A Contribution TO THE PATHOLOGY OF THE THYROID GLAND.

BEING AN ORATION DELIVERED BEFORE THE MEDICAL SOCIETY OF LONDON, MONDAY, MAY 21ST.

BY PROFESSOR KOCHER,
BERNE.

MR. PRESIDENT AND GENTLEMEN,—When I was honoured by the invitation of your former President to deliver the annual oration before this highly reputed Society I was deeply impressed by the fact that some of the most important contributions to the knowledge of diseases connected with the thyroid gland have come out of this Society, and that the Society has been the first to acknowledge my own merits on this field of investigation by offering me the Honorary Fellowship. Allow me to offer to your members my admiration for the first and my sincere thanks for the second.

Thanks to the scientific work done, we are pretty well informed about all affections depending on deficiency of thyroid tissue or thyroid function, including cachexia thyropriva and tetania parathyropriva.

We cannot say the same of another category of diseases connected with alterations of the thyroid body—I mean exophthalmic goître. There exists still such a divergence of opinion as to the nature of the disease, that it influences our practice strongly, and in part in a regrettable way.

Many neurologists adhere firmly to the idea that exophthalmic goître is a neurosis and is to be treated as such, because they see frequently the first symptoms appear after severe mental shock

Sir Victor Horsley first in 1885 brought forward the theory of the thyrogenous origin of exophthalmic goître, asserting that the thyroid body is first affected, and that all the symptoms are to be explained by a dysthyrosis. Möbius has taken up this theory, ascribing a greater importance to the simple but excessive hyperactivity of the gland—that is to say, to hyperthyrosis. Surgeons in general agree with the idea of a combination of hyperthyrosis and dysthyrosis.

Before I try to bring before you the facts which seem to render it possible to come to a decision between those theories, it is absolutely necessary to explain what we mean by the expression exophthalmic goître. There will indeed be no doubt about diagnosis in a very severe case in the worst moments of the disease; but even here we always find a good many other symptoms as important and constant as are exophthalmos and goître—nay, more important than the first-named symptom.

I have never seen a severe case of the disease without an alteration of the thyroid gland. There is always some swelling of the gland, and the vascular phenomena, consisting of dilatation of the vessels, the arteries especially, with a characteristic bruit (*bruit de souffle*), often combined with thrill on putting the finger slightly on the artery, are to be observed very early.

It is only in later periods of the disease, and especially after treatment, that the vascular symptoms may disappear, and then we have only the swelling (much larger at this period) characterized by the uniform diffuse increase of all parts of the gland and by its coarse granular surface. At this period the gland has become harder than normal, whilst in the beginning the great development of vessels makes the organ feel softer than usual.

I would not accept the diagnosis of exophthalmic goître in the absence of characteristic swelling of the gland and the vascular symptoms at the beginning. I think we may affirm that clinically there exists a specific type of goître which presents itself in the beginning in the form of what I call vascular goître.

We cannot say the same of the exophthalmos. It is the most striking symptom, and in Germany people give the name of "*glotzaugen krankheit*" to the disease. There is no doubt, however, that, especially in the first period of the disease, except in very acute cases, exophthalmos may be entirely absent and come on only later. It is true that even in these cases the medical man will be able to make out a series of ocular symptoms well known as Stellwag's, Gräfe's, and Möbius's signs, and especially a sign which I consider one of the earliest symptoms of the disease in many cases, that is, a sudden retraction of the upper lid when the patient is made to look steadily at you or to look upwards suddenly. I think it worth while to take note of this symptom as a help in the early recognition of the disease.

In admitting that exophthalmos is frequently absent at the beginning of the disease and may be absent for a long period, it is impossible to continue the use of the term exophthalmic goître, as there is a risk that the term may cause the medical practitioner to overlook the first symptoms of the disease when treatment would have a most excellent effect.

There are other symptoms which are of greater importance than exophthalmos. In addition to the ocular symptoms already mentioned, tremor may be one of the most constant symptoms, combined with nervous agitation, the impossibility of keeping quiet, congestion of the lips, eyes, and face, perspiration with every effort or every emotional influence, in hot rooms or in society. The eyelids may be red and swollen, yellow-brown pigmentation may be noticed at the lids and round the mouth. The patient may complain of headache, want of sleep, vomiting, diarrhoea, extreme psychical susceptibility or depression, or may have undergone rapid emaciation.

I will not go on enumerating those well-known symptoms which have been described *in extenso* in monographs, and also by Dr. Albert Kocher. But I wish to emphasize the fact that there are a number of symptoms which may enable the medical practitioner to make his diagnosis when the most striking symptom—exophthalmos—is absent, and which for this reason have a greater importance.

But there is one symptom besides the characteristic goître which is never wanting—that is, the heart trouble in the form of tachycardia. The combination of heart trouble with goître is so constant that the name of goître heart (*Kropfherz*) has recently been introduced to collect together all affections of the heart which depend upon the formation of a goître.

Buschan has tried to show in a monograph on Basedow's disease that the good results of operations are to be explained by the fact that the cases really benefited by excision of goître are not true cases of the disease, but that they are examples of those heart troubles in which the heart is affected indirectly by a goître pressing mechanically on the great vessels or the cardiac nerves at the base of the neck or on the windpipe, affecting the heart by producing some degree of suffocation.

It is perfectly true that we may see cases of large goîtres, especially the more or less intrathoracic forms, presenting the symptoms of tachycardia and irregular heart action with obstruction of the venous circulation, so that the eyelids swell and a certain degree of exophthalmos comes on. These are very important cases, inasmuch as by excision of the goître in due time we can certainly obtain a perfect cure.

Buschan proposes the name of pseudo-Basedow for these cases, but it is better to say that they have nothing whatever to do with exophthalmic goître in the proper sense of the word. They are an excellent illustration of the fact that the combination of goître and exophthalmos is not the essential feature of the so-called exophthalmic goître. It is much better, therefore, to give up the term altogether and to use a more indifferent term until we have cleared up the theoretical cause of the disease so far as to enable us to use a rational designation.

I do not wish to enter here on a discussion of the historical question who was the first to describe exophthalmic goître. I am willing to acknowledge that there are as good reasons for giving the name of Graves's disease to true exophthalmic goître as the name of Basedow's disease. If I use the latter name, you will excuse it by the fact that it is the most common designation in medical literature.

What I mean to sum up under the names Graves's or Basedow's disease, includes all the affections in which the symptoms, including the most constant, goître and heart trouble, are dependent directly on the alteration of thyroid tissue and thyroid function. And here I should like to add one word to define at the outset my opinion as to the nature of this influence.

If I exclude from true Basedow's disease all the goître hearts depending merely indirectly on goîtrous changes owing to the mechanical effect of the swelling on the surrounding organs, I shall also exclude for the moment the theory stated in a very able monograph by one of my former pupils, Dr. Minnich, who, basing himself on the experiments of the distinguished Russian physiologist Cyon, has tried to prove that goître heart is a consequence of diminished function of the thyroid gland. On this theory even Basedow's disease, as well as cachexia and tetania thyropriva, would come under the head of hypothyrosis.

I have seen seventy cases of cachexia strumipriva after total or partial excision, and sixty-six cases of spontaneous cachexia thyropriva or myxoedema, but I have never in uncomplicated cases seen any analogous affection to Basedow's disease. On the contrary, the contrast between the two series of symptoms is complete, as I pointed out when I first described the consequences of total excision of the thyroid gland in April, 1883. I should therefore say that we are in no way justified in placing true goître heart and the milder and severe forms of Basedow's disease under the head of hypothyrotic affections.

But what I should like to lay stress on is this, that when we wish to form a clear judgement as to the effect of treatment in Basedow's disease, we must absolutely distinguish the different degrees in which the disease presents itself at the moment of our examination. We may have to examine a patient quite at the beginning, when there is not much more to be seen than a characteristic alteration of the thyroid body, with some heart trouble and slight indications of the other symptoms. We may see the patient when, owing to concomitant alterations of different kinds, the symptoms are mitigated, and some of the most striking features, like exophthalmos, are wanting, or where, on the contrary, by the influence of previous changes in the nervous system, the symptoms are particularly severe. I have therefore classified my material for the statistical reports I wish to bring before you under the following three forms:

I. *Vascular Goître (Struma Vasculosa).*

This variety consists of a very characteristic change in the thyroid body, which swells rather rapidly in the form of a more or less soft tumour with great dilatation of the vessels and systolic bruit and thrill. The tumour is nearly as characteristic as the swelling of the gland in ordinary cases, but the general symptoms are much less pronounced than in a typical case of Basedow's disease. Tachycardia is always present, tremor as a rule, but exophthalmos is often wanting, and only some of the ocular symptoms (Stellwag's or Gräfe's) indicate the beginning of the influence on the general system.

Here the chance of a favourable result from medical treatment by small doses of iodine or, better, with phosphates, is particularly favourable, and the outlook for radical cure by operation is excellent.

I have had 14 of these cases under treatment; 4 have been treated internally, 10 have been operated upon either by ligature or excision on one side, and all have been cured.

II. *Struma Gravesiana Colloides.*

The second variety of the disease, which we have to separate from typical cases, may be placed under the head of what Marie proposed to call (not quite in the same sense as I use it) "goître Basedowifié" = basedowified goître (Struma Basedowificata or Gravesificata). This is a rather frequent form, and its characteristic feature is that an ordinary goître exists before the development of the Basedow changes, which are, so to speak, grafted on the common form of colloid goître. We might give it, therefore, the less barbarous name of Struma basedowiana (gravesiana) colloides.

In these cases I have found the symptoms less severe even when all were present. If all be not present it is especially the exophthalmos which may be wanting. Tachycardia is always present, but even here the dilatation of the heart is less. There can be no doubt that we have to do with real Basedow's disease in a mitigated form, because the other ocular symptoms are frequently present, and so are most of the typical symptoms. Why all the symptoms exist in lesser degrees must be explained by the degenerative changes in the gland; it seems especially, as Dr. Albert Kocher has shown, that the ordinary colloid material is to a certain degree an antibasedowian agent, when patients are fed on it, or when we produce it artificially in the gland. It may be, also, that some direct influence on the sympathetic nerves is diminished by the presence of colloid material. At any rate, I have seen cases in which the symptoms of true Graves's disease have been greatly ameliorated when an ordinary colloid goître developed. This seems to me to be a rather important feat.

Buschan did not make a clear distinction between this form and the mechanical goître heart, but mixed these forms together under the head of pseudo-Basedow's disease. This was a mistake, and has been the cause of much confusion in judging of the effect of treatment.

I have myself seen 72 cases of this mitigated form of Basedow's disease, or struma basedowificata. Of these, 60 have been operated upon without one death. Of 7 cases there is no news to be had; 2 cases are better, and 51 cases are cured. The operation consisted in 32 cases in excision of one side, in 8 cases in excision of one side and one ligature on the other side, in 3 cases in excision of one side and partial resection of the other, in 4 cases in ligation of both superior arteries, in 6 cases in ligation of the two superior and one inferior thyroid arteries.

III. *Typical Basedow or Graves's Disease.*

The cardinal symptoms already described, developing frequently very rapidly—even suddenly—after mental shock, give rise to such a change of aspect that it strikes even inexperienced people at once. The exophthalmos is in this respect the most striking symptom; but it is quite certain that even here in the beginning it may be absent, and the diagnosis has to be made by the other ocular and general symptoms.

Of this form, which may be called struma basedowiana, where every medical man would recognize clearly the disease after a short examination, I have seen 140 cases and operated on 106 of these. There have been 9 deaths; 5 cases have died later of different affections, partly without any relation to the disease; 6 have had tetany after the operation without a death; 7 cases are better than before the operation; 9 cases are greatly or even extraordinarily improved according to the letters received, 62 cases are cured and in 34 of these the cure is perfect. So we have had, with the exclusion of 10 cases in which the operation was performed only a short time ago and which are as yet only ameliorated, and 9 cases in which I have so far failed to get any news from the patient, a perfect or very satisfactory result in 81 per cent., or a good result in 89 per cent. We may say (excepting the nine patients who died) that there has been no patient who has not in reality been benefited a great deal by the operation. I have had news from a very hysterical person, who thinks herself in much the same condition as before the operation, but when I saw her she was cured of her Basedow's disease.

If we take all the cases which can be classed together under the head of Basedow's disease, the typical and severe cases in later periods as well as the milder beginning forms, we have a total of 175 operations with 9 deaths, equal to 5 per cent.; cure or extraordinary amelioration in all milder forms, and in 70 per cent. of severe; in deducting 26 cases in which the time since the operation does not seem long enough to warrant us in speaking of a definite result and in which no records can be secured, the figures show in the remaining 149 cases 131 cures and 9 notable ameliorations.

With such statistical results at hand, and considering the fact that in taking away the diseased thyroid gland we are able to cure even the severest cases of Basedow's disease, when the operation is done in due time, we can scarcely come to the conclusion that we have to do with a neurosis which is cured by such a serious operation, and still less may we approve the idea of Buschan that in cases of true Basedow's disease the operation acts only by way of suggestion. We must, on the contrary, admit that with the thyroid body we take away the source of the mischief and the organ in which the disease is localized. This is practically the most important fact, to be able to say once and for all—Graves's (Basedow's) disease means a thyrotoxic affection in opposition to cachexia thyreopriva. The question whether the functional disorder consists in a perverse activity of the gland in the sense of dysthyrosis or in a simple exaggeration of the normal function (hyperthyrosis) is still open to discussion.

Horsley is the propounder of the first theory, which he

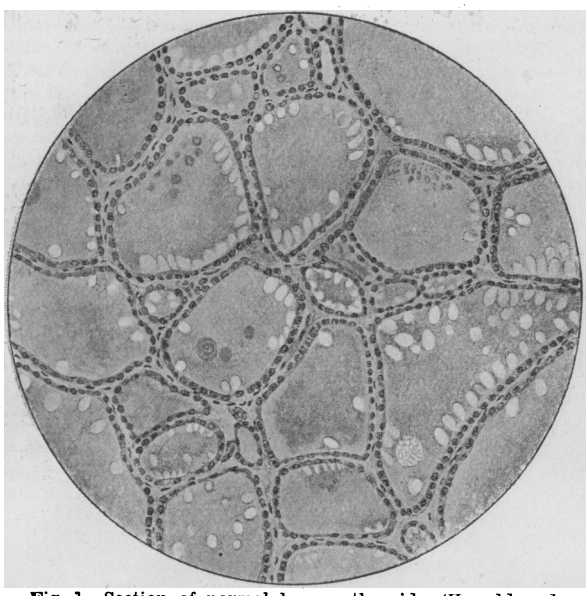

Fig. 1.—Section of normal human thyroid. (Howald and A. Kocher.)

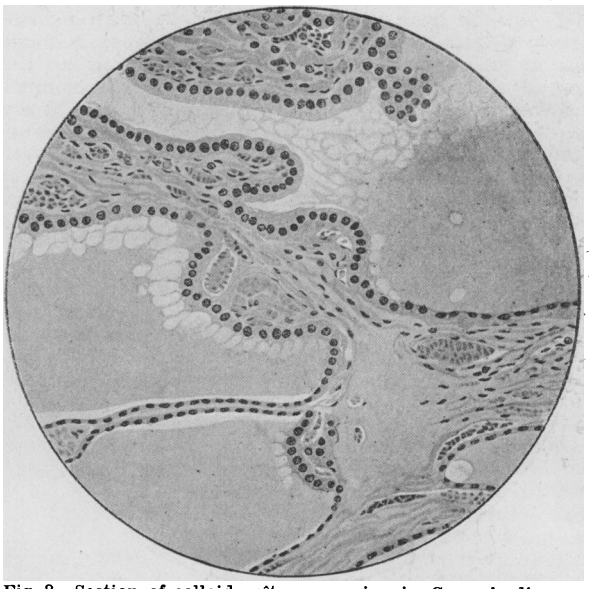

Fig. 2.—Section of colloid goitre occurring in Graves's disease. (Howald and A. Kocher.)

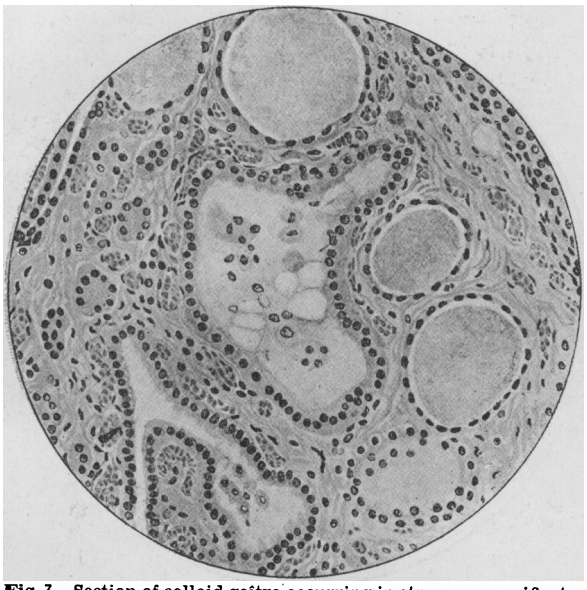

Fig. 3.—Section of colloid goitre occurring in struma gravesificata. (Howald and A. Kocher.)

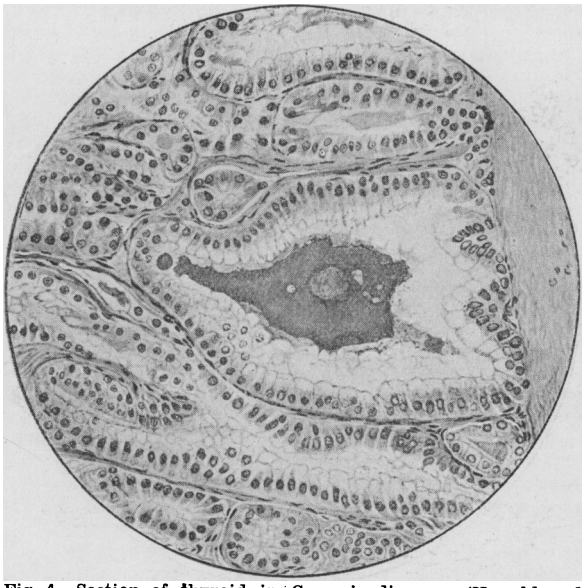

Fig. 4.—Section of thyroid in Graves's disease. (Howald and A. Kocher.)

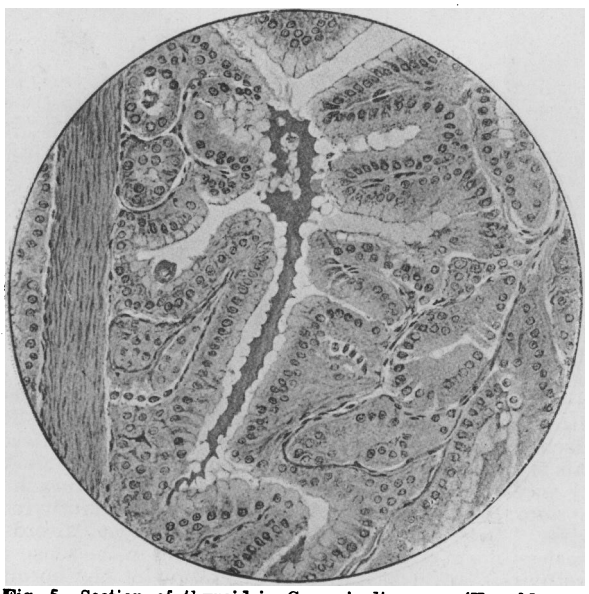

Fig. 5.—Section of thyroid in Graves's disease. (Howald and A. Kocher.)

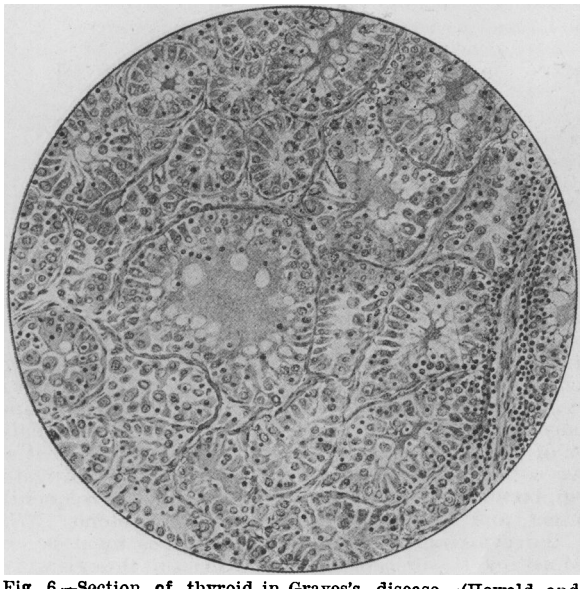

Fig. 6.—Section of thyroid in Graves's disease. (Howald and A. Kocher.)

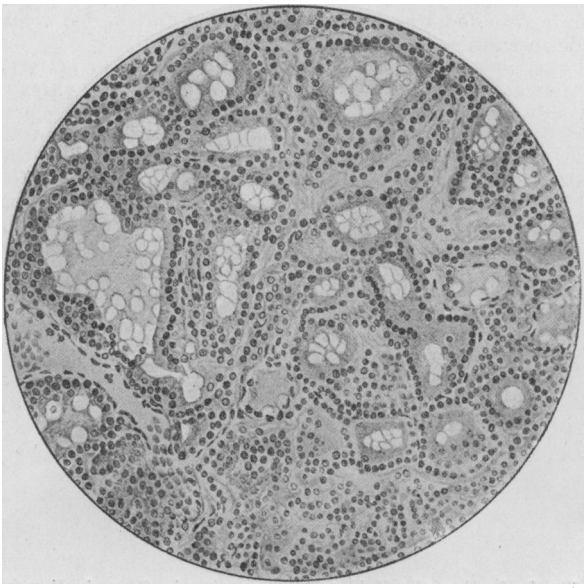

Fig. 7.—Section of thyroid gland of dog 13 weeks old. (De Ligneris.)

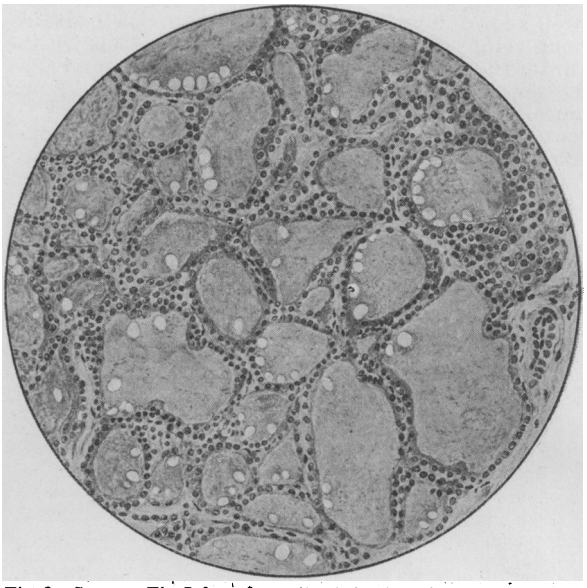

Fig. 8.—Same as Fig. 7, four days after injection of Lugol's solution (De Ligneris.)

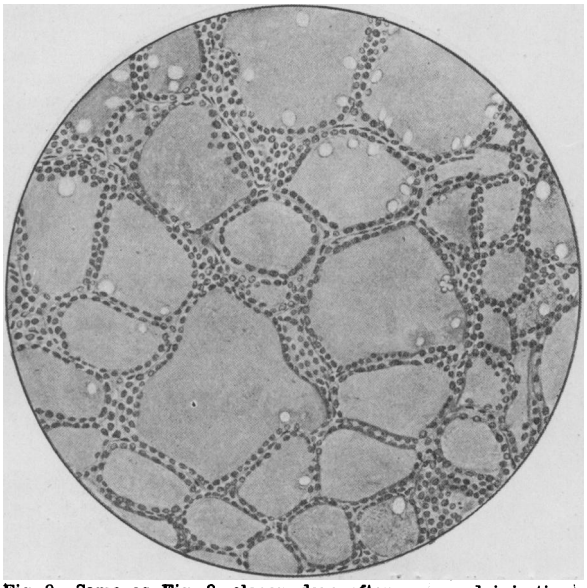

Fig. 9.—Same as Fig. 8, eleven days after a second injection. (De Ligneris.)

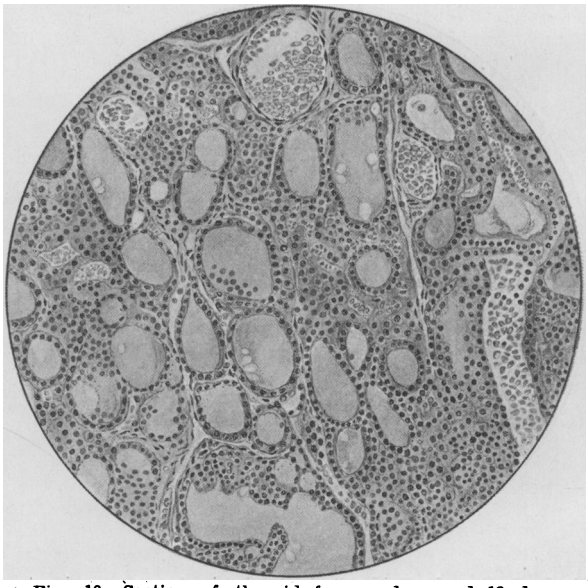

Fig. 10.—Section of thyroid from a dog aged 18 days. (De Ligneris.)

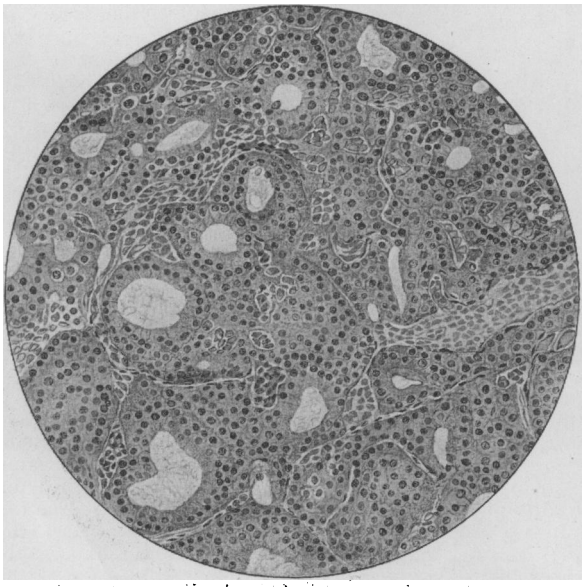

Fig. 11.—Section of thyroid: Hyperplasia of the part of the gland left. (De Ligneris.)

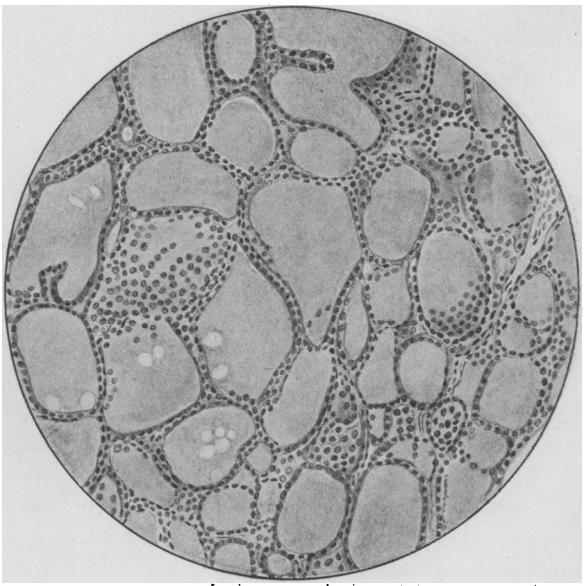

Fig. 12.—The same as Fig. 11, six weeks later, after treatment with potassium iodide internally. (De Ligneris.)

put forward a good while before Moebius combined both in his well-known thyrogenous theory of Basedow's disease, without being able to furnish convincing proofs for the one or for the other. Let me try to submit to your judgement some more facts, drawn from histological and chemical examination of the gland and of the blood.

Does the thyroid gland in Basedow's disease offer histologically such specific changes as justify us in thinking of an increased or altered activity of its parenchyma and secreting cells?

I may call your attention to investigations undertaken by Sir Victor Horsley, Friedrich Muller, McCallum, and many others, and to a paper which is about to be published by Professor Howald in collaboration with Dr. Albert Kocher on this difficult question. I show a few histological drawings of characteristic forms of true gravesian goître and of the colloidal form of it (struma basedowiana vera and struma basedowiana colloides).* The extraordinary development of the epithelium will be observed (Figs. 4, 5, 6). It assumes a high cylindrical form, and has formed papillary excrescences in the lumen of the vesicles; the lumen does not contain the ordinary colloid material, but seems empty because the secretion was liquid. The great vascularity of the gland, and the capillary hyperaemia will also be remarked. A very different picture is seen when preparations of colloidal form are examined (Fig. 2); the follicles are filled in the ordinary way with colloid material, and the epithelium quite flattened. Fig. 3 is from a case of a mitigated form of Graves's disease grafted on colloid goître, and you can recognize distinctly in some places the transition of the one form into the other by the elevation of the epithelium and the formation of low papillae.

It must not be forgotten that the operation which furnishes the pathological specimens is performed at very different periods and for very different degrees of the disease, and that in consequence the anatomical substratum must vary to a great extent.

The second piece of evidence in favour of the increased activity of the gland is the constant swelling of the lymphatic glands in the neighbourhood of the thyroid body in severe Basedow's disease and the changes we have been able to trace in the composition of the blood. In a great many cases during the operation I have seen the lymphatic glands swollen, and pathological examination has proved this swelling to be merely hyperplastic. Now, according to the theory of Asher, this indicates always a greater irritation of the glands by the lymph of the vasa afferentia as a consequence of greater activity of the organ which furnishes the lymph and with it the products of its metabolism.

Further evidence of a greater irritation of the lymphatic glands by the toxic products of increased metabolism in the thyroid body is afforded by examination of the blood. I have had the blood examined many times by my assistants, especially by Dr. Bacilieri, Dr. K. v. Steiger, and by the well-known and renowned haematologist, Dr. Nägeli, of Zurich. We have found in many of these cases an increase in the lymphocytes even up to 60 per cent. of the white corpuscles. In one case, examined by Dr. Nägeli, even 74 per cent. lymphocytes with mononuclear forms were found; as a rule the proportion is from 30 to 40 per cent. This increase does not mean an increase of the leucocytes *in toto*, on the contrary the whole quantity is much the same as normal, or even a little less.

What adds strength to the belief that this lymphocytosis† is a consequence of an irritation of the lymphatic system, is the fact that among the lymphocytes there are a good many atypical forms, with larger nuclei and greater quantity of protoplasm (large mononuclear forms).

Owing to the poisonous effect of the abnormally increased secretion of the thyroid body on the bone marrow (medulla ossea) Dr. Nägeli has found 2 to 3 per cent. of myelocytes with diminution of the neutrophiles and a certain amount of anaemia of the red corpuscles in some cases. These investigations suggest an interesting analogy between the severe forms of Basedow's disease and what is called "status lymphaticus"; in both diseases any operation is attended by a risk of sudden and unexpected death under certain conditions, especially narcosis.

I may mention another indication of the great activity of the gland which is furnished by chemical analysis. Dr. Oswald, and especially my son, Dr. Albert Kocher, have investigated the iodine content of the thyroid in cases of Basedow's disease. The result is that in the cases in which the follicles are found empty after excision much less iodine may be found in struma basedowiana than in the normal gland or in ordinary goître, sometimes almost none at all. That this is only the consequence of the rapid resorption of the thyroid secretion is proved by those cases in which the follicles are filled with colloid material. Albert Kocher has found an extraordinary quantity of iodine—40 to 50 milligrams—in one lobe of the gland in such cases, though the gland was not much more enlarged than in other cases of Basedow's disease. We may conclude from these investigations that the production of one of the specific constituents in basedowian goître is greatly increased.

From a consideration of the fact that, according to Nägeli, chronic lymphocytosis and eosinophilia are characteristic features of other chronic infections and intoxications, and that we can produce the same by hypodermic injections of iodine, we arrive at the conclusion that there is good evidence of hyperactivity of the thyroid body as the cause of Graves's disease.

Clinically, struma basedowiana presents characteristic features in the vascular symptoms (dilatation of arteries and systolic bruit and thrill), with diffuse and uniform swelling of all parts of the gland which has a coarse granular surface, and is at first softer, but later rather harder than ordinary goître. This is quite in accordance with the fact that by taking away the diseased thyroid body the symptoms may disappear completely. There is only one exception to this rule, when in later periods secondary changes have taken place in the fatty tissue of the orbit, in the cardiac muscle, etc., which hinder the complete re-establishment of normal conditions.

There is one more point which affords still stronger evidence of the theory of hyperthyrosis. If we ask why all cases are not attended by complete success, we may answer: We know quite well which cases we may hope to cure entirely, and which will show only more or less amelioration; the improvement is in exact relation with the amount of hypertrophied tissue we take away or destroy by our operation—that is to say, with the amount of diminution of the function of the gland produced.

If we ligature one artery we will get some, but only a slight, amelioration of the symptoms. If we ligature two arteries the effect will be exactly so much greater as more of the function is inhibited. If we take away one lobe of the gland the effect is still greater. If we put a ligature on three of the four arteries, we may have a very good result, and a still better if we excise one lobe and put a ligature on the superior thyroid artery of the other side; it will be even more complete when we combine unilateral excision with the resection of the upper and lower half of the other lateral lobe.

If we have begun with one or two ligations, and have had an unsatisfactory result, we are sure to complete it by adding a third ligature or by excision of one half of the gland. In short, we may say that by operation it is in our hands to guarantee a more or less complete result.

This absolute parallelism between the degree of diminution of morbid symptoms and the quantity of thyroid tissue removed seems to prove that the abnormally increased activity of the gland throws some poisonous substance into the circulation; but the question still remains open whether it is exclusively the excess of the normal secretion which exerts that poisonous influence on the nervous, and especially the sympathetic, system, or whether it is some abnormality of the secretion plays a certain part. In favour of the theory of pure hyperthyrosis we may add that the administration of extracts of the normal gland or of iodothyrin give rise to the same symptoms as basedowian goître. In a case of myxoedema the administration of thyroidin or of iodothyrin was followed by a rise in the pulse and temperature, the urine became more abundant, more nitrogenous substances being excreted, and there was palpitation of the heart, trembling, emaciation, diarrhoea, and perspiration.

* The preparations are made by Professor Howald and Dr. Albert Kocher.

† According to Nägeli, Cabot found in 1 case out of 15 pronounced lymphocytosis (8.5 per cent.). Neusser has made a similar observation. Fapport (like Neusser) has found in 1 case out of 4 eosinophiles (50 per cent.). Besançon and Labbé have seen leucocytes with special increase of mononuclear forms after feeding with thyroid.

If we give to a cretinoid or a myxoedematous individual with atrophy of the thyroid gland the quantity of thyroid extract his body needs, he will become like a normal person; but if we give him much larger doses for a long time, he will go to the other extreme and become a Basedow patient.

So we may state positively that over-activity of the thyroid gland would, for one reason or another, be quite sufficient to explain the appearance of the symptoms of Graves's disease and their disappearance after operation.

Are we, then, bound to propose the operation to every patient affected with symptoms of Basedow's disease, regardless of the stage to which the disease has advanced? In attempting to answer this I must point out that undoubtedly the first change is in the nervous system in many cases; in others the disease dates from an acute infection. Prolonged or sudden nervous exhaustion is frequently the cause of the appearance of the first symptoms, and it is probable that a suddenly increased metabolism in the nervous tissue brings toxic substances through the circulation to the thyroid gland, and gives rise to irritation and reaction, causing increased activity of the parenchyma. This influence must never be forgotten, and has its share in affording indications for treatment. We must in these particular cases do everything to diminish influences tending to exhaust the nervous system, and, above all, keep the patient perfectly quiet in every way for a long time. At the same time we may try to compensate the loss of phosphates accompanying nervous disorders by the administration of phosphates, one of the best treatments for Basedow's disease. In addition, a well-chosen diet and good food are necessary.

On the other hand, it is important not to delay the operation so long that it becomes a danger to life. Whilst in my last 1,000 cases of excision of ordinary goître (excluding malignant diseases) I have only lost 3 patients, I have lost 9 in 175 operations for Basedow's disease. Shall we be able ever to avoid all fatal results after operation? In all the fatal cases, besides the irritation of cardiac nerves, organic changes of the muscle of the heart, with more or less dilatation and irregularity of action existed, and to these alterations of the heart is to be attributed the fact that there have been more deaths than in ordinary cases. It is therefore necessary not to delay the operation until these organic changes have set in.

Table of Cases of Thyreotoxic (Graves-Basedow's) Disease.

Total number of cases seen 225
Total number of cases operated upon ... 176

	Operated Upon.	Mortality of Operation.	No Further News.	Amelioration.	Great Amelioration.	Cured.
1. Struma vasculosa, commencing Basedow's disease; symptoms mainly local	10	0	0	0	0	10
2. Struma basedowificata; milder form developed on a pre-existing ordinary goître	60	0	0	0	2	49
3. Struma basedowiana; typical Basedow's disease	103	9	9	17*	9	62

Total mortality ... ... 5 per cent.
Immediate recovery ... ... 95 ,,
No later news ... ... 10 ,,

Of the remaining 158 cases:
Died later... ... ... 2 ,,
Improved ... ... 10 ,,
Greatly improved ... ... 7 ,,
Cured ... ... 81 ,,

*In 1 of these only preliminary operations have been performed up to the present time.

In all severe cases of Basedow's disease there is much more reaction after operation than after excision of ordinary or even malignant goître. There is a sudden rise of the temperature, and more sudden increase still of the action of the heart. If the heart has already been weakened by degenerative changes it may suddenly fail and death follow very rapidly, sometimes unexpectedly. As an explanation of this excessive tachycardia and fever, I think we must accept the view that besides the influence of the exaggerated sensibility of the vascular nervous system there is a sudden increase of intoxication, because all the other symptoms of Basedow's disease may also be greatly exaggerated, producing great agitation, congestion with profuse perspiration, trembling, diarrhoea, and excessive weakness. It is probable that, owing to the manipulation of the gland during the operation, there is a suddenly increased resorption of thyroid secretion. You are aware of what that means in cases of excess of iodine shown in Albert Kocher's patients. The reaction is still worse after simple ligature. In my fatal cases, in 4 out of 9 I performed simple ligature on one, or two, or three arteries; in two of the other five cases ligation of the other side was combined with unilateral excision. When the veins are ligatured there follows—as Dr. Verebegy has shown experimentally at my clinic—a notable increase of resorption by the lymphatics as the immediate result. The reaction therefore is decidedly less when we ligature the isolated artery alone than when the veins are ligatured together with the artery. This increase of intoxication only lasts for a few days, and the effect of the operation on the action of the heart some days later is excellent.

Operation in the early stages of Basedow's disease does not expose the life of the patient to any danger. I have not lost one case, when the operation could be performed early, even in very bad cases, but I have been very careful to secure judicious medical treatment for these patients for weeks before the operation. A judicious use of very small doses of iodine for a short time, the continuous use of phosphates* (sodium phosphate from 2 to 10 grams a day), and absolute mental and bodily rest are the most important features of it. Figures 7 to 12 are reproductions of drawings of microscopical preparations from experiments by my assistant, Dr. de Ligneris; they show the effect of the iodine treatment on the increase of colloid material.

I often begin with the ligature of one superior artery, perform the second operation ten days or a fortnight later when the patient shows improvement, and undertake excision of one side only when, after some weeks more, the symptoms of the disease show a decided diminution. In this way operative treatment may be made successful, even in severe cases, if care be taken to avoid any danger from the general anaesthesia, which is very risky in cases of great dilatation of the heart, due either to overwork or to toxic fatty degeneration. The latter may exist at the same time in the liver and kidneys.

I saw a few days ago the husband of a lady affected with severe Graves's disease. The diagnosis had been made some months after the appearance of the first symptoms by an excellent medical practitioner. After having examined the patient with the doctor of the family, the consultant went into another room and told the husband: "Your wife has a very serious illness, called Basedow's disease, and there is absolutely no hope for a cure as we have no remedy for it." If I have succeeded in making medical practitioners present at this meeting appreciate the results of my long surgical experience, I hope that they may find themselves justified in telling a poor husband, waiting for the verdict of a medical consultation in an analogous case: "Sir, your wife has a very serious illness; but if you are willing to have an operation performed we may, with the help of proper medical treatment, expect a perfect recovery."

* According to the experiments of Barbera, sodium phosphate is an antagonist to iodine in its action on the regulatory system of the heart.

THE Pasteur Institute at Tunis has begun to publish *Archives*; the first number contains a general account of the institution and its work. It began in 1893 as a viticulture laboratory only, but has grown steadily in all directions and now undertakes antirabic inoculations, the supply of vaccine for all Tunisia, and general clinical research work. It also supplies serums of all varieties if required. A good deal of original research is being carried on within its walls by M. Nicolle and three assistants, the principal subject of investigation being ferments. Altogether since the work was taken up 1,695 presumed cases of human rabies have been treated, with a death-rate of 0.29 per cent.

MEDICINE AND MATRIMONY.—A meeting of the class of 1905 of the Faculty of Medicine, University of Toronto, was held recently, at which it was decided to adopt as "class boy of 1905" the first male child born to a member of the class married subsequently to graduation. This is intended as an encouragement to the young doctors to marry.