A Lecture ON GRAVES'S DISEASE.

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GENTLEMEN,—Graves's disease, the main features of which I propose to discuss to-day, is one of the most interesting of maladies. While it is easy, as a rule, to diagnose it, it is often most difficult to treat it successfully, or to make a correct prognosis. Although we know something about the pathology, there are many points, such as the origin or exciting cause of the disease, which remain obscure. At one time it was generally considered to be a disease of the nervous system, with changes in the brain or the sympathetic, and you will find it still included in textbooks of neurology. It is only of recent years that it has been recognized how the various symptoms of the disease hang together and are dependent on and have their origin in changes of the thyroid gland.

PATHOLOGY.

Let me first remind you of the facts which are known relating to the morbid anatomy of the disease. If we have the opportunity of examining a case after death we observe that the body is emaciated sometimes to an extreme

Fig. 1.—Section of normal thyroid of dog.

degree. We notice that the thyroid gland is enlarged, that this enlargement is general, that the veins on its surface are dilated, and that its nutrient arteries are dilated and tortuous. Its substance, we probably find, is rather softer in consistence than normal, but in an old-standing case it may be firmer than

Fig. 2.—Section of thyroid from a case of Graves's disease.

normal from growth of fibrous tissue. If we cut a section of the gland we probably are able to see that there is a marked hypertrophy of the blood vessels. Under the microscope we observe that the vesicles, instead of being, as they are normally, round or square, have become branched or stellate, and their lining membrane has become involuted. The secreting cells, instead of being cubical, are columnar, and the colloid matter, which normally fills the interior of the vesicles, has partly or entirely disappeared, its place being taken by a mucous substance which stains badly.

Mr. Walter Edmunds, to whose kindness I am indebted for the accompanying illustrations, has shown the striking similarity there is between the microscopical appearances of the gland tissue in Graves's disease and in the case of an animal from which the greater part of the gland has been experi-

Fig. 3.—Normal secreting cells lining vesicles of dog's thyroid.

mentally removed. After the operation the small portion left behind undergoes changes of the nature of compensatory hypertrophy; and if you compare the two you will find that a section of gland from a case of Graves's disease is practically indistinguishable from one from the gland of an animal with this experimental compensatory hypertrophy. It would,

Fig. 4.—Altered secreting cells lining vesicles in a case of Graves's disease.

therefore, seem that in Graves's disease the thyroid, for some reason at present obscure, takes on increased functional activity and undergoes hypertrophy.

Attention has lately been directed to certain small bodies which anatomically are in intimate relation with the thyroid, and have been called parathyroids. Although in man

Fig. 5.—Changes in remaining portion of thyroid of dog after partial thyroidectomy.

actually embedded in the thyroid, these bodies differ from it entirely in their microscopic structure. Instead of being made up of colloid-containing vesicles they are formed entirely of cells which are arranged in columns separated by capillaries. It has been suggested that they are embryonic thyroid tissue, but as they develop in advance of the thyroids

Fig. 6.—Thyroid from a case of Graves's disease.

themselves, this cannot be the case. Physiologically these bodies are of great importance. It is found that their removal, although the thyroids themselves are left intact, almost invariably causes the death of an animal, preceded by symptoms which very closely resemble those we see in some

Fig. 7.—Altered secreting cells lining vesicles after partial thyroidectomy.

Fig. 8.—Normal parathyroid of monkey.

Fig. 9.—Normal parathyroid of dog.

Fig. 10.—Section of thyroid of dog from which parathyroids had been removed.

Fig. 11.—Monkey previous to thyroid feeding.

Fig. 12.—Monkey after nine weeks' thyroid feeding.

fatal cases of Graves's disease. Changes are found to have taken place in the thyroid glands like those of compensatory hypertrophy, save that the glands do not enlarge. It seems probable that the parathyroids play an important part in the pathology of Graves's disease, and that their atrophy may be the cause of some of the more serious symptoms. Atrophy of the parathyroids has been observed in some cases of Graves's disease, but we cannot say as yet whether it is an essential feature or not.

As regards the morbid anatomy, there is another important matter to which I must refer: that is the persistence of the thymus gland. In all the fatal cases of Graves's disease in which I have had the opportunity of seeing or making a *post-mortem* examination, the thymus gland has been found to be persistent, and I think that all pathologists who have looked for the thymus in fatal cases of Graves's disease have noticed the same persistence. Sometimes the thymus is more than persistent—it is hypertrophied. Here is a drawing which Mr. Lapidge made for me in one of those fatal cases, showing the persistent thymus spread out in a thin layer over the surface of the pericardium. The microscopical appearances of the thymus in Graves's disease differ in no way from those of the ordinary gland. The persistence of the thymus in adult life is a curious matter. The persistent thymus has been there before obvious symptoms of the disease manifested themselves. Perhaps every case of persistent thymus is one of potential or latent Graves's disease.

Other changes which are found in Graves's disease are few. Sometimes the spleen is found enlarged; sometimes there is increased connective tissue in the neck; sometimes there is swelling of the lymphatic glands in the neck, in the thorax, and in the abdomen. The heart may appear normal, but usually there is dilatation of the left ventricle, or there may be evidences of old endocarditis, the latter, however, a lesion which has originated independently of the disease.

There are no obvious naked-eye changes in the nervous system, but in some cases certain microscopic lesions have been found after death, such as minute haemorrhages in the neighbourhood of the medulla. My belief is that these are secondary changes, the result and not the cause of the disease. The great probability is that the hypertrophy and over-activity of the thyroid is the cause of the symptoms of the disease, and of most of the changes in the organs of the body, just as the atrophy and loss of activity of the gland is the cause of myxoedema, or its non-development the cause of cretinism.

What it is that starts the hypertrophy of the thyroid and what part the persistent thymus plays we do not know. In some cases the disease seems to be set up by shock or by emotion, which we know may be followed very rapidly by swelling of the thyroid gland. It is possible that the disease in some cases may be due to microbic infection. That the most conspicuous symptoms of Graves's disease are the result of over-activity of the thyroid is shown by the effects which have been obtained by the administration of large doses of thyroid gland in human beings and in the lower animals. Mr. Walter Edmunds has shown that, if dogs or monkeys are fed with large doses of thyroid, there results accelerated action of the heart, increased metabolism, loss of weight, increased action of the skin, and sometimes marked exophthalmos. Indeed, you find that practically all the symptoms of Graves's disease, including exophthalmos, can be produced in animals by the administration of large doses of thyroid gland. I do not know of any case in man in which exophthalmos has been caused by the administration of thyroid gland, but I have observed the production of practically all the other symptoms. Of course, we could not give the extremely large doses of thyroid gland to human beings which have produced exophthalmos in lower animals.

SYMPTOMS.

I propose now to consider the symptoms of the disease. The disease is met with much more commonly in the female than in the male; but it is not so rare among men as is generally supposed. For 5 cases in women I see about 1 case in a man. It may occur at any age, but it is rare in children or over the age of 50.

The chief symptoms of the disease are no doubt familiar to you all. Exophthalmic goitre is one of the first diseases which the medical student learns to recognize by simple inspection, for the diagnosis can generally be made as soon as you set eyes on the patient. There are, as you know, four cardinal symptoms, goitre, palpitation, exophthalmos, and tremor, which are all present in varying degree in most cases.

The goitre as a rule is only of moderate size, although it may be very large. It is important to remember that in some cases while the other symptoms are well marked the goitre may be small or hardly perceptible. The enlargement is usually more apparent on the right side than on the left, just as the right lobe of the normal thyroid is larger than the left. You often find that the goitre pulsates, and if you put your hand over it you feel a thrill. If you listen with the stethoscope you will likely hear a long whiffing systolic murmur. Often the goitre has not been noticed by the patient until the doctor has looked for it and pointed it out, but it will probably have been observed that the collar or the dress was too tight round the neck. The goitre itself seldom causes serious inconvenience, and very rarely produces pressure symptoms.

Rapid action of the heart is an almost invariable symptom, but the patient is not always conscious of palpitation. One finds on examining the pulse that it is abnormally rapid—from 90 to 140; 110 to 120 being about the average rate. As a rule, however, you do not get such an extreme degree of rapidity of the heart as you get in those cases of purely nervous functional disturbance, known as tachycardia. The rate of the heart is increased, and palpitation induced, by emotion or any form of excitement. You can usually see pulsation in the carotids.

The exophthalmos is generally obvious, but you may get all degrees of it, and in some cases it is only the trained observer who will detect it. It is quite common to find it more marked in one eye than the other. In some cases you will notice that the eyes have merely a staring and glistening look, due to some oedema of the conjunctiva, and to a slight retraction of the upper lid. It is hardly necessary to refer to what is well known to you as von Graefe's sign. When the patient follows with the eyes the finger or a pencil held in front of them and gradually lowered, the upper lids lag behind, so that the sclerotic becomes exposed between the lid and the iris. Another interesting eye symptom is known as Stellwag's sign, the retraction of the upper lid, producing widening of the palpebral fissure, and accompanied by fixity of the eyelids under reflex excitement. If you wave your hand or a paper before the patient's eyes you will notice she does not blink. The prominent eyes are apt to water, and to become inflamed. Sometimes more serious troubles ensue, such as ulceration of the cornea, which has led to the loss of the eye in some of my patients. In a few cases there has been oculo-motor paralysis. Difficulty of convergence first noticed by Möbius is not uncommon. You will notice in some cases that there is swelling of the eyelids. This is most marked in chronic cases, and is due to a kind of solid oedema. You will also observe raising and arching of the eyebrows. The pigmentation to which I shall presently refer is often specially marked in the neighbourhood of the eyelids.

Tremor is present in practically all cases of Graves's disease. If you get a patient to put out the hands you will see a fine tremor affecting them. In addition to this form of tremor of the extremities the patient suffers from greater degrees of trembling affecting the whole body, liable to come on with any excitement or emotion. Restlessness is another common symptom closely associated with trembling.

Besides these four cardinal symptoms there are other symptoms which are somewhat less known but are hardly less important. In all acute cases of Graves's disease, and in chronic cases which are doing badly, there is general emaciation, and this may be extreme. You will always be anxious about a case of Graves's disease if the patient is emaciating, for as long as weight is being lost the patient is going downhill. An emaciated patient is one who is doing badly. If, on the other hand, you find the weight of the patient is increasing, you can feel more satisfied. The emaciation of Graves's disease is directly related to an increase in the metabolism of the body. It is not simply the result of less food being taken, for it may occur even when patients are eating well. Excessive metabolism is one of the observed effects of taking large doses of thyroid gland. There is increase in the intake of oxygen, with a corresponding increase in the output of carbonic acid. Along with the emaciation goes progressive loss of strength.

Slight degrees of pyrexia are not uncommon, the elevation of temperature generally not exceeding 1° or 1.5° F.; higher temperatures, however, are uncommon. But even when the temperature is not above normal, the patient often complains of feeling abnormally hot, in contrast with the patient with atrophied thyroid gland, who generally feels abnormally cold. The patient with Graves's disease, moreover, is intolerant of

heat, but is tolerant of cold, while the reverse is the case in myxoedema.

You know what marked changes in the skin occur in myxoedema, and those occurring in Graves's disease are no less interesting. In myxoedema, as you know, there is arrested action of the sweat glands, and the skin becomes coarse, dry, and scaly. In Graves's disease there is increased action of the sweat glands, and the skin is generally supple and moist, as a result of which we find there is diminution in the electrical resistance of the body. Perspiration is unusually freely induced by exertion. The patient readily flushes on excitement or when conscious of being under observation, and a bright blush sometimes appears on the body as well as on the face. Pigmentary changes are common, and the skin sometimes becomes as bronzed as it does in Addison's disease. The complexion usually becomes sallow, and there may be a uniform or irregular darkening of the skin over nearly the whole of the body. The pigment may be irregularly distributed, giving rise to what is called leucoderma or vitiligo. Another symptom affecting the skin which I have sometimes observed is itching. It may be very troublesome and annoying, like that which occurs in jaundice or after the administration of opium. That it is a toxic symptom due to the thyroid secretion is shown by the fact that similar itching of the skin is sometimes experienced by patients who are taking medicinal doses of thyroid gland. Itching is sometimes accompanied by an urticarial eruption. Too much thyroid seems nearly as bad for the hair as too little, for the hair very commonly becomes thin and dry; but I have never seen actual baldness as in the case of myxoedema.

No important blood changes have been observed as the result of the disease. I have had the blood examined in a good many cases, and, as a rule, it has been found to be normal, which gives no support to the theory put forward at one time that Graves's disease was the result of anaemia. It is true that in some cases of Graves's disease the patient is obviously anaemic; that, however, is probably a coincidence owing to the fact that Graves's disease is commonly met with among girls just at the age at which anaemia prevails among them. Although we find no characteristic blood changes, patients with Graves's disease occasionally suffer from haemorrhages, such as epistaxis and menorrhagia.

Respiratory troubles are uncommon, with the exception of dyspnoea, especially felt on exertion, due to the cardiac weakness, and nervous cough, which may be due to the pressure of the thyroid on the trachea and the nerves adjoining, although, as I said, serious pressure symptoms are unusual.

I should like to call your attention next to the occasional occurrence of oedema. Oedema may be very marked in the extremities, and sometimes you find a considerable degree of ascites. It is usually met with, as far as I have observed, near the commencement of the disease and appears to be due to cardiac weakness. At a later stage you will notice some patients get a somewhat solid form of oedema. I have observed a number of cases in which the lower extremities have become very much thickened from solid oedema infiltrating the subcutaneous tissues, like the thickening which you see in myxoedema. It occurs in patients who, instead of getting thin, appear as the result of the disease to increase in bulk. There is no pitting, but the circumferences of the thighs and calves are much increased, and the patients will tell you they find it difficult to get stockings large enough to fit them.

The digestive functions are nearly always altered in some way or another. The appetite generally remains good, but sometimes it is voracious, which is partly accounted for by the increase of the metabolic changes in the body to which I referred just now. Unfortunately in some cases the appetite fails or becomes perverted and the patient may exhibit, like a pregnant woman, a taste for unwholesome or almost unprocurable forms of food. Sometimes there is almost complete loss of appetite, and when that is the case it is a bad sign. There is often excessive thirst, and patients will gulp down almost greedily large quantities of liquids. This, no doubt, is partly due to the increased action of the skin. A symptom which sometimes makes one anxious is vomiting. Vomiting is common in severe and acute cases, and very often precedes a fatal termination. I am always much concerned when vomiting occurs in an emaciated subject. In chronic cases also you may find that the patient has bouts of vomiting without apparent cause. Another trouble which tends to occur all through the course of the disease is looseness of the bowels, alternating sometimes with constipation. In cases which are doing badly there is often troublesome diarrhoea.

Occasionally you may observe some abnormality in the

urine in the disease. Sometimes there is albuminuria, which may be intermittent and variable in degree, or there is polyuria, and sometimes you find glycosuria. In connexion with the latter, it is an interesting fact that glycosuria can be more readily produced by administering glucose in a case of Graves's disease than in a normal person. In a person with Graves's disease a smaller dose of glucose will cause sugar to appear in the urine than in the case of a healthy person. In severe cases you may find diacetic acid in the urine, as shown by Gerhardt's reaction with ferric chloride. None of these urinary symptoms are of much clinical importance.

The catamenial functions frequently become irregular, and menstruation is too profuse or too scanty, or is in abeyance altogether.

The toxin of the disease has evidently a marked affinity for the nervous system, which, as a rule, is profoundly affected, and the mental condition of the patient is seldom quite normal. The tremor and trembling have already been described. Painful cramps are sometimes a source of trouble, and when walking the patients complain of a feeling of giving way of the legs. Paresis of the lower extremities may be observed in severe cases. Patients with Graves's disease are nearly always restless, excitable, irritable, and emotional. One of the first duties of the physician, to which I shall again refer, is that of prescribing rest for them, and preventing them from overtaxing the small reserve of strength they possess. Their sleep is often disturbed and unrefreshing. More serious mental changes, unfortunately, may occur. Cases of Graves's disease sometimes develop symptoms of insanity, and require treatment in asylums, the type of insanity being either melancholia or mania. I may say, however, that out of the many cases I have seen in hospital and in private practice, I can recollect only one case which required removal to an asylum.

We may speak of two varieties of the disease, the acute and the chronic, and we may divide the cases of each variety into the severe and the mild. The acute type is comparatively rare. The symptoms of the disease become well marked in the course of a few weeks or even a few days. As a rule, in the chronic cases it is months or in some cases years before the symptoms become well marked. Acute cases not infrequently terminate fatally after a few weeks' duration, exceptionally they end in recovery, but usually they become chronic. Chronic cases may have exacerbations or relapses of an acute type. We have an important variety of the disease—the incomplete type, or *forme fruste*—in which some of the characteristic symptoms of the disease are wanting, in which exophthalmos is absent, or there is little or no enlargement of the thyroid. This type is not an uncommon one and you will see many cases if you look for them. At least two of the cardinal symptoms, and some of the other secondary symptoms which I have mentioned, should be present before you can justifiably make the diagnosis of this incomplete type. Another division which you can make of the disease is into primary and secondary cases, the secondary cases being those in which the symptoms of the disease come on after an ordinary goitre has lasted for a considerable length of time. Here in London we see far more primary cases than secondary. A very important clinical division, I think, is into the lean type and the fat type, the *forme maigre* and the *forme grasse*. In diabetes we are familiar with these two types, and we are generally satisfied as to the outlook if we have to deal with a well-nourished person, and the reverse when we have to treat an emaciated person. The same holds in Graves's disease—if we have a thin patient to treat we feel much more anxious than when we have a well-nourished patient to look after.

PROGNOSIS.

As regards the prognosis, you should give a guarded one in all cases but especially in acute cases. You can never tell how an acute case is going to do. Sometimes, even although the symptoms are not very severe, an acute case will all at once rapidly go to the bad, and sudden death may occur without obvious cause. The proportion of deaths among the acute cases is very considerable—I should say, roughly, about 30 per cent. In chronic cases, the prognosis as a rule is good as regards life, but not favourable as regards the complete disappearance of the disease. It is very seldom, after the disease has lasted several years, that you get anything like a complete cure or a complete removal of the symptoms, but the proportion of deaths among the chronic cases is much less than that among the acute cases. Another point is that the prognosis is considerably better in patients who are well-to-do than among the poorer classes. Of all cases of Graves's

disease, one may say about 25 per cent. die from the disease sooner or later, 25 per cent. drift on in a condition of chronic illness, and about 50 per cent. make a fairly good recovery.

TREATMENT.

We must now consider the treatment of the disease. Whenever you find that for a particular disease there are innumerable remedies, you may know that there is something doubtful about the action of the remedies, and that probably none are particularly efficacious. Graves's disease is a malady for which many remedies have been employed and suggested from time to time, and I think we may admit that drugs hold an altogether secondary place in the treatment.

The first essential when there are signs of serious illness is to give the patient rest of mind as well as of body. As long as the patient is losing flesh let the rest be absolute, for you have to husband the strength as much as possible. Remember how impressionable the patients are. You must therefore keep away from them all disquieting influences. You must help them with encouragement and cheer them with the hope of recovery by and by. But you must let the friends clearly understand that it will take long to recover and that time is an all-important element in battling with the disease. Of hardly less importance are good food and an abundant supply of fresh air. At St. Thomas's Hospital I find that cases of Graves's disease do best when kept out on the balconies in the open air.

The open-air treatment is perhaps more easily carried out in the case of Graves's disease than in almost any other disease, because, as I have already pointed out, the patients are very tolerant of cold, always feeling better when the weather is cool, and they thoroughly enjoy being out in the fresh air. If you carry out open-air treatment in cases of Graves's disease I am sure you will be doing what is good for the patients.

You must feed them carefully and give them an abundant, wholesome and nourishing diet. If weight is being lost, you may supplement the ordinary food with milk, so that they get an addition to their diet of 2 to 4 pints of milk a day. An adequate amount of fat in the food is very important. In cases where there is vomiting you may try citrate of potash or bismuth to check it, but if it be frequent it is advisable to suspend feeding by the mouth and to feed for a time by the rectum. Diarrhoea, which is sometimes a difficulty in acute cases, must be treated by the careful selection of food and the administration of bismuth or preparations of tannin, such as tannalbin or tannigen.

Massage may prove beneficial in the case of patients who are confined to bed, as well as in the case of those who are able to go about, but massage must be judiciously employed. You must pay great attention to the skin, remembering the excessive sweating, and if the patient is confined to bed she should be washed over twice daily. In other cases you may with advantage allow a warm bath (temperature 98° to 100° F.) to be taken every night. Warm sea water or brine baths are sometimes useful, or you may try the effervescent saline baths which can be prepared with Sandow's tablets. The latter seem sometimes to have a quieting influence on the heart.

Later on we have to consider whether good may not be done by a change of air and climate. When a patient is able to be up and about I think change of climate often proves beneficial. But there is no rule as regards what climate will suit a patient with Graves's disease. One case will do well at the seaside, another inland, one at a high elevation, another at a low. You cannot predict what will suit any given case. But the patient's own knowledge of the kind of place that suits is a guide. I think I have seen more cases benefit by residence at the seaside than elsewhere. Sometimes, however, the seaside is too exciting and too stimulating. In summer the glare of the sun may be very trying, and shelter from the sun and wind and protection from dust should be provided. A few cases I have sent to the higher altitudes in Switzerland have done well, but I can conceive nothing worse for a patient than one of the popular Swiss resorts in the month of August. Care, on the whole, is of far more importance than climate. The great thing is to get our patients to a place where they can get peaceful quiet and rest, with freedom from noise and nuisances, where they can have real comfort and wholesome food, and where they can enjoy pure and bracing air among pleasant and cheerful surroundings. Sea voyages, as a rule, are prejudicial, and, of course, can only be sanctioned where the patient is well on the road

towards recovery, is known to be a good sailor and can travel in comfort.

I must now say a few words about drugs. One of the drugs which I have found useful is potassium bromide. In a case where the nervous symptoms predominate, and you have to deal with a restless, excitable, emotional subject, bromide of potassium may be given with benefit in doses of 20 to 40 gr. at bedtime.

Preparations of iodine are useful in cases where the goitre is large, or where it is increasing in size. Lately I have been giving the syrup of hydriodic acid, which is better borne than iodide of potassium, and seems as effective. The syrup can be given in doses of a drachm three times a day. The tincture or liniment of iodine may be applied externally over the goitre, but has the disadvantage of sometimes making the skin sore. I now use for the same purpose iodipin, which is a solution of iodine in sesame oil; 20 minims of the 20 per cent. strength is gently rubbed into the skin over the gland every night. If you find that during treatment with preparations of iodine the patient is not doing well, is losing flesh, or is having an aggravation of the cardiac or nervous symptoms, then you should at once discontinue their use.

Another drug which I have found useful is belladonna, of which one generally gives the tincture in doses of $\frac{1}{4}$ x three times a day. Patients say they feel better when taking it, and it seems to act best in cases where the cardiac symptoms predominate. I have thought that perhaps its action might be due to its lessening the activity of the thyroid gland. I do not think that under any circumstances it is wise to continue the administration of belladonna for any very long time, and I recommend that if you do use it you should suspend it from time to time. Professor Möbius, I notice, says he has found belladonna useless, and considers it strange that we in England should think at all highly of it as a remedy. I may mention that digitalis is well spoken of by a good many authorities. You give the tincture or infusion, or, as some prefer, Nativelle's digitaline. I have never seen the administration of digitalis make any difference in the rate of the heart, and one may say the same of strophanthus.

Phosphate of soda has come into favour of recent years, and is given in doses of 15 to 20 gr. three times a day. One can say that it will do no harm, and in some cases I fancy that it has done good, although it is difficult to say why. Chloride of calcium is another drug which is said to have been found to be useful. If anaemia be present you may prescribe iron and arsenic. Strychnine is useful when the heart needs stimulation. Cod-liver oil and pancreatic emulsion may be given in the case of poorly-nourished subjects.

Treatment with thyroid gland, I think, usually makes the patient worse, but there are certain cases where I have seen it beneficial. These are cases of old standing where the symptoms seem to be due rather to deficient than to excessive secretion. The cases with solid oedema, for instance, are nearly always benefited, and I have seen the swelling to which I have referred almost entirely disappear under its use. Thymus gland I have used fairly largely, but I cannot say that I have had any very marked results from it. I treated 20 cases with thymus, and compared them with 20 similar cases treated without thymus, but could see no decided difference in the results obtained. Suprarenal gland has been thought to be useful by some physicians.

Extract of spleen has also been tried. I believe I was the first to make use of the animal glands in the treatment of Graves's disease; for in 1892, as soon as I had satisfied myself of the activity of thyroid gland when given by the mouth in myxoedema, I tried it in the fullest doses in cases of the malady we are now considering. I then gave pituitary body, cerebral tissue, orchitic extract, as well as thymus, but found them all without effect.

I must not omit to mention a preparation called thyreoid serum, which was introduced a year or two ago on the suggestion of Professor Möbius. It is a serum derived from sheep which have had the thyroid gland removed by operation six weeks previously. It is supplied in sealed phials containing 10 c.cm., the dose by the mouth being from 1 to 5 c.cm. three times a day. I have made a very complete trial of this in a series of cases, but I am sorry to say that I obtained no good effects from it whatever. The remedy is expensive, and, as far as I can judge, is quite useless, but I see it is still advertised, and I suppose it is still being employed.

In addition to or in place of general remedies, treatment may be directed locally to the thyroid, the eyes, or to the heart. The application of cold compresses or of Leiter's

tubes over the thyroid seems sometimes to be followed by diminution of the swelling. I have already referred to the local use of iodine. We may also employ for the same purpose glycerine of belladonna, or, what is a cleaner preparation, glycerine of atropine (St. Thomas's Hospital Pharmacopoeia). The latter may be applied over the precordium for the relief of palpitation.

Local electrical treatment and light treatment have also been tried. Electrical treatment has proved disappointing, and my belief is that any beneficial effect it has depends on the impression made on the patient's mind. Electrical treatment has been diligently applied to the neck to influence the cervical sympathetic as well as over the thyroid, the eyes, and the heart. Recently the x rays have been used, being applied locally over the thyroid gland; and reports of benefit obtained have been published, especially where the x rays have been used after thyroidectomy.

Medical treatment, general or local, it must be admitted is sometimes most disappointing. In spite of all our efforts the patient occasionally does not improve. Our best results are obtained in cases which have required least help from drugs. Where we most want them, drugs seem to fail us. It is not surprising that surgical methods of treatment have long been advocated and employed, with the object of bringing about a more certain and speedier cure.

If we could assure ourselves that the disease was nothing more or less than a hypertrophy of the thyroid gland it would seem that the most rational method of treatment was to reduce the enlarged gland to something like normal proportions by surgical means. But we cannot altogether ignore the part obviously played by the thymus in the disease. It is many years since partial thyroidectomy was first performed for exophthalmic goitre, and a good many successful results have been published. Unfortunately, the operation is, even in the hands of the most skilful surgeons, a dangerous one, and the risks are greatest in the class of case which responds least to medical treatment. Some surgeons, such as Kocher of Berne and Friedheim of Hamburg, appear to have been particularly successful with their operations, but even Kocher speaks of the operation as *sehr gefährlich*.

In cases where there has been little or no exophthalmos I have had good results from thyroidectomy, but I have also had lately two patients who have died as the direct result of the operation. The risk from operation is an immediate one, the patient dying usually within twenty-four hours. Kocher and others maintain that the operation should be performed under local anaesthesia, and that a general anaesthetic adds greatly to the danger. I have, however, no personal experience of operations on exophthalmic goitre performed in this country under local anaesthesia which enables me to form a judgement as to the comparative merits of operations done under local and general anaesthesia. My friend Dr. Nicholson of Marlow has informed me that one of his patients was greatly benefited by thyroidectomy performed by Professor Kocher.

The statistics of Allen Starr, published some years ago, showed that there was a mortality of 16 per cent. directly from operation. I am indebted to Dr. P. Frank, and to my house-physician, Dr. Inman, for the following references to more recent surgical literature.

Of Kocher's cases, 59 in number, there were:

Cured	...	...	...	76	per cent.
Improved	...	...	...	14	"
Slightly improved	...	...	...	3	"
Died	...	...	...	6	"

A general anaesthetic was only employed three times, and in every case marked thyroidism followed, 2 being fatal.

Friedheim of Hamburg has recently reported observations on 20 cases treated by thyroidectomy, and says a lasting cure has been effected in 14 and in 5 others improvement has occurred. He thinks that the cases in which only a betterment has occurred have still too much gland left behind. In the report which I have seen no details, either of the cases or of the technique of the operation, are given.

Thomas Huntingdon, in reviewing the detailed histories of a considerable number of cases resulting fatally within a short time after operation, says: "We cannot escape the conviction that general anaesthesia is in a very large proportion of them seriously at fault. There is no difference of opinion among operators as to the impropriety of general anaesthesia in this relation, and especially in advanced cases."

Thyroidectomy, however, often fails to cure the disease. A patient was recently shown at one of the provincial medical

societies in whom the exophthalmos became much worse after the operation. It may be, as Friedheim argues, that in those patients who are not cured too little of the thyroid has been removed.

Various other operations, such as resection of the sympathetics, have been performed. Sympathectomy appears to be quite as dangerous as thyroidectomy, and although the immediate results, if the patient survives, are said to be far superior to those of the latter operation, it is difficult to understand how it can exercise a curative effect.

Ligature of the thyroid arteries is another operation which has been frequently performed, but, if less dangerous than thyroidectomy, it is also less likely to cure.

On the whole, I consider the risk attending thyroidectomy is too great to justify the adoption of the operation save in exceptional circumstances. For the present, one must trust to medical treatment on the lines I have indicated, and, with good care and perseverance, there is a fair chance of our efforts being rewarded by the recovery of the patient.

A CASE OF ADDISON'S DISEASE

IN WHICH GREAT IMPROVEMENT TOOK PLACE UNDER OPEN-AIR TREATMENT AND THE ADMINISTRATION OF SUPRARENAL EXTRACT.

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THE beneficial effects of the open-air treatment in many tuberculous affections, and especially in phthisis, is now well established. So far as I know, this plan of treatment has not been as yet employed in Addison's disease. In the following case remarkable improvement took place under the open-air treatment and the simultaneous administration of suprarenal extract. The notes of the case are as follows:

R. W., aged 36, married, a ship's steward, was admitted to the Edinburgh Royal Infirmary on November 2nd, 1903, complaining of great weakness, loss of weight, and occasional pain in the stomach.

HISTORY.

The patient stated that he had been ill for eighteen months; during this time he had lost 4 st. in weight, but recently had gained 8 lb. of this loss. The fact that the patient had gained weight seemed to negative the view that the symptoms might be due to malignant disease of the stomach. The examination of the abdomen and the subsequent progress of the case confirmed this view, and showed that there was no malignant disease.

CONDITION ON ADMISSION.

On examination the patient was found to be well covered with fat. The loss of weight was evidently due to loss of muscle, not to loss of fat. The asthenia was extreme. The pulse was small and soft, the heart's impulse could not be felt, and the heart sounds were very faint and difficult to hear.

The appetite was good. There had been no vomiting. The pain in the stomach was not aggravated by food, and was only occasionally felt. The tongue was clean. There was slight tenderness on pressure in the upper part of the epigastric region, but no hardness nor tumour could be felt. Chemical analysis showed that the stomach contents contained no free hydrochloric acid—a fact which has been previously observed in cases of Addison's disease, and which is presumably due to impaired digestive function.

The mucous membranes were somewhat anaemic. The red blood corpuscles numbered 3,800,000 per c.mm., the white blood corpuscles numbered 8,000 per c.mm., and the haemoglobin equalled 70 per cent. Stained films showed that there was a considerable excess of lymphocytes (40 per cent.); this was suggestive of a tuberculous lesion.

The skin of the face, hands, and wrists which had been exposed to air was deeply pigmented; the nipples and scrotum were deeply pigmented, and there were two or three pigmented spots on the lips, both the upper and lower lips, at the junction of the skin and mucous membranes, but no pigmented patches on the interior of the mouth. There were several brown patches on the abdomen, which were, the patient said, the result of poulticing.

The patient complained of some pain in the back over the region of the suprarenal capsules, but there was no tenderness on pressure in the lumbar region.