Trial of Mefruside

SIR,—Drs. W. H. R. Auld and W. R. Murdoch (25 December 1971, p. 786) have clearly demonstrated the differing actions of mefruside and frusemide. The diuretic response to mefruside is similar to that of hydrochlorothiazide and other medium-acting thiazides both in its time course and in the pattern of electrolyte excretion, particularly the high concentration of sodium and chloride in the urinary increment. They are therefore on solid ground in predicting that mefruside, like the thiazides,[1] will probably exert a more powerful hypotensive action than frusemide alone.

Some caution is needed, however, in interpreting their comparison between the drugs as diuretics. The authors state that they compared the drugs in "equal" doses. The 50-mg doses were certainly equal in weight but by no means equivalent. Weight-for-weight comparisons between diuretics are not of great importance to clinicians. By this criterion cyclopenthiazide is about a thousand times more powerful than chlorothiazide, but the two drugs have similar effects in optimum dosage and in practice the choice between them is made on grounds of cost and convenience not of potency.

Drs. Auld and Murdoch state that the maximum effective dose of mefruside is about 100 mg. If mefruside has a similar dose-response curve to other diuretics the 50 mg dose they administered must have produced a nearly maximum effect. The dose-response curve to frusemide has never been fully established in men with normal glomerular filtration rate, because of the profound diuresis produced by even submaximal doses. The maximum effective dose is certainly well in excess of 400 mg.[2] The 50-mg dose of frusemide used in this study was therefore a comparatively small one.

To date frusemide is unique among the benzene sulphonamide derivatives in having sites of action in the tubule additional to those of the thiazides,[3-5] a much greater maximal activity than the thiazides,[6] and consequently a very useful diuretic activity even in the presence of severely depressed renal function.[7 8] No evidence has yet been presented to suggest that mefruside shares these properties.—I am, etc.,

DAVID KERR

Department of Medicine,
Wellcome Research Laboratories,
Royal Victoria Infirmary,
Newcastle upon Tyne

1 Anderson, J., Godfrey, B. E., Hill, D. M., Munro-Faure, A. D., and Sheldon, J., *Quarterly Journal of Medicine*, 1971, **40**, 541.
2 Kleinfelder, H., *German Medical Monthly*, 1963, **8**, 459.
3 Suki, W., Rector, F. C., and Seldin, D. W., *Journal of Clinical Investigation*, 1965, **44**, 1458.
4 Aukland, K., Johannesen, J., and Kill, F., *Scandinavian Journal of Clinical and Laboratory Investigation*, 1969, **23**, 317.
5 Rado, J. P., Szende, L., Tako, J., Bános, C., and Borbély, L., *Journal of Clinical Pharmacology*, 1969, **9**, 99.
6 Robson, A. O., Kerr, D. N. S., Ashcroft, R., and Teasdale, G., *Lancet*, 1964, **2**, 1085.
7 Elliott, R. W., Kerr, D. N. S., and Lewis, A. A. G., *Postgraduate Medical Journal*, 1971, **47**, (*Suppl.* April).
8 Allison, M. E. M., and Kennedy, A. C., *Clinical Science*, 1971, **41**, 171.

Screening for Mental Disorder

SIR,—The leading article on this subject (25 December 1971, p. 763) describes the increasing interest being taken in psychiatric screening. Recently we have carried out mental health screening procedures in both local authority and general practice multiple-screening clinics. In Rotherham county borough (population 87,000) recognized screening procedures for certain physical illnesses were originally offered,[1] and it was felt some attempt should be made to detect mental illness, a major public health problem, at such clinics. A short inventory of 13 items together with seven buffer items had been shown to distinguish effectively between normal people and psychiatric patients, regardless of diagnosis.[2]

A total of 4,319 people took this mental health test at the Rotherham screening clinics in 1966 and 1967. The value of the test results was investigated by means of a psychiatric interview and further personality assessment using the Minnesota Multiphasic Personality Inventory (M.M.P.I.). A high degree of agreement was found between the screening test results and these further investigations. In 1966 the clinic was organized on an open-door principle and clients shopped around to choose the test they wished to take. This meant that known psychiatric patients were included. In 1967 the clinic was by appointment only and clients were asked about previous mental illness, and if the answer was in the affirmative, they were excluded. The accuracy of the test was equally high on both occasions.[3]

Mental health screening was also used in a country general pactice multiple-screening clinic.[4] On this occasion 961 clients took the mental health test. The test was again checked by the M.M.P.I. and the general practitioner's assessment. The validity was again found to be high, as in the Rotherham studies.[5] The studies quoted give details of the problems involved in identifying false positives and false negatives. We found that the mental health test was most sensitive in registering conditions of anxiety, depression, and social difficulties. The test, not surprisingly, uncovered a lower than expected rate of schizophrenia and psychopathic disorder.

It is sometimes suggested that screening for mental health is not a practical proposition. Nevertheless, the magnitude of the mental health problem is such that techniques should be investigated. The test referred to here is simple and cheap to use. It has been found to be useful in local authority and general practice clinics involving over 5,000 subjects. Though agreeing with Eastwood that screening for psychiatric disorder remains in an experimental phase, we feel that in selected practices where there is sufficient enthusiasm psychiatric screening can be included.—We are, etc.,

R. J. KERRY
J. E. ORME

Northern General Hospital,
Sheffield

1 Donaldson, R. J., and Howell, J. M., *British Medical Journal*, 1965, **2**, 1034.
2 Orme, J. E., *British Journal of Medical Psychology*, 1965, **38**, 269.
3 Donaldson, R. J., Kerry, R. J., and Orme, J. E., *Acta Psychiatrica Scandinavica*, 1969, **45**, 198.
4 Evans, S. M., Wilkes, E., and Dalrymple-Smith, D., *Journal of the Royal College of General Practitioners*, 1969, **17**, 237.
5 Kerry, R. J., Orme, J. E., and Wilkes, E., *Practitioner*, 1970, **205**, 217.

Trimethoprim-sulphamethoxazole in Typhoid Fever

SIR,—The article by Drs. J. N. Scragg and C. J. Rubidge on trimethoprim-sulphamethoxazole in typhoid fever in children (25 September, p. 738) prompts us to report similar effects of the use of this drug in the treatment of typhoid fever in a number of our African patients. Of 92 cases, three, all children under 10 years, exhibited neutropenia in the peripheral blood during therapy.

In one case the neutropenia was complete, but on continuous treatment recovered to 17% of a total white blood count of 6,150/mm³. In another case an absolute neutropenia was noted without any apparent effect upon the remaining series apart from the fact that approximately 20% of the cells were eosinophils, due to concomitant infestation with *H. nana*. There was no leucopenia at any time, and four days after completion of treatment the neutrophil count was 1,140/mm³. In another case in a child of 10 years the neutropenia reached 96/mm³, the remaining cells being lymphocytes in a total count of 3,200/mm³. This child continued on treatment making an uneventful recovery both of her primary typhoid fever and also of her relative neutropenia.

Our 92 cases (range 2 years to 71 years, mean 16 years, mode 10 years) generally seem to have been far better nourished than the group of 144 patients described in the report by Drs. Scragg and Rubidge. In all our cases the neutropenia responded within a matter of days of discontinuing the drug. In only one case was the absolute neutrophil count less than 1,000/mm³ one week after discontinuing treatment. We certainly could not attribute any deaths to this cause. We wonder whether the fatality reported by Drs. Scragg and Rubidge was not in fact due to typhoid septicaemia, which has itself an adverse effect upon bone marrow function.

We are of the opinion that the minimum dosage for the initial febrile period should be not less than 8 mg trimethoprim and 40 mg sulphamethoxazole per kg body weight per day, reducing to 4-6/mg trimethoprim, 20-30/mg sulphamethoxazole per kg body weight per day after five days or upon defervescence, whichever is the later.

We have generally found 14 days subsequent treatment at this level to establish a satisfactory permanent cure. We have, however, established that certain cases do not respond to trimethoprim-sulphamethoxazole, and in view of this fact would feel that the lack of a positive improvement in well being within 72 hours, coupled with a definite response towards defervescence within five days, indicates a need to reassess the therapeutic regimen.—We are, etc.,

T. J. STAMPS
A. C. B. WICKS

City Health Department,
Salisbury,
Rhodesia

Hospital Advisory Service

SIR,—I am grateful to Sir Desmond Bonham Carter for the important points he has raised in his letter (18 December 1971, p. 746). I would also like to thank him for his advocacy of advisory services generally. I agree with his comment that it is important that an advisory team should be regarded by those visited as one of "us" rather than visitors on behalf of some other external body. Equally I agree that one of the most valuable aspects of the advisory service is the stimulus it gives to critical self-examination and the opportunity to contribute to the general pool of experience and knowledge. I do not agree, however, with his proposal that the Hospital Advisory Service should become part of the Department of Health. I think there would be a