co-trimoxazole has only a bacteriostatic action—as was observed in their own experiments.

Both their experiments and their conclusions can, however, be criticized from several points of view. A bactericidal action cannot be determined in the liquid medium used by these authors (Oxoid nutrient broth no. 2), presumably because it contains thymidine, as do a variety of commercially available media.³ The bactericidal efficacy of co-trimoxazole is inseparably connected with the available thymidine (and thymine) concentrations. Though there are only a few data published on the thymidine content of human tissues and fluids we should nevertheless like to draw some conclusions from our present knowledge.

In recent experiments with *Escherichia coli* we found that the addition of 0.05 µg/ml thymidine prevents a bactericidal effect of co-trimoxazole in human blood and urine. Thymine is 10 to 100 times less effective. Microbiological determinations showed that thymine and thymidine concentrations are below 0.1 and 0.05 µg/ml respectively in the blood and urine from healthy persons—quantities insufficient to antagonize a bactericidal effect. This is in accordance with the opinion of other investigators, who have found that thymidine concentrations in mammalian tissues are extremely low,^{4,5} a fact which is further supported by the well known very short half-life of administered ³H-thymidine.⁶ The possibility remains, however, that these conditions change during infections.

Treatment of bacteria with aminopterin or trimethoprim is a widely used selective technique for the isolation of thy⁻ mutants, which are frequently obtained in the presence of thymine.⁷ This is, however, exactly what one would expect to occur under treatment with co-trimoxazole, assuming that thymidine is present. Thy⁻ mutants should develop very rapidly and lead to an appreciable number of clinical failures. This sequence, however, has not been observed and until recently the occurrence of such mutants has not been reported in spite of the widespread use of the drug for several years.

The observation that only wild type strains were isolated after withdrawal of co-trimoxazole in those few cases where co-trimoxazole resistant thy⁻ mutants appeared² underlines our assumption that thy⁻ strains do not normally survive in vivo. Though Okubadejo and Maskell² did not recover any such mutants. Such isolates, however, would than 100 patients under long-term therapy with co-trimoxazole, it may be expected that the isolation of thymine auxotrophs during co-trimoxazole treatment may occur more frequently in the future, if one looks for such mutants. Such isolates, however, would not necessarily mean co-trimoxazole-resistance or therapy failure.

The selection of thy⁻ mutants in vivo which are able to survive and are due to the use of co-trimoxazole is obviously a rare event of little importance for clinical therapy, even if one assumes that many of these mutants may have been overlooked in the past¹ owing to their atypical growth characteristics. This is in accordance with the remarkably low rate of co-trimoxazole-resistance^{8,9} and the constant high efficacy of this drug in clinical use. The incidence of drug failures due to such occurrences is

therefore not expected to increase in the future.—We are, etc.,

RUDOLF THEN
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Basle

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- 3 Koch, A. E., and Burchall, J. J., *Applied Microbiology*, 1971, 22, 812.
- 4 Cleaver, J. E., in *Frontiers of Biology*, ed. A. Neuberger and E. L. Tatum, vol. 6, p. 60. Amsterdam, North Holland Publishing Company, 1967.
- 5 Jaffe, J. J., McCormack, J. J., and Meymarian, E., *Biochemical Pharmacology*, 1972, 21, 719.
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- 7 Bertino, J. B., and Stacey, K. A., *Biochemical Journal*, 1966, 101, 32c.
- 8 Fruensgaard, K., and Korner, B., *Chemotherapy*, in press.
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Battered Children

SIR,—It is disturbing that in the eight issues following your leading article on battering (13 October, p. 61), only one correspondent (24 November, p. 493) has queried your statement that the family doctor's first duty is to refer a child to hospital in case of suspicion.

There may be a moment in time when the disturbed people who act out their personal difficulties in this violent fashion recognize that they need help. It is just possible that by contacting a sympathetic and non-judgemental counsellor at this critical moment they can be reached and helped more meaningfully in terms of the total problem than by referral to another institution or one of the authoritarian agencies. One never knows when tragedy has been avoided.

One will always wonder which alternative could have provided the greater good to the greatest number. Hard and fast rules have no place in the management of this difficult problem.—I am, etc.,

M. S. LANE

Rushden, Northants

The Dog in Our Midst

SIR,—At long last Dr. O. A. Borg and Professor A. W. Woodruff have provided us with alarming evidence that the dog may not be man's best friend but a reservoir of infection causing blindness and at times death to his master (24 November, p. 470). Their paper, reporting that about one-quarter of soil samples from public places in Britain contained the ova of toxocara and that all incubated samples produced viable embryos, gives rise to deep concern about our prevalent attitude towards dogs. Perhaps the most horrifying aspect is that the vast amount of contamination is not on soil, where it can be presumed that some of the faecal organisms are destroyed by soil bacteria, but on the large impervious surfaces of our roads and pavements, remaining for considerable periods in dry weather.

Every year we spend millions on sanitation, hygiene, and drinking water, pass laws to deal with pollution in rivers, air, and food, and demand that noise should be controlled and streets kept free of litter. The sacred dog is allowed to foul at his leisure so that we are exposed to all types of infestation, hydatidosis, tuberculosis, leptospirosis, and salmonellosis to say nothing of the possibilities of viral infection. Surely the time has now arrived when we should demand better legislation to protect us from man's best friend.—I am, etc.,

E. G. CLARK

Wollaton, Nottingham

Points from Letters

Medical Immigration

Dr. M. M. HASAN (Member, Executive Committee, Redbridge Stratford Division, B.M.A.) writes: The letter from Dr. J. N. Docherty (22 December, p. 735) on the above subject cannot be allowed to go unchallenged, especially when he has used his position as Press Secretary of a B.M.A. Division. These uninformed comments with a racial flavour have become almost a fashion recently. He says in essence that a loss of 2,000 British doctors during the last five years is solely due to poor pay and this is because the "politicians" can obtain "cheap" and "ill-trained" foreign graduates to cover up the vacuum. How dare the G.M.C. accord registration to these inferiors?

Let us be clear about the identity of the unfortunate men and women to whom he refers, who are not Irish or Continentals but are mainly drawn from the countries of the Indian subcontinent. It is a slur to the good name of these countries. May I ask what personal experience Dr. Docherty has of the training methods that obtain in these foreign universities? . . .

Dr. K. RAGHAVAN (Edinburgh) writes: I

read with deep regret the letter from Dr. J. N. Docherty (22 December, p. 735) . . . If British doctors need more pay, let them fight it out in a rational and honourable way, without slandering foreign medical graduates. I hate to imagine what would happen to the National Health Service if it were not for the services of these same doctors, whom he calls "cheap" and "ill-trained". While I admit that all foreign doctors may not be highly educated, so also all British doctors are not brilliant. For every good British doctor, there is one equally good foreign doctor. I hope Dr. Docherty can back up his statement with facts and figures, since it is going to lose the goodwill of many foreign doctors in Britain.

As for the E.C.F.M.G. examination, I know of many doctors, including myself, who took this entrance examination to the United States and yet decided to come to Britain for academic reasons. The passing of this examination is no criterion whereby to judge the professional ability of a doctor. I also know of many doctors who went to the States after serving in the National Health Service, and not without some regret. . . .