# PLASMA RENIN CONCENTRATIONS IN CASES WITH RENOVASCULAR HYPERTENSION*

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There has been a great deal of controversy over the role played by renin-angiotensin in causing and maintaining hypertension in patients with renovascular abnormalities. It has been suggested that narrowing of the renal artery stimulates the release of renin from the juxtaglomerular cells. The renin acts upon plasma substrate to produce the pressor peptide angiotensin, which then raises the arterial pressure by a direct vasoconstrictor effect.[1-3]

This theory has been criticized by various workers, mainly because concentrations of renin and angiotensin in experimental hypertension have been inadequate to cause significant pressor response.[4-6] It is currently felt that the renin-angiotensin system regulates aldosterone secretion, and that the aldosterone plays an important role in maintaining the hypertension.[7-9]

The three cases of renovascular hypertension to be discussed in this paper proved very good experimental models for the study of renin excretion. Renin estimations were done before and during surgery on all cases.

## CASE REPORTS

*Case 1*

Mr A. M., a 52-year-old White masseur and part-time karate instructor, incurred an injury to the left side of his abdomen while taking part in a karate exhibition during 1968. Four months after this injury he was seen in the outpatient department because of severe headache and loss of vision. He was found to be hypertensive and was placed on antihypertensive therapy (guanethidine, methyldopa and hydrochlorthiazide) for a period of 2 weeks. At reassessment he was still severely hypertensive, and it was decided to admit him for a full investigation. In the ward he was agitated and was prone to attacks of violence. His blood pressure was 220/130 mm.Hg in both arms and 240/140 mm.Hg in the legs. No abdominal bruits were heard. His fundi showed grade IV KW changes. There were no other abnormalities found in any other system.

*Laboratory and radiological tests.* The full blood count was within normal limits. Urinalysis showed a SG of 1·010 with a 4+ proteinuria and 4 - 5 red blood cells per high-power field. Further pertinent laboratory data are summarized in Table I. An intravenous pyelogram showed normal excretion from the right kidney but non-visualization of the left (Fig. 1).

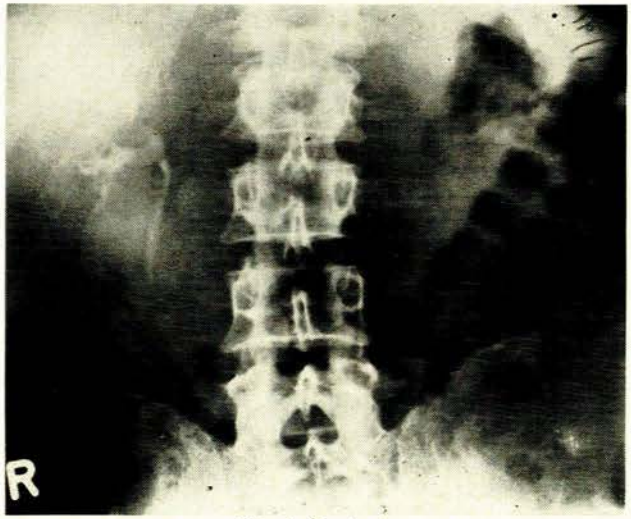


*Fig. 1.* See text.

A retrograde pyelogram showed a normal-sized right kidney, but a small left one. A right femoral aortogram showed normal vasculature on the right, but absent vasculature on the left.

A hippuran renogram done on this patient showed a flat curve over the left kidney, with a normal-appearing pattern over the right kidney. Systemic venous blood had

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TABLE I. BIOCHEMICAL CHANGES IN BLOOD AND URINE BEFORE AND AFTER SURGERY

| | *Before surgery* | | | | | | *After surgery* | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *Creatinine Cl ml./min.* | *Serum (mEq./litre)* | | | *24-hr urine (mEq./litre)* | | *Creatinine Cl ml./min.* | *Serum (mEq./litre)* | | | *24-hr urine (mEq./litre)* | |
| | | *Na* | *K* | *Cl* | *Na* | *K* | | *Na* | *K* | *Cl* | *Na* | *K* |
| Case 1 | 33·3 | 132 | 2·7 | 102 | 60 | 27·2 | 50 | 139 | 4·3 | 104 | 64·8 | 9·05 |
| Case 2 | 60·0 | 136 | 3·9 | 99 | 93 | 25·5 | 74·7 | 140 | 5·5 | 95 | 126 | 33·4 |
| Case 3 | 1·6* | 137 | 4·0 | 95 | 122·6 | 29·9 | 1·2* | 134 | 3·7 | 98 | 86·9 | 24·6 |

* Serum creatinine mg./100 ml.

a renin concentration of 1,500 nanograms/100 ml., the left renal vein had a concentration of 12,000 nanograms/100 ml. and the right renal vein had a concentration of ±800 nanograms/100 ml.

*Operative findings.* The vasculature and form of the right kidney appeared normal. The left renal artery was completely obstructed by a thrombus, and the left kidney was very small and atrophic. A nephrectomy was performed, and tissue was obtained from both kidneys.

Macroscopic and microscopic findings of the specimens taken at surgery showed a laminated thrombus in the left renal artery and bilateral changes of malignant-on-benign nephrosclerosis.

Six months postoperatively the patient's vision had improved and his blood pressure had stabilized at 140/90 mm.Hg on methyldopa 250 mg. twice daily.

*Case 2*

Mr J. S., a 19-year-old White clerk, gave a 2-year history of headache and generalized malaise. He is a first-class sprinter and his trainer suggested that his performance might improve if he were to increase his dietary intake of sodium chloride. This he has done for the past 3 years. On examination his blood pressure in both arms was 210/130 mm.Hg and in the legs 220/140 mg.Hg. On fundoscopy he was found to have early papilloedema. All other systems were within normal limits and there was no abdominal bruit.

*Laboratory and radiological tests.* Blood count and urinalysis were within normal limits. Further pertinent laboratory data are summarized in Table I. An intravenous pyelogram showed delayed appearance of contrast medium in the right kidney which was also significantly smaller than the left one. A retrograde pyelogram verified the above findings of a difference in size between the kidneys.

A translumbar aortogram showed right renal artery stenosis with a moderately significant collateral circulation (Fig. 2).

A hippuran renogram showed diminished blood supply on the right side. A renal scintogram proved the right kidney to be significantly smaller than the left one.

The pre-operative systemic renin value was 460 nanograms/100 ml. The right renal vein had a concentration of 950 nanograms/100 ml., and the left renal vein had a value of 380 nanograms/100 ml.

*Operative findings.* A stenosed segment was resected from the right renal artery and was replaced with a venous graft. A biopsy specimen was taken from each kidney. On histological examination there was no juxtaglomerular apparatus hyperplasia, and the renal tissue was within normal limits.

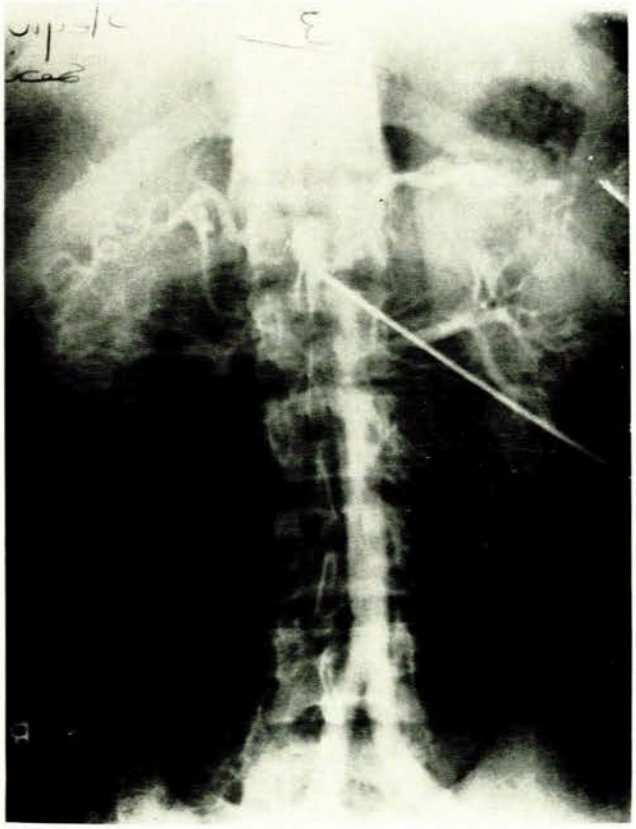

*Fig. 2.* See text.

The blood pressure has now stabilized at 140/85 mm.Hg without any form of therapy. His fundus picture is markedly improved.

*Case 3*

Mr L. B. de W., a 59-year-old White clerk, presented with a history of having had a few dizzy attacks over the preceding 5 years, and severe supra-orbital headache for 6 months before admission. He had also had intermittent claudication of the left leg. This was alleviated by a sympathectomy done in 1963. On examination his blood

pressure in both arms was 240/140 mm.Hg and in his right leg 250/150 mm.Hg. Fundoscopy showed grade 2 KW changes. Peripheral foot pulses were absent on the left side, and on the right the dorsalis pedis was weakly palpable. There were no abdominal bruits.

*Laboratory and radiological tests.* He was polycythaemic, with a haemoglobin of 19·1 G/100 ml. Urinalysis was within normal limits. The pertinent laboratory findings are summarized in Table I. An intravenous pyelogram showed a normal left nephrogram, with a normal-appearing kidney. No nephrogram was obtained on the right side.

A hippuran renogram showed no blood flow to the right kidney. The blood supply to the left kidney was within normal limits. With a renal 'Scintiscan' the right kidney was not visible but the left kidney appeared normal. A translumbar aortogram showed no vasculature of the right kidney, with a possible narrowing of the left renal artery, and severe atherosclerosis of the aorta and its main branches

The pre-operative systemic renin value was 450 nanograms/100 ml. The right renal renin concentration was 7,000 nanograms/100 ml. The left renal vein had a renin concentration of 700 nanograms/100 ml.

*Operative findings.* There was generalized atherosclerosis of the aorta and its main branches. A right-sided nephrectomy was done because it was felt that it was impossible to salvage this kidney. No repair was necessary to the left renal artery.

The right kidney showed hyalinization of some glomeruli, interstitial fibrosis and hyaline atherosclerosis with narrowing of the vascular lumen. The left kidney showed only mild atherosclerotic changes of the blood-vessels.

Three weeks after surgery the blood pressure had stabilized at 140/90 mm.Hg. The patient was asymptomatic, and he was discharged without any antihypertensive therapy.

*Sampling for Renin Estimations*

Where possible the blood samples for renin estimations were all obtained from the patients under similar conditions, i.e. all patients were placed on a constant ward diet containing ±120 mEq. sodium chloride per day for one week before sampling. All antihypertensive or diuretic therapy was stopped for the same length of time.

The pre-operative blood sample was obtained in the morning from a forearm vein with the patient in a recumbent position. (Mr J. S. had unfortunately been walking about before sampling.) At operation blood was obtained from both renal veins and where possible from both renal arteries. Table II is a summary of the renin estimations.

*Method of Renin Estimation*

Except for minor modifications, plasma renin activity was determined according to the method of Helmer and Judson,[10] as modified by Gunnells and Grim.[11] About 10 ml. of heparinized blood was collected in pre-chilled glass tubes and immediately centrifuged at 3,500 r.p.m. at 2°C for 30 minutes. The plasma was then removed and dialysed in 10 litres of de-ionized water at 2°C for 20 hours. An electric stirrer was employed.

After dialysis the pH of the plasma was adjusted to 5·5 with normal HCl. The plasma was then centrifuged, and the supernatant was removed and made isotonic by adding saturated sodium chloride. This plasma was then incubated for one hour at 37°C and immediately tested for renin activity.

TABLE II. RENIN ESTIMATIONS BEFORE AND DURING CORRECTIVE SURGERY*

| | *Pre-operative venous blood* | *At operation* | | | |
|---|---|---|---|---|---|
| | | *Renal artery* | | *Renal vein* | |
| | | *L* | *R* | *L* | *R* |
| Case 1 | 1,500 | — | 1,500 | 12,000 | ±800 |
| Case 2 | 460 | 280 | — | 380 | 950 |
| Case 3 | 450 | — | 1,950 | 700 | 7,000 |

* All figures in nanograms/100 ml. Normal value in supine position is 250 nanograms/100 ml.

The pressor activity of the plasma samples thus prepared was determined by injecting some of it intravenously into an anephric male Sprague-Dawling rat, while the blood pressure was being recorded. Nephrectomy was carried out 16 hours before the test; food and water were withheld postoperatively.

During the experiment, the blood pressure was constantly being monitored by means of an Elema transducer (EMT 34) and recorded on a Hitachi recorder. Commercially available valine-5-angiotensin 11 was used as a standard.

## DISCUSSION

A pre-operative diagnosis of renovascular hypertension was made in these 3 cases. This was verified by the adequate postoperative improvement in blood pressure in all cases.

Case 1 had markedly increased venous renin excretion from the left kidney and presented with the classic changes of the 'hyponatraemic hypertensive syndrome'. This condition is the only form of hypertension in which plasma renin concentrations are consistently raised. The other manifestations of this condition are: low serum sodium, raised serum levels of aldosterone and low serum potassium levels. In this syndrome the level of circulating renin correlates well with the degree of vascular involvement and the extent of hyponatraemia. The hypokalaemia is indirect evidence of increased excretion of aldosterone.

Retinal evidence of malignant hypertension is a usual accompaniment of this condition. This case showed a very satisfactory postoperative improvement in blood pressure, creatinine clearance, serum sodium, serum potassium and 24-hour excretion of potassium (Table I).

Cases 2 and 3 had a normal serum electrolyte picture. Case 2 had papilloedema on fundoscopy, and case 3 had grade 2 KW changes. Effluent plasma renin from the right kidney was markedly increased in case 3. Case

2 had a moderately raised systemic venous renin and effluent plasma renin in the right kidney (Table II). Both cases have shown a very good postoperative drop in blood pressure which has been maintained for the last 4 months.

We feel that the biological method used in this study for the assessment of renin is reliable, but requires a trained staff and adequate laboratory facilities. This estimation should not be a routine, investigatory tool, but it should be done where routine studies to diagnose renovascular hypertension are inconclusive. As can be seen from the 3 patients studied, there is a significant increase in renin in the effluent blood of the ischaemic kidney. This is unfortunately not a constant finding in cases of renovascular hypertension. If it is decided to obtain pre-operative renin samples, they should be taken from both renal veins, possibly applying the method as described by Mickelakis *et al.*[12] The reason for this differential sampling of the renal veins is that the systemic renin values can often be misleading (falsely low values), and this method of sampling helps to delineate the ischaemic kidney.

SUMMARY

Three cases of renovascular hypertension are discussed in this paper. Renin estimations were done on each case before and during surgery. The method of renin estimation used in these cases is discussed, and it is suggested that to adequately assess renovascular hypertension, blood should be differentially sampled from each renal vein.

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