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

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IRRADIATION THERAPY IN THE TREATMENT OF MALIGNANT DISEASE*

BY

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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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come to certain working conclusions in the matter, as a demonstration that the money it had expended in recent years—no small sum—in the equipment and support of centres of radiation throughout the British Isles was being used to afford the maximum relief to patients. Secondly, the answers to these questions would provide the general practitioner with the kind of knowledge he needs, if he is to give sound advice to his patients in a matter in which he is likely at present to be at sea, or swayed by the tone of the last article which he may happen to have read. Thirdly, surgeons—particularly the younger ones—would receive guidance on the problem as to whether they should seek to acquire, at some cost to life, perhaps, in their earlier cases, proficiency in all the recognized major operations for cancer, or in those for cancer in certain organs only. They would be encouraged also to become familiar with the surgical procedures required in

1927—that is, cases dealt with five or more years ago. Such value as they may possess rests, in my judgement, upon two features: (1) that they represent the results not of an individual surgeon of perhaps special skill and extended experience, but of all members of the surgical staff of the hospital; (2) that figures good, bad, and indifferent are all there.

RESULTS

Out of a grand total of over 1,100 cases of malignant disease of all kinds it appears that only 455 were considered fit for radical surgical treatment. Of these we have failed to trace forty-five only. The figures relating to cases of disease of individual organs and, in some sites, of different stages of the disease in the same organ, have all been plotted upon the same form as that used for the last two years in our radium reports. A blank specimen of this form is here presented.

MIDDLESEX HOSPITAL

Disease
Stage

Year	TOTAL Applying for Treatment	TOTAL Treated	Alive Years After Treatment					Untraced at 5 Years	Died of Opera- tion	Died of Other Causes 0-5 Years	Died of Cancer					TOTAL Died of Cancer 0-5 Years	Alive 1932	Died After 5 Years	
			1	2	3	4	5				0-1	1-2	2-3	3-4	4-5			Cancer	Other Causes
1925																			
1926																			
1927																			
1928																			
1929																			
1930																			
1931																			

cases where radium is the main agent—for example, preliminary diathermy, or the removal of post-radiation residual masses. Finally, the radiotherapist, together with those who are in a position to supply him with his cases, would receive clear indications as to the classes of cases whose treatment for the present should form his routine practice.

The answers to our questions must be found in a critical study of the data afforded by radiologists and radium workers of the results of their treatment of a sufficient number of cases, of clearly definable site and stage, whose diagnosis has been confirmed by histological examination, treated by a method in which the variables have been reduced to the minimum, and followed up for an adequate period. But a critical study means not chiefly a dissection of such figures to see how far they conform to these requirements, but their comparison with surgical data of a strictly comparable kind.

Through the courtesy of the board and medical staff of the Middlesex Hospital I am able to present certain figures of this kind, which emerge as the result of a follow-up investigation of all cases of malignant disease not treated by radium or x rays, to contrast with the statistics of our radium cases which we prepare year by year. It is the intention of the hospital authorities to publish the result of the inquiry in full in the autumn. I propose to give here only those, dealing with a few sites in the body, of cases treated in the three years 1925, 1926, and

As will appear, with one or two exceptions, the number of cases of disease in any one organ out of the above total is too few to be worth much, and far too few to justify quotation in percentages. It is to be hoped that other hospitals dealing with cancer cases in large numbers may be able to add comparable figures so that sufficient numbers are available in all groups upon which to base conclusions of weight.

Cancer of the Breast.—Of 151 cases operated upon with two operative deaths seventy-three were free from the disease after three years and fifty at the end of five years (48.3 per cent. and 33.1 per cent. respectively). Analysed into Stage 1 cases—that is, those with no palpable glands—and Stage 2—those with glands involved—the figures are: Stage 1. Operated upon, forty-seven—free at end of three years, thirty-one, at end of five years, twenty-seven (65.9 per cent. and 57.4 per cent. respectively). Stage 2. Operated upon, 104—free at end of three years, forty-one, at end of five years, twenty-three (39.4 per cent. and 22.1 per cent. respectively).

Carcinoma of Tongue.—Of thirty-eight cases operated upon eight died of the operation, eleven were free at the end of three years, and nine at the end of five years.

Carcinoma of Floor of Mouth and Mucosa of Lower Jaw.—Fourteen were operated upon; three died of the operation, five were free from the disease at the end of three years, and four at the end of five years. (The one death was due to "other diseases.")

Carcinoma of Lip.—Out of ten cases operated upon, with no death, seven were free at the end of three years, and five at the end of five years.

Carcinoma of Parotid.—Six were operated upon without operative death. Two were alive and well after three years, and also at the end of five years.

Carcinoma of Stomach.—Out of 132 cases only eighteen were found suitable for operation. Eight died of the operation, two were alive at the end of three years and also at the end of five years.

Carcinoma of Colon.—Out of seventy-eight cases thirty-eight were submitted to operation, of whom eleven died. Sixteen were free from the disease at the end of three years, and thirteen at the end of five years.

Carcinoma of Rectum.—Out of 123 cases twenty-eight only were submitted to operation, of whom nine died. Five were alive at the end of three years and two at the end of five years.

Squamous Carcinoma of the Skin.—Sixteen were operated upon with no deaths. Nine were alive at the end of three years and also at the end of five years.

CONCLUSION

I have chosen these figures from the complete investigation as affording some evidence of the results of surgery (1) in the field in which radium is making definite claims—namely, the skin, mouth, and breast—and (2) in organs in which radium has so far claimed but little—the stomach, colon, and rectum. It is a striking fact that it is in the first group that surgery can show encouraging results, and in the latter it is so disappointing. If a much larger collection of surgical results were examined I believe that the same would hold good. Evidence is so far lacking that either radium or x rays are more than local remedies. It would appear that anatomical and pathological considerations impose much the same limitations upon their usefulness as they do upon that of surgery. The great advantages they offer over operative treatment, in the way of complete freedom from risk to life, avoidance of a period of invalidism, of mutilation, and of the infliction of pain, are in these days of heavy dosage, prolonged treatment, marked local reactions, and complementary surgical procedures, less convincing.

Radium and x rays are unquestionably of service as "palliative" agents in the more advanced cases of malignant disease in those organs in which surgical treatment of the disease when less advanced is most hopeful. How far they are producing lasting freedom from the disease which equals or exceeds that resulting from surgical methods alone, subsequent speakers in this discussion will doubtless endeavour to make plain.

THE RADIATION TREATMENT OF MALIGNANT DISEASE*

BY

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As the other two openers of this discussion are a surgeon and an x -ray therapist, I will, as far as possible, confine my remarks to radium therapy. At the outset it may be well to stress the fact that radium is not a substitute for either surgery or x rays in the treatment of malignant disease. All three methods play their parts, and a correct choice can be made between them only if the principles underlying each are understood.

A study of cancer statistics shows that in the treatment of many forms of malignant disease there is little difference between the results obtained by surgery, by x rays, and by radium when each is in the hands of an expert. This is really not surprising, for success in medicine is obtained by the skill and judgement of the individual

worker, and not by the media in which he works. On account of this, the treatment of cancer will never be standardized; for example, should a clinic be fortunate enough to possess an outstanding surgeon or x -ray therapist cases will naturally be referred to him which under ordinary circumstances would be treated with radium, and vice versa. Of course, when treatment is planned, material and equipment must be considered besides individual skill. Limitations in this direction often make it impossible to use an ideal technique.

Any consideration of radium therapy must begin with the all-important fact, so well demonstrated by Regaud and his fellow workers, that γ rays act on the dividing cell and not on the resting one. It would seem safe to assume from this that an actively mitotic tissue will be sterilized by a dose which will affect relatively stable tissue to a much lesser extent; it is on this assumption that modern radium therapy is based. While rapid cell division and malignancy are usually found in the same tumour, active mitosis does not necessarily connote malignancy. In general, the less complex the function of the cell and the more primitive the tissue from which it arises the shorter is its life, and consequently the higher its karyokinetic activity. Thus, in order to permit growth mitosis must be very active in a rodent ulcer, for it is composed of primitive basal cells which wear out rapidly. On the other hand, a tumour such as a gastric carcinoma is composed of complex cells which wear out slowly, so that, although as compared with a rodent ulcer the rate of cell division is usually low, the malignancy or rate of spread is very high. But we know that the effect of radium depends largely on the rate of cell division, and this explains why a rodent ulcer, which is relatively benign, is often more amenable to radium treatment than a malignant gastric carcinoma.

It is important to remember that γ rays merely sterilize, or partially sterilize, the tumour cells; they do not actually destroy the growth, but they do decrease the rate of cell production in it that the natural resistances of the body and the tissues of the tumour bed are able to effect its destruction. Bearing this in mind, it will be seen that a tumour is most easily destroyed by radium in healthy vascular tissue with good lymphatic drainage. To illustrate the importance of a good blood supply it may be stated that the application of radium to a growth involving bone should, if possible, be avoided, because the dose which sterilizes the malignant cells as a rule damages the blood supply of the bone, causing osteonecrosis.

Local sepsis and inflammation are unfavourable because they interfere with lymphatic drainage; hence radium should not be used to treat a cancer on a tongue which shows signs of severe chronic glossitis. Such tumours rarely respond well to irradiation, and other methods of treatment are preferable.

Another important consideration is the radio-sensitivity of the surrounding normal tissue. Such organs as the intestine and the liver are extremely sensitive to γ rays, and it is almost impossible to give an adequate dose to tumours arising in, or lying adjacent to, these organs without causing them permanent damage. Epidermis is particularly resistant, and even when destroyed by radium it regenerates, whereas other normal tissue becomes necrotic when heavily irradiated. The patient's general condition is also of great importance; to irradiate a patient who shows signs of general carcinomatosis or cachexia is merely to make matters worse.

The radium worker's difficulties do not end when he encounters a radio-sensitive tumour lying in healthy tissue. All parts of the growth must be given an adequate dose of γ rays, and at the same time permanent damage to surrounding healthy tissue must, as far as possible, be avoided. This is comparatively simple when the growth

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