THE TECHNIQUE OF RADIUM THERAPY TO-DAY.*

BY

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Radium therapy has been dealt with largely by the lay press, which has done much good in educating people in the subject, but, as is so often the case, a false impression has been given by the application of the journalistic touch to a most important subject. Two erroneous views are, I think, widely held by the laity in consequence: one is that radium will cure all cases of carcinoma, and the other is that for want of radium many unfortunate people are dying daily throughout the country.

The use of radium has now reached a position where we know that in the treatment of carcinoma it is on a par with the knife, and in certain cases surpasses the use of that instrument; but even the knife has never been able to deal with all cases of carcinoma. In the second place, there is at the moment more radium in this country than there are people trained and capable of using it. On the Continent radium has been studied for many years, while in this country scientific methods have been comparatively lately introduced.

Radium gives off three forms of rays: alpha rays, which are of no importance; beta rays, which are disadvantageous for medicinal purposes, and must be screened off by platinum, lead, or other impermeable metals, since they destroy normal as well as abnormal tissues; gamma rays, which produce therapeutic effects, but must be as pure as possible. The gamma rays act more powerfully on immature tissues than on fully developed and highly differentiated ones. Cancer cells, being immature and hardly differentiated—in many cases consisting of masses of almost wholly undifferentiated cells in stroma—are very much more sensitive than the normal tissues. They can therefore be killed without permanent injury being inflicted upon the normal tissues. We also know that cells in the course of rapid division, such as cancer cells, are more sensitive than cells which divide and multiply at longer intervals.

METHODS OF APPLYING RADIUM.

General radium therapy is the introduction into the system of radio-active substances which will circulate throughout the body and act upon the primary growth, the glands, and the metastases. It is the ideal method, but unfortunately at present it is beyond our powers, since the introduction of such substances would injure vital organs and the individual would be killed before the carcinoma could be destroyed. The future may reveal to us a means of treating carcinoma by this method, and the introduction of a vaccine, a serum, or a metal such as lead, or selenium may open up to us a way of approaching our ideal. Meanwhile we are limited to the introduction of radium foci locally. Radium acts in accordance with Newton's law—that is, its action is the inverse of the square of the distance from the substance on which it operates; these foci must therefore be brought into close contact with the carcinoma, and in order to do this it is convenient to have many foci so that the dose may be evenly distributed over a large area.

Radium must not be confounded with its emanation—radon—which is collected in capillary glass tubes and which acts like radium, though only for a very limited time. In twenty-four hours it loses 18 per cent. of its power; in three days 50 per cent.; in eight days 80 per cent.; while in fourteen days only 8 per cent. remains. This limits its use to centres where a radon plant is available, otherwise exact dosage is difficult or impossible to calculate, since

it is not always known when it was prepared and how much has been dissipated.

Seeds are tiny glass tubes filled with radon, which may be enclosed in a platinum sheath to shield the tissues; they are about 6 mm. long and less than 1.5 mm. thick. Various instruments have been invented for their introduction. They are inserted into the tissues and left there, the radon dissipating in the usual time; if they contain radium they must be attached to a silk thread and recovered.

Needles contain radium in metal capillary tubes called "cells," which are enclosed in platinum tubes, sharpened at one end and with an eyelet at the other. They are of different lengths, and contain one, two, or more cells, each containing 0.5 to 1 mg. of radium. Needles range in length from 20 mm. to 60 or 80 mm., and differ in strength according to the number of cells they contain. The needle is threaded with a flexible substance or thin wire, and is then thrust into the tissues; after a certain time it is recovered by traction on the thread. The thickness of the wall of platinum in each needle varies from a minimum of 0.5 to 0.8 mm., or even 1 mm. for longer needles.

Tubes are composed of platinum, and contain larger quantities of radium ranging from 5 to 100 mm. or more. As a rule they are of no great length, 20 to 40 mm., while their walls may be 2 mm. in thickness. As a rule they are placed in special containers of silver, which fit the situation in which it is desired to place them—the uterus, rectum, or oesophagus.

Bombs are thick leaden cavities, sometimes six inches in thickness, in which large quantities of radium (perhaps 4 grams), suitably screened, are placed; a window can be opened, and the rays allowed to act upon the area required for a very short time. They have been tried in Brussels and Paris, and now there is one at the Westminster Hospital. Though they have been in use for some years abroad it is significant, I think, that, so far, no results have been published.

The dose of radium should be distributed as equally as possible over the malignant cells so as to destroy them, while avoiding injury to the surrounding tissues. This is not always easy to effect. In a large tumour the cells in the centre cannot escape, and can probably do nothing but degenerate; they are therefore not to be feared, for the actively growing and infiltrating cells at the margin are the agents by which spread and metastases are brought about.

In a flat ulcer needles can be introduced into the tissues underneath, and can be placed parallel; but in deeply situated growths infiltrating the tissues, such as the tongue, the needles have to be arranged parallel with the sides, so that they gradually converge from the surface.

1. *The Internal Method of Application, or Intra-cavity-tion*.—This is the introduction of radium into a natural cavity such as the vagina, uterus, rectum, mouth, or oesophagus. The radium is kept in place a certain time to allow it to take effect, and special apparatus may be required; for instance, a dental plate may have to be used to keep the radium in contact with a growth of the palate. Considerable experience is needed to gauge the dose required.

Internal radium therapy is limited in action by many factors, such as the depth from the surface in the oesophagus and rectum, by the thinness of the walls in the oesophagus, or the narrowness of the tube in the urethra. For instance, in the urethra or oesophagus it is almost impossible to destroy a growth on one side and not injure the wall of the canal on the other; this has been a frequent cause of death in cases of disease of the oesophagus.

Perhaps the best results have been obtained in cases of carcinoma of the cervix. The uterus is an organ possessing great radio-resistance, and will stand ten times the dose that the skin will tolerate, so that there is a large margin to work on. The figures of Paris, Stockholm, and Brussels do not differ materially, so I will take those of Paris.

The cases are divided into three classes: degree 1, operable cases in which the carcinoma is apparently early and local; degree 2, borderline cases where the disease is in a more advanced state on the cervix, and the glands

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are possibly affected; degrees 3 and 4, inoperable cases, where the disease is still more advanced, and the adnexa of the uterus are infiltrated. In degree 4 other metastases are present, and the case is hopeless.

In the Paris report there were 61 available cases; the number freed from symptoms was 37, or 60 per cent. of clinical provisional cures. The percentage of five-year cures increased from 20 in 1919 to 81 in 1923. In degree 2 there were 176 available cases, of which 66 were freed from symptoms, or 37 per cent. of clinical provisional cures. The percentage of five-year cures increased from 33 in 1919 to 43 in 1923. In degrees 3 and 4 there were 373 available cases; 81 were freed from symptoms, or 28 per cent. of clinical provisional cures. The percentage of five-year cures increased from 3 in 1919 to 31 in 1923.

These figures are as good as those of the best surgical clinics, and have improved remarkably during the last few years. They probably will improve still more, but all cases will not be cured. There is a great difference in the percentage of cures among those seen and diagnosed and treated early and those seen at a later date. Although squamous-celled carcinoma of the cervix gives such good results, adenocarcinoma of the body of the uterus is highly resistant and gives very bad results; indeed, its treatment by radium has practically been abandoned.

2. *Interstitial Method.*—This consists in the introduction of needles into the tissues. In order that the dose may be evenly distributed a large number of foci or needles are required. Interstitial radium therapy is applied to a host of tumours throughout the body—to either carcinoma or sarcoma of the tongue, the breast, the prostate, or to superficial ulcers and metastases. Carcinoma of the skin gives perhaps the best results; about 90 per cent. can be cured either by this method alone or in some combination.

The tongue yields very striking results, and again I will cite the Paris figures. Of 344 available cases complete cure ensued in 82 (23 per cent.); cure of the tongue, with death from glandular involvement, in 69 (20 per cent.); and failure in 193 (56 per cent.). This far surpasses any results produced by surgery so far.

Interstitial radium therapy has been developed by what is termed "radium surgery" or "surgery of access"; in this the tumour is exposed so as to allow the needles to be inserted. This is best exemplified in carcinoma of the rectum where a modified Kraske operation is performed; the bowel containing the growth is exposed, the needles are inserted so as to form a barrage round the tumour, and the wound is temporarily closed. At the end of a week the wound is reopened, the needles are removed, and the wound is then permanently closed. Very accurate dosage is needed to destroy the tumour, and the method so far is inferior to the knife. Investigation is rapidly travelling along these lines; carcinomas of the larynx and of the prostate are being treated thus; the first with unexpectedly good results.

3. *Surface Irradiation.*—If radium is applied close to the skin an erythema dose is delivered over a very small area, and a burn is rapidly produced. Columbia paste or wax, consisting of 100 grams each of beeswax and paraffin, with 200 grams of fine sawdust, is used, either 1.5 or 2 cm. in thickness. This allows the rays to spread out sufficiently so that an erythema dose will take some time, and the radium can act longer on the subjacent tumour. The wax is warmed in hot water of about 117° F. until it is as soft as a piece of cloth; it is then moulded to the part, a cold cloth being applied to harden it, and the hardening completed by plunging the mould into cold water. The needles are warmed and applied to the outer side; they will stick to the mould or can be fastened to it by plaster, and are covered with a thin layer of lead to protect other parts of the body. The mould is kept in place for fourteen to twenty-one days; until an erythema dose has been administered. Large areas can be irradiated in this manner with very excellent results, especially in superficial metastases.

4. *Distance Radiation.*—This consists of a similar apparatus to the last, but large doses are placed upon blocks of wood at a distance from the skin. It is becoming less and less used. Bombs are a development of this method.

DOSAGE.

The dose of radium given is usually stated in milligram hours; the number of milligrams applied is multiplied by the number of hours of exposure given. Thus 1,000 mg. of radium applied for one hour will equal 1,000 mg. hours, but the same dose can be given by 1 mg. of radium applied for 1,000 hours, or 500 mg. for two hours, or 100 mg. for ten hours, but the clinical results will not be the same.

In early days large doses were given for short periods, but the work of Professor Regaud of Paris showed that large doses with short exposures did not sterilize rabbits, while smaller doses for longer periods did so. This is probably connected with the division of cells, for more mitoses will take place over a long period than over a short one. On the other hand, we know that exposure to radium stops mitosis at once, so there must be some other factor not yet understood. This has revolutionized our dosage, and we are using smaller doses over longer periods. Such a method of dosage is only rough-and-ready, for while needles inserted into the tissues give off energy all round to the tissues, when radium is applied to the skin, the skin will receive less than half the energy given off. In Brussels an attempt is being made to measure accurately the dose received by the tissues, and it seems probable that our methods of dosage will be altered very considerably in the near future.

All degrees of burn can be produced by radium. The first degree is called the erythema dose, and it is tried to bring about a severe first degree of burn where the skin peels afterwards. More than this destroys the tissues, and such burns take long to heal and are painful; they should therefore be avoided. Radium is believed to act best in a virgin soil, and a second dose some months later does not seem to produce as good results as the preceding one. If a second dose follows after only a short interval the same good results are seen. Gynaecologists have developed this idea; they give three doses at intervals of a few days, with excellent results, in carcinoma of the breast.

RESULTS OF RADIUM THERAPY.

The results of radium are well seen on superficial growths on the skin and mucous membranes; the surface cleans up, and becomes smooth and healthy-looking; the rolled-over edges of an ulcer disappear, the mucous membrane becomes white like leukoplakia, and within a week a marked improvement is seen. These changes remain for a period of five to eight weeks, during which time healing advances, and in about two to three months a carcinoma of the tongue may quite disappear. A superficial rodent ulcer will heal in the same time; if, however, it is of long standing and the bone is affected it may take longer to clear up completely. Tumours of the breast will disappear if not too large, and superficial recurrences will certainly clear up, while carcinomatous ulcers can be made to heal, but others may form, or the patient may succumb to internal metastases which have previously started to grow.

One remote result must be remembered. After exposure to radium the tissues are altered, and some quite slight injury may cause their death and necrosis. What this change is we do not know, but we see necrosis of the jaw develop from wearing false teeth, death of areas of skin appear after too hot a bath, and other results ensuing months after the treatment. Healing is very slow, and subsequent operations have to be very carefully considered. This change is not seen earlier than two months, and sometimes more.

THE LIMITS OF RADIUM TREATMENT.

Many of the present limits of radium treatment will probably be overcome in the future; accessibility of the growth is a fundamental necessity. For this reason carcinoma of the oesophagus defies us, though surgery of access enables us to expose the rectum. This may soon render it possible to deal with intestinal carcinoma, but at the moment we can do little. Gastric cancers have been brought to the surface, stitched under the skin, and then treated, but prolonged relief can scarcely be looked for in internal carcinomata which are only suspected from symptoms and which are therefore diagnosed late. Cancer

of the prostate is in the same unenviable position, being diagnosed late and being inaccessible.

Sometimes a carcinoma in its primary form readily reacts to radium, but the glands when infected may not react at all; block dissection of the glands still seems the best treatment in carcinoma of the tongue. Some carcinomata, such as that of the body of the uterus, are resistant and not apparently affected by radium. Accuracy of dose in all cases is essential, and that is the great difficulty at the present moment.

Cure is a term we hardly like to use in connexion with carcinoma, for though a round-celled sarcoma may disappear in a few weeks, the patient will probably die from secondary infection in the lungs, just as after an amputation. Delay, however, is less likely with radium, for there should be less shrinking from radium treatment than from amputation. If it can be impressed upon the public that early diagnosis will remove the disease without a mutilating operation a bigger step forward will result than has ever been made in the history of this disease.

THE FUTURE OF RADIUM TREATMENT.

It must be clearly understood that the treatment of carcinoma by radium requires the knowledge and the experience of a specialist. Haphazard administration must involve disappointment and bring the method into contempt. It is a regrettable thing to have to say that radium treatment in this country has survived in spite of, rather than because of, institutions which have loaned radium to people totally ignorant of the subject; the indiscriminate

distribution of radon about the country must cease, and radium centres are now being established to supply the needs of different areas. France has already formed a large number of such areas; an expert visits the centres and even subcentres at regular intervals.

Post-graduate teaching is now available at the Mount Vernon Hospital, which, it is hoped, will become the cancer centre of the Empire, and attract research students to it from all parts. This institution has linked itself with the Radium Institute, and a school will be opened in the autumn for the instruction of post-graduates in radium treatment. Very close co-operation is needed between the different branches of the profession, including surgeons, laboratory workers, biologists, and physicists; this has been brought to a high state of efficiency in Paris, Brussels, and Stockholm, and the results there are correspondingly good.

No carcinoma investigation is worth anything unless a really good follow-up department is in use. A patient may be relieved for a time, and a secondary mass appear, which can be dealt with efficiently if seen and recognized at once; patients must therefore be examined at all centres periodically. It is hoped that special travelling facilities by rail may be arranged so that they can come for examination at the London centre of the hospital at a reduced fee. In Sweden all carcinoma patients can travel to the centres free of charge. Results cannot be expected until five years have elapsed, so patience is needed, but it is hoped that organization will soon place London in the forefront of the battle against malignant disease.

THE TREATMENT OF PRURITUS ANI AND ANAL FISSURE.

BY

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Recent communications to the *British Medical Journal* by J. P. Scatchard (June 28th, p. 1203) and by A. S. Morley (July 12th, p. 79) indicate that the treatment of anal pruritus and fissure by the method which I described a year ago¹ is proving successful. The method recommended was the subcutaneous injection of a solution composed of anaesthetin 3 per cent., benzyl alcohol 5 per cent., and ether 10 per cent., in sterilized oil, and termed "A.B.A." Since the publication of that paper I have had a large experience of this method, and the present time seems favourable for the elaboration of certain points in the indications and technique which I have found of value.

Pruritus Ani.

In pruritus ani it is only the intractable cases which need treatment by injection of A.B.A.; the majority of cases will clear up by simple attention to cleanliness, by the use of lotions and powders rather than ointments, and by careful search for and treatment of any local cause of the pruritus. The attention which has recently been drawn

FIG. 1.—Showing injection of 10 c.cm. of A.B.A. into the two posterior quadrants at the first treatment.

by Colonel W. P. MacArthur (*Journal*, June 28th, p. 1195) to the importance of thread-worms in this connexion is very opportune. In cases of pruritus ani of long standing in which no local cause can be found, I believe the injection of A.B.A. to be the method of choice, and superior in every way to under-cutting operations. With increasing confidence in the use of this solution, I have found that 10 c.cm. may safely be employed at the first treatment. This amount is injected in relation to the posterior half of the perianal region through four punctures, 2½ c.cm. being injected at each point indicated in the accompanying diagram (Fig. 1). The reason for selecting this part for the first injection is an anatomical one. The sensory nerve supply to the anus and anal canal is supplied by the

inferior haemorrhoidal nerve, and by the perineal branch of the fourth sacral nerve; these nerves approach from the posterior and postero-lateral aspects of the anus. An injection of 10 c.cm. of A.B.A. as described above gives the pruritus, so to speak, an immediate knock-out blow, and very little more has to be done. A week later 5 c.cm. of A.B.A. are injected by two punctures into the right anterior anal quadrant (Fig. 2), and the left anterior anal quadrant is dealt with similarly during the following week. Perianal dermatitis is treated on the accepted lines: cracks and fissures are swabbed with silver nitrate solution, iodine, or friar's balsam, and the patient applies a simple lead or magnesia lotion. Relief of irritation is experienced within a few hours after the first injection. A feeling of numbness

FIG. 2.—Showing injection of 5 c.cm. of A.B.A. into the right anterior quadrant at the second treatment. At the third session the left anterior quadrant is injected in a similar way.

develops and lasts for many weeks, so that ample time is afforded for treatment of the dermatitis, and for the patient to forget his anal troubles.

In the average case, therefore, I find that the injection of three doses—10, 5, and 5 c.cm.—of A.B.A. is sufficient for cure. I have given this large dose many times and have had no complications. The solution must be injected deeply in a fan-like manner as described in my original paper, with strict attention to asepsis, and the injection should be made so deeply that no superficial swelling is noticeable afterwards. I might add that A.B.A. is now dispensed by Messrs. Allen and Hanburys in 5 c.cm. ampoules, which is a more effective amount for use than the original 2 c.cm. ampoules.

As an alternative to A.B.A., I have for some months been trying a solution of percaïne in oil; the remarkable anaesthetic properties of this substance in regard to duration of anaesthesia are well known. The new solution has been prepared for me by Allen and Hanburys, and is composed as follows: percaïne 0.5 per cent., benzyl alcohol 10 per cent., phenol 1 per cent., in 5 c.cm. of sterilized oil. The phenol was added in order to assist the solution of percaïne, alkalis having to be avoided, and also on account of its antiseptic effect. Goldbacher² has shown that 5 per cent. phenol in oil can safely be injected subcutaneously in pruritus cases. This new solution produces a more rapid effect than A.B.A., and the duration of the