

# Results Of A Colposcopic Evaluation After A Repeated Papanicolaou Smear Demonstrating Atypical Squamous Cells Of Undetermined Significance (ascus)

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## Abstract

### Abstract

**Objective:** The management of patients who present atypical squamous cells of undetermined significance (ASCUS) on Pap smear remains controversial. Should a colposcopic evaluation be carried out immediately or should the Pap smear be repeated ? We chose to repeat the Pap smear after four to six months. If ASCUS were revealed by this second test, the patient was advised to undergo a colposcopic examination. The objective of this study was to determine the clinical significance and the prediction of neoplasia among these patients through a colposcopic examination.

**Patients and Method:** Between January 1996 and December 1997, a total of 29'827 patients underwent a Pap smear. ASCUS was diagnosed in 1'387 of them (5 %). A second Pap smear was proposed to these patients; 225/1'387 patients showed repeated ASCUS (16%). A colposcopy was performed on 186 /225 patients. Thirty-nine patients could not be included, because they refused the examination. All cytologic and histologic examinations were screened by the same laboratory.

**Results:** Colposcopy was normal in 91/186 patients (49%) and confirmed with a new Pap smear. Colposcopic examination was abnormal in 95/186 patients (51%), corresponding to 40 ASCUS (21%), 38 low-grade squamous intraepithelial lesions (L-SIL) (21%) and 17 high-grade squamous intraepithelial lesions (H-SIL) (9%). Among these latter 17 H-SIL, 3 carcinoma in situ (CIS) were found.

**Conclusion:** A colposcopic evaluation after a repeated Pap smear with ASCUS is an appropriate cost-effective management. Finding 30% of L-SIL or H-SIL justifies this additional investigation.

## INTRODUCTION

With the adoption of the Bethesda system in 1989, a new definition has emerged in cervical pathology : the borderline diagnosis termed as "atypical squamous cells of undetermined significance " (ASCUS) (1,2). The management of women with such cytologic modifications remains controversial (3,4,5,6,7,8). Moreover, a considerable increase in the incidence of ASCUS has been observed on Pap smear

(9,10,11,12). Commonly, the diagnosis of ASCUS occurs in up to 5 % of routine cervical cytologic smears (13,14,15,16). The clinical management of these patients is a complex gynecological problem as this group can present up to 20 to 30 % of low- (L-SIL) and high-grade squamous intraepithelial lesions (H-SIL) and up to 1 % of carcinoma in situ (CIS) (13,14,17,18,19). One option is to proceed with a colposcopic investigation of all these women after the first diagnosis of ASCUS, resulting in a large number of costly

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consultations (3,20,21,22,23,24). Another option is to repeat a Pap smear three to six months later and, if it is still abnormal, to perform a colposcopic evaluation (25,26). Following current guidelines, we chose the second option with a repeated Pap smear, knowing that a high percentage of ASCUS return to normal on the second Pap smear.

The purpose of this study was to determine the clinical significance and prediction of neoplasia among patients with a repeated ASCUS on Pap smears through colposcopic follow up.

### METHODS

Between January 1996 and December 1997, a total of 29'827 patients underwent a Pap smear (ThinPrep(r) Pap Test(tm)) in our institution (27). If ASCUS were diagnosed, the patients were reevaluated four to six months later with a repeated Pap smear. If ASCUS were reconfirmed, a colposcopic evaluation was proposed and the patients were included in the study. If the second Pap smear was normal, the patients were reexamined one year later. We did not use HPV DNA testing as an routine adjunct to abnormal Pap smear.

The colposcopic examination was performed with a Leica colposcope, after applying 3% acetic acid solution and painting with Lugol's solution. If the examination suggested any cervical abnormality, a driven biopsy was conducted. If no significant lesions were visible, a new cytologic smear was made. All cytologic and histologic specimens were screened by the same laboratory.

Standard demographic variables were entered prospectively into a computerized database. For each patient, the following information was recorded: Pap smears diagnosis, age, contraception use, sexually transmitted disease history, smoking history, parity, menopausal status, hormonal replacement therapy, description of the colposcopic examination and cervical biopsy result.

2 tests and Students' t tests were used to assess statistical significance in an univariate analysis as appropriate.

### RESULTS

ASCUS was diagnosed in 1'387 of 29'827 patients (5%) after the first Pap smear. A second Pap smear was proposed to these patients, but 225 patients (16%) could not be followed-up or refused to come back. Results of the distribution of the second Pap smear are presented in Table

1. The second Pap smear returned to normal in 787/1'387 patients (57%), whereas 225/1'387 patients (16%) showed repeated ASCUS. In the latter group, the remaining 186/225 patients (83%) underwent a colposcopic examination and were included in the study, whereas 39 patients (17%) refused it.

{image:1}

The mean age of the 186 patients was 33 years old (range: 16 to 76 years), 160 of which were premenopausal (86%). Thirty-three (18%) patients had a prior history of abnormal Pap smear and a prior history of colposcopic evaluation. Sixty-five women (35%) were smokers. The mean parity was 1.5 children (range: 0 - 4) and 74 / 186 (40%) were nulliparae. Among the 160 premenopausal patients, 94 (59%) were using hormonal contraception, 8 (5%) had undergone a prior tubal ligation and 9 (6%) had an intrauterine device. The remaining 49 patients (30%) were using barrier methods. Out of the 26 postmenopausal patients (14%), 13 were receiving hormonal replacement therapy.

Out of 186 colposcopic evaluations, 91 patients (49%) had normal evaluation, which was confirmed with a new Pap smear. The colposcopic examination was abnormal in 95 / 186 patients (51%) and confirmed by driven biopsy (Table 2). Histology revealed 38 L-SIL (21 %), 17 H-SIL (9 %), three of which being CIS. ASCUS was revealed for the third time in 40 patients (21%).

{image:2}

ASCUS: atypical squamous cells of undetermined significance, L-SIL: low-grade squamous intraepithelial lesion, H-SIL: high-grade squamous intraepithelial lesion.

All patients with H-SIL were treated by laser or LEEP conization five to seven months after the first Pap smear had demonstrated ASCUS. Seven of the 40 patients with ASCUS and 10 of the 38 patients with L-SIL preferred to be treated, whereas all others were followed by colposcopic evaluation at six-month intervals.

### DISCUSSION

The cytological diagnosis of ASCUS was found in 5% of the conventional Pap smears routinely performed. This incidence was similar to that of other studies (13-15). It has been claimed that the Thin Prep method lowers the percentage of borderline Pap smear diagnoses such as

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ASCUS and increases the percentage of more accurate Pap smears diagnoses such as squamous intraepithelial lesions (28,29). Opting to carry out a colposcopic evaluation only after repeated ASCUS on Pap smear allowed us to avoid a great number of colposcopic evaluations, as 787/ 1'387 cases of ASCUS (57%) returned to normal on the second Pap smear. This rate is slightly lower than in other series (13-18). In Switzerland, a colposcopy costs US \$113, whereas a routine Pap costs US \$ 20. Applying this strategy, we saved US \$ 73'453, did not overload our colposcopic consultation and reduced our waiting list. The disadvantage of this strategy is that we performed a second Pap smear on 150 / 1'387 cases who eventually did present L-SIL and therefore did require a colposcopy. We can consider that the time "lost" is not a significant factor, because the interval between the first Pap smear and the colposcopic examination or treatment was less than seven months. The additional cost of the second Pap smear is insignificant compared to the savings on the colposcopy amounting to US \$ 70'453 over a two-year period.

Our study has a lower percentage of normal results after colposcopic evaluation, 49%, as compared with other studies, whose normal results range between 55 and 81% (Table 2) (4,8,9,13,14,18,19,23,24). This could be partially explained by a higher percentage of repeated ASCUS (21%). Combining these percentages, a rate of 70% is found. It has been established that approximately 10 to 30% of ASCUS may present L-SIL or H-SIL, independently of the chosen strategy (13,14,17-19). We found a comparable rate of L-SIL and H-SIL: 21% of L-SIL versus 7 to 25% in other studies, and 9% of H-SIL compared to 4 to 17% (4,8,13,14,18,23,24,30). The risk of H-SIL, and especially CIS, among ASCUS cases cannot be ignored and justifies further aggressive evaluation. The incidence of carcinoma in situ or invasive cervical cancer among patients with ASCUS varies between 0.14 and 0.46% (30,31). We consider the delay of 5 to 7 months between the first Pap smear and the colposcopic treatment for the H-SIL patients to be reasonable and cost effective.

In order to determine a high-risk group, we compared 17 patients with H-SIL to 169 patients with ASCUS, L-SIL, or normal Pap smear (Table 3). No significant prognostic factors were found. Other authors have tried to define a risk group with different categories of ASCUS: reactive, premalignant or unqualified (14,17,32). However, the results were not conclusive and better criteria in the triage of

ASCUS patients are necessary. It will be interesting to include screening for human papillomavirus (HPV), the relationship of HPV to cervical neoplasia being well established (33,34). HPV typing will probably help to discriminate between low risk and high risk patients in order to treat the latter earlier (35,36,37,38,39). This option however must be proven of value in clinical practice (40,41).

{image:3}

ASCUS: atypical squamous cells of undetermined significance, L-SIL: low-grade squamous intraepithelial lesion, H-SIL: high-grade squamous intraepithelial lesion.

### CONCLUSION

Performing a colposcopic evaluation after a repeated Pap smear with ASCUS is appropriate, economical management. Immediate colposcopic evaluation is an expensive screening procedure, which may lead to excessive treatment and a greater psychological burden for the patient, as over 50% of the ASCUS returned to normal on a repeated Pap smear four to six months later. Our findings of 9% of H-SIL on colposcopic examination after a second Pap smear demonstrating ASCUS justifies additional investigation by colposcopy and aggressive treatment. In the future, patients with abnormal Pap smears will be screened for HPV. However, we still need to define at which positive threshold the triage will be cost-effective and at what point of the management the HPV screening would be carried out.

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