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COMPLICATIONS AND DANGERS OF RADIUM AND X-RAYS IN GYNÆCOLOGICAL CONDITIONS*

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THIS TITLE IS, I feel, an appropriate one, because radiotherapy has a place in the treatment of some common diseases on which the gynæcologist has to advise. Radiotherapy is a comparatively young specialty—its evolution from general radiology is proving to be a somewhat prolonged labour and at least in North America is suffering from some dystocia. My experience has been that few gynæcologists appreciate the principles underlying our specialty and I hope therefore to cover this broad field by summarizing the problems which I feel will be of most interest and use to you.

I shall at least begin logically, by starting with the effects of low doses of radiation and working up to high doses. Even very low doses have effects on the human organism, and with these, we are concerned mainly with the effects on the germ plasm. Radiations produce mutations in the genes, and it is generally taught, though recent evidence throws doubt on it, that these are additive. Which means, that once a mutation has been produced, the change is irreversible, which is contrary to what occurs in other tissues with low doses of radiation. Note therefore what this means. If an individual is exposed throughout his life to radiations, then his sperm or her ova have an increasing chance of carrying an altered character to their offspring. Most of these are recessive characters, so that they would not be seen in the first generation.

This accounts for all the hubbub that is going on about the enormous increase in exposure to radiation to which the human race is being subjected. Atomic warfare, radio isotopes, mass radiography and radiotherapy are all adding to this. Are we altering the characters of our descendants in a way that will only be proved when it is too late? But we should keep a sense of proportion when discussing this, because radiation is really no new thing, for we are all being bombarded at this very moment by natural radiations from cosmic rays, radiations from radioactive materials in the walls of rooms and indeed from radioactive materials in our own tissues. All this amounts to some 1/300 r per day or 50 times less than the amount that is regarded as producing no obvious effects in radiation workers, such as radiotherapists. It may be of interest here, that a therapeutic dose of radio iodine for thyrotoxicosis gives a dose of 5 to 10 r to the ovaries, whereas a lateral radiograph of the pelvis gives a dose of 2 r to these organs. Repeated radiographs and fluoroscopy will give an exposure close to that from radio-iodine and if surgeons continue to do thyroidectomies on young women because of the danger from radiation to the ovaries, they should, to be logical, avoid ordering radiographs of the pelvis.

According to Ellis,[1] 10 r to the ovaries may increase the chance of abnormal conception due to a recessive mutation by 0.05% and the chance due to a dominant mutation by 1%. He also states that to double the natural mutation rate, 140 r would have to be given to the whole population per generation for 2,000 years. The consensus is therefore that at the present level of exposure, the risk to the human race is negligible.

But doses of the order of 200 r such as are given to women for the treatment of sterility may cause an increase of 25% in the number of abnormalities due to dominant mutations. Also, and this to me seems of real importance, if the woman should have recently conceived, there is a definite chance of damage to the fetus and abnormalities have been reported after such an occurrence.* Of course, if one is treating a young woman for a malignant condition, then the dose used will destroy the germ cells permanently, so there is no risk to their offspring. But, what I am worried about is the treatment with radiation for sterility or the induction of a temporary menopause. Also, in treating a woman under the age of 40 for menorrhagia, by attempting to produce a menopause, we have found that with customary doses, one cannot guarantee that the amenorrhœa will be permanent. I would also point out that the use of radium means irradiation to the doctor's germ plasm, as well as the patient's. X-ray treatment gives a negligible amount to the doctor who is outside the room when the machine is turned on. I cannot resist

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*Since this paper was written, Russell and Russell—*Radiology*—March 1952, have shown experimentally that young embryos in various animals can be affected by radiation and that the type of abnormality to be produced can be picked out at will by irradiating when that organ is developing most rapidly. Doses as low as 25 r produce an obvious effect.

pointing out that, it has been shown statistically that radiotherapists are much younger on the average than are gynæcologists, and seeing that the former are therefore at a more reproductive age, it may account for why radiotherapists tend to prefer x-rays to treat menopausal menorrhagia, whilst gynæcologists are content to use radium.

We now turn to the tumour bogy, and the oft-quoted example of the girls who developed bone tumours following ingestion of radium while painting luminous dials on watches. In those cases, there was a long continued constant low dose of radiation. Similarly, when superficial x-rays were used to treat thyrotoxicosis, followed by epitheliomata, the course of radiation lasted over several months. In gynæcological treatments, we have short courses of radiation, and using isotopes, we have short acting substances. It is like comparing the chance of carcinoma in the person who is splashed with tar once, and with the man who works in tar constantly.

Several authors have reported an increase in ovarian and mammary malignancy after irradiation of mice.[2, 3] But the mouse seems to be particularly unfortunate in this respect and a similar action can be demonstrated with administration of œstrogens. Glucksman[2] in a review of this problem states that there is no evidence of an increase in ovarian malignancy from radiation of women. But you will be wanting to quote the reports of an increased incidence of endometrial carcinoma in patients who have been treated for menopausal bleeding by radium.[4 to 7] This is reported to be three times the normal, or about 8% of treated patients will develop the tumour.

However, it is by no means sure that the radiation is the causative factor, for Corscaden[4] believes that the endometrial hyperplasia is itself the premalignant factor. I know little about the mortality and morbidity of total hysterectomy in the menopausal age group but when one considers the high curability of endometrial carcinoma both by radical operation and radiation, I feel that we should await proof before the simple radiation induction of the menopause is abandoned in favour of hysterectomy.

Going on from this, I can now discuss the question I hinted at earlier, that we prefer the use of x-rays to induce a menopause. Most gynæcologists use a thin walled tube around their radium, but though the dose to the ovaries is small, the dose close to the radium is enormous. If, however, you surround your radium by a ½ cm. of rubber, it pushes the endometrium away, but the dose at the ovaries remains the same. The local dose on the endometrium is reduced about one hundred times by this simple interposition of the rubber. The dose is still many, many times greater than the ovaries receive, and there is a risk of telangiectasis being produced, and this may cause hæmorrhage later. Also, if an early carcinoma of the endometrium be missed by the curette and radium is inserted, thinking that it is a case of benign uterine bleeding, then the local high radium dose will produce a temporary resolution of this early tumour, and it may have spread through the wall, by the time it next produces a warning hæmorrhage.[8] Using x-rays, we never accept a patient without a preliminary curettage but seeing that the dose given to the pelvis is uniform, the uterus only receives the same low dose as the ovaries, and this small dose will not prevent a carcinoma from continuing to bleed, prompting a further curettage.

In Manchester, we treat nearly all our menopausal bleeders with a central dose of 450 r by two ports, taking 20 minutes to give. The common practice is, for all gynæcologists in the area to investigate their patients in their own departments and then send them to us for this simple x-ray sterilization. To give those who still use radium for these conditions a little comfort, I must report however, that Kottmeier[9] of the Swedish School has measured the urinary output of sex hormones following both radium and x-ray sterilization, and shown that radium leaves some ovarian function behind, and he thinks that the menopausal symptoms are less because of this. We followed our patients, trying to get confirmation of this, but we could not establish that there was any difference in the symptoms with the two techniques.

Now I turn to the more burning question of the complications following the high dosage necessarily given to cervical carcinoma. I shall follow Todd's[10] work on this, which he did at my own hospital. At the Holt Radium Institute, we treat with radiotherapy 300 carcinoma of the cervix each year which I think you will agree gives sufficient material to satisfy even the statisticians.

Firstly, I should emphasize that one must always be careful to distinguish between damage produced by the tumour, and that produced by

the radiation. For instance, when the recto-vaginal septum consists only of tumour, then removal of the tumour is sure to leave a fistula.

Prof. Todd divided radiation reactions into immediate and late. Almost every patient develops diarrhœa and tenesmus shortly after completion of treatment, and with a sigmoidoscope, an inflammatory reaction is seen on the anterior rectal wall. Similarly, some degree of cystitis develops. Both these usually clear rapidly and are hardly to be regarded as complications. Late reactions are the more important, usually appearing within a year of treatment but often many years later. The commonest late reaction is the pseudo-carcinoma of the rectum, so called because of its similarity to an early carcinoma. This is seen opposite the cervix and is a direct result of too high a dose on the rectal mucosa. In view of its similarity to a carcinoma, abdomino-perineal resections have occasionally been performed for this lesion, but if the patient escapes this fate, the prognosis is good, for with rest, instillation of mild antiseptics and mineral oil, and with penicillin systemically, the lesion heals.

A similar lesion occasionally occurs higher in the rectum, where a retroverted uterus containing radium lay against the bowel. Todd described these as intrinsic rectal reactions to distinguish them from a more serious complication, which he called the extrinsic reaction.

The rectum has a relatively poor blood supply, and seeing that this level of radiation causes sclerosis of blood vessels, a high dose in the region where the branches of the internal iliac artery cross the pelvis towards the rectum, can jeopardize the whole of the blood supply to the posterior half of the pelvis. When this occurs, the rectum becomes surrounded by semi-necrotic tissue, and becomes very indurated. This he called the "frozen pelvis". The prognosis of this type of reaction is more serious, in that recto-vaginal fistulæ commonly occur. Also, there is sometimes considerable hæmorrhage and always persistent pain. Most patients eventually need a colostomy.

Another common late reaction is bladder damage, leading to recurrent attacks of cystitis and hæmaturia which settle with rest and an alkaline urine. Uretero-vaginal fistulæ are rare and in the one case I have seen, she was symptomless, except for the fistula. It being a unilateral fistula nephrectomy was chosen as the best treatment. Many cases of intestinal damage are described in the literature particularly from loops adherent to the uterus or Pouch of Douglas following gynæcological operations. Radiation-induced fractures of the neck of the femur are also described, but I have not seen a single case. With accurate beam direction, it is possible to avoid any high dose on the femur, and such accidents should be unknown with a proper technique.

We do however, see occasional necrotic areas of the abdominal skin, following the use of x-rays. These are usually in stout patients, where it is difficult to get in the required depth dose without raising the skin to a considerable reaction. When machines with increased penetration come into general use, the skin reactions will be minimal.

I shall, now, describe some of the factors which influence these reactions and how they can be minimized. The simplest mistake is for the uterine radium to slip out and lie on the vaginal radium. This gives, of course, an enormous dose to the rectal mucosa, so that every patient should have radiographs of the pelvis and thus this accident can be easily seen, and the radium removed immediately. We also always insert radium with the patient anæsthetized in the knee-chest position. This allows the applicators to be placed easily against the cervix and also facilitates packing behind the vaginal radium to give the essential distance from the rectal mucosa. Sometimes the posterior fornix is involved by carcinoma, and then one must not pack the radium away, if one wishes to cure the tumour.

However, the essential feature of any dosage system must be to avoid the high dosage likely to cause the frozen pelvis I mentioned, or ureteric damage, and therefore in the Manchester system, we assess our doses at the point where the ureter crosses the uterine artery. Experience has shown that this is the critical area. The uterine cavity and vaginal mucosa can withstand enormous doses themselves, because they have either given up their physiological functions or are about to give them up. Making use of this great tolerance, we attempt to throw a curative dose into the parametria, but at the same time, a certain dose can not be exceeded at this critical point, which we call Point A.

Point A is defined as being 2 cm. above the mucosa of the lateral fornix and 2 cm. from the mid line, and treating in two separate applica-

tions of 3 days, with 4 days' interval, 8,000 r must not be exceeded at this Point A. (This is using radium alone). Notice that I state any dose in roentgens for, in this day and age, the use of mgm. hours as a unit of dosage, is an antiquity.

A so-called dose in mgm. hr. only means a quantity of radium there for a certain time. For instance, if one measures the dose on the rectum a cm. away from a radium container for a given number of mgm. hr., it will be so many roentgens, but if the distance is 2 cm. then the dose in roentgens will be a quarter of the former value. Whenever a patient in a ward has a radium treatment, every patient is that ward gets the same number of mgm. hr. as that patient. But the dose anyone gets varies according to how close they are to these mgm. hr. A dose measured in roentgens is a measure of ionization, and it is this ionization which produces tissue reactions, so the roentgen is the obvious measure.

If, after a treatment for carcinoma of the cervix, a necrosis appears, then one must know what dose produced it, so as to avoid such a dose in the future. Reading through the many reports of such occurrences in the American literature, one can not assess their doses for they give their mgm. hr., but without an indication of the distances involved, therefore, every patient who has radium inserted should be radiographed, and the dose at definite points calculated by a physicist. The treatment should be done in at least two sessions, so that any high doses on the rectum or at Point A can be corrected during the second treatment. Similarly, if a radium container is noticed lying towards the sacrum with a retroverted uterus, at the second treatment a shorter tube can be used to cut down the risk of a necrotic dose on the upper rectum. Finally, when x-ray therapy is added, the exact dose contributed should be added to the other, so that less radium dose must be given. It is also most important to state the time over which any course of radiation is given, as the biological effect of any dose will vary as this time. And one should use standard times, so that one's doses are comparable in effect.

Now briefly to mention ovarian carcinomata. Here we have a very different problem, because the tumours involve wide areas, and with ascites the whole abdomen contains potential tumour. Some of these tumours are very radio-sensitive, especially the dysgerminoma, but apart from this, one can not be sure in advance what kind of a response there will be, so that if the surgeon reports that he left tumour behind, one is forced to treat them. The doses used are much lower, because of the large volumes treated—the so-called bath technique. There is now no chance of tissue necrosis, but the blood count must be watched carefully, because agranulocytosis can be produced.

Carcinoma of the vulva is disappointing radiotherapeutically, the skin stands radiation poorly, and if any reasonable dose is given, there is a tendency for repeated trouble with small necroses. Where excision is possible, this is the treatment of choice. Occasionally when the tumour involves the urethra, excision is inadvisable and then a radium implant can be used.

Finally, I would add a warning. It is possible to practice radiotherapy without causing any necrosis, but this only can be done by reducing the doses given, to below an average curative level. If one's aim is to cure as many as possible, then the chance of necrosis is the risk that a patient has to take, at any rate with radiotherapy at its present development, and this compares with mortality and morbidity following radical surgery.

As my chief, Dr. Ralston Paterson states: "A necrosis is not always reason for blame, but a necrosis where the dose which caused it is unknown certainly is reason for blame".

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Now, thieving Time, take what you must—
Quickness to move, to hear, to see:
When dust is drawing near to dust
Such diminutions need must be.
Yet leave, O leave exempt from plunder
My curiosity, my wonder!

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