A British Medical Association Lecture ON THE PROBLEM OF THE RADIUM THERAPY OF CANCER.*

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[In the earlier portion of the lecture Dr. Burrows dealt with the physical properties of radium; he then went on as follows:]

A few facts have been established in respect to the action of radium on cancer cells during the last twenty years. The first is that cancer cells can be destroyed by rays, but this statement is modified by the knowledge that, given a sufficient dose, practically all tissue cells can be killed by radiation, and so arises the second point—namely, that there is a minimum dose which will just kill a cancer cell and will not, as a rule, kill an ordinary tissue cell. This is called the "minimum lethal dose," the "lethal dose," or the "cancer dose." This lethal dose varies with different tumours and different conditions.

Theoretically, given a known quantity of rays, the lethal dose of the cells of a certain cancer, and the size and situation of the tumour to be treated, it is possible to destroy almost any cancer, but unfortunately all these three conditions are variable and are made up of variables. Thus, with regard to rays, the beta rays from radium are not uniform, but are made up of groups of rays which are of different penetrability. Similarly the gamma rays are mixed, as also are x rays. Beta rays can be screened off entirely by using metal plates of a definite thickness, or they may be partially cut off by using thinner or less dense material. It is very difficult to cut off all gamma rays, but certain of them can be eliminated by a process of screening and an attempt made to obtain rays of a certain minimum penetrating power. In the same way by screening and by improving and standardizing apparatus an attempt is made to keep x rays as constant as possible, but unfortunately it is not known exactly what is the right type of ray for each tumour. A few facts are known—for example, that a rodent ulcer will do well with unscreened radium (that is, mostly beta-ray treatment), but gamma-ray treatment is also effective. I think, however, that if beta rays fail in the treatment of a rodent ulcer gamma rays will rarely be successful. Skin diseases are obviously most suited for rays of a longer wave-length. Most rays seem to affect lymphosarcomata, while carcinoma of the tongue as a rule yields best locally to beta rays, but of course with beta rays there is a strong caustic or destructive action. One of the claims of the Erlangen x ray treatment is that a correct ray for the destruction of carcinoma of the cervix of the uterus has been established. But the size, density, and depth of a tumour obviously affect not only the quantity of rays penetrating the whole of a growth—for that can be rectified—but also the quality, which cannot be thus adjusted when radiation is being applied from a distance. The actual insertion of a varying number of suitably screened radium tubes into a tumour is the only method of ensuring uniformity in the quality of the radiation applied. Some tumours are not suitable for the burying of tubes in their substance, and it is then seen how complicated the whole subject is, and how the question of the quality of the rays used, and the dosage, merge into a consideration of the size, density, nature, and position of a tumour.

Lethal Dose.

Assuming that beta rays are used to kill a cancer cell, it is probable that the lethal dose for these would be different from the lethal dose for gamma rays; or, pushing the matter farther, the lethal dose of soft x rays would be different from the lethal dose of hard x rays, as the destructive action of radiations must depend on the quantities of them which are actually stopped in the cells of a growth. Therefore, in fixing a lethal dose for a certain tumour, it must be established for a definite type of ray, and this does not in practical therapy depend altogether upon the operator, but upon the size, nature, and position of the growth he has to radiate. Thus, change the position of the growth by one centimetre and it may be necessary to alter the type of ray used, and

with that the dosage if raying is being carried on from a distance. Then, again, the lethal dose for a tumour may be very near that of the ordinary tissues, and a very fine or no margin left between the quantity and type of rays destroying the normal tissue and the cells of the tumour.

As an example of this last possibility the secondary nodule which may be present on the chest wall following an amputation of the breast may be given. Over this may be stretched a thin and delicate covering of epithelium, and any application of rays given to the nodule may destroy the skin beyond repair long before the tumour cells in the nodule itself are killed.

Nature of the Tumour.

It is an established fact that some tumours are destroyed by rays more easily than others—for example, a small round-celled sarcoma is more easily caused to disappear by irradiation than a squamous-celled carcinoma; but absolute uniformity in respect to the behaviour of groups of growths under radiation does not exist, as other factors, such as the patient's general resistance to tumour growth, or the situation of the tumour, alter its susceptibility to rays and possibly also the stage of development and age of the tumour itself. Is, for instance, a rodent ulcer growing in the skin a different growth from one growing in bone? The same treatment will not cure them both. In fact rodent ulcers of the skin are easily cured by radium; rodent ulcers invading bone are only exceptionally cured.

Nor must the fact be forgotten that rays seem most markedly to affect the reproductive functions of cells. Therefore let the tumour grow quickly, and most often the local growth will rapidly diminish, and vice versa; but unfortunately the local tumour is not the only consideration, for growths such as encephaloid carcinoma of the breast, which grow very rapidly and respond well to radium, soon form secondary deposits, so that the ultimate result is not so good. Or again round-celled sarcomata are usually quoted as types of tumours which respond well to radium treatment, but the more slowly growing and difficult to treat spindle-celled sarcomata with perseverance give the best results in the end.

Size and Density of Tumours.

The size of a tumour is important from several points of view. If a tumour is exceedingly large commonly there is a poor blood supply at the centre (if it is a carcinoma), and there is a great tendency for the tumour to break down and slough under treatment, while at the same time a poor blood supply does not give adequate chance of repair following the treatment. Again, the size of the tumour has a marked effect upon the size of the dose of radiation which is given if an attempt is to be made to destroy all the cells it contains. A small tumour can fairly easily have an even radiation applied throughout its substance, but if it is very large, provided the rays are applied from one direction, the quantity falling on the near side of the tumour will be very much greater than that emerging from the far side. It is also apparent that the density of the growth will have a similar effect, for the denser the tumour the greater will be the difference between the entering and emerging rays.

In the early days of radium treatment Wickham and Degrais suggested the method of cross-fire as one of the means of getting over this difficulty—for instance, if a tumour can be treated from two sides, all other factors being equal, double the dose can be given to the tumour by applying radium to it on those two sides. If the tumour is accessible it may be radiated from more than two sides. What is done by the Erlangen method of x -ray treatment is very much the same thing. In order to get a sufficient quantity of x rays to the tumour, rays are directed through several different areas of skin towards the tumour, which areas are called "ports of entry." It is thus seen that the method is the same as the cross-fire system used by Wickham and Degrais.

With radium and radium-emanation treatment the difficulty is also partly met, as has already been mentioned, by burying radium or radium emanation in the growth, or by varying the distance of the applied radium from the external skin. In the foregoing reference to the size and density of a tumour it has been more or less assumed that the tumour has been regular in outline and of uniform density throughout. But in practice, of course, malignant growths are of many and varied shapes, and they have near and distant secondary deposits; also they are by no means of uniform density, so that the problem of dosage becomes very complicated, and the most that can be hoped for is to obtain an approximation to what is desired which will work in practice.

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The Position of a Tumour.

Its position has a very similar influence to the size and density of a tumour upon its susceptibility to radiations. If, for instance, it lies beneath or in tissues such as muscle and bone, it may become almost impossible to give it adequate radiations from the surface. If such factors as these are not present it may be possible that radiations from one side where the tumour is nearer may, at least in part, make up for deficiencies in radiation from the other side from which the tumour is farther away; but to get a proper quantity of rays traversing the growth many ports of entry may have to be used, and it becomes very difficult to get absolute accuracy of dosage. When cancers invade or are adherent to certain structures and organs such as bone, the stomach, bowel, liver, or lungs, treatment is rendered much more difficult, and often at the present time fails to produce a good result. It seems that not only is the nature of the tumour an important factor in ray treatment, but also the nature of the tissue and organs that it invades. The more accessible a growth is, as a rule, the better are the results, but growths of certain organs, such as the oesophagus, rectum, and tongue, seem to resist radium treatment more than elsewhere.

The consideration of the preservation of the skin is an ever-present problem to the radiologist. It has been already mentioned that under certain conditions it is possible that a stretched or ill-nourished skin may be more rapidly destroyed than a tumour, and, moreover, if the blood supply or ability of the skin to repair is bad, unless proper care is used the last condition may be worse than the first, from the formation of an intractable ulcer—not an x-ray or radium ulcer but a malignant one. That is to say, it may not be possible to give a suitable destructive dose to the ill-nourished tissues without risk. If one could be sure of destroying such a malignant growth beneath the skin there would be less difficulty in dealing with the factor of the skin, for it is almost certain that scar tissue would eventually form and fill up the gap; but the uncertainty of destroying the growth under these conditions makes the radiologist take more care in endeavouring to preserve the skin, and hence has arisen the so-called "erythema dose." The burying of radium tubes will often, but not always, obviate this difficulty. In the case of rodent ulcers and epitheliomata of the skin not invading bone or cartilage, the skin, as a rule, has been modified or destroyed by the growth. In such cases the preservation of the epithelium need not be considered and marked local destruction produced if necessary, with knowledge that good repair will take place afterwards and a soft, supple scar be formed.

It will be seen from the foregoing remarks that the whole system of ray treatment is exceedingly complicated. The difficulties of dosage are modified by nearly all the usual things which may take place in a tumour from its nature or position. The possibility of actually stimulating an outlying portion of a growth which has been only partially radiated must always be borne in mind, although it is not as a rule a difficult problem in practice, because fortunately the range of dosage producing stimulation is an exceedingly small one.

What is needed is a large number of physical measurements of the different parts of the human body and of pathological growths, and a full and complete investigation of the nature of the lethal dose for cancer cells; when these have been made an approximate idea may be obtained of the method of treating tumours in different situations, although even then it seems that a number of imponderable biological problems, such as the resistance of the organism as a whole and the resistance of tissues locally to cancer growth, remain to be solved.

But in spite of all these difficulties, and the disadvantageous position in which radiologists are placed in this country of treating practically only inoperable cases, many good results are obtained from radium treatment: 7½ per cent. of all the cancer cases (mostly inoperable) which come to Manchester for radium treatment are alive and well to-day after periods varying from two to seven years, and many cases of carcinoma of the cervix of the uterus, breast, skin, lip, and other regions are in perfect health who would but for radium be dead; while endothelioma of the parotid gland and spindle-celled sarcomata show still more gratifying results. Moreover, short of cure much valuable palliative work is done, while in non-malignant conditions, such as exophthalmic goitre, Hodgkin's disease (when young), keloid, cavernous and capillary naevi, the percentage of cures is high; finally, radium is specific for excessive uterine haemorrhage and spring catarrh.

THE SURGICAL TREATMENT OF CHRONIC ULCER OF THE BODY OF THE STOMACH.

BY

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THE surgical treatment of duodenal ulcer and pyloric ulcer can now be regarded as standardized and relied upon to give almost uniformly and permanently satisfactory results. Such a statement cannot yet be made in respect of ulcers situated in the body of the stomach. Their treatment has been difficult and disappointing, and the many and varied operative procedures advocated and practised have been gradually discarded as failing to give the results hoped for. Partial gastrectomy, involving excision of the segment in which the ulcer is situated, together with the portion of the stomach on the distal side of it, is strongly recommended by such eminent authorities as Sir Berkeley Moynihan and Mr. James Sherren as being the only method that can be relied upon to cure. On general grounds such a drastic remedy is only justifiable if we admit inability to succeed by simpler measures. The routine excision of an organ for a non-malignant lesion is at variance with the principles governing conservative surgical practice and is rather a confession of failure. That gastrectomy is advisable in certain cases of gastric ulcer may be admitted, but unless we are prepared to regard such ulcers as precursory of cancer its necessity in every case can only be accepted with great reserve. Further, even though partial gastrectomy is held to be the procedure of election the problem is not solved, for it is inapplicable in many of the worst cases of gastric ulcer and proves useless when most required.

For many years I was impressed by the uncertainty of the results that followed operations for gastric ulcer. Immediate and permanent relief of symptoms was obtained in some cases, while in others the results were only partially good or wholly unsatisfactory. Good or indifferent results bore no definite relationship to the size and character of the ulcer, nor to the particular operation performed. I tried posterior gastro-enterostomy with and without excision of the ulcer, excision of the ulcer without gastro-enterostomy, excision of the segment of the stomach in which the ulcer was situated by the "sleeve" method, and various other procedures that have been advocated from time to time. None of these methods gave uniformly good results, and it is of interest that my worst results occurred in a series of twenty-five cases in which small ulcers were excised freely and the opening carefully closed without the production of any appreciable deformity of the stomach. A very small proportion of these cases derived any benefit from the operation, and I have subsequently had to operate a second time upon nearly half of them.

Careful consideration of my cases gradually brought out the fact that the chief determining factor as regards result was the situation of the ulcer. My experience, which I believe to be in accord with that of surgeons generally, was that the relief of symptoms due to gastric ulcer becomes increasingly difficult the farther from the pylorus the ulcer is situated. The farther the ulcer from the pylorus the less satisfactory were the results obtained by the same operative procedure. There is no evidence that this is due to any essential difference in the morbid anatomy or the pathology of the ulcer. An ulcer in any part of the stomach is more or less subjected to the same physical conditions as regards chemical and mechanical irritation of gastric contents. If, then, there is a difference in the response of such ulcers to surgical treatment it can only be accounted for by variations of site and not of pathology, and treatment must be varied in accordance with that principle.

Following up the clue provided by clinical and operative experience, with the valuable assistance of Dr. Harold Black, radiographer to the Queen's Hospital, Birmingham, an endeavour was made to ascertain in what way an ulcer modifies the physiology of the stomach. That from a surgical standpoint any essential modification was in respect of its motility and not its chemistry I was convinced, and that the chemical part of gastric digestion could be modified by a surgical operation to the advantage of the patient appeared highly improbable on general grounds, and my operative experience confirmed this opinion.

Radiography brought out clearly the fact that an ulcer of the stomach causes spasm of the segment in which it is