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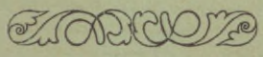
On "Internal Secretions."



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ON "INTERNAL SECRETIONS."

ARMOUR & COMPANY,
CHICAGO.

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THE following article by Prof. Chittenden, of Yale, appeared in *The Dietetic and Hygienic Gazette* of September, 1895:

INFLUENCE OF THE THYROID GLAND ON NUTRITION.

For years the so-called ductless glands were looked upon as having little physiological importance, but gradually evidence has accumulated which indicates that these structures have the power of forming substances endowed with marked physiological action; substances which undoubtedly play an important part in the ordinary metabolism going on in the body. Anyone who has witnessed the action of a simple aqueous extract of the suprarenals on the heart and on general blood-pressure will be convinced that these glands, however small and insignificant they may have been considered in the past, unquestionably manufacture one or more very potent substances which must have some function to perform in the general metabolism of the body. In other words, these ductless glands evidently give rise to a secretion which, unlike ordinary secretions, does not pass out of the body or into any particular channel, but is a true internal secretion, the components of which may be absorbed and thus distributed throughout the body, with possible manifold action.

With regard to the thyroid gland, attention was attracted to its functional power when observations showed that its operative removal from man was attended with a diseased condition of the body—the so-called Cachexia thyreopriva—which showed close similarity to myxœdema, where the thyroid is found to be atrophied and in a completely functionless condition. Experiments on carnivorous animals have shown that its complete removal is generally followed by the appearance of tetanic spasms and finally death. Again, it was found by numerous observers that the transplantation of a thyroid from a normal animal to one suffering with myxœdema, either under the skin or in the peritonæal cavity, was followed by rapid amelioration of symptoms. Further, the same results were obtained when the juice from the gland was introduced by intravenous injection, or when a glycerin extract of the gland was employed. These facts are to-day well known, and made use of in a variety of ways in the treatment of disease; but we would especially emphasize the fact that the dead gland, even when dried or cooked, still possesses its peculiar properties, thus indicating that its activity is due to the formation of some chemical substance which is of primary importance for the well-being of the body. In other words, the cells of the thyroid gland are the seat of chemical changes by which a physiologically active substance is produced, in the absence of which the animal body is unable to keep up its physiological balance. Thyroid glands fed to a healthy but obese individual cause a marked diminution in the body weight, even though the method of living remains unchanged; *i. e.*, the thyroid substance has a distinct influence either upon the normal production of fat in the body or upon its consumption.

These, and many other observations which cannot be mentioned here, indicate that the substance elaborated by the thyroid gland may have a manifold action upon nutrition, and Roos, working in Baumann's laboratory, has attempted an experimental study of the specific action of the thyroid or its extracts upon general metabolism. Working with dogs, it was found that the ingestion of dry thyroids by a healthy animal produced a noticeable change in the quantitative relationship of the more common excretory products. Thus, in one case the daily examination of the urine for ten consecutive days prior to feeding thyroid gave the following results as the daily average:

Nitrogen	3.038 grams.
Sodium chloride	0.907 "
Phosphoric acid (P_2O_5)	0.663 "

After feeding 3.0 grams of dry thyroid the daily average composition of the urine for seven consecutive days changed to the following:

Nitrogen	3.801 grams.
Sodium chloride	1.122 "
Phosphoric acid (P_2O_5)	0.739 "

In another experiment with a healthy dog the average daily composition of the urine for five days was found as follows:

Nitrogen	3.394 grams.
Sodium chloride	0.968 "
Phosphoric acid (P_2O_5)	0.733 "

On feeding six grams of dry thyroid to this animal the average composition of the urine for the following five consecutive days changed to

Nitrogen	4.146 grams.
Sodium chloride	1.192 "
Phosphoric acid (P_2O_5)	0.845 "

In other words, the ingestion of the thyroid gland by a healthy animal is at once followed by a marked increase in proteid metabolism, as indicated by the increased excretion of nitrogen and of phosphoric acid. Further, the thyroid substance causes at once a marked diuresis, which in time gradually disappears and finally gives place to a diminished secretion of urine. If the dosage of thyroid is increased and continued for some days the above action is still more marked.

When fed to an animal from which the thyroid gland has been removed the thyroid substance causes a still greater excretion of nitrogen and of chlorine, plainly inciting to a high degree the consumption of proteid matter by the body, in a manner somewhat similar to that observed after the administration of phosphorus. Further, it is to be noticed that the feeding of thyroid extracts or substance causes a marked decrease in the body weight, far greater than can be accounted for by the increased consumption of proteid matter. This is manifestly due to a direct influence upon the consumption of the body fat; a view which is in accord with previous observations that the thyroid substance gives rise to an increased output of carbonic acid, due obviously to an increased combustion of the adipose material.

Moreover, the results obtained indicate that the thyroid gland has an important influence upon the excretion of phosphoric acid, although it is not quite clear in what manner the gland exercises its influence in this direction. Roos considers that the substance which is responsible for the action of the thyroid is a more or less resistant and stable body, not an enzyme, but having rather the nature of a proteid substance—thyro-proteid—although there is at present no very concise information on this point. Enough is known, however, to indicate quite clearly that this ductless gland, which is assuming such importance as a remedial agent, unquestionably possesses a marked influence upon the metabolic changes going on in the body; a fact which may be taken as an illustration of the view that the nutrition of the animal body is subject to a variety of modifying influences of which as yet we have a very limited knowledge.

We quote, by the kind permission of Dr. E. Fletcher Ingals, from the article read by him before the American Laryngological Association, at its Seventeenth Annual Congress, and printed in the *New York Medical Journal* of September 7, 1895.

THE TREATMENT OF GOÎTRE AND EXOPHTHALMIC GOÎTRE BY THYROID EXTRACTS AND DESICCATED THYROIDS.

By E. Fletcher Ingals, M. D.,
With the Collaboration of Henry G. Ohls, M. D., Chicago.

I feel it almost necessary to apologize to this Association for bringing before it so old a subject, but as my own experience in the medicinal use of the thyroid gland is comparatively recent, and as there are many things about the subject not yet settled, I think it possible that it may be of interest to some others of this Association as well as to many practitioners.

In looking over the histories of my private patients for the last fifteen years I find eighty-one cases of bronchocele and exophthalmic goître that I have treated, sometimes with very indifferent success, but often with most gratifying results.

My usual plan of treatment has been to place the patient affected with goître upon the iodide of potassium, in doses of from five to ten grains in water after each meal. In the course of two or three weeks, if there has not been decided amelioration of the symptoms, this has been substituted by the tincture of iodine, given in doses of from five to twenty-five drops, which was placed in a capsule just before the patient took it, the dose being followed by a full glass of water, and given three or four times a day. Five drops were given at a dose the first day, six the second, and so on until the maximum dose was reached. If this did not speedily effect diminution in the size of the gland, I have also injected the enlarged thyroid with a three-to-five per cent. solution of carbolic acid in glycerin and water, using from twenty to thirty or even fifty minims of the solution at each injection, usually about thirty minims once a week.

Since the thyroid extract was recommended by G. R. Murray, in October, 1891, and the entire gland by F. Howitz in March, 1892, I have been much interested in the report of cases treated by this method, but on account of the inconvenience of obtaining the thyroid juice and from fear that it might become contaminated before used, I have not employed it. It was only recently that my attention was directed to the desiccated thyroids as prepared by Armour & Company, which, from the reputation of this firm for doing whatever it does in the best possible manner, I concluded would be reliable. I procured some of the desiccated thyroids about ten weeks ago and began their administration to two or three patients who were

then under my care. I have since used the remedy all told in six cases of goître, the histories of which I will presently give.

The employment of these animal products seems to have had its origin in the experiments of Ewald and Schiff, who, in 1887, removed the thyroid gland from dogs, and found that death occurred after a period of hypnotic apathy, followed by tetanic contractions of muscles.

Schiff found that by removing the two lobes at intervals of twenty-five to thirty-five days the animal might survive. Ewald also found that a thyroid extract injected into a healthy dog hypodermically caused a similar but temporary condition of apathy.

The survival of some thyroidectomized animals may have been due to accessory thyroids, as pointed out by F. Fuhr. A close relation between the normal action of the nervous system and functional activity of the thyroid was here apparent, but whether it was due to the presence in the blood of a substance secreted by the thyroid or whether the glands metamorphosed something derived from other organs was not determined.

Horsley's experiments on monkeys indicated that the changes due to the removal of the thyroid were caused by impaired nutrition. His further conclusion that the gland had a hæmatopoietic function is disputed by Virchow and Waldeyer.

As to the ætiology of goître, Lustig professes to have found a specific bacillus in water from the Aosta Valley, where cretinism and goître are endemic, but it seems very doubtful whether this theory can be substantiated.

As pointed out by the Reverdins, of Geneva, removal of the thyroid in man is followed by myxœdema, and in children by arrest of development. Sanquirico and Oreccia note that herbivorous animals stand the removal of the thyroid better than carnivora. Biondi, basing his opinion on histological study, maintains that the alveoli of the thyroid secrete a colloid material which passes into the lymphatic channels. Albertoni and Tizzoni state that the blood corpuscles acquire in the thyroid the power of fixing oxygen.

Mobius contrasts Graves's disease with myxœdema, the former being due to excitation and the latter to arrest of the functions of the thyroid. Ord says that myxœdema, sporadic and endemic cretinism, cachexia strumipriva, and operative myxœdema of animals are all due to annihilation of the function of the thyroid body.

The myxœdema committee, appointed by the Clinical Society of London in 1887, reported, after an exhaustive study of this disease, that one condition common to all consisted in destructive changes in the thyroid.

William Robinson, in the *British Medical Journal*, vol. i, 1893, tabulates the following conditions associated with or resulting from deficiency of the thyroid secretions:

1. Cretinism.
2. Congenital goître.
3. Atrophy of the thyroid gland in childhood (semicretins).
4. Goîtrous degeneration symptoms in proportion to the amount of the thyroid gland destroyed.

5. Extirpation of the thyroid causes cachexia strumipriva.

The use of the thyroid gland as a medicament was naturally suggested by the ascertained pathology of myxœdema, and the relation of myxœdema to goitre doubtless suggested its use in the latter. Among the earlier experiments Eiselberg saved two animals from the development of myxœdema after removal of the thyroid by grafting a thyroid under the peritonæum. The first operation on man to an account of which I have had access was that reported by M. Lannelongue, of Paris, in the *Transactions of the Biological Society*, March 7, 1890. This consisted in the transplantation of two-thirds of a sheep's thyroid subcutaneously under the breast. In England, Victor Horsley, following the experiment of Eiselberg (*British Medical Journal*, February 8, 1891), suggested grafting the thyroid gland.

The first successful transplantation of the gland in England was performed by J. W. Collins, May 2, 1892, at the Temperance Hospital, Hampstead Roads. He reported that in cases so treated menorrhagia, headache and melancholia were relieved in twelve hours. His ultimate results are not recorded. The permanence of effect depends upon the vitalization of the gland. If the gland becomes absorbed the effects are temporary.

G. R. Murray (*British Medical Journal*, October 2, 1891) suggested the hypodermic use of thyroid juice made by mincing a gland from the sheep, covered with one cubic centimetre of equal parts of glycerin and a five per cent. solution of carbolic acid, and straining or decanting the pinkish juice that rises on standing twenty-four hours. Of this juice enough should be used to supply the normal secretion of the thyroid gland, which he estimates at about one minim a day, but the exact dose was not determined.

F. Howitz, professer of clinical surgery at Copenhagen, claims priority in the internal use of the entire gland (March, 1892).

Dr. H. W. G. Mackenzie, in 1892, suggested the internal use of two fresh glands daily, minced with beef tea or with glycerin; later to be taken twice a week, then at longer intervals. No ill effects were recorded; but when a large amount was taken for several days the pulse was increased in frequency and the heart was apparently somewhat enfeebled.

The results of the treatment of myxœdema by thyroids seem favorable when the glands are given internally, or hypodermically in the form of a carbolized glycerin extract, or in the form of desiccated thyroids, the dose depending upon the concentration of the preparation.

The use of this substance in obesity was reported by H. W. G. Mackenzie in the *British Medical Journal*, July 21, 1894, but the results were doubtful. His patient lost eight pounds and a half during the first month, but subsequently gained five pounds within three months, although the remedy was still continued. He had no bad effects from the remedy, but thought it had little influence on the condition.

W. Towers-Smith, in the *British Medical Journal*, July 14, 1894, reports a case of obesity improved by the remedy, though it caused some illness and he considered it unsafe. Of Ewald's three cases, reported in *Berlin klin. Woch.*, January 14 and 21, 1895, the first patient exhibited no change; the second lost 3·5 kilogrammes, and the third lost 9·2 kilogrammes; this

case had a superficial appearance of myxœdema, but not the characteristic symptoms.

I speak of the use of these remedies in myxœdema because this is the first disease in which they were considered of benefit, though I have had no experience with that affection. I speak of their use in obesity because reports show that they sometimes have a good deal of influence upon the weight; but I desire specially to call attention to the medicinal use of the thyroid gland in the treatment of goitre, and incidentally in the enlargement of the thyroid existing in what is known as Graves's disease, or exophthalmic goître. Reported cases of goître treated by thyroid glands seem somewhat rare in medical literature, though, no doubt, there have been some that I have not been able to discover in the journals to which I have had access in the Newberry Library, of Chicago.

As late as April 14, 1894, the editor of the *British Medical Journal*, vol. i, page 839, said, in answer to a query as to the effect of the thyroid treatment, that "only amelioration has been noticed, as far as we are aware, and no actual cure in exophthalmic goitre"; but Dr. P. Bruns, in *La Semaine medicale*, 1894, vol. xiv, page 968, reports the cure of nine cases of goître out of twelve treated. He used an extract of raw glands, in doses of one and a quarter to two and a half drachms, every two to eight days. Parenchymatous enlargement was reduced, but cysts were not affected.

W. B. O. Ferguson, in the *British Medical Journal*, vol. ii, 1894, reports a case of exophthalmic goître improved by the internal use of a quarter of a thyroid gland twice a day. Treatment was begun on December 14th, 1893, and extended to July, 1894, but it had to be discontinued for a short time on account of diarrhœa and nausea.

A. G. Auld, of Glasgow, reports in the *British Medical Journal*, July 7, 1894, a case of exophthalmic goitre of two years' standing, in which the thyroid was much enlarged, with slight exophthalmia. This was treated by him and Dr. Charteris with Burroughs and Wellcome's thyroid tabloids, given every three days. The dose was increased to two tabloids daily for nine days. The patient was nauseated and perspired freely. They thought the tabloids caused increase in the Graves's disease, due to an increase in the thyroid secretion.

H. W. G. Mackenzie reports little effect in a case of exophthalmic goître associated with obesity. As to the toxic action of the thyroids, Ewald noted a case of glycosuria during treatment, which ceased when the remedy was discontinued.

In *La France medicale*, January 25, 1895, we find the statement that "thyroid juice poisons the heart and may cause death by syncope, one adult and two children having died in Paris hospitals from its exhibition. The juice has a cumulative effect, like digitalis, and great care is necessary to avoid excitement or exertion during treatment and for some time afterward. Sudden deaths in England took place several days after treatment was discontinued. The pulse may reach 110, or even 160, under exertion during treatment, and its rapidity and quality should be carefully watched."

In the *Revue des sciences medicales* of April 15, 1895, E. Gley notes as the result of administration of thyroid extract in some cases loss of weight; in others signs of Basedow's disease.

Langendorff, in 1889, noted sudden death, with coma and convulsions, following hypodermic or intravenous injections in animals of the thyroid extract.

Alonzo's and Horsley's experiments are negative.

Fred Gourlay, in *British Medical Journal*, vol. ii, 1892, expresses the opinion that the active principle of the thyroid extract is a globulin which may be prepared by mincing and drying the gland at a low temperature Ewald suggests peptic digestion and dialysis.

Just as I was completing this paper an address on the thyroid therapy, by Dr. S. J. Meltzer, before the German Medical Society of New York, March 4th, came to hand (*New York Medical Journal* of May 25th). He reviews at length the earlier literature of animal extracts, giving particular attention to the use of thyroids in myxœdema. He concludes that in the absence of the normal secretion of the gland the patient will need continuous treatment by thyroids, with occasional intermission, to supply the deficiency.

He considers a feeling of chilliness the earliest symptom of return of myxœdema requiring treatment, as this is noticed before weight increases. He states that the poisonous effects so often noted are due to overdoses, and that they can be absolutely avoided by giving at first only the equivalent of a grain of the powder. The dose may be gradually increased, while carefully noting the pulse and temperature. In his cases the more serious symptoms were avoided, but he met some acceleration of pulse, fatigue, some tremor, headaches and diffuse pains, and in some cases urticaria. Iron and strychnine relieved the weakness, salicylate of sodium and phenacetine the pains and aches. A sixteenth of a grain of pilocarpine, three times a day, relieved the urticaria.

For obesity he considers thyroids the best remedy. By limiting the dose to three grains three times a day he avoided unpleasant effects while reducing the patient's weight about a pound a week.

From the fact that dyspnœa and palpitation, when present, were promptly relieved, he infers that the first disappearance of fat occurs in the heart, and, further, concludes that small doses will prove to be effective in the treatment of *cor adiposum*.

I have used only the desiccated sheep's thyroids already referred to, twelve grains of which represent one entire average gland (two lobes) and in quite a large number of cases which I will summarize the same preparation has been employed. Armour & Company kindly furnished me the addresses of a number of physicians who had applied to them for the remedy. I have written to these gentlemen, and have obtained a number of replies, stating the effects obtained in numerous cases which I will summarize. My own cases are only six in number, and all of them, with one exception, are still under treatment, but the results are so marked as to indicate a decided influence upon the disease by this remedy. In several of the cases it will

be noted that they were first placed under the treatment which I have used for a number of years, and in two it will be observed that they had already been relieved or apparently cured from the same disease by this treatment in former years. The cases are as follows:

CASE I.—L. A. W., a man, aged thirty-six years, came to me February 19, 1889, complaining of a sense of fullness in the throat, hoarseness, and difficulty of breathing, though his general health was good; weight, two hundred and twelve pounds. At that time he was suffering from laryngo-bronchitis. On February 28th it was noted that he had acute swelling of the thyroid gland, for which he was given the iodide of potassium, in doses of from five to eight grains, after each meal, with a twenty-fourth of a grain of arsenious acid, a third of a grain of extract of nux vomica, and three grains of extract of quebracho. Four days later the left lobe was smaller and the breathing was somewhat easier. The iodide was increased to ten grains at a dose. Similar treatment was continued for the next twelve days, when he was placed upon the tincture of iodine, in doses of from five to twenty drops, given in capsule after each meal. A week later the gland was injected with thirty minims of a five per cent. solution of carbolic acid. Six weeks later the swelling in the thyroid had mostly disappeared. Two weeks later it is noted that the neck measured eighteen inches and five-eighths, and there was no difficulty in breathing. The treatment was continued, and two weeks later, May 8th, he stated that he thought the neck was well. Ten weeks later it was noted that the swelling of the thyroid had very nearly disappeared, and he had lost twenty-five pounds in weight. A month later, no return of the enlargement of the thyroid; weight, a hundred and eighty-five pounds.

The patient disappeared, but returned on the 10th of October, 1891, when it was stated that the neck had been swelling for the last four or five weeks; this soon disappeared under treatment similar to that used formerly.

I saw the patient in March, 1894, but there had been no return of the goître. On May 13, 1895, the patient called upon me again, saying that for three or four weeks there had been some difficulty in breathing. The collar seemed very tight, and it was observed that there had been considerable enlargement of the thyroid gland. The neck at this time measured seventeen inches and a quarter at the largest place. The patient weighed two hundred and six pounds.

He was given the desiccated thyroids, in doses of three grains, three times daily. He returned twelve days later, stating that at the end of two days the difficulty in breathing had disappeared, and since commencing the medicine the swelling had steadily decreased. His neck at this visit was of normal size, measuring sixteen inches. He departed apparently well and has not since been heard from.

CASE II.—E. M., a woman, aged twenty-one, came under my care in April, 1890, because of an enlargement of the thyroid that had lasted ten or twelve years. She had been frequently troubled with violent cough. There

was neither exophthalmia nor heart symptoms, but the pulse was 108, though regular; general health and digestion were good; there were no abnormal signs over the chest; the neck measured sixteen inches.

The enlarged gland was injected with thirty minims of a five per cent. solution of carbolic acid, and she was given seven and a half grains of potassium iodide in water after each meal. A week later there had been no change in her condition; the injection was repeated and tincture of iodine given in doses of five to twenty-five drops after eating.

I did not see the patient again until three years later, April, 1893. She stated that she had been fairly well during the interval, but that the gland had begun to swell again recently. The gland was again injected with twenty-five minims of a five per cent. solution of carbolic acid, and the tincture of iodine was ordered to be taken in doses of from five to twenty-five drops after each meal. She returned in about a week and the treatment was continued. I did not see her again until February 22, 1894. She stated that from the last treatment the swelling in the gland had much diminished and that she had no trouble for a long time, until about a week previous to this call, when the gland suddenly began to enlarge and caused some difficulty in swallowing. At this visit the gland was injected with twenty-five drops of a three per cent. solution of carbolic acid and she was again given tincture of iodine. The treatment was continued, the injection being given about once a week for the next six weeks. During this time there was very little improvement, though the difficulty in swallowing diminished. In the early part of May I found that the uncomfortable symptoms had disappeared. The iodine had been used continuously and there had been another injection of the carbolic acid solution. June 14, 1894, the neck measured only thirteen inches, and she appeared to be cured. I did not see her again until May 14, 1895, when the neck measured fourteen inches and a half. She was given at this time two grains of the desiccated thyroids after each meal, and a few days later the dose was increased to three grains. A week later it was noted that the circumference of the neck had diminished a quarter of an inch. At that time the desiccated thyroids were increased to four grains three times daily. A week later, pulse 104; neck measured the same. Seven days later, pulse 116; neck measured only fourteen inches. She had been taking only two grains of the desiccated thyroids three times daily for the past week and no injections had been used. She is still under treatment.

CASE III.—W. R., a lad, aged fifteen years, came to me January 9, 1895, complaining of shortness of breath and wheezing respiration upon exercise, with enlargement of the thyroid gland, which had been present for five years.

I found that his mother apparently had consumption, and a maternal great-aunt and cousin had suffered from goître. The patient's general health was good; he weighed one hundred and forty-seven pounds, and the pulse was 90; action of the heart regular, with no abnormal physical signs. The neck measured at this time fifteen inches and a half. Patient was

given five grains of iodide of potassium after each meal, and thirty minims of a three per cent. solution of carbolic acid were injected into the thyroid gland. Similar treatment was continued, the injection being made weekly until the 16th of February. At that time, after five weeks' treatment, the neck still measured fifteen inches and a half, and no perceptible improvement could be noted. He was then placed upon the use of desiccated thyroids, three grains three times daily; the carbolic acid injections were continued once a week. A week later he had noticed a decided decrease in the size of the gland, and the neck measured only fifteen inches. The dose of desiccated thyroids at this time was increased to four grains after each meal. A week later the patient was too ill to come to the office, but it was reported that the neck had gradually decreased in size. He had suffered from faintness and much from headache all the week. A week later, March 9th, he was still feeling so poorly that the dose of the desiccated thyroids was decreased to two grains.

He complained of having felt very weak and faint during the last few days. A week later he was free from headaches and faintness, therefore the desiccated thyroids were increased to three grains three times daily.

The gland was still decreasing in size. One week later, March 26th, about five weeks after the treatment was begun, he reported that he had lost fourteen pounds in weight, but he was feeling pretty well, excepting for frequent headache. At one of his recent visits I had noticed that he trembled a great deal during the consultation, and that he had the nervous appearance and arterial pulsations of one suffering from exophthalmic goître, but there was no prominence of the eyes. At this time the desiccated thyroids were reduced to two grains three times daily. The next week he again reported having had headaches two or three times during the week.

The neck was found to have been reduced to fourteen inches and an eighth, and about four-fifths of the enlargement of the gland had disappeared.

April 6th.—The neck still measured fourteen inches and an eighth; he had at this time gained three pounds in weight; his pulse was 140, and he was quite tremulous. Two weeks later the trembling had all disappeared, and there were no unpleasant symptoms; the treatment was continued.

May 4th.—Patient has had no headache the past week; the neck measures only thirteen inches and three-fourths.

He is still taking two grains of desiccated thyroids three times a day, and is also taking bitter tonics most of the time. He has had the gland injected with the carbolic acid solution nearly every week.

11th.—The dose of the desiccated thyroids was increased to four grains three times daily. On May 19th he again reported having had headaches, nevertheless the desiccated thyroids were increased to five grains four times a day.

25th.—He had a headache nearly every day after the last prescription. The neck was found to measure fourteen inches and a quarter, half an inch increase in the last two weeks; weight, a hundred and thirty-four pounds and a half, twelve pounds and a half less than when he began treatment. The desiccated thyroids were decreased to four grains three times daily.

June 1st.—The patient's general health is good, and there is no exophthalmia or trembling. The thyroid gland has been reduced at least four-fifths.

14th.—The patient has no unpleasant symptoms, and the size of the goître has been reduced fully ninety per cent. He is still under treatment.

CASE IV.—R. P., a woman, aged twenty-seven years, came to me on January 17, 1895, complaining of swelling of the right lobe of the thyroid gland, which had existed for about five years. It had caused no special inconvenience, but was slowly enlarging. There was no hereditary predisposition to the trouble; her general health was good; weight, one hundred and twenty-two pounds; pulse 95; no exophthalmia; digestion natural.

The neck, over the largest part of the thyroid gland, measured fourteen inches and five-eighths, and the swelling was limited to the right lobe. At this time she was given tincture of iodine internally, in doses of from five to twenty-five drops, to be taken in capsules after each meal, and the gland was injected with twenty-five minims of a three per cent. solution of carbolic acid.

The treatment was continued until February 12th; the solution of carbolic acid, however, had been increased in strength to four per cent. At this time there had been no diminution in the size of the gland. It was injected with thirty-five minims of a five per cent. solution of carbolic acid, and the tincture of iodine was continued. About a week later, on February 21st, the injection was repeated, and she was given the desiccated thyroids, in doses of from two to six grains, after each meal. The iodine was also continued. At this time the neck measured fifteen inches, three-eighths of an inch more than when treatment began. Six days later the neck measured only fourteen inches and three fourths. She had been taking six-grain doses of the desiccated thyroids for the last few days. The gland was then injected with fifty minims of a five per cent. solution of carbolic acid, and the iodine was discontinued. A week later she said she noticed a very marked improvement. The gland was injected; the measurement of the neck had diminished to fourteen inches. One week later the digestive organs were much disturbed, she was feeling very poorly, the pulse was 120, and the temperature was 100·2°. She had been taking six grains of the desiccated thyroids three times daily. At this time the dose was reduced to four grains. One week later she reported herself as feeling considerably better; treatment continued. A week later she complained that she had a bad headache every morning for the last week, though she had hardly ever suffered from it previously. The dose of the desiccated thyroids was reduced to three grains after each meal. The injection of the gland was repeated. A week later the amount of the desiccated thyroids was increased to four grains three times daily; the injection was repeated, and it was noted that she had lost three pounds in weight. At the next visit she complained of being very tired, though she suffered but little from headache.

Maltine with the hypophosphites, in doses of from one to four drachms, was given after each meal. A week later the dose of the desiccated thy-

roids was increased to five grains four times a day, and the injection was repeated. A week later she reported herself as feeling well; she had lost no more weight; a week later, on May 7, she weighed a hundred and twenty-nine pounds, or seven pounds more than when treatment was begun. A week later, on May 14, the neck measured only thirteen inches and a half. She had been taking five grains of the desiccated thyroids three times daily; the dose was increased to six grains, and she was given the injection of five per cent. solution of carbolic acid, thirty minims as before. Subsequently the patient called once a week and treatment was continued.

June 11th.—The appetite good, the weight as before; there has been little headache and no other unpleasant symptoms; the measurement of the neck remains the same, thirteen inches and a half; but the gland seems to have diminished in size about eighty-five per cent. from the beginning of the treatment with the desiccated thyroids. Still under treatment.

CASE V.—B. W. G., a man, aged twenty-six years, came under my care on March 18, 1895, complaining of palpitation of the heart and occasional dyspnœa. He exhibited marked exophthalmia and enlargement of the thyroid gland, the latter varying with exercise. He had been affected for three years, but had never suffered from any other disease excepting rheumatism, of which he had an attack the previous fall, lasting two weeks.

His mother and two sisters have also had goitre. He used neither stimulants nor tobacco, but took about three cups of coffee daily. His general health was good; weight, one hundred and fifty-two pounds; pulse, 102, very irregular; temperature normal; at times wheezing respiration and slight cough; he had been troubled somewhat with looseness of the bowels ever since the goître was first noticed. Over the upper portion of the goître the neck measured fourteen inches and three-quarters; over the lower portion fifteen inches and three-quarters.

Upon examination of the chest the cardiac pulsations were noticeable all over the præcordia, and cardiac dullness was found to extend three-quarters of an inch to the left of the normal position. There was some want of synchronism in the action of the two sides of the heart noticeable at times, but there were no abnormal murmurs. Upon examination, the rapidity of the heart's action increased to 160 or 170 a minute. He had been taking ten-minim doses of tincture of strophanthus for some time. He was given desiccated thyroids, two grains with each meal; also tincture of strophanthus, ten minims; fluid extract of cactus grandiflora, three minims; tincture of digitalis, seven minims and a half, in elixir of pepsin enough to make two drachms, three times a day. Coffee was interdicted. He was directed to report in a week, but he did not return until two weeks later, when he stated that he had taken cold shortly after the last visit and had been coughing ever since.

The swelling of the thyroid gland had markedly diminished. The neck measured half an inch smaller at the upper part and five-eighths of an inch smaller at the lower part. During this time he had lost eighteen pounds in weight. He complained of poor appetite and frequent vomiting after break-

fast. He was given maltine with hypophosphites, the use of desiccated thyroids was continued, and he was also given for two or three days ten-minim doses of tincture of strophanthus with a third of a grain of extract of nux vomica, two-thirds of a grain of extract of hyoscyamus, one grain of camphor, and four grains of ingluvin. He was directed to return in four days, but he did not. About a week later I was informed that he had become very ill and seemed in a critical condition. I told his friends to have the medicine discontinued at once, and I think this direction was followed. I did not see him again for four weeks, when he stated that he had lost five pounds since the last weighing, but his cough had ceased and he was feeling very much better. He told me that he had been confined to the bed for two weeks after the last visit, but subsequently had much improved, the appetite returning shortly after discontinuing the desiccated thyroids. There had been no renewed enlargement of the thyroid gland up to this time; the pulse was slower, and the exophthalmia about as at first. All told, the diminution of the thyroid gland appeared to be about seventy-five per cent.

CASE VI.—B. E. J., a woman, aged fifty years, came under my care on May 3, 1895, complaining of difficulty in breathing for the last two years, apparently from obstruction in the larynx. She complained also of cough, especially when eating. There was no pain, the appetite and general health were good, and the digestive organs were in an excellent condition.

Upon examination I found marked thickening and hardness of the isthmus of the thyroid gland, which measured about an inch from above downward and about three-quarters of an inch in thickness. There were no abnormal signs over the lungs, heart, or aorta. Over the largest part of the growth the neck measured thirteen inches. She was given a third of a grain of extract of nux vomica and two grains of the desiccated thyroids three times daily. She returned eleven days later, reporting that she felt much better. Her cough was looser, though at times she still suffered from shortness of breath. She was given at this time half a grain of extract of nux vomica, half a grain of extract of hyoscyamus, and three grains of desiccated thyroids. A week later she returned, reporting that she felt much improved, but that she had a weak spell a few days previously, and that her appetite was not very good. The enlarged gland had considerably diminished in size, it felt much softer, and the neck at the most prominent part measured only twelve inches and a half.

June 14th.—She is still under treatment and professes to be steadily improving.

I have received personal letters from physicians in various parts of the country containing the following records:

Dr. W. O. Taylor, of Princeton, Ontario, reports twenty-five cases of goitre treated by internal administration of the thyroid gland in the last twenty weeks. The patients were all females, and in age ranged from fourteen to sixty-one years. The duration of the disease in seven cases extended from six to fifteen years, the rest running from three months to three years. These cases were treated from seven to twenty weeks each, with an average

of from five to ten grains of the desiccated thyroids three times a day for three weeks. All except seven cases were improved.

The greatest reduction in the size of the neck noted was two inches and three-quarters. In six cases it was reduced two inches or over; in ten cases an inch and a quarter or less.

As to the weight, three patients lost an average of fifteen pounds, while a few others lost from one to four pounds. Headache was noted in thirty per cent. of the cases, dizziness in thirty-seven per cent., trembling in twenty-five per cent. while rapid pulse was noted in five cases and weakness in five cases, the weakness being so great in one case as to render the discontinuance of treatment necessary.

Dr. Taylor attributes the prevalence of goitre in his locality to the very hard water, and states that in the use of thyroids he obtained little effect unless the patients drank distilled water. He has had the very large number of two hundred and seventeen cases of goitre in eight years.

In addition to the twenty-five cases of goitre reported he has also treated with the thyroids three cases of myxœdema in one family — a brother, sister, and a cousin. These cases were under treatment from three to seven months with doses of from five to ten grains three times a day, the disease having existed from four to seven years and a half. One patient was improved for seven weeks, then became worse. In the second the symptoms were kept stationary. In the third case he found treatment very satisfactory; the mental condition was decidedly improved, and the general swelling of the body largely disappeared.

Dr. J. Williamson, of Ottumwa, Ia., reports two cases of goitre treated for twenty-one days, first with five grains, later with two grains and a half, without effect on the goitre, and with the usual headache, etc. The weight diminished perceptibly.

Dr. F. A. Packard, Kearney, Neb., reports one case of goitre treated with ten-grain doses three times a day, but it caused so much trembling, dizziness and nausea that he gave it no further trial.

Dr. S. W. Connell, of Milwaukee, reports one case in which the circumference of the neck was reduced an inch and three-quarters by two months' treatment with five-grain doses. This patient had suffered with chronic headaches for years, so that the influence of the thyroid on that symptom is uncertain.

Dr. H. M. S. Byron, of Whiteside, Tenn., reports one case of rapid reduction of the goitre of twelve years' standing, and some loss of weight, without headaches or dizziness, but with some trembling, rapid pulse, and weakness, under sixteen weeks treatment with two-grain-and-a-half doses.

Dr. Thomas H. Briggs, of Battle Creek, Mich., treated four cases of goitre with the desiccated thyroids for six to eight weeks with excellent results, beginning with five-grain doses given at least two hours from meal time, three times a day, for the first week; he later reduced the dose to two or three grains. The goitres were all much reduced in size, and the weight was usually slightly reduced without headache or other disagreeable symptoms, except nausea and dizziness. He found that the disgust for the rem-

edy could be overcome by giving solution of strychnine with it. He had also used the remedy in a case of lymphadenoma, one of carcinoma, and one of tubercular glands of the neck, but without material results.

Dr. Steele Bailey, of Stanford, Ky., treated one case each of goitre and of myxœdema, giving five-grain doses three times a day for three months. Treatment then had to be discontinued in both cases on account of the usual ill effects from such large doses, though the goitre decreased in size, while the total weight of body increased five pounds. The myxœdema grew worse in spite of thyroid, belladonna, and other medicaments.

Dr. J. K. P. Rogers, of South Portland, Me., treated a case of myxœdema of nine years' standing in a woman fifty-seven years old. Two months' treatment removed all evidence of the disease, beginning with three grains, given on alternate days, reduced a grain and a half after the first week, and later five grains twice a week. The weight was reduced fifteen pounds in the first month and three pounds in the second. By the use of such small doses at longer intervals the unpleasant effects were entirely avoided; but the case is remarkable for a symptom I have not elsewhere heard described. The patient was seized with intermittent pains, the exact duplicate of those of the third stage of labor, both in appearance and in severity. These persisted for four days after treatment had been discontinued, and required morphine hypodermically to control them. Later the dose was diminished on account of sciatic pains and stiffness, which prevented the patient from standing erect, and lastly on account of epigastric pain and palpitation.

Dr. George W. Hall, of Chicago, reports a case in which I recommended the desiccated thyroids, in which the goitre, which had existed for six years, was completely cured by four weeks' treatment by doses of two to three grains. The patient during the treatment had suffered much from headache, with slight dizziness, but no other unpleasant symptoms.

Dr. C. H. Ott, of Chapman Quarries, Pa., treated a case for ten days with thyroids, with improvement.

Dr. C. A. S. Prosser, of Boise City, Idaho, treated one case for five days with a sample only, without appreciable change.

Dr. A. C. Webber, of Cambridge, Mass., treated one case for four weeks with five-grain doses, with almost complete disappearance of the goitre and without headaches or other symptoms but rapid pulse.

Dr. P. F. Metz, of New Haven, Conn., treated two cases with improvement, with two grains two or three times a day.

Dr. Stanley P. Warren, of Portland, Me., gave a few five-grain doses, when the patient became frightened at the terrific face and head congestion and stopped treatment. However, within two weeks the tumor decreased half an inch.

Dr. F. L. Shaw, of Machias, Me., reports one case treated for a month by five-grain doses, the swelling being reduced half an inch, and no disagreeable symptoms except headache.

Dr. C. Walliser, of Sonoma, Cal., reports one case of goitre treated by

three two-grain tablets daily for a week without effect, except all the disagreeable symptoms; for this reason treatment was discontinued. He also reports a case of myxœdema treated for two weeks, the result being unknown so far.

Dr. C. S. Bolton, of Richmond, Ky., treated a consumptive patient with goitre, with improvement.

Dr. R. B. McKeage, of Shickshinny, Pa., treated one case of myxœdema of thirteen months' standing with five-grain doses for twenty days. Patient improved enough to return to work.

Dr. R. A. Lancaster, of Gainesville, Fla., gave the remedy for a short time, but the patient was nauseated and quit treatment.

Dr. Henry G. Ohls, of Chicago, noting the general loss of weight in the treatment of goitre by the thyroids, gave two patients with obesity the remedy in doses of two to four grains three times a day. One used the remedy ten days and gained five pounds, but stopped the treatment on account of severe backache and stiffness of limbs, but without headache or other symptoms. The other lost five pounds in two weeks' treatment, but discontinued it at that time on account of daily rather severe headache. The last patient has recently begun with smaller doses, but I cannot yet report results.

Dr. G. L. Williamson, of Homer, Ill., reports one case of twenty-five years' duration, treated for three weeks with six-grain doses, reduced an inch and a half. In this case there was some puffiness of the face, which disappeared under treatment, and the patient, a minister, thought that his mind was more acute.

Dr. B. F. Van Valkenberg, of Long Prairie, Minn., had a fatal case of exophthalmic goitre, which he treated for two weeks with the thyroid, with negative results.

Summary.—With my six cases treated by internal administration of the desiccated sheep's thyroids, and those reported to me by personal letter, I have, all told, fifty cases of goitre, not including one case of advanced exophthalmia, in which the patient died one month after treatment began. In these I find the following results: The swelling was reduced in thirty-eight cases; swelling not affected in eleven cases; no report in one case.

Of the cases where no improvement was noted the remedy was used only five days in one and a week in another. In four cases the goitre had existed from six to twenty-five years and perhaps was largely cystic, though not specified.

I have reports of seven cases of myxœdema, with the following results: Improved, five; not affected, one; unknown, one.

Of these, in one case the patient improved for seven weeks and then deteriorated, though treatment was continued for three months. Two cases of obesity without other disease are reported. One of the patients lost five pounds; one gained five pounds.

The symptoms noticed after the administration of this remedy, observed in the various cases reported by me and reported by personal letter, have been: Headache in eighteen; no unusual symptoms in eight; no report, twenty-four; dizziness in twenty; no unusual symptoms in five; no report in

twenty-five; trembling in fourteen; no unusual symptoms in five; no report in twenty-one; rapid puise in eleven; no unusual symptoms in six; no report in thirty-three; weakness in seventeen; no unusual symptoms in ten; no report in twenty-three; backache in one; nausea in seven; no report in forty-three; lost weight in twenty-five; gained weight in two; mind improved in two; nervousness in one; uterine contractions in one.

Conclusions.—From a consideration of the history of this subject and an analysis of the cases which we have presented, the following conclusions seem to us justifiable.

1. Thyroid products produce marked physiological effects upon the nervous and circulatory systems, as indicated by headache, dizziness, pains in other portions of the body, and great weakness, and by flushing of the face and rapidity of the heart's action.

2. Some of these unpleasant symptoms usually occur when a daily dose is reached corresponding to one and a half or two entire thyroid glands of the sheep.

3. If the administration of the remedy in doses that cause such symptoms is continued for a few days, constitutional effects are produced indicating that persistent use of doses of from six to twelve grains of the dried thyroid (equivalent to one-half or one thyroid gland), three times daily, might produce fatal results.

4. Desiccated thyroid glands appear quite as active as the liquid extracts and more stable.

5. Internal administration appears quite as effective as hypodermic medication.

6. For internal use, the adult dose of the desiccated thyroids should not exceed two grains three times daily at first, but the dose may be gradually increased to two or three times this quantity, provided it does not cause unpleasant symptoms. There is no evidence that moderate doses have an injurious effect.

7. The remedy in some cases has a pronounced effect on the body weight, but this is very uncertain and varies so greatly in different persons, and in the same individual at different times, that there is strong reason for suspecting that the loss of weight which sometimes follows this administration may be due entirely to disturbance of the digestive organs.

8. In the treatment of myxœdema the remedy has undoubted value and appears to benefit quite a large percentage. In these cases it is probable that the best results will be obtained by giving it at intervals for a long time.

9. In exophthalmic goitre the remedy causes rapid reduction in the size of the gland, but it has no perceptible effect upon the exophthalmia, and it apparently aggravates the heart symptoms. In this disease it must be used guardedly and its effects must be carefully watched.

10. In many cases of goitre internal administration of full doses of the products of the thyroid is followed by a most remarkable diminution in the size of the diseased gland. Improvement or cure may confidently be expected in seventy-six per cent. of the cases, but sufficient time has not yet elapsed to determine what the final results will be. It is probable that cystic growths in the thyroid gland would not be influenced by this remedy.

11. Clinical experience has not yet demonstrated that this remedy is of value in other diseases, but its effect in diminishing the size even of very firm and hard enlargement of the thyroid gland would certainly justify experimentation in other directions.

34 Washington Street, June 14th.

The British Medical Journal of August 10, 1895, treating editorially of Professor Schäfer's (University College, London) Address on Internal Secretion, delivered at the Annual Meeting of the British Medical Association, at London, July–August, 1895, says:

In selecting the subject of internal secretions for his address Professor Schäfer is to be congratulated, for the study of this deeply interesting problem is not only important to the scientific physiologist, but is of the greatest practical value to the practitioner. Those in busy practice formed the great bulk of the audience, and they have often but little leisure to study the rapid advances of science; they therefore owe a deep debt of gratitude to Professor Schäfer for placing before them in a concise and lucid form the main facts relating to the subject.

The term "internal secretion" is of recent origin, though many of the main facts have long been recognized. Removal of the organs of generation markedly modifies the whole build and temperament of an animal; such an operation causes more than a mere cessation of the generative function. This, of course, has been known for centuries; the effects of the removal of the thyroid have not been known so long, but forty years ago Schiff did the experiment, and noted many results; his work was forgotten until it was unearthed subsequently to the important researches of Ord, Kocher and Horsley. So, too, in the case of the pancreas, the association of pancreatic disease and diabetes was noted by clinicians long before the time of von Mering and Minkowski. Professor Schäfer points out that some glands can be removed without injury to life, such as the salivary and and mammary glands. If these organs produce an internal secretion similar to that produced by other glands, the loss after removal must be repaired vicariously.

The address may be subdivided into sections, according to the different glands considered, and evidence is adduced that the liver, the kidneys, the pancreas, the thyroid, the pituitary body, and the suprarenals all produce a something which is poured into the venous blood, and is of benefit to the whole body, producing widespread effects on nutrition. In the case of the pancreas, there is also the external secretion, the pancreatic juice, to be considered, and Professor Schäfer makes a new point when he suggests that the newly discovered internal secretion of the pancreas, the removal of which produces diabetes, is connected with the epithelial islets, in the organ, which have for so long puzzled histologists.

The thyroid naturally comes in for a large share of notice, for it is in relation to this organ that the best practical results have followed close on the heels of experimental investigation. Professor Schäfer is, however, careful to point out that the successful treatment of myxœdema with thyroid injection or thyroid grafting does not necessarily mean a similar success in the treatment of diseases of other organs by injections of extracts of those organs. He, however, has a small amount of evidence to show that cases of Addison's disease are benefited by the exhibition of extracts of suprarenal capsules taken by the mouth.

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