to the drug. However, today I received in the post a new data sheet on cefamandole nafate (Kefadol)—the most recent addition to the ever-growing ranks of cephalosporins—and was disturbed to find that it contained a fundamentally important statement that is contradicted by reports available seven months ago. The antibiotic is described in the data sheet as being "resistant to degradation by penicillinases from *Staphylococcus aureus* and by β -lactamases from certain members of the enterobacteriaceae"; moreover, the promotional letter which accompanied the sheet states unequivocally that "cefamandole has greater resistance than earlier cephalosporins to β -lactamases."

In reality my colleagues and I have shown that cefamandole is highly susceptible to β -lactamases from both Gram-positive and Gram-negative bacteria with the exception of the relatively unimportant type Ia enzyme of *Enterobacter cloacae*, to which the antibiotic possesses a modest degree of resistance.¹ In contrast, greater stability to most enzymes is a feature of some of the well-established cephalosporins, notably cephadrine and to a lesser extent cephalexin. The findings in relation to the enzymes from Gram-negative bacteria have been corroborated by Vuye and Pijck,² who concluded that "cefamandole nafate displayed the highest vulnerability among the cephalosporins tested against the broad-spectrum enzyme" (IIIa or TEM-type). The ability to produce this clinically most important enzyme has evidently been transmitted by plasmids from *Escherichia coli* to the gonococcus and *Haemophilus influenzae* in recent years.³ This alarming trend is likely to negate the one undoubted advantage that cefamandole possesses over other cephalosporins—its enhanced activity against fully sensitive strains of *H. influenzae*.

Unfortunately the manufacturers of this antibiotic are not the only authoritative source of potentially misleading information; in a very recent general review on antibiotics we read that cefamandole is "extremely stable to β -lactamases, especially those produced by Gram-negative organisms."⁴ The general confusion surrounding the cephalosporins has been greatly heightened by the fact that the company in question now markets four of these antibiotics simultaneously in Britain and at least six throughout the world (and yet another new one, cefuroxime, was introduced by a different company last month). A rational choice in this group depends largely on antibiotic stability to β -lactamases.⁵ Cefamandole fails on this score, but several other essential considerations also apply.⁶ In particular, pharmacokinetic features are very important. However, again the picture presented by cefamandole is not very promising since it is relatively highly protein-bound and has a short half life in the body and a relatively low volume of distribution.⁷ This particular "second-generation" cephalosporin seems, alas, ill-qualified to replace the more sprightly of its older relatives.

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¹ Geddes, A, *Medicine* (3rd series), 1978, No 3, p 155.
² Williams, J D, *Journal of Antimicrobial Chemotherapy*, 1978, 4, 109.
³ Selwyn, S, *Lancet*, 1976, 2, 616.
⁴ Gower, P E, and Dash, C H, *European Journal of Clinical Pharmacology*, 1977, 12, 221.

* * * We sent a copy of this letter to the medical adviser to the manufacturers of cefamandole, whose reply is printed below.—Ed, *BMJ*.

SIR,—As Dr Selwyn himself points out, not everyone agrees with his assessment of the stability of cefamandole to β -lactamases,¹ but the more important question is the extent to which such properties are relevant outside the laboratory. For example, later in Vuye and Pijck's paper is the statement that "cefamandole was shown to be by far the most active compound, a property that may probably compensate for the vulnerability of this compound to other resistance mechanisms." Also, in the article by Professor J D Williams is an admission that, unlike penicillins, a clear association of β -lactamase with resistance to cephalosporins is often not obvious even in vitro and that correlations between in-vitro tests and in-vivo results have yet to be established. Specifically in relation to *Haemophilus influenzae* there is, fortunately, clear evidence that strains which produce TEM-type enzyme do not show any increased resistance to cefamandole,² which must cast doubts on the relevance of tests showing cefamandole to be inactivated by that enzyme.

A recent editorial in the *Lancet*³ explained that there are at least three factors to be considered: (1) stability to β -lactamase, (2) penetration through the cell wall and periplasmic space, and (3) inherent antibacterial activity. It is a combination of these factors, not any one of them alone, which determines the effectiveness of cephalosporins; and there is ample evidence, which we would be happy to supply on request, that cefamandole is very well qualified to be considered for use in patients with appropriate infections and as a possible replacement for earlier cephalosporins.

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¹ Farrar, W E, et al, *Journal of Infectious Diseases*, 1976, 133, 691.
² Kattan, S, et al, *Journal of Antimicrobial Chemotherapy*, 1975, 1, 79.
³ *Lancet*, 1978, 1, 863.

The MRCP (UK) examination in Commonwealth countries

SIR,—Since taking up the post of professor of medicine in this university four months ago I have become acutely aware of the problems faced by my junior medical staff when they decide to sit the MRCP (UK) examination. This diploma is highly regarded in Malaysia and Singapore and, now that the Australasian college has changed its regulations, is the only internationally recognised higher qualification in medicine available to postgraduates in South-east Asia.

When I came to Kuala Lumpur I was under the impression that there was no barrier to trainee specialists sitting the part I examination locally, thus sparing them the enormous expense of a journey to the United Kingdom, which could then be deferred until they were ready to sit the part II examination and would allow them to undertake a period of

postgraduate training at the same time. I have since discovered, however, that the part I examination is held only once a year in Kuala Lumpur (Singapore candidates have also to come here for the examination). Thus in the event of failure (and this fate can befall even a very well-prepared candidate) he or she cannot sit the examination again locally for a period of 12 months. This, as can be imagined, places an immense strain on candidates and interferes seriously with their hospital training programme. All that is bad enough, but it has now come to my notice that the number of candidates admitted to the part I MRCP (UK) examination in Kuala Lumpur is restricted to 150 and that because of the demand for places the list is closed almost as soon as it is opened. Consequently many excellent candidates (and the standard of medicine in Malaysia and Singapore is not far behind that of the United Kingdom) are, through no fault of their own, being denied the opportunity of even sitting the part I examination.

I took up this matter with the president of the Royal College of Physicians of Edinburgh, who made the rather lame comment that because of administrative difficulties the number being allowed to sit the part I examination overseas is severely restricted. While I can appreciate that it might be difficult (although not impossible) to increase the number of part I examinations per year in countries like Malaysia, it would surely not be beyond the capability of the royal colleges to relax the restrictions imposed on the number of candidates. It cannot be much more difficult to collect and correct (by computer) 200 instead of 150 multiple-choice question papers.

In these days of declining British commercial influence it is very encouraging that British medicine and British medical qualifications should enjoy such a high reputation in this part of the world, and I feel sad that the royal colleges are apparently not prepared to make a positive effort to help young Commonwealth medical graduates and the medical schools which are training them by easing the present restrictions on the part I MRCP (UK) examination. This would, I suspect, be of much more practical value than "goodwill" visits by presidents to countries where these restrictions exist.

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The Rothschild principle

SIR,—In reviewing the results of applying the Rothschild recommendations to medical research (6 May, p 1167), you not only ignore what was just and sensible in Rothschild's criticism of the previous system but fail to make any constructive suggestions about how they might be met.

We are particularly concerned by at least one aspect of the manner in which the Medical Research Council categorises and organises its coverage of medical research and, as representatives of the British Paediatric Association, have expressed this long ago to the council. Although such important clinical areas as obstetrics and embryological and fetal growth are concealed by the incomprehensible title of the responsible "cell biology and disorders" board, these subjects do appear to be

¹ Imambaccus, Y, et al, in *Current Chemotherapy*, ed W Siegenthaler and R Lüthy, vol 1, p 495. Washington, D C, American Society for Microbiology, 1978.

² Vuye, A, and Pijck, in *Current Chemotherapy*, ed W Siegenthaler and R Lüthy, vol 1, p 492. Washington, DC, American Society for Microbiology, 1978.

³ *British Medical Journal*, 1977, 1, 1618.