

1989, asking whether they were likely to refer more patients with myocardial infarction or suspected myocardial infarction after thrombolytic treatment became available in hospital. Sixty practitioners (67%) replied, of which 31 stated an intention to refer more patients, but 29 thought that their referral habits would be unchanged. The important role required of general practitioners in the co-ordinated management of acute myocardial infarction with the advent of thrombolysis treatment has been emphasised.² Our survey, however, suggests that there is a considerable dichotomy of opinion on this subject and that an appreciable proportion of general practitioners are still uncertain about advising hospital treatment in patients with acute myocardial infarction.

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- 1 Burrell CJ, Skehan JD, Cowley ML, Barrett CW, Mills PG. Districts' use of thrombolytic agents. *Br Med J* 1990;300:237-8. (27 January.)
- 2 British Heart Foundation Working Group. Role of the general practitioner in managing patients with myocardial infarction: impact of thrombolytic treatment. *Br Med J* 1989;299:555-6. (26 August.)

Node negative breast cancer

SIR,—The review by Drs S M O'Reilly and M A Richards is based on node negative breast cancer as a clinical entity defined by using histological examination of axillary lymph nodes. These nodes constitute only one of the groups of nodes that drain the breast, and the size in error in using them alone should be kept in mind. The best evidence on this point comes from a review of one thousand cases of modified radical mastectomy at the Middlesex Hospital (R Handley, unpublished data). This material provides a complete pathological examination of the axillary lymph nodes, and in addition Dr Handley performed biopsy on the internal mammary lymph nodes in every case (see tables).

Table I shows the extent of internal mammary lymph node invasion in relation to the site of the tumour within the breast. As expected the internal mammary nodes are more commonly affected in inner quadrant tumours, being positive in more than a quarter of the patients. Table II shows the incidence of internal mammary invasion in the subgroup of patients from table I in whom the axillary nodes were not affected. Table II shows that 22 patients (12%) with tumours in the inner quadrants of the breast had a positive result on internal mammary lymph node biopsy. As the complete axillary contents are delivered to the

TABLE I—Presence of internal mammary node invasion in women who had had modified radical mastectomy in relation to site of tumour

Site of tumour	No of patients	No (%) with internal mammary invasion
Inner quadrants	309	87 (28)
Outer quadrants	475	66 (14)

TABLE II—Presence of internal mammary node invasion in women who had had modified radical mastectomy and had no axillary node invasion

Site of tumour	No of patients	No (%) with internal mammary invasion
Inner quadrants	179	22 (12)
Outer quadrants	210	9 (4)

laboratory because of the nature of the operation there is no sampling error likely from that source, and if there is a sampling error from the medial half of the breast the true figure could only increase the percentage upwards from 12%.

Though not wishing to introduce further uncertainties into the management of breast cancer, I feel that it seems important to bear in mind that more than one in eight of patients with a tumour in the inner half of the breast will be wrongly staged by present techniques. The rest of Dr Handley's data are available by return from me.

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- 1 O'Reilly SM, Richards MA. Node negative breast cancer. *Br Med J* 1990;300:346-8. (10 February.)

Crisis in our hospital kitchens

SIR,—The appraisal by Drs Allyson M Pollock and Paula M Whitty of an outbreak of diarrhoea in a long stay hospital¹ highlights the problems that are emerging in ancillary services that have been contracted but omits to mention the importance of an effective infection control team in departments such as psychiatric and geriatric continuing care units.

The Cooke report emphasised the crucial role of the infection control nurse as the only full time member of the infection control team, with her primary duty being that of preventing infection by surveillance, research, teaching, and liaison with all departments.² Most infection control nurses would visit all food handling areas routinely.

The financial costs of outbreaks of enteric food poisoning are often underestimated—an average of £2500 per patient was quoted at 1986 prices. This does not take any account of possible litigation costs.

Moves to disperse patients and services from large hospitals to the community, including private nursing homes, have made surveillance of infection much harder. We suggest that if ancillary services or beds are contracted to the private sector infection control measures and surveillance should be written into agreements and costed. In the long term, consideration of this aspect would be cost effective.

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- 1 Pollock AM, Whitty PM. Crisis in our hospital kitchens: ancillary staffing levels during an outbreak of food poisoning in a long stay hospital. *Br Med J* 1990;300:383-5. (10 February.)
- 2 Joint Department of Health and Social Security and Public Health Laboratory Service Hospital Infection Working Group. *Hospital infection control—guidance on the control of infection in hospitals*. London: DHSS, 1988.
- 3 Yule BF. Costing of a hospital based outbreak of poultryborne salmonellosis. *Epidemiol Infect* 1988;100:35.

Geographic variations in blood pressure

SIR,—Dr Jonathan Elford and colleagues showed with data from the British regional heart study that the geographic differences in cardiovascular mortality are accompanied by regional differences in levels of arterial blood pressure: mean systolic and diastolic blood pressures in middle aged men followed a trend, with higher values in those examined in Scotland and the north of Britain than in those seen in the midlands or the south.¹ The place of examination was a more important determinant of blood pressure than the place of birth.

Seasonal variation in blood pressure was first

described in Britain by Rose² and was subsequently confirmed by Heller *et al*³ and Brennan *et al*.⁴ By using blood pressure readings that were recorded in the Medical Research Council mild hypertension trial and meteorological measurements provided by the Meteorological Office Brennan *et al* showed that the seasonal variation in blood pressure was greater in old than in young subjects, was present in both sexes, and was highly significantly inversely related to environmental temperature.

Dr Elford and colleagues suggest that regional variations in alcohol intake, physical activity, and socioeconomic state all contribute to their findings. It would probably be worth examining the role of ambient temperature also.

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- 2 Rose G. Seasonal variation in blood pressure in man. *Nature* 1961;189:235.
- 3 Heller RF, Rose G, Tunstall-Pedoe H, Christie DGS. Blood pressure measurement in the United Kingdom Heart Disease Prevention Project. *J Epidemiol Community Health* 1978;32:235-8.
- 4 Brennan P, Greenberg G, Miall WE, Thompson SG. Seasonal variation in arterial blood pressure. *Br Med J* 1982;285:919-23.

Lymphomatoid granulomatosis

SIR,—Minerva's column¹ included a photograph of a man with non-pulmonary lymphomatoid granulomatosis, together with a comment and a supporting reference.² In the 18 years since the publication of this reference no fewer than six studies have shown that lymphomatoid granulomatosis (also known as polymorphic reticulosis and lethal midline granuloma) is a form of malignant lymphoma of peripheral T cell type; the most recent of these studies was that of Troussard *et al*.³ This form of lymphoma may masquerade as a chronic inflammatory condition, but it is important to be aware of its true nature and to treat it accordingly. Suboptimal treatment can lead to distressing local consequences.

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- 1 Anonymous. Views. *Br Med J* 1990;300:410. (10 February.)
- 2 Liebow AA, Carrington CRB, Friedman PJ. Lymphomatoid granulomatosis. *Hum Pathol* 1972;3:457-558.
- 3 Troussard X, Galateau F, Gaulard P, *et al*. Lymphomatoid granulomatosis in a patient with acute myeloblastic leukemia in remission. *Cancer* 1990;65:107-11.

Detection of intravenous drug use

SIR,—In the follow up study of Dr C A Skidmore and colleagues on HIV seroprevalence among intravenous drug users and changing patterns of drug use recent drug users were significantly more likely to use buprenorphine, dihydrocodeine, and temazepam.¹ Other recent reports have drawn attention to the increased intravenous use of temazepam.^{2,4} They suggest that the particular formulation of temazepam may lend it to intravenous use. Before the recent change in the formulation of this drug (to tablet and hard capsule forms) we surveyed, by using a questionnaire, 38 intravenous drug users on their preference of drugs. Of the 38, 19 had taken temazepam and 14 had used it intravenously. When asked to rate intravenous use of temazepam three of the 14 liked injecting temazepam, two did not mind injecting it, while nine said that they did not like injecting despite having injected it more than once. Thus only three rated taking temazepam intravenously as an

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 demoralised¹ 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.¹ 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,² 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."³

Ramazzini would also have known Horace's reference to bad poetry³: 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."

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

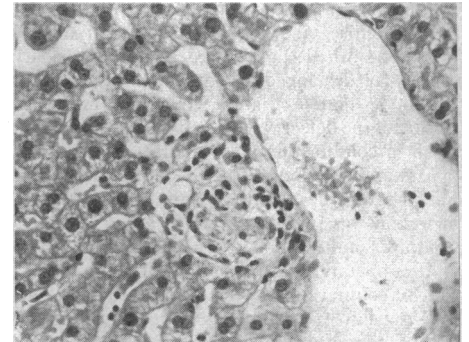
Quinine induced granulomatous hepatitis and vasculitis

Drs SANDIP MATHUR, JAMES DOOLEY, and PETER J SCHEUER (Royal Free Hospital, London NW3 2QG) write: Quinine produces a wide range of adverse effects.¹ Its D-isomer, quinidine, has been reported to cause granulomatous hepatitis, but this hepatic lesion has been reported only once with quinine sulphate,² and the histological diagnosis was later challenged.³ 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 6.0×10⁹/l, platelet count 438×10⁹/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.⁵ Drugs are responsible for about 2% of cases of granulomatous hepatitis,⁵ 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.

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- 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 Chajek 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-