Eight normoventive males (age 19-46 years) were investigated during three levels of sodium intake (1 week each). As sodium excretion (mmol/day) decreased from high (310 ± 43; mean ± se) to medium (186 ± 24) to low (21 ± 4) activity of the renin–angiotensin system (RAS) increased fivefold and packed cell volume increased significantly (P < 0.05). Plasma catecholamines were measured radioenzymatically and titrated L-noradrenaline was infused intravenously at a suppresor dose to equilibrium over 90 min to measure the apparent rate of entry of noradrenaline (NA) into, and clearance from, plasma (Elder et al., 1979, Life Sciences, 25, 1461). During sodium restriction, supine and upright NA increased by 35% (P < 0.05) compared with medium and high intake (isoprenaline values (nmol/l): low 1-78 ± 0.23; medium 1-31 ± 0.14; high 1-35 ± 0.24). This reflected increased rate of entry of NA into plasma (5-86 ± 1.12 against 4.44 ± 0.65 mmol/min, P < 0.05); clearance remained constant (2.99 ± 0.18 litres/min). Plasma adrenaline was unchanged.

Variation in salt intake did not significantly alter cardiac autonomic activity as measured from chronotropic responses to graded intravenous isoprenaline boluses and cardiac autonomic blockade (propranolol, 0.2 mg/kg, and then atropine, 0.04 mg/kg). The increase in sympathetic activity which accompanied sodium restriction was modest compared with changes in the RAS and was not associated with altered autonomic control of cardiac rate.

35. EFFECT OF ALTITUDE ON WATER EXCRETION

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Antidiuresis occurs in individuals with acute mountain sickness (AMS). We investigated the effect of altitude on water excretion and its relation to AMS in 20 healthy males aged 23-52 years during a 10 day non-strenuous ascent and descent to 5000 m. Half the group took acetazolamide-sustained release (500 mg/day) and the other half a placebo. Subjects were given an oral water load (20 ml/kg body weight) after overnight (9 h) fast and fluid deprivation in Birmingham at 150 m and after rapid ascent to 2800 m; 15 subjects underwent a third water load at 5000 m or, on descent, at 3800 m. Measurements were made of plasma osmolality before and 1 h after the load and urine volume and osmolality before and at hourly intervals for 4 h after the water load. AMS was assessed clinically by two experienced observers.

The percentage of water load excreted by 4 h at 150 m was 90-8 ± 5-2% (mean ± SEM). At 2800 m there was a significant reduction in the percentage of the water load excreted in both groups. This was 59-3 ± 7-2% for those on placebo and 65-4 ± 3-5% for those taking acetazolamide (P < 0.01). The difference in the response to the water load at these two altitudes was not significantly correlated with the severity of AMS (r = -0.29, P > 0.05). Minimum urine osmolality at 150 m was 98-8 ± 9-3 mmol/kg. At 2800 m it was 152-4 ± 59-6 mmol/kg for those on placebo and 93-6 ± 7-6 mmol/kg for those on acetazolamide. These differences were not significant (P > 0.05). At 5000 m the response was similar to that at 2800 m whereas on descent to 3800 m there was no significant difference from the response at 150 m.

AMS of moderate severity developed in six subjects, one of whom was taking acetazolamide; three had to descend to a lower altitude. Of the six who were minimally affected by AMS, five were taking acetazolamide.

These results suggest that excess vasopressin does not contribute to water retention at high altitude or to the development of AMS. These findings are further supported by the results from a previous expedition in which plasma vasopressin levels did not correlate with AMS.

36. URINE FREE DOPAMINE IN NORMAL PREGNANCY

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Dopamine is present in the human urine in amounts greater than can be accounted for by simple filtration of plasma dopamine by the kidney. Our previous studies in normal volunteers have demonstrated that dietary salt loading produces a marked rise in urine dopamine but that fludrocortisone administration produces little change in urine dopamine concentrations; neither experimental condition produces any change in plasma dopamine (Oates, Perkins & Lee, 1980; Clinical Science, 58, 77). Pregnancy is characterized by vasodilatation and an increase in effective renal plasma flow (ERPF) yet is associated with a marked rise in the circulating components of the renin–angiotensin system.

Twenty primigravida patients (mean age 25-8 years), who had been routinely referred to the antenatal clinic at 8–12 weeks, were studied at monthly intervals throughout pregnancy. Urine specimens (24 h) were collected on an out-patient basis for analysis of sodium, creatinine and dopamine. All pregnancies progressed satisfactorily to term without the development of hypertension or oedema. Urine dopamine was measured by a radioenzymatic method; plasma and urine sodium and creatinine were measured by conventional Autoanalyzer techniques.

The mean 24 h urine free dopamine was elevated throughout pregnancy when compared with postnatal values (P < 0.05; week 12; P < 0.025, weeks 16, 24 and 40; P < 0.01, weeks 32 and 36; unpaired t-test). In contrast there appeared to be no sustained elevation of 24 h urine sodium output that could account for the rise in urine dopamine. These results demonstrate that urine dopamine is increased during pregnancy compared with postnatal values; our tentative hypothesis is that this increase may be related to the increase in ERPF in pregnancy.

37. EFFECT OF PROLONGED ISOMETRIC EXERCISE ON THE CIRCULATION AND ON RENAL EXCRETION OF SODIUM AND POTASSIUM IN MALES GENETICALLY PREPENSI TO HYPERTENSION

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At the last meeting of the Medical Research Society we showed that relative renal retention of sodium and potassium occurred after prolonged isometric exercise in mild essential hypertension. Any abnormality demonstrable in the children of hypertensive parents which cannot be demonstrated in the children of normotensive parents may be related to the pathogenesis of hypertension. Therefore we studied the effect of prolonged isometric exercise on the circulation and on the renal excretion of sodium and potassium in 16 male medical students, whose parental blood pressure was less than 140/85 mmHg, and in 17 male students with one or two parents whose blood pressure was greater than 150/90 mmHg.

After an initial resting period of 90 min, basal measurements of pulse rate, blood pressure and of the rates of sodium and potassium excretion were made. A 1 h period of isometric exercise involving all four limbs in rotation ensued, followed by 5 h of rest, during which the above observations were recorded at half-hourly intervals for the first 2 h and at hourly intervals for the last 3 h. The studies were repeated on another day with the subjects resting instead of exercising for 1 h. The responses of each subject were then expressed as the ratios of the changes from the basal values observed on the exercise and rest days.