

experience they would wish to repeat. This rating was lower than we expected.

Dr Skidmore and colleagues state that they used urine tests to detect intravenous drug use. Urine analysis will detect which drugs have been consumed but hitherto has not provided information on the route of drug use. It would be a very interesting development to have a urine test that could distinguish between oral and intravenous drug use.

In the past 18 months we have noticed a steady rise in the number of urine specimens containing polyethylene glycol, which was detected by thin layer chromatography. This macromolecule is a constituent of the temazepam soft capsule formulation. We initially thought that the presence of polyethylene glycol in the urine was particular to users of intravenous temazepam, but recently we have detected it in the urine of two patients taking very high doses of oral temazepam (400 mg daily). Thus the presence of polyethylene glycol in a urine specimen should remind the doctor to examine the patient for evidence of fresh injection marks.

In the era of HIV and AIDS investigations that could distinguish between oral and intravenous drug use would help to monitor progress in encouraging drug users to stop injecting. Further work is required to explore the feasibility of such developments.

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- 1 Skidmore CA, Robertson JR, Robertson AA, Elton RA. After the epidemic: follow-up study of HIV seroprevalence and changing patterns of drug use. *Br Med J* 1990;300:219-23. (27 January.)
- 2 Robertson JR, Roberts JJK, Black H, Davitt B, Stewart N. Management of drug abuse. *Lancet* 1987;iii:284-5.
- 3 Start C, Sykes R, Mullin P. Temazepam abuse. *Lancet* 1987;iii:802-3.
- 4 Farrell M, Strang J. Misuse of temazepam. *Br Med J* 1988;297:1402.

## Demoralised doctors

SIR,—Small wonder that Dr Debbie Parker and her contemporaries are demoralised<sup>1</sup> when the BMA, the Hospital Junior Staff Committee, and their unnamed parliamentary ally have failed to persuade the Department of Health to reduce the hours of junior staff to an average of 72 a week. It may interest readers to know that junior hospital resident medical officers in Queensland, Australia, obtained from the Industrial Court in that state a working week of 56 hours as long ago as 1944. Last year the Industrial Commission made further reductions to 88 hours a fortnight from March, 84 from July, and 80 with effect from 1 January 1990. The present salary of a first year resident medical officer in the metropolitan area is \$A1093.70 (about £500) a fortnight.

Perhaps the HJSC should request an entry in the *Guinness Book of Records* to the effect that at the start of the last decade of the twentieth century junior hospital staff in the NHS were the most exploited body of workers in the Western world.

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- 1 Parker DF. Demoralised doctors. *Br Med J* 1990;300:56-7. (6 January.)

## Use of newsprint to wrap fish

SIR,—Minerva notes my publication of Ramazzini's *Diseases of Printers* and asks whether his reference to the use of printed paper to wrap fish

is the first.<sup>1</sup> The answer is no. Education in the seventeenth century would have entailed a large dose of the classics, and Ramazzini almost certainly would have been familiar with Catullus (circa 50 BC), who wrote a poem about the bad poetry of some other poets,<sup>2</sup> ending with the lines: "But the Annals of Volusius will die by the river Padua where they were born, and will often furnish a loose wrapper for mackerels."<sup>3</sup>

Ramazzini would also have known Horace's reference to bad poetry: that the works of a bad poet would be taken to "where they sell frankincense and perfume and pepper and everything else that is wrapped in useless paper."<sup>3</sup>

I am indebted to Mr Desmond Costa of the University of Birmingham for these references.

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- 1 Anonymous. Views. *Br Med J* 1990;300:410. (10 February.)
- 2 Catullus. *Poem* 95. 2nd ed. Loeb Classical Library, 1988. (Translated by F W Cornish.)
- 3 Horace. Epistle 1. In: *Epistles book II*. Loeb Classical Library, 1978. (Translated by H R Fairclough.)

## Drug Points

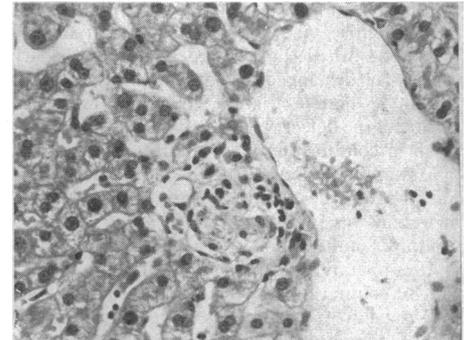
### Quinine induced granulomatous hepatitis and vasculitis

DRS SANDIP MATHUR, JAMES DOOLEY, and PETER J SCHEUER (Royal Free Hospital, London NW3 2QG) write: Quinine produces a wide range of adverse effects.<sup>1</sup> Its D-isomer, quinidine, has been reported to cause granulomatous hepatitis, but this hepatic lesion has been reported only once with quinine sulphate,<sup>2</sup> and the histological diagnosis was later challenged.<sup>3</sup> We describe another patient who developed granulomatous hepatitis with histological features identical to those described in the first report.

A 67 year old man presented with a 10 day history of fever and polyarthralgia. Joint pains had started insidiously and resolved five days before admission. The fever was intermittent with temperatures of up to 38.5°C but no rigors. One day before admission he developed a vasculitic rash over the front of his legs. There was no history of liver disease, jaundice, or alcohol abuse. He had never received blood transfusions and was heterosexual. He suffered from glaucoma, which was treated with carbachol hydrochloride. For two months he had taken quinine sulphate 300 mg at night for muscle cramps but stopped this medication one week before admission because of flatulence.

On examination he appeared well. He had a palpable vasculitic rash over his shins. His blood pressure was 140/90 mmHg. There was pitting oedema of both feet extending to just above both ankles. Investigations showed haemoglobin concentration 125 g/l, white cell count 6.0×10<sup>9</sup>/l, platelet count 438×10<sup>9</sup>/l, erythrocyte sedimentation rate 75 mm in the first hour. Urea, electrolyte, and creatinine concentrations were normal. Liver function tests showed total bilirubin 11 μmol/l (normal 5-17), aspartate aminotransferase 100 U/l (normal 5-40 U/l), alkaline phosphatase 1668 U/l (normal 35-130), γ-glutamyl transferase 1140 U/l (normal 10-43), total protein 73 g/l (normal 60-80 g/l), albumin 30 g/l (normal 30-50). Histological examination of a liver biopsy specimen showed normal liver architecture with prominent Kupffer cells and a few small foci of liver cell necrosis and inflammation as well as small epithelioid cell granulomas which showed no necrosis (figure). There was no cholestasis or fatty change. The portal tracts contained a few lymphocytes and eosinophils. There was nuclear vacuolation in

some hepatocytes, and increased numbers of mitoses were seen. Liver cell nuclei varied considerably in size. The skin biopsy showed a leucoclastic vasculitis.



Small granuloma composed of epithelioid cells and lymphoid cells is seen next to a terminal hepatic venule. Haematoxylin-eosin

All drugs were withdrawn and within a few days he was free of symptoms. The vasculitic rash disappeared over three days. By the fifth day of his illness platelet levels were normal and his erythrocyte sedimentation rate had fallen to 42 mm in the first hour. The aspartate aminotransferase returned to normal the day after admission, the alkaline phosphatase fell to 409 U/l by the fourth day, and the γ-glutamyl transferase to 447. When reviewed a month later his liver function values had returned to normal except γ-glutamyl transferase, which returned to normal six months later.

Our patient's symptoms, biochemical profile, and histological features closely resemble those described in the previous report of granulomatous hepatitis associated with quinine sulphate. In both cases the patients had been taking quinine sulphate in doses normally prescribed for treating nocturnal leg cramps—that is, 300 mg at night. Both presented with fever and polyarthralgia, and the symptoms were episodic with the arthralgia settling spontaneously. The erythrocyte sedimentation rate was raised in both cases, and liver function tests showed cholestatic features. The presence of small granulomas and an infiltrate including eosinophils is consistent with a drug reaction. These features also resemble the report of quinidine induced granulomatous hepatitis.<sup>5</sup> Drugs are responsible for about 2% of cases of granulomatous hepatitis,<sup>5</sup> and those implicated include sulphonamides, penicillin, erythromycin (personal observation), allopurinol, methyldopa, hydralazine, phenylbutazone, carbamazepine, isoniazid, nitrofurantoin, and diazepam. It is important therefore to look specifically for a drug as the causal factor in patients with cholestatic liver disease and hepatic granulomas, and quinine should be added to the list of drugs that may cause these features.

- 1 Joint Formulary Committee. *British national formulary*. No 17. London: BMA, 1989:233.
- 2 Katz B, Weetch M, Chopra S. Quinine induced granulomatous hepatitis. *Br Med J* 1983;286:264-5.
- 3 Nirodi NS. Quinidine induced granulomatous hepatitis. *Br Med J* 1983;286:647.
- 4 Chajck T, Lehrer B, Geltner D, Levij IS. Quinidine induced granulomatous hepatitis. *Ann Intern Med* 1974;81:744-66.
- 5 McMaster KR, Hennigar GR. Drugs induced granulomatous hepatitis. *Lab Invest* 1981;44:61-73.

### Convulsions induced by enoximone administered as a continuous intravenous infusion

DRS IAN APPADURAI, MAIR EDMUNDS, RICHARD WYATT, and THOMAS J SPYT (Department of Cardiothoracic Surgery, Groby Road Hospital, Leicester) write: Many neurological complications, including insomnia, agitation, anxiety, and headaches, have been documented after intra-