detected; serum complement concentrations, DNA binding, and urate concentration were within the normal range; a test for hepatitis B surface antigen was negative. Radiography of the hands, neck, and sacroiliac joints showed no abnormality. Tissue type was HLA-B27.

He was treated with indomethacin 50 mg twice daily. One week later the Silastic peritoneal catheter (Tenckhoff) was replaced. Three weeks later he had an upper gastrointestinal haemorrhage from an acute duodenal ulcer. This did not respond to conservative treatment, and vagotomy and pyloroplasty were performed. He had an uneventful postoperative course, though the arthritis persisted for a further week.

Two months later he was still undergoing continuous ambulatory peritoneal dialysis and had had no further episodes of peritoneal infection or acute arthritis.

Comment

The clinical features in this case suggest that the polyarthritis was reactive to the *S epidermidis* peritoneal infection. The arthritis started three weeks after the onset of peritonitis and was self-limiting, resolving spontaneously after five weeks. Other known causes of acute arthritis were excluded, and there was no evidence of infection with organisms more commonly associated with reactive arthritis. Furthermore, this patient was positive for HLA-B27, and such individuals are more at risk from this complication.¹ We know of no other reports of reactive arthritis associated with *S epidermidis* infection, though *S aureus* is arthritogenic in the rat.² With increasing numbers of patients undergoing continuous ambulatory peritoneal dialysis such a complication may be diagnosed more often in the future.

We thank Dr A J Rees for allowing us to report this case.

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(Accepted 12 October 1982)

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Lithium-induced constructional dyspraxia

Lithium has a narrow therapeutic range, and the likelihood of serious neurotoxicity and encephalopathy increases as blood concentrations rise above 1.4 mmol(mEq)/l. After 14 days' dosage within the therapeutic range the drug causes subtle cognitive impairment in normal volunteers,¹ but evidence from controlled studies of chronic administration in patients with manic depression, though conflicting,^{2,3} generally suggests that any cognitive changes at normal doses are not clinically important. We report here a case of constructional dyspraxia occurring at lithium concentrations within the therapeutic range after a year's previously uneventful administration.

Case report

A 50 year old housewife presented with endogenous depression of two years' duration. She had had episodes lasting about three months yearly for the previous five years. When first seen she was taking amitriptyline 150 mg a day. The total plasma amitriptyline and nortriptyline concentration of 231 µg/l was possibly just above the therapeutic range, but reducing the dose to 125 mg a day did not produce any improvement.

Amitriptyline was stopped and lithium carbonate started, but this did not produce a sustained remission. Thereafter she responded to combined amitriptyline 125 mg a day and lithium 600 mg a day. After remaining well and taking both drugs for the succeeding 14 months she began to complain of difficulties in finding words in conversation and of memory impairment, in the absence of any recurrence of depressive symptoms. Serum thyroxine concentration and free thyroxine index were normal, as was an electroencephalogram. Her 12-hour lithium concentration was 0.80 mmol/l and during the previous 14 months had ranged from 0.66 to 0.89 mmol/l. Psychological testing showed a Mill Hill verbal IQ of 108 and a progressive matrices performance IQ of 98. Her logical memory, paired associate learning, and memory of an array of pictures were normal both on immediate recall and after 30 minutes' delay. She had difficulty in finding words in

ordinary conversation but not on formal testing for aphasia. A striking abnormality was her inability to copy the Rey picture (score on standard scoring criteria 14 out of 36). These findings indicated appreciable constructional dyspraxia and slight dysphasia.

Lithium was stopped but amitriptyline continued. One month later her word-finding difficulties had disappeared and her copy of the Rey picture (alternative form) was considerably improved, her score being 36 out of 36. There were no appreciable differences in the results of the other tests. She remained affectively well on amitriptyline alone at follow-up after six months.

Comment

These findings indicate slowly developing constructional dyspraxia and mild dysphasia with difficulties of subjective memory occurring at lithium concentrations below 1.0 mmol/l and during concomitant use of amitriptyline. The impairment resolved completely when lithium was stopped and the tricyclic drug continued. Although these side effects may have been due to an interaction of both drugs, lithium and a tricyclic antidepressant are commonly prescribed together and the combination is usually regarded as being safe.

The possibility of cognitive difficulties caused by chronic administration of lithium at concentrations within the therapeutic range has not been discussed in recent reviews of lithium. Cases such as that reported here may be uncommon but nevertheless have practical implications: clinicians unaware of reports of research and particularly those not using the drug frequently may mistake cognitive impairment caused by the drug for a relapse of depression or early dementia. In cases of doubt formal psychological testing and retesting after the drug has been stopped are indicated.

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(Accepted 21 September 1982)

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Why patients were lost from follow-up at an urban diabetic clinic

Patients who have frequent contact with a diabetic clinic have a better prognosis than those who do not.¹ We aimed to discover why patients stopped attending a diabetic clinic and what sort of supervision such patients were receiving.

Methods and results

Appointment records of the diabetic clinic from 1 January 1979 to 31 May 1980 were studied. Patients who had not attended for 13 months or more were identified, and non-attendance confirmed from the last entry in the hospital notes. If the reason for non-attendance was not apparent information was obtained from the general practitioner directly or by questionnaire.

A total of 972 patients had appointments during the study period. Forty-seven patients (4.8%) were non-attenders: information was available on 44 (94%), 13 of whom (30%) had in the past missed at least one appointment.

Two of the 44 patients had died.

Eighteen patients (12 men, six women; age range 17-78 years, mean 44) had moved to another area or clinic. Five of these patients were on a diet, two were also receiving tablets. The remaining 13 were being treated with insulin (mean dose 46 units/day): five of these patients were aged under 30 and five were in the age range 30-50. In 14 cases a further appointment was arranged. One patient was pregnant; another was admitted to hospital with self-poisoning.

Ten patients (eight men, two women; age range 18-74, mean 49) were subsequently returned to hospital care. Five were on a diet, two were also receiving tablets. The remaining five were being treated with insulin (mean

dose 54 units/day). All 10 patients had been issued with a further appointment. Three were subsequently admitted as emergencies, and seven returned to the clinic.

Eleven patients (eight men, three women; age range 40-71, mean 56) were under the supervision of their general practitioner, who did not know why they had ceased to attend. Seven patients were on a diet, all but one were also receiving tablets. The remaining four were being treated with insulin (mean dose 38 units/day); none were aged under 30 and three were in the range 30-50. Nine patients were issued with a further appointment. Four were contacted through the district nurse, who took blood samples for estimation of haemoglobin A₁ (HbA₁) (upper limit of normal 8.5 g/dl). One patient, whose HbA₁ concentration was 5.6 g/dl said he had been told by the doctor not to return to the clinic. Two patients (with HbA₁ concentrations of 9.9 g/dl and 7.5 g/dl) said they did not attend unless they felt unwell. The fourth patient (HbA₁ 14.9 g/dl) thought everything was under control.

The remaining three non-attenders (one man, two women; age range 36-55, mean 46) were under no supervision, and their general practitioner did not know why they had ceased to attend. One was on a diet and two were being treated with tablets. Two had been given another appointment.

Comment

The interval between visits for diabetic patients attending our clinic is very variable: some stable patients have annual appointments, while problem patients may be seen after intervals of two to three months, or even less. If patients fail to attend they automatically receive at least one further appointment by post. If a patient continues to default, the doctor at the clinic usually writes to the general practitioner. The clinic studied may have a lower drop-out rate than the diabetic clinic of other centres, but we have no hard evidence to confirm or refute this.

Some 5% of diabetics were lost from follow-up over the period studied. The true loss to hospital follow-up, however, was only 1.4%, as 0.2% had died, 1% returned subsequently to hospital care, and 1.9% moved to another area or clinic (assuming those who moved to another area establish hospital contact). Of the remainder, 1.1% were being seen by their GP and only 0.3% (none of whom were taking insulin) were under no supervision whatsoever. It is noteworthy that three patients required subsequent emergency admission (one with diabetic ketoacidosis and one with an ischiorectal abscess). Men seem more likely to stop attending than women. The mean age was similar for all groups except for those attending their GP, who were slightly older.

If a recall system such as we describe existed for patients who fail to reattend a diabetic clinic, surprisingly few patients would be under no sort of medical care whatsoever and most (67%) would return to hospital care somewhere. Our findings suggest that a more detailed system is probably unnecessary.

Requests for reprints should be addressed to: Dr I N Scobie, Department of Medicine, St Thomas's Hospital Medical School, London SE1 7EH. We thank Staff Nurse Eleanor Brown for visiting patients at home.

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(Accepted 12 October 1982)

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Valproic acid and fetal abnormality

Infants born to women with epilepsy have an increased incidence of fetal abnormality. There are several possible causes for this including inherited factors and the effects of convulsions during pregnancy. Some fetal abnormality, however, may be attributed to the teratogenic effects of anticonvulsants, and phenytoin and phenobarbitone are the drugs most commonly blamed for this. Valproic acid and carbamazepine have been recommended in preference to phenytoin and phenobarbitone as anticonvulsants for women of childbearing age.¹ We report two cases that may call into question the wisdom of this advice with respect to valproic acid.

Case reports

Case 1—The mother of this infant was a 20 year old primigravida with idiopathic epilepsy. During pregnancy she had taken valproic acid 400 mg twice daily and had no convulsions. Serum valproic acid concentration at 35 weeks' gestation was 340 mg/l. There was no family history of congenital abnormality, and the only other medication (apart from iron and folate) had been six tablets of Distalgesic (dextropropoxyphene hydrochloride 32.5 mg, paracetamol 325 mg) taken four weeks after the last menstrual period. The infant was male and born at term weighing 3000 g. He had bilateral finger-like thumbs. One thumb was triphalangeal. A rudimentary extra digit arose from the base of the right thumb. A median cleft of the left foot was present with syndactyly of the first and second toes. Subsequent investigation of failure to thrive showed bilateral renal hypoplasia.

Case 2—The mother of this infant was a 22 year old primiparous woman of subnormal intelligence who also suffered from idiopathic epilepsy. A previous pregnancy had ended in spontaneous abortion at eight weeks. In both pregnancies she had taken valproic acid 600 mg thrice daily. In the second pregnancy she had had four grand mal convulsions during the last trimester. Serum valproic acid concentration at 32 and 36 weeks' gestation was 540 mg/l and 140 mg/l respectively. There was no known family history of congenital malformations. The infant was male and born at 38 weeks' gestation weighing 2400 g. He had micrognathia, bilateral undescended testes, and glandular hypospadias. There was a flexion deformity on the left wrist with shortening of the forearm. The left fifth digit was elongated and proximally inserted. The thumb was finger like. He also had moderately severe valvular aortic stenosis. Intravenous pyelography and chromosome analysis yielded normal results.

Comment

In each of these two cases the mother had taken valproic acid throughout the pregnancy. There are few data on the outcome of pregnancies in which valproic acid was the sole drug taken, but facial, digital and skeletal abnormalities as well as developmental delay have been described.^{2,3} The manufacturers of the drug have collected data on 33 pregnancies in which valproic acid was the sole anticonvulsant (Labaz, personal communication). These pregnancies resulted in 25 normal babies, four spontaneous abortions, and four infants with congenital malformations (two with meningomyeloceles, one with syndactyly, and one with a small ventricular septal defect). Recently eight participants in the International Clearinghouse for Birth Defects Monitoring Systems reported that valproic acid was associated with neural tube defects in about 1% of fetuses exposed in early pregnancy.⁴

In case 1 dextropropoxyphene as well as valproic acid had been taken at the critical period of differentiation of fetal limb buds. Abnormalities including skeletal and thoracic malformations have been recorded after the use of dextropropoxyphene, usually in combination with other drugs.⁵

We cannot be certain that valproic acid was responsible for the abnormalities in our two cases but wish to draw attention to the occurrence of appreciable congenital malformations in two infants born to mothers who took valproic acid throughout pregnancy and to the possibility that yet another drug is hazardous for women in their childbearing years.

We thank Dr J L Wilkinson and Dr R J Rowlett for permission to report case 2. The Congenital Malformations Registry is supported by the DHSS.

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(Accepted 24 November 1982)

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