Renal Transplantation in Infants and Children

JOHN S. NAJARIAN,* M.D., RICHARD L. SIMMONS,* M.D., MARION B. TALLENT, M.D., CARL M. KJELLSTRAND, M.D., THEODORE J. BUSELMEIER, M.D., ROBERT L. VERNIER, M.D., ALFRED F. MICHAEL, M.D.

From the Departments of Surgery and Pediatrics, University of Minnesota, Minneapolis, Minnesota 55455

YOUNG children have not generally been considered ideal candidates for renal transplantation although excellent results have been reported by a number of investigators.[5, 6, 18] The small caliber of vessels and active social behavior of children make their management on hemodialysis extremely difficult. Long-term immunosuppressive therapy is also thought to interfere with normal growth with resultant social problems. Renal failure in children is an extremely common cause of death, however, long-term hemodialysis is seldom satisfactory,[2] and such patients almost always have a parent who is willing to donate a kidney.[15] The present study is designed to document the results of 58 infants and children age 16 and younger who have been transplanted at the University of Minnesota Hospital since 1963. As a readily available comparable control group a series of 80 patients age 17 to 45 were transplanted within the same period of time.

Materials

Fifty-eight infants and children were transplanted between 1963 and March of 1971. These included two infants aged 2 to 4 months, six children aged 1 to 6, 18 aged 7 to 10, 16 aged 11 to 13, and 16 aged 14 to 16. Donors included 33 parents, two siblings, three aunts, and 20 cadavers. In addition, 11 transplants were carried out to nine of these children for a second or third time; four from parents, one from an aunt and six from cadavers.

Methods

The standard technics of renal transplantation have been thoroughly discussed elsewhere.[16] The kidney and a length of ureter are removed from the donor and transplanted into the retroperitoneal space of the recipient pelvis by anastomosis of the recipient's hypogastric artery to the renal artery of the donor kidney, and the iliac vein of the recipient to the renal vein of the donor kidney. Utilizing a submucosal tunnel technic, the ureter is then implanted into the bladder.[17] No major modification of this technic is required for children weighing more than 20 kilograms. Frequently, however, the child's hypogastric artery is so small that the donor renal artery is better anastomosed to the side of the common or external iliac artery.

In children weighing less than 20 kilograms operation is carried out via a midline incision into the peritoneal cavity. The cecum is mobilized, and the aorta and vena cava is dissected free. The renal vein is anastomosed to the side of the vena cava or common iliac vein, and the arterial anastomosis is performed to the side of the aorta or the common iliac artery (Fig. 1).

*John and Mary R. Markle Foundation Scholar in Academic Medicine.

Address reprint requests to Doctor Najarian, Department of Surgery, Box 195 Mayo, University of Minnesota, Minneapolis, Minnesota 55455.

Supported by Grant #1 PO1 AM13083-02 from the United States Public Health Service.

Presented at the Annual Meeting of the American Surgical Association, March 24-26, 1971, Boca Raton, Florida.

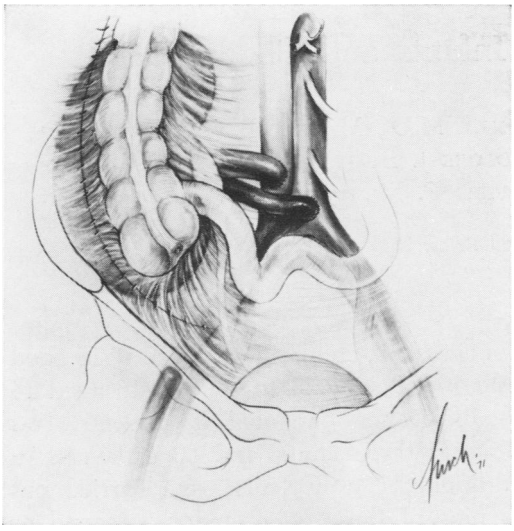

FIG. 1. Technic for transplantation of adult kidneys to infants or small children. A mid-line abdominal incision is made, both kidneys and spleen removed, the colon mobilized as shown and the anastomoses made to the aorta and vena cava or the ileac vessels. Appendectomy is performed and the colon is replaced as shown. The transplanted ureter must be placed in the retroperitoneal position.

The ureter is anastomosed to the bladder in the usual manner, but care is taken to tunnel it in the retroperitoneal space, rather than to pass it across the peritoneal cavity to the bladder. If this latter technic is utilized, distal necrosis of the ureter may occur [18] due to the fact that the collateral blood supply from the surrounding retroperitoneal tissues is not available when the ureter traversed the peritoneal cavity. Following completion of all anastomoses, the cecum is sutured in place in order to fix the kidney in position. The appendix is then removed to avoid post-traumatic appendicitis (Fig. 1).

Technics of Hemodialysis. Hemodialysis is now used exclusively to prepare pediatric patients for transplantation. Peritoneal dialysis superimposes the problem of peritoneal adhesions and possible intraperitoneal infections.

Between 1968 and 1971, 40 children under the age of 15 were hemodialyzed at the University of Minnesota. Two were infants weighing 3 to 4 Kg.; another five children weighed less than 15 Kg., and four less than 20 Kg. There are some special technical problems involved with dialysis of these small children.

(a) *Shunts.* Generally speaking, patients weighing more than 20 Kg. can be shunted using common adult shunt material and the usual peripheral shunt sites, brachial artery to cephalic vein, or the posterior tibial to distal saphenous vein. For the smaller children special pediatric shunt material has been developed.[3] This allows cannulation of the peripheral vessels in children as small as 8 Kg. In infants, the smaller shunts can be used in more proximal sites, either the brachial artery to the cephalic vein, or the profunda femoral artery (or superficial femoral artery) to the saphenous vein. In two instances a shunt from the superficial femoral artery to superficial femoral artery has been used. In no instances have we had any severe ischemic problems with the use of the proximal shunt site.[3] Despite success with the proximal shunts, and the clotting problems in peripheral veins we recommend the use of peripheral shunt sites first, reserving the more proximal shunt sites in order to prolong the potential period of dialysis.

(b) *Dialyzers.* Children weighing more than 30 Kg. can be hemodialyzed with the same equipment as adults without any particular problems. We have used EX-01 dialyzers or one coil of the Ultra-Flow 145 dialyzer. Special precautions are necessary in using this equipment in children weighing 8 to 30 Kg. First of all, it is crucial to have accurate weighing equipment so that blood loss into the dialyzer can be rapidly discovered. Secondly, slow flow should be used in order to avoid the disequilibrium syndrome. For infants special pediatric dialyzers with small priming volumes (20 to 50 ml.), low compliance (10 to 50 ml.) and with lower clearance of creatinine and BUN (20 to 40 ml./min.) have been developed. Mannitol (1 Gm./Kg.) is infused during the dialysis to offset the fall in

serum osmolality secondary to fall in BUN. With this method, no convulsions have occurred in any child and osmolality can be maintained constant during dialysis. A separate report regarding the dialysis of small children is being prepared.

Almost all the recipients of transplants since January 1968 have undergone bilateral nephrectomy and splenectomy. Splenectomy was not generally utilized prior to 1968. In patients weighing more than 20 kilograms the nephrectomies are performed as a first-stage procedure. Following preparation by dialysis a bilateral nephrectomy and splenectomy is carried out, and transplantation is scheduled 1 to 2 weeks later via the retroperitoneal approach. The ureters in all patients with vesico-ureteral reflux are resected at the time of nephrectomy: Ureterectomy is not necessary in patients without vesico-ureteral reflux.

In patients weighing less than 20 Kg., in whom a transperitoneal approach to transplantation is utilized, the nephrectomy and splenectomy are carried out at the time of transplantation. The exception to this rule is in patients with active urinary tract infections. In these patients bilateral nephrectomy, ureterectomy, and splenectomy is carried out via the transperitoneal route at least 3 weeks prior to the transplantation. In this way infection can be cleared from the urinary tract by the surgical excision of the infected organs, antibiotic treatment and repeated irrigation of the bladder with antibiotic solutions.

A related donor is preferred whenever possible in pediatric transplantation. This is impossible in infants weighing less than 5 or 6 Kg. since an adult kidney will not be tolerated within the infant's abdomen. Adult cadaver donors can be utilized for children weighing more than 7 or 8 Kg. Pediatric cadavers have been utilized in several instances and function well despite early reservations concerning the adequacy of function of the immature kidney.

The immunosuppressive regimen utilized prior to January 1968 consisted of azathioprine, prednisone, Actinomycin D, and local irradiation.[10] Since January 1968, almost all patients have received a 2 to 4 week course of intravenous antilymphoblast globulin (ALG) (4 to 40 mg./Kg./day) as previously described.[14] Initial azathioprine dosages of 5 mg./Kg./day are used, the dosage being rapidly reduced to 2 to 3 mg./Kg./day . Prednisone is begun prior to transplantation in doses of 1 mg./Kg./day, and is rapidly reduced to a maintenance dose of 0.2 to 0.3 mg./Kg./day. Double doses of prednisone are initially used in recipients of cadaver kidneys. Methyl prednisolone given in doses of 20 mg./Kg./day intravenously for the first 3 days following transplantation. Local irradiation of the kidney is carried out only during rejection episodes (150 rads/day every other day for 3 doses). During rejection episodes prednisone levels are raised to 2 mg./Kg./day and are rapidly cut within a week to 0.5 mg./Kg. Methyl prednisolone doses of 20 mg./Kg./day are once more given for 3 days at the time of rejection. Identical regimens have been utilized for adult kidney recipients.

Results

Two periods of kidney transplantation have taken place at the University of Minnesota: the first was prior to January 1968 prior to the organization of the present team and the institution of routine ALG therapy. The second period began on January 1968, at which time pediatric hemodialysis was established, the present team was complete, and antilymphoblast globulin was initiated. Tables 1–4 list all patients younger than 16 years transplanted during both those periods.

Figure 2 is a life table construction of the functional survival of kidneys transplanted to children aged 1 to 16 years (excluding infants). The improvement of results of transplantation is apparent but one must take into consideration the fact that

TABLE 1. *Results of Renal Allotransplantation to Children from Related Donors Prior to 1968*

No.	Patient	Age	Sex	Primary Diagnosis	Condition	Serum Creatinine (Mg./100 ml.)	Prednisone (mg./Kg.)	Blood Pressure	Anti-Hypertensive Drugs*
Parent Donors:									
1	D. F.	12	M	Anaphylactoid nephritis	Well—7½ years	1.4	0.0	118/98	None
2	B. M.	9	F	Vesico-ureteral reflux; pyelonephritis	Rejected day 270. Died after 3rd transplant. (see Table V)				
3	R. P.	8	M	Glomerulonephritis	Died day 29—Aspergillosis				
4	V. W.	9	F	Vesico-ureteral reflux; pyelonephritis	Thrombosed renal artery day 2. Well after 2nd transplant. (See Table V)	1.6	0.22	118/84	HDI 25 mg.
5	J. A.	15	F	Vesico-ureteral reflux; pyelonephritis	Well—6½ years	1.2	0.05	134/90	Hydralazine 10 mg.
6	M. S.	11	M	Anaphylactoid nephritis	Well—4½ years	1.9	0.24	120/78	Aldomet 750 mg. HDI 100 mg.
7	T. B.	14	M	Steroid resistant nephrotic syndrome	Well—4½ years	4.3	0.5	162/124	Aldomet 2 Gm. HDI 100 mg.
8	W. B.	12	M	Membrano-proliferative (hypocomplementemic) nephritis	Well—4 years	1.2	0.2	110/78	None
9	B. A.	13	F	Glomerulonephritis	Died day 20—Klebsiella sepsis				
10	S. B.	13	F	Vesico-ureteral reflux; pyelonephritis	Rejected at 1½ years. Died on dialysis 2 years				
11	M. J.	11	F	Vesico-ureteral reflux; pyelonephritis	Rejected at 6 months. Died on dialysis 3 years				
12	J. M.	13	F	Vesico-ureteral reflux; pyelonephritis	Well—3½ years	1.4	0.12	110/78	None
Aunt Donors:									
13	R. J.	7	F	Medullary cystic disease	Well—7 years	0.8	0.0	130/90	None
14	S. S.	15	M	Membrano-proliferative (hycomplementemic) nephritis	Died 2 years—Cryptococcosis				

* HDI = Hydrochlorothiazide.

* Aldomet = Methyldopa.

TABLE 2. *Results of Renal Allotransplantation to Children from Related Donors Since January, 1968*

No.	Patient	Age	Sex	Primary Diagnosis	Condition	Prednisone (mg./Kg.)	Serum Creatinine (mg./100 ml.)	Blood Pressure	Anti-Hypertensive Drugs*
Parent Donors:									
15	J. J.	8	F	Glomerulonephritis	Well—38 months	0.25	1.8	120/92	None
16	S. D.	16	F	Glomerulonephritis	Well—37 months	0.20	0.8	94/60	None
17	C. W.	10	M	Vesico-ureteral reflux; bladder neck obstruction	Well—29 months	0.20	0.7	102/68	HDI 100 mg.
18	C. T.	11	F	Glomerulonephritis	Well—29 months	0.35	4.6	142/98	HDI 50 mg.
19	S. B.	8	M	Glomerylonephritis; hypertensive encephalopathy	Dead at 1 year of cerebral hemorrhage				
20	P. B.	13	F	Glomerulonephritis	Well—24 months	0.15	1.4	98/72	None
21	S. P.	10	F	Cystinosis	Well—22 months	0.20	0.8	122/70	None
22	B. L.	8	F	Vesico-ureteral reflux; pyelonephritis	Well—21 months	0.15	0.7	108/72	None
23	L. F.	6	F	Hypoplasia-dysplasia; vesico-ureteral reflux	Well—20 months	0.4	1.6	120/86	None
24	B. S.	16	F	Glomerulonephritis	Well—18 months	0.20	1.1	112/70	None
25	C. C.	14	F	Glomerulonephritis	Well—13 months	0.15	1.1	124/90	HDI 100 mg.
26	J. O.	8	M	Steroid resistant nephrotic syndrome	Recurrent nephrotic syndrome-kidney removed on day 48. Well after 2nd transplant (See Table V)				
27	S. J.	4	M	Hypoplasia-dysplasia	Well—11 months	0.25	0.5	104/66	None
28	M. K.	11	M	Hereditary interstitial nephritis	Well—9 months	0.20	1.0	124/88	HDI 50 mg.
29	K. L.	13	F	Neurogenic bladder; meningomyelocele	Well—7 months	0.45	2.2	110/76	None
30	J. K.	15	M	Hereditary interstitial nephritis	Well—7 months	0.35	1.4	134/80	None
31	G. L.	10	F	Membrano-proliferative glomerulonephritis; hyperparathyroidism	Well—6 months	0.25	0.9	125/80	None
32	M. E.	10	F	Hypoplasia-dysplasia	Well—3½ months	0.33	1.8	110/80	Aldomet 1.5 Gm. HDI 100 mg.
33	P. W.	3	M	Hypoplasia-dysplasia	Well—3 months	0.55	0.6	130/75	Hydralazine 40 mg. Aldactone 20 mg.
34	B. K.	10	M	Hereditary interstitial nephritis	Well—3 months	0.50	0.9	140/80	Aldomet 500 mg.
35	D. L.	10	M	Hypoplasia-dysplasia	Well—1 month	0.7	0.6	140/90	Aldomet 750 mg.
Sibling Donor:									
36	R. G.	16	M	Subacute glomerulonephritis	Well—27 months	0.1	4.0	120/84	HDI 100 mg.
37	R. F.	16	M	Glomerulonephritis	Well—39 months	0.0	1.2	110/68	None
Aunt Donor:									
38	J. O.	14	M	Glomerulonephritis	Well—30 months	0.44	1.7	104/70	HDI 50 mg.

* HDI = Hydrochlorothiazide.
* Aldomet = Methyldopa.

TABLE 3. *Results of Renal Allotransplantation to Children from Unrelated (Cadaver) Donors before 1968*

No.	Patient	Age	Sex	Primary Diagnosis	Condition	Prednisone (mg./Kg.)	Serum Creatinine (mg./100 ml.)	Blood Pressure	Anti-Hypertensive Drugs*
39	T. B.	16	F	Glomerulonephritis	Died 4 years with rejection				
40	B. S.	14	F	Bladder neck contracture; vesico-ureteral reflux; pyelonephritis	Rejected 1st transplant. Died after 2nd transplant. (Table 5)				
41	J. B.	10	M	Steroid resistant nephrotic syndrome	Rejected 1st and 2nd transplant. Well after 3rd transplant. (Table 5)	0.30	1.1	110/74	HDI 50 mg.
42	C. S.	10	F	Vesico-ureteral reflux; pyelonephritis	Well—6 years	0.15	1.2	134/90	None
43	R. B.	14	M	Vesico-ureteral reflux; pyelonephritis; ? neurogenic bladder	Died 6 years—pyelonephritis of the transplant to an ileal bladder				
44	M. A.	12	M	Bladder neck contracture; vesico-ureteral reflux; pyelonephritis	Died day 29—Klebsiella and pseudomonas sepsis				
45	M. G.	13	F	Bladder neck contracture	Died day 49—Klebsiella and pseudomonas sepsis; ileal bladder				
46	C. T.	1½	F	Hypoplasia-dysplasia	Hyperacute rejection. Died after 2nd transplant (Table 5)				
47	D. G.	13	F	Glomerulonephritis	Technical failure. Died after 2nd transplant (Table 5)				
48	R. H.	14	M	Glomerulonephritis	Well—5 years	0.15	1.5	112/90	HDI 25 mg.
49	J. P.	10	F	Glomerulonephritis	Rejected day 155. Well after 2nd transplant. (Table 5)	0.21	1.6	124/90	Aldomet 750 mg. HDI 50 mg.
50	S. H.	6	M	Steroid resistant nephrotic syndrome	Steroid resistant nephrotic syndrome recurred. Died 2 years with pneumocystis carinii pneumonia				

* HDI = Hydrochlorothiazide.
* Aldomet = Methyldopa.

TABLE 4. *Results of Renal Allotransplantation to Children from Unrelated (Cadaver) Donors after 1968*

No.	Patient	Age	Sex	Primary Diagnosis	Condition	Prednisone (mg./Kg.)	Serum Creatinine (mg./100 ml.)	Blood Pressure	Anti-Hypertensive Drugs*
51	R. A.	12	F	Vesico-ureteral reflux; pyelonephritis	Well—1 year	0.25	0.7	120/92	HDI 50 mg. Aldomet 1.5 Gm.
52	W. A.	6 wks	M	Hypoplasia-dysplasia	Died 3 years with rejection				
53	D. S.	12	M	Vesico-ureteral reflux	Well—7 months	1.0	3.0	130/100	Aldomet 1.5 Gm. HDI 100 mg. Hydralazine 100 mg.
54	B. J.	8	F	Medullary cystic disease	Thrombosed renal artery—well on peritoneal dialysis				
55	R. R.	5	M	Wilms' tumor	Well—4 months	0.33	1.1	128/70	Aldomet 750 mg. HDI 50 mg. Furosimide 80 mg. Aldactone 50 mg. Ismelin 5 mg. Apresoline 75 mg.
56	A. F.	12 wks.	F	Acute congenital glomerulonephritis	Died day 2—respiratory arrest				
57	M. B.	16	F	Hereditary interstitial nephritis	Well—3 months	0.45	1.2	128/70	None
58	S. P.	13	F	Hypoplasia-dysplasia	Well—1 month	0.70	1.0	120/90	Aldomet 750 mg.

* HDI = Hydrochlorothiazide.
* Aldomet = Methyldopa.

more cadaver donors were utilized prior to 1968. Figures 3 and 4 are life table constructions designed to compare the results of transplantation in children 1 to 16 and adults aged 17 to 45. Since few children received sibling transplants, only individuals who received parental kidneys or cadaver kidneys are included in these figures. All causes of renal failure (i.e., technical failures, rejection, or death of the patient) are included in these groups. Figures 3 and 4 demonstrate that renal transplantation is as successful in children as in adults who received comparable grafts from parental or cadaver donors at similar periods in the development of transplantation. It thus appears that children are not a high risk transplantation group, with respect either to kidney loss or to life in the face of immunosuppressive therapy.

Figures 3 and 4 also demonstrate a marked improvement of results in more recent years: Of the 12 patients less than 16 years old, who received renal trans-

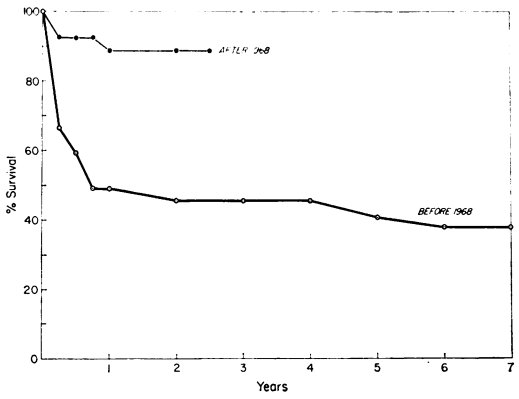

FIG. 2. The survival of functioning kidneys in children aged 1 to 16 years old. Only first transplants are considered and all renal loss due to technical complications, rejection, or the death of the patient are included. Transplants followed less than 3 months are not included in this figure but are included in Tables 1–5.

plants from their parents prior to 1968, ½ are clinically well, 3½ to 7½ years later (Table 1). Five of the 12 died; two of sepsis in the early post-transplant period. Two rejected after 6 months to 1½ years and died on dialysis, and one died after a third transplant, several years later. Patient 4 is well 6 years after a second transplant (Table 5). Of the six patients surviving their primary transplant, good renal function is present in five, but patient 7 (a patient with steroid resistant nephrotic syndrome) has poor renal function and hypertension although he is clinically well.

In contrast, 24 have received transplants from parents or other relatives since January of 1968 (Table 2). Twenty of these have been followed at least 6 months. Of these 20 only two have lost their kidneys. Patient 26, an 8-year-old boy with steroid resistant nephrotic syndrome, developed massive (20 to 70 Gm./day) proteinuria soon after the transplantation from his mother; the kidney was removed on the 48th post-transplant day. Apparently, this kidney developed recurrent nephrotic syndrome. The second patient (19) developed hypertensive encephalopathy, coma, and convulsions, which required an emergency bilateral nephrectomy prior to transplantation. He later received a transplant from his father, recovered and returned to school. Unfortunately rejection episodes were accompanied by recurrent hypertension and the patient died with cerebral hemorrhage 1 year following transplantation.

Of the 22 remaining patients with related grafts, all but three (18, 29, 36) have good renal function. Patient 18, an 11-year-old Indian girl, received a kidney from her father. She has shown slow progressive renal functional deterioration with hypertension. Experience indicates that she will probably lose her kidney and require retransplantation. Patient 29 developed stenosis of the anastomosis between the transplant ureter and ileal bladder. Renal function has not yet returned to normal since the stenosis was repaired. Patient 36 received a transplant from his HL-A identical brother but demonstrated early deterioration of renal function consistent with rejection on renal biopsy. He is clinically well, however, and his renal function has been stable for approximately 2 years. In summary, 24 children have received transplant from related donors since 1968 only two of which have lost their kidneys; only three others have chronic renal functional deteriorations associated with rejection.

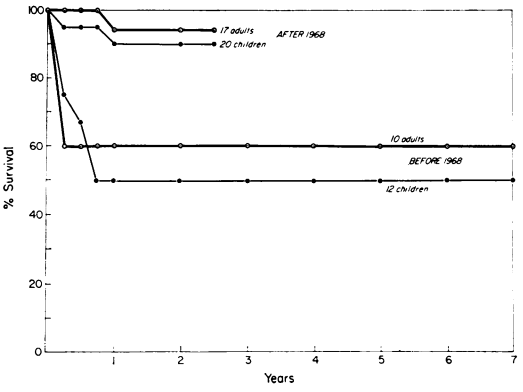

FIG. 3. Comparative survival of functioning kidney transplants in adults (ages 17–45) and children (1–16) who received kidneys from their parents. All causes of kidney loss are included, but only transplants followed at least 3 months are included in this figure.

Tables 3 and 4, and Figure 4 show a similar early improvement of results since 1968 for transplants from unrelated (cadaver) donors. Of 12 children receiving kidney transplants from unrelated donors prior to 1968 (Table 3), only two are now well with the first transplant. An additional two rejected first transplants but are now well with second or third transplants (Table 5). The remaining eight patients are dead; two (Nos. 44, 45) died in the early postoperative period with disseminated sepsis; three (Nos. 40, 46, 47) died after multiple transplants; and three died after a prolonged survival (2, 4, and 6 years). These three late deaths are interesting. One 6-year-old child (50), with stenosis resistant nephrotic syndrome, developed recurrent steroid resistant nephrotic syndrome of the transplanted kidney. Multiple attempts at immunosuppressive treatment of this disease resulted in the development of fatal pneumocystis carinii pneumonia 2 years following transplantation. The second patient (39) has been recently reported in detail.[13] She developed a malignant dysgerminoma which was cured but she died of rejection after refusing to take her medication. The third patient (43) had perfect renal function for 6 years following transplantation. He had had an ileal bladder constructed because of vesico-ureteral reflux and a possible neurogenic bladder. Six years later, he developed pyelonephritis at the transplant with renal calculus formation and died following the transplant nephrectomy.

Table 4 lists the eight patients who have received kidney transplants from unrelated donors since 1968; two of these are infants in the first 4 months of life and will be discussed separately. Of the six children one patient developed thrombosis of the renal artery anastomosis and is now awaiting second transplantation. The remaining five patients are well with normal renal function 2 months to 1 year following transplantation.

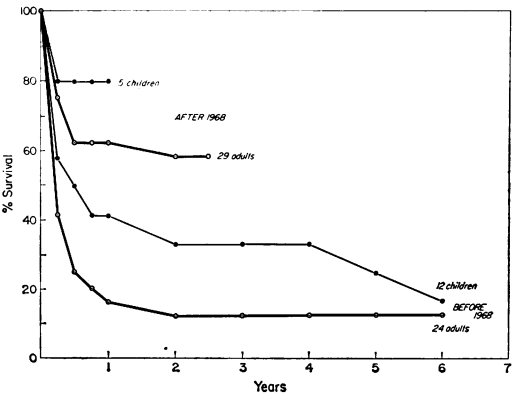

FIG. 4. Comparative survival of functioning kidneys in children (ages 1–16) and adults (17–45) who received first transplants from cadaver donors. All causes of kidney failure are included, but only patients followed more than 3 months are included in this figure.

Multiple Transplants. Table 5 lists those patients who received more than one transplant. The function of these transplants is noted in Tables 1–4. Of seven second or third transplants prior to 1968, only one is functioning well (4) although long-term second transplant function had been established in two other patients (14, 41). Of four second or third transplants performed since 1968, three are functioning well. All patients who received two consecutive cadaver transplants died. The combination of two successive related kidneys or a related kidney followed by a cadaver kidney appear to be more successful.

Effect of Primary Disease on Results of Transplantation

Obstructive Uropathy. Table 6 summarizes the indications for transplantation in the 58 infants and children. These indications are considerably different from those found in the Kidney Registry which mainly includes transplants to adults. The majority (31/58) of the patients in the present series had congenital disease and most of these (25/31) involved vesico-ureteral reflux or obstructive propathy of one type or another. A lesser number of patients (25/58) had acquired disease, usually glomerulonephritis, the pathogene-

TABLE 5. *Results of Multiple Renal Transplants to Children*

No.	Patient	Sex	Age	No. of Trans-plant	Previous Trans-plant Donor	Fate of Previous Transplants	2nd Transplant Donor	Condition
Before 1968:								
41	J. B.	M	11	2	Cadaver	Rejected	Father	Rejected 38 months—received 3rd transplant
14	S. S.	M	15	2	Aunt	Technical Failure	Mother	Died 2 years of cryptococcosis
47	D. G.	F	13	2	Cadaver	Technical Failure	Father	Died day 35 of rupture of mycotic aneurysm iliac artery
4	V. W.	F	9	2	Father	Technical Failure	Cadaver	Well—7 years
2	B. M.	F	9	2	Mother	Rejected 18 months	Cadaver	Rejected—received 3rd transplant
2	B. M.	F	9	3	Cadaver	Rejected	Cadaver	Died day 11 of staphyloccal sepsis
40	B. S.	F	14	2	Cadaver	Rejected	Cadaver	Died day 57 of pseudomonas sepsis
After 1968:								
49	J. P.	F	12	2	Cadaver	Rejected 5 months	Father	Well—38 months
46	C. T.	F	4	2	Cadaver	Technical Failure at age 1½	Cadaver	Died day 19 of mixed sepsis
26	J. O.	M	10	2	Mother	Original disease recurred 1 month	Cadaver	Well—1 month
41	J. B.	M	15	3	Father	Rejected 38 months	Mother	Well—13 months

sis of which may involve immune processes. Table 7 demonstrates that there is no difference in the functional survival between children with obstructive or non-obstructive primary renal disease. The incidence of sepsis is no higher in those with vesicoureteral reflux as long as the ureters have been completely excised. Similarly the incidence of recurrence of the original immune disease is not high enough to prejudice the survival of kidneys in patients with nephritis.

Twenty-five of the 58 patients had obstructive uropathy associated with vesicoureteral reflux. This finding presents several problems: it is extremely difficult to evaluate bladder function in the presence of dilated ureters which reflux freely. Consequently bilateral nephrectomy and total ureterectomy must be performed pior to complete bladder evaluation. When reflux has been alleviated, a simple voiding cystogram will prove the competence of the bladder. Only rarely are cystoscopy or cystometric studies indicated. If a ureterectomy is not complete, urinary infections will occur in the post-transplant period. This was most strikingly seen in patient 23, a 6-year-old girl who underwent right nephroureterectomy but in whom her left aplastic kidney was left. Recurrent urinary tract infections with septicemia appeared 6 months post-transplant. After the left kidney and ureter were removed, the urine became sterile. Therfore, total ureterectomies were performed in almost all patints with reflux.

Table 8 lists the additional lower urinary tract procedures required in eight other patients with obstructive uropathy prior to transplantation. In two patients (17, 44) bladder neck resections enabled the ureter to be implanted into a functioning bladder. In two other instances (12,

TABLE 6. *Indications for Renal Transplantation in 58 Children*

Congenital diseases	
Vesico-ureteral reflux producing pyelonephritis	11
Hypoplasia-dysplasia with vesico-ureteral reflux	8
Bladder neck obstruction with vesico-ureteral reflux	4
Hereditary interstitial nephritis	4
Medullary cystic disease	2
Cystinosis	1
Meningomyelocele with neurogenic bladder	1
Acute congenital glomerulonephritis	1
Acquired diseases	
Chronic or subacute glomerulonephritis	16
Steroid resistant nephrotic syndrome	4
Membranoproliferative (hypocomplementemic) nephritis	3
Anaphylactoid nephritic	2
Wilms' Tumor	1

19) urinary diversion had been necessary but bladder function was unimpaired and transplant ureterocystostomy was performed successfully.

Total urinary diversion of the transplant was necessary because of non-functioning bladders in four patients. Two of these patients (40, 45) died in the early post-transplant period of sepsis. Leakage at the uretero-ileostomy contributed to death in one instance. Successful transplants to ileal loops were carried out in two children (43, 29) as well as three older patients.

The technics of transplantation to dissecting ileal loops has previously been described.[9] Briefly, the infected host kidneys should be removed at a pretransplant operative stage. If a previous urinary conduit had been constructed, this bowel segment should be excised. In this way all infected tissue can be removed without contamination of retroperitoneal spaces. At a second stage operation a new ileal bladder can be constructed and placed within the retroperitoneal space, either behind the cecum or the sigmoid. At the third (transplantation) stage the kidney should be positioned in the iliac fossa with the ureter directed cephalod. Using a short segment of ureter the anastomosis can then be performed to the ileal loop previously placed in the retroperitoneal position. A Foley catheter placed down to the blind retroperitoneal limb of the ileal loop aids in its identification.

Although total urinary diversion of transplanted kidneys can be successfully carried out, an increased incidence of complications can be expected. All three transplants to ileal loops in adults are functioning well. One child (43) survived for 6 years with normal renal function after transplant to an ileal bladder. However, he developed a urinary pelvic calculus and sepsis, and died recently. A second child (29) developed stenosis of her uretero-ileostomy which damaged the kidney and required repair. Renal function has not yet returned to normal.

Membrano-proliferative Glomerulonephritis (Hypocomplementemic Nephritis). The disease responsible for renal failure in four children was membrano-proliferative glomerulonephritis.[8] Such patients may have extremely low serum complement levels during the active phase of the disease. Although complement can be found deposited on the glomerular basement membrane of such patients, it is unknown whether this finding represents immune process directed against the kidney or some other process. Immune globulins are seldom found in this location.[8] There has been a reluctance to transplant patients with this disease because of the suspicions that it may recur within the transplant.

TABLE 7. *Effect of Obstructive Uropathy on Transplant Outcome*

	Clinical Results*			
	Pre-1968		Post-1968	
Indications	Good	Poor	Good	Poor
Obstructive Disease	4	8	11	0
Non-Obstructive Disease	8	6	16	3

* Infants excluded.

TABLE 8. *Urological Reconstructive Procedures Preceding Transplantation in Children with Obstructive Uropathy*

No.	Patient	Procedures	Result
12	J. M.	Ileal bladder	Well; urinary diversion from transplant not necessary
17	C. W.	Suprapubic cystostomy Transureteral resection	Well; bladder function excellent
10	S. B.	Colon bladder	Urinary diversion from transplant not necessary. Rejected 1½ years; died on dialysis 2 years.
29	K. L.	Ileal bladder	Well; stenosis ureteral-ileostomy required repair
40	B. S.	Suprapubic cystostomy YV plasty bladder neck Ureterostomy Ileal bladder	Died after 2nd transplant
43	R. B.	Ileal bladder	Ileal bladder function excellent. Died 6 years post-transplant.
44	M. A.	YV plasty bladder neck Ureterectomy and reimplantation of ureter Nephrostomy	Died day 57 of sepsis
45	M. B.	Ileal bladder	Leaked at ureteroileostomy. Died day 49 of sepsis.

When nephrectomy is performed in the pretransplant period most patients will show increases in complement levels. All three children with membrano-proliferative glomerulonephritis had excellent early response to transplantation (8, 14, 31) as have four adults. One child (14) died 2 years after transplantation with miliary cryptococcosis.

Wilms' Tumor. Several transplantation groups [11] have transplanted patients with Wilms' tumor. In general, the strategy has been to perform bilateral nephrectomy for bilateral Wilms' tumors, and to maintain the patients on dialysis for at least one year. In the absence of metastases, transplantation is then carried out from a cadaver donor. One patient (55) with bilateral Wilms' tumor and a pulmonary metastasis received a renal graft only 4 months after nephrectomy and resection of his pulmonary lesion. His progressive development of antibodies against histocompatibility antigens within the population necessitated premature transplantation from the first cadaver donor to whom the patient was not immune. Renal function has been excellent, without evidence of the tumor recurring. Should the metastasies appear, triple chemotherapy and radiotherapy will be used to attempt to control the metastasis even while continuing the needed immunosuppression. Kountz has reported one patient with Wilms' tumor well 3 years after transplantation.[11]

Hereditary Interstitial Nephritis. Four patients (28, 30, 34, and 57) received kidneys because of hereditary interstitial nephritis, without deafness. Two brothers (28, 34) are included in this series and another (30) has a sister who obtained a kidney transplant at another center. These

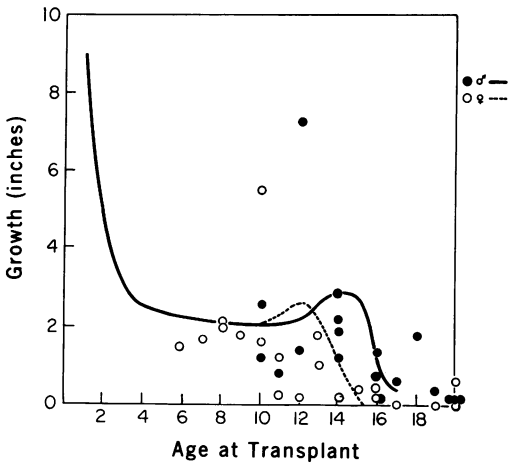

FIG. 5. First year growth after renal transplantation in children: The curve represents normal yearly growth in children at the specified age. The growth occurring in each child during the first year following transplantation is indicated. Only children followed for more than one year are included.

patients have not developed recurrent disease.

Cystinosis. Cystinosis is a congenital systemic disease with cysteine crystals deposited in the renal tubules, as well as in other tissues of the body, leading to progressive functional deterioration and renal tubular acidosis. One 11-year-old girl (21) had cystinosis with severe renal rickets and growth retardation, A growth spurt of 6 inches took place within the first year after transplantation from the mother; and renal rickets has completely been cleared. Function appears to be normal in all respects. Mahoney, *et al.*,[12] have reported four similar patients with cystinosis. Cysteine crystals have been found in the interstitial cells of the transplanted kidney but they were not deposited in the renal tubular cells. Renal function in these patients remains normal despite deposition of cysteine within the kidney.

Medullary Cystic Disease. Two sisters have developed medullary cystic disease. The first (13) received a kidney from an aunt and is well 7 years later. The second (54) developed a severe hypercoagulable state (PTT = 23 seconds), and clotted three Scribner shunts, despite technically adequate operations. Transplantation was carried out without dialysis; on the second post-transplant day renal arterial thrombosis occurred. Coagulation studies of this patient have revealed a persistent hypercoagulable state with thrombocytopenia, but Factor V and Factor VIII levels are five times normal. Whether the hypercoagulable state is associated with medullary cystic disease, or not, is unknown. The possibility exists that this renal disease is associated with chronic release of thromboplastic substances, low grade intravascular coagulation, and a hypercoagulable state. Consequently, peritoneal dialysis, bilateral nephrectomy and a second attempt at transplantation is planned. This patient represents the single technical failure in the 32 patients transplanted within this age group since 1968.

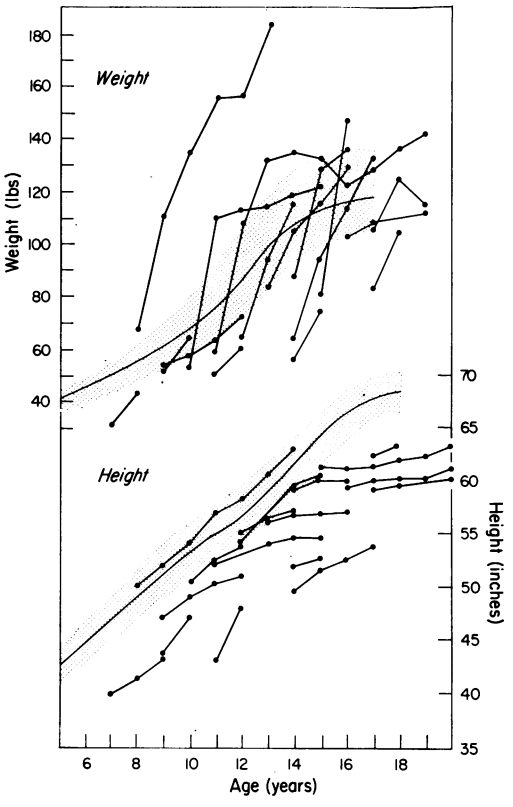

FIG. 6. The growth pattern of girls following transplantation: Growth generally parallels normal growth between the ages of 7 and 13. Thereafter, it levels off rapidly regardless of the age at which the patient was transplanted.

Steroid Resistant Nephrotic Syndrome. Four patients (7, 26, 41, 50) had severe nephrotic syndrome with massive proteinuria which ultimately progressed to renal failure. The syndrome was resistant to high steroid doses and other cytotoxic drugs.[7] Immune globulins and complement are not deposited in these kidneys and an auto-immune pathogenesis is not suspected. The four patients have had very poor results after transplantation; two have apparently had recurrence of the nephrotic syndrome.

S. H. (50), a 6-year-old boy, received a cadaver kidney transplant. Although the creatinine clearance was normal, massive proteinuria appeared soon after the trans-

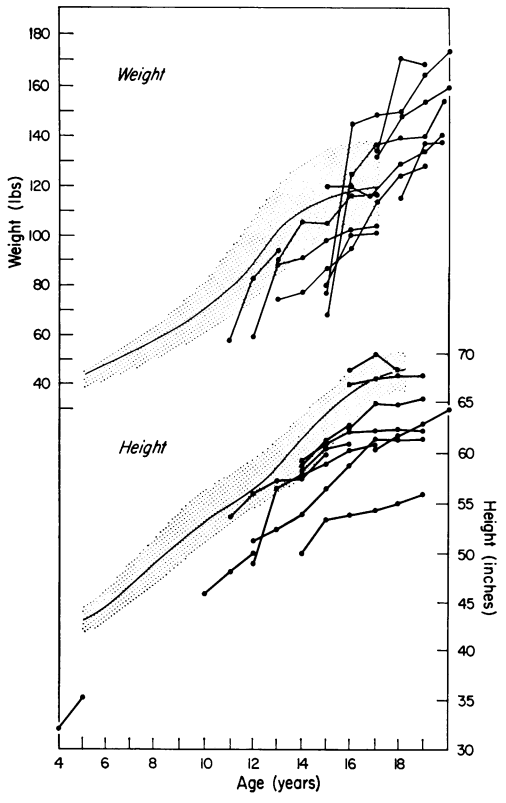

FIG. 7. The growth pattern of boys after transplantation: Growth generally parallels normal growth and levels off rapidly after age 15 or 16.

plant despite immunosuppressant drugs and large doses of steroids. Renal failure progressed slowly and he died 2 years later of pneumocystis carinii pneumonia. J. O. (26) is an 8-year-old boy who received a kidney from his mother. Massive proteinuria (20 to 70 Gm./day) appeared immediately, despite normal creatinine clearances and the kidney required removal on the 48th post-transplant day. A third patient (41) rejected his first kidney 6 months after transplantation and a fourth patient (7) has chronic renal functional failure. Two patients (26, 50) have apparently accepted subsequent transplants without nephrotic syndrome after prolonged dialysis. It is therefore possible that the tendency of the disease to recur may be temporary and that nephrectomy should be followed by rather prolonged periods of dialysis in these children prior to transplantation.

Technical Problems. There has been concern that technical problems would be frequent in pediatric renal transplantation. Since 1968, only one of 32 consecutive primary transplants have been lost for technical reasons. This patient (54) was discussed in the section on medullary cystic disease. The renal artery thrombosed on the second post-transplant day. The patient had a hypercoagulable state which has precluded hemodialysis and she is now maintained on peritoneal dialysis.

Fine has reported nine ureteral complications in 23 primary pediatric transplants, including six leaks from ureteroneocystostomies.[5] No urinary fistulas have developed after first transplants at the University of Minnesota since 1968. One patient (4) developed ureteral stenosis, necrosis, and leakage approximately one month following his third transplantation. The kidney was placed high within the peritoneal cavity and the ureter traversed the free peritoneal cavity. The leakage in this case could be the result of a failure to establish collateral circulation to the distal ureter since it was not placed in the retroperitoneal position. The patient is well one year after ureteral reimplantation into the bladder.

Growth after Renal Transplantation. Figures 5, 6, 7 summarize growth characteristics of children following transplantation. Figure 5 plots the first year's growth of the transplanted child against the average yearly growth curve of children. It is clear that occasional massive growth spurts will occur in the first year following transplantation. Most children, however, grow slightly slower than normal. The adolescent growth spurt is absent in the transplanted children and adolescent growth is particularly depressed in girls. Figures 6 and 7 demonstrates that the first year's growth is continued in the younger children. These children are much smaller

TABLE 9. *Effect of Donor Source, Renal Function, or Prednisone Dose on First-Year Post-transplant Growth (Inches ± S.E.)*

	Donor Source		Serum Creatinine		Prednisone Dose	
	Cadaver	Related	≤1.5	>1.5	≤0.25 mg/kg	>0.25 mg/kg
Girls	1.33 ± 0.6	1.31 ± 0.4	1.34 ± 0.46	1.44 ± 0.38	0.83 ± 0.5	1.03 ± 0.4
Boys	1.75	1.44 ± 0.25	1.13 ± 0.32	1.95 ± 0.21	1.07 ± 0.25	2.0 ± 0.13

than normal, but post-transplant "catch-up growth" is rare. The growth patterns generally parallel normal growth. After age 13 or 14, girls grow very little and boys stop after ages 15–16 whatever age the transplantation took place. This early cessation of growth results in the typical appearance of transplanted girls who are very short and more Cushingoid than the boys.

Sexual maturation in boys appears to be normal although the period of observation is short. Similarly, only two girls now aged 13 and 14 have failed to menstruate at the usual age despite relatively normal renal function and only moderate doses of prednisone. All other girls have resumed menstruating, if previously mature, or have undergone a normal menarche upon reaching age 13 or 14.

Table 9 attempts to correlate the amount of first year post-transplant growth with the kidney donor, renal function, or prednisone dosage. No such correlations can be made.

Rehabilitation. All patients but one have returned to school by 3 months following transplantation. Most patients have noted marked improvement in their school grades, a number of patients have finished high school and a few have entered college or obtained full-time jobs. Chronic rejection, however, with frequent rehospitalization, institution of high doses of steroids, development of Cushingoid faces and the stunting of growth is an occasional severe social, as well as medical, set back. This is an additional indication for removal of the transplant and retransplantation in certain selected children. C. T. (18) is clinically well almost 3 years following transplantation from the father but maintains a serum creatinine of 4, is hypertensive, and severely Cushingoid. She requires tutoring at home because of embarrassment about her appearance. This is the single failure of patients to return to school in these children. The psychological problems of these transplanted children have been reported by Bernstein.[1]

Bone Disease. A number of investigators have commented on muscular and skeletal abnormalities following transplantation. There is an occasional problem among our children as well: Two children have developed severe aseptic necrosis. In one (20) this has involved the tali of both feet. The patient is considerably overweight and Cushingoid but steroid dosage has been kept within reasonable range (0.15 mg./Kg.). A second patient (41) who has received three kidney transplants and has been on dialysis intermittently for 7 years, developed severe necrosis of both hips. After the third transplant he developed bilateral spontaneous ulnar fractures and an asymptomatic intertrochanteric fracture of the femur. This patient rejected his second kidney (from his father) because steroid dosage was drastically reduced when aseptic necrosis of the hips appeared. We have not noted improvement in aseptic necrosis either in children or young adults with reduction of the steroid dosage, although the pathogenesis appears to involve steroid administration. The etiology is obscure as yet and it is not clear whether the avoidance of weight bearing will alleviate the progression of the disease.

A number of factors are thought to con-

tribute to the development of bone disease in these children. Uremia prevents the absorption of calcium from the gut resulting in hyperplasia of the parathyroids, and resorption of the bone. Dialysis against low calcium dialysate solution aggravates the problem and may also deplete ascorbic acid leading to changes consistent with scurvey. Rachitic changes in children with renal disease are frequently severe but after transplantation the changes are usually rapidly reversed despite immunosuppression.

Hyperplasia of the parathyroid glands can be found in all patients with uremia. The secondary hyperpathyroidism usually reverts toward normal after transplantation but a number of investigators have encouraged parathyroidectomy to aid in the management of these children. One patient in our series developed overt hyperparathyroidism with osteitis fibrosis cystica and gross metastatic calcification. Parathyroidectomy was not performed but the hyperparathyroidism managed with a low calcium, high phosphate diet, phosphate containing antacids and diuretics. The calcium has not exceeded normal levels in the 6 months following transplantation and there has been almost complete resolution of the metastatic calcification and bone disease. Thus, even with pre-existing severe secondary hyperparathyroidism it may not be necessary to remove the parathyroids of patients in whom transplantation is imminent. The danger has always been thought to be calcification of the transplant, but medical management should minimize this possibility.

Hypertension. Hypertension can be a severe problem in children with renal disease. In one patient (19) hypertensive encephalopathy, coma and convulsions preceded transplantation and required emergency nephrectomy. Although the hypertension was relieved by the nephrectomy, complete recovery required renal transplantation. Thereafter the child returned to school. Unfortunately, repeated rejection episodes led to recurrence of hypertensive encephalopathy, cerebal hemorrhage, and death 9 months following transplantation.

Hypertension is usually relieved by nephrectomy followed by successful transplantation. The early post-transplant period, however, may be accompanied by hypertensive problems requiring antihypertensive medication. Tables 3 and 4 document this finding. Of seven well children transplanted less than 6 months ago, six are taking antihypertensive medication. This medication can usually be reduced or eliminated after the first 6 months (Tables 1–4).

Even so, children's blood pressures are labile. Five patients (6, 32, 38, 50, 53) developed a single episode of convulsions associated with hypertension 2 months to 5 years following transplantation. In each instance the episode was preceded by a mild rejection episode, slight elevation of serum creatinine, gain in weight, development of hypertension with convulsions. For apparently similar reasons, patients with chronic renal functional deterioration may have hypertension which is difficult to control. This is true of patients 7, 15, 18. Others despite low doses of prednisone and apparently perfect renal function have persistent mild asymptomatic hypertension (5, 13, 25, 42, 48, 51). In this latter characteristic children appear to resemble adult transplant recipients.

Transplantation in Infants. Many children are born each year with renal disease incompatible with life. It is unrealistic to expect to be able to dialyze these infants for prolonged periods. Nevertheless, it is possible to hemodialyze them for several months in expectation that pediatric cadaver kidneys will become available for transplantation. We have recently maintained two newborn infants on dialysis for 1 and 2 months, respectively. These children then underwent renal transplantation on an experimental basis.

W. A. (52) was born of a full-term normal pregnancy. He failed to thrive at

home and returned to the hospital aged 2 weeks. A diagnosis of renal hypoplasia-dysplasia was made. Peritoneal dialysis was required for one week and hemodialysis was instituted age 1 month when the patient weighed 3 Kg. Bilateral nephrectomy, splenectomy, and renal transplantation was carried out 16 days later. The kidney donor was a 12-year-old girl with a double renal artery requiring two anastomoses. Initial renal function was perfect and immunosuppression included anti-lymphoblast globulin, azathioprine and prednisone in reduced doses because of thrombocytopenia. Multiple sequential rejection episodes appeared 6 weeks to 3 months post-transplant. These could not be controlled with steroids and the patient died age 4½ months. At autopsy all anastomoses were patent.

A. F. (56) developed a nephritis of unknown etiology within the first 2 months of life and required a period of 2 months of hemodialysis while weighing 3.9 Kg. A bilateral renal transplant was carried out aged 4 months from a newborn cadaver. The technic is shown in Figure 8. The kidneys did not function immediately and the patient died suddenly during endotracheal suctioning on the second post-transplant day.

Cerilli *et al.*,[4] have reported a successful case of transplantation in an infant nine months old who is well more than a year later. The technical feasibility of hemodialysis and transplantation in these infants has thus been clearly demonstrated.

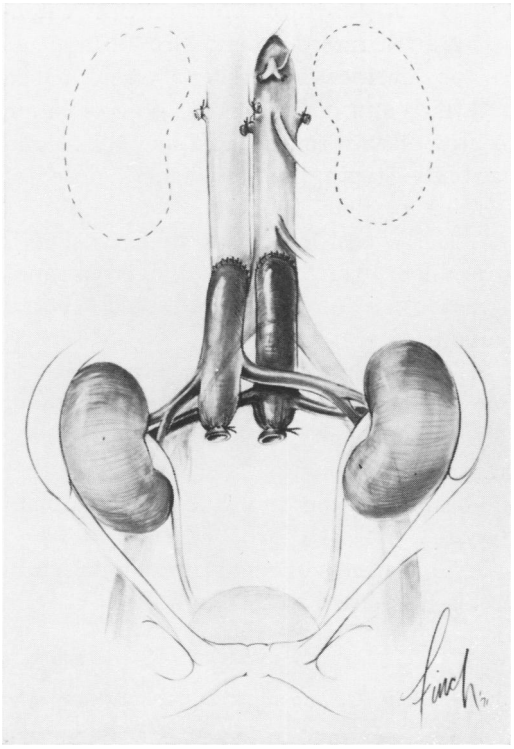

FIG. 8. Technic of transplantation of two newborn cadaver kidneys to newborn recipient. Aorta is anastomosed to aorta, and vena cava to vena cava. The kidneys are fixed by the sigmoid mesentery on the left, and the cecum on the right. The Ureters are implanted separately into the bladder by conventional tunneling technics.

Summary

1. Fifty-six children aged 1–16 and 2 infants have received renal transplants at the University of Minnesota since 1963.

2. Of the 24 patients transplanted between 1963–1967, 50% of recipients of related kidneys are well with their first transplant and 15% are well with second transplants. 16% of recipients of cadaver kidneys are well with first kidneys and 16% are well with second kidneys.

3. Of 24 children aged 1–16 transplanted with kidneys from related donors since 1968, only one has died, and only one has lost his kidney. Of six children aged 1–16 transplanted with cadaver donors since 1968 all are alive and five have good renal function.

4. Patients with obstructive uropathy do as well as patients with nephritis if refluxing ureters have been removed and bladder function restored. Diverting ileal bladders have been constructed for four pediatric transplants.

5. Patients with steroid resistant nephrotic syndrome seem to have poor prognoses and the disease may recur in the transplants. Prolonged dialysis may reduce this tendency.

6. Growth after transplantation parallels

the normal growth of children but "catch-up" growth rarely occurs. Growth appears to stop several years earlier than normal in both girls and boys. There is no correlation of growth with source of kidney, histocompatibility typing, maintenance dose of steroids, or renal function.

7. Early post-transplant hypertension is a problem which requires vigorous antihypertensive measures to avoid central nervous system changes.

8. Transplants have been carried out in two infants aged 2 to 4 months without technical difficulty. One infant rejected the transplant 3 months later and the other died suddenly on the 2nd post-transplant day.

9. The success of renal transplantation in children is equal to that in adults.

References

1. Bernstein, D. M.: After Transplantation—The Child's Emotional Reactions. Amer. J. Psych., 127:1189, 1971.
2. Broyer, M., Loirat, C., Kleinknecht, C., Rappaport, R. and Raymbault, G.: Eighteen Month's Experience with Hemodialysis in Children. Proc. Europ. Dialysis Transplant. Assos., 7:261, 1970.
3. Buselmeier, T. J., Santiago, E. A., Simmons, R. L., Najarian, J. S. and Kjellstrand, C. M.: Arteriovenous Shunts for Pediatric Hemodialysis. Surgery (In press).
4. Cerilli, G. J., Nelsen, C. and Dorfmann, L.: Renal Homotransplantation in Infants and Children with the Hemolytic-Uremic Syndrome. Surgery (In press).
5. Fine, R. N., Korsch, B. M., Stiles, Q., Riddell, H., Edelbrock, H. H., Brennan, L. P., Grushkin, C. M. and Leiberman, E.: Renal Homotransplantation in Children. J. Ped., 76:347, 1970.
6. Gonzalez, L. L., Martin, L., West, C. D., Spitzer, R. and McEnery, P.: Renal Homotransplantation in Children. Arch. Surg., 101:232, 1970.
7. Grupe, W. E. and Heymann, W.: Cytotoxic Drugs in Steroid-Resistant Renal Disease. Amer. J. Dis. Child., 112:448, 1966.
8. Herdman, R. C., Pickering, R. J., Michael, A. F., Vernier, R. L., Fish, A. J., Gewurz, H. and Good, R. A.: Chronic Glomerulonephritis Associated with Low Serum. Medicine, 49:207, 1970.
9. Kelly, W. D., Merkel, F. K. and Markland, C. A.: Ileal Urinary Diversion in Conjunction with Renal Homotransplantation. Lancet, 1:222, 1966.
10. Kelly, W. D., Lillehei, R. C., Aust, J. B., Varco, R. L., Leonard, A. S., Griffen, W. O., Markland, C. A., Herdman, R. C., Vernier, R. L., Michael, A. F. and Levitt, J.: Kidney Transplantation Experiences at the University of Minnesota Hospitals. Surgery, 62:704, 1967.
11. Kountz, S.: Personal Communication.
12. Mahoney, C. P., Striker, G. E., Hickman, R. O., Manning, G. B. and Marchioro, T. L.: Renal Transplantation for Childhood Cystinosis. New. Eng. J. Med., 283:397, 1970.
13. Simmons, R. L., Kelly, W. D., Tallent, M. B. and Najarian, J. S. Cure of Dysgerminoma with Widspread Metastases Appearing After Renal Transplantation. New Eng. J. Med., 283:190, 1970.
14. Simmons, R. L., Moberg, A. W., Gewurz, H., Soll, R., Tallent, M. B. and Najarian, J. S.: Immunosuppressive Assay of Antilymphoblast Globulin in Man: Effect of Dose, Histocompatibility, and Serologic Response to Horse Gamma Globulin. Surgery, 68:62. 1970.
15. Simmons, R. G., Hickey, K., Kjellstrand, C. M. and Simmons, R. L.: Family Tension in the Search for a Kidney Donor. JAMA, 215:909, 1971.
16. Starzl, T. E.: Experience in Renal Transplantation. Philadelphia, W. B. Saunders Company, 1964.
17. Weil, R. W., III, Simmons, R. L., Tallent, M. B., Lillehei, R. C. Kjellstrand, C. M. and Najarian, J. S.: Prevention of Urological Complications Following Kidney Transplantation. Ann. Surg. 174:154,, 1971.
18. Williams, G. M., Lee, H. M. and Hume, D. M.: Renal Transplants in Children. Transplant. Proc., 1:262, 1969.

Discussion

Dr. Joseph E. Murray (Boston): Dr. Najarian and his group, who have produced such a high standard of excellence in clinical transplantation, have presented a timely resume of this subject today. It was Dr. Starzl, I believe, who first popularized the technics of kidney transplants in infants and children, and Dr. Hume who first presented a series of transplants before the Transplant Society a few years ago. Today's study is really a magnificant review of this pediatric experience, and I will only make comments on two aspects: first, the need for extra-careful assessment of the lower urinary tract in prospective recipients of this age group; and secondly, the special socio-economic aspects of donor selection, usually a parent, in these young recipients.

Regarding the lower urinary tract, uremia and dilatation *per se* can produce bladder malfunction and ureteral reflux and dilatation without any anatomical abnormality; and Drs. Harrison and Gross may recall a girl we studied about 7 years ago when we wondered whether or not we ought to transplant because of the presence of ureteral reflux and poor bladder function. Both of them