

Rate of Endometrial Adenocarcinoma in Women Screened Before and After Implementation of the Bethesda 2001 Reporting System

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Objective

To assess the impact of the recommendation of the 2001 Bethesda System to report all benign-appearing endometrial cells seen in women aged ≥ 40 years on the frequency with which endometrial carcinomas are potentially detected as a consequence of Pap test reports that mention endometrial cells.

Study Design

We identified all women diagnosed with endometrial adenocarcinoma who also had a Pap test during the preceding 6 months. The search was performed for 3-year periods before and after the date of implementation of Bethesda 2001.

Results

Benign endometrial cells were reported for 589 women in the 3 years before Bethesda 2001 and for 3,810 women in the 3 following years. The number of endometrial malignancies found on follow-up in these women decreased from 8 in the 3 years before Bethesda 2001 to only 4 subsequently. The frequency of reporting atypical or malignant glandular cells, as well as the likelihood of finding endometrial malignancy on follow-up, did not significantly change.

Our data indicate that the Bethesda 2001 recommendations have not had the desired effect, though the reason remains a matter of speculation.

Conclusion

Despite a 6.5-fold rise in the frequency of reporting benign

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endometrial cells after Bethesda 2001, the frequency of subsequent diagnosis of endometrial malignancies did not increase. (Acta Cytol 2008;52:1–7)

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One of the significant changes in the 2001 Bethesda System is the mandated reporting of all benign-appearing endometrial epithelial cells present in Pap

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tests of women aged ≥ 40 years.¹ This recommendation brought uniformity to an area of Pap test reporting that had previously been muddled, with various standards of reporting formulated by each individual laboratory. Despite this benefit, however, the new requirement has generated some controversy, especially regarding the cutoff age of 40 years.

The authors of the 2001 Bethesda System moved to require reporting of endometrial cells largely because of groundbreaking studies correlating Pap test results with follow-up endometrial histology. These studies showed that, among postmenopausal women, endometrial cells on a Pap test quite frequently corresponded to endometrial hyperplasia or adenocarcinoma.^{2–5} Although the Pap test is universally acknowledged to have low sensitivity and specificity for endometrial lesions, the possibility that a test already widely employed to screen for squamous lesions might help to identify otherwise occult adenocarcinomas and precursors could not be ignored. Common sense indicates that endometrial cells seen on the Pap tests of actively menstruating women would not indicate pathology, but the inconsistent inclusion of last menstrual period on Pap test requisitions made the use of an arbitrary age cutoff necessary. Seeking to ensure that no women would have potentially meaningful endometrial cells go unreported, the authors chose a cutoff age of 40 years.

The aim of the current study is to evaluate the clinical outcomes of the change in Pap test reporting of endometrial cells mandated by the 2001 Bethesda System. We reviewed the 3-year period before and the 3-year period after the implementation of Bethesda 2001 by our institution. We determined the number

of women with endometrial adenocarcinoma diagnosed by surgical pathology within 6 months of a report of any endometrial cells (benign-appearing, atypical or malignant) on a Pap test and compared the number of endometrial carcinomas diagnosed before and after the introduction of the Bethesda 2001 System. Our hypothesis was that the more consistent reporting of benign-appearing endometrial cells introduced by the 2001 Bethesda System would lead to an increase in the number of endometrial carcinomas diagnosed in the follow-up of such tests or in a change in the stage at diagnosis, hopefully a diagnosis at an earlier stage. We also attempted to evaluate the impact of the change in reporting of benign-appearing endometrial cells on the number of endometrial biopsies performed at our institution.

Materials and Methods

A search of all Pap test results reported as benign-appearing endometrial cells, atypical glandular cells and adenocarcinoma from the centralized cytology laboratory of the Fairview Health System was undertaken for the time period between December 1, 1999, and November 30, 2005. A second search was performed for surgical pathology specimens diagnosed as endometrial carcinoma for the period from December 1, 1999, to March 31, 2006. The searches were cross-referenced to find women who had a Pap test performed in the 6 months before a diagnosis of endometrial carcinoma.

The Fairview Health System is a large multiinstitutional health-care organization in the state of Minnesota, U.S.A. It encompasses multiple hospitals and clinics primarily serving a suburban population, but also includes an urban university-based tertiary care hospital. The demographics of the patient population are similar to those of the state of Minnesota as a whole. The institutional review board of the University of Minnesota approved this study.

The centralized cytology laboratory of the Fairview Health System made liquid-based Pap testing available to its affiliated clinics in 2000. The number of liquid-based specimens increased steadily, such that by the start of 2003, liquid-based Pap tests accounted for over 90% of all specimens. Nearly all of the affiliated clinics currently use the SurePath Pap test system, but a few prefer the ThinPrep system, and < 1% continue to collect conventional smears.

Before the implementation of the 2001 Bethesda System, the Fairview Cytology Laboratory rules for reporting benign-appearing endometrial cells in Pap tests were complex. Among women < 55 years but > 40 years, the date of the last menstrual period was a consideration. If the woman was in day 1–14 of her cycle, any observed endometrial cells were not reported or

commented upon. If the woman was at day 15 or greater in her cycle, or the date of the last menstrual period could not be determined, endometrial cells were included in the report in the form of a comment. Among women aged ≥ 55 years, hormone replacement therapy with estrogen was a consideration. For those women known to be taking estrogen, the presence of endometrial cells elicited only a comment. Women not on estrogen or with unknown hormone replacement status received the top-line interpretation of benign endometrial cells. All Pap tests including benign-appearing endometrial cells in women ≥ 40 years, and not known to be in the first 14 days of the menstrual cycle, were reviewed by a pathologist.

Cytologically atypical glandular cells were reported as atypical glandular cells of undetermined significance (AGUS), with an indication sometimes given as to the probable origin of the cells from the endocervix or endometrium. Malignant glandular cells were reported as “adenocarcinoma.” As with AGUS, indications of the possible sites of origin were sometimes included.

The Fairview Health System began reporting Pap test results according to the 2001 Bethesda System on December 3, 2002. After this change, for any woman aged ≥ 40 , regardless of menstrual or hormone replacement status, the presence of endometrial cells on the Pap test elicited an interpretation of “other, see comment,” followed by a uniform comment stating “Benign endometrial cells present” and mentioning the possibility that those cells may correspond to normal menstrual shedding, estrogen therapy, or an underlying endometrial malignancy or hyperplasia. A pathologist reviewed any Pap test with benign-appearing endometrial cells present for which the tested woman did not have a known menstrual period within the previous 14 days.

Under Bethesda 2001, AGUS was replaced by the new term *atypical glandular cells* (AGC). Following the new guidelines, this interpretation always included indication of a probable site of origin in the endocervix or endometrium or, in the absence of certainty, the designation *not otherwise specified* (NOS). “Adenocarci-

noma” persisted as a category. Here also, the designation of a probable site of origin or the inclusion of NOS applied. *Adenocarcinoma in situ* (AIS) was added to the terminology to describe the appropriate subset of what had been AGUS.

During the 6-year period of the study the cytologic preparations were screened by 15 different cytotechnologists, 9 of whom worked throughout the study period. All cytotechnologists were trained and certified in interpreting liquid-based Pap tests (both SurePath and ThinPrep). The slides were then reviewed by the 14 pathologists, 2 academic pathologists and 12 community practice pathologists who did not change during the study period. All pathologists were trained and certified in interpreting liquid-based Pap tests (both SurePath and ThinPrep).

The methods of obtaining and processing histologic specimens did not change significantly over this period, nor did the reporting of diagnoses. Of the 18 pathologists (6 academic pathologists and 12 community practice pathologists) who diagnosed these specimens, 17 were the same during the entire study period. The endometrial specimen types included in this study were biopsies, curettings and hysterectomies. Surgical pathology follow-up specimens were correlated with previous Pap tests even in those instances when the procedures occurred within different parts of the Fairview system.

We also sought to assess the potential change in the number of endometrial biopsies and curettings being performed 1 year before and 1 year after the implementation of the 2001 Bethesda System at our institution that could be attributed to the increased reporting of benign-appearing endometrial cells in Pap tests. We searched our computerized surgical pathology database for endometrial histologic diagnoses rendered within 6 months of a Pap test report mentioning benign-appearing endometrial cells.

Statistical Analysis

Descriptive statistics were presented as counts and frequencies for categorical variables and mean and ranges for age. Odds ratios for bivariate comparisons were

Table I Distribution of Pap Test Interpretations of Reportable Glandular Cell Abnormalities Before and After Implementation of the 2001 Bethesda System

Pap test interpretations	Before Bethesda 2001 (12/1999–11/2002)		After Bethesda 2001 (12/2002–11/2005)	
	Total (EM, EC, NOS)	Age range (Mean)	Total (EM, EC, NOS)	Age range (Mean)
Benign endometrial cells	589	16–87 (47)	3,810	40–76 (46)
AGUS/AGC	315 (65, 61, 189)	16–87 (47)	326 (48, 68, 210)	18–84 (44)
Adenocarcinoma	30 (15, 1, 14)	28–81 (60)	30 (5, 2, 23)	26–86 (62)

EM = malignancy.

Table II Frequency of Pap Test Interpretations Preceding Histologic Diagnosis of Endometrial Carcinoma Before and After Implementation of the 2001

Pap test interpretations	Total (staged)	Before Bethesda 2001 (12/1999–11/2002)						
		Grade			Stage			
		1	2	3	1	2	3	4
No. of endometrial cells	38 (27) ^a	22	10	6	22	1	4	0
Benign endometrial cells	10 (6) ^a	8	0	2	5	0	1	0
AGUS/AGC	22 (15) ^a	11	8	3	14	1	0	0
Adenocarcinoma	17 (16) ^a	8	6	3	8	3	5	0

^aNot all women had staging information available for review.

determined using logistic regression. Multivariate analyses of associations with a diagnosis of benign endometrial cells were accomplished using multivariate logistic regression. Appropriateness of models was assessed using a Hosmer-Lemeshow goodness-of-fit test. There were no indications that the data did not fit the reported models. Analysis was accomplished using SPSS 14 (SPSS, Inc., Chicago, Illinois, U.S.A). Results were considered significant at $p < 0.05$.

Results

Between December 1, 1999, and December 2, 2002, there were 685 Pap tests performed that had benign endometrial cells mentioned in the report. Including only women aged ≥ 40 years, there were 589 Pap tests (Table I). In the same time period, there were 315 Pap tests interpreted as AGUS, excluding those designated "favor reactive." Of these, 216 were from women ≥ 40 years. There were 30 Pap tests interpreted as adenocarcinoma, of which only one was from a woman < 40 years old. From December 3, 2002, to November 30, 2005, there were 3,810 Pap tests in women age ≥ 40 with a comment referring to the presence of benign endometrial cells. During the same 3-year period there were 326 Pap tests in women ≥ 40 years whose reports included the interpretation of AGC. Among these, there were 193 in women aged ≥ 40 years. There were 30 Pap tests interpreted as adenocarcinoma, of which 3 were from women < 40 years. Seven Pap tests were interpreted as endocervical AIS. Over this 6-year span, the total number of Pap tests received by the Fairview cytology laboratory decreased slightly, from 198,766 (65,377, 32.9% liquid-based Pap tests) in the first 3 years to 188,562 (183,036, 97.1% liquid-based Pap tests) in the latter 3 years.

Surgical pathology specimens demonstrated the presence of endometrial malignancies in 160 women who had a Pap test performed within the previous 6 months, including 87 in the 3 years before the implementation of Bethesda 2001 and 73 in the 3 years after (Table II, Figure 1). This total includes 2 carcinosarcomas, 1 of which was preceded by a Pap test inter-

pretation of benign-appearing endometrial cells before the implementation of Bethesda 2001, whereas the other was preceded by an interpretation of adenocarcinoma under the Bethesda 2001 system. Some of the Pap tests during this 6-year period interpreted as AGUS, AGC, AIS or adenocarcinoma corresponded to squamous lesions, endocervical adenocarcinoma or carcinoma metastatic to the uterus. These cases have been excluded from the analysis. The grades and stages of the adenocarcinomas diagnosed following Pap tests including reportable glandular cells do not appear to have differed meaningfully between the 2 3-year periods (Table II).

The odds ratios for the discovery of endometrial carcinoma following a prior Pap test, before and after the implementation of Bethesda 2001, were calculated for each of the following interpretations: no reportable endometrial cells, benign-appearing endometrial cells, AGUS/AGC, and adenocarcinoma (Table III). We observed a statistically significant decrease in the frequency of a prior Pap test interpretation of benign-appearing endometrial cells and adenocarcinoma after the implementation of Bethesda 2001.

We used logistic regression analysis to determine the impact on the likelihood of diagnosing endometrial malignancies following a Pap test mentioning benign-appearing endometrial cells, as opposed to all other Pap test interpretations, for not only the 2001 Bethesda System, but also several confounding factors: conventional vs. liquid-based Pap testing, low-grade (FIGO I) vs. high-grade (FIGO II–III) tumors, interval to histologic diagnosis of < 1 month vs. > 1 month (30 days), and diagnoses made at the University of Minnesota vs. other Fairview sites (Table IV). Only the Bethesda System used to report Pap tests was statistically significant as an independent variable. There were 20 (23.0%) liquid-based Pap tests in women subsequently shown to have endometrial malignancy in the first 3-year period, compared with 71 (97.3%) liquid-based tests in the latter 3 years ($p < 0.001$).

In the 3 years following the implementation of Bethesda 2001, we compared the likelihood of finding

Bethesda, with Corresponding FIGO Grade and Stage

Total (staged)	After Bethesda 2001 (12/2002–11/2005)							
	Grade			Stage				
	1	2	3	1	2	3	4	
41 (30) ^a	23	10	8	26	0	3	1	
4 (4)	3	1	0	3	1	0	0	
20 (12) ^a	11	6	3	6	2	4	0	
8 (8)	0	2	6	3	0	5	0	

an endometrial malignancy following a Pap test report mentioning benign-appearing endometrial cells compared with the remainder of the population receiving cervical screening. Over that time, there were 91,385 Pap tests performed on women aged ≥ 40 years. Thus there were 4 adenocarcinomas found in 3,840 Pap tests mentioning benign-appearing endometrial cells, compared with 73 adenocarcinomas found in the entire screened population. There was not a statistically significant difference between these proportions (odds ratio 1.3, 95% CI 0.49–3.7, $p=0.58$).

The number of endometrial biopsies and curettings performed on women aged ≥ 40 years with benign-appearing endometrial cells reported on Pap tests was 72 in the 1-year period between December 1, 2001, and December 2, 2002. In the first year after the implementation of Bethesda 2001, from December 3, 2002, to November 30, 2003, the number of endometrial biopsies and curettings following a Pap test showing benign-appearing endometrial cells was 150, a 2.1-fold increase from the previous year.

Discussion

The essential finding of this study is that the changes in Pap test reporting of benign-appearing endometrial cells implemented as a result of the 2001 Bethesda System have not produced the desired outcome. We have not found an increase in the number of endometrial adenocarcinomas discovered in the screened population. On the contrary, despite a marked increase in the frequency of reporting endometrial cells, with a concomitant increase in the endometrial biopsy rate, the number of adenocarcinomas diagnosed in follow-up materials actually declined.

A few confounding factors need to be considered. The most obvious is the switch from conventional to liquid-based Pap testing that occurred during the time interval under study. Published reports indicate that liquid-based testing more readily allows differentiation of atypical from benign glandular cells.^{6,7} This finding would support the hypothesis that, as our specimens shifted from predominantly conventional

to almost entirely liquid-based, we would more readily classify cells shedding from endometrial malignancies as atypical rather than benign-appearing. This would mean that, regardless of the Bethesda System used for reporting, there would be an expected decline in the number of adenocarcinomas found following Pap tests containing only benign-appearing endometrial cells. Although our data do not support this hypothesis, both based on the results of the logistic regression analysis and the remarkable stability of the rate of reporting atypical glandular cells in Pap tests over the 2 time periods, we cannot completely rule out this possibility because the reporting according to the 2001 Bethesda System was highly related to liquid-based Pap tests in our data set.

We are currently working on a study meant to further clarify the implications of the shift to liquid-based Pap testing for glandular malignancies. In the context of this study, the available data seem to indicate no major role for this change in the explanation of our findings regarding endometrial malignancies.

The second confounding factor is the decline in the

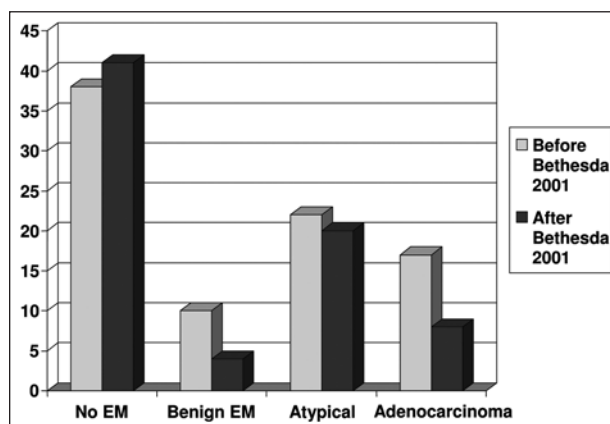


Figure 1 Change in frequency of Pap test interpretations preceding a histologic diagnosis of endometrial carcinoma before and after the implementation of the 2001 Bethesda System.

Table III Proportion of Papanicolaou Test Interpretations with Follow-Up Endometrial Carcinomas Before and After Implementation of the 2001 Bethesda System

Pap test interpretations	Before	After	OR (95% CI)	p Value
	Bethesda 2001 (12/1999–11/2002)	Bethesda 2001 (12/2002–11/2005)		
	Carcinoma (%)	Carcinoma (%)		
No. of endometrial cells	38/197,832 (0.019%)	41/178,870 (0.023%)	1.2 (0.77, 1.9)	0.43
Benign endometrial cells	10/589 (1.7%)	4/3,810 (0.1%)	0.06 (0.02, 0.20)	<0.001
AGUS/AGC ^a	22/315 (7.0%)	20/326 (6.1%)	0.87 (0.47, 1.6)	0.66
Adenocarcinoma ^a	17/30 (57%)	8/30 (27%)	0.28 (0.09, 0.82)	0.02

^aMany women with a Pap test interpretation of AGUS, AGC or adenocarcinoma had positive follow-up, including cervical or extrauterine carcinomas, not included in this study.

number of malignancies diagnosed and treated in the Fairview system, as shown by the overall decrease of endometrial malignancies from 87 to 73 over the 2 3-year periods. Although we have no clear explanation for this, it may be related to a change in the practice and referral patterns of gynecologic oncologists working at the University of Minnesota over the course of the 6 years we studied. Our data do not indicate, however, a substantial role for this change in the declining frequency of diagnosis of endometrial adenocarcinoma in women with Pap tests showing benign-appearing endometrial cells. Our logistic regression analysis of the role of University of Minnesota diagnosis, and interval to diagnosis, show statistically nonsignificant trends in the direction opposite that which would be expected if the gynecologic oncology practice patterns at the University of Minnesota explained our findings in regard to benign-appearing endometrial cells.

Potential confounding factors appear not to be sufficient to explain the decline in the number of endometrial malignancies diagnosed following a Pap test report mentioning benign-appearing endometrial cells. Our data indicate that the Bethesda 2001 recommendations have not had the desired effect, though the reason remains a matter of speculation. It is our hypothesis that the lack of clear recommendations for

the follow-up of benign-appearing endometrial cells reported in Pap tests is the likely explanation. Gynecologists and family practitioners do not have authoritative guidelines generated by their professional societies regarding this matter, leaving this issue to the discretion of individual practitioners. Based on our discussions with clinicians who send us Pap test specimens, many of them are confused as to why benign-appearing cells might indicate a risk for underlying malignancy, and as a consequence do not know the proper response to this finding. Based on our experience, a few clinicians frequently get endometrial biopsies and others repeat the Pap test. Most, however, appear to ignore the finding most of the time. This is not surprising, given the very low frequency with which endometrial cells on a Pap test corresponds to an underlying malignancy. We fear that increased frequency of reporting of benign-appearing endometrial cells has had the perverse and unintended effect of making many clinicians less inclined to follow up on the finding than before, especially because such cells are so often reported in young, menstruating women in whom there is no reason for suspicion.

What should pathologists do to make sure that the finding of benign-appearing endometrial cells on Pap tests leads to the greatest likelihood of finding occult

Table IV Logistic Regression Analysis of Pap Test Characteristics of Women Diagnosed with Endometrial Carcinomas Following a Report Mentioning Benign Endometrial Cells as Opposed to Any Other Interpretation, Over the Entire 6-Year Period

Pap test characteristics	Benign EM (n = 14)	All others (n = 146)	OR (95% CI)	p Value
Post-Bethesda 2001	4 (29%)	69 (47%)	0.23 (0.05, 0.99)	0.048
Liquid-based Pap test	9 (64%)	83 (57%)	3.1 (0.75, 12.7)	0.12
Grade 2 or 3	3 (21%)	71 (49%)	0.30 (0.08, 1.2)	0.09
Interval > 30 d ^a	11 (79%)	73 (50%)	2.8 (0.69, 11.2)	0.15
University of Minnesota ^b	5 (36%)	92 (63%)	2.0 (0.59, 6.9)	0.27

^aInterval refers to the delay between the Pap test and the histologic diagnosis of endometrial carcinoma.

^bUniversity of Minnesota refers to cases for which the diagnosis of endometrial carcinoma occurred at the University of Minnesota, the tertiary-care referral center for the Fairview Health System.

EM = endometrial malignancy.

adenocarcinomas without burdening the medical system or patients with excessive follow-up? In the past, we have recommended that clinicians should evaluate the presence of endometrial cells in the broader clinical context, proceeding to follow-up only in situations in which other factors contributed to a suspicion of pathology.⁸ Others have come to similar conclusions.^{9,10}

Interestingly, the only study with a design similar to ours that has been published to date, by Browne et al,⁹ found a slight, nonsignificant increase in the number of adenocarcinomas discovered after the implementation of the 2001 Bethesda System. Although there may be many explanations for the differences between the findings in this study and those of Browne et al,⁹ including differences in patient populations, we believe that they may also be related to differences in practice patterns of clinicians. The increase in the number of adenocarcinomas discovered after the implementation of Bethesda 2001 in the study by Browne et al⁹ could reflect a better understanding of the significance of benign-appearing endometrial cells found in Pap tests of women over age 40 by academic clinicians, working closely together within a single institution, that resulted in more consistent further evaluation of such women. This in turn would support the notion that better guidance in the form of national guidelines may lead to increased detection of asymptomatic and hopefully earlier stage endometrial carcinomas and decrease the number of unnecessary endometrial biopsies.

A recent review and commentary co-authored by one of the members of the committee that wrote Bethesda 2001 recommended that postmenopausal women with benign-appearing endometrial cells on a Pap test should have follow-up, such as transvaginal ultrasound or endometrial biopsy, whereas otherwise healthy menstruating women should not.¹¹ This seems both simple and reasonable. Similar guidelines have been proposed by other organizations¹² and will hopefully be part of the soon-to-be-published revised American Society for Colposcopy and Cervical Pathology (ASCCP) guidelines. The recent sharp decline in the number of women undergoing hormone replacement therapy has largely eliminated a major complicating factor. Our colleagues in gynecology, family practice and other specialties should be encouraged to adopt and disseminate this recommendation. In the meantime, pathologists should consider chang-

ing the standard comment to provide clearer information to clinicians regarding the response to benign-appearing endometrial cells. A standard comment such as "benign-appearing endometrial cells seen in a Pap test from a postmenopausal woman should prompt consideration of the possibility of endometrial adenocarcinoma" would, we believe, prove very helpful to our clinical colleagues.

References

1. Solomon D, Davey D, Kurman R, Moriarty A, O'Connor D, Prey M, Raab S, Sherman M, Wilbur D, Wright T Jr, Young N: The 2001 Bethesda System: Terminology for reporting results of cervical cytology. *JAMA* 2002;287:2114-2119
2. Ng AB, Reagan JW, Hawliczek S, Wentz BW: Significance of endometrial cells in the detection of endometrial carcinoma and its precursors. *Acta Cytol* 1974;18:356-361
3. Gondos B, King EB: Significance of endometrial cells in cervicovaginal smears. *Ann Clin Lab Sci* 1977;7:486-490
4. Cherkis RC, Patten SF Jr, Andrews TJ, Dickinson JC, Patten FW: Significance of normal endometrial cells detected by cervical cytology. *Obstet Gynecol* 1988;71:242-244
5. Yancey M, Magelssen D, Demazure A, Lee RB: Classification of endometrial cells on cervical cytology. *Obstet Gynecol* 1990;76:1000-1005
6. Guidos BJ, Selvaggi SM: Detection of endometrial adenocarcinoma with the ThinPrep Pap test. *Diagn Cytopathol* 2000;23:260-265
7. Schorge JO, Hossein Saboorian M, Hynan L, Ashfaq R: Thin-Prep detection of cervical and endometrial adenocarcinoma: A retrospective cohort study. *Cancer* 2002;96:338-343
8. Thrall MJ, Kjeldahl KS, Savik K, Gulbahce HE, Pambuccian SE: Significance of benign endometrial cells in Papanicolaou tests from women aged > or = 40 years. *Cancer* 2005;105:207-216
9. Browne TJ, Genest DR, Cibas ES: The clinical significance of benign-appearing endometrial cells on a Papanicolaou test in women 40 years or older. *Am J Clin Pathol* 2005;124:834-837
10. Bean SM, Connolly K, Roberson J, Eltoum I, Chhieng DC: Incidence and clinical significance of morphologically benign-appearing endometrial cells in patients age 40 years or older: The impact of the 2001 Bethesda System. *Cancer* 2006;108:39-44
11. Greenspan DL, Cardillo M, Davey DD, Heller DS, Moriarty AT: Endometrial cells in cervical cytology: Review of cytological features and clinical assessment. *J Low Genit Tract Dis* 2006;10:111-122
12. Institute for Clinical Systems Improvement: ICSI Health Care Guideline: Initial Management of Abnormal Cervical Cytology (Pap Smear) and HPV Testing. Bloomington, Minnesota, Institute for Clinical Systems Improvement, 2006