East.⁵⁻⁹ Fifthly, far from having no side effects as stated by Dr Haworth, mepacrine in doses of 100 mg/day is well known to cause in a proportion of persons mental disturbances, aplastic anaemia, and dermatoses.¹⁰

Finally, not one but six of the seven signatories have recent experience of practising medicine in the tropics.

This brings us to the substance of our recommendations. In areas of chloroquine resistance our first recommendation would be Fansidar, but there is need for an alternative during pregnancy and for those sensitive to sulphonamides. In our view the risks from malaria are greater than the risks from twice-weekly Maloprim. Nevertheless, it is only fair to state that whereas our recommendations were made in conformity with those of a committee at the London School of Hygiene and Tropical Medicine, that committee decided at a subsequent meeting on 14 January to err on the side of caution and to recommend a once-weekly dose of Maloprim for those who need to take it. The subject needs further study. However, on the basis of our own and other people's experience we believe that the recommendations were the best available in the light of current knowledge.

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SIR,—Maloprim (pyrimethamine 12.5 mg and dapsone 100 mg) is both useful and not dangerous as implied by Dr James Haworth (3 January, p 70). Since 1968 it has been the means of controlling *Plasmodium falciparum* and *P vivax* infections throughout the rubber and oil-palm plantations under my supervision in South Johore. The populations concerned would be in the thousands and there are and have been no cases of agranulocytosis, neither have there been any cases of malaria in those taking Maloprim routinely, as directed.

Maloprim was the optimum drug combination chosen by the joint Thai-American expedition in South Thailand and was originally recommended by a visiting professor of WHO in 1968. The dose is still one tablet weekly, though the initial dose and final dose can be doubled. Maloprim effectively gives protection to all visitors to the malarial areas of the South-east Asia region, and is taken with complete safety.

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Group R streptococcal infection

SIR,—We were interested in the report (14 February, p 523) by Dr C H C Twort of a further case of group R streptococcal meningitis in a 61-year-old meat inspector. We have recently seen a case of septicaemia due to this organism in a 47-year-old abattoir worker and another case of meningitis in a 44-year-old housewife who had no history of contact with pig meat. Both recovered on treatment with penicillin but the woman had residual hearing loss. There has only been one previous report of group R streptococcal meningitis in a patient without a history of contact with pig meat: this was the case of a 61-year-old manager of a sawmill in Denmark in the first report of human group R streptococcal infection by Perch.¹

Zanen and Engel² have now analysed 36 cases of human group R streptococcal infection, 19 in The Netherlands, 11 in Denmark, five in England and Wales, and one in France. Peel *et al*³ report an additional case of septicaemia in a 51-year-old veterinary surgeon in Suffolk which responded to treatment with ampicillin. More disturbing, however, is the case reported by Shneerson *et al*⁴ of a 60-year-old West Indian worker in a dog-food factory who developed meningitis due to a group R streptococcus that was resistant in vitro to penicillin.

Group R streptococcal infections are increasing in frequency. Although they are undoubtedly an occupational hazard of pig meat handlers, we should like to stress that this is not invariably so, and that the organism may be resistant to penicillin.

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Recurrent renal calculi

SIR,—The leading article "Recurrent renal calculi" (3 January, p 5) was important, as it highlights a field where so far research efforts have not always pointed the way to clinical success.

A depressing aspect is the extremely high recurrence rate¹ of stones formed in association with infection of the urinary tract by urease-producing bacteria. The incidence of stone formation through infection is not as low as some reports² imply: 15-20%³ of all urinary stones may be due to infection, and a figure as high as 40% has been mentioned.⁴ In another article⁵ infection stone was not touched on, a point recognised by Will,⁶ who admits that it is the calcium oxalate stone that has received most attention.

Recurrence of infection stone poses a particular problem to the urologist. It is thought that stones recur frequently because residual microcalculi remaining after surgery harbour urease-producing bacteria, which go on to cause fresh deposition of magnesium ammonium phosphate (sometimes referred to as struvite).⁷ Thus a vicious circle can occur—infection leading to increased calculus forma-

tion, which may in turn need further surgical intervention. Inhibition of urease has been suggested as a means of preventing stone recurrence,³ but at present the only practical inhibitors are hydroxamates. All hydroxamates give positive results in conventional mutagenicity testing,⁸ and thus at present will be a cause of concern to drug-regulating authorities.

Much of the work on the inhibition of urease has been carried out by Griffith and his colleagues,³ who have concentrated on acetohydroxamic acid, which is at present undergoing restricted clinical evaluation.⁹ Other hydroxamates have been developed, but there is clearly a need for a non-toxic, non-mutagenic urease inhibitor which will be effective clinically for both prophylactic and therapeutic use in infection stones. Bacterial urease may also be implicated in such diverse human conditions as hepatic encephalopathy (due to ammonia production in the intestine) and dental caries, as well as pyelonephritis in cattle, which is caused by *Corynebacterium renale* (see review⁷). An effective urease inhibitor would thus have a wide application in the therapy of these conditions. Our own findings¹⁰ suggest that use of a urease inhibitor alone may be inadequate, and that a combination with an antibacterial agent may be more effective.

Thus research into prevention of infection stone follows entirely different lines from that successfully directed against metabolic stones, where the xanthine oxidase inhibitor allopurinol has been highly successful for specific indications. Obviously the need for an agent to deal in a similar way with infection stones is urgent.

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Haemophilus influenzae endophthalmitis

SIR,—Dr A R J Bosley and others (3 January, p 22) have drawn attention to *Haemophilus influenzae* facial cellulitis in infancy. The organisms were isolated by blood culture in these cases. We would like to report a case of *Haemophilus influenzae* endophthalmitis.

A previously healthy 20-month-old girl was admitted with a temperature of 40°C and malaise. General examination was normal, but she was noted to have a red right eye, a hazy cornea without ulceration, and a hypopyon which obscured the fundus. The left eye was normal. Conjunctival swabs grew *Staphylococcus aureus*. However, *Haemophilus influenzae* type B was subsequently isolated in all three bottles of the blood cultures taken on admission. She was treated with subconjunctival gentamicin and with ampicillin, cloxacillin, and gentamicin systemically. Topically she received chloramphenicol, atropine, and later betamethasone eye drops. She made a satisfactory recovery.

As there was no corneal ulceration or external injury, this endophthalmitis was