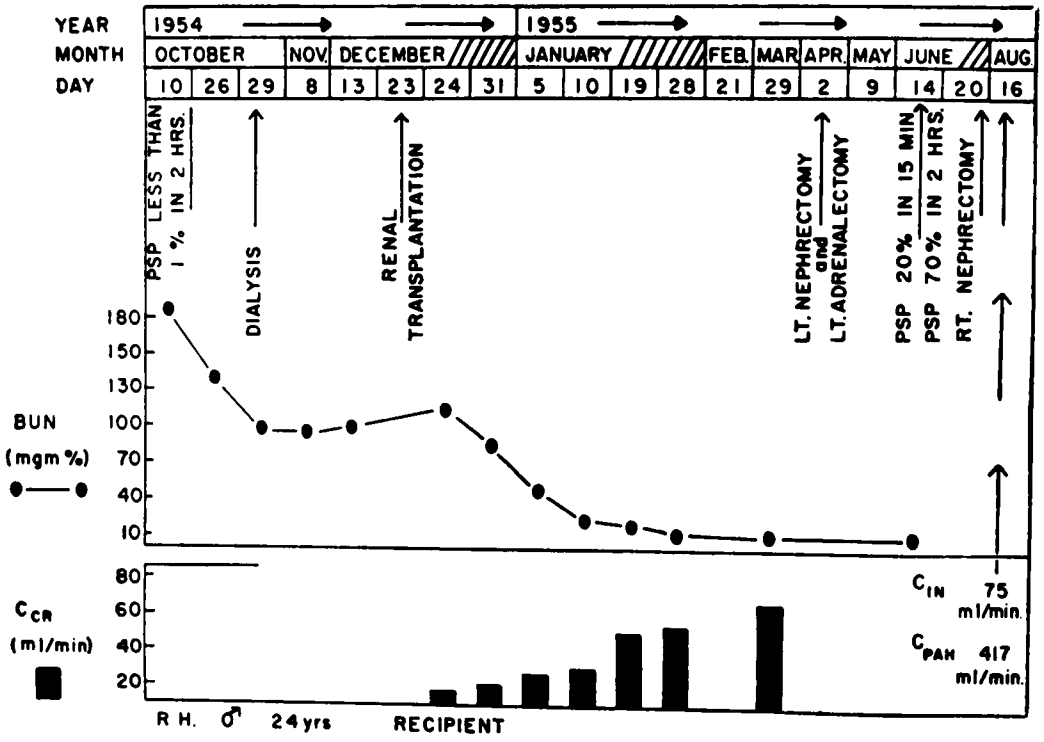

FIG. 4. Disappearance of azotemia and improvement in renal function after renal homotransplantation. There is a progressive decrease in blood urea nitrogen and an increase in serial creatinine clearances (shown in solid bars at the bottom of the diagram). In October 1954, there was almost no discernible phenosulfonphthalein excretion. On June 15, 1955, phenosulfonphthalein excretion was normal. In August 1955, filtration rate and renal plasma flow as measured by the clearances of inulin and *p*-aminohippurate were at near normal values. From Merrill, J. P. *et al.*[7]

to control hypertension with antihypertensive medication. Addititonal advantages of spinal anesthesia are the lack of systemic reaction to the drug itself, avoidance of tracheal intubation, lack of sympathetic or stress response, and elimination of the need for reactive substances such as intravenous barbiturates or muscle relaxants. The latter, particularly, during a long operative procedure, require a satisfactory urinary output for elimination. Small amounts of thiopental were given intravenously when the patient became anxious. It is worth noting that headaches owing to lumbar puncture and neurological sequelae were not encountered in the postoperative period.

Further explanation of the operative sequences shown in table 3 is necessary. Following the first successful transplantation, it was found necessary to remove serially the recipient's own kidneys when he showed signs of recurrence of hypertension and development of proteinuria. This was likewise necessary to avoid infection of the transplanted kidney. Subsequently in other transplants, as theoretically predicted, it became obvious that a disease such as acute or subacute glomerulonephritis could affect the newly transplanted kidney. This was observed in two cases.[21] For this reason removal of the recipient's own kidneys was subsequently performed in various sequences. In one instance both recipient kidneys were removed several days before transplantation. *It is startling to discover on an operating schedule that a bilateral nephrectomy has been scheduled.* In several cases, one of the recipient's kidneys was removed before transplantation and the second kidney removed at a later date at the time of transplantation. Another plan was to remove

both of the recipient's own kidneys at one sitting as soon as possible after transplantation. These secondary procedures were to a large extent accomplished under conduction anesthesia, save in the youngest of the patients in whom clinical improvement permitted the safe administration of general anesthesia. It is not within the scope of this paper to discuss the reasons why additional anesthetics and operations were required in a few instances. These were needed for surgical complications of various types. One patient required rib resection for empyema and pericardiectomy for adhesive pericarditis six weeks after transplantation and bilateral nephrectomy. The eldest patient, and the one most seriously ill, was given seven spinal anesthetics within the course of the year.

Postoperative Course

Of the 17 twins operated upon, 14 are alive at the time of writing and 12 are completely well. One survives with a ureterostomy up to six years and another with proteinuria and nephritis after seven years. One child died within four months of operation owing to contraction of glomerulonephritis in the transplanted kidney. She had been totally anuric for over a week and desperately ill before transplantation. A second child died because of failure of the transplant owing to anomalous blood vessels in the donor kidney and never underwent removal of his own kidneys. Only one patient shows evidence of incipient disease in the transplant related to the original disease. The longest survival is now over seven years. This man, although demonstrating proteinuria, has been married, is gainfully employed, and the father of two children. A female recipient has since delivered two normal babies by caesarean section and her donor has had three normal babies. One of the pairs of twins operated upon represents a transplantation procedure between twins not quite identical in nature. This experience has been reported elsewhere.[1] The postoperative course of a recipient is best illustrated by the charts shown in figures 3 and 4. The gradual improvement may be seen as the transplanted kidney takes over normal function subsequent to removal of the diseased kidneys.

Summary and Conclusions

This is a report of anesthetic management for renal homotransplantation in man with emphasis on the care of the uremic patient. In sequence, the historical background of the procedure, the problems presented by donor and recipient, a description of the operation, and lastly, the anesthetic management and outcome were presented. This account encompasses 17 transplantations between identical twins, except for one pair whose genetic identity was not quite the same. It is believed that transplantation of organs and tissues between individuals will become commonplace once the problem of the tissue-immune response is solved. Anesthesiologists will contribute to the care of these patients in this multidisciplined approach to the solution of many of man's ills.

The authors wish to express their appreciation to Dr. Thomas K. Burnap and to many others on the anesthetic service for their ideas and excellent anesthetic care of the patients described in this report.

References

1. Merrill, J. P., Murray, J. E., Harrison, J. H., Friedman, E. A., Dealy, J. B., Jr., and Dammin, G. J.: Successful homotransplantation of the kidney between nonidentical twins, New Engl. J. Med. **262**: 1251, 1960.
2. Grossman, H. J., Sugar, O., Greeley, P. W., and Sadove, M. S.: Surgical separation in craniopagus, J. A. M. A. **153**: 201, 1953.
3. Lillehei, C. W.: Controlled cross circulation for direct vision intracardiac surgery, Postgrad. Med. **17**: 388, 1955.
4. Murray, J. E., Merrill, J. P., Dammin, G. J., Dealy, J. B., Alexandre, G. P. J., and Harrison, J. H.: Kidney transplantation in modified recipients, Ann. Surg. **156**: 337, 1962.
5. Hume, D. M., Merrill, J. P., Miller, B. F., and Thorn, G. W.: Experiences with renal homotransplantation in the human: report of nine cases, J. Clin. Invest. **34**: 327, 1955.
6. Murray, J. E., Merrill, J. P., and Harrison, J. H.: Renal homotransplantation in identical twins, Surg. Forum **5**: 432, 1955.
7. Merrill, J. P., Murray, J. E., Harrison, J. H., and Guild, W. R.: Successful homotransplantation of the human kidney between identical twins, J. A. M. A. **160**: 277, 1956.
8. Brown, J. B.: Homografting of skin: with report of success in identical twins, Surgery **1**: 558, 1937.
9. Murray, J. E., Lang, S., Miller, B. F., and Dammin, G. J.: Prolonged functional sur-

vival of renal autotransplants in the dog, Surg. Gynec. Obstet. **103**: 15, 1956.
10. Gates, R. H.: Human Genetics. New York, Macmillan & Co., 1946.
11. Metrakos, J. D.: The twin method and its application to the study of genetic and environmental factors in some human diseases, Thesis for Ph.D., McGill University, 1951.
12. Addis, T.: Glomerulonephritis, Diagnosis and Treatment. New York, Macmillan & Co., 1958, p. 184.
13. Masden vs. Harrison, No. 68651 Eq., Mass. Sup. Jud. Ct., June 12, 1957.
14. Curran, W. J.: A problem of consent: Kidney transplantation in minors, N. Y. Univ. Law Rev. **34**: 891, 1959.
15. Murray, J. E., and Harrison, J. H.: Surgical management of fifty patients with kidney transplants including eighteen pairs of twins, Amer. J. Surg., In press.
16. Locke, S., Merrill, J. P., and Tyler, H. R.: Neurologic complications of acute uremia, Arch. Intern. Med. **108**: 519, 1961.
17. Merrill, J. P.: The Treatment of Renal Failure. New York, Grune & Stratton, 1955.
18. Balch, H. H., and Evans, J. F.: The influence of acute renal failure on resistance to infection, Ann. Surg., **144**: 191, 1956.
19. Murray, J. E., Merrill, J. P., Dammin, G. J., Dealy, J. B., Walter, C. W. Brooke, M. S., and Wilson, R. E.: Study on transplantation immunity after total body irradiation. Clinical and experimental investigation. Presented before the Society of University Surgeons, Minneapolis, 1960.
20. Smith, G., Calne, R. Y., Murray, J. E., and Dammin, G. J.: Observations on the renal vessels in man with reference to kidney transplantation, Surg. Gynec. Obstet., In press, 1962.
21. Murray, J. E., Merrill, J. P., and Harrison, J. H.: Kidney transplantation betweeen seven pairs of identical twins, Ann. Surg. **148**: 343, 1958.

METHOHEXITAL One hundred and fifty outpatients were alternately given thiopental and methohexital anesthesia after premedication with 0.65 mg. of atropine alone. No patients were given any other hypnotic or anesthetic drug unless necessary. The operation performed was cystoscopy, pyelography or passage of sounds. Oxygen was not given and respiration was not augmented. In 40 per cent of the females and 86 per cent of the males tremors of the lower limbs caused difficulty to the operators. Methohexital was found to be three times as potent as thiopental. It also produced more hiccups, coughing, and involuntary movements. Methohexital produced a smaller incidence of lowering of systolic blood pressure. Complete recovery with clearheadedness was more rapid with methohexital. Six cases under methohexital anesthesia and none under thiopental required supplementary anesthesia. (*Whitwam, J. G., and Manners, J. M.: Clinical Comparison of Thiopentone and Methahexitone, Brit. Med. J. 1: 1663 (June 16) 1962.*)

OCULAR TENSION Administration of halothane causes a progressive fall of intraocular pressure. In most of the cases studied the tension became stable after ten minutes; in a few instances a continuous fall occurred for about 30 minutes. Regardless of whether the intraocular pressure was initially elevated, normal, or low, a proportional decrease was always observed. After cessation of halothane administration the tension rose to the original reading within 30 minutes. It is believed that the decrease in tension is due to circulatory factors facilitating the passage of fluid. (*Reinhold, H., and Collet, J.: Fluothane on Chirurgie oculaire. Action sur la tension oculaire, Anesthésie, Analgésie, Réanimation 19: 147 (Jan.–Mar.) 1962.*)