SOME THOUGHTS ON GOITRE

R. E. McKechnie, M.D.

Vancouver

THE subject of goitre is one that interests everyone of us, both because of its prevalence and because of the obscurity about its causation. No one will dispute the relatively large proportion of cases found among children and young adults, and a lesser proportion among the more adult. This latter would suggest that a large number of these cases, seen in the young, become spontaneously cured before middle life.

In opening my subject, I do not intend to take up the development or the anatomy of the thyroid, but rather bring to your remembrance the work-a-day facts in connection with goitre, which we as busy practitioners are constantly encountering.

There is no doubt that, in the North Pacific States and British Columbia, we have more than our share of goitre. The reports of our school inspectors show, from 20 to 80 per cent. of the female children in our schools are affected with goitre; a much less proportion of males. With us in British Columbia, it is as prevalent in the dry belt as in the wet coast districts.

While cases of goitre may be found anywhere, still, there are certain areas in the world which are notoriously goiterous. But looking for a local cause we do not seem to find one. Some areas are thought to owe their goiterous characteristics to a chalky soil, others to the presence of limestone. Elsewhere a mountainous district blames its hills while another of sedimentary basin formation, thinks it finds the cause, in excess of organic material present in its soil. No two goiterous districts seem alike, even the same range may vary. Thus British Columbia, Washington and Oregon are distinctly goiterous—but I am informed by a Sacramento practitioner that he rarely sees a case there. So it can't be hills or plains or chalk or limestone or excess of organic material in the soil, that accounts for an over proportion of cases of goitre, for these conditions are not constant in the goitre areas. Perhaps no one cause for goitre will ever be found, and perhaps our troubles are of our own making, in trying to find one cause to fit all cases.

However, I shall seek to prove that an absence of iodine is the main cause of the prevalence of goitre on the north Pacific coast. The coast range of mountains is composed of granite, from which iodine is absent. Granite is a plutonic rock, and one can easily see, how, so volatile a substance as iodine, could never lodge in such a matrix. Hence, the waters derived from such rocks must in turn be free of iodine. The Vancouver water supply has been analyzed and no trace found. Hence, locally, we have a population drinking an iodine free water, and in most instances living on an iodine free food. Some years ago, at the Colony Farm at Essondale, only twenty miles from Vancouver, there were many cases of goitre among the livestock, many calves and lambs being born with it. One calf had so large a goitre that assistance was necessary at its birth. This state of affairs was eradicated by the use of iodine, a small dose of a very few grains of sodium iodide given weekly to the pregnant animal, being sufficient to ensure absence of goitre in their offspring. As further evidence, two years ago, at the Dominion Experimental farm at Summerland, all the pigs born that year were goiterous and all but two died. The following year the pregnant sows were given two grains of sodium iodide daily and not a pig was born with goitre.

The experimental work of Marine and Kimball at Akron, Ohio, is also confirmatory. They found 56.4% of enlarged thyroids among 3,872 school children. Six months after a month's treatment with sodium iodide had been given, they found that one third of the small goitres had disappeared, and one third of those marked as moderate goitres, had decreased 2 c.m. or more, thus showing a curative effect. But the prophylactic effect was just as positive. Not only had iodine been given to those with goitre, but a large number without goitre had also been put under the influence of iodine while a third group, also without goitre had had no treatment. Of those without goitre who took treatment, not one at the end of six months showed any thyroid

enlargement, but of those without goitre who had no treatment, no less than 26% at the end of six months from the beginning of the observations, shewed enlargement.

Empirically, iodine has been used for a long time in treating goitre, and there seems by these late experiments to have been some basis for its use. In the treatment of tropical dysentry in the past, heroic doses of ipecac were given, often with good effect, a true empirical form of treatment. Now the present day treatment by means of emetine derived from ipecac, proves that our predecessors in the profession, shooting in the dark, had hit the mark. So the Akron experiment at least encourages the belief that prophylaxis may be the successful means of eradicating goitre.

Speaking of iodine I am reminded of an observation of Dr. Pearson at one of our local Vancouver meetings. He pointed out, that our local Japanese did not have goitre and also drew our attention to the fact, that in the food consumed by them, quite a proportion was obtained from the sea; *e.g.*, fish and the dried seaweeds used in soups, etc., and these have a well known iodine content.

In confirmation of Dr. Pearson's idea the following letter to me from Dr. Everett O. Jones, of Seattle, is interesting:

"Ten years ago the valley of the White River, which is south of Seattle, was occupied by white farmers. The occurrence of goitre amongst these people was very common. I used to average two or three cases every month from that district. Since then the Japanese truck farmers have come in and crowded out the whites, so that now the whole district is inhabited by Japanese. So far as I know, no case of goitre has ever been seen in any of these people.

"Last summer I was consulted by a middle-aged Japanese woman who was suffering from a very toxic adenoma. It being the only case of goitre I had encountered in a Japanese, I made some enquiries as to her family, mode of living, etc. I was informed that she and her family belonged to the 'Tony Japs'. They had discarded the ways of their own people and were living as much like Americans as they possibly could to the extent of even employing a white cook. These two occurrences would certainly suggest the thought that there is something in the food or the mode of living of the Japanese which protects them from goitre."

As further evincing the growth of the idea that absence of iodine in the food has some influence in the formation of goitre, or in permitting the formation of goitre, it is only recently I noticed in the public press a note by one of your Winnipeg doctors, who blamed the purity of present day refined salt as a factor. Iodine is found in the brine of salt wells and careful refining removes it from the salt.

In view of the foregoing, would it not be a valuable experiment to have every pregnant woman take short iodine treatments, and would it not be a good plan in childhood, to substitute yearly a course of iodine for the familiar sulphur and molasses; I am beginning to believe that goitre might become a rarity if such plans were universally carried out.

I am well aware that the iodine theory will not fit all cases, as for instance the classic goiterous wells in Styria, drinking of whose water cause goitre; of the statement that the goitre producing element cannot be filtered out, but can be destroyed by boiling, thus suggesting a living organism. My only suggestion would be that a re-checking of these various statements would not come amiss and the result might enhance the value of the iodine suggestion. But looking at the subject from another angle more light may be obtained. Granted that no one excitant cause can be found; that what produces goitre in the sedimentary basin of Akron, Ohio, is different from that at Vancouver or Seattle; still in both cases the influence of iodine is marked. Then we must suppose that iodine acts as a protective agent, enabling the thyroid gland to combat or neutralize the evil influences of the unknown agents which are the causes of goitre.

Classification.—A good deal of confusion has arisen in classifying the various types of goitre, owing to a tendency to multiply these types, and make the classification all embracing. Fortunately a very simple classification suffices for ordinary work, and that as used at the Vancouver General Hospital is all that is wanted.

All goitres are there divided into two classes; Symmetrical and Asymmetrical.

The Symmetrical are divided into: (a) Diffuse colloid goitre; the so-called parenchymatous of Mayo. (b) Diffuse hyperplastic goitre; or the typical exophthalmic goitre.

The asymmetrical consists almost exclusively of adenomatous goitres, with their various degenerations. But in addition, in asymmetrical goitre, we have those cases of malignancy; of abscess, etc., which naturally would create an

asymmetry but which being few in number leave the field almost alone to the adenomata. These adenomata in turn are of two kinds—(leaving out the degenerate forms), namely: simple adenomata, and hyperplastic adenomata. Hyperplasia is taken to mean an increase in the epithelial elements lining the acini of the thyroid, and hence when the terms diffuse hyperplastic or hyperplastic adenoma are used they signify toxicity.

It is thus seen that the classification is reduced to simple elements. The thyroid does not increase in size by a multiplication of its acini but either by an increase in the contents of the acini, when we have colloid goitre; or an increase in the cellular elements when we have hyperplasia or toxic goitre.

Based on the foregoing, our pathologist, Dr. Hunter, classified a series of fifty of my cases recently and found as follows: Symmetrical, 36; consisting of: Diffuse colloid, 19; Diffuse hyperplastic, 17. Asymmetrical, 14, consisting of: Simple adenoma, 7; Hyperplastic adenoma, 7. It is thus seen that out of these fifty cases, there were twenty-four hyperplastic, or toxic, and twenty-six non-toxic; nearly half toxic; a higher proportion of such cases than is usually found in a goitre series. But, my observations over a number of years, lead me to believe that this is not exceptional on the Pacific slope, although it does not agree with the published results of some Eastern clinics, *i.e.*, the Mayo's.

Our pathologist, in working over the specimens, made frequent attempts to demonstrate the presence of mitochondria, which Goetsch affirmed were always found in toxic goitre and always in proportion to its toxicity. But failure was recorded, and the hyperplasia, demonstrated by the excess of the epithelial cells lining the acini, was taken to prove the toxicity of the cases. In fact, Dr. Hunter essays to demonstrate the degree of toxicity, microscopically, by noting the degree of infolding of the acinar epithelium. Thus, if the infolding is marked with a consequent increase in the cellular elements there is a high degree of toxicity, while a distention of the acinar cavity with colloid material and a smoothing out of the infolded epithelium denotes a lesser degree of toxicity.

Personally, I think the microscope has missed a number of mildly toxic cases, yet cases which presented the classical picture of Graves' disease. Two years ago, at Spokane, I presented an eleven months' record of sixty-five cases, of which forty-five were clinically toxic; over two and one-half times as many toxic as non-toxic. My last fifty cases rely on the microscope for confirmation and less than half are designated toxic. The discrepancy is too great to be explained away, and I am old fashioned enough to have faith in my clinical findings, even if not backed up by the microscope. However, in my next series I trust to be on firmer ground, having the aid of the basal metabolism tests in diagnosis.

Metabolism is essentially a process of oxidation and it has been found that the excretion of carbon dioxide, as noted in the expired air, furnishes a reliable guide in estimating the rate of metabolism. Thus, if the amount of carbon dioxide is greater than normal, we have increased metabolism. If less than normal, then we have lessened metabolism. This works out in practice, for hyperthyroidism is accompanied by increased metabolism in direct ratio to its gravity, while hypothyroidism is accompanied by metabolism below the normal. The value of this knowledge is so great, that, Charles Mayo says, "a failure of diagnosis is almost impossible if the metabolic rate is taken into consideration with other general symptoms."

It seems that the estimation of the basal metabolism rate as applied to goitre is proving the most valuable aid in diagnosis and treatment elaborated in recent years. Enumerating the various advantages of this method, Eberts, in the *C.M.A. Journal*, of March, 1921, says:

"In hyperthyroidism, basal metabolic methods are of great value clinically in the following ways: (1) In determining the degree of toxicity in cases of toxic goitre. (2) In determining the operative risk judged by the degree of toxicity. (3) In determining whether in a given case of toxic goitre, especially the exophthalmic type, the individual is approaching or receding from a crisis—information of great importance where an operation is under consideration. (4) In determining whether, in cases of large goitre with symptoms resembling hyperthyroidism, these symptoms are due to hyperthyroidism or not. (5) In differentiating, in the presence of goitre, between tachycardia of nervous origin and that due to increased thyroid activity. (6) In discovering the effects of operation, *x*-ray treatment, the administration of thyroxin, or other modes of therapy."

Abbott, in the same issue, has the following to say:

"A word only can be said, on the clinical import of alterations in the basal metabolic rate, as

revealed in the very large number of observations, which the literature cited here represents. Normal changes lie between the relatively narrow limits of −10 and +10 per cent. following a similar range, although with somewhat greater fluctuations, to that of the body temperature. Variations appear to depend upon alterations in the active principle of the thyroid secretion, which has to do with the regulation of heat production, and very high values as +80 to +100 per cent. may be said to be pathognomonic of hyperthyroidism. The converse applies to hypothyroidism, in which the rate may be depressed to the lowest figure consistent with life (−40 to −45 per cent.). A raised rate is most useful in the differentiation of thyrotoxic from adenomatous goitres, and in the diagnosis of those "borderline cases" of thyroid toxicity without exophthalmos which demand treatment, yet frequently escape recognition. In the "irritable heart of soldiers" the normal rate has supplied a valuable negative point against the hyperthyroidism sometimes hypothecated. Alterations in the rate with corresponding changes in the clinical picture, follow administration of thyroid with almost mathematical accuracy, and supply an invaluable index in the gradation of therapeutic doses of thyrotoxin, which is cumulative in its effect. Similarly, in hyperthyroidism, the surgeon is guided to a definite knowledge of what cases demand interference, and of the effect of lobectomy or *x*-ray treatment, when these steps have been taken, by estimations of the metabolic rate. Without it he will operate unnecessarily on many cases, and on many others without the success that should be his due."

From the foregoing it would appear, that the use of this method, both in diagnosis and in estimating the danger of operation, in hyperthyroid cases, is imperative and its non-use almost criminal. I may be radical in my views but I believe that if the profession could be educated to believe in early operation in toxic cases, a great advance would be made. We all remember the discussion about the right time to operate in appendicitis, and know that many lives were lost by waiting for the optimum time to arrive. Murphy crystalised the growing opinion of the profession when he enunciated his dictum that, "the best time was as soon as appendicitis was diagnosed."

Similarly in cases of hyperthyroidism, if instead of waiting until the case got serious, an early operation was performed, many lives would be saved. The majority of these cases demand operation, probably a larger proportion than in appendicitis, so why not at once face the question boldly and enlarge Murphy's dictum to include toxic goitre?

Having diagnosed the case, it is then open to discussion as to what form of treatment is advisable. Physicians contend that many cases are susceptible to treatment and I will not dispute that view with them. Certain forms of treatment I would condemn—as the injection of boiling water—an unsurgical procedure and not without danger; *x*-ray treatment which seems to benefit for a time but whose benefit is not permanent, and which renders a subsequent operation much more difficult, etc. The former practice we hear little about to-day, but the latter is still extensively practised as the surgeons can testify.

Personally, I have but little faith in any form of treatment after a goitre is fully established, say for one to two years. The goitre of adolescence is the most favourable and it is that type that Marine and Kimball found to re-act so readily to sodium iodide.

Toxic goitre is also in a class by itself. The exophthalmic type is more vicious than the toxic adenoma. This latter has remissions when the growing adenoma, with its poor blood supply, finally starves the cortical hyperplastic cells. But a recrudesence is apt to occur as other adenomata begin to grow and the cycle is repeated; repeated many times in the one patient perhaps. These remissions do not occur in the diffuse hyperplastic goitre, but the patient is continuously ill, the seriousness of the symptoms varying with the virulence of the case.

As to treatment in such a case, rest is the most important, but rest and all the drugs in the pharmacopœia will not definitely cure. Surgery offers the only positive treatment. If undertaken early, before extensive myocardial degenerations have taken place, a 100% cure should be looked for; if delayed too long, these degenerations will remain, the patient's condition being improved somewhat by the operation, but never regaining normal. Hence my plea earlier in this paper, for early operations in toxic goitre and the earlier the better. And since by means of the basal metabolism test we have a sure means of proving whether a given case is toxic goitre or not, our opinions should be strengthened and confirmed when a positive result is obtained, and no hesitation should take place in urging an early operation. Until the profession takes this advanced

position, many a case will drift into hopeless invalidism and some to an early death. And in my opinion both forms of toxic goitre should be treated alike.

As for the non-toxic forms there is no such urgency. Some of you will recommend operation on account of disfigurement, some for pressure symptoms. As regards these latter death is not unknown from the continuous pressure on the trachea and atrophy of its cartilaginous rings, caused thereby.

As for the risks of operation, in the non-toxic cases they are almost nil; but in the toxic, you have to do a major operation on a patient seriously weakened in the most vital organ, the heart, and the victim of chronic poisoning. Here then the risk is grave, and operation is not to be lightly undertaken, without thoroughly investigating the patient's condition. And here again the basal metabolism test gives the best guide to go by in deciding when to operate. It is very pleasant to read the tests, from time to time, at intervals of three days, after the patient has been put to bed with an ice collar over the gland. Perhaps our first reading was plus 66, with a heart rate of 140, and then dropping to 60, 55, 45, 40, with perhaps the pulse down to 100 with the latter. One can safely operate when this stage is reached, that is if it is ever entirely safe in toxic cases which have been allowed to advance too far.

I do not intend to try your patience any further. The technique of the operation you all know and probably all I have told you to-night you know too. But it is well sometimes to be reminded of things and I trust my paper will have answered in that respect if in no other.

THE GOITRE PROBLEM—FROM THE PATIENT'S STANDPOINT

F. N. G. Starr, C.B.E., M.B., F.A.C.S.

Toronto

An old Greek proverb says: "You can pick your olives, but you cannot pick your company." We in this old world of modern medicine, while we may pick our treatment, we cannot pick our cases.

If an expectant mother has a goitre of any kind she must needs have the greatest care lest a simple adenoma, or a simple general enlargement, under the stress of pregnancy become hyperplastic, and thus not only ruin the health of the mother, but militate against the health of the child soon to be born. As in the domestic animal, so in the human being, the exophthalmic mother may give birth to an infant with hyperplastic goitre.

I am not sure, now that our salt is so purified that it contains no iodine, the milk so pasteurized as to lose some of its vitamine A, and the flour so white that much of its food value is lost, but that in the prenatal care mothers should have a course of iodine at varying intervals during pregnancy, whether they show any sign of goitre or not. A useful means of bringing this about would be to have them learn to eat seaweed. Dulse can now be procured in many of the shops of inland towns, and when the taste is cultivated people may learn to eat it as a vegetable, raw or cooked. It seems to me that the great problem of the family physician is to maintain the fat-thyroid-iodine balance, and the day may come when goitre, even in childhood, will be unknown

There are but few cases recorded of hyperplastic goitre in infants under five years of age. The probability is that few are recognized before the infant has passed to the Great Beyond. From five years of age to puberty there are more cases. In some goitre areas as many as fifty per cent. of the school children under twelve years have some form of goitre. Buford[1] reports a case of hyperthyroidism in a child of six years, for the cure of which it was necessary to resort to surgery. At least seventy-five per cent. of the goitre cases seen in early childhood or early adolescence can be cured before the age of twenty by proper hygienic surroundings and by the judicious administration of the iodides; while if neglected and advised to leave them alone to be "grown out of"—whatever that may mean—fully seventy-five per cent. of them will cause