thalidone, a low-salt diet, and a salt substitute containing 46% potassium as a food additive which he discontinued on leaving Australia. He was also taking a hay-fever remedy which contained liquorice. He was not generally dehydrated but had a dry mouth. Blood pressure was 160/100 mm Hg and the cardiovascular system was otherwise normal. The muscles were normal in appearance and consistency but he had tenderness of the thigh muscles and global weakness of trunk and limbs which was greater distally than proximally and greater in the legs than in the arms. He was unable to sit unaided or to walk. Extremes of gaze produced diplopia, and muscles of mastication were weak. Cranial nerve function was otherwise normal. Reflexes were depressed, ankle reflexes were absent, and plantars were flexor. There were no clear objective sensory findings although there was some patchy subjective sensory impairment.

Investigations showed a plasma potassium concentration of 1·8 mmol/l (1·8 mEq/l) with a 24-hour urinary excretion of 24 mmol potassium. Electrocardiogram (ECG) showed widened QRS complexes, slightly depressed ST segments in some leads, and asymmetrical T waves fused with U waves. The record was "compatible with" rather than "typical of" hypokalaemia.[1] The serum creatinine phosphokinase concentration (SCPK) was 3050 IU/l (normal 0-130 IU/l). Clinical response to oral potassium supplements was dramatic and within four days recovery was complete. The plasma potassium concentration was 3·5 mmol/l and the ECG normal. Five days later SCPK was 68 IU/l. Oral potassium was discontinued, the plasma potassium concentration fell, and the ECG abnormalities recurred. Fifteen months later he remained asymptomatic on debrisoquine, chlorthalidone, and potassium supplements, but the plasma potassium concentration was 2·7 mmol/l and 24-hour urinary excretion was raised at 119 mmol. No other defect of renal function was found, nor was primary hyperaldosteronism after adrenal function studies.

Comment

The ingestion of chlorthalidone and perhaps of liquorice and a defect of renal conservation of potassium contributed to the hypokalaemia in this patient. The clinical illness was precipitated by discontinuing a potassium-containing salt substitute. The raised SCPK concentration suggested a myopathy. A history of gastrointestinal disturbance followed by a progressive ascending, centripetal paralysis affecting bulbar musculature, associated with muscle pains and minimal sensory impairment, is highly compatible with a diagnosis of the Guillain-Barré syndrome,[2] although other possibilities such as polymyositis might be considered. Constipation was a clue to the hypokalaemia in this patient, but sphincter disturbances also occur in the Guillain-Barré syndrome.[2] In contrast to the dramatic clinical picture the ECG findings were unhelpful. In the investigation of paralysis it is essential to estimate the plasma electrolyte concentrations early.

I thank Dr P D Robertson for permission to report on his patient and for his advice; also Dr A F Lever and Dr A Calvert, who kindly supplied information, including the results of adrenal investigations.

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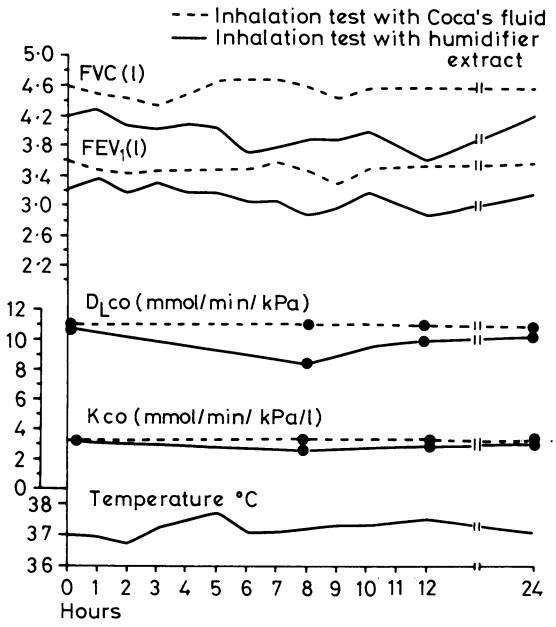
Caithness Central Hospital, Wick, Caithness
CHRISTOPHER D WARD, BA, MRCP, senior house officer (present address: Department of Neurology, Royal Free Hospital, London NW3)

Respiratory allergy to a factory humidifier contaminant presenting as pyrexia of undetermined origin

We report a patient who had attacks of fever which were particularly acute upon return to work after a weekend or other absence, but which improved during the working week. They were probably attributable to a reaction to contaminants growing in the factory humidifier system.

Case report

A 41-year-old man employed for four years in a printing factory had for 2½ years suffered from recurrent attacks of fever with malaise, headaches, and breathlessness, which always started in the afternoon and persisted for up to 72 hours. At first they occurred about once a month, but more recently they had increased to three to four times a month. The results of extensive investigations were normal. After the fourth hospital admission his symptoms recurred whenever he returned to work, particularly after a prolonged absence, but improved during the working week. His symptoms were associated with a rise in temperature and fall in vital capacity. He was referred to the Brompton Hospital. He had no finger clubbing, and no wheezes or crackles in his chest. Results of chest radiography and lung function tests were normal. Two out of 32 other factory employees who were exposed to the same conditions had had similar but less severe symptoms.



Reactions to inhalation tests with Coca's fluid and humidifier slime extract.

The high quality printing work done at the factory required a constant level of humidity, which was achieved by passing air through water sprays in a chamber and then through ducts to the whole factory. The chamber had an unpleasant-smelling dark green slime on the walls below the water level, from which *Phialophora* sp, *Fusarium* sp, and *Cephalosporium* sp were isolated on culture. Freeze-dried extracts were prepared from the slime. Agar-gel double-diffusion tests gave positive precipitin reactions to an extract of the slime with the sera of the patient and four of the other 32 employees, including the two with symptoms. The patient's serum and two of these four positive sera also gave a positive reaction to *Phialophora* sp. Sera from 100 exposed control subjects gave no reaction.

Skin prick tests on the patient with common inhalant allergens and with freeze-dried humidifier slime extract in Coca's fluid plus 50% glycerol at concentrations of 0·1, 1, and 10 mg/ml elicited no reactions. The control inhalation test with Coca's fluid gave no reaction. Solutions of the freeze-dried extract of humidifier slime in Coca's fluid were tested at 0·1, 1, and 10 mg/ml on separate days. The concentration of 10 mg/ml provoked a parallel fall in FEV_1 (forced expiratory volume in 1s) and FVC (forced vital capacity), with a drop in the CO gas transfer factor (D_LCO) and in the CO gas transfer factor per unit alveolar volume (KCO) associated with a rise in temperature and recurrence of his symptoms (figure). No wheezing or prolongation of forced expiratory time was observed during the reaction.

Comment

The results of the inhalation test, supported by the occupational history and the precipitins, show that the patient was reacting to contaminants in the factory humidifier water. Of 32 comparably exposed workers, only four had precipitins, of whom two also had symptoms similar to those of the patient, suggesting a hypersensitivity reaction. The functional changes provoked by the inhalation test, with parallel falls in FEV_1 and FVC and an associated fall in KCO, suggest that this reaction occurred predominantly in the peripheral lung tissue, although the site of reaction can be identified with certainty only by histological evidence.

This pattern of reaction to the inhalation test is similar in nature, speed of onset, and duration to the "late alveolar reaction" elicited by appropriate antigens in extrinsic allergic alveolitis,[1] but this patient's illness differs from typical allergic alveolitis in several important respects. Whereas in allergic alveolitis continued antigenic exposure is associated with progressive symptomatic, functional, and radio-

graphic deterioration, in the patient and others affected by aerosols of contaminated water in other factories[2 3] no radiographic changes were evident after several years' exposure, and no functional abnormalities persisted when away from work. Furthermore, the symptoms were prominent in the early part of the week, improving while continuing at work, but recurring on return to work after an absence. This pattern is similar to the "Monday fever" of byssinosis, but differs so far as we know in the site of reaction, being predominantly bronchial in byssinosis and peripheral in "humidifier fever."

The source of the antigens was identified in this case but the precise causal agent was not, and it may, as Edwards suggested, be derived from free-living amoebae.[4] Awareness of this unusual pattern of reaction should allow earlier identification of its cause, although confirmation may be obtained only by systematic observations at work or by inhalation testing.

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Brompton Hospital, London SW3 6HP
A NEWMAN TAYLOR, MB, MRCP, consultant physician

Wythenshawe Hospital, Wythenshawe, Manchester
C A C PICKERING, MRCP, DIH, consultant physician

Cardiothoracic Institute, London SW3 6HP
M TURNER-WARWICK, MD, FRCP, professor of medicine (thoracic medicine)
J PEPYS, FRCP, FRCPATH, professor of clinical immunology

Prophylactic low-dose heparin by jet injection

Subcutaneous low-dose heparin is a popular and effective method of prevention of postoperative thromboembolism.[1 2] Complications include pain and bruising at injection sites, wound haematomas, and occasionally serious bleeding due to accidental overdosage.[3] Little attention, however, has been paid to the increased nursing work load in giving multiple injections, and this may lead to missed doses. As the prophylactic dose of heparin is standard (5000 IU) we thought that a multidose jet injector might be employed. Jet injection has been used successfully for mass inoculation[4] and for giving insulin[5] and was known to be rapid and accurate.

Patients, methods, and results

A lightweight hand-held injector was used (Med-e-Jet, System Micro-jet). The drug phial fixes to a detachable, autoclavable head and fluid is ejected at high velocity through a 0·15-mm orifice. Power is provided by a small disposable carbon dioxide cylinder. If cylinder pressure drops below 21 kg/cm^2 (300 lb/in^2) a spring device prevents firing and precludes inadequate penetration when the cylinder nears exhaustion. About 25 shots are obtained from a 16-g cylinder. Injection pressure and dose volume are adjustable. With heparin of 25 000 IU/ml strength, dose volume was 0·2 ml. The actual volume delivered was found to be accurate and reproducible. By in-vitro dye injection experiments a pressure setting was found at which the entire 0·2-ml dose was deposited into subcutaneous tissue throughout the life of the gas cylinder.

Injections were made into flat skin cleaned with alcohol. The flank proved a suitable site, avoiding striae gravidarum in women, and both nurses and patients found jet injection acceptable: it was less painful than needle injection and bruising was no more frequent. Thirteen volunteers received 5000 units of sodium heparin by jet injection. Mean plasma heparin concentration (by assay of antifactor Xa activity) was 0·08 (SD 0·0440) IU/ml in the third hour after injection.

A research nurse gave the evening injections of subcutaneous heparin on three surgical wards. The time taken was recorded using three methods: multidose phial, needle, and syringe; single-dose ampoule, needle, and syringe (Wedpack); jet injection. A total of 479 doses given on 192 heparin rounds was timed (see table). With all methods the time taken per patient fell as the number of patients per round increased. Jet injection was considerably more rapid with all numbers. With over five patients, the time taken was cut to one-third.

Nursing time for subcutaneous heparin administration (mean injection time per patient in minutes and seconds)

No of patients per round	Method of administration		
	Multidose phial, needle, syringe	Single-dose ampoule, needle, syringe	Jet injection
1	4-03	4-06	2-14
2-5	3-15	3-20	2-14
6-10	3-07		1-05

Jet injection is a closed system and contamination is unlikely. In addition, multidose phials of heparin contain antiseptic, so it was not thought necessary to autoclave injection heads whenever the phial was changed. Regular bacterial cultures were taken from empty phials and of ejected heparin. No organisms were isolated. As the injection head makes contact with different patients, contamination with blood or tissue fluid during injection might theoretically lead to spread of hepatitis B if used on a carrier. Multiple injections were therefore made in vitro, into tissue infiltrated with radioactive isotope. No increased radioactivity was found on the injection heads. In the demonstrated absence of contamination with blood or tissue fluid, the risk of spreading hepatitis appears remote.

Jet injection incurs an initial capital cost, but thereafter operation is economical because no heparin is wasted in priming syringes. The capital cost would be amortised in a short time on most surgical wards.

Comment

Jet injection offers several advantages over traditional methods of giving prophylactic low-dose heparin, provided that it is as effective in preventing thromboembolism. Studies to investigate this are in progress.

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Department of Surgery, Queen Elizabeth Hospital, Birmingham B15 2TH
J BLACK, FRCS, lecturer
C J NAGLE, technician (at present medical student, University of Bristol)
C J L STRACHAN, FRCSED, senior lecturer

Hypostatic ulceration and Klinefelter's syndrome

Hypostatic ulceration of the leg is uncommon in men. Deep vein thrombosis (DVT) associated with childbirth accounts to some extent for the greater incidence in women, but hormonal factors may also be concerned. Two men of unusual but similar body type presented at the same time with hypostatic ulcers and were identified as having Klinefelter's syndrome. Subsequently four further cases were seen.

Case reports

In each case the physical signs were suggestive of Klinefelter's syndrome. The patients were tall and obese, with scanty facial and body hair, gynaecomastia, normal pubic hair and penis, and small testes. In cases 1 and 6 there was a mosaic 46,XY-47,XXY karyotype. The other cases showed a 47,XXY karyotype. The leg ulcers were all hypostatic associated with varicose veins, chronic oedema of the leg, pigmentation, and sometimes eczema. There was no evidence of arterial insufficiency in any of the patients.

Case 1—Born 1905, married, height 1·8 m, weight 95·3 kg. Ulceration of