A British Medical Association Lecture ON SOME PROBLEMS OF THYROID DISEASE.

DELIVERED BEFORE THE ULSTER BRANCH ON APRIL 30TH
BY

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THE problems to which I desire to direct attention relate (1) to certain causes of thyroid disorder; (2) to the influence of iodine in preventing either thyroid hyperplasia or undue accumulation of colloid material in the gland; and (3) to the types of simple goitre with which we have to deal when employing iodine as a prophylactic agent.

CAUSES OF THYROID DISORDER.

An essential function of the thyroid gland is the manufacture, and supply to the body tissues, of a secretion containing certain active principles or hormones. This endocrine activity is generally believed to constitute the gland's sole function; but it may be doubted whether it has not some other part to play in the metabolic cycle, and whether the administration of the whole gland substance, or of its extracts, provides a complete substitute for the gland itself. Thyroxin, which contains 65 per cent. of iodine, is regarded as the chief, if not the only, active principle of the gland; but it has not yet been definitely proven that thyroxin is produced as such *in vivo*. Nevertheless, most, if not all, of the thyroid gland's activities are exhibited by this substance. Assuming that thyroxin is the gland's active principle, it may be said that the essential function of the thyroid gland is to produce thyroxin, to maintain a definite concentration of it in the tissues, and by its means to ensure a higher rate of metabolism than would exist in its absence. But it can hardly be doubted that the gland has more to do than to control combustive processes. Its anabolic activities and its regulation of the growth and repair of the body tissues are no less important. The thyroid gland is essential to the normal metabolism of iodine, a matter about which very little is known at present. It provides some substance which controls the distribution of iodine within the body and maintains a normal concentration of iodine in the blood. In the absence of the thyroid iodine accumulates in the blood, while the administration of thyroid substance restores the amount of iodine in the blood to normal limits (Hudson). On the other hand, iodine is essential to the functional activity of the thyroid gland. But it does not appear that it is essential to the functional activity of thyroxin, at least in so far as mammalian metabolism is concerned. The effects which thyroxin exercises on metabolism are, according to Kendall, independent of the iodine it contains:

"The function of iodine within the molecule is to increase the reactivity and sensitiveness of the functioning groups present, viz., carboxyl and imino; any other function of iodine is highly problematical."

There is reason to believe that besides thyroxin the thyroid produces other physiologically active substances. Thus, Kendall has extracted one which has no effect on the metabolic rate, although it contains about one-half of the total iodine in the thyroid proteins; it is mainly concerned with the nutrition of the skin and its appendages. Besides these there may be others exercising specific effects on certain organs and tissues; so that the composition of the thyroid gland's secretion is a very complex problem, and one which is far from being definitely settled. It is for this reason, and because the precise part played by the thyroid gland in the metabolic cycle is still so little understood, that the difficulties in the way of elucidating the causes of its disorders are so great. But it would seem to be fairly obvious that such disorders may be brought about by factors which interfere with the normal

elaboration of the gland's secretion or with the normal utilization of its products.

The efficient operation of the thyroid gland is dependent not only on the adequate provision of the raw materials from which its hormone-containing secretion is elaborated, but on a balanced adjustment of ions in its fluids and membranes. The composition of the food is a matter of the greatest importance to the organ, since it is from the food that it derives not only the iodine and other essential constituents of its secretion, but those mineral elements on which the balanced adjustment of ions in its fluid and membranes, and in the cell and tissue plasma of the body generally, depends. It is not enough that the composition of the food should be normal; conditions in the alimentary tract must be such as admit of the adequate absorption of all those elements and complexes which are necessary to the thyroid gland's normal operation. It is, therefore, at the threshold of absorption in the intestine that we must first seek for sources of the thyroid gland's disorder.

The second great source of interference with the thyroid gland's normal operations is disturbance at the threshold of utilization of its products in the tissues. Evidence is beginning to accumulate which suggests that the action of these products may vary at different age periods, in different individuals, and be profoundly influenced by the concentration of certain ions in the cell and tissue plasma. We are accustomed to think of thyroid disease in terms only of "hypo-" or of "hyper-" or of "dys-thyroidism"; but it seems not unlikely that the chemical constitution of the cell and tissue plasma has an importance no less than the paucity or excess or imperfect synthesis of the gland's secretion. Recently Professor Klose of Danzig placed at my disposal two photomicrographs of the thyroid gland from two subjects of "puberty goitre": the one from a case of "unmistakable myxoedema," the other from a case of "unmistakable Graves's disease"; yet both presented histological appearances typical of "primary Graves's disease." It is always dangerous to reason from structure to function, but judged by the histological features of these two specimens both appeared to be glands in active secretion, yet the one was from a case of "hypothyroidism," the other from a case of "hyperthyroidism." Might it not be that the diversity of symptoms in these two cases had its origin in some part outside the gland, and that it was due to biochemical differences in the cell and tissue plasma in these two subjects of puberty goitre? I do not say that this was so; I merely suggest that this point of view is worthy of investigation in regard, not only to puberty goitres, but to other disorders of the thyroid gland. In this connexion one is reminded that severe crises in the course of Graves's disease are sometimes associated with acidosis, and that relief may be afforded the sufferer by measures directed to the relief of the acidosis.

In regard, then, to the causes of thyroid disorder there are these two thresholds to be considered: the threshold of absorption in the intestine, and the threshold of utilization in the tissues. The medium of communication between them is the tissue plasma. Let us now consider very briefly what factors are known to interfere with the normal operation of the thyroid gland at these two thresholds, and to what extent iodine may be expected to counteract their harmful influence.

Disturbances at the Threshold of Absorption.

1. The gland may become deranged because of the inadequate ingestion of iodine or of tryptophane. Interest at the present time chiefly centres round the former. There may be a deficiency of iodine in soil or in the water supply or in the food. Sophisticated foods, such as white flour, contain little or no iodine; while most cereals and vegetables grown on soil fertilized by artificial manures which are not of marine origin are deficient in this element. Goitre is believed to be due to this deficiency of iodine, whether it be common to all the inhabitants of certain localities or peculiar to some individuals no matter what their place of residence may be. To my mind its etiology is not always so simple as this. Nevertheless, the additional provision of iodine may in such circumstances prevent the occurrence of goitre both in man and in domestic animals. It does not, however, always appear to do so. Thus in parts of New

Zealand, where deficiency of iodine has been definitely traced to the soil and water supplies, and to the food grown on this soil, it has been found by Hercus and Baker that in one locality (Timaru) the prophylactic use of iodine for a period of six months was without effect in preventing the appearance of thyroid swellings in previously non-goitrous school children. In another locality (Christchurch) its use for a period of one year reduced the incidence of first attacks of goitre in children from 55 per cent. in those who did not receive iodine to 39 per cent. in those who did. The point of interest and importance in these observations is that 39 per cent. of previously non-goitrous children developed thyroid swellings, despite the prophylactic use of iodine for a period as long as one year. It follows, therefore, either that iodine want was not the cause of the thyroid swellings in these children, or that there was a failure of absorption of iodine at the intestinal threshold, or an imperfect utilization of iodine by the thyroid gland or elsewhere in the body.

2. Another potent source of goitre is the confinement of animals in unhygienic surroundings which involve the ingestion with their food and drink of substances derived from their own alvine discharges. There is, indeed, no more potent source of hyperplastic goitre than this. Fish confined in dirty tanks, animals confined in dirty cages, goats tethered on the same plot of ground for many months, and man living on ground contaminated by his own excreta and that of his domestic animals, are all subject to goitre. In all these instances the goitres are more prone to arise if the food be on the borderland of insufficiency so far as iodine is concerned; at least we assume it to be so, since in all, or almost all, the goitre is preventable by the additional provision of iodine. The point of importance is this: that an amount of iodine which may suffice to keep the thyroid gland in health when the animals are living under hygienic conditions of life may not suffice to prevent goitre when they are living under unhygienic conditions of life. In the latter circumstances the iodine ingested is relatively insufficient for the needs of the thyroid gland or of the body generally. Looking at the problem purely from the point of view of iodine want, it would seem that the presence of certain bacterial agents or their products in abnormal situations in the gastro-intestinal tract may interfere with the adequate absorption of iodine. McClendon has found that bacteria are capable of removing iodine from organic media containing it. It may be, therefore, that the continual ingestion of such bacteria, as in polluted water, may cause a part of the iodine in the food to be lost by way of the faeces.

But the problem does not end with iodine intake nor with iodine absorption, for Gaylord has shown, in the case of fish confined in dirty tanks, that the goitre from which they suffer can be prevented as well by the addition of arsenic or of mercury perchloride to the water as by the addition of iodine; while I myself have shown that goitre is preventable in like circumstances by scrupulous cleanliness. It would seem that the biochemical products of certain intestinal bacteria may be absorbed into the system and cause such changes in the biochemistry of the blood and tissue plasma as to make the thyroid glands hypertrophy and hyperplasia imperative; or they may cause atrophic and degenerative changes in the gland. They may, in short, cause impairment of the gland's capacity as a machine or disturbances at the threshold of utilization of its products. Many, indeed, are the possible ways—in the intestine, in the gland itself, and in the tissue plasma—in which intestinal bacteria or their products may cause derangement of the thyroid gland besides their probable interference with iodine absorption and assimilation. But in whatever way they act it is clear that the additional provision of iodine in the food is a potent means of counteracting their action.

3. There is a third means whereby disturbances at the threshold of absorption may cause goitre—namely, by want of balance of the food in certain directions. Thus, the excessive ingestion of proteins, or of certain fats, or of both, may cause hyperplastic goitres in animals, and presumably also in man. But here again goitre is much more likely to arise if the animals be of a certain age and if

living under unhygienic conditions, or if the diet be such as favours constipation and intestinal putrefaction. In circumstances of protein or of fat excess in the food thyroid hyperplasia is preventable by the additional provision of iodine. There is, however, one exception to this rule: opossums kept in captivity and fed on a protein-rich diet develop thyroid hyperplasia whether or not additional iodine be supplied with their food (Bensley); so that metabolic differences in different species, and possibly also in different individuals, are not without their influence in determining what effect iodine shall have. It may be mentioned that cod-liver oil will prevent thyroid hyperplasia in animals no matter how unhygienic their conditions of life may be. Cod-liver oil not only provides iodine in suitable form, but vitamins in abundance, while it favours the absorption of calcium and phosphorus, both of which have a part to play in ensuring the normal operation of the thyroid gland.

4. Again, the excessive ingestion of lime for prolonged periods may cause the appearance of "colloid goitres" of small size in some animals. This also is preventable by the additional provision of iodine.

It may therefore be stated as a general rule, to which, however, there are exceptions, that goitres arising in consequence of abnormal conditions at the threshold of absorption are preventable by the additional provision of iodine, provided the iodine be adequately absorbed; but this adequate absorption is dependent on a healthy state of the gastro-intestinal tract; and this, in its turn, on the provision of a well balanced food.

Disturbances at the Threshold of Utilization.

Turning now to the threshold of utilization: Mention has already been made of the possible influence which the concentration of certain ions in the cell and tissue plasma may have on the action of the thyroid gland's products. There are certain other facts to which reference may now be made. If the thyroid gland be removed in lambs or kids aged 2 to 3 weeks, nothing much happens for eighteen days; thereafter growth ceases (Simpson). And since the phenomena of growth are essentially those of organic synthesis, it may be said that in animals of this age the withdrawal of the thyroid gland's influence impairs organic synthesis and causes the accumulation in the body of the products of an abnormal metabolism. If, however, the animals be 3 or 4 months old growth is but little affected; the withdrawal of the gland's influence is then evidenced chiefly in failure of nutrition of the skin and in loss of intelligence. In these also abnormal metabolites accumulate in the body. The gland's function thus appears to vary with the age of the animal. The effects of thyroidectomy certainly vary with age, with species, with the nature of the food, with the state of nutrition, with external temperature, and other metabolic factors, as Horsley demonstrated in 1885.

Now if instead of removing the whole gland the major part of it be removed in guinea-pigs—an amount sufficient to initiate compensatory hypertrophy in the remainder—then it is found that again nothing much happens for fifteen to eighteen days. Thereafter hypertrophy and hyperplasia occur in the remnant; and this goes on until the deficiency caused by the thyroidectomy is made good, when the regenerated organ settles down to the normal routine of the gland's cycle of activity: storing colloid, resorbing colloid, and secreting moderately and inconspicuously. It is to be noted that the thyroid hyperplasia occurs only after the lapse of a latent period of about eighteen days—that is to say, just at that time when the normal growth and repair of the body tissues are beginning to be imperilled. During this latent period such changes have taken place in the biochemistry of the tissue cells and plasma as to make hypertrophy and hyperplasia of the remnant of thyroid tissue imperative. In this remnant a "goitre" has been produced, inasmuch as it has been called upon to increase its size. The process by which this increase in size has been brought about is, so far as we know, essentially the same as that occurring in the whole gland when parenchymatous goitre is produced. This is an example of how thyroid hypertrophy and hyperplasia may be caused by disturbances at the tissue threshold

—namely, by the presence in the cell and tissue plasma of abnormal metabolites. Similar effects may be produced in the whole gland when similar biochemical changes are brought about at the tissue threshold by other means; as, for instance, by the injection into normal animals of the biochemical products of bacteria, or by the excessive ingestion of these products, or by the absorption of the proteoses produced in the raw surfaces caused by burns, or by the absorption of other abnormal metabolites, as from toxic foci.

INFLUENCE OF IODINE IN PREVENTING THYROID HYPERPLASIA.

As to the effects of iodine in preventing thyroid hyperplasias such as these, it is generally believed that thyroid hyperplasia is due to iodine want. But in the experiment on guinea-pigs above mentioned hyperplasia occurs in the remnant of thyroid tissue although it has at its disposal all the iodine derived from the food, which sufficed to keep the whole gland in health. It cannot be said, therefore, to undergo hyperplasia because of want of iodine. Further, the additional provision of iodine will not prevent the hyperplasia in these animals; indeed, if anything it tends to increase it (Loeb). It may, however, be modified, but not wholly prevented, by the administration of the preformed active principles of the thyroid gland; while Loeb observed the remarkable fact that it is wholly prevented by the administration of the anterior lobe of the pituitary body. We see, therefore, that the metabolic need which determines the compensatory hypertrophy and hyperplasia is in this case so imperative that no amount of iodine can prevent the thyroid enlargement, and that it is one which concerns other endocrine structures as well as the thyroid gland. Similarly, in dogs iodine will prevent compensatory hypertrophy in the remainder of the gland provided not more than five-sixths of it be removed. But if less than one-sixth to one-ninth be left behind no amount of iodine will prevent compensatory hypertrophy in the fragment that remains (Marine). It would seem, then, that thyroid hyperplasias which result from disturbances at the tissue threshold are not always amenable to control by iodine. In this respect they are in marked contrast to those resulting from disturbances at the threshold of absorption. They are not due to iodine want, nor to a drop in the gland's store of iodine below a certain level; but this drop occurs as a result of the hyperplasia, and the hyperplasia itself is the result of biochemical changes in the cell and tissue plasma.

Etiologically speaking, we have, then, to deal with two types of thyroid hyperplasia: the one, resulting from disturbances at the threshold of absorption, which is usually preventable by the additional provision of iodine in the food; the other, resulting from disturbances at the threshold of utilization, which is usually not preventable by the additional provision of iodine in the food.

So much, then, for what iodine will and will not do in preventing thyroid hyperplasias. I have presented both sides of the picture, since if iodine be used indiscriminately the same fate may overtake it as befell it more than fifty years ago; it may fall into undeserved disrepute unless its limitations be realized. So far as my own investigations permit me to form an opinion, I have come to regard iodine as a substance which initiates and maintains the normal cycle of the thyroid gland's activities—it is, so to say, the oil of the thyroid engine—but I do not regard the efficient working of the thyroid mechanism as a matter solely of lubrication, important though this be.

TYPES OF SIMPLE OR NON-TOXIC GOITRE.

I have observed three types of goitre to arise under experimental conditions in animals: the first, in which there is a balanced exaggeration of all the normal features of the gland's cycle of functional activity—that is, of both active secretion and colloid storage; the second, in which active secretion occurs to the almost complete exclusion of colloid storage; the third, in which colloid storage occurs to the almost complete exclusion of active secretion. The first may be described as hypertrophic goitre; the second as

hyperplastic, parenchymatous, or adeno-parenchymatous goitre; the third as diffuse colloid goitre. In animals under experimental conditions the first or purely hypertrophic type is an early stage of the second or adeno-parenchymatous type. It has been observed to arise particularly in young animals kept under insanitary conditions of life or fed on faecal material or on cultures of faecal bacteria. The second arises under similar conditions; its histological features being well marked in older animals and in congenital goitres experimentally produced by feeding the parent throughout pregnancy on cultures of faecal bacteria. It arises also in adult animals, especially if they be kept under insanitary conditions of life, whose food contains an excess of proteins or of certain fats or of both. The third arises in animals whose food contains an excess of lime. These three types of goitre have their counterpart in man:

(1) *Hypertrophic goitre* may be a purely physiological condition occurring in childhood, at puberty, during pregnancy or the menopause, and in the course of ovarian disorder; or it may be pathological, as when it represents the beginnings of adeno-parenchymatous goitre.

(2) *Adeno-parenchymatous goitre* is the true endemic goitre of such mountainous regions as the Alps and Himalayas; it may also occur sporadically.

(3) *Diffuse colloid goitre* may occur sporadically or endemically, the latter usually in lowland areas.

Adeno-parenchymatous Goitre.

The characteristics of this type of goitre are these: it has its favourite endemic haunts in the great mountain ranges of the world; it is associated with certain forms of cretinic degeneration—congenital goitre, cretinism, deaf-mutism, and idiocy; in the regions where it prevails as an endemic it is rarely or never associated with exophthalmic goitre; the incidence of the acquired disease is low in childhood, but increases gradually with advancing years (Fig. 1); it is

FIG. 1.—Age incidence of adeno-parenchymatous goitre in females: Gilgit, Himalaya.

essentially a hyperplastic goitre; it is of the diffuse, parenchymatous, but often unsymmetrical, type in young subjects; of the adeno-parenchymatous type in older subjects (in the latter the enlarged organ almost invariably contains one or more adenomata); it usually leads to some degree of hypothyroidism in the adult—the cretinic degenerations with which it is associated are the outcome of this thyroid deficiency in the mother; it may be associated, as in Himalayan India, with symptoms referable to other endocrine glands, particularly the parathyroids (endemic tetany and tetanic cretinism are examples); the greater the degree of endemicity the more does the sex incidence approach the ratio 1 to 1, the lesser the degree of endemicity the more does the incidence of the disease in females exceed that in males; newcomers to an endemic area may acquire the disease in as short a period as fifteen days to six weeks, although the "incubation period" is usually longer.

These are the criteria on which the endemicity of this form of goitre is to be based. In Himalayan India, and in other localities where I have had an opportunity to study this malady, it is associated in its origin with insanitary conditions of life, particularly with contaminated water supplies; and is the same disease which occurs under experimental, and like, conditions in animals. It may be that the bacterial agents which are the cause of the disease are favoured in their operation by a deficient intake of iodine in the food and water. This I do not know from actual analysis of the food and water in those regions where I have observed the disease; but judged from the effect of an additional supply of iodine in preventing the hyperplastic goitres which arise in animals under like conditions of insanitation, it seems almost certain that the iodine intake with the food is deficient relatively to the unhygienic conditions of life under which the malady develops in man. It is curable in its early stages by the oral administration of such drugs as thymol. It is preventable by the provision of pure and protected water supplies without increasing the iodine intake with the food. It is to be remembered that the administration of iodine to adults who are the subjects of adeno-parenchymatous goitre is likely to cause hyperthyroidism; this harmful effect of iodine appears, however, to vary in different localities.

Diffuse Colloid Goitre.

This malady may occur sporadically or endemically. It differs in its distribution from the "endemic goitre" of mountainous regions. In this connexion the following passage from De Quervain's writings may be quoted:

"The histological structure of goitre varies according to locality. In certain countries, especially in level regions, the diffuse colloid goitre, with or without hyperthyroidism, and exophthalmic goitre predominate. In more mountainous countries the toxic goitre is the exception, and the nearer one approaches the centre of the endemic area (as in the Alps and Himalayas) the less one meets with colloid goitre. It is replaced by the colloid-poor, diffuse parenchymatous goitre in childhood and by the adeno-parenchymatous nodular goitre with its degenerative forms in adults."

In general, then, colloid goitre would seem to be most often found in lowland localities. It appears to be the common variety of goitre in America, and possibly also in the British Isles, but in the latter no attempt has been made, so far as I am aware, to separate it from the adeno-parenchymatous type, or to determine the distribution of either. It is commonly associated in the same locality with exophthalmic goitre. It does not appear to be associated with, or to be a cause of, cretinic degenerations; at all events true endemic cretinism is said to be unknown in America (Gordon). The nearest approach to the experimental production of a similar condition in animals has been arrived at by feeding them on food containing an excess of lime. In these circumstances colloid storage occurs to the almost complete exclusion of active secretion: but the enlargements so produced were small, and the amount of lime used to produce them was large. I am not prepared to state that colloid goitre in man is due to such excess of lime in the food or to do more than say that my experimental production of colloid goitre in animals by this means affords some indication of the factors which may be concerned in its causation in man. Colloid goitre in animals is preventable by the additional provision of iodine in the food; it appears also to be preventable by this means in man.

Both adeno-parenchymatous and colloid goitre may occur in the same locality. The only attempt to separate them with which I am familiar is that of Levin in a certain region of the Great Lakes of North America, where he found 1,146 cases of goitre in a community of 1,783 persons. His work has brought to light several very interesting facts in regard to the course and behaviour of these two types of goitre. In one of his charts (reproduced in Fig. 2) he separated the adeno-parenchymatous goitres from the diffuse, non-adenomatous goitres. The latter include the diffuse hypertrophies of childhood and

diffuse colloid goitres. It will be observed that the age incidence curve of the adeno-parenchymatous goitre is practically identical with the age incidence curve of the disease as it occurs endemically in Himalayan India (Figs. 1 and 2); in both localities the malady is due to causes the effects of which become more and more manifest as age advances. The other group, which includes the thyroid swellings of childhood and the diffuse colloid goitres, is seen to have its highest incidence in early life, tending to disappear after full maturity has been attained. This tendency is more marked, and sets in earlier, in males than in females. Colloid goitre is thus in marked contrast to adeno-parenchymatous goitre: it would appear to be due to causes whose effects become less and less evident as age advances; adeno-parenchymatous goitre to causes whose effects become more and more evident as age advances. If the former be due solely to iodine want then it would seem that the effects of this want become less conspicuous after full maturity has been attained. If the latter be due solely to iodine want then it would seem that the effects of this want become more conspicuous after full maturity has been attained. There must, therefore, be more in the problem of the causation of these two types of goitre than iodine want.

FIG. 2.—Age incidence of (broken line) adeno-parenchymatous goitre, and (continuous line) diffuse colloid goitre, including childhood goitres, in females: Great Lake Area, U.S.A. (After Levin.)

Again, if this be the cause of both types, then we have the remarkable fact of iodine deficiency producing two diametrically opposite effects in the thyroid gland: (a) hyperplasia to the almost complete exclusion of colloid storage, and (b) colloid storage to the almost complete exclusion, or greatly in excess, of hyperplasia. Yet, paradoxical as it may seem, this can actually occur. Thus, if in adult animals the iodine deficiency be relative to an excess of fats in the food, or to certain conditions of bacterial infection of the intestinal tract, goitres may result in which hyperplasia occurs to the exclusion of colloid storage. If, however, the iodine deficiency be relative to an excess of lime in the food, then colloid storage may occur to the exclusion of hyperplasia. In both cases the administration of iodine restores the normal cycle of the thyroid gland's activities, and for practical purposes both may be said to be due to relative deficiency of iodine. But it is the factors which give rise to the relative deficiency of iodine, rather than the iodine deficiency itself, that are of importance in determining the histological character of the goitre; and, as would seem from the course in man of the two types of goitre with which we are dealing, it is these factors also which determine the persistence of the goitre in the individual. Important, then, as iodine is in preventing either type of goitre, it is to be remembered that, in the causation of both, other factors are concerned which impart to each its own particular characters.

Childhood Goitre.

It was my intention, had time permitted, to refer in some detail to childhood goitre, since many of the observations hitherto recorded in regard to goitre prevention by iodine relate to the thyroid swellings of childhood. I must, however, content myself with the mention of a few points. Many of these swellings in children are physiological hypertrophies often normal to the individual, and have no title to be classed as "goitre"—a term which signifies thyroid disease. The great majority of them—as many as 98 per cent. (Olin)—are slight, some so slight that but a fleeting glimpse of the gland's outlines are caught as the child swallows. If all these be classed as goitre a wholly erroneous idea of the prevalence of thyroid disease may be gained. Further, estimates as to the prevalence of goitre may vary within wide limits according to what the observer may regard as a goitre. Thus, in a school where goitre was endemic, I have known the malady suddenly to assume epidemic proportions with the advent of one school medical officer, and the epidemic to disappear as suddenly with the advent of another.

A small minority of thyroid swellings in children are true goitres; in Himalayan India these goitres are conspicuous, often unilateral and right-sided, but sometimes regular and bilateral enlargements of the gland, which not infrequently are associated with engorgement of the veins of the neck; they may persist through puberty into adult life and begin to show adenomatous nodules in their substance as early as the twelfth year. They are as obviously true "goitres" as similar swellings in older subjects. "Childhood goitres" attain to their highest incidence in boys at the age of 9 and in girls at the age of 10 in Himalayan India; but the peaks of highest incidence appear to differ in different localities and appear also to be related to the prevailing type of goitre. Thus, where colloid goitre is the prevalent type, childhood goitre is said to be at its highest incidence in boys about the age of 8 to 10, and in girls about the age of 12. The incidence of thyroid enlargement in children below the age of puberty is not of itself a true index of the endemicity of goitre; its incidence may be low and yet the endemicity of adeno-parenchymatous goitre be high, or the incidence of childhood goitre may be high and yet goitre may not be a conspicuous feature in the adult population.

The incidence of childhood goitre is only of value as evidence of prevailing thyroid disease when considered in relation to the other criteria of endemicity and to the prevalence of goitre in the adult population. A marked characteristic of the thyroid swellings of childhood is their tendency to spontaneous disappearance. This tendency varies in different localities, and is probably related to the prevailing type of goitre; in endemic foci in Himalayan India I have found 11 per cent. of these swellings to disappear spontaneously in boys and 9 per cent. in girls; Nicholson has placed the figure as high as 50 per cent. in a certain endemic area in the Himalayan foot-hills; while Bircher reports that although 70 to 100 per cent. of children may be the subjects of swollen thyroids in certain parts of Switzerland, not more than 3 to 9 per cent. of young men are rejected because of goitre when they present themselves for military service. It is necessary to bear these facts in mind, not only when inaugurating iodine prophylaxis in any locality, but when attempting to form an estimate of its value.

CONCLUSION.

I have endeavoured to indicate the broad lines on which we must, in my opinion, view diseases of the thyroid gland. It is, I believe, rare that any metabolic disorder such as goitre is due to a single cause. There is, as a rule, a multiplicity of factors involved. The thyroid gland cannot be considered apart from the rest of the body, nor iodine apart from other food constituents. The time has come when we must search more closely for causes of the thyroid gland's disorders in disturbances at the threshold of absorption in the intestine, in disturbances at the threshold of utilization in the tissues, and in disturbances in the cell and tissue plasma of the gland itself.

An Address ON DUODENAL AND GASTRIC ULCERATION:

SOME PERSONAL EXPERIENCES.*

BY

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(With Special Plate.)

I HAVE chosen this subject for two reasons. In the first place, whether we be general practitioners, physicians, or surgeons, its problems are constantly coming before us, and have to be dealt with. No one can believe that the methods of treatment are so standardized that the right and only thing to be done in each instance is settled, and we have all lived long enough to know that what we have done has not invariably turned out to be the best. Men of large experience have written and spoken extensively on this subject, and I make no pretence of saying the final word on this occasion; but we each in our different capacities have to accept responsibility towards those patients who come to us for advice. In the second place, I have for some years tried, in conjunction with my colleagues, to attain the maximum degree of accuracy in diagnosis of gastric and duodenal ulcers by means of x-ray examination. The skiagrams are typical of the results that are to be expected whenever a patient is well enough to have the examination made.

I shall not attempt to cover all the ground. This short address must perforce be discursive. In any surgeon's experience sometimes questions of diagnosis appear to him to be of rather more than ordinary interest; the result of x-ray examination often surprises him; and always he has to adapt his surgical procedures to the material which confronts him. It is around these aspects of the question that I propose to speak.

Before saying anything more I want to acknowledge my personal debt to Sir Berkeley Moynihan (whose work has always been open to visiting surgeons, and whose friendly help has been given to many of us), to Mr. Sherren, and to Mr. William Mayo. To some extent we evolve our individual methods in the course of dealing with our own patients, but certain trails have already been blazed for us, which lessen our anxieties and save our patients from some dangers. To these pioneers our debt is deep.

In dealing with gastric and duodenal ulcers, as with osteo-arthritis, exophthalmic goitre, tuberculosis, and many other diseases, the aim of our profession is to prevent their occurrence, and one by one we may hope to see them disappear; but in the meantime we find our patients seriously ill, being already in a condition which hampers their activities, gives them pain, and puts their lives in danger. Usually they have not consulted a surgeon until their disease has become well established, but many of them have come to you earlier, and some of them reach the surgeon without having had sufficient guidance. Therefore etiology should always be present in our minds. The hygiene of the mouth, arrangement of diet, treatment with drugs, limitation of smoking, and proper rest, may cure in the early stages, and will relieve in all. No surgical operation should be undertaken until all these points have been attended to; for by these means operation may sometimes be rendered unnecessary, and operation will fail to achieve its object if the cause of the condition is not removed.

At what stage, then, are we to say, "This patient should be subjected to operation?" For myself, that time is when the patient, in spite of efficient medical treatment, suffers

* Given at Felixstowe to the Suffolk Branch of the British Medical Association, October 31st, 1924