values in the premenstrual phase may result in symptoms of water retention. Treatment should, therefore, be aimed at preventing both the natriuretic effect of progesterone in the postovulatory phase and the sodium-retaining and water-retaining effects of aldosterone in the premenstrual phase.

References

1 Tonks CM. Premenstrual tension. *Br J Psychiatry* 1975;Special Number 9:399-408.
2 O'Brien PMS, Craven DJ, Selby C, Symonds EM. Treatment of premenstrual syndrome by spironolactone. *Br J Obstet Gynaecol* 1979;**86**: 142-7.
3 Ghose K, Coppen A. Bromocriptine and premenstrual syndrome: controlled study. *Br Med J* 1977;i:147-8.
4 Dalton K. *The premenstrual syndrome and progesterone therapy*. London: Heinemann Medical Books, 1977.
5 Backstrom T, Mattson B. Correlation of symptoms in premenstrual tension to oestrogen and progesterone concentrations in blood plasma. *Neuropsychiatry* 1975;**1**:80-6.
6 Smith SL. The menstrual cycle and mood disturbances. *Clin Obstet Gynecol* 1976;**19**:391-7.
7 Munday M. Hormone levels in severe premenstrual tension. *Curr Med Res Opin* 1977;**4**, suppl 4:16-22.
8 Gillman J. The nature of subjective reactions evoked in women by progesterone with special reference to the problem of premenstrual tension. *Clin Endocrinol Metab* 1942;**2**:157-60.
9 Furuyama S, Nugent CA. A radioimmunoassay for plasma progesterone. *Steroids* 1971;**17**:663-8.
10 Landau RL, Lugibihl K. Inhibition of the sodium-retaining influence of aldosterone by progesterone. *Clin Endocrinol (Oxf)* 1958;**18**:1237-45.
11 Coppen A, Shaw DM, Malleson A, Costain R. Mineral metabolism in mania. *Br Med J* 1966;i:71-5.
12 Sampson G. Premenstrual syndrome. A double blind controlled trial of progesterone and placebo. *Br J Psychiatry* 1979;**135**:209-14.

(*Accepted 15 February 1980*)

SHORT REPORTS

Neutropenia during allopurinol treatment in total therapeutic starvation

Allopurinol, a xanthine oxidase inhibitor, has been recommended to prevent the development of hyperuricaemia during total therapeutic starvation.[1] Leucopenia and even fatal agranulocytosis have occasionally been noted in patients treated with allopurinol for gout,[2] while neutropenia occurs quite often during prolonged fasting, although its exact causation remains obscure. We report here three patients who developed neutropenia during therapeutic starvation when allopurinol was prescribed to prevent hyperuricaemia.

Case reports

We studied three obese patients, all of whom underwent prolonged total therapeutic starvation resulting in pronounced, progressive weight reduction. During the fast all received supplements of potassium (as Slow K), allopurinol (300 mg/day), folic acid, and vitamins A, B, C, and D (as Multivite). One patient (case 1) also received oral iron treatment. Throughout the period of starvation all patients maintained normal serum vitamin B_{12} and iron concentrations.

Case 1—A 23-year-old woman weighing 134 kg underwent a three-month fast. Before starting the fast her white blood cell count was normal ($6{\cdot}8 \times 10^9$/l) but fell as low as $3{\cdot}5 \times 10^9$/l (neutrophil count of $1{\cdot}7 \times 10^9$/l) when allopurinol was started. On refeeding the patient continued to receive allopurinol for a further month and a minimal neutropenia persisted ($2{\cdot}4 \times 10^9$/l). When allopurinol was withdrawn the neutrophil count returned to normal. Sternal marrow biopsy performed during the fast showed normal maturation of the granulopoietic series but rather scanty numbers of polymorphs and precursors.

Case 2—A 20-year-old man weighing 113 kg had a white cell count of $8{\cdot}3 \times 10^9$/l before fasting. Neutropenia (neutrophils $1{\cdot}7 \times 10^9$/l, total white cell count $3{\cdot}6 \times 10^9$/l) developed after 34 days' starvation. Allopurinol was withdrawn and the white cell and neutrophil counts returned to normal (white blood cell count $5{\cdot}8 \times 10^9$/l) after three weeks.

Case 3—A 19-year-old man weighing 130 kg had a white blood cell count of $8{\cdot}5 \times 10^9$/l before therapeutic starvation started. After four weeks of total fasting and treatment with allopurinol he developed leucopenia ($3{\cdot}9 \times 10^9$/l), which persisted until the end of the fast. The lowest neutrophil count recorded was $1{\cdot}3 \times 10^9$/l. Allopurinol was continued for nine days of refeeding, during which time the neutropenia persisted. Thereafter the drug was withdrawn and his neutrophil count returned to normal after two days.

Comment

Neutropenia has often been observed during total therapeutic starvation and is known to occur in starving patients who have never received allopurinol. Hypotheses to explain its appearance during fasting have included the effects of protein deficiency on marrow activity[3 4] and intravascular redistribution of the neutrophils.[4] Some dispute exists about whether neutropenia may be caused in starving patients by folate deficiency, but clearly this could not have been a factor in our patients, all of whom received regular folate supplements.

The evidence of our present study suggests that allopurinol was either an initiating or an aggravating factor in the neutropenia we observed. In particular, the persistence of neutropenia after the fast was broken points strongly to this drug as the cause of the phenomenon. In view of the very low neutrophil counts recorded in the patients whom we studied, we suggest that the white blood cell and neutrophil count should be estimated regularly in fasting patients receiving allopurinol.

1 Schatanoff J, Duncan TG, Duncan GG. Effects of allopurinol on hyperuricaemia secondary to fasting. *Metabolism* 1970;**19**:84-6.
2 Greenberg MS, Zambrano SS. Aplastic granulocytosis after allopurinol therapy. *Arthritis Rheum* 1972;**15**:413-6.
3 Aschkenasy A. On the pathogenesis of anaemia and leucopenia induced by dietary protein deficiency. *Am J Clin Nutr* 1975;**5**:14-25.
4 Drenick EJ, Alvarez LC. Neutropenia in prolonged fasting. *Am J Clin Nutr* 1971;**24**:859-63.

(*Accepted 28 January 1980*)

Department of Medicine, Royal Infirmary, Glasgow G4 0SF
I N SCOBIE, MB, MRCP, medical registrar
A C MACCUISH, MD, FRCP, consultant physician

Departments of Medicine and Haematology, Southern General Hospital, Glasgow G51
C M KESSON, MB, MRCP, senior medical registrar
I R MCNEIL, MB, MRCPATH, consultant haematologist

Lorazepam withdrawal seizures

Reports of seizures after benzodiazepine withdrawal have been appearing since 1961,[1] yet despite recent publicity[2] it is not widely appreciated that withdrawal seizures can occur with these drugs. Seizures after lorazepam withdrawal have not been reported; prescription of lorazepam is increasing, and it is now fourth in the benzodiazepine-prescribing league. For these reasons I report the following cases.

Case reports

Case 1—A 22-year-old woman had no history of seizures or brain damage. She had been taking at least 7·5 mg of lorazepam daily for four years because of anxiety. She decided to stop taking lorazepam, and one day

later myoclonic jerking began in her arms; she felt frightened, and had episodes of panic. A nocturnal tonic-clonic seizure followed 48 hours after the last dose. Her family doctor gave her an anticonvulsant and referred her to the neurology outpatient clinic, where clinical examination and an electroencephalogram (EEG) showed no abnormality. The anticonvulsant was stopped gradually, and there have been no seizures in the four months since the single attack. Symptoms of anxiety continued for weeks, but she has not taken any tranquillisers.

Case 2—A 27-year-old woman had an eclamptic seizure after her first delivery seven years earlier. For four years she had been taking lorazepam 7·5 mg daily but it was stopped abruptly so that she might start a new tranquilliser. Twenty-four hours later, before she had taken the new drug, she had a tonic-clonic seizure and was admitted to hospital. Physical examination and an EEG were normal, and she was discharged without drugs. Once home she restarted lorazepam because of feelings of panic. Two months later she stopped the lorazepam, again abruptly, and 24 hours later had another tonic-clonic seizure. She was admitted under the medical firm who had managed her before, and an anticonvulsant was prescribed. It was weeks before she was able to leave her house because of anxiety and tremor. These symptoms settled spontaneously, the anticonvulsant has been withdrawn gradually, and there have been no seizures in the three months since her last attack.

Comment

Both these patients had been taking lorazepam for years but not in excessive doses. In each case abrupt withdrawal produced unpleasant symptoms and a seizure. The possibility that the seizures were due to drug withdrawal was not considered by the doctors who first saw the patients, and anticonvulsants were started.

In a study of abrupt withdrawal of chlordiazepoxide by placebo substitution all the patients experienced mild symptoms,[3] but seizures seem more likely to occur after prolonged use or overdose. Although withdrawal seizures are not common, patients taking benzodiazepines should be warned to withdraw the drugs slowly. The possibility of drug withdrawal should be considered in any patient presenting with a seizure, for if this seems the likely cause prognosis and management will be radically altered.

I thank Dr S Currie, consultant neurologist, for permission to report these patients; and Mr J Cooke of the drug information unit, St James's Hospital, for his help in the preparation of the report.

[1] Hollister LE, Motzenbecker FP, Degan RO. Withdrawal reactions from chlordiazepoxide. *Psychopharmacologia* 1961;**2**:63-8.
[2] Kendall MJ. Hazards of abrupt withdrawal of drugs. *Prescribers J* 1978; **18**:25-34.
[3] Covi L, Lipman RS, Pattison JH, Derogatis LR, Uhlenhulth E. Length of treatment with anxiolytic sedatives and response to their sudden withdrawal. *Acta Psychiat Scand* 1973;**49**:51-64.

(*Accepted 5 February 1980*)

Department of Medicine, St James's University Hospital, Leeds LS9 7TF
J G HOWE, MB, MRCP, tutor in neurology

Meningitis caused by Campylobacter fetus ssp jejuni

Campylobacter fetus, formerly classified as *Vibrio fetus*, are bacteria well known to cause enteritis and, occasionally, systematic infections in man.[1] We report a case of meningitis caused by *Campylobacter fetus* ssp *jejuni*, a species not previously associated with this condition.

Case report

The patient was a 34-year-old American who had been operated on when aged 5 years for a neuroblastoma. He had suffered since from dysarthria and ataxia but his mental development was normal. In July 1979, when visiting Scandinavia, he developed fever and increasing ataxia and dysarthria. On admission to hospital after 24 hours he had signs of dehydration and meningitis. The cerebrospinal fluid (CSF) was clear and yellowish, and contained monocytes 184×10^6/l (184/mm^3), polymorphonuclear leucocytes 155×10^6/l (155/mm^3), protein 6·5 g/l, and glucose 0·5 mmol/l (9 mg/100 ml). Concurrent blood glucose was 7·0 mmol/l (126 mg/100 ml). CSF microscopy was negative, but cultures yielded a spirochete-like organism that was later identified as *Campylobacter fetus* ssp *jejuni*. The organism was resistant to ampicillin but sensitive to chloramphenicol and metronidazole. On suspicion of a cerebellar tumour or abscess a computer-aided brain scan was performed. It showed a catheter running from the fourth ventricle through the ventricular system to the parenchyma of the right frontal lobe, a slight enlargement of the ventricular system, and a postoperative bone defect.

Treatment with chloramphenicol 1 g intravenously thrice daily for 11 days brought rapid recovery and a normal CSF. The patient was discharged and told to seek medical attention in the United States as soon as possible. For various reasons he did not do so until a week later and did not take any antibiotics during that period. He relapsed and was admitted to hospital with increased cerebellar symptoms and signs of meningitis. The CSF findings were almost identical to those described above, but cultures were sterile and microscopy did not show any micro-organisms. He did not respond to chloramphenicol 2 g intravenously twice daily, and his fever remained at about 39°C. The chloramphenicol was increased to 2 g four times a day. The symptoms then subsided and he recovered over the next seven days, after which he was afebrile and his CSF normal. Treatment was maintained for 14 days, and he was then followed up for six weeks without showing any further signs of relapse.

Comment

Campylobacter is well known to cause veterinary diseases and is one of the commonest causes of gastroenteritis in man.[1] A relatively large number of systemic infections caused by it, especially septicaemia, have been reported.[1] Most of these infections have been caused by *Campylobacter fetus* ssp *intestinalis*. The subspecies identified in our patient, *jejuni*, has only rarely been associated with systemic infections but seems to be the organism normally causing enteritis.[1] Our patient was compromised by his previous brain operation and by the resulting catheter in his ventricular system. Importantly, campylobacter systemic infections seem to be most prevalent in the type of patients who are at risk of developing infections caused by *Listeria monocytogenes*—that is, neonates and compromised adults. Since the clinical symptoms can be similar in these two infections, and since ampicillin is normally the drug of choice for treatment of listeriosis but is often inactive against *Campylobacter*,[2] this organism should be considered in the differential diagnosis in these patients.

We thank Dr M B Skirrow, Worcester Royal Infirmary, Worcester, England, for identifying the causative organism in this case.

[1] Rettig PJ. Campylobacter infections in human beings. *J Pediatr* 1979; **94**:855-64.
[2] Butzler JP, Dekeyser P, Detrain M, Dehean F. Related vibrio in stools. *J Pediatr* 1973;**82**:493-5.

(*Accepted 1 February 1980*)

Department of Infectious Diseases, University of Gothenburg, East Hospital, S-416 85 Gothenburg, Sweden
R NORRBY, MD, PHD, associate professor

Division of Infectious Diseases, Department of Medicine, Thomas Jefferson University, Philadelphia, USA
R V McCLOSKEY, MD, MS, professor of medicine

Department of Clinical Bacteriology, University of Gothenburg, Gothenburg, Sweden
GUNILLA ZACKRISSON, MD, registrar in clinical bacteriology
E FALSEN, PHD, civil engineer

Differences in serum ampicillin concentrations among patients under constant-rate infusion

Continuous infusion of a drug at a constant rate is supposed to maintain its serum concentration at a constant and predictable level. We investigated the truth of this in patients treated with ampicillin for severe purulent meningitis.