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THERAPY FOR CARCINOMA OF THE UTERINE CERVIX; PART I: IRRADIATION

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RECENT enthusiasm for the surgical treatment of carcinoma of the uterine cervix has resulted in a tendency to forget the continuing place of irradiation for cure or for palliation, and sometimes as a complement to surgical therapy. This report presents our current use of irradiation in the treatment of cervical carcinoma. A second communication will present the indications for surgery for this condition.

General Indications for Irradiation

We do not hold to strict rules for the treatment of cervical carcinoma, beyond adhering to the concept of individualization of treatment for each patient. It is as wrong to subject all patients to irradiation as it is to subject all to surgery. The individually appropriate therapy involves consideration of: the extent of the patient's disease, her general physical condition, her age, her marital status, and the quality of available irradiation or surgical technics.

At present we use irradiation as primary therapy for most of the League of Nations stage I and stage II uterine cervical carcinomas. An additional major indication for irradiation is advanced disease that is not amenable to surgery or

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to curative radiotherapy. Irradiation is particularly valuable in the control of potentially exsanguinating bleeding and intractable deep pelvic pain.

Pretreatment Evaluation

Uterine cervical carcinoma is more than a gynecologic disease, for it may spread to involve the rectum, the bladder, or the deep pelvic nerves. Thus, the patient may be evaluated by a urologist, a proctologist, an internist, and a neurologist, in addition to the gynecologist and the radiologist. Pretreatment laboratory studies include a urinalysis, complete blood count, and blood sugar and urea determinations. Roentgen examinations of the chest and of the urinary tract are performed. These procedures indicate the extent of the primary lesion, help to establish whether or not there is metastasis, and also furnish valuable information in regard to the pretreatment status of these systems. Roentgenograms taken before treatment are invaluable records to consult a year or two later, when it may be necessary to differentiate advancing disease from the late effects of irradiation. Such records may also be of medicolegal importance. When all of these studies are completed, a gynecologist and a radiologist consult and decide on an appropriate therapeutic approach. When indicated, either a urologist or a colon surgeon or both participate in the consultation and ultimate decision.

When irradiation is the elected treatment, the gynecologist's responsibility is not transferred to the radiologist. The patient is seen weekly during therapy so that the gynecologist may observe the patient's progress and may treat complications of irradiation. Psychological assistance to the patient is of the utmost importance, and the physician can aid the patient materially in her formulation of a proper perspective in relation to the disease.

Limitations of Irradiation

Irradiation is potentially lethal to all living tissue. Its therapeutic effectiveness lies in the difference in sensitivity between normal and neoplastic tissues. The tolerance of normal tissues is in most instances greater than that of carcinoma, but the margin of safety is not great. In spite of the reports of sensitivity-reaction and radiation-reaction determinations in assessing irradiative sensitivity, there is, at present, no generally available method for determining whether a specific tumor will or will not be sensitive to irradiation.

It has been determined by trial and error over many years that from 6,000 to 8,000 r will destroy most carcinomas originating in the uterine cervix. About 12 per cent of these tumors will be radioresistant and will not be killed by many times this number of roentgens. In view of this cancerocidal dose, our objective is to deliver a minimum of 6,000 r not only to the primary tumor, but also to the parametrium and the lymphatic drainage areas in the pelvis. In accomplishing this, the bladder, rectum, small bowel, and bones of the pelvis also are irradiated. Each of these structures can be injured permanently if care is not used in giving treatment. In order to take advantage of the more rapid recovery rate of normal tissues, irradiative therapy is administered in multiple doses over a period of

several weeks. Thus, neoplastic tissues receive a lethal dose before the normal structures do.

In the past, skin reaction has limited the amount of external irradiation that could be given, for if the dose exceeded that which produced erythema, permanent damage to the skin might result. When erythema was achieved, it was hoped that the tumor itself would have received sufficient irradiation to destroy it. Using a 250-kilovolt roentgen machine the "erythema dose" is reached at approximately 3,000 r. When this dose is given both through anterior and posterior portals, a maximum parametrial depth dose of from 2,000 to 2,500 r is attained.

Radium generally is used to supplement external irradiation, by delivering a cancerocidal dose to the primary tumor and to the tissue immediately surrounding it. Some of this irradiation reaches the lateral walls of the pelvis, but the amounts are small because of the inverse relationship between the distance and the dose. If a dose of from 6,000 to 7,000 r is delivered to the cervix, only from 2,000 to 2,500 r will reach the lateral pelvic walls. Thus, by combining the maximum dosage attained with a 250-kilovolt roentgen machine and that delivered by radium, a lethal dose can be reached at the cervix, but at the same time there is a 2,000 r deficit at the pelvic wall (Table 1). Consequently, 250-kilovolt roentgen therapy is inadequate for the control of carcinoma at the lateral wall.

Table 1. — *Comparison of radiation dosages delivered by 250-kilovolt roentgen therapy and cobalt-60 teletherapy*

Treatment		Number of roentgens delivered to	
		Paracervical tissue	Pelvic wall
250-kilovolt		2,000	2,000
Radium		6,000	2,000
	Total	8,000	4,000
Cobalt-60		4,000	4,000
Radium		6,000	2,000
	Total	10,000	6,000

Cobalt-60 (Co-60) teletherapy and 2,000,000-volt roentgen therapy have several advantages over the 250-kilovolt therapy unit. This is not due to any specific biologic effect of the shorter and more powerful rays, but is due to several physical assets inherent in the super-voltage apparatus. These are: (1) greater penetration with a consequent increase in the depth dose; (2) less back and side scatter, thereby decreasing the integral dose and radiation reactions; (3) skin-sparing effect because of the occurence of maximum ionization (which causes tissue reaction) at a level of from 4 to 5 mm. below the surface of the skin;

(4) no increased absorption of irradiation by bone; this permits the use of lateral fields. Because of these factors a lethal dose of irradiation can be administered to carcinoma at the lateral pelvic walls (Table 1).

A Method of Irradiative Therapy

Since October of 1954, we have employed cobalt-60 teletherapy instead of 250-kilovolt roentgen therapy. Four portals are used, one anterior and one posterior, each 10 cm. by 15 cm., and two lateral portals, each 10 cm. by 12 cm. Lateral fields are used to produce a more homogeneous dose to the parametrium and lateral pelvic walls. We believe that these portals are preferable to sacrosciatic or other angled fields, and we have not encountered aseptic necrosis of the head or neck of the femur as a consequence of this therapy. Rotational therapy was tried and has been discarded because it does not provide homogeneous dosage.

In planning the course of pelvic irradiation we attempt to deliver 5,000 r to the central portion of the parametrium on each side in an 18-day period. Two fields are treated each day. The anterior portal and right lateral portal are treated on one day, and the two remaining fields are treated on the following day. Treatment is given five days a week until a maximum dose of from 2,500 to 3,000 r has been delivered to the skin of each portal. The midportions of the anterior and of the posterior fields are blocked with lead after a depth dose of 1,000 r has been delivered to the cervix. This is done to decrease the irradiation to the bladder and the rectum and to avoid overtreatment of the cervix and nearby tissues.

The above dose does not result in any skin reaction. There may be diarrhea in the first week of therapy but this rapidly disappears when the lead block is applied. There have been no delayed effects either on the small or on the large bowel.

In addition to the cobalt-60 teletherapy, radium is applied either before or after the external therapy, the sequence depending sometimes on anatomic considerations and sometimes on convenience. It is desirable to have a variety of radium applicators available in order that treatment can be individualized according to the anatomic variations occasioned by the disease. We have used the London type of ovoids together with a tandem, the Ernst applicator, the Silverstone colpostat, and low-intensity radium needles. Radium applications are made by a gynecologist with a radiologist in attendance in order that the technical skills of both specialists may be utilized.

When the Ernst, the modified London, or the Silverstone applicator is used, the radium is left in place for about 72 hours, and from 5,500 to 6,000 mg.-hours of irradiation is given. An average of 6,000 gamma roentgens is thereby delivered to point A, which is 2 cm. lateral to the cervix, and 2 cm. above the vaginal vault. When low-intensity radium needles are used, the dosage is varied in accordance with the number of needles used and the distribution of radium.

Radium treatment presents the greatest risk to the bladder and the rectum, and it is for this reason that the radium is carefully positioned under optimal conditions of relaxation obtained by general anesthesia. Adequate packing is employed to separate these structures as far as possible from irradiation sources, and the patient is confined to bed. In spite of all precautions, irradiation cystitis and proctitis do occur occasionally, but we believe that these sequelae constitute a justifiable risk of irradiation and are not completely avoidable.

Irradiation for Palliation

External irradiation may also be used for palliative purposes in treating persistent disease manifested by potentially exsanguinating vaginal bleeding or by leg and pelvic pain requiring narcotics. In many instances when patients have had previous external irradiation with 250-kilovolt equipment, the abdominal skin is so scarred and thickened that it is not wise to deliver further treatment by this method. In those cases, Co-60 teletherapy can be used in either of two ways. On some occasions total pelvic irradiation is used through conventional portals with dosages limited to from 2,000 to 3,500 r to the pelvic wall. In others, a single portal is treated in order to reach the source of pain or bleeding; treatment is administered to the extent of the desired therapeutic effect, but not in excess of 3,500 r. The use of Co-60 teletherapy may obviate the need for cordotomy with its not infrequent undesirable side effects.

Posttreatment Follow-Up

It is too early to evaluate the over-all effectiveness of Co-60 teletherapy, yet we have noted the advantages outlined above. With more radical forms of surgical therapy now generally available, close follow-up study is indicated so that those patients who have radioresistant lesions may be offered further treatment. Since a homogeneous dosage of irradiation is given throughout the pelvis, it is now possible to follow patients with greater assurance, since if the primary tumor is controlled, the tumor in the lateral pelvis generally will be controlled. It is our practice to see patients six weeks after the completion of therapy, every three months for the first year, every six months for the next four years, and then at yearly intervals. Our follow-up examinations include not only the standard pelvic examination but also routine cervical cytologic studies and, when indicated, roentgen studies of the urinary tract, cystoscopy, and proctoscopy.

Summary

Irradiative therapy is an important method of treatment of cervical carcinoma at the Cleveland Clinic, and the use of cobalt-60 teletherapy has made more intense and homogeneous therapy possible. The treatment of any cervical carcinoma should be individualized. An integrated approach through use of various medical and surgical specialties is presented.