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THYROID SECRETION AS A FACTOR

IN

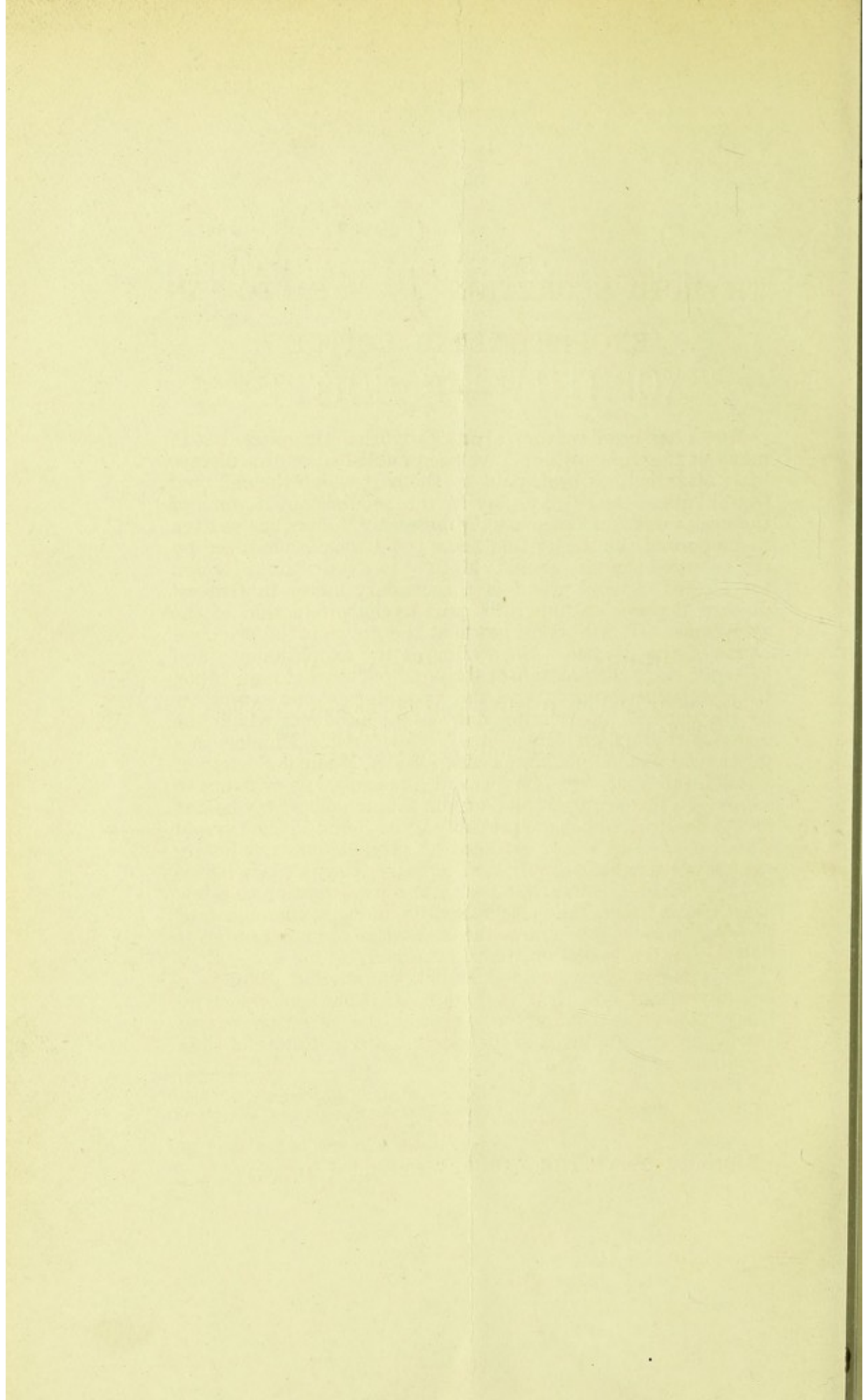
EXOPHTHALMIC GOITRE /.

BY

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THYROID SECRETION AS A FACTOR IN EXOPHTHALMIC GOITRE.

MUCH has been written about exophthalmic goitre, but in many of the papers which have been published on this disease little attention has been paid to the part which the enlarged thyroid gland itself may play in the production of some of the symptoms which are usually present. Möbius has written in support of the theory that there is a toxæmia produced by the enlarged thyroid gland. Müller¹ maintains that, though the altered thyroid gland is a secondary factor in Graves' disease, it plays an important part in the production of the symptoms. Wette² considers that the goitre is the principal cause of the disease. He attributes the exophthalmos and palpitations to the pressure of the enlarged thyroid gland upon the sympathetic nerve, and the variable nervous symptoms to "a general intoxication due to the products which the diseased thyroid gland secretes." Mr. Arthur Maude,³ in a paper read at the opening meeting of the Medical Society of London this year, brought forward some valuable evidence to show that the symptoms of exophthalmic goitre may be due to a general nerve poison, probably to be found in the thyroid gland. The evidence possessed at present does not justify the supposition that the thyroid gland is the primary factor in exophthalmic goitre, but I wish to draw attention to a few facts which, when taken together, do indicate that some of the symptoms may be due to the absorption of an excessive or possibly altered secretion from that gland.

There is now strong evidence that the thyroid gland is a secretory gland—ductless, it is true; but it has been shown by King,⁴ Baber and other observers that the secretion passes along the lymphatics into the general circulation, and so is

¹ Deutsches Archiv für Klinische Medicin, li., 4 und 5.

² Archiv für Klinische Chirurgie, xlv., 3.

³ THE LANCET, Oct. 31st, 1893.

⁴ Professor Victor Horsley: Remarks on the Function of the Thyroid Gland, Brit. Med. Jour., Jan. 30th, 1892.

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distributed all over the body. The effects of atrophy or removal of the thyroid gland in man and in many of the lower animals are now well known, the symptoms of the resulting condition of myxœdema or cachexia strumipriva being due to the loss of thyroid secretion. That this is the correct explanation of that condition is shown by the fact that the symptoms of cachexia strumipriva following thyroidectomy can be considerably lessened, if not entirely removed, by hypodermic injections of thyroid juice. In the case of dogs this has been shown to be the case by Vessale and by Gley. In the monkey I have recently shown⁵ that the usual symptoms of cachexia strumipriva, first described by Professor Victor Horsley,⁶ which came on after removal of the thyroid gland—viz., swelling of the face, hebetude, tremor, anæmia, and subnormal temperature—were all removed by hypodermic injections of thyroid extract. After the injections were discontinued the symptoms of course returned, and the animal died of acute myxœdema and dysentery. The total removal of the thyroid gland was proved by post-mortem examination.⁷ In man the results of the treatment of myxœdema have shown that in a favourable case the symptoms of this condition can be entirely removed by the administration of thyroid juice in one form or another. We have thus the strongest evidence of the secretory function of the thyroid gland, for there appears to be no other supposition by which the action of the thyroid juice in the above instances can be explained. In exophthalmic goitre the thyroid gland is nearly always enlarged and, as Professor Greenfield⁸ has stated, there is "an enormous increase in the secreting structure of the thyroid and also of the colloid material in the spaces of the gland." It may reasonably be supposed that an increase of gland substance of this character indicates an increase of secretion, and even in those cases where the gland is not as yet appreciably enlarged it is quite possible that a hypersecretion may be going on. Mr. Maude, who has been able to watch cases of Graves' disease for long periods, has found that the thyroid gland may vary in size from day to day. Such variations are doubtless due to alterations in the

⁵ Brit. Med. Jour., Sept. 23rd, 1893.

⁶ Brown Lectures, 1885.

⁷ Towards the expenses of this research a grant was made by the British Medical Association on the recommendation of the Scientific Grants Committee of the Association.

⁸ Edinburgh Medical Journal, May, 1893.

vascular supply, the temporary increase in size thus being similar to the turgescence which takes place in the other glands—such as the salivary glands—during active secretion, a similarity which was pointed out to me by Dr. F. W. Mott. In support of this view it is a significant fact that over-doses of thyroid extract produce symptoms similar to those which occur in exophthalmic goitre. As a result of these I have observed acceleration of the pulse, tremor, headache, slight sweating, rise of temperature above normal, and prostration, all of which are symptoms which occur in exophthalmic goitre. One of the most usual effects of overdoses of thyroid juice is considerable acceleration of the pulse. This may occur during both the first and the second stages of the treatment of a case of myxœdema with thyroid extract. Thus in the case of a woman aged fifty-six who has had myxœdema for several years, a daily dose of ten minims of thyroid extract accelerated the pulse from 80 beats to 120 or 130 a minute. Dr. Hector Mackenzie⁹ has observed the same symptoms after the administration of large doses of the thyroid gland itself. The occurrence of tremor, with accelerated pulse, hot flushings, and sweating, after prolonged administration of thyroid extract was well illustrated by one of my cases. This patient first began to be treated with thyroid extract in April, 1891. She was the first case of myxœdema which was treated with this remedy, and for long has been free from symptoms of myxœdema. Since the beginning of this year she has taken one drachm of thyroid extract every week in six daily doses of ten minims each without intermission, as this was found to be a suitable dose for her in the winter. At the end of last July she came to see me complaining of "hot flushes." On examination I found that the pulse was 112 and the temperature 98.4° F. The skin was flushed and moist, and there was a fine tremor of the hands, just like that which is often present in exophthalmic goitre. I attributed these symptoms to her having taken doses of thyroid extract, which, though suitable for winter, were larger than was necessary during a hot summer. This view was confirmed by the rapid disappearance of the symptoms when the doses were diminished. The symptoms of myxœdema nearly always improve without any treatment during the summer, so that it might be expected that less thyroid juice would be necessary to maintain a condition of health then than during cold weather, when the symptoms,

⁹ Brit. Med. Jour., Oct. 29th, 1892.

as a rule, become aggravated. A rise of temperature above the normal as a result of taking thyroid juice occurs both in man and in the lower animals. In rabbits and monkeys I have found that a rise of temperature, sometimes to as much as 2° or 3° above the normal, follows a hypodermic injection of thyroid extract. This influence of thyroid secretion upon the temperature is further illustrated by the way the temperature falls below normal when that secretion is no longer formed, as in myxœdema and cachexia strumipriva.

If some of the symptoms of exophthalmic goitre are due to over-activity of the thyroid gland it should be expected that any method of treatment which leads to diminution of the size of the enlarged thyroid gland or to a lessening of its secretory activity would improve the condition of the patient, and this has been found to be the case. Operative treatment undertaken with this object in view has been followed by recovery. As an example of this Dr. Credé's case¹⁰ may be mentioned, in which, after total extirpation of the thyroid gland, the symptoms of exophthalmic goitre entirely disappeared. Stierlin has collected twenty-nine cases of exophthalmic goitre in which an operation upon the thyroid gland had been performed, and in twenty-two of these complete recovery took place. Then medical treatment directed towards the reduction of the enlarged thyroid gland is useful. My father, who has seen a large number of cases of exophthalmic goitre, finds that the inunction of the red iodide of mercury ointment over the thyroid gland brings this about and is a valuable aid to other methods of treatment in this disease. Belladonna checks secretion in other secretory glands, and Dr. Gowers¹¹ says that it "is the drug that has seemed most often distinctly useful" in exophthalmic goitre, probably because it also checks thyroid secretion. It has been shown experimentally by Wyss that thyroid secretion can be influenced by drugs, for he found that injections of pilocarpine increased the secretory activity of this gland considerably. The beneficial action of this latter drug in myxœdema is, I believe, largely due to the promotion of increased activity in the small portions of glandular structure which still remain in the diseased thyroid gland, such remnants of gland structure being visible even in the thyroid glands of those who have died from myxœdema.

The relationship of exophthalmic goitre to myxœdema also throws some light upon this subject. I refer especially to

¹⁰ Clinical Society's Report on Myxœdema, p. 110.

¹¹ Diseases of the Nervous System, vol. ii., p. 893.

those cases in which the symptoms of exophthalmic goitre have disappeared and those of myxœdema have developed afterwards. Dr. Gowers¹² has observed "myxœdematous swelling of the eyelids and pigmentation of the skin to follow permanent recovery from exophthalmic goitre." Dr. Corkhill¹³ has recorded a case in which symptoms of Graves' disease were followed by myxœdema. In the discussion on Mr. Maude's paper Dr. Ord said that he had seen symptoms of myxœdema develop after the enlarged thyroid gland had been too rapidly reduced in size by treatment, and Dr. Bowles mentioned two cases in which there had been Graves' disease in early life followed by myxœdema afterwards. It is an interesting fact that the disappearance of the symptoms of exophthalmic goitre in these cases should be followed later by distinct symptoms of myxœdema due to atrophy of the thyroid gland; and may it not have been a gradual failure in the supply of thyroid secretion which led to the disappearance of the symptoms of the former disease, as it did to the production of those of the latter at a later period?

Dr. Byrom Bramwell¹⁴ has clearly pointed out the striking contrast which exists between some symptoms of exophthalmic goitre and those of myxœdema. This is what should be expected if the former are due to an excessive supply of thyroid secretion, an exactly opposite condition to that which obtains in myxœdema. This contrast is well shown when the symptoms are arranged in parallel columns.

Exophthalmic Goitre.

Myxœdema.

Hypertrophy of thyroid gland.	Atrophy of thyroid gland.
Acceleration of pulse.	Slowing of pulse.
Excessive perspiration.	Perspiration diminished or absent.
Electrical resistance of skin is diminished.	Electrical resistance of skin is increased.
Temperature normal or above normal.	Temperature subnormal.
Excitable temperament.	Stolid temperament.

If further observations also tend to show that the various symptoms mentioned in this paper can be explained in the manner indicated, it will simplify the problem which still remains to be solved as to the causation of other symptoms

¹² Loc. cit., p. 880 ¹³ Brit. Med. Jour., Jan. 7th, 1893.

¹⁴ Edinburgh Medical Journal, May, 1893.

and of the change in the thyroid gland itself. However, the evidence which exists seems to indicate clearly that any line of treatment which is adopted for exophthalmic goitre ought to include special measures directed to the improvement of the abnormal condition of the thyroid gland which is developed in this disease.

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