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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, and check the accuracy of all* references in Journal style.**

ANTIPARKINSONIAN DRUGS AND DEPOT NEUROLEPTICS

DEAR SIR,

I was alarmed to read (*Journal*, February 1982, **140**, 210) Dr Bennie's assertion that "recent work has confirmed the need for anti-parkinsonian medication in neuroleptic treated schizophrenia". This statement implies that anti-parkinson drugs should be given to all such patients routinely. I was alarmed on three counts: first, I do not believe that Dr Bennie's statement is a true reflection of research evidence on this matter; second, the methodological problems involved in assessing the effects of drugs used in the control of drug-induced extra-pyramidal syndromes are considerable and not fully overcome; and finally, there are dangers in the course Dr Bennie recommends.

Dr Bennie quotes from the recently reported study of Manos and his colleagues. This study reports the effects of withdrawal of anticholinergic drugs from chronic schizophrenic patients who were receiving treatment with a variety of neuroleptic drugs, alone and in combination. Seventy-five per cent of the patients were withdrawn to receive placebo and the remainder to receive trihexyphenidyl. The patients were then assessed weekly for severity of drug-induced Parkinsonism and other changes over a period of six weeks. Although the results of this study show that patients withdrawn from anti-parkinson drugs more frequently show evidence of distress from drug-induced Parkinsonism than those given an alternative anti-parkinson drug; this does not mean that the patients would have shown the same clinical picture had they never received anti-parkinson drugs. A withdrawal effect is in part due to the removal of a substance to which a subject has become habituated and not solely to a pathological condition or the effect of another medication. Thus, although the clinical management of patients already receiving anti-parkinson drugs with neuroleptics might be smoother if the drugs are continued, this cannot be said to imply that all patients, including those recently given the drugs for the first time, should be managed in the same way. Apart from the findings of this study there have been many similar withdrawal studies which have given different results (Marsden *et al*, 1982). This contrary evidence might at least have tempered Dr Bennie's sweeping generalization.

One has only to read a few of the published studies of the use of anticholinergic and other drugs in controlling the symptoms of drug-induced Parkinsonism to realize how difficult it is to carry out satisfactory studies in this field (Mindham, 1976). Problems in methodology make it difficult to justify general claims for the efficacy and routine use of anti-parkinson drugs. The study reported by Dr Bennie is deficient in several respects: the interval between the injection of neuroleptics and assessment for drug-induced Parkinsonism is not specified; two neuroleptics were employed and may show different patterns of extra-pyramidal syndrome after administration, and may not be evenly distributed between the patients receiving the two anti-parkinson treatments; the cross-over of anti-parkinson treatments was not carried out at a specified time after the injections of neuroleptics and introduces problems arising from the order of administration of remedies and the persistence of the effect of the drugs withdrawn; a crude method of assessment was used and the details not given; a comparison of supposedly active substances was made which allows of the possibility that only a small therapeutic effect or no effect was produced by either treatment.

Apart from the general undesirability of giving patients drugs which are not strictly necessary, the administration of anticholinergic drugs is not without its dangers. Some workers believe that they increase the risk of the development of 'tardive dyskinesia' (Klawans, 1973; Kiloh *et al*, 1973). Similarly, these drugs have been reported to play a part in the causation of hyperthermia, an occasional, but serious complication of the drug treatment of schizophrenic patients in hot countries (Westlake and Rastegar, 1973). Furthermore, it has been claimed that anticholinergic drugs may interfere with the therapeutic effects of phenothiazines (Singh and Kay, 1976). This effect may be mediated by a reduction in the plasma level of phenothiazine caused by an effect on its

metabolism (Rivera-Calimlim *et al*, 1973). These two pieces of evidence suggest that reduction of the dosage of neuroleptic might be a more appropriate way by which to combat drug-induced Parkinsonism.

In his final sentence, Dr Bennie suggests that anti-parkinson drugs be administered to neuroleptic treated schizophrenic patients who appear to be depressed. Certainly it is easy to confuse the mask-like facies of Parkinsonism with retardation attributable to depression and in such cases the administration of anti-parkinson drugs, might be useful. Some anti-parkinson drugs have been claimed to possess anti-depressant properties but the evidence for this is weak (Onuaguluchi, 1964; Mindham *et al*, 1972).

For the reasons given here and elsewhere, I do not believe that patients receiving long-term medication with neuroleptics should also be given anti-parkinson drugs on a routine measure. Firm recommendations, such as that made by Dr Bennie, require better evidence than is at present available.

R. H. S. MINDHAM

The Johns Hopkins Hospital,
The Henry Phipps Psychiatric Clinic,
600 N. Wolfe Street,
Baltimore, Maryland 21205

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DAYTIME ENURESIS

DEAR SIR,

Dr Barton and Dr Felker have responded to my *Comments* article Child Psychiatry and Enuresis (*Journal*, September 1981, **139**, 247–8) with a letter (*Journal*, March 1982, **140**, 325) in which they suggest that imipramine is effective in treating diurnal enuresis. However, they admit that they have no evidence from a controlled trial to support their view. I have, to support mine.

I recently participated in a randomized, double blind controlled trial of imipramine in diurnal enuresis, carried out by Professor Roy Meadow, Paediatrician in Leeds. This has not yet been published. Twenty-seven children were included in the study. Although there was some improvement in day wetting during treatment there was no difference in response between the placebo and the active drug groups of cases. In my view, considering the dangers for children of overdose with this hazardous drug, until there is some real evidence for its efficacy in treating diurnal enuresis it should not be used for this condition.

IAN BERG

The General Infirmary at Leeds,
15 Hyde Terrace,
Leeds LS2 9ET

PROPRANOLOL IN SCHIZOPHRENIA

DEAR SIR,

In a recent article in this *Journal* (August, 1981, **139**, 105–11), Peet *et al* concluded that propranolol did not improve schizophrenic symptomatology relative to placebo, while the effects of chlorpromazine were small and inconsistent. It is not the purpose of this letter to question the effects of these drugs, but rather to examine the quality of the evidence marshalled to draw these conclusions.

Finding that treatments do not differ from each other may arise from two different circumstances: they do not in fact differ, and the authors have arrived at the correct conclusion; or they do differ, but the investigators have failed to detect this difference. The reason for the latter result (known in statistical jargon as a Type II error) is that the power of the