A DOSAGE SYSTEM FOR USE IN THE TREATMENT OF CANCER OF THE UTERINE CERVIX

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IN 1933, Paterson and Parker[1] published from the Holt Radium Institute, Manchester, a dosage system for surface applicators of radium which has since been extended to cover interstitial and other forms of radium treatment. This system, as it stands, cannot be used for the treatment of cancer of the cervix, and an attempt is now made to formulate rules which will allow the condition to be included among those to which a dosage system is applicable.

The problem of the dose received in the treatment of carcinoma cervix presents special difficulties because of the variable size and shape of the parts to be treated, and of the tumours found, but an approach from a different angle has been made, and, as a result, we believe that a dosage system can be applied to this locality with approximately the same degree of accuracy as to surface and interstitial applications.

This article attempts to show that it is possible by arranging the radium in specially designed intracavitary applicators so to fix the relationship of the radium to certain important points within the pelvis that the dose received at these points can be pre-calculated.

Two main subjects are considered:—

(1) The Dosage System.

(2) The Application of the Dosage System to Therapeutic Technique.

(1) THE DOSAGE SYSTEM

A dosage system, to be useful, must make it possible to obtain, by following certain reasonably simple rules, a relatively homogeneous dose of radiation in the zone of tissue selected for treatment, this dose being expressed as röntgens delivered in a stated period of time. To make the rules suggested for cancer of the cervix clear, it is necessary

(*a*) To define the zone of tissue and the reason (normal tissue tolerance) for selecting it for treatment.

(*b*) To consider the individual variations in size and shape of the organ and their relation to dosage.

(*c*) To describe the intracavitary applicators.

(*d*) To describe the method of assessing dosage.

(*e*) To relate the anatomical position to simple geometrical conceptions.

(*a*) With the exception of very early cancer of the cervix (Stage I, League of Nations), for which less radical therapy can be justified, all observers agree that it is necessary to treat the cervix itself, the uterus, the vaginal vault, and the parametria, including, if possible, the lymph node on the lateral pelvic wall, usually called the obturator node. This is done by putting radium applicators in the uterine cavity and in the vault of the vagina. For the

techniques at present in general use, the dose is stated in milligramme hours, taking no cognisance of the different arrangements made necessary by the variations in size and shape of the organs, but dosage is limited here, as elsewhere, by the tolerance of the normal tissues, and the anatomical factors which we believe to determine this tolerance must be examined.

Normal Tissue Tolerance

The most common histological form seen in cancer of the cervix is squamous cell carcinoma, and in spite of the varying degrees of differentiation there is as yet no valid evidence that squamous cell cancer can ever be treated as a very sensitive tumour, so that the full tolerance of the normal tissues must always be used. Fortunately, the local tolerance of the uterus is very high. The function of the organ must be lost in any case, because the irradiation received by the ovaries is far beyond the castration dose, and all that remains after treatment for cancer is a small, fibrous uterus with the central canal opening through a ring of fibrous tissue which represents the cervix, and a narrow vagina with obliterated fornices. Necrosis of the uterus, cervix, or vaginal vault, except as part of a massive necrosis due to gross overdosage, does not produce serious symptoms, although slight hæmorrhage from telangiectatic vessels or small patches of ulceration may be seen.

It is sometimes said that the dose received locally on bladder and rectum gives the limit of tolerance, but local necrosis of the bladder is in our experience rare, while the effect of a local overdose, described as "intrinsic rectal reaction" by T. F. Todd,[2] after a detailed investigation into the nature and course of radiation necrosis made in this Institute, is usually the result of a slipped applicator or a persistently retroverted uterus carrying the radium too near the rectal mucous membrane. This is due to a fault in technique, not to a constant limiting tolerance. The presence of such a limiting tolerance is, however, certain, and to overstep it spells disaster in the form of extrinsic rectal reaction in mild cases and massive necrosis, becoming dangerous to life, in severe cases.

To distinguish the factors involved it is necessary to look at the anatomical relationships of the uterus. The cervix is in the centre of the true pelvis, and the uterus is anteverted and anteflexed so that it lies at right-angles to the vagina and resting on the bladder. The uterus projects upward from the pelvic floor, raising a fold of peritoneum, which is reflected at a higher level in front than behind, and this fold extends out to the pelvic walls on either side to form the broad ligament. The pelvic organs are invested and supported by the pelvic fascia, condensed in places into fibro-elastic bands, which form suspensory ligaments; such a band runs through the broad ligament with the uterine vessels. The looser areolar fascia between the folds of the broad ligament is the parametrial fascia, and the firmer supporting tissue which surrounds the cervix is the paracervical fascia. Through this paracervical fascia the uterine artery on either side enters the wall of the uterus, the ureter passes below the vessels to enter the bladder, and the efferent veins from a plexus on the uterus and a plexus on the anterior rectal wall pass to join the hæmorrhoidal veins. Blood vessels are sensitive to irradiation, one of the earliest changes seen in

normal tissue being endarteritis, while fibrosis and contraction of the elastic fascia probably accounts for the stricture of the ureter, which is described as a sequel to treatment.

The work of T. F. Todd, already referred to, supports the contention that the initial lesion of irradiation necrosis is always due to high dose effects in this paracervical region, and not a direct effect on the rectum. It therefore seems reasonable to regard tolerance here as the limiting factor of normal tissue tolerance in the irradiation of the uterine cervix, and it is on this assumption that the principles to be outlined are based. The area described will be referred to as the "paracervical triangle," but should really be regarded as roughly pyramidal in shape, with its base resting on the lateral fornix and the apex curving round with the anteverted uterus (Fig. 1).

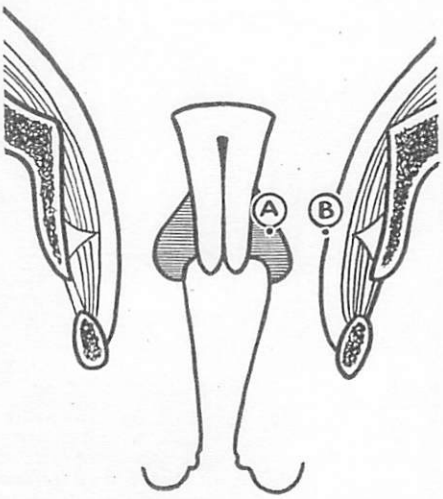

Fig. 1.—Diagram showing paracervical triangle points A and B.

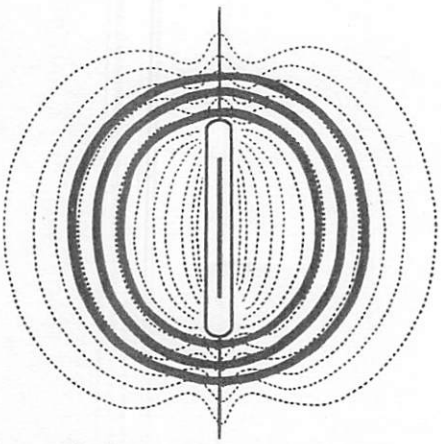

Fig. 2.—Isodose curves round tube of radium to show corresponding shape of ovoids.

It is necessary for the measurement or calculation of dosage to fix a definite point in the paracervical triangle, and that selected and designated point A is 2 cm. lateral to the central canal of the uterus and 2 cm. from the mucous membrane of the lateral fornix in the axis of the uterus. The dose at Point A gives, as will be shown later, an average figure for the dose received throughout a considerable zone in the paracervical triangle.

(*b*) (i) *Individual Size and Shape of Organs*

Having decided that Point A is the point of limiting tolerance, and that the dose must be measured here, it is necessary to find out how much the dose received is influenced by variations in the size and shape of the uterus and vagina. Sandler[4] examined 100 pelves, and divided his cases into:

Large .. Transverse diameter, 6·5 to 7·5 cm.
Medium .. Transverse diameter, 5 to 6·5 cm.
Small .. Transverse diameter, less than 5 cm.

The ratios of the different sizes were found to be present in the following proportions:—

Large .. 18 per cent.
Medium .. 24 per cent.
Small .. 58 per cent.

(*b*) (ii) *Size of Vagina and Dosage Point B*

It is always an advantage to place the applicators as far laterally in the vaginal fornices as possible. The main lymphatic pathway from the cervix lies along the base of the broad ligament, and the first lymph node usually occupies the upper end of the inner surface of the obturator membrane. These lymph nodes, already referred to, are frequently involved, and an effort should be made to include them in the volume of tissue raised to lethal dosage, so that advantage must be taken of the large vagina to place the radium so as to obtain the highest proportional depth dose. This dose received by the obturator node becomes so important that it is advisable that it should be measured, and a secondary point, designated B, five centimetres from the mid-line and on the same level as Point A, is either in or near enough the node to be used to give a measure of the dose received by it.

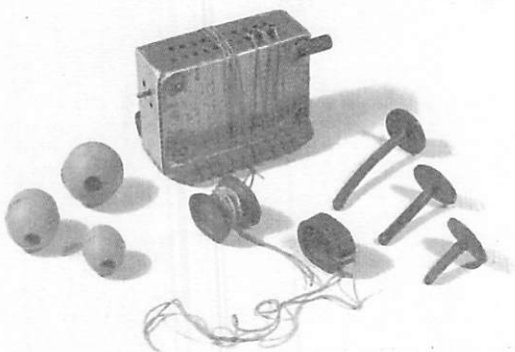

Fig. 3.—Photograph of applicators and radium tubes.

We believe that the limiting tolerance at Point A, and the desirability of giving a sufficient dose at Point B, are so important that the problem of calculating dose received, and determining dose to be delivered, can be discussed in terms of safe, yet adequate, dosage at these points.

(*c*) *The Vaginal Ovoids*

The applicators used in the vagina are essentially a modification of the corks described by Regaud, and used in the Paris technique. They play an essential part in the dosage system. Made of rubber, they have certain special features, so for the sake of brevity have been given the name "ovoid." They are approximately ellipsoids of revolution made of hard rubber, and bored along the axis of revolution to take one or more radium tubes of actual length 2·2 cm., active length 1·5 cm. The shape of the ovoid follows the distribution in three-dimensional space of the isodose curves round a radium tube of 1·5 cm. active length, the shape thus ensuring that the dose is homogeneous over the whole surface of the ovoid (Fig. 2).

Three sizes of paired ovoids are made to fit the three sizes of vagina—large, with shortest diameter 3 cm.; medium, shortest diameter 2·5 cm.; and small, shortest diameter 2 cm. The pairs are held apart by a "spacer,"

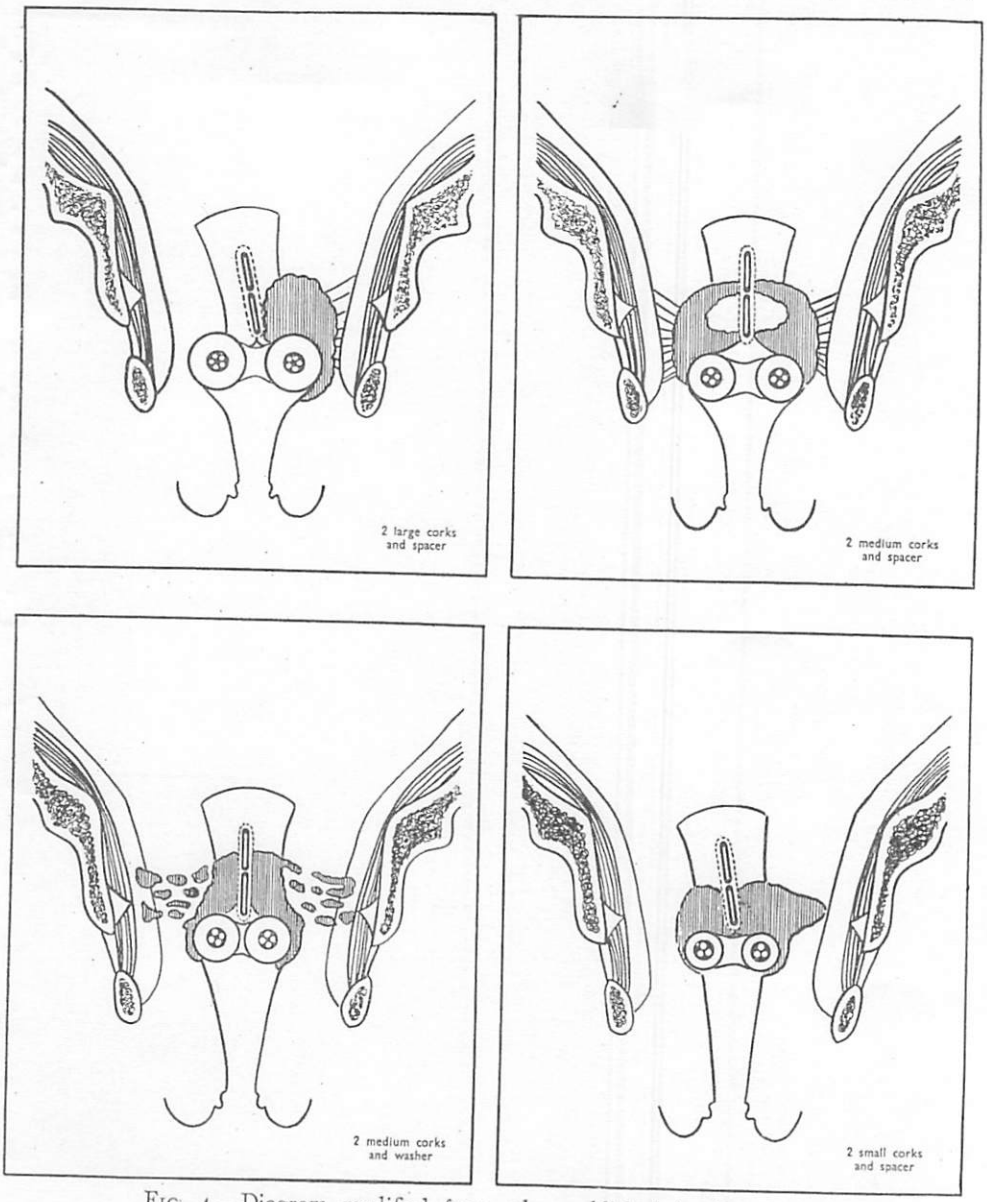

FIG. 4.—Diagram modified from atlas published by League of Nations Health Organisation, showing adaptation of ovoids to different stages of cancer of the cervix.

also made of rubber, which fixes the distance between them at 1·0 cm. If the vagina is too narrow, the ovoids are held in position by a "washer," which allows them to lie almost in contact. The ovoids lie in the lateral fornices, the spacer over the cervix.

It is clear that the largest possible size of paired ovoids must always be used, as this will not only carry the radium nearer to Point B, but will also give a better proportional depth dose. The design of the vaginal ovoids is such that, although easy to insert, the relationship once they are inserted remains constant between the radium foci, yet the different sizes make possible full lateral distention of any vagina, large or small (Fig. 3).

The Intra-uterine Applicator

In this Institute it is considered so important to avoid dilatation of the cervix, with the attendant risks of tearing open a way for sepsis and for the dissemination of malignant cells, that any attempt to increase the depth dose by distance is contra-indicated, and the thinnest possible intra-uterine tube is used. It is convenient to have a thin rubber tube with a flange at the end, which is held by the spacer and packing, and does not slip out during treatment. The cavity of the uterus varies in length, and takes one, two, or three radium tubes of 2·2 cm. actual length.

(*d*) *Assessment of Dose*

The paired ovoids have been designed to take full advantage of the variations in size of the vagina (Fig. 4), but it is clear that if the old method of prescribing so many milligramme hours is used, the dose received at the surface of the ovoid will be higher if the small, and lower if the large, ovoid is taken. This difficulty could be avoided by putting different quantities of radium in the different sizes, so that the dose on the surface of each size of ovoid is the same. The dose is then said to be balanced on the surface of the ovoid. When this form of applicator was first devised, it was thought that the surface would prove to be the correct position for the balanced dose, and experience was gained with a considerable number of cases. It was then observed that the effect of irradiation was more marked when the vagina was large, and the dosage at Point A was computed for over 500 cases. This established clearly that the tolerance of the normal tissues was related not to the surface dose but to the dose received at Point A, which thus becomes of much greater importance than the vaginal mucous membrane. It was then decided that an attempt should be made to balance the dose at Point A, and it was shown by the calculations, details of which follow, that this balance could be achieved by putting the radium in ovoids and uterine tubes in these proportions:—

Large ovoids	.. 3 cm.	.. 5 units each.
Medium ovoids	.. 2·5 cm.	.. 4 units each.
Small ovoids	.. 2 cm.	.. 3 units each.

Uterine tube units, in series, counting from fundus to cervix:—

Long tube	.. 2 units, 2 units, 1 unit.
Medium tube	.. 2 units, 1 unit.
Short tube	.. 2 units.

The intra-uterine applicator only takes single tubes in tandem, and it is therefore necessary to have some double units of radium to load these tubes correctly.

(*e*) *Relationship of Anatomy to Geometrical Concepts*

Before any calculation of dosage is possible, some geometrical basis for the calculations must be established. In the present problem, the external os

is taken as the geometrical origin, and the axis of the uterus as the general axis of reference (or x-axis). At right-angles to it, as shown in Fig. 5, is the axis of the vagina, designated the z axis, while the third, y axis, is the horizontal lateral axis through the cervix. The Point A, at which dosage is to be balanced, is thus the point (2, 2) in the xy plane. The positions of the radium in vagina and uterus are shown in Figs. 4 and 6, the latter being a diagram in the xy plane. The uterine radium in one, two, or three tubes starts at a distance along the x axis depending upon the length of the "dead" end of the tube being used—usually about 0·5 cm. The vaginal radium is taken as being high enough in the vagina to be symmetrical with the xy plane.

The dosage at any point in this geometrical framework was calculated by means of the Sievert formula. It has been assumed that the linear absorption coefficient of platinum-iridium is 2 cm.$^{-1}$ for gamma radiation. The factor for converting the Sievert formula into röntgens per hour is then 9·3, equivalent to 1 Imc. = 8·4 r/hr. Absorption in the radium salt, the rubber ovoids, and tissue has been neglected.

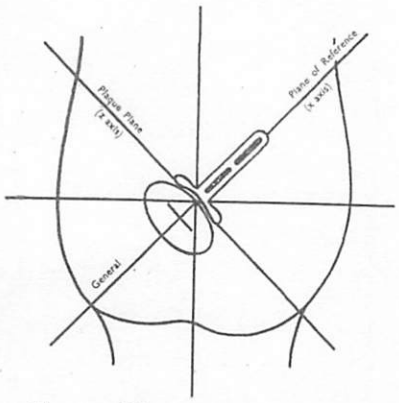

Fig. 5.—Diagram showing axes of references.

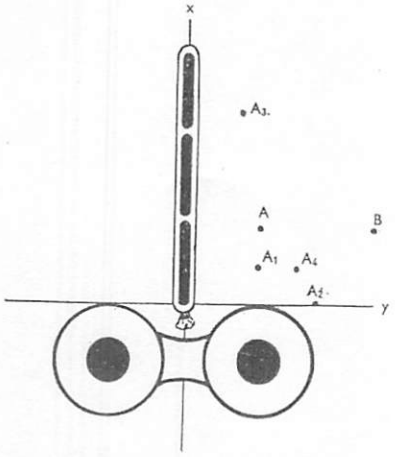

Fig. 6.—Diagram showing x–y axes and points where dose was calculated for balance.

The dose at Point A was calculated assuming the vaginal radium to be in the positions of the centres of the large, medium, and small ovoids taken two at a time, both with and without the spacer. In the uterus was a tube containing three units in the order, fundus to cervix, 2, 1. It was found that the dosage rate at A was practically the same for each ovoid combination if the ovoids and intra-uterine applicator were loaded in terms of "units" of radium tubes, the numbers of the units being as stated above. Using only one tube of two units in the uterus, the dose at A is reduced by 5 per cent., whilst the use of three tubes of respectively 2, 2, and 1 units in uterus increases the dose at A by 10 per cent. It is unfortunate that so wide a variation has to be introduced, but we consider the treatment of the whole length of the uterine canal to be so important that we advise the use of the two units at the fundus except in cases where X-ray films show the uterus to be retroverted, when a

TABLE I

DOSAGE RATE PER MILLIGRAMME OF UNIT AT VARIOUS POINTS IN THE PARACERVICAL TRIANGLE

Ovoid Systems*	Point A $\begin{cases} x=2 \\ y=2 \end{cases}$	Point A_1 $\begin{cases} x=1 \\ y=2 \end{cases}$	Point A_2 $\begin{cases} x=0 \\ y=3\frac{1}{2} \end{cases}$	Point A_3 $\begin{cases} x=3 \\ y=1\frac{1}{2} \end{cases}$	Point A_4 $\begin{cases} x=1 \\ y=3 \end{cases}$
	r/hr.	r/hr.	r/hr.	r/hr.	r/hr.
Two large Ovoids, loaded 5 units, with spacer ..	7·97	8·20	7·02	7·63	7·87
Two large Ovoids, loaded 5 units, with washer ..	8·07	8·30	7·06	7·75	8·03
Two medium Ovoids, loaded 4 units, with spacer..	7·48	8·01	6·65	7·41	7·32
Two medium Ovoids, loaded 4 units, with washer..	7·60	7·85	6·74	7·50	7·49
Two small Ovoids, loaded 3 units, with spacer ..	7·42	7·80	6·57	7·25	7·25
Two small Ovoids, loaded 3 units, with washer ..	7·41	7·53	6·45	7·02	7·03
Average	7·65	7·97	6·75	7·42	7·49

* 3 units, 2, 1 in uterine tube.

shorter uterine tube should be used at subsequent application to avoid intrinsic rectal reaction.

The actual dosage rate at A naturally depends upon the size of the unit used, but the equality between that from the various systems does not, so long as the active length of each unit lies between 1·0 and 2·0 cm. Further calculations at points around A showed that this type of loading gives a comparatively even dose over quite a large volume of tissue in the parametrium. The extent to which the even dose is spread, and also of the balancing of the dose at A for the different combinations, may be judged from Table I, whilst Fig. 6 shows the relative positions of the chosen points. The table is corrected for multiple filtration, but if double units of radium are available, this can be reduced, an advantage if large ovoids are to be loaded, as the variation may be as high as 15 per cent.

It may be asked why two ovoids are used instead of the mechanically simpler single ovoid, more heavily loaded. There are three reasons:—

(1) The above-mentioned volume of even dose throughout a zone round Point A is much smaller in the case of a single ovoid technique.
(2) The paired system produces a depth dose towards the pelvic wall superior to that from a single ovoid.
(3) The splitting of the radium into the two ovoids reduces the dose at the ovoid surface, and hence the dose on vaginal mucous membrane.

An additional advantage of dividing the radium between two ovoids is that this reduces the number of tubes which are bunched together. When two or more radium tubes are used in an ovoid, the ovoid may be distorted, and there will be mutual filtration by the several tubes. Allowance has been made for these effects (± 10 per cent.) in Table I.

Rigorous calculation would only be possible if a supply of geometrically identical tubes, loaded with two or more units of radium, were available.

Ideal placing of the applicators has been assumed in the discussion, but in practice may not always be obtained. For example, an ovoid may rotate so that the contained radium is no longer at right-angles to the *xy* plane, or the uterus treated may be retroverted. The maximum error due to ovoid rotation is less than 10 per cent., but retrovertion may increase the dose at A by 20 per cent., in addition to the possible 10 per cent. due to a tube containing 5 units. This must be allowed for in subsequent treatments. On occasion it may be impossible to place the corks symmetrically on either side of the cervix, one cork being closer to the *x* axis than usual: the maximum variation in dose between either side of the uterus is now 15 per cent. All these variations are found by radiography, as will be described later.

It is sometimes impossible to find the uterine canal at the first attempt. It is then necessary to treat the vagina first, and to give a separate application in the uterus on another occasion, as the treatment of the uterus should not be omitted, and the dose from the intra-uterine units is included in our calculations.

Having ascertained the dose delivered at Point A, it is necessary to find the dose received at Point B, representing the obturator lymph node. This can equally well be calculated by the method described for Point A, making

use of the geometrical postulates for relative positions and Sievert's formula for the actual calculation. When, however, the figures so obtained are compared, it is seen that they fall into a range so close that the distribution of the radium in large or small ovoids loses its importance, except in relation to the quantity of radium used, a point made clear by the following table.

TABLE II
DOSAGE AT POINT B*
USING UNITS OF 10 MILLIGRAMMES

Ovoid Systems	Dose at B	Milligramme Hours per 1,000 r at B
	r/hr.	
Two large Ovoids, loaded 5 units, with spacer ..	29·7	4380
Two large Ovoids, loaded 5 units, with washer ..	28·2	4610
Two medium Ovoids, loaded 4 units, with spacer	25·8	4260
Two medium Ovoids, loaded 4 units, with washer	24·6	4470
Two small Ovoids, loaded 3 units, with spacer ..	21·6	4300
Two small Ovoids, loaded 3 units, with washer ..	20·7	4350
Average	25·1	4400

* Three 10-milligramme units in the uterus.

TABLE III
DOSES RECEIVED AT POINTS A AND B
IN 24 HOURS FROM VARIOUS UNITS*

Size of Radium Unit	Dose at A	Dose at B	
milligrammes	r		r
6·66	1,200	Ovoids	large 470 medium 400 small 330
10	1,800	Ovoids	large 710 medium 600 small 490
13·33	2,400	Ovoids	large 940 medium 800 small 660
20	3,600	Ovoids	large 1420 medium 1200 small 980

* Three units in uterine tube.

Assessment of Dose

It is now possible, using Table I, to find the dose received at Point A per milligramme of unit, and a fair average figure which is convenient is 7·5 r per hour if the uterine tube contains 3 units. The allowance which must be made for uterine tubes containing 5 or 2 units has already been mentioned.

The dose at Point A, with the units system, is balanced, and does not vary, but the dose at Point B is not balanced. Table II shows, however, that the correspondence of the dose at Point B and the quantity of radium at the source is so close that this dose can be calculated in terms of the milligramme hours to deliver 1,000 r. A fair average figure derived from the table is 4,400 milligramme hours per 1,000 r. Using these two basic figures, a simple table shows the doses received at Points A and B in twenty-four hours from units containing varying quantities of radium.

(2) Application of the Dosage System to Therapeutic Technique

It is not claimed that the units system and ovoid applicators offer a new technique for the treatment of cancer of the cervix; the advantage is the delivery of a pre-calculated dose which is accurate within the limits imposed by clinical variations. Techniques previously described have two main features, the applicators employed (boxes, corks, pessaries, etc.) and the use made of the time factor. If the two well-known European techniques, the Paris and the Stockholm, are considered, it is clear that the applicators could be replaced by ovoids without in any way interfering with the particular time spacing preferred, and using the same quantities of radium.

Paris Technique

The technique practised at the Fondation Curie, and associated with the name of Regaud, varies to some extent from case to case, but a typical treatment described by Lacassagne[3] consists in the use of 2 tubes of 13·33 milligrammes in the uterus and the same in the vagina, carried in two corks. The time is 120 hours of continuous irradiation, only slightly split by daily removal of the radium for douching. The dose here is almost 8,000 milligramme hours, and if the balanced dose system, with medium ovoids and a long 5-unit uterine tube, is used, this can be given in 110 hours, 22 hours daily for five days, by using units of 6·66 milligrammes. The actual doses delivered are 6,150 r at Point A and 2,180 r at Point B. Should the vagina be large, and ovoids containing 5 units be inserted, the dose would be almost 11,000 milligramme hours, which would again deliver approximately 6,150 r at Point A, but 2,500 r at Point B. If only small ovoids and a short uterine tube, with 2 units, were possible, the dose remains approximately 6,150 r at Point A, but becomes 1,210 r at Point B.

Stockholm Technique

The technique of the Radiumhemmet is more difficult to define, because Heyman has made it very clear that, in his hands, it is modified to suit the individual case. It seems, however, fair to take an arrangement which is very often described as being the "Stockholm Technique," and which consists of a tube of 50 milligrammes in the uterus, and three boxes, each containing 20 milligrammes, in the vagina, for three insertions of 24 hours in an overall

time of three weeks—7,920 milligramme hours in three weeks. If units of 10 milligrammes are used in a medium-length uterine tube, and medium ovoids, the milligramme hours and time spacing can be made identical with that described, and the dose delivered at Point A is 5,400 r in three weeks, and 1,800 r at Point B. The effect of varying the ovoids would be the same as for any other method; the dose at Point A is unaltered, but that at Point B varies with the milligramme hours.

Technique of the Holt Radium Institute, Manchester

The possibility of pre-calculating the dose to be delivered to a considerable zone of tissue in the true pelvis has allowed a technique to be evolved here which may be regarded as a study in the maximum tolerance of these tissues. The importance of time in the biological effects produced—that relationship

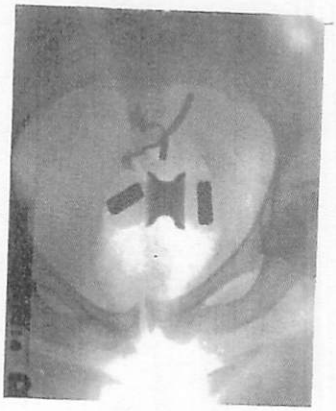

FIG. 7A.
Three tubes, 5 units, in uterus. Two large ovoids and spacer, 10 units, in vagina. Barium in rectum to show relative position.

FIG. 7B.
Lateral of same case. Note spacer for packing between radium and rectal wall.

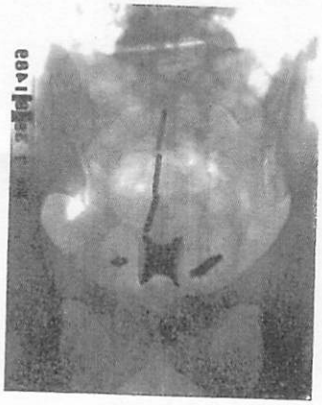

FIG. 7C.
Three tubes, 5 units, in uterus. Two medium corks and spacers, 8 units, in vagina.

FIG. 7D.
Lateral view of same case. Note relation of *x–y* axis. Uterus retroverted, allowed for at second treatment.

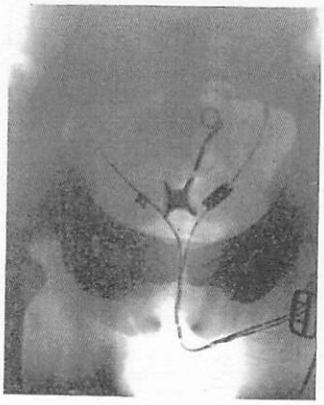

Fig. 7E.
Radium and urethral catheters in position. Case in stage 4—note lateral displacement of uterus and seed for identification in obturator gland. Radiograph blurred by stereoscopic shift for reconstruction.

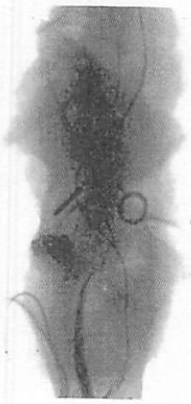

Fig. 7F.
Lateral view of same case. Note seeds in obturator gland and Pouch of Douglas.

Fig. 7 (A) to (F).—X-ray photographs.

of time and dose sometimes referred to as the cumulative dose—must form part of the study, and for cases treated with radium only the time spacing adopted is two applications of 48 hours, with an interval of five days between the removal of the radium and its re-insertion. The dose delivered at Point A by any size of tube and paired ovoids is 7,200 r in nine days. It is believed that this dose approaches the maximum tolerance level, and that there is not a large margin for error, so that it is very important that the placing of the paired ovoids should be carefully controlled. The best method of inserting the ovoids with real accuracy is to do this with the patient in the knee-chest position. Evipan is used as an anæsthetic, and with a little practice and some simple fixtures on the operating table, even heavy women can quite easily be maintained in this position, which allows an excellent view of the cervix. Dilatation is minimal, the intra-uterine tube is inserted, and, next, the ovoids are placed one in each lateral fornix, with the spacer, or washer, between them. The uterus falls forward, and it is an easy matter to pack above and behind the ovoids so that the rectum is held well away from them. This method of insertion of the ovoids in the knee-chest position must be regarded as an integral part of the treatment, as only in this way can the organs fall into the position required by our geometrical postulates used for the calculation of the doses. Variations in position, due to infiltration and displacement by the tumour, are not uncommon at the first treatment, but are not usually gross enough to alter the amount of radiation received to a serious extent, particularly as high dose spots tend to fall in the tumour itself. As soon as the ovoids have been fixed in position by the dry sterile pack completely contained within the vagina, the patient is taken from the operating room direct to the X-ray department, where antero-posterior and lateral views of the pelvis are

taken. These are examined as soon as possible, and if the radium is not in a reasonably good position, it is at once removed, to be re-inserted for another complete treatment on a future occasion. Such radiographs are absolutely essential, not only because gross displacement of the radium is sometimes found, but they also make it possible to allow for the variations in position caused by infiltration when assessing the actual dose received. Fig. 7 shows correct and incorrect position, and the relationship of the uterus to Point A is demonstrated by placing radio-opaque catheters in the ureters. This method has been of great value in determining our anatomical relationships. Films have also been taken just before the radium is removed, to make certain that the position of the radium does not alter. No gross change of position has been found.

We believe the dose of 7,200 r in ten days to be adequate for the zone of paracervical tissue described, but the dose at Point B remains to be considered. Even if the dosage is so large that it has been possible to use the largest ovoids and longest uterine tube, the milligramme hours are 14,400, approximately 3,270 r at Point B, but 2,400 r is a much more usual delivered dose. This cannot be regarded as adequate for squamous carcinoma when delivered over ten days, so that if it is desired to treat the obturator nodes, some form of external radiation is essential. In this Institute X radiation is used to deliver a dose of 4,000 r minimum to the parametria, but this dose cannot always be obtained without exceeding the limiting tolerance of the skin. It has been found in practice that working with 200 to 250 K.V. and a focal skin distance of 40 cm., it is only possible to give a dose of 4,000 r to the parametria in five weeks without reactions too severe to be justified, if the measurement of the patient's pelvis, from the anterior surface of the symphysis pubis to a point midway between the posterior iliac spines, is 18 cm. or less. The summated γ- and X radiation at Point B is then about 6,500 r in 5 to 6 weeks, a figure unlikely to exceed maximum tolerance, even allowing for the increase in the volume irradiated, but the dose at Point A already received from the radium is 7,200 r, and the dose within the cervical tumour is much higher. It is thus unnecessary to increase the cervical dose, and although the tolerance at Point A will be greater because of the longer time taken to deliver the dose, it is certainly undesirable that the full 4,000 r be received here. This is avoided by using an oval applicator with a strip of lead 5 cm. wide running across it, which completely shields the centre and allows only scattered radiation to reach Point A. This oval applicator is used for anterior and posterior fields and, in addition, two anterior and two posterior diagonal fields, 10 $\times$ 5 cm., are placed on either side of the oval, so that each parametrium is actually cross-fired from four portals (Fig. 8). The X-radiation is given between the two applications of radium.

Patients whose measurements are such that X-ray treatment is contra-indicated are treated with radium only, and this allows two separate studies in tolerance to be carried out, and yet gives to each individual patient a treatment which we believe to be well suited to her case. The first technique, which uses radium only, delivers 7,200 r throughout the selected zone of paracervical tissue in ten days, the second delivers approximately 7,200 r from

radium and approximately 2,500 r from X rays in the paracervical zone, and 6,500 r from radium and X rays combined at the obturator node in five to six weeks.

It has already been pointed out that in the treatment of squamous carcinoma it is always necessary to make full use of the normal tissue tolerance. We believe that this system of balancing the dose at a selected point, by taking a ratio of units of radium required to deliver the same dose from specially designed applicators (ovoids) of varying size, is a contribution to the treatment of cancer of the uterine cervix, because it allows a study of the maximum tolerance of the vulnerable surrounding tissues.

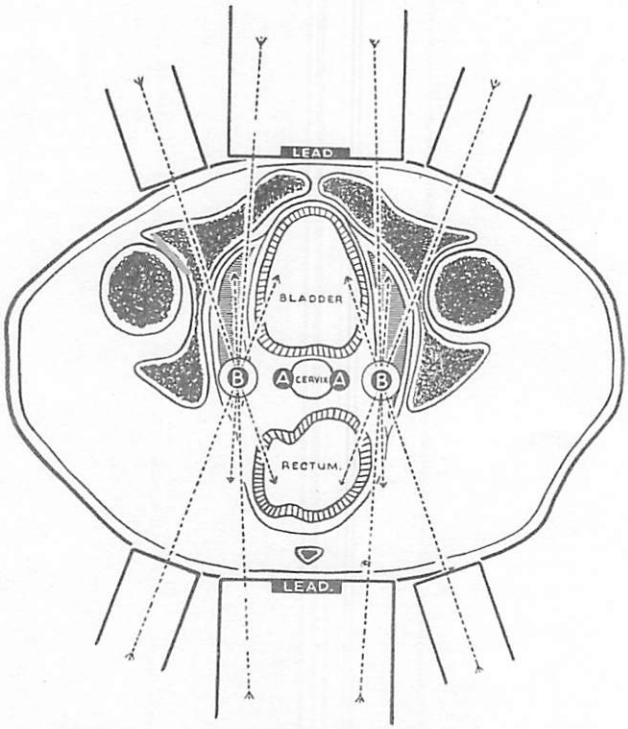

FIG. 8.—Diagram of horizontal section of the pelvis, showing the X-ray fields with beams converging on Point B.

SUMMARY

A dosage system expressed in terms of röntgens is proposed for the treatment of cancer of the uterine cervix.

The anatomy of the part is considered in relation to spread of disease and to normal tissue tolerance.

The vaginal and uterine applicators are described.

Calculations are given to show how the dose may be balanced at selected points in the pelvis.

The relation of such a system to the Paris and Stockholm techniques is discussed, and the Manchester technique for the study of maximum tolerance is described.

ZUSAMMENFASSUNG

Ein Dosierungssystem in Röntgeneinheiten für die Behandlung von Cervixcarcinomen wird beschrieben unter Berücksichtigung der Anatomie, der Ausbreitung der Erkrankung und

der normalen Gewebstoleranz. Die vaginalen und uterinen Radiumbehälter werden beschrieben. Berechnungen zeigen wie die Dosis sich an verschiedenen Punkten des Beckens aufbaut.

Die Beziehungen eines solchen Systemes zur Pariser und Stockholmer Technik werden besprochen und mit der Manchester Methode für die Ermittelung der maximalen Toleranzdosis verglichen.

RÉSUMÉ

L'auteur propose un système de dosage pour la roentgenthérapie dans le cancer du col de l'utérus. Il étudie l'anatomie de la région par rapport à l'ètendue de la lésion cancéreuse et la tolérance du tissu normal.

Les applicateurs vaginaux et utérins sont décrits. Des calculs sont établis pour montrer combien la dose doit être pesée pour certains points précis du pelvis.

Enfin après avoir etudié les relations de ce système avec les techniques utilisées à Paris et Stockholm, l'auteur décrit celle de Manchester pour l'étude de la tolérance maxima.

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ABSTRACT

On the Therapy of X-radiation Leucopenia. By C. Carrié, *Strahlentherapie*, September 1938, Vol. 63, 1, p. 183.

The author draws attention to the similarity between leucopenia produced by benzol and that due to radium, and notes that Friemann found experimentally, in animals, that the leucopenia due to benzol could be prevented by giving Vitamin C. The author investigated the action of Vitamin C in certain patients undergoing X-ray treatment. He chose fever-free cases suffering from tumours of the neck region.

The radiation factors were K.V. 180, ma. 5, ·5 Cu, 1 Al Field size 6 × 8 to 10 × 10. Dose 200–240 r daily. The author indicates that there are normal rises and falls in the white blood count during the day, and emphasises the necessity for remembering this. He states that, in the course of daily X-radiation, one commonly gets a progressively rapid fall in the white blood count.

He then gives five illustrations where the white blood count was strongly influenced by injection of 500 mgm. of 1-ascorbutic acid (Cebion or Redoxon) with, in some cases, concurrent oral administration of the acid (50–100 mgm. 3–6 times daily).

The author believes that a Vitamin C defect occurs during radiation treatment, and he believes that the leucopenia can be greatly influenced by giving Vitamin C, especially at the beginning of treatment.

He is also of the opinion that radiologists and others exposed to danger should take Vitamin C prophylactically.

He states, in conclusion, that his impression was that tumours react better where Vitamin C is given. He indicates that these last observations can only lead to conclusions when a greater number of patients have been observed.

A.G.M.