liable to provoke symptoms of anxiety. Common examples that come readily to mind are respiratory alkalosis associated with hyperventilation, respiratory acidosis associated with lung disease, metabolic acidosis associated with uraemia, hyper- or hypocalcaemia associated with parathyroid disorders, and so on. The common denominator seems to be some deviation from the norm in the patient's internal bio-physical environment. This leads us to believe that *anxiety-prone subjects, and perhaps anxiety neurotics, may essentially suffer from an excessive sensitivity or intolerance to disturbances in their internal bio-physical homeostasis.* They may react with symptoms of anxiety and with compensatory homeostatic efforts to changes that may remain unnoticed or ignored by others.

Viewed in this light (*Arch. gen. Psychiat.*, November 1969, **21**, 611–9), Pitts and McClure's experiment does little more than illustrate what happens when anxiety-prone subjects are suddenly exposed to major perturbation of homeostasis—in this case to major electrolyte and acid-base balance disturbances. The facts that anxiety symptoms can be induced with lactate infusions even without bringing about significant blood lactate elevations, and that similar symptoms can be brought about with bicarbonate infusions admittedly refute Pitts and McClure's hypothesis. However, these factors offer no ground for any 'extension or refinement of the hypothesis of Pitts and McClure', as Friedhoff suggests, nor for that matter do they provide support for any other hypothesized specific mechanism.

More recently, some experimenters have used sodium lactate infusions as an experimental model to test the effectiveness of anti-anxiety drugs. The rationale for this seems to be based on the erroneous belief that lactate-induced anxiety provides a sound laboratory model for clinical anxiety. Since lactate infusions induce anxiety symptoms that are associated with electrolyte, pH and body fluid disturbances the like of which are found in nature only in physically quite ill people, and ordinarily not at all in anxiety neurotics, the validity of using lactate-induced anxiety as an experimental model from which to extrapolate findings to clinical populations is more than doubtful. (In fact, as we will report elsewhere, some of the lactate-induced effects are not only unusual but also hard to explain.) *In fine*, Pitts and McClure's laboratory model can hardly generate clinically valid conclusions.

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THIAMINE DEFICIENCY IN THE AETIOLOGY OF THE HALLUCINATORY STATE COMPLICATING ALCOHOLISM

DEAR SIR,

The paper by Blackstock *et al.* (*Journal*, October 1972, **121**, 357–64) on the role of thiamine deficiency in the aetiology of hallucinatory states complicating chronic alcoholism provides a welcome addition to the thiamine deficiency/alcohol withdrawal debate. Their findings are not so dissimilar to those from my own study (1) as one might suppose from the way they have presented their data.

Our results agree in concluding that hallucinatory states may be induced by alcohol withdrawal alone, in the absence of any clinical and biochemical evidence of thiamine deficiency (Blackstock *et al.*, 6/15 cases, Morgan 4/8 cases with hallucinations).

The precise role, if any, of thiamine deficiency remains problematic. My own findings, based on clinical assessment and pyruvate studies on a very small series, suggest that hallucinatory states which develop while drinking is continuing (and which I have termed 'subacute' because they may extend over several weeks) might be closely associated with thiamine deficiency. Blackstock *et al.*, on the basis of their pyruvate findings, clearly do not subscribe to this view. However, if the criteria of thiamine deficiency in their study are widened to include either pyruvate or transketolase abnormalities, or both, then their findings show a trend in favour of my hypothesis. I suggest that this has still not been put out of court and should remain a matter for further investigation.

There are certain very real problems besetting this particular field of study. Not only are the subjects unreliable as a source of information, but there is also a pressing need for more precise definition of the mental phenomena involved, as Blackstock *et al.* rightly point out. Further, the biochemical tests of thiamine deficiency need further development. The transketolase test, itself superior to the pyruvate tolerance test, is still an indirect method of thiamine assay. Of course, it does not follow that direct assay of thiamine is necessarily any better; for example, isolated blood thiamine estimations fluctuate very widely with the thiamine intake over the previous few days, and are of doubtful value in assessing states of true clinical deficiency of thiamine. Some kind of thiamine tolerance test may eventually prove to be the most sensitive index. Preliminary data using such a technique, with spectrofluorometric assay of thiamine, have been published by Dewhurst and myself (2), but it is not yet clear whether the method can distinguish thiamine-deficient from normal

subjects. Close collaboration between biochemists and clinicians might clarify this issue.

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DEPRESSIVE ILLNESSES IN LATE LIFE

DEAR SIR,

In his recent paper Dr. Post (*Journal*, October 1972, pp. 393–404) considered the distribution of the scores of 92 depressed patients on the Newcastle diagnostic index (Carney *et al.*, 1965). He found that this distribution did not depart significantly from normality and concluded that there was, therefore, no evidence from this data that a dichotomy exists between unipolar and bipolar affective psychoses on the one hand and neurotic depressions on the other.

However, Dr. Post's distribution, and his value of χ^2 obtained ($\chi^2 = 11{\cdot}3$, d.f. $= 8$, $P = {\cdot}2$) suggests that the corresponding population distribution may not be normal, and that additional data might well have produced a significant departure from normality. Accordingly I asked Dr. Kendell to let me have the distribution of 130 depressed patients on the Newcastle index, referred to by him in his 1968 paper (Kendell, 1968). Dr Kendell has kindly given me this distribution, which is reproduced below together with Dr. Post's, with the sum of the two and with the expected normal frequencies.

Although Dr. Post's patients were all over sixty, and Dr. Kendell's patients were younger, the means of the two distributions are very similar (3·86 and 3·79 respectively), so are their variances (10·69 and 10·39), and so are their distributions ($\chi^2 = 4{\cdot}98$, d.f. $= 10$, $P = {\cdot}89$). It is therefore reasonable to add them together, and any departure from unimodality found in the combined distribution cannot be due to differences between Drs. Kendell and Post, or their data. The two sets of data are also similar in that there is a distinct dip at the score of 5 in both distributions. The distribution of the summed frequencies in the Table definitely departs from normality ($\chi^2 = 24{\cdot}5$, d.f. $= 11$, $P = {\cdot}011$). (Dr. Peter Britton has kindly checked this result for me). Thus the hypothesis that the population distribution of depressed patients is normal can be rejected. But this does not necessarily mean that the population is non-unimodal; in general the distribution might be skewed, or flat, rather than bimodal.

The present data, however, appear to be non-unimodal. In particular, frequency of only 16 at the score of 5 is considerably less than either of the two adjacent frequencies (26 and 27). If the population distribution is unimodal, the frequency at score 5 should be at least a third of the sum of the three frequencies at scores 4, 5 and 6, since the scores of 4 and 6 have the highest frequencies and are therefore between the points of inflexion, if they exist. The sum of the sample frequencies at the three scores is 69. Thus the expected frequency at score 5 (given the unimodal hypothesis) is 23 or more. But it is only 16, and the exact probability of obtaining this frequency, or less, given an expected frequency of 23, is only ·045 —a significant result. Thus the hypothesis that the population frequency at score 5 is a third or more can be rejected. This frequency must, therefore, be less than a third of the sum of the frequencies at scores 4, 5 and 6. So it may be concluded that the population distribution is not unimodal.

The distribution of depressed patients is, therefore, neither normal nor unimodal. This is an important finding, because the data upon which it is based are certainly not biased in such a way as to generate a spurious departure from unimodality; it is clear that neither Dr. Post nor Dr. Kendell favour a bimodal view of depression. Dr. Kendell (1968, p. 21) concluded that the bimodal distribution obtained by Carney *et al.* (1965) might well be due to 'the strength of their original convictions and the pernicious influence of the halo effect, rather than any characteristics inherent in the patients'. This suggestion of Kendell's can now perhaps be rejected.

There is one further point which needs to be considered. Dr. Post (1972, p. 402) states 'it should in any case seem obvious that an analysis of data

Score	−3	−2	−1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	Total
Post's data	1	1	6	11	6	9	10	8	6	13	9	6	2	3	0	0	1	92
Kendell's data	1	5	9	10	11	8	14	18	10	14	14	10	1	3	1	1	0	130
Sum	2	6	15	21	17	17	24	26	16	27	23	16	3	6	1	1	1	222
Expected	5·8	5·6	9·1	13·3	18·7	23·3	26·6	27·1	25·5	22·0	16·4	12·0	7·8	4·4	2·4	1·1	0·9	222·0