case one week free from drugs must be left between discontinuing the monoamine oxidase inhibitor and starting the combined antidepressants.

When patients have received three types of treatment without benefit it becomes difficult to decide where their best interests lie. For both bipolar and unipolar groups one can repeat the treatments already given, proceed with different therapies as in the scheme suggested, or do nothing at all, while awaiting spontaneous remission. If this should occur, the subsequent treatment of choice might be lithium, to lessen the chances of a further attack of what has proved to be a refractory illness. In a small group of 'non-responders' we have not experienced much success with various selections of drugs when courses of treatment which have included a tertiary amine tricyclic, bilateral ECT and a monoamine oxidase inhibitor (plus L-tryptophan) have failed. If the combined antidepressants also prove ineffective we feel there is little to offer patients with bipolar illness other than to hope for natural remission.

For unipolar patients we re-examine the diagnosis yet again and usually ask a colleague to reassess the patient, since any long and apparently intractable illness often has its dynamic and social consequences, and it is not uncommon for the situation to be slightly clouded by some changes in the pattern of symptoms. Where the symptoms and basic problem are those of a resistant episode of unipolar affective disorder, it is unlikely that remission will result from manipulation of psychosocial/environmental factors, which appear to be largely secondary phenomena in this particular group of patients.

Decisions on subsequent treatment are not helped by our inability to say with any confidence when spontaneous recovery can be expected in patients who are so refractory to treatment; if remission occurs, how complete it will be and for how long it will be maintained; whether lithium salts will prevent recurrences, and if not whether any subsequent attacks will be as resistant as the current illness.

When attempts to treat patients have been unsuccessful for nine months or more, we have advised stereotactic tractotomy (as described by Mr. Geoffrey Knight, 1972) rather than await remission. This is because of the need to prevent further psychological and physical deterioration resulting from more prolonged illness, to alleviate intense suffering, to prevent suicide, and also because we know so little about the natural progression of the illness in these individuals. In the small group for whom we have requested stereotactic tractotomy the treatment has been most successful, as might be predicted from the review by Strøm-Olsen and Carlisle (1971).

However, we would be interested in other people's views on alternative methods of treatment for this selected group of affective illnesses. Specifically, we would question the value of successive attempts at therapy when the first three or four treatments have been given without success, but as yet we are unable to say when therapeutic defeat should be accepted. We would like to hear of the outcome in similar patients for whom the decision has been to await natural remission.

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CREATINE PHOSPHOKINASE ACTIVITY IN PSYCHIATRIC PATIENTS

Dear Sir,

Loebel and Robins in the May number of the *Journal* (1) report no significant differences in the serum CPK levels of 8 newly admitted female psychotic patients compared with 10 non-psychotic female psychiatric patients. Their conclusion that raised CPK levels are not a distinguishing characteristic of psychotic patients can be disputed on at least two grounds. Firstly, the authors excluded all patients who had received intramuscular injections. Such injections would be likely to be given to the group of patients with the greatest probability of having increased serum CPK activity, namely the most severely disturbed acutely psychotic patients (2, 3). If no effort had been made to avoid the use of intramuscular injections in such patients, it could have happened that the group of psychotic patients left for inclusion in the study would have been the less sick acute patients or chronic psychotic patients with less florid symptoms who would be unlikely to have increases. Secondly, because the period of increased serum CPK activity in acutely psychotic patients is generally for only 1–10 days after the onset of the psychosis (2), it is necessary to indicate whether the serum CPK activity of the patients in the study was determined during this period. For example, although CPK levels are an excellent indicator of a myocardial infarction when the plasma is obtained

up to 48 hours after the infarction, less than 10 per cent of myocardial infarct patients still have increases 96 hours after the infarct (4). There is no indication in the report of Loebel and Robins that they studied recent onset acute patients.

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HALOPERIDOL IN THE TREATMENT OF STUTTERERS

DEAR SIR,

Having read the letter from P. T. Quinn and E. C. Peachey, University of New South Wales, Australia, on haloperidol in the treatment of stutterers (1), we would like to convey some further information.

We have followed-up nine of the 12 patients who originally received haloperidol in our trial (2). More than three years after haloperidol was taken, it was found that fluency alone remained significantly improved; the other two measures, repetitions and interjections, though much improved failed to show significance or improvement.

Side effects were a serious problem: orphenadrine controlled extrapyramidal side effects but depression and drowsiness occurred in more than half the patients. The abrupt withdrawal of medication brought about some subjective and objective worsening and the question of maintenance therapy needs to be considered further.

Imipramine taken with haloperidol reduces its efficacy but subsequently the value of flupenthixol has been explored, producing good results with minimal side effects.

It seems highly likely that the more severely handicapped, i.e. those who are slow and show tic-like movements, may have some biochemical lesion in the basal ganglia (3); this would account for their response to haloperidol and flupenthixol. To clarify this we are shortly undertaking a double-blind cross-over trial of diazepam and flupenthixol.

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TARDIVE DYSKINESIA

DEAR SIR,

We should like to comment on Dr. George M. Simpson's letter on the subject of tardive dyskinesia published in the *Journal*, May 1973, **122**, 618.

Recently a survey has been carried out of all psychogeriatric patients (aged 65 and above) at the St. Louis State Hospital to study the incidence of tardive dyskinesia and drug-induced neurological syndromes. In all, 160 patients were studied of whom 35 patients were noted to have tardive dyskinesia. In view of Dr. Simpson's interesting observation that female patients with Eastern European Jewish background may be more liable to develop tardive dyskinesia when exposed to neuroleptics, we studied the ancestry of our 35 patients of whom 30 were females and 5 males. Only 2 were Jewish (1 male and 1 female), 31 patients were Caucasian, 1 Chinese and 2 Negroes. Of the Caucasian patients 1 was of Austrian descent (female), 1 of Polish descent (female), 3 of Irish descent (1 male, 2 females), 1 of Italian descent (male), 2 of German descent (both females), 1 of English descent (female), 1 of Russian descent (male), 1 of Bohemian descent (female). The rest of the patients were third or fourth generation Americans born in the United States, and no detailed information of their ancestry was available. Taking into