Extracorporeal Renal Transplantation in Man

A. R. Lavender, MD; Marvin Forland, MD; James J. Rams, MD; John S. Thompson, MD; Henry P. Russe, MD; and Benjamin H. Spargo, MD

The kidney of a 9-year-old child was transplanted extracorporeally to the forearm of a 35-year-old anephric man. The kidney was perfused in a sealed chamber by blood from chronically cannulated forearm vessels. Immunosuppressive drugs and heparin sodium were administered during the transplantation period. Renal function was maintained satisfactorily until acute vascular rejection occurred on the 25th day. There were no untoward signs or symptoms attributable to the procedure, and the patient improved markedly. It is suggested that extracorporeal renal transplantation may be useful as a test for viability and functional competence of cadaver kidneys. It also may be helpful in study of immune rejection mechanisms.

Cadaver kidney transplants have the advantage of avoiding removal of an organ from a living donor. They have the disadvantage of adding technical and biological problems to the procedure. Since transplantation must be performed soon after donor death, the procedure is always an emergency and requires coordination of a large number of skilled personnel. Nevertheless, postmortem ischemia either may induce tubular necrosis with delayed onset of function, or may result in a nonviable organ with failure of function.

Temporary extracorporeal transplantation might overcome some of the disadvantages of cadaver kidney transplants by serving as a test for viability and functional competence. If the kidney's vascular supply could be joined to chronically cannulated vessels in the recipient's forearm, transplantation could be performed as easily as chronic hemodialysis and with minimal risk. Access to the kidney would simplify differentiation among causes of functional failure and would facilitate serial evaluation of hemodynamic, excretory, and structural changes. Should the organ fail, it could be removed easily, and periodic hemodialysis could be resumed. Should the organ function satisfactorily, it could be transferred to the iliac fossa.

Using the dog as an experimental model, a technique was devised whereby extracorporeal renal autografts could be maintained structurally and functionally normal in anesthetized animals for as long as 73 hours.[1] This technique now has been applied in man, and our first extracorporeal allogeneic renal transplantation is reported here.

Materials and Methods

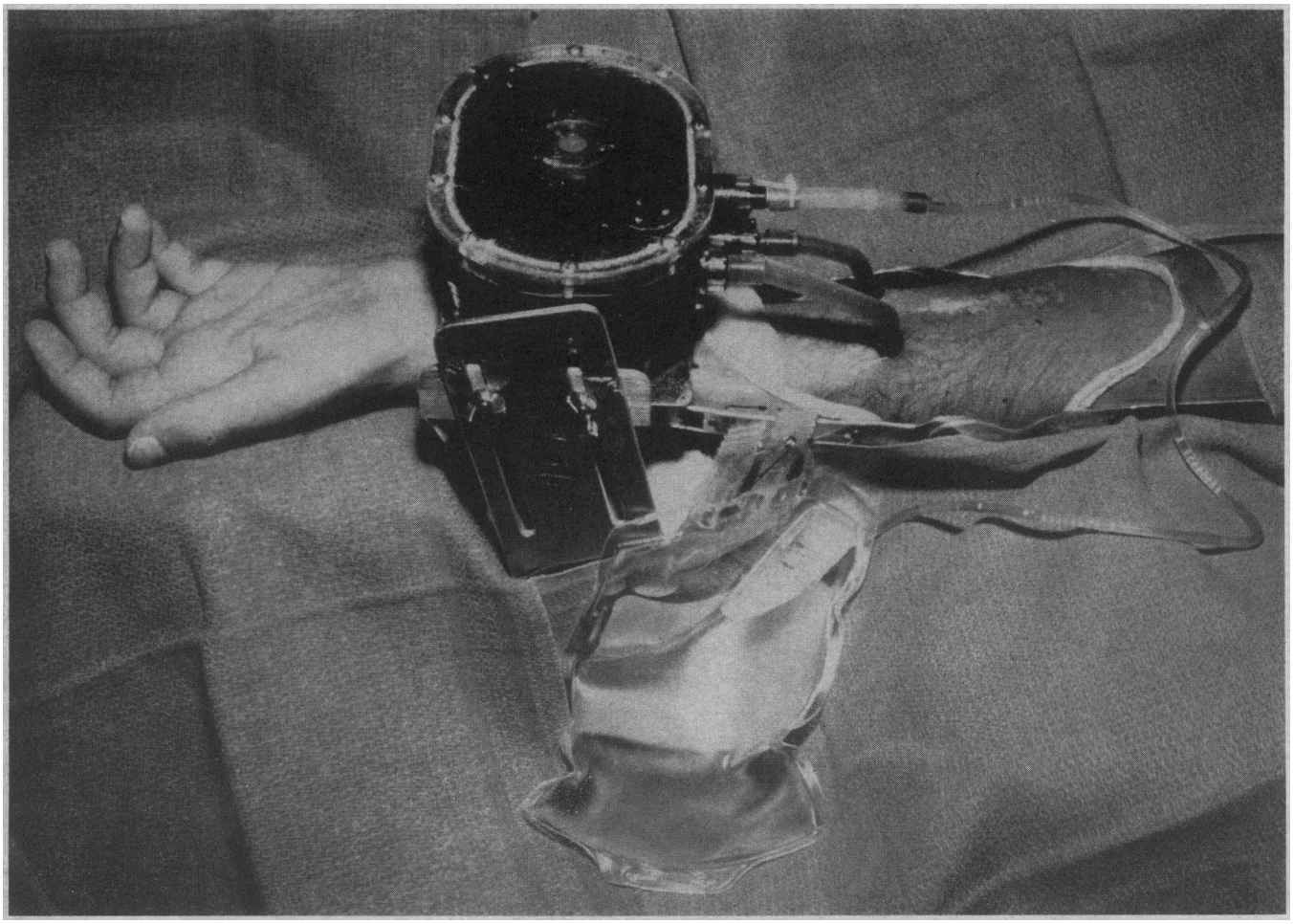
Case History.—A 35-year-old white man first learned of proteinuria at age 20. In June 1962, hypertension and azotemia were discovered. Nausea, vomiting, and diarrhea responded to dietary protein restriction and limited activity. He first was hospitalized at the University of Chicago Hospitals, October 1965, for the complaints of hypertension and numbness of the hands and feet. Significant findings were hypertension, hypertensive retinopathy, cardiomegaly, pedal edema, and neuropathy. Azotemia, proteinuria, and anemia were present. In the following three months, gastrointestinal symptoms persisted, and neuropathy progressed. The patient failed to improve during a subsequent hospitalization, and in February 1966, large-bore arteriovenous shunts (p 261) were implanted into the right forearm. Two days later, the first of 40 pretransplantation hemodialyses was begun with a twin-coil dialyzer.

See also page 261.

Persistent pyuria and bacteriuria were refractory to antibiotic therapy. Since infection would have been a hazard when immunosuppressive therapy was initiated, bilateral nephrectomy was performed one month after beginning chronic hemo-

From the departments of medicine, surgery, and pathology, University of Chicago, and Argonne Cancer Research Hospital, Chicago. Dr. Lavender is the recipient of a Public Health Service career development award from the National Heart Institute. Dr. Rams is now with the Veterans Administration Hospital, Lexington, Ky. Dr. Spargo is the recipient of a Public Health Service research career award from the National Heart Institute.

Reprint requests to 950 E 59th St, Chicago 60637 (Dr. Lavender).



1. Extracorporeal renal transplant in second week. Chamber rests on a stabilizer beneath arm.

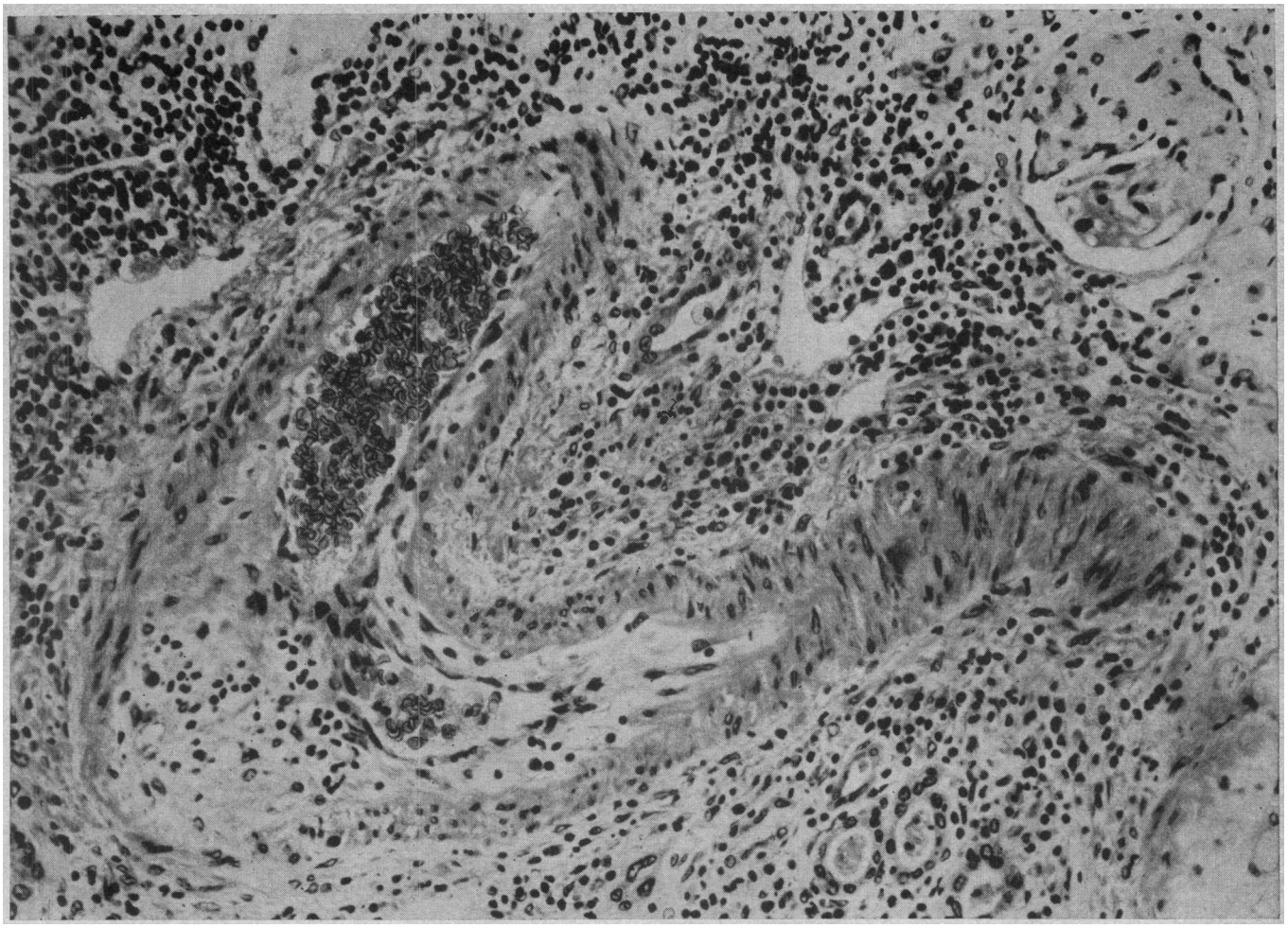
dialysis. Histologic examination was compatible with chronic glomerulonephritis and superimposed pyelonephritis. The postoperative course was complicated by suspected pulmonary embolism and a subcutaneous hematoma in the abdominal nephrectomy wound. On July 5, extracorporeal renal transplantation was performed.

Perfusion Apparatus.—Cannulae were machined from trifluorochloroethylene (Kel-F), etched with a plastic-etching solution (Tetra-Etch), and coated with graphite-benzalkonium-heparin (GBH) by the method of Gott et al.[2] Thin-walled, renal arterial cannulae were taper-bored to reduce turbulence. Their tips were cut square to minimize intimal damage. The largest cannula possible was inserted into the renal artery. Ureteral cannulae were tapped on one end for a female Luer fitting. They were thin-walled, straight-bored, and cut square at the tip. The largest cannula possible was inserted into the ureter. The venous cannula drained blood from the chamber but was not inserted into the renal vein. The cannula's orifice was fitted with a disk to prevent luminal occlusion by invagination of fatty or renal tissue. All cannulae were fitted with silicone rubber gaskets and flanges which seated into recesses in the perfusion chamber.

The oval-shaped perfusion chamber was carved from a block of methylacrylate. Three orifices were provided for ureteral, arterial, and venous cannulae. The cannulae were seated into chamber projections, and only the venous cannula protruded into the chamber. The chamber was lined with GBH, and its rim was fitted with a silicone rubber gasket. The clear siliconized methylacrylate lid had three orifices. The center one was fitted with a self-sealing silicone rubber plug for sampling and injections. The remaining orifices were fitted with plugs for which hemodialysis cannulae could be substituted. This arrangement would permit hemodialysis in parallel with the renal vein. When the kidney was placed in the chamber, the renal artery and ureter were cannulated, but the renal vein was not. Venous blood filled the chamber and surrounded the kidney before egressing through the venous cannula.

The chamber was mounted on a lightweight forearm brace. The brace was hinged at the elbow and had a setscrew to lock the joint. Urine was collected in 600-ml sterile plastic bags. Silicone rubber tubing was secured to vascular cannulae by tying ligatures over grooved Kel-F split-rings.

Protocol.—The donor kidney was obtained from a 9-year-old child undergoing a cephalo-ureteral shunt procedure for hydrocephalus. The donor's



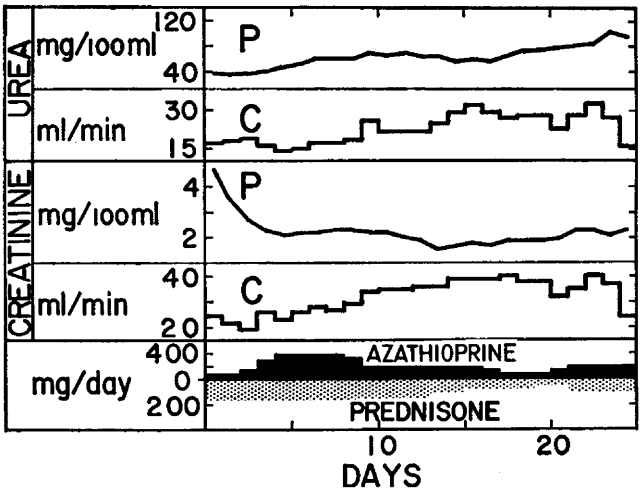
2. Endothelial proliferation and mononuclear periarterial infiltration in rejected transplant (hematoxylin and eosin, ×275).

blood group was OD and the recipient's, BD. The donor kidney was exposed through a left-flank incision, and the ureter was severed about 4 cm distal to the renal pelvis. The distal stump was used for insertion of the cephalo-ureteral shunt. A ureteral cannula for the perfusion chamber was inserted into the proximal stump. An intravenous injection of 50 ml of 25% mannitol was given to the donor. When diuresis began and the kidney was distended, the artery and vein were clamped simultaneously to prevent renal decompression. The vessels were ligated and severed, and the organ was removed.

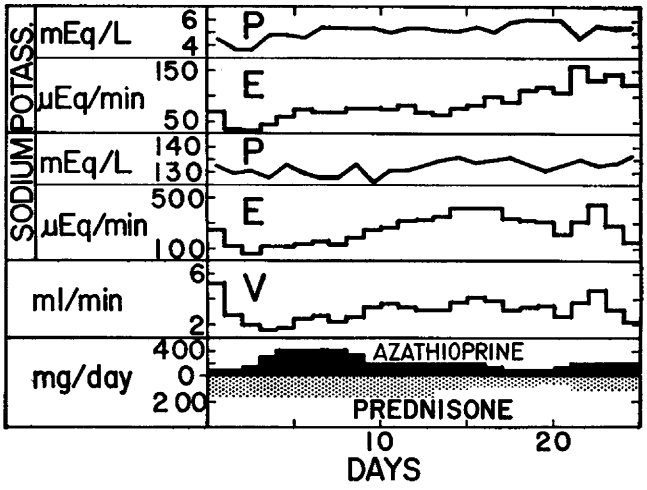
The renal artery was cannulated with the largest possible cannula (0.19 inch, outside diameter), and the kidney was placed in the perfusion chamber. Arterial and ureteral cannulae were positioned carefully to avoid twisting of the artery and ureter. Slow perfusion was begun was room-temperature, bank blood which contained 30 mg of heparin sodium per 500 ml. The renal vein ligature was severed immediately after instituting perfusion at an approximate pressure of 80 mm Hg. Two vials of soluble B antigen were added to each 500 ml of blood to reduce the possibility of intravascular agglutination of B cells by anti-B in the donor kidney's plasma.

When venous blood had expelled all air from the chamber through a needle placed in the silicone rubber plug, the vascular cannulae were attached to tubing on the recipient's forearm. Mannitol, 50 ml of 25% solution, was injected intravenously into the recipient just prior to attachment of the kidney. Perfusion with bank blood was begun 13 minutes after excision, and perfusion by the recipient was begun 27 minutes after excision. Urine appeared 20 seconds after recipient blood flow was initiated. The recipient was returned to a protective isolation room.

Heparin sodium was administered intravenously throughout the transplant period. Administration of azathioprine and prednisone was begun immediately after transplantation. Initial daily doses were prednisone, 150 mg, and azathioprine, 200 mg. On the third day, chlorothiazide, 1 gm/day, and hydralazine hydrochloride, 200 mg/day were begun. Antibiotics were not administered initially. During the first two weeks, fibrinolysin was injected daily into the chamber. Both urine and chamber blood were cultured daily. Blood samples were drawn daily for chemical analyses and hematologic studies. Urine collection bags were changed as necessary, usually nine to ten times a day. The transplanted kidney during the second week is



3. Mean urea and creatinine clearances. P signifies plasma concentration; C, clearance.



4. Mean sodium, potassium, and water excretion. P signifies plasma concentration; E, excretion; V, urine flow.

shown in Fig 1.

Chemical Methods.—All analyses were performed on both plasma and urine. Sodium and potassium levels were determined by indirect flame photometry. Calcium and phosphate levels were estimated in trichloroacetic acid filtrates by modification of the methods of Kingsley and Robnett[3] and Fiske and SubbaRow,[4] respectively. Levels for creatinine were estimated by the method of Bonsnes and Taussky.[5] Levels for glucose were determined by the method of Dubowski.[6] Uric acid and urea nitrogen determinations were performed by the clinical laboratory.

Calculations.—Plasma values for clearance calculations were estimated from a semilogarithmic plot of plasma concentration vs time, taking the midpoint of each three- to four-hour collection period. Daily clearances and solute excretion rates were calculated as means of all collection periods during each 24-hour interval.

Results

Clinical.—The kidney pulsated freely in the chamber when blood flow was reestablished. A jet of renal venous outflow was observed. Ureteral peristaltic activity was evidenced by periodic spurts of urine into the collection bag. Flow in the median basilic vein was visibly and palpably pulsatile.

At no time after transplantation did the patient experience any untoward symptoms. He remained afebrile, his sense of well-being improved, and his appetite increased. Daily caloric intake rose to as high as 6,500 calories. There was no evidence for venous thrombi or embolization. Daily cultures of urine and perfusion chamber blood were negative.

Approximately seven hours after transplantation, blood in the chamber suddenly solidified into a gelatinous mass. Fibrinolysin, 50,000 units, was injected into the chamber. Within three minutes, lysis occurred, and blood flow resumed. Heparin sodium was increased to 500 to 600 mg/day, in six divided doses. From 100,000 to 200,000 units of fibrinolysin were given daily into the chamber for 13 days. On the second day, the right arm became moderately edematous, and slight pedal edema was noted. On the fourth day, blood pressure rose precipitously from 170/110 to 190/145 mm Hg. Chlorothiazide, 1,000 mg/day, and hydralazine, 200 mg/day, were begun. Azathioprine was increased to 400 mg/day. Blood pressure ranged from 160/100 to 175/110 mm Hg thereafter.

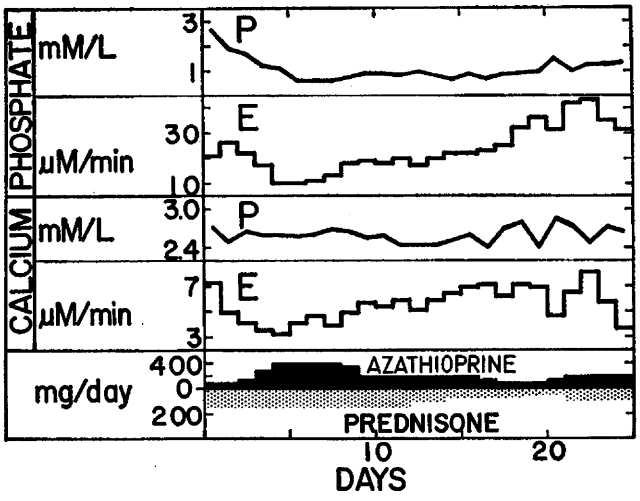
Urinalysis consistently showed microscopic hematuria. Beginning on the 13th day, gross hematuria appeared. All urines had an acid pH, and urine reaction for protein was 1+ to 2+. Glucose was also present.

On the 25th day, urine flow abruptly stopped. Ureteral cannulation revealed no obstruction, but blood flow appeared to be diminished. The patient was taken to the operating room where the chamber was opened aseptically. Several large cortical infarcts were seen, and the organ was removed. The arteriovenous shunt was reestablished, and the patient was returned to his room for hemodialysis.

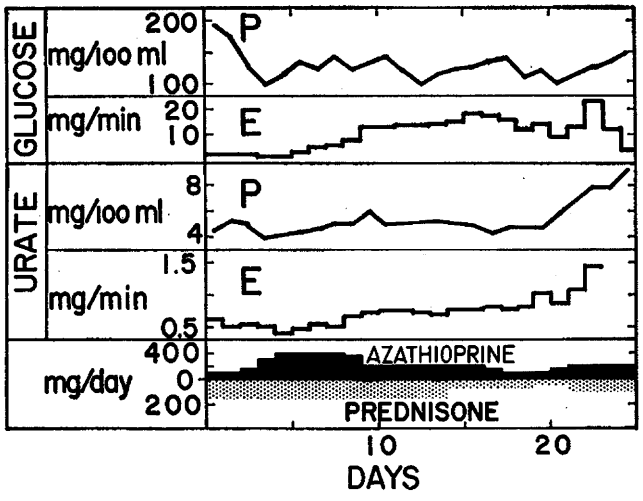
Biweekly hemodialyses have been continued to date. The patient has returned to work, and he remains in good health.

Pathologic.—The rejected kidney weighed 120 gm. Several large infarcted areas were present over the lower pole. Their age was estimated as one, two, and three weeks. The oldest infarct extended 1 cm along the capsular surface and through the cortex. Nearby was a smaller hemorrhagic infarct. A larger area of opacification represented the most recent infarct. The medulla was irregularly pale, but papillary necrosis was absent.

Prominent lesions were present in the interlobular and arcuate arteries near the infarcted areas (Fig 2). Intimal widening and luminal narrowing had nearly obliterated the lumen of some vessels. The thickened intima was poorly cellular and contained scattered fibroblasts, histiocytes, and small collections of white blood cells, including



5. Mean calcium and phosphate excretion. P signifies plasma concentration; E, excretion.



6. Mean glucose and urate excretion. P signifies plasma concentration; E, excretion.

small numbers of neutrophils. Mucinous material, resembling that reported in scleroderma, separated capillaries and stromal fibers in the intima. The intact endothelium contained no fibrin aggregates on its luminal surface. There was no evidence that thrombosis and organization caused arterial narrowing and occlusion. The internal elastic membrane was irregularly reduplicated and focally disrupted. The media was intact except where the entire vessel was necrotic in infarcted areas. Most affected vessels were conspicuously cuffed by round cells, predominately lymphocytes and plasma cells, that extended widely into interstitial tissue. Occasional venous thrombi, observed in small veins near an infarcted area, did not propagate.

In viable parenchyma, slightly enlarged glomeruli had dilated capillary tufts. Glomeruli were not hypercellular, and the ultrastructure of the capillary was normal. An occasional tubular cell was necrotic, and cytoplasm was lost through the ruptured luminal surface. Proximal tubular cells were swollen, the brush border was simplified, and the usually elongated and palisaded basal mitochondria were globoid and dispersed. There was cristae lysis with dense aggregation in the mitochondrial matrix. The tubular basement membrane was intact. In the medulla, collecting tubules had occasional focal obstructions by granular debris. A few focal collections of interstitial round cells were present.

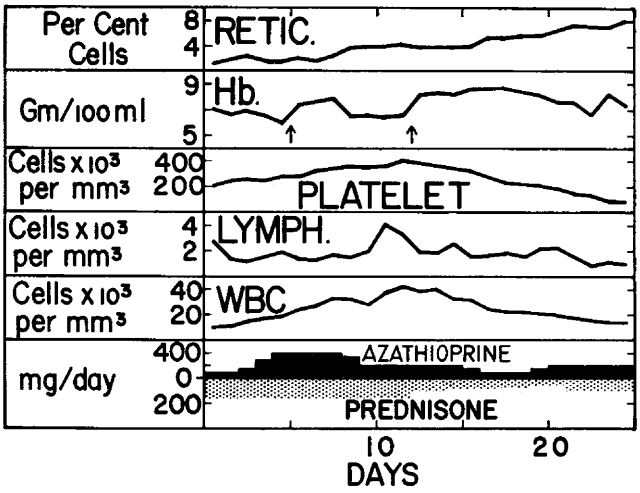
Hemodynamic (Fig 3).—Donor creatinine clearance prior to nephrectomy was 30 ml/min. Donor creatinine clearance two weeks after nephrectomy was 22 ml/min. Recipient clearance the first day was 24 ml/min. This decreased progressively to 18 ml/min on the third day. Azathioprine was increased, and creatinine clearance then rose. By the 15th day, mean creatinine clearance reached 40 ml/min and remained at this level. Individual clearance values were as high as 45 ml/min. Plasma creatinine values fell from about 5 mg/100 ml on the first day to 1.6 mg/100 ml on the 13th day. The value rose slightly thereafter despite maintenance of high clearance values. Urea clearance paralleled creatinine clearance but, because of protein intake as high as 200 gm/day, blood urea nitrogen values rose steadily to 110 mg/100 ml.

Solute and Water Excretion.—The levels for sodium excretion ranged from 100 to 500µEq/min (Fig 4). Potassium excretion levels varied from 30 to 150µEq/min. Urine flow was 1.6 to 5.4 ml/min. Plasma sodium level was 125 to 136 mEq/liter. Plasma potassium level was 3.6 to 6.0 mEq/liter. Sodium, potassium, and fluid intake were not restricted during the transplant period.

Phosphate and calcium excretion levels were high (Fig 5). Mean calcium excretion level was initially 7µM/min and fell progressively to 3µM/min on the fifth day. It subsequently rose steadily until rejection occurred. Phosphate excretion levels paralleled calcium excretion. Plasma calcium levels varied from 2.4 to 2.8 mM/liter. Plasma phosphate values fell from a high of 2.7 to 0.6 mM/liter on the fifth day. On the 24th day, the value rose to 1.2 mM/liter.

Urate excretion value was initially about 720 mg/day, but on the ninth day it began rising and reached 2,160 mg by the 23rd day (Fig 6). Levels for plasma urate varied between 4 and 5 mg/100 ml until the 19th day, when it rose progressively to 8.5 mg/100 ml on the day of rejection. Glucose was present in all urines, and the excretion rate rose to a high of 29 gm/day on the 22nd day. Plasma glucose level was initially high but fell to values of 100 to 150 mg/100 ml.

Hematologic (Fig 7).—White blood cell count was 10,000/cu mm on the first day. The count rose steadily to 40,000/cu mm by the 12th day, despite an increase of azathioprine to 400 mg/day. The count then fell slowly to 17,000/cu mm. Platelet count rose from 200,000 to 400,000/cu mm on the 13th day and then fell gradually to 90,000/cu mm on the last day. Hemoglobin levels varied between 6 and 8.8 gm/100 ml and showed a slight trend up-



7. Hematologic changes during transplant period. Blood transfusions of 500 ml each are indicated (arrows).

wards. Reticulocyte counts rose progressively from an initial low of 1% to 8%. Transfusions were given on the sixth and 13th days. There was no evidence for hemolysis, but stools were consistently positive for occult blood.

Comment

In 1947, Hufnagel et al, as reported by Moore,[7] successfully anastomosed a cadaver kidney's vessels to the brachial vessels of a patient with acute tubular necrosis and demonstrated the adequacy of large forearm vessels for renal perfusion. Perfusion systems resembling that described here have been reported by several groups using experimental animals. Hume et al[8] isolated the kidney in a plastic bag and perfused it with blood from femoral vessels. The first report was optimistic, but a later report[9] stated that renal blood flow could not be maintained at normal levels for longer than 60 to 90 minutes. Marceau et al[10] and Gilsdorf et al[11] utilized a pump in the venous line of exteriorized kidneys. Baitz et al[12] developed a system similar to the one described here and perfused kidneys with femoral blood. Linn et al[13] perfused kidneys with carotid arterial blood. In general, techniques previously used have been either technically difficult or suitable only for short-term perfusions. Most of them were devised with the aim of testing for the viability and functional competence of cadaver kidney transplants.

The data reported here demonstrate that a human kidney transplanted extracorporeally can maintain adequate renal function. Although the kidney underwent immunologic rejection, this was a biological failure, not a technical one. The risk to the patient was minimal. He was not submitted to a major operation, either to transplant the kidney or to remove it. Should a complication have occurred, such as systemic infection, the organ could have been removed easily.

The kidney was not perfused with a synthetic solution nor cooled prior to transplantation. Although the donor's blood contained no anticoagulant during the ischemia period, intravascular clotting did not occur. This corroborates our experience in dogs.[1] Specific B substance was added to bank blood, type BD, which was used to perfuse the kidney and fill the chamber. Soluble B antigen decreased the probability that anti-B in donor kidney plasma would cause intravascular agglutination of red blood cells from the bank blood.

The technical features which contributed to successful perfusion were large-bore tubing and cannulae, GBH coating of surfaces contacting blood, and avoidance of renal vein cannulation. In animal experiments, uncoated cannulae and chambers accumulated fibrin deposits despite heparinization.[1] Fibrin deposits or clots were never observed in properly coated cannulae and chambers, and none were present in this study after 25 days of perfusion.

Avoidance of renal vein cannulation offered several advantages. Blood bathing the kidney prevented cooling from surface evaporation, provided thermal insulation, minimized mechanical shock, and served as an accessory blood supply for the cannulated ureter and artery. Should dialysis have been necessary, the chamber could have been connected to a hemodialyzer without interfering with renal blood flow. Absence of a renal vein cannula reduced time required to initiate perfusion and prevented venous obstruction. Lymphatic obstruction and subsequent edema with functional deterioration were averted by draining renal vein blood into the chamber. Renal lymphatics drain through hilar and capsular vessels, and these vessels are severed when the kidney is excised. If the kidney were enclosed in a sealed chamber and its renal vein cannulated, lymphatic drainage would soon cease as a consequence of increased pressure. Intrarenal rupture of lymphatics with rise in renal tissue pressure would result in impaired venous drainage, tissue swelling, and functional failure.

Venous drainage into the chamber also minimized extrarenal pressure changes. Kidney volume waxes and wanes with systole and diastole, and increased systolic volume would increase extrarenal pressure if the renal vein were cannulated. The detrimental functional effect would be analogous to that of a collodion wrapper around the kidney.[14] When the kidney was surrounded by venous blood, changes in volume had minimal effect on extrarenal pressure and were buffered by simultaneous changes in venous outflow from the chamber. Cyclical changes in venous outflow were evidenced by a pulse in the median basilic vein.

As a tool for study of allogeneic renal transplantation in man, this technique offers several advantages. With the use of large-bore cannulae and tubing for arteriovenous shunts in chronic hemodialysis patients, it will be possible to draw upon a large panel of potential recipients when a donor kidney becomes available. The procedure requires minimal preparation of the recipient and can be initiated as

easily as hemodialysis. Designed for utilization of cadaver kidneys, the technique will permit trials of locally administered drugs and irradiation therapy. Techniques for early detection of rejection can be utilized, such as continuous monitoring of renal blood flow and renal vein pressure.

Although developed for renal perfusion, the chamber should be suitable for perfusion of any organ with a solitary arterial blood supply. The principle of free lymphatic and venous drainage into the chamber should be of value in perfusion of organs such as the pancreas and liver. This principle has been applied advantageously by Eiseman et al[15] in studies of porcine liver perfusion.

This investigation was supported in part by Public Health Service research grant HE-07969 from the National Heart Institute.

Patient care was provided by Public Health Service research grant FR-65 to the Clinical Research Center, University of Chicago.

The prednisone used in this investigation was supplied as Meticorten through Roger W. Cooper, MD, of the Schering Corp., Union, NJ. The azathioprine was supplied as Imuran through George H. Hitchings, PhD, of Burroughs Wellcome & Co. (USA), Inc., Tuckahoe, NY. The plastic urine collection bags and hemodialysis equipment were supplied by the Artificial Organs Division, Travenol Laboratories, Inc., Morton Grove, Ill. The fabrication of the silicone rubber plugs was done by Jack L. Boone of Dow Corning Corp., Midland, Mich.

Surgical assistance was provided by Anthony J. Raimondi, MD, Edward S. Lyon, MD, and Peter V. Moulder, MD.

Generic and Trade Names of Drugs

Mannitol—*Osmitrol.*
Azathioprine—*Imuran.*
Prednisone—*Deltasone, Deltra, Meticorten, Paracort, Cotone, Lisacort, Metasone, Delta-Dome.*
Chlorothiazide—*Diuril.*
Fibrinolysin (human)—*Actase, Thrombolysin.*

References

1. Lavender, A.R.; Berndt, A.A.; and Stupka, J.J.: Extracorporeal Renal Transplantation, *Trans Amer Soc Artif Intern Organs* **12**:246-253, 1966.

2. Gott, V.L.; Whiffen, J.D.; and Dutton, R.S.: Heparin Bonding on Colloidal Graphite Surfaces, *Science* **142**:1297-1298 (Dec 6) 1963.

3. Kingsley, G.R., and Robnett, O.: New Dye Method for Direct Photometric Determination of Calcium, *Amer J Clin Path* **27**:223-230 (Oct) 1957.

4. Fiske, C.H., and SubbaRow, Y.: Colorimetric Determination of Phosphorus, *J Biol Chem* **66**:375-400 (Dec) 1925.

5. Bonsnes, R.W., and Taussky, H.H.: On Colorimetric Determination of Creatinine by Jaffe Reaction, *J Biol Chem* **158**:581-591 (May) 1945.

6. Dubowski, K.M.: An *o*-Toluidine Method for Body Fluid Glucose Determination, *Clin Chem* **8**:215-235 (July 6) 1962.

7. Moore, F.D.: *Give and Take,* Philadelphia: W.B. Saunders Co., 1964, pp 14-15.

8. Hume, D.M., et al: Studies of Renal Homotransplantation in Man, *Ann NY Acad Sci* **120**:578-606 (Nov 30) 1964.

9. Cleveland, R.J., et al: Preservation of the Cadaver Kidney for Renal Homotransplantation in Man, *Surg Gynec Obstet* **119**: 991-996 (Nov) 1964.

10. Marceau, J.P., et al: A Comparison of Autoplastic, Allogeneic and Xenogeneic Perfusion of Isolated Kidneys, *J Surg Res* **5**:492-502 (Nov) 1965.

11. Gilsdorf, R.B.; Clark, S.D.; and Leonard, A.S.: Extracorporeal Recipient Shunt Homograft Kidney Perfusion: A Model for Organ Resuscitation and Function Evaluation, *Trans Amer Soc Artif Intern Organs* **11**:219-223, 1965.

12. Baitz, T., et al: Preservation of Kidneys for Transplantation, *Arch Surg* **91**:276-287 (Aug) 1965.

13. Linn, B.S., et al: Plug-In Kidneys for Dialysis of Uremic Dogs, *Amer J Surg* **111**:498-501 (April) 1966.

14. Collings, W.D., and Swann, H.G.: Renal Clearances in Dogs With Reduced Renal Distension, *Fed Proc* **8**:29 (March) 1959.

15. Eiseman, B.; Liem, D.S.; and Raffucci, F.: Heterologous Liver Perfusion in Treatment of Hepatic Failure, *Ann Surg* **162**: 329-345 (Sept) 1965.

BICHAT, DISCIPLE OF DISSECTION.—"No one has done so much and so well in so short a time," said Jean-Nicholas Corvisart, surgeon to Napoleon, in speaking of Marie François Xavier Bichat (1771-1802), French surgeon and anatomist. In his short 31 years of life, which encompassed the French Revolution of 1793 and the resultant disorganization of medicine, he laid the foundation for modern histology and histological pathology.

Bichat's philosophy was: "Dissect in anatomy, experiment in physiology, follow the disease and make the necropsy in medicine. This is the threefold path, without which there can be no anatomist, no physiologist, no physician." (Disciples of Dissection, editorial, *JAMA* **173**:261-262 [May 21] 1960).

Bichat was born in Thoirette, France, the son of a physician. His education in anatomy and surgery was interrupted by draft into the French Revolutionary Army. The revolution, with its wholesale executions by the guillotine (invented by a French physician, Joseph Ignace Guillotin), provided him with about 600 human bodies. These, he dissected meticulously at the Hôtel-Dieu, a charity hospice in Paris. The knowledge gained gave him the background for his last great literary work, the five-volume *Anatomie Générale.* In this, he gave detailed descriptions of the tissues in healthy and in diseased bodies, establishing him as the founder of modern histology and histopathology.

After the revolution, Bichat became a pupil of Pierre-Joseph Desault (1744-1795), physician at the Hôtel-Dieu, and at the latter's death was appointed to the post. The revolution had left medical practice and education in France badly disorganized. To correct the situation, Bichat in 1796 formed the Société Médicale d'Emulation de Paris for young doctors, who met in debates. Later, he undertook electrophysical studies and electrocuted corpses.

Tuberculosis and overwork took its toll. Bichat collapsed one day and death came rapidly. By order of Napoleon, a bust of Bichat was placed at the Hôtel-Dieu.—Mirt, J.A., "Medical Pathfinders on Postage Stamps."