INTENSIVE CORTISONE THERAPY IN SCHIZOPHRENIA

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CORTISONE therapy has been claimed to produce favourable results in clinical schizophrenics (Cohn and Karnosh, 1951; Cohn *et al.*, 1953). Rees and King (1952) carried out a controlled investigation on the effects of Cortisone given in moderate doses over a four-day period to a group of schizophrenic patients and found no significant changes in symptomatology, behaviour or in a series of psychological and physiological tests.

In a personal communication Dr. Cohn suggested that Cortisone given in higher doses over a longer period would probably be therapeutically more effective in chronic schizophrenia.

The present paper describes a controlled investigation into the therapeutic effects of Cortisone given in high dosage over a relatively prolonged period.

EXPERIMENTAL GROUP

The investigation was carried out in a group of 18 schizophrenic patients consisting of nine pairs matched for age, sex, clinical status, duration of illness and previous treatment.

METHODS

1. *Clinical Assessment*

A detailed assessment of clinical status was carried out on all members of the group. An item sheet of some 200 items relating to social, family and personal history, personality, aetiology and symptomatology, was completed for all patients. The various aspects of schizophrenic symptomatology were rated in a 7 point scale by the method of Rees (1949). This detailed analysis of clinical status enabled accurate matching of patients into pairs. One member of the pair received Cortisone therapy and the other was utilized for control purposes.

Clinical data relating to each group on the Item analysis shown in Table I.

2. *Assessment of Recovery or Improvement*

In addition to the above detailed clinical assessment, a modification of the Worcester State Hospital Psychiatric Rating Scale was used. The rating rate consists of 14 traits relating to behaviour and symptomatology which can be rated and scored in terms of deviation from the patients pre-psychotic state.

This method provides a quantitative method of expressing and recording a patient's behaviour and clinical state. The sum total of the scores gives a convenient index of abnormality. The rating scale completed before, during and after treatment, provides a graphic standardized method of recording any

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TABLE I

	Per cent.	Symptomatology	Per cent.
Sex:		Introversion rating:	
Male	77	High	88
Female	23	Low	11
Age:		Intellectual disconnection rating:	
20–29 years	77	High	66
30–39 years	11	Moderate	22
39–40 years	11	Low	11
Family history (Parents and siblings):		Emotional disconnection rating:	
Negative	67	High	22
Psychosis	22	Moderate	11
Neurosis	11	Low	77
Personality:		Conduction disconnection rating:	
Stable	33	High	66
Somewhat unstable	33	Moderate	11
Very unstable and ill-adjusted	33	Low	22
Onset:		Paranoid disposition rating:	
Sudden	22	High	55
Prodromata then acute	11	Moderate	22
Gradual	77	Low	33
Aetiology:		Type:	
Psychological causes important	22	Simple	11
Exogenous factors contributing	11	Catatonic	33
Mainly endogenous	77	Paranoid	55

changes in clinical status or symptomatology during the period of observation.

In view of the importance of multiple recording in investigations of this kind, doctors' and nurses' reports made independently of the above were available for the final assessment of results.

3. *Psychological Tests*

The tests used in our previous investigations (Rees and King, 1952) were included in the present investigation.

(*a*) Personal tempo:

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 Rorschach card in 30 seconds.
IV. Number of responses to uncoloured Rorschach card in 30 seconds.

(*b*) Persistence: this was measured by the time the patient could hold outstretched leg with knee 3 inches above a chair, according to method of Eysenck (1947).

4. *Physiological Tests*

These included eosinophile counts, blood-pressure readings, water intake and output records, electroencephalography and electrocardiography.

The above tests were carried out before, during and after Cortisone therapy.

CONTROL PROCEDURE

In this investigation we employed both the method of paired controls and the method of using the patient as a self control.

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The method of paired controls in psychiatry presents inherent difficulties as it may be quite impossible to make certain that the two members of the pair correspond in clinical status and prognosis.

It is of paramount importance to ascertain that the members do not differ in important prognostic indicators. In this investigation the patients were matched by age and sex, symptomatology, duration of illness and previous treatment received. This ensured that the groups did not differ significantly in these important prognostic indicators. In spite of all attempts at detailed accurate matching of patients in the paired series, it remains a possibility that the capacity for spontaneous improvement may still differ in the two groups. It is therefore clearly desirable to institute other controlled procedures as well.

In the present type of investigation, the method of self control is valuable.

This method has recently been described in detail by Hogben (1954).

The following procedures were applied:

Double Blind Trial

In order to avoid the possibility of bias in recording and assessment of the clinical changes on the part of nurses or doctors, the investigation was carried out blind, neither the nurse nor the doctor making the assessment knew when inert or active injections were being given.

The trial can be divided into three phases:

1. Period of inert injections given to all members of the series during which the tests and assessments were carried out.

2. Inert injections continued with the control series and Cortisone therapy given on the other series.

3. Inert injections given to total group.

This method enables the effect of suggestion or therapeutic influence of the general procedure and regime to be assessed and also enables the possibility of spontaneous improvement during the period of the trial to be controlled.

Dosage

The following dosage was used: 8 c.c. (200 mg.) of Cortisone acetate intramuscularly twice daily (400 mg. daily) for 21 days.

8 c.c. saline was given intramuscularly twice daily for seven days before onset of Cortisone administration and for seven days afterwards and in the control series was given throughout the five-weeks trial period.

Results

Six out of nine patients receiving Cortisone therapy showed no significant change in clinical state or behaviour assessed from observation in wards by medical and nursing staff in the more objective method of the Psychiatric Rating Scale. One female patient showed a temporary exacerbation of symptoms returning to previous state after termination of Cortisone therapy.

Two male patients showed a very slight improvement in behaviour and attitude, became more alert and co-operative but without significant change in schizophrenic symptomatology.

One patient in the control series showed a similar slight degree of improvement.

The results are unequivocal and provide no evidence that Cortisone therapy had a significant therapeutic effect on our group of schizophrenics.

No significant changes occurred in psychological tests or electroencephalography.

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Complications and Side Effects

In eight out of the nine patients receiving Cortisone, marked side effects occurred usually from 8th–14th day of dosage at 400 mg. The most constant effect was water retention, sudden increase in weight, oedema of dependent parts and, in some, puffiness and oedema of facial subcutaneous tissues.

A tendency to bradycardia was found in four patients, the pulse rate falling to 45–50 per minute after a previous level of 70–75.

When these side effects appeared the dosage had to be reduced and potassium chloride medication by mouth instituted. The dose of Cortisone was later gradually increased again but usually with return of symptoms.

This high dosage therefore imposes a severe strain on the homeostatic mechanisms in the body and these side effects constitute a serious disadvantage.

Discussion

The results of our controlled investigation are unequivocal and provide no evidence to support claims that Cortisone given in high doses over a relatively prolonged period is therapeutically valuable in chronic schizophrenia.

The results are in striking contrast to those of Cohn (1953) who reported that six out of twenty-one chronic patients who had been ill for over six years were discharged from hospital after intensive Cortisone therapy.

He found that paranoid patients showed the best therapeutic response. We were unable to confirm this in our series in which five out of nine patients were paranoid schizophrenics.

Furthermore the marked side effects accompanying continued high Cortisone dosage constitute a severe strain on the organism's homeostatic methods and are a serious disadvantage of this method of treatment.

It is noteworthy that none of our patients developed euphoria which many observers have reported in patients with physical disease during Cortisone therapy and also that only one patient showed exacerbation of symptoms, the majority showing no significant change in symptomatology or behaviour.

It is a possibility that future research may provide an indication for the use of Cortisone in certain selected schizophrenics. Thus if it could be demonstrated that endocrine disequilibrium was causally important in some schizophrenics and that if Cortisone, either by substitution or indirectly by influencing the functions of other endocrines, helped to restore homeostasis in endocrine functions and if this in turn resulted in clinical improvement, a scientific basis for its use in such patients would be established.

It is clear from our results that whatever biochemical, physiological or endocrinological changes are produced by massive Cortisone therapy these did not result in any clinical improvement in our series of chronic schizophrenics.

In conclusion we may say that our findings provide no evidence in support for the general use of this method of treatment in chronic schizophrenia.

Summary

(1) The paper describes a controlled investigation of the therapeutic effects of Cortisone given in high dosage over a period of three weeks.

(2) The experimental group consisted of 18 schizophrenic patients comprising nine pairs matched after detailed clinical analysis for age, sex, clinical status, duration of illness and previous treatment.

(3) The experiment was carried out as a double blind trial, neither doctors making clinical assessments nor nurses knew when active or inert injections were being given. All patients were given inert injections for the first week during which all tests were carried out. Inert injections were continued in the control series for three weeks and Cortisone given to the other series. Finally inert injections were given to both groups.

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(4) Psychiatric rating scales, psychological tests of personal tempo and persistence and physiological tests such as blood-pressure and water balance records, electro-encephalography and electrocardiography were carried out before, during and after the period of clinical trial.

(5) No significant clinical improvement was noted in patients receiving Cortisone therapy or in the control series. One female patient showed a temporary exacerbation of symptoms, returning to her previous state after termination of Cortisone.

(6) No significant changes occurred in psychological tests for personal tempo and persistence. In eight of the nine patients marked side effects occurred consisting of water retention, sudden increase in weight, oedema, and in four patients a marked bradycardia developed. No changes in electroencephalograph recordings were noted during Cortisone administration.

(7) The results of the investigations lend no support to the claims that Cortisone given in high dosage for a relatively long period has any beneficial therapeutic effect in chronic schizophrenia.

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