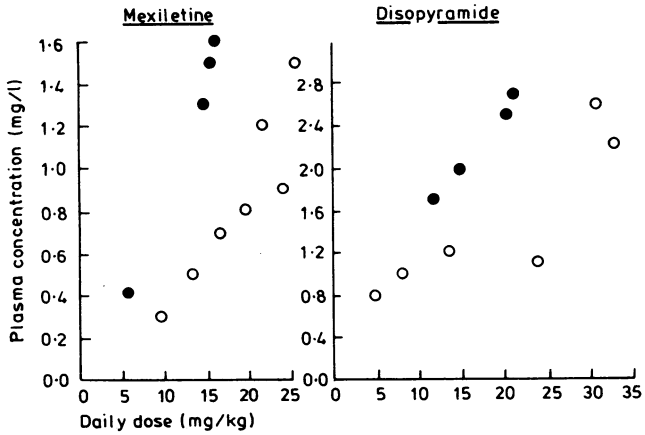
apex rate was still 250 beats/min. Two intravenous doses of practolol had no effect. Digoxin was stopped and direct current shock, verapamil, disopyramide, and lignocaine were given to control her heart rate—all without success. When transferred to Guy's Hospital, aged 2 weeks, intracardiac electrophysiological studies showed the arrhythmia to be an ectopic upper His-bundle tachycardia with two components—a fast rate (250-300/min), which was sensitive to both lignocaine and disopyramide, and a slower rate (200-240/min), which was well tolerated but which could not be terminated either electrically or by drugs. Chronic oral therapy with mexiletine and disopyramide was started. Plasma drug concentrations were monitored and the doses of both drugs were modified until plasma concentrations were similar to those known to be therapeutically effective in adults, using doses of 25 mg/kg (mexiletine) and 30 mg/kg (disopyramide) (figure). At this point her heart rate was stabilised at 170-180 beats/min. She has maintained this rate since she was discharged home, aged 5 months, continuing to thrive on both drugs.



Trough plasma concentrations of mexiletine and disopyramide with respect to weight-related daily doses. Open circles refer to data from case 1, closed circles to case 2.

Case 2—A 20-month-old boy was admitted to hospital with a febrile illness. While in hospital he developed a paroxysmal tachycardia (240/min) which was originally diagnosed as being supraventricular but was not controlled by digoxin, lignocaine, or disopyramide. Intracardiac electrophysiological studies showed the arrhythmia to be ventricular tachycardia responsive to bolus doses of lignocaine and disopyramide. He was therefore given intravenous lignocaine and disopyramide and changed rapidly to mexiletine and disopyramide by mouth. Dosage of these drugs was adjusted according to plasma drug concentrations, and his tachycardia was well controlled when concentrations were stabilised within the therapeutic range using doses of 15 mg/kg (mexiletine) and 20 mg/kg (disopyramide) (figure).

Comment

Daily adult maintenance doses of mexiletine and disopyramide are about 8·6 mg/kg and 5·7 mg/kg respectively. Plasma concentrations associated with therapeutic effect are in the range 0·75-2 mg/l[1] (mexiletine) and 2-4 mg/l[2] (disopyramide). In these two children this dosage regimen produced very low plasma drug concentrations associated with a poor clinical response. Indeed, in both cases disopyramide and lignocaine (a drug with electrophysiological properties similar to mexiletine) had been abandoned as ineffective when they were given in conventional doses. Large doses were needed to control the tachycardia, at which time plasma drug concentrations were in the ranges produced by typical adult doses. Titration of these drugs according to plasma concentrations is therefore crucial for their safe and effective use in children.

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(*Accepted 13 September 1979*)

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Serum IgE concentrations in rheumatoid arthritis: lack of correlation with gold toxicity

Chrysotherapy for rheumatoid arthritis is restricted by its potential toxicity. Some of the side effects, particularly the cutaneous, may be mediated by a type I hypersensitivity response and monitoring serum IgE concentrations may be helpful in their early detection.[1] This topic is complicated by the fact that increases in serum IgE concentrations have been reported as part of rheumatoid disease itself[2] and by the wide variation in serum IgE concentrations in normal populations.[3] The aim of this study was to examine the range of serum IgE concentration in patients with active rheumatoid arthritis and their value in predicting gold toxicity.

Patients, methods, and results

Serum IgE measurements were made with a commercially available paper radioimmunosorbent kit test (Phadebas).

(1) Initial studies on 30 consecutive outpatients with active, definite, or classical rheumatoid arthritis (RA)[4] were carried out. Twenty-three were women and none was receiving gold or penicillamine therapy. The presence or absence of rheumatoid disease exacerbations or extra-articular manifestations was noted. Patients with a personal or a family history in a first-degree relative of asthma or eczema were excluded from this part of the study. Nineteen age-matched patients (17 women) with primary osteoarthritis (OA) were similarly studied for comparison. Serum IgE concentrations in RA (range 87-900 IU/ml, mean 354 IU/ml) were significantly higher than those in OA (range 11-137 IU/ml, mean 73·3 IU/ml) ($P<0·001$). The concentrations in the 13 rheumatoid patients with extra-articular complications of their disease (Sjögren's syndrome 7, Sjögrens syndrome+ cutaneous vasculitis 2, extensive subcutaneous nodules 2, upper limb oedema 1, and fever 1) did not differ significantly from rheumatoid patients without these complications.

(2) Serial serum IgE concentrations were measured before and during treatment with intramuscular gold injections (Myocrisin) in 17 patients with RA. Two of these had been excluded from the first study because of a family or personal history of hayfever. Myocrisin 50 mg weekly was given after incremental test doses. Serum IgE measurements were repeated at least at each three-monthly outpatient visit, or earlier in the case of gold toxicity, in parallel with other immunological and clinical measurements. Eight patients developed adverse reactions during gold therapy (table). The serum IgE did not rise in any of the patients who reacted with a rash. With another adverse reaction (leucopenia, case 7) there was only a minor rise. The baseline IgE measurements were of no value in predicting which patients would develop adverse reactions to chrysotherapy.

Baseline and reaction serum IgE concentrations in patients developing side effects during chrysotherapy

Case No	Reaction	Cumulative gold dosage (mg)	Serum IgE (IU/ml)* Baseline	Follow-up
1	Rash	100	650	265
2	Rash	400	750	260
3	Rash	1500	315	16
4	Rash	1075	289	240
5	Rash+ proteinuria	440	215	80
6	Proteinuria	540	196	10
7	Leucopenia	140	99	230
8	Thrombocytopenia	1350	178	5

*Note that serum IgE concentrations fell with gold therapy in all but one patient.

Comment

Serum IgE concentrations were raised in our patients with active rheumatoid arthritis even when those with personal or family histories of atopic diseases were excluded. Serum IgE was raised in all but four patients in association with rises in other immunoglobulins, and thus seemed in keeping with the immunological hyperactivity that occurs in active rheumatoid disease. There was no evidence from this study that rises in serum IgE were significant in the appearance of disease exacerbations or of extra-articular complications. Lastly, our study suggests that significant rises in serum IgE concentrations are not the rule in patients developing gold-induced skin eruptions, and therefore measuring serum IgE, at least in New Zealand caucasian patients, will not give warning of such toxicity. Whether all or some of the recognised gold reactions may be immunologically related is arguable. Experimental evidence for an immunological basis to an adverse reaction was obtained in only one patient,

who developed thrombocytopenia and in whom a lymphocyte transformation test to gold in vitro was positive. Probably a direct toxic mechanism was responsible for at least some of the adverse reactions to Myocrisin.

We thank the Medical Research Council of New Zealand for financial support, and Karen Chaney, working under the supervision of Dr M Sears, for the IgE estimations.

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(*Accepted 24 September 1979*)

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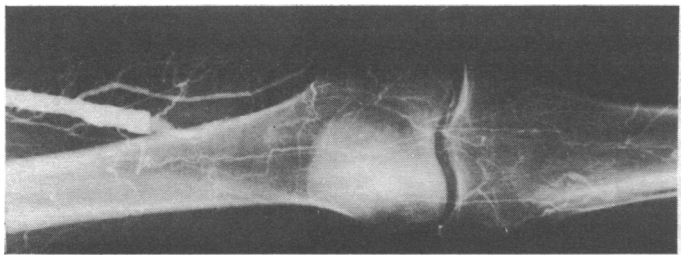
Thrombosis of leg arteries after prolonged travel

Venous thrombosis and subsequent pulmonary embolism after prolonged sedentary travel have been reported.[1-3] We describe three cases of thrombosis of leg arteries after prolonged travel.

Case reports

Case 1—A 68-year-old man presented with pain in his right calf similar to cramp after a flight lasting at least 20 hours from Australia to England. After arriving home his calf became more painful and the foot cold and numb. There was gradual improvement over the next few days, but seven days after arrival in England he sought hospital treatment. He was fit, blood pressure 140/80 mm Hg, in sinus rhythm, with no ankle oedema or calf tenderness. All pulses in the left leg were present and normal. The right common femoral pulse was present, but all pulses below this in the right leg were absent. There was reduced sensation in the right foot, which was cool. He had a block of his right superficial femoral artery. He was given intravenous heparin and subsequently warfarin. A right femoral arteriogram taken six days after admission (see figure) showed a complete block of his right superficial femoral artery, and there were signs of thrombosis. Interestingly there were multiple collateral channels suggesting earlier arterial disease. There was no popliteal artery filling, though, lower down the calf there was filling of an attenuated posterior tibial artery. His leg remained viable and gradually improved. He was discharged after two weeks, though he experienced subsequent ischaemic symptoms.



Case 1. Right femoral arteriogram showing a complete block of superficial femoral artery in region of adductor canal; presence of collateral vessels suggests pre-existing atheroma at this site. There is no filling of popliteal artery.

Case 2—A 70-year-old woman was in excellent health until she arrived in Perth, Western Australia, in July 1978, after a flight from Great Britain. On arrival her left leg was numb and she experienced cramp in her calf after walking about 50 yards. There was a delay of three weeks before referral to hospital, by which time her claudication distance was 300-400 yards. Clinical examination showed classic signs of a left superficial femoral artery thrombosis. There were no signs of embolic disease. Because of her improved condition arteriography was not performed. She was advised to remain as mobile as possible on her return flight to Britain.

Case 3—A 44-year-old man underwent external iliac artery disobliteration in November 1977, which restored all leg and foot pulses. In February 1978 he undertook a five-day coach trip from Perth to Sydney, Australia, and found that he was unable to walk on arrival. He was referred in March 1978 on his return to Perth. Clinical examination failed to detect any pulses in his right leg. Arteriography and operation disclosed another thrombosis at the site of the disobliteration. Thrombectomy was performed. Subsequently all pulses were restored, and he was discharged well.

Comment

Two of these patients showed evidence of pre-existing arterial disease; in the third patient, this was not investigated. On long flights, such as those between Europe and Australia, patients with established peripheral arterial disease may benefit from being offered prophylaxis against arterial thrombosis as well as the more commonly recognised venous problems. Several factors, apart from being unable to walk about for many hours, may be concerned, particularly dehydration and excessive smoking that act by increasing blood viscosity and fibrinogen values.[4]

Thus travellers with peripheral arterial disease should be advised to remain as mobile and well hydrated as possible during prolonged travel. Sleeping tablets are probably contraindicated as these may exacerbate prolonged immobility and cause a concomitant fall in blood pressure. There may be a case for offering such patients aspirin or even low-dose heparin injections.

ADDENDUM—One of us (WMC) has been notified of a 68-year-old man who required an amputation below the left knee in Perth in July 1979 after arriving on the direct London-to-Perth flight. He had had a one-month history of left intermittent claudication.

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(*Accepted 27 September 1979*)

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Disappearance of uraemic pruritus after lowering dialysate magnesium concentration

Uraemic pruritus is well known in patients receiving chronic haemodialysis (CHD). Itching may be distressing and resistant to treatment. We report the case of a patient in whom all common treatments failed and whose pruritus completely disappeared after the concentration of magnesium in the dialysate was lowered.

Case report

A 59-year-old man with chronic glomerulonephritis had for two years been dialysed for six hours three times weekly with a 1·8 m^2 capillary kidney against a dialysate bath containing 1·0 mmol/l (2·4 mg/100 ml) magnesium. He had had pruritus before starting CHD but it worsened afterwards. Although aluminium hydroxide 12 g/day was needed to control serum phosphorus concentration, parathyroid hormone was only slightly raised at 6·7 mU/ml (normal range 2-6 mU/ml). Bone radiographs showed no uraemic osteopathy, so parathyroidectomy seemed not to be indicated. The itching, after briefly improving with antihistamine treatment, became worse. Ultraviolet phototherapy was tried without effect and was stopped after four weeks. Cholestyramine 4 g thrice daily also failed to give relief and was stopped after three weeks. We tried cimetidine, because it relieves pruritus in polycythaemia vera,[1] but without success. Beginning in January 1979 we lowered the magnesium concentration in the dialysate from 1·0 mmol/l to 0·2 mmol/l (2·4 mg/100 ml to 0·48 mg/100 ml). Consequently the serum magnesium concentration fell from 1·4 mmol/l (3·36 mg/100 ml) to a predialysis concentration of 0·57 mmol/l (1·36 mg/100 ml) and a postdialysis concentration of 0·37 mmol/l (0·88 mg/100 ml). After about a week the pruritus completely disappeared and had not relapsed after eight months.