*Brit. J. Psychiat.* (1979), **135**, 82–83

# *Comments*

This is the third of a series of short reviews and reports on topical matters. They are intended to be useful in some aspect of clinical practice or to report an interesting new growing point in neuroscience, or to give a synopsis of the current situation in some area of psychiatry. They should reflect topical interests, what people talk about both informally and at society meetings. Some may be valuable in the training of young psychiatrists, others in the further education of consultants, and yet others will prove starting points for new investigations.

## PIMOZIDE AS A NEUROLEPTIC

Pimozide is one of the diphenylbutyliperidines, a neuroleptic group which also includes penfluridol and fluspiriline; their chemical structure is closely related to that of the butyrophenones and gives a relatively prolonged action.

Although pimozide was clinically available in Europe from 1970, systematic evaluation of it occurred slowly. Jimerson *et al* (1976) reported a study of seven patients with manic illness; substantial improvement occurred during the first week in six, particularly in terms of decreased psychomotor activity. Otherwise, however, no reliable basis exists for the use of pimozide in affective illnesses, neuroses or personality disorders. As far as schizophrenia is concerned, Pinder *et al* (1976) had found evidence only for its value as maintenance therapy in chronic patients, but this may have been because of the dosages used. Shopsin and Selzer (1977) and Piyakulmala *et al* (1977) both reported series of acutely ill schizophrenic patients who were treated with up to 60 mgm daily, i.e. ten times the mean dosage of most previous studies. On the whole, results were very satisfactory in the short term and no significant problems were encountered from side-effects. Ross and Moldofsky (1978) carried out a double-blind placebo-controlled study in nine patients with Gilles de la Tourette's Syndrome; whilst both pimozide and haloperidol produced a significant and lasting decrease in the frequency of tics, pimozide did not cause the marked lethargy often found with haloperidol and so was better accepted.

Further information of much potential clinical interest has emerged from the study by McCreadie *et al* (1979) in which plasma pimozide levels were measured by radioimmunoassay in nine chronic schizophrenics. The drug was found to be slowly absorbed, reaching peak plasma levels after about eight hours, and was then slowly eliminated with a mean half-life of 53 hours, i.e. very much longer than that of chlorpromazine. The peak plasma level after a single oral 24 mg dose was four times higher than after the first of a series of four daily doses of 6 mg. Plasma levels after the single 24 mg dose did not fall below levels obtained with the four 6 mg daily doses until at least 72 hours after the single dose. There was also a thirteen-fold inter-individual variation in bioavailability, which might require giving higher doses in certain patients to produce a therapeutic effect; no serious side effects were observed after the single large dose. Although the relationship of neuroleptic plasma levels to therapeutic response is still uncertain, these findings suggest it might be possible to administer oral pimozide less frequently but at higher than usual dosage.

In relation to the maintenance treatment of schizophrenia, discussion has centred on two controversial points—the efficacy of an oral regime compared with injections, and the risk of tardive dyskinesia. Falloon *et al* (1978a) carried out a double-blind study of 44 schizophrenic patients during twelve months after discharge from hospital in which either pimozide tablets or fluphenazine injections were given; this was followed by six months in which 20 patients received either pimozide or placebo tablets. On the principal criteria of schizophrenic relapse, rate of relapse, depressive symptomatology, adverse effects and regularity of medication, it was concluded that oral pimozide, given once daily, is at least as effective as depot injections of fluphenazine decanoate. During the additional period four further relapses occurred—three of them among the eight patients taking placebo. A further report on the same sample (Falloon *et al*, 1978b) stated that patients treated with pimozide were superior to those on fluphenazine decanoate in respect of several aspects of social adjustment, possibly due to a lower prevalence of

extrapyramidal side-effects, particularly rigidity. However, the difficulties of finding normative data for social functioning were emphasized.

In view of considerable earlier evidence on the unreliability of oral regimes over long periods these results appeared rather surprising, especially as Watt (1978) refuted any suggestion that follow-up had been more diligent than that usually provided. However, patients actually entering the trial numbered only about one-third of those who were selected as being eligible, whilst Hogarty (1979) found a lower relapse rate in patients on fluphenazine decanoate than in those on oral drugs from the *second* year of treatment onwards, so that length of time may be significant.

Gibson (1978) carried out a prospective study on 374 schizophrenic out-patients, receiving depot fluphenazine or flupenthixol and found that the proportion showing tardive dyskinesia (TD) rose from 8 per cent to 22 per cent over three years—though only to a mild extent in 75 per cent of affected cases. Costall and Naylor (1977) had reported that pimozide reversed dyskinesia produced in experimental animals and Gibson found that 41 out of 50 patients whose medication was changed to pimozide or fluspirilene lost their TD. Unfortunately, it had recurred in all cases followed-up for three years; halving the dose of depot neuroleptic produced remission in all of a further 19 patients, but ten of these had relapsed three years later. In the study of Falloon *et al*, mild TD was equally present with both drugs used, but otherwise, reports of this complication with pimozide have so far been few.

In 1975, Riding and Munro first reported the virtually complete disappearance of somatic delusions in five cases of monosymptomatic hypochondriacal psychosis when they were treated with 2–6 mgm pimozide daily. In several cases there had been a previous failure to respond to other neuroleptics and indefinite prescription of pimozide seemed to be necessary. Further studies are proceeding on this question, but the present author has also treated a similar case with equal success for nearly three years and Reilly *et al* (1978) have reported the same in a case of delusional parasitosis.

**Acknowledgement**

I would like to thank Messrs Janssen Pharmaceuticals Ltd. and particularly Mrs Helen Massey for their help with information for this paper.

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