samples were also drawn at indwelling venous cannula three samples each were drawn for was analysed by radiometric assay with PNMT. Noradrenaline Hosome Hospital, Glasgow. Scotland, U.K. by the use of an pressure was monitored with a Bosomat conclusion that plasma noradrenaline concentration increases higher in normotensive elderly compared with the young. It is decreased clearance of noradrenaline was responsible for the increased concentration in elderly subjects. Eight young men (28.7 ± 5.3 years) and nine elderly men (69.7 ± 4.3 years), all with normal biochemical indices, were studied. By the use of an indwelling venous cannula three samples each were drawn for determination of supine and standing noradrenaline. Six samples were also drawn at 30 min intervals during a steady-state noradrenaline infusion (0.06 µg min⁻¹ kg⁻¹). Blood pressure was monitored with a Bosomat 11D. Noradrenaline was analysed by radiometric assay with PNMT. Noradrenaline release and clearance were determined as described elsewhere (Fitzgerald et al., Clinical Pharmacology and Therapeutics, 1979, 26, 669-675). Data were analysed by the Wilcoxon rank sum test. We confirm that plasma noradrenaline increases with age as follows. Supine position (nmol/l): young, 2.44 ± 0.76; old, 4.09 ± 1.19 (P < 0.01). Standing position (nmol/l): young, 4.31 ± 1.44; old, 7.21 ± 1.68 (P < 0.01). There was no difference in clearance between the two groups. This was true both when clearance was expressed as 1/min (4.59 ± 1.33, young; 5.82 ± 3.71, old; P > 0.05) and as ml min⁻¹ kg⁻¹ (64.9 ± 21.2, young; 73.7 ± 37.2, old; P > 0.05). The rate of noradrenaline release (nmol/min) was significantly increased in the elderly group: Young supine, 10.82 ± 3.71; old supine, 23 ± 14.58 (P < 0.05). Young standing, 19.1 ± 8.2; old standing, 41.9 ± 33.1 (P < 0.01). Four of the elderly subjects were normotensive (B.P. < 160/95 mmHg) and four were hypertensive. There was no difference between the normotensive and hypertensive elderly subjects in clearance, rate of release or plasma concentration of noradrenaline. However, in both supine and standing positions plasma noradrenaline was significantly higher in normotensive elderly compared with the young. It is concluded that plasma noradrenaline concentration increases with age because of increased release. Hypertension was not associated with higher noradrenaline concentrations.

8. COMPARISON OF THE KINETICS OF INFUSED WITH EXCERCISE-RELEASED PLASMA NORADRENALINE IN MAN

L. COPE, I. B. DAVIES, S. L. LIGHTMAN AND P. S. SEVER
Department of Clinical Pharmacology and Medical Unit, St Mary's Hospital Medical School, London
Noradrenaline (NA) released into plasma from sympathetic nerves (Rosenthal, Birch, Osikowska & Sever, 1978, Cardiovascular Research, 12, 144-147) and blood pressure responses to infused NA (Philipp, Distler & Cordes, 1978, Lancet, II, 62-67) respectively, may reflect sympathetic activity and noradrenergic sensitivity. It seemed important to identify differences in the elimination of NA which has entered plasma by these routes. Therefore we compared the kinetics of NA released during dynamic exercise with that producing a similar pressor response during intravenous infusion in five normal male subjects (23-35 years).

Venous blood samples were taken at rest and after (30 and 60 s intervals for 5 and then 20 min respectively) bicycle-ergometry (50 and 100 W for 1 and then 2 min) at 14.00 hours. Seven days later, at 14.00 hours, the NA dose necessary to maintain (4 min) a similar blood pressure increase and a steady-state plasma NA concentration was determined by incremental infusions (0.025, 0.05, 0.10, 0.15, 0.20 µg of NA base min⁻¹ kg⁻¹). Samples were taken during (1 min intervals) and after the final increment (30 s and then 1 min intervals for 10 and then 15 min respectively). NA was measured radioenzymatically (Henry, Starman, Johnson & Williams, 1975, Life Sciences, 16, 375-384).

During exercise, pressure, heart rate and plasma NA increased from respectively 124 ± 6/80 ± 4 mmHg, 66 ± 2 beats/min and 2763 ± 1501 pmol/l (mean ± SEM) to 161 ± 1279 ± 8, 128 ± 11 and 7416 ± 2963. NA elimination was multiphasic: for the first phase, half-time and elimination constant were 2.6 ± 1.3 min and 0.46 ± 0.11 pmol min⁻¹ l⁻¹. NA entry rate into plasma was 1.5 ± 0.26 pmol min⁻¹ l⁻¹. The final NA infusion changed the pressure, heart rate and plasma NA from respectively 104 ± 28/65 ± 5, 61 ± 3 and 888 ± 139 to 145 ± 3/92 ± 5, 48 ± 4 and 39 550 ± 9887. The half-time was not different (0.92 ± 0.07) but the elimination constant was greater (0.77 ± 0.06), despite the faster NA entry rate into plasma (2.57 ± 0.32) (P < 0.02 and P < 0.05 respectively). Volume of distribution and clearance were 32 ± 6.1 and 25 ± 6.3 respectively.

9. COMPARISON OF HEMODYNAMIC EFFECTS OF PRENALTEROL IN PATIENTS ON OR OFF β-ADRENERGIC-RECEPTOR-BLOCKING DRUGS

M. F. SHIU, M. A. IRELAND AND W. A. LITTNER
Department of Cardiovascular Medicine, University of Birmingham and East Birmingham Hospital, Birmingham, U.K.

The haemodynamic effects of prenalterol, a β₁-adrenoceptor agonist, were studied in 24 patients with ischaemic heart disease. Nine patients, three of whom had congestive heart failure, were not on β-adrenoceptor-blocking drugs. In these prenalterol (5 mg), given intravenously over 5 min, increased heart rate by 28% and left ventricular max. dp/dt by 72%. Systolic blood pressure rose slightly and wedge pulmonary artery pressure was unchanged. Angiographic ejection fraction increased from 0.49 ± 0.08 to 0.61 ± 0.08 (P < 0.02). Fifteen patients were studied while on chronic β-adrenoceptor-blocking drugs. In these patients the heart rate and max. dp/dt responses were similar, but systolic blood pressure did not change and wedge pulmonary arterial pressure fell significantly. Angiographic ejection fraction was increased from 0.49 ± 0.08 to 0.61 ± 0.08 (P < 0.01). With heart rate fixed at 110 beats/min, by atrial pacing in seven patients, max. dp/dt increased from 1803 ± 682 mmHg to 2600 ± 272 mmHg after 5 mg of prenalterol. Patients on β-adrenoceptor-blocking drugs tolerated a higher total dose of prenalterol without undue tachycardia. The study showed the specific β₁-adrenoceptor agonist property of prenalterol and demonstrated its powerful inotropic effect in patients with or without left ventricular dysfunction.

10. LONG-TERM EFFECTS OF DIURETIC TREATMENT IN HYPERTENSION: REVERSIBILITY OF CHANGES IN PLASMA RENIN

S. S. SWART, R. F. BING, H. THURSTON AND J. D. SWALES
Department of Medicine, University of Leicester, U.K.

There are probably important differences between the short- and