of patients with a combination of streptomycin and isoniazid to be more effective than treatment with either drug alone, even in the early stages, when development of resistant strains of tubercle bacilli would probably not have occurred.

When either streptomycin or isoniazid alone was added to our cultures, in most experiments resistant strains eventually replaced the sensitive bacilli which had been killed. When the two drugs were added together resistant strains did not emerge. These results are analogous to the observation that a combination of streptomycin and isoniazid prevents or delays the development of resistant strains in pulmonary tuberculosis (Medical Research Council, 1953a).

Summary

At concentrations four to eight times those necessary to inhibit growth of tubercle bacilli the bactericidal activities of streptomycin and isoniazid were the same. At concentrations ten times higher, corresponding to maximal serum levels, the activity of streptomycin was greater than that of isoniazid. The activity of the combination of both drugs was higher than that of either alone, and prevented the growth of resistant strains of tubercle bacilli.

REFERENCES

- Elmendorf, D. F., Cawthon, W. U., Muschenheim, C., and McDermott, W. (1952). *Amer. Rev. Tuberc.*, 65, 429.
Garrod, L. P. (1950). *Ibid.*, 62, 582.
Mackness, G. B., and Smith, N. (1953). *Ibid.*, 67, 322.
Medical Research Council (1948). *Lancet*, 2, 862.
— (1953a). *British Medical Journal*, 1, 521.
— (1953b). *Lancet*, 2, 213.
Mitchison, D. A. (1952). *Ibid.*, 2, 858.
— (1953). *J. gen. Microbiol.*, 8, 168.

PROGNOSIS OF DEPRESSION TREATED BY ELECTRIC CONVULSION THERAPY

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Electric convulsion therapy (E.C.T.) is now widely used in psychiatric practice, and its efficiency, especially in the treatment of depressive states, would seem to be beyond dispute. It is certainly the commonest method of treatment employed by the in-patient psychiatric unit.

In England and Wales approximately 60,000 people are admitted to mental hospitals annually, and probably at least one-third have E.C.T. at some time during their stay; nor does this figure take into account the number who receive it as out-patients or in private practice.

It is therefore a matter of some importance that the long-term results of this treatment should be critically assessed. The present paper describes the position at the end of three years of a series of cases of depression treated in a mental hospital, the majority of which received E.C.T., and the effects of that treatment are evaluated.

Material and Method

The patients studied consisted of 114 "typical" cases of a series of 130, the clinical features of which have already been published (Jarvie, 1950). They represented the routine admissions to the Cheadle Royal Hospital of people suffering from depression who came under my care from May, 1947, to April, 1949. Of the 130 cases, 16 were regarded as "atypical" in that they showed unusual, bizarre, or

schizophrenic features, and the diagnosis of "depressive state" would probably not have been accepted in their case by many psychiatrists. The results in this atypical group will be published elsewhere, as they are of more specialized interest.

The 114 cases were an entirely heterogeneous group of consecutive admissions and included cases which could have been placed in most of the recognized clinical subgroups—manic-depressive, involutional, anxiety-depressive, reactive. Their ages ranged from 21 to 78, but the majority (74) at the time of admission were 50 years of age or older. They included cases having both recurrent and first attacks. The age and sex distribution is shown in Table I. In view

TABLE I.—Age and Sex Distribution of Cases Studied

Group	No. of Cases	Sex		Age Group					
		M	F	20-29	30-39	40-49	50-59	60-69	70-79
No E.C.T.	17	9	8	2	—	2	4	7	2
E.C.T.—Recovered	71	28	43	2	7	16	23	21	2
„ Improved	26	12	14	—	6	5	7	6	2
Totals	114	49	65	4	13	23	34	34	6

of the difficulty that exists, except in extreme cases, of making a rigid differentiation of clinical types, it was felt it would be of little value to attempt an analysis of the effects of E.C.T. on different subgroups. Consequently the results presented here are those of the whole series without reference to diagnostic grouping.

The method of inquiry was as follows. On the third anniversary of the patient's discharge from hospital a questionnaire was sent to the nearest relative and to the patient's doctor. The information asked for was the same in both cases, except that the doctor was asked to give the certified cause if death had occurred. The purpose of the double questionnaire was to obtain a cross-check on the information received. From the results obtained in this way any further sources of information were followed up—for example, by inquiry to hospitals or consultants who had been concerned with the patient. The case-notes of the parent hospital also form a source of information when, as in many cases, the patients had returned for further in-patient or out-patient treatment.

Results

Of the 114 cases, 97 received a course of E.C.T., after which 71 (73%) were discharged recovered and 26 (27%) were discharged improved. The number of convulsions administered and the duration of stay in hospital (in weeks) are shown in Table II. The remaining 17 patients either did

TABLE II.—Number of Convulsions and Duration of Stay in Hospital of Cases Receiving E.C.T.

Group	No. of Convulsions			Stay in Hospital (Weeks)		
	Min.	Max.	Median	Min.	Max.	Median
Recovered	2	14	7.5	2	23	7
Improved	6	21	7.5	3	37	8

not receive E.C.T. or received such small amounts that it was regarded as not affecting the course of the illness. This last group is considered first.

Cases Not Receiving E.C.T.

In seven cases treatment with E.C.T. was withheld for physical reasons, all cardiovascular—atheroma, congestive cardiac failure, aortic aneurysm, aortic stenosis, cardiac syncope, and hypertension. In one other case the treatment was stopped after four convulsions, as the patient developed Stokes-Adams attacks during its administration. At the end of three years six of these eight patients were dead—

four from natural causes and two from suicide; one was a patient in another mental hospital, and one was well so far as the psychiatric illness was concerned.

Of the nine remaining cases which did not receive E.C.T. the following was the position at the end of three years: no information, 3; still in hospital, 1; completely well, 3; fairly well, 2.

E.C.T.—Cases Discharged Recovered

At the end of three years the position with regard to the 71 cases which received E.C.T. and were discharged recovered was as follows:

No adequate information	..	7 (10%)	
Dead	..	5 (7%)	
Well—Completely	..	25 (35%)	} 34 (48%)
Fairly*	..	9 (13%)	
Relapsed	..	25 (35%)	

*Nine cases were regarded only as fairly well for the following reasons: (a) still on sedatives, 2; (b) failed to return to work, 1; (c) evidence of unstable episodes of short duration, usually of depression and/or elation, 6.

Of the five deaths, four were due to coronary artery thrombosis and one to lobar pneumonia.

Cases Relapsing

The interval (in months) between discharge and recurrence of symptoms is shown in the Chart. It is interesting to note that the relapses reached a peak within the first six months, then became less frequent, so that between 18 and 24 months none was recorded. From then onward the incidence of relapses began to rise again. This suggests that cases relapsing within 18 months of discharge are mainly true "relapses" of cases apparently well but really inadequately treated, while those whose symptoms recur later are having further genuine attacks.

Seven cases were still well after a further single course of treatment, in six consisting of more E.C.T. and in one

Interval between discharge from hospital and recurrence of symptoms in 25 cases which relapsed after being discharged recovered.

of symptomatic treatment with sedatives and euphoriant drugs. In all seven cases the recurrence of symptoms occurred within a year of discharge.

Four cases had broken down again just at the end of the three-year period and were under treatment in hospital at the time of inquiry.

One patient had been admitted to another hospital, where she still remains. In her case the symptoms recurred six weeks after discharge from the Cheadle Royal Hospital.

Of the remaining 13 cases, 12 had required further in-patient or out-patient supervision on two occasions: four of them had received one further course of E.C.T., and the remainder two further courses. Subsequently two of these cases had the operation of prefrontal leucotomy. Only one of these 12 cases was regarded as being well at the time of inquiry. The remaining patient had been readmitted to hospital on seven occasions within the three-year period and had received seven courses of E.C.T., consisting of a total of 39 convulsions.

E.C.T.—Cases Discharged Improved

Twenty-six cases were discharged only improved after what was regarded at the time as an adequate course of E.C.T. At the end of three years the position with regard to this group was as follows:

No adequate information	..	7 (27%)	
Dead	..	2 (7.7%)	
Well without further treatment	..	1	} 4 (15.4%)
Well after relapse treated with E.C.T.	..	3	
Still not symptom-free:			
In same condition as on discharge; no relapse, no more E.C.T.	..	6	} 10 (38.4%)
Still unwell after relapse treated with E.C.T.	..	4	
Prefrontal leucotomy	..	3 (11.6%)	

Of the two deaths, one was due to carcinoma of the colon and the other to a glioblastoma.

Physical Sequelae

Apart from the deaths and the one patient who developed epilepsy, organic sequelae which could even be remotely ascribed to the treatment were surprisingly few.

In this series the treatment had in every case been given *unmodified*—that is to say, without the aid of muscle relaxants or anaesthetics. In only one case was a definite fracture encountered during the administration of the treatment. This was in a lady of 65 who fractured her right humerus. Since then she has developed a painful swelling of both hands, presumably arthritic, although she had not been troubled with this before. It is of course difficult to decide how much these changes are due to the effects of the fracture or E.C.T. and how much to the natural processes of ageing.

Two patients complained of pain in the back which seemed to be genuinely organic in origin. Although minor degrees of compression fracture of the mid-dorsal vertebrae may have been missed, it is again difficult to decide without fuller investigation whether these complaints were not based on natural changes unconnected with the treatment.

Although not specifically asked for in the questionnaires, no complaints of persisting amnesia or other intellectual defect were recorded. Most of the patients in this series came from the Registrar-General's social classes I and II, and many have returned to work of considerable responsibility which they have carried on effectively and efficiently.

The deaths require some comment. Four of the seven were due to coronary artery thrombosis. Again it is difficult to implicate the treatment as an aetiological factor in precipitating death in these cases. One patient was known to have a pre-existing heart lesion, while the other three died at intervals of 3, 16, and 24 months after treatment. They were aged respectively 42, 61, and 66 at the time of death. It is not surprising that cases of unsuspected cardiovascular anomaly pass unnoticed in patients of the older age groups.

As has already been stated, the actual administration of E.C.T. in the crude and unmodified form gave rise to anxiety in only one case—namely, that of the lady in whom it was stopped because of the development of Stokes-Adams attacks during it. Even she managed to survive for two years after its administration.

The patient who developed a glioblastoma complained of symptoms two and a half years after discharge and died nine months later. The tumour, of considerable size, was found at necropsy in the temporal lobe.

One patient developed epilepsy. On discharge she was known to have received the largest number of convulsions—

a total of 60. Her case was complicated by the fact that a few weeks before her initial treatment with E.C.T. she appeared to be recovering from some infection involving the nervous system, as the following case history shows. There was no family history of epilepsy in her case.

A woman of 27 was admitted to the Cheadle Royal Hospital in November, 1942, suffering from melancholic stupor. She remained a patient until the early part of 1944. During this time she received 54 convulsions. Two months before admission she was reported to have had "catarrhal jaundice," and on admission she had nystagmus and bilateral extensor plantar responses. A lumbar puncture produced a clear fluid with 64 cells per c.mm., lymphocytes predominating, and a raised protein. Blood and C.S.F. Wassermann reactions were negative. Six months later the C.S.F. was normal, and when she was examined on readmission in 1947 there were no persisting neurological signs. A further course of six convulsions was given, and 21 months later she had her first grand mal attack.

Discussion

This study confirms the value of E.C.T. as a therapeutic agent in the treatment of depression.

It has to be remembered that most of the cases in this series were severely ill, otherwise mental hospital treatment would not have been regarded as necessary. Many on admission to hospital were calculated suicidal risks, and several had made an active attempt at suicide before admission. In the 71 cases discharged recovered after a course of E.C.T., 15 (21%) had made such an attempt, while in the 26 cases discharged improved 9 (34.6%) had done so. Only two attempts at suicide, both unsuccessful, were reported in the available follow-up material of these 97 cases.

On the grounds of suicidal risk alone, therefore, treatment with E.C.T. can be said to have returned many socially useful people to a happy and effective life much more quickly than would have been the case if a natural remission had been awaited. Nevertheless, the limitations of the treatment must be recognized. In the first place, although the number of cases of depression which make a good initial response to E.C.T. is high (73%), every case does not respond completely, although on the whole nearly all of them show sufficient response to be regarded as improved. Secondly, a high proportion (35%) of cases discharged recovered relapse within the relatively short period of three years. Many of these cases are true "relapses" in that they represent the recurrence of symptoms in an attack which has been inadequately treated and in which superficial improvement has been regarded as recovery. Several of these cases respond to a further single period of supervision (on the average, of 10 weeks' duration) and an additional course of E.C.T. (on the average, eight more convulsions).

In any unselected group of depressions treated with E.C.T. there will be a hard core of cases in which the administration of this form of treatment will be of only limited value. These cases will consist of two main groups—those which fail to produce more than a minimal response to E.C.T. although apparently adequately treated, and those which seem to respond to E.C.T. but which relapse after a short time and continue to relapse at intervals, in spite of further courses of E.C.T. Thus one woman in the series had received a total of 39 further treatments and had been readmitted to hospital on seven occasions during the three-year period. In the 10 years which had passed since her first attack she had a total of 11 admissions to hospital and was known to have had 65 convulsions.

In chronic relapsing cases of this nature, with decreasing intervals of well-being, it is obvious that the continued administration of E.C.T. can hardly be justified. In such cases cerebral surgery must be seriously considered as an alternative form of treatment, and the good but limited response to E.C.T. which these cases show gives the measure of probable success. The reasons why a number of cases of depression should make only a limited initial response to E.C.T., so that they can be regarded as having improved rather than recovered, are obscure and probably complex. While a few of the 26 cases discharged improved were probably inadequately treated, reasons other than this must be adduced to explain the failure of response in the

remainder. From the study of this group there was some evidence that many were people of poor personality caught up in serious personal difficulties.

In spite of the fact that the mode of action of E.C.T. is apparently physiological, it is important that we should not get too far away from the concept of depression as a dynamically orientated illness.

The assessment of any form of treatment must be made against the background of the natural history of the illness. It should therefore be remembered that depression is a self-limiting disease, and patients often come for treatment when the brunt of the illness is over. Nevertheless, the response of most cases of depression to E.C.T. is rapid and effective and can be observed after the first few convulsions.

On the whole, E.C.T. is an effective form of treatment for the majority of cases of depression uncomplicated by serious physical disease, although its limitations in 30-40% of cases should be recognized. Physically, it is fairly innocuous, and apart from traumatic events in the course of its administration and the occasional disturbing cardiac episode, it is very safe. These events should be materially reduced by the administration of the treatment in the modified form. The only serious complication would appear to be epilepsy, and this cannot be a common one. It does not occur unless large numbers of convulsions are administered (Sundqvist, 1951). On the whole, for this and other reasons, the continued administration of E.C.T. as a therapeutic agent in any one case over a long period of time is undesirable.

Summary

The results of a three-year follow-up study of 114 cases of depression treated in a mental hospital are reported.

Ninety-seven cases were given E.C.T., and the immediate and remote results of this treatment are analysed.

It is concluded that E.C.T. is an effective form of treatment in most cases of depression, but its limitations in some 30-40% of cases should be recognized.

Physically, it is an innocuous form of treatment, but one serious complication reported is epilepsy.

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REFERENCES

- Jarvie, H. F. (1950). *J. ment. Sci.*, **96**, 208.
Sundqvist, I. (1951). *Acta psychiat. neurol., Kbh.*, suppl. 60, p. 151.

New regulations made under the National Insurance (Industrial Injuries) Acts by the Minister of Pensions and National Insurance extend the insurance cover against pneumoconiosis. The regulations, which came into operation on January 11, give effect to recommendations made by the Industrial Injuries Advisory Council in their report on pneumoconiosis (Cmd. 8866). Up till now benefit for pneumoconiosis has been available only to persons who since July 5, 1948, have worked in occupations which have been scheduled because they are known to be capable of giving rise to the disease. Under the new regulations benefit is also available to persons who have never worked in a scheduled occupation but who are suffering from pneumoconiosis due to the nature of their work since July 5, 1948, in some other dusty occupation. Before being referred to the pneumoconiosis medical panels, claimants from unscheduled occupations will be required to provide a medical certificate or similar evidence to show that there is a reasonable cause for suspecting they are suffering from pneumoconiosis. Those who are totally disabled by pneumoconiosis but whose period of exposure ended before July 5, 1948, may be entitled to an allowance under the Pneumoconiosis and Byssinosis Benefit Scheme, 1952.