A Paper ON FOOD AND GOITRE*

SIR ROBERT McCARRISON, C.I.E., M.D., D.Sc.,
LL.D., F.R.C.P.

HONORARY PHYSICIAN TO THE KING; COLONEL, INDIAN MEDICAL SERVICE;
DIRECTOR, NUTRITION RESEARCH LABORATORIES, PASTEUR
INSTITUTE, COONOR, S. INDIA

In some circumstances the thyroid gland is among the most, in others it is among the least, variable of all organs with respect to its weight and proportionate size in the body. There is no stable biometric constant of variability associated with thyroid glands under all conditions. It is not an organ whose size is unalterably fixed, but one designed to adapt itself to environmental conditions. Some latitude must therefore be allowed it, some arc through which the pendulum of its normal activities may swing without the charge of abnormality. These activities involve variations both in size of the gland and in its histological appearance, the latter varying with the phases of its activity. At one extreme its vesicles are filled with colloid; at the other its store of colloid is dispersed and active secretion predominates. It is essential to be aware of these extremes of histological variation, lest normal appearances be described as pathological.

Similarly, it is necessary to recognize that the gland has a normal range of size. Recent biometric studies have defined the limits of this range (McCarrison and Madhava, 1932).¹ It is demarcated by the formula: $M \pm 2.5$ times the standard deviation from M , where M is the mean size of the gland in a normal universe of animals or men, or in any section of that universe. Glands not exceeding the value given by the formula $M + 2.5\sigma$ are not abnormally large, however else they may be altered histologically. Supposing we take a sufficiently large number of thyroid glands from individuals comprised within a normal universe, estimate their weights or proportionate size in the body, and construct a frequency distribution diagram of these weights or sizes, then we find that this diagram can be fitted by a normal probability curve. But it is different when the universe is one in which goitre prevails; then the frequency distribution diagram exhibits positive "skewness" in proportion to the prevalence of thyroid enlargement.

The factors influencing the size of the thyroid gland are multiple and their interactions manifold. They include hereditary influences, individual idiosyncrasy, age, sex, sexual activity, psychic factors, season, locality, altitude, distance from the sea coast, sanitary condition, and diet. Of these diet is the most important. There are two aspects of the relation between food and the thyroid gland: the influence of the gland on the metabolism of food and the influence of food on the gland. The latter is my main theme, but brief mention may be made of certain known facts relating to the influence of the thyroid on the metabolism of the proximate principles of food—proteins, carbohydrates, fats, mineral salts, and water—since these have a practical interest for the physician.

INFLUENCE OF THE THYROID GLAND ON THE METABOLISM OF FOOD

The relation of the thyroid to the metabolism of nitrogen is exemplified by the increased urinary excretion of nitrogen as urea, which occurs in Graves's disease and experimental hyperthyroidism. This loss of nitrogen can, to some extent, be prevented by the increased ingestion

of fats and sugars. As is well known, a meat diet is harmful in Graves's disease and other states of hyperthyroidism, but the casein of milk is definitely beneficial. Rats fed on a milk diet are resistant to hyperthyroidization: excessive increase in metabolism and the nervous symptoms, occasioned by thyroid administration to these animals, are markedly lessened (Abelin).

The mobilization of hepatic glycogen, consequent on hyperthyroidization, is evidence of the gland's relation to carbohydrate metabolism. Here also this mobilization can be prevented by the increased ingestion of animal fat, such as beef fat or cod-liver oil, although it is not prevented by the increased ingestion of carbohydrate; it can also be prevented by the increased consumption of casein (Abelin). Another evidence of this relation is afforded by the increased consumption of glucose by the perfused heart (cat) under the influence of hyperthyroidization.

One of the most important of the thyroid gland's metabolic relationships is that to the katabolism of fats. This is illustrated in the well-known effect of thyroid administration on obesity. There seems to be little doubt that an antagonism exists between thyroid activity and the metabolism of fats; an excess of thyroid hormone inhibits the anabolism of fats, and, inversely, the enrichment of the organism in fats diminishes the activity of the thyroid hormone. The favourable effect of fats in hyperthyroidism depends upon the phase of this condition; "so long as the cells have lost only in part the capability of using up the fat or of depositing the fat, just so long does the supply of fat act favourably" (Abelin). When the metabolism is already abnormally high the administration of fat is not beneficial and may be harmful (Abelin).

The gland's relation to mineral metabolism is also close, especially in regard to calcium and phosphorus. Witness the increased excretion of calcium consequent on hyperthyroidization, the negative calcium balance in Graves's disease when the diet is low in lime, and the effect of iodine administration in diminishing the excretion of calcium in this disease. The thyroid secretion appears to have a direct stimulating katabolic effect on the calcium deposits in the bones (Aub). The administration of inorganic phosphates intensifies the effect of thyroid medication, that of calcium diminishes thyroid action. Rats can consume much larger quantities of thyroid substances without an excessive increase in metabolism if they be given calcium at the same time; other symptoms of hyperthyroidization—nervous hyperexcitability, perspiration, disturbance of respiration, etc.—are also minimized (Abelin).

The gland's relation to iodine metabolism is likewise close, though still not fully understood. It controls the utilization of iodine in the body—an important function, since iodine, apart from the fact that it is an essential constituent of thyroxine, is an essential element in nutrition. The thyroid has also a concern with the metabolism of water; the diuresis produced in myxoedematous subjects by thyroid administration and the loss of water by the skin, bowels, and lungs in hyperthyroidism are examples of it. Thyroid administration diminishes the capacity of the tissues to retain water; thyroid deprivation augments it (Blanchard).

INFLUENCE OF FOOD ON THE THYROID GLAND

With the possible exception of the thymus and adrenal glands no organ of the body is more sensitive to food conditions than the thyroid gland. Under varying conditions of diet its moods are as variable as the sea, being stirred to heights of activity by some and lulled to placidity by others. Its sensitivity is greatest in early life, when the gland is growing rapidly. At this period its rate of growth outstrips that of the body as

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a whole. The gland attains to its acme of size, relative to that of the body, about puberty. It is then that it is in greatest need of all those elements and complexes which are necessary for its normal nutrition and for the normal exercise of its functions.

There are two main directions in which food may influence the gland: it may impose upon the organ a burden of work greater than it can bear without undergoing hypertrophy and subsequent strain fibrosis, or, because of the food's improper constitution, the physiological efficiency of the gland may become impaired. In these circumstances retrograde changes may occur and the thyroid be less able to withstand the attacks of toxic agents. This aspect of the genesis of goitre—the nutrition of the gland itself—is, I think, sometimes forgotten. Food and function, faulty food and faulty function, faulty function and disease—these are sequences applicable as much to the thyroid as to the body as a whole.

The first principle to which I would direct attention is this: the more perfect the constitution of the diet the more normal and the less variable is the size of the thyroid gland, and the less the scope for the operation of individual idiosyncrasy as a factor causing variation in the size of the thyroid. The more normal also is the frequency distribution of thyroid weights or sizes in any given universe of animals and the less likely is goitre to occur. A diet that fulfils these requirements is one composed of freshly ground whole-wheat flour, milk, butter, sprouted legumes, root vegetables, green leafy vegetables, and water, with fresh meat occasionally. Starting with a universe of hygienically caged rats, fed in this way and therefore goitre-free, the size of the thyroid gland and the incidence of goitre can be altered at will by varying the composition and quality of the diet. The following table shows ten groups of rats taken from the same goitre-free stock and fed in different ways; they are arranged in order of increasing size of the thyroid gland and of increasing incidence of goitre:

	Mean Thyroid Size, mg.*	Percentage of Incidence of True Goitre†
(1) Complete synthetic diet, containing iodine as potassium iodide	6.63	0
(2) Well-balanced vegetarian diet with whole milk	6.69	0
(3) Well-balanced vegetarian diet without milk	7.13	0
(4) Synthetic diet, as in (1), containing 40 to 80 per cent. of protein	8.05	0
(5) The perfectly constituted diet described above	8.18	0
(6) Cabbage, oatmeal, and wheat diet (60:20:20)	8.45	2
(7) As in (5), but with much less milk ...	9.76	2
(8) Cabbage, sorghum, and wheat diet (60:20:20)	10.38	7
(9) As in (1), but with soya bean as the sole source of vitamins	17.20	33.3
(10) As in (1), but with ground-nut as the sole source of vitamins	21.69	

* Weight per 100 grams of body weight.

† By true goitre is meant an increase in size of the gland over that yielded by the formula $M + 2.5\sigma$.

These results are instructive. They illustrate clearly: (a) that the size of the thyroid gland is profoundly influenced by the composition and quality of the diet; (b) that true goitre can arise despite the adequate ingestion of iodine as potassium iodide; and (c) that vitamin insufficiency has an important relation to goitre.

The next most important principle relates to the balance of the diet: excesses in one direction or deficiencies in another. Of the excesses the chief are excess of fats, of lime, of iodine, and of certain unidentified substances contained in some vegetable food-stuffs. An excess of animal protein (in the form of a fat-free meat residue) in an otherwise complete diet does

not cause thyroid enlargement. On the contrary, the gland tends to be smaller than normal, normal being taken as that of rats fed on the perfectly constituted diet. Deficiency of suitable protein is more likely to be associated with goitre than is its excess, especially if it be combined with vitamin deficiency.

An excess of fats is favourable to goitre production, but the thyroid enlargement so caused is preventable by the additional provision of iodine. Butter has different effects on the thyroid gland, depending on the composition and quality of the diet to which it is added. When added to diets deficient in fats and fat-soluble vitamins it makes good these deficiencies, and counteracts the tendency to increase in the size of the thyroid induced by such diets. But when it is added in excess to complete diets it has a definite goitrogenic action. There is, as I pointed out many years ago, a fat-iodine balance in nutrition, disturbance of which is reflected in the thyroid gland. This is well illustrated in tadpoles. When their diet is too rich in butter they fail to grow normally; so do their thyroids. When their diet is too rich in iodine they likewise fail to grow normally; so do their thyroids. But the addition to the diet of iodine in the one case and of butter in the other restores the fat-iodine balance, and growth both of the thyroid and of the body proceeds normally.

An excess of calcium has a definite goitrogenic action; this, too, is counteracted by the additional provision of iodine. On the other hand, an excess of iodine may also cause a 50 per cent. increase in the size of the thyroid gland (pigeons), and this can be counteracted by the additional provision of calcium. There is thus a calcium-iodine balance, the disturbance of which in either direction may affect the thyroid gland unfavourably.

There are certain unidentified substances contained in some vegetables whose action may be goitrogenic when ingested in excess. They are present in cabbage and other members of the Brassica family, as well as in some Cruciferae. Some rabbits when fed on an exclusive diet of cabbage develop goitre within a very short time; others do not, or the resultant goitres are small. Two factors are concerned in bringing about these different results: the varying content of the goitrogenic substance in the vegetable, which is certainly related to season and probably related to rainfall, and the varying susceptibility of the animals themselves. The goitres produced by the cabbage diet are of the work-hypertrophy or hyperplastic type, and, like all such types, are preventable by the additional provision of iodine. The administration of thyroxine also prevents them, so does the administration of manganese chloride or of thymol, but the latter is less constant in its action. Although the ingestion of additional iodine prevents these goitres, they are not due to deficiency of iodine in the vegetable. If iodine be administered to rabbits already suffering from "cabbage goitre," it may cause their death within a few days owing to the greatly enhanced metabolism it brings about (Webster). This is apparently due to the excessive production of thyroxine. It has been suggested (Marine) that the goitrogenic substance or substances in cabbage are such as depress cell oxidation, and are probably cyanides. Cyanogen, probably in the form of cyanogenetic glucoside, does occur in cabbage, but the amount of cyanide generated from it on enzyme hydrolysis is relatively small, far smaller than the amount needed to cause goitre in rabbits by the subcutaneous injection of methyl cyanide. The "cyanide goitres" produced in the latter way occur in only approximately 50 per cent. of these animals in Coonoor; the remaining 50 per cent. do not become goitrous, suggesting that to cause the goitre some other factor besides cyanide is

needed. Further, I have not found (in Coonoor) that the subcutaneous injection of methyl cyanide in sublethal doses for a period of thirty-five days will cause goitre in well-fed and hygienically housed albino rats. During the past year evidence has accumulated in my laboratory which appears to suggest that the goitrogenic potency of these vegetable foods may be in inverse relation to the amount of sulpho-cyanides—substances much less toxic than cyanides—which is generated, from their cyanogen, by enzyme action in the gastro-intestinal tract. In other words, the more sulpho-cyanide generated the less is the goitrogenic action of the vegetable; the more cyanide the greater the goitrogenic action. There is thus much evidence tending to connect cyanide with "cabbage goitre," but not enough to incriminate it as the essential or direct cause of this type. Nevertheless, it may possibly be ancillary to this cause.

There is another aspect of this matter. Among the ten diets scheduled above there are two into which soya bean or ground-nut entered. Both caused goitre, although the rats were ingesting large quantities of iodine in the form of potassium iodide, and both were deficient in vitamins A and C. The goitres exhibited on section the characteristics of vitamin A deficiency (epithelial keratinization, etc.) Soya bean and ground-nut are relatively rich in cyanogen, and both yield considerable quantities of cyanide on enzyme hydrolysis. The question therefore arises whether the vitamin deficiency favoured the action of the cyanide or whether the cyanide favoured the action of the vitamin deficiency. Recently, I have found that while well-fed rats receiving daily injections of methyl cyanide, subcutaneously in sublethal amounts, did not develop thyroid enlargement, those fed on vitamin-A-deficient diets did; but the enlargement did not amount to true goitre.

Cyanides are not the only substances that have come under suspicion in connexion with "cabbage goitre." It has been suggested (Stiner) that saponins—glucosides widely distributed throughout the vegetable kingdom—may be the goitrogenic factors. The suggestion has attractions, but so far as I am aware no experimental evidence has yet been advanced in support of it. Besides these positive goitrogenic substances present in certain foodstuffs there are others, also of an unknown nature, that are "anti-goitrogenic," and whose anti-goitrogenic action does not appear to depend on their iodine content. Among them are milk, oatmeal, green grass, sprouted legumes, alfalfa, carrots, etc. Here also is a new field for exploration, in which the hexuronic acids, vitamins, enzymes, and other substances, probably not yet identified, obtrude themselves.

Turning now to the effect of food deficiencies on the thyroid gland, there are three to which brief reference must be made: oxygen deficiency, vitamin deficiency, and iodine deficiency.

OXYGEN DEFICIENCY AND GOITRE

Certain states of anoxemia produced by the injection of hydrocyanic acid, by diminution of the partial tension of the oxygen of the air, or by bleeding, give rise to hyperfunction of the thyroid gland (Mansfield and Muller). Twenty years ago Blauel and Reich showed that if the trachea of the rat be carefully constricted by means of a silk ligature the vesicles of the thyroid become distended with colloid. This observation was subsequently confirmed by Breitrner and others. Some years ago I observed that rats fed on diets deficient in vitamin-A-bearing food materials developed adenoid-like growths in the upper part of the trachea; sometimes so extensive as to reduce the lumen of the air passage by more than one-half.² Associated with these growths

there was often much accumulation of colloid material in the vesicles of the gland, giving rise to their overdistension and frequent distortion. These observations are sufficient to indicate that anoxemia or restricted intake of air may cause goitrous changes in the thyroid gland.

VITAMIN DEFICIENCY AND GOITRE

The vitamins whose deficiency is known to affect the thyroid gland unfavourably are vitamin A, vitamin B, and vitamin C. There is some evidence that vitamin D may not be without effect, but up to the present I have not been able to satisfy myself that deficiency either of vitamin D or of sunlight has any noteworthy effect on the gland. Others have reported hyperplasia of the thyroid in rats which had been kept in the dark, an observation I have so far failed to confirm. Deficiency of vitamin A, or, more properly, deficiency of vitamin-A-bearing materials, in the diet is one of the main dietetic factors concerned in the production of thyroid weights which are increased relative to that of the body. A statistical explanation of this finding is the disparity in the adjustment of thyroid weight to body weight as a result of subsistence on such diets. In these circumstances true goitre is likely to arise, and it seems not unlikely that it is related to the infections which are so commonly associated with this deficiency. Like other epithelia throughout the body, that of the thyroid gland is likely to undergo degenerative change and functional impairment in consequence of deficiency of vitamin A. The characteristic change is one of epithelial keratinization. The epithelial degeneration may be associated with the aggregation of lymphocytes in the gland, and ultimate fibrosis may occur. A condition—to which the term "lymphadenoid goitre" has been applied—may thus be produced. The round-celled infiltration of the gland is not a constant feature, and when it does occur it seems to be due to the action of an additional factor, probably of microbic or toxic nature. Sometimes the enlarged glands are of the colloid type; sometimes they are hyperplastic, with areas of keratinization occurring here and there. The final picture appears to depend on other factors, dietetic and toxic, besides the actual vitamin deficiency itself. These changes and the goitres resulting from them can occur despite the adequate ingestion of iodine, as, for example, in Groups 9 and 10 of the above schedule. Further, the administration of iodine to rats fed on such vitamin-A-deficient diets may actually favour the occurrence of goitre.³ Iodine is a thyroid stimulant, and too much stimulation of a physiologically inefficient organ is bad practice.

Guinea-pigs fed on a scorbutic diet (consisting of crushed oats and autoclaved milk) not infrequently exhibit thyroid enlargement (in Coonoor, 6,000 feet above sea-level). The goitre is of the colloid type, and, weight for weight, there is a fourfold increase in its iodine content over that of the normal organ—another example of the occurrence of goitre in the midst of iodine plenty. "Scurvy goitre" is of great interest in view of the identity of vitamin C and hexuronic (or ascorbic) acid, for the biological activity of this acid is probably due to its double function of oxidation and reduction (Cox, et al., 1932).⁴ Associated with this type of goitre there are characteristic changes in the adrenal cortex (McCarrison, 1919). A combination of vitamin deficiencies is more potent in favouring the development of goitre than deficiency of a single vitamin.

Another matter of great interest may be referred to here. The pH of "scurvy goitre," in which colloid accumulates in the gland, is significantly reduced. The pH of "cabbage goitre," in which colloid is dispersed from the gland, is significantly increased. To what extent

is colloid storage or colloid dispersion related to variations in pH of the organ? Certain it is that its pH is related to diet, and that a perfectly constituted diet prevents both undue accumulation and undue dispersion of colloid.

IODINE DEFICIENCY AND GOITRE

Enough has, I think, been said to show that there is more in goitre production than iodine deficiency. No one who has closely studied the question will wish to deny the part played by iodine deficiency; but it is not the whole orchestra, as some would have us believe. Here I must enter a protest in regard to the laxity with which use is made of such phrases as "iodine-free diets," "removal of all iodine from the diet," etc. There is no such thing as an iodine-free diet, and the removal of all iodine from the diet is an achievement incompatible with the existence of the diet as a source of sustenance. It surprised me also to read, as I did the other day in

FIG. 1.—"r" curves of the thyroid gland in four groups of rats. One group was fed on a well-constituted (control) diet and distilled water; another on this (control) diet and a grossly polluted water; a third on a diet of cabbage, wheat, sorghum (C-W-S), and distilled water; and a fourth on this (C-W-S) diet and the same grossly polluted water. Note the high degree of protection afforded by the well-constituted diet against the goitrogenic action of the polluted water, and the summation of goitrogenic action of the C-W-S diet and the polluted water.

one of our leading medical journals, that "all types of experimental goitre are preventable by iodine"; this is not so.

Let us consider briefly what iodine deficiency does and what it does not do. There is no invariable association between the iodine content of drinking water, soil, or food and the endemic occurrence of goitre. In certain localities where there is an undoubted inverse relation between goitre incidence and soil iodine, this relation applies only to school children up to the age of 13 or 14 years; after that age the inverse relation does not apply. Further, the incidence of goitre in such localities is never nil, whatever the level of soil iodine may be. Side by side with localities in which this inverse relation exists there are others in which it does not: places where soil iodine is high and yet goitre prevails; places where it is low and yet goitre does not prevail or its incidence is low.

There is no incontrovertible evidence that iodine deficiency is, by itself, the cause of goitre. Both Hellwig (1931) and Jackson (1932) have failed to find that diets low in iodine do cause goitre under carefully con-

trolled experimental conditions in rats. I reached a like conclusion some years ago. Nevertheless, a low intake of iodine may, in certain conditions of diet and of hygiene, predispose to the occurrence of goitre, and may even be a determining cause of its endemicity.

Iodine is a stimulant of the thyroid gland, both of its growth and of its metabolism. The cultivation of thyroid tissue *in vitro* makes this abundantly clear, apart altogether from the fundamental observations of Leo Loeb and his associates. This being so, it is difficult to credit a view which attributes to want of iodine a direct stimulating, or hyperplasia-producing, action on the thyroid gland. On the other hand, in all conditions giving rise to an unusual demand on the part of the body for thyroid products the additional provision of iodine in physiological amounts makes it easier for the thyroid to supply them.

Iodine will prevent all goitres which are of the work-hypertrophy type; such, for instance, as those caused

FIG. 2.—To show the summation of the two goitrogenic agencies: faulty food and grossly polluted water: "r"-values of the thyroid gland as in Fig. 1; fitted with smooth curves. Glands above 15 mg. in size are goitrous. A=thyroids of rats fed on the well-constituted diet and distilled water. B=thyroids of rats fed on the ill-constituted (C-W-S) diet and distilled water. C=thyroids of rats fed on the ill-constituted (C-W-S) diet and the grossly polluted water. Note that the goitrogenic action of C-W-S diet is exercised mainly in rats of the lighter body weights (or earlier ages), while that of the polluted water is exercised at all ages.

by insanitary condition, or by the excessive ingestion of fats, or by the unidentified substances contained in certain vegetable foods. It will prevent the hyperplasia that follows injection of alkaline extracts of the anterior pituitary lobe. It will not prevent, and may even favour, the occurrence of goitres arising in consequence of malnutrition and physiological inefficiency of the gland. Its fourfold increase in the gland does not prevent the occurrence of "scurvy goitre." It will not prevent the compensatory hypertrophy which follows partial thyroidectomy in guinea-pigs (Leo Loeb, 1929) nor the colloid goitre which results from ligation of the pancreatic duct in dogs (Sweet and Ellis, 1915).

INTERACTION BETWEEN FAULTY FOOD AND INSANITARY CONDITION IN THE CAUSATION OF GOITRE

If rats be confined in roomy cages, admitting of free exercise and efficient ventilation, and fed on a perfectly constituted diet they rarely, or never, develop goitre when living under conditions of gross insanitation. But when fed on an ill-constituted diet, such as one composed of cabbage,

sorghum, and wheat, a high proportion of them become goitrous. The results of two recent experiments will suffice to illustrate these points.

Two groups of rats were fed on the latter diet during the summer months, when the goitrogenic potency of cabbage is *nil* in Coonoor. One group was caged under conditions of gross insanitation, the other under conditions of meticulous cleanliness. In the former the mean size of the thyroid gland was 15.74 mg. per 100 grams of body weight, in the latter it was 6.69 mg. The incidence of true goitre was 46.6 per cent. in the former group and *nil* in the latter. In the second experiment two groups of rats were caged under conditions of gross insanitation, one group being fed on a perfectly constituted diet, the other on the cabbage-sorghum-wheat diet referred to above. The mean size of the gland was 8.6 mg. in the former group and 16.7 mg. in the latter, the incidence of goitre being *nil* and 56.2 per cent. respectively.

The results of another experiment will serve to illustrate the way in which faulty food and polluted drinking water may combine to cause goitre.

During the winter months (in Coonoor) the goitrogenic potency of cabbage is at its highest. A diet composed of 60 parts of this vegetable with 20 parts of whole wheat and 20 parts of sorghum is then definitely goitrogenic. Two groups of rats were fed on this diet during the winter season. One was given distilled water to drink, the other

an extract in distilled water of rat excreta and decaying food taken from certain insanitary rat cages. The first group exhibited the effects of the diet alone, the mean size of the thyroid gland being 14.4 mg. and the incidence of goitre 38.9 per cent. The second group exhibited the effects both of the food and of the impure water, the mean size of the gland being 17.8 mg. and the incidence of goitre 88.9 per cent. These results are illustrated graphically in the accompanying figures (1 and 2).

CONCLUSION

The facts I have laid before you are sufficient to indicate the intimate association which exists between food and the thyroid gland and the complexities of this association—how the organ influences the metabolism of food and how in its turn it is influenced by food. But great as these complexities are, and difficult as it is to maintain a right judgement in all things relating to them, this truth stands pre-eminent—the more perfect the constitution of the diet the more normal is the thyroid gland, both as to its size and as to its action.

REFERENCES

- ¹ *Indian Medical Research Memoirs*, No. 23, 1932.
- ² *British Medical Journal*, 1931, i, 966.
- ³ *Ibid.*, 1930, i, 989.
- ⁴ *Nature*, 1932, p. 888.

IRRADIATION THERAPY IN THE TREATMENT OF MALIGNANT DISEASE*

BY

E. PEARCE GOULD, M.D., M.Ch., F.R.C.S.

SURGEON TO THE MIDDLESEX HOSPITAL,

It is now thirty-odd years since radium and α rays were first used in the treatment of malignant disease. It would appear that the war years mark a dividing line between the first and the later chapters in the history of this branch of therapeutics. Until the war the use of both agents was in the hands of a few pioneer enthusiasts, who, paying but scant attention to the comments of sceptical colleagues, succeeded in at last winning a general recognition of the fact that, in spite of many failures and disappointments, their successes were of a kind that could not be ignored. Radiation therapy had come to stay. Since the war the few have become the many, α -ray tubes have multiplied in number and potency, and radium is dealt with in grams rather than in milligrams. And yet we are still waiting for anything approaching general agreement throughout the profession as to the true place of radiation methods in the treatment of cancer. Some of us who are neither radium and α -ray enthusiasts nor brilliant cancer surgeons are a little tired of the partisan claims emanating from both sides, which in their narrow, immediate scope appear to lose sight of the larger problem.

The time has come when a serious attempt should be made to face the larger problem, and this joint discussion may prove of great moment if it succeeds in finding a working answer to the question: "What is the place of radiotherapy in the treatment of malignant disease?"

In passing it is worth noting that radiotherapist and surgeon have each had a share in postponing so long the day when this question may be answered. Radiotherapy came upon the scene at a time when the increasing safety of standardized major surgical procedures had given this line of attack a hopeful outlook, and encouraged surgeons to talk in terms of the "surgical cure of cancer." At

such a time the radiotherapist was naturally denied access to early cases of the disease, the only type of case in which the surgeon was taking any interest. On the other hand, the technique of, and dosage in, radiotherapy has changed and developed with a rapidity that has been in one sense its own enemy. No sooner were the results of a particular method followed up for a sufficient time to be of any value than they lost their significance because the method by which they had been obtained was already out of date.

SCOPE OF RADIATION

It has been wisely said that "no patient is to be considered as cured of cancer until he is safely dead of some other disease." We shall do well, I think, if in this discussion we avoid the word "cure" and speak in terms of either "palliative" treatment, or treatment affording "lasting freedom" from the disease. If the former needs a definition I would suggest that we use the word to imply a temporary alleviation of a local condition with an addition to the expected period of tolerable life. By the latter I would suggest a period of freedom from demonstrable disease materially in excess of the known average duration of the *untreated* disease.

I would submit, therefore, that our discussion should endeavour to afford answers to the following four questions:

1. In what groups of clearly definable cases of malignant disease does radiation offer the best chance of prolonged freedom from the disease?
2. In what groups of cases does the combination of radiation with surgery offer the best chance of lasting freedom?
3. In what other groups of cases have radiation methods a purely palliative but none the less valuable effect?
4. In what groups of cases have radiation methods proved so far of negative value?

Clearly, with the science and practice of radiotherapy still in its infancy, and making notable advances almost every year, any answers we are able to formulate to-day can have but a temporary value. I would like to suggest that, even if temporary, their value would, none the less, be great in many directions. First, because—from a scientific point of view of the least importance—the lay public would welcome the news that the profession had

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