of eclampsia as long as 17 days after delivery, unless the renal failure had delayed the excretion of a substance responsible for eclamptic fits. These were associated with a marked rise in the blood pressure, and, although the treatment used in this patient caused a marked drop in the blood pressure with the cessation of the fits, it is no explanation simply to attribute the fits to the raised blood pressure, for this only leaves unsolved the aetiology of the sudden hypertension.

It is well known that overhydration with water can cause convulsions of an epileptiform type, but the fluid-balance investigations did not indicate an excessive intake of water, and certainly no clinical evidence of overhydration occurred. These findings were supported by the fact that rapid intravenous injection of 3 g. of sodium chloride failed to control the fits. Indeed, prior to the onset of the fits sodium had already been administered in the form of the ion-exchange resin.

From the evidence available it can only be assumed that the fits were associated in some way with the anuria and progressive uraemia, for after restoration of renal function the fits ceased and did not recur.

The treatment of the convulsions was entirely empirical, and was based on the management of eclampsia. Thiopentone was used as an emergency, followed by a full dose of bromethol. This was effective in controlling the fits initially, and a further small dose of bromethol was given three hours later, when the blood pressure began to rise again. Fortunately no harm came from the use of these drugs despite poor renal function.

Nature of the Residual Renal Lesion

The presence of proteinuria even one year after the episode of anuria suggests that the renal lesion was of some magnitude, and this is supported by the lowered inulin and P.A.H. clearances. The presence of pus cells also requires further explanation. No organisms were found in the urine either during the period of anuria or subsequently. Cystoscopy revealed no abnormality, and a retrograde pyelogram was essentially normal in the follow-up period. Perhaps the pus cells are the result of gross renal damage undergoing repair.

Future Pregnancies

In the chronic phase of Ellis type I nephritis the chances of foetal survival are very poor, and deterioration of the maternal condition is very great when the blood urea level is raised above 40 mg./100 ml. at the beginning of pregnancy (Dodds and Browne, 1940; Hamilton, 1952). In chronic pyelonephritis of comparable severity, on the other hand, the prognosis for the infant would not be so poor, and the maternal risk would lie more in the danger of superadded acute renal infection. In any case, the possibility of a recurrent pre-eclampsia and even accidental haemorrhage has to be considered. It would seem, therefore, that there would be considerable risk to mother and foetus in a further pregnancy. If the husband and wife are still determined to try again we could only keep a close watch, and offer termination of pregnancy immediately signs of deterioration develop.

Summary

A case is described of anuria for 11 days and oliguria for a further six days following severe concealed accidental haemorrhage.

Epileptiform fits occurred on the 17th day of reduced renal output. They were associated with a sudden rise of blood pressure.

The detailed management of the anuria and of the fits is described.

The results of renal investigations one year later are given. They showed persistent proteinuria and pyuria, with considerable impairment of renal function.

The management of anuria, the possible aetiology of the fits, the nature of the residual renal lesion, and the prognosis for future child-bearing are discussed.

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CORTICOTROPHIN IN TREATMENT OF HYPERTHYROIDISM

BY

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Harris and Woods (1956) reported that electrical stimulation of the tuber cinereum of rabbits by remote control rarely produced the expected increase in thyroid activity unless preceded by adrenalectomy. After reviewing other evidence for the possible inhibitory action of the adrenal cortex on thyroid function, they concluded that further investigation of the effects of corticotrophin administration in early and previously untreated cases of Graves's disease would be of interest. This communication records such an investigation, a preliminary report of which was given by Richardson (1957).

Methods

Eight patients with hyperthyroidism were admitted to hospital. The clinical diagnosis was confirmed by observation for at least 10 days, during which time radioiodine studies and protein-bound iodine estimations were made. Basal metabolic rate (B.M.R.) estimations were also carried out on three days towards the end of the observation period. Corticotrophin gel was then given by intramuscular injection for from two to five weeks, the initial dose of 20 units b.d. being halved in some cases after 7 to 11 days. At the end of the period of treatment the laboratory studies of thyroid function were repeated (Table I). The potency of the batch of corticotrophin which was used throughout had previously been demonstrated on a healthy subject. Confirmation of the efficiency of the adrenocortical stimulation was provided by the fluid retention which occurred and by the increases which were detected in the urinary excretions of 17-ketosteroids and 17-ketogenic steroids. Excessive retention of fluid was combated in the thyrotoxic subjects by injections of mersalyl, but such injections were not given when radioiodine or urinary steroid excretion studies were being made. However, in spite of precautions, pulmonary congestion developed at the end of the course of treatment in two patients.

A ninth patient with hyperthyroidism was treated with prednisone, 20 mg. b.d., for 14 days and studied in a similar way.

Results

A significant improvement in the hyperthyroid state was observed in only one patient, a man aged 40 with mild hyperthyroidism, a diffuse goitre, and symptoms of short duration (Case 2). Even though the improvement was only

TABLE I.—Clinical Details of Nine Hyperthyroid Patients, with Results of Laboratory Tests of Thyroid Function Before and at End of Treatment

Case No.	Age in Years	Sex	Goitre	Duration of Symptoms (Months)	B.M.R.* %		Serum P.B.I. μ g./100 ml.		Radioiodine Studies (% of Administered Dose)									
									Urine Excretion				Thyroid Uptake at 24 Hours		Plasma Radioiodide per Litre		Plasma P.B. Radioiodine per Litre	
					0-8 Hours		8-24 Hours											
					C	T	C	T	C	T	C	T	C	T	C	T	C	T
1	55	F	N	18	+37	+58	7.5	6.8	7.8	7.5	0.6	3.1	77.5	73.5	0.8	—	0.68	—
2	40	M	D	4	+27	+6	11.6	8.6	9.7	23.3	1.3	3.2	52	31.3	0.73	0.59	0.71	0.58
3	45	F	D	9	+44	+33	9.5	10.3	—	5.7	0.6	0.6	73.5	84	1.04	1.05	0.95	—
4	43	F	D	6	+51	+50	21.2	16.4	—	3.4	0.9	0.4	76	78	0.81	—	0.79	—
5	57	F	N	6	+40	+41	9.4	12.2	6	9.7	2.6	3.4	47.8	40.5	3.4	—	3.4	—
6	29	M	D	2	+69	+66	10.5	7.9	7.7	8.3	1.1	2.6	74.5	70.5	1.26	1.5	1.18	1.43
7	35	F	D	2	+57	+46	11.8	14.8	3.1	6.3	1.1	1.1	66.1	82.4	2.83	2.49	2.75	2.28
8	48	M	D	18	+37	+55	9.6	8.5	4.1	7.0	1.0	2.0	75	67.3	1.87	1.86	1.86	1.6
9	40	F	N	5	+30	+47	—	—	6.4	6.3	0.9	1.1	70.6	86.5	0.86	—	0.97	—
Normal Range							3.5-7.5		25-50		7-20		19053		<0.6		<0.3	

D=Diffuse goitre. N=Nodular goitre. *Lowest of three measurements. C=During control period. T=At termination of treatment.

slight it was apparent clinically and on each of the laboratory assessments of thyroid function.

Reduction in the size of the goitre was thought to have occurred in Case 3 during the first fortnight of treatment, but further reduction was not seen, although corticotrophin was given for another three weeks. The goitres of the other patients did not alter in size nor was any lessening of proptosis noted.

Although in Case 8 the patient, who had a typical thyrotoxic myopathy, showed no improvement in the hyperthyroid state, a definite increase in the power of the affected muscles occurred during treatment. The electromyographic abnormalities, however, persisted unchanged.

The results in the patient treated with prednisone (Case 9) were equally negative.

Discussion

Hill *et al.* (1950) treated six patients suffering from Graves's disease with corticotrophin in doses of 40 to 200 mg. a day for 5 to 23 days. Two showed an improvement amounting almost to complete remission, in two there was some reduction in hyperthyroidism on laboratory tests only, while two showed no improvement in any respect. Engel (1950) reported a single case of hyperthyroid heart disease in which a 10-day course of corticotrophin produced an immediate improvement in the general condition and was followed in three weeks by disappearance of all clinical evidence of thyroid overactivity. Excellent clinical responses to corticotrophin in single patients were also noted by Means and Stanbury (1950) and by Sideman (1951), although the latter's case relapsed two months after the end of treatment.

Szilagyi, McGraw, and Smyth (1952) investigated the effect of corticotrophin on five patients with hyperthyroidism who had proved unmanageable by the usual medical measures. A definite improvement in the laboratory tests accompanied by slight clinical improvement was noted in one case, deterioration occurred in another, and the three remaining patients showed no clear response. Similarly unsatisfactory results were described by Werner (1950), who treated two patients, and by Moseley and Merrill (1950) and Charvat *et al.* (1952), who reported single cases. More recently Wisniewski and Górowski (1957) gave corticotrophin as a preparation for thyroidectomy to five patients who were intolerant of antithyroid drugs. A reduction in hyperthyroidism was seen in four of the cases. Euthyroidism was never achieved, and relapse quickly followed cessation of therapy.

Thus in 10 of 23 patients with hyperthyroidism significant clinical benefit was obtained from the use of corticotrophin therapy, and this does not accord completely with our experience of only one moderately successful result after the treatment of eight patients. The fact that none of the authors of the single case reports have subsequently described larger series implies that the promise of their earlier successes has not been fulfilled. An unexpected feature revealed by the

analysis of the published results of corticotrophin treatment was the reduction in the size of the goitre in eight patients, often without any reduction in the hyperthyroidism. A doubtful effect was observed in only one patient in our series. The apparent improvement in muscle power in our patient with thyrotoxic myopathy is probably a non-specific effect; Maczynski and Sporny (1956) have described a temporary improvement in general strength in a hyperthyroid patient given 90 mg. of corticotrophin over 20 hours.

There have been several descriptions of the use of corticotrophin and adrenocortical steroids in malignant exophthalmos and in thyrotoxic crisis. In the former most writers agree that a reduction in the local oedema occurs without any improvement in proptosis or ophthalmoplegia. In the latter all observers believe that corticotrophin played an important part in ensuring and accelerating recovery, although all admit that, as other forms of therapy were given concurrently, clinical impressions form the only evidence for this beneficial effect.

The assessments of the function of the adrenal cortex in our patients (Table II) confirm the studies of the majority of preceding workers (Levin and Daughaday, 1955). Two of our cases (Nos. 3 and 4) had definitely subnormal levels of urinary excretion of 17-ketosteroids, while all other

TABLE II.—Adrenocortical Function in Nine Hyperthyroid Patients

Case No.	Sex	17-Ketosteroids* (mg./24 hours†)	17-Ketogenic Steroids† (mg./24 hours‡)
1	F	6.5	9.5
2	M	7.0	12.3
3	F	2.0	6.4
4	F	2.4	5.5
5	F	6.3	8.6
6	M	8.2	11.1
7	F	6.3	6.4
8	M	6.0	12.0
9	F	9.1	12.1

* Method of Norymberski *et al.* (1953). Normal (80%) range: males, 7-20; females, 5-15.

† Method of Gibson and Norymberski (1954). Normal (80%) range: males, 5-18; females, 5-15.

‡ Mean of at least two estimations.

patients had levels in the lower ranges of normality. Glucocorticoid activity as demonstrated by the urinary excretion of 17-ketogenic steroids was not significantly abnormal, and the rather low levels found in our cases are not uncommon in patients with normal adrenocortical activity after a short period of bed rest. As Harris and Woods (1956) pointed out, the surprising feature of these findings is that the urinary excretion of adrenal steroids is not increased in hyperthyroidism, a condition in which the patient would appear to be under physical and emotional stress.

It would seem, therefore, that significant improvement in hyperthyroidism is not to be expected after corticotrophin treatment, except possibly in mild and early cases. For these patients other more satisfactory and safer methods of treatment are available. In patients whose preoperative management is difficult or who develop thyrotoxic crises, the addition of corticotrophin to other therapeutic measures is probably worth while.

Summary

There is much evidence for the association of adrenal cortical underactivity with hyperthyroidism.

Nine hyperthyroid patients had subnormal or low levels of urinary excretion of 17-ketosteroids. The excretion of urinary 17-ketogenic steroids was not reduced.

Eight of the patients were treated with corticotrophin in full doses for two to five weeks. Only one patient showed any significant clinical benefit; this was accompanied by an improvement in all laboratory tests of thyroid overactivity. The ninth patient received treatment with prednisone without benefit.

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WAX KERATOSIS IN CHILDREN'S EARS

BY

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It was some time before penicillin became easily available in forms which could be used by general medical practitioners, but once this happened it was used freely in the treatment of acute otitis media. In 1953 it was stated that nearly all such cases were being treated by general practitioners, only the failures being seen by otologists (Black, 1954). One of the causes of failure was due to a mistaken diagnosis in that the patient—a child—did not have otitis media, but infection and suppuration in a mass of wax deeply impacted in the external auditory canal. It had long been known that wax did occasionally become impacted against the tympanic membrane, where it became covered by sheets of desquamated epithelium, and we had come to call this a "wax keratosis." This was thought to be the early stage of the so-called keratosis obturans, a condition well enough known to appear in the textbooks, although there was discussion about its cause and origin and even about its nature.

This wax keratosis seemed to be of interest in itself, in that we did not know how the wax got into the deeper

external auditory canal, nor quite what troubles it could cause when it got there. Another curious feature was a known association with chronic respiratory tract suppuration, that of sinusitis and bronchiectasis. Morrison (1956) stimulated further interest with a paper on keratosis obturans, in which he suggested an explanation for the presence of the wax against the tympanic-membrane and noted some of the facts of the condition.

Altogether, it seemed to justify some attempt at obtaining further facts, and accordingly an analysis of a collection of such cases has been made, and this forms the basis of the present paper.

Incidence and Location of Wax in Children's Ears

It was important at the outset to have some information concerning wax in children's ears, whether normal or otherwise.

The hair follicles and glandular elements in the skin of the external auditory canal are confined essentially to its outer half or so. Collins (1951) supported previous views that the waxy or more solid secretion of the sebaceous glands is softened by the secretion of the ceruminous glands so that it can find a way to the outside. Therefore it would be expected that wax would normally be found in the outer part of the external auditory canal or not at all (Fig. 1).

An investigation was carried out in 1,000 consecutive children seen for the first time in 1957 in three E.N.T. out-patient departments, perhaps not an entirely normal cross-section of the whole. Three different classes were recognized in these children, as follows: (1) no wax present anywhere in the external auditory canals; (2) wax present in the area which normally produces it; and (3) wax impacted in the deep part of the external auditory canals—that is, wax keratosis.

FIG. 1.—So-called normal wax in outer half of external auditory canal.

TABLE I

Class	First Series		Second Series	
	No. of Cases	%	No. of Cases	%
1	828	82.8	489	88.4
2	146	14.6	45	8.1
3	26	2.6	19	3.5
Total	1,000	100.0	553	100

A further series of over 500 children were seen in two more E.N.T. out-patient departments. The results in the two series are shown in Table I. It will be seen that 2.6% of the first series had wax firmly impacted against the tympanic membrane. When the wax was removed under general anaesthesia from these 26 children, 14 were found to have a well-formed wax keratosis, and in the remaining 12 the wax had formed a complete cast of the canal, but no epithelial envelope was present as yet. It is probable that these 26 cases represent degrees of the same process, which has been termed wax keratosis. In the second series 3.5% showed the presence of a wax keratosis.

It will be seen that these two series bear a striking similarity, and confirm the incidence of wax keratosis in about 3% of all children attending an E.N.T. out-patient department for a variety of reasons.