

Dr. ALBERT KOCHER (Berne) : It was with great pleasure that I accepted the very kind invitation of the Secretary of your Society to take part in to-night's debate on "Exophthalmic Goitre." There are but few diseases on which more has been written in medical papers than Graves's disease. I am pleased to say that there is to-day nearly unanimity as to the pathogenesis of the disease being a functional trouble of the thyroid gland. The very different features, degrees, and course of the malady have, however, made it difficult up to the present to fix the exact functional change in the gland. Some pioneers, of whom I will only mention Sir Victor Horsley, Moebius, and Rehn, have, according to their own observations on different lines, described the disease as dysthyreosis or hyperthyreosis. The latter view, however, has gained ground very much by the results of surgical treatment, and my father, Theodor Kocher, who has been operating for thirty years on the thyroid gland in Graves's disease, is the main advocate of the theory of hyperthyroidism, basing his opinion on his extensive operative experience, of which he spoke at the meeting of the British Medical Association in 1910. The operations for Graves's disease in the surgical clinic at Berne up to date amount to 865, performed on 669 patients. With my father's kind permission I will speak of the whole of these cases, and not merely of my own, as we have observed and operated together on the great majority of these cases. As already mentioned by some of those who have spoken in the debate, it is difficult to class all the cases under one head. Allow me, therefore, to tell you in a few words how the different features of the disease have to be explained according to our present knowledge. (A) First, the different kinds of Graves's disease according to the condition of the thyroid gland itself (the following views are based on histological and chemical investigations on 200 glands of Graves's disease which will be published shortly in *Virchow's Archiv*). (1) The change in the thyroid gland in Graves's disease consists in the more rapid and more abundant absorption of the material stored in the gland-follicles. There is a considerable difference in the quantity and quality of the stored material present in the gland at the time of the outbreak of the disease. (2) There is a marked hypertrophy of the epithelium. Both these changes are connected with a hypervascularization of the gland. (3) If the disease is progressive all the stored-up material is sooner or later absorbed, according to its quantity and the rapidity of progress, and under further progression there is no more storing of material in the gland-follicles, but the proliferation of the epithelium is still progressive all through the gland, and degenerative changes of the epithelium can take place

together with formation and proliferation of lymphatic tissue. (B) The different kinds of Graves's disease as regards ætiology. In the outbreak of the disease we distinguish neurogenic causes which act through the vascular nerves, and toxic causes of chemical and infectious nature, acting through the blood. They can be acute or chronic, and they can also be combined.

I will not take up your time any longer with this complicated matter; you may judge from these few remarks that a large, if not *the* largest, part of the different features of the disease lies in the thyroid gland itself. I wish, however, to draw your attention to one more point. There are a great many cases, especially combined with nodular goitre, which present a few symptoms of Graves's disease, and only occasionally (especially after iodine treatment) show exacerbation or pronounced hyperthyreosis. Since surgical treatment of the disease has become more common a great many surgeons operate, and all *these cases* are apt to be registered as Graves's disease cured by operation. This is not quite right; we should always make the following distinction. (1) Cases with symptoms of hyperthyroidism presenting only occasionally pronounced hyperthyreosis, which, however, does not last and is not progressive, being usually the consequence of unlimited iodine treatment; (2) cases of steadily progressive, and (3) of periodically progressive Graves's disease. The first also come from sudden or very rapid and abundant absorption of the thyroid secretion stored in the gland-follicles (thyroid diarrhœa, as my father calls it), but when the cause of the outbreak has passed by the gland does not undergo further change—the disease is not progressive. In the cases of the second and third type this takes place, and after a certain time of duration degenerative changes may come on, not only in the thyroid gland itself, but also in other glands with internal secretion such as the adrenals, pancreas, thymus, spleen, liver, ovaries. In other organs also permanent changes are established, such as fatty degeneration of the muscles, especially of the heart muscle, also of the kidneys and of the liver. We can, therefore, before looking upon the results, presume that in progressive Graves's disease it is *most important at what period* of the disease we operate, whilst in simple hyperthyroidism we do not risk so much in postponing operation.

Amongst our list of 669 cases, 130 were of simple hyperthyroidism, mostly combined with nodular goitre of nearly every size, some presenting no extraordinary difficulty during the operation; some, however, partly or totally intrathoracic, and being combined with hyperthyreosis, very vascular and technically very difficult operations. These cases

have *all been entirely cured* of their symptoms of hyperthyreosis after the operation, with the exception of two, who died from post-operative pneumonia. In these cases we remove the cause of the disease with the goitre, and, more than that, we remove with the goitre the reservoir of the poison. Histological and chemical researches have shown that the goitre removed contains a large quantity of rather liquid colloid, in which an unusual amount of iodine is present. These cases are all suitable for operation if they are not complicated with other serious pathological changes in the lungs, heart, or kidneys. But it is advisable also to prepare these patients for operation by a short course of treatment, keeping away every toxic and nervous influence, because it is to be borne in mind for the operation itself that we have to deal with very sensitive people who are poisoned by toxins.

Five hundred and thirty-nine cases have been operated upon for steadily or periodically progressive Graves's disease. We are collecting the ultimate results, but with such a number they cannot be obtained as quickly as we should wish. We can at present give the ultimate results of 360 patients operated upon for progressive Graves's disease: 160 of these (45 per cent.) are radically cured, so that there is at the present time not one symptom of the disease left, and the function of the rest of the thyroid gland is normal. These cures last up to twenty-five years after the operation. The patients are leading a normal life, some working hard. Several lady patients have given birth to one or more healthy children since. Not all of these cases have been early ones; more than half were very severe and of long duration. The latter have been cured only after some time, during which several (up to five) operations have been performed on the same patient. The early cases have been cured a short time after *one* operation. One hundred and forty-nine cases (41 per cent.) show at the present moment, months or years after the operation, a few symptoms of the disease, but have been greatly benefited by the operation, inasmuch as patients of the working class, for instance, can earn their living without any difficulty. (a) Amongst these 149 cases there is first of all a considerable number in which a more extensive—that is to say, a second—operation would give complete recovery. Most of these patients, however, feel so well that they are unwilling to submit to any further operation. (b) In a small number of cases the only symptom still present is the exophthalmos, but they are not cases in which the bulb was most protruded before the operation, but cases in which the exophthalmos underwent no more change. They were sometimes combined with paresis of the bulbar muscles. I must mention here that among the 160 cases

radically cured, a very large number have had an extremely marked degree of exophthalmos; in one instance the bulb came quite out one day and had to be replaced. At the present time the eyes are normal. (c) A further group of cases show symptoms which had been present before the operation and were the result of the toxic influence on some of the organs, due to the severity and long duration of the disease, such as chronic myocarditis, chronic nephritis, and some degenerative trouble in other glands, such as diabetes, but all symptoms of Graves's disease have disappeared. (d) Some patients still show symptoms of functional trouble of the thyroid gland. There is no more progressive disease, but the part of the gland left does not seem able to adapt itself to the various demands. We sometimes find symptoms of hyperthyroidism and sometimes of hypothyreosis. The gland seems to be in a labile state. The cause of this is that the progressive changes in the gland, during the Graves's disease, had gone so far that it had lost its power of storing material in the gland-follicles, and the part of the gland left after operation was not able to regain this power.

However, all these 149 patients are cured of the great majority of the symptoms of Graves's disease and are able to lead a normal life. If we add this 41 per cent. to the 45 per cent. of complete cures, we can say that in 86 per cent. the ultimate result of operative treatment has been satisfactory. In 28 cases (8 per cent.) the ultimate result cannot be called a satisfactory one. (a) Amongst these we find cases in which the operative treatment has not been carried on so far as to obtain a satisfactory result. Some of these patients object to further operation, not having been benefited by the first one. In some, however, the disease has gone so far, and also the shock of the first operation—sometimes only ligation of one or two arteries—has been such that a more extensive operation seems too risky and is therefore abandoned. (b) The remaining cases of this group comprise those who have had recurrence of the disease. There are about 5 per cent. in all. In none, however, has the second attack been as severe as in the first instance—that is, before the operation. Amongst the cases registered as cured there is a number in which a second operation has cured the recurrent disease. Most of those also who show symptoms of recurrence might in a similar way be benefited by a further operation. But we have to bear in mind that partial removal (resection) of the remaining lobe of the gland in a recurrent case is extremely difficult, and therefore dangerous. It is true that in a few cases an excellent result has been obtained with it, but naturally the small part of the gland left has more difficulty in resuming its normal function. Twenty-two patients (6 per

cent.) have died since from other diseases. Only in a few instances does the former Graves's disease seem to be connected with the ultimate death. Five patients died very suddenly from what is called heart-stroke, after a fright or over-exertion, or in the course of an otherwise not dangerous (mostly infectious) disease. In all these cases Graves's disease had been of a very long standing, and had caused degenerative symptoms; however, after the operation the pure symptoms of the disease had disappeared. One patient died from diabetes. Whether this is in connexion with the degenerative influence of the severe Graves's disease on the pancreas remains doubtful.

This leads to the question "*What cases are suitable for operation?*" If we could operate in all cases within a short time, say half a year after the outbreak of the disease, and the sooner the more acute the outbreak is, I dare say *all* might be *cured* by operation. A short rest, with avoidance of all the things likely to cause progression of the disease, such as nervous strain and toxic influences, combined with more or less vegetarian diet and internal phosphorus preparations, is the proper preparation of these cases for operation. During this time a careful examination of the patient should be made, and this is *the chief point* to decide—whether an operation should be done or not in severe cases and of such long duration of the disease. Special attention must be paid to the heart, kidneys, liver, adrenals, pancreas, lymphatic organs (thymus, spleen, lymph-glands), and to the blood. A constantly irregular pulse, the persistence of a notable amount of albuminuria, very frequently fatty stools, distinct and constant, not only alimentary, glycosuria, low blood-pressure, marked status lymphaticus (especially the form without the otherwise characteristic lymphocytosis of the blood), a very high lymphocytosis of the blood, combined with very marked leucopenia, very slow coagulation of the blood—are conditions that *forbid* an operation unless they can be made to disappear under proper treatment during the time of preparation for the operation.

The operation itself consists either in the reduction of functional gland tissue by partial thyroidectomy or in the reduction of arterial supply by ligation of arteries. In early cases this will bring about a cure. In slightly enlarged, but very vascular glands, ligation of two or three arteries should be done; in larger glands hemi-thyroidectomy may be preferable. But one cannot fix any scheme, the most suitable operation for each case has to be decided upon individually. In severe cases of long duration the combined—that is to say, the consecutive—use of both operations is the method of choice. The ligation of the superior artery is best done from a small collar incision across the upper part

of the lateral lobe, between omohyoid and sternocleido-mastoid, the upper pole of the gland is set free and the artery tied or cut between two ligatures. The effect seems to be better if ligation of the thyroidal veins is omitted. In partial thyroidectomy the larger lobe with the middle part and pyramidal process should be removed. This is done with Kocher's symmetrical collar incision across the middle of both lobes. After dividing the straight muscles above the entrance of the nerve branches, the gland is carefully detached under exact hæmostasis of all the numerous accessory veins passing from the capsule to the gland. It is an advantage if the superior and inferior artery can be tied soon. Special care is to be taken at the back, where the recurrent laryngeal nerve and the upper parathyroid gland are adjacent. The best plan is to leave a sheath of gland tissue behind. Next, with regard to ligation of the inferior artery. The ligation of the inferior artery alone is as a rule a very difficult procedure, as it can only be done on the main branch, when the lateral lobe of the thyroid is lifted up. We do not therefore consider it the best method to be chosen, although it is the one lately chosen by most French surgeons. It has exceptionally to be done in cases where one lobe has been removed and the upper artery of the other tied. It is the same with the *partial removal or resection of the second lobe*. It is only exceptionally necessary and on account of the difficulty of hæmostasis not a safe procedure. The removal of one lobe and the partial removal of the other *in one operation* is a procedure which should not be undertaken. In early cases it is not necessary, in severe cases it is frequently the cause of death. We are sure that most of the cases lost after this operation could have been saved by consecutive operations performed at the necessary intervals.

All operation *can* and *should* be done under local anæsthesia. In early cases, where no symptoms of degeneration in the organs are present, general anæsthesia, ether and oxygen, may be given, but there are always two disadvantages: the recurrent laryngeal nerve cannot be spared with certainty, and the sickness after the operation, considering the slow coagulation of the blood, makes the healing slow, and has a bad general influence. The local anæsthesia is done by injections of  $\frac{1}{2}$  and 1 per cent. novocain solution with 2 drops of 1 per cent. adrenalin solution for 10 grm. of novocain. This is injected under the skin at the place of the incision, in the muscles where they are to be cut, and in the periglandular tissue, especially at the upper pole. It is important to calm the patient before the operation, not so much with drugs such as veronal, medinal, codein, and valerian, but more by mental influence. I can assure you that during the above-mentioned preparatory rest cure

in the house, which lasts from two to several weeks, we nearly always influence the patient so that he is anxious to have the operation and fears it no more. After most operations, even if not the slightest irregularity, not to speak of complication, takes place, when no antiseptics and no general anæsthetic have been employed, the patient shows a very severe reaction; the more so, the more severe the case is. Rise of temperature and pulse-rate, irregularity of pulse, albuminuria, glycosuria, restlessness, sweating, and oppression are quite usual, and sometimes very alarming. We find this reaction sometimes even more severe after ligation than after partial removal. If antiseptics have been largely used, or if the wound has had to be packed with gauze, or general anæsthesia has been given, this reaction is much more severe. On four occasions, in cases where we have had to give general anæsthesia because of the lack of self-control of the patient, we have seen this reaction go on for a period up to twenty-four hours, and ending in coma and death; and here the necropsy revealed fatty degeneration of the heart muscle, kidneys, and liver, with circumscribed necrosis, such as is found experimentally in the liver after chloroform death. Besides cases of death following the operation under general anæsthesia we lost 5 patients from pneumonia, 3 from nephritis (extensive fatty degeneration), 2 from embolism, and 4 who died, with the above-mentioned symptoms, very suddenly, and showed marked status lymphaticus, together with fatty degeneration, at the necropsy. If you consider the cause of death in all these cases and compare with it what I said of the special attention that must be paid to the condition of the heart, liver, kidneys, adrenals, lymphatic organs, and blood, before operating, you may conclude that the majority of deaths could have been avoided. If we had omitted general anæsthetics in the four cases, if we had refused to operate on the three patients who had distinct signs of kidney degeneration before, and on the four patients who showed status lymphaticus in very marked degree, all these would have been spared, and our statistics showing 2.6 per cent. mortality from 865 operations would be only a little over 1 per cent.

We come to the conclusion that early diagnosis of Graves's disease is *the* important task of a medical man. If this is established an early operation should be performed by an experienced surgeon. After the operation treatment with rest, proper food, good air, especially mountain air, avoiding any nervous or toxic influence, will bring about radical cure in a fairly short time. Thus we shall not only avoid recurrence of the disease, but the patient will be spared the toxic influence on his heart, kidneys, and liver, of which he will die sooner or later. The

thyroid gland will resume its normal function, whilst, if the disease is progressive, it may reach such a point that the gland is no longer able to do so. In severe cases and in those of long duration a careful examination, according to our modern knowledge of the disease, must be made. Cases with distinct symptoms of functional degeneration cannot be operated upon without risk. Only surgeons who have great experience in the surgery of the neck, who are able to make complete hæmostasis, and who can guarantee complete asepsis, should operate in Graves's disease. A difference should be made between cases of goitre with symptoms only of Graves's disease, and the progressive full disease. The results of operative treatment in the first should not be published as results of operation in Graves's disease, without adding that they were rather cases of hyperthyroidism grafted on ordinary goitre.

MR. WILFRED TROTTER: My contribution to this discussion is made with a good deal of diffidence and hesitation, because my experience of the operative treatment of Graves's disease is quite a small one, and I regard many of the most interesting problems of the subject as being so far from solution as not profitably to be entered upon here. Limited as one's experience is, and it is based on less than fifty cases, it has enabled one to come to certain rough practical conclusions which I will attempt briefly to put before you.

In comparing the medical and surgical treatments of Graves's disease it must be kept clearly in mind that the former does not attempt to influence directly the course of the disease, but is limited to putting the patient under favourable conditions while the disease runs its natural course, to end in arrest, spontaneous cure, or death. Operative treatment, on the other hand, is intended to be specific and to deal directly with the disease itself. It is clear, therefore, that we have to take into account not merely the comparative mortalities of the two methods, but also the length of the natural course of the disease and the condition of the patient during its progress. That the condition of a patient with severe Graves's disease is a very miserable one is common knowledge, and is strikingly shown by the willingness of the patients to submit to operation, although they are rendered morbidly nervous by the disease and have usually been told before they come to the surgeon that the operation is an excessively dangerous one.

While I do not attempt to minimize the fact that the mortality of the operation is a considerable one, and possibly greater than that of the untreated disease, I am convinced that it would be justifiable to run a good deal of risk if it were the means of avoiding the years