REFRESHER COURSE FOR GENERAL PRACTITIONERS

THE MANAGEMENT OF THYROTOXICOSIS

BY

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The diagnosis of thyrotoxicosis and the division of the disorder into its component syndromes lie outside the scope of this paper. Nevertheless, a few introductory words on these subjects are necessary if misunderstanding of what follows is to be avoided.

Pathological Types

It has been customary in the past to lay some stress on the consistence of the thyroid gland, and especially on the presence or absence of nodules. There is little doubt that nodularity is of great pathological significance and academic interest, but until it has been subjected to far more study it is wise to avoid exaggeration of its clinical significance. It should be remembered that almost all diffusely enlarged glands become nodular with the passage of the years. Moreover, it is a common experience that glands considered to be diffusely enlarged before and even during operation are found under the microscope to be in fact nodular. It is therefore justifiable to attach significance to the presence of nodules, but not to their absence.

It is also unwise to be influenced too greatly by the size of the gland, unless severe pressure symptoms occur. Severe thyrotoxicosis may exist in patients whose thyroid glands are impalpable either because of their position or the shape of the neck or because they are in fact not enlarged.

Symptomatology

The sufferer from classical Graves's disease is easy to recognize. He complains of sweating, anxiety, irritability, palpitations of the heart, breathlessness on exertion, excessive activity followed by undue fatigue, loss of weight, and intolerance of warmth, and shows the signs of thyroid enlargement, exophthalmos, upper-lid retraction, vasodilatation, tremor, and tachycardia. Many patients present few of these symptoms and signs, and all too often are stigmatized as malingerers or hysterics, experiencing years of avoidable invalidism. Most often unrecognized are those in whom the brunt of the disease falls upon the heart, in whom no evidence of thyrotoxicosis may be found except tachycardia, fibrillation, and even congestive heart failure, and in whose thyroid glands may be found a nodule too small or too deeply placed to have been obvious even to the patient. There is no more satisfying experience in medicine than the discovery, treatment, and actual cure of patients such as these.

It is important to remember that even when the disorder is fully developed all the symptoms and signs may not be due to thyrotoxicosis. In foretelling the results of treatment, knowledge of the patient's physique and personality before the onset of the disease is of great importance. In many instances thyrotoxicosis attacks the constitutionally inadequate. Indeed, many of us believe that it is sometimes the result of the impact of shocks and strains upon patients ill formed by nature to bear them. In such circumstances we cannot expect to make a silk purse out of a sow's ear. In a few patients the anxiety state or other original inadequacy may remain, expressing itself perhaps by an auto-

nomic or psychological imbalance which both patient and doctor had assumed to be part of the thyrotoxic state. Nevertheless, even these patients are better able after treatment to cope with the difficulties of their lives.

Factors Bearing on Management

Before any definite conclusions can be reached about the ideal management of a case of thyrotoxicosis the disease must be considered historically. The heredity of the patient (for thyrotoxicosis is often familial), his environment before the disease developed (for this may be alterable), the immediate predisposing causes (which may never be repeated), and the nature of the disease itself must be examined.

From the practical point of view a family history of thyroid disease is important because it suggests that the thyroid once having "gone wrong" is likely to go wrong again, should similar circumstances arise. It is one point in favour of the partial removal of the offending organ. The previous environment is important, because careful inquiry may elicit the reasons for the thyroid gland's persistent overactivity—the earlier straws which weakened the camel's back. Such straws may be avoidable, or they may be unavoidable and therefore a continuing risk. The immediate predisposing causes—the last straws which broke the camel's back—are often obvious. Among these are puberty, childbirth, the menopause, severe infection, psychological shock, and the unwise administration of thyroid in the treatment of obesity. Often these are causes against which the patient can be protected, but unfortunately they are frequently interchangeable, and in avoiding one the patient may encounter another. Any last straw will do. Indeed, however successful may be our treatment for the time being, the thyrotoxic patient remains at risk while he retains his thyroid gland, for ever watching the wind to see which way the last straws are blowing. There is much to be said for the dictum of Mr. Charles Donald. At a meeting at the Royal Society of Medicine he criticized the medical treatment of thyrotoxicosis with its claim for remissions lasting several years, and stated his belief that all patients so treated would eventually relapse. Certainly at the New End Thyroid Clinic we have seen scores of middle-aged patients with a typical exacerbation or—a still more serious event—with auricular fibrillation, and sometimes with cardiac failure, who had had thyrotoxicosis in their youth.

Medical Treatment

Despite this proviso, we are still justified in considering the desirability of medical treatment in the individual case, and our justification is likely to remain until we have had an opportunity of examining the after-history of "successfully treated" patients for half a century. Even before the introduction six years ago of the thiouracil derivatives, there were patients who recovered without operation, and some of these have not so far relapsed. My own experience in those days was slight, but it was large enough to leave an impression on my mind clear enough for comparison

with those of older physicians, many of whom formed, with better reason, a similar opinion. In the days when surgery was very risky, physicians often attempted to treat their less severely ill patients by means which are still an essential part of the medical treatment of thyrotoxicosis; means, I would add, which are often unjustifiably neglected by those who are content with the straight choice between thiouracil and thyroidectomy. They attempted to secure for their patients the maximum of physical and mental rest by confinement to bed, sedation, advice on the replanning of their lives, and simple psychotherapy.

My earlier memories suggest that those who responded by a prolonged remission were usually young women with mild thyrotoxicosis and small, diffusely enlarged, or impalpable thyroid glands, with no family history of thyroid disorder, and with an apparently obvious "last straw" from the weight of which they could be easily relieved. My experience in the last six years suggests that this type of patient may have a prolonged remission after treatment with thiouracil derivatives, but whether this remission will prove permanent only time will show. Even when patients are carefully selected and treatment is continued, as it should be, for at least a year, relapse within a year, and usually within six months, is common. Those who relapse can be treated again by the same means, with equally satisfactory results, but, again, relapse is common. In a disorder characterized by undue anxiety it seems unjustifiable thus to play cat-and-mouse with the patient, and it is better to recommend thyroidectomy when the first relapse occurs.

When treatment with thiouracil is chosen, all those general measures which were a part of the older medical treatment should be instituted, though rest in bed is no longer necessary, except in the severest cases. In this country the methyl derivative of thiouracil is generally used, in the United States of America the propyl derivative. The latter is said to be less toxic, but, as serious toxic symptoms are rare with either, more prolonged controlled observations will be needed before a final conclusion can be reached. Methyl thiouracil, 200 mg., is given morning and evening until all signs of thyrotoxicosis have been controlled. During this initial period of a few weeks no reduction can be expected in either the size of the thyroid or the degree of exophthalmos, both of which may indeed be slightly increased. The dose is then gradually reduced to 50 mg. daily, at which level it is kept for at least a year.

Complications of Thiouracil Treatment

It was formerly the custom to perform frequent white cell counts during treatment with thiouracil, as once it was during the administration of the sulphonamide group of drugs. This is now considered neither necessary nor helpful. The dreaded complication of agranulocytosis is very rare, occurring with the modern derivatives of thiouracil and with the small doses now employed in less than 2% of cases. Moreover, agranulocytosis does not usually develop gradually, but strikes suddenly. In one example it occurred only two days after a white cell count of 10,000 had been recorded. Instead of frequent examinations of the blood, a warning is issued to the patient that in the event of his throat becoming sore he should take no more of the drug and report immediately to hospital. Should the white cells then be found to be greatly reduced he is immediately admitted, and massive doses of penicillin and blood transfusions are given.

Other complications of treatment are less serious and rarely enforce discontinuance of the treatment. They include a variety of rashes, such as purpura and urticaria,

swelling of the joints, nausea, drug fever, and enlargement of the lymphatic glands. The rashes usually respond to the antihistamine drugs such as promethazine hydrochloride ("phenegan"). The frequency of these complications in two series of 200 patients are as follows:

	Edinburgh*	New End
Agranulocytosis	4	2
Leucopenia	2	2
Purpura	1	0
Urticaria	Not stated	7
Fever and vomiting	5	0
Conjunctivitis	5	2

*Reported by Professor Derek Dunlop.

A different class of complication occurs which should be regarded as evidence of overdosage. It includes obvious increase in the size of the gland or in the degree of exophthalmos, and the appearance of oedema and myxoedema. If these occur treatment should be stopped until the undesirable effects have passed off, when it should be continued in smaller doses.

Contraindications to treatment with methyl thiouracil are the presence of large goitres, causing pressure symptoms, and of retrosternal goitres. In the opinion of the team working at the New End Thyroid Clinic, obvious nodularity is also a contraindication. In our experience, though the signs and symptoms of hyperthyroidism are in such cases easily controlled, relapse invariably occurs. The intelligence of the patient and his willingness to co-operate must be considered seriously, and the slightest deviation from the rules laid down for his safety is an indication for thyroidectomy. But perhaps the most serious contraindication to medical treatment is the fact that it imposes on a patient, already as a rule unduly anxious, a period of prolonged reliance on his doctor, which cannot fail to exaggerate any hypochondriacal traits which may be already present.

Surgical Treatment

The indications for surgical treatment are implicit in what has already been written. After a preliminary enthusiasm for medical treatment on my part, the members of the team at the New End Thyroid Clinic, which has the advantage of treating over 300 patients suffering from thyrotoxicosis per annum, are of the opinion that in most cases thyroidectomy after proper preparation is the ideal method of treatment. In skilled hands (a point referred to below) the risks by either method are too small for comparison. The results of surgery are more certainly and more rapidly achieved. The economic position of the patient is better protected by a method which in most cases rids him within two months of the necessity for further treatment. The cosmetic results, except for the inevitable risk of keloid scars (a risk we shall shortly be able to eliminate), are unexceptionable. Within a month or two the scar in most cases is invisible, or almost invisible, at a normal conversational distance.

The statement that the risks by either method are equal and negligible requires qualification. It implies in the first place a close and friendly collaboration between physician and surgeon, and in the second place a surgical technique of the first order. Even to-day the risk of surgery to the life of the patient and to the integrity of his recurrent laryngeal nerves and of his parathyroid glands is by no means negligible in the hands of one who has been called by Linnell "the occasional thyroid surgeon," however competent he may be to perform the other operations of surgery. In certain areas the general practitioner, dealing with a patient suffering from gastric ulceration, for whom he feels that a partial gastrectomy is the operation of

choice, may decide for similar reasons that his patient had best be dealt with by a gastro-jejunostomy or even by purely medical treatment. I have been forced to make such a choice in circumstances in which the gastric operation would perforce be performed by myself. It is impossible to discuss a question like this except on the assumption that both medical and surgical treatment will be of the highest order.

When, with this assumption granted, it has been decided that the treatment of choice is thyroidectomy, the preparation for operation, important though it may be, is straightforward. Admission to hospital is no longer necessary until a day or two before operation. Patients suffering from mild symptoms and signs of thyrotoxicosis can safely be prepared by means of iodine alone. Lugol's solution in the unnecessarily large dose of 5 minims (0.3 ml.) three times a day is usually given for a period of two to three weeks. The patient is then admitted to hospital and the operation performed almost immediately.

When, however, the degree of toxicity is moderate or severe, it should first be controlled by means of methyl thiouracil. The thiouracil derivatives have the disadvantage of rendering the operation of thyroidectomy more difficult in the occasional case. This disadvantage—a small one in comparison with the enhancement of safety which accompanies it—can usually be overcome by the administration of iodine for two to three weeks before operation. Some physicians prefer to combine the iodine in the pre-operative period with methyl thiouracil; some (as at New End) forgo the thiouracil for the final period and use iodine alone; others overlap the two drugs for various periods, giving at first methyl thiouracil alone, then a combination of methyl thiouracil with iodine, and, finally, iodine alone. Others administer thyroid as well. So far it seems that no advantage is attached to any one of these methods. All are excellent in their results, and it will be many years before any valid comparison can be made between them. Whichever method is adopted, the patient is usually out of bed in four or five days and out of hospital in from nine to twelve days.

There seem to be few contraindications to operation. Certainly auricular fibrillation is not one of them. In from 60 to 80% of cases the fibrillation ceases, almost always in paroxysmal fibrillation, as a result of thyroidectomy alone or of thyroidectomy followed by a short course of quinidine. Even congestive heart failure is no contraindication, though it may call for a longer pre-operative period, perhaps in hospital. The operative death rate in skilled hands is under 1%, the incidence of other complications is negligible, recurrence is of the greatest rarity, and a return to normal life and work almost invariable.

The use of radioactive iodine may well be the method of the future, but no useful purpose would be served in discussing it here. Even in centres in which it is available it is still in the experimental stage. It is not generally available in Great Britain. When it is, it will be beyond the scope of the general practitioner because of the special knowledge and equipment which it requires.

In no other disorder is the judgment of the general practitioner, with his knowledge of the background, character, and economic situation of his patient, of greater value than in thyrotoxicosis. It should be largely his responsibility to decide upon the best method of treatment. On the assumption that an expert thyroid surgeon is at his disposal, he will probably decide on thyroidectomy, after adequate medical preparation, as the best treatment for most of his patients.

A DIFFERENT VIEW OF THE TUBERCULOSIS PROBLEM

BY

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Nearly all those who have written in the lay or medical papers about the tuberculosis problem, as it exists to-day, have emphasized the need for more institutional beds and for more nurses to staff them. While everyone will agree that there is a shortage of beds and staff, and that there are long lists of sick and often infectious persons waiting for admission, it must not be forgotten that the provision of hospital and sanatorium accommodation is but one aspect of the matter in considering any truly comprehensive scheme for the prevention and treatment of tuberculosis.

A few contributors have mentioned what may be called the other end, or perhaps the beginning, of the problem. They have written of the housing situation and particularly of overcrowding. While agreeing with them, most of us on reflection would like to extend the idea to improving the whole environment of the people, whether in the home, school, office, shop, or factory. Many of the early triumphs of preventive medicine were won on the environment front, and there is still plenty to be done there.

Let it be agreed, then, that at one end of the situation we want more functioning beds and at the other end better environmental conditions, especially housing, not overlooking such matters as milk-borne infection.

Sir Robert Philip's Scheme

What is lacking is uniform and purposive control. That kind of control can be produced and maintained only by restoring the tuberculosis dispensary to its proper position in each clinical area as the directional centre of what the late Sir Robert Philip called many years ago a co-ordinated tuberculosis scheme.

It is to be doubted if many of the younger men and women practising medicine to-day, even those working in the tuberculosis field, have any clear conception of what the tuberculosis dispensary should be and should do. It is certain that many members of local health authorities, hospital management committees, and regional hospital boards have only the vaguest ideas about the whole matter, and yet they are the bodies that are supposed to be directing policy. Up to the appointed day there were areas with excellent schemes, and there are still some; but they were never numerous, and many more local authority units were content with poor or indifferent arrangements. In these latter it will be found that the dispensary has become an isolated and degraded out-patient department, falling very far short of the kind of dispensary conceived in Philip's mind as long ago as 1887.

Below is shown how Philip defined the tuberculosis dispensary, and I am able to reproduce from my tuberculosis scrapbook the diagram which accompanied the description. Both pamphlet and diagram were given out to his classes in the University of Edinburgh after the foundation of the chair of tuberculosis.

Under the heading "Co-ordinated Tuberculosis Scheme—Edinburgh Pattern" the tuberculosis dispensary is described as "an institution for the detection of tuberculosis, and for the treatment and guidance of persons and households suffering therefrom. It is a 'reception house' and 'clearing house,' and a centre of information regarding