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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(Accepted 15 March 1978)

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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 inoculation⁴ and for giving insulin⁵ 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/cm² (300 lb/in²) 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

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

rapid with all numbers. With over five patients, the time taken was cut to one-third.

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 radio-active 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.

CJN was in receipt of a Weddel Pharmaceuticals research scholarship.

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(Accepted 30 March 1978)

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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, gynecomastia, 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

the right leg at age 52 and later of left leg. No history of DVT; no family history of leg ulcers. Left inguinal herniorrhaphy at age 45.

Case 2—Born 1915, single, height 1.8 m, weight 95.3 kg. Ulceration of left leg at age 39. Mild eczema of the right leg. No history of DVT. Mother and maternal aunt had leg ulcers.

Case 3—Born 1944, single, height 1.8 m, weight 93.9 kg. Ulceration of the right leg at age 29. Four years previously he injured the right foot. This was followed by DVT and pulmonary embolus.

Case 4—Born 1918, married, height 1.77 m, weight 92.1 kg. At age 53 ulceration of the left leg developed and later eczema of the right leg. Thrombophlebitis of the left leg occurred before ulceration. History of varicose veins in his mother's family.

Case 5—Born 1924, height 1.77 m. Ulceration of right leg at age 40. Operation for varicose veins at 27. No history of phlebitis or thrombosis. His mother had varicose veins and his maternal grandmother leg ulcers. Two brothers had no leg trouble.

Case 6—Born 1907, very tall, weight 76.9 kg. Ulceration of legs present with a generalised rash at age 44. Subsequently he had eczema of both legs and a small ulcer on the medial aspect of the left ankle.

Comment

Leg ulcers, both venous and arterial, have been reported in patients with Klinefelter's syndrome. Vogt and Breit¹ described three patients in whom arterial insufficiency was considered a major cause of the ulcers and Palou *et al*² reported two similar cases. Zuppinger *et al*³ found varicose veins in eight of 24 patients with Klinefelter's syndrome, four of whom had leg ulcers. Thomsen⁴ described four patients attending a dermatology clinic, two of whom had hypostatic ulcers. Federman⁵ recorded varicose veins in eight of 24 patients, three having hypostatic ulcers.

Other conditions, particularly chronic bronchitis and emphysema and diabetes, seem to be common in these patients. The incidence of Klinefelter's syndrome is possibly 1 in 400 male live births. The statistics of hypostatic ulcers are very uncertain, perhaps 0.2-0.5% of the population being affected, with a female preponderance of 2-4:1. Peripheral vascular disease, both venous and arterial, appears to be common in Klinefelter's syndrome and should be considered in men presenting with chronic leg ulcers.

I am grateful to Dr R E Bowers, for information about cases 5 and 6.

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³ Zuppinger, K, *et al*, *Acta Endocrinologica (Copenhagen)*, 1967, **54**, suppl, 113.

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(Accepted 15 March 1978)

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Treatment of hypertensive emergencies with oral labetalol

The blood pressure may be controlled rapidly in severe hypertension by giving intravenous labetalol (Trandate), which is effective within minutes. Three out of 16 patients treated in this way complained of faintness and sweating from the prompt fall in blood pressure.¹ To prevent this tendency a constant infusion technique has been developed, which gradually reduces blood pressure over several hours of careful adjustment of infusion rate and incremental dose against recorded blood pressure levels.² The complexity of this regimen makes it unsuitable for use in a general medical ward, and we have used oral labetalol, which is effective within two hours,³ to achieve satisfactory control of blood pressure in hypertensive emergencies.

Patients, methods, and results

Eleven consecutive patients were treated, eight men and three women, aged from 32 to 68 (mean 55) years. Grade IV fundi were present in four patients and grade III in one. One patient with a grade II fundus had

hypertensive encephalopathy. All patients had "essential" hypertension with normal renal function.

Only patients admitted acutely to the general medical ward with a diastolic blood pressure (DBP) exceeding 130 mm Hg were included in the study. Starting dose of oral labetalol was either 400 mg when DBP was 140 mm Hg or higher; or 300 mg when DBP was 130 to 140 mm Hg. Subsequent doses were given at eight-hour intervals for the first 24 hours. The size of the second or third dose was dictated by the blood pressure at the time. 200 mg was given when DBP was 120 to 130 mm Hg and 100 mg when DBP ranged between 100 and 120 mm Hg. The dose was omitted when DBP fell below 100 mm Hg. Frequent blood pressure recordings were made by an Arteriosonde ultrasound apparatus, and pulse rate was taken by a trained nurse during the first 24 hours. All observations were performed in the recumbent position, and simultaneous standing blood pressure readings were made in five patients with starting dose of 300 mg.

Results are summarized in the figure, which plots the mean values ($\pm$ SEM) of blood pressure for the whole group of patients as a function of time after starting treatment with labetalol. The results of measurements in the standing position are shown separately. The graphs indicate rapid control achieved in the lying position after six hours and the steady maintenance of this level over 24 hours. The results in the standing position were less satisfactory, particularly for systolic pressure, although control was still achieved at 24 hours. Only minor changes in pulse rate were observed. No side effects or complications of treatment were noted.

The initial 24-hour period of treatment with oral labetalol in severe hypertension.

Comment

The simplicity of oral administration has obvious advantages, providing a promising alternative to parenteral treatment, which requires intensive care monitoring. Labetalol, a combined beta- and alpha-receptor blocking drug, produces good reduction in blood pressure with a first dose of 400 mg or 300 mg in severe hypertension, with a smooth and gradual effect over hours. Sustained control over the first 24 hours occurred without mishap. In this small series the rare pressor response⁴ was not observed, but a careful watch for complications should be kept at all times.

We are grateful to the shop floor workers at Smith's Industries Ltd of Ystradgynlais for purchasing the Arteriosonde; Sister M Morris of ward 9 for nursing care; and Mrs M Penhallurick for secretarial help.

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(Accepted 30 March 1978)

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