classified as either "black" or "white" (with an occasional allowance made for "grey"), even though referring to complex phenomena (like "personality", "precipitating factors" or "course independent of events"), would lead to equally simple and clear-cut results, e.g. the existence of a dichotomy'.

This is only true when the items of the scale are perfectly or very highly correlated amongst themselves. If the items are independent, or only slightly correlated, then, in view of the central limit theorem, the distribution of the summed scores will tend to normality, as Maxwell (1971) has pointed out (see also Guilford, 1956, p. 452). The average intercorrelation of the items of the Newcastle diagnostic index is only about ·18. Thus, given an homogeneous population, the distribution of this index will tend to be normal, not bimodal. This is also true of the Depressive Category-Type Scale (average intercorrelation = ·14) on which Garside *et al.* (1971) and Sandifer *et al.* (1966) found bimodal distributions. If this were not so, then such scales as those of the EPI and MPI would tend to have bimodal distributions, whereas in fact they have unimodal distributions.

Thus the finding that Kendell's and Post's data, when added together, are inconsistent with both the normal and unimodal hypotheses clearly indicates that there are at least two distinct populations of depressed patients. These populations, of course, may overlap to some extent, but they are nevertheless distinct in the sense that the majority of patients can be classified as belonging to particular groups.

Finally, as Dalén, a lucid exponent of Popper's ideas, has recently (1972) pointed out, a theory or hypothesis can be *dis*proved, but 'nothing can prove a theory is *true*: collecting facts which are favourable to a theory does not lead to any conclusive result'. The unimodal hypothesis of depression is a satisfactory hypothesis in that it is capable of being disproved. But it cannot be proved, as Drs. Kendell and Post have tried to do. Indeed, when their separate data are increased by adding them together, the resulting distribution is inconsistent with the unimodal hypothesis, as were the data of Carney *et al.* (1965), Sandifer *et al.* (1966), Fahy *et al.* (1969), Gurney (1971) and Garside *et al.* (1971). Thus six sets of data, collected by three independent groups at different places, are all inconsistent with the unimodal hypothesis of depression. Is it not now disproved?

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SUSTAINED RELEASE AMITRIPTYLINE (LENTIZOL) IN DEPRESSIVE ILLNESS

Dear Sir,

As Medical Director to the Company responsible for the production of sustained-release amitriptyline (Lentizol), and having been associated with Dr. Haider in the study reported in the *Journal* (May 1972, **120**, 521–2), I feel that there are several points which require comment in the letter from Dr. Arthur Rifkin *et al.* in the October 1972 issue of the *Journal*, **121**, 457. I am sure that Dr. Haider himself will wish to reply personally to this letter, but as he is now resident in Pakistan and there may be some delay before his reply is received I should like to make the following comments:

1. At the present time, to my knowledge, there are no published clinical trials demonstrating that ordinary amitriptyline given in a single daily dose is efficacious. It seems that the authors of this letter feel that the new sustained form of amitriptyline, which is a recognized advance in the formulation of the drug, should be matched against ordinary amitriptyline given in an as yet unproved dosage

regime. In the absence of such evidence, Dr. Haider can firmly claim that a single evening dosage of sustained release amitriptyline is an advantage over the thrice daily dosage of ordinary amitriptyline, used in current therapy.

2. A very important point has been ignored, or perhaps has been unappreciated by Dr. Rifkin and his colleagues, that equal therapeutic effect is obtained in the case of the sustained release form at two-thirds of the dosage of ordinary amitriptyline. Clinical trials have demonstrated this. Sims (1972), Gomez (1972), Wheatley (1972), Sedman (1972). This represents a definite advance, especially with regard to psychotropic drugs.

3. Reference to the effectiveness of imipramine given in single dosage is based on a retrospective and somewhat impressionistic study covering 43 patients by one of the co-authors (Dr. D. F. Klein) at their own hospital. This study, and your correspondents' interpretation thereof, are open to criticism on the following points:

(a) Findings with imipramine cannot be taken to imply that amitriptyline given in single daily doses would necessarily produce similar results. This is especially true in regard to side effects.

(b) Data are retrospective in both groups studied. In the first group 12 or 22 subjects received concomitant drugs, several of which would inevitably influence the outcome of the patient's depression. All patients in this first group had psychotherapy.

(c) We are not told how the patient's progress was assessed.

(d) The authors' claim that a single daily dosage of imipramine 'can give fewer side effects' is based on data (unstated) from *three* patients.

4. Dr. Rifkin *et al.* ignore the important point that even if one were to give ordinary amitriptyline as a single dose and attempt to compare it with the same or two-thirds of the dose of the sustained release form, there could be no true comparison, as the two formulations are quite different. One is a normal film-coated compressed tablet of amitriptyline hydrochloride, the other is a gelatine capsule containing the active principle in small coated pellets each of which is a microdialysis unit diffusing out a fixed amount of drug over a specified period. A much more sophisticated process than ordinary tablet disintegration is surely an advance by any standards.

My Company is, of course, aware that both forms of amitriptyline should be compared in a once daily dosage, and are at present conducting such clinical studies.

Lastly, I would remind Dr. Rifkin and his colleagues that the object of Dr. Haider's study was not to demonstrate an advantage over ordinary amitriptyline given in an empirical and as yet unproved dosage, but to show that sustained release amitriptyline given once a day and producing equal therapeutic effect at two-thirds of the dosage of ordinary amitriptyline on a thrice daily dosage basis is an advance in the treatment of depressive illness.

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FLUPENTHIXOL IN THE TREATMENT OF DEPRESSIVE STATES

DEAR SIR,

In a recent report on the treatment of chronic schizophrenia with flupenthixol decanoate (1), 11 of the 13 schizophrenic patients whom we treated reported a significant elevation of mood. We suggested that flupenthixol might therefore prove useful not only as an antipsychotic drug but also as an antidepressant, and similar suggestions had been made previously in the columns of your *Journal* (2, 3).

We subsequently treated 25 patients suffering from sustained depression of mood, average duration of depression being 7·5 years. Twenty patients showed diurnal variation of mood, 21 depressive hypochondriasis, 15 depressive sleep disorder and 14 psychomotor retardation. Twelve had made suicidal attempts and most of them were regarded as suffering from long-standing 'mixed' depressive illnesses (i.e. showing both 'endogenous', 'reactive' and neurotic features). Twenty were female, 5 male, and mean age was 47 years (range 18·78 years). All but one had previously been treated with various tricyclic antidepressants and 14 with monoamine oxidase inhibitors, whilst 14 had been treated with electroplexy.

Sixteen patients were treated with oral flupenthixol at a dose of 0·5–2 mg. per day, and 9 with flupenthixol decanoate 20–40 mg. intramuscularly every 2–3 weeks. Of the latter, 5 developed parkinsonism