Relation of plasma noradrenaline to blood pressure, age, sex and sodium balance in patients with stable essential hypertension and in normotensive subjects

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Summary
1. Plasma noradrenaline was measured in 125 patients with stable essential hypertension (WHO I–II) and in 107 normotensive control subjects lying and standing.
2. In normotensive subjects and in patients with essential hypertension no sex-related differences of plasma noradrenaline were found between age-matched groups.
3. Plasma noradrenaline was not related to sodium balance indexed by urinary sodium/creatinine ratio.
4. In patients with essential hypertension plasma noradrenaline increases with age.
5. Mean plasma noradrenaline concentrations are significantly higher in patients with essential hypertension compared with age-matched normotensive subjects both lying and standing.
6. In patients with essential hypertension diastolic blood pressure and heart rate correlated significantly with supine plasma noradrenaline concentrations.

Key words: age-dependence, essential hypertension, plasma noradrenaline, sodium balance.

Introduction
The significance of the sympathetic nervous system in the pathogenesis and maintenance of essential hypertension is still a matter of controversy. Lack of appropriate control groups and varying test conditions in some studies may partly account for contradictory findings.

Methods
107 normotensive healthy subjects (58 women, 49 men) with a mean age of 42 years (15–81 years) and 125 patients with stable essential hypertension (WHO I–II; 57 women, 68 men) with a mean age of 40 years (17–70 years) were studied. All had a creatinine clearance above 70 ml/min 1.73 m⁻² and no clinical signs of heart failure. Antihypertensive drugs including diuretics were discontinued 14 days before the study. All probands underwent the same test-procedure, which consisted of two consecutive phases: (1) 4 h supine from 08.00 hours to 12.00 hours; (2) 7 min standing. Blood pressure, heart rate and blood samples were taken after each phase. Plasma noradrenaline was measured fluorometrically according to the method of Renzini, Brunori & Valori (1970) with modifications described by Brecht, Banthien & Schoeppe (1976).

Urinary sodium excretion expressed per g of urinary creatinine during the resting period was taken as a measure of sodium balance (Goldberg & Spierto, 1973; Skrabal, 1975).

Results
No significant difference was found between 43 men and 43 age-matched women (normotensive or...
hypertension) in plasma noradrenaline concentration either standing or after resting supine. Plasma noradrenaline concentration was not related to urinary sodium/creatinine ratio in 105 normotensive subjects ($r = 0.18$, N.S.) and in 116 patients with essential hypertension ($r = -0.07$, N.S.).

In 107 normotensive subjects plasma noradrenaline concentration did not increase with age under basal conditions ($r = 0.10$, N.S.), but increased significantly with age when standing ($r = 0.27$, $P < 0.01$).

In 125 patients with essential hypertension plasma noradrenaline concentration was significantly correlated to age both when recumbent ($r = 0.27$, $P < 0.005$) and standing ($r = 0.26$, $P < 0.001$).

Basal resting diastolic blood pressure correlated highly with the corresponding plasma noradrenaline concentration in patients with essential hypertension ($r = 0.48$, $P < 0.001$) but not in normotensive subjects ($r = 0.09$, N.S.) (Fig. 1). Since both plasma noradrenaline and blood pressure increased with age, the influence of age on this correlation was eliminated by partial regression analysis. With age being eliminated the correlation between diastolic blood pressure and plasma noradrenaline concentration remained significant ($r = 0.45$, $P < 0.001$). Under basal conditions heart rate and plasma noradrenaline concentration were positively correlated in patients with essential hypertension ($r = 0.24$, $P < 0.01$) but not in normotensive subjects.

Mean plasma noradrenaline concentration in 87 patients with essential hypertension was significantly higher than in 87 age-matched normotensive subjects under basal [201 ng/l (135–298) vs 128 ng/l (95–171), $P < 0.001$] and orthostatic conditions [405 ng/l (268–613) vs. 278 ng/l (194–400), $P < 0.001$].

**Discussion**

In patients with stable essential hypertension mean plasma noradrenaline concentration was significantly higher than in age-matched normotensive subjects both recumbent and standing. Moreover, diastolic blood pressure and heart rate correlated significantly with the corresponding plasma noradrenaline concentration in patients with stable essential hypertension but not in normotensive subjects. Even after elimination of the influence of age by partial regression analysis the correlation between diastolic blood pressure and plasma noradrenaline remained highly significant. Increased plasma noradrenaline concentrations in patients with essential hypertension have been reported by Geffen, Rush, Louis & Doyle (1973), Louis, Doyle & Anavekar (1975), Lütold, Bühler & Da Prada (1976), and Philipp, Cordes, Zschiedrich & Distler (1977). Sever, Birch, Osikowska &

![Fig. 1. Correlation between diastolic blood pressure and plasma noradrenaline concentration in recumbent patients with essential hypertension (●, $n = 125$, $r = 0.48$; $P < 0.001$) and in normotensive recumbent subjects (○, $n = 107$, $r = 0.09$; N.S.) under basal conditions.](image-url)
Tunbridge (1977) could only detect higher plasma noradrenaline concentrations in younger patients (less than 50 years of age) with essential hypertension. Some reports, however, did not confirm increased plasma noradrenaline concentrations in essential hypertension (Pedersen & Christensen, 1975; Lake, Ziegler, Coleman & Kopin, 1977; Franco-Morselli, Elghozzi, Joly, Di Giulio & Meyer, 1977). The results of these three study groups, however, cannot indiscriminately be compared with ours. In the study by Pedersen & Christensen (1975) some of the control subjects were hypertensive with systolic values of 160 and diastolic values of 100 mmHg. Further, some hypertensive subjects must be classified as WHO stage III with a reduced kidney function and Grade III retinopathy. Plasma catecholamines have been shown to depend on kidney function and Grade III retinopathy.

The discrepancies in the reports of plasma noradrenaline concentrations in essential hypertension might also be due to the use of patients with labile essential hypertension. This group of patients is characterized by excessive noradrenaline responsiveness to various stimuli (Esler & Nestel, 1973 a,b) but may also exhibit lower than normal plasma noradrenaline concentrations under basal conditions (H. M. Brecht & W. Scheppe, unpublished results). Our data suggest a significant pathophysiological role of sympathetic neurogenic activity in stable essential hypertension. However, as 60% of patients with stable essential hypertension show noradrenaline concentrations within the normal range additional factors contribute to the hypertensive state.

References