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CERVICAL CONIZATION AS A METHOD OF
DIAGNOSIS AND TREATMENT OF CARCINOMA OF THE CERVIX

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Introduction

Cancer of the uterine cervix should, at present time, be classified as a preventable disease. Early diagnosis and treatment should lead to 100% survival of patients with this disease.⁷ This malignant lesion will attack approximately 2.2% of the female population, killing more than 50% in whom the disease occurs.¹² According to the statistical research department of the American Cancer Society, there would be 26,000 new cases of carcinoma of the cervix in 1961.⁹

If then invasive cancer of the uterine cervix is to be classified as a preventable disease, how may this process be prevented? The development of vaginal cytology according to Papanicolaou has fostered a developmental concept of cervical cancer which may enable very early diagnosis of cervical cancer.⁵ If then the suspicion of cervical cancer can be detected with cytology, what methods are available for further definitive tissue diagnosis of this process? The random punch biopsy has been used but a study by Thornton et al. in 1954, revealed that of 30 patients who had in situ carcinoma of the cervix diagnosed by punch biopsy, 5 of these women subsequently had invasive cancer found in larger specimens obtained by cold knife cervical conization.

For a biopsy to be adequate, of the cervix, it must include a generous amount of tissue on either side of the squamocolumnar junction of the cervix and possibly also to include material derived from an endocervical curettage to further localize the possible lesion. This is required because the site of origin of most cases of squamous carcinoma in situ of the cervix is at or near the junction between the endocervical columnar epithelium and the squamous epithelium of the portio. Histologically, this junction may be sharply defined varying within which endocervical surface epithelium and glands intermingle with portio squamous epithelium. The location of this junction often does not correspond with the anatomical os of the cervix. The literature also indicates that the majority of cases of carcinoma in situ of the cervix arise in a field of abnormal epithelium rather than from a mutation in a single cell or small group of cells.¹¹

A histologic diagnosis of carcinoma of the cervix must be made. Clinical judgment must not be entirely relied upon.⁸

Two questions will be answered in the following thesis:
1) Does the cold knife cervical cone fulfill the requirements of an adequate tissue biopsy specimen for diagnosis of cervical carcinoma?, and 2) Is the cold knife cervical cone an adequate method of definitive treatment of carcinoma in situ of the uterine cervix?

Methods and Materials of the Study

The patients in this study were obtained from the records of the University of Nebraska College of Medicine in Omaha, Nebraska from a period of 1958 to 1963. Reference was not made as to marital status, race, parity, or age of the patients. This study also does not include the indications for the cervical conization performed on these patients. Research into the pathological findings of these patients included:

1. Reference to the pathological code file to obtain the diagnosis, surgical number, and year of the cervical specimens.
2. Correlating the above surgical number with the surgical report volumes to learn the patients name.
3. Reference to the pathological master file to learn the type of procedure used to obtain the cervical specimen and to determine if a subsequent hysterectomy was performed and the diagnosis of the uterine specimens.

The cervical specimens that were of interest were those obtained by the cold knife conization procedure. The method of obtaining the cervical cone is discussed below.

General anesthesia, spinal, and paracervical analgesia are used and the patients are placed in dorsal lithotomy position. The perineum is prepped and there is no internal or vaginal preparation. Following this a pelvic exam is done and described in relation to examination and palpation. A Schiller test is then done on the cervical epithelium. The cervix is then grasped with a tenaculum and a solution of 3 mgm. of neosynephrine diluted to 30 ml. with isotonic sodium chloride is injected submucosally for hemostasis. Two number II-0 general chromic sutures are placed in the cervix at 3 o'clock and 9 o'clock. Sharp conization of the cervix followed with a Fleming cold knife taking care to include a generous portion of the squamous columnar junction of the cervix. A partial curettage of the endocervix follows this and is sent to the pathology laboratory as a separate specimen from the cervical cone. Dilatation of the cervix and sounding of the uterine cavity precedes a uterine curettage and this specimen is also sent to the pathology laboratory.

Obvious bleeding points at the squamo-columnar junction about the cone site are then cauterized by electrocautery. The diagnostic cone must not be taken with electrocautery because of loss of cellular detail which results from the coagulation current of the electrocautery.



Diagram of Cone Biopsy Method

In pathology, the cervical cone specimen is placed flat with the mucosal surface upward and a tissue block is taken out about every 2 mm., each properly labeled. Slides are made from each tissue and stained with H. and E. stain.

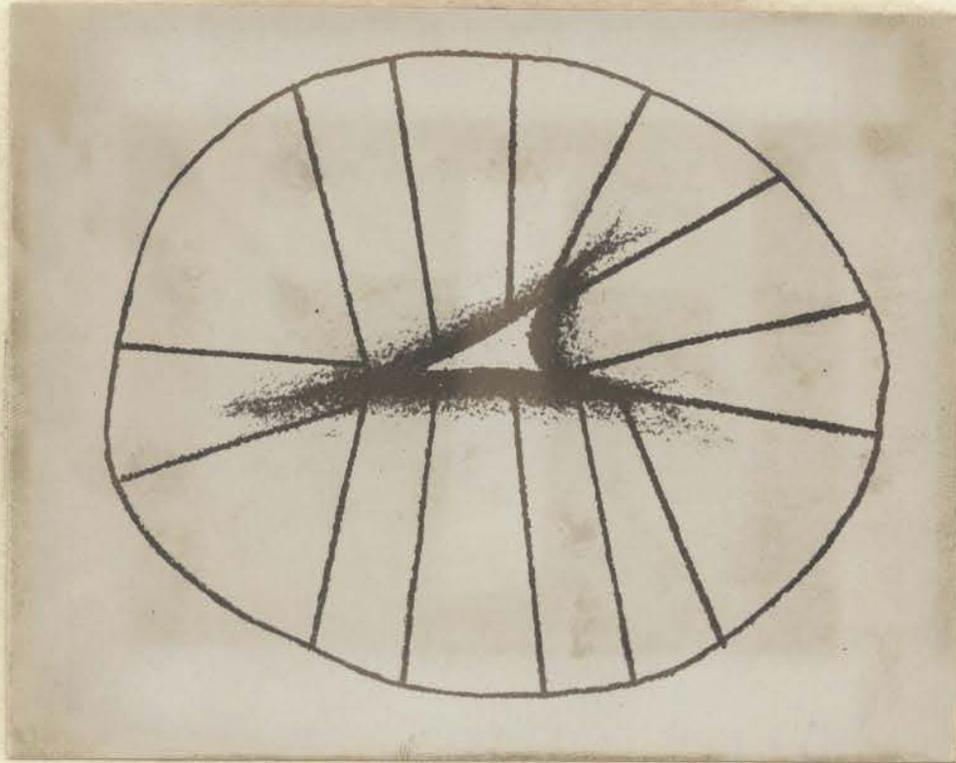


Diagram of the cuts made of the cone biopsy to
prepare blocks for Microscopic Examination.

The next step is the microscopic examination of the properly prepared surgical specimens.

Dysplasia of the uterine cervix is a term applied to all differences or disturbances of differentiation of the cervical squamous epithelial lining that cannot be classified as either carcinoma in situ or invasive carcinoma. Dysplasia and basal cell hyperplasia are often used interchangeably. Microscopic findings in this condition include: 1) some increase of basal cell activity that extends for varying distances through the epithelium, 2) a zone of basal cells rather than a single layer as seen in normal squamous epithelium, 3) mitotic figures throughout the area involved, 4) associated loss of normal polarity of the cells⁸, 5) variations in staining properties with the development of hyperchromatism, and 6) the process may involve varying thicknesses of the epithelium.

Intraepithelial or in situ carcinoma of the uterine cervix includes the following microscopic changes:

1. Loss of normal cellular stratification of the full thickness of the epithelium.
2. Anaplasia.
3. Hyperchromasia.
4. Loss of normal polarity.
5. Mitotic figures through all areas of the surface involved.

6. Inflammatory reaction of the underlying stroma.
7. No break through of the basement membrane.
8. May involve the endocervical glands.
9. Sharp demarcation from normal epithelium that lies alongside.

Invasive carcinoma of the uterine cervix includes the following: 1) extension of anaplastic abnormal epithelium into the stroma of the cervix, 2) the endocervical glandular tissue is often involved, 3) ulceration and inflammation are hall marks of malignancy, 4) invasion of the stroma takes the form of buds of malignant surface epithelium that break through the underlying basement membrane and also larger columns and nests of malignant tissue.^{7,1,4}

Pathology reports of subsequent hysterectomy specimens were then reviewed to determine the remaining pathology in the uterine specimen after the cold knife conization biopsy.

Results

One hundred thirty-one conization specimens were reviewed and of these 58 women subsequently had a hysterectomy after the diagnostic conization procedure. The diagnoses of the surgical specimens were divided into three groups. One group showed a more serious lesion in the uterus than in the cone. Another group showed the same lesion in the uterus as in the cone, and another group showed a less serious lesion in the uterus than in the cone (Table 1).

There was only one case where there was a more serious lesion in the subsequent hysterectomy specimen than in the cone (Table 2).

In 25 of the 58 cases, the cones showed the same pathologic diagnoses as the uterine specimens (Table 3).

In 32 of the 58 cases, there was a less serious lesion in the uterine specimens than there was in the diagnostic cones (Table 4).

The total of Table 5 exceeds the total number of cones because some of the cones had more than one diagnosis.

Discussion

The diagnostic cervical cone specimen and the hysterectomy specimen correlated well in 25 of the 58 cases of the series. The same lesion was found in both at pathological examination. In 32 of the 58 cases, a lesser lesion was found in the uterus after hysterectomy had been performed. Both of these findings would indicate that there is a high degree of accuracy of diagnostic results with the cone biopsy if taken properly.

The finding of the lesser lesion in the uterus subsequent to conization would be explained by the fact that the diagnostic cone had removed the more serious lesion. Because most of the cervical carcinoma arises at the squamo-columnar junction, and a good diagnostic cone includes a

generous portion of the area, at least the major portion of a stage 0, early invasive carcinoma, or dysplasia may be removed at the time of the diagnostic cone. Then 57 patients in this series would have derived benefit from the diagnostic conization procedure.

In only one case of the 58 was there a more serious lesion in the uterine specimen than was found in the cone. A diagnosis of stage 0 carcinoma was made in the cone specimen and a diagnosis of early stage I carcinoma of the cervix was made in the hysterectomy specimen. This could mean that possibly inadequate treatment was rendered to this single patient by the performance of a simple hysterectomy on the basis of the diagnosis of stage 0 carcinoma of the cervix in the cone specimen. This would then indicate that 1 case in 58 cases of the series would not benefit from the results of diagnostic conization.

The problem of diagnosis of early stromal invasion is sometimes difficult. Areas of invasion may be present in or beneath an area of histological and clinical leukoplakia. Sometimes there is marked variation in both the horizontal and vertical planes in the tissue sections of the hyperplastic epithelium overlying the focus of invasion. One study revealed that in a series of 60 patients with diagnosis of borderline invasion or early stromal invasion, 20 of the 60 on further semi-serial sections showed definite stromal invasion.³

Then 57 of the cases of this study showed good correlation of cone and uterine specimens as related to the same lesions or lesser lesions in the uterine than in the cone specimen. These patients would have "benefited" from the cone procedure. To think of beneficial results one must realize an important concept that intraepithelial carcinoma of the cervix may follow dysplasia of the uterine cervix. Also the concept must be borne in mind that in situ carcinoma of the cervix does develop into invasive carcinoma of the cervix.

Peterson⁷ followed a group of 127 patients with carcinoma in situ of the cervix which were not treated and found that after one year 4% had developed invasion and by five years, 22% had invasive carcinoma. Hall⁷ revealed that 16% of the cases of carcinoma in situ which he followed developed invasion. From this it is seen that the diagnosis of dysplasia and carcinoma in situ must be made to prevent the development of invasive cervical carcinoma.

One patient would not have benefited from the cone procedure as a more serious lesion was found in the uterine specimen after conization. From the above, the cervical cold knife cone does appear to be an adequate method of diagnosis of cervical carcinoma.

Twenty-three of the 58 cases of the series had residual carcinoma in the uterine specimens after the diagnostic conization. Seventeen of the cases had residual stage 0

carcinoma of the uterus or 10%. Five of the cases had residual dysplasia of the uterine specimen or 9%.

Then 39% of the cases would have had residual carcinoma in the uterus after diagnostic conization which would indicate that the diagnostic cone as practiced in this study is not a good method of definitive therapy of carcinoma of the uterine cervix.

The comparison of this study with the Ferguson² study of diagnostic cervical conization yields the following results:

	Present Study	
	Ferguson Study	Present Study
Number of cone specimens	235	131
Subsequent hysterectomies	118	58
More serious lesion in uterus than in cone	8	1
Same lesion in uterus as in cone	28	25
Less serious lesion in uterus than in cone	82	32

The present study then compares favorably with the Ferguson study in that the trend in each of the specified categories of comparison of the cone specimens is in the same direction.

The following are factors which may cause errors in interpretation of carcinoma in situ of the cervix:

1. Surgical Errors

Removal of the entire lesion by the initial cone biopsy. Therefore, residual carcinoma may not be demonstrated by clinical, cytologic, or histologic means.

2. Technical Errors

Cellular distortion may result from improper staining technique and tangential sectioning and even give the false impression of stromal invasion. If there is any doubt about technique, the tissue should, of course, be reblocked, resectioned, and restained.

3. Inadequate tissue.

There may be insufficient tissue for the pathologist to fairly make a diagnosis even though pre-invasive or invasive carcinoma may be suspected. Additional tissue should be obtained. If the diagnosis is made on inadequate tissue, it may mean that the biopsy was taken from the periphery of an advanced carcinoma or that invasive carcinoma may be present elsewhere in the cervix.

4.

By far the majority of errors in histologic diagnosis

are incident to incorrect differentiation between benign atypical, intraepithelial or invasive carcinoma or those mentioned below.

- a. associated inflammatory reactions.
- b. pregnancy with its hyperhormonal state may produce cellular changes which may mimic carcinoma in situ.
- c. postmenopausal cervix.
- d. Trichomonas infections.

Summary

Cancer of the uterine cervix is a killing disease if undetected and untreated. Methods are now at hand, however, which can lead to early detection and cure of this disease if only these methods were put into practice. The cytologic method of Papanicolaou has led to early suspicion of possible cervical cancer. More definitive tissue diagnosis is needed, however, than that furnished by the cytological technique. Adequate tissue is needed for good tissue histologic diagnosis before treatment is to be instituted.¹⁰

The cold knife cervical cone has been proposed as a method of adequate tissue biopsy of the uterine cervix. An adequate tissue biopsy must include a generous amount of tissue on either side of the squamo-columnar junction of the cervix because the site of origin of most cases of squamous carcinoma in situ is in this area.¹¹

Essentially two questions are to be answered:

1. Is the cervical cone an adequate method of diagnosis of cervical carcinoma?
2. Is the cervical cone adequate as method of therapy of carcinoma of the cervix?

The cases in this study included 58 patients of the University of Nebraska College of Medicine in a period from 1958 to 1963. Each had a conization biopsy of the cervix. The subsequent hysterectomy specimens were then compared with the conization specimens as to pathologic diagnoses. They were compared to: 1) a more serious lesion in the uterus than in the cone, 2) same lesion in the uterus as in the cone, and 3) less serious lesion in the uterus than in the cone.

Dysplasia of the uterine cervix is a term applied to all disturbances of differentiation of the cervical squamous epithelial lining that can not be classified as either in situ or invasive carcinoma. In situ carcinoma includes cancerous cellular changes that do not invade the basement membrane but may involve the cervical glands. Invasive carcinoma has invaded through the basement membrane.

One case exhibited a more serious lesion in the uterus than in the cone. Twenty-five cases showed the same lesion in the uterus as in the cone and 32 showed a less serious lesion in the uterus than in the cone. The findings of the cone

biopsies then correlated well with the subsequent hysterectomy specimens except for one case. The finding of a less serious lesion in the uterus than the cone could be the results of removal of the more serious lesion by the cone biopsy. Adequate treatment at the present time could have been instituted in all cases except one.

Twenty-three of the 58 uterine specimens exhibited residual carcinoma. This included both stage 0 and stage I carcinoma. Therefore, the cone biopsy as practiced in this study would not be an adequate form of therapy for carcinoma of the uterine cervix.

This present study does compare favorably with the Ferguson² study of diagnostic cervical conizations.

Conclusions

1. Invasive carcinoma of the cervix should, to a certain degree, be classified as a preventable disease; but if left undiagnosed and untreated incurs a high mortality rate.
2. Methods are at hand which enable early diagnosis and treatment of carcinoma of the cervix.
3. Adequate cervical tissue is needed at the squamo-columnar junction before accurate diagnosis is possible.
4. Cold knife cervical conization is a rewarding method of diagnosis of cervical carcinoma.
5. Cold knife cervical conization is not an adequate method of treatment of cervical carcinoma.
6. Several pit falls are present in the diagnosis of in situ carcinoma of the cervix.
7. Cervical dysplasia is a premalignant lesion of the cervix.
8. In situ carcinoma of the cervix does lead to invasive carcinoma of the cervix.
9. This present study does compare favorably with the Ferguson study of diagnostic cervical conization.

Table 1. Comparison of Diagnosis of Conization and
Hysterectomy Specimens

Diagnosis	Number of Cases
More serious lesion in uterus than in cone.	1
Same lesion in uterus as in the cone.	25
Less serious lesion in uterus than in the cone	32
Total	58

Table 2. More Serious Lesion in the Uterus Than in
the Cone as Demonstrated by Biopsy.

Cone Biopsy	Uterus	Number of Cases
Stage 0 carcinoma	Early stage I carcinoma	1
Total		1

Table 3. Same Lesion in the Uterus as in the Cone
As Shown by Biopsy

Cone Biopsy	Uterus	Number of Cases
Stage 0 carcinoma	Stage 0 carcinoma	15
Invasive carcinoma	Invasive carcinoma	5
Dysplasia	Dysplasia	1
Chronic cervicitis	Chronic cervicitis	4
Total		25

Table 4. A Less Serious Lesion in the Uterus
Than in the Cone Biopsy

Cone Biopsy	Uterus	Number of Cases
Stage 0 carcinoma	No residual carcinoma	18
Stage 0 carcinoma	Chronic cervicitis with dysplasia	2
Stage 0 carcinoma	Chronic cervicitis	2
Dysplasia	No dysplasia	6
Stage I carcinoma	No residual carcinoma	1
Stage I carcinoma	Stage 0 carcinoma	3
Total		32

Table 5. Overall Diagnoses of Cone Biopsies

Cone Biopsy	Number of Cases
Chronic cervicitis	47
Dysplasia	50
Stage 0 carcinoma	41
Invasive carcinoma	16
Total	154

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