increased population in this age group is taken into account. Accident rates per million population at risk in all other age groups were remarkably similar between the two periods.

Comment

The fact that the improvement was confined to school-age children shows that measures taken between these periods had a major impact on this age group, which is that most exposed to advice and perhaps the group most receptive to it. Other water safety measures than those instituted by the 1971 conference were taken or increased at about this time and the improvement is likely to have resulted from several factors, including better training in swimming. Whatever the precise contribution of these, the figures make it clear that older and younger age groups were not effectively reached by any of the measures taken to reduce deaths in water. The high proportion of good swimmers among those who die suggests that many may be made over-confident by their swimming ability and be unaware of the specific dangers of cold water and how to minimise them.

Additional measures are clearly needed to reduce the death rates in those over 15. Warnings such as those which the BBC broadcast recently, when weather forecasts predicted particularly hazardous combinations of sunny weather and cold water, may be the best way of catching people's attention at relevant times. These could be reinforced by compulsory attachment of brief warning notices to all new small craft and all ships' bridges, giving advice about survival in cold water. Both the broadcast warnings and notices could include advice always to wear lifejackets in small craft in cold waters; if immersed, to float still rather than swim about, and to keep on warm clothing as well as a lifejacket in the water²; and never to take even small quantities of alcoholic drinks after exercise in exposed conditions unless a large meal is eaten at the same time.³

Traditional campaigns to teach swimming should certainly still be encouraged and extended to the youngest possible age groups. Nevertheless, there seems a special need to tackle the high accident rate among those who can swim but are unaware that it has limited power to preserve life—and in fact often hastens death in cold water.

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Giardiasis and peripheral neuropathy

Comprehensive investigation of two patients showed no cause for their peripheral neuropathy. Both had giardiasis, and the neurological symptoms resolved after treatment of the infestations.

Case reports

Case 1—A man aged 27 years had had progressive numbness and painful paraesthesiae of the feet for 9 months. Toe dorsiflexion was weak and the feet were numb distally. Reflexes and the results of motor and sensory conduction studies were normal, but distal muscles showed denervation. The peroneus brevis showed denervation atrophy. Histological appearances of the sural nerve were normal by light and electron microscopy. Three-day faecal fat excretion was 29.5 g (normal <18 g). Small-bowel biopsy showed normal findings; numerous motile *Giardia lamblia* trophozoites were seen in the duodenal aspirate. After treatment with 4.2 g metronidazole for 7 days the faecal fat excretion became normal. The neurological symptoms gradually improved after 4 months. The course of metronidazole was repeated after a year and the symptoms and signs completely resolved shortly after. He has remained asymptomatic for 18 months.

Case 2—A man aged 33 years had had intermittent diarrhoea and abdominal discomfort for eight years. Stools contained *G lamblia* cysts, and he fully recovered after treatment with 8.4 g metronidazole for 14 days. Eighteen months later he required two further courses one month apart of

metronidazole 4.2 g for recurrence of abdominal symptoms. One month after the third course numbness of fingers and toes developed and slight pressure on nerves produced tingling and numbness. This implicated the peroneal and ulnar nerves, and several times he awoke with a wristdrop lasting for several minutes. Modest alcohol intake induced transient numbness distally, sometimes spreading up the arms and legs. There was numbness to pin prick of the toes and fingers but no other signs.

The results of nerve conduction studies were normal, but electromyography showed denervation of distal muscles. Denervation atrophy was present in the left peroneus brevis. Histological appearances of the sural nerve were normal on light microscopy but electron microscopy showed an excess of collagen fibres, consistent with a chronic neuropathy. Duodenal histology and faecal fat excretion were normal. Six months after onset of his neurological symptoms he was given 6 g metronidazole for 10 days. Three months later the neurological symptoms rapidly improved. He has remained asymptomatic for 13 months.

Comment

A causal rather than a chance association of giardiasis and peripheral neuropathy is suggested by the failure to identify an alternative cause of neuropathy; the striking similarity in the two patients of the symptoms, signs, investigative findings, and clinical course; and the return to normal of neurological symptoms after treatment for giardiasis. Malabsorption, a recognised cause of peripheral neuropathy¹ and common in giardiasis, is a possible explanation for the neuropathy. Our first patient had steatorrhoea, but faecal fat excretion in the second patient was not estimated before the giardiasis was treated. Serum folate and vitamin B₁₂ concentrations and radioactive vitamin B₁₂ absorption were normal in both when they presented with neurological symptoms. Deficiency of other vitamins was not investigated.

Metronidazole is unlikely to have contributed to the neurological symptoms in our two cases since in all patients so far reported the dose has been much larger than that given to our patients.²⁻⁴ Furthermore, both improved after receiving further courses of the drug.

If further studies indicate a firmer link between peripheral neuropathy and intestinal giardiasis, patients with peripheral neuropathy of no apparent cause should be screened for giardiasis because gastrointestinal symptoms may be absent, as in case 1. Furthermore, giardiasis is easily treated, and may be another treatable cause of peripheral neuropathy.

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Requests for reprints should be addressed to Dr G Danta.

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Ankylosing spondylitis presenting as PUO*

Constitutional disturbances have been reported in ankylosing spondylitis but are usually minor. Fever is usually absent or slight, rarely exceeding 38°C. We have recently seen four patients with ankylosing spondylitis, presenting with severe constitutional upset, high fever, weight loss, and disease of the hip joints. All showed a good response to phenylbutazone and all were positive for the HLA-B27 antigen.

*Based on a paper at the Joint Heberden/British Association for Rheumatology and Rehabilitation/RSM Section of Rheumatology and Rehabilitation/Irish Society for Rheumatology and Rehabilitation Meeting, Carlisle, 13-14 October 1977.

Case reports

Case 1—A 22-year-old Kenyan Asian man presented with pain in the right hip for one month, weight loss of 9 kg, and lassitude. He was pale and thin, with a fixed flexion deformity of 15° in the right hip and little movement because of intense pain. Temperature was 38.5°C, chest expansion 4 cm, haemoglobin concentration 10.1 g/dl, ESR 96 mm in the first hour. The results of all serological tests were negative. Histological and bacteriological examination of inguinal node and hip synovial biopsy specimens failed to confirm tuberculosis. X-ray films showed loss of joint space in the right hip with obliteration of the right sacroiliac joint. The patient remained very ill and a trial of antituberculosis treatment was ineffective. He developed polyarthritides, and further x-ray films showed bilateral sacroiliitis. Phenylbutazone produced considerable improvement.

Case 2—A 26-year-old Pakistani man presented with malaise, fever (39°C), night sweats, and severe left hip pain for four months. He was thin, with his left hip fixed in a flexed and adducted position. Chest expansion was 4.5 cm, ESR 87 mm in the first hour, the results of serological tests negative, and chest x-ray film normal. All cultures of an open synovial biopsy specimen failed to confirm tuberculosis. A trial of antituberculous treatment failed. Repeat x-ray films two months later showed bilateral sacroiliitis, and his lumbar spine was stiff. Phenylbutazone produced rapid improvement.

Case 3—A 35-year-old British woman presented with left hip joint pain, early morning stiffness, fever (38.6°C), anorexia, and weight loss for six weeks. She was toxic and ill with pallor and painful restriction of all hip movements. The haemoglobin concentration was 8.9 g/dl, ESR 70 mm in the first hour, and the results of serological and antinuclear factor tests were negative. Cultures were sterile apart from klebsiella isolated from the faeces. She then developed polyarthritides, and x-ray films showed bilateral sacroiliitis. Phenylbutazone produced a considerable improvement.

Case 4—A 36-year-old British man presented with lassitude, weight loss (9 kg), fever (38.5°C), night sweats, and right hip pain for four months. There was painful limitation of movement of the hip, and effusion of the right knee. The ESR was 113 mm in the first hour and the haemoglobin concentration 13.1 g/dl. The results of serological tests and cultures were negative and x-ray films were normal. High-dose salicylates were ineffective and the patient continued losing weight, with a falling haemoglobin concentration and fever. Despite exhaustive investigations, no firm diagnosis was made. Trials of antituberculous and antituberculous treatment failed. He gradually developed stiffness of the lumbar spine and early kyphosis. When reviewed seven months after the onset of symptoms he had early morning stiffness, chest expansion 5 cm, and reduced lumbar spine movements. The clinical picture now suggested ankylosing spondylitis, and phenylbutazone produced dramatic improvement. Recent x-ray films, apart from showing bilateral calcaneal spurs, have still shown normal appearances.

Discussion

Unilateral sacroiliitis has been observed in early ankylosing spondylitis, and symptoms may precede sacroiliitis by some years.¹ Chest expansion of under 5 cm is an important physical sign in ankylosing spondylitis.² Cases No 1 and 2 may represent spondylitic forms of juvenile chronic arthritis in view of histories of "arthritis" at the ages of 12 and 15, respectively. Alternatively, they could represent incomplete forms of Reiter's syndrome progressing to sacroiliitis and spondylitis.³ Ebringer⁴ has reported an association between klebsiella infection, ankylosing spondylitis, and the possession of HLA-B27 antigen. This organism was isolated in patients 3 and 4.

Ankylosing spondylitis may present with severe systemic upset and pyrexia of undetermined origin, but these manifestations are poorly recognised. Sacroiliitis should be looked for in undiagnosed fever.

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Neural tube defects and immunoreactive β -melanocyte-stimulating hormone in amniotic fluid

Our recent findings of large amounts of β -melanocyte-stimulating hormone (β -MSH) in the human brain¹ and cerebrospinal fluid (CSF)² suggested that neural tube defects might be detected by finding MSH peptides in amniotic fluid.

Patients, methods, and results

Amniotic fluid was obtained at diagnostic amniocentesis (2nd trimester) or at artificial rupture of the membranes (3rd trimester) from 66 patients. There was a neural tube defect in 10 (anencephaly seven, meningocele three) and there were three stillbirths. A modification of the method of Thody and Plummer³ was used to measure immunoreactive β -MSH in blood and amniotic fluid and in three placentas and the attached umbilical cords from full-term normal deliveries. The tissues were homogenised in 1M HCl, the extracted β -MSH separated by centrifugation, and the supernatant lyophilised for immunoassay. In each case curves parallel to the standard were obtained.

β -MSH concentrations were significantly higher in amniotic fluid than in normal plasma (mean = 66.3 $\pm$ SE 5.9 ng/l compared with 16.2 $\pm$ 1.2 ng/l for plasma) and fell (figure) with increasing length of gestation. In the seven with neural tube defects the β -MSH concentration in the second trimester was 80.9 $\pm$ 19.6 ng/l, compared with 83.1 $\pm$ 7.3 ng/l for the normal pregnancies. The amniotic fluid β -MSH concentration from the three stillbirths was higher than normal (118.3 $\pm$ 32.0 compared with 83.1 $\pm$ 7.3), but the difference was not significant. The β -MSH content of the three placentas and corresponding cords were 553 and 582; 526 and 120; and 674 and 0 μ g/g.

Immunoreactive β -MSH concentrations in amniotic fluid at various weeks of gestation. The decrease with gestation is significant ($r = 0.64$, $P < 0.001$).

Comment

We have confirmed the presence of immunoreactive β -MSH in the amniotic fluid⁴; furthermore, our finding that its concentration in amniotic fluid is higher than in plasma suggests a concentrating mechanism or a source of β -MSH other than maternal plasma. The fetal pituitary contains β -MSH, corticotrophin-like intermediate lobe peptide (CLIP), and β - and γ -lipotrophin⁵ which cross-reacts with β -MSH in most immunoassays. Nevertheless, the higher concentrations of β -MSH found after fetal death make this source unlikely. The detection of immunoreactive β -MSH in full-term placentas suggests that the placenta may be the source of amniotic fluid β -MSH. If this surmise is correct the differential is unlike that for placental lactogen, which occurs in lower concentrations in amniotic fluid than in maternal plasma and increases in the latter with the increasing size of the placenta: by contrast, β -MSH in amniotic fluid decreases with length of gestation.

Increased amniotic fluid β -MSH concentrations were not found in association with neural tube defects, although human nervous tissue¹ and CSF² contain large amounts of MSH peptides. Presumably,