THE CLINICAL RESPONSE OF PSYCHONEUROTICS TO CHLORPROMAZINE

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CHLORPROMAZINE hydrochloride (3-chloro-10 (3'-dimethylamino-propyl)-phenothiazine) or "largactil" is being widely tried out as a form of therapy in psychiatric disorders. Papers have appeared describing its use in comparatively severe conditions encountered in in-patient mental hospital practice (e.g. Anton-Stephens, 1954) and in psychoneurotics (e.g. Garmany, May and Folkson, 1954). In the psychoneurotic group in particular, the drug is reported to be helpful in reducing tension and diminishing pre-occupation with worries, fears, and concomitant symptoms. These two properties—the reduction of tension and the production of a feeling of relative indifference to distressing stimuli—were amongst those originally attributed to chlorpromazine by Sigwald and Bouttier (1953) and, of course, they approximate to the characteristic changes resulting from prefrontal leucotomy (Partridge, 1950). The effects of this operative procedure have been extensively studied in relationship to such factors as the previous personality of the patient and the duration of the illness involved (e.g. Baker and Minski, 1951) and it was considered that it might be of value to investigate similar factors in patients treated with chlorpromazine. It is true that prefrontal leucotomy entails structural damage as a result of which the previous personality, for example, may be expected to have a significant bearing on the therapeutic outcome, but even with patients treated by chlorpromazine the ultimate result may depend, at least to some extent, on the inherent make-up of the individual or the symptom-complex from which he is suffering. It was in order to study the relationship between factors of this nature and chlorpromazine treatment that the following investigation was undertaken.

MATERIAL AND METHODS

The fifty patients included in this report were treated in out-patient departments of general hospitals. All were suffering from psychoneurotic disorders, their clinical conditions, age, and sex being summarized in Tables I, II, and III

TABLE I

Diagnosis and Clinical Response

			Obsessional State			
Diagnosis	Anxiety State	Hysterical Reaction	Mainly Ruminative	Mainly Compulsive	Neurotic Depression	Total
Remission ..	8	2	—	—	1	11
Improved ..	10	8	2	1	1	22
Unchanged ..	2	10	1	—	4	17
Number ..	20	20	3	1	6	50

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TABLE II
Age Group and Clinical Response

Age Range in Years	11–20	21–30	31–40	41–50	51–60	61–70	71–80
Remission	—	4	4	—	2	1	—
Improved	—	8	7	3	3	—	1
Unchanged	—	2	2	4	7	1	1

TABLE III
Sex Distribution and Clinical Response

	Males	Females
Remission	2	9
Improved	8	14
Unchanged	9	8

respectively. In addition, an assessment was made of the presence or absence of overt neurotic traits in the previous personality, and the duration of the current illness, prior to commencing chlorpromazine treatment, was also computed (Tables IV and V respectively).

TABLE IV
Previous Personality and Clinical Response

Previous Personality	Overt Neurotic Traits Present	Overt Neurotic Traits Absent
Remission	5	6
Improved	16	6
Unchanged	10	7

TABLE V
Duration of Illness and Clinical Response

Duration of Illness	Less than 1 Year	1–3 Years	Over 3 Years
Remission	4	3	4
Improved	6	9	7
Unchanged	2	6	9

In view of the fact that the subjects were out-patients, administration of chlorpromazine was limited to the oral route. The initial dose in each case was 25 mg. t.d.s. the patients being asked to lie supine for 30 minutes, after taking the drug in order to avoid side-effects. Depending on the response of the patients, the dosage of the drug was subsequently raised in many cases; the maximum dose given being 75 mg. t.d.s. The majority of patients, however, received only 25 to 50 mg. t.d.s.

All the patients included in this study were kept on chlorpromazine medication for three months. At the end of this period an assessment was made of the clinical response on the basis of the following three broad groupings (Table I):

1. *Complete Remission.* This, of course, applied to those cases which became symptom-free. Case No. 34 may be taken as an example. Patient was a 40-year-old woman with overt anxiety symptoms for the previous five years. There was marked fear of crowds, pre-occupation with physical disease, and specific phobic ideas concerning cancer. Tension, irritability, and tiredness were in evidence. Following chlorpromazine medication (25 mg. t.d.s.) she became placid, composed and cheerful. She no longer mentioned any phobic symptoms. When asked about her fears, she smiled and readily stated that they had ceased to worry her. She was running the home without difficulty for her husband and young son and coping quite satisfactorily with her normal household chores.

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2. *Improved.* This assessment referred to cases in which some clinical alleviation of symptoms was obvious to the patients and the writer. This category can be illustrated by Case No. 29. The patient was a 31-year-old married man with a history of severe obsessive–compulsive symptoms, and marked fears of fainting, for the previous twelve months. He had always been of typical obsessional make-up. His presenting symptoms were precipitated by promotion to the position of foreman and consisted of excessive checking and re-checking of work done in the factory with resultant difficulty in coping with his responsibilities. Subjective tension complained of but not obvious at interview. Placed on chlorpromazine (25 mg. t.d.s.). Fear of fainting subsided and there was a marked decrease in compulsive symptoms. It remained evident, of course, that he still had his obsessional tendencies but these had receded so much into the background that they did not materially interfere with his ability to carry on with his normal work.

3. *Unchanged.* This group included those cases in which there was no obvious improvement in the presenting symptoms.

Results

More than three-fifths of the cases gained material benefit from chlorpromazine treatment. Approximately one-fifth became completely symptom-free. Anxiety states showed the most favourable response to treatment, especially in relationship to complete remission of symptoms. Taking the categories of "remission" and "improved" together, application of the exact χ^2 test showed that the difference between the response of anxiety states and the other diagnostic categories was significant ($P=0\cdot0035$).

Those cases under 40 appeared to respond better than the older age groups. By combining the "remission" and "improved" categories, this difference was shown to be significant (Difference/S.E.$=41\cdot7/13\cdot4$).

Table III suggests that females fared better than males, but on the comparatively small number of patients studied, the figures were not significant. ("Remission" and "improved" taken together: difference/S.E.$=21\cdot6/13\cdot8$.)

The previous personality did not appear to exert any significant effect on the therapeutic outcome. (Combination of "remission" and "improved" categories: difference/S.E.$=4\cdot5/13\cdot8$.)

The duration of the illness involved was not shown to have any material influence on the chances of remission or improvement. ("Remission" and "improved" taken together: $\chi^2=2\cdot71$.)

Comment

In this series, patients suffering from anxiety states showed a significantly better response to treatment than those in the other diagnostic categories. This is in line with the finding of Garmany, May and Folkson (1954), that the best results are obtained in cases in which tension is the most conspicuous feature. They stated, however, that patients with predominantly obsessional symptomatology did badly, though their clinical summaries of cases with obsessional features showed some relief of tension in all the patients concerned. In view of the latter, one would have expected that their cases would have shown a somewhat better response to treatment, especially taking into account the fact that prefrontal leucotomy, largely as a result of reducing tension, is frequently successful in obsessional states. In the present study, though the numbers are small, three out of the four patients with obsessional states showed a

material degree of improvement. With the relief of associated tension, the obsessional tendencies became correspondingly less troublesome and in one case they virtually disappeared. These observations lend some support to the views of Sigwald and Bouttier (1953b) and Winkelman (1954), concerning the beneficial effects of chlorpromazine in obsessional conditions. In fact, Winkelman states that no obsessional patient should undergo prefrontal leucotomy until chlorpromazine has been given a trial. A somewhat similar opinion has been expressed elsewhere. (Leading Article, *British Medical Journal*, 1954, **2**, 581.)

When depressive or hysterical features predominated in the symptom-complex, the results were not good, these findings being similar to those of Garmany *et al.* (1954).

As with prefrontal leucotomy (Baker and Minski, 1951; Gillies, Hickson and Mayer-Gross, 1952), there is a suggestion that females respond better than males, but the relevant figures in this series are not significant. Unlike the results of leucotomy (*ibid.*), younger patients fared better than those in the older age groups.

The presence of neurotic traits in the previous personality, and the duration of the illness involved, were not shown to be significant factors in the short-term response to treatment.

Summary

Fifty psychoneurotics were treated on an out-patient basis for 3 months with oral doses of chlorpromazine ranging from 25 mg. t.d.s. to 75 mg. t.d.s.

Approximately three-fifths of the cases gained substantial benefit from treatment.

Anxiety states showed a statistically significant better response than the other diagnostic groups. This supports the view that the main effect of the drug is in the relief of tension. Some obsessional states showed material improvement. Hysterical and depressive reactions did not respond well.

Patients in the first four decades fared better than the older age groups.

There was no evidence that the previous personality, or the duration of the illness involved, were significant factors influencing the clinical response.

The findings, especially in relationship to prefrontal leucotomy, are briefly commented upon.

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References

Anton-Stephens, D., *J. Ment. Sci.*, 1954, **100**, 543.
Baker, A. A., and Minski, L., *British Medical Journal*, 1951, *ii*, 1239.
Garmany, G., May, A. R., and Folkson, A., *Ibid.*, 1954, *ii*, 439.
Gillies, H., Hickson, B., and Mayer-Gross, W., *Ibid.*, 1952, *i*, 527.
Leading Article, *Ibid.*, 1954, **2**, 581.
Partridge, M., *Prefrontal Leucotomy*, 1950. Oxford.
Sigwald, J., and Bouttier, D., *Ann. Med.*, 1953b, **54**, 150.
Winkelman, N. W., *J. Amer. Med. Ass.*, 1954, **155**, 18.