Comparative Value of Bemegride and Thiopentone

An attempt was made in the 28 patients receiving both bemegride and thiopentone to evaluate which of the two had proved the more useful technique: in five bemegride was more useful, in eight thiopentone was more useful, in 8 they were deemed equally useful, in two the routine record was more useful than either of the two records, and in five patients no assessment could be made.

Discussion

This investigation has confirmed the experience of Pampiglione and Kerridge (1956) that the sphenoidal recording is both a useful and a safe procedure. It would also seem that bemegride, which has now been used in this department in over 50 patients, is a comparatively safe drug in the doses used, giving only a small incidence (14%) of fits. The onset of these fits is not alarming to the patient or to the observer. It should again be stressed that the onset of the fit is slow and gives time to take adequate precautions—for example, removal of the sphenoidal electrodes.

From the small number of controls investigated it would seem that, in the dosage used, abnormalities which might be interpreted as being due to epilepsy are uncommon in a non-epileptic patient. The sensitivity of various subjects to this drug must vary. It would not be surprising to find epileptic discharges in the E.E.G. of a normal patient if a sufficiently large dose of bemegride was given. With the present technique it is likely that at least 150 to 200 mg. of bemegride would be needed to produce abnormal discharges in any reasonable proportion of normal subjects.

Compared with thiopentone, bemegride has two advantages: firstly, that the patient is conscious throughout, provided a fit does not occur, and can walk away immediately after the record is taken; secondly, unlike thiopentone, it can be given if the patient has had a meal recently. Bemegride has the disadvantage of producing an occasional fit, and if this does occur the recording may be interrupted.

Bemegride is a useful addition to the activators used in electroencephalography, as it can demonstrate focal as well as generalized abnormalities in a reasonable proportion of patients (43% of 40 patients in this series showed an epileptogenic focus following bemegride). It may be that by using a modified technique a greater proportion of abnormalities will be demonstrated with bemegride. This series has been concerned mainly with the demonstration of temporal-lobe foci, but the use of bemegride to demonstrate foci elsewhere in the brain may be of value, and this has not been investigated.

Bemegride is not a substitute for thiopentone in sphenoidal recordings, but makes a useful addition to this technique. It can also be used after the administration of thiopentone in order to arouse the patient rapidly from his state of sleep.

Summary

The history of the use of bemegride in connexion with electroencephalography is summarized.

Bemegride was used as an activator in recording the E.E.G.s of 40 patients and 10 controls. Most of the patients had temporal-lobe epilepsy and sphenoidal electrodes were used.

Bemegride appears to be a safe drug and a useful activator in that it can demonstrate epileptogenic foci as well as produce generalized epileptic discharges.

Fits were induced in 7 out of 50 subjects to whom bemegride was given.

I thank Dr. D. A. Pond for his continued help and encouragement throughout this investigation, Mrs. E. Moody for her technical assistance, and the medical students who volunteered as control subjects. A. & G. Nicholas Ltd. kindly made supplies of bemegride available for this work.

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BENACTYZINE IN PATIENTS WITH VIOLENT TEMPER AND PATIENTS WITH PARKINSONISM

BY

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In the early experiments with benactyzine ("suavitil," "parasan," "nūtinā"), Larsen (1955) noted in himself and his colleagues to whom the drug was given "a certain insusceptibility to unpleasant impressions"; and Jacobsen (personal communication), who worked with Larsen, informed me that the drug gives one a feeling of distance from reality, so that problems with which one is occupied do not seem to be so urgent or so demanding. Jacobsen and Skaarup (1955) showed that in cats which have been rendered "neurotic" in a conflict situation the drug tends to bring about a return to normal behaviour and a diminution in neurotic reactions. Jacobsen agreed that it would be worth testing this drug in that small group of patients, usually epileptics, who have violent outbreaks of temper. As the drug has anticholinergic properties, and as atropine and other anticholinergic drugs are useful in cases of Parkinsonism, it was also decided to test the drug on patients with this malady.

The drug was given orally in tablets, each containing 1 mg. of benactyzine. Control tablets were made up to look identical with the tablets containing the drug, and an equivalent number were given. In half the patients the first supply of tablets consisted of benactyzine, and in the other half it consisted of the control tablets; on subsequent occasions the opposite kind of tablets was given, so that those patients who had received the control tablets received the benactyzine, and vice versa. No patients ever discovered that some of the tablets they were receiving were blanks.

Patients with Tempers

Twelve patients were collected who were attending the out-patient department of this hospital and whose outbreaks of temper formed an important feature of the clinical picture and of which complaint was made. Two patients had developed these outbursts following closed head injuries; the other 10 had epilepsy. Of the epileptics, three had idiopathic epilepsy, two had temporal lobe lesions, and five had infantile hemiplegia. The drugs which the patients were receiving—phenobarbitone, primidone, hydantoin sodium—to combat their fits were given throughout the

period of administration of the benactyzine and the control tablets. The dosage of benactyzine for this group of patients varied between 3 and 12 mg. a day.

In two of these patients the investigation lasted four months, and in one patient it lasted two and a half years; in all others it lasted between one and two years. The patients were given supplies of the drug or the control tablets sufficient for two or three months. The two patients in whom the investigation lasted four months were seen and the drug and the control tablets were changed at fortnightly intervals.

In all cases the opinion of another member of the family was taken regarding the patient's general irritability and liability to lose his temper. The patient, or, if the patient was a child, his mother, kept a record of the number of outbursts of temper which occurred.

The results are shown in Table I. The terms "no change or worse" explain themselves; "improved" means that the patient was less apt to be bad-tempered and/or had

TABLE I.—*Effects of Benactyzine and Control on Outbursts of Temper*

Patient	Benactyzine		Control	
	Improved	No Change or Worse	Improved	No Change or Worse
Epileptics:				
C	+		+	+
P	+		+	
Re	+	+		+
Bl		+		+
Ga		+		+
L	+		+	
A		+		+
F		+		+
By		+		+
Gr	+		+	
Head injury:				
L	+			+
E	+	+	+	+
Total ..	7	7	5	9

fewer outbursts of temper. It can be seen that an equal number of patients were improved as were not improved by benactyzine. Two patients on some occasions were improved and on other occasions received no benefit from benactyzine; and, similarly, two patients were on different occasions improved and received no benefit from the control tablets; one of these patients appeared in both groups and received the drug or the control tablets for two and a half years; on various occasions he received benefit and no benefit from the drug and from the control tablets. Five of the 12 patients received benefit from the control tablets, whereas nine received no benefit. It will be noted, however, that 5 of the 12 patients were better both on the control tablets and on the benactyzine. Thus it seems that these patients benefited from having tablets of any sort; 7 of the 12 patients were no better on either sort of tablet. Only one patient showed an improvement on benactyzine on all occasions while showing none on the control tablets.

As benactyzine failed to be of use in helping patients in controlling outbursts of temper or in preventing their being irritable, further details of this trial need not be given.

Patients with Parkinsonism

The drug was tested on 18 out-patients with Parkinsonism. The dose varied from 3 to 10 mg. a day. The drugs which the patients were receiving to combat the manifestations of Parkinsonism—benzhexol hydrochloride, hyoscine, stramonium—were given throughout the period of administration of the benactyzine and the control tablets.

The duration of the investigation on these patients was as follows: on two patients three months, on five patients six months, on three patients eight months, on six patients one year, and on two patients one and a half years. The drug or the control tablets were given for periods of one or two months, after which the other sort of tablet was given for the next period.

C

The results are shown in Table II. The term "improved" means that one or more than one of the symptoms from which the patient suffered was less irksome, or that the

TABLE II.—*Effects of Benactyzine and Control on Symptoms of Parkinsonism*

Patient	Benactyzine		Control	
	Improved	No Change or Worse	Improved	No Change or Worse
BAR		+		+
DA		+		+
I		+		+
BAL		+		+
EV		+		+
G		+		+
L		+		+
DO		+		+
KN		+		+
T		+		+
H	+		+	
J	+		+	
A	+		+	
M		+	+	+
E	+	+	+	
KE	+	+		+
W	+	+		+
F			+	
Total ..	7	14	6	13

patient felt better in some way, such as feeling stronger, or less anxious and tense, or less tired. Twice as many patients received no benefit from benactyzine as noted an improvement; four patients during some periods on benactyzine considered that they were better while during other periods on the drug they were no better or worse; about as many felt better on the control tablets as on the benactyzine; twice as many received no benefit from the control tablets as received benefit from them. Ten patients were helped by neither the benactyzine nor the control tablets, and five patients were helped by both. No patients were improved by benactyzine who were not also improved by the control tablets or who, on other occasions, received no benefit from benactyzine. Thus benactyzine was shown to have no value in combating the unpleasant manifestations of Parkinsonism.

Undesired Side-effects

No effects on the skin or the kidney were encountered. There were no sensitivity reactions, repeated total and differential white counts were normal, and no casts or red blood corpuscles were found in the urine of patients receiving the drug. No patient complained of difficulty in focusing, of palpitations, or of dryness of the mouth.

Two patients considered that the benactyzine made them "dopy" and "unclear in the head"; one had these symptoms with 4 mg. daily and the other with 6 mg. daily. However, two patients got these identical symptoms on the control tablets. A further patient reported that the control tablets made her so sleepy that she could neither wake up nor get up in the mornings; she did not get this effect from the benactyzine itself. Another patient found that on the control tablets she felt so dizzy and dull-witted that she did not know what she was doing; she stopped taking these tablets as she said they terrified her. One patient, however, obtained the opposite effects when on the control tablets; he found they made him "clearer in the head." Two patients complained that the benactyzine tablets made them sweat. One patient complained that the rigidity of Parkinsonism was worse both on the benactyzine and on the control tablets, and another complained of lack of libido and of impotence both on the benactyzine and on the control tablets.

Discussion

Seager and Leitch (1956) found that benactyzine was no more effective than control tablets in neurotic patients in whom anxiety and tension predominated. And Raymond, Lucas, Beesley, O'Connell, and Roberts (1957), in a similar group of patients, found that there was no significant difference between control tablets and meprobamate, benactyzine, and chlorpromazine. The same result—that benactyzine

is of no value—was found here in the two groups investigated—those with outbreaks of violent tempers and those with Parkinsonism. Once again this minor investigation shows that inert substances produce the same effects as drugs with pharmacological properties; they are useful to patients who believe they will get benefit from them, and they cause undesired side-effects; and the side-effects may be present only with the inert tablets and not with the actual drug.

Summary

Benactyzine was tested in patients with outbreaks of violent temper and in patients with Parkinsonism. It was of no greater value than control tablets.

I thank Drs. Eliot Slater, John Marshall, and John Walton for referring cases to me for this investigation, and Dr. E. A. Carmichael for opportunities to carry out this investigation.

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TRIAL OF A NEW REMEDY (CIBA 10870) IN PARKINSONISM

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In the treatment of Parkinsonism we are always glad to hear of a new remedy. Current therapy leaves much to be desired, and our most effective drugs have unpleasant or dangerous side-effects. We have recently studied the effects of a parasympatholytic drug on a series of Parkinsonian cases. The compound—preparation No. 10870 (Ciba)—is 3-phenyl-3-(β -diethyl-amino-ethyl)-2,6-dioxopiperidine hydrochloride, with the structural formula:

It has already been tried on a series of patients by Giannotti, Gilberti, and Spizzirri (1956). They have reported favourably on its effects in Parkinsonism, alone and in combination with reserpine and methyl phenidate ("ritalin").

Material and Methods

Ten cases of Parkinsonism (four males and six females) were observed in Snowdon Road Hospital, Bristol, by all three of us. Their ages ranged from 47 to 82 years. In six cases the Parkinsonism was attributed to encephalitis lethargica dating from the epidemic in the 1920's and in four cases to idiopathic paralysis agitans. No case of "arteriosclerotic" Parkinsonism was included.

It was decided to stop all current therapy for a day before the trial began. When this decision was taken it was not expected that withdrawal symptoms would be so troublesome. Actually they were severe in three cases. It is difficult to distinguish withdrawal symptoms from basic

symptoms in such cases. The chief symptoms noted were intense salivation, perspiration, and mental depression. One of the three patients threatened suicide unless he was put back on his previous treatment. In other cases these symptoms may have prejudiced the patients against the new tablets.

The compound was dispensed in small white tablets, each containing 2.5 mg. of active drug. Tablets the same size and colour containing an inert substance (ascorbic acid) were used as controls. There was a slight difference in appearance between the two tablets, so that some of the doctors knew which was genuine and which dummy on the first day. It is doubtful if any of the patients recognized the difference in appearance between the two tablets. The tablets were given orally in a dosage of six daily to every patient. The patients were divided into two groups, one taking the dummy tablet (tablet A) for four days, while the other took the genuine tablet (tablet B). At the end of four days the tablets were changed round and each group put on the alternative treatment. In two cases withdrawal symptoms were severe, and tablet A had to be discontinued after one and three days respectively and previous treatment re-instituted. This did not occur with tablet B.

The condition of each patient was assessed by all three observers before and at some time during the trial. On a chart provided for each case points were scored for effects on tremor, rigidity, dribbling, oculogyric crises, facial mask, walking, feeding, reading, and bladder and bowel functions.

Table I gives a general assessment of the results in our 10 patients.

TABLE I

Sex and Age	Type	Previous Therapy	Result with Placebo (Tablet A)	Result with 10870 (Tablet B)
F 49	Post-enceph.	Hyoscine and benzhexol	Worse	Better
F 79	Paralysis agitans	Mephenesin and benzhexol	"	"
F 68	" "	Benzhexol	"	"
F 82	" "	Hyoscine	Mentally confused	No change
F 52	Post-enceph.	Benzhexol	Worse	Better
M 68	" "	"	"	"
M 50	" "	"	"	"
M 47	" "	"	"	"
F 50	" "	Benzhexol and belladonna	"	"
M 63	Paralysis agitans	Hyoscine	"	Better. Euphoria

In addition to these 10 patients we were able to try out the preparation on a further six in outlying hospitals in Thornbury, Wells, and Axbridge. One of us (W. H.) had these patients under observation before and after treatment, but the assessment of results observed at the time is based mainly on observations by the medical officers in charge of these hospitals and by the nursing staff.

The results in these six cases are set out in Table II.

TABLE II

Sex and Age	Type	Previous Therapy	Result with Placebo (Tablet A)	Result with 10870 (Tablet B)
F 45	Post-enceph.	Benzhexol and chlorpromazine	Severe withdrawal symptoms	Excellent
F 75	Paralysis agitans	Barbiturates	Worse	Better
F 74	Post-enceph.	Ethopropazine	"	Better. Euphoria
M 67	" "	Chlorpromazine	Same	Better
F 76	Paralysis agitans	Benzhexol	Worse	"
F 71	" "	Nil	Same	Better. Dry tongue

The general impression was that the new preparation was equal if not superior to any therapy in current use. The best result in individual cases was its effect on salivation in post-encephalitics. One patient who used to soak a pillow on most days dried up completely. Another who