considerations may also apply to coma in myxoedema, especially as there is evidence that adrenocortical failure may occur in myxoedema (Statland and Lerman, 1950; Hill *et al.*, 1950; Hubble, 1955), and there is a possibility of pituitary hypofunction too (Statland and Lerman, 1950; Hubble, 1955).

The treatment successfully employed in Case 3 relied on the early administration of thyroxine and corticotrophin together with the application of warmth. Alternatively a regime of management described by Caughey and Garrod (1954) for treatment of hypopituitary coma could on empirical grounds be suggested for treatment of coma in myxoedema. Early recognition of hypothyroidism with adequate and continuous therapy should prevent the occurrence of coma.

Summary

Three cases of coma with hypothermia in myxoedema are described. Hypothermia can be recognized clinically by appreciation of the extreme dry coldness of the skin and can be confirmed by measuring the temperature with a low-reading thermometer. Factors connected with the causation of hypothermic coma in myxoedema are discussed and the similarity to coma in hypopituitarism is considered.

ADDENDUM.—Since this paper was submitted for publication an additional case has come to my attention. A woman of 67 was admitted to the Royal Hospital, Sheffield, in February, 1955. The clinical features were similar to those in the above cases. There was no pitting oedema. The rectal temperature was 80° F. (26.1° C.). By application of electric blankets it was raised to 92° F. (33.3° C.). The patient did not shiver. Serum electrolyte concentrations were: Sodium, 118 mEq/l.; potassium, 3.5 mEq/l.; chloride, 76 mEq/l. Blood urea was 30 mg., and blood sugar 102 mg. per 100 ml. She was diagnosed as a case of Simmonds's disease, but at necropsy the pituitary and adrenal glands were normal. The thyroid gland showed advanced atrophy.

My thanks are due to Dr. D. V. Hubble, Dr. H. T. Howat, and Dr. S. Oleesky for permission to publish a description of cases under their care, and for their help and encouragement in the preparation of this paper. I am indebted to Dr. A. D. Smith for clinical observations on Case 3.

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The *St. Raphael Quarterly*, the journal of the Guild of St. Raphael (the Anglican guild for the promotion of the Ministry of Healing), has been issued under a new format, with Mr. P. Shuffrey as editor. Obtainable from the Guild of St. Raphael, 33, Wilton Place, S.W.1, the subscription is 3s. 6d. While the Church has come again to regard healing as part of her function, "her understanding of the matter has been mostly concerned with the results, a little with the how, but hardly at all with the why of it. The purpose of this journal . . . is to try to fill that gap." It is hoped that doctors, psychiatrists, priests, and theologians will contribute. In the autumn issue, 1955, three doctors and three priests write a joint article stressing that, while "a distinction must be drawn between the cure of a specific malady and the larger concept of healing," both doctor and priest are concerned with the issue of total health. The authors believe that the concept of psychogenic origins of illnesses has made a *rapprochement* between Church and Medicine easier.

MYXOEDEMA COMA IN A PATIENT WITH HASHIMOTO'S STRUMA

BY

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Coma as a complication of thyroid myxoedema is not a frequent occurrence and is not often mentioned as a terminal event in the natural history of the disease. Summers (1953) described four cases of coma leading to death in patients with thyroid myxoedema. He suggested that hypothermia might be the cause of death and pointed out that treatment was ineffective once coma had developed.

We wish to report a case of coma, without discernible precipitating factor, occurring in a patient with myxoedema who died despite hormonal treatment and in whom the diagnosis was confirmed by radioactive tracer studies and post-mortem examination, including examination of the pituitary body.

Case Report

A 63-year-old white woman was admitted to the Institut Jules Bordet on March 14, 1954, with the chief complaint of constipation and asthenia. The onset of the disease dated back about six months before admission, when she experienced constipation alternating with periods of diarrhoea. She had several fainting spells during the week preceding admission. A detailed history was difficult to obtain because of her profound asthenia and lack of attention and interest. However, she did not complain of pain, and a review of the various systems was negative except for moderate ankle oedema at night and mild dyspnoea on exertion. She had always been sensitive to cold. The family history failed to reveal any significant fact: the patient was married and had two healthy children. Her past history was negative except for a strangulated hernia which was operated upon in 1940.

Physical examination showed a well-developed woman in a satisfactory state of nutrition. She was lying in bed quietly, paying little attention to her surroundings, fully conscious, but slow in answering questions, which she did in a monotonous and deep voice. The blood pressure was 160/100; temperature 99° F. (37.2° C.); pulse 68, regular. The skin and hair were dry and the patient looked anaemic. There was a puffiness around the eyes, and the face appeared somewhat swollen and was inexpressive. Examination of the head, neck, and chest showed nothing else of significance. The thyroid gland was not felt and there was no tenderness. The extremities were normal. Axillary hair was lacking, but pubic hair had a normal distribution. Neurological examination was negative. The patient was able to walk, but did not volunteer to leave her bed.

X-ray examination revealed the presence of residual fluid in the stomach with no other abnormality, a normal intestinal tract, and a moderate enlargement of the heart.

The urine was free of sugar and albumin, but contained a few white blood cells. The blood showed: haemoglobin, 13.6 g. per 100 ml.; white cells, 8,200 per c.mm., with a normal differential count; urea nitrogen, 34 mg. per 100 ml.; total cholesterol level, 336 mg. per 100 ml. of serum. The cephalin flocculation test was negative after 48 hours and thymol turbidity was 0.5 MacLagan unit. The complement-fixation test for syphilis was negative.

A diagnosis of myxoedema was made on admission. The basal metabolic rate was minus 8%. Examination by radio-

active iodine tracer was carried out on the ninth day : the patient was given 200 microcuries of ^{131}I by mouth, following which the maximum thyroid concentration, measured locally, amounted to 4.5%. Concentration was less after three hours than after one hour. The radio-iodine did not concentrate more in the region of the thyroid than in the surrounding area. Urinary excretion of radio-iodine could not be measured accurately because part of the urine was inadvertently discarded in the ward.

During the next few days the patient's condition deteriorated gradually. She became disorientated and incoherent in her speech. However, she never was agitated. On the 13th day after admission her pulse was 92, respirations 24, and blood pressure 100/70. There was a marked degree of myasthenia, with almost complete inability to move the extremities. Tendon reflexes disappeared. The patient's condition appeared serious. In an attempt to correct the myasthenia, 1 mg. of neostigmine was injected under the skin, with no improvement. The temperature rose to 100.4° F. (38° C.) in the afternoon and 400,000 units of penicillin and 0.5 g. of streptomycin were given twice a day until death ensued. On the 16th hospital day the patient was in coma with complete areflexia. The respiration rate was 32 a minute, pulse 112, and blood pressure 83/60. The eyelids were half closed and there was a convergent strabismus. Measurements of serum electrolytes gave the following results : potassium, 4.1 mEq/l.; sodium, 139 mEq/l. The blood urea was 61 mg. per 100 ml. The eosinophil count on this day was 28 per c.mm. These results seemed to rule out the possibility of an Addisonian crisis.

At 11 a.m. the patient received 1 mg. of thyroxine intravenously, followed by 100 mg. of cortisone by mouth 90 minutes later. By that time the patient was in deep coma and she died three hours later.

Post-mortem Findings

The principal post-mortem findings were as follows :

Macroscopic Examination.—The lungs showed some hypostatic congestion. The heart weighed 310 g. and the pericardium was normal. There was no pericardial effusion.

Section of the thyroid ; Masson's trichrome.

The myocardium was normal except for a small subendocardial haemorrhage near the septum. There was marked atheroma of the aorta and the two coronary arteries, but no coronary occlusion. The thyroid gland weighed 9 g. and had an atrophic appearance, especially the left lobe. The middle lobe contained a small adenoma, 1 cm. in diameter. There was some hypertrophy of the parathyroids. The abdominal cavity was normal. The spleen weighed 40 g., the pancreas 110 g., and the liver 1,250 g. : all these organs were normal. The left adrenal gland weighed 3.7 g. and the right 5.1 g. The kidneys, pelvic organs, brain, and pituitary were normal.

Microscopic Examination.—**Thyroid** (see Fig.): The medium-sized branches of the thyroid artery showed a pronounced hypertrophic endarteritis with calcium deposition

encircling the vessels. The gland itself was markedly fibrosed. The glandular structure was much altered : very few vesicles were left ; they were small and contained little colloid ; the lining epithelium was necrotic in spots, with thinning and pyknosis of the nuclei. At other places the thyroid tissue was dissected by an abundant lymphoid infiltration, and, in addition, lymphadenoid nodules with germinal centres were present. An aberrant thyroid nodule in the neck showed the same structure as the thyroid. The *parathyroids* showed a simple hypertrophy. The *lymph nodes* in the mediastinum contained small foci of fibrous tuberculosis. The *adrenals* had a normal appearance and there was no depletion of lipoids. The *pituitary* body showed abnormalities confined to the anterior lobe, which contained numerous acidophilic cells, characteristic of severe thyroid deficiency : the cytoplasm, stained by the method of MacManus, had a sponge-like structure with bright red granules, sometimes containing vacuoles. This sponge-like structure is explained by the dissolution of lipid material by the histological reagents. The basophil cells were normal. **Central nervous system:** The supraoptic nuclei contained numerous cells with an eccentric nucleus, and large Nissl bodies at the periphery : the cytoplasm showed a very fine granular structure. Other organs had a normal structure.

In summary, the post-mortem examination showed an atrophic thyroid with marked lymphoid infiltration : the appearance was that of a Hashimoto's struma.

Discussion

The diagnosis of myxoedema in this case was based on the characteristic clinical symptoms and signs of the disease : the most striking were the constipation and the mental apathy. Constipation was so severe that prior to her admission it led to a diagnosis of intestinal obstruction. The patient was very apathetic during her stay in hospital, although she responded to questions and stimuli, and was in no distress. The basal metabolic rate was within normal limits, but the results of the iodine tracer studies, although incomplete, definitely confirmed the diagnosis. Especially significant in this respect was the lack of concentration of ^{131}I in the region of the thyroid. Post-mortem examination confirmed the diagnosis of thyroid myxoedema by demonstrating an atrophic thyroid gland with the lymphoid infiltration characteristic of Hashimoto's struma. The myxoedema was not of pituitary origin ; the changes in the anterior hypophysis were secondary to and confirmatory of the primary thyroid disease.

The clinical course and the post-mortem findings strongly suggest that the patient succumbed to myxoedema coma. No other cause for death could be discovered. The adrenals could not be implicated, since no evidence of adrenal failure was observed before or after death. The myxoedema coma appeared to be caused by failure of the thyroid gland.

This case differs from those previously reported (Le Marquand *et al.*, 1953 ; Summers, 1953) in that there was no hypothermia preceding death. If our case is really one of myxoedema coma—a diagnosis supported by the data reported here—then hypothermia does not provide a general explanation for the death of myxoedematous patients. Our data allow very little speculation regarding the mechanism responsible for the fatal outcome. Some thought should be given to a possible neural factor, as suggested by the abnormal histological structure of the supraoptic nuclei in our case. Of interest in this respect is the fact that our patient, in contrast with those previously reported, had a pyrexia at the time of death. A more precise discussion of the mechanism involved is not possible on the basis of the available facts.

So far as treatment is concerned, previous reports have pointed out the apparent irreversibility of myxoedema coma with the available therapeutic measures. The treatment of our patient was not energetic enough to justify any conclusion on this point. It would seem that large amounts of thyroid preparations should be given to these patients. In

view of the recent report suggesting a more immediate action of L-triiodothyronine as compared with L-thyroxine in myxoedema (Rawson *et al.*, 1953) it might be advisable to administer this new compound to patients of the type described here. Certainly an expectant attitude is not justified when coma develops in a patient with myxoedema.

Summary

The case is reported of a patient with myxoedema, as proved by clinical and laboratory studies as well as by post-mortem examination, who died in coma. No other cause of death than myxoedema could be found. Myxoedema coma is a rare occurrence which appears to be irreversible with the available therapeutic means. The disease responsible for the myxoedema in the present case was Hashimoto's struma.

We are indebted to Dr. Dor for performing the radio-iodine concentration test.

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TAY-SACHS DISEASE IN TWO SINHALESE CHILDREN

BY

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Until recently the infantile type of this disorder had been described almost exclusively in children of Hebrew stock, but at the Ophthalmological Congress in London in 1950 Franceschetti and Klein (1951) recorded a number of cases in "Swiss peasant families which certainly have no Jewish blood." They mentioned the following authors: Schmuziger, Scheidegger, Bing, Fanconi, Hanhart, and Bamatter and Sierro. Roos (1935) mentioned two cases in the literature and added one of his own in a Norwegian child. Van Creveld (1953) has reported three personally observed cases in non-Jewish children. One of us (de Silva, 1951) reported a case in a Sinhalese boy aged 3 years. His illness began with convulsions one week after birth, and the disease was of slow progress. The macula showed dark plum-coloured areas—larger than the usual spot and surrounded by a greyish-white circle. There were no blood vessels in this area. There is no reason any longer to state that Tay-Sachs disease arises almost exclusively in Jewish infants.

Case 1

A Sinhalese boy aged 2½ years was admitted to the Children's Hospital, Colombo, on September 27, 1952, with a history of fits from the age of 2 months and inability to hold up his head. Since he was a year old his limbs had been observed to be spastic. When he was 2 months of age his mother noticed that he was easily startled by noises, more so than a normal child would have been. She stated that there was a transient tremor of the limbs and a rolling of the eyes. These were interpreted as "fits" by her. Each "fit" lasted only a moment or two, but there were two or three such spasms a day. These occurred daily till admission to hospital—that is, for two and a half years.

Family History.—The patient was the youngest of eight children. The first and second children had died after prolonged illnesses with cough, fever, and emaciation, the first at 1 year of age and the second at 1½ years. These deaths had occurred over 17 years ago, and no further details could be elicited from the parents, who were illiterate peasants. There was no consanguinity.

Milestones.—The child first raised his head about the sixth month, rolled over in the seventh, sat up in the eighth, and stood up with help just before his first birthday. Soon after this his mother noticed that he had difficulty in holding up his head. Later he lost his ability to raise it at all. At this time he also became irritable and cried often. Two to four weeks after the onset of the weakness of the neck muscles one leg became spastic and paralysed, and was kept in a position of flexion; within a week the other leg was similarly affected. At this stage the patient was unable to sit up by himself. On being passively sat up, he adopted the tripod-stand posture with the arms behind his back to take the weight. Very soon after this the arms too became paralysed, spastic, and flexed. At this time (at 13–14 months of age) he made inarticulate noises and showed no interest in his surroundings and could not even recognize his mother. After the age of 18 months these noises also ceased. The number of daily seizures increased from two to three to more than ten to fifteen. The patient continued to be in this state of flexion and spasticity, with excessive salivation, till his death at the age of 2 years and 10 months—that is, four months after admission to hospital. The duration of the disease was therefore two years and eight months.

On examination the child was severely underweight—13 lb. 4 oz. (6 kg.)—and thin. The liver and spleen were not palpable. He was very quiet, apathetic, and completely uninterested in his surroundings. On hearing any noise or on being touched, he would get a sudden extension of all four limbs—like an exaggerated Moro's reflex—a drawing out of the angles of his mouth, a rolling up of his eyes, and an extension of the spine as in a case of opisthotonos, and frothy fluid would exude from his mouth. There was, however, no loss of consciousness. The tendon reflexes were all exaggerated, more so on the left than on the right. The plantars were extensor on both sides. The fundal examination was done by Dr. K. J. de S. Devaditya, to whom I am indebted for the following report: "Optic disks—marked pallor, edges clear-cut; appearances suggest primary optic atrophy. Blood vessels show attenuation of retinal arterioles. Macular region—there is marked oedema over both maculae (that is, pale white areas) with a purplish coloured spot over the fovea centralis. This appearance is suggestive of cerebro-macular degeneration. There is no evidence of any choroidal tubercles or active choroiditis." Radiographs of the skull showed no calcified areas.

Laboratory Findings.—Blood calcium and serum sodium, potassium, and phosphorus were within normal limits. The Wassermann, Kahn, and cardiolipin reactions on the cerebro-spinal fluid on September 29 were negative. Total protein in the C.S.F. was 25 mg. per 100 ml. The Lange colloidal gold curve was 3222111100. The C.S.F. on culture produced no organisms.

The child lived in this vegetable-like state with intermittent rises of temperature to 99–100° F. (37.2–37.8° C.) until January 23, 1953, when he died. Necropsy showed a small brain with flattened gyri. There was no other abnormality to the naked eye. Microscopical report: All parts of the brain showed swollen ganglion cells with a foamy cytoplasm and a small nucleus. These cells were, however, less numerous than those seen in Case 2. There were no hyaline or calcified masses.

Case 2

A Sinhalese boy aged 2 years and 1 month was admitted to the Children's Hospital, Colombo, on September 23, 1953. About a month before admission the parents noticed a few abnormal movements—extension of the limbs with jerking. These recurred about 25 times a day, each attack being accompanied by frothing from the mouth, which lasted for