SHORT REPORTS

Physiological response to parachute jumping

The metabolic and hormonal responses to stress in racing drivers, airline pilots, rock climbers, public speakers, and parachutists have been reported.¹ Most studies have concentrated on catecholamine concentrations and their effects on heart rate; little information is available about changes in the concentrations of other hormones and intermediary metabolites.

Subjects, methods, and results

Eight healthy subjects (two women, six men) took part in the study. None had made a parachute jump before. Their ages ranged from 23 to 29, and all were within 10% of their ideal body weight. All subjects fasted from 1300 and jumped between 1900 and 2100. Venous blood was taken through an indwelling cannula before they left for the airfield (basal values); on arrival; after 30 minutes' exercise training on the ground; in the aircraft at 610 m immediately before they jumped from a static line; within 30 seconds after landing; and at 10, 20, and 30 minutes after landing. A Tracker Holter monitor was attached to each subject to give a continuous electrocardiogram, and the tapes were analysed on a Pathfinder 3 analyser.

Concentrations of intermediary metabolites were measured fluorimetrically and spectrophotometrically (acetoacetate). Non-esterified fatty acid concentrations were measured by a radiocobalt soap method, potassium concentrations by flame photometry, and hormone concentrations by radioimmunoassay or high performance liquid chromatography (catecholamines).² Data were classified by subject and time and analysed by two way analysis of variance. When the variance ratio for a time effect was significant the change from basal values was assessed by Student's *t* test for paired samples.

All eight subjects showed three clear peaks in heart rate: on arriving at the airfield, during ground training, and on jumping out of the aeroplane (the greatest increase). Heart rates increased from a basal mean of 78 (range 62-91) beats/min to a peak of 160 (150-183). No ventricular arrhythmias or ST segment abnormalities were recorded.

The table shows the changes in concentrations of intermediary metabolites and hormones. In six subjects peak concentrations of non-esterified fatty acids were greater than 1.4 mmol/l, and three had lactate concentrations greater than 5 mmol/l. Concentrations of adrenaline and noradrenaline rose in parallel, reaching peak values when the subjects were in the aeroplane and on landing, respectively. After landing the concentration of adrenaline fell to basal values within 10 minutes but the concentration of noradrenaline was still significantly raised 30 minutes later ($p < 0.05$).

Comment

The metabolic response to the stress of parachute jumping seems similar to the response to other forms of stress studied. The rise in concentrations of glucose and fatty acids with a fall in the insulin concentration results from increased concentrations of circulating catecholamines. We observed a rise of three to 15 times the basal value in both adrenaline and noradrenaline concentrations in the aircraft immediately before the jump.

The popularity of parachuting is increasing, especially now that people are often sponsored for jumping. In our fit young subjects the heart rate rose to a mean of 160 beats/min; concentrations of catecholamines increased fivefold and those of non-esterified fatty acids reached values associated with cardiac arrhythmias.³ In subjects with undiagnosed coronary artery disease the

demands on the heart of a sustained tachycardia, a low grade hypoxia caused by reduced oxygen pressure depending on the height at which the jump is made, and a simultaneous rise in the concentrations of catecholamines and non-esterified fatty acids could cause cardiac arrhythmias.⁴ Doctors asked to perform medical examinations to assess fitness to jump should be aware of the extreme nature of the stress of parachute jumping.

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Endogenous digoxin-like immunoreactivity in congestive heart failure

Material cross reacting with antidigoxin antibodies has been found in several clinical settings, including the third trimester of pregnancy, the neonatal period, liver disease, and chronic renal failure.¹ Though the exact nature of this material is not known, we have shown recently that digoxin-like immunoreactive substance is probably a steroid.²

Several observations have suggested a pathophysiological role for digoxin-like immunoreactive substance. Firstly, it has been found in several hypertensive states, including toxemia of pregnancy and experimental hypertension in rats. Secondly, the hypertension in aortic coarctate rats is reversed by antidigoxin antibodies.³ Thirdly, gel filtration fractions of serum which contained digoxin-like immunoreactive substance from volume

Mean (SD) concentrations of intermediary metabolites and hormones in eight subjects before and after a parachute jump

	Basal	On arrival at airfield	After exercise training	In aeroplane immediately before jump	On landing	10 Minutes after landing	20 Minutes after landing	30 Minutes after landing
Glucose (mmol/l)	4.9 (0.3)	4.6 (0.4)	4.6 (0.5)	5.3 (0.3)	5.8 (0.5)**	6.2 (0.6)**	5.7 (0.4)**	5.3 (0.3)*
Lactate (mmol/l)	0.84 (0.12)	0.75 (0.17)	1.13 (0.51)	1.47 (0.36)	4.48 (1.39)**	3.32 (1.02)**	1.66 (0.70)*	1.08 (0.21)
Pyruvate (mmol/l)	0.07 (0.01)	0.06 (0.02)	0.09 (0.05)	0.09 (0.02)	0.18 (0.04)**	0.18 (0.05)**	0.10 (0.02)*	0.08 (0.01)
Alanine (mmol/l)	0.31 (0.05)	0.28 (0.03)	0.31 (0.05)	0.27 (0.04)	0.29 (0.05)	0.31 (0.05)	0.29 (0.04)	0.27 (0.04)
Non-esterified fatty acids (mmol/l)	0.60 (0.12)	0.75 (0.29)	0.93 (0.10)**	1.47 (0.37)**	1.45 (0.38)**	1.43 (0.28)**	1.06 (0.23)**	1.06 (0.25)**
Glycerol (mmol/l)	0.07 (0.03)	0.10 (0.06)	0.15 (0.05)**	0.15 (0.06)**	0.21 (0.09)**	0.23 (0.09)**	0.15 (0.05)**	0.13 (0.04)**
Total ketone bodies (mmol/l)	0.05 (0.03)	0.10 (0.06)	0.14 (0.05)	0.35 (0.24)**	0.34 (0.23)**	0.30 (0.20)**	0.25 (0.15)*	0.25 (0.17)*
Adrenaline (nmol/l)	0.50 (0.26)	0.57 (0.19)	0.82 (0.37)	2.21 (1.06)**	2.11 (1.11)**	0.71 (0.17)	0.56 (0.20)	0.41 (0.21)
Noradrenaline (nmol/l)	1.76 (0.58)	2.40 (0.43)	2.66 (0.55)	4.24 (1.23)**	6.35 (1.93)**	4.87 (1.38)**	4.46 (1.33)**	3.35 (0.90)*
Insulin (mU/l)	6.79 (3.81)	3.03 (1.55)*	2.34 (1.41)**	3.31 (0.74)*	4.35 (2.96)	7.65 (1.54)	5.91 (3.61)	4.11 (1.26)*
Growth hormone (mU/l)	3.06 (3.28)	1.39 (0.56)	17.00 (6.16)**	4.18 (4.08)	5.21 (6.47)	6.69 (5.90)	8.53 (5.63)*	6.30 (4.39)
Cortisol (nmol/l)	359 (120)	248 (141)	221 (197)	466 (289)	561 (333)*	680 (327)**	685 (334)**	632 (354)**
Prolactin (mU/l)	280 (129)	188 (93)	193 (114)	453 (328)*	648 (529)**	505 (271)**	356 (228)	296 (170)
Potassium (mmol/l)	3.9 (0.2)	3.8 (0.4)	3.7 (0.2)*	4.3 (0.4)**	3.6 (0.2)*	3.8 (0.2)	3.6 (0.3)*	3.8 (0.2)

Significance of change from basal value: * $p < 0.05$, ** $p < 0.001$.

expanded dogs inhibited sodium-potassium adenosine triphosphatase.⁴ Finally, digoxin-like immunoreactive substance has been shown to have natriuretic activity.⁵ This last finding prompted us to study whether concentrations of digoxin-like immunoreactive substance would be increased in a clinical setting such as congestive heart failure, in which natriuretic activity would be expected to be high.

Subjects, methods, and results

Plasma and urine were obtained from 15 patients with congestive heart failure (New York Heart Association class III or IV at time of study) who were not receiving digitalis or other drugs known to cross react with antidigoxin antibodies—for example, spironolactone. Twelve had ischaemic heart disease and three dilated cardiomyopathy. Plasma and urine samples were also obtained from 10 normal volunteers. Liver and renal function values were normal in all subjects.

Concentrations of digoxin-like immunoreactive substance were measured by a double antibody radioimmunoassay for digoxin (RIANEN, New England Nuclear, Billerica, MA, USA). The assay was slightly modified by including additional standards at the lower portion of the standard curve. The lower limit of detectability with 95% confidence limits was 0.06 nmol/l. In this assay there was no or insignificant cross reaction with hydrocortisone, deoxycorticosterone, 11-deoxycortisol, dehydroepiandrosterone, androstenedione, 17-hydroxyprogesterone, progesterone, aldosterone, or oestradiol. All samples were assayed in duplicate. In view of the observation of Valdes and Graves that the bulk of digoxin-like immunoreactive substance is protein bound and can be detected only after diluting and boiling serum,¹ we measured concentrations in native serum and in serum diluted to 1/4 in deionised water and boiled for 10 minutes. We also measured digoxin-like immunoreactive substance in untreated urine, and corrected for urine creatinine concentration.

In native serum of normal subjects no digoxin-like immunoreactive substance was detected. In native serum of the patients with congestive heart failure digoxin-like immunoreactive substance was detected in 11 cases with a mean concentration of 0.125 (SD 0.1) nmol/l (Student's *t* test, $p < 0.001$) (table). The concentration of digoxin-like immunoreactive substance in diluted and boiled normal serum was 1.09 (0.15) nmol/l compared with 1.34 (0.29) nmol/l in congestive heart failure ($p < 0.001$). Urinary concentrations of digoxin-like immunoreactive substance after correction for creatinine were significantly higher in patients with heart failure ($p < 0.001$).

Digoxin-like immunoreactive substance in serum and urine

	Native serum (nmol/l)	Boiled serum (nmol/l)	Urine (nmol/l: creatinine, mmol/l)
Congestive heart failure:			
Mean (SD)	0.125 (0.10)	1.34 (0.29)	0.34 (0.08)
Range	(0.0-0.30)	(0.93-1.61)	(0.2-0.46)
Normal subjects:			
Mean (SD)	0	1.09 (0.15)	0.23 (0.08)
Range	—	(0.86-1.34)	(0.09-0.36)

Comment

Our results show that congestive heart failure must be added to the clinical states associated with increased concentrations of digoxin-like immunoreactive substance. Using the RIANEN assay for digoxin we found detectable concentrations of digoxin-like immunoreactive substance in 11 of 15 patients. In patients receiving digoxin digoxin-like immunoreactive substance is additive in the digoxin radioimmunoassay. Hence the presence of endogenous cross reacting material would falsely increase measured values, albeit only slightly. Impaired hepatic or renal function, which is often found in conjunction with heart failure, has been shown to increase the concentration of digoxin-like immunoreactive substance. The combined effects of congestive heart failure and hepatic or renal disease on digoxin-like immunoreactive substance may lead to more pronounced overestimation of true digoxin concentrations in patients receiving this drug.

Valdes and Graves found that diluting and boiling serum increase measurable concentrations of digoxin-like immunoreactive substance.¹ They suggested that these procedures liberate protein bound digoxin-like immunoreactive substance and allow determination of the total amount. We have shown that total digoxin-like immunoreactive substance is increased in the serum of patients with congestive heart failure and that the amount excreted in urine is also increased. These results suggest that the raised concentrations of digoxin-like immunoreactive substance found in congestive heart failure reflect increased synthesis of this material.

In view of the suggested physiological role of digoxin-like immunoreactive substance our results raise the intriguing possibility that concentrations of the substance are increased in patients with congestive heart failure as an adaptive phenomenon, analogous to similar alterations noted in concentrations of atrial natriuretic peptide in congestive heart failure.

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Hypophosphataemia: a feature of malaria?

Many patients with malaria admitted to this hospital have unexplained low serum phosphate concentrations. I report on 17 such patients; in one the phosphate concentration seemed to be related to treatment.

Patients and findings

Case 1—A 36 year old Welshman was admitted after returning from Kenya with a history of fever and headache. On examination his fever was confirmed and he was unwell but alert. A blood film showed a 10% parasitaemia with *Plasmodium falciparum*. His condition initially improved with oral quinine and the parasite count fell, but his blood film remained positive until day 5. On day 3 his condition deteriorated and he developed headache and drowsiness. He was given quinine 3 g in saline intravenously, as is recommended for patients with this degree of parasitaemia,¹ and sulfadoxine 3 g and pyrimethamine 150 mg (Fansidar) orally over days 3-5. Capillary glucose concentrations were estimated every three hours and ranged between 4.5 and 6.5 mmol/l. On day 5 he was alert and free from headache, and his condition then improved steadily.

Of 28 patients with malaria admitted between January 1984 and December

Serum phosphate concentrations in patients with malaria by plasmodial species. Vertical bar indicates mean concentration with 95% confidence interval in patients with malaria; solid horizontal bar indicates control mean; hatched area indicates normal range for the laboratory.