TREATMENT OF HYPOTHYROIDISM

A NOTE ON THE USE OF CORTISONE

BY

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The occurrence of adrenocortical deficiency in myxoedema has received increasing attention during recent years, and a number of papers (Hubble, 1955; Statland and Lerman, 1950; Hill *et al.*, 1950) have been published on this subject. From this work, the question naturally arises whether all the symptoms of hypothyroidism are due to thyroid deficiency or whether some are due to the associated adrenocortical deficiency. In an attempt to determine if some of the changes produced in the body in severe hypothyroidism were caused by deficiency of corticosteroid hormones, a series of five cases of myxoedema were treated with cortisone for a month. It was, of course, realized that symptoms due to adrenocortical deficiency might be due to lack of hormones other than cortisone.

Present Investigation

All the five cases treated were typical examples of myxoedema and had characteristic facies, dry scaly skin, slowness of movement and cerebation, thickened speech and often deafness, and sparse head hair. In addition, radio-iodine tracer studies, basal metabolic rate, and serum cholesterol estimations were carried out. As a final safeguard in diagnosis the patients were photographed before treatment was started. At the end of the cortisone therapy, thyroid treatment was instituted. The comparison of the original photographs with the appearance of the patient after several weeks' thyroid therapy left no doubt about the accuracy of the diagnosis.

In order that full clinical and biochemical observations could be made all the patients were admitted to hospital for some time before treatment was started. A varied diet of constant electrolyte content was given. All patients had a standard course of treatment, 25 mg. of cortisone being given orally for 28 days. This dosage was decided upon in view of previous experience of treating hypopituitarism with oral cortisone, the most effective dose in those cases being between 12.5 and 25 mg. of cortisone daily. The ages of the patients treated ranged from 73 to 39 years; two were male and three female. All were regarded as examples of severe hypothyroidism.

Clinical State.—Before treatment was begun all the patients were lethargic, slow of movement and speech, and content to lie in bed all day without any occupation. None displayed much interest in the daily activities of the ward or took much part in them. Even reading seemed to be too much effort, and their physical state could only be described as torpid. All were extremely sensitive to cold; one of the males was normally covered in bed by five flannelette sheets and three blankets. Axillary sweating was slight or absent in all the cases and the hands felt cold.

Physical and Mental Activity.—Within 48 hours of the start of cortisone therapy there was a remarkable change. These patients became active, mentally and physically. They read newspapers and books, the women knitted, and all showed marked activity about the ward instead of the inertia that had formerly characterized them. They all noted increased physical strength and a decreased sensitivity to cold. The appearance of extremely busy and active patients who apparently still remained myxoedematous was most remarkable. One patient said that she was unable to sleep, particularly if she took her cortisone at night.

General Appearance

No change was noticed in the facial appearance of any of these patients, and even at the end of treatment they remained quite myxoedematous. The dryness of the skin persisted, although sweating of the palms of the hands was observed after a few days' treatment. Axillary sweating, which in most cases had been slight or absent, became noticeable within four or five days of beginning treatment. The voice became less hoarse in one case, but this change was not observed in any of the others. The hearing did not improve in any of the patients, but a marked improvement took place in their powers of concentration. Mental activity that would have been too much for them before cortisone therapy was now undertaken without any effort whatsoever.

One of the female patients had had rheumatoid arthritis for 25 years which did not appear to be very active. Before treatment she did not complain of joint pains, although there was a moderate typical deformity of the hands due to rheumatoid arthritis. Within three days of beginning cortisone treatment she began to complain of joint pains; these persisted, and indeed became worse as long as the treatment continued. It is of interest to note that in this case the reactivation of the rheumatoid arthritis persisted after thyroid was substituted for cortisone and even when all clinical evidence of hypothyroidism had disappeared. The association of rheumatoid arthritis with hypothyroidism is, in my experience and in that of many physicians with whom I have discussed this question, very uncommon. The reactivation of the arthritic condition by means of cortisone, an anti-rheumatic remedy, is therefore of interest.

No change in weight occurred in any of the patients even at the end of treatment, and no diuresis was present. There was an increase in pulse rate, averaging about 10 a minute in all cases, and this increased rate occurred at the end of about seven days' treatment; no further increase in pulse rate was observed during the remainder of the treatment period. There was no increase in the temperature or in the respiration rate. The electrocardiogram remained unaltered at the end of treatment (apart from a slight increase in heart rate), and no change in the size or shape of the heart was seen radiologically. No alteration in the blood pressure took place.

Appetite improved in all of the patients, usually at the end of about a week. Four who had complained of severe constipation noticed considerable improvement in this symptom towards the end of the second week of treatment with cortisone.

Biochemical Changes

Biochemical and other investigations were carried out in all cases to assess various aspects of the disordered physiology resulting from loss of thyroid secretion; the effect of cortisone therapy on adrenal function was observed with particular interest.

The basal metabolic rate was estimated in all cases before and at intervals of 10 and 20 days after treatment. No change in the basal metabolic rate was noted. Similarly, no change in the uptake of radioactive iodine or in its excretion was produced by cortisone. In two cases there was a rise in the serum cholesterol levels. The initial average pre-treatment level in one patient was 330 mg./100 ml.; after 19 days of cortisone therapy the level was 415 mg./100 ml. and at the end of a month's treatment the serum cholesterol had reached 550 mg./100 ml. In another case the initial cholesterol level was 350 mg./100 ml. and after 21 days it was 480 mg./100 ml. The serum cholesterol in the remaining three cases remained unaltered or showed a slight fall. The significance of the unusual behaviour of the cholesterol levels in these two cases is difficult to assess. The cases did not appear either clinically or biochemically different in any way from the others.

Investigations of particular interest were those that might have been expected to throw light on the adrenocortical function. Kepler water-diuresis tests were made on four of the cases. Their average water excretion before treatment

was 2.1, 2.1, 2.3, 3 ml./min. When these tests were repeated after three weeks' treatment the average water excretion was 3, 3.5, 4.5, and 6 ml./min respectively. There was an increase in 17-ketosteroid excretion in all cases. Before treatment the output ranged from 2.8 to 4.7 ml. a day; after treatment it was from 5.5 to 11 mg. a day.

No significant changes were observed in the levels of serum sodium, potassium, or chlorides, and these levels were usually within normal limits both before and during treatment. Insulin sensitivity tests revealed a hypoglycaemic unresponsiveness in all cases, and this was unaltered by treatment.

No change was produced in the blood picture; in no patient was the anaemia of severe degree. The effect of administration of cortisone over a prolonged period might be worth observing, particularly as it is known that the anaemia of myxoedema responds very slowly to the administration of thyroid extract.

Summary

The effect of cortisone treatment in five cases of myxoedema has been observed. No change was produced in the physical or biochemical state of these patients. A marked quickening of mental processes was, however, noticed. There does not appear to be any good reason for using cortisone as an adjuvant to thyroid extract in most cases of hypothyroidism. The quickening of mental activity produced in these patients by cortisone might make this drug helpful in those cases of myxoedema in which drowsiness is marked and in which the development of coma is a possibility.

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PERCEPTIVE DEAFNESS IN HYPOTHYROIDISM

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Deafness is a recognized symptom of hypothyroidism, and Means (1948, quoting Lerman) states that it occurs in 30% of cases, and that it may be a conductive, perceptive, or mixed type of deafness. Vertigo in addition to deafness has also been reported in hypothyroidism (Moehlig, 1927; McLaurin, 1945; Athens, 1946). We have been able to find few published records of investigation into the hearing of hypothyroid patients, and standard textbooks, beyond noting the occurrence of deafness in some of these patients, rarely mention that it may be perceptive in type. The usual aetiological factors quoted are: hypertrophy and oedema of the mucosa of the nose and eustachian tubes causing eustachian obstruction, hypertrophy of the mucosal lining of the middle ear, and thickening of the tympanic membrane. General cerebral retardation is also thought to be of importance (McMahon, 1947; Means, 1948; and others).

Apart from this last factor, all the others would give rise to some degree of conductive deafness. This type of deafness was found in 45 patients treated by Barnes (1947). However, in less than half these patients was there definite evidence of hypothyroidism, and no details of the hearing tests are given. In those patients whose hearing improved, eustachian catheterization, and often repeated catheterization, as well as thyroid medication, was used.

Perceptive deafness in hypothyroidism has received less attention, although in cretins deafmutism is common and it is certain that a purely conductive deafness would never be sufficient to give rise to deafmutism. Gray (1910) examined the temporal bones from four deaf-mutes, and in each there was marked degeneration of the cochlear branch of the auditory nerve. The outer and middle ears appeared normal and the vestibular branch of the auditory nerve and the facial nerve were normal. The appearances of the labyrinth suggested increased intralabyrinthine pressure. In hypothyroidism it is known that chromatolysis of nerve cells does occur (Brun and Mott, 1913).

In adults the only report that we can find of investigations in a patient with hypothyroidism and perceptive

Summary of Cases

Case No.	Sex and Age	Duration of Symptoms	B.M.R. (Robertson Reid)	Rinne Test	Pure-tone Audiogram	Improvement in Hearing (Assessed from Audiogram after Treatment)
1	F 64	1 year	-30%	+	Very severe perceptive deafness	Marked
2	F 54	6 months	-28%	+	Moderate perceptive deafness	Nil
3	F 75	2 years	-23%	+	Severe perceptive deafness	"
4	F 52	1 year	-33%	+	Moderate perceptive deafness	Slight
5	F 31	2½ years	-23%	+	Slight perceptive deafness	"
6	F 56	3 "	-33%	-	Severe mixed deafness	Marked
7	F 58	75 "	-24%	-	Very severe mixed deafness	Nil

Deafness is assessed as:

Slight = 0-20 db. loss

Moderate = 20-40 " "

Severe = 40-60 " "

Very severe = over 60 db. loss

(Average of frequencies 512, 1024, and 2048 c.p.s.)

Hearing improvement is assessed as:

Nil = 0-5 db. improvement

Slight = 5-10 " "

Fair = 10-20 " "

Marked = over 20 " "

(Average of frequencies 512, 1024, and 2048 c.p.s.)

deafness is by Rau (1947). This patient was a man aged 38 whose chief complaint was deafness; it was perceptive in type, and his hearing returned "practically to normal" after thyroid medication.

In this paper we wish to record five cases of perceptive deafness and two of mixed conductive and perceptive deafness. All seven patients were women with symptoms of hypothyroidism, and were seen at the Middlesex Hospital recently. The Table shows the features especially studied in these patients.

Case Histories

Case 1.—Referred to E.N.T. department complaining of hoarse voice, dysphagia, deafness, and lack of energy. A hearing-aid was issued, but she was found to be hypothyroid. Because of the known sensitivity of hypothyroid patients to thyroid, treatment was started with a small dose