successful than linoleic acid has yet to be proved.

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¹ Seaman GVF, Swank RL, Tambllyn CH, Zukoski CF IV. *Lancet* 1979;ii:1138-9.

² Millar JHD, Zilka KJ, Langman MJS, et al. *Br Med J* 1973;ii:765-8.

³ Bates D, Fawcett PRW, Shaw DA, Weighman D. *Br Med J* 1978;ii:1390-1.

Retrospective versus prospective controls in clinical trials

SIR,—It has happened again. Many a time now, in my relatively short medical career, I have accepted as gospel truth medical knowledge without personally examining its foundations, only to find some time later that those foundations are almost non-existing. Examples include tonsillectomy, anticoagulant therapy for infarction, and cleansing the skin with alcohol before venepuncture. The most recent example was the attack on the holiness of prospective trials launched by Dr Lawrence Cranberg (17 November, p 1265). His article fills one's heart with fear, for no longer will one be able to stand up at Grand Rounds and put down some bright young whippersnapper: "Yes, but were those findings confirmed in a prospective trial?"

In spite of such disadvantages, Dr Cranberg's article has one great advantage: it leads us to examine the postulates on which clinical trials are based. In physics and chemistry there is no need for concurrent controls, for the variables are few and well known. Experiments are designed in serial fashion, altering one variable at a time. A careful record of the critical variables is kept and the experiment can be repeated time and time again, with identical results. In biology, however, we not only have a greatly increased number of variables, we also understand them less well. Indeed, sometimes we are not aware of variables that may effect the outcome of the experiment. This problem has been circumvented by the process of matching experimental preparations and then introducing a known controllable variable (administration of a chemical, the making of a lesion, etc) to one of the matching pair only, usually in a randomised fashion. The effect of the introduced variable is then determined by observing any difference between the pairs that did not exist initially. It is necessary only to match for those variables that might be affected by the experimental process. Thus sex, weight, age, concentration of certain metabolites, and the presence and severity of certain characteristics such as symptoms and signs of disease are among the more important variables. Duration of a disease may be important, but the point in time at which a variable is tested rarely is (provided ambient temperatures, etc, are treated as different variables). Yet the only advantage of the use of concurrent controls is to be able to say that the two experiments were done at the same point in time in the life of the universe. Other apparent advantages, such as ease of comparison for sameness, are important only in experiments where the variables are improperly recorded. Generally, the result of such work is as sloppy as the record keeping. Finally, it has been suggested by some reviewers of grant applications—not, of course, any associated with agencies to

which I apply for funds—that a temptation exists in retrospective trials to select the controls and experimental subjects on the basis of the expected or desired outcome. To those individuals I would say: "The null hypothesis states that there is no difference in the inherent honesty of researchers using retrospective and concurrent controls." Until the latter is disproved in a prospective, double-blind crossover trial, I shall feel justified in using retrospective or concurrent controls as dictated by the variables of the experimental situation.

In conclusion, thank you, Dr Cranberg.

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Rehabilitation

SIR,—May I take up some points from Dr D H Bossingham's letter (8 December, p 1508)?

It is certainly the responsibility of doctors, at both primary and secondary care level, to think about any necessary stages in rehabilitation that their patients might need during recovery, and to direct their patients in the desired direction and to the appropriate agencies for any help needed after (or during) clinical treatment. Unfortunately, rehabilitation is considered to be a "soft" subject and, perhaps partly for this reason, often induces an apparent occupational deafness in harassed clinicians.

If the subject is to become more scientific, thought and attention must be given to developing valid measures of outcome and evaluating different rehabilitation procedures. The recently founded Society of Research in Rehabilitation provides a forum for many disciplines (not only medicine but others including the remedial professions) to look critically at work that is being done not only in medical rehabilitation but in other fields, such as those of occupational assessment and employment rehabilitation.

Dr Bossingham points out that many doctors do not make use of the Manpower Service Commission's employment rehabilitation centres to help their patients return to work, if such an assessment is needed. While the employment rehabilitation centre does not provide training, a skilled occupational assessment can be given by a team which includes not only medical and nursing advice but also that of occupational psychologists and skilled workshop supervisors. Such an assessment may be followed by a placement directly into suitable work or possibly by training.

The number of referrals of patients to these centres from doctors has steadily declined over the last few years. There are many possible reasons for this, and to try to counteract this trend the Employment Medical Advisory Service (EMAS), which now provides medical and nursing services for 25 of the 27 employment rehabilitation centres, has recently agreed with the Employment Service Division (which manages the centres) the introduction of an additional method of direct medical referral of patients to the employment medical adviser at the centre. This referral could come from doctors working at either primary or secondary health care level.

I would like to draw your readers' attention to the further information about this new facility on p 193.

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Drug names that look or sound alike

SIR,—In the issue of 17 November (p 1297), Drs R N Palmer and F V Simpson cite instances of similar sounding drugs causing confusion. It is thus ironic that on the following page (1298) "Minerva" is confused by one of the very drug pairs listed by Dr H McNulty and Mr P Spurr (6 October, p 836). In the letter she quotes¹ Montello and her colleagues at the Children's Hospital of Philadelphia used clotrimazole and not co-trimoxazole to treat their patient's oral thrush. Dr W T Houlsey (p 1297) should note that these *are* the approved names—surely an unnecessary confusion but one which may lessen if trimethoprim alone replaces co-trimoxazole in common use.

An oral preparation of clotrimazole appears not to be available in this country^{2,3} but there is a suitable formulation of miconazole. Dakatrin Oral Gel (Janssen Pharmaceutical Ltd) is designed to persist in the mouth and might thus be a candidate for prescription "by thumb."

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¹ Montello JM, Darby MH, Faubel K, August CS. *New Engl J Med* 1979;301:1005.

² *Data Sheet Compendium 1979-80*. London: Pharmind Publications Ltd.

³ *MIMS* 1979;21, No 10. London: Haymarket Publishing Ltd.

Iatrogenic collapse

SIR,—I would like through your columns to discuss points brought up by Dr M J Boscoe (24 November, p 1367). A complication of profound respiratory depression is serious indeed, but I felt somewhat reassured after reading the references quoted in his letter.

In the fifth edition of *The Pharmaceutical Basis of Therapeutics*¹ respiratory depression is mentioned as a complication of Pamergran (pethidine hydrochloride 100 mg, promethazine hydrochloride 25 mg, and atropine sulphate 0.6 mg), but no statistics are given. In a large series² respiratory depression of short duration occurred in two patients out of 774 receiving the drug parenterally. This covers 10 320 doses of the drug, an incidence of 0.02%. One of these two patients was suffering from advanced carcinoma of the oesophagus and the second was markedly debilitated with generalised arteriosclerosis.

Comparing seven analgesic drugs, Prescott *et al*³ showed that all of them had caused some depression of respiration, a fact that is of great importance in obstetric practice owing to possible depressant effects on the respiration of the newborn. He quotes that, of the more established drugs, pethidine is the most useful obstetric analgesic. Of the eight medical students he investigated, respiratory depression was shown by asking volunteers to breathe a gas mixture containing 0.5% carbon dioxide in oxygen, the analgesics being injected intramuscularly after an initial record had been taken. No subject suffered profound respiratory depression.