DESOXYCORTONE ACETATE AND ASCORBIC ACID IN THE TREATMENT OF SCHIZOPHRENIA.

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DURING recent years there has been a revival of interest in the possible role of the adrenal cortex in the pathophysiology of schizophrenia.

There is now considerable evidence indicating a relative hypo-activity of adrenal cortical function in schizophrenia and a lower reactivity than normal subjects of the adrenal cortex to various forms of stress (Freeman *et al.*, 1944; Hoagland *et al.*, 1946; Pincus and Elmadjian, 1946; Pincus *et al.*, 1949). Increased adrenal cortical activity has been shown to occur in electroconvulsive therapy, electronarcosis and insulin therapy. Direct evidence of increased adrenal cortical activity during electroconvulsive therapy was obtained by Ashby (1949) who found a brisk outpouring of cortical steroids during the first few days of treatment. Similarly measurements of lymphopenia and eosinopenia has given evidence of enhanced adrenal cortical activity during the above methods of treatment (Mikkelsen and Hutchins, 1948; Rees, 1949*a*; Parson *et al.*, 1949).

It is concluded by Hemphill and Reiss (1942) and Hoagland *et al.* (1949) that electroconvulsive therapy mobilizes adrenocorticotrophic hormone (ACTH) endogenously resulting in increased formation of adrenocortical hormones.

While there is considerable evidence of increased adrenal cortical activity occurring concomitantly during the application of various physical methods of physical treatment, it is not yet known whether it is partly or wholly the therapeutic agent.

Further interest has been stimulated in adrenal cortical function in mental illness by the work of Hans Selye (1937, 1942, 1946, 1949), emphasizing the importance of the adrenal cortex in adaptation to stress, and the dramatic discovery by Hench *et al.* (1949) that cortisone was therapeutically valuable in rheumatoid arthritis.

Carlisle (1950) reported that a definite improvement in mental attitude of patients receiving cortisone usually occurs, often with acceleration of the alpha waves in the electroencephalogram, whereas in rare instances pre-existant

or latent mental disorder such as schizophrenia seems to have been intensified or precipitated.

In view of the fact that cortisone is virtually unobtainable and ACTH is in very short supply, substitutive methods were sought.

Lewin and Wassen (1949) claimed that desoxycortone acetate (D.C.A.) given with ascorbic acid produced beneficial results in rheumatoid arthritis. It was assumed that ascorbic acid acted on desoxycortone to produce cortisone or other active anti-rheumatic substances. Hallberg (1950) considers the interaction to be oxidation of D.C.A., whereas Landsberg (1950) maintains that the action is one of reduction. Some workers have confirmed the results of Lewin and Wassen (Lavery and Loxton, 1949 and 1950), Fox (1949), but the investigations of many workers did not support their claims (Kellgren, 1949 ; Hartfall and Harris, 1949 ; Lloyd and Starer, 1949 ; Currie and Weil, 1950 ; Spies *et al.*, 1949 ; Bywaters *et al.*, 1950).

Cranswick and Hall (1950) treated a series of psychiatric patients with D.C.A., and ascorbic acid and found a fall in eosinophile count, a change in the urinary uric acid/creatinin ratio and regarded this as suggesting the production of a cortisone-like substance. They found that some patients improved and pointed out the need for further investigation.

This paper describes a controlled investigation into the value of D.C.A. and ascorbic acid in the treatment of schizophrenia.

Method.

The possibility that the mere procedure of giving a series of injections might have therapeutic effects by suggestion or otherwise, makes it particularly important to institute a control series of patients receiving inert injections by a similar procedure. The control and treated groups should participate equally in the general hospital regime and should correspond in age and sex distribution, mental status and tendency to spontaneous recovery.

The experimental group consists of 28 schizophrenics comprising 14 pairs of patients matched for age, sex, mental state, duration of illness and previous treatment. The matching was carried out after a detailed assessment of clinical status, utilizing an item sheet of some 300 items relating to history, clinical state and prognosis. Mental status was rated in terms of components in accordance with the method of Rees (1949*b*) whereby such features as introversion, intellectual or emotional disconnection, paranoid disposition, etc., are rated on a seven-point scale according to severity. Data collected and recorded in this way enabled the matching of patients to be carried out readily and effectively.

An analysis of salient features is shown in Table I.

An additional technique was used to record clinical progress. This was a modification of the psychiatric rating scale of the Worcester State Hospital and involved rating each patient on some 15 traits in terms of deviation from the patient's previous behaviour and personality. The sum total of the scores on the rating scale gives an abnormality index which computed before, during and after treatment, provides a graphic and quantitative expression of behaviour

TABLE I.—*Item Analysis.*

	Per cent.
Sex distribution.	
Male	57
Female	43
Age.	
15–19	7
20–29	32
30–39	36
40–49	25
Family history.	
Negative	83
Psychosis	13
Neurosis	4
Previous mental health.	
Normal	50
Definite illness	13
Personality.	
Stable	43
Very unstable and illadjusted	39
Broad interests	5
Very touchy and suspicious	27
Very schizoid	23
Cyclothymic	9
Duration of illness.	
Less than 1 year	28
1–3 years	12
Over 3 years	60
Onset of illness.	
Sudden	28
Prodromata then acute	7
Gradual	65
Aetiology.	
Psychological causes important	18
Aetiology—cont.	
Exogenous factors contributing	18
Mainly endogenous	54
Mental status.	
Introversion.	
High (4+)	65
Low (0–2)	35
Intellectual disconnection rating.	
High (4+)	73
Low (0–2)	18
Emotional disconnection rating.	
High (4+)	39
Low (0–2)	45
Conduct disconnection.	
High (4+)	37
Low (0–2)	45
Paranoid disposition.	
High (4+)	14
Low (0–2)	59
Depression rating.	
(2+)	9
Excitement (all ratings)	4·5
Intelligence rating.	
Below average	13
Average	78
Above average	9
Diagnostic subtype.	
Simple and hebephrenic	72
Catatonic	14
Paranoid	14

changes during and after treatment. The item sheet and rating scale were completed by one of us (L.R.) and the matching of pairs carried out in consultation.

One member of the pair was given an intramuscular injection of 5 mg. D.C.A. followed by an intravenous injection of 1 gm. ascorbic acid. The other member was given, for contro purposes, an intramuscular injection of arachis oil and an injection of saline intravenously in similar quantities, and in precisely the same way. The treatment and control procedure was given thrice weekly for 4 weeks. To eliminate the possibility of subjective bias, assessment of clinical state and behaviour during and after the treatment was carried out by the assessor without knowing which patient had received the active injections and which was the control.

All patients participated in a full regime of occupational and recreational therapy.

Results.

No significant changes were noted in clinical state or behaviour of patients receiving D.C.A. and ascorbic acid either from observation in the wards by medical and nursing staff, or by the more objective method of the Psychiatric Rating Scale. The only person in the series showing any significant change was a member of the control group, an early schizophrenic who improved during the period of administration of the inert injections.

Discussion.

The results are unequivocal and provide no evidence that D.C.A. and ascorbic acid when given by the technique described had any therapeutic effect on the group of schizophrenics studied.

The group contains a number of patients with a long duration of illness and other unfavourable prognostic features, and it might be held that these patients would be unlikely to respond to any treatment. It is therefore particularly noteworthy that no improvement occurred in patients with an illness of less than one year's duration, and other favourable prognostic features.

The need for caution in attributing improvement accompanying or following therapeutic trial to the particular treatment under investigation, is indicated by the recovery of one of the patients whilst receiving the course of inert injections. This might be due to coincidence with spontaneous recovery, or possibly suggestion may have had therapeutic effects.

The investigation throws no light on the possibility that other products of adrenal cortical activity may be therapeutically valuable in schizophrenia. Hoagland (1950) reporting the results obtained by giving ACTH to a small group of schizophrenics found improvement in one case only out of five, and the improvement ceased when the ACTH was discontinued. It is possible that the therapeutic effects of the various shock therapies are not due entirely to release of endogenous ACTH. Further research is urgently needed to ascertain the effects of adrenal cortical products on functioning of nervous tissue and whether any particular product of adrenal cortical activity is responsible for the beneficial effects of shock methods of treatment.

Summary.

1. The experimental population of the study consists of 28 schizophrenics, comprising 14 pairs of patients matched, after detailed clinical analysis, for age, sex, mental state, duration of illness and previous treatment.

2. One member of the pair was given thrice weekly injections of 5 mg. of desoxycortone acetate (oily) and 1 grm. of ascorbic acid intravenously (aqueous) and the other member serving as a control was given a similar quantity of arachis oil intramuscularly and saline intravenously. Both groups participated equally in a full regime of occupational and recreational therapy.

3. Each patient was assessed before, during and after the course of injections by means of a psychiatric rating scale. In order to avoid the possibility of subjective bias, the assessments were made without knowing which patient had received the D.C.A., and ascorbic acid and which was the control.

4. No significant changes were noted either on clinical observation by doctors or nurses, and no significant improvement was noted in the abnormality ratings given by the psychiatric rating scale.

5. The investigation, therefore, provides no evidence to suggest that desoxycortone acetate and ascorbic acid given in the manner described has any material beneficial therapeutic results in schizophrenia.

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