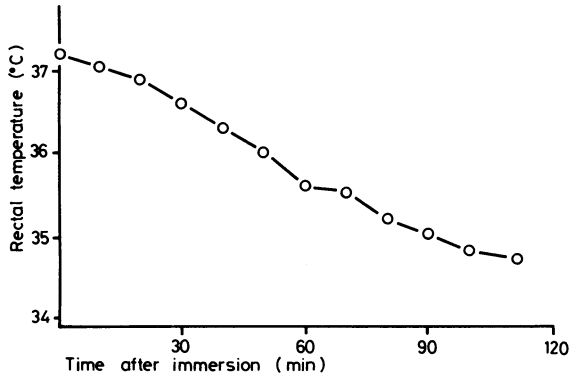
SHORT REPORTS

Progressive symptomless hypothermia in water: possible cause of diving accidents

Unexplained loss of consciousness, often followed by death, has been common during diving in British waters. Forty-two such deaths were noted by Childs and Norman[1] and no likely cause for them has been established. We describe here progressive symptomless hypothermia which developed during one of a series of fully monitored laboratory experiments designed to assess individual responses to mild surface cooling in water.

Case report

The subject was a physically fit, thin man aged 20. He was cox of a rowing eight and had been repeatedly exposed to cold air, close to or below 0°C, for about one and a half hours three times a week for one month before the experiment on 1 February 1979. His subcutaneous fat thickness measured by ultrasound averaged 3·8 mm over the upper chest and 4·1 mm over the lower abdomen at the level of the iliac crests. The figure shows that when he was immersed in water at 29°C wearing only bathing trunks his rectal temperature fell from an initial value of 37·20°C to 34·70°C after 112 minutes. This temperature was still falling, though at a reduced rate, at the end of this time.



Progressive fall of body temperature during immersion in water at 29°C.

Towards the end of the immersion the electrocardiograph showed ventricular and supraventricular ectopics.

The subject did not feel uncomfortably cold at any stage of the immersion. His metabolic rate during the last 10 minutes of the immersion, estimated from O_2 consumption, was 1·65 kcal/m²/min compared with 0·90 kcal/m²/min during an immersion in warm water at 37°C. His metabolic rate rose to 2·40 kcal/m²/min during another immersion in water at 26°C. Total body conductance in the last 10 minutes of the immersion at 29°C was 0·34 kcal/°C/m²/min compared with 1·36 kcal/°C/m²/min in water at 37°C. It fell to 0·27 kcal/°C/m²/min in water at 26°C. The subject therefore showed metabolic and vasoconstrictor responses to cold in water at 29°C which were less than he was capable of producing and were insufficient to stabilise body temperature during the immersion. The experiment was ended because of the continuing fall in temperature and the cardiac irregularities. The subject was then rapidly rewarmed in water at 42°C, when the ectopic beats ceased.

Comment

Two features about this subject are likely to have contributed to his failure to stabilise body temperature in water as warm as that of tropical seas. Firstly, thin people cool much more rapidly than fat people in cold water, because even when fully vasoconstricted they have less insulation from subcutaneous fat.[2] This alone would not account for his hypothermia, however, in which there was a failure of adequate metabolic response and of adequate vasoconstriction and appropriate sensation of cold, even at body temperatures below 35°C. Secondly, the subject's previous repeated exposure to cold probably contributed to hypothermia. Cold acclimatisation of different patterns may alter responses in complex ways but its commonest effect is to reduce reflex responses to cold. For example, repeated immersion in water at 15°C greatly reduces metabolic and respiratory responses to such immersion.[3]

There are no doubt several reasons for unexplained confusion and bad judgment leading to diving accidents, and for unexplained unconsciousness and death during dives, but "silent" hypothermia of the kind seen in this immersion could readily account for such cases. Such hypothermia would not be detected in a routine dive since standard practice during deep dives is to flood the suit continuously with warm water pumped down from the surface and to assess the adequacy of heating by the diver's own report of thermal comfort. Monitoring of body temperature seems highly desirable during deep dives in spite of the practical difficulties which it presents.

We are indebted to Mr A Gin and Mr M Rai for their help in the experiment and to the North-east London Polytechnic for making them available; to Miss G S Howard for technical help; and to the MRC for financial support.

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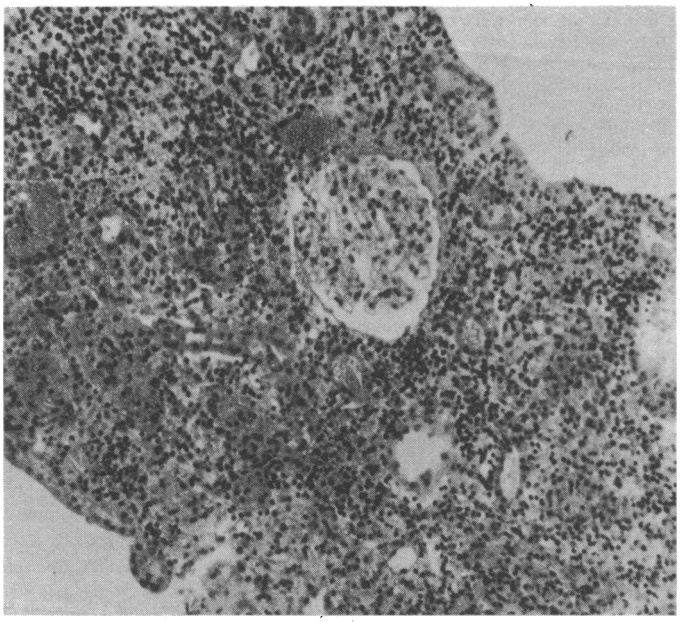
Recurrent acute renal failure due to antibiotic-induced interstitial nephritis

Acute renal failure due to antibiotic-induced interstitial nephritis is uncommon but increasingly recognised. We believe this is the first report of recurrent episodes due to different antibiotics occuring in the same patient.

Case report

Between June 1974 and February 1978 a 55-year-old man with previously normal renal function had three attacks of non-catabolic, non-oliguric acute renal failure. On each occasion clinical examination was normal, but intravenous urography showed bilaterally enlarged kidneys with normal drainage tracts. Percutaneous renal biopsy specimens showed normal glomeruli but much interstitial oedema with an intense infiltrate of eosinophils, plasma cells, lymphocytes, and histiocytes in association with patchy tubular damage—changes typical of acute interstitial nephritis (figure).[1] The first attack was initially thought to be due to septicaemia after cystoscopy for recurrent urinary tract infection. During the previous four months, however, he had taken courses of co-trimoxazole, ampicillin, cephalexin, and nalidixic acid.

On admission he was taking co-trimoxazole. Investigations showed haemoglobin 13·2 g/dl; total WBC $8·6 \times 10^9$/l (8600/mm³), eosinophils 2%; blood urea 71 mmol/l (426 mg/100 ml); serum creatinine 1459 μmol/l (15·9 mg/100 ml); urine cultures sterile with excess erythrocytes and leucocytes; urine output 60 ml/h. Peritoneal dialysis was begun and methyl prednisolone 1 g intravenously given on two successive days after biopsy. After 72 hours he had a diuresis of 140 ml/h. Subsequent recovery was uneventful. One month later creatinine clearance was 68 ml/min. Nevertheless he became unwell with fever (38·9°C), and urine culture grew *Escherichia coli*. Intramuscular gentamicin was given, keeping serum concentrations within recommended limits. On the fourth day the serum creatinine concentration was 578 μmol/l (6·3 mg/100 ml) although urine output was 90 ml/h. After biopsy 1 g methyl prednisolone was given intravenously for four days. Recovery began on the second day and 16 days later creatinine clearance was 70 ml/min.



Pronounced diffuse interstitial inflammatory infiltrate with groups of histiocytes, some tubular degeneration, and normal glomerulus (H and E. × 28.)

He remained well until he was admitted in February 1978 with a one-week history of fever, myalgia, and productive cough. After persistent questioning he admitted taking co-trimoxazole. Investigations showed blood urea concentration 18·6 mmol/l (112 mg/100 ml); serum creatinine concentration 390 μmol/l (4·25 mg/100 ml); urine output 28 ml/h; urine osmolality 330 mosmol/kg. After biopsy peritoneal dialysis was started and methyl prednisolone 1 g given intravenously for two days and then 0·5 g for another two days. Recovery was rapid. Creatinine clearance was 70 ml/min on discharge. Two months later intravenous urography showed normal-sized kidneys and biopsy showed only a few foci of lymphocytes and mild patchy interstitial fibrosis. On each occasion immunoglobulins, complement, antistreptolysin O titre, DNA binding, and eosinophil count were normal.

Comment

Antibiotic-induced interstitial nephritis leading to acute reversible renal failure has been ascribed to sulphonamides,[2] penicillins,[3] and co-trimoxazole.[4] The characteristic histological changes of interstitial nephritis and their relation to acute renal failure after streptococcal and diptherial infection were first described in 1898.[5] The appearances are the same in drug hypersensitivity reactions. We believe our patient's acute attacks were due to co-trimoxazole and gentamicin, although the aetiological agent in the first attack is uncertain. Cases due to gentamicin have not, we believe, been reported. The absence of one or more of the classical features of fever, rash, eosinophilia, haematuria, and proteinuria should not, as our case shows, bar a diagnosis of antibiotic-induced acute interstitial nephritis. When suspicion exists early renal biopsy is advocated. From the results of treating this patient and others with high doses of corticosteroid we strongly recommend their use in these cases.

We thank the Director General of Medical Services (RAF) for permission to report this case, and Dr I Chorlton and the pathology department of IPTM PMRAF (H) Halton for assistance with the histology.

[1] Heptinstall, R H, *Pathology of the Kidney*, 2nd edn. Boston, Little, Brown and Company, 1974.
[2] Black-Schaffer, B, *Archives of Pathology*, 1945, **39**, 301.
[3] Gilbert, D N, *et al*, *Annals of Allergy*, 1970, **28**, 378.
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Glycosylated haemoglobin in chronic renal failure

The observation that haemoglobin in the erythrocyte undergoes progressive glycosylation with the aging of the erythrocyte and that the rate of glycosylation is enhanced by hyperglycaemia has led to the concept that raised concentrations of glycosylated haemoglobin (HbA_1) indicate poor glycaemic control in diabetic patients.[1 2] Since information on other factors or pathological conditions which may alter HbA_1 concentrations is limited, the clinical application of this test has been confined to diabetic patients. We report here a study in which we measured HbA_1 concentrations in patients with chronic renal failure (CRF) and those with renal transplants.

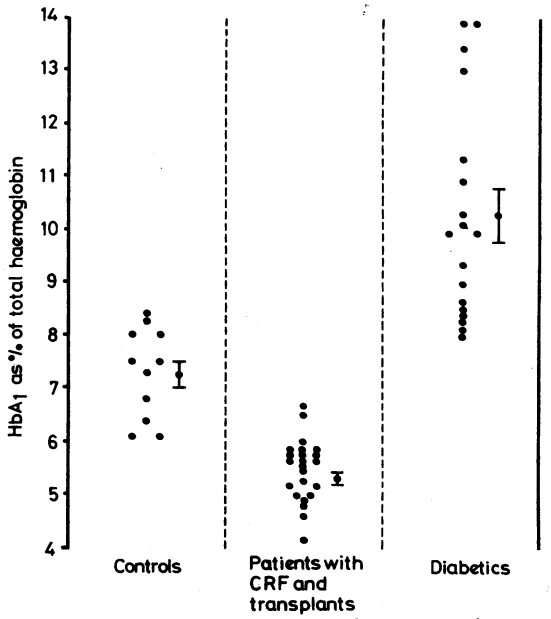
Patients, methods, and results

Seventeen patients with CRF (age range 10-53 years, mean 34 years) on long-term haemodialysis of variable duration (two months to five years) and from different causes were studied. Five patients who had had renal transplants (creatinine clearance range 10-53 ml/min) for less than three months were also studied. None of these patients had fasting or postprandial hyperglycaemia, glycosuria, or hypoglycaemia. Blood samples were collected in heparin and were stored in a refrigerator at 4°C before HbA_1 measurement. All estimations were carried out within three days of collection of the sample. HbA_1 was measured by a kit (Isolab Laboratories) which used chromatographic separation of HbA_1 from HbA on a biorex microcolumn. This microcolumn method has recently been shown to produce results similar to those obtained with the macrocolumn method[3] of Trivelli *et al.*[4] All HbA_1 results were expressed as percentage of total haemoglobin and not as absolute concentrations. To demonstrate that uraemic plasma did not interfere with the mobility of HbA_1, estimations of HbA_1 in the normal blood diluted with normal and uraemic plasma were carried out.

All but one of the patients with CRF or a renal transplant had low HbA_1 concentrations (see figure). The remaining patient had been transfused with four units of blood two days before the collection of his blood sample. All patients with renal transplants had HbA_1 concentrations similar to those observed in patients with CRF (see figure). There was a direct correlation between HbA_1 and total haemoglobin concentrations ($r=0·6$, $P=0·001$). Dilution of normal blood with normal and uraemic plasma did not alter HbA_1 concentrations.

Comment

This is the first demonstration of low HbA_1 concentrations in CRF. Since there was no obvious abnormality in the glucose homoeostasis in any of these patients, the low concentration of HbA_1 was probably related to the shortened life span of erythrocytes known to



HbA_1 concentrations in patients with CRF and renal transplants compared with those in controls and diabetic patients (with blood glucose concentrations >7·1 mmol/l). Means ± SE of means are shown. CRF *v* controls: $P<0·001$; diabetics *v* controls: $P<0·001$.