

## Correspondence

*Correspondents should note that space is limited and shorter letters have a greater chance of publication. The Editors reserve the right to cut letters and also to eliminate multitudinous references. Please try to be concise, strictly relevant and interesting to the reader.*

### CARDIAC ARREST IN A YOUNG WOMAN TREATED WITH AMITRIPTYLINE COMBINED WITH LEVOPROMAZINE

DEAR SIR,

Some authors such as Herzmann (1978) compare the influence of the tricyclic antidepressants (TAD) on the heart to that of quinidine, talking about a quinidine-like effect as a result of which atrioventricular block may occur or which may lead to ventricular fibrillation and even cardiac arrest. Most cases of cardiac arrest among patients treated with TAD and, less frequently, with neuroleptics take place in older people or in people with a history of heart disease. There is a much smaller number of reports of sudden disturbance of cardiac rhythm, ventricular fibrillation and even death in young patients treated with the above mentioned drugs but who did not previously suffer from heart disease (Mocchetti, 1977; Hollister, 1978). Some authors express doubt that such cases exist, e.g. Sack (1977). The risk of cardiac complications becomes greater when the doses of TAD are large or when TAD is given in combination with neuroleptics (Hollister, 1978). There has been no mention in the literature of clinical death following cardiac arrest as a result of an unfavourable interaction between amitriptyline and levopromazine (an aliphatic phenothiazine) given in therapeutic doses. It is worth stressing the fact that the case discussed here concerned a young woman who had never had heart disease. For both these reasons the case seemed worth reporting.

A 34-year-old single female engineer was admitted in depressive stupor. She had been previously healthy and free of heart disease, and many routine ECGs in psychiatric departments had been normal. On admission she had a normal tracing, with tachycardia. Eight days after admission amitriptyline was started in doses rising to 250 mg daily on the 10th day of treatment. Because of insomnia she also had levopromazine 100 mg at night. She improved markedly, being in better contact and less depressed. On the 12th day she had unheralded cardiac and respiratory arrest at 10.30. Anaesthetists were by chance at hand and immediately began resuscitation by intubation,

assisted respiration and cardiac massage, followed by defibrillation, which restarted the heart at 11.15. The patient's ECG then showed normal axis, sinus rhythm at 96 per minute, non-specific ST deflections, T<sub>1</sub> plane, and T waves in leads V<sub>2</sub> to V<sub>6</sub> flattened. That afternoon the patient recovered consciousness and recognized her parents. At 20.05 ventricular fibrillation returned very briefly but ceased without intervention. A xylocaine infusion was started, at 22.55 defibrillation again had to be applied for ventricular fibrillation, and at 24.00 tracheotomy for accumulation of bronchial secretions. The next day the patient's general condition improved greatly, and five days after that the ECG was normal.

ROBERT TEODOR HESE

*Psychiatric Department,  
Miners Hospital,  
41-902 Bytom, Roosevelta 10,  
Poland*

### References

- HERZMANN, C. (1978) Zur Frage der kardiotropen Wirkung von Antidepressiva insbesondere bei Altpatienten. *Aktuelle Gerontologie*, **8**, 481–5.
- HOLLISTER, L. E. (1978) *Clinical Pharmacology of Psychotherapeutic Drugs*. New York: Raven Press.
- MOCCHETTI, T. (1977) *Kardiotoxische Medikamente unter besonderer Berücksichtigung der Phenothiazine und Imipraminderivate*. Stuttgart: Verlag Hans Huber.
- SACK, R. L. (1977) Side effects of and adverse reactions to psychotropic medications. In *Psychopharmacology. From Theory to Practice* (eds. J. D. Barchas, P. A. Berger, R. D. Ciaranello and G. R. Elliott), p 279. New York: Oxford University Press.

### NEUROENDOCRINE RESPONSES AS AN INDICATOR OF RECURRENCE LIABILITY IN PRIMARY AFFECTIVE ILLNESS

DEAR SIR,

The assessment on clinical grounds of the liability of affective disorders to recur has not been satisfactory. Clearly, if we had a laboratory test which would detect biological propensity for relapse before it manifests in psychopathology and behaviour, the management of recurrent affective disorders could be

much more effective. Instead of being treated continuously with medication, as they are now, patients could be monitored by neuroendocrine tests and many treated intermittently. Affective episodes could be prevented by early treatment, which could be discontinued once the laboratory tests became negative. In contrast with current practice, this approach would introduce an individually tailored, more effective treatment with fewer long-term side-effects.

Several recent observations indicate that some neuroendocrine responses may become useful in this respect. It has been suggested recently that the dexamethasone suppression test (DST) may change in parallel with the severity of primary depression (1) and that a positive DST may even precede clinical depressive episodes (2-6). Furthermore, the TSH response to TRH has been reported (7-10) to have predictive value for impending affective recurrences.

We have recently made another observation along similar neuroendocrine lines: in bipolar patients increased prolactin response to hypoglycemia was significantly associated with subsequent manic relapses (Table).

TABLE

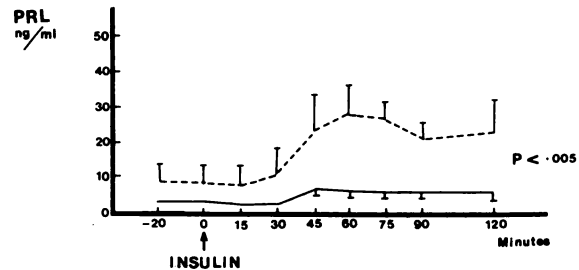
Fourteen patients with bipolar affective disorder. Prolactin response to hypoglycemia tested during free interval, patients divided according to maximum prolactin response greater or less than 10 ng/ml. Manic relapses counted in subsequent three months. Chi-Square Test with Yates' correction.

Bipolars stabilized on lithium		
	Relapse	Non-relapse
PRL increased > 10 ng/ml	4	1
PRL increased < 10 ng/ml	0	9
P < 0.05		

This observation took place during a systematic study of the neuroendocrine effects of lithium in humans. All subjects reported here were patients with the RDC diagnosis of bipolar affective disorder, free interval, and were tested during long-term lithium treatment. All were given insulin and later TRH and LHRH stimulation. After testing, some of the patients qualified for intermittent treatment with lithium.

Of the 14 stabilized patients tested during lithium treatment, 4 had an acute manic relapse within 3 months after testing, while 10 remained stable. Hormonal responses were compared in the relapsed and non-relapsed groups. The prolactin responses to insulin hypoglycemia were significantly greater in the 4 patients who subsequently relapsed, than in the 10 who did not (Fig). Neither prolactin responses to

TRH, nor growth hormone responses to hypoglycemia differentiated between these two groups.



FIG—Prolactin response in bipolar patients stabilized on lithium. Patients who remained stabilized ( $n = 10$ ); solid line. Patients with subsequent manic relapses within 3 months ( $n = 4$ ); interrupted line. Analysis of variance.

These observations did not take place within a randomized lithium discontinuation trial, hence replication is required. Therefore, we have now embarked on a systematic study of the value of prolactin responses to insulin hypoglycemia in predicting recurrence.

All in all, the above-mentioned observations raise the interesting possibility that one or more neuroendocrine responses may be more sensitive than overt psychopathology in assessing the propensity for recurrences, and therefore may be useful for decisions about treatment. If these observations are further validated, it may be desirable to monitor prolactin, cortisol and TSH responses during the treatment of recurring affective disorder: cortisol non-suppression may be particularly sensitive to future depressive, and prolactin to future manic recurrences.

EVA GROF  
GREGORY M. BROWN  
PAUL GROF

Departments of Psychiatry and Neurosciences,  
McMaster University, Hamilton, Ontario

#### References

- (1) CARROLL, B. J., FEINBERG, M., GREDEN, J. F., TARIKA, J., ALBALA, A., HASKETT, R., JAMES, N., KRONFOL, Z., LOHR, N., STEINER, M., DEVIGNE, J. P. & YOUNG, E. (1981) A specific laboratory test for the diagnosis of melancholia. *Archives of General Psychiatry*, **38**, 15-22.
- (2) ALBALA, A. A., GREDEN, J. F., TARIKA, J. & CARROLL, B. J. (1981) Changes in serial dexamethasone suppression tests among unipolar depressives receiving electroconvulsive treatment. *Biological Psychiatry*, in press.
- (3) DE LA FUENTE, J. & ROSENBAUM, A. H. (1980) Neuroendocrine dysfunction and blood levels of tricyclic antidepressants. *American Journal of Psychiatry*, **137**, 1260-1.

- (4) GOLDBERG, I. K. (1980) Dexamethasone suppression test as an indicator of safe withdrawal of anti-depressant therapy. *Lancet*, *i*, 376.
- (5) — (1980) Dexamethasone suppression tests in depression and response to treatment. *Lancet*, *ii*, 92.
- (6) GREDEEN, J. F., DEVIGNE, J. P., ALBALA, A. A., TARIKA, J., BUTTENHIEM, M., EISER, A. & CARROLL, B. J. (1981) Post-dexamethasone plasma cortisol levels among lithium treated rapidly cycling bipolar patients. In *The Prediction of Lithium Response* (ed. H. Dufour). Paris: Economica, in press.
- (7) KIRKEGAARD, C., NORLEM, N., LAURIDSEN, U. B. & BJOERUM, N. (1980) Prognostic value of thyrotropin-releasing hormone stimulation test in endogenous depression. *Acta Psychiatrica Scandinavica*, *52*, 170–7.
- (8) — & BJOERUM, N. (1980) TSH responses to TRH in endogenous depression. *Lancet*, *i*, 152.
- (9) LANGER, G., SCHONBECK, G., KOINIG, G., SCHUSSLER, M. & REITER, H. (1980) Neuroendocrine status of depressed patients at admission and during anti-depressant drug treatment (Clomipramine). *Neuropsychobiology*, *6*, 153.
- (10) — — & ASCHAUER, H. (1981) Neuroendocrine mechanisms in therapeutic effects of anti-depressant drugs: The "Thyroid axis" hypothesis. Presentation—3rd World Congress Biological Psychiatry, Stockholm. Abstracts S-211.

#### PLACEBO-CONTROLLED STUDIES OF ECT

DEAR SIR,

In his discussion of placebo-controlled studies of electroconvulsive therapy Professor Kendell (*Journal*, October 1981, *139*, 265–83) referred to the six studies reviewed by Barton (1977) and adds to this number the four double-blind studies published over the past four years.

In a recent review of placebo-controlled studies of ECT (Mendelson, 1981) I discussed two other studies which were only mentioned in passing by Barton and omitted by Kendell, namely the reports of Sainz (1959) and of Fahy *et al* (1963). Sainz reported on 20 patients with depressive illness, of which ten were treated with ECT while the remainder received 'mock' treatment. He found that in the electrotherapy group nine patients recovered and one improved; in the placebo group one patient improved, six were unchanged, and three became worse. Fahy and his colleagues compared groups of depressed patients treated with imipramine, electrotherapy, and 'thiopentone sleep'; there were 17 patients completing treatment in each of the three groups. Although ECT was more effective than 'thiopentone sleep', this difference did not reach statistical significance. This study was perhaps biased against ECT in that severely depressed patients who were considered high suicide risks were excluded from

the trial, and it is a widely held clinical belief that these patients show the most striking response to electrotherapy.

Professor Kendell's comment about "conflicting results of recent comparisons of the effect of real and simulated ECT in the treatment of depressive illness" is ill-founded. Three of the four recent studies have shown ECT to be clearly superior, whereas the study by Lambourn and Gill (1978) used brief pulse stimuli, applied unilaterally with the rating of improvement made on the day following the last treatment, although it has been shown that unilateral ECT has a poorer therapeutic effect within the first week of therapy when compared with bilateral ECT (Heshe *et al*, 1978).

I would suggest that the results of placebo-controlled studies of ECT pose no serious challenge to the accepted clinical view that electrotherapy is a specific and effective treatment of depressive illness in the presence of indications as discussed by Kendell.

GEORGE MENDELSON

Suite 7,

30 Queens Road, Melbourne 3004, Australia

#### References

- BARTON, J. L. (1977) ECT in depression: the evidence of controlled studies. *Biological Psychiatry*, *12*, 687–95.
- FAHY, P., IMLAH, N. & HARRINGTON, J. (1963) A controlled comparison of electroconvulsive therapy, imipramine and thiopentone sleep in depression. *Journal of Neuropsychiatry*, *4*, 310–14.
- HESHE, J., RÖDER, E. & THEILGAARD, A. (1978) Unilateral and bilateral ECT. *Acta Psychiatrica Scandinavica*, Suppl. 275.
- LAMBOURN, J. & GILL, D. (1978) A controlled comparison of simulated and real ECT. *British Journal of Psychiatry*, *133*, 514–19.
- MENDELSON, G. (1981) Electrotherapy and "placebo" electrotherapy: a review. *Medical Journal of Australia*, *2*, 125–8.
- SAINZ, A. (1959) Clarification of the action of successful treatment in depression. *Diseases of the Nervous System*, *20*, 53–7.

#### BENZODIAZEPINES AND EFFECTIVENESS OF ECT

DEAR SIR,

I have read with much interest the magisterial review article "The Present Status of Electroconvulsive Therapy" by R. E. Kendell, (*Journal*, October 1981, *139*, 265–83).

I agree with him about the continued utility of ECT in psychiatric treatment and the necessity for accurate and conscientious routines in its use. I also agree with him about the necessity for further research in this form of treatment, still the most effective in some types of depressive states.