RADIUM THERAPY OF CARCINOMA OF THE CERVIX UTERI.*

AN ANALYSIS OF RESULTS OBTAINED AT THE WOMAN'S HOSPITAL, NEW YORK.

BY

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I HAVE no apology to offer for having the temerity to bring to your attention this subject, as the therapy of cancer of the uterus is by no means accepted and standardized as are most of our gynaecological problems, and because the literature is full of conflicting opinions as to the results obtained, and as to what is the most efficient technique. Therefore, in the hope that our few drops of clinical experience in the radium therapy of carcinoma uteri during the past ten years at the Woman's Hospital in New York may act as a reagent to help clarify the hazy mixture of the various clinical reports, I beg leave to give you a survey of our observations and viewpoint as a small contribution towards bringing about the stabilization of the therapy which I am sure we all ardently desire.

Before the discovery of radium by Mme Curie the treatment of cancer of the cervix uteri was by local destruction of the carcinomatous tissue with some form of cauterization or by operation. The technique of the radical operation, as developed by Wertheim, gave so much better results than other operative procedures that up to the last ten years practically no other treatment has been used. The question to-day before us is, Can we with radium obtain the same result in treating cancer of the cervix as can be obtained by the Wertheim operation without its high primary mortality? No one questions the palliative effect of radium in the inoperable cases of carcinoma of the cervix, but to ascertain the true value of irradiation one must compare the results by operation with the results by irradiation in operable cases of carcinoma of the cervix uteri.

At this time there are only a few large clinics using radium alone for operable cases of cancer of the cervix, and consequently only a few series of operable cases of carcinoma of the cervix treated with radium five years or more ago to compare with the large number of cases operated upon radically and observed for a period of five years or longer. The object of this paper is, therefore, not only to report the results obtained in the Woman's Hospital of New York by irradiation of all cases of cancer of the cervix, but especially to show our results by irradiation of operable cases in the ten years that we have had radium in the hospital.

In the past year two statistical studies on surgical and radiological treatment of cancer of the cervix uteri, of great importance to physicians concerned directly or indirectly with this disease, have been published—one in England and one in Sweden. The first study mentioned is an exhaustive report by Dr. Janet E. Lane-Claypon, published by the Ministry of Health in England and based on the data published in sixteen different countries relating to the records of some 80,000 cases of cancer of the uterus treated by operation or radium. This is a work of great magnitude, and includes a most valuable bibliography. The second study is a comparative analysis by Heyman of the Radium-Hemmet in Stockholm, which he presented before the Scandinavian Surgical Society at Gothenburg in June, 1927. This is an admirable review and comparison of the published statistics of the results obtained in twenty surgical clinics and seventeen radiological clinics in Europe and America in operative or radium therapy of carcinoma of the cervix uteri.

In his comparative study of published statistics Heyman has reduced the figures of all the clinics to one uniform standard. He has left out all doubtful statistics and does not deduct intercurrent deaths or non-traced cases, and

quotes only the accepted five-year cure. His combined summary of twenty surgical clinics and seventeen radiological clinics shows:

For total cases—			
Operative treatment	...	approximately	18.0 per cent.
Radiological treatment	...	...	16.3 "
For operable and borderline cases—			
Operative treatment	...	...	35.6 "
Radiological treatment	...	...	34.9 "
Primary mortality—			
Operative treatment	...	...	17.2 "
Radiological treatment	...	less than	2.0 "
Operability—			
Operative treatment	...	...	43.0 "
Radiological treatment	...	less than	30.0 "

While these figures apparently approach each other very closely it must be evident that it is not fair to consider them as similar when we take into account the great difference in the character of the initial material as shown by a 43 per cent. operability in the operative statistics as compared with less than 30 per cent. in the radiological figures.

The above general averages are interesting when compared with the results obtained at the Radium-Hemmet at Stockholm by Forsell and Heyman. From 1914 to 1921 inclusive they reported for all cases 22.4 per cent. free from symptoms after five years, and borderline cases with a five-year cure of 44.4 per cent. Their primary mortality from irradiation was 1.59 per cent.

These results, contrasted with the general average of the operative treatment, are certainly to the advantage of irradiation therapy, especially when we consider the character of the initial material from which these figures are compiled.

TECHNIQUE AT THE WOMAN'S HOSPITAL CLINIC, NEW YORK.

We have not a large amount of radium at our disposal at the Woman's Hospital, New York. Our armamentarium consists of some 280 milligrams of the salt in tubes and needles, and our average initial dosage has been from 2,400 to 4,200 milligram hours. It is of interest to note that the Radium-Hemmet at Stockholm also uses the salt in similar dosage, and does not use the emanation with massive amounts. Our experience convinces us that the employment of massive doses cannot show any better results than the intelligent application and reapplication of smaller doses.

We start with the principle that every case of cancer of the cervix is a study in itself, and that the *frequent personal observation* by the surgeon directing the treatment is absolutely essential to obtain results, and this personal contact must continue throughout the period of cure. As we cannot say when any case is permanently cured, this means the patient should be under observation at regular monthly intervals throughout her life, if she would be safe, as we believe we have obtained our results by this constant watching enabling us to discover a recrudescence of the disease in its early stages long before the patient would be aware of symptoms. Thus we have the opportunity of putting out the fire while it is yet a small blaze by prompt re-radiation, instead of having to try and extinguish the serious conflagration which would be present when the patient had developed symptoms. If there is an opportunity to plant a radium needle in a suspicious area at the onset of a recurrence the problem is much simpler, as the chances of smothering the fire in its incipency are greater. We therefore believe in repeated re-radiations as often as indicated; 50 per cent. of our cases have had more than one application, and many of our successful cases have had three or more irradiations. It is upon this personal frequent follow-up of our cases that we have based our treatment, and attribute to it whatever success we have had.

As we are familiar with what the post-radiation picture should be at the end of each month, we think we can tell from the general appearance of the growth whether the several stages of hyperaemia, local sloughing, separation of the slough, and healing process with final cicatrization and marked contraction, which represent the phenomena

* Read in the Section of Obstetrics and Gynaecology of the Annual Meeting of the British Medical Association, Cardiff, 1928.

of irradiation of the cervix by radium, are progressing satisfactorily. This process, as we have observed it at our clinic, has been graphically shown in a paper published by Farrar. Our technique of application is simple and has been described in a previous report. We employ brass and rubber screening of the radium tube and distance screening with vaginal gauze for the protection of the bladder and rectum. We believe anchoring of the radium tube by suture is an important detail. We prefer the short needles to the long model for implantation in the periphery of the growth, and we believe the needles should not be closer to each other than 2 centimetres. Usually four needles are sufficient, unless the growth is very large. We have found a self-retaining catheter inserted in the bladder during the time of the radium application is most satisfactory to all concerned.

Many of these patients are suffering from toxic absorption and are cachectic and anaemic. During the sloughing stage of the radiation process there is necessarily an increased absorption of these toxins with resulting septic fever and an increase of the debilitated state. We have found that blood transfusion is an important adjunct to the irradiation in enabling these patients to combat this sepsis more successfully. Wherever possible we give these cases 500 c.cm. of blood before their discharge from the hospital.

Important details are to get the patient up early to favour drainage, and to give careful instructions as to repeated daily douches of potassium permanganate solution to favour separation of the slough, to deodorize it, and to stimulate tissue growth.

Our results have been obtained without the employment of high voltage x-ray therapy as an adjunct, as we have not the apparatus, and our employment of a moderate voltage as a post-radium treatment in some of our cases seemed harmful, and gave us less satisfactory results than when we used radium alone. So for the present we do not use x-ray therapy in conjunction with radium as a routine. We believe, however, that high voltage attack on the lymphatic glands to produce a lymphatic block as an adjunct to radium therapy is theoretically correct, and if it can be done without associated injury to the adjacent viscera it would be ideal.

Each patient is requested to report once a month in the follow-up clinic. Dr. Farrar and myself attend this clinic in person, and one or the other of us palpates and inspects each cervix with its adjacent tissues.

PROGNOSIS FROM THE TYPE OF CELL.

In view of the interest that has been aroused by Martzloff, Cutler, and others on the possibility of making a prognosis as to the probable reaction to irradiation in accordance with the predominating type of cell in cervical carcinoma, I have had Dr. Plaut, our pathologist, study the type of cell in our series. We have not found it possible to predict the result from the type of cancer cell, for we have observed when several pieces of tissue have been taken from different places in the growth that different types of cancer cells are present. While we hope that the grading of the type of cell may prove to be as reliable an index of prognosis as some pathologists expect, still we are inclined to believe with Dr. Plaut that there is at present a bewildering mass of contradictory evidence as to its value.

In 1925 we reported our results at the Woman's Hospital in New York of two five-year series of radium therapy for carcinoma of the cervix before the American Medical Association. Our percentage of cures of all cases was 23.6, and for the early and borderline (operable) cases it was 52.9, based on cases traced, or 22.4 and 50 when including the non-traced cases, to accord with Heyman's uniform standard, with a mortality of 1.6 per cent. Since that date we have completed two more five-year series, and are now able to report on all cases treated in 1919, 1920, 1921, and 1922, and the first five months of 1923. Our records and follow-up end-result cards have been audited by professional statisticians, and the figures I present to you have been compiled by them and certified as correct.

It has seemed well before giving our statistics to state definitely the character of the cases we are reporting. We have included only cases of carcinoma that have originated in the cervix and have not been operated upon or treated with radium elsewhere, so that we may compare our method of radium treatment with the radical operative treatment in similar classes of carcinoma of the cervix uteri.

TABLE I.—Primary Carcinoma of the Cervix Uteri: Radium Five-Year End-Results.

Gynaecological Service, Woman's Hospital, May, 1928.

	Treated.	Traced.	Living.	Percentage Living.	
				Cases traced.	Cases treated.
Classes 1, 2, 3, 4 ...	134	126	31	24.6	23.1
Classes 1 and 2 (limited to cervix)	32	30	17	56.7	53.1

Primary mortality, 0.44 per cent.

Comparing these results with the statistics of seventeen clinics as given by Heyman in his report, and also with the results obtained by Forsell and Heyman at the Radium-Hemmet in Stockholm, we have as follows:

TABLE II.—Comparative Results of Radical Operative and Radiological Treatment of Carcinoma of the Cervix (Five Years).

TOTAL CASES TREATED.

*All Clinics:	Per cent.
Operative treatment ...	18.0
Radiological treatment ...	16.3
*Radium-Hemmet ...	22.4
Woman's Hospital Clinic, May, 1928 ...	23.1
Primary Mortality:	
Radiation operation ...	17.2
Radiological treatment ...	2.0

*From Heyman's Report, 1927.

TABLE III.—Operable Cases (Five Years).

*All Clinics:	Per cent.
Operative treatment ...	35.6
Radiological treatment ...	34.9
*Radium-Hemmet ...	44.4
Woman's Hospital Clinic, May, 1928 ...	53.1

*From Heyman's Report, 1927.

Although our total series is small as compared with the Radium-Hemmet, still it is encouraging to know that our last two five-year series maintain the percentages achieved in our previous report. It must be borne in mind that the percentages given for the borderline cases must always be of uncertain value, as "borderline" means confusion, because it must depend entirely upon the personal equation of the surgeon, and we are inclined to agree with Jeff Miller that it is a useless classification for practical purposes, and that we should simplify our statistics by having only two types—early and advanced. Likewise there must be uncertainty as to the term "operability," because one surgeon will consider operable, and will operate on, cases with definite involvement of the parametrial tissues—as, for instance, Victor Bonney—while many of us who are conservative will not consider a case operable unless the uterus is mobile and without infiltration beyond the cervix. Consequently the figures given for "operable" cases will always be of unstable value for comparison also.

The lack of standardization of statistical reports is what complicates the problem of making fair comparisons. A cursory glance at the various reports published in the literature will show what a great variability exists in presenting the subject. Two-, three-, and four-year results only add to the confusion, and should be abandoned. Only five-year observations should be considered.

In giving the report of our cases of carcinoma of the cervix treated with radium we have felt the need of standardization of statistics, and would urge that we have—

1. A uniform classification of the growth itself. Schmitz's classification of groups from I to IV gives a sufficiently definite anatomical description of the extent of the tumour itself, and this grouping we have adopted in our work.

2. The report of only five-year results—total cases and early cases. For comparison with the operative results obtained, we must take the same period that surgical clinics do—that is, five years.

3. Inclusion in statistics of all patients that either have not been traced, or are dead from any cause, as *dead from cancer*. This may seem unfair in some instances where it is difficult to trace cases, or in hospitals that do not have a "follow-up," but if the rule applies to everyone it can only affect a small percentage of cases, and may lead to a better follow-up system. Heyman, in his statistical analysis of over 8,000 cases, has followed this procedure.

4. Operability rate and primary mortality. These should be given for comparison with cases treated by radical operation.

PROPHYLAXIS.

The role of chronic irritation as an etiological factor in the development of carcinoma makes it imperative that lacerations and erosions of the cervix should not be neglected. In a study by Farrar of 300 consecutive case histories of cancer of the cervix at the Woman's Hospital in New York it was found that pregnancy had occurred in 96 per cent. In 288 cases 11.1 per cent. of the patients had had the last pregnancy less than five years and 20.3 per cent. less than ten years before entering the hospital for the malignancy. We believe that the immediate repair of cervical lacerations, when done under proper conditions as in a hospital, will lessen the danger of subsequent development of carcinoma in the cervix.

CONCLUSIONS.

In conclusion, I wish to draw attention to the following creed which I hold.

There is less primary mortality, less morbidity, less loss of time with radium therapy than in the radical operation for carcinoma of the cervix.

The palliative results in cases not permanently cured are an important advantage not to be ignored.

The morbidity results of the radical operation—fistulae, thrombosis, suppuration, etc.—are not to be forgotten.

Vesical and rectal fistulae should be increasingly less frequent in radium therapy as the technique develops.

Repeated irradiations are of distinct value, and subsequent treatments should be based on the reaction to the initial or test dose.

A personal monthly inspection or follow-up is an essential throughout the period of observation, in order that by a watchful waiting we may discover a recurrence in its incipency and thus extinguish the fire before it has gained headway.

Large amounts of radium are not necessary to produce results.

A standardization of statistical reports on irradiation of cancer of the cervix is needed for comparison of results in different clinics.

We believe that our results show that radium is preferable in all classes of cervical carcinoma. We also believe that in the very early cases the radical operation will give the same result as radium, but at the cost of high primary mortality and greater morbidity.

As to the early cases—and how few we see!—with the present statistical figures available it is not yet proved which gives the best results, but the available figures do not show that the operation is any better than radium.

LITERATURE.

Schmitz: The Classification of Uterine Carcinoma for the Study of the Efficacy of Radium Therapy. *Amer. Journ. Roentgenology*, 1920, vii, 383.

Farrar: Preliminary Report of Primary Carcinoma of the Cervix Uteri Treated with Radium in the Woman's Hospital. *Amer. Journ. Obstet. and Gynecol.*, 1925, x, 205.

Ward and Farrar: Radium Treatment of Carcinoma of the Cervix Uteri. *Journ. Amer. Med. Assoc.*, 1925, lxxxv, 159.

Farrar: The Reaction of the Tissues to Radium in Treatment of Cancer of the Cervix and the Importance of Lacerations in Producing Cancer in this Location. *Surg., Gynecol. and Obstet.*, 1925, 719.

Heyman: Radiological or Operative Treatment of Cancer of the Uterus. *Acta Radiologica*, vol. viii, Fasc. 5, No. 45, 1927.

Lane-Clayton, Janet: Cancer of the Uterus. Ministry of Health, London, 1927.

RADIUM IN THE TREATMENT OF CARCINOMA CERVICIS AND INTRACTABLE MENORRHAGIA.*

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CARCINOMA CERVICIS.

THESE observations are based on a study of over 200 cases treated with radium since January, 1926, and an experience of 130 radical operations (Wertheim). All the cases were checked by pathological report.

Radium bromide (100 mg.) was applied for twenty-four hours to the external os, if it was ulcerated, or into a crateriform cavity if one existed. In a few cases 200 mg. was used. After the application the patient rested for fourteen days, took potassium iodide, 5 grains thrice daily, and had a douche every day.

Pathology.

Forty-five uteri which had been exposed to radium and had been reported to be malignant were sent for a further report after removal. Radium had been applied at least fourteen days previously, and in some cases one or two months had elapsed. Nine reports, when referring to the malignant growth, contained such terms as "disorganized," "retrogressing," "some necrosis," "being phagocytosed," and three stated that there was no evidence of malignancy. In the remaining thirty-three uteri the malignant cells were apparently unaltered.

Radium applied directly to the growth can produce a beneficial result, but my operative experience makes me doubt its practical value in dealing with glandular deposits.

In order to appreciate the results the terms "operable," "borderline," and "inoperable" must be defined. These are based on the local condition as judged by the possibilities of the radical operation (Wertheim), and without reference to the age or general condition of the patient. For the benefit of those who are not conversant with operative technique it might be useful to state that the radical operation entails removal of a cuff of vagina with the cervix, as well as the extirpation of the lymphatic glands. An ordinary total hysterectomy, sometimes called panhysterectomy, does not allow of this.

Operable means that the growth is limited to the cervix, or has involved the vagina only to a limited extent, and that there is little, if any, infiltration of the cellular tissue.

Inoperable implies (1) that the ulcer extends so far down the vagina or into the broad ligaments as to prevent removal, or (2) that the cellular tissue in the ligaments or round the cervix is densely infiltrated.

Borderline refers to the intermediate cases. This classification will, to some extent, depend upon the individual operator.

1. Operable Cases.

In 20 cases considered operable prior to January, 1928, radium alone was used. These cases were not submitted to operation owing to such causes as age, general condition of the patient, or the presence of heart disease or diabetes; in two cases operation was refused, and in two others the application of radium made the condition clinically inoperable.

Results.

Excluding two cases which have been lost trace of, the after-history of the 18 at the present date is as follows:

Improved	...	...	...	...	...	...	3
Stationary	...	...	...	...	...	...	3
Worse or dying	...	...	...	...	...	...	6
Dead	...	...	...	...	...	...	6

* Read at the Annual Meeting of the British Medical Association (Section of Obstetrics and Gynaecology), Cardiff, 1928.