Letters to the Editor

Group B streptococcal meningitis in an adult

Sir,

Group B streptococcal infection causing acute septicaemia and meningitis is rare in adults and accounts for less than 1% of cases. Group B streptococcus is a very invasive organism which seldom causes acute inflammation at the site of entry to the body and the appearance is usually unheralded.

A 45-year-old woman was admitted for varicose vein surgery. She had a history of varicose eczema and left deep vein thrombosis. She was allergic to penicillin. Spinal anaesthetic was performed aseptically and lignocaine was injected through a bacterial filter. Stripping of varicose veins was performed satisfactorily. Prophylactic subcutaneous heparin was used.

Six hours post-operatively she developed a sore throat and 18 hours later she became confused, restless, had a temperature of 38°C, neck stiffness but no focal neurological signs. A clinical diagnosis of meningitis was made and she was given intravenous ceftazidime and chloramphenicol after blood cultures had been taken. Lumbar puncture was performed aseptically under sedation. Cloudy cerebrospinal fluid (CSF) was obtained with 2000 white blood cells per ml (95% polymorphs), 1000 red blood cells per ml, 6 g/l protein, glucose 0.4 mmol/l; Gram-positive cocci were seen. Venous blood glucose was 10.1 mmol/l and white blood count 13.2×10^9 /l. Urea and electrolytes, liver function tests and arterial blood gases were normal. She was commenced on vancomycin and ceftriaxone and transferred to the intensive care unit.

At this point she was protecting her own airway and was haemodynamically stable; an erythematous rash developed on her right leg. A retained tampon was removed. She remained restless and was sedated with a propofol infusion. Computed tomography (CT) of the head showed slight cerebral oedema. On day 2 she was making spontaneous purposeful movements with her left side but only localising pain with her right side. She remained restless. Right plantar response was extensor. Repeat head scan showed no focal lesion. She was commenced on dexamethasone, 4 mg intravenously qid, for suspected cortical thrombophlebitis.

The following day group B streptococci were isolated from the two sets of blood cultures, high vaginal swab and the CSF. On day four she had three grand mal fits and was commenced on phenytoin. Magnetic resonance imaging showed a small lacunar infarct. Her antibiotic regime was changed from vancomycin to clindamycin.

Over the following few days she improved with resolution of her confusion and hemiparesis. On day 15 she developed left-sided pleuritic chest pain and shortness of breath, strongly suggestive of pulmonary embolus. This was confirmed by a perfusion scan which showed a large perfusion defect at the left base. Treatment was commenced with heparin and warfarin. On day 23 she was discharged home with no evidence of focal neurological deficit. Intravenous antibiotics had been continued for a total of 14 days; dexamethasone was reduced and stopped over this period and she remained on phenytoin and warfarin on discharge.

The reported mortality rate in adults with group B streptococcal meningitis is 27%, 45% in patients with a comorbid condition, and 0% in patients without underlying disease; 30% of those with bacteraemia die. The presentation is similar to that of other bacterial meningitides. It is usually very sensitive to penicillin but has a relatively high mean inhibitory concentration. More than 50% of reported cases have a comorbid condition such as diabetes, or malignancy. Although infections associated with the female reproductive system form a considerable proportion of the cases in young adults, overall, a greater number of males and patients over 45 years are affected.

Meningitis after lumbar puncture and spinal anaesthesia is very rare. In two reported cases^{1,2} no organisms were grown in the CSF and the patients made a full recovery. The postulated causes are shown in box 1.

It has been suggested that lumbar puncture creates a site of low resistance to infection across the blood–brain barrier. In this case we postulate that the retained tampon was responsible for the entry of group B streptococci into the bloodstream from the female reproductive system. The spread of infection into the CSF was then facilitated by the spinal anaesthetic having created a site of low resistance. Although she developed a skin rash the skin swabs were negative, making this very unlikely to be the source of infection.

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Learning points

- rare in adults but high mortality
- often comorbid conditions
- high index of suspicion
- look for upper respiratory tract symptoms and ensure tampons are removed pre-operatively
- strict asepsis for spinal anaesthesia
- treat early with intravenous antibiotics and fluids on the intensive care unit; anticonvulsants may be required

Box 2

Causes of meningitis after lumbar puncture or spinal anaesthesia

- aseptic meningitis from disinfectants and detergents
- introduction of bacteraemia from the bloodstream of a septicaemic patient
- introduction of foreign material due to coring
- use of certain local anaesthetic solutions
- coincidental viral infection

Box 1

- 1 Dunne DW, Quagliarello MD. Group B Streptococcal meningitis in adults. *Medicine* (Baltimore) 1993; 72: 1–10.
- 2 Roberts SP, Petts HV. Meningitis after obstetric spinal anaesthesia. *Anaesthesia* 1990; 45: 376–7.

Genetic predisposition of ischaemic heart disease

Sir,

Wat *et al* reported a 29-year-old man who developed acute myocardial infarction.¹ Another recent publication reported a 28-year-old Olympic champion, without any conventional risk factors for coronary heart disease, who died of acute myocardial infarction associated with coronary heart disease.² Wat *et al* reported that their patient had no coronary heart disease risk factors other than hypercholesterolaemia.¹ Patients with hypercholesterolemia of 7.1 mmol/l are commonly observed in out-patient clinics. However, it is quite rare that they develop such severe coronary heart disease, or fatal acute myocardial infarction, at this age. Genetic predisposition for the development of coronary heart disease is largely unknown, but recent observations have revealed that some genetic variants are associated with coronary heart disease in Caucasians.^{2–4} We propose that there is a marked ethnic difference in a coronary heart disease susceptibility gene variant.⁵ Whether such genetic alterations are associated with coronary heart disease in Chinese is currently unknown. However, an involvement of some genetic factors other than hypercholesterolaemia in the pathogenesis of his acute myocardial infarction is probable in Wat *et al*'s patient. Judging from the absence of a family history of acute myocardial infarction, he may have inherited genetic abnormalities from each of his parents. Compound heterozygosity of more than two mutations or homozygosity of one genetic mutation may have thus led to his acute myocardial infarction of juvenile onset.

It is obvious that conventional risk factors for coronary heart disease, such as hypercholesterolaemia should be controlled, but investigation of genetic predisposition is likely to contribute to decreasing fatal coronary heart events. Other than conventional risk factors, genetic analysis of patients for coronary heart disease susceptibility genes will be important for the prevention of fatal coronary heart events.

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- 1 Wat M, Tai Y, Lam K. Ischaemic heart disease in a young man. *Postgrad Med J* 1996; 72: 510.
- 2 Goldschmidt-Clermont, Shear WS, Schwartzberg J, Varga CF, Bray PF. Clues to the death of an Olympic champion. *Lancet* 1996; 347: 1833.
- 3 Gardemann A, Weiss T, Schwartz O, *et al*. Gene polymorphism but not catalytic activity of angiotensin 1-converting enzyme is associated with coronary artery disease and myocardial infarction in low-risk patients. *Circulation* 1995; 92: 2796–9.

- 4 Ruiz J, Blanche H, James RE, *et al.* Gln-Arg 192 polymorphism of paraoxonase and coronary heart disease in type 2 diabetes. *Lancet* 1995; 346: 869–72.
- 5 Odawara M, Matsunuma A, Yamashita K. Platelet glycoprotein IIIaP1 polymorphism and Japanese diabetic patients with coronary heart disease. *Lancet* 1996; 348: 1310.

Carbon monoxide poisoning

Sir,

The recent review of carbon monoxide poisoning by Balzan *et al*¹ provided helpful advice about this sometimes difficult diagnosis. We would, however, hesitate to follow the recommendations made about the treatment of CO poisoning. Their assessment of the benefit of hyperbaric oxygen (HBO) does not appear to be based on the presented evidence and the potential complications of transporting critically ill patients to HBO facilities do not receive the attention they merit.

The authors cite one randomised trial assessing HBO in patients who were not pregnant.² The indications they propose for HBO include two (impaired consciousness and cardiovascular instability) that were the exclusion criteria in this trial. Case series are also cited.^{3,4} We do not believe these provide sufficient information to allow clinically useful comparison between different treatments. Their rôle is to generate rather than to test hypotheses. We conclude with the observation of Thom *et al* (our italics): "Questions that should be addressed include whether treating patients [with hyperbaric oxygen] more than 6 hours after poisoning is effective and whether the benefits outweigh the costs of transportation and treatment."

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- 1 Balzan MV, Agius G, Debono AG. Carbon monoxide poisoning: easy to treat but difficult to recognise. *Postgrad Med J* 1996; 72: 470–3.
- 2 Thom SR, Taber RL, Mendiguren II, Clark JM, Hardy KR, Fisher AB. Delayed neuropsychologic sequelae after carbon monoxide poisoning: prevention by treatment with hyperbaric oxygen. *Ann Emerg Med* 1995; 25: 474–80.
- 3 Myers RAM, Snyder SK, Lindberg S, Cowley RA. Value of hyperbaric oxygen in suspected carbon monoxide poisoning. *JAMA* 1981; 246: 2478–80.
- 4 Norkool DM, Kirkpatrick JN. Treatment of acute carbon monoxide poisoning with hyperbaric oxygen: a review of 115 cases. *Ann Emerg Med* 1985; 14: 1168–71.

This letter was shown to the authors, who responded as follows:

Sir,

In our article we attempted to reproduce widely accepted recommendations in the current literature for the use of HBO in CO poisoning. These are based mainly on clinical experience and retrospective case series comparing outcomes in patients treated with HBO with historical controls receiving normobaric oxygen (NBO). These have shown clear-cut, often dramatic improvements with HBO in severely intoxicated patients.

I agree with Hardern *et al* that, in principle, any therapeutic measure and its indications should be tested in a large prospective randomised controlled trial. However, in view of the evidence in retrospective case series for the greater effectiveness of HBO, it is unlikely that any ethical committee would permit such a trial in severe CO intoxication. It is also

unlikely that a properly informed patient or his delegate would give his consent to participate in such a trial.

Probably for these reasons, two recent prospective randomised controlled trials comparing HBO with NBO have excluded patients with severe poisoning (those with loss of consciousness or myocardial instability) and concentrated on moderate intoxication. Both these studies have confirmed the utility of HBO, compared to NBO, in accelerating recovery and preventing delayed neurological sequelae.^{1,2}

However, does it make sense in clinical practice to treat moderately intoxicated cases with HBO and not severe cases for the simple reason that a trial cannot be performed as treatment is considered potentially life-saving? Would such a position be tenable in a court of law? Is it logical to treat moderately intoxicated women, except when they carry a foetus very vulnerable to hypoxia, when it has been shown that HBO is safe in pregnancy?

As regards the transport of critically ill patients, it is accepted that supportive care must never be compromised in transport and that the logistics of every case must be considered individually and carefully evaluated in a local context. However I feel strongly that, in line with guidelines in the literature, comatose patients, or patients with prolonged loss of consciousness should, whenever possible, be offered HBO.

HBO treatment in patients presenting late is still debatable. Whether the cost of an HBO unit or the transport expenses are justified or not by the benefit of therapy depends on the logistics and health rationing priorities of different healthcare setups.

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- 1 Thom SR, Taber RL, Mendiguren II, Clark JM, Hardy KR, Fisher AB. Delayed neuropsychologic sequelae after carbon monoxide poisoning: prevention by treatment with hyperbaric oxygen. *Ann Emerg Med* 1995; 25: 474–80.
- 2 Dugas JL, Izard PH, Celsis P, *et al.* Moderate carbon monoxide poisoning: hyperbaric or normobaric oxygen? In: Baker DJ, Schmutz J, eds. *Proceedings of the 2nd Swiss Symposium on hyperbaric medicine* 1990; pp 289–97.

Heart failure in the elderly

Sir,

Although I enjoyed reading the well-researched review of the management of heart failure in the elderly,¹ I disagree with the emphatic restatement of the conventional view that adjunctive treatment with spironolactone is absolutely contraindicated in patients already co-prescribed angiotensin-converting enzyme (ACE) inhibitors and loop diuretics. The reality is that amongst patients already co-prescribed ACE-inhibitors and loop diuretics, there will always be a few with refractory, and potentially life-threatening hypokalaemia, due, in some instances, to hyperaldosteronism,² for which corrective treatment could either be resection of an adrenocortical adenoma or co-prescription of spironolactone and ACE-inhibitors.²

In my own register, dating back to 1984, comprising 349 patients co-prescribed ACE-inhibitors and loop diuretics for heart failure, three women, now aged 81, 81 and 79, respectively, had coexisting hypertension and hypokalaemia, the latter refractory to ACE-inhibitors. In the first patient, with a nadir serum potassium of 2.7 mmol/l, following co-

prescription of spironolactone 25 mg/day, frusemide 40–80 mg/day and enalapril 10 mg/day followed by lisinopril 20 mg/day, the serum potassium was maintained in the range 3.9–4.4 mmol/l during the last six months of a 30-month period of 'triple' therapy. Prior to commencement of 'triple' therapy, her 24-hour urinary aldosterone was 7 nmol (reference range 10–50) in 1050 ml urine, and her 09.00 h serum cortisol was 516 nmol/l.

In the second patient, the co-prescription of spironolactone was precipitated by a fall in serum potassium to 2.2 mmol/l whilst taking enalapril 20 mg/day and frusemide 80 mg/day. Her 24-hour urinary aldosterone output was 25 nmol (in 1620 ml urine), but neither 24-hour urinary cortisol nor serum cortisol were requested due to the (peroneous) perception that a serum potassium of 2.6 mmol/l, 11 years previously, rendered the diagnosis of Cushing's syndrome unlikely in the absence of the development of clinical stigmata over that period. Ultrasonography had also not identified any adrenal abnormality. This patient was subsequently prescribed spironolactone 25 mg/day, in addition to frusemide 80 mg/day, and enalapril was increased to 40 mg/day; 28 months later her serum potassium had increased to 3.2 mmol/l.

The third patient had an initial blood pressure of 280/100 mmHg in association with plasma potassium of 2.9 mmol/l, urea of 16.5 mmol/l, creatinine of 139 µmol/l and body weight of 47 kg. Unfortunately, her 24-hour urinary aldosterone and cortisol levels were quantified when she was already taking spironolactone 50 mg/day, frusemide 120 mg/day, ramipril 10 mg/day, and lacidipine 4 mg/day, yielding values of 2.0 nmol and 71 nmol, respectively, in 800 ml urine. Computed tomography showed that she had right-sided hydronephrosis, but no adrenal adenoma. During the subsequent three months, spironolactone was progressively increased to 200 mg/day, frusemide reduced to 80 mg/day, whilst ramipril was maintained at 10 mg/day and lacidipine increased to 6 mg/day. Consequently, her blood pressure fell to 200/90 mmHg, but her plasma potassium remained at 2.9 mmol/l, with urea 17.1 mmol/l and creatinine 130 µmol/l. Due to the subsequent development of a pruritic maculopapular rash, losartan 50 mg bid was substituted for ramipril, and she is now undergoing titration of the spironolactone dose, due to a 75% reduction in frusemide requirements (based on transient development of reversible prerenal uraemia).

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- 1 King D. Diagnosis and management of heart failure in the elderly. *Postgrad Med J* 1996; 72: 577–80.
- 2 Geist M, Dorian P, Davies T, *et al.* Hyperaldosteronism and sudden cardiac death. *Am J Cardiol* 1996; 78: 605–6.

This letter was shown to the author, who responded as follows:

Sir,

I make no apology for stating that the use of spironolactone (and other potassium-conserving diuretics), in conjunction with ACE-inhibitors should be discouraged in the elderly. This combination in older people