SUMMARY

1. In patients with essential hypertension plasma renin concentration (PRC) was assessed in relation to age, plasma volume, extracellular fluid volume, aldosterone secretion rate, renal vascular resistance, filtration fraction and excess sodium excretion after acute salt loading.

2. Up to a calculated renal vascular resistance of 20,000 dyn s cm\(^{-5}\), PRC was found to be inversely related with the above-mentioned variables except plasma volume, extracellular fluid volume and aldosterone secretion rate.

3. It is concluded that the phenomenon of renin suppression is not dependent on mineralocorticoid excess. Instead, a decrease in PRC together with hypernatriuresis appears to reflect a progressive switch in intrarenal haemodynamic relationships. Renin suppression should therefore be considered to be a feature of progressive, but still uncomplicated, essential hypertension.

Key words: renin, sodium excretion, renal haemodynamics, age, aldosterone, filtration rate.

Renin suppression is mostly defined as the presence of an abnormally low plasma renin level, which fails to respond to various stimuli; for instance dietary sodium restriction and head-up tilting. The mechanism involved has not been clarified. Many investigators are inclined to assume that renin suppression in hypertension is caused by mineralocorticoid activity. But with a few exceptions hypersecretion of aldosterone has not been demonstrated in these patients and the role of other mineralocorticoids is far from having been established. Alternatively, renin suppression could be the consequence of increased intrarenal pressure in the presence of systemic hypertension. The statement that patients with renin suppression represent a distinct pathological entity, is still lacking proof. In this study we have assessed the relationships between plasma renin concentration and the following variables: age, plasma volume, extra-
cellular fluid volume, aldosterone secretion rate, renal vascular resistance, filtration fraction and sodium excretion.

SUBJECTS AND METHODS

Sixty-three hypertensive patients (thirty-three men, thirty women, aged 20–63 years) were studied. The diagnosis of essential hypertension was made after screening the patients for overt endocrine disorders, renal disease or renal artery stenosis. Renal arteriography was omitted in most cases, the results of intravenous pyelography and isotope renography being normal. Serum electrolytes were normal in all cases. In fifty-five patients the hypertensive process was considered to be uncomplicated. The others showed evidence of impaired renal function, serum creatinine values being elevated (1.4–27 mg/100 ml), but these values were known from the outpatient clinic to be normal (below 1.4 mg/100 ml) at an earlier stage of their hypertension. Renal arteriography did not show evidence of renal artery stenosis in these patients. The patients were hospitalized and received a diet with 3 g of salt daily. All drugs had been omitted at least 3 weeks before admission, and long-acting drugs (reserpine) had not been prescribed at all.

Plasma renin concentration (PRC) and the other variables were measured in a way similar to that reported previously from our department (Birkenhager, van Es, Houwing, Lamers & Mulder, 1968; Schalekamp, Schalekamp-Kuyken & Birkenhager, 1970; Schalekamp, Krauss, Schalekamp-Kuyken, Kolsters & Birkenhager, 1971; Birkenhager, Schalekamp, Krauss, Kolsters, Schalekamp-Kuyken, Kroon & Teulings, 1972). All values relevant to body surface were converted into 1.73 m². Blood samples for renin were taken between 9 and 10 a.m., after the patients had been kept in the lying position throughout the night.

Aldosterone secretion rate was measured in fourteen patients with a double-isotope derivative method.

RESULTS

With respect to renal vascular resistance and filtration fraction patients fell into two rather distinct categories. Group 1 comprised fifty patients with a calculated renal vascular resistance up to 20 000 dyn s cm⁻⁵. Filtration fraction tended to rise with increasing resistance. In group 2 (thirteen patients) where calculated renal vascular resistance exceeded 20 000 dyn s cm⁻⁵, this tendency was absent (Fig. 1). There was also a marked difference in PRC between these groups of patients. PRC ranged from 2.0 to 16 ng ml⁻¹h⁻¹ in group 1, and from 2.6 to 260 ng ml⁻¹h⁻¹ in group 2. Values obtained in thirty-five control subjects (twenty-five men and ten women, aged 19–63 years) under similar conditions, ranged from 5.2 to 18 ng ml⁻¹h⁻¹. The responsiveness to 45° head-up tilting during 1 h was definitely reduced in most patients as compared with control subjects and it was nil in patients with a PRC below 4.0 ng ml⁻¹h⁻¹. In group 1, PRC was inversely correlated with renal vascular resistance ($r = -0.69, P<0.001$) and filtration fraction ($r = -0.65, P<0.001$). An inverse relationship was also found between PRC and age in these patients ($r = -0.52, P<0.001$), but not in the control subjects. When PRC values in both groups are plotted against the entire range of values calculated for renal vascular resistance, a biphasic pattern emerges (Fig. 1). PRC in group 1 was definitely unrelated to plasma volume (range 2.07–3.38 litres), extracellular fluid volume (9.0–14.6 litres), and aldosterone secretion rate (52–260 μg/24 h). Eight out of twenty-two patients from group 1 showed an exaggerated natriuretic response to the intravenous administration of 300 ml of
FIG. 1. Values of plasma renin concentration, glomerular filtration rate and filtration fraction in sixty-three hypertensive patients, plotted against estimates of renal vascular resistance. Values relevant to body surface area have been converted into 1.73 m².

5% saline, the increase in sodium excretion being more than 40 mEq/2 h. Excess sodium excretion was inversely related to PRC \((r = -0.78, P<0.001)\).

DISCUSSION

In this study no relationship was observed between plasma renin concentration and plasma
volume or extracellular fluid volume. The hypothesis that hypervolaemia is the cause of renin suppression in essential hypertension therefore appears to be untenable. Neither did we find an inverse relation between renin and aldosterone secretion rate. Such a relationship was hardly to be expected anyhow in view of the results of the volume studies. The majority of patients with primary hyperaldosteronism exhibit expanded body fluid volumes (Novak, Strong & Hunt, 1972). In view of the missing link of volume expansion it is also highly improbable that some other mineralocorticoid hormone is involved in renin suppression. Instead, our observations fit into the baroreceptor theory of renin secretion. In the present series renin suppression parallels progressive changes in renal vascular resistance up to a point of 20,000 dyn s cm\(^{-5}\). This trend is accompanied by an increase in filtration fraction, presumably reflecting an increase in pressure at the glomerular level. These changes in renal haemodynamics are known to progress in the course of hypertensive disease. Thus, renin suppression may be stated to reflect a rather advanced stage of hypertensive disease. This view is supported by the inverse relationship between plasma renin concentration and age, a relationship which was absent in the normotensive subjects.

Beyond the point of a renal vascular resistance of about 20,000 dyn s cm\(^{-5}\), PRC tends to rise, and this again would be in accordance with the baroreceptor theory, because then lesions are expected to occur in the larger intrarenal segments.

Definite proof for the applicability of the baroreceptor theory is still lacking, because direct pressure readings at the juxtaglomerular level are not obtainable. Still, it has been observed that systemic hypertension is transmitted throughout the renal vascular tree (Loewenstein, Beranbaum, Chasis & Baldwin, 1970). Moreover, exaggerated natriuresis is supposed to be pressure-dependent (Cannon, 1968) and this phenomenon occurred in the present series specifically in patients exhibiting renin levels in the lower range.

REFERENCES