Roentgen Treatment of Diseases of the Generative Organs

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The use of the x ray as a therapeutic agent in diseases of the female generative organs is no longer new. Already a vast literature, experimental, biological, röntgenological and surgical has accumulated on the subject, but among the profession the method of application of treatment and its limitations, is not generally understood.

After Albers-Schönberg's discovery in 1902 of the sterilization effect of the rays on the testicles of rabbits, and Halberstadter's demonstration of the greater sensitiveness of the ovary of the female of animals to the agent, it was not long before the occurrence of similar changes in human beings was proved and not long before a mass of evidence had accumulated to prove that the application to the pelvic structure of a certain x ray dose caused temporary or permanent cessation of menstruation.[1]

It is to this end that the x ray has its greatest field of applicability. The gynecologist and the radiologist are both concerned in this application of the x ray as a therapeutic agent, and a close cooperation between the two is essential if effects are to be obtained and the treatment is to be properly and honestly applied. Without a correct diagnosis, without proper control by the gynecologist, without a proper selection of cases, the radiologist works blindly and often to the detriment of his patient. In fact, the radiologist is but the assistant of the gynecologist in these cases. The knowledge of the actual pelvic conditions must come from the gynecologist and the keener his diagnostic ability, the closer his scrutiny of the case, the more effective are the results and the higher the percentage of cures.

In reference to the radiologist, there is this to be said—that he must apply the rays with brains and talent; that, although certain fundamentals must be adhered to, which will be indicated later, and which are the essentials of technic, he must remember that he has a living human being to deal with, who responds and reacts in manifold ways to the application of this powerful agent.

What is the function of the gynecologist in this cooperative treatment? The answer will define for us the limitations of the applicability of this treatment. The function of the gynecologist is to select the cases for treatment.

[1] The first to apply the röntgen ray for the treatment of uterine fibroids was Foveau de Courvelles (1904). Longfeller (1906) was the first to make definite observations upon the menstrual changes produced by radiation of the generative organs. Albers-Schönberg (1909) was the first to attempt to apply a definite systematic technic to this therapeutic procedure. Kronig and Gauss carried the technic a step further by their introduction of filtration with aluminum (the use of which was first suggested by Thompson) and the dosage through numerous ports of entry. Friedrich, Seitz, and Wintz showed the importance of the secondary radiations in the tissues, and indicated methods of increasing these by the use of higher voltages, heavier filtration and greater focal distances and larger fields. They also established a unit of dosage.

Of the five great causes of uterine bleeding, pregnancy, infection, displacements and lacerations, neoplasms of the uterus and ovaries, and endocrine disturbances (which are usually ascribed as the cause where no gross pathological change is discernible and which are due to dysfunction of ovary, thyroid, hypophysis or adrenal) we are concerned with the latter two only. The remainder are not within the province of the radiotherapist. Of the ovary it may be stated that dysfunction of this organ is an overwhelmingly important factor in the pathogenesis of affections of the generative organs.

CONDITIONS IN WHICH X RAYS SHOULD BE USED.

The x ray is applicable to the treatment of the following conditions:

1. Excessive or prolonged hemorrhage:
   a. From a uterus showing no gross pathological lesions, at puberty, at the menopause, during the whole child bearing period.
   b. From a uterus showing pathological changes.
2. Benign tumors.
   a. Fibroids of the uterus.
   b. Myofibrosis.
3. Malignancy.
   a. Carcinoma.
   b. Sarcoma.
4. Sterilization.
   a. For severe dysmenorrhea with infantile development of the uterus.
   b. After Cæsarean section.
   c. For osteomalacia.
   d. For systemic diseases, tuberculosis, carcinoma (extrapelvic) and heart disease.
   e. For social indications.
5. Diseases of the vulva.

Having selected the cases, the radiologist applies a certain dosage of rays to the pelvic organs. In order that the rationale of the method be clearly understood, it is necessary to recall certain primary considerations.

1. That the reaction of the cell depends upon the absorption of x rays. 2. That the reaction of the cell is apparently the same to rays of different wave lengths, if the same amount of energy is actually absorbed. 3. That the cells vary in their reaction to the same amount of energy absorbed, certain cells being destroyed, others stimulated to growth, others showing no changes. 4. For certain cells, both malignant and benign, the amount of radiation of a certain wave length which will cause degeneration and death has been established. 5. That applying the ray as a therapeutic procedure both the reaction of the organism as a whole to the radiation and the local effect on the organ treated must be studied. The general effects are due to the entire absorption by the portion of the body irradiated, while the local effects are the result of the varying amounts of radiation reaching the various tissue layers.

If the amount of energy of a certain quality which will cause the degeneration and death of the normal or aberrant cell is established, we know the dose which will give the maximum effect. This is comparable to the effect of the maximum dose of a drug. The maximum dosage may be applied in one continuous period (massive method), or it may be divided into several periods (the fractional method). The biological effect of the fractional radiation is cumulative. The x ray acts in small doses to stimulate, in moderate doses to inhibit, and in large doses to destroy. Normal and pathological tissues differ as regards their reaction to the radiation. The lymphocytes and glandular tissue are more sensitive than the connective tissue cells; the ripe graafian follicle is more sensitive than the spermatoza, skin more sensitive than mucous membrane, while muscle fibre and brain tissue are relatively insensitive. So also, pathological tissues vary in their sensitiveness to the ray.

The sarcoma cell requires only sixty to seventy per cent. of the dose of the carcinoma cell for its destruction. Tumors of embryonal cell origin are relatively susceptible. Ovarian carcinomata of embryonal origin are very sensitive to radiations. The rodent ulcer or basal cell epithelioma responds to a smaller dose than does the squamous cell epithelioma. The Hodgkin's gland responds to a smaller dose than the tuberculous gland.

The more vascularized a growth the more susceptible it is to radiation. In general the greater the karyokinetic activity and the shorter the karyokinetic interval the more sensitive is the cell to radiation. There is, therefore, no one general standard maximum dose.

TECHNIC.

Until recently, because of the lack of accurate methods of measurement, the technic of the application of the radiation to the treatment of pathological conditions of deep structures was more or less a matter of individual experience and observations. No precise data based on scientific measurements were possible. Through the use of instruments of relative precision fairly exact data are now obtainable and the entire technic is being established on sound scientific basis.

THE PHYSICAL DOSE.

This may be defined as the energy absorbed in a volume unit of substance. It is directly proportional to the surface energy of the radiation and indirectly proportional to the hardness. It is estimated by subtracting the quantity of energy remaining on the under surface of the absorbing media from the total energy falling on the upper surface of the media. Such a unit of physical dosage is, however, the average dose and it becomes necessary to distinguish, a, the surface dose, that is, the dose absorbed by a very thin uppermost layer of the irradiated medium from the, b, deep dose, the energy absorbed in a very thin lower layer of the absorbing media. The surface dose is the intensity of the energy falling on a square centimetre of surface in a unit of time, whether this is on the upper or lower surface.

If all structures reacted similarly to an equal dose of the x ray, the technic of treatment would be simple. A single dose to the area in which the involved tissue existed would be sufficient. This is not the case. We are limited in the application of the ray by the skin, a barrier which must be taken into consideration in making our attack. The administration of such a single dose as might cause a severe

skin reaction (superficial or surface dose) might have but little effect on the organs located at a depth. There are many factors which must be taken into consideration in the determination of the superficial and the deep dose. Before these can be considered, it is necessary to understand certain primary conceptions relating to dosage.

THE ESTIMATION OF AN ERYTHEMA DOSE.

Since it was found that the amount of chemical and biological action produced by the x ray is in direct proportion to the amount of electrical energy applied to the tube, and since with modern apparatus it is possible to measure this, and since the method is more accurate than the methods previously used and more easily applied, the standard erythema dose, that is to say the quantity necessary to produce an erythema of the skin in a certain number of days after exposure, may be measured by estimating the voltage or spark gap, the milliamperage, the time and the distance. The measurement by chemical, photographic and color reactions are in this country at least abandoned.

This method is of value only for the estimation of the skin effects. It gives no clue whatever to the dosage underneath the surface. Estimations by these formulas are of value in protecting the skin from deleterious effects when the lower voltages are used.

The energy absorbed, therefore, is the deep dose, subtracted from the surface dose and divided by the volume of the absorbing media. If the thickness of the irradiated layer is made equal to the semireducing layer value of the ray (that height of a layer of water which will reduce its intensity to half), then the intensity of the energy at the depth is half that of the surface energy. If the hardness of the radiation is expressed in semireducing layer values, the physical dose is inversely proportional to this. Now it has been established that the semireducing layer value is equal to the absorption coefficient of the ray for the same absorbing media. Therefore, the physical dose may also be expressed in terms of surface energy and absorption coefficient to both of which factors it is directly proportional.

THE BIOLOGICAL DOSE.

The biological dose is the physical dose multiplied by the sensibility coefficient of the tissue. If, therefore, the sensibility coefficient of a certain cell is known, then the biological dose may be estimated from the physical.

According to Wetterer the ovarian follicle is seven times more sensitive to the ray than the skin, ten times more than connective tissue, twenty times more than muscular tissue. Myoma cells are much more sensitive than normal muscular cells and more sensitive than the skin. Since the skin acts as the barrier which must be taken into consideration in estimating the dose, the biological skin dose has been taken as a unit of dosage. Taking the sensibility coefficient of the skin as 1, the sensibility coefficients of the remaining tissues may be estimated.

1. For the skin..... 1.0
2. For the ovary..... 2.5
3. For the sarcoma cells..... 1.6 —1.4
4. For the carcinoma cells..... 1.0 —0.8
5. For the intestines..... 0.74
6. For the muscles..... 0.55
7. For the tuberculous tissue..... 2.0

There was, until recently, no practical method of measuring the deep biological reaction by physical means. It cannot be estimated by mathematical formulæ because of the essential rôle played by the secondary radiations (scattering) in producing the biological effects below the surface. Recently, however, the ionization chamber has been made practical for this purpose.

By this iontoquantimeter, as it is called, estimations of the number of units of ionization required to obtain a skin erythema have been estimated.[1] This value was then itself taken as a unit. Now, by applying the iontoquantimeter to various levels of human tissue irradiated, the intensity of the rays reaching the depth at various levels, in percentages of the intensity necessary to produce the skin unit have been determined. It is thus that the dose in terms of surface intensity for various conditions was estimated.

Calling this radiation necessary to produce such a reaction as one hundred per cent., Seitz and Wintz have with this dose as a basis determined a biological dosage which, in spite of its deficiencies, is nevertheless useful.

TABLE I.

Dose	*Per cent.*
1. Skin unit dose	100
2. Castration dose	35
3. Sarcoma dose	60-70
4. Carcinoma dose	90-110
Irritation dose for carcinoma	35-40
5. Intestinal dose	135
6. Muscle dose	180
7. Tuberculosis dose	50

These figures for castration and malignancy doses should not by any means be accepted as absolute. Depending on the characteristics of the individual and the characteristics of the type of malignancy the doses given in the table may need considerable modification. There is surely a certain percentage of sarcoma and a greater percentage of carcinoma which is not affected by the above dosage. There is considerable variation in the sensitiveness of the ovary to radiation, even in individuals of the same age.

THE DOSE QUOTIENT.

The dose quotient is that quotient of surface dose over deep dose and gives the ratio between the surface dose and the deep dose. The aim of the deep therapy technic is to keep this quotient as small as possible, or, in other words, that the dose at a particular depth small approach that which was received by the surface at the time of administration as closely as possible. The value of the deep dose is expressed in percentage of the value of the surface dose. The deep dose percentage is the reciprocal of the dose quotient. The aim in modern therapeutic technic is to get as high a deep dose percentage as possible. Striving for this has been responsible for the striking changes in technic. The value of the dose depends on three factors: 1. On the absorption of the rays in the overlying tissues. 2. On the dispersion of the radiation. 3. On the scattering of the radiation.

[1] The "skin erythema" of Seitz and Wintz which is the basis for their measurement is apparently too low.

1. For the same thickness of absorbing media and the same focal distance, the dose quotient will be smaller the less the absorption by the media irradiated, that is to say, the more penetrating the primary radiation. The characteristics of the primary radiation may be changed: a, through increasing the penetration; b, through filtration, attempting to attain homogeneity.

2. For the same thickness of absorbing media and the same ray quality the dose quotient will be smaller the further the source of radiation is from the absorbing object. Increasing dispersion, therefore, diminishes the difference between the surface and the deep dose.

3. For the same thickness of absorbing media and the same focal distance and with the same ray quality, the dose quotient will be smaller the greater the scattering. The production of secondary radiations in the tissues which tests have shown greatly improves the effective dosage is increased, a, through increasing the focal distance, b, through increasing the size of the portal.

1. THE CHARACTERISTICS OF THE RADIATION.

The penetrating quality of the rays depends on the voltage by which the tube is energized. For standardization of technic and for relative accuracy in estimating dosage, practical homogeneity is necessary. A ray which is no further hardened (average penetration unchanged) after passing through ten cm. of human tissue, a desirable qualitative homogeneity for therapeutics, can only be obtained by higher voltages and heavier filtration. Until recently the voltages used for the generation of x rays with the tubes available varied from eighty to one hundred thousand volts. Recently, however, transformers have been developed which generate from one hundred and eighty thousand to two hundred and eighty thousand volts, with the production of rays of very great penetrating power, making it possible to deliver a considerable quantity of qualitatively homogeneous radiation in the tissue depth and to produce considerable scattered radiation, which augments the percentage of radiation absorbed at the depth. When qualitative homogeneity is maintained the reaction of the different tissue is then dependent only on two variables ,intensity and time.

The time necessary to produce a given dose with various voltages, other factors being the same, may be estimated as follows:

Gap	20 cm.	25 cm.	30 cm.	35 cm.	40 cm.
Time	7 1/2 min.	5 1/6 min.	3 1/6 min.	2 1/2 min.	1 5/6 min.

It is thus seen that it takes four times as long to get the same dose with an eight inch gap as it does with a sixteen inch gap. The translation of spark gap equivalents into numerical voltage values is responsible for much confusion in thought. The mean square voltage has usually been stated in this country. Abroad the peak voltage has been given. The measuring of air gaps between blunt points has been used in this country, while abroad the measurement is made between point and disc. Because frequency and wave shape have no appreciable effect in varying the discharge between sphere gaps, these are now being utilized for the measurement of voltages. With the proper sized spheres, voltages from 10,000 to 500,000 may be measured with an accuracy of about two per cent. (Kaye). The sphere gaps read peak voltage. The values are about as follows:

Blunt points	*Needle points*	*Sphere gaps*	*Peak voltages*
10 inches	6.96	1.6	110 K.V.
12 inches	9.4	2.25	140
14 inches	11.1	2.62	160
16 inches	13.6	3.50	195
17 inches	14.0	3.64	200
18 inches	15.5	4.25	220
20 inches	17.8	5.32	250

The x ray spectrometer measurements show a simple relationship between the voltage applied to the tube and the shortest wave length of the emitted radiation, namely, that voltage is equal to 12,400 divided by the wave length in Augstrom units.[2] By measuring the wave length of the radiation the maximum effective voltage applied can be determined and vice versa, by knowing the maximum voltage the wave length can be determined by dividing 12,400 by the voltage. Thus with a 200,000 peak voltage there would be a wave length of .062 A°. It would perhaps be advisable in the future to speak of wave lengths of the radiation.

FILTRATION.

To still further increase the absorption at the depth, the ray is filtered with the view of cutting out the rays of longer wave length. The filtration utilized with the old technic consists of three to five millimetres of aluminum. With rays of greater penetrating power, heavier filtration is necessary. Ten millimetres of aluminum, five tenths millimetres of copper or zinc are used.

To obtain practical homogeneity so that the ray is not changed after passing through ten cm. of water or bakelite, a five mm. zinc filter is necessary. Such filtration is practical only with currents of very high voltages, such as are being used in the most modern therapeutic methods.

The socalled deep dose percentages with various gaps and filters have been estimated as follows:

	Equivalent spark gap		
Filter	*30 (12 in.) Percent.*	*35 (14 in.) Percent.*	*40 (16 in.) Percent.*
Unfiltered	..	5.2	..
Aluminum—3 mm. ...	..	12.2	..
Zinc—0.5 mm.	18.5	19.	20.5
Zinc—1.0 mm.	..	20.5	..
Zinc—2.0 mm.	..	22.	..
Copper—1.0 mm.	21.4	..	22.5
Copper—2.0 mm.	21.3	..	22.6

These measurements have been obtained by Seitz and Wintz by iontoquantimeter tests.

FOCAL DISTANCE.

The further the source of radiation is from the absorbing media for the same quality of radiation, the smaller the dose quotient, in other words, the less the difference between surface and deep dosage. With the same radiation through the same portal, the absorption at a depth of three centimetres will vary with the focal distance as follows:

At a depth of 3 centimetres	*At a depth of 5 centimetres*	*At a depth of 10 centimetres*
30 cm.—77%	30 cm.—70%	30 cm.—47%
50 cm.—86%	50 cm.—79%	50 cm.—59%
100 cm.—93%	70 cm.—83%	70 cm.—65%

With the increase in focal distance there is a loss in intensity which varies inversely with the square of the focal distance. To get the same intensity at an increased distance, it is necessary to increase the time directly as the square of the distance, with certain exceptions, which will be noted later.

[2] The Augstrom unit is equivalent to one hundred millionth part of a centimetre.

The appended table of Voltz gives the intensity and time factors for various distances, from 23 to 100 cm., the focal distances usually employed.

F. D.	23	25	28	30	35	40	45	50	55	60	65	70	75	80	85	90	95	100
I.	1.00	0.85	0.67	0.58	0.43	0.32	0.26	0.21	0.17	0.15	0.12	0.11	0.09	0.08	0.07	0.065	0.060	0.055
T.	1.00	1.18	1.48	1.70	2.32	3.02	3.83	4.73	5.72	6.81	7.99	9.26	10.63	12.10	13.66	15.31	17.09	18.89

Checked by iontoquantimeter measurements, Wintz states increasing the focal distance from twenty-three to fifty centimetres, the time is five to eight per cent. less than calculated and trebling the size of the field under the same conditions the time fourteen to eighteen per cent. less. Beyond a focal distance of fifty centimetres, the time required to obtain a skin dose is about twenty-five per cent. longer than calculated. As judged by skin reaction and epilation this apparent exception to the law above stated cannot be corroborated. Judged by biological tests the distance square law may be said to be valid with this consideration. With long focal distances and small fields the rule does not hold. But with long focal distances and large fields it does hold. Seitz and Wintz use small fields. The size of the focal spot on the anticathode plays an important part in these considerations.

PORTALS.

The absorption quotient may be improved by increasing the size of the portal. This also increases the width of the cone of rays and a greater extent of tissue is radiated with an increase in the scattering. This scattering comes not only from the tissue overlying the object treated but from the tissues beneath. The shorter the wave length of the primary beam the greater the scattering. It has been estimated that as much as fifty to one hundred per cent. can be added to the dose in this way.

The extent to which varying the size of the portal varies the percentage of absorption at the depth is indicated in the accompanying table.

With a peak voltage of 200,000 and one and a half milliamperes of current with a filtration of 1.3 copper the percentage of absorption at various depths for different sized portals for various focal distances is as follows:

Portal	*Depth*					
	1 cm.	*2 cm.*	*3 cm.*	*5 cm.*	*7 cm.*	*10 cm.*
30 CM. FOCAL DISTANCE						
5.7 x 7.6	90	80	70	60	50	40
9. x 12.	90	80	75	65	55	45
18. x 24.	95	90	80	70	60	50
40 CM. FOCAL DISTANCE						
6.1 x 8.1	91	82	75	65	55	45
9.7 x 12.9	92	83	80	70	60	50
19.3 x 25.7	95	91	85	75	67	55
50 CM. FOCAL DISTANCE						
10.1 x 13.4	93	90	80	72	65	55
20.1 x 26.8	95	92	88	80	72	60
60 CM. FOCAL DISTANCE						
10.4 x 13.8	95	90	80	70	65	55
20.7 x 27.6	97	93	90	80	74	63

By increasing the focal distance either to 80 or 100 cm. the dose at 3 cm. may be increased from ninety to ninety-five per cent. These figures would indicate that in order to approximate the hundred per cent. deep dosage the more superficial the growth, the longer the focal distance and the larger the portal necessary, while the deeper the growth the more numerous and smaller the portals.

Increasing the size of the portal of entry from of three cm. the increase is about sixty per cent. Under certain conditions, by increasing the focal distance to either eighty or one hundred centimetres, 1.5×2 cm. to 10×15 cm. gives nearly four times the dose at a depth of ten cm. while at a lesser depth the dose at a depth of three centimetres can be increased from ninety to ninety-five per cent., which is over a maximum sarcoma dose and a minimal carcinoma dose. The maximum effects may, therefore, be obtained by combining the requisite portal with the proper focal distance.

The general findings of Dessauer regarding this latest technic of röntgen therapy is of interest. 1. With hard rays and large portals, deeply placed and centrally situated points receive more radiation through scattering from the direct rays. 2. While the direct intensity decreases with the depth, according to rules, the scattered intensity increases with the hardness, with the size of the radiated volume, with the proximity of the area to the central radiation with the thickness of the overlying layer. 3. Definite intensities due to scattered radiation are present lateral to the directly radiated volume.

LOCALIZATION.

The ideal method of application is that which concentrates the x rays upon the particular organ it is desired to affect. Such concentration of energy can only be obtained by the most exact orientation regarding the position of the organ in the particular individual. Thus, if it is the ovaries upon which the radiation must be concentrated in the treatment of uterine hemorrhages, it is advantageous to locate the ovaries and to administer the dose directly to these organs.

The treatment as generally administered in practice is not so accurately localized and the effect obtained is through secondary and scattered radiation upon the organ attacked. With a view to more accurate direction of the radiation, the technic for the application to ovaries, includes their localization. It becomes necessary then to determine the following facts: 1. The relative position of the ovaries to each other and their projection upon the surface of the body in relation to certain fixed points. 2. The depth of the ovaries from the external abdominal wall.

Hoehne and Lizenmeyer have determined the position of the ovaries in relation to the interspinous line and the median line. By means of bimanual examination in the living, controlled by operative findings, measurements have been made indicating the position of the ovaries in anteflexion both in the nonpregnant and the gravid uterus and in retroversion of the uterus.

The average distance between the ovaries is about nine and a half centimetres. In individuals with small transverse measurements of the pelvis, it may vary from seven to eight centimetres; in those with very large and broad pelves it might be as much as thirteen centimetres. The right ovary is usually more lateral than the left, five to four and a half

centimetres. The more the uterus is anteverted, the greater the displacement of the ovary below the interspinous line.

The distance between ovaries in the second and third months of pregnancy is the same as in the non-pregnant state, nine and a half centimetres. This also holds true for relationship of the right and left ovaries to the median line. In the second month the average is about five centimetres, for the right and four and a half centimetres for the left; the third month five and one third centimetres for the right and four centimetres for the left. As the uterus enlarges the interovarian distance increases; in the fourth month it measures twelve centimetres; in the sixth month eighteen centimetres. The distance below the interspinous line is relatively great in the second month but gets smaller with increasing size of the uterus, in spite of greater anteversioflexion and at about the fourth month is above the line. The interovarian distance grows smaller in the retroverted position of the uterus, and so does the distance below the interspinous line. The measurements hold true only in the absence of a fixation of the ovaries by an inflammatory process.

The measurements given above permit us to state that in the average case—a square three centimetres in size so drawn that its inner border is three centimetres from the median line, its upper border at the interspinous line, will in ninety per cent. of the cases include the position of the ovary. In practice this square is used as a centre for a portal six by eight centimetres in size. The depth of the ovary below the skin was similarly obtained. The distance varied from four and a half to seven and a half centimetres. On the average it was six and a half centimetres on the right side and about six centimetres on the left side.

Though no marked displacement of the ovaries occurs with the myomata of average size, in the presence of large myomatous uteri the localization of the ovaries is difficult, if not impossible.

Therefore, in the square outlined, it is necessary that the ray be so gauged that the required biological dosage is administered at a depth of six centimetres.

In the localization of the uterus for carcinoma, the maximum depth of the organ is considered to be ten centimetres beneath the skin. Taking into consideration the necessity of reaching the pelvic lymph nodes and of applying the ray to the whole pelvis in carcinoma, the localization is unnecessary. In the localization of the uterus for carcinoma, the maximum depth of the organ is considered to be ten centimetres beneath the skin. Taking into consideration the necessity of reaching the pelvic lymph nodes and of applying the ray to the whole pelvis in carcinoma, accurate localization is unnecessary. But in certain tumor formations where localization becomes necessary, in order that the radiation be directed with accuracy, the area to be irradiated must be accurately mapped out. This is essential so that, firstly, all parts of the tumor may receive the required radiation and secondly, that no normal tissue about the tumor receive an overdose. To this end such devices as those of Holfelder (1) or Dessauer (2) may be utilized, the latter method, consisting of carefully constructed charts, giving the dosage at various centimetre levels, with various types of radiation, through various portals, with various filters, based on numerous measurements made with photographic emulsion. Its accuracy in practical work has not, however, been completely verified, though it is extremely useful as a basis for dosage. Where crossfiring becomes necessary, the various cones of radiation must be transferred to the tracing of a cross section of the part of the body and the portals so selected as to obtain sufficient radiation to all parts of those tissues which are under treatment without overdosage to the other parts which are not under treatment.

APPLICATION.

As a rule the skin of the lower abdomen from the umbilicus to the pubis is divided into a number of areas or portals of entry. The number varies, depending on the condition under treatment, and the dose desired at a particular depth. With the old technic the portals were very small, and the whole of the lower abdomen was marked off. Through each such portal, with the voltage equivalent of a nine inch gap, was applied five milliamperes of current with filtration of four millimetres of aluminum at a distance of twenty-five centimetres in ten minutes by a method the intent of which was to crossfire. Though with this technic, in which there was a great aimlessness in crossfiring, castration was accomplished with ease, since the thirty-four per cent. absorption was thus attained. Nevertheless the malignancies were practically unaffected. The iontoquantimetre measurements indicated the necessity for greater, more accurate and more certain dosage, for such conditions and a complete revision of the technic followed. Now the size of the field depends upon the condition treated and upon the depth of the focus to be reached by the particular radiation at hand. The number of portals depends on the biological dose desired. It may be administered through one portal as for castration under certain conditions, or through many portals as in carcinoma of the uterus, with lymphatic involvement.

When the requisite portals have been mapped out, a quantity of radiation is applied at a certain focal distance, through a certain portal and given a certain direction in order to reach the tissues under treatment. The radiation is administered over such a period of time as to obtain the requisite absorption and administer the effective dose at the particular depth at which the structure to be treated lies limited, of course, by the skin reaction. As a rule for benign conditions the skin limit is a first degree reaction but in the treatment of carcinoma it is necessary to administer such a dose through each area as will produce a second degree reaction in the skin, even with vesiculation and complete alopecia. The regeneration of the epidermis, if the dosage is carried no further, is complete without sequela and the skin restitutes to normal. There are at the present time two great methods of dosage: a. By complete dosage at one session; b, by divided doses through several lesions.

(To be concluded.)

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In determining the number of series and the intervals of the series, there are two considerations: First: The local changes in the pelvic organs. Second: The systemic response.

1. It must be conceded that in carcinoma it is a great advantage gained to be able to administer the full dose in as short a time as possible with the aim of overwhelming the affected tissue. On the other hand, when castration is the result desired and no urgency exists, the mental and physical shock resulting from a prolonged session is an indication for the utilization of divided doses and only the total minimal dose necessary to produce the result.

With the modern therapeutic methods, at the distances utilized, the effective dose may require eight to twelve hours. If patients cannot stand this prolonged session, it may be divided into two to four days. In order to shorten the actual duration of the treatment the radiation may be simultaneously applied by two or more tubes each, adjusted over a separate portal, or when the carcinomatous lesion is superficial, by two tubes operating over the same portal.

However given, when a full dose has been administered through each skin area, the series is complete. It then becomes necessary to wait until the reaction, both skin and systemic, have subsided. At the end of this interval, if necessary, a second series is similarly applied, and after another interval a third. (A portion of the skin or "a portal of entry" which becomes the seat of a third degree reaction is closed as far as further treatment through this portal is concerned. In fact, a severe röntgen dermatitis due to previous radiation is an indication in favor of operability of the pelvic condition.)

We have at the present time in the ultraviolet light a method of "doping" the skin whereby severe dermatitis is prevented, even by an overdose. In dosage with the very penetrating radiations and heavy filtration now in use, the erythema may be very transitory and the bronzing very intense.

The administration of all the areas at one sitting, even in carcinoma, where the growth is to be effectively dosed in as short a period as possible is not always feasible. Radiation sickness, which a great number of patients have, to whom are administered the large doses, may make it impossible. This "sickness" is due in part to the breaking down of the cellular elements of the blood and the organs and the liberation of nucleins in the blood (these leucotoxins have a destructive influence on the leucocytes themselves and a markedly irritating effect on the kidney epithelium) and also to the disturbance of the secretion of the organs attacked. This, however, is not the only factor concerned in this troublesome condition. The static discharge distributed over the surface of the patient's body, as a result of long treatments, also plays a part as do numerous psychical factors.

Such patients are made very uncomfortable for some time. This is avoided if the number of doses given in one day is limited. The organism then has an opportunity to eliminate the destroyed products. In some conditions (leucemia) the administration of a very large dose in a short period is actually dangerous. (The reaction of the blood cells to the röntgen ray is striking. According to Murphy, Ross, Chambers, Scott and Mottram, the most striking effect is that which it has on the total number of lymphocytes to the centimetre of blood. At first there is marked diminution in the number of circulating lymphocytes which reaches its lowest level forty-eight hours after the administration of a röntgen dose. There is then a primary rise which reaches its height in from three to five days, due to the contribution of the blood of lymphogenic cells from the lymph glands, bone marrow, etc., and then a secondary fall occurs which reaches its lowest level in from five to twelve days. This again is followed by a secondary but permanent rise which persists for at least six or seven weeks and represents the complete regeneration of all lymphogenic tissues. When, however, the treatments are given a successive number of days these phases may overlap and the permanent increase is much delayed. This selective affinity of the röntgen ray for the lymphocytes is occasionally also accompanied by destructive changes in the granular blood cells. The repeated large doses, by diminishing the number of lymphocytes, lower the power of resistance of the patient, for the lymphocytes play an important rôle in defending the body against the invasion of many malignant growths and their destruction predisposes to metastasis. Small doses, however, will rapidly increase the lymphocytic content of the blood and fortify the body against secondary deposits. An increase in the polynuclear neutrophilic elements has also been reported. A breaking down of the lecithin in the blood with the formation of certain by-products has been reported. This may account for the symptoms of weakness which are sometimes present. Though the significance of these changes is not yet completely understood, the above data suggest a more complicated technic than is now followed.)

The modern treatment with highly penetrating rays through large portals, particularly so when the full dosage over several areas is applied in one session, has resulted in such a terrific destruction of the red blood cells as to produce fatal anemias. An attempt has been made to cope with this "röntgen cachexia," as it is called by transfusion.

This heroic measure, however, only becomes necessary when the radiation attack is made upon a blood already impoverished as a result of the condition for which the radiation is applied. It is, therefore, advisable in all cases to make a preliminary examination of the blood and then by suitable means, rest,

forced feeding, arsenic and iron injections, to bring the red cell condition to as nearly normal a state as possible. This will be referred to later, in the consideration of carcinoma.

During the radiation period and afterward attention should be paid to the general body hygiene. Rest (enforced in cases of carcinoma), regulated diet, mild catharsis are very important. After every series, particularly when heavy dosages are given for malignancy, it becomes exceedingly important to indicate to the patient the impending changes in the skin and the necessity for carefully observing certain precautions, as regards irritation, mechanical, chemical or physical of the skin over the portals through which therapy has been administered. A lotion such as the following (Dodd) should be applied daily for three weeks:

Zinc oxide	½ oz.
Carbolic acid	½ dram
Glycerine	1 dram
Aqua calcis, q. s.	8 oz.

or an ointment consisting of

Cera alba	2.1
Cetaceum	2.4
Ol. olivæ	18.0
Aq. dist.	7.5

The series should not be repeated until the skin reaction has subsided. So also the blood must return to as nearly a normal state as possible. This may take three to six weeks. When large fields have been used, it may be twelve weeks before restitution is accomplishd.

The general tonic effect on the whole system which is often observed during and after x ray treatment is not only due to the result of the local curative action but to a regulating general effect on the endocrine secretion. There is also apparently a decided change in the chemistry of the blood, which shows itself frequently by an absorption of metastasis at a distance from the focus treated.

TREATMENT OF MYOPATHIC HEMORRHAGE.

This type of bleeding is associated with an exaggerated form of the normal changes in the endometrium during menstruation. The cycle of changes through which the endometrium passes is coincident with the cycle of development and recession of the corpus luteum, therefore, in pathological as well as under normal conditions, uterine bleeding is controlled by the corpus luteum. This in turn is probably affected by other glandular secretions. This pathological bleeding is merely a variation in amount, duration, character and periodicity from the normal. This being so, the logical procedure to be followed, if it is desired to cause a cessation, is to destroy that element which controls the menstrual cycle, namely, the graafian follicle, the forerunner of the corpus luteum. Since this ripe follicle is more sensitive to the ray than is the primordial follicle, a smaller dose may destroy only the mature follicles and produce temporary amenorrhea, a larger dose will destroy the primordial follicles and give a permanent amenorrhea. It must be conceded, however, that since radiotherapy acts by destroying the graafian follicles and causing sterility, it is not the ideal treatment, therefore, since the excessive hemorrhage in the grossly normal uterus is due to a disturbance in the proper balance between the various elements controlling menstruation, the aim first should be to restore this.[8] A restitution to their normal condition of the factors governing menstruation may be attempted by endocrinological therapy, for the menorrhagias at puberty, not produced by myomata or retroflexion are undoubtedly ovarian in their origin; while the climacteric bleeding is also associated with dysfunction of the ovary at this critical period.

Though only a small proportion of the cases will be benefited, nevertheless this should first be attempted if the bleeding is not severe. In severe hemorrhage radiotherapy is the method of treatment. In persistent hemorrhage and dysmenorrhea the production of menopause is justifiable even in young women, when the emotional and mental stability is threatened. The therapeutic aim in the metrorrhagia being to bring about a normal restitution of the menstrual function, the radiation should be administered serially, in sufficiently divided dosage to permit the control of the effect. A three weeks' interval is suited to most cases.

The degree of amenorrhea which can be produced depends upon the period of time in relationship to the physiological climacterium in which the symptoms are manifested. The nearer a woman is to this period, the more easily will amenorrhea be produced and the more difficult the production of oligoamenorrhea. At puberty the production of the desired effects is fraught with difficulty. In women under thirty, a partial amenorrhea can be produced. In women between thirty and forty a partial amenorrhea will result once for every five cases in which complete amenorrhea takes place. Even one series at this period may produce a permanent amenorrhea, particularly in individuals who belong to the class in which menopause takes place early. As a result of similar series of radiation the effect, depending on the age, varies as follows:

10-20 years	oligoamenorrhea 80%	amenorrhea 20%
20-30 years	oligoamenorrhea 66%	amenorrhea 33%
30-40 years	oligoamenorrhea 33%	amenorrhea 66%
40-50 years	oligoamenorrhea 3%	amenorrhea 97%

Even in the small percentage of cases where amenorrhea occurs in youthful individuals, menstruation usually reappears after a short interval, but its characteristics are relatively normal.

In women near the menopause age—thirty-eight or over—radiotherapy will produce immediate menopause and the general physical and mental disturbances resulting from the irregular uterine hemorrhage will be avoided. Radiation is the treatment *par excellence* for climacteric hemorrhage. It cannot be denied that with careful technic all cases in this category can be benefitted by the x ray.

FIBROMYOMATA.

What the causal relationship between fibroids and the uterine bleeding is, is not clear. The ovary is a gland of internal secretion and a trophic centre for the whole genital apparatus. It is undoubtedly intimately concerned in the production of neoplasms in the uterine musculature. Apparently the hemorrhage is an accompanying symptom—which owes its origin to a similar if not the same cause.

[8] In amenorrhea, associated with Basedow's disease, a small dose applied to the ovary may bring on menstruation. A preliminary curettage has been suggested in all cases of climacteric bleeding, in search of a possible malignancy.

There are three theories as to the mechanism by which fibroids, subjected to the rays, diminish in size.

1. The fibroid undergoes an artificially produced atrophy—similar to the normal atrophy at menopause. The latter is associated with ovarian changes.

2. There is a direct action upon the smooth muscle cells by the rays, causing them to degenerate and to become replaced by connective tissue. (Fibroids shrink more rapidly after radiation than after castration or following natural menopause.)

3. The endarteritis produced is severe enough to starve the myomatous growth.

The ray undoubtedly calls into play all three factors, though the first and second are the most potent. The reduction in the size of the fibroids may be appreciable before the advent of amenorrhea and fibroids in women who have already had their menopause may be reduced by radiation.

The factor to be considered in the determination of the mode of treatment depends on: 1, age of individual; 2, characteristics of tumor, age, location, size, rate of growth; 3, complications. A. Functional disturbances, a, menstrual disturbances, b, pressure symptoms, and c, pregnancy. B. Organic disease.

THE AGE OF THE PATIENT.

The bleeding from a uterus, the seat of a myoma, just as the bleeding from a uterus showing no gross pathological lesion, is more easily controlled the nearer the patient is to the menopause. The hemorrhage of fibroids usually appears, however, later than the myopathic hemorrhages; therefore, the latter are more responsive to the treatment. In general it may be stated that the hemorrhage due to fibroids should be treated by radiotherapy in those women in whom a permanent menopause is not objectionable. In women about forty with slow growing tumors and symptoms of hemorrhage, pain and pressure, the beneficial effects are striking in their rapidity and permanency. Some observers do not approve of the treatment of cases under the age of thirty, because of the production of premature menopause. This point must be taken into consideration with all the other factors in the case. Because the uterus is preserved for child bearing, it is held by some that myomectomy is the preferable procedure in young women with fibroids and menorrhagias.

The contraindications (phlebitis, obesity, anemia, disease of the heart, lungs, liver and kidney), which before radiotherapeutic days were considered, but nevertheless risked, should now be considered as indications for the radiation treatment, irrespective of age. Even if severe, the menopause symptoms are to be preferred to any operative risk, for they can be fairly well controlled by organotherapy.

LOCATION.

The location of the mass influences the method of treatment.—Thus: 1, Interstitial fibroids are most amenable to this treatment; 2, subserous fibroids are best treated by surgery, and 3, submucous fibroids are amenable to x ray treatment but had better be treated surgically. (These tumors have a tendency to malignant degeneration.)

But pedunculated myomata, partially extruded from the cervix, myomata, the seat of cystic calcareous, gangrenous degeneration, or associated with carcinoma, large, rapidly growing myomata, producing severe pressure symptoms and rapidly growing myoma with severe hemorrhages and not rapidly responsive to radiation, are surgical conditions requiring surgical treatment. These indications are, however, not sharply defined. A subserous growth, if small but the cause of pain, may be attacked with x ray with excellent results, producing marked shrinkage in the growth with cessation of symptoms. Similarly, submucous growths in patients in whom severe operations cannot be performed, may result in shrinkage and extrusion of the growth and its removal by simple surgical means. These cases must, however, be closely watched for dangerous hemorrhages may occur after radiation. (Such submucous, pedunculated myomata are frequently overlooked clinically.)

In the interstitial growths, the results are uniformly good. There is amenorrhea, marked shrinkage of the growth and general systemic improvement. The dysmenorrhea of interstitial metritis may be greatly relieved by radiation.

Size.—A tumor reaching midway between the symphysis and umbilicus may be successfully treated by radiation unless pressure symptoms exist, for these tumors of long standing with compression of the adjacent viscera had better be treated surgically. Some operators will not treat tumors whose size exceeds that of a four months pregnant uterus, because of the slow retrogression and the possible danger of later degenerative changes.

Rate of growth.—If the tumor grows and the hemorrhage persists, in spite of treatment, a complication, a wrong diagnosis, or a malignancy should be suspected and operative measures instituted. (It has been suggested that a temperature record during the x ray therapy is advisable in the attempt to determine the onset of infection, softening, necrosis or thrombosis.) Small but rapidly growing tumors respond more readily than large, slowly growing tumors.

Condition of tumor.—Necrotic or degenerated myomata, producing cachexia and toxemia from absorption and an anemia out of proportion to the menorrhagia, are best treated by operative proceduce. So also are tumors showing calcareous degeneration and characterized by intense menstrual and intermenstrual pain. The existence of an associated malignancy is not always an indication for operation.

COMPLICATIONS.

FUNCTIONAL.

Menstruation.—In rare cases severe hemorrhages may require immediate treatment and unless contradindications exist, operation is indicated.

Pressure.—Severe pressure symptoms demand quick relief and therefore indicate operation.

Pregnancy.—Is a distinct contraindication to röntgen therapy of myoma, for the pregnancy may be interfered with and fetal development disturbed.

ORGANIC DISEASE.

The presence of an associated acute or chronic adnexal inflammatory condition is a direct contraindication to the treatment. Severe anemia and

myocarditis, either as a result of the myomata or the hemorrhages, are conditions which indicate the necessity of radiation, particularly when the hemoglobin falls as low as twenty-five per cent. In these cases, in order to avoid the increase in bleeding after the first series, a larger dose than usual should be given. (Hemotherapy either by drugs or transfusion preliminary to the x ray treatment has been suggested.) Diseases of the heart, lungs, liver, kidney or blood-vessels are indications for the application of radiation in fibroids.

TECHNIC.

The old technic of many small fields has given way to the more modern method of large fields and heaver filtration. The results with this latter method have been very striking. The complete dosage may be administered in one to four sittings and rarely is more than one series necessary.

The Coolidge tube is energized with a peak voltage of two hundred thousand, with five milliamperes of current at a focal distance of thirty-five centimetres.[4]

The ray is filtered through one millimetre of aluminum and five tenths of a millimetre of copper. The treatment is adminstered through four fields, two abdominal and two dorsal, each on either side of the median line in four sessions in two to eight days at the end of the menstrual period. Fifty per cent. of the full skin dosage is applied to each portal. In many cases this treatment is followed by complete cessation of menstruation, even in women under thirty. In some cases the exposure must be repeated but only a smaller dose is then necessary. While the tumor and the hemorrhage may be controlled by frequent and continued small doses, nevertheless the complete dosage applied within a short period has many disadvantages from the viewpoint of accuracy of dosage and economy of means and time. The systemic effects during and after radiation are not more severe, if the proper technic is used, than with the older methods.

Where only radium is available it may be used as a substitute for x rays in the treatment of myomata and myopathic hemorrhages with the limitations above enumerated. Fifty mg. of radium, properly filtered, are inserted into the uterine cavity, for twenty-four hours or less, depending on the age of the individual. It may be definitely stated that for the purpose of producing menopause the x ray is superior as a therapeutic agent to radium.

The results to be expected from radiotherapy are:

1. *Cessation of the bleeding.*—When the bleeding is very excessive and time is a factor, operation is indicated. The hemorrhage due to fibroids should be treated by radiotherapy in those women in whom a permanent menopause is not objectionable. In younger women, up to the age of thirty-eight, the resultant premature menopause must be considered unless a surgical operation is contraindicated. The contraindications (phlebitis, obesity, anemia, disease of the heart, lungs, liver and kidney), which before radiotherapeutic days were considered, but nevertheless risked, should now be considered as indications for the nonoperative treatment. While the menopause symptoms are not desirable, they are to be preferred to any operative risk, for they can be fairly well controlled by organotherapy. Fibroids in a woman over forty should be treated only by röntgen therapy. While the tumor and the hemorrhage may be controlled by frequent and continued small doses, nevertheless, complete doses should be applied quickly for the avoidance of prolonged period of attendance and to prevent the development of complications.

2. *The shrinking of the growth.*—This shrinkage is a slow process, though it begins almost immediately. Marked shrinkage following radiation occurs in about sixty per cent. of the cases. The extent of the shrinkage depends both on the age of the tumor and the age of the patient.

3. *Improvement in the general condition,* the cessation of pain, the relief of insomnia, the cure of the constipation, an increase in weight and general increase in vigor definitely follow in the cases in which the treatment is effective.

With the older method of administration of the radiation through many fields at a distance of twenty-three centimetres with a nine inch gap and five ma. and filtration of four mm. of aluminum the result of the first series is rarely an amenorrhea without return, usually an increase of symptoms, with increased and profuse menstruation, or no change at all. The result of the second series is usually an amenorrhea, sometimes a marked diminution in the flow or no change.

The result of the third series is usually amenorrhea in women over thirty or the treatment is ineffective.

Two or three series are usually necessary to obtain the desired result. With the modern method if the radiation is applied in the first half of the intramenstrual period, the desired effect is produced after the first series.

In the myofibrosis cases, with diffuse thickening of the uterine wall, the effects may not appear after the first session but always after the second.

When the cases are properly selected and all proper indications exist and the technic is properly carried out, the desired clinical result, namely ammenorrhea, diminution in the size of the myomatous uterus, frequently a restitution to normal and disappearance of all symptoms, is obtained in one hundred per cent. of the cases.

Generally speaking the röntgen method of treatment has its disadvantages as well as advantages. The gynecologist should weigh these in determining the method of treatment to apply.

ADVANTAGES.

1. The treatment is painless.

2. There are no failures in the properly selected cases.

3. The menopause is not usually attended by any

[4] The transformer apparatus used consists of two separate closed core transformer units, energized in parallel and capable of producing a voltage of 300,000. There are two rectifying mechanisms, one for each of the transformers. The current is so rectified that both impulses are delivered unidirectionally to the terminals of the tube, while the ground potential is maintained between the two transformers. The rectifying mechanism consists of a cross-shaped mica spider at the ends of which are mounted the segments and conducting strips. The frictional resistance of this form of commutating switch is much less than that of a full circular disc of the same diameter, which permits both discs to be mounted on the opposite ends of a single motor shaft. The voltage control consists of a heavy variable ballast resistance in the primary circuit. The filament transformer is provided with a voltage stabilizer. Damping resistances are placed in the secondary circuit for the prevention of surges and for the symmetrical distribution of the load in the circuit.

severe nervous symptoms, the psychical equilibrium is maintained and the vasomotor changes are insignificant.

4. It takes one to eight weeks and if it fails the operation may be carried out under the same conditions as before.

5. There is practically no mortality if the cases are properly selected, while the operative mortality with abdominal extirpation is about three per cent.

DISADVANTAGES.

1. There is a definite time period before the cure is effected.

2. The fibroid may only partially disappear after several months, and in rare cases a recurrence may occur.

3. Malignant changes may be present in the uterus or in the fibroid tumor and overlooked or malignant changes may take place in the fibroid under treatment.

The last is urged as the most important objection to the use of radiotherapy. It is true that a sarcomatous degeneration may, except in cases of rapidly growing tumors, be overlooked in determining the proper treatment. But sarcoma is rare and the danger of operation is surely greater than the possible danger of overlooking a sarcoma. Greater stress is laid on the coincidence of carcinoma or epithelioma with fibromyoma. Though it is obvious that an undiscovered cancer of the uterus will lead to fatal results, unless the radiotherapeutic procedure is especially applied for this purpose, it is also obvious that the discovery of cancer in the specimen after hysterectomy has been performed, presents the problem of surgical treatment in a new aspect.

Just as any form of treatment outlined for the fibroid is altered when the cancer is discovered, so the röntgen treatment must be altered if the response to intensive treatment is such as to indicate that malignancy exists. This phase of the case is in the hands of the gynecologist, whose constant scrutiny of the case by all the available methods will minimize the possibility of an erroneous diagnosis. It must be conceded that where the slightest doubt as to the correctness of diagnosis exists the interest of the patient demands operation followed by immediate röntgenization. Not infrequently are tumors of the ovary radiated in the belief that it is a fibroid, which apparently does not respond to treatment. The crux of the entire treatment of fibroids by this method is correct diagnosis. By that test, the value of this treatment stands or falls. In some gynecological clinics, eighty-four per cent. of all myoma cases are submitted to röntgen therapy. There are still, however, in this country, a number (though rapidly diminishing) of gynecologists, who operate the vast majority of cases and refuse to acknowledge the value of radiation, even now when the consensus of opinion holds that it is the method of choice in the treatment of fibroids.

CARCINOMA.

GENERAL CONSIDERATIONS.

Preparation.—The patient with carcinoma, to be submitted to radiation, must be considered in the same light and from the same viewpoint as the patient about to undergo a severe surgical operation, both as regards preliminary management, radiation and postradiation treatment.

It is surprising that this viewpoint is not more generally considered and that patients suffering from a malignant disease are not managed with the same consideration as would be given to a severe surgical condition. It is necessary, firstly, that the patients be primarily put in as excellent a physical condition as possible, both by rest, diet, and the administration of hemotherapy, with the intention of bringing the blood to about as nearly a normal point as possible and of increasing the general resistance and vitality of the individual. An enforced rest in bed, proper regulation of the excretory functions, forced and regulated diet, and the administration of iron and arsenic, preferably by subcutaneous injection, should be instituted. During the treatment there should be rest in bed, liquid diet and thorough elimination. For at least six weeks after the treatment has been completed the patient should be put to bed on a regulated diet, with plenty of fluids and the blood constantly examined and treated.

Technic.—Too great emphasis cannot be laid on the necessity of accurate technic in the application of radiation to the treatment of carcinoma. While in the treatment of nonmalignant conditions, there is considerable latitude in the size of the dose by which the desired effects may be obtained and while no very accurate localization of the radiation is essential, in the treatment of malignancies not only must the type of malignancy be known and the pathological field be accurately topographed, but the dose must be accurately measured so that it is neither too large or small and the quantity received by each particular portion of the body traversed by the ray must be known.

The technic of successful radiation of cancer demands: 1. A radiation of the proper quality and quantity. 2. The administration of the lethal dose of this radiation to all the cancer cells at the varying depths at which they exist. 3. The administration of the dose in such a way that, a, the local resistive power of the normal cells about the tumor are not depressed and, b, the general resistance of the whole organism is not appreciably lowered.

The minimal lethal dose for a carcinoma cell, Seitz and Wintz assert, has been established with a fair degree of exactitude. In terms of surface erythema dose it is ninety to one hundred per cent. At least this quantity of radiation and possibly a minimal lethal dose of 140 per cent. may need to be administered to a particular cell. The aim to administer a lethal dose at the desired depth through a portal as small as possible, to avoid general effects, and at a distance as small as possible in order to shorten the duration of exposure.

The question of dosage of the cancer cell would be a relatively simple matter if the various types of cancer cells all reacted similarly to the radiation. At present, however, with the means at hand the sensibility of the cancer cell may vary from an extreme sensitiveness to absolute radioresistance. Then, also, there are periods when the cancer cell has a low vital resistance, as during the period of karyokinesis. But it is not possible to attack all the cells at this particular period. If the radiosensitive-

ness of the particular type of cancer cell under consideration were known, if the degree of activity of its karyokinesis could be estimated, or the karyokinetic interval determined, then the cell might be attacked in its vulnerable period, with the particular type of radiation which would be most effective. The vulnerable period is during mitosis and the vulnerable point is the nucleus and the action is on it directly. In other words, growth stops because the nuclear structure is damaged and the action is a physicochemical one, taking place as a change in the atomic structure of the nuclear substance, due to bombardment of the secondary electrons excited by the primary radiation. Though, because of its selective affinity for the radiation, the neoplastic cell will react as indicated, the normal cell, on the other hand, because of its low degree of sensitiveness, is excited to increased cellular activity and plays an important defensive or reconstructive rôle against the activities of the tumor. This defensive or reconstructive power of the normal cell can be inhibited or destroyed by overdosage and cannot be aroused when the general bodily vitality is low. No definite statement regarding the actual dosage necessary in a particular case or for a particular type of tumor can as yet be accurately given and any sweeping statement regarding carcinoma dosage must be taken with caution. The clinical study of the case is now the sole guide in the determination of the size and the frequency of the dose.

In the determination of the focal distance, the size and number of portals, the size of the mass, its location and the size of the overlying and underlying tissue layers must be studied.

Though to those portions of the tumor at the immediate surface or which, by destruction of the skin, has reached the surface, the necessary one hundred per cent. may be administered with ease, the extension of the growth towards the deeper structures, however, creates a problem—that of obtaining as much absorption at the depth as at the surface itself. If the growth in its deeper or peripheral parts receives a dose less than the minimal lethal dose, the effect is to irritate rather than inhibit its extension. The lethal dose can be administered through several portals by crossfire, if the growth is at a considerable depth below the surface, as in the uterus. The nearer the growth is to the surface, the more difficult the technic. Thus, for instance, given a growth having a diameter of five centimetres, and located well below the surface (more than five centimetres) it is possible to administer forty to forty-five per cent. of the surface dose at the required depth through each of the two portals of entry, measuring six by eight centimetres, so that the mass may receive eighty to ninety per cent. dosage, with the focal distance as small as twenty-three centimetres. But when such a mass is superficially situated, a crossfire attack is not possible, because of the resulting necrosis which would occur from overdosing of the normal overlying and underlying tissues. This holds true with greater force when the mass is smaller and situated at or a short distance (one to two centimetres) below the surface. Such a mass cannot be effectively crossfired through two portals at the usual focal distance of twenty-three centimetres.

If the radiation were applied through a single portal, however, at this focal distance, the cells at the base of the tumor might receive only about fifty per cent. of the surface dose, depending on the size of the portal. The upper layers would receive the minimal carcinoma dose of ninety per cent. and heal, but the deeper layers (five centimetres) would be irritated to proliferation. In order to administer a dose of one hundred to one hundred and ten per cent. at a depth of five centimetres through this single portal of six by eight centimetres a focal distance of twenty-three centimetres according to Seitz and Wintz, the surface would need to receive two hundred per cent. with certain skin necrosis.

By increasing the size of the portal to ten by fifteen centimetres at twenty-three centimetres focal distance a dose may be obtained at the required depth which is above the irritation dose but less than the minimal lethal dose and by repeating the dose within two weeks it may be possible to produce some destruction of the carcinoma. Yet this method is uncertain, for in the two weeks' interval proliferation may occur.

However, by increasing the size of the portal of entry and the focal distance, the required minimal lethal dose may be administered. In other words, a minimal dose of ninety per cent. may be administered at three centimetres depth, through fields varying from 108 to 225 square centimetres area, at a distance varying from eighty to one hundred centimetres focal distance. Each case, therefore, requires individual consideration, the mass must be measured and the portals carefully plotted and the dosage at various depths estimated.

CARCINOMA OF THE UTERUS.

Though in some cases of primary carcinoma the tumor in its primary stage is limited to the uterus, in the vast majority of cases, even with small carcinomata, the pelvic lymphatics and lymph nodes are infiltrated. With extensive growths this is always the case. It becomes necessary, therefore, in every case not only to attack the primary growth but every portion of the pelvic structures must be thoroughly radiated, including the lumbar, iliac and sacral and inguinal lymph nodes.

The surgical viewpoint classifies carcinoma of the cervix into operable, borderline and inoperable cases, utilizing the radiation for postoperative treatment in the first group, preoperable treatment in the second group and agreeing to the submission of the third group entirely to the treatment by radiation and electrical means. The radiological viewpoint would consider the first surgical group as clearly defined radiation cases, the second surgical group as radiation cases, to be followed by electrical and surgical treatment, and the inoperable group as radiation cases, to be treated with the aid of electrical means.

The treatment by irradiation is one which demands very careful scrutiny of the patient for a prolonged period, in order to detect the earliest evidence of recurrence, either locally or in the lymphatics. Of the three types of carcinoma of the cervix, the medullary, the ulcerative and the fungating, the former is the most malignant and when submitted

to treatment usually already has lymphatic involvement. The radiation of the fungating type is markedly simplified and aided by a removal of the friable masses by diathermy.

In reference to carcinoma of the body of the uterus, the routine may be followed which has been in vogue for the treatment of breast tumors, the radiation being applied before and after surgical intervention of the carcinoma may be treated entirely by radiation. Whether of the cervix or of the corpus, whether prophylactic or radical, the full dosage of the radiation must be applied within as short a period as possible, notwithstanding the reaction of the patient.

Preoperative radiation may be applied either four weeks or four days before the operation, depending upon the extent of the infiltration. If the primary tumor is definitely circumscribed and the proper radiation is applied only with the intent of devitalizing any deposit which may exist in the lymphatics, then the operation may be performed four days after the radiation. When, however, the primary lesion is not localized and there is considerable infiltration in the parametrium and the lymphatics, the purpose of the radiation is only to circumscribe the extent of the growth and devitalize the infiltration in the lymphatics, the operation should be performed four weeks after the radiation. In both instances, however, it is important that the fields be so mapped out on the abdominal wall as to leave an unradiated area in the median line, in order that a clean surgical incision be made possible and that healing of the incision be not interfered with. Recurrences, whether in the uterus, parametrium, vagina or lymphatics, should be treated promptly and vigorously.

The mapping out of the fields and the arrangement of the tube in its proper position should not be done without a careful orientation as regards the situation of the carcinomatous mass. Whether of the cervix or the fundus, the arrangement of the tube in relation to the field and the pelvic structures must be made with the aid of a bimanual examination, with one finger in the vagina over the mass and the other on the abdominal wall. Every portal must be carefully mapped out in this manner.

Seitz and Wintz utilize the voltage corresponding to a sixteen inch spark gap at a focal distance of twenty-three centimetres with five-tenths millimetre zinc filtration, each portal measuring six by eight centimetres, receiving from twenty-five to thirty-eight minutes' exposure, which is repeated after six weeks' interval. The treatment is administered through three fields anteriorly and three posteriorly and one over the vulva. The middle field is located above the symphysis, and somewhat toward the right of the median line. The two lateral fields are placed crossways. When the pelvis is small the lateral fields extend outside the iliac fossa. They seek to obtain a destructive dose which they calculate at 135 per cent. Because in the raying of the primary tumor the rectum receives the full carcinoma dose, 110 per cent., therefore, in the second series the right parametrium is treated first, through three portals in front and three in back. This is done because as there is only six weeks interval between the first and second treatments, it is imperative to avoid injury to the rectal mucous membrane by overdosage. In the third series, when the left parametrium is treated, in the same way through three portals, fourteen weeks have elapsed and the rectal reaction has had time to disappear. If the left parametrium is more involved than the right, then the left must be treated first, regardless of the danger of the rectal mucous membrane. It must be stated that this technic, even if carefully applied, is not usually successful without local radium treatment. The radiation administered through the portals above described appear to be insufficient. Another method is to apply the radiation through four fields, one in front, one behind, taking in the entire pelvic abdominal wall, and one to either side, measuring twenty-four centimetres by nine centimetres at fifty centimetres focal distance, filtering through one millimetre of copper, with a peak voltage of 200,000. The result of the treatment must be carefully studied and radium inserted if necessary.

If the uterus is extensively involved and there is marked infiltration in the parametrium and the glands, both the above methods seems to deliver insufficient dosage.

At least four portals in front, five posteriorly and one over the vulva are necessary. The bladder and rectum are emptied. The pelvis is elevated. The abdominal wall from the symphysis to the umbilicus and as far lateral as the posterior axillary line is mapped out as the field of operation. The curved surfaces of this anterior and lateral portion of the abdominal wall are built up by the use of wet tissue paper, aluminum silicate, or by a compound of paraffin, until rectangular surfaces are obtained. The anterior surface is now divided into four equal portals. The posterior abdominal wall is similarly built up and similarly mapped out. The two lateral aspects are each considered as one portal. And the radiation administered over an additional portal over the vulva with the upper edge of the 6 by 8 cm. field at the lower border of the symphysis. For each of these portals a full dose is made up as follows: the voltage 45 cm. gap between points; filtration 1 mm. copper, 3 mm. aluminum; distance 30 cm. milliamperage minutes, sufficient to administer the maximum dose the skin can safely tolerate—a second degree erythema.

Eight to twelve weeks after an area has been treated the dose is repeated. The frequency of the repetition of the series and the interval between series depends upon the general and local clinical condition and the condition of the skin.

If the treatment is given after surgical operation, the same routine must be used in the application of the rays, subjecting the part to complete dosage in as short a time as possible. Lengthening the duration of the series and insufficient dosage predisposes to fresh invasion. The affected tissues must be completely overwhelmed by the ray.

Radium has its important and valued place in the treatment of carcinoma in association with the x rays. The gamma rays of radium and the x rays are similar agents and equal wave lengths of the same radiation may have the same effect. It is true that the wave length of the gamma rays of radium represent the maximum penetrative power of any radiation now known. To produce x rays having

a penetrating power of the gamma rays a Coolidge tube with a voltage of about one and one half million would be necessary.

The intensity of the gamma radiation is, however, exceedingly feeble. So that even though with 220,000 or 250,000 volts a radiation having a penetrating power of the gamma rays is not produced, still there is made up in intensity what is lacking in penetration. The x rays perhaps are the more generally useful therapeutic agent, in that, besides the local action, there is much desired action on distant tissues, for which radium is ineffective. The gamma rays and the x rays now available do not, however, have an identical therapeutic value. The lymphocytes are more readily reduced by the x rays than radium while the cells of the liver and spleen are more susceptible to the gamma rays.

Radium is of great value as an adjuvant in the treatment of carcinoma of the uterus, but the effect on the distant lymphatics and on pelvic metastasis can only be obtained by crossfire by x rays—unless enormous quantities of radium are at hand. Six hundred milligram hours' irradiation with the gamma rays will kill cancer cells for a distance of one centimetre. A dose at least four times as great is necessary if the malignant cell lies at a distance of two centimetres, an extremely unsatisfactory dose quotient, which cannot be increased by increasing the focal distance, due to loss of intensity. Increasing the quantity of radium is likely to produce a burn of the rectal mucosa, which is as sensitive as the carcinoma cell. Unless the tumor is larger than three centimetres in diameter over 100 mg. should not be used and the rectum and bladder must be pushed away. To destroy a cancer of the cervix three centimetres in circumference, 3,200 milligram hours are necessary; one hundred mg. for thirty-two hours. Observations in the dead house on cases of deep cancer treated with radium clearly indicate that without the additional use of x rays, the treatment by radium alone is likely to produce superficial healing with active and progressive infiltration in the depth. In these cases mere reduction in the size of the tumor does not warrant the deduction of the retrogression of the tumor. The effect by this combined treatment, depending on the growth and the reactive powers of the body of the particular case, is either a clinical cure, a prolongation of life and amelioration of symptoms, discharge and pain, or an improvement to such an extent as to make the case easily operable and diminish the possibility of recurrence.

The final verdict regarding the effect of this combined treatment cannot as yet be given. The Wertheim operation in good hands shows forty per cent. (Bonney) of the patients alive after five years. The combined radiation treatment, judging even by present results, will surely better this.

CARCINOMA OF THE VULVA.

The lesions may vary from flat growths three quarters of an inch in diameter to masses half an inch thick by three inches in length. Though the erosion is apparently on the surface, the invasion is through the fascial planes. This infiltration extends beyond the visible evidences of the growth.

Here the method is that outlined with large portals at great focal distances. The field to be treated is blocked out with lead. The target skin distance utilized is from 75 to 100 centimetres, the central ray being directed to the middle of the field. An exposure of eight to twelve hours is given at one time with 200,000 volts.

STERILIZATION.

a. In all but infectious dysmenorrhea, the radiation has the effect of diminishing the discharge and pain. The dose must be carefully applied in order to avoid complete castration. However, when the uterus is infantile, no such contraindication exists and then sterilization may be produced. The degree of permanency will depend upon the age of the individual and the size of the dose.

b. The röntgen treatment may also be utilized after Cæsarean section, where resection has not become a part of the operation.

c. The application of the radiation to the ovary for the purpose of treatment of osteomalacia was first advanced by Ascarelli. Wetterer obtained a marked improvement by systematic x ray treatment. The pains diminish or entirely disappear, motion improves and the general condition improves remarkably. Further bone deformation does not occur but existing bone deformities are not, however, influenced. The treatment is continued until complete and permanent amenorrhea is obtained.

d. Cases of severe tuberculosis or where an operation for carcinoma has been done or where x ray therapy is being applied for carcinoma of the breast, may be sterilized by the röntgen ray effectively. This procedure is to be preferred to the surgical means.

e. The attitude regarding the sterilization for social reasons is rapidly changing. As a rule sterilization may be rapidly accomplished in multipara, when such measures are justifiable and permissible, according to the numerous indications which need not be outlined here.

PRURITUS VULVÆ.

Here the ray should be applied filtered in small dose, with a voltage of 90 to 100,000, three millimetres of aluminum, at thirty cm. distance, one treatment a week. A single skin unit, less than an erythema dose may be sufficient. This should not be repeated until an interval has elapsed sufficient for the subsidence of every trace of reaction. By this technic the production of the desired result, though somewhat delayed, is nevertheless, because of the permanency and the absence of later skin changes, the preferable method of application.

CONCLUSIONS.

Anyone reviewing the rapid progress of the röntgen therapeutic methods in gynecology in the last few years, must be driven to the conclusion that though much has already been accomplished, there is no finality to progress. Considerable modification in the scope and the technic of this form of therapy will undoubtedly take place in the near future. Already a great quota of the cases have been removed from the realm of the surgeon and the solution of the many unsolved problems in technic will surely widen the field of röntgenology.

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