THE THYROID AND THYROID THERAPY.

By Haldor Snévé, M. D.

St. Paul.

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In the midst of the conflict it is not so easy to take stock of the exact situation and to prognosticate the ultimate direction of the currents of opinion. Today we are right in the flood of a lot of new facts and new theories about the "internal secretions," and especially concerning the thyroid gland and its perversion of function, to which last I wish to direct your attention through the medium of a brief resumé of the subject.

HISTORICAL.

For years the frequent occurrence of the goitre in mountainous countries, especially in the valleys of the Alps, was noted, and attention was directed almost exclusively to the drinking water for the noxious element which caused the disease; chemistry was exhausted in the vain effort to explain its origin, and later bacteriology was appealed to, culminating in the apparently important discovery of the over-successful Klebs of flagellates (cercomonas globulus and navicula), which caused goitre in dogs who were given water containing them. The physiology of the thyroid was a sealed book until the dawn was heralded by Schiff, who described the effects of complete thyroidectomy in dogs in 1859. In 1882 and 1883, after Reverdin's description of operative myxœdema resulting from removal of the thyroid for disease, Schiff again took up his experiments in 1884, and found that the grafting of a thyroid in the peritoneal cavity of a dog allowed him to remove the thyroid without the train of symptoms following, which he had described in his first experiments. Then came the intravenous injections of thyroid extracts by Vassale and Gley and then the subcutaneous use in England in a case of myxœdema with marvellous effect by Geo. R. Murray in 1891.

Howitz, of Copenhagen, first began the use of thyroid per os in 1892, and this is the mode of administration today. The occurrence of tetany was noted by Weiss in Billroth's clinic after total extirpation of the thyroid, and Reverdin described the cachexia following its extirpation giving us the conception "cachexia strumipriva." Kocher also enriched our knowledge along this line, and von Eisselsberg, at Vienna, made a series of studies and presented the whole subject of experimental extirpation of the thyroid in a masterly manner. Brown-Sequard, a few years in advance of the rest of the world, published his ideas on the influence of the secretions of the ductless glands on nutrition and especially on injection of testis and ovary, which bade fair in the mouths of the ignorant to raise a cloud of ridicule which would darken the monument of gratitude the world owes to that most brilliant investigator. Brown-Sequard has given us the name internal secretion as applied to the ductless glands, meaning thereby that in these some sort of secretion was elaborated, absorbed into the blood tó exert through this and the nervous system an effect especially on the nutritive functions of the cells. How correct he was is apparent when we view the changes occurring in the organism consecutive to castration (eunuchs, oxen, capons), and when we see the effect produced in so-called "backward children" (sporadic cretins), by thyroid feeding, and the marvellous changes effected in myxœdema by the same treatment. Horsley's experiments on monkeys connected myxœdema with total extirpations of the thyroid. Kocher took the ground in 1892 that cretinism, both sporadic and endemic, is due to loss of function of the thyroid. Osler collected sixty cases of sporadic cretinism in America, in many of which thyroid had been used with marvellous results. Chemistry came to the aid of experimental pathology to explain why thyroid gland could be swallowed, exposed to the digestive juices and still exert the same wonderful effect on nutrition that could be produced by injections into veins and subcutaneously, and to further explain why iodine and its salts frequently exert a curative action on simple goitre. For the first time iodine was found in the tissues as an organically united constituent, united with the colloid substance manufactured by the thyroid.

In 1896 Baumann found in the colloid secretion material containing iodine, which when

*Read before the Ramsey County Medical Society, April 25, 1898.

decomposed yields a non-proteid substance to which he gave the name of iodothyrin, a substance unaffected by digestive juices and exposure to acids. The experiments of Roos on dogs, and Ewald and Bruns on clinical cases have pretty thoroughly demonstrated that this is the active principle, so to speak, of the thyroid secretion.*

ANATOMY.

The thyroid gland has no excretory duct and hence is classed among the ductless glands. It was formerly described as consisting of two lateral lobes about two inches in length and an inch in breadth, joined together at the lower third by the isthmus, half an inch in breadth and the same in length, but a Swedish anatomist, Sandström, described two accessory glands connected with the lateral lobes which he called parathyroids. In 1891, Gley, of Paris, confirmed these researches, and later Kohn demonstrated the existence of four of these glandules, two at each lobe.

I have here a dissection of the sheep's glands in order to show you the thyroid and parathyroids. Sometimes there is a third lobe of conical shape arising from the isthmus or left lobe. The gland is made up of connective tissue septa dividing the organ into lobes and lobules, the last consisting of acini lined with a single layer of cubical epithelium surrounded by a very vascular connective tissue containing large lymphatics and blood vessels. These acini contain a viscid, homogeneous, semi-fluid, slightly yellowish material.

The nerves are probably derived from the sympathetic (cervical ganglia).

PHYSIOLOGY.

It is one of the triumphs of vivisection that practically all we know concerning the function of the thyroid together with all the beneficial results of treatment based on such knowledge is derived from experiments on animals. What a triumph for experimental pathology that myxœdema, a terrible affliction, is now amenable to treatment and that idiotic children can be reclaimed through scientific therapy! The function of the thyroid is now partly revealed by the discovery by Baumann of iodothyrin, and the beautiful studies of Baumann and Roos on its relation to the gland and to the functions of the body. It appears from their experiments that "the thyroid gland gives off something to the blood which in some way affects favorably all or part of the tissues of the body." When this substance is lost through atrophy or by extirpation of the gland we get the picture of cachexia strumipriva; the hair grows thin, coarse and dry, the lymph spaces under the skin fill up with a semigelatinous substance which gives a brawny feel to the touch, there is loss of the teeth and nails, of perspiration, muscular and mental weakness, and disturbances of the organs of special sense. On the other hand when the gland apparently hyperfunctionates we get the picture of exophthalmic goitre so-called; here the vaso-motor system is irritable, there is a subjective feeling of heat, the sweat is increased, the patient is mentally irritable, reacts quickly to external impressions, there is nervous restlessness, the eyes protrude and their normal action is interfered with; there may be tremor of any or all the limbs, the skin may become pigmented, the pulse greatly augmented and the patient grows thin through destructive metabolism and excretion; the administration of iodothyrin produces an increased elimination of carbonic dioxide and nitrogen in the urine, which also is increased in amount. At present we can only speculate on how the secretion of the thyroid acts on the tissues of the body. Two main hypotheses have been advanced: First, that the tissues form toxic substances which are neutralized by the thyroid secretion; this is the antitoxic theory; second, that the thyroid secretion promotes or regulates normal metabolism; this is the trophic hypothesis. All the newer evidence seems to point to the latter as the more probable one.

In 1892, Gley, of Paris, made experiments on rabbits, which showed that the extirpation of the thyroids without removing the parathyroids did not produce the symptoms of complete thyroidectomy ending in death. These results have been confirmed by Vassale and Generali in Italy, who further stated that removal of the four parathyroids in dogs and cats, leaving the thyroids intact, produced the acute symptoms of complete thyroidectomy and finally death. Rouxeau on rabbits partly confirmed Gley's statements. Finally Moussu made fifty-three experiments on dogs and cats and stated that from removal of the parathyroids acute symptoms supervened which rapidly ended in death, while those in whom these were left, and the thyroid body removed, survived with symptoms of cretinism. All this seems to give the thyroid and the parathyroids different functions. There seems to be conclusive evidence that ingestion of thyroid or iodothyrin prevents or averts the effect of removal of the thyroid in human subjects and in animals, but Stabel, in Prof. Munk's laboratory, carried out researches on the iodothyrin in thyroidectomized dogs which contest this view. In three out of twenty-one experiments this preparation exerted a perceptible effect on the survival of the animals, whereas in all the other dogs death occurred in spite of the administrations of large doses of iodothyrin. These results are in direct conflict with clinical experience.

Dr. de Cyon reported to the French Academy of Sciences, June 28 and September 13, 1897,

that researches he had made on the depressor nerve of the heart showed that filaments exist which can influence the thyroid gland directly through the laryngeal nerves, and by reflex action, accelerator nerves and the oculo-motor apparatus, maintaining that disease of the depressor nerve is the fundamental trouble in exophthalmic goitre, explaining the principal manifestations of the disease, viz.: the goitre, the exophthalmos and the cardiac symptoms. He says that the thyroid glands situated at the base of the skull at the entrance of the carotids form an apparatus for the protection of the brain from the dangers resulting from a sudden afflux of blood. By determining extensive dilatation of the thyroid vessels the thyroid intervenes for the protection of the brain in two ways, viz.: (1) by opening the flood gates in cases of sudden danger; (2) by increasing the production of iodothyrin in cases of permanent danger. Dr. de Cyon believes that iodothyrin stimulates the functions of the nerve centers which regulate the beating of the heart and the circulation. "The function of the thyroid gland is to form iodothyrin from the iodine salts in the blood, thus ridding the nerve centers of a dangerous toxic substance." His views are mentioned not for any particular value that I place on them, but to show how tangled are the opinions concerning the physiology of the thyroid.

PATHOLOGY.

The pathology of the thyroid in exophthalmic goitre, myxœdema and cretinism, as Prof. J. G. Adami demonstrated in his paper at the Congress of Physicians and Surgeons of last year, consists principally of certain queries for the future to elucidate.

In simple goitre there is hyperplasia of the glandular follicles with secondary fibroid, colloid or cystic changes. In exophthalmic goitre there are the same conditions without the secondary changes; hypertrophy of the parenchyma of the thyroid and in all probability increased secretion, the latter differing only from the simple in being more mucinoid than colloid. In myxœdema all pathologists are agreed that there is an atrophy of the gland. In cretinism opinions are more mixed. Bircher maintains that there is no etiological relation with the thyroid gland, but nearly all others believe that the disease is due to one of three conditions: absence, atrophy, or goitre. Examinations of the cervical sympathetic have up to this time been negative.

SIMPLE GOITRE.

Many of you are familiar with the results of thyroid feeding in simple goitre. Nearly all observers agree that in simple hypertrophy of the gland, thyroid administration causes a diminution in the size, although cysts, fibrous tissue and large collections of colloid material are apparently unaffected.

Simple goitre is supposed not to cause general symptoms, but the experience of one of my confréres and a number of cases observed by myself would seem to indicate that frequently, if not always, there are present various nervous symptoms in the form of general weakness, irritability, a modified Von Graefe symptom, nervousness, and sometimes irritability of heart.

I would strongly urge every practitioner to observe carefully the condition of the thyroid gland in making physical examinations, as a small goitre is generally not noticed by the patient.

Dr. E. F. Ingalls, of Chicago, reported fifty cases in the New York Medical Journal, September, 1895, treated by various observers, in which the swelling was reduced in thirty-eight cases; swelling unaffected in eleven; no report in one.

In 1894 Bruns reported sixty cases treated by this method, curing fourteen, improving twenty-nine and leaving seventeen unaffected. Phosphate of soda combined with thyroid is extolled by Kocher; Ewald and Bruns, from the use of thyroid in over a hundred cases, found that it produced a very noticeable effect. In the parenchymatous form a few days treatment sufficed to greatly reduce the size of the swelling. Baumann has found, from a series of remarkable investigations, that the iodine content of the thyroid and the occurrence of goitre have a certain definite relationship. In most cases of goitre the amount of iodine present is very small, but he has found in addition that in certain cases the content of iodine is far beyond the normal, thus implying the existence of two conditions, one in which the iodine content is below, and another in which it is far above, the normal. As we all know iodine and its salts has a remarkably curative effect in most cases of goitre, probably those in which the iodine content is small.

Dr. Marie, of Paris, speaks of two kinds of exophthalmic goitre, in one of which the symptoms develop in cases of long standing simple goitre, a so-called Basedowified goitre.

MYXŒDEMA.

There appear to be two great classes of this disease, one congenital and the other acquired (atrophy or operation). The congenital form is probably that which we now call sporadic cretinism. The pathological condition is probably the same in both varieties, and the thyroid treatment is a specific. Since I have had no experience in the treatment of acquired myxœdema I shall not refer to it further. You are all familiar with the classical symptoms of this disease.

SPORADIC CRETINISM.

This is really a retardation of growth affect-

ing the bony tissues as well as the soft parts, and accompanied by varying degrees of idiocy, accompanied or caused by loss or absence of function of the thyroid gland. One of the most common names for this disease occurring in our practice is "backward children." Dr. Hertoghe, of Antwerp, has written a mongraph in 1896, in which he advocates the theory that not only arrest of growth due to myxœdema, but also arrest of growth due to rickets, hyperazoturia, congenital syphilis, etc., can be counteracted by the administration of thyroid, maintaining that all deleterious influences capable of interfering with growth attack in the first place the thyroid gland, and that the latter, being variously affected in its functions, determines, according to the degree of its lesions, obesity, rickets, chondrodystrophy, and ultimately more or less complete myxœdema. The theory of infantilism is thus markedly simplified.

The author also discusses the influence of the thyroid gland on the morphological development of the organs of reproduction. He shows that hypertrophy of the thyroid is the first symptom of puberty, and that this hypertrophy is indispensable for the definitive evolution of the special sexual apparatus. It has hitherto been assumed that the development of the thyroid coincided with puberty. Dr. Hertoghe proves apparently that thyroid hypertrophy is the direct cause of the formation of the sexual organs. From a practical and therapeutical point of view this fact is of considerable importance, the administration of thyroid juice in cases of retarded puberty being clearly indicated.

I have personally under treatment two cases of cretinism in which remarkable results are being attained by the administration of five-grain doses of thyroid gland. I show you herewith photographs of two of these cases.

CASE I.

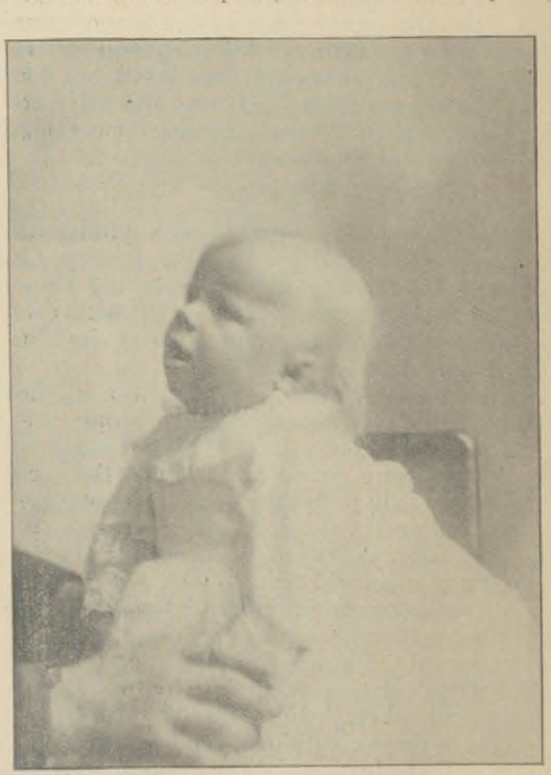
The first of the two is a little girl, æt. six years, whose family history on the paternal side is good; on the maternal side the grandfather died of paresis, one aunt was insane and one had epilepsy.

The mother suffers from sick headaches and the patient's brother at birth had apparently just escaped having a hairlip, but is otherwise normal. Patient's height in shoes is forty-five inches; there is a thick, bony ridge extending along the coronal suture, the muscular system is fairly well developed and locomotion is good; the child began to walk at the age of three; the subcutaneous fat was thick and the abdomen was protuberant. The lips thick and the mouth, as you see in the picture, is usually open, with the tongue frequently out and saliva flowing out at the angles; the expression resembled somewhat the imbecile, and the child's vocabulary was very limited. The hair was thin and dry for a long time after birth, but is now thicker and more soft; the skin was apparently normal. Palpation of the throat revealed a slight indication of the thyroid gland. This patient has been taking thyroid tablets for six months, beginning with three grain tablets t. i. d. for the first three months, and since then taking five grains t. i. d. There is a gradual growth of the skeleton, the protuberant abdomen is gone, the mentality is markedly improved, and the prognosis appears to be very favorable.

In this case it seems that the patient was a typical cretin, but that some remains of the thyroid existed, which three years after birth began to assume some part of its function.

CASE II.

A. S. F. Female, æt. twenty months, is a typical sporadic cretin. In November, 1897, at fifteen months the child was fat, with protuberant abdomen, red cheeks, no teeth, skin dry, and unable to crawl. The head is square, the anterior fortanelle is open (size of a five-cent piece),



TWO MONTHS AFTER TREATMENT.

scalp rough and dry, hair scanty and coarse, mentality low, mouth open, tongue nearly always protruded, drooling of saliva and unable to speak a word. No thyroid palpable.

Two months treatment with three grains of sheep's thyroid, t. i. d., produced a truly marvel-

lous change. The masses of fat began to disappear rapidly, the skin to become soft, the hair to grow, the expression to change, the tongue to remain within the mouth and the child could say "papa" and "mama." This picture was taken two months after treatment.

The child began with three grains, t. i. d. which was increased to five grains t. i. d., and it is progressively growing in every way, and five teeth have erupted after four months treatment. The dose is a little large because the child is rather restless and always hot and perspiring, but now resembles children of its age. In cretinism as in adult myxœdema, treatment must be continued indefinitely, but large amounts are not require. Just how much thyroid must be administered after the patients have "caught up" is a question for the future to decide.

SIX MONTHS LATER.

In a general way, all cases of retarded growth indicate thyroid therapy. At the present state of our knowledge, it is impossible to differentiate between the cases of so-called endemic and sporadic cretinism with regard to the influence of thyroid treatment. Bircher maintains that thyroid therapy has no influence upon the endemic form. It may be true, but that should not deter us from using thyroid in all cases of retarded growth.

It will be necessary for us to differentiate between cretinism and the various forms of idiocy dependent upon faulty development of the brain hemispheres in fœtal life, the hydrocephalic and the microcephalic idiots, and the forms of imbecility associated with the cerebral palsies of children. In these last it will undoubtedly not avail us to use the thyroid treatment. At the present status of our knowledge of the subject, the conclusion is that we should use thyroid gland in all cases of retarded periods of life.

EXOPHTHALMIC GOITRE.

In 1835, Graves, of Dublin, described a disease which, in English speaking countries, bears his name. In 1840, Basedow, in Germany, gave a more full account of the affection, and on the Continent exophthalmic goitre is usually spoken of as Basedow's disease. There are three cardinal signs of the affection, exophthalmos, tachycardia and goitre. There are many other symptoms. Von Graefe described a symptom which bears his name; in these cases the eyelids do not follow the excursions of the eye properly. Stellwag described a greater divergence than normal between the upper and lower lids and defective winking. Marie called attention to tremor; Charcot-Vigouroux to decreased electrical resistance; other symptoms are diarrhœa, obstinate vomiting, sensations of heat, flushing and irritable mental and vaso-motor system, emaciation, various paralyses, local œdema, fever, pigmentation of the skin, or leucoderma, and urticaria.

Trousseau extended the range of the disease by describing abortive cases, meaning that the disease may be present without all of the cardinal signs. This conception has been of the greatest value to me in my practice, because a great many cases that I have heretofore classed as neurasthenia, are undoubtedly abortive forms of Graves' disease, and the recollection of this fact, inducing me to use the same treatment for them that I have used in exophthalmic goitre, has given me success, and if I do nothing else in this paper but call your attention to this fact, I hope it will aid you in your treatment of a number of anomalous cases which hitherto have been baffling. The signs that have been of the greatest value to me are those connected with the sympathetic system, especially those connected with the vaso-motor apparatus, in cases with flushings, increased perspiration, sensation of heat, and frequently some prominence of the eyes, with a modified Von Graefe symptom. Lastly, the exhibition of thyroid gland increases the symptoms of the disease. Many cases of neurasthenia, traumatic or acquired otherwise, may be complicated with sympathetic disturbance due to an effect upon the thyroid gland, and the ordinary treatment, supplemented by that used in exophthalmic goitre, will give you success in a remarkably short time; in fact, it is

now my practice to try to separate my cases of neurasthenia into those with or without symptoms described as belonging to disturbances of the thyroid gland (Graves' disease).

I will refer to the three theories which have held the boards in the etiology of this disease. Basedow promulgated the hæmatogenic theory, the disease, in his opinion, being due to a chloroanæmic condition. In 1879, Filehne showed that a lesion of the restiform body caused tachycardia, exophthalmos, sometimes goitre, and believed, therefore, that the disease is a nervous one. Later Jaboulay, of Lyons, and Abadie, of Paris, located the disease in the cervical sympathetic system. Möbius has propounded the thyreogenic theory, maintaining that the products of the thyroid gland either neutralize the tissue poisons or furnish a toxic material which reacts upon the nervous system. In 1897, Dr. Jaboulay, of Lyons, operated upon nine women suffering from exophthalmic goitre by division or resection of the cervical sympathetic. Adding to these nine operations those performed by Reclus, Gerard-Marchant, Quenu and Jonnesco under similar conditions, we arrive at a total of fourteen divisions or resections of the cervical sympathetic for the relief of Graves' disease. In all these fourteen cases the operation was simple and invariably resulted in improvement. The operation has never been followed by ill effects of any kind, there having been no trophic disturbances, no changes in any organ or tissue, and no impairment of the power of visual accommodation. Dr. Jaboulay thinks that the operation is more successful in aged persons than in young people, because the question of age appears to be connected with a physical condition of the moderating and accelerating systems of the heart, which differ according to the age of the subject, in that the accelerating system predominates in youth. He maintains that the imperfect recoveries after division of the cervical sympathetic are due to anatomical abnormalities. Sometimes there are two columns connecting the upper and the middle cervical ganglia. The former may be split in two. In such cases the operation should be repeated. He believes the operation indicated in those cases refractory to medical treatment and hydrotherapy, and especially where there is very marked exophthalmos. He insists that whatever may be the exact nature of Graves' disease, its effects are transmitted through the cervical sympathetic. Abadie explains the goitre through the vaso-dilatation of the arteries from stimulation of the cervical sympathetic, which furnishes too much nourishment to the gland. Exophthalmos is due to vaso-dilatation of the retro-bulbar vessels. We all know that disease of the cervical sympathetic affects the heart through the pneumogastric, and that excessive stimulus produces diarrhœa; also that the vaso-motor system is affected by such derangement. Before this operation of Jaboulay's extirpation of part or all of the thyroid has been used in the treatment of the affection. Dr. Lejars removed the right lobe of the thyroid gland in a girl of eighteen, Oct. 12, 1896, who died in an attack of extreme dyspnœa soon afterwards. At the autopsy nothing abnormal was found. Dr. Quenu removed the entire thyroid gland in a case which recovered, but later developed myxœdema, which was successfully treated by means of thyroid. Dr. Tillaux pointed out that exophthalmic goitres due to the existence of a tumor in the thyroid gland which compressed the cervical bundle of blood vessels and nerves, should be operated upon by excision of the tumor, while exophthalmic goitre without intrathyroid tumors is not amenable to surgical treatment. Dr. Goris removed completely a goitre of the mediastinum without myxœdema and ending in recovery. Dr. Picque operated on a woman in 1894 by removal of the goitre, with recovery, and again in 1897 on another case, with the same result. Dr. Schwartz removed an intrathyroid tumor in the right lobe of the thyroid gland where symptoms of exophthalmic goitre existed, in May, 1896, resulting in a cure. Dr. Tuffier performed partial thyroidectomy in two cases, one on July 31, 1894, the other January 24, 1897. In the first a cure was effected; in the last only improvement. Prof. Poncet has operated on several cases, in some of which there have been severe nervous disturbances, and even death after the operation. Dr. Doyen reports removal of the entire thyroid gland in two cases, with complete and lasting subsidence of all symptoms.

All operators are agreed that removal of the thyroid gland is a very dangerous operation, causing death from hemorrhage or toxæmia. Kocher advises ligation of three of the thyroid arteries in preference to thyroidectomy. He has treated thirty-one cases surgically and has seen varying degrees of improvement, sometimes even complete recovery. Of 187 cases surgically treated collected by Kinnicutt, thirteen died as a result of the operation, sixty recovered, forty-seven improved, eleven unimproved and in twenty-five the result is unknown.

I will not burden you with theories favoring the thyreogenic or the nervous origin of this affection more than to point out that the pathological condition in simple goitre and exophthalmic goitre are apparently identical as far as the gland is concerned; that nervous shock is a frequent exciting cause of exophthalmic goitre; that Graves' disease occurs most frequently in women (4.6 to 1.7), the sex that suffers most from neuropathic conditions; that the symptoms of the disease can well be explained by an affection of

the sympathetic system (cervical sympathetic), and finally, that operations on the cervical sympathetic and those on the gland producing the same effect on the sympathetic fibres distributed to it, seem to cure the disease. The fact that exophthalmic goitre is the antithesis of myxœdema does not prove anything more than that in the last there is loss of function and in the first apparent hyperfunction; but why not the same symptoms from simple goitre? And how about Basedowified simple goitre?

But how shall we explain the non-occurrence of cachexia strumipriva in cases where apparently complete removal of the thyroid has been practised? The simplest explanation is, probably, that the parathyroids have not been completely removed, and it would seem that the operations upon the thyroid gland for the relief of exophthalmic goitre should be limited to cases of neoplasm occurring in the same. The remarkable results following resection of the cervical sympathetic bid fair to throw new light upon the causation of the disease, and give us a successful mode of treatment. I append a table of eleven cases of exophthalmic goitre treated by me during the last three years.

From this table it will be seen that this disease predominates in the female—nine out of eleven cases.

From the ages it will be seen that the disease is one of middle life, and strangely enough, one case which developed in a woman of seventy-one years.

Among the causes it will be noted that heredity in these cases has played no rôle. In five out of the eleven there have been mental causes. In the form of worry (three cases); fright (two cases); la grippe (two cases); chronic diarrhœa, general nervousness, each one case; no causes (two cases).

In the eleven cases both lobes were pretty symmetrically enlarged in seven cases, the right usually a little larger than the left; in one case no enlargement; in two cases the left lobes were enlarged; in one case, slight enlargement both lobes.

In two of these cases the pulse was practically normal as regards rate, but the rhythm was disturbed in all by the least excitement.

In nine out of the eleven cases Graefe's symptom was present; in two it was absent.

In one case the remarkable difficulty existed that the patient could hardly turn the eyes downward from the horizontal plane. In six out of the eleven cases exophthalmos was present.

In five of these cases (numbers one, two, four, five and seven), the administration of thyroid produced a marked exaggeration of all the symptoms on the part of the nervous system. In other cases it was not tried. In cases four and seven, which were the worst and most marked, galvanization of the neck with administration of thymus resulted in remarkable improvement, seemingly coincident with the use of the thymus, but since I have used with it galvanism (a treatment of great value), my cases are of little value in the elucidation of the question as to whether the thymus gland is of value in the treatment of exophthalmic goitre. In case ten, great improvement has occurred after four months thymus treatment alone.

I think that we can safely say that the administration of the thyroid gland produces a reaction in cases of exophthalmic goitre in cases where the gland is apparently hyperfunctionating. The symptoms are those of a sensation of heat (rarely cold), headache, tremor, irritability of the nervous and circulatory systems, and nausea, sometimes vomiting.

The mode of administration that I have adopted consists in giving the capsules of pulverized thyroid or compressed tablets just before meals upon an empty stomach, followed by a half-glass of hot water, hoping thus to secure a more complete and speedy absorption of the remedy. The tabloids I have used are those of Parke, Davis & Co.

OBESITY.

The elimination of nitrogen and carbonic acid in large quantities of urine and its effect on the pathological fat deposits in cretins led to a trial of thyroid extract in cases of this kind, and many cases have been reported in literature where great diminution of weight has occurred from its use.

My own experience is limited, owing to failure of my cases to report results. In one case I administered five grain tablets four times a day for two weeks without appreciable result, then the dose was increased to eight tablets a day with a loss of two pounds in a week. The next week twelve tablets daily caused a further loss of one pound, and the next week sixteen tablets a day produced irritability of mind, sense of heat, nervousness, asthenia and tremor; and the tablets were reduced to three daily for two more weeks with subsidence of the nervous symptoms and also a loss of weight down to fourteen pounds less than it was at the beginning of the treatment. The urine was greatly increased all the time. My data are incomplete in other cases that I have treated, and I shall not weary you with a recital of them. I think that the future will discover that obesity is of various kinds on the basis of its eiology, and that certain cases will be adapted to thyroid therapy, as an adjuvant to removal of the cause. Under thyroid therapy after a discontinuance of the treatment relapse follows if the cause of the obesity be not

Sex	Age	Causes.	Enlargement of Gland.	Pulse.	Eyes.	Vaso-Motor and Other Symptoms.	Treatment.	Result.
Female	18	Nervous heredity. No exciting.	Both lobes moderately large.	Normal.	Stellwag. Prominent. V. Graefe.	Feels cold. Insomnia. Shortness of breath.	Galvanism. Thymus, 5 gr. t. i. d.	Great improvement in three months. One and one-half years later good health.
Female	19	Accident two years before onset. Hurt head some.	No enlargement.	96-104.	Normal except pain in eyeballs.	Flushes easily. Tachycardia. Muscular weakness.	Massage of eyes. Sponge baths. Thymus 5 gr. t. i. d.	One year later is quite well.
Female	25	La grippe four years ago. Has been feeling badly since.	Great enlargement of both lobes.	140	Prominent. Stellwag and V. Graefe.	Sense of heat. Flushings of skin. Tachycardia. Muscular atrophy of arms. Asthenia. Melancholia. Reflexes exaggerated. Electrical resistance lowered. Diarrhœa. Temperature 100° to 101°.	Fowler's sol. Galvanism.	Continued treatment but one week.
Female	26	Worry about slander concerning her character.	Enlargement of both lobes and isthmus, especially of right.	110-149	Exophthalmos. V. Graefe. Stellwag,	Asthenia. Flushings. Heat. Perspiration. Tremor of hands. Tachycardia. Dyspnœa. Temperature usually 100°.	Galvanism every other day for six months. Thymus 5 gr. t. i. d.	Disappearance of exophthalmos. Pulse down to 90.
Female	33	Proof reading. Worry.	Moderate enlargement.	89	Exophthalmos. V. Graefe. Stellwag.	Tachycardia. Flashes of heat. Slight tremor of hands. Diarrhœa. Temp. 100 1-5°.	Thymus, 5 gr. t. i. d. Galvanism.	Recovery.
Female	36	Badly frightened in runaway two years ago.	Left lobe somewhat enlarged.	134	Graefe sign only. Very difficult to look down.	Tachycardia. Dyspnœa. Heat sensation. Nervousness. Tremor of hands.	Thymus, 5 gr. t. i. d. Galvanism.	
Male	41	Chronic diarrhœa (?).	Enlargement of both lobes; right larger.	90	Exophthalmos. V. Graefe. Stellwag. Mobius well marked.	Tachycardia. Flashes of heat. Excessive perspiration. Dyspœna. Attacks of diarrhœa.	Thymus t. i. d. Sponge baths. Galvanism.	Pulse 82. Exophthalmos practically gone one year later.
Female	48	None.	Slight enlargement.	82	Eyes normal.	Nervousness. Flashes of heat. Tachycardia.	Bromide of arsenic. Galvanism.	
Female	48	None.	Right lobe somewhat enlarged.	100-170	Exophthalmos. Graefe. Stellwag. Conjunctivitis.	Tachycardia. Tremor of hands. Nervousness. Insomnia. Heat sensation. Temp. 101½°.	Thymus, 5 gr. t. i. d. Sponge baths. Galvanism.	Slight improvement.
ale	54	La grippe five years ago.	Left lobe size of a large apple.	88	Marked V. Graefe.	Irritability. Nervousness. Poor sleep. Tachycardia.	Thymus, 5 gr. t. i. d. Sponge baths.	Marked improvement four months after beginning treatment, and subsidence of nervous symptoms.

Sex	Age	Causes.	Enlargement of Gland.	Pulse.	Eyes.	Vaso motor and Other Symptoms.	Treatment.	Results.
Female	71	Great worry over a daughter five years before onset.	Great enlargement of both lobes and isthmus.	120	Graefe's sign only.	Tachycardia. Dyspnœa. Nervousness. Emaciation. Tremor. Heat. Excessive perspiration.	Rest in bed. Tonics. Strophanthus and arsenic.	Treatment just begun.

removed, and small doses must be continued indefinitely. The heart should always be watched.

The study of the subject of the internal secretions has forced upon me the view that the physiological function of the ductless glands of the body is one of intimate connection with the sympathetic system which presides over vegetative life; over nutrition, broadly speaking. We have seen what an important part the thyroid bodies play in the economy; the adrenals either directly (?), or more probably indirectly through the abdominal sympathetic have also an important place (in nutrition be it remarked), as evidenced by the disturbances following pathological conditions (Addison's disease, etc.); the testicles and ovaries must exert a profound influence on the nutrition of the body, as their period of activity corresponds to nutritional changes of profound nature: growth of the hair, change in the voice, etc., and their ablation produces a retrograde change in the individual: a return to a lower type corresponding to that existing before puberty, and not, as generally stated, to the opposite sex, i. e., masculine to feminine, etc.

The hypophysis of the brain, like the thyroid, is a compound tubular gland with excretory ducts in fœtal life, which later, also like the thyroid, becomes ductless. Disease of the hypophysis is associated with, if not the cause of the nutritional diseases we call acromegaly and giantism, where a peculiar overgrowth of bone exists. The thymus gland has its mysterious function to perform in fœtal life, the period of most active morphological change, and later it disappears.

All these glands are richly supplied with nerves from the sympathetic system. Recent histological research indicates that the secreting cells of organs have nerves ending directly in them. Nearly all we know of the animal organism indicates that its activities, including also the vegetative, are liberated by and performed through the nervous system, and any view which does not take cognizance of this fact, like the one now so glibly popular, that because feeding the body gland substance which is absent from the organism restores function, therefore, these glands are to be looked upon as small chemical laboratories, where substances are produced which sail around in the blood stream to find places that need repairing, or to antagonize toxines.

How much more in accord with what we know of the human economy to assume that these glands provide substances which act upon the body through the sympathetic, just as the carbonic dioxide of the blood acts upon the respiratory centre, stimulating it to increased activity. How radical a change to suppose that the cells of the body increase or decrease their activity because of a humor carried about in the blood stream.

The conclusions that I should like to draw after this fragmentary consideration of the thyroid are as follows:

First. The thyroid gland produces a secretion of the greatest importance to the metabolism of the body. Absence of function produces cretinism if congenital, myxœdema if acquired.

Second. Simple hyperplasia (simple goitre) does not produce marked pathological disturbances, but I believe it to be a larvated form of exophthalmic goitre, and I think that so-called "nervousness" can be found in the vast majority of cases.

Third. Hyperplasia associated with disturbance of the cervical sympathetic is the disease known as exophthalmic goitre.

Fourth. Surgical interference in diseases of the thyroid gland should be limited to the removal of neoplasms; thyroidectomy in exophthalmic goitre is unphysiological, irritational and dangerous.

Fifth. In the majority of cases of exophthalmic goitre, medicinal and hygienic treatment, rest, galvanism through the neck (two to five M. A.), tonics, sodium phosphate and thymus gland will effect amelioration. In cases refractory to medical treatment where life is threatened, section of the cervical sympathetic should be practised.

Sixth. Many cases of neurasthenia are cases of masked exophthalmic goitre and should be treated accordingly.

Seventh. Thyroid therapy is specific in sporadic cretinism, myxœdema and simple goitre, and removes obesity.

Eighth. Thyroid extract increases the unpleasant symptoms in exophthalmic goitre, and is a reliable test also in the masked form of this disease.

Note. In the NORTHWESTERN LANCET of November 15, 1885, is a report by Dr. D. W. Hand, of St. Paul, of an epidemic of goitre occurring at the State Reform School, at that time situated in the outskirts of St. Paul. Dr. Hand visited the school on July 3, 1885, and found that during the past two weeks a considerable number of the boys had become afflicted with a swelling of the neck, which upon examination proved to be enlargement of the thyroid gland, both lobes and the isthmus being involved in most cases. The enlargement in different cases varied from a slight tumor to a protuberant deformity. There was no prominence of the eyes and in but few cases any acceleration of the pulse. The Superintendent stated that he had a few boys with swelled necks every year, but that the number at this time was extraordinary. The boys all claimed to be in good health. Of the 140 boys in the institution 44 had the goitre. There were 19 girls in a separate building a quarter of a mile away, and of these but one had goitre, and she gave a history of the disease on entrance. Both boys and girls used the same water supply, from a bored well, 156 feet deep. The only change made recently in the food was in the brand of flour. No local cause for the epidemic could be discovered.

The treatment adopted was the administration of Lugol's solution of iodine. The cases improved rapidly and were nearly all well by the end of August. An examination on the first day of October showed but five boys with any traces of the old enlargement.

DISCUSSION.

Dr. Schwyzer: Dr. Snévé has developed before us a very neat picture of the different questions and discoveries which interest the medical world today as concerns the thyroid gland. The subject is a very large one and would take us a very long time to discuss in any complete way. I can, therefore, only pick out a very few things in the doctor's paper.

As concerns the etiology of goitre, the doctor does not say much about it, and leaves this question completely open. It seems that the infectious character or at least the transmission through water has most believers. Kocher found certain springs in certain regions that showed an unfavorable influence in this direction. The well established fact in Switzerland, that healthy families moving into goitre regions becomes affected after staying there for a while, is not to be forgotten.

The parathyroids, that the doctor mentions, have importance only in certain animals, like dogs and cats, upon which Vassale and Generali operated. Blumenreich and Jakoby publish experiments that show the parathyroids to be of no benefit after removal of the principal gland in rabbits. The parathyroids did not show any vicarious qualities, and the pictures, after operations, were not changed, whether the parathyroids were left behind or removed with the thyroid. They claim that the parathyroids are not related historically to the thyroids.

In human beings parathyroids do not come into consideration. We have the thyroid with its double embryological origin, the median part originating from an epithelial tube at the base of the tongue and this thyroglossal tube sometimes persists. The two lateral parts, which form after this the principal part of the lateral lobes of the human thyroid, originate from the lower border of the sixth bronchial cleft on each side. There are now a number of aberrant thyroids found in the region of the hyoid bone, the larynx, pharynx, even in the supraclavicular fossæ, or near the aorta. The upper horns of the lateral lobes run sometimes very high up on the sides and are troublesome in goitre operations. Such aberrant parts of the thyroids as I have mentioned are not constant and have to be considered as seclusions. Of the parathyroids, in the sense of Vassale and Generali, in men, we do not know anything so far.

It might be of interest to add to the anatomical and physiological remarks that E. Brian (Paris, Bailliere and Fils, 1898), has studied the nerve supply of the thyroid recently in a minute manner. He always found the sympathetic sending branches from the region of the middle cervical ganglion. There were also constantly filaments from the superior laryngeal, and the recurrens to be found. On section through the

sympathetic above the inferior cervical ganglion he noticed the blood vessels of the thyroid to be contracted, while section below it made hyperæmia. If the cervical sympathetic was divided on one side he found this side of the thyroid much larger and darker than the opposite side. This shows an importance influence of the sympathetic nerve on the thyroid and helps to strengthen the neurogenic theory of exophthalmic goitre, and to justify the division of the cervical sympathetic in exophthalmic goitre.

Speaking of this latter disease Dr. Snévé mentions only a hyperactivity of the thyroid. This is most probably for the majority of cases, but in other cases we probably have not simply a too abundant but a wrong (pathological) secretion. Instead of a hyperthyreosis we would have to speak of a dysthyreosis. This alone could explain some cases of exophthalmic goitre which were reported as cured or benefited by thyroid tablets. Hyperthyreosis seems, however, to be the most frequent, and it is interesting to compare the different symptoms individually between exophthalmic goitre and cachexia strumipriva, or as we should better say, cachexia thyreopriva.

In the one there is protrusion of the eyes, that are widely open; in the other they are deep and less open than normally. In the one you see the circulatory system wildly active, the skin flushed; in the other the circulation is lacking, the skin is pale and the extremities are somewhat cyanotic. In the first the skin is moist, in the other dry. In the one there is sensation of heat; in the cachexia thyreopriva the patient always feels cold, where normal people are very comfortable. In pronounced exophthalmic goitre you notice emaciation, in the other case you find the myxœdematous thickening. The one patient is irritable, hasty; the other phlegmatic and slow, and so forth. There is direct opposition in the two clinical pictures.

As concerns thyroid feeding in common goitres, I would like to mention one point. As the nodules with larger colloid masses are less influenced, the goitre becomes smaller, but in the meantime the nodules are more distinct and easier to be felt. They appear more isolated from each other, as the more normal, diffusely hyperplastic tissue between them becomes very much reduced in size. This palpatory sign is more important than the diminution in the circumference of the neck, which we are very apt to measure wrongly, and where other causes may change the width of the neck.

Dr. Snévé has shown us that he had quite a few cases of exophthalmic goitre where not all the cardinal symptoms were present. Those cases are very valuable and interesting. They lead us from the picture of typical Graves' disease over a number of stepping stones to the picture of neurasthenia and hysteria. There is a strange combination of nervous and metabolic disturbances, and as the cases vary in form, the therapeutic measures have to be changed. I do not dare to agree with the doctor when he says that the only justified surgical interference is division of the cervical sympathetic and that operations on the thyroid are irrational in exophthalmic goitre. The results of the division of the cervical sympathetic are striking, I will admit; but as we stand today we have good reports from both sides. Riedel, that careful observer, reported last year his cases (eleven with four cured and two almost cured) of partial thyroidectomy in Graves' disease, and declares all the misresults caused by recurrence of the goitre. Schulz, of Hamburg, reported last year fourteen cases with twelve cures and two improvements after operating upon the thyroid exophthalmic goitre. On the other hand we find a case of resection of the cervical sympathetic nerves, including the upper ganglion, where the protrusion of the eyes disappeared very rapidly but reappeared later on (Gérald-Marchant et Abadie, reported in the Centralblatt fuer innere Medicin, Dec., 1897). I think, therefore, that we have to let larger practical experience say the last word on this question.

I agree, however, with Dr. Snévé's thesis denouncing operations upon the thyroid in exophthalmic goitre as dangerous. They may indeed be very dangerous for two reasons: First, we do not have an ordinary goitre but a vascular goitre, the blood vessels buzzing frequently on all the sides and the hemorrhage may be frightful. Second, and this is very important to remember, we may have a very bad general effect following immediately the operation and showing itself principally by further rise of the pulse. It is the consequence of handling, pulling and squeezing the thyroid, as we have to do it in resections. The cases of death after this operation, without further causes found at the autopsy, are explained by the pressing of the gland out, forcing the secretion of the gland into the general circulation and therefore poisoning the body by accumulation of the toxic substances which had caused the disease, i. e., exophthalmic goitre.

The ligation of three thyroid arteries after Kocher avoids these dangers to a considerable degree, and for this reason I used it in a very severe case of exophthalmic goitre. Cases of this degree are not common, and I will therefore relate it in short.

A lady of twenty-three years consulted me in June, 1896, for headache, nervousness, restlessness and weakness; protrusion of the eyes had existed for about six years and a thickened

neck for about a year. Pulse 100. Palpitations. Tremor of fingers. After trying different measures the patient began to be gradually worse throughout the fall, and finally she had to remain in bed towards the middle of October, 1896. She was then moaning almost constantly from headache, ate almost nothing for several days, vomited sometimes, and had diarrhœa. The hair fell out. There were neuralgic pains in the lumbar and occipital regions, and combined with the great emaciation and an extreme exophthalmos she offered a frightful picture. The exophthalmos had reached such a degree that one of the rectus muscles could not give way as much as his antagonist and marked strabismus was the consequence. [I will add right here that the strabismus disappeared when the exophthalmos went down later on.] The pulse ranged from 124 to 132, sometimes going down to 114 in the evening.

On October 21, 1896, I ligated without narcosis, the right lower thyroid artery, after injection of one per cent. cocaine into the skin. The right lobe of the thyroid was the largest. Even the next day after the operation you could notice a decrease in the pulse rate. On the fourth day after the operation the pulse went down to 92 and did not go beyond 100 until I ligated one week after the first operation the right, upper thyroid artery, which was hard to find and rather small. For about two weeks the pulse remained at 100 or a little above. But then things grew worse again.

In the middle of December, 1896, the pulse ranged between 140 and 150 with no interruption. The headache, which had been unreasonably severe at the time of the first operations, existed yet, though not quite to such a degree. Temperature 100.2 degrees; pulse 152 in the morning of December 18, 1896, when I operated for a third time. Ligation of a strong branch coming from the right hyoid artery downwards and ligation of the left inferior thyroid artery, so that only the left superior thyroid remained united. Again I did not use any general anæsthetic, but locally cocaine in a very small does. In the afternoon of the following day the pulse dropped to 120 and the following days it ranged from 100-110-120. While the rest of the symptoms gradually improved, the pulse remained the same (110-132) for several months, and only towards the latter part of 1897 became normal (70 to 80). Long before this the formerly emaciated lady had gained from about 100 pounds to 151 pounds. The goitre became very slowly smaller and the exophthalmos has gone down considerably; it still exists, however, to a marked degree.

In a medical way I had tried about all I knew of. Galvanization of the cervical sympathetic, though not long enough, as the patient grew worse under its use; calomel and intestinal antiseptics as praised for exophthalmic goitre in the New York Medical Journal, 1896; then bromides, quinine; Overbach's migranine, fresh thymus gland, one-half ounce daily. Then tablets of ovarian substance and even iodides (!) for a while. After all I tried there seemed to be only one remedy that had any favorable effect, and that was phosphate of soda, two to six grammes daily, as advised by Traczewsky, of Bern.

I will not take up your time any longer, but let me mention that I had not better but much worse results than Dr. Snévé with cases of thyroid feeding for obesity. I got very serious toxic effects on the heart in the three cases I treated in this way. One tablet of sheep's gland (5 grains, Burroughs, Welcome & Co.) daily produced trouble. The thyroids of hogs are much more harmless, and I have not seen any ill effects where I used these.

Dr. Burnside Foster: I have listened with much pleasure to this paper and to Dr. Schwyzer's remarks, and I have learned much that was new to me. I have always been and still am very skeptical concerning the value of treatment by the animal extracts, especially when administered by the stomach. I admit, of course, the reasonableness of the iodothyrin theory, and the accumulated experience of many eminent investigators leaves no room to doubt that on certain diseases where the thyroid gland has undergone pathological change a very remarkable effect is produced by administering thyroid extract.

Some two years ago when the animal extract boom was very active, several European dermatologists reported remarkable results in certain chronic affections of the skin by thyroid feeding. At that time, stimulated by these reports, I gave the treatment what seemed to me a fair trial. During a period of about four months I treated twenty-two cases of psoriasis, suspending local treatment entirely, by the internal use of thyroid extract. I used both the raw gland and the powdered extract. I watched the cases carefully, and I was unable in a single instance to note any effect upon the disease from my treatment. In one case, where the eruption was very abundant, I selected a few patches for local treatment, leaving the rest of the body untreated. In this case the patches treated locally speedily improved, but the other patches were unchanged. In a number of these cases where I could see the patient frequently, I watched the pulse and the temperature and the general condition carefully, but could see no effect of any kind.

I also tried the treatment on four or five cases of late syphilis which had obstinate skin lesions, but I could not see that any effect was produced.

This is the extent of my experience with thyroid treatment, and while it proves nothing, I desire to record it because it is absolutely different from the recorded experiences of certain observers who have so enthusiastically recommended thyroid feeding in many chronic affections of the skin. I cannot believe that these men have deliberately misrepresented facts, but rather that they allowed themselves to be carried away by their enthusiasm for a novel method of treatment and came too hastily to an unwarranted conclusion.

Dr. Courtney, of Brainerd, wished to say a word about the heredity of simple goitre. He knew of a family where a mother and four children suffered from goitre, and where the iodine treatment produced complete recoveries in all but one. As far as the surgical part of it was concerned, he had operated on a little girl who was very anæmic, after having first placed her upon an iron tonic. Ether was the anæsthetic used, and the patient developed pneumonia a short time after the operation, and the query arose, did not this patient become infected with the pneumococus from the saliva, a little of which accidentally got into the wound, because the patient acted badly under the anæsthetic, and the contamination occurred during the efforts at resuscitation.

Doctor C. Williams spoke of an epidemic of enlargement of the thyroid which occurred a number of years ago in the Reform School, affecting the majority of the inmates and lasting a number of weeks. He was called by the late Dr. Hand to see if there were symptoms on the part of the eyes, but none were found.

Dr. Dunning referred to a case of sporadic cretinism in a girl sixteen years old who weighed sixty pounds, in whom he had used the thyroid treatment with undoubted improvement and an increase in weight. He concurred in the main with Dr. Snévé's ideas on neurasthenia. Dr. Dunning also said the manner in which he administered iodine was to expose a few grains in an open jar in the patient's sleeping room at night, and he thought this was the best mode of treatment for simple goitre.