Management of Invasive Cervical Cancer Following Inadvertent Simple Hysterectomy

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During a 20-year period from 1940 to 1960, 84 women were referred to our hospital after having undergone elsewhere a simple or subtotal hysterectomy in the presence (usually unrecognized) of invasive carcinoma of the cervix. The annual incidence of such referrals to this hospital has unfortunately remained fairly constant, despite the many educational programs in cancer detection sponsored for physicians throughout the country and the increasingly widespread use of the cytologic smear as a routine screening method for early recognition of cervical cancer. The types of inadequate operation performed included:

| Operation                     | No. of patients |
|-------------------------------|----------------|
| Total abdominal hysterectomy   | 60             |
| Supracervical hysterectomy    | 13             |
| Vaginal hysterectomy          | 5              |
| Cervical amputation           | 3              |
| Excision of cervical stump    | 3              |
| Total                         | 84             |

In the majority of these patients, no diagnostic appraisal whatever of the status of the cervix had been made prior to carrying out hysterectomy for benign conditions, most often uterine leiomyomas, coexisting with the unsuspected cancer. In a number of patients who had complained of abnormal bleeding, simple hysterectomy had been undertaken without preliminary vaginal cytologic examination, cervical biopsy, or curettage—and occasionally without even speculum examination of the cervix. In one patient, continuous, painless, third-trimester pregnancy bleeding, presumed before operation to be due to marginal placenta praevia, was found at cesarean section-hysterectomy to be due to Stage II carcinoma of the cervix.

In some instances invasive cancer had been found in the specimen after hysterectomy for presumed carcinoma in situ, the diagnosis having been established by punch biopsy only, without proper additional evaluation by curettage and cone biopsy.

Regrettably, in a few cases simple hysterectomy was done despite the known presence of invasive cancer of the cervix. In some, "Wertheim" hysterectomies were said to have been performed; however, after review of the operative notes and examination of the patients, it was quite obvious that these procedures, in fact, had been merely

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Reprinted from OBSTETRICS AND GYNECOLOGY 32: 784-789, 1949.
simple hysterectomies combined with removal of a few iliac lymph nodes. Omitted entirely had been the all-important, wall-to-wall, deep pelvic dissection and removal of the parametrial, paracervical, and paravaginal tissues together with an adequate amount of upper vagina, which is the essence of the true Wertheim-Meigs radical hysterectomy. In the remainder of patients, simple hysterectomy had been done deliberately in the mistaken belief that, because the invasive lesion appeared to be small, this would be adequate surgical treatment. A few of these patients were given postoperative X-ray therapy at their local hospitals. All the patients in this small group in whom simple hysterectomy had been done, despite the known presence of invasive cervical cancer, had developed obvious clinical recurrence of cancer by the time they were later referred to our hospital.

Only 40 of these patients were referred for further treatment within 6 months of their inadequate operations. Twelve others received their additional therapy after an interval of 6-12 months, 17 after an interval of 2 years, and the remaining 15 after periods of from 3 to 7 years. Early referral for adequate treatment in this unfortunate situation is imperative, for delay in further treatment seriously affects the ultimate prognosis (Table 1). The five-year cure rate for 33 patients undergoing additional therapy within 4 months of their inadequate hysterectomy was 42 percent, whereas it was only 18 percent for the 51 patients treated after 4 months. The overall five-year cure rate for the entire group of 84 was 27 percent (23 of 84 patients).

Methods
Each of the 84 patients was reevaluated thoroughly and the histologic diag-

| TABLE 1—INTERVAL BETWEEN INADEQUATE OPERATION AND TREATMENT |
|-------------------------------------------------------------|
| Interval | Months | Years | Total |
|----------|--------|-------|-------|
|          | 1 2 3 4 5 6 7 8 9 10 11 12 | 2 3 4 5 6 7 |     |
| Patients (No.) | 13 7 6 7 4 3 2 2 1 – 1 6 | 17 8 3 3 – 1 | 84 |
| 5-yr. cure (No.) | 7 2 2 3 1 1 – – – – | 4 1 – – – – | 23 |
| 5-yr. cure (%) | (42%) | (18%) | (27%) |
nosis of invasive carcinoma was confirmed by biopsy of lesions of persistent or recurrent disease, if present clinically, or by review of the slides from the original hysterectomy specimen. The extent of residual tumor was estimated by pelvic examination under anesthesia together with cystoscopy, sigmoidoscopy, intravenous pyelography, barium enema, and chest and skeletal survey X-ray films. A tentative decision then could be reached regarding proper additional treatment, either with the hope of cure, or with a view to worthwhile palliation. A summary of the further treatment and ultimate results in these 84 patients is presented in Table 2. Twenty-two women with widespread recurrent and metastatic tumor received palliative and supportive care only. Patients with no evidence of extrapelvic spread of tumor were carefully individualized and considered for either radical operation or radiation therapy.

Thirty patients were selected for definitive radiation therapy and received a full course of treatment employing local radium applications as well as external irradiation. Of those women, 3 also underwent bilateral, extra-peritoneal pelvic lymphadenectomies. Of the 30 patients, 9 (30 percent) who were treated by radiation achieved five-year cures.

Thirty-two women were selected for surgical therapy. At laparotomy 11 tumors were found to be inoperable and these patients later received palliative irradiation, all dying of disease within 5 years. In 21 patients, definitive radical operation was possible and consisted of a Wertheim procedure with pelvic lymphadenectomies in 15, a Schauta-Amreich vaginal operation in 3 (2 of whom also underwent bilateral, extra-peritoneal pelvic lymphadenectomies), and pelvic exenteration in 3. A summary of the results of definitive, radical surgical treatment is presented in Table 3. Of these patients, 14 (67 percent) (11 who had had Wertheim's operation and all 3 who had had Schauta's procedures) achieved five-year cure. In the

| Type of treatment                                      | Number of patients | 5-year cure (number) |
|-------------------------------------------------------|--------------------|----------------------|
| Non-surgical                                          |                    |                      |
| No treatment                                          | 21                 | —                    |
| Inoperable at laparotomy                              | 11                 | —                    |
| Chemotherapy only                                     | 1                  | —                    |
| **Total**                                             | **33**             |                      |
| Radiation                                             |                    |                      |
| Radiation only                                        | 27                 | 7                    |
| Radiation and pelvic lymphadenectomy                   | 3                  | 2                    |
| **Total**                                             | **30**             | 9 (30%)              |
| Surgical                                              |                    |                      |
| Wertheim and pelvic lymphadenectomy                    | 15                 | 11                   |
| Schauta and pelvic lymphadenectomy                     | 3                  | 3                    |
| Exenteration and pelvic lymphadenectomy                | 3                  | 0                    |
| **Total**                                             | **21**             | 14 (67%)             |
| **Total**                                             | **84**             | 23 (27%)             |
Wertheim group, six patients had positive nodes, and although all six ultimately died of distant metastases, three lived for eight, eight, and six years, respectively. Of the nine negative-node patients, eight are still living and well six to twenty-three years after their radical operations, one dying of postoperative complications (Table 4). In the Schauta group all had negative nodes and all 3 are living 7, 10, and 15 years after operation. None of the three total pelvic exenteration patients—two of whom had positive nodes—is alive, although one survived two years, and the one with negative nodes, who appeared to have been cured, succumbed to postoperative complications. Nevertheless, it is clear that pelvic exenteration can be curative in selected patients with cervical cancer in whom accidental simple hysterectomy has unfortunately been done. Several such patients, not included in this report because their treatment was given after 1960, are living and well, having had pelvic exenteration done more than five years ago—shortly after they had the misfortune to undergo simple hysterectomy in the face of cervical cancer.

**Discussion**

There are three aspects of our experience with this problem which merit discussion. First, though further confirmation hardly seems necessary, it has demonstrated again the inadequacy of simple total hysterectomy in the management of invasive cervical cancer irrespective of how small the clinical lesion may be. Not only is simple hysterectomy inadequate, but its prior performance seriously diminishes the patient's ultimate chances for cure, even when followed promptly by more adequate treatment employing conventional full radiation therapy or reoperation with radical surgical resection. Thus, even though it was possible to give additional treatment with a view to cure by either full radiation therapy or radi-

**TABLE 3—RESULTS IN SURGICALLY TREATED PATIENTS**

|                   | Wertheim | Schauta | Exenteration |
|-------------------|----------|---------|--------------|
| Number of patients| 15       | 3       | 3            |
| Survival length (years) | 23,19,15,10 | 0 | 2 yrs., 4 mos. |
| Living            | 10,8,6,6 | 15.7    | 8 wks.       |
| Died              | 8,8,6,3,3,2,1 | 10^2 |              |
| Five-year survivors| 11       | 3       | 0            |

^1 Died of postoperative complications.  ^2 Died of pneumonia.

**TABLE 4—CLINICAL AND PATHOLOGIC FINDINGS IN PATIENTS WITH WERTHEIM OPERATION**

| Nodes | Number of patients | Clinically diseased patients | Positive biopsies | Died | Survival length (years) |
|-------|--------------------|------------------------------|------------------|------|-------------------------|
| Negative | 9               | 4^1                         | 4                | 1    | 3                       |
| Positive | 6               | 6                           | 6                | 6    | 8,8,6,3,3,2              |

^1 In the other five patients no clinical disease was present when examined at our hospital; review of the hysterectomy specimen revealed it to be positive in these patients.
cal pelvic operation, in 51 of these 84 patients, only 23 were alive at the end of 5 years, an overall salvage rate of only 27 percent.

Jones and Jones reported a series of 36 women with early Stage I cervical cancer (all lesions were less than 1 cm. in diameter) deliberately treated by simple total hysterectomy, and they observed a five-year cure rate of only 41.6 percent. Schmidt reported on a similar group of 36 patients, 21 of whom had had the simple hysterectomy inadvertently done in the face of unrecognized cervical cancer. He recorded five-year cure rates of 16 percent for those in whom the tumor had extended beyond the cervix, 60 percent when the lesion had been confined to the cervix, and 82 percent when only carcinoma in situ had been present. These authors concluded that ordinary total hysterectomy was not adequate treatment even for selected patients with early invasive cervical cancer.

Daniel and Brunschwig have also reported the results of a detailed study of the specimens from the radical Wertheim operations of 202 women with clinical Stage I cervical cancer who received their primary treatment at Memorial Hospital in New York during the period 1947-1955. These authors pointed out that, in at least 50 percent of the specimens, it was clearly demonstrated by histologic studies that simple total hysterectomy would not have removed all the malignancy.

On the basis of the extensive data accumulated during the past two decades on end results of the radical Wertheim hysterectomy, as well as cure rates achieved by modern radiotherapy, one would certainly expect a 90-95 percent cure rate of Stage I lesions measuring less than 1 cm. in diameter—either by radical hysterectomy with pelvic lymphadenectomy or properly administered radiotherapy.

Our experience thus reaffirms the observations of these previous reports and should serve again to inject an appropriate note of caution into current discussions regarding the possibility that so-called "microinvasive" cervical cancer may require only simple hysterectomy for control. Such a compromise ignores the lessons of the past and would seem to be unsound from an oncologic viewpoint. Furthermore, it is not really in the best interests of the patient who, as a result of modern methods and programs of cancer detection, is fortunate enough to have her cervical cancer discovered at an early stage when cure rates approach 100 percent—if adequate treatment is given.

Secondly, the importance of proper evaluation of the cervix before performing simple total hysterectomy for whatever indication, particularly if the patient has noted abnormal bleeding, seems self-evident. Had this been done prior to hysterectomy in the patients subsequently referred to our hospital for further treatment, the diagnosis of cervical cancer could have been established readily in essentially all of them before their unfortunate, accidental simple hysterectomy.

In each of the 84 patients in this series, one or more of the following errors were made: (1) cancer was not suspected, although abnormal bleeding was a symptom in many of these women; (2) cytologic examination, biopsy, curettage, and conization were not utilized properly to exclude the presence of invasive cervical cancer; (3) simple hysterectomy was erroneously believed to represent adequate treatment in the few instances when diagnosis of invasive cancer was made; and (4) referral to an institution with facilities available for adequate treatment was delayed when unsuspected invasive cervical carcinoma was found in the simple hysterectomy specimen.

Finn, reporting 21 patients, and Moore, presenting a series of 14 pa-
tients, all of whom had undergone accidental simple hysterectomy in the presence of unsuspected cervical cancer, also emphasized that routine cytologic examination and cervical biopsies or endocervical curettage could have resulted in the correct preoperative diagnosis in almost all of their patients.

Finally, the experience with our 84 patients does permit comment regarding what seems to represent the most effective additional therapy in this unfortunate situation. In our experience, the best results have been afforded when prompt reoperation and radical surgical removal of all potential areas of residual disease has been performed (when it has been possible to do so) or, if recurrence is already clinically present, a radical resection encompassing all known, as well as potential, areas of persistent cancer is done. Obviously, in the latter group pelvic exenteration will be required in many instances, if the patient is to be offered any chance of cure.

Even in the patient referred immediately following discovery of an unsuspected cervical cancer in her simple hysterectomy specimen and in whom there is as yet no positive evidence of persistent tumor, a radical Wertheim type of dissection of the parametrial, paracervical, and paravaginal tissues, with upper vaginectomy and pelvic lymphadenectomy, is strongly recommended and will offer the best chance for cure. This conviction is based on knowledge of the high ultimate rate of recurrence following inadvertent simple hysterectomy and our observation in this series that a delay of more than four months in proceeding with adequate treatment yields a five-year cure rate of less than 20 percent. This figure is indeed a sobering one when it is remembered that almost all these patients originally had small Stage I lesions, clinically unsuspected, many of them of the so-called microinvasive variety.

Daniel and Brunswig reached similar conclusions after reviewing the outcome in 78 women with recurrent carcinoma of the cervix following simple total hysterectomy referred to Memorial Hospital during the years 1947-1955. In 30 of their patients simple hysterectomy had been performed inadvertently; in 30 it had been done deliberately, presumably "because the lesion was small or microinvasive"; and in 18 the circumstances were unknown. External irradiation already had been given elsewhere to 60 of the 78 women and had not proved effective. Operation was possible in 45 patients, although in only 36 was it felt to be potentially curative. Twelve patients underwent a radical Wertheim dissection, accompanied in three instances by segmental resection of the adjacent bladder wall or lower ureters; 10 of these women were living and well 5 years later. Of the 33 patients with pelvic exenterations, there were ten postoperative deaths (33 percent mortality), and 7 of these patients were living and well at 5 years. The five-year cure rate for the women undergoing radical reoperation was 38 percent—for the entire group it was only 22 percent. Only 3 of the 42 patients in whom only palliative treatment or additional radiotherapy was feasible lived more than 1 year, the longest survival in this group being 15 months. Thus, Daniel and Brunswig have also advised prompt surgical intervention in this difficult and often tragic situation, the type of operative procedure to be determined by the extent of the recurrence.

Moore has also reported a group of 14 patients in whom total hysterectomy was done accidentally in the presence of early, invasive epidermoid cervical cancer. All 14 of the cervixes were blocked and sectioned serially for detailed histologic study; 12 of these lesions were described as minimal, only two showing deep penetration in the cervical stroma.
operation by means of a radical surgical procedure tailored to the individual circumstances of each patient offers the best hope of cure in this difficult situation. Needless to say, avoidance of this tragic error by proper evaluation of the cervix before performing simple total hysterectomy is even more important in preventing avoidable mortality from early cervical cancer.

**Conclusions**

Apparently, physicians are not yet universally aware that the presence of cervical cancer must be excluded before performing simple total hysterectomy for whatever reason, and that in the face of abnormal bleeding it is imperative to evaluate the cervix first by means of cytologic and speculum examination, Schiller's test, punch biopsy, D&C, and cone biopsy, where indicated.

It behooves all gynecologists to promote the following concepts among their surgical and medical colleagues:

1. Cancer is overlooked most often when it occurs "unexpectedly"—e.g., in young women, during pregnancy, and in association with leiomyomas or pelvic inflammatory disease. Even when its presence is obvious to the trained eye, it surely will be missed if it is not "looked for."
2. Simple hysterectomy has no place in the primary treatment of invasive carcinoma of the cervix.
3. The first chance to treat cancer offers the best chance to cure it, but a second chance for cure is better than none. The error of inadvertent simple hysterectomy in the face of cervical cancer should not be compounded by a subsequent ineffectual course of "postoperative X-ray therapy" with resulting delay in referral to an institution where adequate treatment is available.

**Summary**

Eighty-four women in whom simple hysterectomy had been performed accidentally in the presence of invasive cer-
vical cancer, unsuspected in most instances, were referred to our hospital during the twenty-year period, 1940-1960. Early reoperation with radical surgical removal of the residual tumor-bearing area by means of the Wertheim, Schauta, or pelvic-exenteration procedure appears to offer the greatest chance of salvage in this unfortunate situation. In this series, 21 patients underwent radical reoperation with a view to cure, and 14 (67 percent) survived 5 or more years. Radiation therapy has proved less successful in our hands, quite probably because of the technical obstacles to effective local application of radium which absence of the uterus poses. Thus, although 30 patients were given a full course of radiotherapy with a view to cure, only 9 (30 percent) survived 5 or more years.

Bibliography

Daniel, W. W., and Brunnerwig, A.: The management of recurrent carcinoma of the cervix following total hysterectomy. Cancer 14: 582-596, 1961.

Finn, W. F.: The postoperative recognition and further management of unsuspected cervical carcinoma. Am. J. Obst. & Gynec. 63: 717-729, 1952.

Jones, H. W., and Jones, G. E. S.: Panhysterectomy versus irradiation for early cancer of the uterine cervix. J.A.M.A. 185: 920-922, 1962.

Moore, D. W.: Unintentional removal of invasive epidermoid cervical carcinoma in total hysterectomy. A ten year survey at a private hospital. Am. J. Obst. & Gynec. 89: 320-327, 1961.

Schmidt, R. T. F.: Panhysterectomy in the treatment of carcinoma of the uterine cervix: evaluation of results. J.A.M.A. 146: 1810-1812, 1951.

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**IMMUNOTHERAPY AS AN ADJUNCT TO CANCER SURGERY**

Since it has been difficult or impossible to cause regression of established tumors in animals by immunologic means, it is unlikely that immunotherapy alone will ever play the major role in the treatment of cancer. Furthermore, Southam’s studies on the autotransplantability of cancer in man indicate that inoculation of $10^8$ cells almost uniformly results in tumor growth at the inoculation site. A neoplasm, only one centimeter in diameter, contains approximately $10^6$ tumor cells. Therefore, by the time most tumors are clinically detectable, they have already outgrown the patient’s immune defenses, and it is unlikely that immunotherapy alone will ever bolster host defenses sufficiently to reverse this process in the patient with advanced disease.

However, immunotherapy is a logical adjunct to definitive cancer surgery for several reasons: (1) Patients who have only small foci of cancer cells remaining after surgical removal of the bulk of tumor are those most likely to benefit from immunotherapy because the tumor mass which must be destroyed by host immune responses is smallest at that time. (2) Surgical patients are most likely to respond from the immunologic standpoint to any immunotherapeutic maneuvers, since the cancer patient’s immunological competence is greatest in the stage of localized cancer and progressively declines with advancing disease. (3) Immunotherapy would be expected to complement rather than to interfere with other currently available methods of managing cancer recurrences following surgery, such as irradiation and chemotherapy.

—Donald L. Morton, M.D., “Cancer immunology and the surgeon.” Surgery 67: 396-398, 1970. Page 398.