

## A CASE OF CARCINOMA UTERI BENEFITED BY RADIUM EMANATION.

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On Friday, October 2, 1914, I had the good fortune to be present at a lecture on radium delivered by Professor John Joly, Sc.D., F.R.S., to Post-Graduate Students of Medicine in the School of Physic in Ireland, Trinity College, Dublin. That discourse was intensely interesting and most instructive. It was published in the number of the *Dublin Journal of Medical Science* for November, 1914 (Vol. 138, No. 515, Third Series, page 321).

After hearing Professor Joly's lecture I felt bound to ascertain whether radium therapy might not benefit a female patient who had been under my care in the Meath Hospital from September 24, 1914. She was suffering from malignant disease of the womb and neighbouring parts, and her case had been declared to be inoperable by my colleague, Dr. Frederick W. Kidd, Gynæcologist to the Hospital.

Accordingly, I spoke to Professor Joly on the subject. He referred me to Dr. Walter Stevenson, who kindly visited the patient with me, and, after examination, arranged to give radium therapy a fair trial in the hope that it would relieve the poor woman's suffering.

CASE.—Mrs. Ellen H., aged sixty-five years, wife of a sergeant in the Royal Irish Constabulary, was admitted to the

Meath Hospital on Thursday, September 24, 1914. She stated that she had enjoyed good health up to the middle of last June, when she was suddenly attacked by a profuse bleeding from the womb. This was soon followed by agonising pain in the lower part of the belly and about the private parts. She lost her appetite, had a bad taste in her mouth, and rapidly lost flesh and strength. When admitted, she was much wasted and very bloodless, and presented the aspect of one who had gone through much and long-continued suffering. She was of medium height, and weighed 6 stones 13 lbs. On admission the pulse-rate was 120 per minute, respirations 28, and temperature subnormal (96° F.). The bowels were constipated. The right side of the abdomen was prominent, and a tumour could be felt on palpation in the right iliac fossa. The urine, examined on September 28, was pale, faintly acid, and of rather low specific gravity. It contained some albumen, was turbid from the presence of both phosphates and pus and threw down a deposit which became viscid on the addition of liquor potassæ.

To relieve irritability of the stomach, flatulence and pain, a mixture was prescribed containing solution of citrate of bismuth and ammonium, bicarbonate of sodium, tincture of nux vomica, and compound tincture of chloroform and morphine—the last-named in only 4-minim doses thrice daily. In consequence of loss of sleep through pain a hypodermic injection of morphine and atropine was given at night as required.

On October 6, my colleague, Dr. F. W. Kidd, examined the patient very thoroughly. He found the uterus and adnexa extensively involved in a new growth, which seemed already to have invaded the posterior wall of the bladder. The new growth was extremely vascular, and was partly disintegrating. Dr. Kidd's opinion was that the condition of the parts precluded operative interference.

In view of this unfavourable opinion, and with a strong desire to relieve the patient in some way, I asked Pro-

fessor Joly about the feasibility of treating the case by radium emanation. At his suggestion, I conferred with Dr. Stevenson, who had been getting good results from radium therapy in various cases of superficial new growths. Dr. Stevenson very kindly visited the patient in the Meath Hospital, and on Friday, October 23, inserted six radium needles, each carrying an initial charge of 4 millicuries, into the growth. They were left *in situ* for twenty-four hours. There was scarcely any constitutional disturbance or reaction—for the three following evenings the axillary temperatures were  $99.4^{\circ}$ ,  $99.0^{\circ}$ , and  $99.3^{\circ}$  respectively. The needles were inserted into the posterior lip of the cervix uteri in the first instance—that being the most difficult part to reach—then into the anterior lip, and finally into the left vaginal wall. The needles were inserted for the second time on the afternoon of October 28, and their position was changed on each of the three succeeding days. They were removed on November 1. In connection with this second *séance* there was a somewhat decided constitutional reaction, the evening temperatures being  $99.4^{\circ}$  on October 29,  $101.0^{\circ}$  on the 30th,  $101.2^{\circ}$  on the 31st, and  $100.5^{\circ}$  on November 1. From the last-named date the temperature range became, if anything, subnormal, coincidentally with a certain looseness of the bowels, which in turn was followed by improved appetite. The patient also was freer from pain, slept better, lost the haggard, dragged look which she had previously worn, and began to regain colour. This last change seemed to depend on a cessation of the bleeding which had been almost constant during October.

An interval of four weeks was now allowed to elapse before the third insertion of the needles, which took place on November 27. The position of the needles was

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changed next day, and again on November 30, and they were removed on December 1. A longer-continued but less active febrile disturbance followed, but the highest reading of the clinical thermometer was only 100.4°.

Mrs. H. felt so much better after this third application that she consented to a fourth instalment of the treatment only after much persuasion. The needles were inserted for the fourth and last time on Christmas Eve. They were removed and re-inserted on Christmas Day, and again on December 27, and were finally removed on December 29. An irregular subfebrile temperature followed, lasting till January 6, when the body temperature became subnormal for a week. The patient left hospital for her home in the County Kildare on January 17, driving off in state in a taxi provided for the occasion by her sons.

I have already stated that the new growth became much less vascular as the treatment went on. This is confirmed by Dr. Stevenson, who tells me that the first insertion of the needles was followed by free hæmorrhage, but that later on there was less and less bleeding after their insertion.

The average amount of radium emanation introduced from each needle was estimated by Dr. Stevenson at three and a half millicuries—the initial strength of four millicuries ebbing quickly from day to day. He has very kindly furnished me with the following technical details as to the radium treatment :—

Mrs. H., from October 23 to December 29, 1914 (sixty-seven days), was under treatment by an average of twenty millicuries for thirteen and a half days. During all this time she had six old capillaries in a little metal case inserted into the cervical canal. They contained an average

of 4.17 millicuries. She received altogether 6602 milligramme hours of radiation. Six needles were inserted eleven times, twenty-four each into the anterior and posterior lip of the cervix and fornix and eighteen into the vaginal wall. Posterior fornix and lip of cervix, treated for four days twenty-one hours, received 1872 milligramme hours—average 16 millicuries. Anterior fornix and lip of cervix, treated for six days twelve hours, received 2162 milligramme hours—average 13.8 millicuries. Vagina, treated for four days four hours, received 1218 milligramme hours—average 8.1 millicuries. Cervical canal and uterus, treated for thirteen days six hours, received 1350 milligramme hours—average 4.1 millicuries per hour.

The constitutional febrile disturbance which followed the various *séances* is noteworthy. Dr. Stevenson suggests that the rapid disintegration of the cells of the new growth and the absorption of the resulting *débris* may account for this.

Dr. Kidd has kindly furnished me with the following note as to the condition of the patient before and after the radium treatment:—

“I was afforded the opportunity of making a pelvic examination in the case of Mrs. Ellen H. One examination was made before any treatment had been adopted, and on that occasion, even with the greatest care, the examination was followed by profuse hæmorrhage. I arrived at the conclusion that the case was inoperable as infiltration had taken place on both vaginal walls, and the posterior wall of the bladder seemed to be implicated along with the vesico-vaginal septum. I made a second examination after Dr. Stevenson had inserted the radium needles and certainly found a marked improvement. The infiltration seemed much diminished and the examination

was conducted very thoroughly without being accompanied or followed by any hæmorrhage whatever.”

In the Thirteenth Report from the Cancer Research Laboratories, published in the thirty-third volume of the *Archives of the Middlesex Hospital*,<sup>a</sup> will be found a paper by A. Clifford Morson on “The Changes which occur in Malignant Tumours on Exposure to the Gamma Rays of Radium.” This paper originally appeared in the “Proceedings of the Royal Society of Medicine” (1914, Vol. vii., Pathological Section. Pp. 97-108). I quote Mr. Morson at some length, as his observations throw such a light on the happenings in my patient’s case. Mr. Morson writes :—

“For some months I have been carrying out an investigation into the changes which take place in the cells of malignant growths when exposed to the gamma-rays of radium. The procedure which I have adopted in this investigation is as follows :—A small portion of the growth is removed before exposure to these rays for the purpose of comparison between the radiated and the non-radiated cancer cell. On removal of the tube of radium, which in every case was embedded in the tumour for periods varying from fifteen to twenty-four hours, that part of the growth in actual contact with the tube of radium was excised. Further portions of the tumour were removed for microscopical examination at intervals of forty-eight hours to two months.

“The tissues submitted to the action of the gamma rays when removed by the scalpel appeared to be completely insensitive, and it was not found necessary to make use of either general or local anæsthesia in performing the operation. I have had personal experience of the anæsthesia

<sup>a</sup> London : Macmillan & Co., Dec., 1914.

produced by the gamma rays, for last July, as a result of handling radium daily over a period of two months, changes occurred in the skin of the forefinger and thumb of my right hand, which caused a temporary loss of tactile sensation, but marked sensibility to heat and cold.

“ Within fifteen hours of the commencement of radiation the malignant cells in the immediate vicinity of the tube of radium begin to degenerate. The nuclei become irregular in shape, and in places are broken up into two or more fragments. Twenty-four hours later all that can be seen is a structureless mass, embedded in which are a number of cells in various stages of degeneration. In the region of the growth where the intensity of the rays is less the cells may also be seen to be altered. Their normal arrangement is lost and the malignant mass is broken up into isolated groups of cells.

“ In some microscopic sections a definite line of demarcation has been seen between fully degenerated cells and the relatively unaltered malignant cells. It is possible that this observation may assist in determining the radius of action of a known quantity of radium, when inserted into a growth whose microscopic characters have been previously investigated. If, three days following radiation, a part of what remains of the growth be removed, further changes will be noted. The connective tissue cells have commenced to proliferate, and those malignant cells which have escaped immediate death show apparent vacuolation with greatly enlarged nuclei.

“ In a considerable number of cases, within fourteen days of the application of the radium, absence of cancer cells can be demonstrated. On the other hand, some growths appear more resistant to the action of the gamma-rays, and if microscopic examination be made as long as

two months after radiation, malignant cells will be detected, though changed from the normal. The cells show a peculiar vacuolated appearance, with swollen nuclei. Around the malignant cells will be observed dense fibrous tissue."

The radium emanations used in the treatment of my patient were obtained from the Royal Dublin Society's stock of radium from which the needles are charged under the skilful and skilled supervision of Mr. R. J. Moss.

In conclusion, I can but re-echo the closing words of Professor Joly's Address on "Radium," to which I have already referred. They are as follow :—

"This—the first Radium Institute in Ireland—has already done good work for the relief of human suffering. It will have, I hope, a great future before it, for I venture, with diffidence, to hold the opinion that with increased study the applications and claims of radio-active treatment will increase."

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DR. W. C. STEVENSON said that, with regard to the extract from Mr. Morson's paper in which it was indicated that it was the gamma rays that caused the effect, he had recently read a paper in the *Practitioner*," by Lazarus Barlow, in which it was questioned whether it was the gamma or beta rays which produced the effect in cancer. He (Dr. Stevenson) said the beta rays were present in any case, so that they could not be avoided. He referred to a paper by Abbé, who separated the beta from the gamma rays, and who proved to his own satisfaction that the gamma rays had very little effect, and that the beta rays had great effect in retarding cell growth.

He had noticed the effect of handling radium on the tips of the fingers, which became quite insensitive.

DR. SOLOMONS expressed regret that the paper had not been brought before the Section of Obstetrics. He was also sorry that Dr. Kidd, who had expressed the opinion that the case



was inoperable, was not present, as it would have been of interest to know his idea as to what was an inoperable case.

DR. C. M. O'BRIEN said the whole virtue of radium depended on the action of radium emanation on the cancer cells and also on the stimulation of the connective tissue cells. He thought that Barlow, summing up in his last paper, said that no matter what might be the future of radium every operable case of cancer should be operated upon. He recalled a case of his which was treated in 1906 for epithelioma of the right cheek, which was looked upon as cured and remained well for six years, and at the end of that time the patient returned with large infiltrating glands absolutely inoperable from the surgical standpoint.

DR. CROFTON said that one would think that radium would produce a local effect only on the cancer, but it appeared that there was always a general reaction, and he suggested that part of this was due to the absorption from the cancer cells into the circulation, so that not only might the radium act as a destructor of the cancer cell, but that it might lead to a certain amount of immunity.

DR. W. GEOFFREY HARVEY said Dr. Crofton's point should not be lost sight of. He found that when a tumour in a mouse disappeared after treatment with *x*-rays, it was almost impossible to reinfect that mouse with cancer. From that he considered that the absorption of the cancer did produce some kind of protective bodies.

DR. SPENCER SHEILL said that if it was assumed that the diagnosis was correct without microscopic examination, Sir John Moore was to be congratulated. He had spent some time in studying the effects of radium, and had seen results with which he considered this case compared favourably. If nothing more than the cessation of pain and apparent improvement had been achieved, he considered that a distinct gain.

THE PRESIDENT said the physics of radium was a complicated subject, and the question of its physiological action, which was of greater interest, was still more complicated. It seemed to him that the most fundamental thing as to the possible line of radio-activity was that it was a branch of photo-therapy, and might be brought into line with Finsen

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light. He suggested that it was a photo-electrical treatment influenced largely by the wave-length of the light, and possibly acting on the tissue. He considered that it was possible in all those radio-active elements there might be a stimulant action, and suggested the possibility of too feeble application of radium stimulating cancerous growths.