generally and in temporal lobe epilepsy has recently been re-emphasized in Ounsted's (1955) preliminary report on his survey of epileptic children, but the point at which this would be operative is still obscure. It may be that Ammon's horn sclerosis or any other focal lesion in the temporal lobe would give rise to epilepsy only if additional factors were present. It is pertinent in this respect to observe that, even in animal experiments, during electrical or chemical stimulation of the medial centres of the temporal lobe it may be necessary sometimes, in order to produce temporal lobe attacks, to lower the animal's seizures threshold with small doses of leptazol.

Summary

Ammon's horn sclerosis has been encountered in resected temporal lobes of 19 out of 27 cases (70%) suffering from temporal lobe epilepsy. The mean age of onset of the epileptic history when Ammon's horn sclerosis was present lay at the fourth year of life, but in less than half of the cases only a history of birth trauma could be elicited. The association with a history of status epilepticus preceding the psychomotor seizures was encountered in at least 64% of these cases; this association was not encountered in those cases without Ammon's horn sclerosis.

The importance of the various pathogenetic mechanisms is discussed, particular stress being laid upon cerebral oedema as a major factor.

The association between Ammon's horn sclerosis and temporal lobe epilepsy is of considerable interest; although this relationship is not yet fully understood, it is probably not simple or direct. The possible mechanisms involved are briefly discussed in the light of recent conceptual developments concerning temporal lobe epilepsy.

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BENACTYZINE IN PSYCHONEUROSIS

A CONTROLLED CLINICAL TRIAL IN HOSPITAL PATIENTS

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Ross (1949) has commented at length on the difficulties inherent in the evaluation of the results of treatment where psychoneurotics are concerned. He was discussing the results obtained by the Weir Mitchell method, but the remarks he then made apply equally well to-day in the assessment of the new group of drugs named by Fabing (1955) the "ataractics," also described as "tranquillizing agents." These drugs are stated to relieve the tension and anxiety so often complained of by psychoneurotic patients, and have been used singly, in combination with each other, with psychotherapy, and with E.C.T.

Benactyzine is a new member of this group, and work has been done in Denmark to demonstrate its activity in "normalizing" the behaviour of disturbed experimental animals (Jacobsen and Sonne, 1955; Jacobsen and Skaarup, 1955) and also in relieving the symptoms of human patients (Munkvad, 1955; Jensen, 1955). The drug is pharmacologically a member of the anticholinergic group, with a mild atropine-like action, and its peripheral effects have been long established. Work on its central effects was first carried out in Denmark, and led to its trial clinically because of its activity in increasing the emotional threshold for external stressful influences and its ability to induce a blocking of thoughts, which suggested that it would be useful in cases where there is persistent rumination.

The series of cases so far published have included only one controlled trial (Raymond and Lucas, 1956) on psychiatric patients. Munkvad gave placebo tablets during his work with the drug, but points out that he was aware that the patient was on a placebo. It has been shown (Wolf and Pinsky, 1954) that it is very easy for the investigator to be led astray in spite of all his efforts at objectivity when this method is used. For this reason we have used the self-controlled, self-recorded clinical trial, which has proved its value on previous occasions (Hogben and Sim, 1953; Hare *et al.*, 1956).

Case Material

The patients studied were all in-patients of a neurosis unit which is organized for the treatment of acute non-psychotic illness. The usual duration of stay in the unit is from 4 to 12 weeks. The patients were all of average or above average intelligence and were fully co-operative in the trial. Patients were selected for the trial if anxiety and tension were prominent symptoms, and the diagnoses of the group were as follows: anxiety state 6, neurotic depression 7, obsessional state 2, hypochondriacal state 1.

Sixteen patients started the trial, but only 13 completed it. Of the three who failed to complete it, all were on benactyzine and gave up during the first period of the trial; two of these became worse clinically and it was considered advisable to stop the administration of the drug; one of

them became so depressed that he was given E.C.T. The third patient took her discharge against medical advice on the eleventh day of the treatment. Most of the subjects were new cases, recently admitted to the hospital for the first time. Symptoms had been present for less than a year in six men and three women, from one to three years in one man and two women, and over three years in one woman. The ages of the group ranged from 17 to 58, the average age being 41; seven were male and six were female.

During the trial the patients conformed to the usual therapeutic programme, including occupational therapy, etc., but received no other special treatment, although when they had been receiving a hypnotic such as quinalbarbitone ("seconal") 1½ or 3 gr. (0.1 or 0.2 g.) at night, this was continued if necessary. Two minor exceptions to this are mentioned later.

Method

After the usual history and physical examination all patients had an E.E.G., and then received two tablets three times a day for four weeks. The tablets were either benactyzine hydrochloride in a dosage of 2 mg. three times a day, or an inert placebo. Each patient received benactyzine for two weeks and placebo for two weeks, in a random order of starting. During the trial, only the hospital pharmacist was aware of which tablets a patient was receiving at the time. He arranged that approximately equal numbers should start on controls and on benactyzine. Because three patients withdrew from the trial before completion, it was found that eight patients began on controls and five on benactyzine, as the three who had withdrawn were all on benactyzine. Each evening they were requested to fill in a form commenting on their general state of well-being during the previous 24 hours, and to mark a number of symptoms listed (see Table) as "absent," "mild," "moderate," or "severe." These were scored for rating purposes as 0, 1, 2, and 3 respectively—that is, the lower the score the better the result, and vice versa. This method of scoring was used for all ratings. Thus the scoring for each symptom and each assessment had the same pattern—low scores denoting good results and high scores poor ones. However, there is no relationship necessarily between the scores obtained in the different sections. There was opportunity for comment about fresh symptoms and for others not listed. Each patient also completed a weekly sheet on which he was asked to summarize his feelings during the week in terms of a five-point scale, from "much better" (1) to "much worse" (5). The sister/charge nurse in charge of the ward kept a daily note of the patients' state and the night nurse a nightly report of hours slept, if restless, and any sedatives needed. A score of one indicated each half-hour awake between 10.30 p.m. and 6.30 a.m. The doctor made a twice-weekly clinical summary of the patients' condition. Repeat E.E.G.s were carried out after 12 and 26 days of the trial.

The patients were told that they were to receive a course of treatment with tablets for four weeks and that we wished to follow their day-to-day state carefully, hence the form which they filled up each evening. There was no suggestion that the treatment was experimental, and the patients were told that they might have some ups and downs. Some patients are reluctant to admit to their doctor that they are no better, or worse, as they feel that they ought to get better with treatment and blame themselves if not doing so. The knowledge that the doctor is quite prepared to receive even adverse reports on their condition leaves them freer to make objective assessments of their state without a feeling of guilt for worsening or lack of improvement.

The trial was planned so as to avoid invalidation of the findings by suggestion, and the conditions were kept unchanged during both phases of the trial. The basis of the trial was a comparison between the placebo phase and the active drug phase, and not an absolute assessment. Under these conditions, this type of trial acts as a combined treatment and research project, and there is nothing to be gained by telling the patient that this is a new treatment and the physician does not know whether or not it will be helpful.

The period of two weeks on each phase was regarded as sufficient to assess improvement or otherwise, since this allows ample time for the pharmacological effects of known sedative drugs to exert themselves.

The benactyzine dosage of 2 mg. three times a day is in line with the recommendations of other workers, although some workers regard 1.5 mg. thrice daily as adequate (Jensen, 1955; Munkvad, 1955). Much higher doses have also been given, although the incidence of side-effects, such as dryness of the mouth, paralysis of accommodation, depersonalization, etc., becomes considerable.

Results

The Table shows the totals of the scores obtained by the 13 subjects who completed the trial. It should be remembered that a low score means a good clinical response, and vice versa.

Combined Rating Scores for 13 Neurotic Patients Receiving (a) a Placebo and (b) Benactyzine. A Low Score Indicates a Favourable Response

Symptom or Sign	How Often Rated	Rated by	Total Score for Each Fortnightly Period on:	
			Placebo	Benactyzine
General condition	Daily	Patient	333	350
	"	Nurse	326	351
	Weekly	Patient	65	74
Headache	Twice weekly	Physician	138	152
	Daily	Patient	180	212
Palpitation	"	"	50	91
Sweating	"	"	121	115
Dizziness	"	"	132	147
Trembling	"	"	166	199
Indigestion	"	"	78	76
Drowsiness	"	"	192	175
Depression	"	"	171	225
Anxiety and tension	"	"	232	249
Other somatic signs	Twice weekly	Physician	150	165
	"	"	65	72
Sleep	Weekly	Patient	38	38
	Daily	"	310	319
	"	Nurse	597	685

The results obtained showed clearly that the pharmacological and therapeutic effects of benactyzine were no better than those of the placebo. If anything, the results were less good, and in only two cases (both males) were more favourable scores obtained. The actual differences were not great, but with the number involved it was not possible to apply statistical methods to the results. Of the two patients who showed favourable scores for the benactyzine period, one was suffering from an anxiety state and the other from a neurotic depressive illness.

There was a distinct trend for the scores of female patients to be higher than those of the male patients while on benactyzine, the scores of the males more often being approximately equal. In no case did a female patient have a more favourable—that is, lower—score on benactyzine than on control.

As has been reported by other observers, no euphoriant action could be detected, and there were no abstinence symptoms after cessation of treatment. Little was observed in the form of side-effects with the dosages used, the most that can be said being that there was some increase in the incidence of complaints of headache, palpitation, trembling, and in one case a spontaneous complaint of thought-blocking. The rating scores for anxiety and tension were little changed, the slightly higher scores being for the benactyzine period.

The low score for drowsiness is interesting, since most sedative drugs in effective doses tend to induce drowsiness. This would suggest a different kind of pharmacological action from that of the barbiturates, which is of course claimed to be the case. Jacobsen (1955) suggests that the drug may temporarily block intracortical and cortico-thalamic pathways.

Two patients during the second fortnightly period, and while receiving benactyzine (on the second and the third day respectively of the active drug period), became so tense and anxious that it was necessary to give them amylobarbitone

sodium, 2 gr. (0.13 g.) twice daily for a day or two (from which they received much benefit), followed by 1 gr. (65 mg.) three times a day, in order to avoid dropping them from the trial; it was considered justifiable, however, to include them in the series, since they had completed more than half of the trial. It is of interest also that three patients who started on benactyzine in the first fortnightly period gave up with complaints of adverse effects, whereas no patients gave up in either period while on placebo. This reinforces the conclusion that the benactyzine administration gave no better results than the placebo; actually, the results were probably less good.

Ten patients had the three E.E.G. recordings necessary to compare the resting record with that after 12 days' benactyzine by mouth and 12 days on placebo (not necessarily in that order). Eight of these had normal baseline records, one an immature type of record, and the other a complex record of no specific pathological condition. Three records showed no change with drug or placebo, while the other records showed varying change in the alpha rhythm. In five placebo records the alpha rhythm was less persistent and in two it was more persistent, while in three benactyzine records it was less persistent and in four more so. There was thus no evidence that the drug taken by mouth in this dosage had any consistent effect on the E.E.G.

These findings indicate that benactyzine hydrochloride was no better than a placebo, and in some cases probably worse, in relieving the symptoms of tense, anxious psychoneurotic patients in hospital.

Discussion

It had been intended to continue the trial until there were sufficient patients from whom results of statistical significance could be derived, but in view of the unequivocal nature of the results obtained it was felt to be unjustifiable to continue the trial.

These results must be considered in the light of other workers' findings, and they do in fact bear out some of the observations hitherto published. Munkvad first pointed out that results on in-patients were unsatisfactory, while Raymond and Lucas found that their cases of neurotic depression were not helped. Patients with this type of psychoneurotic illness are those most often admitted to hospital, and in this series seven were cases of neurotic depressions and one was a case of hypochondriasis. Raymond and Lucas noted that the duration of symptomatology was a factor; the longer the symptoms had been present the less likely were the patients to respond, as was found in this series.

Age range is also important, as in the older patients the diagnosis of psychoneurosis usually implies an illness of prolonged and fluctuating course. This would explain the differences obtained in the male and female groups in this series. The difference is one of age rather than of sex, because the men are in a younger age group (17 to 57, average 36), while the women's ages range from 33 to 58, average 44.5.

From our findings, this drug is of no appreciable value in dealing with illnesses with more deeply rooted features—that is, more constitutional in type. Any action found by other workers is probably only that of a therapeutic barrier between the patient and minor external stresses in such cases as one is more likely to find in out-patients.

In comparing our results with those of other workers, it must be kept in mind that the seeing of patients by the therapist for prolonged periods in itself exerts an effective therapeutic pressure, so that good results can very often be achieved irrespective of any drug administration. In psychiatric cases the true pharmacological action of a drug may probably be evaluated more accurately in a carefully controlled trial over a relatively short but effective period than in more prolonged studies, where other variables become increasingly important. Once the pharmacological effect is assessed, its value as an adjunct, for example, to psychotherapy is more apparent.

Conclusion.—The conclusion which can be drawn from this series is the negative one that benactyzine hydrochloride was not an effective drug for the 13 typical in-patient psychoneurotics studied in this paper, although the small number treated renders caution necessary before making dogmatic statements. Nevertheless, it seemed unethical to continue the trial, since no apparent benefit was derived from the drug.

Summary

A self-controlled, self-recorded clinical trial involving 13 patients suffering from neurotic illness in which anxiety and tension symptoms predominated was carried out. Each patient received 2 mg. of benactyzine hydrochloride three times a day for two weeks and an inert control tablet of similar appearance and taste for a further two weeks, approximately equal numbers of patients starting on the active and inert drugs.

No difference was found in the therapeutic result, and, while the small numbers involved militated against a dogmatic conclusion, we thought that the drug was of no appreciable value in the treatment of the 13 relatively typical psychoneurotic in-patients under the conditions of this trial.

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APICOLYSIS WITH FASCIAL FIXATION

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In the surgery of pulmonary tuberculosis the recent trend has been towards excision rather than collapse. Nevertheless, for some forms of upper lobe disease many believe that collapse is the treatment of choice. The ideal operation would be one which achieves this with the least possible mutilation, while at the same time preserving the maximum respiratory function. Thoracoplasty, extrapleural pneumothorax, and plombage comprise the surgical armamentarium.

Thoracoplasty as originally described by Sauerbruch has undergone considerable modification. The modern thoracoplasty, with a mortality in the region of 2%, causes the patient little upset, and with adequate post-operative management there is little residual disability. The results of this operation are good. Nevertheless, the removal in part or *in toto* of the upper four or five ribs is still, for the patient, a formidable procedure, and we