Papanicolaou Smear Adequacy: The Cervical Cytobrush And Ayre Spatula Compared With The Extended-Tip Spatula

Michael L. Noel, M.D.

Abstract: Papanicolaou smears have false-negative rates of 6 percent to 56 percent that are due, in large part, to inadequate sampling of endocervical cells. A randomized, prospective trial was conducted comparing the adequacy of Papanicolaou smears obtained with the cytobrush and Ayre spatula with smears obtained with the extended-tip spatula, as measured by the presence of endocervical cells. One hundred of 111 Papanicolaou smears obtained with a cytobrush and Ayre spatula contained endocervical cells (90.1 percent), compared with 68 of 105 smears obtained with the extended-tip spatula (64.8 percent) ($\chi^2 = 18.6$, $P < 0.0001$). There were no other significant differences between the two study groups for age, gravidity, parity, and hormone usage. The combination of the cytobrush and Ayre spatula appears to be superior to other methods that are currently used to obtain Papanicolaou smears. (J Am Bd Fam Pract 1989; 2:156-60.)

A number of studies have reported high false-negative rates for detecting cervical cancer on Papanicolaou (Pap) smears, ranging from 6 percent to 56 percent.[1,2] Approximately two-thirds of these false-negative smears were due to inadequate sampling of the cervix, while one-third were due to laboratory error.[3,4] The primary cause of sampling error was failure to obtain cells from the squamocolumnar transition zone, where cervical cancer is known to develop.[5,6]

As the percentage of Pap smears containing endocervical cells increases, so does the detection rate for cervical intraepithelial neoplasia and carcinoma. In 1983, Elias, et al.[7] found that the rate of detection of dysplasia and carcinoma increased by more than 60 percent in smears with endocervical cells compared with smears without endocervical cells. They suggested that smears that do not contain endocervical cells should be repeated. These findings were confirmed by Vooijs, et al.[8] and Boon, et al.[9] Both reports agreed that endocervical cells are one of the best indicators that an adequate Pap smear has been obtained.

Seventy-five percent of early cervical cancers are found only above the external os in the endocervical canal.[6] The squamocolumnar transition zone migrates with age, moving up into the endocervical canal in menopausal women.[10] This migration of the squamocolumnar transition zone is one of the causes of the lower recovery rate of endocervical cells from such patients.[11-13] Therefore, the endocervical canal must be sampled in all instances.

Four percent of cervical cancers are found only outside the external os, on the ectocervix.[6] Because the location of the squamocolumnar transition zone cannot be detected by visual inspection alone, the ectocervix must also be sampled.[6,14] In 273 patients with known cervical neoplasia, Richart and Vaillant found that the false-negative rate for Pap smears decreased to 1 percent when both the endocervix and ectocervix were sampled, as opposed to false-negative rates of 12 percent and 20 percent, respectively, when each technique was used alone.[1] The Ayre spatula has been shown to obtain ectocervical cells better than an extended-tip spatula.[14]

The cervical cytobrush (Figure 1) was developed to improve cell recovery on Pap smears.[15] Compared with the combination of an Ayre spatula and cotton swab, the cytobrush improves en-

From the Department of Family Medicine, Baylor College of Medicine, Houston. Address reprint requests to Michael L. Noel, M.D., 5510 Greenbriar, Houston, TX 77005.

Funding for this study was provided by the Department of Family Medicine, Baylor College of Medicine, Houston. Materials for the study were supplied by International Cytobrush, Inc., P.O. Box 7733, Hollywood, FL 33081 and Milex Southern, Inc., 3410 Hidden Creek, Houston, TX 78478.

J Am Board Fam Pract: first published as 10.3122/jabfm.2.3.156 on 1 July 1989. Downloaded from http://www.jabfm.org/ on 8 May 2025 by guest. Protected by copyright.

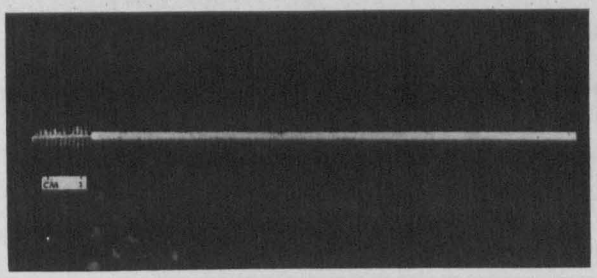

Figure 1. The cervical cytobrush.

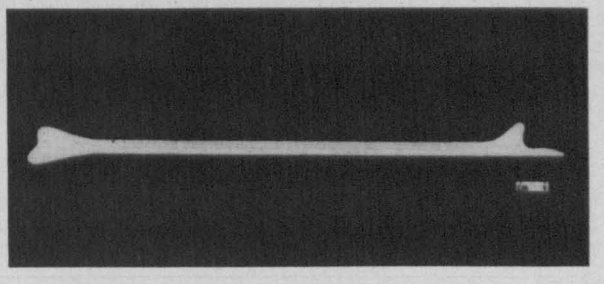

Figure 2. The extended-tip spatula.

docervical cell recovery, whether used alone[16] or in combination with the Ayre spatula.[17] Compared with the extended-tip spatula (Figure 2), used alone[9] or in combination with a cotton swab,[12,18] the combined cytobrush and extended-tip spatula also improves endocervical cell recovery.

Both the extended-tip spatula[11,19-21] alone and the combination of the cytobrush and Ayre spatula[17] have been shown to provide better endocervical cell recovery than the combination of an Ayre spatula and cotton swab. What is needed now is a comparison of these two methods. The purpose of this study was to compare the adequacy of Pap smears obtained with the cytobrush plus Ayre spatula with smears obtained with the extended-tip spatula alone, as measured by the presence of endocervical cells.

Materials and Methods

Patient Recruitment and Randomization

Between August 1987 and February 1988, women coming to the Baylor Family Practice Center for routine Pap smears were asked to participate in this study. Patients who had a hysterectomy or were currently pregnant were ineligible for the study. Health maintenance organization (HMO) members were also ineligible because their laboratory was unable to provide the data needed for the study.

Sample size calculations were based on the ability to detect a 15 percent difference in successful outcomes between the two methods, with an α level of 0.05 and a β level of 0.20 (power = 0.80). Using the appropriate equations for the comparison of two proportions, estimates of 88 participants per diagnostic method were derived.

Eligible patients who gave written informed consent were randomized (using a blocking factor of four) either to the extended-tip spatula method or to the experimental cytobrush and Ayre spatula method of obtaining a Pap smear.

Data Collection

Patients completed a questionnaire requesting information about age, gravidity, parity, current hormonal therapy, menopausal status, and previous cervical surgery. Pap smears were obtained by the faculty or resident physician with whom the patient's appointment was made. All smears were analyzed for the outcome variable, the presence or absence of endocervical cells, by a cytotechnologist registered by the American Society of Clinical Pathologists. The cytotechnologist was blinded to the patient's diagnostic method assignment.

The Pap smears were obtained using the techniques recommended by the instrument manufacturers. The cytobrush was inserted into the endocervix and rotated slowly one-half to one full turn. The Pap smear was prepared by nurses rolling and twisting the cytobrush on a glass slide. A sample was also obtained from the ectocervix using an Ayre spatula and smeared on a separate slide. The slides were then were fixed with spray immediately.

The Milex™ extended-tip spatula was inserted into the endocervical canal, rotated clockwise (360°), and removed. The method of insertion and removal of the Milex™ extended-tip spatula varies with the position of the cervix. When the cervix has a normal curve or anterior position, one presses posteriorly on the smooth part of the spatula toe, and when the cervix is in a posterior position, one presses anteriorly on the spatula toe. The Pap smear slide was prepared by nurses by holding the spatula head at a 45-degree angle, pressing the serrated edges on the glass slide, moving the long toe of the spatula from right to left, then the

Table 1. *Descriptive Statistics for the Entire Sample and by Papanicolaou Smear Method Assignment.*

Variable	Entire Sample (n = 219) Mean ±1 SD	Brush Method (n = 111) Mean ±1 SD	Spatula Method (n = 108) Mean ±1 SD
Age (years)	32.15±10.6 ($P = 0.40$)	32.02±10.3	32.29±11.0
Gravidity	1.11±1.5 ($P = 0.53$)	1.01±1.4	1.22±1.5
Parity	0.77±1.1 ($P = 0.70$)	0.76±1.2	0.79±1.1

flange part of the spatula from left to right. The spatula is then flattened to the slide to obtain additional material.

Statistical Analysis

Frequencies, means, and standard deviations were calculated for all variables for the entire study group and within each diagnostic method using the SPSS/PC+ software package. Student's t-test was used to assess differences in age, gravidity, and parity. Chi-square analysis was used to compare the two groups for differences in menopausal status, current hormonal therapy, previous cervical surgery, Pap smear classification, and presence or absence of endocervical cells.

A subgroup analysis was used to determine if there were significant differences in outcome between the two methods for menopausal women, because it tends to be more difficult to obtain endocervical cells in this group.[11,12,22]

Results

Comparison of Equivalence of Groups

Table 1 provides descriptive statistics. The mean age (± one standard deviation) was 32.3 (±10.6) years for all participants. The mean gravidity was 1.1 (±1.5), and the mean parity was less than one (0.7 [±1.1]). One hundred nine (50 percent) of the participants were nulligravidas, and 132 (60 percent) were nulliparous. Eighty (36.6 percent) patients were taking some form of hormonal therapy; 77 of them were using birth control pills, and 3 were receiving estrogen replacement therapy. Two hundred five (94 percent) patients were premenopausal, and 14 (6 percent) were postmenopausal. Five patients had previous cervical surgery (3, cryosurgery; 2, conization). All of the Pap smears were reported as "negative," except two that were inconclusive due to air drying. No smears showed dysplasia.

Using the Pearson χ^2 statistic and Student's t-test, P values ≤ 0.05 were considered significant. The only factor for which there was a significant difference between the two experimental groups was a history of previous cervical surgery ($P < 0.05$), and the majority of these patients were in the cytobrush group. There were no significant differences in age ($P = 0.40$), gravidity ($P = 0.53$), parity ($P = 0.70$), hormonal therapy ($P = 0.61$), or menopausal status ($P = 0.74$) between the two groups.

Primary Study Findings

Two hundred twenty-two patients were enrolled in the study; 112 were randomly assigned to the combined cytobrush and Ayre spatula method and 110 to the extended-tip spatula method. Three ineligible patients were inadvertently randomized. Two of these patients were HMO members and were randomized to opposite diagnostic methods. One patient was recruited and randomized twice, on two separate occasions, to the same method (extended-tip spatula). Her second visit, as well as the two HMO cases, were dropped from the analysis. All of the other participants' data were analyzed according to their initial method assignment.

Pap smears obtained with the combination of cytobrush and Ayre spatula had a significantly greater number of endocervical cells than the smears obtained with the extended-tip spatula alone ($\chi^2 = 18.6$, $P < 0.0001$). One hundred of the 111 Pap smears obtained with the combination of a cytobrush and Ayre spatula contained endocervical cells (90.1 percent) compared with 68 of the 105 smears obtained with the extended-tip spatula (64.8 percent) (Table 2). Three smears, all in the extended-tip spatula group, were inadvertently not analyzed for endocervical cells. The combination of a cytobrush and Ayre spatula obtained endocervical cells in 5 of 6 (83 percent) postmenopausal patients,

J Am Board Fam Pract: first published as 10.3122/jabfm.2.3.156 on 1 July 1989. Downloaded from http://www.jabfm.org/ on 8 May 2025 by guest. Protected by copyright.

Table 2. *Recovery of Endocervical Cells by the Cytobrush Plus Ayre Spatula versus the Extended-Tip Spatula.*

	Method		
	Combined Cytobrush and Ayre Spatula	Extended-Tip Spatula	Row Total
Endocervical cells			
Yes	100	68	168 (77.8%)
No	11	37	48 (22.2%)
Column total	111 (51.4%)	105 (48.6%)	216 (100.0%)

$\chi^2 = 18.6$, $P < 0.0001$.

compared with 4 of 8 (50 percent) patients for the extended-tip spatula.

Discussion

The cervical cytobrush yields a greater quantity and quality of endocervical cells than the cotton swab.[15,23] In a study of 100 patients, Gupta, et al.[16] reported that the brush alone provided satisfactory smears in 97 percent of cases compared with 39 percent done by the combined Ayre spatula and cotton swab. Taylor, et al.[17] found that a combination of the Ayre spatula and brush was superior to a combination of the Ayre spatula and swab, as measured by the presence of endocervical cells, in both pre- and postmenopausal females. The rate of suboptimal smears (those without endocervical cells) fell from 12 percent to 1.7 percent when the endocervical brush was used. In a cohort of patients undergoing repeat Pap smears after an initial smear yielded no endocervical cells, Trimbos and Arentz[18] found that the combination of an extended-tip spatula and brush obtained endocervical cells in 27 of 30 patients compared with the combination of an extended-tip spatula and cotton swab, which obtained endocervical cells in only 9 of the same 30 patients ($P < 0.001$). Boon, et al.[9] showed that the combined extended-tip spatula and brush yielded endocervical cells more often (98 percent of the smears) than the extended-tip spatula alone (84 percent of the smears). Their multicenter sample population included almost 6000 in the combined extended-tip spatula and brush group and 24,000 in the extended-tip spatula alone group. In 1988, Reissman found that the combination of the extended-tip spatula plus cytobrush improved endocervical cell recovery by 200 percent in women older than 45 years and by 57 percent in women aged 45 and younger.[12]

Cotton swabs trap endocervical cells and thereby contribute to false-negative smears.[24] The use of a cotton swab in addition to the extended-tip spatula for endocervical sampling does not improve endocervical cell recovery.[12] Cotton swabs, however, are useful for removing excess mucus from the cervix before obtaining the Pap smear: this has been shown to increase the yield of endocervical cells (70 percent versus 62 percent, $P < 0.02$).[22]

The yield of endocervical cells with the extended-tip spatula in this study (64.8 percent) was within the range reported in previous studies (43 percent to 88.3 percent).[21,22] The yield of endocervical cells with the Ayre spatula alone is very poor when compared with the extended-tip spatula.[11,19,21]

Limitations

There are several potential sources of bias in this study; e.g., the physician's skill in obtaining Pap smears might have improved during the study. However, the methodology provided for random selection of patients in groups of 4; for every 4 patients, 2 were assigned the cytobrush and 2 the extended-tip spatula. Therefore, levels of physician skill were likely to be spread evenly between the two experimental groups. Similarly, one physician may have been more likely than another to have had a patient who needed a Pap smear. However, because patients were randomized to the experimental methods, those physicians who performed a greater number of Pap smears were just as likely to use one method as the other method. To avoid potential bias, the registered cytotechnologist was blinded to the technique used to obtain the sample. Near the end of the study, a different registered cytotechnologist screened the slides for endocervical cells, but she, too, was blinded.

The 3 ineligible patients who were dropped from the study would not have significantly affected the results, nor would the 3 smears that were not analyzed for endocervical cells. Because of the small number of postmenopausal women, there was insufficient statistical power to test ef-

J Am Board Fam Pract: first published as 10.3122/jabfm.2.3.156 on 1 July 1989. Downloaded from http://www.jabfm.org/ on 8 May 2025 by guest. Protected by copyright.

fectively the subhypothesis that there was a difference between methods for this group.

There are some limitations of the cytobrush technique. First, it is not recommended for use with pregnant patients; however, this is not a major limitation, because screening with the cytobrush can be performed postpartum. Second, there may be mild painless spotting for 1 to 2 days after the Pap smear. This is common to other methods that sample the endocervical canal (for example, the extended-tip spatula) and does not represent a major limitation if the patient is forewarned. Third, in at least one patient, the cytobrush could not be inserted into the endocervical canal because of cervical stenosis.

Conclusion

The 6 percent to 56 percent false-negative rate of Pap smears is unnecessarily high, primarily because of inadequate sampling.[3,4] Using the cervical cytobrush for Pap smears increases the rate of recovery of endocervical cells, which has been shown to improve the detection of cervical dysplasia.[7-9] The cost of the cytobrush is 20–30 cents each, which is small when compared with the cost of repeat smears. Other methods of obtaining endocervical samples, such as the cotton swab or extended-tip spatula alone, are inferior to the cytobrush and should be abandoned.[15,23] In addition to cytobrush sampling of the endocervix, the Ayre spatula should be used to sample the ectocervix.[6,14]

Statistical consultation was provided by Haley Kaplowitz, Ph.D., Department of Family Medicine, Baylor College of Medicine, Houston, TX.

References

1. Richart RM, Vaillant HW. Influence of cell collection techniques upon cytological diagnosis. Cancer 1965; 18:1474-8.
2. Berkowitz RS, Ehrmann RL, Lavizzo-Mourey R, et al. Invasive cervical carcinoma in young women. Gynecol Oncol 1979; 8:311-6.
3. Beilby JO, Bourne R, Guillebaud J, Steele ST. Paired cervical smears: a method of reducing the false-negative rate in population screening. Obstet Gynecol 1982; 60:46-8.
4. Morell ND, Taylor JR, Snyder RN, Ziel HK, Saltz A, Willie S. False-negative cytology rates in patients in whom invasive cervical cancer subsequently developed. Obstet Gynecol 1982; 60:41-5.
5. Fluhmann CF. The squamocolumnar transitional zone of the cervix uteri. Obstet Gynecol 1959; 14:133-48.
6. Marsh M. Original site of cervical carcinoma. Topographical relationship of carcinoma of the cervix to the external os and to the squamocolumnar junction. Obstet Gynecol 1956; 7:444-52.
7. Elias A, Linthorst G, Bekker B, Vooijs PG. The significance of endocervical cells in the diagnosis of cervical epithelial changes. Acta Cytol 1983; 27:225-9.
8. Vooijs PG, Elias A, van der Graaf Y, Veling S. Relationship between the diagnosis of epithelial abnormalities and the composition of cervical smears. Acta Cytol 1985; 29:323-8.
9. Boon ME, Alons-van Kordelaar JJ, Rietveld-Scheffers PE. Consequences of the introduction of combined spatula and cytobrush sampling for cervical cytology. Improvements in smear quality and detection rates. Acta Cytol 1986; 30:264-70.
10. Briggs RM. Dysplasia and early neoplasia of the uterine cervix. A review. Obstet Gynecol Surv 1979; 34:70-99.
11. Wolfendale MR, Howe-Guest R, Usherwood MM, Draper GJ. Controlled trial of a new cervical spatula. Br Med J 1987; 294:33-5.
12. Reissman SE. Comparison of two Papanicolaou smear techniques in a family practice setting. J Fam Pract 1988; 26:525-9.
13. Gondos B, Marshall D, Ostergard DR. Endocervical cells in cervical smears. Am J Obstet Gynecol 1972; 114:883-4.
14. Garite TJ, Feldman MJ. An evaluation of cytologic sampling techniques. A comparative study. Acta Cytol 1978; 22:83-5.
15. Ros E, Jimenez AM, Vilaplana E, et al. New technique for endocervical cytological sampling with Stormby's brush. Preliminary results. Citologia 1983; 3:9-20.
16. Gupta RK, Naran S, Bakalar J, Fauck R, Buchanan A. Improvement in the quality of gynaecological smears using a cytobrush. N Z Med J 1987; 100:532-4.
17. Taylor PT, Anderson WA, Barber SR, Covell JL, Smith EB, Underwood PB Jr. The screening Papanicolaou smear: contribution of the endocervical brush. Obstet Gynecol 1987; 70:734-8.
18. Trimbos B, Arentz NP. The efficiency of the cytobrush versus the cotton swab in the collection of endocervical cells in cervical smears. Acta Cytol 1986; 30:261-3.
19. Bounds W, Grubb C, Metaxas N, Vessey M. A randomized comparative trial of the performance of the Ayre and the Armovical cervical spatulae. Br J Obstet Gynaecol 1976; 83:981-7.
20. Colon VF, Linz LE. The extended tip spatula for cervical cytology. J Fam Pract 1981; 13:37-41.
21. Pistofides GA, House FR, Shepherd JM, Vale JC. The multispatula: a new dimension in sampling the cervix. Lancet 1984; 1:1214-5.
22. Hamblin JE, Brock CD, Litchfield L, Dias J. Papanicolaou smear adequacy: effect of the different techniques in specific fertility states. J Fam Pract 1985; 20:257-60.
23. Glenthoj A, Bostofte E, Rank F. Brush cytology from the uterine cervix. Acta Obstet Gynecol Scand 1986; 65:689-91.
24. Rubio CA. A trap for atypical cells. Am J Obstet Gynecol 1977; 128:687-8.

J Am Board Fam Pract: first published as 10.3122/jabfm.2.3.156 on 1 July 1989. Downloaded from http://www.jabfm.org/ on 8 May 2025 by guest. Protected by copyright.