THYROTOXICOSIS: ITS SURGICAL ASPECTS*

BY

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Our thoughts, and mine especially, turn this morning to him who should have been the chairman of this discussion; for the faculty which raised him above his fellows was essentially that of kindling in his associates and his students the desire to acquire more accurate knowledge, and in some subtle and quite unconscious way transmitting to them an eagerness in its pursuit. It never occurred to him or us that work was laborious. It was the very essence of life, and it was nowhere more obvious than in his attitude to this disease thirty years ago. With Osler he realized that it was a disease from which "few recover and many die." It hurt him to feel that years of the best part of a patient's life were slipping away, and that, for some patients, those years were irreplaceable. One of Richard Stawell's phrases is often in my mind, "Youth does not endure." It was his way of saying, "Life is short and time is fleeting."

At this stage I should like to make some acknowledgements—to Dr. Murray Morton, who placed a bed at my disposal for my first operation; to the late Mother Berchmans, Rectress of St. Vincent's Hospital, who subsequently made it possible for this case to be followed by others; and to two—no longer with us—Dr. Cecil Rothera and my brother. Together throughout a long night in 1908, walking up and down Collins Street, we discussed the necessity, the wisdom, and the safety of cutting through the second lobe of a thyroid gland in order to obtain a higher level of health, something more nearly approaching normal than we had been able to obtain by resection of a single lobe. Resection of one lobe had not given us the results reported elsewhere. At that time, cutting across the second lobe seemed a risky procedure, for methods of controlling haemorrhage had not then been perfected. In that year (1908), and in each succeeding year, we published our practice of resecting an adequate amount of both lobes. Four years later (1912) Halsted's article on "The Necessity for Double Lobectomy in the Treatment of Exophthalmic Goitre" was published in the *Annals of Surgery*.

The subject of thyrotoxicosis has been discussed to such an extent in the last thirty years that it may well be asked whether anything of value can be added. We would all deprecate taking up the time of this meeting with the iteration of accepted procedures, but, as with everything else, as we learn and begin to think that we can standardize our knowledge fresh problems arise and they are difficult. These difficulties should form the basis of our discussion this morning.

Lest we be too satisfied with achievement the recent report of the Registrar-General comes to disturb our complacency. The number of deaths from Graves's disease in England and Wales in 1922 was 653. In each succeeding year an almost regular increase occurred, until in the last year of that decade the number of deaths was 1,404. That the death rate should have more than doubled in ten years is startling; but that is not all. The Registrar-General is only concerned with the deaths, and if the cold facts of the death rate are such the unrecorded morbidity can be imagined. The problems of this disease are not finally settled, and there is still much to discuss. Some of us can contribute experience, some will bring the freshness of young and inquiring minds—both are needed. The first problem is that of aetiology.

Aetiology of Thyrotoxicosis

The disease is not standardized because human beings are not standardized. The protoplasm of each individual has its predestined frailties, as well as its vigour, handed down through the ovum and the sperm of countless generations. Surely this determines to a great extent which system gives way under strain, and why; and for the same reason the wonder is, not that endocrine balance is sometimes upset, but that in the majority it is reasonably good. Also in the matter of environment there are influences beyond our capacity to measure behind the face and figure of the simplest individual. Experience does give us more skill in sensing the background.

It is accepted that the secretion of the thyroid gland causes the manifestations which constitute this disease. The gland has to stand up to the buffetings and vicissitudes of life. We can no longer doubt that its deviation from the normal sometimes dates from a severe shock; nor that worries and anxieties are detrimental to a patient suffering from the disease. But we still have no accurate knowledge of the mechanism that stimulates—or fails to restrain—its activities. The more we know of heredity, environment, and associated conditions the better will we be fitted to deal with a condition of which our knowledge must for a long time yet remain imperfect; and it is well for us to remember that while it is so imperfect some patients will fail to regain completely normal health, whatever method of treatment is followed.

That leads to the question of dogmatic statements and exaggerated claims. It is so frequently stated and written that with rest and iodine preparation every patient may be made safe for operation; and that with adequate operation every patient will be cured. Even your own *Journal of Surgery*—with its very high standard—was somewhat scathing in its review of a well-known and ably written two-volume system of operative surgery because the author of the latter spoke with caution. It cannot be emphasized too much that some patients *cannot* be made safe for surgery; and the sooner the word "cure" is dropped in this disease the better. Greatly improved—yes; saved from landslide and death—yes; but cured? Kipling wrote:

"Light your pipe and have a look among the files.
You've a better chance to guess
At the meaning of success
When you've seen it in perspective in the files."

When Kipling wrote that Governments alone kept records. Since physicians and surgeons have organized follow-up departments not only has the practice helped our patients, but we also have been kept sane—and more truthful. Exaggeration serves no useful purpose. It is a disservice to our profession and to our patients.

The Severer Complications

The second problem is that of the severer complications. How can we detect when the slide is likely to occur? These complications do not become less frequent or less severe. The larger the population the more likely it is that some cases will slip without being spotted, and of these some are likely to become severely ill before they reach a knowledgeable physician who will pilot them aright, and so the severity of the complication increases. These complications fall into groups. (? Is this due to inherited predisposition?)

1. The commonest complication is cardiovascular—with auricular fibrillation, often followed by congestive heart failure.
2. Glycosuria is, in my experience, the next most common.
3. Mental derangement may be severe.
4. Emaciation may be extreme and resistant to treatment.

* Read in opening a discussion at a combined meeting of the Sections of Medicine and Surgery at the Annual Meeting of the British Medical Association, Melbourne, 1935.

5. The condition which, for want of a name that would more exactly describe it, has been called quite wrongly "localized myxoedema" is interesting rather than serious, although it is annoying to the patient.

6. Pruritus may be so persistent and severe that the patient scratches the whole body until it bleeds.

The disease occurring in children is full of interest and difficulties, and so are the "formes frustes."

In the paragraphs that follow, discussing individual complications, the numbers of patients are taken from my own series.

Cardiovascular Complications

Regarding cardiovascular complications, I see fewer patients now who are severely waterlogged. By that I mean, with oedema well above the waist, with fluid in the serous cavities, and reduced output of urine; but I see many more with established auricular fibrillation in whom gross heart failure has not yet occurred. From that I infer that when auricular fibrillation is first detected it is more generally recognized that the thyroid gland is a possible cause and is therefore examined; and that when the thyroid is the cause more patients are offered and accept surgery as a method of treatment. Furthermore, when regular rhythm has been restored patients are wise enough to submit to stricter observation and to some limitation of their activities. Naturally the exact amount of limitation demanded varies with each individual, and it cannot be foretold either by the extent of the preceding heart failure or by the duration of the symptoms. We see patients who have suffered from congestive heart failure—and for a long time—living active lives for years afterwards, while others, apparently not so ill, do not regain the same robust health. Is this due to the inherited protoplasm of the individual, or differences in the strength, quantity, toxicity, or length of action of the gland secretion, or to some associated condition of cardiac musculature?—for not every heart is sound before Graves's disease commences. The number of patients with established auricular fibrillation upon whom I have operated is 260. Of these, 218 have regained regular rhythm following operation—that is, 84 per cent.; seventeen have died, that is, 6.5 per cent.; twenty have not regained regular rhythm; and five are untraced. A few who had regained normal rhythm have relapsed.

Glycosuria

The second most common complication is glycosuria (fifty-two patients). Discussion of this belongs more appropriately to our medical colleagues. Before operation glycosuria may become difficult or impossible to control, even with insulin. I have not known a case where operation has failed to give considerable relief. A striking case was that of a girl aged 24, who was admitted with toxic goitre, emaciated, and with severe glycosuria. A sister aged 14 and a brother aged 8 had each died from diabetes; her grandfather and an uncle both suffered from it. Following operation ten years ago this patient is in normal health and free from glycosuria. An illustrative case in which relief was not all that could be desired is a woman aged 46, well-to-do and therefore able to have every care, who was advised operation in 1921 when glycosuria and fibrillation were both present. She refused operation for twelve years, until March, 1933, when the glycosuria had become uncontrollable. Following operation the glycosuria is controllable, but some insulin is still required. In this patient normal rhythm has not been regained.

Mental Derangement

Mental derangement (forty-three patients) is possibly the most pathetic complication. The question to be decided is whether this might have occurred apart from the thyrotoxicosis or whether it is due to the disease—an increase (gradual or sudden) of the change in temperament or the irritability so often present. The family and personal history must be carefully examined, and the help of a colleague skilled in mental disorders sought. The choice of this colleague is a matter of importance. It is essential that he should be open-minded enough to know what is possible. One so conservative that he would refuse consent to operation in any sort of mental disorder would be useless. On the other hand, he should be firm if he considers the state of mind is due to causes other than the thyroid. Even when it is certainly a complication of Graves's disease, the management may be difficult. A patient of Sir Walter Langdon-Brown of Bart's and Dr. R. D. Gillespie of Guy's had suddenly slipped from a condition apparently manageable to one almost unmanageable—acute mania, fibrillation, and an almost complete refusal to take food. Operation was only made possible by giving morphine to induce sleep sufficiently deep to permit avertin being given. One artery was ligated at a time, and later an adequate resection. Some days after the third and final stage the first glimmer of intelligence returned, and later every trace of mania disappeared. There are few in whom the mania is so wild and so complete as it was in this patient. To operate on a patient foredoomed to mental derangement would be unpardonable—and we have all made errors of judgement. To illustrate the risks in operating when this complication is present, I must state that three patients, who appeared to be mentally stable, became demented following operation for periods up to three months, and then regained normal mentality. One other—unstable before operation—committed suicide some months later, and one has failed to recover. I believe that all the others—and they number forty-three—have regained normality. I do not include in this series patients with mental irritability, however severe.

Extreme Emaciation

Probably the most difficult cases for either physician or surgeon, and the most dangerous for operation, are those with extreme emaciation, who, in spite of rest in a nursing home or hospital and every resource at our command, continue to lose weight. In these patients iodine has no influence whatever, either on the pulse rate or on the loss of weight. Patients of this type are usually agitated as well, and with a high pulse rate. In the most extreme case the weight had fallen from 8 st. 7 lb. to 4 st. 1 lb. before operation was performed, and in another from 8 st. 13 lb. to 4 st. 7 lb. In the last three years I have had twenty patients in whom the loss of weight has been over 3½ st. In four of these the loss was as much as 5 st. Possibly the usefulness of iodine had been exhausted by its indiscriminate use earlier in the history of the illness, although, as Henry Plummer pointed out long ago, some patients do not respond to it. It is chiefly because of patients in this group that there must always be a death rate of about 3 per cent.—if very ill patients are to be given a chance by operation. When considering the death rate of operation it is to be remembered that sudden deaths are not infrequent in this disease apart from operation. Death in very ill patients may be precipitated by seemingly slight causes, and therefore when severe cases are operated upon some deaths must occur.

Skin Complications

Pruritus in Graves's disease can be severe (twenty-three patients). Many of these were unable to refrain from scratching themselves until they bled over a considerable part of the body, and could not obtain relief until the disease itself improved.

Bilateral symmetrical patches of mucinous degeneration in the skin. This is usually situated just above the ankles on the antero-lateral aspect of the legs, but sometimes it extends to the toes and almost to the knees. This has been described—wrongly—as "localized myxoedema." Myxoedema is a generalized disease, differing entirely from this. This condition does not occur apart from thyrotoxicosis. In many patients it improves or disappears after adequate operation. Our American colleagues state that it reappears later. That has not yet been my experience. My first case was operated upon nine years ago. The condition slowly disappeared and has not recurred, nor has it in five others. In one patient—a very recent case—it was extensive, though still symmetrical and confined to legs and feet. Operation has been performed, but it is too early to judge the result. It is too much to hope that the condition can be materially improved when it is so extensive, although the improvement has been so definite in all the others. One must speculate sometimes. Seeing that this condition is bilateral, symmetrical, confined to limited regions, a swelling of tissues that scarcely interferes with function, disappearing slowly in many patients after operation but intractable in others, is it possible that the swelling in the tissues behind the eyeballs that causes the proptosis is of the same nature?

The Time for Operation

One of the great difficulties of this disease is to recognize when a downhill slide is about to occur. The complications are severe, and in some patients their results irremediable. For this reason some surgeons here and many abroad consider that operation should be performed early—that it is preferable to prevent rather than have to deal with complications. The time at which operation is performed has steadily been advanced; but while family practitioners and physicians know that occasional cases undergo spontaneous cure, and while human nature is still—perhaps fortunately—rather averse from surgical operations, patients will continue to come with the severer complications.

The average patient gives us no anxiety at the time of operation. Among those who are very severely ill there are some whom I personally can only hope to get safely through by making, in the beginning, the smallest inroad that can be depended on to achieve some good. It is not true to say that all patients can be made safe with iodine, at any rate at the late stage at which we frequently see them. Also, it is not true to say that all the poison is in the thyroid gland, and that therefore the best way of dealing with the patient is to remove the greater part of the gland at one operation. This is a misstatement of facts, a misinterpretation of physiology. Henry Plummer showed that one injection of thyroxine will keep up the basal metabolism of a myxoedematous patient for thirty days. Is that injection of thyroxine stored up in the thyroid gland and gradually liberated as required? I think not; surely it is carried to, and stored in, the cells of the body; and in a case of severe toxic goitre the cells of the body are charged—supercharged—with secretion. If in such a person—poisoned, desperately ill—a severe inroad is made—a subtotal thyroidectomy performed—we do not remove all the toxin; on the contrary, we fire the charge and make an explosion. I used often to be asked by surgeons, "Why

did a patient upon whom I operated die?" The reply should have been "Killed by the operation." I have done it; and if experience counts for anything it is in judging how much an ill patient can tolerate.

Results of Operations

If I do not spend time in stating the excellent—generally really remarkable—results of thyroidectomy, it is because at this meeting it is of more importance to say that sometimes we cannot hit it off exactly. I know several patients who, after operation, are still on a border line. Sometimes in the same patient the portion remaining is not adequate and a little thyroid extract has been necessary temporarily; at another time the remaining portion of gland has still been too active and a little x-ray treatment has been sufficient to reduce its activity. Again, in some patients the remaining portion undergoes too much hyperplasia and a second operation is necessary. We should not regard these as failures. As stated earlier, individuals are not standardized. We have to go back to inherited protoplasm, environment, or sometimes to associated pathological conditions for a possible explanation.

The "formes frustes" present a difficult problem. It is one condition where the basal metabolic rate is of great value. Operation in an unsuitable case is worse than a mere failure to do good, and, as regards the so-called "masked" hyperthyroidism, I am entirely unconvinced. Hyperthyroidism is only "masked" when enlargement of the gland, if present, is so deeply placed that its presence is difficult or impossible to detect.

The Disease in Children

The disease occurring in children presents problems in management. It has not been our experience that it can be held in check medically. I have seen fifty-one cases under the age of 17, and of these fourteen have been under the age of 12, and nine under the age of 8—the youngest was aged 4. It has been our aim to control the condition with the smallest interference while development is incomplete. With one child of 8 we continued medical treatment too long and he died. In six x-ray treatment has been sufficient thus far. One of these was aged 6. Only in one patient has ligation of arteries sufficed, and in sixteen partial thyroidectomy has been necessary after the less radical measures had failed.

Sexual Disturbance.—I do not want to emphasize this unduly, but I must not ignore it. In one child of 7 sexual precocity was so insistent that it presented a grave difficulty. Following adequate operation (I say adequate because it was performed in stages and the effect of each observed) the child became normal. I think this was not coincidence. The condition before the final operation was too distressing and the improvement quite definite. Sexual problems have not infrequently been present in adults.

X-Ray Treatment

Some patients have undoubtedly been cured, and some patients upon whom I have operated, and who were not as well as they and I would have liked, have been further improved by x-ray treatment. One hundred and forty patients who had had x-ray treatment given under favourable conditions have ultimately come for operation. Of these, in twenty-three auricular fibrillation had occurred subsequent to the x-ray treatment. In seventeen of the twenty-three in whom fibrillation was present the heart rhythm has become normal following operation. X-ray treatment has a place in the management of Graves's disease, and in my view its chief value is in the early stages and in young people. In severe cases

and in older patients I do not think its results compare with those of surgery.

Regarding the basal metabolic rate, while it is always interesting to have information as complete as possible, I should not regard it as indispensable in a straightforward case. It is invaluable in the "formes frustes," in differential diagnosis, and in deciding whether an incomplete result is due to continuance of hyperthyroidism; but with private patients whose means are limited it should not be demanded as a routine if the clinical condition is clear or unless the information desired is actually necessary.

CONGENITAL PYLORIC STENOSIS

WITH OBSERVATIONS BASED ON 209
CONSECUTIVE CASES

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The clinical features of a typical case of congenital pyloric stenosis are well known. An infant suffering from this condition is usually healthy at birth: some authorities, indeed, maintain that it is unusually so, and will weigh nearer 8 than the average 7 lb. Typically, the infant is the son and heir, and for the first two weeks behaves normally, taking feeds well, gaining weight, not vomiting, and having normal motions. Then, in the third week, without evident cause, he begins to go downhill. First there is cessation of weight gain, then an occasional vomit, and less regularity of the bowels; soon there is actual weight loss, the vomiting becomes more frequent and copious and rapidly acquires projectile characteristics. At this time constipation is a definite feature, and the napkins are wet much less frequently than before.

Vomiting does not necessarily occur after each feed. One or more feeds may be retained, and then an unusually large vomit empties the stomach of the last and previous feeds together. The vomitus occasionally contains blood, either in the form of fine streaks or intimately mixed, giving a "coffee-grounds" effect. This has occasionally been observed for one or two days after operation. There is a distinct facies in this disease—the furrowed brow, pale face, prominent sucking-pads, over-ready lip reflex, and constant fist-gnawing, being readily recognized by anyone accustomed to seeing many cases. The consistently keen appetite, even after large vomits, and the absence of retching or evidence of indigestion are also helpful diagnostic points.

On physical examination the visible waves of peristalsis are perhaps the most striking feature. These may be seen at any time if the abdomen is examined in a good light—either spontaneously, usually after a feed, or elicited by flicking the skin with the forefinger. They appear as golf-ball-like waves of contraction, commencing beneath the left costal margin, and slowly progressing across the epigastrium towards the umbilicus, clearly outlining the shape and position of the stomach. The point where the waves cease is an indication of the locality of the pylorus, and here the tumour is to be palpated. The tumour is *always* palpable, but whether it is actually felt in any given case depends on a variety

of circumstances. It is sometimes tucked up under the liver and can only be appreciated when the stomach has either been emptied or filled, or is actively contracting. Several examinations may be necessary before the olive-like tumour is felt with certainty. There has to be complete relaxation of the abdominal wall, and this may not be readily obtained. The more often each case is examined the nearer will the number of tumours felt approximate to 100 per cent. One other striking feature on abdominal inspection is the marked hollowing of the lower half of the abdomen in comparison with the upper, which is usually distended by the dilated stomach. While the skin turgor is poor, as it is in marasmus, the striking difference between the upper and lower halves of the abdomen is only seen in pyloric stenosis.

Variations in the clinical history are frequent. First, in the time of onset of vomiting, which not infrequently occurs before the third week. In two of our cases it was first observed while the infants were still in the maternity hospital (that is, they were less than 10 days old), in one case, a doctor's child, it occurred on the fourth day: in two more it had quite certainly commenced in the first week. Bilderback has reported a case starting as early as the fourteenth hour after birth. At the other extreme we had three cases in which no vomiting occurred until the sixth week. Ibrahim¹⁴ found that out of 266 cases only five started as late as the eighth week, while Sauer¹ found that not more than 1 per cent. started after the eighth week. Secondly, while absolute constipation is the rule, diarrhoea may occur, and this may be due to one of two causes—(a) infection, or (b) hunger. The infective type of case occurs earlier—while there is still a fairly patent lumen—and does not differ from other infective diarrhoeas of infancy. The second type manifests itself in frequently passed, small greenish-brown stools, containing little faecal matter and consisting largely of mucus.

Pathology

The pathology of this condition is still unexplained. There have for long been three main theories: (1) that there is a congenital hypertrophy; (2) that there is a primary spasm, with hypertrophy occurring only secondarily; and (3) that there is in every case a combination of both hypertrophy and spasm. The third postulate is almost certainly correct, but the underlying cause has not been fully explained. That there may be a primary hypertrophy is undoubted, for cases have been reported in which a tumour has been present at birth, and even in premature babies. Hyperadrenalism, phimosis (Tyrrell Gray¹⁰), lack of vitamin B in the maternal diet during pregnancy (leading to a delayed myelination of the pyloric nerve), and many other theories have been propounded.

As regards the cause of the spasm there are even more interesting theories. Ernberg¹¹ holds that trauma is the basis of every case, the trauma usually arising from over-distension of the stomach. White¹² thinks all these infants are hypertonic, and that there is, in addition, an autonomic incoordination (John Thomson¹³) which leads to contraction of the pyloric sphincter, instead of relaxation, when food reaches the antrum; this continued incoordination rapidly increases the hypertrophy and causes dilatation of the stomach with consequent retention of food and mucous gastritis.

It is a fact that in every case there is dilatation of the stomach and a varying degree of gastritis with swelling of the pyloric mucosa. The swelling usually takes from two to three weeks to reach its maximum. It coincides with the *complete* obstruction of the pyloric lumen, and accounts for the fairly constant time of onset of acute symptoms of the condition. The pressure exerted on the pyloric capillaries may easily cause thromboses and