SHORT REPORTS

Hypothermia during saturation diving in the North Sea

We recently suggested after laboratory experiments¹ that undetected hypothermia might account for unexplained casualties during working dives in the North Sea. At depths greater than 50 m in the North Sea water temperature is below 10°C. Heat is usually supplied by flooding the diving suit continuously with warm water pumped from the surface via the diving bell; its temperature is monitored at the bell, but not at the diver, and is regulated mainly on the basis of the diver's report of feeling hot or cold. We found that simulation of this with warm water at 29°C around a thin man could produce progressive hypothermia with cardiac irregularities but without any serious sensation of cold.

We are now reporting the body temperatures of divers during saturation diving operations using the conventional heating system at a depth of 130-145 m in the North Sea in August-November 1979.

Subjects, methods, and results

The divers breathed helium and oxygen throughout. Their urine temperatures² were measured within eight minutes of their return to the bell after working dives with a maximum-reading Digitron thermistor with a response time of under 10 seconds in at least 50 ml of urine flowing through the outlet of a perforated funnel. This volume had been found with this apparatus to yield readings accurate to within 0.2°C. Skinfold thicknesses were measured with Harpenden callipers.³

The table shows that the thinnest diver in the group developed hypothermia at 34.7°C during a dive lasting only 55 minutes. He had felt a little cold and shivered at one point during the dive, but when the temperature of the warm-water supply, measured at the bell, was increased by 4°C he had stopped feeling cold. Two of the other divers cooled to near hypothermia with temperatures below 35.5°C at the end of 4-4½ hour dives, in one of which the warm-water system had failed for the last hour. That diver felt cold and shivered, but the other did not. In contrast, one relatively fat diver had a normal body temperature even after a one-hour failure of the warm-water supply; he reported considerable shivering and sensation of cold at that time. Body temperature after other dives was usually normal; in one instance it was a little high at 38.3°C.

Physical characteristics and body temperatures of divers, temperatures of warm water, and duration of dives

Diver	Height (m)	Body weight (kg)	Skinfold thickness* (mm)	Approximate temperature of warm water at bell (°C)	Duration of dive (min)	Body temperature at end of dive (°C)
1	1.80	74.8	9	40-44	55	34.7
2	1.73	68.9	13	41	207	36.6
				38	76	38.3
3	1.83	79.4	27	44	189	37.2
				42	216	35.6
				42	118	36.6
				44	235	37.1
4	1.83	82.6	23	42†	265	36.4
5	1.70	78.0	19	44	210	36.4
6	1.91	85.7	11	42	240	36.0
7	1.85	87.0	28	42	240	35.2
				42	182	37.6
8	1.73	79.4	19	42†	278	35.3

*On abdomen 50 mm below and lateral to umbilicus.
†Supply failed for last hour.

Comment

Even in dives in which the warm-water supply functioned normally, one diver cooled to near the point of hypothermia and another thin diver cooled below this without reporting any serious discomfort. The second, like the thin subject in our experiments,¹ cooled to 34.7°C, a temperature at which our subject developed an atrial arrhythmia of the heart—and at which mental impairment can be expected to present an increasing hazard. Any failure of the warm-water supply at that time, or continuation of such dives without raising the diver's temperature, could have rapidly caused confusion and unconsciousness as body temperature fell further.

Such changes produced by hypothermia could readily account for unexplained incidents in working dives. On average in 1974-9 over six divers died yearly in the North Sea, mainly in the British sector. At least half of these deaths were partly or completely unexplained. Many other divers survived periods of unexplained confusion and loss of consciousness.⁴ A heating system that kept skin temperature reasonably uniform and mean skin temperature and inspired gas temperature at an optimal level near 35°C could make hypothermia impossible. A control system on the outside of the diving suit supplying a closed circulation of warm water under the suit, with hard-wired sensors to monitor temperature in the suit and circulating system, could probably achieve this most simply.

We are greatly indebted to the divers for their co-operation and to Mr T L Gosling and Mr T A Cardale, of Star Offshore Ltd, for arranging for the measurements to be taken.

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² Fox RH, Woodward PM, Fry AJ, Collins JC, Macdonald IC. Diagnosis of accidental hypothermia of the elderly. *Lancet* 1971;i:424-7.

³ Edwards DAW, Hammond WH, Healey MJR, Tanner JM, Whitehouse RH. Design and accuracy of calipers for measuring subcutaneous tissue thickness. *Br J Nutr* 1955;9:133-43.

⁴ Childs CM, Norman JN. Unexplained loss of consciousness in divers. *Médecine Subaquatique et Hyperbare* 1978;17:127-8.

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Immunological studies of minimal-change nephropathy

The pathogenesis of minimal-change nephropathy (MCN) is unknown, partly because examination of affected kidneys has yielded no important information. Clinical data, however, have led to the postulation that lymphocytes of patients with minimal-change nephropathy can release a factor (lymphokine) that increases vascular permeability, particularly in high-pressure glomerular capillaries, thus causing proteinuria.¹ Supportive results have been reported² but have proved difficult to repeat.³ We have attempted to determine whether lymphocytes in minimal-change nephropathy do release such a factor.

Subjects, methods, and results

Lymphokine production—Peripheral blood lymphocytes were separated on a Ficoll Hypaque gradient, washed three times in mixture 199, and re-suspended to a final concentration of 1×10^6 cells/ml in mixture 199 and 10% heat-inactivated normal human AB serum. Phytohaemagglutinin (PHA) 5 µg was added to test cultures and 50 µl physiological saline to control cultures, all of which were performed in duplicate or triplicate and maintained at 37°C for 48 hours (reduced to 24 hours in later experiments). At the end of the culture period the cells were removed and the supernatant stored at -80°C after PHA 5 µg had been added to control ("reconstituted") supernatants.

Vascular permeability assay—The backs and flanks of Hartly-strain guinea-pigs (weighing 250-300 g) were shaved 24 hours before assay. Supernatant (0.1 ml) was injected intradermally at eight sites. Evan's blue 1 ml (1% in 0.15 mol sodium chloride/l) was injected through an ear vein and the animal killed 30 minutes later. Each supernatant was assayed in duplicate. The diameters of areas of blueing around each injection site were measured on the reflected skin surface and areas of blueing calculated.

The table shows the results of the assay. Seven assays were done in five patients whose cells were taken during relapse of minimal-change nephropathy before steroid treatment began; 10 were done in controls. The difference in mean areas of blueing for reconstituted supernatants between controls (R₁) and patients (R₂) was significant ($p < 0.001$) as was

Mean (± 1 SD) vascular permeability (as mean areas of blueing) caused by cultured lymphocytes taken from normal subjects and from patients during relapse of minimal change nephropathy before treatment with steroids

	Mean areas of blueing (mm ²)
R ₁ : reconstituted supernatant from cultures from controls	32.8 $\pm$ 22.2
R ₂ : reconstituted supernatant from cultures from patients	105.4 $\pm$ 32.7
S ₁ : supernatant from PHA stimulated cultures from controls	60.2 $\pm$ 38.1
S ₂ : supernatants from PHA-stimulated cultures from patients	113.8 $\pm$ 24.9

PHA = Phytohaemagglutinin.

that for PHA-stimulated supernatant (S₁ v S₂; $p < 0.005$). In seven control assays S₁ was significantly higher than R₁ ($p < 0.05$, Student's dependent t test). The difference in values for R₂ and S₂ was not significant; nor was there any difference in production of vascular permeability factor between cells taken from patients in remission and those taken from controls.

Comment

Our results show that lymphocytes taken from patients during relapse of minimal-change nephropathy produced significantly more vascular permeability factor than lymphocytes of normal subjects when both sets of cells were stimulated with PHA in vitro (S₁ v S₂). This confirms the findings of Lagrue *et al.*² The production of vascular permeability factor by patients' unstimulated cells, however, was not significantly lower than that by cells cultured with PHA (R₂ v S₂), which suggests that during relapse patients' lymphocytes are already stimulated to produce vascular permeability factor in vivo and cannot be further stimulated by PHA in vitro. Conversely, lymphocytes of normal subjects produced more vascular permeability factor when stimulated by PHA, though by small amounts (R₁ v S₁).

These data suggest that Shalhoub's hypothesis should be modified. If the main abnormality in minimal-change nephropathy were an overproduction of vascular permeability factor by lymphocytes this should have been detected in patients studied during remission. More probably, lymphocytes in controls and patients with MCN can produce vascular permeability factor but in the patients its production is not inhibited. Clinically, this may constitute the difference between febrile proteinuria and frank nephrotic syndrome. A factor has been detected in the sera of patients during relapse of minimal-change nephropathy that could substantially inhibit PHA-induced transformation of lymphocytes.⁴ This factor disappeared when patients went into remission and was absent from the sera of patients with other forms of nephrotic syndrome. This inhibitory factor may serve to stop production of vascular permeability factor, and the basic abnormality of minimal-change nephropathy may be unresponsiveness of vascular permeability factor-producing lymphocytes to this factor. Measles, which induces remission of minimal-change nephropathy, inhibits lymphokine production in vitro.⁵ The importance of these results rests on the ability of vascular permeability factor to induce proteinuria, which has yet to be confirmed.

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Requests for reprints should be sent to Dr J M Boulton Jones.

¹ Shalhoub RJ. Pathogenesis of lipid nephrosis: a disorder of T-cell function. *Lancet* 1974;iii:556-9.

² Lagrue G, Xheneumont S, Branellec A, Hirbec G, Weil B. A vascular permeability factor elaborated from lymphocytes. 1. Demonstration in patients with nephrotic syndrome. *Biomedicine* 1975;23:37-40.

³ Trompeter RS, Barratt TM, Layword L. Vascular permeability factor and nephrotic syndrome. *Lancet* 1978;iii:900.

⁴ Moorthy AV, Zimmerman SW, Burkholder PM. Inhibition of lymphocyte blastogenesis by plasma of patients with minimal change nephrotic syndrome. *Lancet* 1976;ii:1160-2.

⁵ Joffe MI, Rabson AR. Dissociation of lymphokine production and blastogenesis in children with measles infections. *Clin Immunol Immunopathol* 1978;10:335-43.

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Temporal arteritis in association with the Guillain-Barré syndrome

A symmetrical polyneuropathy and mononeuritis both occur as manifestations of temporal arteritis,^{1,2} but the Guillain-Barré syndrome has not been reported in association with this condition. The following is a report of such a case.

Case report

A 71-year-old woman presented with a four-week history of bilateral facial weakness followed by a gradually progressive proximal limb weakness, which had begun in the legs and spread to the arms. There were no associated sensory symptoms, nor did she have muscle or joint pains. From the onset of the facial weakness she had had sore red eyes, and for three months she had also complained of anorexia, weight loss, and mild bilateral deafness associated with giddiness. Throughout this time she had not suffered from headaches.

She had bilateral conjunctivitis but her fundi and visual acuity were normal. There was a slight perceptive deafness present bilaterally. She had an almost complete facial diplegia and a definite proximal weakness of the limbs. There were no sensory abnormalities in the limbs, but all her tendon reflexes were absent and the plantar responses were flexor.

Investigations showed: haemoglobin concentration (Hb) 9.9 g/dl, red blood cells normochromic and normocytic; white blood count $7.8 \times 10^9/l$, neutrophils 86%, lymphocytes 14%; erythrocyte sedimentation rate (ESR) 125 mm in one hour; plasma urea, electrolytes, and calcium concentrations normal; and plasma albumin concentrations 25.8 g/l. Serum protein electrophoresis showed: albumin low, a pronounced increase in α_1 - and α_2 -globulins with a diffuse increase in γ -globulins, and no paraprotein band. Serum concentration of IgG was raised, but that of IgA and IgM normal. She was positive for antiparietal cell antibodies but negative for other autoantibodies. Serum iron concentration 8.5 mmol/l (47.5 $\mu g/100$ ml), iron binding capacity 37.5 mmol/l (209.4 $\mu g/100$ ml), and vitamin B₁₂ concentration 354 pmol/l (480 ng/l). Bone marrow examination showed an increase in stainable iron but was otherwise normal. Glucose tolerance was normal and the Wassermann reaction was negative. Muscle enzymes values were normal. The cerebrospinal fluid was acellular and contained 0.1 g/l protein. Sputum cytology and a chest radiograph showed nothing abnormal. Barium meal showed a hiatus hernia and barium enema diverticulosis. A skeletal survey was normal, as were nerve conduction studies and slit lamp examination of the eyes. Audiometry showed a bilateral sensorineural hearing loss.

After admission there was a gradual spontaneous improvement in her symptoms and signs, and the Guillain-Barré syndrome was diagnosed. Extensive investigations for an underlying neoplasm were carried out in view of the weight loss, anaemia, and raised ESR but all proved negative. Two weeks after discharge, however, she developed severe bilateral fronto-temporal headaches followed within a week by an appreciable deterioration in the vision of the left eye and blurring of vision on the right. When examined she could not distinguish light from dark with the left eye and had greatly reduced visual acuity in the right eye (J 14). She had bilateral papilloedema, which was more pronounced on the left. The left retina was generally pale, indicating the presence of retinal oedema, and there were some haemorrhages close to the optic disc. Both temporal arteries were tender to touch. She still had a mild left facial weakness, a mild proximal limb weakness, and absent tendon reflexes. Her haemoglobin concentration was 10 g/dl and her ESR 134 mm in one hour. Temporal arteritis was diagnosed and steroid treatment started immediately (prednisolone 80 mg/day). By the next day her headache had improved greatly and after three days her haemoglobin concentration had risen to 13.4 g/dl and her ESR fallen to 52 mm in one hour. Her visual acuity improved progressively to J4 on the left and J2 on the right after six weeks. Her ESR continued to fall and her symptoms were subsequently controlled by a reduced dose of prednisolone (10-20 mg daily).

Comment

The patient presented initially with the clinical picture of the Guillain-Barré syndrome, a diagnosis which was acceptable despite the presence of a normal protein concentration in the cerebrospinal fluid and normal results of nerve conduction studies.³ She also gave a three-month history of anorexia and weight loss and had an unexplained anaemia associated with a high ESR. It was only some weeks later, when her facial diplegia and polyradiculoneuropathy had greatly improved, that she developed the clinical features of temporal arteritis. This association does not seem to have been reported and, although it may be a mere coincidence, both disorders are thought to have an immunological pathogenesis.^{4,5} The neuropathies reported in association with temporal arteritis have been attributed to ischaemic lesions of the nerves due to an arteritis of the vasa nervorum.^{1,2} Nevertheless, the clinical picture in this patient, with a symmetrical