meratran at the present time could result in distressing medical and social sequelae. For while we have found the means of combating a flare-up of anxiety by the addition of barbiturates or chlorpromazine, it remains to find out how the occasional severe psychotic episode resulting from its use can be predicted and so prevented. Further clinical research may indicate more clearly the type of patient in which this is likely to happen.

Summary

An extensive clinical trial of the new stimulant drug "meratran" is described and its value in the treatment of reactive depression confirmed.

Unlike the amphetamine group of drugs, meratran generally causes little disturbance of appetite or sleep, and in this respect would seem to be superior to any stimulant drug at present available.

Promising results were obtained with it in the treatment of spasmodic torticollis and post-leucotomy anergia. This requires further investigation.

The value of the drug reported by American workers in endogenous depressions is not confirmed. It is our experience that such patients are often made worse by meratran.

The chief drawback to this drug's therapeutic usefulness is its tendency to exacerbate pre-existing anxiety; this necessitates exact diagnosis before administering it. Fortunately, combination with other drugs (chlorpromazine hydrochloride or amylobarbitone sodium) will often prevent this.

Psychotic episodes which can only be attributed to the action of meratran itself are reported in this series. Owing to the poverty of bodily side-effects, no warning of their imminence is given, and they can occur on minimal doses of the drug. At present there is no way of anticipating these disturbances.

We wish to record our thanks to Dr. William Sargent for helpful advice and criticism, and to the Wm. S. Merrell Co., of Cincinnati, U.S.A., for the generous supplies of meratran.

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A second edition of the historical record of the King Edward VII's Hospital for Officers (Sister Agnes's) has now been published; the price is 2s. 6d. a copy and the proceeds will go to the hospital, which is independent of the Health Service. The new edition brings the history of the hospital up to date, since it reopened in Beaumont Street, London, W.1, in 1948 after the bombing of 17, Grosvenor Crescent in 1941. This "postscript" shows that the tradition of royal interest in the hospital, which began when King Edward VII insisted that the work of the Sisters Fanny and Agnes Keyser for the wounded officers of the Boer War should be continued in peacetime, has continued strongly. In 1950 Princess Margaret paid the hospital an informal visit, and shortly before his death King George VI came to invest a patient with the G.C.V.O. Her Majesty the Queen is the fifth sovereign to become its patron. Last year 761 patients were admitted, and a gift from the British War Relief Society, Inc., of America has made the planning of a new nurses' home possible. This should be ready in 1957.

GROUP BEHAVIOUR IN CHRONIC SCHIZOPHRENICS TREATED WITH "MERATRAN"

BY

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A new drug, α -(2-piperidyl) benzhydrol hydrochloride ("meratran") with the following formula

has been described in the U.S.A. as being an anti-depressant similar to the amphetamines in its central action but without their peripheral sympathomimetic effect. In clinical trials conducted by Fabing *et al.* (1955) a group of 25 chronic patients, of whom 19 were schizophrenics, were given meratran, the experiment being controlled by placebo tablets. They showed improved co-operativeness and ward adjustment, but the results were not analysed statistically. Delusions and anxiety were said to be contraindications (Schut and Himwich, 1955). Similar claims were made in cases of depression, narcolepsy, and long-term schizophrenia with deterioration and psychomotor retardation—active delusions, anxiety, and agitation being regarded as contraindications (Fabing, 1954, 1955)—with average doses of 2 mg. three times a day orally (Andren, 1955) and with resultant increase in activity unaccompanied by euphoria (Forster *et al.*, 1955).

It was thought opportune to study the action of a new drug such as meratran on group behaviour in chronic deteriorated schizophrenics, and to determine what effects were produced and, if any improvement resulted, whether it was reasonable to conclude that any of this was due to the drug or whether it could be shown to be due to some other factor.

For this project a group of 20 chronic male schizophrenics, the most deteriorated and withdrawn patients in a hospital of 900 patients, were selected. They were all more or less retarded, and were lacking in any sense of self-consciousness or group feeling, though they were in the same ward. Their ages ranged from 31 to 72 (average 46.3 years) and their duration of stay in hospital ranged from 3 to 38 years, with an average of 16.6 years.

These 20 patients formed part of a big rehabilitation and occupational research project, in which they in particular spent most of the day in some activity on the farm or in the ward, but on an average eight patients were quite unemployable in any fashion. They were also subject to habit-training which had freed them from nocturnal incontinence, and their night sedation had been cut down to nil.

Design of the Experiment

The 20 patients were divided at random into two groups of 10. Their behaviour was studied, being tabulated under the headings of feeding, letter writing, reading, conversation,

mutual aid, washing, and dressing. These are the forms of social behaviour that could be studied objectively. The patients were graded on a three-point scale according to whether the particular form of behaviour was shown spontaneously (3 points), in response to urging (2 points), or not at all (1 point). For example, if the patient ate his food without prompting he was given 3 points, if only when prompted 2 points, if he had to be fed 1 point, the score thus indicating the degree of spontaneity, highest marks being given for most spontaneity. The same method applied in regard to letter writing, reading, conversation, washing, and dressing. In regard to mutual aid, if patients offered to help each other to wash or dress, or offered them a light for a cigarette, or showed any other spontaneous desire to help others they scored 3 points, if they helped others only when told to do so they scored 2, and if they refused to help others they scored 1.

All this was explained to the nursing staff, who remained the same throughout the experiment. A trial period was then embarked on for six weeks before the tablets were available and practice was thus gained in charting the results.

The first 10 patients were then given the meratran (2 t.d.s., the dose recommended by the manufacturers) from a box labelled "A tablets." The second 10 patients were given the placebo tablets, which appeared the same (bright pink) and tasted the same. These were given from a box labelled B. I was the only one who knew which were the real tablets, and only the nursing staff entered the observations in the charts, so that my knowledge could not prejudice the entries.

The patients were given these tablets in this order for a four-weeks period. A two-weeks period free from tablets then ensued to allow any effects to pass off. A further four-weeks period of tablets followed, reversing the order so that the first 10 patients now had B tablets and the second 10 patients had A tablets (meratran). In this way any bias caused inadvertently by the method of selection was neutralized. The scores on the three-point scale of each of the seven days of the fourth week of A (meratran) tablets—that is, the fourth week of the first course and fourth week of the second course—were added together, and the daily scores were similarly added for the fourth weeks of B tablets. The least possible score for seven days is seven, and the greatest 21. The fourth week was chosen because any effects of meratran would then be maximal. The two groups were then compared and the differences analysed statistically.

Results

The results are shown in Table I. The almost complete lack of response to letter writing and mutual aid after

TABLE I

Case No.	Age	Feeding		Reading		Conversation		Washing		Dressing	
		A	B	A	B	A	B	A	B	A	B
1	52	21	21	7	10	12	14	14	21	21	21
2	44	21	21	14	20	16	20	19	21	21	21
3	53	21	21	11	12	14	15	20	21	21	21
4	72	21	21	7	8	14	14	20	21	21	21
5	34	21	21	14	21	17	20	13	21	21	21
6	43	19	21	16	21	19	21	20	21	21	21
7	45	19	21	8	7	10	9	14	21	18	21
8	32	21	21	16	21	14	17	16	21	20	21
9	42	20	21	7	7	9	8	9	21	13	21
10	43	21	21	14	21	13	15	13	21	14	21
11	49	21	21	7	8	9	9	21	7	21	10
12	31	21	21	17	17	17	19	21	16	21	19
13	55	21	21	7	7	8	8	21	7	21	15
14	46	21	21	7	7	8	8	21	10	21	14
15	37	21	21	9	8	13	14	21	13	21	18
16	50	21	21	16	12	18	17	21	15	21	20
17	55	21	11	21	11	21	11	21	11	21	12
18	46	18	7	7	7	7	7	14	7	19	7
19	62	20	14	7	7	14	14	18	9	20	14
20	35	7	7	7	7	15	14	16	14	21	14
Standard error		1.245		1.45		1.257		1.35		1.13	
Diff. between means		1.1		1.0		0.3		1.7		1.25	

A=Meratran. B=Placebo.

meratran made an analysis unnecessary. The means, difference between means of groups treated by A tablets and groups treated by B tablets, standard deviation, and standard error were calculated = $\sqrt{(S.D._1)^2/n_1 + (S.D._2)^2/n_2}$ (Bradford Hill, 1955). The difference between the means was not significant at all for any of the behaviours studied as between meratran and the placebo tablets.

A comparison was then made between the second week of the preliminary trial period before tablets were given and the final week of the project, when the first 10 patients were having B and the second 10 patients were having A tablets, and the results were charted as before. (The second week was chosen, as the nurses had by then become accustomed to the method of scoring.) The results when the scores for the seven days of the second week were added together were labelled I, and those for the final week were labelled II (Table II).

TABLE II

Case No.	Feeding		Reading		Conversation		Washing		Dressing	
	I	II	I	II	I	II	I	II	I	II
1	16	21	14	10	14	14	14	21	17	21
2	20	21	12	20	14	20	16	21	19	21
3	21	21	7	12	14	15	21	21	19	21
4	21	21	7	8	14	14	16	21	19	21
5	21	21	12	21	15	20	16	21	18	21
6	17	21	11	21	14	21	12	21	18	21
7	20	21	7	7	9	9	14	21	15	21
8	18	21	7	21	14	15	14	21	16	21
9	19	21	7	7	10	8	12	21	14	21
10	21	21	13	21	13	14	12	21	14	21
11	19	21	8	7	7	9	11	21	14	21
12	18	21	12	17	15	17	13	21	16	21
13	20	21	7	7	8	8	8	21	12	21
14	20	21	7	8	8	8	9	21	12	21
15	18	21	7	9	11	13	9	21	14	21
16	17	21	7	16	14	19	8	21	14	21
17	21	21	14	21	19	21	14	21	21	21
18	9	18	7	7	7	7	7	14	7	19
19	11	20	7	7	9	14	7	18	7	20
20	7	7	11	7	14	15	12	16	14	21
	P=0.05		P=0.0027		Not significant		P=0.0027		P=0.0027	
Standard error	1.1		1.5		1.24		0.89		0.937	
Diff. of means	2.4		5.0		1.9		8.0		5.75	

I = 2nd week

II = Final week

The results here are extremely interesting. Feeding shows an improvement of 2.4—that is, greater than twice the standard error of 1.1—and is therefore significant at the 0.05 level of confidence. Reading shows an improvement of 5.0—more than three times the standard error of 1.5—namely, at a 0.0027 level of confidence, or more than would occur by chance 1 in 370 times (Bradford Hill, 1955). Conversation shows an improvement of 1.9, which is not greater than twice the standard error of 1.24, and therefore is not significant at a 0.05 level of confidence. Washing shows an improvement of 8.0—more than three times the standard error of 0.89—and is highly significant. Dressing shows an improvement of 5.75—more than three times the standard error of 0.94—and is highly significant. Of course, feeding was at a fairly high level to begin with and had less leeway to make up, but the improvements in reading, washing, and dressing since the project began are indisputable.

Notes on individual patients show that certain patients who were hallucinated and deluded became more so at times. One patient in particular, who had always been somewhat anxious and preoccupied with feelings of sexual guilt and who masturbated continuously, became vividly hallucinated, seeing visions of his mother in every window and calling out for her while frantically rushing backwards and forwards from one window to the next. This began on the tenth day after he received meratran but subsided spontaneously within a few days, only to recur in a milder form on the last three days. It did not occur with the placebo tablets. Only two other patients showed similar psychotic outbursts of activity,

though to a much less degree. No change in blood pressure, temperature, pulse, or respiration was noted at any time in any patient.

Discussion

New tablets are constantly being brought on to the market and clinical trials made of them, in some cases without a controlled experiment and in many cases without statistical analysis of the results. As in the present project, improvement takes place, particularly in disturbed psychotic patients, and it is assumed that this is caused by the tablets.

The present experiment shows that a group of chronic deteriorated schizophrenics improved measurably in spontaneity in certain activities during a four-months period, during which time the nursing and medical staff showed great interest in details of their patients' behaviour. All of these activities were ones in which the nursing staff approved of the greater spontaneity shown—and in many ways they actively encouraged it, for it made their own nursing work easier.

If spontaneity meant that patients were to feed themselves, dress themselves, wash themselves, and help one another, the nurses welcomed it. More reading, more letter writing, and more conversation were also desirable as signs of recovery, and did not in any way cause difficulty. Only one patient became so overactive as to be a nuisance; but this was not enough to imperil the popularity of the "clinical research." It should be added that such a control experiment had not previously been carried out in this hospital, and was the focus of considerable discussion, feeling, and approval.

How the improvement comes about it is difficult to tell. The results bear a close resemblance to those in the famous Hawthorne experiment (Urwick and Brech, 1948), where the productivity of a group of factory workers, studied under varying physical conditions, rose steadily regardless of whether the conditions were made better or worse; it was later shown that this rise in production was due to the high morale of the experimental group under the attention of the management and to the high prestige of the experiment itself.

There it was possible to question the operators and elicit their increased happiness, heightened morale, and raised "we-feeling." Whether this has happened with the schizophrenics in the present study must be a matter of conjecture, for most of them are too "demented" or withdrawn to sustain a conversation, far less to give an insightful account of their feelings toward the group. That the morale of the nursing staff was raised is undoubted; they were deeply interested in such prestige-laden activity as "clinical research" and they were delighted with the progress made by the poor confused people in their charge. The fact that senior members of the medical staff were taking consistent and maintained interest in the minor details of the lives of these patients was also a new and important change in the social situation of the ward. Traditionally the interest of the doctors was limited to the vocal and "interesting" patients; the "dements" were merely seen when annual notes were due or when they developed some physical ailment. Their names and such personality as they manifested were known only to the nursing staff—not to the doctors.

The relationship between patients and staff as it affects schizophrenic behaviour has been studied sociologically and the conclusion reached that when the staff realize that they contribute to patients' behaviour they can help to modify it (Stanton and Schwartz, 1955). If a doctor concentrates on a neglected ward of chronic psychotics with a desire to eliminate some form of behaviour objectionable to him he can succeed in doing it. As attention concentrates on it, as questions are asked day after day, as the nursing staff get to know the bee in this new doctor's bonnet, the manifestation—be it incontinence, destructiveness, excessive sedation, masturbation, or untidy clothing—diminishes rapidly; it may even disappear entirely. Unfortunately, however, there

is a tendency for doctors to move on to other hospitals, and then reaction may set in and all the manifestations of faulty behaviour return. This is analogous to the return of instruments of restraint at Hanwell after the resignation of Sir Wm. Ellis in 1838 because the officers at Hanwell had not partaken of his benevolent spirit (Walk, 1954). Popular demand and overriding social needs may prevent such regression and consolidate the gains made, though it is a fundamental characteristic of hierarchical organizations to resist change.

It can be predicted that anything on which attention is focused will change in the direction desired, merely because of that focusing of attention. Myerson's (1939) concept of "total push" was an elaboration of this fact. Many current "rehabilitation" programmes (Martin, 1950; Klemes, 1951; Galioni *et al.*, 1953) derive much of their early satisfaction from this. It can be said that a true change has been brought about in a group of chronic psychotic patients only if changes occur in other manifestations which cannot be directly related to the efforts of the staff. For example, if after a habit-training drive it is found that some of the patients are writing letters home (without overt encouragement) then this can be regarded as a real improvement. The results of the present experiment in this regard are ambiguous. The improvements in feeding, in dressing, and in washing are all direct results of pressure by the nursing staff.

It may be that the increase in spontaneous reading is an indication of a definite change. One of the problems of such researches in mental hospitals is to devise measures of improvement that are valid and yet not directly due to the nurses' efforts.

The main lesson that emerges from this study is that caution and adequate control procedures are essential before any therapy or drug is accepted as beneficial in chronic psychotics, and that statistical analysis of results is essential, for in this particular group of schizophrenics it showed that meratran was no more effective than placebo tablets, yet an improvement in the behaviour of the patients had occurred during the project that would otherwise have been attributed to meratran. To understand the factors that will improve chronic schizophrenics in mental hospitals prolonged sociological studies are necessary.

Summary

A new drug, meratran, said to be antidepressive without the disadvantage of amphetamines, is described. This drug was tested on a group of 20 male chronic schizophrenics by studying their behaviour under headings of feeding, letter writing, reading, mutual aid, conversation, washing, and dressing, using a three-point scale. After six weeks' preliminary charting, 10 patients were given meratran and 10 were given placebo tablets for four weeks. After a two-weeks interval the meratran and placebo order was reversed, thus eliminating any bias due to the chance selection, and administered for four more weeks.

The results in the fourth weeks of the two courses of treatment with meratran and placebo were compared and found not to differ significantly. The results in the second week of the project were compared with the results in the final week and a significant improvement in reading, washing, and dressing was noted. This was attributable to increased nursing enthusiasm, and its significance is discussed. A warning is given about the strict analysis of results in a group of psychotics treated by a new drug before a definite conclusion is reached on the value of such a drug.

I wish to thank Dr. D. H. Clark, medical superintendent of Fulbourn Hospital, for his valuable advice and criticism; Riker

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BENACTYZINE IN PSYCHONEUROSIS WITH A NOTE ON THE E.E.G. CHANGES IN NORMAL SUBJECTS

BY

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In this paper we are reporting the clinical effect of benactyzine on a small series of out-patients, and the electroencephalographic changes following the administration of the drug to normal subjects.

Benactyzine ("suavitil") is the hydrochloride of benzilic acid diethylaminoethyl ester. It is rapidly absorbed and excreted, and in addition to its anticholinergic, local analgesic, and quinidine-like actions it has recently been claimed to have a central effect which alters reactions to stress (Jacobsen, 1955; *Danish med. Bull.*, 1955).

Animal Experiments

Jacobsen and Sonne (1955) claim that the drug has a "normalizing" effect on the behaviour of rats rendered "tense and immobile" by a technique involving recurrent electrical stimulation. In other experiments, cats were trained to obtain food by opening the lid of the food box, and "conflict-induced behaviour" was then observed in them when a sudden stimulus was used to interfere with their food-seeking activity. This behaviour was said to be "normalized" by the use of the drug (Jacobsen and Skaarup, 1955).

Effect on Human Subjects

Human subjects given 5-6 mg. of benactyzine by mouth or by injection were reported by Jacobsen (1955) to have experienced giddiness which was occasionally very severe, a feeling of muscular relaxation, and thought-blocking. Experiments showed that patients under treatment with the drug exhibited diminished autonomic response to emotional stimuli, and Jacobsen claims that the drug has a specific action raising the "psychic threshold for irritation." Referring to unpublished work done by Hess in 1955, he states that the electroencephalogram showed partial or complete blocking of the alpha rhythm, which started and disappeared at the same time as the subjective changes experienced.

The use of the drug in the treatment of psychoneuroses and psychoses has been described by Munkvad (1955) and Jensen (1955). Munkvad found no effect on 22 psychotics receiving doses of up to 15 mg. four-hourly. Of 15 psychoneurotics, 10 improved with the drug but not with a placebo. The dosage used was up to 1.5 mg. three times a day, and no side-effects of importance were noted. Jensen claimed improvement in 75% of 110 psychoneurotics treated with a similar dosage. Patients with anxiety reactions, depressive reactions, and obsessive compulsive reactions responded favourably. The side-effects were few and insignificant: slight dizziness, slight thought-blocking, and undefined "queerness."

Clinical Trial

The following pilot study was carried out at St. George's Hospital, where the drug was given to a series of psychoneurotics attending the out-patient department.

Selection.—The only criterion of selection was that, no matter what his other symptoms, the patient complained spontaneously of feeling tense, strung up, or overwrought. Tension was thus prominent though not necessarily predominant in the symptomatology of these patients.

Method of Administration.—Only the pharmacist knew whether the patient was given the drug or a placebo of identical appearance, and the courses alternated at intervals varying from 10 days to one month. At each interview the patient was asked to say whether there was any change and, if so, whether he was better or worse. A definite statement was obtained regarding tension, predominant mood, energy, and irritability.

Response to the drug was assessed on the following basis. Where relief of tension was reported but other symptoms persisted the patient was classified as "improved." Where the overall improvement was such that he no longer needed to attend for treatment the patient was classified as "considerably improved." In both these groups the improvement must be attributed to the drug and not to the placebo. Where the placebo seemed to be equally or more effective the patient was classified with those who reported "no change," while "worse" is self-explanatory.

Of the 19 patients included under "no change," nine had reported no change from the drug or the placebo, six had found benefit from the placebo but not from the drug, while four had reported equal improvement with both drug and placebo. Of the six patients who said they were worse, four were made worse by the drug but not by the placebo, while two said they were worse on both.

As will be seen from Table I, none of those with neurotic depression was improved. Of the obsessive compulsive cases which reported an improvement, none noticed any

TABLE I.—Results

	Total	Worse	No Change	Improved	Considerably Improved
Neurotic depressions	10	2	8	—	—
Obsessive compulsive neurosis ..	8	—	4	4	—
Hysteria ..	4	3	1	—	—
Anxiety neurosis ..	18	1	5	4	8
Miscellaneous:					
Colitis ..	1	—	—	1	—
Pruritus ..	2	—	1	1	—
	43	6	19	10	8

change in the compulsive rituals or ruminations, but simply reported less tension in performing them. Of the four hysterics, three were made worse and one reported no change.

Of 18 cases of anxiety neurosis 12 showed improvement, and eight of them considerable improvement. Those patients who benefited from the drug spoke of "not worrying ahead so much," "developing a couldn't care less attitude," "feeling calmer," and similar changes indicative of diminished tension. Most of the patients with anxiety