

## CONE BIOPSY OF THE CERVIX

A Review of 486 Cases

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A SUMMARY of the experience with 486 diagnostic conizations of the cervix on one hospital service will be presented. The value of these conizations of the cervix will be measured by making comparisons with the punch biopsies and the hysterectomy specimens, when available, in the same patients. The price paid in complications and disabilities for these conizations will have to be considered.

Physicians practising without the benefit of vaginal cytology recognize little or no need for diagnostic conization of the cervix. When one has responsibility for a growing number of patients who have had cytological examinations, he finds he has an increasing number of patients who have a positive cancer smear that is difficult to explain. These puzzling patients may have no lesion, no symptoms suggestive of cancer, and the punch biopsy specimen cannot be considered cancer. It is recognized that possibly only by examination of the entire uterus and the cervix can the exact diagnosis be determined. Because a hysterectomy may be undesirable, or may, as in the presence of invasive carcinoma, be inadequate treatment, hysterectomy is not an accepted method of solving the diagnostic problem. A large specimen of the cervix and a curettage of the remaining cervical-uterine cavity will usually disclose the cause of the positive smear. Conization of the cervix is one method of obtaining the large specimen that is necessary for a true diagnosis.

At the University of Miami-Jackson Memorial Hospital we have had a yearly rise in the number of cytological examinations, reaching 13,000 such examinations in 1960. For over four years we have been obtaining cytological examinations

on all of our obstetric and gynaecological patients, both in-patients and out-patients. With this load has come the increased need to obtain cone specimens in order to explain the increasing number of puzzling positive cytologic reports (Fig. 1). The experience reported here is heavily

EFFECT EXPANDING CYTOLOGY PROGRAM

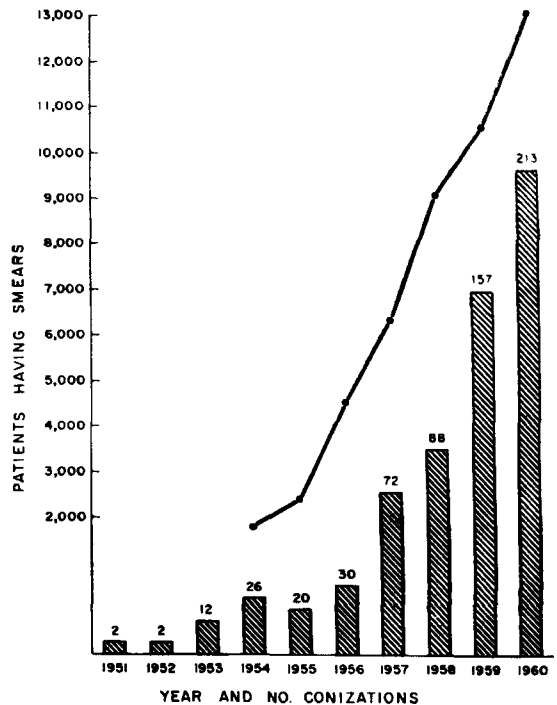


FIG. 1

Effect of expanding cytology programme on number of conizations.

weighted with patients who have neoplasia in its earliest phases. They became the subjects of this study usually because they had a positive cancer smear and the cause of the positive smear could not be determined confidently unless a specimen as large as a cervical cone was examined.

MATERIAL AND METHODS

The 486 women in this study were staff patients at the Jackson Memorial Hospital, a county hospital caring for both staff and private patients. The period covered begins in 1951 and ends 30th June, 1960. At the time of this writing, over 700 conizations have been performed but operations since 30th June, 1960, have been excluded because of the short period of follow-up. All of the patients were in the care of the Department of Obstetrics-Gynecology and were not pregnant; the pregnant patients have been reported elsewhere (Ferguson and Brown, 1960) and continue to be studied as a separate group. The staff patients in this hospital have a concentration of many of the epidemiological factors associated with a high cervical carcinoma rate. They are usually from a low socio-economic group. About 65 per cent are Negroes. They tend to have several pregnancies early in the reproductive years. Characteristically, they are dilatory in seeking medical attention.

Our principal indications for diagnostic conization of the cervix have been: (1) the unexplained positive cancer smear (Papanicolaou Class III, IV or V). We have learned that a positive cancer smear demands a thorough search for invasive carcinoma. A specimen smaller than the conization specimen is not acceptable unless that small specimen did show invasive carcinoma; and (2) a punch biopsy diagnosis of the cervix revealing intra-epithelial carcinoma. Here conization has to be done to be certain that beyond the reach of the punch biopsy there does not exist an area of invasive carcinoma (Schulman, 1959; Ferguson and Demick, 1960).

TECHNIQUE

The excision of a cervical cone specimen ends with a fractional curettage of any endocervical canal that remains and of the uterine cavity. We have tried a number of variations in the opera-

tion, but the operation remains essentially as described earlier (Offen and Ferguson, 1960). Surgicel,\* an oxidized regenerated cellulose, as a light packing in the cervical defect has been a useful addition to the operation. Pitressin has been added to the list of the different haemostatic agents we have used to infiltrate the cervix.

Cone specimen measurements vary according to the size of the cervix, but the average specimen is 3-4 cm. wide at the ectocervix and contains 3 cm. of the endocervical canal; it includes all visible lesions and Schiller-positive areas. A minimum of 12 tissue blocks are made from each specimen and step sections are made from each block. If further treatment is not needed, the patient is usually discharged 24 to 48 hours after the operation.

RESULTS

Our figures on the effectiveness of conization in the diagnosis of cervical disease are remarkably similar to the figures given in our earlier publications dealing with fewer cases. We will describe our results by answering four important questions that are frequently asked about this operation.

1. *Is the Cone Biopsy more Accurate than a Punch Biopsy?*

We believe that our figures emphatically illustrate that the cone biopsy is more accurate than a punch biopsy.

TABLE I  
*Effect of Punch Biopsy on Principal Disease in the Cone Specimen. 345 Cases*

Punch biopsy removed lesion .. ..	51 (15%)
Punch biopsy partially removed lesion .. ..	184 (53%)
Punch biopsy missed principal lesion .. ..	110 (32%)

Table I is an analysis of the 345 of our 486 patients from whom both punch and cone biopsy specimens were taken within a short interval. There are three possible effects the punch biopsy can have on the principal neoplastic disease in the tissue destined to be a cone specimen: (1) the punch biopsy can completely

\* Surgicel, Johnson & Johnson, New Brunswick, New Jersey.

TABLE II  
110 Cases in which the Punch Biopsy Missed the Principal Lesion

	Cone Dysplasia	Cone Intra- epithelial Carcinoma	Cone Invasion
Punch: cervicitis ..	30	30	5
Punch: dysplasia ..	—	17	5
Punch: intraepithelial carcinoma ..	—	—	23

excise the microscopic lesion; (2) it can partially remove that lesion; or (3) it can completely miss the most serious disease that will be found in the cone specimen.

Our greatest concern are cases in which the punch biopsy specimen failed to reveal the most serious disease in the cervix. This happened in 110 (one-third) of the 345 cases. Table II shows that the punch biopsy missed intra-epithelial carcinoma in 47 cases and invasive carcinoma in 33 cases. Some of these 80 patients—23 per cent of all the 345 patients with both punch and cone biopsies—might have suffered grave consequences had we relied solely on the punch biopsy.

Our punch biopsies are made with any one of the several conventional punch biopsy forceps. If a cervix appears normal, we take a specimen from each quarter. If there is a lesion, samples of the lesion are excised. Iodine staining of the cervix sometimes indicates target areas for the punch biopsy.

We perform punch biopsies for several reasons: (1) a lesion was observed when the patient was first seen; (2) the patient had a record of a positive smear but no tissue had been obtained; and (3) to make comparisons with the cone specimen.

## II. Does the Cone Biopsy Alter the Management of the Patient?

Because of the different diagnoses that the cone will sometimes yield compared to the diagnoses obtained by punch biopsy, conization frequently does result in different management of the patient. This will be true as long as the treatment of invasive carcinoma, cervicitis, dysplasia and intra-epithelial carcinoma are so different.

We can consider, with the aid of Table II, what would have happened with 33 patients with invasive carcinoma who without conization would not have had the full extent of their carcinoma recognized. Five women would have been thought to have cervicitis and five dysplasia. Twenty-three women would have been considered to have only intra-epithelial carcinoma and would then probably have had an inadequate simple hysterectomy or perhaps they would have elected simply to be observed for a while, thereby losing valuable time.

A history of a conization does not alter our treatment of invasive carcinoma. We have proceeded with radical hysterectomy or radiotherapy, as we would have if no conization had been necessary for the diagnosis.

## III. How Effective is the Cone Biopsy as a Therapeutic Measure?

This question will have to be given a tentative answer until we have had more time to follow the women who have elected to have no further surgery after conization. At this writing, we are observing 88 such women who have had intra-epithelial carcinoma of the cervix and 104 women who had only dysplasia. These patients are being encouraged to have periodical cytological examinations and, when indicated, punch biopsies.

The above question can be partially answered by a study of the 163 hysterectomy specimens from our patients with intra-epithelial carcinoma of the cervix who have had a previous conization and who have had a diagnosis of intra-epithelial carcinoma made by the punch biopsy or the cone biopsy or both (Table III). The hyster-

TABLE III  
Effectiveness of a Cone Biopsy as a Therapeutic Measure. One Hundred and Sixty-three Cases with Intra-epithelial Carcinoma on Punch Biopsy or Cone Biopsy or Both; Study of Subsequent Hysterectomy Specimen

Diagnosis in Uterus					
Cervicitis .. .. .	..	..	..	..	96
Dysplasia .. .. .	..	..	..	..	18
Intra-epithelial carcinoma .. .. .	..	..	..	..	46
Invasive carcinoma .. .. .	..	..	..	..	3
					30%
Total .. .. .	..	..	..	..	163

ectomy specimen showed 49 (30 per cent) of the patients had residual carcinoma. Conization as a therapeutic measure might be considered successful in only 70 per cent of our cases—not a very comforting figure.

We are studying the ability of repeated cytological studies and biopsies to detect residual neoplastic disease in the women who have had a conization but have not had a hysterectomy. We are not prepared at this time to describe the accuracy of a careful follow-up in such patients.

Comparisons of our operation with those done by others indicate that this 30 per cent residual carcinoma is not the result of our having excised a small cone specimen. Our cones are as large as anyone's. This residual carcinoma is a short-coming of the operation and one reason for this difficulty is the multicentric origin of some carcinomas which make it inevitable that some lesions will be beyond the reach of this particular excision of tissue.

The number of sections made of the cervix that remains in the hysterectomy specimen will, of course, influence the percentage of cases in which a residual tumour will be found. The investigation of our hysterectomy specimens is representative of that generally being done.

In an attempt to predict which patients might have residual tumour after conization, Schulman and Cavanagh (1961), in this department, carefully studied the margins of the cone specimens of 100 of our patients who subsequently had a hysterectomy. They found that by such a method it could not be reliably predicted which patients would have residual carcinoma. In 35 of these cases it was incorrectly predicted that intra-epithelial carcinoma would not be found in the hysterectomy specimen.

We conclude that conization is primarily of value as a diagnostic procedure and that as a therapeutic measure it is risky.

#### IV. *Is Conization a Dangerous Operation?*

The risk involved in a conization operation will have to be described in terms of morbidity, haemorrhage, cervical stenosis, effect on fertility, accidents of the operation and mortality.

*Morbidity.* Our hospital records of the conization patients are inadequate for a true evaluation of morbidity because so many patients remained in the hospital only one to three days after the

operation; post-operative temperature elevations after discharge from the hospital could have been unrecognized or unreported to us. The records of the first 287 patients who had a conization were inspected. (This number happened to be within a time interval and were not selected cases.) So few (12) hospital courses were morbid (temperature to 100·4° F. one or more times) that further investigations seemed unnecessary. Studies in progress in the department on the effect of conization on a subsequent hysterectomy have afforded a continuing opportunity to suggest that conization produces little morbidity—or adds but little morbidity to the hysterectomy.

*Haemorrhage.* The amount of bleeding, immediate or delayed, from the conization operation has concerned many gynaecologists. Our technique of doing the conization has apparently prevented excessive bleeding from being a frequent complication. We believe that our technique of infiltration of the cervix with a haemostatic solution and the avoidance of heavy cauterization of the conical defect in the cervix have contributed to the practical elimination of haemorrhage as a major complication.

*Operative Blood Loss.* The amount of blood loss is estimated, not measured. Only 20 of the 486 conizations had estimated operative blood losses of more than 100 ml.; most of these occurred in the earlier years before present-day improvements in the operative technique and this amount of blood loss has been rare since 1958. The highest estimated loss was 800 ml. The average loss was 25–50 ml. No conization patient required hysterectomy because of haemorrhage.

*Immediate Post-operative Period.* Five patients bled enough during the post-conization hospital stay to demand vigorous attention. Only one of the five had to be taken back to the operating room for cervical suturing. The other four were easily handled in the treatment room by packing the cervix.

*Delayed Bleeding.* After discharge from the hospital, 19 of the 486 patients returned to the Emergency Room or the Out-patient Clinic because of vaginal bleeding. Ten of these 19 did not require hospitalization and the bleeding was controlled with packing or cauterization of the cervix. Nine of these patients did have

to be re-admitted to the hospital because of difficulty in controlling the bleeding or because of anaemia resulting from haemorrhage. They required various treatments such as transfusions, cauterization, tamponage and suturing.

*Accidents at Conization.* Perforation of the uterus during the dilatation of the internal cervical os and the curettage was a much more frequent accident during the conization operation than in the usual dilatation and curettage which is done without a preceding conization. The perforations did not create any serious problems, either immediate or delayed. The rectum was entered twice, but the defect was immediately repaired and no fistula resulted.

*Cervical Stenosis.* We are frequently asked if our conizations cause stenosis of the cervical canal. We define cervical stenosis as the inability to pass a standard uterine sound through the entire cervical canal and into the uterine cavity. Our knowledge of cervical stenosis in our patients is incomplete because some patients failed to return to clinic after their operation. And, our record of cervical stenosis is distorted by the tendency of examiners not to record the sounding of the cervical canal, particularly when there is no obstruction.

By our definition, 17 patients had cervical stenosis after conization. Two of these patients had such severe stenosis that their problem could only be resolved by hysterectomy. The cervixes of the remaining 15 patients were dilated successfully in the clinic.

We recommend that each patient, who has had a conization, have her cervical canal tested frequently with a sound and the canal dilated if there is a tendency to stenosis. We believe this will prevent stenosis in most instances.

*Fertility.* Aside from stenosis, there has been expressed the fear that conization would affect fertility by removing endocervical glands or by some other mechanism. Our comment on pregnancy subsequent to conization will, of necessity, be incomplete. We are not able to correct our figures for the group's fertility potential, age, practice of contraception, length of observation, and other factors that would have to be considered. One hundred and sixty-three of our 486 patients cannot be considered because they have had a hysterectomy.

We have observed 41 pregnancies in these

conization patients. Abortion and premature delivery were no greater than we usually see in our staff patients. There was no case of incompetent cervical os. Two patients had dystocia and severe cervical lacerations presumed due to scarring of the cervix.

From the above comment on pregnancy after conization it seems reasonable to conclude that the operation has no extraordinary effect on the ability to become pregnant and to deliver.

*Deaths.* There have been two deaths following conization, but the deaths were not specifically related to the type of operation. One patient received an inappropriate mixture of nitrous oxide and oxygen. When the error was discovered, the patient had been anoxic for a prolonged period of time. She expired 18 hours after the operation. The second death was a psychotic patient who had been taking large doses of steroids for years without medical supervision. Five days after conization she had an acute asthmatic attack, developed a fulminating pneumonia, and expired suddenly. Autopsy revealed chronic lung disease, bronchopneumonia and a marked atrophy of the adrenals.

In summary, diagnostic conization involves only a moderate number of complications. At present, the knowledge gained by the operation and the advantages of greater accuracy in diagnosis of cervical disease far outweigh its disadvantages.

#### PATIENTS WITH TWO CONIZATIONS

In the period of time of this report, we have had an interesting group of 24 patients who have had two diagnostic conizations. Because there is very little information in the literature on patients who have had a conization more than once, these patients merit a description. Most of them are patients who had their first diagnostic conization with no diagnosis worse than intra-epithelial carcinoma of the cervix found on the punch or cone biopsy specimens. The patients did not wish a hysterectomy. Subsequent periodical cytological examinations produced positive smears suggesting that neoplastic tissue still existed. During this period of observation, some also had punch biopsies. This persistence of positive smears left us in the



TABLE IV  
*Comparison of the Diagnosis of 24 Patients who had Two Conizations of the Cervix*

	2nd Cone Cervicitis	2nd Cone Dysplasia	2nd Cone Intra-epithelial Carcinoma	2nd Cone Invasion
1st cone cervicitis .. .. .	4	2	2	1
1st cone dysplasia .. .. .	4	2	3	1
1st cone intra-epithelial carcinoma ..	1	2	1	1

same position as we were before the first conization in that we wished to have an accurate diagnosis before we decided on definitive treatment—for a safe diagnosis we needed a large specimen, and conization is one way to accomplish this.

A comparison of the diagnosis of the two cone specimens is made in Table IV. Three new cases of invasive carcinoma were found in patients whose intervals of time between the two conizations were four, six and nine months. Five new cases of intra-epithelial carcinoma of the cervix were discovered by the second conization. It may be tempting to conclude that the new cases represented progression of neoplastic disease, but this seems much less likely in that the first cone specimen simply did not include the more serious lesion eventually found. This experience seems consistent with that reported in Table III where we can see that among 163 patients who had the diagnosis of intra-epithelial carcinoma and a conization, there were 49 patients who had some class of carcinoma in a subsequent hysterectomy specimen.

In all patients scheduled for a second conization operation a choice between the conization and hysterectomy certainly existed. Some decisions were made by the patients who agreed to a second conization operation but would not agree to a hysterectomy. We have felt that if the interval of time is short between the first conization and the realization that neoplastic disease still existed, then we could proceed with a hysterectomy. With a longer time interval we have to consider that the residual neoplastic disease may have progressed to invasive carcinoma and the ordinary hysterectomy is not the indicated treatment. As was the situation before the first conization, and explained more fully

in other publications from the department (Ferguson and Cavanagh, 1959), the degree of positiveness of the cancer smear and the punch biopsy diagnosis were not dependable guides as to which of the two different operations was indicated.

As was true with the first conization, the second conization has the potentiality of completely removing the neoplasm.

It should be realized that this problem of the second conization is similar to the first conization in that without frequent cytological testing there are no such problems. Without a large number of cancer smears there are few recognized needs for the first diagnostic conization. If we did not do repeated cytological studies on the patient who had had a conization, we would not have realized that we had a problem on our hands.

DISCUSSION

We have, during these years of increasing number of conization operations, always felt that the financial cost and the complications of the operation were worth the rewards of having accurate diagnosis. Without conization, we would not be able to explain many instances of exfoliation of cancer cells. We presume that the continued exfoliation of such cells from the asymptomatic, normal cervix will usually end with the appearance of a lesion. This lesion that finally appears may no longer be a pre-invasive one.

The conization operation, like punch biopsy or any other excision of cervical tissue, is destroying our ability to study the progression of dysplasia to intra-epithelial carcinoma and to invasive carcinoma. When part of the cervix has been removed we cannot yet accurately decide what type of tissue remains in the cervix

that has not been removed. The only alternative to cone biopsy, in the presence of a positive cancer smear that cannot be explained, is hysterectomy; and hysterectomy is not now accepted on such an indication.

#### SUMMARY

An experience with 486 diagnostic conizations of the cervix was made by comparing punch, cone and hysterectomy specimens. The conization was usually done because of an unexplained positive cancer smear or a punch biopsy diagnosis of intra-epithelial carcinoma of the cervix. The cone biopsy was considerably more reliable than the punch biopsy; in one-third of the women who had both biopsies, the diagnosis was worse on the cone specimen than it was on the punch specimen. Without the cone biopsy, the treatment of many women would have been inadequate. Conization as a treatment for intra-epithelial carcinoma of the cervix is hazardous,

as evidenced by the 30 per cent incidence of intra-epithelial carcinoma in the uterine specimen among the women who subsequently had a hysterectomy.

The rewards of greater accuracy of diagnosis afforded by conization far outweighed the complications of the operation.

Twenty-four patients needed a second conization because of the unacceptability of a hysterectomy as an immediate solution to the problem raised by recurrence of a positive cancer smear.

#### REFERENCES

- Ferguson, J. H., and Brown, G. C. (1960): *Surg. Gynec. Obstet.*, **111**, 603.  
 Ferguson, J. H., and Cavanagh, D. (1959): *Amer. J. Obstet. Gynec.*, **77**, 838.  
 Ferguson, J. H., and Demick, P. (1960): *New Engl. J. Med.*, **262**, 13.  
 Offen, J. A., and Ferguson, J. H. (1960): *Obstet. and Gynec.*, **15**, 396.  
 Schulman, H. (1959): *Bull. Univ. Miami Sch. Med.*, **13**, 7.  
 Schulman, H., and Cavanagh, D. (1961): *Cancer (Philad.)*, **14**, 795.