THE
British Medical Journal.

THE JOURNAL OF THE BRITISH MEDICAL ASSOCIATION.

LONDON: SATURDAY, JANUARY 3RD, 1914.

An Address
ON
RADIUM AND CANCER.

DELIVERED AT THE ANNUAL MEETING OF THE WEST SOMERSET
BRANCH OF THE BRITISH MEDICAL ASSOCIATION,
AT TAUNTON, ON DECEMBER 9TH.

(With Special Plate.)

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MR. PRESIDENT AND GENTLEMEN,—In speaking to you this afternoon upon the subject of radium and cancer, a subject chosen for me by your President, I desire to keep steadily before my mind two or three facts which make it imperative that I should speak with great reserve.

The first of these facts is that, familiar as we all are with the clinical manifestations and the gross and the minute morbid anatomy of malignant growths, we are still in ignorance of their exact pathology. Whether cancer is the result of an infection of the tissues by a bacterial or protozoal parasite, or whether it is the result of a disordered, irregular, uncontrolled cell growth, is not known. Much can be said in favour of each view, but we are still waiting for the actual demonstration that shall remove all doubts and clearly establish the nature of malignant growths. Although this is so, we can say with confidence that a malignant growth begins as a local disease, usually single, and that while tending to spread locally, it also has a special power of causing secondary growths in various parts of the body more or less remote from its primary seat. The cells of which it is composed are derived from, and are very closely analogous to, the cells of healthy tissues. These cells have an enormous power of multiplication but lack a corresponding power of organized and regular development and of functional value. As a general rule, the course of the disease is marked by a steady increase of the cancerous growth, often accompanied by ulceration—particularly of the primary seat of the disease—with increasing interference with the function of various organs, and to this may be added haemorrhages, the wearing effects of pain, later on toxæmia, and in some cases such disastrous consequences as starvation, obstruction, or paralysis. But one of the first facts brought home to any student of this disease is the extraordinary variation in its course, activity, and duration. It is the most protean of all diseases, so much so that it is almost impossible to make any statement about it to which exception may not be taken. Usually beginning in a single tiny focus, it may be multiple from the start; usually steadily enlarging, it may actually diminish in size while it develops; usually showing little power of organization or development, the malignant cells may organize into higher tissues so completely as to make it impossible for the skilled pathologist to recognize the signs of a malignant growth. I was recently consulted about a lady from whom a tumour of the upper end of the fibula had been excised; at the operation it fell on the floor with a resounding noise, and on microscopical examination only apparently normal bone could be detected, so that it was confidently pronounced to be an osteoma; and yet the operation was immediately followed by local recurrence, and the really

malignant nature of the growth was beyond all doubt. Of what form of cancer would one speak of pain as a more constant symptom than of epithelioma of the tongue? And yet a medical friend of mine died from a very extensive epithelioma of the tongue, the floor of the mouth and the cervical glands, and to the last was persistent that he had not suffered any pain. He never asked for, nor had given him, an anodyne, and he slept well without a narcotic. If we speak of the duration of the disease, we have to say that while some cases run their whole course in a few weeks, others extend over a greater number of years. And lastly, while we are all too familiar with the steady downward progress of this disease, there are undoubtedly a few cases which get well spontaneously.

If cancer is thus unknown in its exact nature, and extremely variable in its clinical course and manifestations, what can we say of radium? It is potent; it is wonderful; chemists place it among metals; the physicist can for a short while store its active emanations in liquid air, but it remains still one of Nature's mysteries, and its influence upon living tissues is unexplained and variable, and at present not within our control. Evidently, therefore, when we have to consider the action of unknown and variable radium upon unknown and very variable cancer, it is incumbent upon us to speak with great reserve, and to be constantly checking our observations with what is known of the natural history of the disease. I desire to emphasize this point most carefully, and I beg you to criticize all my statements most rigidly, and to remember that exact therapeutic knowledge can only be obtained when we have exact knowledge of the nature of a disease, and of the physiological action of the medicament.

With this by way of preface, let me now tell you what little I know of radium in its action on cancer, and something of what I have myself seen of its therapeutic uses.

There is no doubt that radium has power over the life-history of animal cells; it can increase or inhibit their rate of multiplication, and it can affect their vitality even to the point of destroying them. But this action is by no means uniform on all animal cells; it can influence certain cells more readily than others, and, speaking generally, it affects cancer cells more powerfully than normal tissue cells, and the cells of certain malignant growths more than those of others. It is upon this great fact that the therapeutic use of radium in cancer is based. Were all living cells influenced alike, by radium we should find it impossible to use it in any other way than we use the knife or caustic, as a means of removing a given area of tissue, in the hope that by so doing we should destroy all the living cancer cells present in the body.

The *selective power of radium*, as I may call it, enables us to use it to remove the cells of a malignant growth, and to leave behind the healthy tissues. It is true that in practice we sometimes come short of this ideal, both in the way of failure to remove all cancer cells, and also in the injury or destruction of other than cancer cells.

But the true therapeutic use of radium rests upon its *selective affinity for cancer cells, and not upon a general caustic or destructive power.*

It is akin to salvarsan with its wonderful selective affinity for the *Treponema pallidum*, and we can even think of it in the terms with which Professor Ehrlich has made us familiar. It follows that radium is not to be used in the treatment of cancer, like many drugs, as a palliative agent for the relief of pain or for the lessening of hæmorrhage or discharge—all of which it does—but as

a curative agent for the arrest of the life and activity of the cancer cell. This will all become clear if I mention to you certain cases, and I will take first the histories of two patients who have been good enough to come to Taunton to-day that you may see the results of radium treatment many months after its completion.

CASE I.—*Adeno-carcinoma.*

Mrs. M. A. H., aged 44, came to me on December 12th, 1911. Her history was that in 1906 a cystic adenoma of one ovary was removed, and that in 1908 a solid tumour of the remaining ovary was removed; this specimen was unfortunately lost before it had been examined. There was prolonged suppuration after the second operation, and healing was accompanied by the development of a solid lump in the abdominal wall. In November, 1911, the surgeon made an attempt to remove this, but found it quite impossible. A portion of the tumour was taken for microscopical examination, and was found to be adeno-carcinoma. When I saw her she looked ill, and there was a considerable tumour of the abdominal wall fixed to the pelvis, and over its centre was an irregular ulcer the size of the palm of one's hand. In each groin were firm enlarged glands. On two occasions she had full pastille doses of x rays, and after that (between the end of February, 1912, and January, 1913) she had five courses of radium-plate treatment, kindly carried out at the Radium Institute. As you see, Mrs. H. is now in robust health; she weighs nearly 3 st. more than when I first saw her. She is living a strenuous life, and shows no sign of her old malady, except the scars.

CASE II.—*Spindle-cell Periosteal Sarcoma.*

Mr. R. G., aged 18, was brought to me on May 4th, 1912, by Dr. Gower Bergin of Bristol. The history was that nine weeks before he had tripped over a peg, fell, and hurt his right knee, but went on running. Three weeks later he tripped on the stairs, and this time he had great pain in the same place. A week later he consulted Dr. Bergin because he still had pain, and walked with a slight limp. Dr. Bergin found a small lump, which he thought might be a haematoma in the rectus femoris muscle; he kept him in bed for a week, and applied iodine to the swelling. Since then very trifling jars to the limb had brought on pain in the same place, and the tumour had got decidedly larger. The patient was a healthy-looking youth. I found an elongated swelling on the front of the right femur just below its centre, with an abrupt upper edge, a less salient lower end; it was absolutely fixed to the bone, and apparently attached to about one-quarter of its circumference. The swelling was firm, without pulsation, slightly uneven on the surface, not tender. I could not detect any enlarged glands in the groin, nor any signs of enlargement of the liver or affection of the lungs. The knee could be fully extended, but could not be flexed beyond an angle of 120 degrees. Dr. Bergin brought with him a skiagram, which showed a shadow on the front of the femur, well defined and uniform in density (Fig. 1).

I diagnosed periosteal sarcoma of the femur, and it was decided to use radium rather than resort to

amputation through the hip-joint. On May 10th, 1912, I cut down on the tumour, which I found to be infiltrating the quadriceps muscle, excised a portion for microscopical examination, and then embedded in the tumour a tube containing 100 mg. of radium, very kindly lent by the Radium Institute. This was removed after twenty-three hours. On June 28th (six weeks later) I saw him again: the tumour was, I thought, a little smaller, with a less abrupt edge to it; it was certainly not larger. I repeated the operation, but this time found the tumour tissue to form only a thin layer under the muscle, with new bone beneath it. I introduced a tube of radium emanations, equivalent to 100 mg. of radium, into the tumour, and left it in for twenty-eight hours. There has been no further treatment. Since October, 1912, he has resumed his studies at Bristol University, and I have heard of him from time to time that he was "quite well."

Dr. Bergin has taken several skiagrams, which indicate diminution of the tumour, with progressive ossification (see Fig. 2). Mr. Gordon Taylor kindly prepared sections of the portion of the tumour removed on May 10th. It shows the structure of a typical spindle-cell sarcoma. Sections of the tumour removed on June 28th

show the cells to be degenerated and quite altered.

Mr. G. tells me to-day that beyond his right thigh being a little smaller than the left, he knows of no difference between the two limbs; he walks for long distances, cycles, plays all games except football and hockey, is quite free from pain, and has full use of the knee; he looks in robust health, and all that can be felt in the thigh is a slight thickening on the front of the femur at the site of the tumour. A skiagram taken this week shows a small bony thickening on the front of the femur (Fig. 3).

It is now nineteen months since the radium was first used, and when we remember the extreme malignancy of these cases—the great rapidity of growth and of the development of metastases—

the fact that the patient shows no signs of local activity or of metastasis warrants, I think, the hope that he is cured.

I will relate three other cases in which radium has proved strikingly beneficial.

CASE III.—*Large Tumour of Tonsil and Pharynx.*

M. L., aged 58, was admitted to the Cancer Charity of Middlesex Hospital on March 31st, 1913. Eight months before she had noticed a swelling on the right side of her neck. Four months later she discovered a swelling in her throat. In January, 1913, she attended the outpatient department of the hospital, and was told that she had a growth in the tonsil, and was advised to enter the Cancer Charity as it was inoperable.

On examining the pharynx, I found a globular growth attached to the right tonsil, the right pillar of the fauces, and the right side of the base of the tongue; it seemed to fill the pharynx, and reached across to the left tonsil. It was soft in consistence, and the mucous membrane covering it was congested, and in places superficially ulcerated. She was only able to swallow liquids, and that with difficulty; her breathing was frequent and difficult, and she had a distressed appearance. The

Fig. 4.—Photomicrograph of a section of the growth of the femur removed on May 10th, 1912. Case II, Mr. R. G.

FIG. 1.—Skiagram of Case II, Mr. R. G., taken in 1912 before treatment, showing the faint shadow of the sarcoma on the anterior surface of the femur.

FIG. 2.—Skiagram of Case II, Mr. R. G., taken in December, 1912, showing the shadow of the ossified sarcoma.

FIG. 3.—Skiagram of Case II, Mr. R. G., taken December, 1913, showing only a slight bony thickening of the femur at the site of the former sarcoma.

movements of the tongue were limited: its tip could be pushed up to, but not beyond, the incisor teeth. There was a firm, enlarged gland behind the angle of the jaw on the right side; none could be felt lower down the neck, nor was there other evidence of secondary growth.

On April 29th a tube containing 82 mg. of radium was inserted into the centre of the growth through the mouth. This remained in place for twelve and a half hours, and then came out. It was reintroduced next day for a further twelve hours.

On May 14th it was noticed that the growth was smaller, and that there was no difficulty in deglutition; the movements of the tongue were still limited. Three days later it was noted that the tongue could be protruded nearly an inch beyond the teeth. The tumour continued to shrink rapidly, and on June 22nd, eight weeks from the introduction of the radium, I made the following note:

There is now no sign of the growth in the tonsil or pharynx, and the glands behind the mandible can no longer be felt. The patient swallows solid food easily, and has no functional defect. Her general health is good. I am, therefore, discharging her from the Cancer Charity.

This patient has attended the cancer out-patient department from time to time, and I saw her there less than a week ago. The pharynx remains quite sound, and the woman feels well and is back at her work; but there is now an enlarged gland beneath the middle of the right sterno-mastoid muscle; this I intend to excise within the next few days.

CASE IV.—*Encephaloid Carcinoma of Testicle.*

Mr. P., a man 30 years of age, was brought to me by Dr. Crawford Aitken, of Carlisle, on July 23rd, 1912, with a tumour of the left testicle. I agreed with Dr. Aitken that it was a malignant growth, and advised its immediate removal. This was done the same month by the late Mr. Jordan Lloyd, who excised the testicle and cord, and carried the dissection up along the retroperitoneal tissues as far as the renal vessels. The tumour was found to be encephaloid carcinoma; the patient made a good recovery.

In September, 1913, Dr. Aitken wrote to say that Mr. P. was very ill, that he had a considerable swelling in the upper left abdomen, and was losing flesh and strength. On October 3rd he brought him to see me. Mr. P. was then very pale, thin, with sunken eyes; he complained of nausea, and of entire loss of appetite; his tongue was thickly furred, and he suffered a good deal of pain, which prevented sleep; he was entirely unable to work, and walked with difficulty. He had a tumour which occupied the left hypochondriac region, projected the abdominal wall below the false ribs, and reached from just to the right of the middle line into the left loin. The tumour was immovably fixed to the spine, was solid, and, of course, dull on percussion. The pulse was 104; I could not discover any signs of other metastases.

I regarded the case as an exceedingly unfavourable one, but consented to try the effects of radium; so on October 9th an incision was made into the abdomen, the colon was separated from the stomach sufficiently to expose the tumour, which was found to be dark in colour, and of the size already stated. Two tubes of radium emanations of 50 mg. each were inserted into it for twenty-four hours. There was speedy improvement in the patient's pain, then he lost his nausea: in ten days we noticed that the tumour was smaller. On October 31st he left the nursing home and went to Bournemouth, and at that time we could not feel any trace of the tumour. His weight was then 8 st. 10 lb. On Friday last, December 5th, he returned home from Bournemouth, and I saw him as he passed through London. He had all the appearance of a healthy man, he had gained flesh, and weighed 9 st. 8 lb., had a very fair colour, could walk five miles at a time, had a good appetite and normal digestion, and on careful examination of his abdomen I could not detect the least sign of the tumour, nor could I find any enlarged glands or signs of metastasis anywhere.

CASE V.—*Malignant Disease of Naso-pharynx.*

On November 11th I was asked to see, with Mr. Marriage and Dr. Rose, a young man, J. T., 18 years of age, who had a growth on the left side of his naso-pharynx, and glands about the size of a hen's egg beneath the upper end of the left sterno-mastoid muscle. He was deaf in the left ear, and had obstruction in the left nasal fossa. We decided to remove the

glands in the neck, and at the same time to explore the naso-pharynx while he was under the anaesthetic. On November 13th this was done. We felt a firm growth occupying the left side of the naso-pharynx, and involving the Eustachian tube, and Mr. Marriage removed a portion of it for microscopical examination; at the same time I excised the glands in the neck. The parts removed were submitted to three pathologists, all of whom reported them as undoubtedly malignant, though there was difference of opinion as to the exact classification of the malignant growth.

On November 19th 100 mg. of radium screened in a metal tube and inserted into a rubber catheter was passed along the nasal fossa into the naso-pharynx, and left in place for eight hours. We saw this patient yesterday (Monday, December 8th)—less than three weeks after the use of the radium, and he told us that on the tenth day he felt a sudden opening of the Eustachian tube, and that from that date began to recover his hearing, which is now practically perfect. There is an entire absence of all obstruction in the nasal fossa.

We examined the naso-pharynx with the finger while the patient was under chloroform, and were unable to feel any sign of the growth which we had felt three weeks before. The only difference between the two sides was that the trumpet end of the left Eustachian tube was just a trifle fuller on the left side than on the right. There was no sign of enlargement of glands in the neck.

These cases are sufficient to illustrate the two results of the treatment of cancer by radium that in my opinion are to be desired—the gradual removal of the growth without sloughing, and the removal of the tumour without injury to the healthy tissues. They show the “selective action” of the radium on malignant cells, its power to inhibit their growth more quickly than that of healthy cells. The cases also show the much more rapid and satisfactory effects of radium when introduced into a tumour than when it is applied as a plate on the surface of the body. A good deal of radium has been and is being wasted—in the sense of not being used to its greatest advantage—by being made into radium plates instead of placed in thin metal tubes. Further, these cases illustrate what was known long before its recent dramatic announcement in the lay press—that radium emanations are as efficient as the pure salt of radium itself. I could relate many other cases in which I have seen evidence of the power of radium to arrest and to remove malignant growths. These cases include cancer of the tongue, lip, maxilla, mandible, breast, chest wall, glands, rectum, muscles, and fascia; some of these I have already published.

DANGERS OF THE RADIUM TREATMENT OF CANCER.

I will, however, devote the time remaining to me to a consideration of some of the dangers and limitations of the radium treatment of cancer. Let me first of all deal with its dangers.

Danger to the Operator.

You will not misunderstand me if in the first place I refer to the danger to the worker with radium. I know one who has definite changes in the skin of his fingertips, and in view of the many disasters that have occurred to x-ray experts, I make no apology for uttering a warning against the careless handling of tubes of radium.

Sloughing.

The first danger to the patient is sloughing. This I have seen in two or three forms. Thus, I saw last week a woman who came to me with a very large inoperable recurrence of a fibro-sarcoma of the leg, which had been twice removed by operation. I have introduced tubes of radium into this tumour on several occasions, and the circumference of the leg has been reduced by $3\frac{1}{2}$ in., and the patient has lost her pain. But at the site of one of the punctures there is now an ulcer as large as a shilling, with a sloughy base. Again, I have under my care a woman who had a large infiltrating mass filling the right iliac fossa and bulging forwards the abdominal wall, into which it extended—a tumour as large as a good-sized melon. I have treated this with radium, and all that is left is a very slight thickening of the abdominal wall, close to the fold of the groin; for six months she had a very painful sloughing indolent ulcer at the seat of the introduction of one of the radium tubes. I am glad to say that

now the ulcer is no longer painful and is healing. These are examples of *superficial radium burns*.

Another form of sloughing occurred in a woman in one of my cancer beds, who had an inoperable and growing cancer of the ovary, forming a considerable abdominal tumour. I put in a tube of radium on three occasions, each time with apparent benefit in the form of lessened pain and diminution in the size of the tumour. But an ulcer formed at the site of the second tube, and through this liquid faecal matter escaped, and the faecal fistula hurried on the fatal end. The radium had "burnt" into an adjacent—probably adherent—coil of small intestine. The same accident happened in another case in the hospital under one of my colleagues. In that case he put a tube of radium into a tumour in the right iliac fossa, which also involved the abdominal wall. A faecal fistula formed and persists, though the tumour is very much reduced in size, and the patient, a member of our profession, is able to get about.

A third form of this sloughing effect is illustrated in a case now in the Middlesex Hospital Cancer Charity. This woman had a large secondary scirrhous carcinoma adherent to the sternum and the ribs on the left side. I treated her first by a single tube of radium, and she was later on admitted to the hospital for further radium treatment, and, owing to a misunderstanding, three tubes of radium, amounting in all to 144 mg., were introduced into the centre of the mass, with the result that this central part quickly sloughed. The slough has now separated leaving a large ulcer, but no beneficial effect has been produced on the surrounding growth. It seems to be an example of a too intense action over a limited area, which is not compensated for by a less intense and beneficent action of the radium outside this area. I regard this as a regrettable accident, and not as an illustration of one of the proper ways of using radium.

Thrombosis.

Another danger is the production of thrombosis. In a case in Middlesex Hospital a tube of radium was passed into a tumour in the right iliac region. Unhappily the patient became very ill, jaundice set in, and death occurred in about forty-eight hours. At the necropsy it was found that thrombosis had occurred in the external iliac vein, and had extended along the vena cava into the right auricle of the heart and into the hepatic veins. I have on more than one occasion put radium into a cancerous gland above the clavicle, fortunately without accident, but I am afraid that it has not been without risk of thrombosis in the jugular, subclavian, or innominate veins.

Haemorrhage.

Another danger is that of haemorrhage. The introduction of a tube of radium into a very vascular growth may be attended with free haemorrhage at the time. This has occurred to me twice—once when I passed a tube into a malignant growth of the thyroid gland, and once in passing a tube into a large fibro-sarcoma of the calf. On each occasion firm pressure over the puncture quickly arrested it. I know of a case where, three days after the introduction of a tube of radium into a growth in the abdomen, there was very free, and even alarming, haemorrhage. The action of radium upon vessels should make us cautious about introducing it into growths close to large arteries or veins. In a case to which I shall presently refer, where I was asked about the use of radium in a case of malignant disease of the pancreas and liver, one of the reasons I gave against the suggestion was that the radium would of necessity be in close proximity to many large and important vessels.

Constitutional Reaction.

The introduction of radium into a tumour is often quickly followed by a slight constitutional reaction—moderate rise of temperature for a day or two; I have known this to develop to quite a dangerous extent—to high fever, very rapid pulse, and jaundice—a condition which obviously threatened life.

THE LIMITATIONS OF THE TREATMENT OF CANCER BY RADIUM.

Inaccessibility.

The first limitation arises from the inaccessibility of many malignant growths, such as cancer of the liver, secondary growths in the spine, etc. I mention these

with some reserve, because, if with more experience we gain greater confidence in the value of radium in the treatment of cancer, we may discover safe means of carrying so beneficent an agent into the most inaccessible regions of the body.

Nature of the Part Affected.

The second limitation arises from the nature of the part affected—for example, the intestine, the stomach, or the bladder. I was recently asked if I thought radium should be introduced into a large mass caused by an inoperable cancer of the caecum, and I replied, "No, because I do not see how it is possible to remove the disease and to leave an intact bowel." The only possibilities of good that occurred to me were: "If radium could so perfectly remove the disease, at the expense of the formation of a fistula, that the surgeon could then excise the affected portion and unite the severed ends of the bowel; or (2) that after a short-circuiting operation the area of disease could be isolated, then treated by radium, and a final less severe operation done to close the remaining wound. At present our experience with radium and its less satisfactory effect on mucous membrane does not, I fear, warrant its use in this way, but more knowledge may give us the power to do something of the kind. The same conditions apply to cancer in the stomach and bladder.

Metastases.

A third limitation in the use of radium arises from the spread of malignant disease in the body and to the presence of metastases. I was recently asked whether I could advise the use of radium for a case of inoperable cancer of the pancreas, with secondary deposits in the liver—I had to say "No." So far as our present knowledge goes I can see no hope of using radium successfully in such a case, nor for such cases as melanotic sarcoma with numerous secondary growths, nor for the late stages of cancer of the breast with metastases in bones, liver, pleura, and many glands.

I believe that what is known as radium water is sometimes prescribed as a beverage with the idea that it may affect beneficially internal and widely diffused malignant growths. It is not for me to criticize the prescriptions of others, but I should certainly consider myself guilty of charlatanism if, with my present knowledge, I ordered radium water for any such purpose. I know of no evidence to justify it.

The Extent of the Influence of Radium on Cancer.

The question of the area over which radium produces a curative influence on malignant growths is a very important one and cannot be summarily dismissed. In the first place, we must remember that it is not unknown for the removal of a primary malignant growth to be followed by the disappearance, or the very long quiescence, of secondary growths. The most striking instances are afforded by operations upon *deciduoma malignum* and upon papilliferous ovarian cysts. I have known it to happen in cancer of the breast, and I have in the hospital just now an interesting example in a case of carcinoma of the maxilla. The patient came in with a tumour in the left maxilla and a definitely enlarged gland beneath the mandible. I excised the maxilla, and intended to dissect out the glands in the neck a few days later. When I examined the neck before this second operation I was unable to feel the gland which before had been quite obvious. I nevertheless carried out the operation upon the neck, and sent the parts removed to the pathologist for examination, and his report was that more than one of the glands removed showed carcinomatous growth.

So far as I have had the opportunity of studying the effects of radium on cancer up to the present, the extent of its influence has appeared to be very variable and often quite limited. I have already mentioned a case of growth in the right tonsil, where radium removed the primary growth, and, apparently, the growth in the adjacent gland, but there is now quite certainly growth in another gland lower down in the neck. I have seen other cases where the diseased glands have been quite unaffected by the successful use of radium for growths close by. In a case of squamous epithelioma of the left maxilla which was removed quite quickly by radium, a secondary growth in the neck was wholly unaffected and had to be excised.

I recently had a case of secondary carcinoma of the chest wall, consisting of an ulcerated growth adherent to the sternum, with a small nodule in the skin about half an inch away. A tube of radium emanations inserted into the larger growth was followed by a healing of the ulcer, and the entire disappearance of the malignant induration beneath and around it, but the little separate nodule of growth was quite unaffected, and continued slowly to enlarge. In this case the influence of radium would appear to have been very limited in range.

Then, again, I have seen the introduction of radium into a carcinoma of the chest wall, for instance, followed by healing of an ulcerated surface and the removal of the more superficial part of the growth, while a deep layer of firm growth has been left behind and required the further use of radium. This limitation of its influence is also seen sometimes in the disappearance of an area of tumour tissue immediately around the tube of radium, without any apparent benefit to the growth further away. And yet, in another case, even a large tumour may disappear after the insertion of radium into it at one spot, as in the instance of Mr. P. (Case iv).

There is, moreover, variation in the time during which beneficial effects are seen. In most cases the good effect is seen soon, and is not observed to increase after a few weeks. In others it seems to continue for many weeks; that is to say, in some cases the diminution of the tumour is quickly at an end, in others it goes on for a very long time. But in this matter we must be careful to distinguish between two separate processes—(1) the arrest of the growth of the cancer cells, (2) the removal of the inhibited or dead cancer tissue. The first is largely, possibly wholly, due to the radium, the second may be independent of the radium—we do not know this—and will certainly vary in rapidity with the proportion of fibrous tissue and other more highly organized tissue to the cellular elements. Arrest of growth is the surest measure of the beneficial influence of radium; the removal of the morbid tissue is a matter of secondary importance.

Variations in the Reaction to the Same Dose of Radium.

Very directly connected, therefore, with this is another of the limitations in the use of radium—the great variation in the reaction to the same dose of radium. This is the most trying circumstance connected with its use. One of my early experiences with radium was the case of an elderly gentleman who had a very extensive papillary squamous epithelioma of the hard and soft palate on the right side, and extending down along the wall of the pharynx below the opening of the larynx. It was treated by a tube of radium introduced into the mouth. The first application was followed by the complete destruction of the lower half of the growth, but the part in the mouth, which was actually closer to the tube of radium, was entirely unaffected by it, and although the application of the radium was repeated, it was never affected at all, and the patient died of his disease.

I have seen cases of scirrhus of the breast remain quite unaltered after the introduction of a tube of radium into them, while others that I could not distinguish clinically from the first, have rapidly melted away under the influence of the same tube of radium. Then, again, cancer affecting mucous membrane appears to be less amenable to radium treatment than cancer of adjacent skin. This is frequently exemplified in the treatment of cases of rodent ulcer by radium. As a class, sarcomata have been more amenable than carcinomata, and the softer growths than the firmer ones, but exceptions to this rule are seen. Thus, several cases of firm scirrhus lumps of the chest wall, secondary to cancer of the breast, have disappeared quite rapidly when a tube of radium was passed into them, and I recently had a patient whose rectum I had excised, and who came back with a firm flat recurrence on one side of the anus that could have been just covered with a florin. A fortnight after the introduction of a tube of radium beneath this disc-like growth I failed to find any trace of it whatever.

On the other hand, I have a patient with a very soft tumour of the maxilla, into which I have twice introduced radium with little, if any, observable benefit.

I must also mention that some cases seem to be made actually worse by the use of radium. This was strikingly

exemplified for me in a man who was under my care for epithelioma of the pinna and parotid region. The introduction of radium into this growth was immediately followed by the much more rapid extension of the growth, and a speedy downward course.

Painful and Persistent Local Reaction.

I must specially mention the painful and often persistent local reaction that sometimes follows the use of radium. This is particularly the case when the radium is used in the rectum; sometimes it happens when introduced into the vagina. The pain caused by the radium may last for many weeks, and add considerably to the patient's distress.

I have made no reference to-day to the effects of radium in uterine cancer, where relief of pain, cessation of haemorrhage, and lessening of discharge frequently result from the introduction of the radium into the malignant mass, even if the disease be not cured. I cannot now deal with the very important practical point of the amount of filtration or screening that it is best to use. This is a matter on which we need a good deal more light.

Ought Radium to be Used as an Alternative to Operation?

Two important questions remain for consideration. The first is: Ought we to use radium for the treatment of cases of malignant disease which we believe can be satisfactorily dealt with by operation—for example, cases of early scirrhus of the breast? I would answer that question with considerable reserve, remembering that we are only on the threshold of our experience and knowledge of this subject; but, so far, I have not felt it right to do so, and for these reasons: Experience tells us that even in a very early carcinoma of the breast there may be secondary growths commencing in the axillary glands or in lymphatics a little remote from the primary growth, though nothing of the kind can be detected by the most careful clinical examination. We do not yet know that even if radium deals satisfactorily with the primary growth it would prevent the usual developments of these metastases, while we do know that a careful and wide operation affords a very good prospect of setting our patient free from the disease. The case, however, is very different when the operative treatment of the disease has proved very far from satisfactory, and of such I would mention particularly periosteal sarcoma of the femur, melanotic sarcoma, and some pharyngeal and laryngeal growths. The success which attended the use of radium in the case of sarcoma of the femur which I treated nineteen months ago (Case II), the subject of which is here this afternoon, has emboldened me to advise radium rather than amputation at the hip-joint in three other cases of a like nature, which I will just mention quite briefly.

CASE VI.—Periosteal Sarcoma.

A girl, S. M., aged 16, was admitted to Middlesox Hospital under my colleague, Dr. Pasteur, in June, 1913, supposed to be suffering from rheumatic fever. She was transferred to my ward on July 3rd, as it was evident that she had a periosteal sarcoma of the left femur. There was a tender swelling of the bone on the front and inner side of the knee, immediately above the epiphysis, and this was the seat of constant and severe pain. There was no pulsation or sense of yielding. A skiagram showed the bone intact and the shadow of a tumour attached to it.

On July 5th I cut down on the tumour, cut out a piece, and then buried in the tumour three tubes, containing in all 144 mg. of radium, which were left in place for twenty-four hours. The pain immediately lessened, and in two or three days was gone. The tumour not only ceased to grow, but became smaller, and its x-ray shadow at the same time became denser.

On July 26th I repeated the operation, cut out a piece of the growth, and put in 60 mg. of radium for another twenty-four hours. I have seen her from time to time since. The swelling on the inner side of the bone has flattened down to a condition of only slight thickening of the bone. Last month she complained of pain on the outer side of the bone, and I found a swelling there, so on November 9th I had 144 mg. of radium introduced there. At this operation a thin layer of sarcomatous tissue was found over the bone. I saw her on November 25th, and she was then free from pain, and I could

not identify any swelling on the outer side. The tumour when first removed was seen to be a mixed-cell sarcoma with many mitotic figures. On the second occasion, only three weeks later, the tumour was harder, and on section was found to be largely ossified and much less vascular than before. Islands of cartilages were seen embedded in small masses of fibrous tissue; there was no evidence of malignant disease. This girl has now been under observation for five months, and the original tumour, instead of being larger, has almost, if not wholly, disappeared.

CASE VII.—*Periosteal Sarcoma.*

G. P., aged 16, was brought to me by his father on November 15th. On October 12th he was knocked down at football and then accidentally kicked on the inner side of his right knee. I saw him just five weeks after his accident. He walked into my room very lame, leaning hard upon his father, with his right knee bent at an angle of 140 degrees. I found a prominent swelling on the inner side of the knee, about the size of an apple, fixed to the femur, with an abrupt, well-defined upper edge. It was solid, without pulsation, a little tender. The skin over it was neither reddened, hot, nor oedematous. The muscles of the thigh were much wasted; the femoral glands were not enlarged. In this case excellent skiagrams were taken; they showed no shadow, the outline of the femur was perfect, but there was one tiny defect in the bone about $\frac{1}{2}$ in. below the surface. I diagnosed a periosteal sarcoma, and advised treatment by radium rather than immediate amputation at the hip-joint.

On November 20th, 1913, I operated, and found the tumour unattached to the muscle over it, and covered by a thin capsule. I cut out a piece of it, and then buried in the tumour for twenty-four hours 100 mg. of radium. I last saw this patient on December 9th, nearly three weeks later. There was some little fluid in the joint, but the swelling was very definitely smaller, and has lost all definite outline; the boy declares that since the operation he has had none of the old pain, and he wants to get up and walk. There is, at any rate, good reason to hope for success in this case, but it is too early to speak with assurance. The tumour in this case is a spindle cell sarcoma with considerable chondrification.

CASE VIII.—*Periosteal Sarcoma.*

My fourth case of femoral sarcoma was brought to me only last week, on December 4th, by Dr. Millar, of Streatham. The patient was a single woman, 30 years of age, who noticed a swelling on the inner side of the left knee five weeks before; beyond that we could not get any history. She walked without a limp, and had practically no pain or disability. There was a prominent tumour on the inner side of the left femur, immediately above the epiphysis. It was firm in consistence, immovably fixed to the bone, measuring nearly 5 in. by $3\frac{1}{2}$ in. The skiagram showed a faint shadow, and the femur intact. I diagnosed a periosteal sarcoma, and advised the use of radium.

On December 6th I cut down on the tumour, found it attached to the bone and infiltrating the muscle, and after removing a bit for microscopic examination, buried a tube of 100 mg. of radium in it for twenty-four hours. Examination of the piece of tumour removed showed it to be a spindle-cell sarcoma.

These cases are incomplete, and I have not put them therefore, alongside of the cases which I mentioned in the earlier part of this paper. I am mentioning them now merely as examples of a class of case in which the choice lay between an extensive and notoriously unsatisfactory operation and the use of radium, and in which I decided to try radium rather than at once resort to the operation.

I have under my care just now a case of melanotic sarcoma of the heel where I have introduced radium into the primary growth, and excised the glands in the groin. As we all know, the operative treatment for melanotic sarcoma has been extremely unsatisfactory. I have also spoken of a case of naso-pharyngeal cancer treated by radium.

Our practice in this matter can only be based upon much longer and wider experience of the use of radium than we have at present. We must "wait and see."

Prophylactic Use of Radium.

The other question is whether, after operating for cancer, we ought to use radium as a prophylactic measure to prevent recurrence. I do not see my way to do this.

In the first place, we do not know where the supposed cancer cells are lurking, and, as I have already said, we have at present no clear evidence that the selective effect of radium on cancer cells is exercised over a wide area. But we do know that radium can produce such active cell growth as will end in cancer. Further, when operating for cancer, I like to approach the case with the conviction that if the operation is well planned and carefully carried out it will succeed in freeing the patient from the whole of his disease. I fear it will have a paralysing effect upon the surgeon in his operation if he is feeling that, after all, he is leaving cancer cells behind, and will use radium in the wound to prevent their further activity. If we operate, let us have faith in the efficiency of our operation. Still, in this as in other matters, I wish to preserve an open mind, and to accept any new light that comes.

In bringing these remarks to a close I think I am justified in stating that the cases I have been able to relate to you to-day from my own experience warrant me in saying that in radium we have an agent that in many cases can be used in the treatment of cancer with great hope of success, and that the selective action upon cancer cells marks it out from all other known remedies for this disease; but this same experience also shows that it would be a gross exaggeration to speak glibly of radium as the "cure for cancer" in the sense that it will deal with any and every case of this disease. Such is not the case, as we use it at present; but remembering what I started with as a preface to this paper—that on the one hand the nature of cancer is unknown and most variable in its manifestations, and on the other hand that radium is almost the youngest of the known chemical elements, and has been studied but for a few years, and by relatively few investigators—there is good ground for hope that in the time, which will surely come, when we shall unravel the secret of the nature of cancer and know more of the properties of radium, and how to use them better and to control them, we shall have a great extension of the therapeutic value of radium in cancer.

A Clinical Lecture

ON

THE TRIPLE SYNDROME IN ABDOMINAL EMERGENCIES.

DELIVERED AT

THE ROYAL VICTORIA INFIRMARY, NEWCASTLE-ON-TYNE,
NOVEMBER 13TH, 1913.*

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It is important, probably of greater practical importance than anything else in medicine and surgery, to know the meaning of an abdominal pain. Such pains are of so common occurrence, especially in children, that most old women seem to think "a dose of castor oil and a hot bottle" are sufficient treatment, and that a diagnosis as to the cause is unnecessary. This is almost as bad teaching as that of those surgeons who say a "diagnosis is impossible, open the abdomen and see"—for both may result in more harm than good.

Those of you who have accompanied me round the wards know that in abdominal emergency cases I expect from my house-surgeon a carefully-taken history, followed by a description of the physical signs, his diagnosis in detail before operation, and a description of the pathological findings after operation to compare with this. By a diagnosis in detail, taking appendicitis as an example, I mean that he shall foretell the position of the appendix, the pathological condition of it and of the peritoneum, and offer an estimate of the vital resistance of the patient. Nothing has interested me more than to note the quickly-acquired and improved diagnostic capacity of a zealous and enthusiastic house-surgeon subject to these apparently exacting demands, for at the termination of his six

*This lecture was delivered also at a scientific meeting of the British Medical Association held on November 20th, 1913.