Neisseria meningitidis or other forms of acute bacterial meningitis.¹

"Pretreatment" of patients with bacterial meningitis is rendering in a significant number of cases blood and cerebrospinal fluid cultures (and in many also smears of CSF) negative for bacteria; these effects have been most notable in patients with *N meningitidis* meningitis.² Although in most patients with bacterial meningitis who have been "pretreated" the initial lumbar puncture on admission to the hospital still disclosed polymorphonuclear predominance, hypoglycorrhachia, and elevated levels of protein in CSF (which is most compatible with bacterial meningitis), occasionally pretreatment has resulted in CSF findings compatible with "aseptic" meningitis.³ Even by using counter-immunoelectrophoresis, the problem of differentiating aseptic from bacterial meningitis in patients with equivocal CSF findings and negative bacteriological studies has not been resolved. This is particularly relevant when commercial antisera have been used for counterimmunoelectrophoresis, since cross-reactions and false positives have occurred, making the interpretation of results difficult at times.⁴ It should also be mentioned that the association of skin petechiae with meningitis is not pathognomonic of *N meningitidis* meningitis, since haemorrhagic skin manifestations have been observed in *Acinetobacter* (*Mima polymorpha*), *Staphylococcus aureus*, and other forms of bacterial meningitis^{5,6} and even in "aseptic" meningitis due to enteroviruses.⁷

Finally, the practice of "pretreatment" of patients with bacterial meningitis prior to hospitalisation has never been shown to reverse the progressive deterioration of untreated disease. We reviewed 1316 cases of community-acquired purulent meningitis admitted during the antibiotic era, and found that antibiotics had been given prior to admission to 54.6% of patients.⁸ There were 103 fatalities, 70.8% of which occurred within the first 48 hours of hospitalisation. Among the 103 fatalities, 49.5% had been pretreated with antibiotics. Thus the practice of pretreatment with suboptimal doses of antibiotics prior to hospitalisation is to be condemned.

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¹ Underman AE, Overturf GD, Leedom JM. *Disease-a-Month*, 1978;24:7-63.

² Geiseler PJ, Nelson KE, Moses VK. *Clinical Research*, 1979;27:344A.

³ Converse GM, Gwaltney JM, Strassburg DA, Hendley JO. *J Pediatrics* 1973;83:220-5.

⁴ Finch CA, Wilkinson HW. *J Clin Microb* 1979;10:519-24.

⁵ Murray HW, Tuazon CU, Sheagren JN. *Arch Intern Med* 1977;137:844-7.

⁶ Fred HL, Allen TD, Hessel HL, Holtzman CF. *Arch Intern Med* 1958;102:204-6.

⁷ Lerner AM, Klein JO, Cherry JD. *New Engl J Med* 1963;269:678-85, 736-40.

⁸ Geiseler PJ, Nelson KE, Levin S, Reddi KT, Moses VK. *Rev Inf Dis*, in press.

*The "blind" administration of oral antibiotics to the febrile, sick child, which often continues for two to three days, in inadequate dosage, should not be confused with the injection of a single therapeutic dose of penicillin at the time the child is sent to hospital. While agreeing that the former may mask the diagnosis of pyogenic meningitis we do not believe that one dose of antibiotic will appreciably alter the cell count or biochemistry of the cerebrospinal fluid over a period of an

hour or so. In some patients, however, meningococcal disease follows a relentless course and may be fatal despite apparently adequate chemotherapy. General practitioners do often administer a single dose of penicillin and this is found to be helpful. In one hospital that recently reviewed 113 consecutive patients admitted with meningococcal meningitis, only three died, a mortality of 2.6%. A haemorrhagic rash may indeed occur in meningitis caused by organisms other than the meningococcus. This, however, appears to be uncommon.—Ed, *BMJ*.

"The Division in British Medicine"

SIR,—Dr S L Loudon (9 February, p 391) has written a thoughtful review of my book *The Division in British Medicine*, and I wish to respond to the criticisms he made.

Most of the faults he finds deal with the years before 1911 and after 1948, periods which I did not attempt to cover comprehensively. Indeed, at the moment I am working on a sequel which will examine the whole period from 1948 in greater detail. Some of his criticisms, moreover, are not clear and the most important reflects a basic misunderstanding. Dr Loudon suggests that I did not give sufficient attention to the influence of the referral principle—but he fails to see that the establishment of this principle was a symptom, not a cause, of the division in British medicine. Furthermore, though the principle was established in the nineteenth century, it did not become fully operational until the Health Service was created in 1948. Dr Loudon does not seem to be aware of the many difficulties encountered before it could be made to work. Until 1948 the GP did not always retain the patient but sometimes lost him in a competitive struggle with consultants and specialists.

With regard to the query raised about the relative influence of the various medical-political groups, I thought my study made clear the central importance of the BMA in the development of health policy. In fact, it was the BMA—in conjunction with the TUC—that set forces in motion which led to the Beveridge Report. This is the most surprising point to emerge from my study and it is one that should be emphasised to a BMA audience. From my book it can be seen that, to a large extent, it was the doctors themselves who created the National Health Service and other aspects of the welfare state. This has great relevance to current problems because the BMA has recently come out in favour of an insurance-financed service. It would be ironic, indeed, if after spending so many years trying to abolish an insurance system the BMA managed to recreate one in the 1980s.

To understand how the alliance between the BMA and the TUC arose, one has to examine closely the development of the panel system and its intimate links with workmen's compensation. This is why my study focuses primarily on the panel doctor. Other aspects of general practice are discussed in less detail because they did not exert the same historical influence. The panel system, in all its essentials, is still with us today—whereas the wide-ranging group practice that flourished between the wars changed character after 1948. Moreover, the panel system occupied a much more important place in the provision of medical care than many have thought. Of the 20-odd thousand GPs in Britain in 1936,

19 000 were on the panel and, before the National Health Insurance Act ended in 1948 they treated half the population.

So far as my comments about social class are concerned, Dr Loudon attaches more significance to them than I intended. Social class differences within the profession were important in the nineteenth century—that is generally accepted—but the main influences in the twentieth century undoubtedly arose from State intervention and the advance of specialisation. My study is concerned primarily with the former but I did not neglect the effect of advancing specialisation (see pp 117, 155, and 163 in particular).

It is unfair to suggest, therefore, that I saw "the hardening of the division entirely as the result of a bitter conflict between the wars." The words "bitter conflict" are Loudon's, not mine. I do not think that the conflict was all that bitter because GPs did not put up much of a fight to enter the hospital world. Most were content to stay in their surgeries.

As for the blank cover on the dustjacket, it appears only on review copies. The completed cover was not ready at the time the book was sent for review.

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Preoccupation with hypertension

SIR,—My fellow Bristolian, Dr J A Moss (26 January, p 251), is worried about the number of "medicated neurotics" from over-diagnosis and over-treatment of hypertension.

A recent leading article (5 January, p 4) indicates that casual blood pressure readings may often be valid, and in any case "catching" the younger male with a borderline blood pressure gives one the opportunity to "grill" him about smoking, weight, and proper exercise, which one needs to be doing whether the patient has a true hypertension or not. Admittedly, one gets some puzzled reactions from the men who "only came in" for their sore throat or sprained wrist, but eventually they even produce a word of thanks for the aggressive approach. After a few months of possibly unnecessary treatment, the patient is delighted if the pills can be stopped, and he is then persuaded to attend twice a year, which I fondly believe gives him an added incentive towards good health behaviour.

The patients don't look the slightest bit neurotic about it, not in East Bristol anyway.

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Blood pressure and ambient temperature

SIR,—Your recent series on blood pressure measurement has emphasised the need for clinicians and epidemiologists to estimate the true biological value of blood pressure as accurately as possible, the former in the interests of the "borderline" patient, the latter to determine more precisely relative and attributable risks for the individual and the community. Ambient temperature has often been reported as affecting observer error. Recently we had the opportunity to confirm this finding in a review of data collected in a longitudinal, multiphasic screening study of the employed and general populations in west central Scotland.^{1,2}

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.

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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.

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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.

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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