Wet and dry bulb temperatures were recorded in examination rooms at the midpoint of each screening session in a number of temporary centres attended by 2178 males aged 40-65 years (approximately 75% response rate). Temperatures ranged from 11-18°C wet and 14.4-25°C dry bulb. Blood pressure was recorded using the London School of Hygiene and Tropical Medicine sphygmomanometer with examinees seated and the appearance and disappearance (phase V) of the Korotkoff sounds were used to observe the mean of two consecutive readings.

The table gives correlation coefficients between wet and dry bulb temperatures and systolic and diastolic blood pressure. A normal

Blood pressure and ambient temperature: correlation coefficients between wet and dry bulb ambient temperatures and systolic and diastolic blood pressure (phase V) in 2178 males aged 40-65 at work in west central Scotland

Age (y)	No	Systolic		Diastolic	
		Wet	Dry	Wet	Dry
40-44	100	0.089	0.028	0.198*	0.190*
45-49	311	0.091	0.093*	-0.036	0.052*
50-54	519	0.019	0.085*	0.006	0.114*
55-59	526	0.045	0.113*	0.001	0.069
60-64	429	0.037	0.125*	0.009	0.089*
65 and over	293	0.045	0.174*	0.063	0.167*
Total	2178	0.033	0.112	0.006	0.106

*Significant at 5% level.

distribution of ambient temperatures could not be assumed, so a non-parametric method was used.³ The analysis shows a significant positive correlation between systolic and diastolic blood pressure and dry bulb temperature.

The data raise questions about the role of blood pressure in the homeostatic control of body temperature and the possible effects of impairment of that mechanism in hypertension, and suggest the need to investigate outcome in the long-term follow-up of this cohort and of other cohorts over a wider range of ambient temperature, including the recording of examinees' temperatures. There could also be implications for the validity of cross-cultural comparisons between populations in tropical and temperate climates.

The multiphasic screening studies reported here were supported by grants from the Scottish Home and Health Department and the Renfrewshire King Edward Memorial Trust.

V M HAWTHORNE

Professor and Chairman

MARY SMALLS

Glasgow Mass Miniature Radiography
Cardiorespiratory Screening Unit,
University Department of Statistics,
Glasgow G12 8QQ

¹ Hawthorne VM, Greaves DA, Beevers DG. *Br Med J* 1974;iii:600-3.

² Hawthorne VM, Beevers DG, Gilmour H, Stewart GM, Watt H. *Clin Sci Mol Med* 1976;51:6535-65.

³ Kendall MG. *Rank correlation methods*. London: Griffin, 1948.

Paraproteins and non-Hodgkin's lymphoma

SIR,—Your leading article (2 February, p 273) did not point out the frequent incidence of paraproteinaemias in non-Hodgkin's lymphoma other than widespread lymphoplasmacytoid lymphoma and chronic lymphocytic leukaemia.

A study of non-Hodgkin's lymphomas based

upon the Kiel classification¹ was carried out at Oxford. Presentation sera and concentrated urines were examined for paraproteins using agarose gel plates and standard antisera. Paraproteins were detected most frequently in the low-grade lymphomas and in particular in the lymphoplasmacytoid lymphomas involving bone marrow. However, there was an appreciable incidence of paraproteins detectable in patients who fulfilled the criteria neither for Waldenström's macroglobulinaemia nor for chronic lymphocytic leukaemia. Thus in low-grade lymphomas the lowest incidence of paraproteins was found in patients with follicle-centre-cell lymphomas and the highest in diffuse lymphocytic lymphomas. In the high-grade lymphomas the most frequent rate of detection was among patients with immunoblastic lymphoma, and here it is of interest to note that the IgA paraproteins (one as part of a double clone) were detected in patients with small-bowel lymphoma. The incidence of paraproteinaemias in other high-grade lymphomas was much less frequent but still well above the expected incidence in this age group. Overall, IgG paraproteins were found almost as frequently as IgM paraproteins, and light chains were detected in urine in association with serum paraproteins but in eight cases alone.

Among patients with widespread lymphoplasmacytoid lymphoma the IgM paraprotein was from 10 to 20 g/l but was frequently lower in the diffuse lymphomas and in the chronic lymphocytic leukaemias. The levels of IgG paraprotein were also 10-20 g/l in most instances, although in one case (a patient with chronic lymphocytic leukaemia) over 40 g/l. Levels of IgA paraprotein were 6-10 g/l.

The incidence of hypogammaglobulinaemia in non-Hodgkin's lymphomas has been reported elsewhere.² There was no association between hypogammaglobulinaemia and detection of paraprotein in the high-grade lymphomas and even among the low-grade lymphomas there was only a slight increase in the tendency for suppression of polyclonal IgG and IgM in association with paraproteins and not at all for IgA. Among the 35 patients who had detectable paraproteins, 18 had no immunosuppression of the other classes.

The purpose of this particular study was to detect the incidence of the paraproteinaemias in relation to the various Kiel histopathology groups. The frequent detection of paraproteins in virtually all the low-grade lymphomas and in the immunoblastic lymphomas is of interest and could be regarded as indirect evidence for a B-lymphocyte origin in these cases.

R C F LEONARD

Royal Victoria Infirmary,
Newcastle upon Tyne NE1 4LP

¹ Lennert K. *Acta Neuropath* 1975;90 suppl:1-16.

² Leonard RCF, MacLennan ICM, Smart Y, Vanhegan RI, Cuzick J. *Int J Cancer* 1979;24:385-93.

Iatrogenic collapse

SIR,—The correspondence (20 October, p 1001; 24 November, p 1367; 19 January, p 185) relating to the use of intravenous pethidine once again emphasises how much is taken for granted with this widely administered drug.

I was surprised at how few controlled studies had been performed to confirm the clinical impression that intravenous pethidine can be a severe respiratory depressant. A study by Orkin and colleagues¹ is probably the best of the few that relate to the common clinical situation where an intravenous narcotic is used as a supposedly short-acting anaesthetic providing analgesia, sedation, and relaxation in the ambulant patient. Ten healthy unpremedicated patients were given pethidine

100 mg intravenously. They found an increase in respiratory rate which persisted for the one-hour study. More importantly, the tidal volume decreased by 55% and the minute volume by 50%, though these returned to 90% of their baseline values within 15 min. They noted periodic respiration in seven out of the 10 subjects. With morphine 10 mg instead, also given intravenously, the tidal volume was depressed by only 30% and the minute volume by 20%. They questioned the value of respiratory rate as a sign of respiratory depression with pethidine and implicated the use of this index as a cause of the widespread belief that pethidine does not cause significant respiratory depression. Age and sex did not prove to be determining factors as severe periodic breathing was seen in an 18-year-old female. Jennet has noted that the interpretation of tests of respiratory depression,² is both difficult and controversial³ but that the two drugs are almost equally depressant in equianalgesic doses. Where they differ is in producing peak effects at different times and in their dose-response relationships. There is no evidence that pethidine is safer than its rivals with regard to either of these.

Concerning Dr Huntington's other points, I would be surprised if anyone sent in a yellow card recording respiratory depression with pethidine 100 mg almost 40 years after the drug's introduction.

Finally, I recommended naloxone (Narcan) as an antidote, rather than nalorphine, because it carries no risk of further respiratory depression and is now the drug of choice.

M J BOSCOE

Department of Anaesthetics,
University Hospital of Leiden,
Leiden, The Netherlands

¹ Orkin LR, Egge RK, Rovenstine EA. *Anesthesiology* 1955;16:699.

² Jennet S. *Br J Anaesth* 1968;40:746.

³ Jennet S. In: Marcus AW, Smith R, Whittle B, eds. *Pain*. Edinburgh: Churchill Livingstone, 1977.

Endocrine aspects of liver disease

SIR,—I read with interest the explanations of liver dysfunction in thyrotoxicosis summarised by Dr R G Long (26 January, p 225). He may, however, have omitted the commonest cause of disturbance of liver function now seen in this condition.

Abnormalities of liver function, especially elevation of serum transaminases and alkaline phosphatase, are common in patients presenting with thyrotoxicosis today, their incidence varying from 8% to 50%.¹⁻⁵ In these patients few of the complications mentioned in the article and in which earlier literature abound^{6,7} are in fact present, such as heart failure, thyroid crisis, "severe untreated disease," or associated liver pathology.

When liver biopsies are done in these patients few of the histological changes mentioned by Dr Long are found but more subtle changes of liver ultrastructure are seen on electron microscopy, including elongation of mitochondria, frequent metamitochondria, and hypertrophy of the smooth endoplasmic reticulum with decreased glycogen.⁸ Similar hepatic changes are evident in patients taking potent enzyme inducers and are associated with elevation of liver enzyme levels in the serum.

The plasma half life of antipyrine, whose decay in serum is known to reflect hepatic microsomal metabolism, is shortened in

thyrotoxicosis⁸—strong evidence for the presence of liver enzyme induction in hyperthyroidism. Although isoenzyme studies of alkaline phosphatase⁹ have shown that at least some of the rise in thyrotoxicosis is of bony origin and is thought to reflect an increased osteoblastic activity, there is direct evidence of liver enzyme induction by thyroxine in animals.^{10 11}

Thus the commonest type of liver abnormality in the thyrotoxic patient appears to be a functional and thus reversible phenomenon unrelated to structural liver damage, the practical importance of which should be to avoid unnecessarily invasive procedures in the investigation of these patients.

R M JENKINS

Selly Oak Hospital,
Birmingham B29 6JD

- ¹ Perin E, Sode J. *Med Ann District Columbia* 1970; **39**:563-7.
- ² Ashkar F, et al. *South Med J* 1971; **64**:462-5.
- ³ Huther KJ, Shilz HR. *Dtsch Med Wschr* 1970; **95**:498.
- ⁴ Weber S. *Praxis* 1968; **57**:1-13.
- ⁵ Klion FM, Segal R, Schaffner F. *Am J Med* 1971; **50**:317-24.
- ⁶ Shaffer JM. *Arch Pathol* 1938; **20**:30.
- ⁷ Beaver DC, Pemberton J. *Ann Inst Med* 1933; **7**:687-708.
- ⁸ Vesell ES, et al. *Clin Pharmacol Ther* 1974; **17**:48-56.
- ⁹ Gerlach U, Paul L, Latzel H. *Enzymol Biol Clin* 1970; **11**:251-6.
- ¹⁰ Freedland RA. *Endocrinology* 1965; **77**:19.
- ¹¹ Rivlin RS. *J Biol Chem* 1963; **238**:3341.

Methylcellulose paint as possible cause of heart failure?

SIR,—Methylcellulose enjoys an immense worldwide use as a food additive, a pharmaceutical, and an industrial aid. Because it is not absorbed from the gut or through the skin it has essentially no toxicity. It has zero vapour pressure and the heavy, water-soluble dust does not reach the alveoli. Finally, it has next to no solubility in organic solvents such as amylacetate. Drs P L Weissberg and I D Green offer no evidence of its existence in the paint blamed for induction of an acute toxic myocarditis (3 November, p 1113) and there is no technical reason to suppose it was there.

MAYNARD B CHENOWETH
J D DEVRIEZE

Dow Chemical Company,
Midland, Michigan 48640,
USA

Hazard of nitrous oxide cryosurgery

SIR,—As I was responsible for introducing nitrous oxide for cryosurgery in this country,^{1 2} I was concerned to read Minerva's note on its hazards (2 February, p 337). I suggested its substitution for carbon dioxide because it is a better refrigerant and is almost universally available in operating theatres, and its acute toxicity is much lower. A reversion to carbon dioxide would therefore be no solution to the pollution problem and the other advantages would be lost.

So far as I know, no cryosurgical equipment emits more than about 15 litres of nitrous oxide a minute, so that the hazard is no more than two and a half times that from an anaesthetic—and, of course, usually lasts for a much shorter time. However, the same arguments that have been used to justify the requirement for control of anaesthetic pollution must apply and either passive or active extraction can be used. Passive extraction is much easier for cryosurgery than for anaes-

thesia because there is plenty of driving pressure, so that small tubes can be used over long distances if necessary. Devices that do not emit the gas from a single tube should be either banned or modified and, of course, not used in unventilated rooms.

B M WRIGHT

Rickmansworth, Herts

- ¹ Wright BM. *Lancet* 1971; **i**:951-2.
- ² Wright BM. *Br J Urol* 1976; **48**:203-6.

In defence of clinical freedom

SIR,—I write to comment on the letter by Dr Mark R Baker, "In defence of clinical freedom" (26 January, p 255). While it is possible that "clinical freedom" has been responsible for the alleged benefits of active and energetic modern hospital geriatric service practice, the corollary is surely that clinical freedom was also responsible for the previous level of activity which Dr Baker feels has with advantage been superseded.

Could it not also be true that "the greater demands on community health services and personal social services have been absorbed less well" because of the tendency to discharge patients more quickly? If clinical freedom is always a virtue it should also be recognised that those who spend public money in other fields are certainly not permitted such licence.

It surely cannot be desirable that some elderly patients should run a "substantial" risk of not being able to manage in the community. In the practice of geriatric medicine it may be more obvious that co-operation with other medical and non-medical services is important, but I believe this to be true in all clinical practice. "Clinical" freedom means precisely that: the freedom of a medical practitioner to take "clinical" decisions. It does not mean that one can take all decisions affecting a patient's admission, length of stay, discharge, and subsequent support services without considering the likely effect on other human and material resources.

N H N MILLS

Pontypool, Gwent

Cutting the drug bill

SIR,—In 1977 you kindly printed a letter by two of us (ML and AKS) drawing attention to the considerable savings that could be made in general practice by the use of generic prescribing rather than using trade names (7 May 1977, p 1218). At that time we assessed over a period of four weeks the savings that were made by prescribing nine commonly used drugs by generic rather than the familiar trade name. Since 1977 we have continued to prescribe generically wherever possible, with virtually complete acceptance and we believe without therapeutic detriment.

Recently there has been considerable national publicity concerning the cost of the drug bill in the NHS and obvious economies that are open to GPs.¹ In the light of this publicity we have reviewed the savings produced in our practice over a four-week period in January 1980. We chose 12 commonly prescribed drugs which we have been prescribing generically for the past three years and made a note of every one prescribed, whether initially or in a repeat prescription.

The drugs chosen were diazepam (Valium), nitrazepam (Mogadon), indomethacin (Indocid), methyldopa (Aldomet), frusemide (Lasix), phenylbutazone (Butazolidin), amitriptyline (Tryptizol), imipramine (Tofranil), chlorpropamide (Diabinese), ampicillin (Penbritin), oxytetracycline (Imperacin), penicillin V (VCIK).

At the end of the four-week period we costed the alternatives and found we had made an approximate saving of £270. This is in a three-man teaching practice of 6000 patients, and represents annual savings of £3500. If this example was followed by our GP colleagues over the whole country the savings to the NHS would be in the region of £24m a year. In times of stringent financial constraints when hospital and community services throughout the country are being subjected to cut-backs which may well have an adverse effect on patient care, we feel that economy in GP prescribing is well worth pursuing. We know that we should all be aware of interaction of drugs, of incompatibility and adverse reactions. We should also be aware of comparative cost.

We would like to see the DHSS take a far more active advisory role in this matter. The GP and receptionist's bible is *MIMS*. This is an excellent up-to-date publication but has to be read very thoroughly to extract comparative costs. The *British National Formulary* is also an excellent book, but is unfortunately infrequently consulted. Perhaps we should have a British National Health formulary produced by the DHSS and kept up to date. This would give prescribing information and comparative cost of generic and trade preparations. Clinical freedom must obviously be cherished and this applied to freedom of prescribing. However, freedom must be accompanied by responsibility and accountability. We believe that, unfortunately, at the moment in general practice there is an element of irresponsibility, perhaps owing to ignorance and laziness. Perhaps we should have DHSS "reps" competing with the pharmaceutical industry in trying to "sell" GPs the idea of prescribing economy. At the moment regional medical officers are concerned only with those doctors whose prescribing costs are above the average, but this is having little impact because the average prescribing costs are unnecessarily high. The Secretary for Social Services recently remarked in Parliament that we are now in an era where patients expect "a pill for every ill." GPs are very aware of this and many are taking a more active role in health education. A few well-chosen words will often be of more therapeutic value and certainly do much less harm than many prescribed pills, and if drugs are indicated perhaps we as GPs can ensure that unnecessary extravagance is avoided.

MONTE LUBEL
A K SINHA
S K MUKHERJEE
M HEATH

Westcliff on Sea, Essex

- ¹ *Daily Telegraph* (leading article) 27 November 1979, and subsequent correspondence.

Illegal immigration and medical confidentiality

SIR,—Under the Immigration Act of 1971 illegal immigration and overstaying are criminal offences.¹ A doctor may break