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Correspondence

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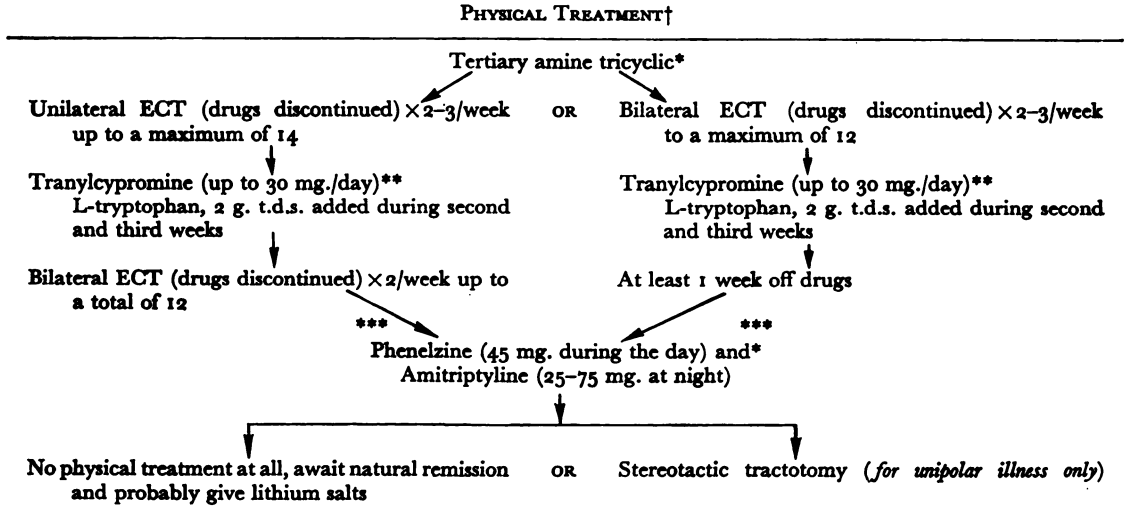
THE MANAGEMENT OF RESISTANT DEPRESSION

DEAR SIR,

Most patients who suffer from the depressive phase of affective illness remit spontaneously or respond to treatment readily, but in a very small number the illness appears to be relatively resistant to therapy. We would like to initiate discussion on this group, mainly because really intractable illness occurs in such a small proportion of depressed individuals that it is difficult to accumulate experience with a large sample.

In those with the clinical picture of the depressive phase of unipolar or bipolar affective illness, characterized by depression, diurnal variation of mood, loss of appetite and libido, early morning waking, diminished energy, interest and concentration, self-blame, etc., there are no known means of distinguishing those who will become 'non-responders'. When such individuals are identified it is obvious that the initial diagnosis, together with any psychosocial factors, drugs, endocrine abnormalities, physical illness, etc. which may be hindering recovery, should be re-examined. Management is easier if the order of treatment caters in advance for the few patients who require a continuous and systematic series of therapies. The scheme tabulated gives two of the possible formats, but each new treatment is considered in the light of the needs and circumstances of the patient at the time.

Both the timing and methods of therapy are tentative. The position of bilateral electroconvulsive therapy (ECT) in the order of treatments poses particular difficulties, especially since Abrams (1972) has suggested that bilateral ECT is more effective than unilateral treatment. We have tended recently to replace unilateral with bilateral ECT for some patients and omit the second course of ECT, in which



* Discontinue at 4 weeks if patient not *beginning* to respond by this time (e.g. to amitriptyline, 150 mg. or more/day).

** Discontinue after 3 weeks if patient not *beginning* to respond by this time.

*** After the first 3 or 4 treatments for intractable depression we have tried secondary amine tricyclics, tertiary and secondary amine tricyclics combined, tricyclic antidepressants and thyroxine, tricyclic drugs and reserpine; but as discussed, we have doubts about the use of drug treatments in general at this stage.

† It is important to remember that MAOI and tricyclic drugs cannot be given sequentially without a period off drugs.

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.

DAVID M. SHAW.
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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