temporal relationship between treatment and the onset of manic symptoms was not entirely coincidental and therefore worthy of report.

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Radioreceptor Assay of Serum Neuroleptic Concentrations in Psychiatric Patients

Sir: We read with interest the report by Krska *et al*, (*Journal*, February 1986, **148,** 187–193), concerning the usefulness of radioreceptor assays for the measurement of plasma neuroleptic concentrations. We have been assessing the usefulness of a similar assay based on a lyophilised calf caudate preparation and ^{3}H-labelled spiperone ligand, which is available from Wellcome Diagnostics as a 200 assay kit (Lader, 1980). We have found this assay simple to use and reproducible, requiring only 0.2 ml of plasma for each duplicate analysis. The assay has been found to be linear between 15 and 1000 neuroleptic units per litre (1 NU/l equivalent to 1 nmol/l haloperidol).

In contrast to Krska *et al*, who investigated patients on long-term therapy, we are investigating the application of this assay to the management of acute schizophrenia and have so far studied nine patients. All our patients were previously untreated, fitted the RDC criteria for schizophrenia (Spitzer *et al*, 1975), and were treated with haloperidol in doses of between 1.5 and 60 mg per day according to clinical judgement. No other neuroleptic or psychotropic medication was prescribed. We found a significant linear relationship between daily dose of haloperidol and plasma dopamine receptor binding activity ($n = 11$, $r = 0.76$) similar to that reported by Krska *et al*. In three patients who were intensively investigated over a 4–6 week period there was a marked clinical improvement, as assessed on the CPRS rating scale (Åsberg *et al*, 1978). We found a direct relationship between dopamine receptor binding activity, dose and clinical improvement. However, due to the small number of patients, statistical significance could not be reached. This improvement was obtained on doses of between 9 and 20 mg/day haloperiodol, which achieved plasma neuroleptic concentrations of 14–48 NU/l.

Extrapyramidal side-effects, as assessed using the Simpson Rating Scale (Simpson & Angus, 1970), were completely unrelated either to dose or to plasma neuroleptic concentrations. This poor relationship between plasma neuroleptic activity and extra-pyramidal side-effects was confirmed in six additional patients. These findings underline the conclusion reached by Krska *et al*, that for chronic schizophrenics there was no simple relationship between plasma neuroleptic concentrations and side-effects. It is interesting that side-effects seem to be so poorly related to total plasma neuroleptic dopamine blocking "activity" as measured in a radioreceptor assay. This may be because the assay measures only the total plasma concentration of "active" drug *in vitro* rather than reflecting dopamine blocking activity in brain *in vivo*. Another major problem with the use of this technique is that dopamine receptor binding activity may differ from one neuroleptic to another by several orders of magnitude despite equivalent clinical effects. The results are therefore meaningless if the patient is on more than one neuroleptic drug at the same time, a situation which pertains frequently in clinical practice.

Although a number of early reports indicated that radioreceptor assays showed promise, more recent work has been equivocal (Dahl, 1986). It is likely that such assays offer very little advantage over alternative techniques, e.g., gas and liquid chromatography which are capable of measuring parent drugs as well as metabolites which may have activities on different neurotransmitter systems. Much more work is required before dopamine blocking radioreceptor assays can offer any useful information in the management of schizophrenic patients.

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Neuroleptic Malignant Syndrome

Sir: In their recent review of the neuroleptic malignant syndrome (NMS) Drs Abbott & Loizon (*Journal*, January 1986, **148,** 47–51) recommended sodium dantrolene and bromocriptine as the best treatment options for this syndrome. We wish to suggest the possible use of electroconvulsive treatment (ECT) in NMS in addition to these treatment modalities.

Case Report: We recently treated a patient who presented a NMS which improved with ECT. This 23 year old male schizophrenic patient developed NMS on the fourth day

of his treatment with intramuscular chlorpromazine (200 mg/day). The clinical features and laboratory results were typical for NMS, including extreme muscle rigidity, severe dysautonomic disturbances, and laboratory findings of rhabdomyolysis. In spite of the discontinuation of chlorpromazine the patients's condition deteriorated over the following week. On the seventh day of NMS a bilateral modified ECT was administered which was followed by a dramatic improvement in hyperpyrexia, diaphoresis and level of consciousness. The patient received a course of five ECT treatments within 2 days. When ECT was stoped fever and stupor recurred. Four further sessions of ECT were administered resulting in a complete recovery.

A survey of the literature revealed four case reports of successful treatment of NMS by ECT, (Powers *et al*, 1976; Jesse & Andersen, 1983; Lazarus, 1986). In another patient (Regestein *et al*, 1977) ECT during NMS was followed by permanent brain damage. This patient, however, had suffered from cardiac arrythmia before ECT, and developed ventricular fibrilation followed by brain anoxia during the ECT. The disastrous outcome did not result, therefore, from a direct action of ECT on the brain. Besides specific contra-indications for ECT, this procedure seems an effective treatment for NMS. The ability of ECT to increase post-synaptic receptors' sensitivity for dopamine (Lerer & Balmaker, 1982) might explain its beneficial effect in NMS. This explanatory model is in line with the aetiological role attributed to an acute reduction in CNS dopamine activity in NMS.

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Sir: We were interested to read the review on the neuroleptic malignant syndrome by Abbott and Loizou (*Journal*, January 1986, **148**, 47–51). Whilst the quotation from Baastrup and colleagues (1976) accurately reflects their finding that none of the 425 patients in their review treated with both lithium carbonate and haloperidol developed the neuroleptic malignant syndrome, we were intrigued to note that the authors had omitted to mention the original report by Cohen & Cohen (1974) which had prompted Baastrup *et al*, to conduct their review. Cohen & Cohen described four acutely agitated manic patients receiving the lithium and haloperidol combination who developed a toxic syndrome which they attributed to a specific haloperidol/lithium interaction.

However, Jefferson & Greist (1980) reviewed the original case reports and noted that the clinical descriptions resembled the neuroleptic malignant syndrome. This similarity has also been noted in other publications (e.g. Frankel & Spring, 1982). Since Cohen & Cohen's original paper, a number of other case reports have appeared in the literature, and other neuroleptics have been implicated in presumed toxic interactions with lithium. Having closely examined 26 similar reports of patients treated with haloperidol and lithium (Hone *et al*, 1985) we concluded that at least seven of the 26 met the criteria for the diagnosis of neuroleptic malignant syndrome, including the four patients originally reported by Cohen & Cohen.

In summary, we can find little or no support for the lithium/haloperidol interaction hypothesis. We consider that there is a need for a detailed epidemiological enquiry to identify the incidence of neurotoxic events resulting from the concomitant use of lithium and neuroleptics, together with other toxic sequelae related to neuroleptic usage. In conducting such a survey, we would hope to provide more information on these phenomena – be they attributable to lithium toxicity, drug interactions, or the neuroleptic malignant syndrome.

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