function. Although our patient was treated with prednisone throughout, clinical improvement seemed to be temporally related to the administration of aspirin and dipyridamole. Central nervous system symptoms disappeared within two days of the initiation of antiplatelet therapy. The subsequent increase of dipyridamole dosage to 600 mg/day was followed by an increase in the platelet count, similar to the experience reported by Giromini et al.[8]

The effectiveness of aspirin and dipyridamole in TTP cannot be established with certainty by a few isolated case reports. However, the studies of Neame et al[10] and Harker and Slichter[11] suggest that the use of antiplatelet drugs in cases of TTP has a sound pathophysiologic basis. For this reason, the favorable results reported here and elsewhere[6-9] are probably not fortuitous and the use of antiplatelet drugs should be strongly considered in the treatment of TTP.

Nonproprietary Name and Trademark of Drug

Dipyridamole—*Persantine.*

References

1. Moschcowitz E: An acute febrile pleiochromic anemia with hyaline thrombosis of terminal arterioles and capillaries. An undescribed disease. *Arch Intern Med* 36:89-93, 1925.
2. Baehr G, Klemperer P, Schifrin A: An acute febrile anemia and thrombocytopenic purpura with diffuse platelet thromboses of capillaries and arterioles. *Trans Assoc Am Physicians* 51:43-58, 1936.
3. Singer K, Bornstein FP, Wile SA: Thrombotic thrombocytopenic purpura: Hemorragic diathesis with generalized platelet thromboses. *Blood* 2:542-554, 1947.
4. Amorosi EL, Ultmann JE: Thrombotic thrombocytopenic purpura: Report of 16 cases and review of the literature. *Medicine* 45:139-159, 1966.
5. Lerner RG, Rapaport SI, Meltzer J: Thrombotic thrombocytopenic purpura: Serial clotting studies, relation to the generalized Shwartzman reaction, and remission after adrenal steroid and dextran therapy. *Ann Intern Med* 66:1180-1190, 1967.
6. Jobin F, Delage JM: Aspirin and prednisone in microangiopathic haemolytic anaemia. *Lancet* 2:208-210, 1970.
7. Zacharski LR, Walworth C, McIntyre OR: Antiplatelet therapy for thrombotic thrombocytopenic purpura. *N Engl J Med* 285:408-409, 1971.
8. Giromini et al: Effect of dipyridamole and aspirin in thrombotic microangiopathy. *Br Med J* 1:545-546, 1972.
9. Amir J, Krauss S: Treatment of thrombotic thrombocytopenic purpura with antiplatelet drugs. *Blood* 42:27-33, 1973.
10. Neame PB, et al: Thrombotic thrombocytopenic purpura: Report of a case with disseminated intravascular platelet aggregation. *Blood* 42:805-814, 1973.
11. Harker LA, Slichter SJ: Platelet and fibrinogen consumption in man. *N Engl J Med* 287:999-1005, 1972.
12. Weiss HJ, Aledort LM, Kochwa S: The effect of salicylates on the hemostatic properties of platelets in man. *J Clin Invest* 47:2169-2180, 1968.
13. Harker LA, Slichter SJ: Studies of platelets and fibrinogen kinetics in patients with prosthetic heart valves. *N Engl J Med* 283:1302-1305, 1970.

Renal Transplantation Between Adults and Children

Differences in Renal Growth

Sherman J. Silber, MD

• There is an impressive but purely compensatory growth response of the child's kidney transplanted into the uremic adult, but no hypertrophy or hypotrophy of the adult's kidney in the uremic child.

Two separate types of renal growth seem to occur. Compensatory hypertrophic growth is a rapid reversible response to a functional nephron deficit. Obligatory growth occurs as one grows up, and is not reversible.

(*JAMA* 228:1143-1145, 1974)

AFTER unilateral nephrectomy, the size and function of the remaining kidney increases dramatically. The cause of this compensatory response remains an enigma. It is clearly a growth process, since RNA metabolism and protein content in the kidney increase considerably.[1-3] This response does not occur in hypophysectomized animals or in animals receiving antimetabolic drugs.[3,4] One could easily speculate that compensatory renal hypertrophy is simply an acceleration of the normal growth process in response to a decreased functioning of the renal mass.

Our study, however, has shown that compensatory renal growth is easily reversible when the nephron deficit is corrected.[5,6] When a hypertrophied kidney of a rat was transplanted four weeks after contralateral nephrectomy into a similar animal that also had only one hypertrophied kidney, each kidney returned rapidly to its original size, glomerular filtration rate (GFR), and renal plasma flow (RPF). In contrast, when normal adult animals were given extra kidneys, there was no decrease in size or function of any of the kidneys, and the animals had persistently increased GFR and RPF. Two types of renal growth can be defined: Obligatory renal growth occurs simply as the animal grows. This type of growth might be modified by "need," but it is definitely not reversible. Compensatory renal growth is a functional response induced only by a nephron deficit. This type of growth is easily reversible when the need is eliminated.

There has been much experience with renal transplantation in the use of children as donors as well as recipients,[7] but the bearing of these results on the understanding of compensatory hypertrophy has received little attention. This study describes the

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Read in part before the 122nd annual convention of the American Medical Association, New York, June 26, 1973.

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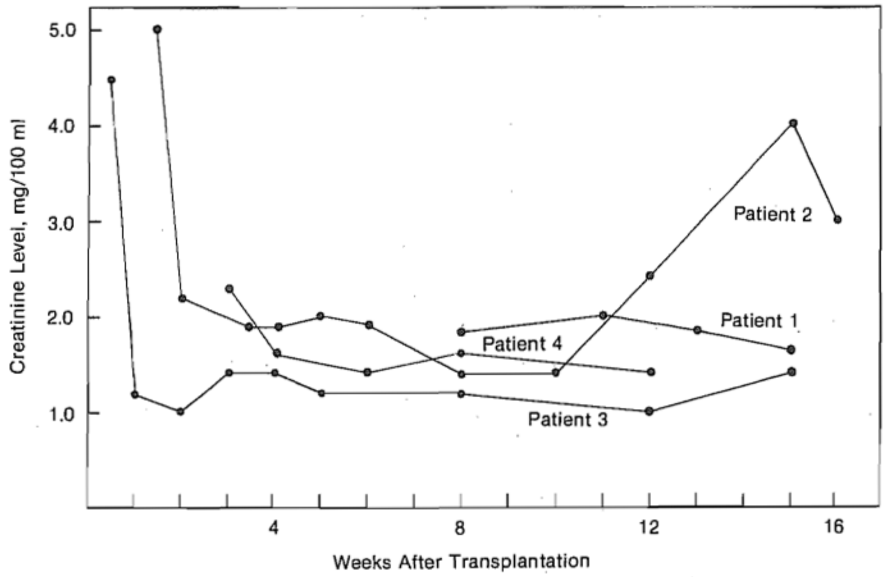

Fig 1.—Serum creatinine levels in adults with transplanted kidneys of children.

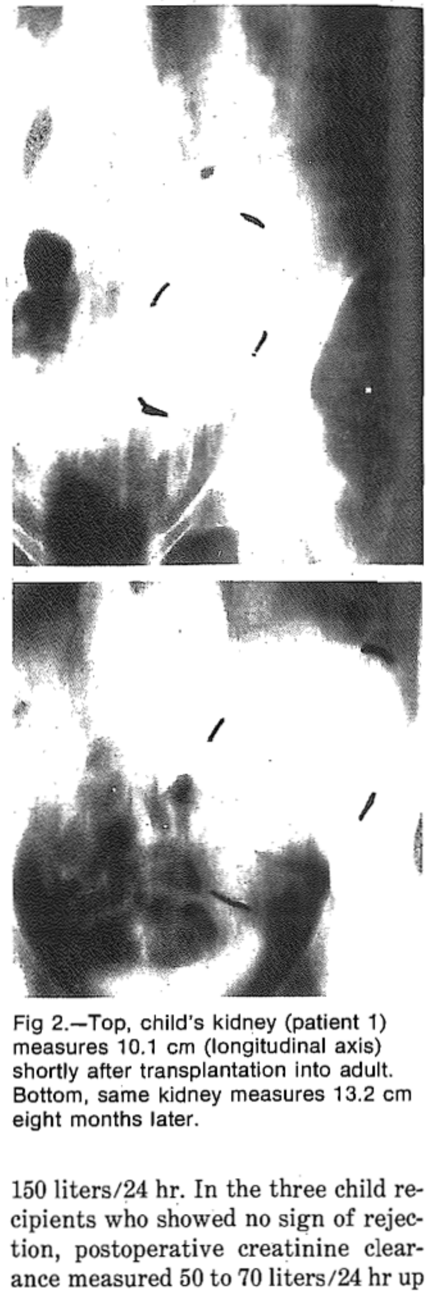

Fig 2.—Top, child's kidney (patient 1) measures 10.1 cm (longitudinal axis) shortly after transplantation into adult. Bottom, same kidney measures 13.2 cm eight months later.

behavior of renal growth in kidneys transplanted from children to adults and vice versa.

Methods

Four anephric adult patients, aged 23 to 39 years and with surface areas of 1.4 to 1.8 sq m, had hemodialysis regularly. Each received an immediate renal transplant from two dead children, aged 4 to 5 years. Renal function was monitored with serum creatinine determination, and renal size was determined by intravenous pyelography.

In addition, four children, aged 6 to 11 years and with surface areas of 0.7 to 0.8 sq m, had hemodialysis regularly. The children received at the time of bilateral nephrectomy a renal transplant from their mothers, who were aged 33 to 47 years and had a mean surface area of 1.7 to 1.8 sq m. Preoperative and postoperative renal functions were determined in the donors by measurements of serum creatinine and creatinine clearance. Preoperative and postoperative renal sizes were determined by intravenous pyelography. Similar studies were carried out with the recipients of the transplants.

Results

Child's Kidney Transplanted Into Adult.—Figure 1 shows that within three weeks of transplantation, three of the four kidneys were functioning well; by eight weeks, all four were. In patient 3, who had a body surface area of only 1.4 sq m, the serum creatinine level was as low as 1.2 mg/100 ml. In the three other patients, serum creatinine values were between 1.6 and 2.1 mg/100 ml. The creatinine level remained stable in all patients except patient 2, who later rejected the kidney. Table 1 and Fig 2 show that the children's kidneys measured 10.1 to 10.8 cm (longitudinal axis) when first placed into the adult, but by one to three weeks, the dimensions were 11.2 to 11.6 cm; by four to six weeks, 12 to 13 cm; and by five to nine months, a maximum of 13.2 to 13.6 cm.

Table 1.—Size (Longitudinal Axis) of Children's Kidneys Transplanted Into Adults

	Size of Kidney, cm			
Patient	At Time of Transplant	1-3 Weeks	4-6 Weeks	5-9 Months
1	10.1	...	12.0	13.2
2	10.4	...	13.0	13.5
3	10.8	11.6	13.0	13.6
4	10.6	11.2	...	13.5

Adult's Kidney Transplanted Into Child.—Figure 3 shows that all child recipients had a rapid drop of serum creatinine level to 0.6 to 0.8 mg/100 ml. All values persisted at this level for more than six months; patient 6, however, showed signs of rejection. Preoperative creatinine clearance in the four adult donors measured 110 to 150 liters/24 hr. In the three child recipients who showed no sign of rejection, postoperative creatinine clearance measured 50 to 70 liters/24 hr up to six months later. Postoperative clearance in the adult donors measured 100 to 130 liters/24 hr.

Table 2 and Fig 4 show that the adult donor's kidney originally measured 13.2 to 13.6 cm (longitudinal axis); dimensions were essentially unchanged four months postoperatively. However, the remaining kidneys of the adult donors measured 14.5 to 15.8 cm by that time.

Comment

The initial size of the cadaveric child donors' kidneys was inadequate for carrying on the normal requirements of the adult recipients. These kidneys, however, very rapidly hypertrophied to 177% of their preoperative

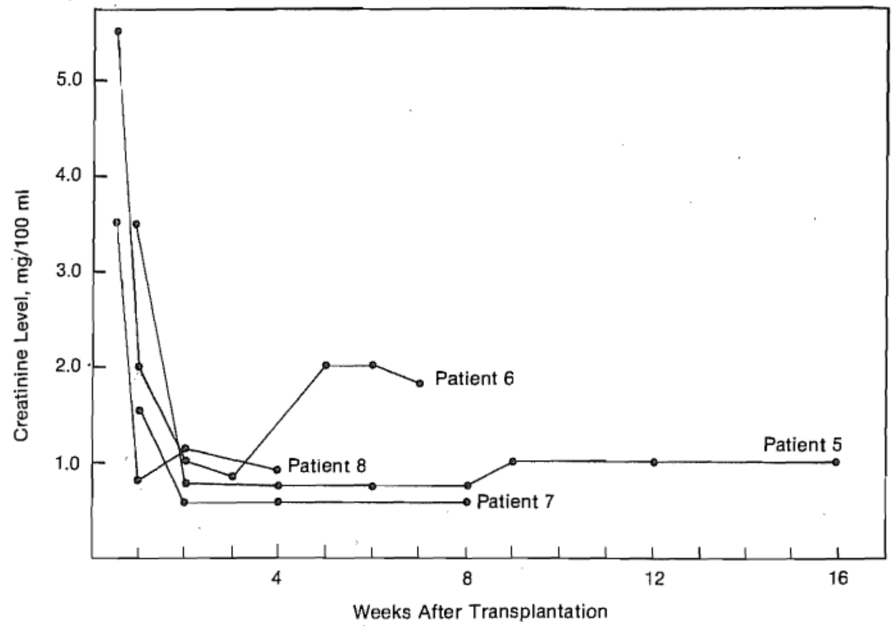

Fig 3.—Serum creatinine levels in children with transplanted kidneys of adults.

Fig 4.—Top, adult's kidney (patient 5) measures 13.2 cm (longitudinal axis) before transplantation. Bottom, same kidney measures 13.8 cm one year after transplantation into child.

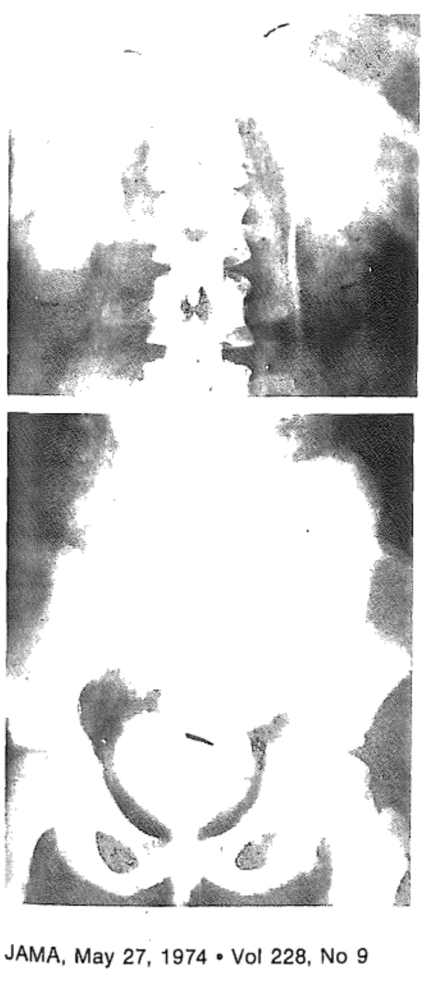

Table 2.—Size (Longitudinal Axis) of Adults' Kidneys Transplanted Into Children

	Size of Kidney, cm			
Patient	At Time of Transplant	1 Week	1 Month	4 Months
5	13.2	13.2	13.4	13.3
6	13.5	13.5	13.5	...
7	13.3	...	13.4	13.3
8	13.6	...	13.5	...

volume. (If volume is proportional to the axis,[3] and if the axis were increased by an average of 33%, the calculated volume would have been increased by 77%.) This dramatic growth is not surprising for two reasons: First, compensatory renal growth is known to be more pronounced in children than in adults.[8] Second, the relative deficit of renal mass in these adult recipients is much greater than when the donor is also an adult. Growth leveled off, however, at 13.2 to 13.6 cm, and did not reach the size of the usual adult's hypertrophied kidney (15 to 16 cm). In these patients, although the compensatory growth process was brisk and greater than usual, there was an upper limit. Serum creatinine values between 1.6 and 2.1 mg/100 ml, corresponding to about one-half normal adult GFR, support this observation. Fine et al[9] noted a similar degree of hypertrophy when transplanting a child's kidney into another child. The greater need of adult recipients, therefore, did not induce acceleration of obligatory growth; instead, simply normal compensatory growth occurred. One cannot draw really firm conclusions, however, from human cadaver transplants, since occult rejection could be occurring, thus preventing a greater growth response.

The size of the adult's kidney did not increase or decrease when placed in a child whose surface area measured only 40% of the donor's surface area. Yet, the donor's remaining kidney hypertrophied to about 150% of its preoperative volume, and the donor's creatinine clearance rose to almost the original value with two kidneys. The child's creatinine clearance, however, remained at half of the donor's original value.

Ogden[10] found that as the donor's kidney hypertrophied, the GFR can be used as a standard to judge the status of the recipient. In the case of an adult donor's kidney that already has a GFR greater than the need of the child recipient, there is no such hypertrophy. In addition, this kidney does not appear to decrease its size or function. Unfortunately, none of our recipients were quite small enough to test critically this latter impression. On the basis of our experiments on rats with three kidneys, however, renal atrophy or reduction of GFR would not be expected in human recipients.

References

1. Lowenstein LM, Stern A: Serum factor in renal compensatory hyperplasia. *Science* 142:1479-1480, 1963.
2. Malt RA: RNA metabolism in compensatory growth of kidney in Nowinski WW, Goss RJ (eds): *Compensatory Renal Hypertrophy.* New York, Academic Press Inc, 1969, pp 131-156.
3. Malt RA: Compensatory growth of the kidney. *N Engl J Med* 280:1446-1459, 1969.
4. Resnick MI, Albert DJ, Persky L: Inhibition of compensatory renal hypertrophy with mithramycin. *J Urol* 108:194-196, 1972.
5. Silber S, Malvin R: Compensatory and obligatory renal growth in rats. *Am J Physiol* 226:114-117, 1974.
6. Silber S, Grudup J: The three kidney rat model. *Invest Urol,* to be published.
7. Fine RN, et al: Renal transplantation in young children. *Am J Surg* 125:559-569, 1973.
8. Barrows CH Jr, Roeder LM, Olewine DA: Effect of age on renal compensatory hypertrophy following unilateral nephrectomy in rat. *J Gerontol* 17:148-150, 1962.
9. Fine RN, et al: Use of pediatric cadaver kidneys for homotransplantation in children. *JAMA* 210:477-484, 1969.
10. Ogden DA: Donor and recipient function two to four years after renal homotransplantation. *Ann Intern Med* 67:998-1006, 1967.