occurs in the absence of clinical or laboratory signs of toxicity. Further studies are necessary to resolve this point.

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EFFECT OF LITHIUM ON DISTURBED SEVERELY MENTALLY RETARDED PATIENTS

Dear Sir,

We wish to report on the therapeutic effects of lithium salts on the disturbed behaviour in severely mentally retarded patients.

Ten patients (six male and four female) were selected for a trial period of twelve weeks to observe the therapeutic effect of 'Lithium Phasal'. All were severely mentally retarded and displayed aggressive and self-mutilating behaviour. Previous treatment with various tranquillizers and behaviour modification therapy had had little or no effect. Two of the patients were well controlled epileptics: The age of the patients ranged between 16 and 58 years and most of them had been in hospital for more than eight years. A simple rating scale was used to assess the patients' behaviour with regard to aggressiveness, self-mutilating tendencies, affectivity, social behaviour and personal habits. During the trial period the patients were assessed every two weeks.

Following a full general physical examination, 'Lithium Phasal' was administered in doses of 900 mg. daily, in addition to the existing medication which was not changed for at least three months preceding the trial. Subsequently the dose was adjusted according to the lithium plasma level. Lithium tests were done weekly for the first four weeks and fortnightly thereafter. Serum lithium was maintained between 0·6–1·4 m.Eq./L. No side effects were observed.

We found that five out of the nine patients who had aggressive tendencies showed significant improvement. Three patients improved slightly and in one there was no change. The outbursts of aggressive behaviour became less frequent and easier to control. The therapeutic effect of lithium treatment was found more evident in patients whose main problem was self-mutilating behaviour. Six of the eight patients with such tendencies improved to a point where self-mutilation ceased. One patient improved mildy and one patient showed no improvement. It was also noted that all the patients became less irritable, and more co-operative, and developed an increase in their social tolerances.

The result of this pilot study suggests that lithium salts have a significant effect on the disturbed behaviour in severely mentally retarded patients. Our findings agree with the findings of T. Dostal and P. Zvolski concerning anti-aggressive propensity of lithium, but we were surprised that self-mutilating behaviour responded even better.

We hope that these findings will stimulate further studies on the use of lithium in this field.

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ABRUPT WITHDRAWAL OF ANTIPARKINSONIAN DRUGS

Dear Sir,

Referring to the paper by McClelland *et al.* (*Journal*, February 1974, **124**, 151–9), I feel that the practice of prescribing antiparkinsonian drugs with neuroleptics, particularly with depot drugs, remains an important safeguard for patients, unless further and longer term studies confirm the authors' findings.

Their reported relapse rate of 8 per cent extrapyramidal symptoms is much lower than that found in previous studies, but only 9 per cent of the patients studied were taking chlorpromazine (or equivalent) in doses of more than 100 mg. three times daily. Patients aged over 70 years were excluded, but these form a large proportion of long stay in-patients, and their exclusion, combined with that of out- and day-patients, may prejudice the relevance of the study. While the deterioration of some patients taking antiparkinsonian drugs may be 'statistically non-significant' this statement could be less meaningful

than it appears. In the group of 27 patients receiving antiparkinsonian medication only one patient developed 'akathasia' compared with four in the untreated group, two 'oral dyskinesia' compared with five, and five 'lost arm swing' compared with eight respectively.

For most of us the possible long-term extrapyramidal side effects of neuroleptic drugs are more important than short term effects, and despite this study's excellent design and the care with which it was carried out a four-week period cannot be expected to shed much light on the long-term issues. Lastly, the side effects which the authors mention apply mainly to older drugs, e.g. benzhexol, and while one agrees that any unnecessary prescribing of antiparkinsonian drugs is wasteful of both time and money, it is important that there should be no unjustified throwing out of the baby with the bathwater.

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CHOREIFORM MOVEMENTS AFTER DEPOT INJECTIONS OF FLUPENTHIXOL

DEAR SIR,

I have two patients who have been treated with depot injections of flupenthixol and have developed choreiform movements. One, a man of 40 who has had schizophrenia for eight years, has been on 40 mg. flupenthixol intramuscularly every three weeks since August 1972. In June 1973 he changed his address without letting his community nurse know. In the autumn he was seen, quite by chance, in a dentist's waiting room by a member of our staff and was noticed to have obvious generalized chorea. This has since slowly and completely disappeared without any treatment. The other, a man of 28, has suffered from schizophrenia for seven years and has been treated with a large number of neuroleptic drugs. In November 1972 he was changed from intramuscular fluphenazine to flupenthixol, 40 mg. every two weeks. In August 1973 he developed extremely severe generalized chorea which affected his limbs more than his body and was not associated with oral dyskinesia. Later he developed athetoid as well as choreiform movements. His condition failed to respond to tetrabenamine, thiopropazate or thioridazine. It was only when he was started on lithium that some amelioration of his condition occurred.

In the two cases investigation excluded thyrotoxicosis and polycythemia; skull X-ray and brain scan were normal, chest X-ray was clear and there was no family history of Huntington's chorea.

If one accepts the view that the tardive dyskinesia which patients show on neuroleptic drugs is due to upsetting of the balance of the dopaminergic-cholinergic transmitter system in the central nervous system, then it was only a matter of time before such an effect was likely to be seen with flupenthixol.

Attention is drawn to the irreversibility of the situation in one of the patients and to the fact that the patients are young, unlike those described previously who seem mostly to have been elderly females.

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WHAT SHALL WE DO WITH THE THE DRUNKENNESS OFFENDER?

DEAR SIR,

In their paper *Journal* (**124**, 327), H. I. Hershon *et al.* use the word 'decriminalize'. How soon will it be before we 'deschizophrenicize', 'dedepressivize', 'defrigidize' (or ? 'defrost') our 'clients'?

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AGRANULOCYTOSIS AFTER TREATMENT WITH CLOMIPRAMINE INFUSION

DEAR SIR,

I write to report the occurrence of agranulocytosis in a woman of 37 who had been treated with clomipramine infusion for a moderately severe depressive illness. A complete agranulocytopenia occurred some three weeks after the infusion. In the intervening time she had received increasing doses of the drug starting at 50 mg. and with a maximum of 250 mg. each day. Sternal bone marrow examination showed neither white cell precursors nor red cell precursors. During the next three weeks she came very near to death, as much from a severe infection of *Candida albicans* following massive antibiotic therapy as anything else, but she survived, with a complete return of function of her bone marrow.

The manufacturers of clomipramine inform me that only one other case of agranulocytosis has been reported with this drug since it came into use in 1965. Because its chemical structure is so similar to chlorpromazine, which has a directly toxic effect on bone