IATROGENIC PARKINSONISM*

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THERE can hardly be a psychiatrist in this country who has not produced parkinsonism in his schizophrenics with reserpine or phenothiazines: Moore, who was among the first in the field in the use of reserpine, spoke of the parkinsonian syndrome, but there was one observation of his that received only passing attention, This was that a small number of his chronic schizophrenics lost their florid schizophrenic symptoms, to be replaced by a clinical picture that he found closely akin to retarded endogenous depression, to the point of contemplated or attempted suicide.

In our view Moore was on the threshold of a discovery that has at best been exploited by only a few isolated individuals. Our experience of the side-effects of reserpine is negligible, as we administer this in a tablet combined with orphenadrine (Disipal) which obviates them; our hypotheses are based on a study of the phenothiazines, which produce identical side-effects. The motor signs of phenothiazine intolerance, rigidity, tremor, tongue-protrusion, head-rolling, torsion-spasm, oculogyric crises, dystonia and akathisia, are familiar enough, with an incidence of 25 per cent. or more among the active phenothiazines other than chlorpromazine. These manifestations are disturbing, but only to the physician or the patient's relatives. Anyone who has interrogated the patient on his feelings will have appreciated that in general he experiences at worst nothing more than a slight embarrassment that his involuntary movements interrupt the flow of conversation with his physician. He is rarely distressed at his symptom; he is much more likely to be distressed by the onlooker's anguish.

There are 3 ways of dealing with this syndrome; the first is to administer phenothiazines in sufficiently minute doses to preclude the possibility of extra-pyramidal symptoms. This one might call preventive medicine; the second is to reduce the dose if these manifestations appear, and so maybe drop below the therapeutic level; the third is to exhibit an anti-parkinsonian agent. This last procedure is tacitly regarded by many as "going too far", with the result that these never know what they are missing.

Nevertheless it is not with this aspect that we are here concerned.

All present, but perhaps those especially with extensive neurological experience, will be aware of the fact that those patients with the less severe motor manifestations of extra-pyramidal disorder exhibit a mental syndrome consisting of dejection, hopelessness, and apathetic inertia. This applies whether the motor disorder is due to paralysis agitans, encephalitis, cerebro-vascular disease, reserpine or phenothiazines. It is our contention that this

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peculiar psychic state, akin as it appears to be to endogenous depression, is an integral part of the extra-pyramidal syndrome. However, this realization did not come to us as a brilliant flash of insight, but rather by the Watsonian method.

We first began by giving Artane or Disipal to those phenothiazine-treated patients who were showing minor extra-pyramidal symptoms. As the motor signs disappeared we observed an increase of psychomotor activity. From this we continued in haphazard way to give one or other of these anti-parkinsonian agents to schizophrenics whose florid symptoms were controlled by phenothiazines, but who were inert and seemingly apathetic. The response was striking, for this state was generally replaced by renewed interest, activity and initiative.

In the course of time many patients were given one of these drugs in addition and we felt that it was time we produced some statistically evaluable evidence.

To this purpose we selected 20 chronic schizophrenics, long stabilized on phenothiazines and long resident in hospital, who had made a good hospital adjustment, who were on full parole, and whom we had not regarded as falling into the category of dejected apathetic inertia. Thus we had not considered them as possibles for anti-parkinsonian drugs.

We ran a double-blind cross-over trial, one month each way, giving in addition to the regular phenothiazine 50 mg. Disipal t.d.s. or its neutral facsimile, and categorized each patient for activity and initiative. In crude terms, for the sake of brevity, our results were: On placebo, 1 much improved, 1 moderately, 0 slightly, 15 not, 3 worse; on active tablet, 4 much improved, 4 moderately, 4 slightly, 8 not improved, 0 worse. This gave χ^2 10·96 and P ·001.

The implication of this is that anti-parkinsonian drugs benefit phenothiazine-treated patients who are not manifestly on the threshold of any extra-pyramidal syndrome. There are 3 possible explanations of this.

1. The abolition of the psychomotor retardation of sub-clinical parkinsonism. This has already been discussed and we believe it to be valid.
2. The exerting of an independent psychotropic action. Freyhan (1958) states "Some of these compounds, notably Disipal, are mild stimulants, or exert a psychotropic action of their own". Our own, admittedly limited experience of Artane and Disipal, each used on its own, is that neither has a detectable action as a psychotropic agent.
3. The potentiation of a psychotropic agent. This we feel is likely and applies in addition of course to the first possibility. It may be that the phenothiazines, in their depression of the reticular formation, and consequently their depression of cerebral systems dependent on it, simultaneously depress mood and activity: thus anti-parkinsonian agents do not potentiate psychotropic activity, but rather do they limit the inhibiting action of the phenothiazine.

Our conclusion is therefore that a large proportion of schizophrenics on phenothiazine therapy gain additional benefit from the concurrent administration of Artane and Disipal.

In this we do not mean to exclude other such agents; it is merely due to the fact that so far we have only had time to evaluate these two. Between them we cannot as yet differentiate. We have used Artane the more often simply because it is the one longer known to us. It may well be that Disipal is the superior or that some as yet untried drug is better than either. We shall feel that we have

achieved something if we have indicated a direction in which further research can be profitably directed.

It is a fault of authors of short papers and even sometimes of long ones, not to practise what they preach. To test this last week we counted up the schizophrenics and paraphrenics on the male division who are not involved in any clinical trial. Of 174 such patients, 29 are on Disipal and 60 on Artane; that is to say 89 of 174 or 51 per cent. are on anti-parkinsonian agents, and even more will be when we get around to it.

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