units are willing to accept cases of carbon monoxide poisoning:

Heatherwood Hospital, Ascot 0990 23333
Whipps Cross Hospital, London E11 01 539 5522
Peterborough District Hospital, Peterborough
0733 67451
Royal Victoria Infirmary, Newcastle upon Tyne
091 232 5131
Monsall Hospital, Manchester 061 205 2393

It would clearly be sensible for the clinical aspects of a given case to be discussed by the referring physician with the consultant or duty registrar at the unit before arranging speedy transfer.

American work has shown the cost effectiveness of this mode of treatment in various conditions, and we would welcome a similar independent study in Britain before decisions are made to increase or decrease its availability under the NHS.

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Drug points

Acute renal failure due to cephmandole

Drs P CSANYI, J P RADO, and M HORMAY (Weil Emil Hospital, Budapest, Hungary) write: First generation cephalosporins have been reported to cause renal effects. We describe here an acute renal complication developing in a patient who was treated with cephmandole, a second generation cephalosporin compound.

A 76 year old woman was admitted with abdominal pain, fever, emesis, and jaundice. She had been aware of cholelithiasis for 20 years. Pronounced tenderness was found in the right hypogastrium. Glutamate transaminase activity was 42 U/l, oxaloacetate transaminase 47 U/l, alkaline phosphatase 180 U/l, and serum bilirubin 93.2 mmol/l. Ultrasound examination showed stones in the gall bladder. Cholelithiasis and cholecystocholangitis were diagnosed. Cephmandole treatment was started at a dose of 1 g four times a day intravenously. In three days the patient became free of fever and symptoms, jaundice disappeared, and laboratory findings became normal; no signs of renal impairment were detectable. Oliguria (day 4) followed by anuria (day 5) then developed (figure) with peak serum urea and creatinine concentrations of 37.4 mmol/l and 707 µmol/l respectively. Frusemide and glucocorticoid treatments were ineffective, and the following day peritoneal dialysis was started and maintained for 10 consecutive days. Urine was excreted again on the fifth day of dialysis. Renal function improved dramatically by the 16th day: the serum urea nitrogen value dropped to 14.4 mmol/l and serum creatinine to 198 µmol/l, and the daily diuresis was 3430 ml. Dialysis was stopped. The patient was discharged on the 23rd day in good general condition and with normal laboratory findings. At no stage of her illness did the patient become dehydrated or hypotensive, and her blood pressure remained between 120/80 mm Hg and 150/80 mm Hg. She did not receive any non-steroidal anti-inflammatory drugs during her stay, though she was given a

Changes in daily urine volume and serum concentrations during and after treatment with cephmandole.

spasmodic analgesic compound containing atropine, codeine, amidopyrine, papaverine, and aminopyrine on the first two days of admission and two ampoules of papaverine intramuscularly on the third and fourth days.

Among the first generation cephalosporin compounds cephalothin and cephaloridine induced dose related severe nephrotoxicity in the form of acute tubular necrosis or acute interstitial nephritis.¹ Second and third generation cephalosporins with broad spectrum bactericidal potential are thought not to impair kidney function and are even recommended in chronic renal failure and dialysis.² In 153 studies on 2640 patients treated with ceftriaxone, a third generation cephalosporin, no cases of nephrotoxicity were reported.³ The results with cephmandole are similarly favourable, and only a few patients with slightly raised serum creatinine concentrations have been reported.⁴ Acute tubular necrosis induced by cephmandole was seen in a single patient treated with high dose cephmandole for endocarditis induced by *Haemophilus parainfluenzae*,⁵ but the dose our patient received was not large. Cephmandole seems the most likely cause of our patient's acute renal failure and we would like to draw attention to this risk of even modern cephalosporin treatment.

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Sulfadoxine-pyrimethamine resistant malaria from west or central Africa

Dr J GUBLER (Medizinische Klinik, Winterthurer CH-400, Switzerland) writes: In vivo malaria resistance to sulfadoxine and pyrimethamine has been reported from South East Asia, the Amazon, and east Africa^{1,2} but not from west Africa (W H Wernsdorfer, WHO Malaria Action Programme, personal communication). We report an imported case of malaria caused by *Plasmodium falciparum* contracted in west or central Africa despite adequate prophylaxis which showed in vivo resistance type R II.³

A 23 year old previously healthy man was admitted on 5 July 1987 with fever and chills lasting three days.

From 20 January to 13 May 1987 he had travelled on a bicycle through Niger, Nigeria, Cameroon, and Equatorial Guinea, taking one tablet of Fansidar (sulfadoxine 500 mg, pyrimethamine 25 mg) a week until 20 June, six weeks after his return to Europe. He took few other precautions. During his trip he had two minor episodes of diarrhoeal disease, and on arrival in Europe on 16 May he had an episode of three days of fever up to 38.8°C and symptoms resembling flu. On 1, 3, and 4 July he had fevers spiking up to 40°C associated with chills and headache not suppressed by antipyretics. On admission (day 0) falciparum malaria was diagnosed by examination of blood smears (parasitaemia of 26/1000). He was given a single dose of three tablets of Fansidar. His clinical state improved rapidly, and he was discharged on day 5. The course of the temperature, parasitaemia, and subsequent plasma sulfadoxine levels are shown in the figure. On

Course of parasitaemia, fever, and plasma sulfadoxine concentrations.

day 8 blood smears showed numerous sexual forms and rare trophozoites. On 17 July (day 12) the patient was readmitted with a new bout of fever up to 39°C, chills, and headache. On physical examination slight hepatosplenomegaly was noted, and blood smears again showed asexual *P. falciparum* parasitaemia of 9%. He was treated with mefloquine, 750 mg initially and 500 mg six hours later, and made a rapid and uneventful recovery. No asexual plasmodium forms could subsequently be identified.

Plasma sulfadoxine concentrations on days 0, 3, and 12 indicated adequate absorption during prophylaxis and after oral therapy,^{4,5} illustrating in vivo resistance to sulfadoxine and pyrimethamine acquired in west or central Africa. With the introduction of new in vitro tests,⁶ monitoring of drug resistance in west Africa should be greatly facilitated. Clinicians should be highly suspicious of *P. falciparum* drug resistance, even in patients returning from areas currently considered free of resistant strains.

We thank Dr Dell of F Hoffman-La Roche (Basle) for determining the plasma concentrations of sulfadoxine.

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