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Treatment-resistant depressives

SIR: Tyrer & Murphy (*Journal*, January 1990, **156**, 115–118) elegantly confirm the success of sequential attempts at pharmacotherapy of an affective disorder in a female patient. However, their article also includes three errors often encountered in the therapeutic history of so-called treatment-resistant patients.

The first is taxonomic: in the abstract they describe the illness as a resistant neurotic disorder while what they summarise seems to be a chronic major depressive disorder in partial remission, possibly due to inadequate pharmacotherapy. While for purely classificatory purposes the four diagnostic categories from DSM-III which the patient satisfies need to be recorded, this ignores the clinical principle of hierarchical classification whereby all these would be residual symptoms of the major depressive disorder which needed to be treated with electroconvulsive therapy (ECT). We apply these concepts daily in outpatients when we see people recovering from major depression going through stages of predominantly 'neurotic' symptoms, and I believe that these ideas may be included in the ICD–10. The problem about using the word 'neurotic' is that, despite evidence to the contrary (Kahn *et al*, 1987; Lydiard & Ballenger, 1987; Zohar & Insel, 1987), many prescribers take it to mean that pharmacotherapy has few chances of success.

The second error relates to the fact that psychiatrists carry on ignoring the effect of dose in prescribing antidepressants. In the article we are not told what kind and how many ECTs the patient received and, more important still, what dose of tablets she had been exposed to. So-called standard doses may be ineffective (Quitkin, 1985), but when increased there is often a response (Kotin *et al*, 1973; Schuckit & Feighner, 1972). Prescribing a tricyclic for instance to a maximum dose of 150 mg daily cannot be considered an adequate trial of the drug, although the British National Formulary still prints this as the maximum dose. What is the point of using combinations when there is no evidence that the single agents have been tried to their full potential (Razani *et al*, 1983) as determined by the patient's tolerance rather than by a theoretical and ill-conceived upper dose limit?

Finally, why wait ten years? Even if the diagnoses of dysthymia and anxiety are upheld, we know that these can respond to antidepressants, and the same end point could have been reached in one year at the most. Based on the doses described in their papers, I calculated this time figure by including regular stepwise increases in the dose of the single agents used, periods of maintenance at high dose and of washout, and then stepwise increases in the combination until the patient is symptom free.

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SIR: The problem of dose and diagnosis were reconsidered on many occasions during our patient's long psychiatric contact. The hierarchical system of classification that Dr Malizia supports was quite inadequate for our patient. Although at times a primary diagnosis of depressive episode was justified, at others she had no depressive symptoms at all and attempts to force her into a depressive diagnostic category would have been Procrustean nonsense. During the ten years in which we have had personal contact with the patient, the most persistent symptom has been severe generalised anxiety, but obsessional rituals dominated her symptoms for nearly a year and at other times her agoraphobia made her almost housebound. Rather than bend all these symptoms into the status of secondary depressive ones, it is much more appropriate to allow the co-existence and changing dominance of different symptoms at different times. This patient is an exemplar of the general neurotic syndrome, a relatively severe neurotic disorder in which the depression, anxiety and other neurotic symptoms are associated with dependent or anankastic personality characteristics (Tyrer, 1985, 1989; Andrews *et al*, 1990).

Dr Malizia's comments about dosage are important and have been reinforced by others (Bridges, 1983; Quitkin, 1985). Our patient had been treated with up to a maximum of 175 mg daily of amitriptyline, but in higher dosage she was extremely handicapped by unwanted effects and on one occasion went into urinary retention. Unusually, these anticholinergic effects persisted even after prolonged dosage. Although it is possible to argue that the efficacy of combined antidepressnt therapy could be achieved by merely increasing the dose of a single antidepressant (bearing in mind that both groups of drugs increase the availability of central monoamines), we feel that this would not be sufficient explanation for the improvement shown in our patient, not least because she responded at relatively low dosage. More particularly, she regarded the improvement that she achieved on combined antidepressant therapy as qualitatively different from all previous treatments, and this had given a new dimension to her life. Although it would have been reasonable at first to regard this as a non-specific effect, the fact that it was still maintained after many years of treatment and that she relapsed during the placebo substitution described in our paper suggests that there are specific effects of combined antidepressant therapy that are not achieved by single drugs.

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Jewish depressives

SIR: I was very interested to read the study on Jewish depressives by Ball & Clare (*Journal*, March 1990, **156**, 379–383); however, I was disappointed, as the conclusions that the authors reach are not justifiable.

The sample population is a highly selected group, and there is no evidence that the Jewish depressives in the study were representative of the depressed members of the whole Jewish population of Hackney, or indeed of the rest of the country. Little information is given of the selection procedure for the study, which may be a main source of bias.

Forty per cent of the Jewish sample were widowed, compared with 19% of the non-Jewish sample. I performed the χ^2 test on this data myself, and the difference between the two groups approached statistical significance. It was remiss of the authors not to mention this fact, as widowed status has a bearing on the nature and course of depression (Parkes, 1965).

Furthermore, we know nothing about the social status, racial mix or types of religion of the non-Jewish sample, nor indeed about their 'religiousness' scores in comparison with the Jewish sample. There is also no indication as to whether this control group is representative of any population, be it Hackney or England in general. Such data would be essential to ascertain any effect that the Jewish religion has on symptoms.

Most of the Jewish sample experienced antisemitic persecution in the 1930s. It might be that this single factor has more bearing on the nature of subsequent depressive episodes than any vague cultural or religious issues centred around being Jewish. But