To the Editor

Barron et al present data and arguments for the introduction of a new category of cytologic interpretation of LSIL-H—low-grade squamous intraepithelial lesion (LSIL)/cannot rule out high-grade squamous intraepithelial lesion (HSIL)—into The Bethesda System (TBS) for reporting cervical cytologic diagnoses. They report that the percent of high-risk human papillomavirus (hrHPV) and the risk of cervical intraepithelial neoplasia grade 2 or 3 (CIN 2/3) for LSIL-H differed from other cytologic categories—greater than for LSIL and atypical squamous cells/cannot rule out HSIL (ASC-H) and less than HSIL. The decision to distinguish LSIL-H from other cytologic interpretations should be based on the answers to two key questions: (1) Does it improve patient care and outcomes? and (2) Is it a reliable cytologic category?

The answer to the first question is no. To improve patient care, the use of any test, measurement, diagnostic, or, in this case, reclassification should accompany a change in care. That is, either a group of patients are identified who are at lower risk such that they would receive less aggressive/invasive care or at higher risk that they would receive more aggressive/invasive care. However, with these cytologic classifications, including LSIL-H, all women would have a colposcopy, and only women with HSIL are at sufficiently high risk that, under specific circumstances, immediate treatment is warranted without histopathologic verification of CIN 2/3 or cancer. Therefore, there is seemingly no benefit to patients.

The answer to the second question is probably no. There are no studies of intra- or interrater agreement of LSIL-H or even ASC-H. In general, the interrater agreement of cytology is only fair, likely because of the lack of agreement for cytologic features that underlie those categorizations. However, we can learn about LSIL-H indirectly from its related cytologic category, ASC-H. In the analysis by Barron et al, the percent of hrHPV was 54.3% and the risk of CIN 2/3 was 17.2% for ASC-H, both significantly lower than previously reported. In fact, the LSIL-H in this analysis more closely resembles ASC-H in risk of CIN2/3 and percent hrHPV positive from those previous reports, suggesting that there is a continuous spectrum of morphologic features, between mild abnormalities of atypical squamous cells of undetermined significance (ASC-US) and LSIL at one end and severe abnormality of HSIL at the other, which are probably poorly distinguished and cannot be reliably divided into subgroups. And because of the rarity of LSIL-H (0.18%), it is unlikely that any cytopathologist will become practiced at making the call of LSIL-H reliably.

Therefore, given the (1) growing complexity of screening and management guidelines, (2) lack of benefit to patients, (3) the likely unreliability of the LSIL-H interpretation, and (4) the rarity of its occurrence (if it is a real, distinct entity), there seems little reason to introduce LSIL-H as a category in TBS. Cervical cytopathology does not need new categories of classification. It needs to make the current categories more reliable.

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References


The Authors' Reply
LSIL-H is not a new category, as we pointed out in our article1 by citing two dozen earlier publications on similar cytologic findings and by referring to often overlooked illustrations in the 2004 second edition of The Bethesda System atlas. These citations as well as our own study consistently have documented a risk for follow-up histopathologic CIN 2/3 that is intermediate between that for LSIL and HSIL; however, since no consensus follow-up recommendations were formulated in 2006 or 2012 follow-up guidelines, clinicians have at times been uncertain about appropriate clinical follow-up. Unfortunately, cytologic recognition of similar cases and use of this or similar terminology have become widespread in US cytopathology laboratories. The College of American Pathologists 2011 PAP Education and PAP Proficiency Testing supplemental questionnaire indicated that most respondents (80.9%) employ the term LSIL-H (unpublished data). We authored another report that documented how HPV detection rates after atypical squamous cells/cannot rule out HSIL vary when cytologic interpretations are those of a single reviewer as opposed to more restrictive consensus panel reviews.2 In our opinion, the most interesting detail of our histopathologic follow-up findings on 347 LSIL-H cases may be the absence of even a single case of invasive cervical carcinoma, especially when one compares follow-up data from HSIL cases, in which a 2% to 3% cervical carcinoma detection rate has been documented in several large studies.3,4 Absence of cervical cancer after LSIL-H cytologic findings also parallels our previous observation that confirmable LSIL cytologic findings are strikingly absent in Papanicolaou tests of women later developing cervical cancer.5 These observation could indicate that CIN 2/3 cases documented after either LSIL-H or LSIL are disproportionately nonprogressive intraepithelial lesions. If confirmed in additional studies, this could be a significant observation in cervical screening risk stratification. Visual observation-based methods such as cytopathology, histopathology, and colposcopy will always have inherent limitations associated with interobserver variability; however, the clinical power of these humble visual tools in the application of medical history’s most successful cancer screening test has been well documented in the medical literature.

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References


