

# AN INVESTIGATION INTO COMBINED ELECTROCONVULSIVE AND CHLORPROMAZINE THERAPY IN THE TREATMENT OF SCHIZOPHRENIA\*

A. H. BOROWITZ, M.B., B.CH. (RAND), D.P.M. (R.C.P. & S. ENG.), *Medical Officer, Fort England Hospital, Grahamstown*

We have found chlorpromazine a singularly useful drug in the treatment of disturbed African female patients in Sterkfontein Hospital. Rapid improvement in the behaviour of noisy, aggressive, resistive, or destructive psychotics has become commonplace; and in patients suffering, for instance, from acute catatonic reaction states it appeared to have exerted a specific action, frequently inducing, as far as could be determined, a complete remission of the illness. It seemed to suppress not only their restlessness, apprehension, excitement and tension but, in many cases, their delusions and hallucinatory experiences as well.

Our chronic schizophrenic patients showed a similar improvement in their behaviour, but quite commonly remained withdrawn into themselves, solitary, indifferent to their surroundings, and emotionally flat. They showed little or no response when encouraged to engage in such work or social therapy as was available to them in the ward. This finding is in close agreement with that of Hine<sup>1</sup> who,

\* This investigation was carried out when the author was a member of the staff of Sterkfontein Hospital, Krugersdorp.

in an excellent study of this problem, concluded 'that chlorpromazine does not alleviate the symptom complex, withdrawal, in the chronic schizophrenic patient and that this is true even for those patients with varying degrees of withdrawal who are improved in their psychiatric status by chlorpromazine therapy'; and 'that withdrawn chronic schizophrenic patients may, as a result of treatment with chlorpromazine, be distinctly benefited in behavioural areas other than withdrawal and thus in their general psychiatric status'.

This symptom complex of withdrawal, however, is often seen *inter alia* in patients undergoing a course of insulin coma therapy. It may occur during the course or as a sequel to it, but in either case its presence is regarded by authorities such as Mayer-Gross, Slater and Roth<sup>2</sup> as an indication for electroconvulsive therapy (ECT), which adjunct is not infrequently found to be effective in dealing with this symptom complex.

A combination of chlorpromazine and ECT as a *specific form of treatment* for this condition therefore appeared to

us to be worthy of a trial investigation in view of the effect of the former on the symptomatology of schizophrenia in general, and the effect of the latter on the symptom complex of withdrawal in particular. We could not find any examples in the literature where this had been done before, although we were aware of the fact that Sargant<sup>3,4</sup> had been treating some of his cases with a combination of ECT, chlorpromazine and modified insulin from as early as 1956.

With regard to the risk entailed by this procedure, some authorities, such as Kalinowsky,<sup>5</sup> felt it was both dangerous and unnecessary, while others, who were in the majority, were of the opinion well summarized by Blair and Brady<sup>6</sup> that 'ECT has a very definite place as an adjuvant to chlorpromazine . . .' in the treatment of chronic schizophrenia.

#### THE EXPERIMENT

##### Background

This enquiry was carried out in a self-contained unit with accommodation for 138 African female patients. In 1958 we admitted over 70 patients, of whom about 50 were suffering from one or another form of schizophrenia. The patients were cared for by 2 trained and experienced European nurses, and 7 untrained, lay African female assistants, 3 of whom had had over 8 years of experience in dealing with them. General medical and psychiatric attention was provided by the writer.

The wards are all managed on the open-door system, started here in 1956.<sup>7</sup> Realistic opportunities are provided for the patients to keep themselves occupied. Thus they begin each day by making their own beds, tidying their wards, washing the verandahs and sweeping the courtyard. Then the majority leave the ward, to tend surrounding gardens, cultivate farm lands, help in the kitchen and laundry, or perform charing duties in the European wards. The better educated patients assist the nursing staff in looking after the more chronic and physically disabled ones. Some who prefer to devote their afternoons to knitting, needlework, plaiting and beading are encouraged to try to get others interested in their skills as well; in this they achieve a certain amount of success.

By way of entertainment they have weekly song and dance sessions, which they virtually conduct themselves, an occasional game of basket-ball, and a monthly cinema performance. Long walks in the grounds are a regular feature for many patients. As far as possible they are encouraged to participate in their activities in groups of 10-20 patients, which is about as many as an assistant can comfortably supervise without unduly restricting the freedom of the groups and yet maintaining a reasonable level of discipline.

##### Case Material and Assessment

Of the 30 African female patients in the test series, 27 were new admissions, and 3 were old cases who had partially responded to ECT and insulin coma but had remained withdrawn into themselves in spite of it. These patients were all found to be free from any form of physical disease and sober in their habits. Five of them whose blood gave positive Wassermann reactions but CSF negative were accepted for the project after a course of penicillin treatment.

Each case was assessed by a conference of doctors after one or two weeks of observation, during which period the provisional diagnosis was kept under constant review. Particular care was taken to exclude schizophreniform

reaction cases.<sup>8</sup> Where there was any doubt the period of observation was prolonged to a month or longer. It was necessary to do this because as yet no realistic effort has been made to assess either the presentation or the natural history of schizophrenia in the African, even from readily available mental-hospital records, so that one has to be guided in diagnosing by information pertaining to Europeans exclusively.

Simon's stricture<sup>8</sup> that 'African mental patients are being admitted to institutions only when violent, uncontrollable, criminal or destitute' is not applicable to our group of patients; almost a third of their number were referred to us from the mental health clinics in and around Johannesburg, and possessed none of the characteristics he enumerates.

Once treatment had commenced patients were seen at weekly intervals in unstructured groups of 10-12, accompanied by a well-educated African female assistant, skilled in both psychiatric nursing and interpreting in Zulu, Sotho, Tswana, Xosa, English, and Afrikaans. An article is in preparation giving full details about this method of seeing patients, but, for the present, it is sufficient to say that patients appear more at ease, converse more readily, and express their symptoms and signs to the doctor with greater freedom, than when seen alone by him in his office, with the sister and interpreter standing by at attention. All conversation with the patient is conducted through the interpreter in the patient's language. We found that after 8 years of experience the interpreter had acquired a good understanding of the patients' complaints. While this conversation is in progress the doctor has an excellent opportunity of observing not only the patient in question, but the effect on the other patients as well.

Once a month a ward conference was held, and each patient's condition marked up in a Parkside behaviour rating scale<sup>9</sup> (PBRS). This enabled us to obtain a comprehensive picture of the nurses' impression of the patient. These findings were then correlated with the weekly clinical notes, and in cases where opinions differed, the PBRS was deferred to.

At the end of the investigation the case was again assessed at a conference of doctors. For purposes of assessing those patients leaving hospital, the following criteria were agreed upon:

A full remission would imply as follows:

1. The patient is symptom-free.
2. She participates willingly in group activities, and is no longer asocial or withdrawn into herself.
3. She keeps herself fully and sensibly occupied in the ward without any undue prompting from the staff; finding work for herself if left alone.

These patients were invariably *discharged* from hospital.

A partial remission would imply as follows:

1. The patient's general behaviour is such as to cause no offence or anxiety to lay people.
2. She participates in routine group activities voluntarily.
3. She is fully cooperative with the nursing staff, needing no undue prompting from them to keep herself fully and sensibly occupied.

These patients were sent out on *leave of absence* for 1 year, in charge of a relative in every case.

### The Combined Treatment (CT)

Symptomatic chlorpromazine treatment and ECT were given concurrently for a period of not more than 3 months in the following manner:

Treatment was begun with a dose of 25 mg. *b.d.*, which was increased to 50 mg. within 3 days. If the patient's behaviour remained restless or aggressive it was, after the lapse of another 3 days, pushed up to 100 mg. *b.d.* or even 200 mg. in 2 cases. Like Blair<sup>6</sup> we found we could establish an 'optimum dose' for each patient, i.e. the dose of chlorpromazine on which they remained for the longest period of time in their 3 months' course without showing any side-effects and, deriving the maximum benefit from the drug. The optimum doses in some of our cases is shown in Table V. The average daily dose taken by each patient over the whole course of treatment agreed closely with that found by Little<sup>10</sup> in his cases, viz. 150 mg. daily by mouth.

If after a week the patient remained disturbed or withdrawn, ECT was commenced. It was administered twice weekly on Mondays and Fridays. The only premedication given was atropine (1/120 gr.) half an hour before treatment. Some markedly withdrawn patients were given 3 ECTs during the first week in an effort to get them to eat or control their sphincters, and this treatment was continued until the patient's symptoms had been relieved or until she had had 20 induced seizures. Such cases as tended to become withdrawn again after the ECT had been discontinued were placed on weekly ECT until apparently stabilized and no longer in need of it. The number of ECTs administered in cases that improved is given in Table V.

We used a 'Pulsacon electro-coma' machine, employing the rheostat to produce a glissando effect up to 12 milliamps, which was held for  $\frac{1}{2}$ –1 second. This treatment programme enabled us to see each patient every Thursday morning with as little post-ECT confusion as possible.

We came across no complications whatever, and found that the patients could carry on their daily routine with a minimum of disturbance.

The patients were followed up for a minimum of 1 month in hospital after cessation of treatment. Having left hospital the majority were seen regularly at monthly intervals at our mental health clinic in Johannesburg. In case any of these cases had relapsed at home, they were issued with a routine form which would have enabled them to be referred back to our hospital with a minimum of delay.

### The Control Series

At the outset of this investigation it was decided to use a matched sample of cases receiving insulin coma treatment (ICT) for control purposes. There are 6 beds available for patients on this treatment, and in this hospital a full course of treatment is considered to be 60 comas. Before receiving this treatment, however, almost every case is subjected to a course of ECT—20 in all—administered at the rate of 3 per week.

Unfortunately, 1 out of every 2 patients receiving ICT was prevented from completing a full course because of 3 main reasons:

(a) They went into a deep coma on doses as small as 5–10 units of insulin.

(b) They fluctuated widely in their response to a fixed dose of insulin—going into a deep coma one day and showing hardly any response to it the next.

(c) Running a course of intermittent pyrexia which would have made the treatment an extremely lengthy one. These patients were all ultimately found to be suffering from hepatic disfunction.

Because of this we had recourse to the records, and examined the case histories of the last 30 patients who had had 30 or more comas and used them as our control series. As Table I shows, the control (ICT) series of cases and the investigation (CT) series turned out to be surprisingly alike. Of the control patients 20 had had 60 comas, 4 had 40–50 comas, and 6 (of whom 5 appeared to have completely remitted) had had 30–40 comas.

Although the above may not reflect the response to ICT by African schizophrenics in general,<sup>11</sup> Wolpowitz,<sup>12</sup> one of the pioneers in its use in this country, is of the opinion that they do not do nearly so well on it as the Europeans. In a series of 12 male and female African patients who had received a full course of treatment at Komani Hospital, Queenstown, in 1953–4, there were no recoveries, and only a slight improvement in two or three cases. This was in spite of carefully selecting young patients whose illnesses were of fairly recent onset.

### Course of the Experiment

During the period of observation our most acute problem was dealing with restless, violent or noisy patients without having recourse to either chlorpromazine or ECT. It is quite a tribute to the nursing staff that we managed to do this with the aid of chloral hydrate and paraldehyde draughts only. Not one of these patients required seclusion in a protective room.

Once CT had commenced, a few of the patients refused to take their chlorpromazine by mouth and it had to be given them by injection. After two or three such injections they invariably became cooperative in this respect. Because of the relatively small doses used, we did not come up against the obstacle of drowsiness and lethargy confusing an already difficult clinical picture, which appears to hamper some American workers especially; Goldman,<sup>13</sup> writes of doses such as 200 mg. or more 6-hourly.

Within 10–14 days of the start of CT some of our patients became inordinately confused. This was neither a regular nor predictable finding, and it passed off within a week or two with continued treatment. It was of no prognostic importance.

The majority of our patients showed a considerable general improvement within a fortnight of commencing therapy. After this, those that were going to remit showed a slow but steady improvement, while the others remained static despite increases in chlorpromazine. One patient had to have more than 200 mg. *b.d.* for longer than three or four days. She became drowsy, listless and anergic on account of the drug, thus presenting a difficult problem for assessment.

With 2 exceptions, all our patients had a 3 months' course of chlorpromazine—the dose being gradually reduced within the last 2 weeks of treatment. One case appeared to undergo a complete remission in 2 months, and another in 10 weeks. The cases that did not remit showed little change in their illness despite their treatment; 2 of these showed an excellent response after a month and then relapsed and remained ill despite further treatment.

Every one of these patients was followed up for 1 month in the ward, with 1 exception—the paraphrenic, who

desired to go home for urgent reasons of employment, but who attended at the mental health clinic on the appointed day and time, apparently quite well.

## DISCUSSION

In order to collect 30 patients who had received a course of 30 or more comas it was necessary to look up the records as far back as September 1955. One difference in the two samples of patients consists in the fact that the CT group contained a higher proportion of paranoid schizophrenics (Table I). We felt that this did not detract from the simi-

TABLE I. COMPARISON OF THE TWO GROUPS OF PATIENTS AS RANDOM SAMPLES

	ICT cases	CT cases
1. Tribal and racial distribution:		
Bechuana .. .. .	6	6
Tswana .. .. .	1	1
Shangaan .. .. .	—	1
Sotho .. .. .	5	10
Swazi .. .. .	1	2
Xosa .. .. .	4	2
Zulu .. .. .	8	5
Coloured .. .. .	3	3
Indian .. .. .	2	—
Totals .. .. .	30	30
2. Age average (in years) .. .. .	31.4	32.2
3. Social conditions in ordinary place of residence:		
Strong European influence (cities and towns) .. .. .	24	22
Weak European influence (farms and reserves) .. .. .	6	8
4. Duration of illness before admission (average):		
Acute cases (months) .. .. .	8.5	8.5
Chronic cases (years) .. .. .	5.2	10.8
5. Syphilitic infection (cases) (blood W.R. +; C.S.F. W.R. -) .. .. .	4	5
6. Diagnostic categories:		
Acute catatonic schizophrenia .. .. .	15	10
Acute hebephrenic schizophrenia .. .. .	3	3
Acute paranoid schizophrenia .. .. .	1	5
Chronic catatonic schizophrenia .. .. .	5	7
Chronic hebephrenic schizophrenia .. .. .	4	1
Chronic paranoid schizophrenia .. .. .	1	3
Paraphrenia .. .. .	1	1

larity of the two groups, because this class of patient is not normally considered suitable for ICT. In fact, because of a paucity of beds and an excess of catatonic and hebephrenic schizophrenics requiring treatment, it very rarely happened that they received this treatment.

With regard to the duration of illness before treatment in chronic cases, the average number of years of those who received CT was inflated by 3 cases—one having been ill for 10 years and the other two 7 years each before admission. In approximately a third of each group the duration of illness could not be ascertained at all.

As is evident from Table II, the results from CT were about twice as good as those from ICT in our acute patients.

TABLE II. COMPARISON OF TOTAL RESPONSES TO THE TREATMENTS

	ICT	CT
Complete remissions (discharged) .. .. .	6	13
Partial remissions (L.O.A.) .. .. .	5	5
Unimproved or relapsed .. .. .	19	12

This finding was subjected to statistical evaluation and was considered to be significant within the 7% level. These

cases had been ill for not more than 3 years or, should they have remitted on previous occasions, had had not more than 3 relapses in their illness regardless over what length of time (Table V).

Our results with CT also compare favourably with that expected from ICT in Europeans as quoted by Mayer-Gross, Slater and Roth,<sup>2</sup> while compared with De Wet's findings<sup>14</sup> in African female cases they are quite promising. According to him, in a patient population of 50 souls, each with a duration of illness of less than 30 weeks, only 7 are

TABLE III. ANALYSIS OF CASES IMPROVED, AS ENUMERATED IN TABLE II

	ICT Cases	CT Cases
Acute catatonic schizophrenia ..	4 out of 15	4 out of 10
Acute hebephrenic schizophrenia ..	2 out of 3	3 out of 3
Acute paranoid schizophrenia ..	1 out of 1	5 out of 5
Totals .. .. .	7 out of 19	12 out of 18
Chronic catatonic schizophrenia ..	2 out of 5	3 out of 7
Chronic hebephrenic schizophrenia ..	0 out of 4	0 out of 1
Chronic paranoid schizophrenia ..	1 out of 1	2 out of 3
Totals .. .. .	3 out of 10	5 out of 11
Paraphrenia .. .. .	1 out of 1	1 out of 1

likely to recover spontaneously within 15 months after admission. This rate of remission does not appear to be improved upon by ECT only given twice weekly on either 15 or 30 occasions. Our most pleasing results were seen in the paranoid schizophrenic cases (Table III), who appeared to do remarkably well. The figures, however, are too small for any conclusions to be drawn from them and this may well have been a chance event.

TABLE IV. AVERAGE DURATION OF TREATMENTS COMPARED

Combined therapy .. .. .	12 weeks
Insulin coma therapy .. .. .	16 weeks
ECT and ICT .. .. .	23.5 weeks

CT is quite straightforward and quick to administer; taking half the time for a full course of treatment compared with the usual procedure of a course of 20 ECTs followed by ICT (Table IV). It greatly increases the number of pa-

TABLE V. TREATMENT OF CASES UNDER CT THAT REMITTED PARTIALLY OR COMPLETELY

Duration of Illness	Diagnosis	ECTs			Chlorpromazine		D or L
		No.	Time (weeks)	Optimum dose (mg. b.d.)	Time (weeks)		
1 13 months	Acute catatonic schizophrenia	13	6	100	8	D	
2 Unknown	Acute catatonic schizophrenia	12	6	100	6	D	
3 Unknown	Acute catatonic schizophrenia	7	5	50	7	D	
4 3 weeks	Acute catatonic schizophrenia	13	8	200	9	D	
5 18 months	Acute hebephrenic schizophrenia	19	10	100	8	L	
6 Unknown	Acute hebephrenic schizophrenia	10	9	100	8	D	
7 Unknown	Acute hebephrenic schizophrenia	4	5	50	9	D	
8 Unknown	Acute paranoid schizophrenia	9	7	100	12	L	
9 2 months	Acute paranoid schizophrenia	16	12	50	12	D	
10 3 months	Acute paranoid schizophrenia	14	8	200	5	D	
11 1 year	Acute paranoid schizophrenia	11	7	100	8	D	
12 Unknown	Chronic catatonic schizophrenia	11	6	50	10	D	
13 4 years	Chronic catatonic schizophrenia	5	3	100	10	L	
14 5 years	Chronic catatonic schizophrenia	14	8	100	3	D	
15 3 years	Chronic catatonic schizophrenia	9	7	100	10	D	
16 4 years	Chronic paranoid schizophrenia	6	4	150	10	L	
17 7 years	Chronic paranoid schizophrenia	5	3	50	8	L	
18 2 months	Paraphrenia	5	4	50	10	D	

D = discharged. L = leave of absence.

tients which a limited number of staff can treat, and seems very much safer than either ICT or massive-dose chlorpromazine therapy. In addition, smaller doses of both ECT and chlorpromazine appear to be necessary than when either is used alone (Table V).

We feel that our results from combined therapy in African females are of interest, and suggest that further work along the lines indicated may contribute more information on the symptomatic treatment of schizophrenia.

We cannot, however, too strongly emphasize that, without the active support of well trained nursing staff who have a good understanding of group methods in the handling of patients, this treatment is bound to fail. It depends, absolutely, on having available for each patient facilities whereby she may relate to other people in a free and relaxed environment if she is fortunate enough to have been brought back to reality by the treatment. Left alone, patients showing any sign of improvement whatever all too readily withdraw into themselves and in at least 2 of our cases this process proved to be irreversible.

#### SUMMARY

The use of combined electroconvulsive and chlorpromazine therapy as a method of treatment of schizophrenia is described.

The importance of employing group methods in the application of this treatment is outlined and emphasized.

This therapy was received by 30 African female schizophrenics, approximately two-thirds of whom remitted partially or completely.

The results of this form of treatment is compared with those obtained in insulin coma therapy.

It is concluded that combining the two therapies is worthy of further investigation in the treatment of schizophrenia.

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#### REFERENCES

1. Hine, F. R. (1958): *J. Nerv. Ment. Dis.*, **127**, 220.
2. Mayer-Gross, W., Slater, E. and Roth, M. (1954): *Clinical Psychiatry*, p. 287 and 283. London: Cassell.
3. Sargant, W. (1958): *Lancet*, **2**, 1370.
4. *Idem* (1957): Personal communication.
5. Kalinowsky, L. B. (1958): *Amer. J. Psychiat.*, **115**, 297.
6. Blair, D. and Brady, D. M. (1958): *J. Ment. Sci.*, **104**, 662.
7. Hurst, L. A. (1958): *Report of the 18th Conference of Physician Superintendents of Mental Hospitals and Institutions for the Mentally Defective*, p. 18. Pretoria: Department of Health, Mental Hygiene Branch.
8. Simons, H. J. (1958): *J. Ment. Sci.*, **435**, 377.
9. Schmidt, K. E. (1957): *Ibid.*, **103**, 200.
10. Little, J. C. (1958): *Ibid.*, **435**, 334.
11. Hurst, L. A. (1959): Personal communication.
12. Wolpowitz, B. (1959): Personal communication.
13. Goldman, D. (1957): *Amer. J. Med. Sci.*, **233**, 137.
14. De Wet, J. S. du T. (1957) *J. Ment. Sci.*, **103**, 739.