gravitational effect. This may be 3, 4, 5, 6, or more times ordinary gravity, according to the speed of the aircraft and curvature of the turn. At about 5 g. blood is driven from his retina and he develops the condition of "black-out"—i.e., he is momentarily blind. At about 6 g. he becomes unconscious, again only temporarily, but during these few seconds he may have covered much space and, since he may be turning to avoid action or chasing an enemy plane, it is of the greatest importance that his wits and eyesight should be perfect during the turn. The problem therefore is to provide the airman with such conditions that his threshold for blacking-out is high, and yet it must not be higher than that which the aircraft will stand. Full consciousness would be no consolation if the aircraft broke up. Another trouble aviators have to meet at high altitude is due to the nitrogen dissolved in their blood coming out of solution and forming bubbles. These cause intense pain in joints and muscles, which may pass on to collapse and unconsciousness; and the condition is known as "bends." It is now known that "bends" can be mitigated by washing out the nitrogen from the tissues before ascent.

You will see that these problems require much research, and it is the object of the physiologist to arrange his investigations so that as performance of aircraft becomes greater so also must the airman be kept provided with better means to increase his own powers of control. So far the physiologist has responded to all calls, and improvement in aircraft performance has been accompanied by equal powers of control. Submarines and tanks also have their own problems, and much work has been done to promote the efficiency of their crews under the many different conditions which may arise. It would be possible to give many other examples of investigations on personnel necessary in wartime—clothing to meet the extremes of heat and cold as met with in Persia or on an Arctic convoy respectively, the best diet for normal and extreme conditions, food for special purposes like commando operations, conditions for optimum vision in the dark. Probably I have said enough to show that this kind of research on fighting personnel is of very great importance.

Conclusion

I have now given a general survey of medical research activities during the war. I regret that, for obvious reasons, I have not been able to include in it an account of many of the more interesting discoveries that have been made, but most of these will come to light in course of time. The advance of medical science, both before and during the war, has been fantastic.

This lectureship has been instituted in memory of a man whose outstanding quality was to apply scientific knowledge to the service of man. The work I have attempted to describe is exactly of this nature, and I am sure it would meet with his approval when I express the wish that this lecture be regarded as a tribute to all those engaged on medical research in this country. Sitting as I do at the centre of all these activities I am in a position to say that this body of men and women—pathologists, bacteriologists, physiologists, biochemists, pharmacologists, and clinicians—deserve well of their country for the unsurpassed quality of their work, for their devotion to its performance, and for their complete unselfishness in carrying out their allotted tasks.

The American Society for Research in Psychosomatic Problems held its first annual meeting on May 9 to 11, when a constitution was unanimously adopted and the following ten research committees were appointed: on psychosomatic problems in obstetrics and gynaecology, in early infancy and childhood, in physiological mechanisms, in war medicine, in internal medicine, and in industrial medicine; psychosomatic implications of animal experimentation; psychosomatic teaching in medical schools; psycho-analytical research in psychosomatic problems; and the psychosomatic approach to social and cultural problems. These committees will correlate and initiate psychosomatic research in their different fields, present an annual report, and suggest programmes for meetings with other medical societies. The papers read to a joint meeting of the Society and the American Psychiatric Association on May 15 discussed new methods of psychosomatic diagnosis, including new Rorschach techniques and a new electronic method for measuring and recording deviations in psychosomatic functions.

PITUITARY HYPOTHYROIDISM WITH IMPAIRED RENAL FUNCTION

BY

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The following case presented certain features suggestive of hypothyroidism and nephritis. A series of investigations confirmed the diagnosis of a clinical syndrome related to a disorder of the pituitary gland which may be called pituitary hypothyroidism. This appears to be a rare condition, and resembles in many respects the few cases of pituitary myxoedema which have been reported.

Case Report

The patient is a female, single, aged 26. The present illness began at the age of 19, and there is little of significance in the history previous to this. The signs and symptoms in order of their appearance were as follows:

Abdominal Discomfort.—This was her first symptom, and she described it as a "fullness" even after small meals (aged 19). She also had acute attacks of diarrhoea.

Thirst.—Two years later (aged 21) she had severe attacks of thirst, especially in the winter. They were periodic, and are still present.

Oliguria.—She noticed that the output of urine fell appreciably with the onset of the thirst. At times micturition was very painful.

Swelling of Legs and Face.—At the age of 23, in the winter, she complained of periodic swelling of the ankles and legs. The leg muscles would become hard "like wood," making walking very difficult. The face and wrists also swelled periodically.

Cramps and Tetany.—She complained of slight cramps in the hands and legs at the age of 25. These became so severe that a tetanic attack in the hand often followed the taking of her blood pressure.

Coma.—A few months after the onset of tetany she became very weak and drowsy, with oliguria leading almost to anuria, bradycardia, marked fullness in the abdomen, and constipation. The attack lasted about 7 days. Two months later she had another and more severe attack during which she slept for three days. She appeared to make gradual recovery from both attacks.

Throughout the course of her illness this patient was admitted to various hospitals for investigation on four occasions. Only on the last occasion was a diagnosis made and treatment instituted. She was considered to be a case of "latent nephritis" because of a diminished urea clearance (an average of 25% of normal) and a urinary protein of 0.08%. She was advised to restrict her fluid intake, avoid salt, and be sparing with protein.

She was first seen by one of us (G. E. B.) on April 10, 1942, or one month after her most recent discharge from hospital. She was then aged 26, her height 5 ft. 3 in., and her weight 84 lb. (i.e., she had lost 17 lb. since the beginning of her illness). She was thin but not emaciated, and neither her mental nor her physical condition suggested anorexia nervosa or myxoedema. Her skin had been very dry, with absence of perspiration, since the age of 16. The pubic hair was of female distribution; eyebrows, axillary hair, and hair on head were normal. She had noticed more hair on the arms and legs during the last four years, and on the thighs and upper arms during the last few months. Her appetite was good. The heart was normal, the blood pressure 110/60, the arteries not thickened, and pulse 60. Micturition occurred on an average only twice a day, and the output was scanty. Her menstrual periods began at the age of 14, and were regular until she was 16. There were no periods from 16 to 17, when they recurred and were almost regular until Feb., 1942 (aged 25). She then missed one period, and had no more after May, 1942, until they returned in Jan., 1943, when she was under treatment. They have since been regular. There appeared to be little else abnormal on physical examination.

It seemed improbable that she was suffering from nephritis of such a severe type as to lower the renal function to 25% (van Slyke), when the urine showed no casts and only an occasional trace of albumin, and there was no other clinical evidence of

nephritis. The periodical swelling of the malar regions of the face and the hardening "like wood" of the leg muscles from time to time suggested the possibility of masked hypothyroidism, a condition to which attention has been drawn by Beaumont and Robertson (1939), Dodds and Robertson (1939), and Beaumont (1941). Unexplained diarrhoea is also sometimes due to this cause. The basal metabolic rate was determined, and was -21 (Aub-DuBois), and the blood cholesterol was 170 mg. per 100 c.cm. It now occurred to us that the low van Slyke reading might be due to hypothyroidism rather than to a primary affection of the kidneys. It is known that in primary myxoedema a diuretic crisis usually occurs as soon as the patient responds to thyroid administration. This suggests that renal function is impaired in myxoedema, at any rate so far as water elimination is concerned. The normal blood cholesterol figure suggested that the hypothyroidism was not primary, for in primary myxoedema the blood cholesterol is almost always raised in untreated cases.

Progress.—As she was not now considered to be suffering from nephritis she was put on a normal diet with as much salt and water as she desired, and thyroid medication was begun with gradually increasing doses, from $1/4$ gr. to 3 gr. daily. At first her condition greatly improved until she had taken 3 gr. a day for a month. She then complained of feeling very ill, with intense lassitude, dizziness, retching, diarrhoea, and acute abdominal discomfort. The pulse was 100, and the temperature 99° to 100° F. The urine output fell to 35 oz. a day. She looked very ill, was dehydrated, and had sunken eyes, a sallow greyish complexion, and dry skin. She was admitted to hospital for further investigation. Her blood chemistry gave the following findings: urea 87 mg., plasma chlorides 450 mg., serum sodium 291 mg. per 100 c.cm. In other words the urea had risen, the chlorides and sodium had fallen—a condition typical of an impending adrenocortical crisis. The urea clearance had fallen to 13% of normal. It is known that the administration of thyroid causes acute adrenocortical failure in cases of Addison's disease and in pituitary myxoedema.

The diagnosis of simple hypothyroidism was now considered as only part of the syndrome, the condition being probably a multiglandular deficiency with the primary lesion in the pituitary gland. When her condition had improved further tests were carried out. A radiograph of the pituitary fossa was normal, and there was no evidence of a suprarenal or renal tumour as judged by clinical abdominal examination, a direct radiograph of the abdomen, and the uroselectan test. An "insulin-tolerance curve" was carried out on the standard lines described by Himsworth (1935), Fraser, Allbright, and Smith (1941), and Fraser and Smith (1941).

Blood Sugars after Intravenous Insulin (the Resting Sugar taken as 100 mg. per 100 c.cm.)

	Resting	After 5.6 Units of Insulin Intravenously					
		20 min.	30 min.	45 min.	60 min.	90 min.	120 min.
Normal	100	45	50	70	80	95	115
Our case .. .	100	55	35	60	60	85	80
Case of pituitary hypofunction*	100	55	40	40	45	75	60

* Lerman and Stebbins.

Our case showed "hypoglycaemia unresponsiveness" and failure of the diabetogenic hormone typical of hypofunction of the pituitary gland. In other words, there is a 50% fall in the blood-sugar level in 20 or 30 minutes, and at the end of two hours the blood sugar is less than 90% of the fasting level.

Urinary System.—A series of tests was carried out on the renal function. The urea clearance was repeated, and was found to be 19% of normal. In addition there was impairment of water elimination—only 350 c.cm. of urine were excreted three hours after ingesting a litre of water—and inability to concentrate urine above a specific gravity of 1011. Despite these signs of renal impairment the blood urea was now normal (33 mg. per 100 c.cm.), the urine contained no albumin, and no abnormalities were found microscopically in the centrifugized urinary deposit. There was no previous history of nephritis, and the blood pressure was normal.

The diagnosis of pituitary hypofunction now appeared to be established. Such a syndrome would explain a combination of a multiglandular deficiency affecting the thyroid, adrenal, and sex glands, giving hypothyroidism, cortico-adrenal insufficiency (accentuated by thyroid therapy), and amenorrhoea. The effects of replacement therapy were then studied.

Treatment and Progress.—The treatment included sodium chloride, cortical extract of suprarenal glands (later desoxycorticosterone acetate), pregnant mares' serum, and thyroid. Sodium chloride was given by mouth in doses of 180 gr. daily. Suprarenal extract (eucortone, Allen and Hanburys) was given daily intramuscularly in doses first of 2 c.cm., increasing by 2 c.cm. every second day up to 10 c.cm. After a month this was replaced by desoxycortico-

sterone acetate (percorten, Ciba) 5 mg. intramuscularly on alternate days for 14 days. Pregnant mares' serum (gonadyl, Roussel Lab.) was given daily intramuscularly in doses of 400 mouse units for two months, and thereafter three times a week for six months; now it is being given three times a week for two weeks every month before her periods are due. Thyroid was stopped for a month in view of its effect on the adrenocortical deficiency, and now is being given in doses of $1/2$ gr. twice daily.

The patient made considerable improvement as soon as the above treatment was instituted. She felt more energetic and looked well. Menstruation restarted. After six weeks of treatment her urea clearance rose to 44% of normal, and five months later it was within normal limits, with a greatly improved water elimination. Her weight has increased by over 16 lb., and she is now (June, 1943) back at work, her periods are regular, and she is feeling very much better in every way.

Discussion

In 1914 Simmonds described a syndrome which manifested itself clinically in a pronounced loss of weight, premature senility, diminished sexual functions, weakness, and loss of hair. The finding at necropsy was almost complete destruction of the anterior lobe of the pituitary gland. The clinical symptoms closely resembled anorexia nervosa, and the differentiation between these diseases was difficult. Cachexia is not now considered a characteristic feature of Simmonds's disease. More recently some unusual types of a pituitary syndrome have been described. Thus Castleman and Hertz (1939) reported a case of pituitary fibrosis with myxoedema. The case looked, and was, myxoedematous, with a blood cholesterol of 374 mg. per 100 c.cm. Although not suggested by the authors, it seems probable that the Simmonds's disease developed in an established case of myxoedema. The parathyroids were fatty, the adrenals and ovaries atrophic, and the anterior lobe of the pituitary and the thyroid showed fibrosis. Lerman and Stebbins (1942) have reported two cases of the pituitary type of myxoedema, with typical myxoedema and the pituitary syndrome, including hypogonadism, adrenocortical insufficiency, and decreased diabetogenic activity. In one case in which it was estimated, the cholesterol was 120 mg. per 100 c.cm.—an unusual finding in primary myxoedema.

Our case possessed the following features typical of Simmonds's disease: hypogonadism, adrenocortical insufficiency, and a decreased diabetogenic activity, together with hypothyroidism. The patient did not look myxoedematous and the blood cholesterol was normal, which suggests that the hypothyroidism was not primary. The only signs of a masked hypothyroidism were the "wood-like" stiffness of the leg and arm muscles and the dry skin. The most prominent sign in our case (and not previously referred to in the literature) was evidence of renal impairment as shown by diminished urea clearance, diminished water elimination, and a urine of low specific gravity. In a further paper it will be shown that only part, and not all, of these renal signs could be due to the hypothyroid factor. In view of the improvement of the urea clearance and in the water elimination after treatment with the various forms of therapy (thyroid, adrenocortical, and gonadal hormones) it seems probable that the renal signs were in fact a manifestation of the disease.

Summary

A case of pituitary hypothyroidism is described which presented the following signs and symptoms. (1) Renal impairment:—This was the most prominent sign, and at first suggested a diagnosis of "latent nephritis." The urea clearance and water elimination were diminished, and there was a urine of low specific gravity. (2) Hypothyroidism:—This is to be distinguished from the typical primary myxoedema, in which the blood cholesterol is usually raised. (3) Cachexia. (4) Adrenocortical insufficiency. (5) Hypogonadism. (6) Decreased diabetogenic activity.

Treatment with sodium chloride and the hormones of the thyroid, gonads, and adrenal brought about a marked improvement in the clinical condition and restored the renal function to normal.

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