recorded. This research is not yet completed and full details of the project will be published in due course. In the meantime it seemed important to give early notice of the following observation.

During 25 days in November and December last year 9253 inspections were made on 481 children on the registers and some 1543 injuries were located and recorded. None of these injuries were found to be bilateral symmetrically about the main axis of the body—for example, affecting both sides of the head or both arms.

This suggests that symmetrical bilateral injury is a comparatively rare occurrence and indicates the need to alert all doctors and staff to be particularly vigilant when seeing children with bilateral trauma.

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Postmenopausal urinary symptoms and hormonal replacement therapy

SIR,—Recent discussion on the management of the menopause has failed to mention the possible effects of oestrogen deprivation on the lower urinary tract. In a study of a large number of women with lower urinary tract symptoms¹ it was shown that a significant proportion first experienced their urinary symptoms after the menopause, often in association with a senile atrophic vaginitis, an association previously noted by Everett.² It was suggested that the urinary symptoms were due to oestrogen-deficient changes in the urethra similar to those producing the senile vaginitis.

The natural variations in oestrogen activity occurring throughout a woman's life are reflected by changes in the maturation of the squamous epithelium covering the distal urethral segment.³ Adequate levels of oestrogen are necessary for maturation of this epithelium, failure of which may give rise to atrophic changes similar to those of senile vaginitis. At first these postmenopausal urinary symptoms were thought to be due to the presence of distal urethral stenosis, and hormone replacement therapy was combined with urethral dilatation.¹ However, in a recent clinical study 18 postmenopausal women with lower urinary tract symptoms were treated by oestrogen therapy alone (Premarin 0.625 mg daily for three weeks out of four, for a total of three months). Of the eight women whose urinary symptoms had been present on average for less than 12 months this treatment relieved the symptoms in six. In the remaining 10 patients symptoms had been present for more than 12 months and only two of these were relieved of their symptoms by this hormone therapy alone.

This suggests that the early symptoms of postmenopausal atrophic urethritis are probably due to epithelial changes alone and hence can be corrected by hormone replacement therapy. At a later stage fibrosis and stricture formation may complicate the epithelial changes and urethral dilatation is required in addition. This hypothesis now forms the basis of a more detailed prospective study, but it would suggest the prompt use of hormone replacement therapy in those postmenopausal women presenting with lower urinary tract symptoms of frequency and dysuria. It would be interesting to hear from other workers whether hormone replacement therapy has

been effective in treating such symptoms and whether the duration of urinary symptoms has been a significant factor in the success of the treatment.

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¹ Roberts, M, and Smith, P, *British Journal of Urology*, 1968, **40**, 694.

² Everett, H S, *American Journal of Surgery*, 1941, **52**, 521.

³ Smith, P, *British Journal of Urology*, 1971, **44**, 667.

Drug treatment of typhoid fever

SIR,—I read with great interest the paper by Surgeon Lieutenant Commander P D Clarke and others on "Mecillinam: a new antibiotic for enteric fever" (3 July, p 14). I agree that further information is required on the question whether mecillinam is also effective in typhoid fever due to organisms with the R-factor-mediated multiple resistance to chloramphenicol, tetracyclines, sulphonamides, and streptomycin which has been known for several years now.¹ I do not agree, however, with the statement of the authors that "chloramphenicol-resistant *Salmonella typhi* strains, such as those that caused the large typhoid epidemic in Mexico, are sensitive to ampicillin." R-factor-mediated ampicillin resistance among *S typhi* strains has been reported from that same typhoid epidemic in Mexico² and, apart from individual cases in France and Algeria, has also been reported from South Vietnam and Thailand.³ Ampicillin-resistant *S typhi* strains have been noted in India⁴ as well. If there exists no cross-resistance to the closely related ampicillin and amoxycillin, then mecillinam could be a valuable "addition to the agents available for treating typhoid." The exact mode of action of this new amidino penicillin is, however, not yet known and the question of cross-resistance is still open.⁵

Considering the risk of irreversible aplastic anaemia, the various drawbacks in the treatment of acute typhoid fever (lack of influence on the relapse rate³ and reconvalescent excretor state³ and the occurrence of a toxic crisis in 5-10% of treated cases^{3 6}) and the alarming spread of R-factor-mediated chloramphenicol

resistance throughout the world (see figure³), I doubt whether it is still justified to call chloramphenicol the drug of choice in typhoid (except for economic reasons—for example, in developing countries). Ampicillin was for years the only valuable alternative agent, but the response of acute typhoid fever to ampicillin is at least 1-3 days slower than that to chloramphenicol and the failure rate can reach 30%.³ Amoxycillin gave promising results,⁷ but there is a complete cross-resistance to ampicillin.

Reviewing the literature on the chemotherapy of typhoid fever³ I found that co-trimoxazole has not only a therapeutic efficacy equal to that of chloramphenicol as measured by the time for defervescence and for improvement of the patient's general condition, but has moreover the advantage of not causing a toxic crisis in the cases treated^{3 6} and of even being effective, although somewhat more slowly, in cases of multiple drug-resistant *S typhi* infections (including sulphonamide resistance).⁷ It is worth noting that the synergistic effect of the two components of co-trimoxazole (sulphamethoxazole and trimethoprim) has been shown not only in infections due to various sulphonamide-resistant bacteria in vitro⁸ as well as in clinical trials in man⁸ but also in R-factor-mediated sulphonamide resistance in *S typhi* in vitro,⁹ the latter finding being, however, contrary to the findings of Anderson.¹ In view of the above-mentioned qualities and its good tolerance¹⁰ co-trimoxazole seems to be at present the drug of choice in acute typhoid fever.

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¹ Anderson, E S, *Lancet*, 1973, **2**, 1494.

² Olarte, J, and Galinder, E, *Antimicrobial Agents and Chemotherapy*, 1973, **4**, 597.

³ Herzog, C, *Infection*, in press.

⁴ Solomon, S, Subramaniam, S, and Madanagopalan, N, *Current Medical Research and Opinion*, 1976, **4**, 229.

⁵ Roholt, K, Nielsen, B, and Kristensen, E, *Chemotherapy*, 1975, **21**, 146.

⁶ Kamat, S A, *British Medical Journal*, 1970, **3**, 320.

⁷ Gilman, R H, et al, *Journal of Infectious Diseases*, 1975, **132**, 630.

⁸ Acar, J F, Goldstein, F, and Chabbert, Y A, *Journal of Infectious Diseases*, 1974, **128**, suppl, p 470.

⁹ Bushby, M R, and Bushby, S R M, in *Proceedings of 9th International Congress of Chemotherapy*, London, 1975. In press.

¹⁰ Havas, L, Fernex, M, and Lenox-Smith, I, *Clinical Trials Journal*, 1973, **10**, 81.

● single cases   ▲ epidemic outbreaks   □ endemic occurrence

Incidence of single cases ● and epidemics ▲, and endemic □ occurrence of typhoid fever due to *S typhi* with R-factor-mediated resistance to chloramphenicol and other antibiotics throughout the world, 1967-74.³