

THE TREATMENT OF DEPRESSIVE STATES WITH DINITRILE  
SUCCINATE.

By A. GILLIS, M.B., B.Sc., M.R.C.P.E., D.P.M.,  
Consultant Psychiatrist, Cherry Knowle Hospital, Ryhope, Sunderland  
and

D. J. SALFIELD, M.D., B.Sc., D.P.M.,  
Consultant Psychiatrist, Winterton Hospital, Sedgfield, Co. Durham.

HARRIS (1951) adequately summarizes the work done on nitrile compounds and their therapeutic use in psychiatric disorder. This work is highly controversial and the results contradictory. He adds a series of thirty cases of his own treated with dinitrile succinate ("Suxil" or "Psychil"), and concludes that no clear evidence of its therapeutic value was obtained. Twenty of his cases were treated by six or less injections of 0.1 gm. for the first, and 0.2 gm. for subsequent injections. He says: "Later, following representations by the manufacturers, this was extended to twelve." He also comments on the suggestibility of some of his patients and the high spontaneous remission rate which make assessment of the efficacy of therapy peculiarly difficult. As far as can be seen from his paper, the assessments were made entirely impressionistically. Our preliminary trials, confirmed by our further experience with this drug, indicated (in complete harmony with Harris's opinion) that the drug is "safe, easy to administer, and quite free from toxic effects in the doses recommended." We felt, therefore, that a further experimental trial was indicated.

Nine patients were selected for treatment in order to obtain a sample comparable in size to Harris's series. A control group of six patients was also chosen, to exclude the effects of suggestibility. In order to exclude day-to-day fluctuations in mood and to nullify the spontaneous remission rate, chronic patients were chosen.

*Method.*—Each treatment case received four times thrice weekly intravenous injections, twelve in all, of 5 c.c. "Psychil" (2 c.c. for the first injection), corresponding to 0.25 gm. per 5 c.c. The control patients were given an intravenous injection of 5 c.c. of 5 per cent. glucose solution during the same session as the treatment cases and with the same amount of care and interest. To exclude entirely subjective assessment, a small battery of tests was applied before, during and after treatment. All our fifteen patients showed depression, a measure of retardation and apathy, and included paraphrenias with these symptoms. It was originally planned to investigate 12 patients to be treated with "Psychil" and 12 controls, but only 15 patients are entered into our

account. The rest had to be discontinued before finishing their course of injections owing to intercurrent disease and clinical deterioration which made the administration of E.C.T. a necessity. It would thus appear that the dice were weighed in favour of findings confirming efficacy of "Psychil."

Brief case notes follow :

Case.	Age.	Admission.	Clinical state before treatment.	After treatment.
1	62	16.viii.31	In mania for 10 years, then gradually dull, retarded, some confusion. Recently auditorily hallucinated	No appreciable clinical change.
2	56	5.vi.51	Depression, delusions of guilt. Thought she was to be punished. Sometimes excited	Ditto
3	56	10.ix.47	Depression. Suicidal attempt before admission. Visual and auditory hallucinations. Dejected. No interests	"
4	57	4.xii.50	Depressed, sometimes confusional and delusional episodes	"
5	40	12.vii.50	Hostile, aggressive; some auditory hallucinations. Lately emotional, depressed and hypochondriacal, some retardation	"
6	47	18.vi.48	Depressed, emotional, ideas of unworthiness, bizarre somatic delusions. History of attempted suicide. Refusing food	"
7	60	16.vi.50	Retarded, depressed, bodily delusions. Agitated and retarded in alternation	"
8	62	27.ii.48	Confused, solitary, depressed, lacking insight, emotional and agitated at times	"
9	63	10.v.49	Manic-depressive, mostly in deep, almost stuporose depression, when she is mute and incontinent. Now depressed	"
10	51	30.viii.50	In spite of 13 E.C.T., agitated, depressed and absorbed in misery. Ideas of guilt and persecutory delusions	"
11	49	18.vi.47	Depressed, retarded, self-absorbed. Ideas of guilt and unworthiness. Actively suicidal since admission. No E.C.T. for physical reasons	"
12	67	19.iii.51	Hypochondriasis with depression. Worrying, self-accusatory. Bizarre pains, fairly severely depressed	"
13	66	9.i.50	Manic-depressive. Attacks in 1940 and 1949, manic in last. Now hallucinated, depressed, retarded, ideas of unworthiness, periods of agitation	"
14	65	18.iii.41	Apprehensive, self-centred, solitary, dull, dejected and mildly depressed	"
15	64	19.viii.49	Suicidal attempt before admission. Pulls hair and bites fingers. Often bursts into tears. Depressed. Responded to E.C.T. temporarily	"

#### ADMINISTRATION OF TESTS.

All patients were tested on 3 occasions: first, on the day before the first injection; second, a fortnight later, when half-way through the course of 12 injections; third, 10 days after the last injection.

TEST BATTERY.

The tests were so selected as to be simple and speedy, in view of the patients' mental state :

1. "Speed of decision" was assessed by sorting a pack of cards into red, and "picture" cards. Score : Time taken and mistakes made.
2. "Fluency" was measured by the number of different words uttered in one minute. Patients were instructed not to use sentences, etc.
3. "Object memory" was assessed by the number of objects remembered out of 15 small common objects after viewing them for ½ minute.
4. Digit span score : number of digits correctly repeated, two trials being given for each span.
5. The Bender Gestalt test, scored according to Pascal and Suttell (1951). The score purports, according to these authors, to correlate with the likelihood of the testee being a psychiatric patient. Raw scores are given for all tests.

It is not intended to undertake a discussion of the validity, reliability and rationale of the employed tests, as this would go far beyond the scope of the present paper. But it may be said that Test 1 reflects mainly motor speed, Test 2 "fluency", Test 3 "object memory" and attention, Test 4 "digit span" memory and attention, while the Bender Test was taken to measure what has been claimed for it.

TEST RESULTS.

"I" designates results before injections started, "II" those obtained after half the course, "III" those 10 days after termination of the course.

Practice effects, which would probably be slight, have been disregarded. At any rate, they may be presumed not to differ greatly in the two groups.

The number of the patients assessed has been too small for formal statistical treatment, but the results (Table I) will be given and discussed.

TABLE I.—*Test Results.*

Case.	Speed of decision test.									Fluency.	Object memory.			Digits.	Bender Gestalt.			
	Time in secs.			Mistakes.			I	II	III		I	II	III		I	II	III	
	I	II	III	I	II	III												
Treatment :																		
1	. 75	81	95	. 2	2	1	. 0	0	0	. 6	9	5	. 4	5	6	. ref.*	ref.	ref.
2	. 60	110	122	. 28	0	1	. 19	21	20	. 4	3	7	. 5	6	7	. 107	123	101
3	. 47	62	57	. 2	0	0	. 13	9	10	. 7	9	10	. 5	7	7	. 47	64	51
4	. 64	91	90	. 0	0	0	. 15	19	14	. 6	10	12	. 5	7	7	. 85	74	75
5	. 145	120	75	. 3	4	3	. 9	8	7	. 3	2	3	. 4	4	4	. 106	82	97
6	. ref.	120	80	. random	10		. 0	4	2	. 1	2	3	. 5	5	3	. 206	180+	194
7	. 90	70	55	. 3	3	1	. 10	16	10	. 5	10	10	. 6	6	6	. 72	77	68
8	. 78	73	95	. 1	0	0	. 17	25	24	. 4	6	8	. 6	6	7	. 131	91	124
9	. 138	535	563	. 1	13	10	. 1	3	4	. 4	8	10	. 5	7	7	. 81	125	111
Control :																		
1	. 58	52	56	. 1	2	1	. 7	6	8	. 4	5	5	. 5	4	4	. 148	99	176
2	. 84	70	52	. 0	0	0	. 16	17	21	. 4	5	9	. 5	5	7	. 83	38	43
3	. 52	61	45	. 0	0	1	. 34	30	42	. 7	8	10	. 6	6	6	. 84	79	57
4	. 75	65	66	. 0	2	0	. 11	26	32	. 4	9	8	. 3	4	4	. 111	88	82
5	. 172	108	108	. 1	1	0	. 6	8	13	. 2	3	7	. 6	6	6	. 49	68	70
6	. 133	115	120	. 3	0	1	. 11	12	7	. 6	7	7	. 6	5	4	. 98	79	154

\* ref. = refused to co-operate.

## DISCUSSION OF TEST RESULTS.

*Speed of Decision Test.*

In Treatment Group, in 5 out of 9 cases the time taken was greater in the II column than the I column, and in 3 cases greater in III than in I. Mistakes made decreased significantly in 2, but increased in 1 case.

In Control Group, time taken almost uniformly decreased. Mistakes cannot be called significant, owing to the very small number made.

Results obtained from "Psychil" treatment can certainly not be considered better than those from Glucose injections, but rather the contrary.

*Fluency Test.*

Whilst there is a slight average increase in the control group the increase in the treatment group is less.

*Object Memory Test.*

In 7 out of 9 cases there is an increase in score in the treatment group, but also in all control cases there is a very similar increase. We are dealing here probably with a practice effect of very similar size in both groups, although there is a slight additional gain in favour of the treatment group.

*Digits.*

In 6 out of nine cases of the treatment group there is a slight increase in digit span, while there is only an increase in 2 of 6 control cases. There is an average increase of one digit in the treatment group of II over I, but *nil* in the control, which is maintained afterwards in III, while the control stay on the same level.

*Bender Gestalt Test.*

6 out of 9 cases show a slight decrease of the III score as compared with the I score, but also 3 out of the 6 controls show the decrease and, at that, to a much more considerable extent. 5 out of 6 controls show a decreased score in II as compared with I, whilst only 4 of the 9 treatment cases do similarly. The first patient refused to co-operate suitably and had to be left out of the count, although the impression was that she had considerably improved, as far as performance in this test is concerned. Averaging the scores, there is a very slight downward trend in the treatment group, and a downward trend, much more marked in the control, as comparing I and II, but this is not sustained. It will be recalled that the score correlated with the likelihood of psychiatric disorder.

## RESULTS.

No clinical improvement of note was obtained in the patients who were given "Psychil" injections. Compared with the control group, there was a slight, probably insignificant, improvement of attention (or decrease of anxiety?) as measured by the digit repetition test. There was a very slight improvement, as measured by the Bender Gestalt test, in the patients' psychiatric state, which is also likely to be insignificant. Even if these results were

borne out by the analysis of larger groups, the improvements by this method of treatment are so slight as to make the administration of this drug hardly an effective procedure to relieve depressive states of the indicated nature. This applies even in chronic patients and to those who do not respond to E.C.T. or cannot be given E.C.T. for various reasons. We feel that other measures are likely to be more effective.

#### SUMMARY.

A course of intravenous "Psychil" injections (dinitrile succinate) was given to a series of 9 chronic mental hospital patients showing depressive features. Six controls received a similar number of intravenous glucose injections. A battery of tests was given to all the patients before, during and after the experiment, which was conducted over a period of 4 weeks. No appreciable clinical change was noted. The improvements in the test scores of the treated group were small. From this and the clinical observations it is concluded that this drug is ineffective in the treatment of depressive states. This does not exclude the possibility of its efficacy in other conditions.

Thanks are due to the manufacturers of "Psychil," who have provided ample supplies for the purpose of this experiment. We are grateful to the nursing staff of Winterton Hospital for their co-operation, and especially Ward Sister Harbinson. Dr. F. D. MacGilp, formerly Medical Superintendent, has encouraged and supported our investigation, for which our best thanks are due to him.

#### LITERATURE.

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HARRIS, A., 1951, *J. Ment. Sci.*, 1951, **97**, 406, 209.