Membrane Disease."[1] Unfortunately, you have seriously misrepresented our results. Our survival figures do not refer to "overall survival rate," they refer to the survival rate for infants who are severely affected by the illness, as defined in the article. Our overall survival rate is much higher.[2] Furthermore, the numbers you quote are wrong. The survival rate for all seriously affected infants in 1970-2 was 69%, not 63%; and the survival rate for the ventilated ones in 1967-9 was 11% and in 1970-2 49%, not 15% and 44% as stated in your article.—We are, etc.,

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**Our leading article recognized the high standards of the neonatal unit at University College Hospital, and we regret that these errors gave a false impression of the results of treatment there.—ED., *B.M.J.*

Jaundice after Halothane

SIR,—There is no doubt that the paper by Dr. W. H. W. Inman and Professor W. W. Mushin (5 January, p. 5), and the associated letter circulated by the Committee on Safety of Medicines to all doctors, dentists, and pharmacists within the United Kingdom has changed the practice of clinical anaesthesia both in Britain and abroad. There is equally little doubt that such change has not necessarily been to the advantage of the patient. The paper by Dr. Inman and Professor Mushin has been widely criticized—a reflection of the major flaws in the data and arguments presented. It is possible that the allegation of a positive direct association between multiple exposures to halothane and postoperative liver damage, supported by Dr. Inman and Professor Mushin, may eventually be substantiated—indeed, we have never dissented from the view that the *possibility* of such a direct relationship exists. However, the evidence presented in their paper did not entitle the authors to draw such a conclusion.

By far the most disquieting feature of this unfortunate affair has been the attitude of the Committee on Safety of Medicines. Implicit in the effective function of this important body is that it must have the confidence, respect, and trust of the medical profession. The position of the present committee in this respect must now be a matter for debate. Why were the members of the committee unable to discern the major limitations of the data on which the analysis by Dr. Inman and Professor Mushin was performed—limitations so readily made apparent in the correspondence columns of this journal? Why did the committee not seek expert opinion before taking the drastic step of issuing its inopportune letter? Perhaps it did?

The committee has maintained an obdurate silence despite the many and serious doubts which have been cast on the validity of Dr. Inman's and Profesor Mushin's conclusions. Furthermore, the committee has ignored not only the temperate and carefully worded statement by the Medical Research Council (27 July, p. 268), but also pleas for the circulation by the committee of a moderated version of its document by the Anaesthetic Research Society, the Association of Professors of Anaesthesia (with one notable abstention), and the Anaesthetists' Subcommittee of the Central Committee for Hospital Medical Services.

The functions of the Committee on Safety of Medicines are fundamentally too important to be prejudiced by such behaviour. We respectfully suggest, therefore, that the present members should offer their services for alternative, less demanding activities.—We are, etc.,

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Dr. Mikhail Shtern

SIR,—I wish to draw the attention of professional colleagues to the appalling case of Dr. Mikhail Shtern of Vinnitsa, Ukraine. The details are as follows.

Dr. Shtern is a leading endocrinologist in Vinnitsa. In November 1973 his son applied for a visa to go to Israel and subsequently Dr. Shtern was advised to forbid his son to emigrate. He refused and consequently lost his job. In May of this year his appartment was searched by the K.G.B. Dr. Shtern was arrested and imprisoned. Every attempt was made to find something to accuse him of. These attempts failed. Finally the authorities resorted to the mediaeval accusation that Dr. Shtern had poisoned some of his young patients. After much difficulty they have found "witnesses" to provide evidence and a trial was due to start on 2 December. This is reminiscent of the infamous "Doctors' Plot" of 1952 and cannot but cause grave apprehension. In addition, Dr. Shtern has been very ill in prison and has had recurrent haemoptyses.

I am sure we are all saddened at the treatment of a professional colleague in this way and I ask for support for him in his difficulties.—I am, etc.,

JOHN COHEN

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Value of Hospital Case Notes

SIR,—Dr. A. A. Lewis does himself and his colleagues in hospital considerable injustice in his letter (23 November, p. 468) on the matter of general practitioners' access to hospital case notes. I recognize and respect his feelings on this subject, but he must not allow the facts to be obscured. He knows very well, for he is on the district medical committee, that it is the district hospital medical committee and not the staff of St. Mary's Hospital alone that has incurred his anger. He knows very well that the hospital staff committee welcomed visits by G.P.s to their patients when in hospital and agreed to free access to the case notes *with the permission of the consultant concerned.* He ignores the very proper reservations of a few consultants in sensitive specialties and instead claims a divine right for the G.P. to read, without consultation, the records made by a specialist colleague. There are some things a patient, rightly or wrongly, wishes to keep from his G.P. but tells a specialist and I am sure there are many things the patient tells his family doctor but keeps from the hospital staff. We both have to respect these confidences and yet work together to help those who put their trust in us.

Dr. Lewis knows that no affront to G.P.s was intended—quite the reverse—and he should also know that working as a team sometimes involves accepting that opinions can differ.—I am, etc.,

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Diagnostic Test for Multiple Sclerosis

SIR,—The absence of technical detail in the commnication from Foster *et al.*[1] denying the specificity of the linoleic acid depression (L.A.D.) test for the diagnosis of multiple sclerosis (M.S.) makes it difficult to analyse the possible sources of the discrepency between their findings and those in the original positive report.[2] However, one of us (B.K.S.) made the actual measurements in Foster *et al.*'s work and is aware of certain differences which obtained in the two series of studies.[3] It now seems that a major factor was their use of tuberculin purified protein derivative (P.P.D.) instead of thyroid as test antigen. The former would have been quite in order had the test animals been free from "spontaneous" sensitization.

We have now repeated a double-blind trial using thyroid (F1 fraction) as well as P.P.D. (as used in the Foster experiments) since the latter has antigenic determinations in common with encephalitogenic factor (E.F.)[4] and guinea-pigs become sensitized to both if

Percentage Reduction in Response to Antigen Brought about by Linoleic Acid (LA) in M.E.M. test with Lymphocytes from Two M.S. Patients and a Normal Control using "Spontaneously" Sensitized and Non-sensitized Guinea-pigs as Source of Indicator Macrophages.*

Antigen	Sensitized guinea-pig			Non-sensitized guinea-pig
	Patient 1	Patient 2	Control	Patient 1
P.P.D.	43·6	32·7	75·5	91·4
Thyroid (F1)	95·0	91·4 (88·0)	51·0 (45·1)	89·7 (84·4)
	Animal Sensitization (Diengdoh and Turk[8])			
E.F.	8·4	—	8·4	—
P.P.D.	6·6	7·8	6·9	1·2

* % reduction = $\frac{\text{\% slowing with antigen} - \text{\% slowing with L.A. + antigen}}{\text{\% slowing with antigen}} \times 100$

Figures in parentheses are those obtained on aliquots by another observer using a different cytopherometer.

exposed to antigens of banal viruses such as influenza.[5 6] Macrophages from animals so sensitized constitute a faulty indicator system for human lymphocyte-P.P.D. interaction. We have, however, found that even with guinea-pigs which have not been rigorously shielded from "spontaneous" sensitization and so show clear evidence of sensitivity to E.F. and P.P.D. it is still possible to obtain positive results in the L.A.D. test if thyroid is used as test antigen for the human lymphocytes instead of P.P.D. Indeed, if the same M.S. lymphocytes are tested with both thyroid and P.P.D., then the high result characteristic of the disease is obtained with thyroid but not with P.P.D. Results with the latter seem to be randomly distributed depending upon a number of factors not as yet studied. Two examples from our protocols are set out in the table. It will be seen that when an animal which is not presensitized to E.F. and P.P.D. is used as the source of indicator macrophages the customary high result is found with both P.P.D. and thyroid. When, however, a presensitized guinea-pig is used for the macrophages then the high result is obtained only with the unrelated thyroid antigen.[1] All these experiments were carried out with the original macrophage electrophoretic mobility (M.E.M.) test.[2]

The importance of these results is that they (1) underline the need for the use of guinea-pigs free from "spontaneous" sensitization, (2) show that it is possible for those who do not have access to a protected source of anmials to carry out M.S. testing with thyroid antigen, and (3) explain the difficulties experienced by Foster *et al.* in their work with P.P.D.—We are, etc.,

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8 Diengdh, J. V., and Turk, J. L., *International Archives of Allergy*, 1968, **34**, 297

All Change

SIR,—The light-heartedness implicit in the heading you award to Dr. H. R. Rollin's letter (9 November, p. 341) epitomizes an inadequate appreciation of the danger in a situation in which administration loses sight of its original purpose to improve the efficiency and efficacy of the artisans it administers and becomes an end in itself.

St. Mary's Hospital, Hampton, to which Dr. Rollin refers in his letter, has seen changes of catchment area within the past five years from Springfield Hospital to Horton Hospital and now again to Long Grove Hospital. These changes have taken place without any reference to local needs, requirements, or wishes, the only reason for them being a desire to tie in with boundaries of one kind or another. The time must surely come when the people affected by these administrative manipulations will simply refuse to co-operate any longer. Let the authorities therefore take notice of this warning and ensure that in the future adequate consultation takes place at *all* levels.—I am, etc.,

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**Neither we nor other long-suffering users of public transport ever hear the cry "All change!" with anything but a heavy heart. —ED., *B.M.J.*

Lincomycin and Clindamycin Colitis

SIR,—Your leading article entitled "Lincomycin and Clindamycin Colitis" (12 October, p. 65) discussed the incidence of pseudomembranous colitis occurring during therapy with the lincomycins. In our first report[1] 10 years ago of studies with lincomycin hydrochloride diarrhoea occurred in two out of 24 patients receiving the antibiotic. In a larger series[2] of 65 patients treated with lincomycin diarrhoea occurred in eight patients, but in only two was it severe enough to necessitate stopping treatment. Fifty-two of these patients had bone or joint infections. The mean duration of treatment in patients with acute osteomyelitis was 3·3 months and 5·4 months in those with chronic infections. More recently[3] we reported the results of treatment with clindamycin of 50 patients, only one of whom developed diarrhoea. A total of 129 patients were included in these three studies (10 patients were included in two of the reports) and diarrhoea occurred in only 11 (8·5%). It stopped immediately lincomycin or clindamycin was discontinued and in none was there evidence of pseudomembranous colitis.

To date we have treated a total of 50 patients suffering from bone or joint infections with relatively prolonged courses of clindamycin, the duration of therapy varying from six weeks to 12 months with a mean of 4·4 months. All were carefully observed for adverse reactions during therapy and followed up after treatment. Three (6%) had transient diarrhoea which cleared when the antibiotic was temporarily discontinued for 48 hours, but none developed pseudomembranous colitis.

Since our initial studies with lincomycin in 1963 and with clindamycin in 1969 we have now treated several hundred patients with these two antibiotics but have confirmed colitis associated with therapy in only one. This was in a 64-year-old man who developed diarrhoea while taking clindamycin for an ear infection. It is of interest that his wife developed diarrhoea before the onset of the patient's symptoms. The patient continued taking clindamycin after the onset of diarrhoea, and barium enema examination revealed ulceration of the ascending and proximal transverse colon. Treatment was started with salazopyrine, with satisfactory response and relief of diarrhoea.

Our experience with the lincomycins therefore differs from that of Tedesco and his colleagues,[4] who found an incidence of diarrhoea of 21% and of pseudomembranous colitis in 20 of 200 patients receiving clindamycin. Other investigators in the United States[5-7] and New Zealand[8] have reported a similar high incidence of diarrhoea and colitis during lincomycin or clindamycin therapy. The low incidence of both in our experience, even in patients receiving prolonged courses of clindamycin or lincomycin, suggests the possibility of a geographical difference in occurrence of these side effects such as has been reported with chloramphenicol. The simultaneous development of diarrhoea in the wife of our patient suggests that an infective agent could trigger off the diarrhoea which might then be perpetuated by clindamycin. In this context it would seem reasonable to avoid the linocomycins in patients with bowel disease and to warn patients to stop treatment immediately diarrhoea develops during lincomycin or clindamycin therapy. Care might also be taken in the elderly because of the possibility of ischaemic colitis or diverticulitis in this age group.—I am, etc.,

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SIR,—We were interested to read your leading article (12 October, p. 65) and the subsequent correspondence. We should like to bring to notice the case of a woman who recently died here of this condition. The patient, aged 60, was admitted with gangrene of the toes and had to have her leg amputated after a femoropopliteal bypass operation had failed. She was treated for a chest infection with lincomycin and Kefzol for three days. Six days after the discontinuation of the antibiotics she developed severe diarrhoea, and sigmoidoscopy revealed complete involvement of the rectal mucosa by thick yellow plaques. Diarrhoea continued until she died of bronchopneumonia some days later. At necropsy histologically typical pseudomembranous colitis was found, involving the entire large bowel from ileocaecal valve to rectum.

Our patient was admittedly in poor general condition, but severe colitis can arise in much younger, fitter people and may lead to perforation or the need for resection. Your leading article refers to a number of previously reported deaths. We were disturbed to see that Mr. D. H. Wilson and Drs. W. J. Cunliffe and S. G. Tan (2 November, p. 288) are using these drugs for preoperative prophylaxis and acne vulgaris respectively. We agree with the implications of your article that they should be prescribed only for bacteroides infections or serious infections for which other antibiotics are not appropriate. This approach would do much to avoid unnecessary morbidity and mortality.—We are, etc.,

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