A GENERAL SURVEY OF RADIOTHERAPY IN MALIGNANT DISEASE.*

BY

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THIS is the fifth annual discussion on radiotherapy since the year when, as President, I suggested that this subject should become a hardy annual until it had been thoroughly thrashed out.

The subject is being discussed in all countries by men who look at it from various points of view. Radiologists are swayed this way and that by new theories and methods which are advocated with persistent regularity. The subject is undoubtedly very complex, and we are apt to lose sight of the wood because of the trees. I propose to outline the wood a little more clearly.

To do this, let us call a halt and take a brief survey of the present position. This survey should embrace the disease, the therapeutic agent, and the patient.

THE DISEASE.

To ensure keeping to the right road, it is essential that we should have a clear conception of the disease we are attempting to attack. I grant we know little as yet as to the cause of cancer, but we do know the usual course it takes, and we must plan our attack accordingly. We cannot expect to attain our object immediately. The high-voltage technique raised our hopes; it was thought that a short cut had been found to our object—a cure for cancer—but sufficient time has now elapsed since its introduction for us to realize that, while a definite advance has been made, we have yet a long way to go before reaching our goal—if ever it is reached. It might be said that prevention would be a short cut to the cure of cancer.

Some try to persuade us that malignant disease is a local disease. This is true within narrow limits; it certainly commences as a local lesion—the primary growth; but radiologists must not lay their plan of attack on this assumption alone. The surgeon very rarely sees early cases and radiologists practically never. We must, in any case, play for safety. The primary growth is but an indication that the patient has malignant disease, and does not by any means give us a correct idea as to its extent. A very small lesion, often undetected even *post mortem*, may give rise to extensive secondary deposits. I have in mind an operation for retrofixation disclosing a very small nodule of one ovary. This was removed. A very small island of malignant cells was detected microscopically, yet in three weeks the abdomen was full of large secondary deposits.

To ensure our plan of attack being developed on sound lines, it must be based on the assumption that malignant disease is a generalized disease and not a local lesion.

Ingenious and elaborate schemes have been devised to ensure the primary growth receiving its lethal dose. Satisfaction may be expressed on its reduction or disappearance, but the patient dies very shortly from secondary deposits. The gland areas are occasionally irradiated, but this is not enough; there are no means of being certain where stray pathological cells have already settled. I maintain that if the primary growth can be destroyed by radiation, metastases will be equally susceptible, possibly even to a much smaller dose, for they are usually less bulky. At present we concentrate on the primary growth; we must go further and endeavour to control the offspring which may be settling down comfortably elsewhere. I do not say that this control will ever be achieved, but it is the ideal we should certainly try to attain. It will, at the same time, ensure our working along the right lines. Surgeons are not content with removing the primary growth; why should radiologists be?

THE THERAPEUTIC AGENT.

I must confine my remarks to α rays. Some radiologists advocate the high, others the low, voltage technique. A better distinction would be homogeneous and heterogeneous

radiation. *Homogeneous* radiation (high voltage) means, briefly, the use of a bundle of rays of one particular penetration. *Heterogeneous* (low voltage), on the other hand, means the use of a large number of rays of all penetrations, filtering out those rays likely to injure the skin. Either of these forms of radiation may be used on the intensive principle, but results do not necessarily depend on this factor. These two forms of radiation cannot be divorced from each other. It would be a tragedy if radiologists were to become divided into two separate schools—the high and the low voltage.

It is important that we should not discard heterogeneous radiation. It is of the greatest value, as those of us who have been utilizing it for many years know. It has its limitations, but the newer method should be an addition, and not a substitute. The reports from various countries make one realize that even under the best conditions the results of homogeneous radiation are, on the whole, disappointing; they may improve as the technique is developed. Let us not scrap our machine guns because a long-range gun has been invented. To be fully equipped we require elasticity in our apparatus, so that each case can be treated on its merits, for in some the heterogeneous radiation will be more suitable than the homogeneous, and vice versa. Every radiotherapeutic department, therefore, to be complete, should be so equipped that radiation at all voltages is available, in order that any desired condition of radiation may be repeated at will. Cannot the physicists investigate the low-voltage technique with the same care and enthusiasm they have bestowed on the high-voltage? The former has by no means been fully worked out.

Professor Wirtz, in his last report on results of radiation of carcinoma of the uterus—the most suitable type of case for high voltage—concludes with the following interesting statement: "In spite of the best technique with favourable initial conditions and good general state of the patient, the results are from time to time inexplicable, so that one is compelled to believe that for the cure of carcinoma with α rays certain unknown biological factors play a certain part." I should like to substitute "an important" for "a certain."

The question as to how radiation affects morbid cells is far too complex to be discussed in detail here. There are, however, several important factors that may be briefly mentioned.

Radiation does not destroy or remove unwanted cells like the cautery or knife. Profound changes are set up which allow them to be absorbed and replaced by healthy cells. This is important to remember, for it means that malignant cells can be made to undergo a change, resulting in their replacement by normal tissues, without necrosis taking place—in short, a metamorphosis without cellular death.

It is clear, therefore, that tissue reaction plays an important part. If, for some unknown reason, this reaction fails, no amount of radiation will succeed in destroying the pathological cells. It is thus evident that there is a local indirect effect of radiation; carried further, is it not possible to create it on a larger scale generally, calling up all Nature's forces to assist in the cure? In other words, may it not be possible by radiating a large area to set free in the body some antitoxin or enzyme that will assist in the desired destruction? The work of many physicists supports this theory. I have myself on several occasions seen lympho-sarcomatous glands in unirradiated parts disappear after large areas have been irradiated. In one case this was manifested in half an hour! Is radiation sickness evidence of the liberation of something of the nature of an antitoxin? I have said enough to indicate a line for future research.

To sum up, let us have all forms of radiation at our command, and apply them with judgement and circumspection, for each case is a study in itself. Uniform dosage for all the various forms of carcinoma or all varieties of sarcoma cannot be entertained. Lastly, our results may be dependent, not only on the direct effect of radiation, but on some as yet unknown indirect phenomena. Experimental data are rapidly accumulating, indicating that the occurrence and nature of immunity to cancer is a field of study from which we may expect much in the near future.

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THE PATIENT.

It is not fit that we medical men should be accused of treating the human body as if it were merely so many cubic centimetres of material. We are all conscious of the so-called "personal element"—that tantalizing something—present, but yet not measurable. A patient for radiation should not only be thoroughly investigated physically, but his age, state of health, and so on, must be taken into consideration before deciding whether radiation will achieve anything beneficial to him.

Radiation being decided upon, the next point is to map out clearly the lines of treatment to be adopted. These may be palliative or curative. Of the patients seen by radiologists, in the majority palliation only is all that can be hoped for. This side of radiotherapy is of great value, but is being lost sight of in our efforts to cure. It is quite impossible, in certain cases, to attempt to eradicate the disease, and the chances are that if we do not discriminate the last condition of the patient will be worse than the first. The therapeutic goal varies, and each case must become a study in itself. I make it a rule to put down the objects I hope to achieve by radiation, and my plan of treatment is arranged accordingly.

Radiation Sickness or Malaise.—Radiation sickness is the bugbear of radiators. We have to inquire what its cause is, and whether it should be regarded as evidence of over-dosage. The results are often disastrous to the patient, being sufficient to turn the scale against him. This puzzling phenomenon may manifest itself in several ways. Actual vomiting may occur as the patient is undergoing treatment, or sudden nausea with or without vomiting may be experienced from one to seventy-two hours after. As hospital patients describe it, "I come all over alike—sudden." Intense headache may be complained of without gastric symptoms. With the high-voltage line of treatment vomiting may become uncontrollable. In its treatment various drugs have been advocated from time to time, but so far I have found nothing to control it. At present I do not consider that we are justified in subjecting a patient to the risk of severe radiation sickness unless we can promise him something substantial in return.

Carcinoma Mammæ.

The majority of cases that find their way to the radiological department of the London Hospital, and probably at most of the hospitals in England, come under this heading. Over two thousand have been treated at the London Hospital in the last fourteen years. For this reason I have always endeavoured to improve the technique for this large class of case. Whether inoperable, recurrent, or requiring prophylactic treatment, malignant disease of the breast illustrates very clearly the problem we have to solve in radiation of cancer.

Prophylactic Methods of Radiation.—After the primary growth has been removed, not by radiation, but by the surgeon, the radiologist is called in. His interest now is not distracted by the presence of a tumour; he has to devise a technique that has a reasonable chance of destroying cells at unknown depths and positions. This is a complex problem, but it must be faced. The surgeon can, in a number of cases, remove the primary growth and glands without our help, but he is not satisfied with the results because he does not necessarily prevent metastases or recurrence. This, then, is where the radiologist can help. Even if it were possible to destroy with certainty every primary growth by radiation or any other method, I personally should not be satisfied. Metastases kill the patient just as rapidly. We must control these in addition to the original cancer.

I consider heterogeneous radiation to be of greater therapeutic value than homogeneous in the prophylactic treatment of breast cancer, for these reasons: It gives radiation absorption at various depths; a large radiation field can be utilized with minimum general disturbance. I readily grant that further development is required on these lines. I have already reached the limit of the toleration of the patient under these conditions.

There are four chief objections to the high-voltage method in this class of case:

1. The radiation field is necessarily much too limited.
2. There is no indication as to the depth at which the dose should be delivered.
3. Damage to the lung tissue is comparatively frequent.
4. General disturbance—such as sickness and blood changes—place too great a strain on the patient.

The response of many a hopeless case is often remarkable if the heterogeneous radiation is carefully carried out.

Radiation of the Whole Trunk.—I maintain that whatever form of radiation is used in cases of breast carcinoma, it is useless and against common sense to limit it to local areas. Radiation should, if possible, include the whole trunk. It benefits the patient but little to check the metastases in a localized area while they go ahead elsewhere. As there is also evidence for the theory that in many cases the patient's tissues—we do not know which—have the ability of producing some beneficial reaction, the larger the field of radiation the better.

As a preliminary effort towards achieving the conditions I consider necessary in the treatment of these cases, I introduced the dual open method at the London Hospital some three years ago. Briefly stated, it consists in placing a tube at the back and front of the patient, both running at the same time, the radiation field including practically the whole trunk. The results show, without doubt, that this arrangement has greatly increased our range of control, benefit being now obtained in cases previously out of our reach, such as secondary deposits in the spine. This is all to the good, but much research is necessary before any further advance can be expected. To my mind this is certainly a logical method of radiation, where stray pathological cells may be at unknown depths and positions. It must be realized that attempts to substitute physics for biology and medicine can only hinder sound progress in radiotherapy.

EMPHYEMA OF THE LEFT SPHENOIDAL SINUS WITH OPTIC NEURITIS AND SUBSEQUENT POST-PAPILLITIC ATROPHY

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WITHOUT actual exploration of the sphenoidal sinuses it is impossible to exclude disease of these cells as the responsible factor in certain cases of optic nerve disease. A very considerable amount of work has been published on this subject, but in spite of careful observations we are still without reliable guides, either signs or symptoms, to lead us to a definite diagnosis in cases of optic neuritis due to sphenoidal sinusitis. The case here recorded is an example of one in which there was little to indicate the true nature of the case; it also emphasizes the value of a routine examination of the sinuses on both sides.

A Hindu woman, aged 40, married, was brought to see me on April 17th, 1923, complaining of loss of vision in the right eye and headache of two months' duration. The vision of the right eye was fingers at 3 metres; left eye vision 6/9 bar one letter with plus 1.0. D.S. = 6/5. The headache was frontal for the most part, but with definite occipital pain, chiefly on the right side. The pupil reactions and tension were normal on either side. The right disc was somewhat swollen and oedematous on the nasal side, pallid and steamy in appearance; the arteries were narrowed and sheathed (subsiding papillitis). The left disc showed quiet neuritis, a red swollen disc with definite venous engorgement. The eye grounds were otherwise normal. There was no history of syphilis or evidence of it clinically; the Wassermann test was negative. There were no symptoms pointing to cerebral disease except headache. The reflexes were normal, as also the urine and blood. There was slight pyorrhoea, but x-ray photographs did not show anything definite either as regards teeth or sinuses. The right field could not be taken; the left was examined with Lister's perimeter in uniform daylight illumination (intense north light over each shoulder), 5 mm. at 33 cm. for white and