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The Treatment of Chronic Depression
An Illustrative Case

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Although chronic depressive illness has not attracted a great deal of attention, it is a source of considerable psychiatric morbidity in the community and occurs in a proportion of the new long-stay patients. Prior to the introduction of specific antidepressant treatments, figures for continued affective illness were high. Lundquist (1945) observed an overall recovery rate of 80 per cent for a first attack. Perhaps the best researched study is that of Winokur who followed up for between two and 20 years 225 depressive patients. He showed that 25–30 per cent of female depressives developed a chronic state, compared with 10 per cent of male patients (Winokur and Morrison, 1973).

However, we suggest that this condition may be successfully treated. The number of drugs and psychotherapies available has considerably expanded over the past few years, and the present case illustrates some of the potential pharmacological strategies available today.

Case Report

J.O., a 60 year old widow, was referred from a local mental hospital where she had been an in-patient continuously for two years with unremitting symptoms of an endogenous depressive illness of psychotic intensity. Her illness began at the age of 28 during the puerperium with an atypical episode in which she was described as "manneristic, with statuesque posture, incoherence and thought disorder." The illness responded to ECT. Following a gap of 10 years, she subsequently had 24 admissions to hospital with increasing frequency. Many were of short duration and responded to ECT and tricyclics. The symptoms in these episodes were more classical of depressive illness. Her social capability between episodes was, however, impaired. A daughter developed a depressive illness during which she killed her own first child. There was no other family history of psychiatric abnormality.

On admission to our unit she presented in a grossly retarded state, being initially mute. She had auditory hallucinations that echoed her delusional guilt. She was poorly orientated with incontinence of faeces and urine. Oro-facio-buccal dyskinesia was also apparent. Because of her mental state, it was not possible to perform a Hamilton rating on admission, although she scored 46 on the Beck Depression Inventory. She was assessed throughout the period of study on the NOSIE rating scale (Honigfeld *et al,* 1966). Each of the 30 behavioural items of the NOSIE scale has been awarded a positive or negative value in order to produce a total (Figure). The greater the negative value of this total, the greater the depth of depression. A non-depressed person would score in excess of 15 on this total.

Treatment

After an initial drug free period of two weeks, she was started on a combination of phenelzine (up to 45 mg/day to maintain a platelet inhibition of 80 per cent), lithium (to maintain a serum level around 0.5 mmol/l) and L-tryptophan (up to 3 g/day). She had an initial dramatic response: after two weeks she showed no symptoms of depression, began baking in occupational therapy and took over the supervision of the patients' tea money (Figure). There was no evidence of hypomania. She remained well for four weeks and was about to be discharged when she developed sodium retention leading to congestive cardiac failure, ventricular ectopic beats and postural hypotension. Investigations showed no intrinsic heart disease and the syndrome was attributed to the side effects of phenelzine and lithium. The former was stopped, and diuretics introduced with close monitoring of plasma lithium levels. Two weeks after the phenelzine was discontinued she began to relapse (Figure). She became mute, with stereotyped movements and a return of urinary incontinence.

Zimelidine (200 mg nocte) a 5HT targeted reuptake blocker was commenced but was without effect after a four week period. An increase in agitation was noted and the patient attempted suicide by self-strangulation. After a further two week period on lithium and L-tryptophan alone, to allow wash out of zimelidine, the monoamine oxidase inhibitor tranylcypromine was

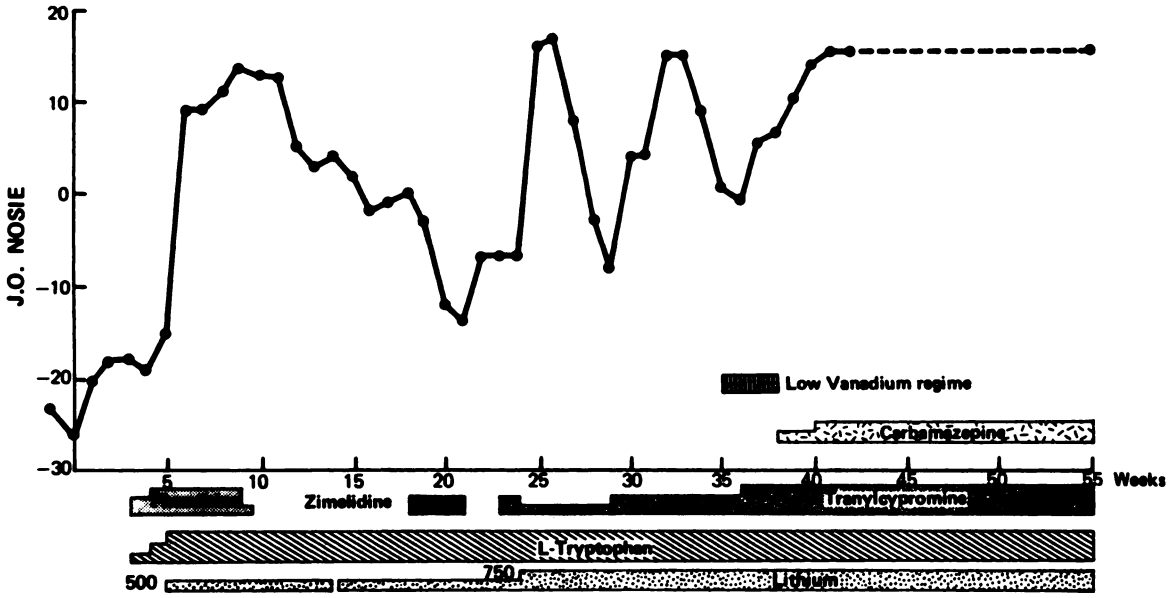

FIG.—Total score on NOSIE rating scale throughout the period study

introduced at a dose of 10 mg a day. A further dramatic recovery occurred after 2 weeks but relapse could only be prevented by increasing the dose of the MAOI, in two stages, up to 30 mg/day which eventually lost its efficacy. A vanadium lowering regime (EDTA 3 g/day and vitamin C 3 g/day with a low vanadium diet) was used but she remained depressed and agitated. At this time there was a very marked diurnal variation in mood from extreme withdrawal in the morning to moderate sociability in the evening. Because of the failure of the vanadium lowering regime carbamazepine (to achieve a plasma level around 5 mg/l at a dose of 200 mg/day) was introduced in its place, and within three days clinical improvement became apparent and she became normal within 10 days.

From this point she remained well and after a trial weekend leave she was discharged home with adequate social support. At follow up two months later she remained well.

Discussion

Although there are many aspects to this patient the discussion can fruitfully be limited to the drug treatment. We had previously noted the efficacy of a combination of lithium, L-tryptophan and phenelzine in a study of 13 chronically depressed patients. Fifty per cent had a good recovery. A recent pilot study in Newcastle of very severe cases of chronic depression supported this observation.

It may well be that this combination is targeted on 5HT mechanisms (Eccleston, 1981). In this case zimelidine did not improve the patient and the use of the triple combination was halted by the development of serious sodium retention, a feature found in other patients in an ongoing trial. The search for a substitute MAOI led to the use of tranylcypromine whose efficacy could not be sustained.

Naylor has studied ATPase in membranes of red cells in bipolar patients. His hypothesis postulates a reduced ATPase activity in membranes, including those of central neurons, leading to elevated intracellular sodium (Naylor *et al,* 1980; Naylor and Smith, 1981a). He feels that vanadium, a potent inhibitor of ATPase, may precipitate illness in these biologically predisposed patients (Naylor and Smith, 1981b). His treatment regimes aim at reducing the pentavalent ion of vanadium (Vn^5) to the less inhibitory tetravalent ion (Vn^4) by use of the reducing agent vitamin C. In addition the intake of vanadium may be reduced using specific diets and the chelating agent Ca EDTA given orally.

Carbamazepine is also a relatively recent introduction (Post, 1982). It has a place in the acute treatment of unipolar and bipolar patients and is a potentially useful prophylactic agent. Its previous use in epilepsy would suggest a mode of action at membrane level, as in the case of lithium.

The above case represents an attempt at a clinical experiment making use of new drugs and combinations

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of well known drugs over the period of a year in an extremely difficult case of chronic resistant depression.

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