

## CYTOPATHOLOGICAL FINDINGS ON VAGINAL PAPANICOLAOU SMEARS AFTER HYSTERECTOMY FOR BENIGN GYNECOLOGIC DISEASE

KATHERINE F. PEARCE, M.D., HOPE K. HAEFNER, M.D., SYEDA F. SARWAR, M.D., AND THOMAS E. NOLAN, M.D.

**ABSTRACT**

**Background** Periodic, routine Papanicolaou smears of cells from the vagina are commonly examined in women who have undergone a hysterectomy for benign gynecologic disease. The benefits of this method of screening are not known.

**Methods** We analyzed Papanicolaou smears obtained from the vaginal apex (cuff) in 6265 women at Charity Hospital in New Orleans between January 1, 1992, and December 31, 1994. Of the 10,595 vaginal smears, an estimated 9610 were obtained during follow-up examinations of 5682 women who had undergone hysterectomy for benign gynecologic disease.

**Results** Among these 9610 vaginal smears, 104, from 79 women, were abnormal. The abnormal smears were categorized according to the findings, as follows: atypical squamous cells of undetermined significance, 52 (0.5 percent of all smears); low-grade squamous intraepithelial lesion, 44 (0.5 percent); high-grade squamous intraepithelial lesion, 6 (0.1 percent); and squamous-cell carcinoma, 2 (0.02 percent). In five women, biopsies revealed vaginal intraepithelial neoplasia type I or II; there were no biopsy-proved cases of vaginal cancer. The probability of an abnormal Papanicolaou smear in this group of women was 1.1 percent, and the positive predictive value of the Papanicolaou test for detecting vaginal cancer was 0 percent (95 percent confidence interval, 0 to 33 percent).

**Conclusions** The prevalence of abnormal findings on cytopathological examination of vaginal Papanicolaou smears after hysterectomy for benign gynecologic disease is extremely low. (N Engl J Med 1996;335:1559-62.)

©1996, Massachusetts Medical Society.

**P** RIMARY invasive carcinoma of the vagina is a rare gynecologic cancer, accounting for between 1 and 4 percent of primary malignant tumors of the genital tract in women.<sup>1-4</sup> Vaginal carcinoma in situ (vaginal intraepithelial neoplasia type III), which may be a precursor of invasive vaginal carcinoma,<sup>1,5,6</sup> is even less common.<sup>6-9</sup> Dysplasia or carcinoma of the cervix is the most common predisposing factor for the development of both vaginal carcinoma in situ and invasive vaginal carcinoma,<sup>1,3,7,10-12</sup> and both are very rare in women with no history of cervical disease.<sup>1,5,7,8</sup> Risk factors for vaginal dysplasia or carcinoma after hysterectomy for benign gynecologic disease may include older

age,<sup>2</sup> a relatively high number of sexual partners,<sup>11</sup> low socioeconomic status,<sup>11</sup> human papillomavirus infection,<sup>11</sup> and immunosuppression.<sup>13</sup>

The Papanicolaou smear has been widely used to screen for carcinoma of the cervix for over 40 years. Despite the lack of any randomized, controlled clinical trial to prove its efficacy, such screening has become common medical practice, and the morbidity and mortality associated with cervical carcinoma may have decreased as a result.<sup>14-16</sup> Since preinvasive and invasive vaginal lesions are thought to follow a clinical course similar to that of cervical lesions, many physicians believe that routine Papanicolaou smears are indicated after total hysterectomy.<sup>1,17</sup> Evidence to support this practice comes from several case series in which vaginal carcinomas developed after hysterectomy,<sup>1-3,18-20</sup> but because of the study design the risk could not be assessed.<sup>21</sup>

The American Cancer Society<sup>22</sup> and the American College of Obstetricians and Gynecologists<sup>23</sup> endorse routine screening with the Papanicolaou smear after hysterectomy, but the benefit of such routine testing in women who have undergone hysterectomy is unknown. We conducted a large, retrospective study of a population of predominantly inner-city women to determine the prevalence of abnormal vaginal Papanicolaou smears and the clinical importance of abnormal cytopathological findings.

**METHODS**

We reviewed the results of all Papanicolaou smears of cells from the vaginal apex (cuff) in women who had undergone hysterectomy. The information was obtained from the computer data base of Charity Hospital in New Orleans and covered the period from January 1, 1992, through December 31, 1994. To estimate the percentage of women who had undergone hysterectomy for benign gynecologic disease, we randomly selected 150 women who had normal vaginal Papanicolaou smears and conducted a limited review of their charts. We hypothesized that the percentage of these women in whom hysterectomy had been performed for benign gynecologic disease was similar to the rate in the hospital's patient population; we confirmed this assumption by examining the pathology reports for 802 consecutive hysterectomies performed between January 1992 and January 1994.

We then identified all abnormal Papanicolaou smears of cells

From the Departments of Obstetrics and Gynecology (K.F.P., T.E.N.), Internal Medicine (T.E.N.), and Pathology (S.F.S.), Louisiana State University Medical Center, New Orleans, and the Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor (H.K.H.). Address reprint requests to Dr. Pearce at the Department of General Internal Medicine, Bowman Gray School of Medicine, Medical Center Blvd., Winston-Salem, NC 27157-1051.

obtained from the vaginal cuff and reviewed the women's medical records to ascertain the results of biopsies of the vaginal cuff and of any other diagnostic tests or therapeutic procedures. Any woman with a history of cervical, vaginal, ovarian, fallopian-tube, or uterine carcinoma or cervical intraepithelial neoplasia type III (cervical carcinoma in situ) was excluded from the study. Women were also excluded if their vaginal Papanicolaou-smear slides were unavailable for review. All abnormal Papanicolaou smears and 1 percent of the normal slides were reviewed by two independent pathologists who were unaware of any prior readings. The slides were classified according to the Bethesda system.<sup>24</sup>

**RESULTS**

The characteristics of the study population are shown in Table 1. A total of 10,595 vaginal Papanicolaou smears were available from 6265 women, for an average of 1.7 smears per woman. Among the 150 women with normal vaginal-cuff smears whose records were reviewed, 97 (64.7 percent) had well-documented indications for hysterectomy. Benign gynecologic disease was the indication in the cases of 88 of the 97 women (90.7 percent), and gynecologic cancer was the indication for 9 women (9.3 percent). None of the 53 women whose medical records did not list the indication for hysterectomy had a history of gynecologic cancer. The percentage of women who were found to have benign gynecologic disease documented in the medical-records review was similar to that determined by the review of pathology reports; of 802 consecutive hysterectomies, 722 (90.0 percent) were performed for benign gynecologic disease.

Therefore, we estimate that approximately 9610 of the 10,595 Papanicolaou smears of the vaginal cuff (90.7 percent) were obtained during follow-up of women with benign gynecologic disease. During the study period, 104 abnormal Papanicolaou smears of the vaginal cuff were obtained from 79 women who had undergone hysterectomy for benign disease. The vaginal cytologic findings in these women, categorized according to the Bethesda system, are

**TABLE 1. CHARACTERISTICS OF THE STUDY POPULATION.**

	VALUE
No. of women	6,265
No. of Papanicolaou smears	10,595
Mean age — yr (range)	52 (19–89)
Race or ethnic group — %	
Black	83
White	9
Hispanic	5
Other	3
Lower socioeconomic status — %*	99

\*Lower socioeconomic status was defined as self-reported annual income at or below the federal poverty level.

**TABLE 2. FOLLOW-UP OF ABNORMAL PAPANICOLAOU SMEARS IN WOMEN WHO HAD UNDERGONE HYSTERECTOMY FOR BENIGN GYNECOLOGIC DISEASE.\***

FINDING	NO. OF SMEARS (%)	NO. OF WOMEN	NO. REFERRED FOR COLPOSCOPY	NO. WITH VAIN ON BIOPSY
Atypical squamous cells of undetermined significance	52 (0.5)	47	5	1
Low-grade squamous intraepithelial lesion	44 (0.5)	30	15	2
High-grade squamous intraepithelial lesion	6 (0.1)	6	6	3
Squamous-cell carcinoma	2 (<0.1)	1	1	1
Total	104 (1.1)	79†	27	5‡

\*The estimated total number of Papanicolaou smears in women with benign gynecologic disease was 9610. VAIN denotes vaginal intraepithelial neoplasia.

†Three women each had Papanicolaou smears classified as abnormal in two categories, and one had a smear classified as abnormal in three categories.

‡One woman had Papanicolaou smears classified as abnormal in three categories, so the abnormal biopsy results were from only five women.

shown in Table 2. The overall probability of an abnormal vaginal Papanicolaou test was approximately 1.1 percent.

The number of abnormal smears in each category, the number of women represented, and follow-up testing received are also shown in Table 2. One woman had three abnormal Papanicolaou tests during the study period (one characterized by atypical squamous cells of undetermined significance, one indicating a low-grade squamous intraepithelial lesion, and one indicating a high-grade squamous intraepithelial lesion). Her biopsy revealed vaginal intraepithelial neoplasia type I to II (mild-to-moderate dysplasia), and she eventually underwent laser ablation of the vaginal cuff. Three of the other 46 women in the group categorized as having atypical squamous cells of undetermined significance underwent biopsy; none had vaginal intraepithelial neoplasia (dysplasia).

Four of the women with evidence of a low-grade squamous intraepithelial lesion on vaginal cytologic study had normal colposcopic examinations, and no biopsy was performed. Five women had normal results on colposcopy with a random vaginal biopsy; none revealed dysplasia. Colposcopic findings consistent with condyloma were present in six women, including the woman with vaginal intraepithelial neoplasia type I to II. In this group, one additional woman underwent a biopsy that revealed vaginal intraepithelial neoplasia type I (mild dysplasia); she was treated with trichloroacetic acid. All the women who were treated subsequently had normal vaginal

**TABLE 3.** CLINICAL COURSE OF WOMEN WITH EVIDENCE OF HIGH-GRADE SQUAMOUS INTRAEPITHELIAL LESIONS ON CYTOLOGIC SCREENING OR DYSPLASIA ON BIOPSY.\*

PATIENT No.	CYTOLOGIC FINDING	RESULTS OF BIOPSY	TREATMENT	FINDINGS ON FOLLOW-UP
1	ASCUS, LSIL, HSIL	VAIN type I to II (mild-to-moderate dysplasia)	Laser ablation	Normal colposcopic examination and biopsy
2	HSIL	Refused biopsy	None	Normal cytologic findings
3	HSIL	Chronic inflammation	None	Normal cytologic findings
4	HSIL	Condyloma	None	Normal cytologic findings and colposcopic examination
5	HSIL	VAIN type I (mild focal dysplasia)	Excisional biopsy	Normal cytologic findings
6	HSIL	VAIN type I (mild focal dysplasia)	Laser ablation	Pending
7	SCCA	VAIN type II (moderate focal dysplasia)	Lost to follow-up	
8	LSIL	VAIN type I to II (mild-to-moderate dysplasia)	Trichloroacetic acid	Normal cytologic findings and colposcopic examination

\*ASCUS denotes atypical squamous cells of undetermined significance, LSIL low-grade squamous intraepithelial lesion, HSIL high-grade squamous intraepithelial lesion, VAIN vaginal intraepithelial neoplasia, and SCCA squamous-cell carcinoma.

smears and normal colposcopic examinations. The women who were not treated were followed with repeated colposcopic examinations or Papanicolaou tests until the results of examinations and tests returned to normal.

Six women had high-grade squamous intraepithelial lesions. All were referred for colposcopic examination. The biopsy results and clinical courses of these patients, as well as two other patients with dysplasia on biopsy, are summarized in Table 3.

Limited follow-up information was available for the woman whose smear was categorized as indicating squamous-cell carcinoma. Her biopsy revealed vaginal intraepithelial neoplasia type II (moderate focal dysplasia). No further treatment was documented, and she was lost to follow-up.

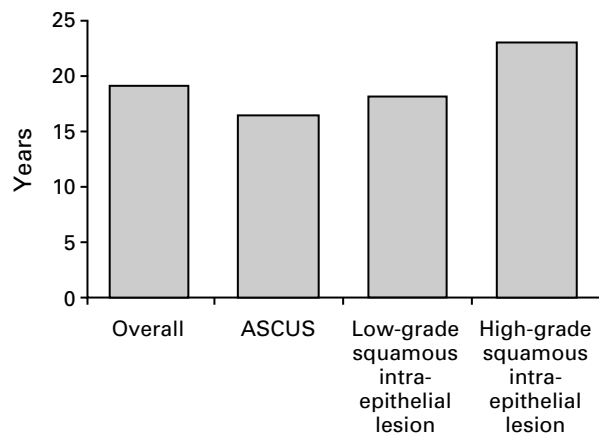
Of the 79 women with abnormal vaginal smears, only 5 had dysplasia on subsequent biopsy (Table 3), and there were no biopsy-proved cases of vaginal carcinoma. Therefore, the positive predictive value of the vaginal Papanicolaou smear for detecting vaginal cancer was 0 percent (95 percent confidence interval, 0 to 33.0 percent). The positive predictive value of the vaginal smear for detecting vaginal intraepithelial neoplasia type I, II, or III (dysplasia) was 6.3 percent (95 percent confidence interval, 3.1 to 18.0 percent).

Figure 1 shows the mean length of time from hysterectomy to an abnormal Papanicolaou smear for each category of abnormality, on the basis of information for 60 of the 79 women; the year of hysterectomy was not documented in the medical records of the remaining 19 women. The mean length of time to an abnormal Papanicolaou smear was 19 years, and there was no significant difference among the groups.

## DISCUSSION

Our data show an extremely low prevalence of abnormal cytopathological findings on routine screening with the vaginal Papanicolaou smear in women who have undergone hysterectomy for benign gynecologic disease. Since the women in the patient population served by the Charity Hospital are almost exclusively inner-city residents at increased risk for abnormal cervical or vaginal cytopathological findings,<sup>11,15</sup> our data probably represent an overestimate of the prevalence of abnormal cytopathological results in the general population.<sup>16</sup>

Five women in our study group had vaginal intra-



**Figure 1.** Mean Time from Hysterectomy to an Abnormal Papanicolaou Smear in 60 Women Who Had Undergone Hysterectomy for Benign Gynecologic Disease.

ASCUS denotes atypical squamous cells of undetermined significance.

epithelial neoplasia type I to II (dysplasia) on biopsy. This represents approximately 0.1 percent of the study population and 6.3 percent of women with abnormal cytologic results. It is clear from our study and others that abnormal cytologic findings on screening with vaginal smears are uncommon in this population; when an abnormal test result occurs, it is usually of little clinical importance.<sup>25,26</sup> Moreover, women who have not undergone hysterectomy are never tested routinely with vaginal Papanicolaou smears.

Cost effectiveness is an important aspect of all screening tests, and routine vaginal cytologic screening after hysterectomy for benign disease may not be cost effective. Because the prevalence of abnormal results is low, the cost per case identified through screening will be high.<sup>27</sup> In addition, the vaginal Papanicolaou smear has a high false positive rate, and each woman with a positive test (whether true positive or false positive) must undergo further evaluation.

Our study has some limitations. It is a one-time survey of the prevalence of disease in a high-risk population and is limited by the lack of long-term follow-up. Since we were able to review the medical records of only a limited sample of women with normal vaginal smears, we may have overestimated the number followed after hysterectomy for benign gynecologic disease. One could argue that women with a history of cancer of the genital tract are likely to be seen more frequently than other women and may, therefore, be overrepresented in our study population. Such an overrepresentation would lead to underestimation of the prevalence of dysplasia among women followed for benign disease. Even if our estimate is off by as much as 20 percent, however, one would still have to screen 1000 women to detect a single case of dysplasia, and many of the cases of dysplasia detected may resolve without treatment.

The data from our study are consistent with those of others, who have found the prevalence of vaginal dysplasia after hysterectomy for benign disease to be between 0.13 percent and 0.15 percent.<sup>25,26</sup> Therefore, because of the low prevalence of disease and the poor positive predictive value of the test, periodic routine screening by means of vaginal Papanicolaou smears is probably not necessary for women who have undergone hysterectomy for benign gynecologic disease. Until more data are available, routine vaginal Papanicolaou smears should be considered only for women with a history of cancer of the genital tract or cervical intraepithelial neoplasia type

III (carcinoma in situ) because of their increased risk for disease.<sup>5,7,18-20,25</sup>

*We are indebted to Suzanne M. Selvaggi, M.D., for her valuable advice during the preparation of the manuscript.*

## REFERENCES

1. Rutledge F. Cancer of the vagina. *Am J Obstet Gynecol* 1967;97:635-55.
2. Johnston GA Jr, Klotz J, Boutselis JG. Primary invasive carcinoma of the vagina. *Surg Gynecol Obstet* 1983;156:34-40.
3. Gallup DG, Talledo OE, Shah KJ, Hayes C. Invasive squamous cell carcinoma of the vagina: a 14-year study. *Obstet Gynecol* 1987;69:782-5.
4. Cramer DW, Cutler SJ. Incidence and histopathology of malignancies of the female genital organs in the United States. *Am J Obstet Gynecol* 1974;118:443-60.
5. Hummer WK, Mussey E, Decker DG, Dockerty MB. Carcinoma in situ of the vagina. *Am J Obstet Gynecol* 1970;108:1109-16.
6. Aho M, Vesterinen E, Meyer B, Puroola E, Paavonen J. Natural history of vaginal intraepithelial neoplasia. *Cancer* 1991;68:195-7.
7. Gallup DG, Morley GW. Carcinoma in situ of the vagina: a study and review. *Obstet Gynecol* 1975;46:334-40.
8. Oliver JA Jr. Severe dysplasia and carcinoma in situ of the vagina. *Am J Obstet Gynecol* 1979;134:133-7.
9. McIndoe WA, Green GH. Vaginal carcinoma in situ following hysterectomy. *Acta Cytol* 1969;13:158-62.
10. Schiffer MA, Mackles AM, Greene HJ. Carcinoma in situ of the vagina after hysterectomy. *Surg Gynecol Obstet* 1972;134:653-4.
11. Brinton LA, Nasca PC, Mallin K, et al. Case-control study of in situ and invasive carcinoma of the vagina. *Gynecol Oncol* 1990;38:49-54.
12. Funnell JD, Merrill JA. Recurrence after treatment of carcinoma in situ of the cervix. *Surg Gynecol Obstet* 1963;117:15-9.
13. Hankins CA, Lamont JA, Handley MA. Cervicovaginal screening in women with HIV infection: a need for increased vigilance? *Can Med Assoc J* 1994;150:681-6.
14. Dickinson L, Mussey ME, Kurland LT. Evaluation of the effectiveness of cytologic screening for cervical cancer. II. Survival parameters before and after inception of screening. *Mayo Clin Proc* 1972;47:545-9.
15. Christopherson WM, Lundin FE Jr, Mendez WM, Parker JE. Cervical cancer control: a study of morbidity and mortality trends over a twenty-one-year period. *Cancer* 1976;38:1357-66.
16. Christopherson WM, Parker JE. Control of cervix cancer in women of low income in a community. *Cancer* 1969;24:64-9.
17. Kvale KM, Remington PL, Lantz PM. Self-reporting of Papanicolaou smear tests among women after hysterectomy. *Wis Med J* 1994;93:275-6.
18. Bell J, Sevin BU, Averette H, Nadji M. Vaginal cancer after hysterectomy for benign disease: value of cytologic screening. *Obstet Gynecol* 1984;64:699-702.
19. Stuart GCE, Allen HH, Anderson RJ. Squamous cell carcinoma of the vagina following hysterectomy. *Am J Obstet Gynecol* 1981;139:311-5.
20. Jimerson GK, Merrill JA. Cancer and dysplasia of the post-hysterectomy vaginal cuff. *Gynecol Oncol* 1976;4:328-34.
21. Fetters MD, Fischer G, Reed BD. Effectiveness of vaginal Papanicolaou smear screening after total hysterectomy for benign disease. *JAMA* 1996;275:940-7.
22. Pap test. Atlanta: American Cancer Society, 1991.
23. Cervical cytology: evaluation and management of abnormalities. ACOG technical bulletin. No. 183. Washington, D.C.: American College of Obstetricians and Gynecologists, 1993.
24. Kurman RJ, Solomon D. The Bethesda System for reporting cervical/vaginal cytologic diagnoses. New York: Springer-Verlag, 1994.
25. Piscitelli JT, Bastian LA, Wilkes A, Simel DL. Cytologic screening after hysterectomy for benign disease. *Am J Obstet Gynecol* 1995;173:424-32.
26. Miller JM, Chambers DC, Miller JM. The need for Pap tests after hysterectomy for benign disease: results of a study of black patients. *Postgrad Med* 1987;82:200-2, 205.
27. Foltz AM, Kelsey JL. The annual Pap test: a dubious policy success. *Milbank Q* 1978;56:426-62.