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Variations in Arterial Blood Pressure after Kidney Transplantation

Relation to Renal Function, Plasma Renin Activity, and the Dose of Prednisone

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SUMMARY

The course of hypertension within the first 2 months after kidney transplantation was correlated with renal function, plasma renin activity (PRA), and the daily maintenance dose of prednisone in 18 homograft recipients. During acute rejection blood pressure (BP) closely correlated with PRA. Patients with normal homograft function showed an increase in BP early after transplantation which in most returned to normal 3–8 weeks later. In the latter group no correlation could be found between the level of BP and PRA, however the BP correlated closely with the dose of prednisone. These observations suggest that during acute rejection the increase in BP may at least partly be mediated by a renal pressor mechanism, whereas with normal renal function the high dose of glucocorticoids may play an important role in the development of hypertension.

Additional Indexing Words:
Hypertension Prednisone Rejection of homograft Plasma renin activity
Kidney transplantation

HIGH BLOOD PRESSURE is a common phenomenon after kidney transplantation.[1–8] In view of its potential detrimental consequences[9–11] effective control of posttransplant hyptertension is of utmost importance.[10] Numerous factors have been implicated as either causing or contributing to the occurrence of hypertension early after kidney transplantation.[5, 7, 12, 13] Renal pressor mechanism may be responsible for high blood pressure in states of impaired homograft perfusion resulting from prolonged ischemia time[12, 14, 15] or renal artery stenosis.[16, 18] Hypertension which occurs during acute rejection has been reported to resemble renal arterial hypertension[11, 19] and is frequently associated with a high plasma renin activity.[15, 20, 22] Retained diseased kidneys have been proposed as another factor responsible for high blood pressure.[23] Reports on cure of hypertension after removal of the residual organs lend support to this notion, although the mechanism is poorly understood.[17, 23]

In a reported series of hypertensive renal homograft recipients, normotension was noticed to prevail as time elapsed and the dose of corticoids was reduced.[24] This observation implied a possible cause and effect relationship between the level of blood pressure and the dose of steroids and warranted a more detailed appraisal of the role of glucocorticoids in posttransplant hypertension. Observations on the early course of hypertension after transplantation, its relation to the variations in renal function, plasma renin activity, and the dose of glucocorticoids, form the basis of the present communication.

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Table 1

Clinical Data and Plasma Renin Activity of All Patients

Pt	Age (yr)	Sex	Diagnosis	Hemodialysis	Bilat NPX	BP (mm Hg)		PRA (ng/ml/hr)		Donor
						Pre-NPX	Post-NPX	Pre-NPX	Post-NPX	
CB	40	F	Chr GN	+	+	140/100	120/70	10.82	0.00	R
RC	41	F	Chr GN	+	−	200/110	−	9.11	−	R
BW	28	M	Chr GN	+	+	160/100	140/90	1.80	0.49	R
UM	16	F	Chr GN	+	+	180/120	120/80	−	−	R
MK	18	F	Chr GN	+	+	170/120	150/90	4.20	0.00	R
KR	46	M	Chr GN	+	−	160/110	−	9.27	−	R
PJ	28	F	Chr rej	+	−	160/100	−	3.00	−	C
WM	42	F	Chr GN	+	+	140/100	120/80	−	0.44	R
NJ	10	F	Med CD	+	−	140/90	−	1.80	−	C
TS	12	F	Chr rej	+	−	140/110	−	7.50	−	C
LL	16	F	LE neph	+	+	180/110	120/70	114.00	0.00	R
VJ	14	M	Med CD	−	−	130/90	−	−	−	R
LN	38	F	Chr PN	+	−	180/110	−	−	−	C
DP	9	F	Cyst	+	−	140/100	−	−	−	C
ML	28	M	Chr GN	+	−	170/118	−	−	−	R
DJ	23	M	Chr rej	+	−	160/100	−	11.70	−	C
CM	24	F	Chr GN	−	−	140/100	−	−	−	R
CE	18	M	Chr GN	+	+	160/110	145/80	−	0.00	R

Abbreviations: Chr GN = chronic glomerulonephritis; Med CD = medullary cystic disease; Chr rej = chronic rejection of homograft; LE neph = lupus nephropathy; Chr PN = chronic pyeleonephritis; Cyst = cystinosis; Bilat NPX = bilateral nephrectomy prior to transplant; BP = blood pressure; PRA = plasma renin activity; R = related; C = cadaver; BP = blood pressure.

Methods

Fifteen patients with chronic renal disease of diverse etiology and three patients with chronic rejection of renal homografts undergoing transplantation were studied. Sixteen patients had diastolic blood pressure in excess of 90 mm Hg. The sex, age, and the source of the organs are listed in table 1. Seven patients underwent bilateral nephrectomy 1–6 months prior to, and six during the transplantation; five retained their original kidneys. The surgical procedure and the immunosuppressive regimen were described elsewhere in detail.[25, 26] Sixteen patients were treated with chronic hemodialysis. All patients were on a low-protein diet (40g/24hr), and the amounts of sodium and

Table 2

Creatinine Clearances, Blood Pressure, Body Weight, Urinary Sodium Excretion, Plasma Renin Activity, and Daily Maintenance Dose of Prednisone during the First Week and 3–8 Weeks after Kidney Transplantation in Patients with Adequate Renal Function

Pt	C_{CR} (ml/min)		BP (mm Hg)		Weight (kg)		$U_{NA}V$ (mEq/24 hr)		PRA (ng/ml/hr)		Prednisone (mg/24 hr)	
	I	II	I	II	I	II	I	II	I	II	I	II
UM	45	68	160/120	120/60	41	45	140	152	4.00	18.10	140	30
RC	40	38	160/100	140/90	45	49	110	130	11.00	1.9	120	45
MK	65	70	160/120	126/70	44	42	135	130	1.44	5.00	200	40
CE	69	80	150/110	130/70	55	57	105	120	1.20	2.41	170	45
BW	60	62	160/110	140/100	59	58	147	132	0.50	5.90	180	90
WM	70	68	140/90	110/80	43	46	140	155	1.10	7.30	140	45
TS	29	63	160/115	110/70	43	41	142	121	0.00	2.30	180	25
DJ	46	50	140/100	130/80	60	55	100	122	0.50	12.20	175	40
CM	56	48	140/100	100/64	52	50	140	120	0.22	2.50	180	40
LL	50	46	120/70	110/70	55	56	130	150	0.60	1.12	40	30
VJ*	42	51	170/105	140/90	40	52	100	104	−	17.90	80	15
KR*	85	75	180/110	140/80	62	65	150	170	−	14.00	170	40
ML*	36	46	160/110	150/100	80	77	160	152	20.0	38.40	180	100
JP	49	52	130/95	120/80	43	47	159	167	−	1.80	170	50

*Patients retaining their original diseased kidneys.

Abbreviations: C_{CR} = creatinine clearances; $U_{NA}V$ = urinary sodium excretion; I = first week after transplant; II = 3–8 weeks after transplant.

potassium were adjusted according to the individual needs of each patient. After transplantation, patients with adequate homograft function were given liberal diets. The calculated amounts of sodium in the diets ranged from 100 to 170 mEq/24hr; these amounts were also reflected in urinary excretion rates as shown in tables 2 and 3. Salt and water intake were restricted only during acute rejection. All patients were weighed daily.

Kidney Function

Endogenous creatinine clearances were used as estimates of glomerular filtration rate. Urine was collected over 24 hours and blood was obtained at the end of the collection periods. Creatinine concentrations in the serum and in the urine were determined with a Technicon autoanalyzer. Creatinine clearances were measured daily during the first 4–6 weeks after surgery and then at least once every week; during episodes of acute rejection, the clearances were measured daily. Sodium concentrations in the serum and in the urine in all specimens were determined with an Instrumentation Laboratory flame photometer model 143.

Blood Pressure

Blood pressure was measured in supine position four to eight times daily during the first 4–6 weeks after surgery and thereafter at least once a week. During acute rejection crises, it was recorded as frequently as during the initial period. The values to be given represent averages of daily measurements.

Plasma Renin Activity

Eighty-five determinations of plasma renin activity (PRA) were made during the study; 18 before and the remainder after surgery. Blood collected directly into EDTA-containing vacutainer tubes was spun in a refrigerated centrifuge and the plasmas were frozen. The patients were in a supine position for at least 1 hour before the blood was withdrawn. The measurements of PRA were performed with a radioimmunoassay.[27, 28] In most of the patients, PRA was determined on two occasions; first, during the first week, and second, 3–8 weeks after transplantation. The dietary sodium intake on these two occasions was very similar; this fact is also reflected in comparable urinary excretion rates of sodium as shown in tables 2 and 3. Additional determinations were made within the course of the study. In several patients, serial values were obtained following bilateral nephrectomy and after surgical removal of the rejected homografts.

Table 3

Average Antihypertensive Therapy during the First Week and 3–8 Weeks after Kidney Transplantation in Patients with Adequate Kidney Function

Pt	Time	Methyldopa (mg/24 hr)	Reserpine (mg/24 hr)	Hydralazine (mg/24 hr)	Guanethidine (mg/24 hr)	Hydrochlorothiazide (mg/24 hr)
UM	I	750	—	100	—	50
	II	—	—	—	—	50
RC	I	500	0.50	80	—	100
	II	500	0.50	40	—	100
MK	I	1000	0.75	100	—	100
	II	500	0.50	—	—	100
CE	I	1000	0.75	120	10	150
	II	1000	0.75	—	—	150
BW	I	1500	—	80	20	150
	II	1500	0.50	80	20	150
WM	I	500	—	60	—	100
	II	—	—	—	—	50
TS	I	750	—	100	—	100
	II	500	—	—	—	100
DJ	I	750	0.50	80	—	100
	II	500	0.50	—	—	100
CM	I	1000	0.50	60	—	50
	II	500	—	—	—	50
LL	I	—	—	—	—	50
	II	—	—	—	—	—
VJ	I	750	0.75	80	—	150
	II	750	1.00	80	—	150
KR	I	1500	1.00	—	20	100
	II	750	0.50	—	20	100
ML	I	1000	1.00	60	—	150
	II	1000	1.00	60	—	150
JP	I	500	—	—	—	100
	II	500	—	—	—	100

Abbreviations: I = first week after transplant; II = 3–8 weeks after transplant.

Antihypertensive Therapy

Antihypertensive therapy after transplantation was instituted in every patient with a diastolic blood pressure exceeding 90 mm Hg. This approach was adopted as a safeguard against the detrimental renal effect of severe hypertension. The antihypertensive regimen was based on the following agents: hydrochlorothiazide, reserpine, methyldopa (aldomet), hydralazine, and guanethidine. The combined dose (usually several drugs were used at the same time) varied in relation to the severity of hypertension, and was reduced or discontinued as blood pressure returned to normal; thus, during the latter part of the study the combined dose of various antihypertensive agents was considerably lower than that employed initially; however, the dose of diuretics (hydrochlorothiazide) did not change throughout the study.

Immunosuppression with Glucocorticoids after Transplantation

Prednisone was given initially in the amount of 100–200 mg/24hr. Only in one patient (L.L.) in the initial dose was 40 mg/24hr. The dose was reduced gradually after surgery. A high dose was reinstituted during episodes of acute rejection. In several patients, corticoids were also given for several days before surgery.

Results

Kidney Function

Fifteen patients had adequate renal function after transplantation (tables 2 and 3). In patient D.P. (not listed in tables 2 and 3) the homograft functioned only for 1 week. Three patients (N.J., L.N., and C.B.) underwent accelerated acute rejection shortly after surgery and the homografts were removed within the first postoperative week. Episodes of acute rejection occurred in another five patients (R.C., B.W., C.M., M.K., and K.R.) during a later part of the study. In M.K., acute rejection led to a total infarction of the homograft with renal vein thrombosis; the remaining four patients recovered and regained normal renal function. The diagnosis of acute rejection was based on clinical and biochemical findings in five and on tissue histology in four patients.

Blood Pressure

All patients who underwent bilateral nephrectomy prior to transplantation showed a decrease in blood pressure (table 1). Hypertension (diastolic pressure 90 mm Hg) was present in most of the patients early during the first week after transplantation (tables 2 and 3). Blood pressure increased during acute rejection in seven patients, did not change in one, and fell in one (B.W.); in the later septicemia could account for the observed hypotension (table 4).

Prednisone and Blood Pressure

Five of six patients who were treated with prednisone for a short period of time prior to transplantation showed an increase in blood pressure (table 5). The latter was not associated with substantial changes in body weights. Five patients were anephric. These patients were treated with hemodialysis three times (8-hr intervals) a week with a Kiil-type hemodialyzer. The listed weights and blood pressure levels were measured before dialysis. The patients were not on antihypertensive therapy during the observation period.

All patients with adequate kidney function showed a decrease in blood pressure as the dose of glucocorticoids was reduced. Table 2 lists the levels

Table 4

Plasma Renin Activity before and during Acute Rejection

Pt	BP (mm Hg) I	BP (mm Hg) II	Weight (kg) I	Weight (kg) II	PRA (ng/ml/hr) I	PRA (ng/ml/hr) II	
CB*	140/100	150/110	47.0	49.0	20.1	69.9	(142.0)†
NJ*	150/100	190/140	26.0	25.5	28.8	148.8	
LN*	140/90	140/110	49.0	42.0	3.9	25.7	
RC	140/100	150/110	42.0	52.0	1.9	26.6	
DP*	140/90	150/105	14.0	15.8	14.0	20.1	
CM	140/95	140/95	51.0	53.0	0.22	2.5	
BW	170/105	90/50	53.5	52.0	5.9	15.6	
KR	130/90	140/115	62.0	66.0	9.0	32.0	
MK	126/70	140/100	36.0	41.0	0.62	0.60	

*In these patients acute rejection started shortly after transplantation; adequate homograft function was never reached.

†PRA value after hemodialysis.

Abbreviations: I = before rejection; II = during rejection; BP = blood pressure; PRA = plasma renin activity.

Table 5

Changes in Blood Pressure following the Administration of Prednisone Prior to Transplantation

Pt	Prednisone (mg/24 hr)	Days	NPX	BP (mm Hg) Pre	BP (mm Hg) Post	Weight (kg) Pre	Weight (kg) Post
CB	200	2	+	120/70	160/110	49.2	49.0
BW	200	2	+	130/50	180/120	59.0	59.4
UM	100	2	+	130/86	148/100	43.5	42.5
KR	200	3	−	130/90	180/120	67.0	66.0
WM	200	3	+	120/80	170/112	49.0	48.6
CE	100	5	+	140/80	140/80	58.0	56.0

Abbreviations: Days = days of treatment with prednisone; NPX = after bilateral nephrectomy; Pre = measurement obtained prior to administration of prednisone; Post = measurement made after administration of prednisone, before transplantation.

of blood pressure in the first postoperative week when the patients were on the peak dose of steroids and at a later period (3–8 weeks after surgery) when the dose was reduced to its lowest value. The blood pressure levels recorded initially were higher than those measured later. Patients who were still on large amounts of prednisone (B.W. and M.L.) during the latter period showed elevated blood pressure. In figure 1, the doses of prednisone were plotted against diastolic blood pressure values in patients with adequate renal function (the diagram contains measurements of blood pressure at three different doses of prednisone and in one patient at four different doses, episodes of acute rejection were not included). A highly significant direct correlation was found between those two variables. Doses of prednisone divided by body weights were plotted against blood pressures. The relationship between these two variables was similar to that noticed in figure 1 ($r=0.72$). Similar plot for blood pressure and body weight showed no significant correlation.

Plasma Renin Activity

Plasma renin activity values measured in a group of normal subjects under varying conditions of posture and salt intake are shown in table 6. Since most of our patients after transplantation were treated with antihypertensive agents which might have affected PRA,[28, 29] the interpretation of the results is complicated and great caution has to be exercised in arriving at definite conclusions. Antihypertensive therapy was reduced substantially during period II as compared with that during period I (table 3). However, the dose of hydrochlorothiazide was not altered and thus could not contribute to the observed changes in PRA. Methyldopa decreases whereas hydralazine increases PRA;[28, 29] both drugs were reduced during the latter period of the study. The effect of this alteration in therapy on PRA is difficult to quantitate, however presumably it was minimal, considering the opposite influences of methyldopa and hydralazine on PRA.

Following bilateral nephrectomy (before transplantation) in six patients, PRA was undetectable in four and below 0.5 ng/ml/hr in two (table 1). Serial determinations of PRA in a patient with lupus nephropathy (L.L.) after bilateral nephrectomy are shown in table 7. During the first week after transplantation, the PRA in the majority of patients with adequately functioning homografts was low or normal (table 2). These values were recorded at the time when most of the patients were hypertensive. PRA values measured 3–8 weeks after transplantation were higher than the initial ones in all but one. These values were obtained when most of the patients were normotensive and the amount of antihypertensive agents was markedly lower than that given initially during the first

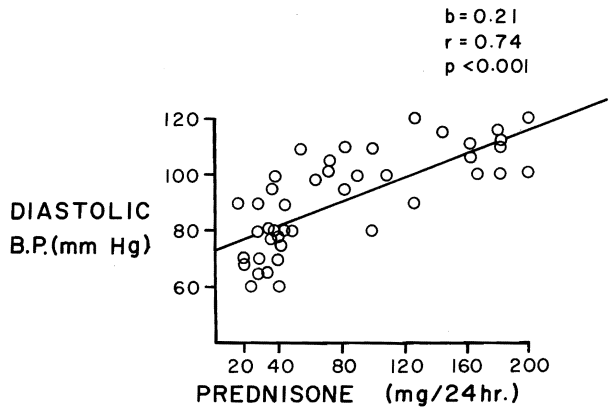

Figure 1

The relationship between diastolic blood pressure and the maintenance dose of prednisone in patients with adequate kidney function.

Table 6

PRA in Normal Subjects

Data	Na intake			
	110 mEq/24 hr		10 mEq/24 hr	
	Supine	2 hrs up	Supine	2 hrs up
Mean (ng/ml/hr)	1.60	5.34	6.76	14.3
SE (ng/ml/hr)	0.40	1.28	1.35	2.1
N	9	10	9	6
P	<0.025	<0.005	<0.01	
Range (ng/ml/hr)	0.23–3.62	0.61–10	2.13–13.8	9.2–20

weeks. Three of five patients with PRA exceeding 10 ng/ml/hr (K.R., V.J., and M.L.) had retained their original damaged kidneys. The changes in body weight and in sodium excretion were relatively small and inconsistent. No significant correlation could be found between diastolic blood pressure and PRA in patients with normally functioning homografts (fig. 2). A marked increase in PRA was noticed during acute rejection (table 4). These changes were noticed before readjustments were made in the dose of antihypertensive drugs and in sodium intake. In two patients (N.J., and B.C.) PRA assumed extremely high levels. An additional increase in PRA was recorded in one patient (C.B.) following a weight loss of 2.5 kg with hemodialysis. In patient M.K., PRA remained low; however, the removed homograft was totally infarcted. This patient gained 5.0 kg during the rejection crisis, and blood pressure was restored to normal after hemodialysis. PRA values during acute rejection crisis correlated directly with blood pressure values (fig. 3). Removal of rejected organs in three patients was followed by a drop in PRA and a decrease in blood pressure. Serial measurements of PRA and blood pressure after the removal of a rejected kidney in patient N.J. are shown in table 8. In this patient, the hypertension which was associated with the acute rejection failed to respond to a marked extracellular fluid volume depletion with hemodialysis but responded promptly to nephrectomy.

Table 7

Changes in PRA following Bilateral Nephrectomy and Transplantation in Patient L.L.

Date	Time	PRA (ng/ml/hr)
12/29/70	Pre-NX	114.50
12/30/70	18 hrs post-NPX	1.09
12/31/70	36 hrs post-NPX	0.03
1/ 2/71	96 hrs post-NPX	0.11
2/ 5/71	Pre-TX	0.00
2/ 8/71	4 hrs post-TX	0.60

Abbreviations: NPX = bilateral nephrectomy; TX = transplantation.

Discussion

The rise in PRA during acute rejection crises as seen in the present study confirms similar observations previously reported by other workers.[15, 20, 21, 23] Although an increase in blood pressure during acute rejection was associated with an increasing PRA, no such association could be demonstrated in patients with normally functioning renal homografts. Similarly, other workers failed to show a definite consistency in the relation between the degree of hypertension and PRA after transplantation.[3, 30, 31] The role of a renal pressor mechanism, mediated by the renin-angiotensin system, in the genesis of hypertension during acute rejection requires further evaluation and cannot be established on the basis of presently available information. However, the prompt relief of severe hypertension following the surgical removal of the rejected homografts as observed in three patients,

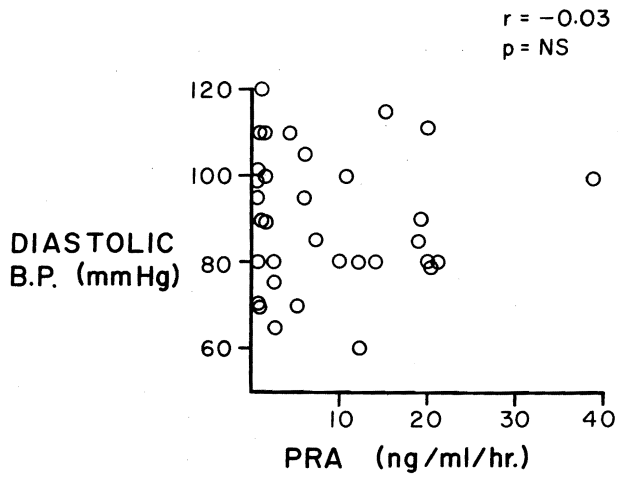

Figure 2

Diastolic blood pressure and plasma renin activity in patients with adequate renal function.

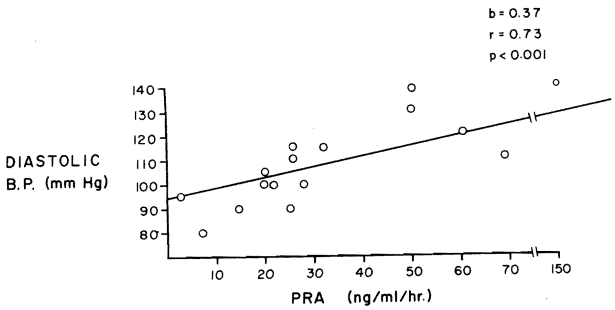

Figure 3

The relationship between diastolic blood pressure and plasma renin activity in patients undergoing acute rejection.

before any appreciable changes in body weight occurred, suggests that a renal mechanism was at least partly responsible for the severe hypertension. Salt and water retention is common during acute rejection and may contribute to the development of hypertension[32] as observed in patient M.K.; however, in patient N.J. marked extracellular fluid volume depletion had no appreciable effect on the severe hypertension. Similar observations were also made in our other patients. A rise in PRA following hemodialysis as noticed in patient C.B., suggests that a homograft undergoing acute rejection preserves its physiologic response to extracellular fluid volume depletion; however, additional observations will be necessary before more definite conclusion can be made. The low PRA in patient M.K., during acute rejection, could be explained by the finding of totally infarcted renal homograft with presumably not enough viable tissue left to secrete the hormone. It is possible, therefore, that the measurement of PRA during acute rejection may provide certain information regarding the viability of the transplanted kidney.

Table 8

*Changes in PRA and Blood Pressure following Removal of an Acutely Rejected Homograft in Patient N.J.**

Date (1970)	Time	BP (mm Hg)	PRA (ng/ml/hr)
7/19	Acute rejection	180/140	148.80
7/24	Pre-NPX	170/135	61.30
7/24	1 hr post-NPX	160/125	78.40
	3 hrs post-NPX	160/100	30.60
	4 hrs post-NPX	140/90	26.60
	12 hrs post-NPX	150/98	18.10
	16 hrs post-NPX	164/90	13.60
7/27	—	160/90	16.40
7/29	—	160/100	6.60
8/ 3	—	130/95	1.80

*This patient had retained her original diseased kidneys.
Abbreviations: NPX = removal of rejected homograft.

The variations in plasma renin activity in patients with adequately functioning renal homografts, showing an increase during the late part of the study 3–8 weeks after transplantation, are not well understood, but several possible explanations are worthy of comment. (1.) Although the denervated transplanted kidney has been shown to be capable of elaborating renin,[33] it is quite possible that initially this capability is limited and improves as time passes. (2.) High doses of steroids which were given during the first week could cause suppression of renin production[34] whereas lowering of the dose during the latter part of the study might have reversed that effect. (3.) The initial blood samples were obtained while the patients were on a bed rest regimen, whereas during the latter part of the study the patients were ambulatory and assumed a supine position only 1 hour before drawing the blood samples. These differences in posture could influence the results. (4.) The alteration in antihypertensive regimen could exert significant effect on PRA.[28, 29]

The present observations strongly support the role of glucocorticoids in the development of post-transplant hypertension. An increase in blood pressure presumably not associated with significant changes in sodium balance was observed in anephric patients awaiting transplantation after the administration of a high dose of steroids for several days. A significant relationship between the dose of prednisone and the diastolic blood pressure was demonstrated in patients with well functioning renal homografts. The reported absence of hypertension in patients who are not treated with glucocorticoids after transplantation[35] are in agreement with the present findings. The possibility that small changes in renal function played a major role in altering the level of blood pressure seems unlikely, since no significant correlation could be found between creatinine clearances and the levels of blood pressure.

Despite the widespread use of glucocorticoids as therapeutic agents in many disease processes and the well known occurrence of various complications, surprisingly, hypertension has received relatively little attention.[36, 37] A study undertaken to assess the incidence and the severity of various side effects associated with prolonged administration of glucocorticoids led to a conclusion that hypertension was not a serious complication.[38] In contrast to the clinical observations, glucocorticoids have been

proved to be highly potent hypertensive agents in experimental animals.[39, 42] It has also been demonstrated that hypertension which was produced experimentally with glucocorticoids, contrary to that produced with mineralocorticoids, was not salt dependent.[39, 41] The latter feature rendered the glucocorticoid-induced hypertension unresponsive to salt restriction. The animal studies also demonstrated severe renal damage associated with glucocorticoid-induced hypertension.[42]

The major difference between the clinical and the experimental conditions is related to the amount of glucocorticoids employed. The dose used in animals to induce hypertension in relation to their body weight was considerably larger than that usually used in humans. However, the doses of steroids which are given to patients to protect their renal homografts may be large enough to account for the hypertension. Our observation that the degree of hypertension was directly related to the dose of prednisone is consistent with that notion. Furthermore patients with renal homografts may differ from subjects with normal kidney by being more sensitive to the hypertensive action of prednisone.

The recognition of glucocorticoid-induced hypertension in renal homograft recipients bears on several important clinical aspects. The appearance of hypertension in patients with adequate renal function who are treated with large amounts of prednisone, early after transplantation, does not necessarily indicate homograft dysfunction and unless other signs of acute rejection are present the dose of immunosuppressive agents should not be increased. The prognosis of that kind of hypertension is usually good and a reduction of the maintenance dose of glucocorticoids, when possible, will eventually result in normotension. However, as long as the hypertension is present, vigorous antihypertensive therapy should be continued. This will likely minimize or prevent the deleterious effect of severe hypertension on the transplanted organ, and on the whole cardiovascular system.

References

1. STARZL TE: Experience in renal transplantation. Philadelphia, WB Saunders Co, 1964
2. STARZL TE, MARCHIORO TL, TERASAKI PL, PORTER KA, FARIS TO, HERRMANN TJ, VREDEVOE DL, HUTT MP, OGDEN DA, WADDELL WR: Chronic survival after human renal transplantation. Ann Surg **162**: 749, 1965
3. BLAUFOX MD, BIRBARI AE, HICKLER RB, MERRILL JP: Peripheral plasma renin activity in renal homotransplant recipients. New Eng J Med **275**: 1165, 1966
4. MERRILL JP: Homotransplantation kidney and other tissues. *In* Proceedings of the 96th Annual Conference on the Kidney, edited by Mecoff J. York, Pennsylvania, Marple Press Co, 1966, p 165
5. HUME DM: Progress in clinical transplantation. *In* Advances in Surgery, vol 2, edited by Welch CE, Chicago, Year Book Medical Publisher, 1966, p 419
6. ROCK R, ROSENAU W, NAJARIAN JS: Clinopathologic study of human renal homotransplantation. Surg Gyn Obstet **125**: 289, 1967
7. WOODRUFF MFA, NOLAN B, ROBINSON JS, MACDONALD MK: Renal transplantation in man: Experience with 35 cases. Lancet **1**: 6, 1969
8. GONZALES LL, MARTIN L, WEST CD, SPITZER R, MCENERY P: Renal transplantation in children. Arch Surg **101**: 232, 1970
9. PARSONS FM, MARKLAND C, RAPER FP, FOX M: Cadaveric renal transplantation. Brit Med J **1**: 930, 1963
10. STARZL TE, MARCHIORO TL, WADDELL WR: The reversal of rejection in human renal homografts with subsequent development of homograft tolerance. Surg Gyn Obstet **117**: 385, 1963
11. MARCHIORO TL, AXTELL HK, LAVIA MF, WADDELL WR, STARZL TE: The role of adrenocortical steroids in reversing established homograft rejection. Surgery **55**: 412, 1969
12. CALNE RY, LOUGHRIDGE L, MACGILLIVRAY JB, SWALES JD: Further observations on renal transplants in man from cadaveric donors. Brit Med **2**: 1345, 1966
13. DOSSETOR JB, MORGAN RO, BECK JC: Observations on the function of a transplanted kidney. Canad J Biochem **41**: 1409, 1963
14. SWALES JD, MORGAN MN: Acute hypertension in dogs following ischemic damage to transplanted kidneys. Lancet **2**: 219, 1965
15. ROGUSKA J, DEL GRECO F, SIMON MM: Serum renin activity in human renal homotransplantation. Nephron **8**: 289, 1971
16. NEWTON WT, KELTNER RM, SHANKEL SW: Acquired renovascular hypertension in a patient with renal allotransplantation. Amer J Surg **113**: 292, 1967
17. PAPADIMITRION M, GRISHOLM GD, SHACKMAN R: Hypertension in patients on regular hemodialysis and after renal allotransplantation. Lancet **1**: 902, 1963
18. DUNEA G, NAKAMOTO S, STRAFFON RA, PIGUEROA JE, VERSAU AA, MASAKATSU S, KOLFF WJ: Renal homotransplantation in 24 patients. Brit Med J **1**: 7, 1965
19. STARZL TE, PORTER KA, ANDRES G, HALGRIMSON CG, HURWITZ R, GILES G, TERASAKI PL, PENN I, SCHROTER GT, LILLY J, STARKIE SJ, PUTNAM CW: Long-term survival after renal transplantation in humans. Ann Surg **172**: 437, 1970
20. GUNNELS JC, STICKEL DL, ROBINSON RR: Episodic hypertension associated with positive renin assays after renal transplantation. New Eng J Med **274**: 543, 1966
21. LUNDGREN G, BOZOVIC L, CASTENFORS J: Plasma renin activity before and after allogenic kidney transplantation in man. Scand J Urol Nephrol **1**: 181, 1967

22. ABBRECHT PH, TURCOTTE JG, VANDER AJ: Plasma erythropoietin and renin activity after canine renal allotransplantation. J Lab Clin Med **71**: 766, 1968
23. MURRAY JE, MERRILL JP, HARRISON JH: Kidney transplantation between seven pairs of identical twins. Ann Surg **148**: 343, 1958
24. STARZL TE, MARCHIORO TL, PORTER KA, MOORE CA, RIFKIND D, WADDELL WR: Renal homotransplantation: Late function and complications. Ann Intern Med **61**: 470, 1964
25. STARZL TE, MARCHIORO TL, DICKENSON DC, RIFKIND D, STONINGTON OG, WADDELL WR: Technique of renal homotransplantation: Experience with 42 cases. Arch Surg **89**: 87, 1964
26. STARZL TE: Experience in hepatic transplantation. Philadelphia, WB Saunders Co, 1969
27. KATZ FH, SMITH JA: Angiotensin I radioimmunoassay: Comparison of two renin activity methods and use for other measurements of the renin system. Clin Chem **18**: 528, 1972
28. HABER E, KOERNER T, PAGE LB, KLIMAN B, PWINODE A: Application of a radioimmunoassay for angiotensin I to the physiologic measurements of plasma renin activity in normal human subjects. J Clin Endocr **29**: 1349, 1969
29. MOHAMMED S, FASOLA AF, PRIVITERA PJ, LIPICKY RJ, MARTZ BL, GAFFNEY TE: Effect of methyldopa on plasma renin activity in man. Circ Res **25**: 543, 1969
30. WEST TH, TURCOTTE JG, VANDER A: Plasma renin activity, sodium balance and hypertension in a group of renal transplant recipients. J Lab Clin Med **73**: 564, 1968
31. NIELSEN I, CLAUSEN E, JENSEN G: Plasma renin activity after allogenic kidney transplantation in man. Acta Med Scand **188**: 355, 1970
32. SWALES JD: Sodium metabolism in relation to changing blood pressure levels in human renal transplantation. Amer J Med Sci **253**: 531, 1967
33. GREENE JA, VANDER AJ, KOWALCZYK RS: Plasma renin activity and aldosterone excretion after homotransplantation. J Lab Clin Med **71**: 586, 1968
34. NEWTON MA, LARAGH JH: Effects of glucocorticoid administration of aldosterone excretion and plasma renin in normal subjects, in essential hypertension and primary aldosteronism. J Clin Endocr **28**: 1014, 1968
35. HAMBURGER J, CROSNIER J, DORMONT J: Renal Transplantation: Theory and Practice. Baltimore, Williams and Wilkins Co, 1972
36. TREADWELL BLJ, SEVER ED, SAVAGE O, COPEMAN WSC: Side-effects of long-term treatment with corticosteroids and corticotrophin. Lancet **1**: 1121, 1964
37. SMYLIE HC, CONNOLLY CK: Incidence of serious complications of corticosteroid therapy in respiratory disease. Thorax **23**: 571, 1968
38. QUAADE F: Undesirable effects of glucocorticoids. Acta Med Scand (suppl 500): 77, 1969
39. KNOWLTON AI, LOEB EN, STOERK HC, WHITE JP, HEFFERMAN JF: Induction of arterial hypertension in normal and adrenalectomized rats given cortisone acetate. J Exp Med **96**: 187, 1952
40. FRIEDMAN SM, FRIEDMAN CL, NAKASHIMA M: The hypertensive effect of compound F acetate in the rat. Endocrinology **51**: 401, 1952
41. KNOWLTON AI, LOEB EN, STOERK HC: Effect of synthetic analogues of hydrocortisone on the blood pressure of adrenalectomized rats on sodium restriction. Endocrinology **60**: 768, 1957
42. CLARKE TD, ASHBURN AD, WILLIAMS WL: Cortisone induced hypertension and cardiovascular lesions in mice. Amer J Anat **123**: 425, 1969