

THE TREATMENT OF CARCINOMA OF THE CERVIX

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On scanning the literature since 1900 on the treatment of cancer of the cervix one finds that three periods are represented. During the first period the surgical treatment was emphasized and the reports consisted chiefly of descriptions of operations and surgical end-results. Then there was the period of controversy concerning the relative merits of surgery and radium. During the past ten years, in this country, and with few exceptions on the continent, most of the literature has dealt with radiation therapy, its technic and end-results. An analysis of these results would seem to indicate that, for the time being at least, radium and roentgen ray is the treatment of choice, not only from the standpoint of the rate of curability but also from the standpoint of palliation, morbidity and economy.

In this paper, I am reporting a series of 420 cases of cancer of the cervix, in which the patients were examined, treated and observed during the period from 1920 to 1931, inclusive. In this group, there were 302 cases of primary carcinoma, in eighty there were recurrences following operation or irradiation elsewhere and in eighteen, the lesions were too far advanced for any possible treatment. Twenty patients in this group refused treatment or sought medical advice elsewhere.

I shall not take time to discuss the diagnosis of carcinoma of the cervix. It has been dwelt upon time after time. Yet, on reviewing my series of cases, it is not pleasant to have to admit that in patients examined in 1931 the disease was just as far advanced as it was in those examined in 1920. This in spite of numerous articles written on the subject and in spite of the publicity given it by The Society for the Control of Cancer. Despite the fact that the cervix is an easily accessible organ, failure to recognize early cervical cancer has occurred in a discouraging number of cases. Delinquency on the part of the patient is sometimes responsible, but with increasing public education this is becoming less frequent and still entirely too many failures are attributable to the remissions of the medical profession.

Diagnostic failures come about in two ways. The symptoms may be attributed to the menopause and frequently consultation with-

out proper examination leaves the patient with a false sense of security which leads to further delay. The lesion may be discovered but may not be recognized as malignant, being mistaken for ulcer, erosion or eversion. In case of doubt a biopsy is imperative. The physician's hesitancy to do a biopsy may have resulted from the active discussion a few years ago of the danger of spreading the cancer in this way. Today that discussion is dead — so are many patients for lack of a biopsy. I have never seen any harm come from it and recommend its use in any doubtful case. It will save far more than it will harm.

Another fallacious opinion has been advanced in an effort to show that irradiation both by roentgen-ray and radium may cause distant metastases not seen heretofore. The literature shows that many distant and bizarre metastases were observed long before radium was used. If metastases are being observed more frequently now, it is because radiation has prolonged the life of the patient for sufficient time to make this observation possible. On noting the cause of death in my series it is found that practically all the patients have died with the disease confined to the pelvis with obstruction to the ureter only. Very few show metastases to the liver, lungs and bones.

Anyone who has treated a large group of cases is at once impressed by the varied individual resistance to cancer. Some patients with apparently advanced lesions respond better than do those in whom the disease is recognized early. This variation in response is undoubtedly attributable to normal body defenses about which little is known. However, Broders has developed a method of evaluation of malignancy histologically, by which the prognosis in a given case may be expressed on a numerical basis, dividing the cases into four groups, according to the degree of cellular differentiation. Following these lines, a tremendous amount of investigation has been carried on by other workers for the purpose of determining whether there is any definite relationship between the histologic structure of carcinoma and its relative malignancy, and of trying to deduce from this finding the best form of treatment for the type in question, and also of determining the prognosis. I have not been able to test this out in my series of cases because I believe that a large personal equation enters into the problem and that direct, personal contact with Broders would be necessary in order to develop a precise duplication of his method. If not done properly, I am sure that such an attempted classification would lead to further confusion. Another complication, of course, is that sections from different portions of the tumor may give different histologic pictures which also may be misleading.

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The clinical classification I use is that of the American College of Surgeons which, for working purposes, is quite practical except in regard to the question of involvement of the broad ligaments. It is often difficult at first examination to decide whether or not such involvement may be inflammatory or malignant, but time generally furnishes this information. I believe that cures in cases in which there is definite infiltration of the broad ligament are relatively few.

RATIONALE AND TECHNIC OF RADIUM THERAPY

For practical purposes, the simple idea that radium is a means of destroying cancer cells without too much injury to the normal cells is a good working hypothesis, but by reason of our accumulating knowledge of the physics of radiation, and of the biologic effects of radiation, we are being led to a better understanding of its action. In brief, radium has a threefold action on malignant tissue. It affects (1) the cancer cells, (2) the connective tissue, and (3) the blood and lymph vessels. The action on the cancer cell is shown microscopically by swelling and vacuolization of the protoplasm and by shrinking of the nuclei. This is followed by phagocytosis and absorption and replacement by an homogeneous connective tissue. This contracts and affects the lymphatic and smaller blood vessels and starves the growth.

There is not sufficient time to enumerate the varieties of technic which have been used since radium therapy was instituted nor to mention all the men who have contributed to the advancement of our present knowledge. Suffice it to say that there are two entirely different schools of thought in regard to the method of treatment. In one, the opinion is that it is best to give large, massive doses within a short space of time, preferably in one, or at most, two treatments. The other is that it is preferable to give very small doses over a longer period of time. I believe that most of the large clinics in this country favor the former view, while protagonists of the latter method are led by Regaud of the Radium Institute of Paris. This difference of opinion undoubtedly will be settled before many years elapse, when the results of both methods may be compared. Standardization of the dosage of radium used in treating uterine cancer is impractical; dosage and technic must vary with the character and location of the lesion.

The technic followed in the Cleveland Clinic has varied but little during the last ten years, the only change being that since a larger amount of radium has been available, larger doses have been given over a shorter period of time, and an effort is made to give the complete dose at one sitting. Previously, the total irradiation was given

in two doses. The average dose given in the first cases in my series was 4200 milligram hours distributed evenly in and against the cervix. In later cases, since radium has been combined with roentgen ray of high voltage the average dose is about 3,600 milligram hours. The standard screen is made of brass, one and one-half millimeters in thickness, and this is encased in a rubber tube three millimeters thick. At the present time a tube is placed in the fundus as well as in the cervix. This is done because in some cases treated earlier it was found that after being free from symptoms for a year or so, the patient suddenly might have bleeding and discharge, and examination would reveal a large undermined cavity at the upper end of the vagina which had not been reached by the radium. It is necessary to anesthetize the patient in order to determine accurately the extent of the new growth. However, it is sometimes impossible, even when the patient is under an anesthetic, to place a tube of radium high in the cervical canal.

In addition to the radium tubes placed in the fundus and cervix, two or three tubes are placed against the cervix and these are held in place by packing the vagina tightly with gauze. If the growth is of the cauliflower type it is frequently curetted away or implanted with radium needles. A catheter is placed in the bladder in order to keep it empty and as far away from the radium as possible. Care should be taken in transferring the patient from the table to the cart and from the cart to the bed. Bending and twisting of the patient during the transfer may dislocate the vaginal tube and may account for bladder and rectal symptoms. The best method is to place the cart alongside the table and to slide the patient on the cart by means of a sheet, and to transfer her from the cart to the bed in the same manner, so that the position is unchanged throughout the procedure. Gold seeds have not been used in the treatment of any of these cases, but they are of great value in cases in which there has been recurrence, because their action is localized to a greater or lesser extent. Large, heavily filtered doses frequently are harmful in the treatment of lesions which have recurred. In this series there has been no case in which gold seeds were placed in the broad ligaments by laparotomy. Three to four weeks after treatment with radium the patient returns to the Clinic for a course of treatments with high voltage roentgen rays, given in five or six doses during a period of five or six days.

After patients have been treated they are requested to return at monthly intervals for three months, and afterwards, every three months during the following year. If local recurrences develop, they are treated by means of implantation of seeds. If the recurrence is deep, roentgen therapy is repeated, with marked relief for a time.

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In cases of intractable pain in the pelvis and down the legs, cordotomy may be done. Section of the sensory column in the cord may afford amazing relief from pain.

COMPLICATIONS

The chief complications in the treatment of carcinoma of the cervix by radium are hemorrhage, symptoms referable to the rectum and bladder, and fistulae, both urinary and fecal.

Hemorrhage may be due to the natural progress of the disease or to ulceration caused by the radium. I believe that the natural progress of the cancer is the principal cause of hemorrhage. In the most serious cases packing and transfusion are sufficient to control the hemorrhage.

Bladder and rectal symptoms are of two types — early and late — and it is quite important that they should be recognized. It is reasonable to assume that if a sufficient dose of radium is given to cure carcinoma of the cervix, it will also be sufficient to produce an erythema in the rectum or bladder. Very often this erythema is slight and passes unnoticed unless the patient is questioned. If it is severe, it is evidenced by a slight burning sensation and a tendency to frequency of urination or defecation. In the mild cases, the condition usually clears up within ten days or two weeks, but in the severe cases from four to six weeks may be required. It is in this group in which the symptoms persist that late rectal and bladder complications may develop, usually six or eight months after the initial irradiation. These late symptoms frequently are mistaken for a recurrence of the carcinoma, and if the patient is given additional treatment with radium, irreparable damage may result. A clue to the true state of affairs is found in the fact that the symptoms are out of all proportion to the findings. There is severe pain and tenesmus and the stool contains considerable blood and mucus. Digital examination causes greater pain than in the case in which there is recurrence of the malignant lesion. The patient is not cachectic. Proctoscopic examination reveals, approximately at the level of the cervix, a puckered scar or small ulcer with telangiectasis and considerable redness of the mucosa. The condition may be compared to an overtreated area on the skin which is healed by the formation of scar tissue through which fine vessels may be seen to course. In the rectum the scarring is subject to trauma and infection with subsequent ulceration which causes the late symptoms.

The same general condition is to be found in cases in which there are late bladder symptoms. Cystoscopic examination may reveal an area of intense redness and, at times, ulceration. I have observed several cases of this type over a period of months, and a

few over a period of two years. Occasionally the urinary salts will be found deposited in the slough in the bladder and stones will be formed. For the rectal symptoms the treatment consists of rest in bed, cleansing of the lower bowel, and the injection of three or four ounces of warm olive oil into the rectum twice a day. Occasionally an opium suppository is necessary. For the bladder symptoms rest, irrigation of the bladder, and the instillation of gomenol are prescribed. Sometimes these bladder and rectal complications may not disappear for four to six months.

Fistula. We know that the natural progression of carcinoma of the cervix will cause a certain number of fistulae into the rectum or the bladder. In some of my earlier cases fistulae may have resulted from treatment of the carcinoma, but with our present knowledge and the improved methods of treatment, I feel sure that the incidence of fistula will be lower than in cases in which the patient has received no treatment at all. If the fistula appears soon after treatment it is interpreted as being due to destruction from the disease. If it appears late, and there is no evidence of recurrence of the carcinoma, it probably is due either to progressive ulceration or to the later complications mentioned above, and hence is the direct result of the radium treatment.

The method of treatment of a fistula in the rectum must depend upon its size and the amount of inconvenience it causes the patient. A small fistula may not require treatment. If a large fistula is present, it may be advisable to do a colostomy before attempting to repair it, and to close the colostomy if and when the repair is successful.

The urinary fistula is more annoying on account of the constant flow of urine. If the fistula is small, it can be repaired easily by operation. If it is irreparable, the patient may be made more comfortable by transplantation of the ureters into the sigmoid.

Of the total number of cases of primary carcinoma of the cervix coming to the clinic some attempt at treatment has been made in 93 per cent. The remaining 7 per cent were in extremis on admission. Below in tabular form are the statistics of the results in 303 cases of primary carcinoma of the cervix treated from 1920 to 1931, inclusive. All patients not traced are counted as dead. It will be seen that of 148 cases treated over five years ago, 37 or 25 per cent are alive and well. Twenty-nine per cent are living from three to five years, and 61 per cent are living under three years.

With increasing facilities throughout the country to take care of these patients, it seems to me that our biggest problem still remains, that of getting the patients to seek medical advice when the disease is still in an early stage.

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RESULTS IN TREATMENT OF CARCINOMA OF THE CERVIX

	<i>Year</i>	<i>Treated</i>	<i>Traced</i>	<i>No. Living</i>	<i>Per Cent</i>
Living over 5 years.	1920	8	8	2	25
	1921	17	15	4	24
	1922	22	21	5	23
	1923	26	23	5	20
	1924	24	21	7	30
	1925	21	17	5	25
	1926	30	25	9	27
		<hr/> 148	<hr/> 130 - 90%	<hr/> 37	<hr/> 25%
Living 3 to 5 years.	1927	32	26	9	28
	1928	13	10	4	30
		<hr/> 45	<hr/> 36 - 80%	<hr/> 13	<hr/> 29%
Living 1 to 3 years.	1929	48	42	24	50
	1930	35	31	19	54
	1931	32	32	28	87
		<hr/> 115	<hr/> 105 - 90%	<hr/> 71	<hr/> 61%