Original Articles.

THE PRESENT STATUS OF THE TREATMENT OF EXOPHTHALMIC GOITER.*

BY JAMES MARSH JACKSON, M.D.,
AND
THEODORE JEWETT EASTMAN, M.D., BOSTON.

IN considering the subject of exophthalmic goiter we are immediately impressed by the tremendous rapidity with which our knowledge of certain aspects of it has advanced, for, unknown and unrecognized comparatively few years ago, its bibliography now numbers many hundreds of articles in all languages. While it must have existed long — perhaps for centuries — before it was first described in medical literature, it was only after the attention of physicians was called to it by Parry that it began to be noticed. Dock,¹ in his comprehensive article on the history of the disease, tells us in a few pages all that we know of its history. The earliest description that he found was by Flajani, probably before 1820. Parry, of Bath, England, gave in 1825 a fairly accurate and keen description of a case seen by him in 1786 of very marked exophthalmic goiter following confinement, and later he saw seven others. No other good descriptions of the disease were given until 1835, when Robert James Graves, a renowned physician of Dublin, described with great fullness three typical cases.

Following this, in 1848, came a very thorough article on four cases observed by Carl A. von Basedow, of Merseburg, a small town in Germany. With this article was a full bibliography, and an inquiry into the pathology of the disease. Graves did not attempt to give a name to the disease, but Basedow called it "goggle-eyed cachexia." The name "Basedow's disease" seems first to have been used by Hirsch in 1858, and "exophthalmic goiter" and "Graves' disease" were first applied to it in 1860 by the great Trousseau, who was a firm admirer of the Dublin physician.

A discussion on the disease in the Paris Academy of Medicine in 1860 created great interest in it, and many articles soon appeared, including those of Von Graefe and Marie and Moebius, and this interest has so grown that when Kocher made his great bibliography on the subject in 1902 he was able to find 1,423 titles.

There have been few diseases as to the origin of which more theories have been advanced than concerning exophthalmic goiter. Heinek² mentions seven theories which have been held, among them the cardiac, which assumes that the tachycardia is primary and the other symptoms are all secondary to it; the sympathetic, which assumes that all the symptoms are due to a disturbance of the sympathetic nervous system; the nervous, which has its basis in the fact that a neuropathic family history is found in some cases; the parathyroid and the thymus theories, which attribute the cause of the disease to disturbances in these glands, and, finally, the thyroid theory, the one which carries greatest weight at present

and which is substantiated by clinical, experimental and pathological evidence.

Of the first four theories, that regarding the sympathetic nervous system is the only one which seems to have any evidence in its favor. Jonnesco³ claims a considerable number of cures of the disease through severing the cervical sympathetic nerves leading to the thyroid gland, but there is practically no other advocate of this practice now. Changes have been found in the parathyroid glands in a number of cases, but injury of these glands has failed experimentally to produce the symptoms of Graves' disease. Falta, who with Eppinger and Rudinger has done the best work on the relation of the glands of internal secretion, explains the occasional occurrence of lesions of the parathyroids by saying "that on account of the close approximation of the parathyroids to the thyroid gland, functional disturbances of the parathyroid may occur as a consequence of rapid strumous enlargement or inflammation of the thyroid." As for the thymus theory, autopsy statistics have not shown any connection between persistent thymus and Graves' disease. The theory that the thyroid gland is alone responsible for the disease is the only one that has survived, and this is borne out by experimental and clinical evidence. It is found that the administration of thyroid extract will produce the symptoms of the disease,⁵ and pathological examination of the thyroid gland in cases of it constantly shows changes, proving that there is a hypersecretion of the thyroid juice either from an increase of normal thyroid tissue, or simple hypersecretion by a normal sized thyroid.

The manner in which the symptoms of the disease are produced by this hypersecretion has been much discussed, but from all the evidence it seems most probable that the secretion acts on the sympathetic system, perhaps directly on the *chromaffin substance* which it contains, which is in itself a gland and, therefore, most likely to be acted upon by another gland, as is so frequently the case. It is not impossible that we are dealing with a vicious circle. It is acknowledged that the glands are controlled by the sympathetic nervous system: something — in many cases apparently a mental shock — excites this system which brings about an increased thyroid secretion; this in turn reacts on the sympathetic system for which it seems to have a special affinity. The thyroid is in this way still further stimulated and we have a vicious circle, the continued sympathetic stimulation showing its effect in the sweating, diarrhea, nervousness, rapid respiration, tachycardia, etc. Another link in the chain of evidence in favor of the sympathetic theory is shown by Falta,⁶ who points out the fact that the cells of the chromaffin system and those of the medulla of the adrenal are similar; that the majority of the symptoms in exophthalmic goiter point to a hyperirritability of the sympathetic system, and so, too, adrenalin exerts its chief influence upon the endings of the sympathetic nerves.

It is perfectly possible for a gland to show great *hyperactivity* without actual enlargement just as

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do the salivary glands in a case of salivation. Furthermore, it is possible that some change in the *quality* of the secretion may produce the symptoms without any increase in the quantity.

The gland may be scarcely perceptible to the touch in a patient with very severe symptoms, and, on the other hand, the victim of a very mild attack of the disease may have a large goiter.⁷ In this latter case the goiter is made up mostly of colloid,⁸ but cystic or colloid degeneration may come on in plain goiter and may cause hyperthyroidism, probably by pressure on the thyroid tissue, just as in a polycystic kidney the pressure causes a nephritis. Again, a colloid goiter may suddenly become active and produce the worst type of Graves' disease, because nature suddenly tries to bring the degenerating gland to life again and creates a lot of new epithelium.⁹

Now a few words as to diagnosis. Palpitation and tachycardia are the commonest early symptoms; then, possibly, an increase in the size of the thyroid. Exophthalmos may be present relatively early and then may follow some or all of the symptoms which we find in the most marked cases. Nervousness, an anxious expression of the face, pallor, tremor, diarrhea, sweating, frequently a slight albuminuria and occasionally glycosuria through a sympathetic disturbance of the pancreas by the thyroid, as has been shown by Falta.¹⁰ The signs (v. Graefe's, etc.) found in the eyes may or may not be present. In practically every case, however, we find some abnormality of the heart. In the earliest stages it is only rapidity of the beat, but before this has gone on very long we are sure to find some evidence of a myocardial affection, — weakness, irregularity in rate, rhythm or strength, and hypertrophy and dilatation. In fact, myocarditis of some degree is one of the most constant lesions of the disease.

In rare cases an abnormality of position of the thyroid may exist. We saw a short time ago a patient with extremely marked symptoms of Graves' disease, but were unable to find by palpation any traces of a thyroid. On percussion, however, there was dullness below both clavicles, and at operation (which was successfully accomplished) it was found that the case was one with a so-called "dipping thyroid," and that the lateral lobes were located in the position shown by percussion. Another case which came to our attention showed a very much enlarged left lobe in its normal situation, whereas the right lobe occupied the position of the apex of the right lung and was nearly the size of a cocoanut. In cases like these we are often mystified by the very marked dyspnea without any sign of an enlarged thyroid. This dyspnea may come on only in attacks following "catching cold" or getting overtired or at the time of menstruation on account of the swelling of the thyroid at those times producing pressure symptoms and is a great element of danger in that the pressure may give rise to emphysema and bronchitis and result in overloading of the heart with consequent cardiac failure, or the thyroid may swell suddenly and to a large size and suffocate the patient.

Kocher¹¹ has shown that there is a characteristic blood picture in the disease. In his analysis of 106 cases he shows that the red cells are somewhat increased and there is, as a rule, no anemia. The white cells are most affected. There is a marked diminution in their numbers, going as low in one case as 3,700 to the cubic millimeter. As a rule, the neutrophils only are affected, being reduced often to as low as 35% instead of the normal 50% to 57%. The lymphocytes, on the other hand, showed sometimes an absolute but more often a relative increase, even to 57% instead of the normal 25%. Werelius¹² says that this picture is characteristic of exophthalmic goiter and is most marked at the height of the disease, and it has been shown in many cases that the blood returns to its normal conditions following a successful operation. This blood picture agrees with the long-recognized fact that starvation, cachexias and nutritive disturbances increase the lymphocytes in the circulating blood. Furthermore, in exophthalmic goiter we have, besides the profound change in nutrition, a marked chemotoxic action on the lymph system by the excessive thyroid secretion thrown into the circulation. The more severe the hyperthyroidism and its constitutional changes, the greater the lymphocytosis, and Kocher¹³ contends that this condition is a contra-indication to immediate operation if such can possibly be avoided. The utmost endeavor, he says, should be made to treat these cases medically and restore their nutritive balance until the fall in lymphocytes shows that the patient's resistance has been so built up as to make the operative risk at least a reasonable one.

As has been already suggested, we may find hyperfunction and degeneration in the same thyroid gland. Thus we may have together the causes of exophthalmic goiter and of myxedema, and it is a fact that we find cases presenting clinically symptoms of both diseases. These are patients in whom the major part of the gland has been destroyed by degeneration and who would be myxedematous were it not for the fact that the preceding hyperthyroidism has produced a myocarditis which accounts for the tachycardia, while the exophthalmos and nervous symptoms persist. It may thus be seen that many cases — in fact, it is stated as many as 50% — are destined to recover from Graves' disease if they can be tided over the acute stage.

How may we best accomplish this? Two methods of treatment are open to us: surgical, by which we remove the cause of the disease, and medical, by which we endeavor to palliate the symptoms and keep the patient going, — and in this connection we want to emphasize the great importance of the medical man and the surgeon studying the cases together, for there is no disease in which each can work more to the advantage of the other than in this one.

Let us consider first the medical treatment, and this means to a great extent the treatment of the tachycardia, for when we allay that we also diminish the other nervous symptoms; and, further, the heart is the organ most needing protection.

In fact, the medical treatment of exophthalmic goiter may be expressed as the treatment of myocarditis: in the early cases we treat it by prophylaxis, try to prevent its occurrence; in the later cases we try to remove its cause, and in very late cases we try to palliate the existing condition and save what heart muscle is left.

The etiology of this myocarditis has been disputed. It is by some regarded as a result of overwork through pressure on the vagus, by others as a result of direct toxic action on the myocardium by the thyroid secretions, and by Romberg and others as a result of nervous stimulation.

In some cases the direct cause of an overworked and later dilated heart may be the emphysema and bronchitis brought about by compression of the trachea or bronchi by a large thyroid, but in the greater number of cases it seems to me that the cardiac condition is brought about by a primary stimulation to greater rapidity by the thyroid secretion, with a resulting malnutrition of the heart muscle on account of the shortened diastole.

In the treatment of this condition we resort to these measures: *to rest the heart and to diminish the thyroid activity*. Here the most important factor is rest, — absolute rest, — not only physical but mental rest as well. Since the patient is usually in a very highly nervous condition we must first insist upon her remaining in bed, in the quietest room in the house, or in some place away from home, especially in cases where there is any exciting or worrying factor in the household, or, indeed, anything to modify the most perfect conditions for mental quiet; in short, the so-called "Weir Mitchell rest cure" should be rigidly enforced in its strictest form. To care for the patient, we must find a nurse whose effect on her will be soothing. The diet must be nourishing and easily digested, tea and coffee forbidden or greatly limited, and alcohol and tobacco absolutely forbidden. The tachycardia and to some extent the nervous symptoms can often be markedly diminished by an ice bag over the precordia, and occasionally constant cold applications over the thyroid are also of value by retarding the action of the gland and thus diminishing the output of secretion. Cold sponges, cold wet packs and in some cases prolonged cool baths are found to exert a marked soothing effect. At times the bromides in doses of 10-30 gr. three times daily may be successful in diminishing the tachycardia and nervous symptoms, but opium should be avoided whenever possible.

The drugs usually used in cardiac cases we find of little avail. Digitalis, our common reliance in slowing the heart beat, has little effect since it does not reach the cause of the tachycardia, and in exophthalmic goiter it easily causes gastric upsets. Strophanthus and spartein sulphate are also of little use, but in some of the more advanced cases with cardiac weakness small doses of strychnia are sometimes valuable. We have found in a large series of cases that the drug which gives the best results has been the neutral hydrobromide of quinine, the use of which was first suggested by Dr. Forchheimer, of

Cincinnati. It is important that a strictly neutral salt be used, as the acid salt which is frequently dispensed does not give as good results, and we have had the best success with that made by Parke, Davis & Co. It is given in capsules containing 5 gr. each, and to the limit of the patient's tolerance, which is rarely more than three or four capsules a day. Toxicity is shown by the appearance of tinnitus, and no further ill effects are experienced if the medicine is temporarily stopped when this appears. The administration of this medicine must be continued for a long time and it is well to tell the patients in the beginning that they will probably have to take it for months or even for two years or so. If this is not done, the patients are apt to become discouraged if they see no marked results after a few weeks. Very frequently the patients notice after a week or two of the treatment a diminution of the palpitation, the sweating, the tremor and other nervous symptoms, and in many cases the thyroid diminishes in size. The exophthalmos seems to be the last of the signs to disappear, and this may not be until the expiration of two or three years, while rarely the exophthalmos and tremor may persist more or less even after all subjective symptoms have disappeared. When this last occurs, the dose of the drug should be cut down even to two or three capsules a week, the patient being cautioned, however, to resume immediately the former dose at the first appearance of any of the old symptoms.

Our cases have often proved to us the close connection between the thyroid gland and the genital organs. For instance, we have noticed that if the patient becomes pregnant the symptoms are often held in abeyance during the pregnancy, returning, however, after confinement. Again, relapses may occur at the menopause, and, in fact, one of us has just seen a case that has been entirely well for seven years but has recently had a relapse coincident with the climacteric. When relapses occur, as is not uncommon, an active resumption of the treatment quiets them quickly. We are not certain how the quinine acts, though it seems most probable that it acts on the sympathetic system and thus puts an end to its stimulation of the thyroid and the vicious circle which has already been mentioned. We can easily assure ourselves of its specific action by discontinuing its administration in any case and noting the prompt return of symptoms.

In tabulating the results of this treatment on our patients at the Massachusetts General Hospital two years ago with Dr. Mead, it was found that of 56 cases under observation for from three to nine years whom we were able to examine and talk with, 76% had had no signs or symptoms for two years, while 13% had been benefited and only 6 cases (11%) could be considered failures. These cases which we regard as cured are able to perform their ordinary daily work. It is, of course, the early cases that do best under this treatment, and in the very advanced cases with organic changes in the heart we can hardly expect a cure, but we do often see a radical change for the better.¹⁴

With thyroidectin, the dried and powdered

blood of thyroidectomized goats, we have not obtained satisfactory results. Moebius¹⁵ reports several cases in which the symptoms have been diminished by this treatment, but he has not published any cures through its use. Some of our early cases were treated by subcutaneous injections of the serum of thyroidectomized goats, and in a few cases we got good results, especially on the exophthalmos and on the goiter. The serum is, however, very expensive, and some patients object to the frequent injections; and, further, it is not a treatment that can be carried out by the patient at home. The milk of thyroidectomized goats in its original or the powdered form, and "Rhodagen," a preparation made by drying the proteids precipitated from the milk by alcohol, have been used to some extent abroad, but they are hard to get, are expensive, for the goats soon become myxedematous, and, furthermore, no marked benefit has ever been reported from their use.

A few years ago Rogers and Beebe,¹⁶ of New York, brought to our notice a serum treatment. Believing that the symptoms of the disease are caused by hyperactivity of the thyroid, they prepare a serum which is to neutralize, as does an antitoxin, the toxic action of the proteid in the thyroid secretion, and also by its specific toxic action on the secreting cells of the gland to diminish or stop the manufacture of these injurious proteids.

To prepare this serum the proteids are extracted from fresh human thyroid and injected into animals. After several doses have been given, the blood of these animals, which has now become loaded with antibodies, is withdrawn and the serum injected into the patient.

In certain types of cases¹⁷ — those in the transitional stage, where the formerly hyperactive thyroid is undergoing colloid degeneration and where we find a curious mixture of the symptoms of Graves' disease and myxedema — Rogers and Beebe use what they term the "combined treatment." In this they use the serum we have just described to combat the conditions of hyperthyroidism, and at the same time give an extract of sheep's thyroid to neutralize the hypothyroidal or myxedematous conditions caused by the degeneration of part of the gland. One would naturally think that the serum would neutralize the extract of the sheep's thyroid, but this, the authors claim, is not the case. Rogers' latest published results¹⁸ are not as good as his earlier ones, for in 480 cases of all grades he claims only 15% of cures, removal of the subjective symptoms in 10%, and 50% improved to such a degree that they disappeared after one or two months' treatment because of the relief of symptoms. These cases, then, are lost, and we do not know whether they are better or worse. Seventeen per cent were unimproved and 8% died from the natural course of the disease.

They lay great stress on the importance of properly selecting the cases suitable for the different treatments and on the amount and frequency of dosage, and say that it is impossible to make hard and fast rules, but each patient must be carefully

studied and treated accordingly. Exophthalmos and goiter are the last signs to disappear, and while the latter persists the patient must avoid mental or physical over-exertion for fear of a return of the symptoms.

The principal objection raised to this form of treatment has been the possibility of injury to the rest of the organism by a cytotoxic serum strong enough to act upon any one of the tissues, as this serum is supposed to act upon the thyroid epithelium.

Electricity in several forms has been used by a good many, but there is very little evidence that any form of it is of value except the x-ray. Cook,¹⁹ Beck,²⁰ Freund,²¹ Price,²² Holland,²³ Garré,²⁴ and others report excellent results from its use, and all report a very great drop in pulse-rate after two or three treatments, in several cases the pulse dropping to normal after a few exposures and with this a great improvement in the subjective symptoms. It is thought that the x-ray causes the secreting tissue to shrink, and perhaps to some extent kills it, and in this way the secretion of the toxins is checked. As an adjunct in certain cases this treatment is certainly of value.

Let us now consider the other alternative, surgery, and first let us emphasize the importance of the surgeon's being an expert at thyroid operative technic, for the liability of injury to the parathyroid or to the recurrent laryngeal nerve and of hemorrhages in the hands of the inexperienced are too great to be overlooked. What are the indications for operation? The opinion of some surgeons is still that *diagnosis is the indication for operation*,²⁵ but that opinion is one which should be considerably modified in view of the success of medical treatment in a good percentage of cases. Certain types of cases require prompt operative treatment. Such cases are those in which the goiter is a mechanical danger, as, for instance, when it compresses the trachea or esophagus, or both. Here you get interference with swallowing or with breathing, and frequently cough and occasionally a dangerous bronchitis. The diagnosis is easy in the ordinary case when the enlarged thyroid can be palpated, but in cases with "dipping thyroid" the diagnosis is sometimes very blind. The greatest danger lies, not in the continued bearable pressure, but in the liability to sudden enlargement of the goiter, which not infrequently occurs, and which may quickly suffocate the patient. This point has been very strongly impressed upon us, for we have seen three cases die in this way while awaiting operation. Furthermore, this danger is so great that immediate operation is indicated in any case in which a dipping thyroid is found, even though the symptoms of exophthalmic goiter be very slight, as may happen.

Operation is also indicated when exophthalmos, by preventing closure of the lids, endangers the eyesight through corneal ulceration, or when after three months of good medical treatment there is no marked improvement in tachycardia or in the patient's general health, or there is an increase in the intoxication by thyroid secretion, even though

no enlargement of the thyroid can be demonstrated.²⁶ Cases with beginning cardiac involvement, — i. e., myocardial weakness, — as shown by a pulse of 130–160, or one that suddenly fluctuates in tension and rate, should be operated upon at once in order to save the heart,²⁷ while in cases that have gone beyond this point, and have arrived at the stage where the myocardium is badly diseased and the aggravating symptoms of exophthalmic goiter are still present, operation must be considered a last resort, not expecting a cure, but merely as an effort to prolong life by taking strain off the heart. If there is anemia with swelling of the feet, Mayo²⁸ puts the patient on rest and belladonna for some days, and in the severer types uses in addition the x-ray for two to six weeks. Riedel²⁹ emphasizes the importance of avoiding operation if possible, if there is any bronchitis from compression, since it increases to so great a degree the liability to bronchopneumonia, but in these cases it is usually better to risk the consequences of an operation than to risk a sudden swelling of the thyroid and a resulting death by suffocation.

Then there is another side of the question that must be considered, — the circumstances surrounding the patient. For instance, if our patient is a business man, dependent on himself and unable to give up the long time necessary for medical treatment and he is unable to go on in his present condition, immediate operation offers the best solution of the problem.

We shall not go deeply into the methods and technic of surgical treatment. Of the procedures³⁰ which remove the thyroid tissue, excision, as done by Kocher, and resection, as done by Mikulicz, are most frequently done, while Porta and Socin's method of enucleation without disturbing the posterior portion of the capsule offers the least liability of injury to the parathyroids with the resulting tetany. This however, is a very uncommon accident at the hands of experts. Horsley's procedure of division of the isthmus on the assumption that it would be followed by atrophy of the lobes has not been successful, and excision of the cervical sympathetic ganglia, as proposed by Edwards and later used by Jaboulay (1896) and Jonnesco, has been proved experimentally by Schiff to have no effect on the thyroid. Curtis,³¹ however, reported in 1903 that Jonnesco had done 17 bilateral operations of this sort with 60% of perfect cures and no deaths. Ligation of the thyroid arteries — Wollfer's operation — is of value. In some cases this alone has produced cures, but it is most valuable as a preliminary to the radical operation in severe cases.³² There is the danger of including the recurrent laryngeal nerve in tying the inferior thyroid artery, with resulting laryngeal paralysis and inhalation pneumonia, so great care should be taken that this does not occur. Ligation of the superior artery and vein, as is now done especially by the Mayos, is safe, but in many cases is not sufficient. In their latest paper³³ they report 2% of deaths within a few days after operation. For some unexplained reason acute thyroid poisoning may follow either of these last two methods of

operation as well as those in which the thyroid tissue is cut and otherwise subjected to trauma.

Crile³⁴ lays special emphasis upon the importance of mental quietude preceding the operation. He so handles the patient by rest and sedatives that she is not worried and excited by the approach of the operation, nor is she conscious of taking the anesthetic, and, indeed, he claims that the patient in some cases does not realize that the operation has been done. This method he terms "stealing the gland," and certainly his results are remarkably good.

Quiet following the operation seems to me to be equally important, for frequently the patient is fuller of thyroid toxin at this time than at any other.

Capelle³⁵ has called attention to the importance of ascertaining when possible the presence of a persistent thymus, for in unexplained cases of death following operation the thymus was found in many cases to be of the size commonly found in the newborn. This gland, lying just behind the upper part of the sternum, is very difficult to make out by percussion, particularly as it lies surrounded by a mass of fat which not infrequently leads to a wrong diagnosis. The x-ray helps us very little if any here, and if we find dullness on percussion over this region we are between two risks, — that of operating in the presence of the apparently present thymus, and that of depriving the patient of the benefit of an operation when the mass is a false thymus consisting merely of fat.

It is well known that persistent thymus predisposes to death under ether, and in many cases collected by Capelle death occurred ten to twenty hours after successful operation, with gradually increasing weakness of the heart without apparent cause. In other cases there was sudden death during the operation. Capelle does not believe that hyperthyroidism has anything to do with the sudden deaths, but considers the thymus responsible. In 60 such cases following operation for Graves' disease, 79% showed a large thymus, and of the cases of Graves' disease which died of intercurrent diseases, 44% had large thymus. Of those who died of exophthalmic goiter alone, 82%, and of those who died during operation, 95% had large thymus. Its presence, then, if it can be made out surely, contra-indicates operation.

Another contra-indication to operation is an acute exacerbation of the symptoms. If this occurs we must treat with rest, baths and sedatives until the symptoms subside. Furthermore, the condition of the heart must be carefully considered and the effect of exercise or excitement studied. In other words, if there is dilatation, marked hypertrophy or myocarditis, operation should be avoided. This means that operation, if done, must be done before any advanced symptoms of cardiac involvement appear; and it is very poor judgment to advise operation in any desperate case.

Following operation, we expect a very marked diminution in the subjective symptoms in a large percentage of cases. The exophthalmos and tachycardia, however, may persist or even increase

after the operation, and a total disappearance of exophthalmos can be expected only in those cases in which operation is done early. A case is occasionally seen in which the exophthalmos has increased after operation, though the pulse may be normal. We have recently seen a case in a girl in whom the operation removed all symptoms; she feels and apparently is perfectly well, her pulse is 80, and she is living her ordinary life, but with a steadily increasing exophthalmos, which may in time endanger her eyesight.

The theoretical course of goiter is to go on to degeneration, which means myxedema in the end. If this is true, it may be said that by removing a large portion of the gland we are merely hastening the advent of myxedema, and yet in the cases in which operation has been done years ago, myxedema has not yet appeared. This may be owing to the fact that other glands, perhaps the chromaffin system (that is, the cells we find in the medullary portion of the adrenals and scattered through the sympathetic system, particularly in the ganglia), takes up some of the functions of the degenerated thyroid.

Now to sum up in a few words: In practically every case it is our duty to treat the patient medically, as I have already outlined, for three months. If at the end of that time no improvement has taken place, preferably ligate the vessels. This may effect a cure. If it does not, and the patient later comes to the operation of partial thyroidectomy, — which is as yet the most satisfactory of the radical operations, — the ligation will make the operation easier and less dangerous. If the goiter is very large, it is well to remove only the larger lobe and then treat the remaining lobe with the x-ray and medical procedures.

Cases that show beginning cardiac failure should be operated upon as soon as possible after putting the patient in fair condition by medical treatment. Many cases, however, come to the doctor only after the myocardial changes have begun. Patients in this condition must be treated as cases of advanced myocarditis, for all treatment beneficial to this condition is also beneficial to the exophthalmic goiter. The treatment which I have mentioned — the strictest rest, with ice bags over the heart and thyroid, a carefully regulated diet, the hydrobromide of quinine, and, if necessary, the cautious use of strychnia and bromides — must be carried out. We must not expect an absolute cure in the cases where the myocarditis is advanced, though symptomatic recovery does sometimes occur, and we can hope only to lessen the symptoms and make life better worth living for the patient and the patient's family. The earlier cases we may be able to cure, and if not we may, by careful medical treatment, improve their condition to such an extent that they can be operated upon with much less danger than before treatment.

Gentlemen, — The last word in the treatment of exophthalmic goiter has not yet been said and we are still a good deal in the dark regarding it, but I hope that I have made clear to you the

indications for treatment which have met with the greatest success so far.

DISCUSSION.

DR. C. FROTHINGHAM, JR., of Boston: As Dr. Jackson's complete paper seems to cover the whole subject, I will simply try to emphasize a few of the points which seem to me to be of special interest. Although it is pretty generally admitted that the disease is due to a hypersecretion of the thyroid gland, the cause of this increased secretion is not clear. From a morphological point of view some pathologists say that there is an increase of glandular epithelium shown by infoldings. Other pathologists, however, deny that this condition is specific for Graves' disease. The chemists find some variation in the chemical properties of the gland in certain cases which might call forth an increased secretion, but no definite condition common to all these cases. Recently Dr. John Rogers, of New York, has worked out an elaborate theory for this hypersecretion dependent upon the interrelation between the chromaffin system, the pancreas and the thyroid. This theory up to the present time lacks confirmation by experimental evidence. In addition to the increase of secretion is the possibility of the increased secretion being abnormal. On this point there is considerable difference of opinion. Thus it is evident that there is a big field open for more work directed towards clearing up the true nature of this disease.

There is one point in regard to diagnosis which should be emphasized, and that is the question of whether the individual case is one of hyper- or hypo-secretion. For after the hypersecretion has ceased and there is even a diminution of secretion, the symptoms of exophthalmos and tachycardia may persist. In these cases the exophthalmos has become permanent, due to structural changes, and the tachycardia is the result of myocardial degeneration. To operate in such cases in order to diminish the secretion would, of course, be useless. Careful history taking and physical examination ought to clear up the point.

Whether or not to advise surgery in the treatment of this disease is difficult to decide. This is due to the fact that the present statistics are unsatisfactory. They are unsatisfactory for two reasons: the same authors rarely compare good medical treatment with the same treatment plus operation, and authors will not confine their reports to only those cases that have been observed many years. That surgical intervention will give more prompt temporary relief seems pretty well established. The uncertainty exists in the end results. Therefore the circumstances of the patients make a considerable difference in the line of treatment to be advised. For proper medical treatment the patient should have absolute rest. This of course is impossible for patients in our big general hospitals and for the poorer classes in their homes. Therefore, unless future statistics show that the end results of surgical treatment are a failure, some form of surgical treatment should be recommended for those who cannot afford proper medical treatment earlier than for those who can.

DR. C. A. PORTER, of Boston: I have just read a paper upon the surgical treatment of exophthalmic goiter, in which I endeavored to make a plea for surgery in selected cases in which adequate medical treatment for a number of months did not prove successful. I tried to bring out clearly that in operating upon cases of Graves' disease, the object of the operation is different from surgery in cases of fibroids of the uterus or diseases of the appendix. In the latter, surgery may properly be said to cure, that is, to remove the cause, but in exophthalmic goiter all the surgeon can attempt to do is to modify the function of a gland which for

various reasons is functioning excessively or abnormally. It must, therefore, be understood that the results will be good or bad, depending upon the wise selection of cases and the operation done; whether it be ligation of the vessels or partial thyroidectomy. I feel quite sure that too many cures have been claimed both to medicine and surgery without waiting an adequate time to see what the end results will be. The general practitioner must remember that there is a mortality from 8 to 10% under medical treatment. This mortality, I believe, could be very distinctly reduced, probably halved, if surgery had been resorted to at an earlier period. We must never forget that this disease, once advanced to a certain stage with accompanying degenerations of the heart, nervous system and vessels, is absolutely incurable, though under medicine or surgery the patient's condition may be somewhat improved. Whoever has seen a case of acute hyperthyroidism successfully operated upon cannot doubt that the diminution of secretion of the gland has struck at the root of the evil. I feel that in Graves' disease we have one of the best opportunities for co-operation between the physician and surgeon, and the use of experience and judgment in the selection of a time when medical treatment should cease and surgery begin.

DR. J. C. MUNRO, of Boston: I have just been congratulating them upstairs on the brotherly love that is dawning between the surgeon and the medical practitioner.

I endorse everything that Dr. Porter said.

DR. EBEN C. NORTON, of Norwood: I would simply add that I have used serum in three cases of exophthalmic goiter, in one case beneficially and in two cases negatively.

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THE SURGICAL TREATMENT OF EXOPHTHALMIC GOITER.*

BY CHARLES A. PORTER, M.D., BOSTON.

WHEN I agreed to read a paper upon the surgical treatment of exophthalmic goiter before this section, I had no idea that such excellent résumés of the whole subject were so soon to appear in our

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MEDICAL JOURNAL, written by Dr. Channing Frothingham, Jr., and Dr. J. G. Mumford. The subject, however, is one of growing importance and no harm will be done by bringing it up again, perhaps from a slightly different point of view.

While in this community the disease is commonly regarded as a medical affection, to be treated along the lines which Dr. Jackson will discuss fully in another section, the advances made by surgery in the past ten years have established without question the superior advantage of operation in properly selected cases. In spite of the newer treatment by sera and other therapeutic measures, a definite proportion of these cases go on to a rapidly fatal issue, or to myocardial and vascular changes which after a longer or shorter time are followed by death. Acute Graves' disease passes unrecognized even now, and a mortality of 5% to 10%, in hyperacute cases 15% to 20%, should teach us that exophthalmic goiter may be far different from the disabling, chronic but perhaps ultimately curable disease which many think it.

The excellent results of Kocher, Charles Mayo, Crile, Klemm, etc., show an operative mortality which varies from 3.5% (Kocher) to 9% in a series of 888 cases gathered from various clinics by Krecke in 1909. Statistics as to the results in the way of cures are numerous and somewhat variable. Heineck claims as end results 63.7% cures in 207 cases. Mumford's analysis of 741 cases, chosen somewhat at random from different surgeons' statistics, gives an immediate mortality of 4.03%; late mortality, .66%; unimproved, .38%; improved, 22.27%; cured, 70.3%. Though these figures are interesting and any argument in favor of operative treatment as against medical treatment halts lamely when not backed up by figures, I must confess to an entire agreement with Dr. George Grile, who states his opinion as follows:

"A study of my series of 72 operations for Graves' disease, presenting as they do numerous and complex symptoms, and involving many organs, as well as the most fundamental vital processes, impresses me with the great, almost insurmountable, difficulty, I may add, the impossibility, of compiling any statistical table that accurately represents the net clinical results."

The disease itself is fatal in perhaps 10% of the cases. Most surgeons select their material for operation, and many cases of temporary hyperthyroidism must be classed in the statistics as cases of Graves' disease. What the physician wishes to know is the particular risk which an individual case runs from operation, and what are the chances of cure as compared with medical treatment. This I claim must depend upon the sound judgment and skill of the surgeon, and the stage of the disease, and cannot be estimated from statistics in per cents. In the same way in regard to cures, when once certain degenerations have developed, a cure by medical or surgical means becomes an impossibility; some cases with very acute symptoms rapidly improve with or without operation; other patients, apparently well after