Plasma noradrenaline concentration in hypertensive and normotensive 40-year-old individuals: relationship to plasma renin concentration

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Summary
1. Forty-year-old individuals with mild essential hypertension, identified during a survey of a population born in 1936, were investigated. Forty-year-old normotensive subjects, drawn from the same population, served as a control group.
2. Plasma noradrenaline concentration and plasma renin concentration at rest supine and after acute stimulation, as induced by frusemide intravenously and ambulation, did not differ from reference values in the 40-year-old normotensive controls. In the hypertensive group a close correlation ($r = 0.77, P < 0.001$) was found between plasma noradrenaline and plasma renin concentration after acute stimulation.
3. Sympathetic nerve activity, as defined by measurements of plasma noradrenaline, is normal in mild essential hypertension. Discrepancies described in the literature are probably related to a lack of comparability between hypertensive and normotensive study populations.

Key words: hypertension, plasma noradrenaline, renin, sympathetic nerve activity.

Introduction
The role of the sympathetic nervous system in the maintenance of high blood pressure remains a subject of continuing debate. Determination of plasma noradrenaline concentration [noradrenaline] is currently thought to be a useful index of sympathetic nerve activity (Christensen, 1979; Lake, Ziegler, Coleman & Kopin, 1977). Whereas some investigators have found increased plasma [noradrenaline] or increased urinary excretion rate for catecholamines (De Champlain, Farley, Cousineau & Van Ameringen, 1976; DeQuattro, Campese, Miura & Mejier, 1976; Esler, Julius, Zweifler, Randall, Harburg, Gardiner & DeQuattro, 1977) in a sizeable fraction of patients with essential hypertension, others have found completely normal values (Berglund, Tibblin & Aurell, 1975; Lake et al., 1977; Pedersen & Christensen, 1975).

The aim of this report is to present our measurements of plasma [noradrenaline] and plasma renin concentration [renin] in 40-year-old individuals with mild essential hypertension and in 40-year-old normotensive subjects.

Patients and methods
All patients and normotensive controls were identified during survey of a population born in 1936. None of the patients had ever received anti-hypertensive treatment. Individuals with an alcohol intake of more than 40 g/day and/or with abnormalities in liver-function tests were excluded.

Two groups of hypertensive and normotensive individuals were studied.

Group I. Thirty-three individuals (seven females, 26 males) with a diastolic blood pressure $\geq 95$ mmHg at the very first examination. The majority of the patients had not been informed about their high blood pressure at the time of blood sampling. In 20 out of these 33 individuals the hypertension was labile, defined as diastolic $\geq 95$ mmHg at the
first examination, but < 95 mmHg in at least one out of three subsequent examinations at 4 weeks intervals. The remaining 13 had sustained diastolic hypertension (≥95 mmHg at no less than three sequential measurements in the outpatient clinic at 4 weeks intervals). Blood samples for determination of plasma [noradrenaline] (Christensen, 1979) were drawn after 10 min rest in the supine position, 10 min after insertion of an indwelling needle. In 31 (17 females, 14 males), normotensive controls (diastolic ≤90 mmHg), randomly selected from the study population, blood samples were collected under the same conditions.

Group 2. Twenty-two patients (six females, 16 males) with sustained diastolic hypertension, defined as above, were investigated in more detail. Ten out of these also formed part of group 1. Plasma [noradrenaline] and [renin] (Giese, Jørgensen, Nielsen, Lund & Munck, 1970) were measured supine at rest, and again after Frusemide, 0.65 mg/kg intravenously, with subsequent quiet ambulation for 2 h. Twenty-four 40-year-old normotensive individuals (10 females, 14 males), served as a control group.

Results are presented as median values, with ranges in parantheses.

Results

In the group of hypertensive individuals with diastolic ≥ 95 mmHg at the very first examination (group 1), mean systolic and diastolic pressures were 144 (120–190) mmHg and 100 (95–122) mmHg respectively. Plasma [noradrenaline] at rest supine did not differ significantly from the values in the normotensive control group: 1.08 (0.25–2.48) nmol/l and 1.15 (0.25–2.17) nmol/l in the hypertensive and normotensive individuals respectively. There was no significant difference between males and females. Plasma [noradrenaline] was identical in patients with labile hypertension (n = 20) and in patients with sustained hypertension (n = 13).

In the patients with mild sustained hypertension (group 2; n = 22) plasma [noradrenaline] at rest and after acute stimulation did not differ from the values in the normotensive controls (Fig. 1). After 2 h rest in supine position, at the time of blood sampling, systolic and diastolic pressures were 152

![Figure 1](https://example.com/figure1.png)

**Fig. 1.** Plasma noradrenaline concentration at rest supine and after frusemide plus ambulation (a) in 40-year-old patients with untreated mild sustained essential hypertension and (b) in normotensive controls.
Plasma noradrenaline and hypertension

(125–186) mmHg and 102 (91–124) mmHg respectively in the hypertensive patients. There was a significant ($P < 0.01$) increase in plasma [noradrenaline] during acute stimulation, in normotensive as well as in hypertensive individuals. Similarly, plasma [renin], measured under identical conditions, did not differ significantly between patients with hypertension and normotensive controls. In the group of patients with hypertension a close correlation ($r = 0.77, P < 0.001$) between plasma [noradrenaline] and [renin] after acute stimulation was found. A similar correlation was found between the absolute changes from resting to acutely stimulated values ($r = 0.72, P < 0.001$). There was no significant correlation between the resting values for the concentrations of the two. In the group of normotensive controls no correlation was found between [noradrenaline] and [renin], neither at rest nor after acute stimulation.

Discussion

The present investigation deals with 40-year-old individuals with mild essential hypertension, identified during a population survey, and with normotensive controls selected at random from the same population. It should be emphasized that fairly rigid inclusion criteria were applied, as detailed above.

Based upon a positive, albeit weak, correlation between age and plasma [noradrenaline] in normotensive controls (Lake et al., 1977; Pedersen & Christensen, 1975) and in patients with hypertension (Pedersen & Christensen, 1975), it has been suggested by some authors (Lake et al., 1977; Pedersen & Christensen, 1975) that the finding of the elevated concentrations in patients with essential hypertension could be explained by age differences between the normotensive controls and the hypertensive patients. However, this point has been refuted by other investigators (Campese, Myers & DeQuattro, 1977). The representativeness of the normotensive individuals has been questioned in other respects in particular the practice of including nurses, physicians, medical students and normotensive patients in the control groups (Lake et al., 1977). Plasma [noradrenaline] did not differ between patients with hypertension and their normotensive controls in the present study. It is thus very likely that discrepancies reported in the literature are, at least to some extent, related to a lack of comparability between the hypertensive and normotensive individuals studied, as far as the source of study populations is concerned.

In our patients with mild sustained hypertension a close correlation between plasma [noradrenaline] and [renin] after acute stimulation was found. However, this does not necessarily imply any cause-and-effect relationship, but the influence of adrenergic activity on renin release has been documented in many physiological conditions (Davis, 1974). Several factors control renin release, one of these being the sympathetic nervous system, but other mechanisms, such as changes in sodium balance or changes in renal perfusion pressure, may override the influence of adrenergic tone (Davis, 1974).

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References


