active treatment and half placebo. Those of us with experience of manipulation in clinical practice know that some patients respond dramatically, having had weeks or months of pain previously; clearly there are subgroups of patients with low back pain who do improve.

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SIR,—It is not surprising that no real differences between treatment and placebo groups were found in the trial of mobilisation and manipulation by Dr H Sims-Williams and his colleagues (11 November, p 1338). As in so many trials of this kind, the investigators selected patients with a symptom, the origin of which was "in doubt," but which included "many different conditions." The mechanism of the treatment used was acknowledged to be "disputed." Under these circumstances how can a trial of treatment produce meaningful results?

To be valid, a trial of treatment in back pain needs to consist of groups of patients selected beforehand as likely to benefit—by clinical or other criteria—from the treatment under investigation. If such criteria are unknown, then the investigator's first task should be to elucidate them and work out the indications for the particular treatment. It seems to me that only in this way will our knowledge of how to help patients with back pain be advanced.

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Clinical trial experience by simulation

SIR,—A further advance in the use of simulation games for medical education has been made by Dr B W Madsen and his colleagues (11 November, p 1333) and I for one am delighted. It would be a pity, however, if first-time readers in this subject were to become confused by the references.

"Instant Experience in Clinical Trials"¹ was first reported in a non-computerised form (not as stated by Madsen *et al*). Later on this was computerised and the working instructions, systems analysis, and computer programs (written in PL1 for an IBM 360/40 with disk drives) were donated, together with the copyrights, to the Trust for Education and Research in Therapeutics (TERT), which published them as a manual.² These are available only from the Trust, c/o Dr D M Burley, Ciba Laboratories, Horsham, West Sussex.

The easier production of very large quantities of authentic-looking data presented problems to Dr Madsen and his colleagues similar to those of Ciccolunghi *et al*³; both systems offer remarkably similar facilities. It is educationally unwise, however, to offer participants many more data than they can reasonably be expected to handle in the time available and organisers should edit protocols ruthlessly on this score to protect their pre-stated teaching objectives.

These games are at their best when a clear drug effect can be discovered by the simplest trial design but perhaps missed by a bad one; additional and more subtle effects should be ascertainable with more sophisticated or more appropriate designs. The inclusion in the

results matrix of subgroup interactions permits genuine differences in the results from several trials to be discussed profitably in terms of methodology, therapeutics, and statistics. The greater reality and freedom offered by these later developments will surely find optimal application by their incorporation into undergraduate and postgraduate training rather than in the short course. If simulated clinical trial results can be analysed and studied over a period of weeks rather than hours it would seem sensible to encourage one parametric variable (and perhaps a second requiring transformation), one amenable to χ^2 testing, and one ordinal variable. The teaching and learning opportunities are expanding rapidly.

Verisimilitude has clearly been advanced by both Dr Madsen and his colleagues and Ciccolunghi *et al* and the former's criticisms of Instant Experience are fair and valid. It should not be forgotten, however, that the non-computerised form still has much to commend it. Although it is crude and simple, it allows more flexibility than its own automated form. Furthermore, its most sophisticated hardware requirement is a photocopier, it can be comfortably managed by two people (or even one if a higher error rate and harder work can be tolerated) and it is as mobile as the dozen or so sheets of paper needed to control it. The generation of results for four simulated trials, each involving two variables in 80 patients, has taken less than six man-hours.

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¹ Maxwell, C, Domenet, J G, and Joyce, C R B, *Journal of Clinical Pharmacology*, 1971, **11**, 323.

² Maxwell, C, Smith, F R, and Shing, L K, *Instant Experience in Clinical Trials: a Computerised Teaching Aid*. Horsham, TERT, 1972.

³ Ciccolunghi, S, Joyce, C R B, and Liebrich, K G, *Proceedings of the 2nd IMPP, Florence, 1975*. Amsterdam, Excerpta Medica. In press.

Contamination of sterile fluids

SIR,—I would like to comment on one of the issues raised in the letter from Dr G A J Ayliffe and others (8 July, p 123).

Their main purpose is to question the necessity for expensive and sophisticated facilities for the preparation of non-injectable fluids. Towards the end of their letter, however, they extend the argument to small-scale aseptic dispensing and say, "For the latter an efficient laminar flow cabinet is all that is necessary and not a plenum-ventilated room." I wonder whether they were aware of Appendix 29 of the *British Pharmaceutical Codex 1973*, which reads as follows:

"For success in aseptic processing, scrupulous care should be taken to reduce the risk of contamination of the materials being processed. If practicable, a room should be set aside for this work and a positive pressure maintained in it by introducing air which has been passed through a bacteria-proof filter. In addition, all manipulations should be carried out under a protective screen or in a current of sterile filtered air.

"Likely sources of contamination include the hair, hands, clothing, and breath of the operator and the air impinging on exposed surfaces. The risk of contamination from these sources should be countered by accepted methods of cleansing and disinfection and by the use of protective clothing."

Bearing in mind that small-scale aseptic dispensing is undertaken for such things as intrathecal injections, intravenous injections,

and bladder irrigation solutions I hope that they would agree that an efficient laminar flow cabinet is not all that is necessary.

I am sure that it is the authors' hope that their major points will be replied to in due course by the Medicines Inspectorate.

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Antibiotics and respiratory illness

SIR,—General practice trainees should be encouraged to do simple research, but their results must be checked and errors explained if the exercise is to be of any value. Dr K R Hutchinson, in his report on a study of the effect of antibiotic prescribing on the demand for repeat consultations for respiratory illness (11 November, p 1342), has been allowed by his more experienced collaborator, Dr J G R Howie, to reach conclusions that are not justified by the findings.

They claim that a policy of high antibiotic prescribing does not appear to reduce the number of patients seeking further consultation; yet, out of 639 patients given antibiotics, 33 (5%) came back whereas of the remaining 217 who were not given antibiotics 20 (9%), returned.

They say that trainees seem less able than more experienced doctors to prescribe effectively for children, basing this on the fact that they had a higher failure rate in the youngest group. Since the trainees only had the same failure rate overall, should they not have also concluded that they were better prescribers when dealing with the older patients?

Finally they compare the total consultations with those of the National Morbidity Survey without any check on the make-up of their practice population or other relevant factors, notice that they are about one-third higher, and ascribe this to above-average antibiotic prescribing without producing any evidence to support this belief.

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Treatment of migraine

SIR,—Dr David Thrush, in his review of the treatment of migraine (7 October, p 1004), does not mention the role of tricyclic and monoamine oxidase (MAO)-inhibiting antidepressant drugs and I should like to make good this omission.

An earlier survey of the disorder¹ does refer to treatment of migraine with amitriptyline and since that time other evidence has accumulated that both tricyclic drugs^{2,3} and MAO inhibitors⁴ may be effective in a proportion of patients. Recent evidence which points to a disturbance of monoamine metabolism⁵ leaves many questions unanswered but supplies a possible explanation of the therapeutic action of antidepressant drugs in this disorder. I have been seeing patients with severe migraine for a number of years, mainly with a view to treatment by autolytic techniques, and such patients have usually failed to respond to a large number of currently used pharmacological treatments. However, while patients are still on the waiting list for the psychotherapeutic treatment I usually try the effect of small doses of a

tricyclic and, if that should fail, of an MAO inhibitor. I have been impressed with the good response of about half of these very severely affected patients to such therapy.

Elithorn¹ stated that migraine is "undeniably a hunting-ground for the drug-happy physician." This, of course, is true, but such a statement should not deter efforts to find an effective treatment for this distressing and persistent disorder.

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¹ Elithorn, A, *British Medical Journal*, 1969, **4**, 411.

² Gomersall, J D, and Stuart, A, *Journal of Neurology, Neurosurgery, and Psychiatry*, 1973, **36**, 684.

³ Couch, J R, Ziegler, D K, and Hassanein, R, *Neurology*, 1976, **26**, 121.

⁴ Anthony, M, and Lance, J W, *Archives of Neurology*, 1969, **21**, 263.

⁵ *Lancet*, 1974, **2**, 703.

Sex and prognosis in adult acute lymphoblastic leukaemia

SIR,—A relationship of sex to prognosis in acute lymphoblastic leukaemia (ALL) was shown in the last report to the Medical Research Council by the Working Party on Leukaemia in Childhood, the girls faring significantly better than the boys (16 September, p 787). This report suggested that testicular relapse accounted only partly for the observed difference. The same relationship had been observed by Baumer and Mott¹ but was lately denied by Evans *et al.*²

All these studies were concerned with childhood ALL. We would like to add information on the relationship of sex to prognosis in adult ALL based on 137 cases (32 patients treated in our division from 1972 to 1977 and 105 patients reported in detail by others³⁻⁵). The distribution of these patients according to age and peripheral blood blast cell count was similar for both sexes. All patients had been treated for remission induction with vincristine and prednisone and

many of them had also received 2-4 doses of daunorubicin or doxorubicin. Most of the patients who had achieved complete remission had received cranial irradiation and intrathecal methotrexate and maintenance chemotherapy with daily 6-mercaptopurine and weekly methotrexate. The complete remission rate was almost identical for males (69/89 or 77.5%) and females (38/48 or 79.1%). Survival and duration of complete remission were also very similar for the two sexes (see figure). No testicular relapse was recorded in the 89 males during the observation period. These data suggest that at present sex has no prognostic value in adult ALL.

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¹ Baumer, J H, and Mott, M G, *Lancet*, 1978, **2**, 128.

² Evans, D I K, *et al*, *Lancet*, 1978, **2**, 522.

³ Willemze, R, *et al*, *Blood*, 1975, **46**, 823.

⁴ Scavino, H F, *et al*, *Cancer*, 1976, **38**, 672.

⁵ Lister, T A, *et al*, *British Medical Journal*, 1978, **1**, 199.

Minimum information needed by prescribers

SIR,—Mr P W Golightly and Dr D C Banks (11 November, p 1366) make a rather doubtful claim when they state that "the number of drugs in routine use is constantly increasing." Although this was probably true a few years ago, the number of medicines in this country now seems to be falling. For example, *MIMS* lists approximately 1000 commonly used prescription drugs. Last year (1977) they recorded only 43 additions to their list, while at the same time they recorded that 97 of their listed drugs had been discontinued.

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SIR,—The article by Dr A Herxheimer and Professor N D W Lionel (21 October, p 1129) elucidates a problem faced by all health practitioners dealing with drugs. The authors' examination of the present void of adequate sources of drug information should be lauded, but their proposal for a manual of minimum information inadequately fills that void.

If, as the authors point out, the manufacturer's current data sheets (package inserts in the United States) are inadequate in disseminating important clinically relevant material, then the concept of providing practitioners with minimum drug information to supplement the information from the manufacturer perpetuates the problem. For example, in the authors' draft of minimum information on tetracycline why are peak plasma concentrations, minimum inhibitory concentrations, half life, protein binding, and metabolism excluded from the section on pharmacology? Similarly, why is erythromycin not mentioned as a first choice of therapy along with tetracycline for mycoplasma? Other areas could be cited, but the emphasis should be to encourage necessary additions which are important when imparting clinically relevant drug information. But even the lack of data in the draft is not as serious as the omission of

the references used in compilation of the data. Possibly owing to space considerations in the journal the authors found it necessary to delete them and I hope this was the case.

Providing clinically relevant drug information to practitioners prescribing and/or administering medication is a necessity governed by the inadequate data published by pharmaceutical manufacturers. Providing minimum information with lack of suitable references as a substitute for or companion to data sheets (package inserts) is perpetuating the problem.

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Opportunity in health visiting

SIR,—It was with some pleasure that I read the proposed Nursing Bill currently passing through Parliament. There is tremendous need to review the training requirements of those working in the health professions. General practice is half way through that review and nurses have only just started.

May I use your columns to question the assumption that the right basic training for a health visitor is a nurse training course to SRN level? Historically, health visitors started separately and only relatively recently became part of the nursing profession. The present situation often encourages a nurse who, after gaining her SRN, has realised that she has made a wrong career choice to change direction and to train to become a health visitor. This surely must be the wrong reason for entering the profession of health visiting. Perhaps poorly motivated health visitors are in large part to blame for the frequent disparaging remarks made by general practitioners and district nurses about health visiting.

I would like to see health visiting as a separate profession with its own defined area of responsibility. I do not doubt that there may be a need for a basic health/nursing training as a component of a health visitor's course, but there should be the opportunity for young people at school to elect to enter either profession, health visiting or nursing. Thus we might see the emergence of a strong professional body of health visitors, willing and able to work in primary care, to provide a lead in tackling the modern epidemics of accidents, alcoholism, coronary heart disease, lack of exercise, smoking, and over-eating. I for one would welcome the opportunity to work with such colleagues.

MICHAEL HALL

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General practice records

SIR,—I would like to congratulate Dr Christopher Maycock (25 November, p 1510) and his partner on their system of record-keeping, but having looked at many general practice records throughout the country I would like to point out that they are enthusiasts and not therefore representative of most GPs. I disagree with Dr Maycock's reasons for preferring the existing medical record envelope (MRE) format to the A4 records. I note, however, that after stating his reasons he adds the rider that the structuring of the MRE records will make any future con-

Life-table analysis of survival and remission by sex in 137 adult patients with ALL.