is at issue. Phobic patients (especially agoraphobics) are liable to spontaneous fluctuation in the severity of their disability and naturally tend to present and start treatment during a phase of relatively severe affliction. It follows that some degree of improvement can be reasonably expected during the period following presentation in many cases. The uncertainty, even in the authors' minds, implicit in the words 'probably' and 'very many' could be resolved, and the magnitude of degree of spontaneous improvement to be expected in any period following presentation measured and taken into account, by—and only by—having a control group.

Furthermore, it is not, in fact, even the difference between the effect of a specific treatment and the degree of spontaneous improvement over the period following presentation that is at issue: it is rather the effect of a specific treatment versus the summed effects of attention and placebo reaction. The authors seek to reassure themselves and (hopefully) their readers, by mentioning that many patients. had had a great variety of treatments before referral. Their contention that the failure of previous treatments indicates that the effects of 'suggestion' or 'the confidence of the doctor' could be more or less discounted is made less convincing when in the same paragraph they contrast their own manner of prescribing anti-depressants ('giving them with confidence') with the unhelpful (but understandable?) anxiety which they say characterizes 'some doctors' when prescribing M.A.O.Is. And their assertion that the latent interval between starting treatment and the occurrence of improvement was 'solid evidence that the improvement seen was due to the specific effect of the anti-depressants' would be more acceptable if one could be certain that patients were never warned to expect such an interval, and that the regular recording of such a latent interval was in no degree consequent upon the expectations of the prescribing doctors.

Dr. Kelly and his colleagues suggest that 'to carry out a trial using a placebo appears unjustifiable in view of the prolonged length of treatment . . . ,' but later they go on to state that 'anti-depressants should generally (be tried) because, when successful, the initial response is quicker than with any other type of treatment available at present'. In fact, given that according to the report 'the change in mean phobic ratings at one month . . . showed a highly significant improvement', and even allowing for the reported latent interval between stopping treatment and relapse, it would be possible to assess the claimed efficacy of M.A.O.I.s adequately and with suitable rigour in a simple sixteen week double-blind crossover trial employing a placebo. It is profoundly to be hoped that Dr. Kelly and his associates will now undertake such a trial.

The last decade has seen a proliferation of Academic Departments of Psychiatry within Britain, and we are looking forward hopefully to the establishment of psychiatry's own Royal College: these developments represent not only the aspirations of British psychiatrists, but also the increasing acceptance by our general medical colleagues of the legitimacy of such aspirations. The execution, reporting and publication of investigations the gross methodological inadequacies of which would be apparent to any final year medical student, cannot but imperil this increasing acceptance. Might I humbly suggest, Sir, that the *Journal* could appropriately celebrate this auspicious year by a firm policy decision that papers combining those pretensions to scientific respectability which a heavy sprinkling of Probability Values always represents with serious and fundamental flaws in experimental design, will have to look elsewhere for publication?

A. B. Mawson.

The Maudsley Hospital, S.E.5

References

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2. Foulds, G. A. (1958). 'Clinical research in psychiatry.' *J. ment. Sci.*, **104**, 259.
3. Laurence, D. R. (1962). *Clinical Pharmacology* London: Churchill.

Dear Sir,

Dr. Mawson appears to make two main points in his letter: first, the weaknesses inherent in our study because of its retrospective nature, and, secondly, its lack of controls. The evaluation of treatment in psychiatry is a slow and complicated process, especially where drugs are concerned. Initially it is necessary to have considerable experience with a drug, to discover its properties and side-effects, the type of patient who would benefit from treatment, and to form hypotheses about its clinical, as opposed to its pharmacological, mode of action. The next step is to test these hypotheses and to decide whether it would be of value to carry out a prospective controlled trial with placebo, and if this were so how it should best be carried out. A retrospective study, which enables large numbers of patients to be examined, is appropriate in this case, in spite of the potential shortcomings, of which we are aware. In our study a control group was not available

because almost all phobic patients seen at St. Thomas' are treated with anti-depressants; however, in spite of this, and the problems of a retrospective study, a great deal of new information was gained which went towards answering a number of questions we considered to be important, namely:

(i) phobic patients improved on the treatment régime.
(ii) panic attacks were reduced.
(iii) there was no difference in the response of agoraphobic patients compared with those suffering from other phobias.
(iv) significant improvement occurred in the first month.
(v) the results appeared to be comparable and in certain respects superior to those obtained in a controlled retrospective study of behaviour therapy, although differences in patient populations limited the value of this comparison.

On the basis of this information it now seems justified to carry out a double-blind controlled trial of phenelzine versus placebo. We now know the type of patients we wish to study in such a trial, the appropriate dosage of medication, the importance of assessing panic attacks, and the duration of treatment which is likely to be necessary to get a partial response. A prospective study is at present being conducted conjointly at the Maudsley Hospital and at St. George's Hospital by one of us (D.K.). This trial should answer the question of whether phenelzine alone is superior to placebo in treating phobic patients, but it cannot be a substitute for the information gained by following as many as 196 adult patients over the course of a year's treatment, or for the unique opportunity of examining the effects of M.A.O.I.s on childhood phobias. The patients are being treated with either phenelzine or placebo for two months, but a crossover design is not being used because of the 'carry-over' effects of initial treatment and because it seems unjustified to substitute a placebo if a patient is improving on active medication and gaining confidence in overcoming phobias. Past experience in substituting placebo for phenelzine in patients who were becoming less phobic resulted in such a high relapse rate that the project was abandoned.

In clinical psychiatry, as in the whole of medicine, new treatment possibilities will continue to be discovered. In our view, it is not only ethically but also scientifically acceptable to establish the potential value of a treatment régime before embarking on a prospective trial in which a placebo is used, because of the many difficulties for patient and therapist which it entails. Our study has done this to our satisfaction.

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WAGIH GUIRGUIS.
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[In his last paragraph Dr. Mawson puts a question to the Editors to which the short answer is 'no'.

There are many ways of advancing our understanding of treatment in psychiatry; and scrupulously conducted double-blind trials, and other efficiently designed experiments, cover only part of our needs. No useful method of treatment was ever yet discovered in a strictly controlled trial, but such trials have their place when the exploratory work has been done. It is to be hoped that there will always be room in the *Journal* for the conscientious retrospective reporting of good pioneer work.

Dr. Mawson expects too much. There is, unfortunately, no work at all, published in this or any other psychiatric journal, which is not open to serious methodological criticisms. Even controlled drug trials contain a large make-believe element, since serum levels of the drug are not monitored over the trial periods.

No doubt the success claimed by authors in uncontrolled studies is generally greater than the success reported in controlled studies. Of course part of the difference will be due to self-deception—optimistic self-deception by the therapist, and also, at times, negativistic self-deception by the anti-therapist. But it seems likely that a large part of the difference in results is real. Though we cannot do without them, controlled studies are unfortunately very insensitive tests of therapeutic potentialities. It is not possible to get, by giving standardized doses at set intervals over a fixed length of time to an arbitrarily selected group of patients, the same results from a psychotropic drug as can be obtained by a clinical expert sensitively selecting his patients and dosages, individual by individual, on a basis of experience. The ethical dilemma cannot be escaped. One cannot both carry out a therapeutic experiment and do one's best for the patient who has placed himself in one's care.

Eds.]

DEPRESSION AND CARCINOMA

DEAR SIR,

In their article in the *Journal* for November, 1969, Kerr, Schapira and Roth report that 'deaths from