

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/7761689>

Clinical Significance of Unsatisfactory Conventional Pap Smears Owing to Inadequate Squamous Cellularity Defined by the Bethesda 2001 Criterion

Article in *American Journal of Clinical Pathology* · June 2005

DOI: 10.1309/GA19KPY3YLMKVWYU · Source: PubMed

CITATIONS

23

READS

1,308

6 authors, including:



Wenquan Wang

56 PUBLICATIONS 3,796 CITATIONS

SEE PROFILE

Some of the authors of this publication are also working on these related projects:



mol path [View project](#)

Clinical Significance of Unsatisfactory Conventional Pap Smears Owing to Inadequate Squamous Cellularity Defined by the Bethesda 2001 Criterion

Amy L. Adams, MD,¹ Jonathan Gidley, CT(ASCP),¹ Janie Roberson, SCT(ASCP),¹ Wenquan Wang, PhD,² Isam Eltoum, MD, MBA,¹ and David C. Chhieng, MD, MBA¹

Key Words: Bethesda 2001; Cervicovaginal cytology; Unsatisfactory; Squamous cellularity; Follow-up

DOI: 10.1309/GA19KPY3YLMKVWYU

Abstract

To determine the incidence of clinically significant lesions in long-term follow-up after a diagnosis of inadequate squamous cellularity using former and new criteria, we reviewed conventional Papanicolaou (Pap) smears (January-December 1998) for adequacy based on the Bethesda System 2001 criterion. Of 23,302 Pap smears evaluated in our laboratory, 114 (0.489%) were classified as unsatisfactory and 245 (1.051%) as "satisfactory but limited by" based on the 10% rule. Follow-up information for 5 years was obtained for 172 patients without a concurrent cervical epithelial abnormality: 25 (14.5%) had squamous abnormalities (atypical squamous cells, 22; low-grade squamous intraepithelial lesion, 2; and high-grade squamous intraepithelial lesion, 1). With the Bethesda System 2001 criterion, 167 (97.1%) of 172 smears had inadequate squamous cellularity and 5 (2.9%) were adequate. No differences in the incidence of squamous abnormalities detected on follow-up were noted between patients with unsatisfactory Pap smears owing to inadequate squamous cellularity and patients with satisfactory and negative smears. Our findings raise the question whether patients with unsatisfactory Pap smears and a negative history of gynecologic diseases require repeated Pap smears within 2 to 4 months as suggested by the American Society for Colposcopy and Cervical Pathology guideline.

When issuing reports for gynecologic cytology (Papanicolaou [Pap] smears), the pathologist or cytotechnologist must provide information about the adequacy and quality of the specimen along with his or her interpretation. Therefore, in addition to defining the diagnostic categories, the Bethesda System also develops criteria for determining the adequacy and quality of Pap smears.¹ According to the Bethesda System, these criteria customarily have included estimations of the number of squamous and endocervical cells present, specimen preservation and fixation, and the absence of obscuring elements such as excessive blood or inflammation. Based on these criteria, Pap smears traditionally have been placed into 1 of 3 categories: satisfactory, unsatisfactory, or satisfactory but limited. Although patients with unsatisfactory smears generally undergo repeated evaluation within a few months of the unsatisfactory smear, the recommendation for patients with smears classified as satisfactory but limited are less well-defined, but most agree that patients should be rescreened at the same interval as patients with satisfactory smears.²

The most recent Bethesda Conference in 2001 redefined some of the criteria for assessing specimen adequacy and eliminated the "satisfactory but limited" category.³ The definition of adequate squamous cellularity for conventional smears is among the many changes made at the conference. Before Bethesda 2001, adequate squamous cellularity was defined arbitrarily as the presence of well-preserved and well-visualized cells covering more than 10% of the slide.¹ This definition proved somewhat confusing, leading to differing interpretations of adequacy based on the squamous component. According to Bethesda 2001, adequate squamous cellularity for conventional preparation is defined as the presence of "an estimated minimum of approximately 8,000-12,000 well-preserved

and well-visualized squamous epithelial cells.”³ The estimation is to be determined not by actual counting of the cells but by comparison with computer-generated reference images.

Sheffield et al⁴ demonstrated that the application of the new criterion along with the use of reference images to determine the adequacy of squamous cellularity on conventional Pap smears significantly improved interobserver reproducibility compared with the 10% rule. However, there is no substantial evidence that the presence of an estimated range of 8,000 to 12,000 squamous cells is the most appropriate cutoff for an adequate squamous component. The goal of the present study was to evaluate conventional Pap smears previously classified as unsatisfactory or “satisfactory but limited by” (SBLB) according to the old 10% criterion to see how the smears would be classified based on the current definition for adequate squamous cellularity. In addition, we compared the incidence of squamous abnormalities occurring within a 5-year follow-up period in patients with unsatisfactory smears based on either criterion with the incidence for patients with satisfactory smears.

Materials and Methods

A computerized search identified all cases with conventional Pap smears designated as unsatisfactory or SBLB as a result of scant squamous cellularity during a 12-month period (January 1–December 31, 1998). For SBLB Pap smears, only cases interpreted as within normal limits or benign cellular changes were included in the study; cases interpreted as atypical or beyond were excluded. Patient records then were reviewed for a 5-year period to determine the number of patients in whom squamous abnormalities were found, including atypical squamous cells of undetermined significance (ASCUS), low-grade dysplasia (low-grade squamous intraepithelial lesion [LSIL]), and high-grade dysplasia (high-grade squamous intraepithelial lesion [HSIL]), during follow-up (Pap smear and/or histologic examination).

The Pap smears originally classified as unsatisfactory or SBLB owing to inadequate squamous cellularity were reviewed and reassessed for adequate squamous cellularity based on the new Bethesda criteria and the use of the reference images.⁴ The latter were computer-generated reference images that exemplified the density of coverage needed for adequacy using a 4× objective for 10 fields, 20 fields, and for an entire slide.

A comparable number of control cases with satisfactory smears and an interpretation of within normal limits or benign cellular changes were chosen randomly from the same 12-month period. For cases to be eligible for the control group, patients were required to have at least 1 follow-up Pap smear or biopsy and no squamous abnormality on the index

Pap smear; however, control group cases were not matched for age, race, or other demographic characteristics.

Follow-up included review of the repeated Pap smears and surgical pathology specimens obtained between January 1998 and February 2004. The incidence of squamous abnormalities detected during the 5-year follow-up period was compared for 3 groups: (1) cases with smears originally categorized as unsatisfactory or SBLB with regard to squamous cellularity according to the 10% rule; (2) cases with inadequate smears based on the 2001 Bethesda criterion; and (3) the control group, with satisfactory smears.

Statistical analyses were performed with the χ^2 test and the Fisher exact test. The level of significance was set at .05 or less.

Results

From January 1 to December 31, 1998, a total of 23,302 Pap tests were evaluated in the cytology department at our institution. Fewer than 5% of the Pap tests were liquid-based preparations. Of the total, 114 (0.489%) were labeled unsatisfactory and 245 (1.510%) SBLB on the basis of inadequate squamous cellularity. Excluding cases that were liquid-based preparations and cases with a concurrent squamous or glandular abnormality on the index smear (the latter was for SBLB Pap smears only), 252 cases were available for review, 172 SBLB cases and 80 unsatisfactory cases.

For the 80 unsatisfactory Pap smears, 22 (28%) were lost to follow-up; 54 patients (68%) had repeated Pap tests; the remaining 4 patients (5%) underwent biopsy. For the 172 patients with SBLB Pap smears, 58 (33.7%) had no follow-up studies. Of the remaining patients with SBLB Pap smears, 104 (60.5%) had repeated Pap tests, and 10 (5.8%) had histologic follow-up (Table 1). Therefore, our study population consisted of 172 patients, 58 with unsatisfactory Pap smears and 114 with SBLB Pap smears. Of the patients with unsatisfactory Pap smears, 6 (10%) had at least 1 subsequent diagnosis of ASCUS, and 1 (2%) had a subsequent diagnosis of LSIL. None had a subsequent diagnosis of HSIL. Of patients with SBLB Pap smears, 16 (14.0%) had a subsequent diagnosis of ASCUS, 1 (0.9%) of LSIL, and 1 (0.9%) of HSIL (Table 2). In addition, 1 patient (0.9%) had a subsequent diagnosis of atypical glandular cells of undetermined significance (AGCUS).

When the slides from the same 58 unsatisfactory and 114 SBLB cases were assessed for adequate squamous cellularity using the 2001 Bethesda criterion, 167 cases (97.1%) were categorized as inadequate. Only 5 cases (2.9%) were reclassified as adequate. Of the 167 patients with inadequate Pap smears, 154 (92.2%) had repeated Pap tests, and 13 patients (7.8%) underwent biopsy. Of the 5 patients with adequate Pap smears, 4 (80%) had follow-up Pap smears, and 1 patient

Table 1
Comparison of Follow-up Studies Performed in Each Adequacy Group*

	No Follow-up	Biopsy	Repeated Papanicolaou Smears	Total
By 10% rule				
Unsatisfactory	22 (28)	4 (5)	54 (68)	80 (58)
SBLB	58 (33.7)	10 (5.8)	104 (60.5)	172 (114)
By Bethesda 2001 criterion				
Adequate	—†	1 (20)	4 (80)	5
Inadequate	—†	13 (7.8)	154 (92.2)	167
Control cases	—†	6 (1.7)	344 (98.3)	350

SBLB, satisfactory but limited by.

* Data are given as number (percentage) except in the Total column, in which the number in parentheses excludes cases without follow-up.

† Cases without follow-up were excluded.

Table 2
Comparison of Follow-up Diagnoses for Each Adequacy Group*

	ASCUS	LSIL	HSIL	Total
By 10% rule				
Unsatisfactory (n = 58)	6 (10)	1 (2)	0 (0)	7 (12)
SBLB (n = 114)	16 (14.0)	1 (0.9)	1 (0.9)	18 (15.8)
By Bethesda 2001 criterion				
Inadequate (n = 167)	22 (13.2)	2 (1.2)	1 (0.6)	25 (15.0)
Adequate (n = 5)	0 (0)	0 (0)	0 (0)	0 (0)
Control cases (n = 350)	39 (11.1)	6 (1.7)	3 (0.9)	48 (13.7)

ASCUS, atypical squamous cells of undetermined significance; HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion; SBLB, satisfactory but limited by.

* Data are given as number (percentage).

(20%) underwent biopsy (Table 1). Within the 167 patients with inadequate smears, 22 (13.2%) had subsequent diagnoses of ASCUS, 2 (1.2%) of LSIL, and 1 (0.6%) of HSIL. In 1 additional patient (0.6%), AGCUS developed. Of the 5 adequate cases, no squamous abnormalities were found in subsequent examinations (Table 2).

Among the control group of 350 cases, 6 patients (1.7%) underwent subsequent biopsy, and 344 (98.3%) had follow-up Pap smears (Table 1). Of 350, 39 (11.1%) had a subsequent diagnosis of ASCUS, 6 (1.7%) of LSIL, and 3 (0.9%) of HSIL (Table 2). In addition, AGCUS developed in 4 patients (1.1%).

Patients with Pap smears thought to be unsatisfactory or inadequate were more likely to undergo biopsy than patients in the control group; the difference was statistically significant ($P = .003$; χ^2). There was a significant increase in the proportion of inadequate smears classified using the 2001 Bethesda criterion compared with those classified by the 10% rule ($P < .001$; χ^2). However, there was no statistically significant difference in the incidence of squamous abnormalities identified in subsequent follow-up using either criterion to assess the adequacy of squamous cellularity. There also was no difference in the incidence of squamous abnormalities during follow-up between patients with unsatisfactory or inadequate Pap smears and those in the control group.

Discussion

Assessment of the adequacy of a specimen is an integral part of the overall evaluation of a Pap smear. Various studies have pointed out that a substantial portion of false-negative Pap smears originally designated as negative were deemed unsatisfactory for interpretation during retrospective review.⁵⁻⁷ Henry and Wadehra⁸ correlated smear quality with the detection of epithelial abnormalities in a series of 68,328 Pap smears. Superior smear quality, in particular the presence of an adequate squamous component, was associated with a higher detection rate of epithelial abnormalities.

In 1988, the Bethesda System recommended the inclusion of a statement regarding the adequacy and quality of the Pap smear in the report. Cytologists were required to classify Pap smears into 3 categories: satisfactory, SBLB, or unsatisfactory, based on their quality. The Bethesda System also came up with criteria for adequacy. The definition for adequate squamous cellularity was the presence of well-preserved and well-visualized squamous epithelial cells covering more than 10% of the slide surface.¹ Although widely accepted by many cytology laboratories, the 10% rule for reporting squamous cell adequacy has its limitations. First, it is an arbitrary value that is not supported by scientific studies. In addition, it is difficult to translate cellularity into the percentage

of surface coverage because of nonuniform distribution of cells on conventional Pap smears. Renshaw et al⁹ reported that cytologists often overestimated visually the percentage of slide coverage by squamous cells compared with the results obtained using an image analysis system. Gill¹⁰ stated that 10% slide coverage was equivalent to the presence of an average of 190 squamous cells per 100× field of view and, therefore, was too high. Another issue is poor interobserver agreement. Most investigators agreed that interobserver reproducibility in assessing squamous adequacy using the 10% rule ranged from poor to fair.^{4,9,11}

In view of the limitations and controversies associated with the 10% rule, Bethesda 2001 proposed a new criterion for adequate squamous cellularity for conventional smears—a conventional Pap smear should have an estimated minimum of approximately 8,000 to 12,000 well-preserved and well-visualized squamous epithelial cells.³ Computer-generated images of known cellular density are used as references to compare with smears to assess adequacy. In addition, Bethesda 2001 also recommended eliminating the category SBLB and classifying smears only as inadequate or adequate; a qualifier can be added to the report for adequate smears.

Sheffield et al⁴ demonstrated that interobserver agreement in determining the adequacy of squamous cellularity was significantly better when the Bethesda 2001 criterion, rather than the 10% rule, was used. They also reported that the proportion of smears designated as unsatisfactory based on the new guidelines was higher than that obtained using the 10% rule.⁴ The mean proportion of smears designated as unsatisfactory was 0.34 using the 10% rule but was 0.51 using the new criterion. In the present study, we again demonstrated differences in the proportion of smears designated as inadequate based on the 2 criteria, with the Bethesda 2001 criterion proving to be a more strict assessment of adequacy, ie, more smears were classified as unsatisfactory because of inadequate squamous cellularity. By using the Bethesda 2001 criterion, all but 5 of 114 smears originally classified as SBLB were reclassified as inadequate, as were all smears originally classified as unsatisfactory.

It seems that observers tend to overestimate the percentage of slide coverage by squamous cells based on the 10% coverage criterion. One group of investigators pointed out that a visual estimate of 10% coverage corresponded to a “true” median coverage of 3% as determined by computer image analysis.⁹ When the evaluation was repeated with the provision of reference smears of different extents of coverage for comparison, the median estimated coverage given by 3 of 4 observers was similar to the results obtained using computer image analysis. Based on our experience and that of others, the advantage of using reference images, smears, or both to determine the squamous cellularity of conventional Pap smears is quite apparent.

The purpose of designating smears as unsatisfactory is to alert clinicians that the particular smear might not be reliable for detecting preneoplastic or neoplastic conditions. Unsatisfactory smears that are diagnosed incorrectly as negative might provide clinicians and patients a false sense of security, resulting in failure to initiate the appropriate follow-up measures.

The next logical question is whether an estimated range of 8,000 to 12,000 squamous cells is the most appropriate and clinically relevant cutoff for an adequate squamous component in conventional preparations. In the present study, we observed no significant differences in the incidence of squamous abnormalities detected during subsequent examinations for patients with unsatisfactory smears based on either criterion. It also is interesting to note that there was no significant difference in the incidence of squamous abnormalities detected on subsequent examination between patients with unsatisfactory smears based on the Bethesda 2001 criterion and the control group.

In 1997, Ransdell et al,¹² from the University of Kentucky and the University of Iowa, reported that in 16% of patients with initial unsatisfactory specimens, SIL or malignancy was found during an 18-month follow-up. The authors also observed that the incidence of SIL during subsequent follow-up in this group was significantly higher than the incidence in patients with satisfactory or SBLB Pap smears. Ransdell et al¹² reported a higher incidence of squamous abnormalities in patients with unsatisfactory smears than found in the present study; however, there are differences between the studies. One of the main distinctions is that Ransdell et al¹² included unsatisfactory smears related to a wide variety of reasons, including inadequate squamous cellularity (based on the 10% rule) and obscuring blood or inflammation; the present study included only unsatisfactory smears owing to inadequate squamous cellularity.

A more recent study by Fidda et al¹³ (reported in 2004) compared the unsatisfactory rate between 2 groups of Pap smears, one with specimen adequacy determined by the 10% rule and the other by the Bethesda 2001 guidelines. In agreement with our findings, Fidda et al¹³ concluded that implementation of the Bethesda 2001 guidelines increased the number of unsatisfactory smears without a significant increase in the number of squamous abnormalities detected on follow-up evaluation.

Although our study specifically addressed adequacy with regard to conventional Pap smears, the issue of specimen adequacy for liquid-based preparations is becoming more important because the use of such methods is more widespread. The Bethesda 2001 guidelines define adequacy of the squamous component for liquid-based preparations as a minimum of 5,000 cells. Since implementation of this new criterion, few studies have looked at the subsequent effect on adequacy of

liquid-based specimens. Stanford et al¹⁴ reviewed the percentage of unsatisfactory smears by liquid-based preparation and noted a 2.3-fold increase in the percentage of unsatisfactory cases (59% vs 26%; $P < .05$) when smears originally classified by the 10% rule were reclassified by the Bethesda 2001 guidelines. In contrast, Bolick and Lin¹⁵ noted an increase in unsatisfactory conventional Pap smears, as defined by the new guidelines, but saw no significant change in the percentage of unsatisfactory smears prepared by the SurePath liquid-based method (TriPath Imaging, Burlington, NC). The same study noted an increase in the unsatisfactory rate with Pap smears performed by the ThinPrep liquid-based method (Cytoc, Marlborough, MA); however, the number of cases prepared by ThinPrep vs SurePath was much smaller (508 vs 19,442).¹⁵

When conventional and liquid-based preparations are considered together, results have been mixed. Basta et al¹⁶ demonstrated an increase in the rate of unsatisfactory Pap smears from 0.6% in 2000 to 1.7% by the first quarter of 2002 with the implementation of Bethesda 2001 guidelines. In contrast, Papillo and St John¹⁷ found no significant increase in the percentage of unsatisfactory Pap smears as defined by the new guidelines, a finding that paralleled the experience in our laboratory in a previous study.¹⁸ Thus, the impact of the new guidelines with regard to liquid-based preparations is less clear. As such preparations become increasingly common, the effect of the Bethesda 2001 guidelines might become more evident.

Until recently, there was no consensus on the management of patients with unsatisfactory or satisfactory but limited Pap smears. In 2002 a task force convened by the American Society for Colposcopy and Cervical Pathology (ASCCP) published guidelines for the management of such patients.¹⁹ The ASCCP guidelines recommend that women with unsatisfactory smears undergo repeated testing within 2 to 4 months. The ASCCP guidelines do not explicitly discuss management for patients with smears with "limited squamous cellularity." For patients whose smears have other limiting factors, such as obscuring blood or inflammation and lack of an endocervical component, ASCCP guidelines recommend that patients undergo repeated testing in 12 months.

With the implementation of the Bethesda 2001 criterion, it seems that a greater proportion of Pap smears will be classified as unsatisfactory. If these additional patients with unsatisfactory Pap smears are required to undergo repeated Pap testing within 2 to 4 months, the increase in health care costs could be considerable. It seems reasonable to question whether such a strategy is appropriate for patients whose Pap smears are classified as unsatisfactory based on inadequate squamous cellularity and who have no history of a cervicovaginal abnormality, given that the risk of developing a subsequent squamous abnormality is comparable in our study population between patients with inadequate and satisfactory Pap smears. Certainly our small retrospective study cannot

answer this question conclusively because of inherent limitations. For example, there exists the possibility of introducing unforeseen bias in the selection of study and control groups. Also, although the rates of unsatisfactory Pap smears at our institution were comparable to those of similar institutions, review of unsatisfactory cases for a 12-month period from our files alone might not provide adequate statistical power to detect significant differences. Therefore, a future study with a larger sample is warranted to validate our findings.

By using the Bethesda 2001 criterion for assessing squamous cellularity, more Pap smears were interpreted as unsatisfactory, particularly those originally designated as SBLB using the 10% rule. Patients without a cervicovaginal abnormality (atypical squamous cells or worse) with unsatisfactory Pap smears had an incidence of squamous abnormalities during subsequent follow-up similar to that for patients with satisfactory and negative Pap smears. Our findings raise the question of whether patients with unsatisfactory Pap smears and a negative history of gynecologic disease require repeated Pap smears within 2 to 4 months as suggested by the ASCCP guideline.

From the Departments of ¹Pathology and ²Medicine-Hematology and Oncology, University of Alabama at Birmingham.

Presented in part at the 92nd Annual Meeting of the American Society of Cytopathology, Orlando, FL, November 2003.

Address reprint requests to Dr Chhieng: Dept of Pathology, 619 19 St S, KB 627, Birmingham, AL 35249-6823.

References

1. Kurman R, Solomon D. *The Bethesda System for Reporting Cervical/Vaginal Cytologic Diagnoses: Definitions, Criteria and Explanatory Notes for Terminology and Specimen Adequacy*. New York, NY: Springer-Verlag; 1994.
2. Davey DD, Austin RM, Birdsong G, et al. ASCCP patient management guidelines: Pap test specimen adequacy and quality indicators. *Am J Clin Pathol*. 2002;118:714-718.
3. Solomon D, Davey D, Kurman R, et al. The 2001 Bethesda system: terminology for reporting results of cervical cytology. *JAMA*. 2002;287:2114-2119.
4. Sheffield MV, Simsir A, Talley L, et al. Interobserver variability in assessing adequacy of the squamous component in conventional cervicovaginal smears. *Am J Clin Pathol*. 2003;119:367-373.
5. Pairwuti S. False-negative Papanicolaou smears from women with cancerous and precancerous lesions of the uterine cervix. *Acta Cytol*. 1991;35:40-46.
6. Paterson ME, Peel KR, Joslin CA. Cervical smear histories of 500 women with invasive cervical cancer in Yorkshire. *Br Med J (Clin Res Ed)*. 1984;289:896-898.
7. van der Graaf Y, Vooijs GP, Gaillard HL, et al. Screening errors in cervical cytologic screening. *Acta Cytol*. 1987;31:434-438.
8. Henry JA, Wadehra V. Influence of smear quality on the rate of detecting significant cervical cytologic abnormalities. *Acta Cytol*. 1996;40:529-535.

9. Renshaw AA, Friedman MM, Rahemtulla A, et al. Accuracy and reproducibility of estimating the adequacy of the squamous component of cervicovaginal smears. *Am J Clin Pathol*. 1999;111:38-42.
10. Gill GW. Pap smear cellular adequacy: what does 10% coverage look like? what does it mean [abstract]? *Acta Cytol*. 2000;44:873.
11. Spires SE, Banks ER, Weeks JA, et al. Assessment of cervicovaginal smear adequacy: The Bethesda System guidelines and reproducibility. *Am J Clin Pathol*. 1994;102:354-359.
12. Ransdell JS, Davey DD, Zaleski S. Clinicopathologic correlation of the unsatisfactory Papanicolaou smear. *Cancer*. 1997;81:139-143.
13. Fidda N, Miron J, Rodgers WH, et al. Impact of the new Bethesda System 2001 on specimen adequacy of conventional cervicovaginal smears. *Diagn Cytopathol*. 2004;30:235-239.
14. Stanford T, Zhang XJ, Stowell SB, et al. Specimen adequacy on liquid-based Pap tests: comparison of two Bethesda systems [abstract]. *Mod Pathol*. 2003;16:82A.
15. Bolick DR, Lin KK. Effectively implementing the Bethesda System 2001 guidelines on specimen adequacy [abstract]. *Acta Cytol*. 2002;46:929.
16. Basta N, Davey D, Banks H. Increase in unsatisfactory Pap tests with adoption of Bethesda 2001 criteria [abstract]. *Acta Cytol*. 2002;46:929-930.
17. Papillo JL, St John TL. The effect of Bethesda 2001 on laboratory statistics [abstract]. *Acta Cytol*. 2002;46:923.
18. Chhieng DC, Roberson J, Gidley et al. Bethesda 2001: impact on reporting of gynecologic cytology. *Acta Cytol*. 2004;48:355-362.
19. Wright TC Jr, Cox JT, Massad LS, et al, and the ASCCP Conference. 2001 Consensus Guidelines for the management of women with cervical cytological abnormalities. *JAMA*. 2002;287:2120-2129.