

Carcinoma Cervix Uteri

by

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The treatment of cervix cancer is important because it attacks a relatively young age group but, even more because in the early stages it is, except for cancer of the skin, the most curable of all the common cancers. This last fact is not as fully appreciated as it ought to be, but it is a statement well supported statistically. Cancer of the cervix is the one disease about which, thanks to Heyman of Stockholm, we have, as you know, world statistics. The results of radiotherapy from a very large group of hospitals in many parts of the world, as collected by Heyman in his League of Nations and later reports are impressive. The number of patients concerned is large, so these results cannot be due to selection of a few favourable cases, and the follow-up is complete so that the cure rates are genuine. These compare favourably with the cure rates published for any large number of cases of cancer in any form other than skin. Detailed analysis shows in addition that steady improvement has taken place year by year.

What has caused this improvement? I think it is the result of a combination of factors:

1. The public in many countries is becoming conscious of the vital importance of early treatment.
2. New methods of early diagnosis are being developed.
3. Treatment is undoubtedly being improved, particularly in regard to calculation of radiation dosage.
4. The risks of treatment are being eliminated.

I propose to discuss certain aspects of each of these factors.

Early Diagnosis

It is now well known that early diagnosis and consequent early treatment are the secret of

the high cure rates of cancer in any site. It is particularly true for cancer of the cervix. All workers in this field are in complete agreement that great advances could be made were it possible to alter the outlook of ordinary people, and to teach them not to be afraid to seek advice as soon as these significant signs appear.

Great efforts have also to be made to improve the education of the General Practitioner in this respect. If he is careless or forgetful, he, too, can contribute to the delay.

The Scandinavian countries lead the world in the treatment of uterine cancer, not only because their technique is good, but also because they have induced much higher percentages of their patients to seek advice early. In contrast we have the consistently advanced growths so all too common in African native populations.

Diagnosis by Vaginal Smear

Another addition to the technique of early diagnosis is diagnosis from vaginal smears—a technique devised and developed by Papanicolaou, and much used—but also abused—in the U.S.A. What is its real value? It is, I believe, a very useful screening test, but it must never be made an exclusive basis for radical treatment. Where positive though seldom wrong it must be confirmed histologically by true biopsy. Where negative it must not be regarded as excluding cancer in the face of suggestive symptoms. A vaginal examination at the right moment remains, therefore, the most important single item in the early diagnosis of this cancer, and far more important than all the laboratory tests in the world.

Problems of Treatment.

Propaganda and early diagnosis give opportunity but in the end success depends on method of treatment. On this subject there is still con-

siderable discussion and some controversy. Is surgery or radiotherapy the better method or is a combination of the two more effective? How should radiation be given and, in particular, what is the place of X-Ray therapy either added to radium or as intra-vaginal treatment in its own right? Can methods based on the use of isotopes be developed to improve on the existing radium techniques? These and many similar questions await an answer, and considerable work is being done on all of them.

The topical question today is undoubtedly the choice between surgery and radiotherapy, or their judicious combination. I am going to say at once that I am strongly of the opinion that for **cancer of the cervix radiotherapy alone can** give better results than surgery. It is not for me to discuss the technique of surgery or to deny that surgery may cure some radioresistant cases in which radiotherapy would have failed. The essential point is that radiotherapy will not only cure more early cases than will surgery but it also cures a considerable proportion of cases which are already inoperable. The main argument against surgery is related to the direction of local extension from primary cancer of the cervix. It is well known that the first line of spread of a cervical cancer is laterally on to the fornices and then into the base of the broad ligament. There is no need for me to remind you of the anatomy of this region, or of how close this site is to the ureter as it passes forward to enter the base of the bladder. Once the tissues near the ureter are involved, the need to separate the ureter from the vessels and preserve it, make it almost certain that malignant tissues will be cut into. Such a process is against all the principles of reliable surgery for malignant diseases, and so limits results. In contrast, cancer round the ureter is well within reach of full doses of radiation from intracavitary radium and may thus be destroyed by radiotherapy even without additional X-Ray therapy. It is this weakness of the older surgical approach which lead to the trial some years ago of more radical operations with ureteric transplantation. The morbidity from these was almost worse than the number of cases radiotherapy fails to cure.

In favour of surgery it is often claimed that secondary deposits in lymph nodes cannot be cured by radiation. I admit at once that it is doubtful whether the old forms of radiotherapy cured many cases of secondary squamous cell cancer in lymph nodes; but present day methods do cure some. In the cases proved to have deposits in pelvic nodes from cancer of the cervix, it seems

to me that surgery does not cure many either. A number of groups of surgical cases have been published showing the incidence of node involvement, but very few show results at 5 years of the treatment of these cases.

The relative safety of modern operating is not disputed, but, even so, the Wertheim operation is an ordeal not without some mortality. Why then use it when another and better method of treatment is available, and is infinitely easier for the patient.

If all this be true, why then do we still see arguments vigorously presented for the retention of some form of surgery in this disease. I think there are many reasons for this but they all amount in some form or other to a comparison between the surgery of **today**, with all its modern assets, and the radiotherapy of **yesterday**—totally oblivious of the fact that in many countries radiotherapy, too, has advanced *pari passu*. Indeed, nowadays, the only excuse for surgery is that in the Centre involved the radiotherapy is bad.

When I talk of the radiotherapy of yesterday I am tactitly admitting that radiotherapy, as practised 10-20 years ago, was **not** all that it ought to be. Many blemishes on actual practice might be mentioned, but the main ones were:—

- First: Even when nominally according to a standard method, such as the Stockholm technique, actual treatment was often in practice most haphazard and casual.
- Second: Post-treatment sepsis was a serious complication.
- Third: High dose effects, with in the worst cases fistulae, did occur.
- Fourth: X-ray treatment, if added at all, was planned on altogether the wrong lines.
- and Fifth: Dosage was in terms of milligramme-hours of radium used. This does not really measure dose and so can be very misleading.

With the passage of the years we have seen each one of these defects corrected.

The **casual approach to treatment** I put first because it used to be very prevalent. Radium was regarded as a superior kind of diathermy. Far, far too often it was considered technically so simple that it was left to internes or junior medical staff. The mere presence of some radium inserted anyhow into uterus or vagina was ranked as acceptable treatment. Even the number and

duration of insertions had often no consistent basis. It was, I think, first demonstrated irrefutably by Dr. Hurdon at the Marie Curie Institute in London, that a meticulous technique could yield real profits. She was a master of detail, pre-operative and post-operative, as well as in regard to the actual insertion and positioning of the applicators and tubes. Using the standard Stockholm boxes but with a perfection of technique and hospital care, she lifted the overall survival to over 40% 5 years, long before anybody else did so. Heyman's successor, Dr. Kottmeier, too, lays great stress on this question of technique, and on the value of experience with **adequate numbers of cases** for those who are selected to control this method of treatment.

Septic complications, including peritonitis, could be minimised by special care with nursing, but right up to the advent of modern chemotherapy, even in the best Centres they remained a major anxiety. Since then this complication has practically disappeared. The radium treatment of the average case of carcinoma cervix now carries a negligible mortality and morbidity equally for radiotherapy as for surgery. Moreover, from the patient's point of view, the course of radiotherapy has become, because of this, remarkably simple in its freedom from discomfort, risk, or immediate after effects.

The incidence of necrosis and high dose effects in the old days presented a similar problem. It is important that we as radiotherapists admit in retrospect how serious a complication this was at one time. This complication can only be **totally** eliminated by underdosage and inadequate therapy. As this would be futile, we must seek ways by which its incidence is kept at minimal levels. Today, where carefully controlled radiotherapy is practised, the incidence of serious necrosis is low and it should, indeed, become even less common in the next two or three years. Its elimination is partly related to the general improvement of treatment technique, which I have already mentioned. It is also due to the radiographic control, immediately post-operative, of the radium to verify correct and safe positioning. A further valuable safeguard, which ought to become universal, is direct rectal dosimetry such as is employed in a number of centres, using scintillation counters.

The diminishing incidence of necrosis, is, however, also partly due to the new conception of dosage to which I will refer later.

X-ray treatment as an adjuvant to radium has steadily improved. In the beginning, if used at

all, it was almost universally applied as "large fields" to the whole pelvis. There was no realisation of the modern principle of radiotherapy that the factor of "volume irradiated" has almost as much bearing on results as the "time factor." This principle can be stated as follows:—

The smaller the volume irradiated, provided the tumour irradiated, provided the tumour bearing zone is covered, the better the results. The older fashioned approach to whole pelvis irradiation, generally using multiple fields of the order of 10 x 15 cms. has gradually been modified to some form of accurately beam directed technique aimed at the lateral parametria only, and sparing the already irradiated central zone. Mega-volt therapy in any form, including cobalt beam units, has been shown to be of great assistance in achieving this purpose elegantly, but is by no means essential nor necessarily superior. We now know that the maximum dosage which could be given by the large field method could scarcely ever have cured lateral pelvic nodes and its use only paid lip service to this aim. With the small field, small volume principle, the summated radium and X-ray dosage in the region of the obturator gland is substantial and probably controls the small, node metastasis in just as many cases as does pelvic surgery.

To these fairly generally accepted changes should be added two others of importance concerning dosage, initiated by the late Dr. Margaret Tod of Manchester. The contributions which I have in mind are the method of measuring treatment in terms of true tissue dose in roentgens instead of MG-hours, and the establishment thereby of some knowledge of optimum dose. The whole scientific basis of any branch of radiotherapy is strengthened when we begin to think of dosage in terms of the radiation absorbed at the tumour and not merely as connoted by some measure of the size or strength of the radiating sources. It is, therefore, entirely fair to credit the original cervix dosage system set out by Tod and Meredith (1938) as a substantial advance.

A true dosage system such as this, however, not only permits us to reproduce our treatments. Its greatest value lies in the fact that it can lead us in time to knowledge of optimum dose—a very important advance.

Another line of advance comes to us through true clinical trials with genuine random selection of cases. We have run quite a number in Manchester over the last ten years. Two of interest related to cervix cancer.

1. For Stage III cases the results of cases treated using X-ray **before** Radium was contrasted with X-rays **after** Radium. The former appeared superior to a statistically significant degree.
2. For Stages I and II the use of X-ray plus Radium was contrasted with the use of Radium only, each technique using its own appropriate optimum dose. There was no apparent difference between the two series.

It looks as if this type of experiment could prove immensely valuable in the future.

Where do we go now becomes our last question, because we must not stand still. It is never easy to envisage the future, but we can, I think, find some suggestive indications. I have been putting emphasis on the value of present-day radiotherapy **on its own**, yet there are some radioresistant cases. A well conceived attempt to devise scientific methods of isolating the resistant case uses Ruth Graham's criteria of radiation response. This is a promising line of investigation, provided one remembers that it is still an experiment and not a proved entity.

Our own studies in this field are too incomplete to publish but do suggest it has great value.

Even without it, however, I feel that greater use should be made of surgery as the second line of defence in failed or failing radiation cases. After all, if I may reverse an argument previously used, surgery has advanced *pari passu* with radiotherapy and is definitely safer than it was. I believe that it does not help to apply it as a routine post-radiation adjuvant in all cases. This second line of defence argument is, of course, not entirely palatable to the practising surgeon, or gynaecologist, but, after all, it is already the established way of things for mouth cancer—and, to a lesser extent, for bladder cancer, so why not cervix?

The other way in which advance could undoubtedly be made is by expansion of our efforts to get both patient and doctor to act on the early symptoms of cancer. Perhaps that way as much could be done as by any purely technical advances.

The main point to remember is that this is one of the diseases which it is infinitely satisfying to treat because it is, by and large, one of the more curable cancers.