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SERUM CREATINE PHOSPHOKINASE ACTIVITY IN ACUTE PSYCHOSIS

Dear Sir,

In a recent paper (*Journal*, October 1972, pp. 351–5) Gosling *et al.* confirmed my previous reports of increased serum CPK activity in acutely psychotic patients and its lack of an increase in non-psychotic patients. They inaccurately stated that I and colleagues had studied only admission serum CPK levels in non-psychotic patients. We have previously published the lack of an increase in serum CPK activity in samples obtained Mon.–Fri. throughout hospitalization from two sizeable groups of severely disturbed, hospitalized non-psychotic psychiatric patients (Meltzer, 1969; Meltzer and Moline, 1970).

Gosling *et al.* also claimed that there was a trend towards a higher percentage of psychotic patients with increased serum CPK activity who were diagnosed manic-depressive, manic phase, or paranoid schizophrenic, as opposed to psychotic depressive or non-paranoid schizophrenic. In our previous studies (Meltzer, 1969; Meltzer, Elkun and Moline, 1969), we have indicated that the incidence of increased serum CPK activity is not significantly different in non-paranoid schizophrenics, paranoid schizophrenics, or manic-depressives, manic phase. We reported on too few psychotic depressions, bipolar or unipolar, of recent onset to know if the enzymes are elevated in depressed patients with equal frequency (Meltzer, 1969; Meltzer, Elkun and Moline, 1969). In our current studies, looking only at patients admitted within one week of the onset of psychotic symptoms, but whose serum CPK activity was studied Monday to Friday throughout hospitalization, I have found increased serum CPK activity in 41 of 53 (78 per cent) acute schizophrenics of non-paranoid types, 29 of 32 (91 per cent) acute schizophrenics, paranoid type, 6 of 7 patients with paranoid states, 9 of 12 patients with manic-depressive psychosis, manic-phase and 3 of 3 psychotic depressives. There are no statistically significant differences between the incidence of elevations in these groups. In approximately one-third of these patients, the increases in serum CPK activity did not occur until after discharge from hospital. I suggest that the data of Gosling *et al.* are best explained by a greater delay in admitting non-paranoid schizophrenics and psychotically depressed patients to the hospital in comparison with paranoid psychotic patients and manic-depressives, manic phase patients.

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UK 3557 IN DEPRESSION

Dear Sir,

Dr. Wheatley's conclusion that UK 3557 'has a similar antidepressant effect to the control drug, amitriptyline, but that there are no therapeutic differences between them' (*Journal*, December 1972, p. 622) is unwarranted. The results of his trial show that amitriptyline was consistently superior to UK 3557 at all periods of assessment, although this did not reach significance. In the absence of a placebo control group no inferences can be drawn about the antidepressant effects of UK 3557, as the improvement shown during the trial could be entirely due to non-specific factors.

Peter Tyrer.

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Dear Sir,

In the interpretation of clinical trial results, it is always necessary to strike a balance between that which is statistically significant (or non-significant)

and that which is clinically significant (or non-significant). However, in a straightforward comparison between the effects of two anti-depressant drugs, using standard rating scales, it is generally accepted that unless the statistical differences between them reach the 5 per cent level of significance then for clinical purposes no differences have been demonstrated.

In this particular trial, although, as was pointed out in the report, 'such differences as were present were always in favour of amitriptyline', there was no single assessment that showed a significant difference in favour of the control drug. Since the report was a short one, the non-specific factors that were recorded were not enumerated, but these were as follows: sex, age, marital status, previous attacks, duration from first attack ever, duration of present attack, religion, educational level, previous treatments, and menstrual status in females. The two treatment groups were well matched in respect of all these factors. Although non-drug variables such as these may play a part in influencing the response to psychotropic drugs, it is doubtful whether such differences are of practical clinical significance (Wheatley, 1973).

I agree with Dr. Tyrer that scientifically it would have been prefereable to include a group treated with placebo only. However, our trial was undertaken in general practice, and it would have been unethical to leave unsupervised depressed patients without specific antidepressant treatment, when it is generally accepted that such treatment is in fact efficacious.

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CONTROL OF GROSS SELF-MUTILATION WITH LITHIUM CARBONATE

DEAR SIR,

Self-mutilation is common in hospitals for the mentally subnormal (1) and is often extremely difficult to control. This is evident from the wide variety of therapeutic measures that have been advocated including sedatives and tranquillizers, intensive individual care, recreation, constructive occupation (1) and behaviour therapy techniques (2, 3).

We wish to report satisfactory control with lithium carbonate of gross self-mutilation in a severely subnormal girl in her early twenties. Brain-damaged at birth and without speech, she was admitted to Strathmartine Hospital, Dundee, in 1963 at the age of 18 with a five year history of hyperactivity and repeated self-injury. In hospital her behaviour became a constant and serious problem; in addition to being withdrawn and negativistic she had frequent bouts of screaming when she threw herself on the floor or down a stone staircase, struck her head repeatedly against sharp corners of furniture, metal radiators or the head and sides of her bed, producing swelling, haematomas and lacerations. She persistently gnawed at the backs of her hands so that they were chronically ulcerated, and at times her general condition gave such cause for concern that she was put into a special jacket. Her conduct failed to respond to intensive individual nursing care combined with a succession of tranquillizing drugs, and in September 1967 it was decided, empirically, to observe the effect of lithium carbonate. She was physically fit; blood examination, including the uric acid level, was normal and all other drugs apart from hypnotics were withdrawn.

Lithium carbonate was prescribed in a dose of 500 mgs t.d.s. (6 days per week) and produced a steady plasma level of 0·9 mEq./l. For a few days there was little change but within a week the patient became quiet, docile and co-operative. Her chronically ulcerated hands healed completely in two weeks, head-banging ceased and for the first time she began to show some interest in her fellow patients. In view of the apparent dramatic response to lithium, consideration was given to the substitution of a placebo, but her parents, gratified by the marked improvement, were unwilling to risk the possibility of serious relapse following withdrawal of the drug.

In late December 1967, she developed a respiratory infection which was associated with relapse into self-destructive behaviour, and lithium was withdrawn for a few days until the infection cleared. Fortunately, the episode was short-lived, and since 6 January 1968 she has remained constantly on lithium, at the above dose, with plasma levels consistently within therapeutic limits. Although she has continued to be rather negativistic, and on three separate occasions each lasting a few weeks was temporarily elated and over-active, self-mutilation has not recurred during the five years she has been treated with lithium. There seems little doubt that lithium has improved very substantially the management problem which