

ALCOHOL-DISULFIRAM REACTIONS

DEAR SIR,

In his discussion on alcohol-disulfiram reactions, Brewer (*Journal*, February 1984, **144**, 200-2) shows that some patients will require more than the recommended 200 mg of disulfiram to experience a reaction. He has had to use up to 1500 mg. This confirms our experience in preparing patients for disulfiram implants (Malcolm *et al*, 1974). We closely studied six patients during alcohol reactions from oral disulfiram, with clinical observations and hourly blood tests. Between 2 and 6 g of disulfiram had been given during the previous five days yet the resulting blood levels of between 0.1 and 0.8 mg% were not proportional to dose of disulfiram taken. However, the severity of clinical response did appear to depend on the disulfiram level and might have been associated with a recorded fall in serum potassium and ST depression on ECG. Alcohol levels up to 158 mg% did not seem strongly relevant. Additional disulfiram levels on outpatients showed no correlation between dose of drug and blood level.

Since we do not know how to predict blood levels in individuals, Brewer's plan of increasing the disulfiram dose until a response is obtained seems appropriate.

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Reference

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AKATHISIA DURING LITHIUM PROPHYLAXIS

DEAR SIR,

The most frequently reported extrapyramidal side effects with lithium alone, at 'therapeutic' serum levels, are cogwheel rigidity and rapid hand tremors (Kane *et al*, 1978). Akathisia, usually a side effect of neuroleptic treatment, has also rarely resulted from lithium-neuroleptic combination, but not with lithium alone (Perenyi *et al*, 1983). This is a report of akathisia occurring during lithium prophylaxis.

A 52-year-old bipolar manic-depressive was taking prophylactic lithium 900 to 1350 mg/day. After two euthymic years, he developed a manic episode. Consequently, lithium was increased to 1500 mg/day. Three days later, he developed severe restlessness, inability to sit still even for a brief time, and an irresistible urge to pace the floor. It interfered with his daily activities and sleep. A local doctor suspected

manic excitement and gave 200 mg of chlorpromazine. This worsened his restlessness further. When he was brought to us after 48 hours, his vital signs, higher mental functions, fundi and superficial and deep reflexes were normal. He had a short, shuffling gait, without associated movements, rapid hand tremors, generalized cogwheel rigidity and dysarthric speech. He could not lie down or sit still at any place, and paced up and down constantly. He attributed this to a 'peculiar' inner restlessness in the legs, not under his control. Manic features were absent in mental status examination.

Twelve-hour serum lithium was 1.2 mEq/L. RBC lithium was 0.6 mEq/L. Complete haemogram, urinalysis, serum electrolytes, ECG and EEG were normal. The patient was given 50 mg promethazine IV stat and again after an hour. Trihexiphenidyl 4 mg/day was added to lithium 1500 mg/day. Akathisia, dysarthria and gait disturbances completely resolved within 36 hours after starting anticholinergics. However, mild cogwheel rigidity and hand tremors persisted for more than 3 weeks. Serial investigations including serum and RBC lithium and renal function tests were normal during the subsequent three weeks.

The hyperkinetic parkinsonian syndrome after addition of chlorpromazine indicates its synergy with lithium. Phenothiazines are known to cause increased influx of lithium intracellularly, possibly by passive leak diffusion. This mechanism is held responsible for toxicity during combination therapy (Pandey *et al*, 1979). But the initial akathisia that developed during lithium prophylaxis in an otherwise drug-free patient is difficult to explain. None of the explanations of lithium neurotoxicity at therapeutic levels offered by Strayhorn & Nash (1977) apply in this case. It appears to be a dose-independent, idiosyncratic reaction to lithium. This is clinically relevant because, as in this case, akathisia is often misdiagnosed as psychotic agitation and addition of neuroleptics makes the situation worse (Van Putten, 1974).

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