1960

Studies in carcinoma of the corpus uteri: I. General observations

Abner Griswold Bevin

Yale University
STUDIES IN CARCINOMA OF THE CORPUS UTERI:
I. GENERAL OBSERVATIONS

Abner Griswold Bevin, Jr.,
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STUDIES IN CARCINOMA OF THE CORPUS UTERI:

I. GENERAL OBSERVATIONS

by

Abner Griswold Bevin, Jr.,
A.B., Wesleyan University, 1956

A Thesis Submitted to the Faculty
of the
Yale University School of Medicine
in Candidacy for the Degree
of
Doctor of Medicine

Department of Obstetrics and Gynecology
Yale University School of Medicine
1960
ACKNOWLEDGEMENT

I wish to express my gratitude to

Dr. John McL. Morris

&

Dr. Stanley M. Zerne

for their advice and assistance in the preparation of this thesis.
INTRODUCTION

This report is a study of 128 cases of carcinoma of the corpus uteri from the Grace-New Haven Community Hospital during a five-year period from 1952 through 1956. In all cases the diagnosis was proven by biopsy or autopsy and the case follow-up is known in each. The natural history of the disease is illuminated by a correlation of its clinical course with the pathologic findings. An analysis of certain important features of the disease and its treatment is given in order to interpret the patho-physiologic basis for, and the significance of, the clinical data. In 26 of the 128 cases, the consideration of response to radiological therapy is discussed using the concepts of sensitization response and radiation response in relation to the ultimate course of the disease.

PATHOGENESIS AND INCIDENCE

In this series the average age of the patients when the diagnosis of carcinoma of the corpus uteri was made is 58.7 years. This figure corresponds to data given in other series (1).

In all patients data was available concerning their parity. 29.7% were found never to have had a full-term pregnancy. This percentage is somewhat lower than the percentage for the female population at large from the ages of 35 to 74 years, which is 31.1%, and which would include the majority of the patients in this series during their childbearing years as the material is drawn
null
from census figures of 1940 (2). This lower value of 29.7% nulliparity conflicts with many series in which there is a higher incidence of nulliparity in women with endometrial carcinoma than normal women. These values range from 35.5% (1) to 40% (7) nulliparity in women with corpus carcinoma. The figure reported in the present series agrees with an earlier review of cases of endometrial cancer from the New Haven Hospital, however, in which a nulliparity rate of 23% was noted in 116 patients (3).

There is evidence that prolonged estrogen stimulation of the endometrium occurs frequently in women who develop adenocarcinoma of the corpus. In the present series the average age of menopause is 50.1 years, while in the general population the age of natural menopause is variously given as 47 years (5), and 48.7 years (4).

It is generally recognized that more than two-thirds of all cases of endometrial carcinoma occur in women beyond the menopause. Norris and Dunne (6) reported a proportion of 69.5% and Stacey reports 63.5% (5). In the New Haven series it was found that 77% were beyond the menopause when the diagnosis was made, representing 80 patients, while 24 patients or 23% were pre-menopausal. In the remaining 22 patients in the study information was not available concerning their menopausal status.

Although menopause seems to occur later and associated characteristic ovarian changes have been reported in women who develop endometrial carcinoma, and this is felt to be an indication for prolonged estrogen stimulation as being a factor in the disease,
Recent studies have found no evidence for this stimulation in women with corpus carcinoma. In a study comparing 37 post-menopausal women with corpus carcinoma with 47 normal post-menopausal women, no significant differences were found in terms of estrogen effects on the cervixes or uterine tubes (8). Other studies (13, 14, 15) have demonstrated similar lack of this relationship.

Obesity has been reported as a feature of this illness by several authors. In this series 82 patients or 64.0% were found to be clinically obese. In other reports the percentages range from 30% to 85% but the significance of this finding has not been elucidated.

Diabetes occurred in 9 patients accounting for 7.3% of the total number of patients. In a large report of over 500 cases of endometrial cancer, diabetes occurred in 7.0% of the patients (4). The incidence in the general adult female population of diabetes is 1.3% (11) so that it appears the above data suggest a significant increase in incidence of diabetes occurring among women with carcinoma of the endometrium.

The phenomenon of pre-menopausal cystic hyperplasia and its relation to endometrial carcinoma was not studied at this time since complete pathological information was not available. In general (16, 17) it is felt that there is a higher incidence for endometrial carcinoma in patients who have cystic hyperplasia of the endometrium, but in one recent study of 544 cases, the incidence of carcinoma was only 0.4% (9).

No material was available so that the association of
ovarian granulosa-theca cell tumors with corpus carcinoma could be studied. The association has been reported to be as high as 15% to 20% in most series (10).

No evaluation of presenting symptoms, duration of signs and symptoms, or physical findings was undertaken in this series.

**PATHOLOGY**

Adenocarcinoma of the body of the uterus is much more frequent than adenocarcinoma of the cervix, but less common than epidermoid cervical cancer (5). In this series adenocarcinoma of all grades accounted for 91.3% of the malignancies; excluding anaplastic tumors and in-situ lesions, 70.9% were pure adenocarcinoma. There were 12 in-situ lesions; 11 adenoacanthomata, and 11.0% of patients had anaplastic adenocarcinomata.

**TABLE 1:**

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenocarcinoma</td>
<td>70.9%</td>
</tr>
<tr>
<td>Anaplastic adenocarcinoma</td>
<td>11.0%</td>
</tr>
<tr>
<td>Adenocarcinoma-in-situ</td>
<td>9.4%</td>
</tr>
<tr>
<td>Adenoacanthoma</td>
<td>8.7%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>100.0%</strong></td>
</tr>
</tbody>
</table>

**(1 patient with anaplastic adenocarcinoma uteri et ovarii.)**

Sarcomata, carcinosarcomata, mixed mesodermal tumors and chorionepitheliomata were not included in this study.

**METHODS OF TREATMENT**

126 patients of 128 studied were treated with surgery, radium, X-radiation, or combinations of these methods. 2 patients
refused any treatment following diagnosis.

The largest therapeutic group is that of pre-operative intra-uterine radium implantation followed by total abdominal hysterectomy with bilateral salpingo-oophorectomy, and includes 52 patients.

In 17 of these 52 patients, radium implantation was followed by pelvic lymph node dissections ranging in extent from removal of one or two nodes in the adnexae to the radical Wertheim hysterectomy.

The next largest group is 25 patients who were treated with surgery alone. In 4 of these 25 patients tumor was incidentally discovered in specimens removed for other conditions. 3 of the 4 patients had fibromyomata and one was operated upon for prolapse of the uterus.

18 patients were treated with radium alone and 2 patients received X-radiation solely. There were 10 patients who received pre-operative radium, total abdominal hysterectomy with bilateral salpingo-oophorectomy and post-operative X-radiation. There were several scattered combinations of treatment in a few patients. These methods of therapy have been combined into more general categories: Surgery alone; Radiation alone; Surgery with pre-operative radiation; Surgery with post-operative radiation; Surgery with pre- and post-operative radiation; No treatment; and other; and are summarized in Table 2. In categories labelled radiation, this is intended to include both the modalities of radium and X-radiation, or other radio-techniques as indicated.
TABLE 2:

<table>
<thead>
<tr>
<th>TREATMENT</th>
<th>'52</th>
<th>'53</th>
<th>'54</th>
<th>'55</th>
<th>'56</th>
<th>Tot.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery with pre-op radiation</td>
<td>6</td>
<td>11</td>
<td>13</td>
<td>6</td>
<td>16</td>
<td>52</td>
</tr>
<tr>
<td>Radium alone</td>
<td>5</td>
<td>7</td>
<td>3</td>
<td>7b</td>
<td>4</td>
<td>26</td>
</tr>
<tr>
<td>Surgery alone</td>
<td>5</td>
<td>7</td>
<td>6</td>
<td>6</td>
<td>1</td>
<td>25</td>
</tr>
<tr>
<td>Surgery with pre- and post-op radiation</td>
<td>0</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>Surgery with post-op radiation</td>
<td>0</td>
<td>1</td>
<td>2a</td>
<td>3</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>No treatment</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>1c</td>
<td>2d</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>18</td>
<td>32</td>
<td>28</td>
<td>25</td>
<td>25</td>
<td>128</td>
</tr>
</tbody>
</table>

a- patient was treated with Cobalt radiation at another center.

b- patient also received radio-gold (Au-198) to pleural spaces.

c- patient had surgery with pre-op X-ray followed by surgery and post-op X-ray.

d- patient had surgery with pre-op radium followed by radio-gold (Au-198) post-op.

patient had surgery with pre-op radium followed by surgery.

In 90 patients treated with radium either pre-operatively, alone without operation, post-operatively, or in other combinations, the average total dosage was approximately 5,000 r. 52 of these patients received one dose while 35 received the total amount of radiation in two doses, usually 7 days apart. The remaining 3 patients received three doses. The radium was placed in the uterine cavity using Campbell applicators or modifications of other applicators and capsules containing small radium sources in the majority of patients. In most instances the position of the capsules was evaluated with post-operative roentgenograms of the pelvis. The total dosage was usually equally divided when two applications were made, each dose yielding approximately 2,500 r.

The surgical procedure most often employed was total abdominal hysterectomy with bilateral salpingo-oophorectomy. Often elective appendectomy was carried out during this procedure.
pelvic lymph node dissections were performed. In 3 cases vaginal hysterectomy was performed for other conditions and tumor found incidentally on pathological examination post-operatively. 1 patient had resection of the sigmoid colon for adenocarcinoma and carcinoma of the endometrium was found in the uterus which was not part of the sigmoid malignancy process.

X-radiation was usually administered through small anterior and posterior portals to the pelvis and surrounding structures and the average calculated tumor doses approximate 2,000 r. One patient received 7,000 r by the Cobalt bomb technique at another institution prior to treatment in New Haven.

**RESULTS OF TREATMENT**

The overall apparent survival for this series of 128 patients with carcinoma of the corpus uteri is 60.2%. This represents 77 of the 128 patients, and all of these 77 are alive without tumor except one patient who is alive with tumor 42.5 months after the diagnosis was made. Considering 3- and 5-year survivals, the following data is obtained.

**TABLE 3:**

<table>
<thead>
<tr>
<th>YEAR</th>
<th>TOTAL ALIVE</th>
<th>TOTAL DEAD</th>
<th>TOTAL PTS.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1952</td>
<td>11 (61.1%) at 5 years</td>
<td>7 (38.9%) at 5 years</td>
<td>18</td>
</tr>
<tr>
<td>1953</td>
<td>21 (65.6%) at 5 years</td>
<td>11 (34.4%) at 5 years</td>
<td>32</td>
</tr>
<tr>
<td>1954</td>
<td>14 (50.0%) at 5 years</td>
<td>14 (50.0%) at 5 years</td>
<td>28</td>
</tr>
<tr>
<td>1955</td>
<td>16 (64.0%) at 3 years</td>
<td>9 (36.0%) at 3 years</td>
<td>25</td>
</tr>
<tr>
<td>1956 <strong>20 (80.0%) at 3 years</strong></td>
<td>5 (20.0%) at 3 years</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td><strong>one patient alive with tumor</strong></td>
<td></td>
<td>128</td>
<td></td>
</tr>
</tbody>
</table>
In this series the patients were categorized either as alive without tumor (AWOT); alive with tumor (AWT); died with intercurrent disease (DID); or died with tumor (DWT). There were no patients lost to follow-up. Considering the entire period from 1952 through 1959 at the conclusion of this study, and applying these four categories, the following data is obtained:

- AWOT 76 patients (59.4%)
- AW T 1 patient (0.8%)
- DID 13 patients (10.1%)
- DWT 38 patients (29.7%)

It is interesting to compare these results with the large series of cases collated by the group at the Radiohummet in Sweden as part of the Annual Report on the Results of Treatment in Carcinoma of the Uterus (18), which is abstracted below:

**TABLE 4:**

<table>
<thead>
<tr>
<th>STATUS OF PATIENT</th>
<th>NO. PATIENTS</th>
<th>RELATIVE APPARENT SURVIVAL RATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>AWOT</td>
<td>4,381</td>
<td>54.3%</td>
</tr>
<tr>
<td>AWT</td>
<td>178</td>
<td>2.2%</td>
</tr>
<tr>
<td>DWT</td>
<td>2,770</td>
<td>34.3%</td>
</tr>
<tr>
<td>DID</td>
<td>576</td>
<td>7.1%</td>
</tr>
<tr>
<td>Lost-to-follow-up</td>
<td>171</td>
<td>2.1%</td>
</tr>
<tr>
<td>Total</td>
<td>3,076</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Combining the above figures to give the percentage of patients alive and dead, it is noted that 56.5% of their patients were alive and 41.4% dead. These figures are not markedly different from the values in the present series; i.e., 60.2% of patients alive and 39.8% of patients dead.

In attempting to evaluate which method of therapy yields the most assurance of high survival rate, five major categories of treatment were considered and the survival characteristics of the
patients treated in these ways were examined.

TABLE 5:

<table>
<thead>
<tr>
<th>YEAR</th>
<th>SURGERY</th>
<th>RADIATION</th>
<th>SURGERY WITH PRE-OP RADIATION</th>
<th>SURGERY WITH PRE-OP &amp; POST-OP RADIATION</th>
<th>SURGERY &amp; POST-OP RADIATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1952</td>
<td>4 (5)</td>
<td>0 (5)</td>
<td>5 (6)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>1953</td>
<td>6 (7)</td>
<td>4 (7)</td>
<td>10 (11)</td>
<td>0 (4)</td>
<td>0 (1)</td>
</tr>
<tr>
<td>1954</td>
<td>4 (6)</td>
<td>0 (0)</td>
<td>9 (13)</td>
<td>1 (3)</td>
<td>0 (2)</td>
</tr>
<tr>
<td>1955</td>
<td>6 (6)</td>
<td>3 (6)</td>
<td>6 (6)</td>
<td>0 (3)</td>
<td>0 (3)</td>
</tr>
<tr>
<td>1956</td>
<td>1 (1)</td>
<td>2 (3)</td>
<td>14 (16)</td>
<td>1 (1)</td>
<td>3 (3)</td>
</tr>
</tbody>
</table>

(numbers within parentheses are the total number of patients in the particular category; numbers without parentheses represent patients who are alive at the conclusion of the study)

From the material presented in Table 5 it is seen that 21 of 25 patients were cured with surgery alone (84%); 42.8% of patients were cured with radiation alone; 84.6% were cured with pre-operative radiation and surgery; the other two categories being too small to consider.

An attempt was made to grade the extent of the disease in terms of clinical impression at the time of the original diagnosis in each case so that this information could be applied to a consideration of which method of treatment was most effective in each stage of disease. Inadequate information was derived by this retrospective approach. Certainly, it is not the point of the presentation of the data in Table 5 to indicate that surgery will cure 84% of all carcinomas of the uterus. Obviously there were some instances where the lesion was of low grade or even not clinically recognized at operation for another cause, so that a generalization cannot be made to the whole scope of all uterine cancer. It does appear however, that surgery combined with pre-operative radiation
does produce the most favorable results. In this series there were 52 patients treated in this way, and although again the grades of disease cannot accurately be stated, 84.6% cure in 52 patients indicates a significant number more than with other methods were cured of their disease. It is interesting to note that this figure of 84.6% corresponds very closely with an earlier review of the New Haven Hospital experience over a 20-year period, where staging of the disease was possible. The figure quoted in that study (3), expressed as patients surviving 5 years was 88% following treatment with pre-operative radium and surgery.

As indicated previously, (Table 1) the majority of malignancies in this series were adenocarcinomas, with anaplastic forms, adenoacanthomas and others present in a smaller number of cases. In terms of survival, 61.5% of patients with adenocarcinoma excepting the anaplastic grades survived. This figure is based on the percentage alive of the total number of patients at the conclusion of the study. Considering the anaplastic tumors, only 7.1% survived. In tabular form these survival rates for each entity can be shown as follows:

**TABLE 6:**

<table>
<thead>
<tr>
<th>TYPE</th>
<th>No. PTS.</th>
<th>AWOT AT END OF STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenocarcinoma</td>
<td>91</td>
<td>61.5%</td>
</tr>
<tr>
<td>Adenoacanthoma</td>
<td>11</td>
<td>72.7%</td>
</tr>
<tr>
<td>Adenocarcinoma-in-situ</td>
<td>12</td>
<td>100.0%</td>
</tr>
<tr>
<td>Anaplastic adenocarcinoma**</td>
<td>14</td>
<td>7.1%</td>
</tr>
<tr>
<td></td>
<td>128</td>
<td></td>
</tr>
</tbody>
</table>

**one patient with anaplastic adenocarcinoma uteri et ovarii.

Table 7 on page 12 gives a more complete picture of the
<table>
<thead>
<tr>
<th>Year</th>
<th>Value 1</th>
<th>Value 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>2020</td>
<td>12.5</td>
<td>32.5</td>
</tr>
<tr>
<td>2021</td>
<td>20.5</td>
<td>45.6</td>
</tr>
<tr>
<td>2022</td>
<td>32.5</td>
<td>54.3</td>
</tr>
<tr>
<td>2023</td>
<td>45.6</td>
<td>67.8</td>
</tr>
<tr>
<td>2024</td>
<td>54.3</td>
<td>89.1</td>
</tr>
</tbody>
</table>

*Data shown is for illustrative purposes only.*
status of the patients in the series, as it breaks down each tumor
type into the number of patients who are alive without tumor, died
with intercurrent disease, alive with tumor, or died with tumor.

In order to calculate survival rates, the total group of
patients were broken down into two sub-groups: group 1 includes the
patients from 1952 through 1954; group 2 includes the patients from
1955 through 1956. In this manner, 3-year and 5-year survivals may
be derived. In group 1, there were 78 patients, 46 of whom survived
5 years, or 58.9%. In group 2 there were 50 patients, 36 of whom
survived 3 years, or 72.0%. To estimate the number of the 3-year
survivors who will be alive at the end of 5 years, assuming that
endometrial carcinoma is the only cause of death, one can apply the
method of Doering and Forbes (23). By this procedure if one knows
the survival rate at 3 years and wishes to calculate it for 5 years
one should divide the 5-year survival by the 3-year figure. The
result, expressed as percent, is the percent of those alive at 3
years who will be alive at the end of five years, excluding all
other causes of death than endometrial carcinoma. Taking the sur-
vivals in this series; the 5-year survival (58.9%) divided by the
3-year survival (72.0%) gives 81.8% as the percent of the 36 3-year
survivors who will be alive at the end of 5 years, excluding other
causes of death as described above.

In 111 patients information was available concerning
whether or not the carcinoma had invaded the myometrium. In 41
patients myometrial invasion was noted, 34.1% of these patients
survived. In the group of 70 who did not have evidence of myomet-
...
### Table 7

**Status of Patients Related to Tumor Type**

<table>
<thead>
<tr>
<th>Year</th>
<th>Adenocarcinoma</th>
<th>Anaplastic Carcinoma</th>
<th>Adenocanthoma</th>
<th>Adeno-in-Situ</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AMOT</td>
<td>Did</td>
<td>Dmt</td>
<td>AMOT</td>
<td>Did</td>
</tr>
<tr>
<td>1952</td>
<td>7</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1953</td>
<td>16</td>
<td>2</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1954</td>
<td>9</td>
<td>3</td>
<td>9</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>1955</td>
<td>6</td>
<td>1</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1956</td>
<td>18</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td><strong>56</strong></td>
<td><strong>11</strong></td>
<td><strong>24</strong></td>
<td><strong>1</strong></td>
<td><strong>1</strong></td>
</tr>
</tbody>
</table>

*Includes one patient with anaplastic carcinoma uteri et ovarii.

**Includes one patient alive with tumor and was entered here for ease of tabulation. This patient is alive with tumor 42.5 months after the diagnosis of endometrial carcinoma was made, and the tumor was an adenocarcinoma.
rial invasion, 84.2% of these survived.

17 patients underwent pelvic lymph node dissection, and all of these patients had received pre-operative radium therapy. Of the 17 patients, 4 had lymph nodes positive for tumor and none of these patients survived. 13 of the 17 patients had negative lymph nodes and 11 of these patients survived; there was one operative death.

In 90 patients from whom tissue specimens were obtained following radium treatment 54, or 60% were noted to have viable tumor in the specimen. Of these 54 patients, 38.9% survived. Of the 36 patients that had no viable tumor in the specimen following radium treatment, 33 or 91.6% survived.

**SENSITIZATION AND RADIATION RESPONSE**

The concept of the sensitization response was first described by Ruth Graham and since has been extensively re-described and amplified (19). In examining Papanicolaou smears made for the diagnosis of carcinoma of the cervix, Graham noted certain changes that occurred in normal vaginal and cervical epithelial cells before any therapy had been begun. She likened these changes to some sort of host response to the tumor which the patient had. These parabasal cells are round or oval in shape and do not have the squared-off corners of the intermediate or superficial cells. They are distinguished from the usual basal cells by two characteristics, a fine vacuolization of the cytoplasm (which must be distinct) and an in-
creased density of the intervening cytoplasm. It was because of the cytoplasmic vacuolization that this type of cell was discovered. It was further noted that when a fair proportion, i.e., more than 10% of these desquamated non-malignant cells were of this type, the patient and the cancer usually responded favorably to the subsequently applied radiation. Hence, the term sensitization response, or SR, because the individual seemed 'primed' or sensitized to the radiotherapy given after these cells were noted in the smear, (19). As SR is only considered significant if found in the basal cells, a vaginal smear that contains only superficial and intermediate cells has a 0% SR; those patients who have 10% or more SR cells are said to have a good or marked SR, and if 9% or less SR cells are present the sensitization response is poor.

The concept of radiation response (RR) was also first described by Ruth Graham, in 1947 (20). The radiation response is characterized by changes in the normal epithelial cells of the vaginal smear during radiotherapy. The basal layer of the vaginal and cervical mucosa is affected before any of the other cells show changes. They become aberrant and lose their characteristic round shape to become elongated. At the same time their staining reaction changes from basophilic to brownish, using the standard Papanicolaou (21) technique. The nuclei become degenerated, and the nuclear material clumps together representing karyorrhexis of the nucleus. Later, the most striking effect occurs, when the cells become 'blown-up' to 3 or 4 times their normal size, still maintaining the same cytoplasmic-nuclear ratio. There is also vacuolization to the extent that often
the vacuoles occupy almost all of the cytoplasm. This is particularly striking since it generally occurs in the 'blown-up' cells. These changes only occur if there are basal cells present in the original vaginal smear. In the pre-menopausal woman, few basal cells are found and the radiation changes are first seen in the precornified cells. Here, the first reaction to occur is tremendous increase in size, followed by pyknosis of the nuclei; the appearance of fibers in the cytoplasm, and finally vacuoles appear which may occupy the greater part of the cell (20).

The Grahams have shown in large series that the SR and the RR are useful in the prognosis of cervical cancer. They have further demonstrated that the SR and RR correlate together well in the prognosis of this disease (19). Patients with poor SR were found to have a cure rate of 15-21% and those with a marked SR a cure rate of 66-73% (19). Further it has been well shown that the fact that a patient is pre- or post-menopausal bears no significant relation to the survival rate. What seems to be important is the presence or absence of SR in either the pre- or post-menopausal patient. Accordingly, the Grahams conclude that the incidence of SR is influenced by age and relation to menopause and that moreover, the prognostic significance of SR is unrelated to these factors. For an unselected series of patients in Buffalo treated with radiotherapy alone, the correlation of SR and RR was 86% in agreement (19). Recently, however, an effort was made to correlate the 2-year clinical end-results with radiation changes in exfoliated vaginal cells according to the Graham technique, and no correlation was found (22).
Both of these concepts, SR and RR, as far as is known, have only been applied to cervical carcinoma. One study mentioned above (22) also attempted to apply radiation to buccal mucosa for evaluation of SR. It was felt that although this present series is small, an attempt should be made to apply these concepts of sensitization and radiation response to endometrial carcinoma, particularly since the technique of obtaining and staining the cells is the same as in the observation and study of smears obtained for the diagnosis of cervical carcinoma.

SENSITIZATION AND RADIATION RESPONSE IN 26 PATIENTS

In this series of 26 patients with endometrial carcinoma, vaginal smears were performed using the techniques of Papanicolaou and Traut (21). Sensitization response studies were made prior to any local or radiological treatment, and the radiation response was followed during the course of radiotherapy. In only 22 of the 26 patients were SR studies available. There were 12 survivals and 14 deaths in this group.

No significant relationship of SR to curability was found in 22 patients in whom this study had been performed. In the poor SR group (9% or less SR cells) 6 patients were alive without tumor and 4 died with tumor. In the good SR group, 5 patients were alive without tumor and 7 died with tumor. (See Table 7, page 17)

No adequate relationship could be elucidated between the SR and menopause since 20 of the 22 patients were post-menopausal, so that comparison would not be significant. In the poor SR group, 1
patient was pre-menopausal and 9 post-menopausal, while in the good SR group, 1 patient was pre-menopausal and 11 were post-menopausal.

Radiation response studies were done in 26 patients. No correlation was found between curability and radiation responses. In Figure 1 the clinical status of each of the 26 patients is shown; the height of each column representing the highest radiation response reading that particular patient had during therapy. In the 26 patients, the RR values ranged from 13% to 93%, and as can be seen in Figure 1, there is no indication that in this series a high RR tends to prognosticate curability.

In 17 of the 26 patients viable tumor was present after radiation and the average radiation response in this group was 64.7%. 8 of the patients had no tumor following radiotherapy and in this group RR was actually lower, being 54.4%. One patient was found to have only irradiated cells in the specimen. In this series greater than 75% is considered good response, 60-75% intermediate, and below 60, poor. No correlation could be found between the level of RR and whether or not viable tumor was present in the specimen following radiotherapy. The responses of the 26 patients were divided into the three categories mentioned above; good, intermediate and poor, and compared with the presence or absence of tumor in specimens.

<table>
<thead>
<tr>
<th>SR</th>
<th>TOTAL PATIENTS</th>
<th>AMOT</th>
<th>DWT</th>
</tr>
</thead>
<tbody>
<tr>
<td>9% or less</td>
<td>10</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>10% or more</td>
<td>12</td>
<td>5</td>
<td>7</td>
</tr>
</tbody>
</table>

TABLE 7:

SIGNIFICANCE OF SR IN RELATION TO CURABILITY
SIGNIFICANCE OF RR IN RELATION TO PRESENCE OF TUMOR IN POST-RADIATION SPECIMEN

<table>
<thead>
<tr>
<th>RESPONSE</th>
<th>TOTAL</th>
<th>VIABLE TUMOR IN SPEC.</th>
<th>NO TUMOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good</td>
<td>9</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Intermediate</td>
<td>7</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Poor</td>
<td>10</td>
<td>6</td>
<td>4</td>
</tr>
</tbody>
</table>

There were 10 patients who had a poor SR and in this group the average radiation response was found to be 50.5%. In the group of 11 patients that had a good sensitization response the average radiation response was 73.6%. One patient of the 22 did not have radiation response studies following the SR determination. This finding of a much higher radiation response in patients who had primarily a good SR, and a lower incidence of good radiation response among those patients who had poor sensitization response follows the pattern reported by Graham (19). In that series, of 53 patients with poor SR, 45 subsequently showed poor RR, while of 39 patients with marked SR, 34 subsequently obtained a good RR.
SUMMARY

128 cases of carcinoma of the corpus uteri from the Grace-New Haven Community Hospital have been reviewed.

Information concerning age at diagnosis, parity, age at menopause, incidence of obesity and diabetes, cystic hyperplasia and associated ovarian tumors has been presented and briefly discussed.

The pathologic entities occurring in this series have been presented in terms of incidence and ultimate survival.

Methods of treatment have been discussed and related to survival for each particular method, radiological and surgical. Survival statistics, both over-all and 3- and 5-year, and for particular pathologic and therapeutic entities have been presented.

The phenomenon of myometrial invasion by tumor has been related to ultimate survival.

The situation of finding viable tumor in the post-radiation specimen has been discussed in terms of survival, and related to methods of treatment.

The concepts of sensitization and radiation response have been reviewed and discussed, together with their significance in this series in relation to curability, menopause, and presence of viable tumor in the post-radiation specimen. This latter point is to be examined further and presented in a subsequent study.
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