inappropriate treatment plasma potassium estimations in patients with acute myeloid leukaemia should be made on plasma separated immediately after venepuncture.

We thank Dr M Qureshi for permission to study his patient and Professor M D Rawlins for his help and advice.

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Brain abscess due to *Arachnia propionica*

Arachnia propionica, a member of the Actinomycetaceae, has rarely been described as an agent of human infections. We report the isolation of this organism from a brain abscess and emphasise the problems associated with its identification.

CASE REPORT

A 32-year-old man presented with a two-day history of severe central headache not relieved by the usual analgesics, falling to the left when walking, and spatial visual difficulties on looking to the left. His medical history indicated that he had developed Eisenmenger's syndrome as a result of an inoperable ventricular septal defect, confirmed by cardiac catheterisation in 1952. During the procedure a left cerebrovascular accident had occurred, which had resulted in continuing convulsions, right-sided hemiparesis, and growth retardation. He had been started on prophylactic phenoxymethylpenicillin 250 mg twice daily.

Four months before presentation he had been admitted to hospital for treatment and control of cardiac failure. Shortly after discharge he stopped the penicillin prophylaxis. On readmission he was subjected to a full examination and special investigations. A computed tomography scan showed generalised atrophy of the left cerebral hemisphere and a lesion in the right occipital lobe compatible with an abscess. No primary focus of infection was found. He was started on intravenous ampicillin 2 g four times daily and gentamicin 80 mg and metronidazole 500 mg thrice daily and underwent craniotomy, when an abscess close to the medial surface and above the calcarine sulcus of the right occipital lobe was drained and the wall excised.

Pus was cultured aerobically on blood agar, CLED agar, and heated blood agar, and anaerobically on blood agar and a supplemented lysed blood agar containing gentamicin 5 mg/l, cysteine hydrochloride 0.05%, yeast extract 0.5%, and vitamin K₁ 0.0002%. Microscopy showed numerous leucocytes, Gram-positive cocci, and branching Gram-positive bacilli. After 48 hours' incubation results of aerobic culture were negative while anaerobic culture produced an anaerobic Gram-positive coccus subsequently identified as *Peptostreptococcus micros* and a branching anaerobic Gram-positive bacillus identified as *A propionica*. Identification of isolates was based on morphological studies, routine biochemical tests, and analysis of the end products of glucose fermentation as described by Holdeman *et al.*³ He was treated with intravenous penicillin and metronidazole and discharged three weeks later taking oral penicillin.

Comment

A propionica isolations have usually been associated with lesions of the cervical lymphocutaneous tissues, lacrimal glands, lung, abdomen,² and bone.³ We have found no reports of a brain abscess

due to this organism. *A propionica* is a resident of the oropharynx, as is *P micros*, and the organisms isolated from the abscess probably originated from this site despite the absence of oral disease.

Identification of *A propionica* in the microbiology laboratory can be difficult. Morphologically and biochemically the organism is similar to *Actinomyces israelii* and clinically may produce a disease that is indistinguishable. Three tests are available to differentiate the two organisms—namely, the demonstration of diaminopimelic acid in the cell wall of *A propionica*, specific fluorescence antibody staining, and the demonstration of the production of propionic acid by gas-liquid chromatography from glucose fermentation by *A propionica*.² As the first two tests are beyond the scope of most clinical laboratories, the importance of carrying out gas-liquid chromatography analysis of a glucose broth for all organisms resembling *Actinomyces* cannot be overemphasised.

Both organisms isolated from the abscess were sensitive to penicillin. Hence an important question is raised regarding the use of prophylactic antibiotics, in this case phenoxymethylpenicillin, in patients with cardiac anomalies, either congenital or acquired. Should the patient take subtherapeutic dosages of prophylactic antibiotics for long periods and risk acquiring resistant oral microflora or stop prophylaxis and risk infection with commensal micro-organisms?

In our patient oral prophylaxis with phenoxymethylpenicillin was justified as we assume that a bacteraemic episode had occurred a few weeks before presentation while he was not taking antibiotics. Although it is recommended that prophylaxis is indicated only when a patient is subjected to some manipulative procedure known to cause bacteraemia,⁴ phenoxymethylpenicillin had been continued in our patient, albeit at subtherapeutic dosages, after he was discharged, in an attempt to prevent a further bacteraemic episode.

We thank Dr M Lee for permission to report this case, and Dr K T Karthigasu for helpful discussion in preparing the manuscript.

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Legionnaires' disease and abscess of appendix

While gastrointestinal symptoms, particularly diarrhoea and abdominal distension, are common in legionnaires' disease,¹ a surgical "acute abdomen" has not previously been reported in this condition. I report on a patient with legionnaires' disease complicated by an abscess of the appendix.

Case report

A 48-year-old engineer was admitted to this hospital with a seven-day history of headache, rigors, and fever. Three days before admission he had developed an unproductive cough without chest pain or dyspnoea; treatment with co-trimoxazole had been started. The next day he had developed central abdominal pain, which had worsened and localised in the right iliac fossa. He had been anorexic and was constipated. He had become ill on the day he returned from a 10-day holiday in Benidorm.

On examination he was seen to be feverish and toxic. He was tachypnoeic with clinical signs of a left basal pneumonia. There was a tender, 3-cm-diameter mass palpable in the right iliac fossa, with guarding and rebound tenderness.

Haemoglobin concentration was 15.9 g/dl and white cell count $10 \times 10^9/l$

(10 000/mm³) with 78% neutrophils. Plasma sodium concentration was 121 mmol(mEq)/l, and urea and potassium concentrations were normal. Serum aspartate aminotransferase activity was 180 IU/l (normal 3-35 IU/l) and serum amylase activity 390 IU/l (normal 40-160 IU/l). A chest x-ray film showed extensive consolidation in the left lung. No pathogenic organisms were isolated from sputum or blood cultures. Indirect fluorescence tests on admission and days 8, 11, and 21 showed antibody titres to *Legionella pneumophila* of 1/8, 1/32, 1/64, and 1/128 respectively. There was no serological evidence of infection with influenza, respiratory syncytial virus or adenovirus, group B chlamydia, or *Mycoplasma pneumoniae*.

As legionnaires' disease was suspected on admission he was given erythromycin 500 mg four times daily for 10 days. The abscess of the appendix was treated conservatively with intravenous fluids, and gentamicin and metronidazole were given for 10 days. On this regimen his condition improved steadily, the pneumonia having cleared clinically and radiologically after 12 days in hospital. Appendicectomy was performed two months later. Histological examination showed a subacute abscess with no specific features. He has remained asymptomatic since the operation.

Comment

Although abdominal symptoms are often present in patients with legionnaires' disease, structural lesions of the gastrointestinal tract have not been found at necropsy. The symptoms of appendicitis were this patient's main complaint—in fact, despite extensive pneumonia, he complained of a dry cough only on direct questioning. While this may have been a chance association, I believe that this complication might be overlooked in a patient severely ill with respiratory failure or encephalopathy, and if not treated correctly might have a deleterious effect on the outcome.

I thank Dr T Rowbotham for the legionella serology, Mr T Brennan for his surgical advice, and Dr J Stevenson for permission to report on this patient.

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Spacing between doses on a thrice-daily regimen

The effect of drug treatment is related not only to the number of doses taken but also to the timing of doses. This is particularly true for drugs with a narrow therapeutic range and a short elimination half-life. While considerable variations in the patients' interpretations of the prescription label have been reported,¹ the spacing between doses has not been studied objectively. We used a recording medication monitor² to study the spacing between doses by patients on a thrice-daily regimen and to study the validity of interview data on the timing of doses.

Patients, methods, and results

The medication behaviour of 82 patients (45 men, 37 women) aged 56-90 years who were being treated with pilocarpine thrice daily for simple glaucoma was studied for three weeks with a medication monitor, which recorded the date and hour each time the medication bottle was opened.² Other sources of the drug were controlled, and the patients were not told that their drug-taking was being monitored until all the data had been collected.

From each monitor record we determined the three times (more than two hours apart) when doses were most frequently taken. For each patient the spacing between doses was then determined as the intervals between these times. Monitor records from five patients were lost for technical reasons. The mean of the first, second, and third intervals was 6.4, 6.5, and 11.1 hours respectively (table). The third interval was 12 hours or more for 30 (39%) patients. Only four patients took the drug at eight-hourly intervals. In the most extreme case the patient took the drug at intervals of three, three, and 18 hours. The patients studied took their drug at relatively similar intervals from day to day: 68 (88%) took at least 80% of their doses within one hour of their usual time.

After the recording period the patients were asked at which hours of the day they usually took the drug. Five patients were lost from these interviews. Comparisons with data from the monitor showed good agreement: for 85% of the intervals the difference was one hour or less. Only nine patients reported an interval with a deviation of more than two hours from that recorded by the monitor.

Comment

Although interview data on missed doses are often inaccurate,³ our findings show that interviews with patients were accurate in determining the spacing between doses. In studies of medication compliance data on the spacing between doses gained at interview may be combined with other methods to determine the number of doses taken—for example, pill count. In routine medical practice interviews may be useful for obtaining information about irregular dosage intervals and as a first step towards improving the situation.

A striking finding was the irregular timing of doses among patients on a thrice-daily regimen. Assuming that the effective duration of the drug is about eight hours,⁴ it is probable that long night intervals unfavourably influence the result of the treatment. Among patients with a twice-daily regimen Hermann found a tendency to spread doses more regularly, with an average night interval of 13.6 hours.¹ There is evidence that the proportion of missed doses is lower with a twice-daily than with a thrice-daily regimen.⁵

Hence, both in terms of missed doses and of spacing between doses, drugs prescribed twice daily will probably be more properly administered than those prescribed three times a day. When it is not possible to reduce the frequency of doses tailoring of doses to daily routines may improve compliance both in terms of spacing and of missed doses.⁵

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Intervals between doses of pilocarpine prescribed three times daily

Duration of interval (hours)	0	-1½	-2½	-3½	-4½	-5½	-6½	-7½	-8½	-9½	-10½	-11½	-12½	-13½	-14½	-15½	-16½	-17½	-18½	-20
No of patients				5	7	11	15	17	16	5	1									
No of patients				3	7	9	19	16	16	6	1									
No of patients							1	8	10	13	15	14	7	2		5	1	1		