consistent with Hamp's (1961) work with normal individuals who displayed evening mood elevation. Perhaps such diurnal variation is more widespread than an occurrence in endogenous depressives.

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REFERENCES

HAMP, H. (1961) Die tagesrhythmischen Schwankungen der Stimmung und des Antriebes beim gesunden Menschen. *Archiv für Psychiatrie*, **201**, 355–77.

KILOH, L. G. & GARSIDE, R. F. (1963) The independence of neurotic depression and endogenous depression. *British Journal of Psychiatry*, **109**, 451–63.

ROSENTHAL, S. H. & KLERMAN, G. L. (1966) Content and consistency in the endogenous depressive pattern. *British Journal of Psychiatry*, **112**, 471–84.

SANDIFER, B. C., WILSON, I. A. & GREEN, L. (1966) The two-type thesis of depressive disorders. *American Journal of Psychiatry*, **123**, 93–7.

STALLONE, F., HUBA, G. J., LAWLOR, W. G. & FIEVE, R. R. (1973) Longitudinal studies of diurnal variations in depression: a sample of 643 patient days. *British Journal of Psychiatry*, **123**, 311–18.

WALDMAN, H. (1972) Die Tagesschwankung in der Depression als rhythmisches Phänomenon. *Fortschritte der Neurologie Psychiatrie und ihrer Grenzgebiete*, **40**, 83–104.

CONTINUED NEED FOR PLACEBOS

DEAR SIR,

The superiority of imipramine over placebo has been clearly demonstrated by Drs Rogers and Clay (*Journal*, December 1975, **127**, pp 599–603) though there are at least two simpler methods of drawing the same conclusion about efficacy: via the overall response rates and via the trends of individual trials.

In their summary, however, the authors state that further drug-placebo trials in non-institutionalized patients with endogenous depression are not justified. This is not so. It is more ethical to use placebo as a control than imipramine.

Consider a new drug which has gone through an exhaustive series of uncontrolled trials from which it could reasonably be expected that 70 per cent of such patients will show a 'greatly or moderately improved' response. The therapeutic benefit is not yet confirmed; there is reasonable doubt and some sort of quantitative evaluation is desirable and justified. A controlled trial is needed. But which control—imipramine or placebo?

Sixty-five per cent of the imipramine patients can be expected to respond adequately (the authors have shown), contrasted with 70 per cent of patients on the new drug. To reach a statistically significant result at the 0·05 level will require a trial with 1,000 patients if the original premise is correct. Five hundred patients will receive imipramine, of whom 65 per cent can be expected to respond and 35 per cent not to do so. Thus 175 patients on the control treatment can be expected to show an inadequate response.

If, on the other hand, a placebo control were to be used with a response rate of say 30 per cent (the first 14 trials in their Table I gave a response rate of ·32 with a standard deviation of ·19) then the controlled trial with the new drug will require about 30 patients. Of these, 15 will be on placebo and 10 of these can be expected to show an unsatisfactory response.

I have no difficulty in justifying the continued use of placebo, even though the value of imipramine is beyond dispute.

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SCHIZOPHRENICS' FAMILIES

DEAR SIR,

Fowler and Tsuang (*Journal*, January 1976, pp 100–1) take issue with our finding (*Journal*, August 1975, **127**, pp 97–108) of more personality disorder in the families of our schizophrenic probands than in the controls. In fact there does not appear to be any substantial point of disagreement between our data and those of Fowler and Tsuang, but rather a difference of terminology. Those relatives whom we regarded as suffering from the kinds of personality disorder which our analyses suggested were biologically akin to schizophrenia they would have called cases of 'suspected schizophrenia'. Those illnesses which we did not think were biologically related to schizophrenia they found in their families to be 'transmitted independently of schizophrenia'. In our study this applied to affective disorders, neurotic reactions (except possibly in females) and neurotic personality disorders, subnormality and suicidal behaviour, while Fowler and Tsuang mention particularly affective disorder and alcoholism. As regards the latter, some but not all of our cases were thought to have arisen on the basis of personality disorder of the kind related to schizophrenia, while Fowler and Tsuang emphasize that 'alcoholism and some personality disorders in the families of