study to test whether, for instance, sulphasalazine is better than placebo in rheumatoid arthritis. In deciding the sample size required to show a difference or that no difference exists between a possibly effective drug and placebo, a statistician requires to know the likely improvement rates both for the drug and for natural remission.

Another reason for publishing carefully conducted uncontrolled trials of this type is that they are feasible and plausible when they come from one hospital. It would be virtually impossible for a single hospital to muster sufficient suitable patients for a controlled study. Once more than one hospital or more than one clinician is involved disparities in case selection and patient management may vitiate the results of the trial. Once we enter the league of multicentre controlled trials we enter a morass of committee work, of anonymity, and often of two-year delays, in which the seeds of originality, such as the use of sulphasalazine, may fail to germinate or may germinate only to become blighted.

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Exercise training in chronic bronchitis

SIR,—We accept Dr J E Cotes's comments (15 March, p 795) that the allocation of patients to exercise and control groups was not randomised. To facilitate the weekly supervision of the exercise group it was necessary to allocate patients according to the geographical position of their homes; to exclude those outwith the city would have greatly reduced the number available for study. The role of the research nurse was to supervise the training and to encourage the patients to continue with their daily training programme. At the conclusion of the study the patients were asked to continue with daily exercise without further supervision. and were told that they would be reassessed in six to nine months' time. After a mean period of eight and a half months, 11 patients in the exercise group were reviewed. The mean 12-minute distance fell significantly from 1104.2 to 992.3 metres ($p < 0.005$). Although this value was greater than the mean 12-minute distance on entry to the study (886.5 metres), the difference was not statistically significant. In 10 patients the walking distance deteriorated, in the other it was unchanged. The mean 12-minute distance in the control group fell from 868 metres to 740 metres, but this was not statistically significant.

These patients did not continue to take regular exercise and the benefits of training were soon lost. For worthwhile improvement to be maintained supervision with constant encouragement, a role principally filled by the nurse, is essential.

We are concerned that your readers' assessment of our study may be unduly influenced by the letter from Dr N R Andersson (29 March, p 942). His criticisms are largely invalid and demonstrate a lack of understanding and misinterpretation of our results. We have clearly stated that all patients were cigarette smokers and were advised to stop at the beginning of the study. As changes in this habit are never predictable it is not surprising that the number who gave up smoking was different in the two groups, but it is hardly something we could control. We referred to the

results of a study of unsupervised exercise in patients with chronic bronchitis¹ and stated the object of our study was to determine whether close supervision would lead to an improvement in exercise rehabilitation. We believe that the value of close supervision has been confirmed.

In the exercise group one patient died and two failed to complete the study while in the control group three patients died, not a drop-out of five and six as stated by Dr Andersson. Recruitment of patients took place over a period of months; as the total time available was limited not all subjects were studied for 12 months, a number completing follow-up after six months—hence the difference in the numbers at the initial and final assessment.

The difficulties of recruiting patients, of repeated physiological testing, and of funding the close supervision of a group of patients with a chronic disabling disease imposed limitations on this study and should be sufficient reason, for those with practical experience of these difficulties, to refute the jibe of "rushing to publication."

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¹ McGavin CR, Gupta SP, Lloyd EL, McHardy GJR. *Thorax* 1977;32:307-11.

Indomethacin treatment of postural hypotension

SIR,—The letter from Dr I B Davies and others (19 January, p 181) prompts observations and questions concerning management of the common problem of hypotension in the elderly where simple causes have been excluded.

A prostaglandin-like substance, probably PGE₂, was released into the renal venous blood when angiotensin II was infused experimentally into the renal arteries of dogs. Release of the prostaglandin-like substance coincided with recovery of renal blood flow and it seemed that PGE₂ might be functioning as a regulator.¹ Drugs such as indomethacin may restore falling blood pressure, and following the paper of Kochar and Itskovitz² seven or eight elderly patients with postural hypotension were treated in this department with indomethacin, the dose varying from 25 mg to 50 mg thrice daily, with elevation in blood pressure and lessening of symptoms.

All these patients had had troublesome falls of systolic and diastolic blood pressure levels of more than 20 mm Hg on standing, without acceleration of the heart rate and often with syncope. Most had an abnormal Valsalva response, pyramidal signs, and some features of Parkinsonism; continence was variable. Serum potassium levels were normal, or if low were corrected without benefit. Poor hydration was corrected and supporting stockings were provided. Cerebellar abnormalities were not seen; none had obvious neuropathy or recent severe ischaemic heart disease. Plasma volume, aldosterone, catecholamines, and metabolites were not estimated. Whether our patients suffered from an incomplete or variant form of the Shy-Drager syndrome we cannot say, and they were not studied as meticulously as those of Professor Abate and his colleagues.³

Flurbiprofen may have a more potent blocking effect than indomethacin⁴: the percentage inhibition of PGE₂ production is reported to be greater than with indomethacin. A small number of our patients were changed from indomethacin to flurbiprofen but did

less well. Other non-steroidal anti-inflammatory agents may well influence hypotension, and one must look forward to the effects of these being studied, perhaps by those with the resources available at St Mary's Hospital, London, and in Wisconsin and Bologna.

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¹ McGiff JC, Crowshaw K, Terragno NA, Lonigro AJ. *Circ Res* 1970;26-27, suppl 1:121-30.
² Kochar MS, Itskovitz HD. *Lancet* 1978;ii:101-4.
³ Abate G, Polimeni RN, Cuccurullo F, Puddu P, Lenzi S. *Br Med J* 1980;ii:1466-8.
⁴ Perkins CM, Lee MR. *Lancet* 1978;ii:1058.

Unrecognised dehydration during parenteral nutrition

SIR,—When drawing attention to the importance of allowing correctly for the water content of certain solutions administered intravenously, Drs R W G Prescott and J C Stoddard (22 March, p 847) failed to emphasise another, more important, cause of inadequate fluid replacement, which I have often seen and which their article illustrates.

In two of their three cases the rise in plasma sodium concentration is shown in the table as having occurred in association with a *positive* water balance and a *negative* sodium balance. There is no way in which this can occur, as both changes lead to hyponatraemia. On the assumption that the plus and minus signs are correct, the explanation would seem to lie in the statement that "... taking insensible losses into account, the fluid replacement was inadequate." This, presumably, was a retrospective assessment, the insensible losses having been ignored when the fluid balance was calculated in order to formulate treatment. It is this which would have been the prime cause of the hypernatraemia, as the cumulative effect of the insensible losses over five days would have far exceeded the 700-1200 ml overestimation of the water intake. To explain the data given, the insensible losses would have to have been very large.

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Bladder cancer as a prescribed industrial disease

SIR,—The article by Sheena N Somerville and others (23 February, p 540) and their letter (22 March, p 867) drew attention to a possible under-claiming for social security benefits in respect of industrially induced primary neoplasm of the epithelial lining of the urinary tract. While we have no other evidence that under-claiming for this prescribed disease (No 39) occurs, the following advice may nevertheless improve the present state of affairs.

If a consultant considers that one of his patients has the condition he should advise him to seek the help of the local office of the Department of Health and Social Security. The patient will then be afforded every assistance in completing a claim form and the office will try to confirm the occupational history. With the patient's consent his clinical history will be obtained from his GP or from hospital, as seems most suitable. A consultant's opinion, normally from the one in clinical