summer at home or at a lower altitude; by so doing they generally become worse, and, returning to us in winter, nearly always show a relapse. Nearly all the good and lasting "cures" have been obtained by continuing the treatment until a sufficiently safe state of consolidation has been reached. There is no need to fear the effect of the snow-melting period at the high altitude health resorts in spring; either the weather is beautifully warm and sunny or snow falls; but even this last is preferable to the treacherous windy and damp weather with April showers which is usual at low altitudes at this time. Early spring weather is an especially risky time for lung patients in the lowlands, and induces every year many severe colds. Another difficulty is that some doctors order their patients home at that time, and are astonished that they then grow worse. Those patients would have continued to improve had they been allowed to remain out during the spring and summer. I cannot over-emphasize the importance of continuous treatment, which is far preferable to the "wintering" only.

The patient's co-operation is essential, and he must have full confidence in his medical adviser. Doctors who send patients abroad can do great harm by being too optimistic at first. To encourage the patient so many say: "Oh, a few months out there will put you all right." The few months pass, the patient feels better, and gets discontented at not being allowed to go home. If they were warned at first: "You will probably get well, but it may take a long time; we cannot know it yet, and you must play the game," people would be spared a false idea and much disappointment. Doctors should also warn relations not to urge patients to come home; several patients under my care were completely upset by injudicious home letters. In 99 cases out of 100 it is quite impossible to "cure" at home faithfully. After many years of attending lung patients I must express my conviction that patients will nearly always do much better in a good sanatorium than at open hotels.

TOXIC GOITRE.*

BY

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THE term "toxic goitre" is used in this paper to include all forms of thyrotoxicosis: primary Graves's disease—that is, where no enlargement of the thyroid gland existed before the onset of the disease—and secondary Graves's disease, where toxic symptoms arise in a patient with a pre-existing goitre. "Toxic adenoma" is used to signify thyrotoxicosis where one or more discrete adenomata are present in the gland.

CLASSIFICATION.

Toxic goitre gives rise to a wide variety of clinical pictures. The symptoms of the disease are numerous, and are combined in varying numbers and severity, so that each case is essentially a study in itself. There is, however, a dividing line between the primary and the secondary types; you may see this clearly illustrated by looking at the cut surfaces of glands removed at operation—the primary shows a uniform surface, the secondary a surface marked by various types of degeneration. Clinically, the primary is characterized by exacerbations or crises, with periods of improvement, and may result, with adequate time and care, in a complete cure; or it may pass into a subacute or chronic state, which is difficult to distinguish from the secondary. The secondary type, including the adenomatous variety, is characterized by steady progress, free from ups and downs. The emphasis in the primary form is on the nervous symptoms, whereas the secondary causes a progressive deterioration of the cardio-vascular system. The two types, however, are so interlinked that in many individual cases it is difficult to place the case definitely in either group.

SYMPTOMATOLOGY AND IDENTIFICATION.

The classical group of symptoms of Graves's disease used to be given as goitre, tachycardia, fine fibrillary tremor of the fingers, and exophthalmos, and where these are present the disease is easily recognized. The chief additional symptoms are easily produced fatigue, palpitation, loss of weight, excessive perspiration, nervousness, digestive derangements, and, in advanced cases, auricular fibrillation and even dropsy.

The patient in many cases never dreams of connecting her symptoms with an enlarged thyroid; she will even say that her present complaints have nothing to do with her goitre, as she has had that for years and it has given her no trouble. Neither is it easy for the doctor in many cases to recognize and convince himself of the causal connexion. Such cases fall chiefly into three groups.

The first group includes patients who complain of some falling off in general health, and on inquiry are found to have some palpitation, nervousness, excessive perspiration, loss of weight, and are easily fatigued. That a goitre is often the cause of such falling off in health can be clearly demonstrated by three facts: first, the marked improvement in general health which often occurs after a goitre, considered non-toxic, is removed for mechanical reasons; secondly, the severe toxic reaction which can occur during the first forty-eight hours after operation in a patient with only slight toxic symptoms; and thirdly, the dramatic improvement in this group of cases after operation. The immediate improvement is nearly always obvious on the third to fifth day after operation, and consists in a feeling of restfulness and general well-being, with cessation of uncomfortable pulsations and throbbing in precordia or neck; the ultimate improvement is a return to normal weight, strength, and general health.

The second group consists of patients with cardio-vascular degeneration who for years have had an apparently harmless goitre. The causal relationship of such a goitre to the premature degenerative changes has in the past been often unrecognized; but if such a goitre (which has become toxic) is operated on, a marked change in the outlook will soon follow, unless the organic degenerative changes have been allowed to become hopelessly advanced.

The third group comprises patients with an anomalous or atypical mixture of symptoms. For example, a man, aged 61, sent in as a case of diabetes, complained of excessive fatigue on very slight exertion. He had almost no exophthalmos, a very coarse tremor of the hands, pulse 96, and a slight symmetrical soft enlargement of the thyroid, without any thrill. After hemithyroidectomy he felt better in three days; nine months later, having increased 3 st. in weight, he resumed his work. A female teacher, aged 55, had fallen off in weight and lost her physical and mental energy, concurrently with a slight increase in size of her parenchymatous goitre; four months after a bilateral resection she had put on a stone in weight, resumed work, and regained, as she said, her *joie de vivre*.

It is essential, of course, in all such cases to form a careful clinical picture. A female patient who was sent to me recently because of loss of strength and weakness of the legs, with an obvious goitre, was suffering from locomotor ataxia. Such diseases as phthisis, diabetes, and carcinoma must be excluded. If this care be taken, operations on a coexisting goitre will in the above groups of cases rarely fail to produce a good, often a spectacular, result. Where cardio-vascular degeneration is the symptom early recognition is of vital importance, since if operation is carried out reasonably early it entirely alters the outlook, and if delayed too long the case becomes an excessively bad risk.

TREATMENT.

We are comparatively ignorant of the causal factors of toxic goitre and of the mechanism by which these causal factors stimulate and derange the thyroid gland, as well as of the natural history of the disease. It is not easy to give a prognosis in an individual case. It follows that definite lines of treatment are not easy to lay down. American surgeons give a brief and clear answer to this question of treatment—namely, toxic goitre has become a surgical disease; operation cures quickly and safely; conservative

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treatment is slow and uncertain, and apt to inflict permanent damage to the heart.

The leaders of surgical opinion in this country take a different view. Dunhill considers that primary Graves's disease should be given a six months' trial of non-operative treatment, and not till then—and then only if such treatment does not seem to present a prospect of cure—should operation be considered. The length of time may be more than the patient can or will afford, and economic reasons may force a decision between incomplete cure and chronic ill health on the one hand, and operation on the other. The wisdom of the conservative treatment of primary cases is shown by the fact that many of these patients return in course of time to apparently perfect and normal health, in possession of a useful thyroid gland. Such a result is no doubt preferable to any that operation can produce, and where the patient is prepared to afford a length of time necessary to endure it she should be given the chance.

In the uncured residue of those primary cases, and to a large extent in secondary Graves's disease, operation is the method of choice. While this opinion is necessarily based on the clinical results, examination of the glands removed shows that it rests on a sound pathological basis. The glands show in varying measure areas of degeneration (colloid, cystic, fibrous, nodular, calcareous), contrasting with the uniform hypertrophy of primary Graves's disease. They are end-results of disease, and their retention within the body is detrimental to health. It is not unlikely that the character of the toxicity alters—that the primary type is really a pure hyperthyroidism which provides an intense but temporary stimulus to the nervous system, whereas the secondary is a dysthyroidism, pouring into the blood a perverted secretion which causes a slow but progressive deterioration in the cardio-vascular system. If this view is correct, operation is definitely indicated in advanced primary and in secondary Graves's disease.

In toxic adenoma operation is essential. The removal of the adenoma relieves the symptoms quickly and with certainty, and, while not repairing organic damage, radically changes the outlook. The rate of progress of toxic adenoma may be illustrated by the following cases.

A. B., female, single, aged 37; complained of intermittent aphonia, "croaky voice," ill health, chronic goitre. The goitre was first noticed when she was 17, when she had typical symptoms of secondary toxic goitre (trembling, nervousness, weakness, sweating, pulse 130-140, no exophthalmos). She was off work for twenty-six weeks. Treated by x rays for two and a half years, supervised another year. Relapse at 21; off work nineteen weeks. She had pneumonia at 27, and had been off work for twenty weeks each year since then. Symptoms had persisted during twenty years: tremulousness, weakness, excessive sweating, palpitation, pulse 106; no exophthalmos. There was complete paralysis of the left vocal cord, and a compressed and displaced trachea, due to a large adenoma the size of a goose's egg, partly substernal, left-sided. This was removed at operation, and after a severe reaction during the first forty-eight hours the patient made a good recovery.

C. D., aged 49. Advanced cardiac disease. Pulse 170 and very irregular. Had a large goitre with multiple adenomata. Was in good health till 41, since when health has deteriorated, with concurrent development and growth of goitre. This patient, after careful medical treatment, failed to improve, and was dismissed as hopeless and inoperable.

E. F., aged 65. Was perfectly healthy and never knew fatigue till two and a half years ago, when for the first time she noticed a commencing goitre, which has steadily grown, and now has several adenomata in the left lobe, and one in the right lobe. She has become weak, thin, breathless, incapable of exertion, depressed. Her pulse was rapid and irregular, and after careful supervision the consulting physician thought the risk of operation too great. The right lobe and part of the left lobe were removed. In the following three months she gained a stone in weight, and though her heart still fibrillates, she is a different woman.

It may be noted that in these three cases the duration before serious complication ensued was, in the patient of 37, twenty years; in the patient of 49 eight years; and in the patient of 65 two to three years—that is, in a definite relation to the activity of the gland.

G. H., female, aged 47, had a large median adenoma and a small adenoma of the left lobe, and wished them removed for mechanical reasons. My house-surgeon records "no toxic symptoms." A lump was first noticed twelve years ago; it was then the size of a marble. It had grown quickly during the last two years. Her only general symptoms were easy fatigue and very slight tremor. After operation her improvement in weight,

strength, and general health was rapid and permanent. She brought with her a man who had increased in weight from 6 st. 2 lb. to 9 st. 7 lb. after a similar operation. Both have scars practically invisible.

Brilliant results such as the above are common in the surgery of the toxic thyroid, and cases could easily be multiplied did space permit. The gratitude of such patients is not easily measured. Many of them enter on a new life, and this is true, not merely of toxic adenoma, but of all forms of toxic goitre.

RISK OF TOXICITY OCCURRING IN A NON-TOXIC GOITRE.

The question arises, What risk is there of the chronically enlarged thyroid becoming toxic? Jackson states that by the time a patient with a non-toxic adenoma reaches 45 the chances are one to two that toxic symptoms will develop; that the adenoma is present for eighteen to twenty-five years before toxic symptoms arise; that their onset is subtle and gradual, and inflicts serious and lasting injury within four years, at an average age of 44 years. He uses "toxic adenoma" in the larger sense of "adenomatous goitre." Dr. Quervain states that after a bilateral resection for parenchymatous goitre (non-toxic) recurrence is comparatively frequent among the young, however thoroughly the operation may have been performed, but in older patients the power to prevent recurrences seems to have become exhausted. This would tend to show that there is a diminution of thyroid activity—a sort of thyroid menopause—round about 40 years of age. With diminished activity degenerations are prone to occur and toxicity to arise. I have observed in a number of cases that toxic symptoms date from about 40 years of age, and believe that from this age onwards they should be kept under supervision with a view to early detection of toxic phenomena.

CONSERVATIVE TREATMENT.

The sheet anchor is time and rest, the length of time varying from six months to three years. Septic foci should, when practicable, be removed. There are many cases which have cleared up or materially improved after this has been done. It is well, however, not to exaggerate the value of this procedure, and in severe cases it should be undertaken with due care, being not entirely free from risk. Even if one takes the view that toxic goitre is due to an infection which selects the thyroid because of the predisposition of the individual, following a disorder of the reactions of the ductless glands from sex trauma or overstrain, the removal of a septic focus whilst the patient is in a state of toxæmia may have a disappointing result.

The following case shows what can be accomplished by treatment of septic foci and their sequelae. It was under the sole care of a general practitioner, who has given me his notes.

History and Examination.—Mrs. W., aged 54. Three years ago this patient came under my care and was almost bedridden; nearly every joint in the body had been stiffened, and most were swollen and painful. There was extremely limited movement of the limbs, and the patient could hardly open her jaws sufficiently wide to take anything but liquid nourishment. The pulse rate was about 150; the pulse was very intermittent and irregular, and the cardiac sounds in keeping. There was a systolic apical murmur with mitral regurgitation. Weight (three years ago) 6 st. Left lobe of thyroid enlarged (about the size of a Tangerine orange)—probable toxic adenoma—and had been steadily enlarging for the past fifteen years. Teeth very foul, spongy, and caked almost to a solid mass. It was impossible to differentiate separately the lower incisors, and the remainder of her teeth were more or less a solid mass. The ankles were markedly oedematous. There were large "rheumatic" nodules at areas of pressure; one nodule, about the size of a hen's egg, over the third lumbar spine, and smaller ones over the first and second dorsal spines. On each elbow was a nodule about the size of a pigeon's egg, and several smaller ones down the ulnar aspect of the arm—pressure nodules. The patient could not reach her chin with either hand, and could not attempt to do her hair or wash her own face. She hobbled on sticks to a chair at her fire-side; that was her sole effort at walking.

Previous Treatment.—As far as could be gathered this had consisted of thyroid tablets, thrice daily after meals, and aspirin at bedtime. She had been forbidden meat and milk.

Treatment (carried out by me).—Intermediate removal of all the teeth, under novocain. She was put on a diet of beef-tea and nourishing fluids, including milk; she could not take solids. Orally collosol sulphur and collosol iodine for alternate fortnights. Six weeks after removal of the teeth the patient received a course

of six injections of mixed streptococcal vaccine. After three months the pulse rate had come down to 100; the heart had become much more regular; the nodules had almost disappeared and the heart murmurs were hardly discernible. The adenoma of the thyroid had diminished by half. Joint movements had slightly improved, especially the jaw, which had markedly improved. During the subsequent three months the patient was kept on collosol sulphur and iodine and as full a diet as possible. At the end of this period she was provided with artificial dentures, and masticated food for the first time for years with comfort. At the end of a further three months I gave another course of six injections of streptococcal vaccine; collosols as before, with full diet, including meat, vegetables, and fruit—the latter in plenty.

One year after beginning treatment the patient was sent to Bath for a six weeks' course of exercises and massage. On her return she was able to come downstairs with the aid of one stick, to perform her ablutions, and to dress herself and to attend to her own hair.

Exercises were maintained at home for another six months. Further course of six injections of streptococcal vaccine, at the end of which time the pulse rate had come down to 84 and was perfectly regular. Heart sounds normal. All signs of adenoma had disappeared and the patient was able to do her own shopping out of doors. The nodules had entirely disappeared, and only slight oedema of ankles reappeared towards the end of the evening.

July, 1929: Patient remains very well. Sleeps well at night, takes hearty meals, and generally is a vastly improved subject. Weight has steadily risen to 8 st. 12 lb. Throughout treatment mag. sulph. in graduated doses was taken to keep bowels regulated.

The value of x rays is a thorny and unsettled question. The surgeon does not as a rule see a big enough series of cases so treated to offer a fair judgement; he sees the bad results, which certainly occur. X rays should not be used for toxic adenoma, probably not for secondary Graves's disease, and their sphere in primary Graves's disease is still a matter of dispute.

Among the numerous drugs recommended there is one of outstanding importance—namely, iodine. As an adjuvant to surgery, lugol (a solution of iodine 5 per cent. and potassium iodide 10 per cent. in water), introduced by Plummer in 1922, has proved its value. In the great majority of cases of toxic goitre it improves the patient (often in a striking degree) before operation, and is a safeguard against post-operative thyrotoxicosis. Whilst as a stand-by to the surgeon it is invaluable, the use of iodine as a continued medical treatment is open to question. Its beneficial effects are apt to be temporary; its excessive use may induce hyperthyroidism, and it loses most of its value to the surgeon should operation subsequently be required. I have seen four patients during the last year who had had careful iodine treatment for about three months; all of them had the characteristically firm gland which the continued use of iodine induces; two, aged 46 and 48 respectively, were inoperable on account of their cardiac condition; the other two, females, aged 26 and 48, had pulses of 160 and 140 respectively, and after being carefully piloted through the two-stage operation made a very satisfactory recovery. It would appear in these four cases that iodine in the amount given had no curative effect, and may even have been injurious. Cases of toxic goitre have been cured by potassium iodide, but possibly the old view of the danger of iodine as a medical treatment of toxic goitre is well founded. The history of one of these cases is as follows.

I. J., female, single, aged 28, a few weeks after an attack of erysipelas had a sudden and very violent onset of Graves's disease, with a running pulse of 180, severe gastro-intestinal disturbance, restlessness, and tremors of marked exophthalmos. She was treated with lugol (2 minims three times a day) for three months. I then saw her for the first time, with typical symptoms of primary Graves's disease, pulse 160, and a firm "iodine" gland showing a slight bilateral enlargement. She was admitted to hospital for a month's observation, and continued very ill, pulse 150-160. Lugol was then resumed for a month (7 minims thrice daily), and she immediately improved in every way, pulse 130. Right hemithyroidectomy was performed, with very marked improvement, the pulse falling as low as 100. After six weeks two very septic enlarged tonsils were removed. This caused a slight relapse. During the next four weeks the patient remained stationary (pulse 115-120), and about three-fourths of the left lobe was accordingly resected. Rapid improvement followed. About three weeks after the operation the patient said to me, "I have not felt so well for seven years." It appears that she had been in indifferent health for seven years, nervous and easily tired.

This period of nervous debility—in reality a mild thyrotoxicosis (what might be called the prodromal stage of

toxic goitre)—lasting some few years, is a not infrequent prelude to an identified attack, and is the period when preventive medicine (or surgery, in adenomatous cases) is of especial value. It is difficult to identify a thyrotoxicosis—possibly the pulse pressure (a convenient and fairly accurate substitute for the basal metabolic rate) might help—and the type of patient is not easily persuaded to rest. I believe the following case is an example of prophylactic treatment.

K. L., female, married, of very active habits, was admitted to a nursing home for fractured patella. She was considered to be "on the borders of a nervous breakdown," was nervous, and had fallen off in weight and strength; pulse 110-120. A consulting physician was unable to say whether or not she was in the prodromal stage of toxic goitre. She was carefully warned and had a few months' complete rest. She regained good health, and is still, two or three years thereafter, strong and robust.

OBJECTIONS TO OPERATION.

Although the operative treatment of toxic goitre produces results as dramatic and as excellent as any other branch of surgery can show, certain objections to this particular operation are often present in the minds of the patient and especially of the doctor.

1. The hope of non-operative cure.
2. The dislike of the removal of such an important organ as the thyroid. The aim of surgery is to remove, not a useful, but a deleterious gland.
3. The risk of operation. At the present day this is certainly small. The death rate depends upon whether the surgeon chooses to accept the very bad risks, especially the late secondary cases with advanced cardiac degeneration and rapid, irregular, and feeble pulse; on careful pre-operative and post-operative care; on gentleness of handling; absence of loss of blood during operation; and drainage of the wound. Of about eighty cases I have operated on from 1921 to 1929, I have lost two only, both before the lugol period. One was a case of primary Graves's disease with extreme emaciation, rapid pulse, and anorexia; the other, a woman, aged 63, with a bilateral adenomatous goitre in which neither the physician nor myself had suspected a toxic element; she died of acute thyrotoxicosis. At the present day, I believe, both would have survived.
4. The scars on the neck. These are wonderfully good, often scarcely visible, and many patients are rather proud of them.
5. Injury to the voice. If one of the recurrent laryngeal nerves should be damaged some change in voice may follow; if both are injured, it is a serious sequel. The risk of injuring one of these nerves is now very small. It is never negligible. Jackson considers that since the patient may have a paralysed vocal cord without being aware of it, laryngoscopic examination should be a routine before operation. Improved technique has reduced this risk to a slight one. I have one patient only with a damaged voice, though cured of a severe primary Graves's disease.

6. Incomplete cure and possible relapse. Dunhill lays down the rule that no surgeon should operate on toxic goitre who is not prepared to remove enough of the thyroid gland to effect a cure, otherwise he will have sufficient bad results to render a serious disservice to surgery. If this rule be followed, relapse need not be feared. It might be asked, What constitutes a cure? Slight remnants of the disease may remain (notably some prominence of the eyes), but a cure may be regarded as a return to active life, with a satisfactory prospect of longevity.

Hemithyroidectomy is sometimes curative; as a rule it effects only a partial cure, and it is generally agreed that the removal of three-quarters to seven-eighths of the gland is necessary. The fact that Nature can carry on satisfactorily with a mere remnant of a gland so important as the thyroid is a tribute to her wonderful adaptability.

Had space permitted I should have liked to quote cases illustrative of clinical opinions expressed above. In conclusion, I wish to express the indebtedness that every surgeon who operates on toxic goitre must feel to the leaders of opinion on the subject.