CORTISONE IN THE TREATMENT OF SCHIZOPHRENIA.

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INTRODUCTION.

RECENT research has given rise to the hope that the secretory products of the adrenal cortex might be useful in the treatment of schizophrenia.

Two main lines of research have stimulated renewed interest in the role of the adrenal cortex in the pathophysiology of schizophrenia. A number of investigations have produced evidence that the responsivity of the adrenal cortex of schizophrenic patients to stress is lower than that of normal controls (Freeman *et al.*, 1944; Hoagland *et al.*, 1946; Pincus and Elmadjian, 1946; Pincus *et al.*, 1949).

Another series of investigations has shown that adrenocortical activity is stimulated by insulin coma therapy, electronarcosis and electroconvulsive therapy (Hemphill and Reiss, 1942; Mikkelsen and Hutchins, 1948; Rees (1949*a*); Parson *et al.*, 1949).

Cranswick and Hall (1950) reported that desoxycortone acetate and ascorbic acid appeared to be therapeutically valuable in schizophrenia. Rees and King (1951) carried out a controlled investigation on the treatment of schizophrenia with desoxycortone acetate and ascorbic acid, and found no evidence that the method was of any therapeutic value. It was pointed out that the investigation did not preclude the possibility that other products of the adrenal cortex might be therapeutically useful in schizophrenia.

The present paper describes a controlled investigation in the therapeutic value of cortisone administration in schizophrenia.

We are indebted to Dr. Ernest Evans, Consultant Physician, East Glamorgan Hospital, for making available a supply of cortisone for the investigation.

EXPERIMENTAL POPULATION.

The study was carried out on a group of 12 schizophrenic patients (6 male, 6 female), consisting of six pairs, matched for age, sex, clinical status, duration of illness and previous treatment.

METHODS.

1. *Clinical assessment.*—A detailed investigation of clinical status was carried out on the group. An item sheet of some 200 items relating to social, family and personal history, personality, aetiology and symptomatology was completed for each patient. Various clinical features and components of schizophrenic symptomatology were rated on a 7-point scale by the method of Rees (1949*b*). This detailed analysis of clinical status permitted an accurate matching of patients into pairs, one member of the pair for treatment and the other for control purposes.

2. *Assessment of recovery or improvement.*—In addition to the above detailed clinical assessment, a rating scale consisting of 14 traits relating to behaviour and symptomatology was completed before, during and after treatment. This method, consisting of making ratings of traits in terms of deviation from the normal, provides a quantitative expression of the patient's behaviour and clinical state. The sum total of the scores gives a convenient index of abnormality, permitting a quantitative expression of any change in symptomatology or behaviour during the period of observation. Doctors' and nurses' reports made independently of the above methods were also available.

3. *Psychological tests.*

(a) *Personal tempo.*

In view of clinical observations that changes in personal tempo appear to develop during cortisone therapy, the following tests were applied :

(i) The number of triangles that could be drawn in 30 seconds.
(ii) Enumeration of objects in 30 seconds, e.g., things to eat, birds, flowers.
(iii) Number of responses to coloured Rorscharch card in 30 seconds.
(iv) Number of responses to uncoloured Rorscharch card in 30 seconds.

(b) *Persistence.*

As a measure of persistence, the time the patient could hold outstretched leg with knee 3 in. above a chair was carried out according to the method of Eysenck (1947).

4. *Physiological tests.*—These included eosinophile counts, blood pressure and water intake and output records.

5. *Electroencephalography.*

The above tests were carried out before, during, and after the period of cortisone administration.

Method of Administration and Control Procedures.

The following procedure was employed : sterile water injections were given to both members of the paired patients for the first week, during which time all the tests were carried out. During the second week cortisone was given to one member of the pair and saline injections were continued with the other member.

Cortisone was given intramuscularly in divided doses amounting to 300 mgm. on 1st day, 200 mgm. on 2nd day, and 100 mgm. on the 3rd and 4th days.

Results.

1. *Clinical status, symptomatology and behaviour.*—No significant improvement was found in any of the patients. One patient receiving cortisone became temporarily worse, returning to his previous state after termination of cortisone therapy.

2. *Psychological tests.*—No significant changes occurred in the tests of personal tempo or persistence.

3. *Physiological tests.*—In all patients receiving cortisone there was a marked fall of circulating eosinophiles, indicating that the cortisone had been absorbed and was active. No significant changes in blood-pressure or water balance occurred.

4. No change in electroencephalograph recordings was noted.

Discussion.

Although there is considerable evidence that adrenocortical activity is stimulated by various physical methods of treatment, such as insulin coma therapy, electroconvulsive therapy and electronarcosis, it is not yet clear what role, if any, this plays in producing improvement or recovery. Hoagland *et al.* (1950) maintain that the adrenal cortex is stimulated by adrenocorticotropic hormone (A.C.T.H.) released endogenously during shock methods of treatment. Hoagland *et al.* (1950) treated five schizophrenic patients for 3 weeks with daily doses of 100–200 mgm. of A.C.T.H. without significant change apart from transient improvement in one patient who relapsed later. They concluded that it was not likely that A.C.T.H. would prove to have any therapeutic value in schizophrenia, and the beneficial effects of E.C.T. might involve entirely different processes.

The results of our clinical trials provide no evidence to suggest that an endogenous release of cortisone like substances from the adrenal cortex produced by insulin coma or electroconvulsive therapy is the underlying process responsible for improvement or recovery. Our findings are similar to those of Hoagland *et al.* (1950) with A.C.T.H., and give no confirmation of the recent report of Cohn and Karnosh (1951) that cortisone produces striking improvements in chronic schizophrenia.

The precise role of the adrenal cortex in the pathophysiology of schizophrenia has yet to be elucidated. There is an urgent need for further research in the effects of adrenocortical products on brain metabolism and their significance in various shock methods of treatment.

Summary.

(1) The experimental population of the study consists of 12 schizophrenic patients (6 male, 6 female), comprising 6 pairs matched after detailed clinical analysis for age, sex, clinical status, duration of illness and previous treatment.

(2) All patients were given injections of sterile water for the first week during which all tests were carried out. During the second week cortisone was given intramuscularly in divided doses as follows: 300 mgm. on the 1st day, 200 mgm. on the 2nd day, and 100 mgm. on the 3rd and 4th days.

(3) Psychiatric rating scales, psychological tests of personal tempo and persistence, and physiological tests such as eosinophile counts, blood-pressure and water balance estimations and electroencephalography were carried out before, during, and after the period of clinical trial.

(4) No significant improvement was noted on the patients receiving cortisone therapy by clinical observation or by means of psychiatric rating scales. One patient became temporarily worse during cortisone therapy and returned to his previous state afterwards.

(5) No significant changes occurred in psychological tests for personal tempo and persistence or in blood-pressure or water-balance measurements.

(6) All patients receiving cortisone showed marked decrease in circulating eosinophiles, indicating that the cortisone had been absorbed and was active.

(7) No changes in electroencephalograph recordings were noted during cortisone administration.

(8) The investigation provided no evidence to suggest that cortisone given by the method described had any material beneficial therapeutic effects in schizophrenia.

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