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Correspondence

A DOUBLE BLIND TRIAL OF PHENELZINE AND AMITRIPTYLINE IN DEPRESSED OUT-PATIENTS

DEAR SIR,

We are pleased that Dr. B. M. King (*Journal*, October 1973, *123*, 492) has drawn attention to the possible importance of dosage in our 'blind' trial of phenelzine and amitriptyline reported in the *Journal* for July, 1973 (*123*, 63–7). In describing the daily dose of 15 mg. of phenelzine as 'cheeseparing', Dr. King wittily hit upon the *mot juste*. So great were the fears of cheese reactions, not to mention complications in the event of anaesthetics being required, at that time (1966) that our colleagues were reluctant to use the drug at all. However, this dosage, i.e. 2 tablets each consisting of either 7·5 mg. of phenelzine or 25 mg. of amitriptyline, was the *minimal* dose permitted, and was intended to allow for the occurrence of unpleasant side-effects. The usual dosage reached was 6 tablets daily, i.e. 45 mg. of phenelzine or 150 mg. of amitriptyline.

In another trial (1), conducted in the regional hospitals, the original idea of comparing the effects of phenelzine and amitriptyline had to be abandoned because risks to patients on MOAI drugs were regarded by the consultants as unacceptable. The pendulum may now be swinging back, and there is at present a trial in progress, conducted by Prof. Sir Martin Roth and Dr. C. Q. Mountjoy in this Department, in which the daily dose of phenelzine increases from 45 mg. to 75 mg. So far, we understand, no serious dose-related effects have been met with. We do not imagine that the last word has been said about the uses and abuses of MAOI drugs.

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REFERENCE

1. KAY, D. W. K., FAHY, T. & GARSIDE, R. F. (1970) A seven-month double-blind trial of amitriptyline and diazepam in ECT-treated depressed patients. *British Journal of Psychiatry*, **117**, 667–71.

THE MANAGEMENT OF RESISTANT DEPRESSION

DEAR SIR,

Drs. Shaw and Hewland are to be commended on raising an issue that has so far received little attention in the literature other than a resigned admission that it exists (1). The percentage of depressed patients who fail to respond adequately to conventional treatments is small, being approximately one in six patients (Medical Research Council, 1965), and often they are written off as 'character disorders' or perhaps 'schizophrenics' by their frustrated therapists. However, as the author suggests, a more comprehensive use of somatic therapy may make the difference between, on the one hand, chronic morbidity with possible suicide and, on the other, improved health with reintegration in the community.

Three points from their letter can be amplified. In treating resistant depression, many would agree that combining MAOI and tricyclic drugs is indicated. If one chooses phenelzine and amitriptyline, as Shaw and Hewland suggest and at the dose they indicate, it can be predicted that many responses will be less than satisfactory. Recent evidence indicates that a maximum dose of 90 mg. of phenelzine may be needed (2) and that a substantial number of people are rapid acetylators of this drug; in these it is probably no more effective than a placebo (3). From a small series of 14 patients treated here within the last year, the best and most sustained response has been found with a combination of tranylcypromine and amitriptyline. In most cases, however, isocarboxazid and amitriptyline are used. The former combination is used only if special indication warrants it. The least satisfactory results have come from using phenelzine and amitriptyline, perhaps for reasons already outlined above.

Another question to be answered relates to the optimal dose of drug for a given patient. In the above series, there was one patient who had absolutely no pharmacological response until a daily dose level of 80 mg. of tranylcypromine and 300 mg. of amitriptyline was reached, at which point she developed nocturnal confusion. This disappeared when amitriptyline was reduced to 200 mg. at night. Although not fully recovered, she was much improved and able to be discharged from hospital. Conversely, one patient derived enormous benefit after her amitriptyline was