

RÖNTGENOTHERAPY IN UTERINE FIBROIDS AND UTERINE HEMORRHAGE.*

BY

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I WAS among the first to employ the Röntgen rays in the treatment of uterine fibroids and uterine hemorrhage (nonmalignant), having treated my first patient in January, 1906. (My first malignant case in 1901.) My experience therefore extends over a period of nine years, and while I have only treated forty-six nonmalignant cases in this time, the duration of my observation and my interest in the subject during these nine years will permit me to speak with a reasonable degree of assurance.

In my previous papers(1) on this subject I have reviewed briefly the history and the theory of the action of the Röntgen rays in the treatment of uterine fibroid and uterine hemorrhage, and in my paper read before the Section on Obstetrics, Gynecology and Abdominal Surgery of the American Medical Association in June, 1914(2), I described the modern technic, and in previous papers I have given detailed reports of cases. Therefore in this paper I shall make an effort to answer some of the questions that continually arise in the minds of the members of the profession and of patients.

During the past nine years there have been treated probably between two and three thousand patients of the class under consideration. Gauss(3) made a statistical summary of 1395 cases that were recorded up to January 1, 1914. Lockyer(4) (published Aug., 1914) from the records of only seven authors collected 1572 cases. If Lockyer is able to collect this number from seven authors it is reasonable to assume that there must be practically twice this number on record. He remarks that almost every article indexed "Myome" during the previous seventeen months in the *Zentralblatt f. Gynaekologie u. Geburtshilfe* related to radiotherapy, and in Germany and France the method of treatment seems to be accepted as one to be considered in every case. It is, therefore, no longer a new and untried method, and if the bad results of treatment,

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subsequent degenerations and serious complications were as prolific following the treatment as some of the authors (Tracy(5)) (McGlenn(6)) seem to think we surely would have met them long before this and would have abandoned the treatment.

The indications for the treatment of hemorrhages due to myomas, as given in my recent paper,(2) are: 1. All cases of myoma in older women in whom there is already a well-advanced anemia, which may be the cause of an anemic heart. 2. All elderly and young women with myomas, in whom there is marked organic heart disease, diabetes mellitus, chronic nephritis, marked lung disease and goiter with cardiac symptoms. 3. All patients beyond the age of forty, in whom there is no contraindication to the treatment. In general, the older the patient and the nearer she has approached the menopause, the more prompt and satisfactory will be the result. Under forty, Röntgenotherapy is not the method of choice, but good results can be obtained, though the younger the patient, the more treatment will be required. Even in patients under forty, if the alternative is complete extirpation of the uterus and adnexa, Röntgenotherapy should be seriously considered, for it is claimed that even with the disappearance of the Graafian follicles and the destruction of the reproductive functions that there is a preservation of the internal secretion (Bordier). It is also possible that there will be a regeneration of the ovaries in young women, with the possibility of subsequent menstruation. This has occurred in one of my patients, a woman of thirty-four, in whom, after all the symptoms of fibroid had disappeared and after complete cessation of the menstrual period for several months, there was a return of normal menstruation which has continued normal for about five years, and now is gradually diminishing. During these five years she has enjoyed excellent health. This possibility should, therefore, be kept in mind. Edelberg(7) reports a case of myoma of the uterus associated with pregnancy in a woman of thirty-eight, six years after her second pregnancy. She was given a course of Röntgen treatment, the ovaries being systematically treated, the total dosage being 146 Kienboeck units. It is estimated that 111 x-units were given before pregnancy and 35 x-units after pregnancy, but the pregnancy proceeded unmolested to normal term and the child seemed absolutely normal and thriving at the seventh week. 4. The intramural or the interstitial variety of tumor gives the best results.

Gauss(3) believes that all cases of myoma should be treated by radiotherapy, because the lowest mortality ever claimed for operative methods is from 3 to 5 per cent., while in his second and third

group, in which the doses were from 175 to 1500 x -units, there were no deaths. He thinks this alone should justify the treatment.

Krönig(8) says his clinic has abandoned the operative treatment of fibroids for the treatment by the Röntgen rays, except in those occasional cases where it appears that myomectomy may leave a functioning uterus for a young woman. The argument is that the Röntgen rays are just as efficient in their action as total ablation and is devoid of all danger to life, while an operation carries with it an operative mortality even if it is small. The artificial menopause symptoms are in general not nearly so pronounced as after operation.

Contraindications.—1. All cases of myomas in which the tumor is pedunculated, or which can be excised without destroying the reproductive powers of the patient. 2. Fibroids that have undergone malignant degeneration, or that have become gangrenous, should not be treated. 3. Fibroids associated with disease of the adnexa. 4. Fibromas which are producing such marked symptoms that the patient is endangered more by waiting two or three months for results of Röntgenotherapy, than by the result of an operation.

The Probability of Cure.—In the critical reviews made by Gauss, he divided the 1395 cases into three groups, according to the dosage given. The first group embraces a total of 693 cases, in which the total dosage amounted to from 50 to 175 Kienböck's x -units. Group II included 544 cases in which the doses varied from 175 to 500 x -units. Group III included 158 patients, who were given doses amounting to from 500 to 1500 x -units. Corresponding to the rise of the total doses in the three groups there is a rise also in the percentage of cures from 72 to 82 and 95 per cent. It can be seen from this that the success attained is greater in proportion to the dose of radiation applied to the surface of the body. To this, however, must also be reckoned the fact that in addition to the increase of the dose, the rays applied in recent years has been more penetrating and more thoroughly filtered. In Group III, so far as he was able to learn, practically all of the cases of myoma and metropathy that presented themselves for treatment were treated, at least this was true at the Freiburg Clinic. Therefore, since all variety of cases in Group III were treated the increase in good results must be due to the improvement in technic. In Group I there was evidence of recurrence in 4 per cent., in Group II of 3 per cent., while in Group III there was no recurrence to record. By recurrence I mean the recurrence of hemorrhage.

It must always be borne in mind that the younger the patient the more treatment will be required. In hemorrhages due to fibroids

I believe it is always desirable to bring about at least a temporary menopause. When the patient is treated from any necessity during the child-bearing period, it will sometimes be an advantage to secure only a temporary cessation of the menses, for it is generally recognized now that the action of the rays is on the tumors as well as on the ovaries. I believe we will find it possible to cause the disappearance of the tumors without actually destroying the action of the ovaries. Fraenkel(9), referring to the treatment of young women, has seen repeatedly amenorrhea produced for a few months, then the patient become pregnant and give birth to perfectly healthy children.

Modern treatment is to-day given in series, each series of doses being separated by an interval of three or four weeks. The menstrual period following the first series of doses is generally uninfluenced, and unless given within ten days preceding the period will probably not be increased. The second period is usually diminished, and the third is usually absent. Therefore one can never judge results inside of two months, and I usually count on from three to six months for the cure. By using the very large doses described by Gauss the duration of treatment can be reduced, but I can see no advantage, and some disadvantage, in bringing about a rapid menopause.

The Tumor.—The tumor is the last to disappear. From a study made in a previous paper(2) I found that 75 per cent. of the tumors had disappeared, but from the fact that in the early cases treated there was a progressive disappearance of the tumors after discontinuing treatment, I am led to believe, but not yet able to prove, that they will probably all disappear. The third case treated was a patient forty-nine years of age, who had a tumor the size of a grapefruit, extending to the umbilicus at the beginning of treatment, at the end of the second year it was the size of an orange, and when last examined, five years after beginning treatment, which is now nearly four years ago, the tumor had entirely disappeared.

Subsequent Degeneration of the Tumor.—The fear of subsequent degeneration of the fibroid has been aroused by a number of men(10), both in personal conversation and in literature. If this were a great likelihood it surely would have developed long before this. This treatment has been in use nine or more years, and the early work was done very much less satisfactorily than it is done to-day, and yet there is no definite records of any such degeneration. Norden-toft(11) remarks in July, 1914, that he has been unable to find on record any evidence of malignant degeneration in the relics of a

myoma or fibroma that has retrogressed under Röntgen treatment. There have appeared, however, two or three cases in which malignancy has been discovered during the course of treatment, which had not been discovered previously. Haenisch(12) reports one case of unrecognized carcinoma. Shoemaker referred to one case in discussion at the Atlantic City Meeting, June, 1914. When one considers the frequent occurrence of carcinoma it is rather remarkable that only so few have shown the development of carcinoma during the course of treatment, for Freund, referred to by Nordentoft, found malignant disease of the uterus or ovary in 6 per cent. of 500 myoma cases, Klein in 7.7 per cent. of 491 cases, and Mackenrodt in 7.7 per cent. in 418 cases. Tracy (referred to by McGlinn(6)) found it in 10 per cent. of his cases. Therefore, if no malignant disease has developed in over 1500 cases that have been treated long enough at least to be placed on record (from 1 to 9 years), and among which with a percentage of 7 per cent. there should have developed over 100 cases of malignant disease if they had been untreated, it would seem to me a rather strong argument in favor of treatment, from the fact that only two or three cases have been recorded in which malignant disease developed during the treatment, or one-fifth of 1 per cent. Since there is apparently 99 or more per cent. less carcinoma in the number of cases treated by the Rontgen rays than are found in the general average, it would suggest very strongly that the rays have a beneficial influence in the prevention of malignant disease or in the cure of early cases of carcinoma. It is true that the most of these cases treated were more or less selected, and carcinoma reasonably eliminated, but in the cases of the Freiburg Clinic, at least, and probably in many others, all patients who applied were treated. Therefore, if we are limited simply to the last 195 cases reported from the Freiburg Clinic there should have been in the ordinary course of events, approximately fifteen cases of cancer develop. There is no record of any such degeneration.

Most patients treated have been more or less under the observation of gynecologists and it is not likely that many cases of carcinoma could have developed, following Röntgen treatment, and not been reported. It seems, therefore, that the fear of subsequent degeneration is entirely without foundation.

The Difficulty of Making an Accurate Diagnosis.—This is an objection that has been raised by most gynecologists, and on the basis of this difficulty and on the statistical basis of the complications that are liable to arise with fibroma of the uterus, a number of papers(5-6) have been written strongly objecting to the Röntgen

treatment. While most Röntgenologists have advised against the treatment of any cases with known complications it does not follow that all these cases with complications are going to die, provided that they are treated with the rays. The statement is often made that it is not the preferable treatment, but it is entirely unfair to assume that any large percentages of these cases will die if treated, for if carcinoma of the pelvis can be made to disappear after it has recurred, following an operation, and if inoperable cases can be made operable or the disease can be made to disappear, as I shall show later, it is surely fair to assume that these early unrecognizable carcinomas may also disappear. Therefore it seems to me an unnecessary fear to be aroused in patients in whom Röntgen treatment has been advised. If complications were as dangerous to the patient as has been indicated, surely many of these 1500 or more patients already recorded would have died and we would know of it. Gauss found death in only half of 1 per cent. in the first group of cases treated, which involved incomplete and undeveloped technic, and no deaths at all in the second and third group, while under operation the operative mortality is at least 2 or 3 per cent., and recurrent mortality much greater.

The action of the rays is effectual on abnormal tissues as well as on the ovary and fibroid. In 75 per cent. of all cases where there had been adhesions of the genital organs, Fraenkel(13) found they had improved or entirely disappeared after Röntgen treatment. Firmly fixed uteri became movable, thick bands in the parametrium softer and less prominent, and bands in Douglas' pouch could no longer be felt when placed under tension. In one case a firmly adherent ovarian cyst became movable. He explains this retrogression of adhesions under Röntgen treatment as being partly mechanical, the myomata as they decrease in size losing the adhesions by traction. In other cases it must be admitted that there is a reduction of the adhesions by the direct action of the Röntgen rays. This was particularly true in adherent uteri and peritoneal tuberculosis, and, in some cases, the retrogression of the adhesions was confirmed on laparotomy.

Complications Arising during Treatment.—There is nothing to prevent an operation if a complication arises during the course of treatment. Generally the patient's hemorrhage will have been controlled, she will be less anemic, and she will stand an operation better than at the beginning. In one of the cases which I have treated, the patient had been extremely anemic from hemorrhage, the fibroid extended to the umbilicus, amenorrhea was produced

and the tumor was reduced to the size of an orange, when she developed symptoms of pelvic abscess. This demanded an operation, which was done at a time when the patient was in much better health than at the beginning, and from which she recovered completely. There was no trouble in the healing of the wound, and the preliminary x -ray treatment had done nothing but good.

POSSIBLE DANGERS FROM THE TREATMENT.

The Skin.—In all Röntgen therapy our first thought is the skin, for the great proportion of the rays are absorbed in the skin and the superficial layers of the tissues, therefore we are limited in the quantity of rays that can be given through any particular area of skin. This has led us to divide the areas, as much as is necessary, so as to get a deep effect by cross-firing, which is nearly or quite equivalent to the effect in the superficial tissues. With good technic, the use of hard rays, filtration by at least 3 mm. of aluminium and a layer of sole leather and careful measurement of dosage, there should be no ill effects on the skin, beyond pigmentation, which disappears and is not objectionable. The degree of pigmentation will vary with the complexion of the patient treated. Dark people show more pigmentation than others, and the light complexioned are apt to show slight redness instead of pigmentation, but a real dermatitis should always be avoided. The pigmentation will disappear just like the tanning from the sun. Fortunately the ovaries and tumor tissue are more sensitive to the rays than the skin, and therefore one can obtain results without damage to the skin.

Visceral Effects.—The possibility of damaging the other viscera has been raised both by gynecologists and Röntgenologists. In a few instances diarrhea has been recorded in literature which lasted for a day or two after treatment, but this probably is a constitutional condition if due to the treatment at all, of which I shall speak later. Accidental diarrhea occurs so commonly, independently of any treatment, and especially in the neurotics, that it can easily be ascribed to any new procedure. There has never been any intestinal irritation in my patients. In two cases of mine slight bladder irritation developed, which lasted a few days, but in one of these, at least, the patient had been subject to this bladder irritation at intervals before this treatment had been instituted. Therefore, I believe it is of no serious importance.

Constitutional Symptoms.—Since we have been using these mass-

ive doses, and giving a great many doses in a short time, a number of patients have complained of lassitude, nausea, and sometimes vomiting, which lasts a day or two, and occasionally three. At first this was thought to be due to an effect upon the ovaries, but I have seen it also in extensive breast treatments, in the treatment of a large sarcoma of the hip and in the treatment of carcinoma of the liver in a man. I believe these effects are due to the inhalation of the gases which are generated in the neighborhood of the high-tension currents. This is noticed now because of the multiplication of doses given on one day, and also because the more penetrating rays now used require a much higher voltage, which gives more brushing from the machine and wires. I am making some investigation along this line and believe that I am gradually eliminating these constitutional effects. I hope to make a more complete report of this subject at a later date.

Menopause Symptoms.—The symptoms associated with the production of an artificial menopause have at no time been severe, and they consist chiefly of flashes of heat and occasional headaches. In some cases these have been practically absent. Krönig says that the symptoms of an artificial menopause are very much less severe after Röntgen treatment than after operation.

Metropathic Hemorrhage.—Metropathic hemorrhage and hemorrhages occurring at the climacterium respond especially well to this form of treatment. Sometimes these hemorrhages occurring at about the normal menopause respond remarkably quickly. Herff⁽¹⁴⁾ says the best results are obtained in climacteric hemorrhage. Of forty-nine patients of this class treated by him all but one were cured. In all of these cases the hemorrhage had resisted the previous measures used. The action is the more prompt the nearer the normal menopause.

Hemorrhage Due to Malignant Disease.—I began the treatment of uterine malignant disease on an advanced inoperable case in 1901. The patient was referred to me by Dr. Elizabeth Peck, at the Philadelphia Hospital. This was at the beginning of Röntgen treatment, at a time when no filtration was used and when we knew little about the control of the rays. I felt justified in treating her very severely, as was done. Two years later she returned to the Philadelphia Hospital because of the degeneration of the skin over the lower abdomen, due to the effects of the rays. At this time all evidence of carcinoma of the pelvis had disappeared, according to the statement made by Dr. Peck. During the subsequent years I treated about fifteen patients, but with only a moderate improvement, and

I abandoned the treatment for about eight years. During the past year I have been much encouraged by the effects of deep Röntgenotherapy and have again treated a few cases of recurrent carcinoma of the pelvis. The patients have improved, but I am not yet prepared to report any specific results in this field.

Amann(15) states that he has applied Röntgenotherapy in fifty-two cases of uterine cancer. In the thirty-one absolutely inoperable cases of cancer of the cervix, five of the patients were completely or nearly cured, 29 per cent. thus being restored to health, when they had been absolutely doomed before. The improved technic accomplishes this, besides without danger of Röntgen burns even with the far more extensive dosage, while the action on the cancer cells is more destructive. When the rays are applied both from front and back to act on an advanced cancer of the cervix, they act on the entire region, all the lymph glands and adjacent tissues feeling the effect, and thus a more thorough clearing out of the malignant disease is possible than could even be realized by operative measures. In one case he had removed a cancer of the cervix three years before and a recurring tumor a year later. Again a tumor as large as a fist developed in the pelvic connective tissue but this was treated with intensive Röntgen exposures and a complete cure followed. The sciatica-like pains and the contracture of the foot from pressure on the nerves vanished and the patient gained in weight. She was in good health for a long time, but died suddenly later without recurrence of pelvic trouble. Amann's experience has been so favorable that he thinks the improved technic for Röntgenotherapy can be applied even in operable cases.

Krönig(8) reports sixty-four cases of carcinoma that were treated for the prevention of secondary growth after operation; of these, forty-three were treated almost exclusively with unfiltered rays, while twenty-one cases were treated partly with filtered and partly with unfiltered rays. Twenty-three of the forty-one cases undoubtedly died of carcinoma. From following the subsequent history of twenty-one cases, in which filtered rays were used, nineteen were undoubtedly free from carcinoma. Sufficient time had not elapsed to speak of them as definite cures, yet the result is so unusual that he says it will have to be credited to the treatment, and that recurrences are not so frequent when filtered rays are used after operation.

Sielmann(16) treated sixteen cases of carcinoma, three were inoperable carcinomas of the cervix, one became free from bleeding and pain and improved in general health, and died of apoplexy at the

age of sixty-one. Two others became free from bleeding and pain with shrinking of the tumor. Six other cases of metastatic carcinoma improved—there was a decrease in bleeding and pain, and a lessening of the malignant discharge. Four cases given postoperative treatment have had no recurrence in the two years. One case of carcinoma of the urethra improved.

Such results as the above, obtained in hopeless cases of carcinoma in which the disease has spread, makes me less fearful of treating a carcinoma that cannot be diagnosed, for if we can cause the disappearance of an extensive distribution of carcinomatous tissue there should be less difficulty in causing the disappearance of an early case. It must not be understood that I am recommending Röntgen treatment in operable cases, but I think that we must not become hysterical and insist upon operating upon every case in which malignant disease cannot be absolutely eliminated. Likewise in sarcoma of the uterus we can act within reason, for it is well known that sarcoma is even more responsive to the Röntgen rays than carcinoma. Miller, writing from the Freiburg Clinic, states that from January 1, 1909, to July 28, 1912, 175 cases of myoma were treated by the rays and none have shown any signs of sarcoma. In 318 myomas operated upon five showed sarcoma. He also showed that of 180 cases of sarcoma operated upon, 79 per cent. failed to be permanently cured. From an analysis of the theoretical probabilities of death from operation or death after *x*-ray treatment, he concludes that eight-tenths of 1 per cent. will probably die after *x*-ray treatment, which will compare favorably with 79 per cent. after operative treatment.

The cautions laid down both by gynecologists and Röntgenologists that Röntgenotherapy must be applied by competent operators is of course very important, and even more important than that care should be used in surgical operations, for all physicians receive a certain definite amount of training, both theoretical and practical, in surgery, while many who buy *x*-ray machines know little or nothing of the theory or the practical applications of the rays in treatment or diagnosis, and a machine will no more accomplish results in this field without the addition of skill than will surgical instruments do good operations, excepting in the hands of a skilled surgeon.

CONCLUSIONS.

1. Röntgenotherapy must be looked upon as a very efficient adjunct to the gynecologist's armamentarium, and while I believe

that the rays should be applied by the Röntgenologist, excepting where the gynecologist has become a Röntgenologist, he should at the same time work hand in hand with the gynecologist.

2. Deep Röntgenotherapy stops the hemorrhage associated with uterine fibroids. This is followed by a gradual disappearance of the tumor. This atrophic process may extend over several years and continues long after the cessation of treatment.

3. The treatment of metropathic hemorrhage is almost uniformly successful.

4. Uterine hemorrhage occurring at the menopause, when not malignant, will usually respond very quickly. There should be an increase in weight and an improvement in the blood condition following treatment, and when this does not occur suspicion of malignancy should be aroused. (Albers-Schönberg.)

5. Some good results can be obtained in inoperable carcinoma. The deep Röntgenotherapy should be especially recommended as postoperative treatment in all cases operated upon for carcinoma.

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