Cytopathology and More | Managing abnormal screening results: highlights of new guidelines

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August 2013—The field of cervical cancer screening saw many developments in 2012. In April last year, the American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology published new guidelines for cervical cancer screening, most notably raising the age at which screening should begin, extending the interval between screening tests, and giving preference to simultaneous Pap and human papillomavirus co-testing in women ages 30 to 65.[1] Almost simultaneously, the U.S. Preventive Services Task Force published similar screening guidelines.[2] Then, in July, the CAP and ASCCP published the results of a joint project recommending a uniform Lower Anogenital Squamous Terminology (LAST).[3] Finally, in September the ASCCP led a consensus conference of 23 participating organizations to update guidelines for managing abnormal cervical cancer screening test results. In April of this year, these updated guidelines were published simultaneously in the *Journal of Lower Genital Tract Disease* and *Obstetrics and Gynecology*.[4,5]

After the new screening guidelines were published last year, it became clear that the 2006 guidelines for managing abnormal screening results needed to be updated accordingly. Given the shift in focus from cytology alone to a combination of cytology and HPV co-testing, the number of cytology-HPV-histology permutations that the management algorithms needed to address had increased several-fold. One option would have been to develop individual guidelines for every possible combination of test results, but that would have complicated the algorithms to such an extent that implementation would have become impractical, if not impossible. For this reason, in several instances different combinations of test results were grouped into the same management category. The common benchmark used to identify similar test result combinations that could be managed similarly was five-year risk for CIN 3 or worse.[6] Once it was determined that a certain combination of test results had a risk for CIN 3+ that was similar to the risk of a Pap result that already had a well-established management guideline, then the new test result combination could be managed similarly.

For example, the accepted management for a Pap diagnosis of low-grade squamous intraepithelial lesion (LSIL) has already been established to be referral to colposcopy, and data from the Kaiser Permanente Northern California (KPNC) database of nearly 1 million women showed that the five-year risk of CIN 3+ for a Pap diagnosis of LSIL is 5.2 percent. The KPNC data also showed that risk for a co-test result of HPV-positive ASC-US is similar, 6.8 percent. Based on the guiding principle of “equal management of equal risk,” it was therefore determined that referral to colposcopy is also the appropriate management for HPV-positive ASC-US.

The focus of the updated management guidelines is on more intensive screening and followup in women at the highest risk for developing CIN 2/3, as determined by their HPV status when co-testing is applied. As a corollary, the extended screening intervals and more conservative management in young women 21–24 years of age and in low-risk and HPV-negative women diminish the possibility that women will be subjected to unnecessary testing or therapy. What follows is a summary of the highlights of the recommendation changes. They do not include all of the changes referring to special populations and management of glandular changes. For more detailed information, the reader is referred to the guideline articles[4,5] and to the ASCCP Web site, www.asccp.org.

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Adequacy, including unsatisfactory cytology and cytology reported as absent or insufficient EC/TZ component. The first grouping of management recommendations address Pap test adequacy. If a Pap test is reported as unsatisfactory, a repeat cytology should be performed in two to four months. If the second, repeat Pap is also unsatisfactory, the recommendation would be for colposcopic evaluation. If co-testing of a cytologically

unsatisfactory Pap reveals high-risk HPV, then either repeat cytology in two to four months or colposcopy is acceptable.

Also related to adequacy is the absence of endocervical/transformation zone component in the Pap test. Women with absent or insufficient EC/TZ component do not have a higher risk for CIN 3+ compared with women with a satisfactory EC/TZ component and should therefore be managed similarly.

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Negative cytology with a positive HPV test. The new guidelines address management of co-testing in women ages 30 to 64. This has been confusing to clinicians, and the new parameters address discrepancies in the co-testing results. The largest category of these co-test results is that of negative cytology with a positive HPV test. In this group the recommendation is for repeat co-testing in one year. Colposcopy is recommended if the repeat HPV is positive or if the repeat cytology is ASC-US or above. When the repeat testing is cytology and HPV negative, repeat co-testing is recommended at a three-year interval. When the results of genotyping are available, colposcopy is recommended if HPV types 16 or 18 are positive and repeat co-testing at one year if 16/18 is negative.

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Atypical squamous cells of undetermined significance (ASC-US). The management guidelines address repeat screening in women with ASC-US based not only on their HPV status but also their age. Women 21 to 24 years are managed more conservatively with repeat cytology at one year if HPV positive and return to routine screening if HPV negative. HPV-negative LSIL in women 21 to 24 are also included in this group. Colposcopy is recommended only when repeat cytology is HSIL, ASC-H, or AGC or if cytology remains abnormal for 24 months at the second annual repeat. In this scenario young women with a repeat cytology of ASC-US or LSIL are not immediately colposcoped even if HPV positive. Management of women 25 to 29 remains unchanged.

In women over 30 the ASC-US cytology is managed somewhat differently. HPV testing is preferred in this age group. If HPV is positive, the ASC-US is managed the same as LSIL with colposcopic referral. If HPV negative, co-testing is repeated at an interval of three years. If HPV is not performed, repeat cytology at one year is an acceptable option.

Management recommendations at the one-year interval in the ASC-US over 30 age group have also been altered. When repeat cytology is performed at one year, any cytology diagnosis of ASC-US or worse, regardless of HPV result, would eventuate in colposcopy. This emphasizes the high-risk status of cytology results of ASC-H, HSIL, and AGC.

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LSIL on cytology. Management of LSIL has also been carved out into its own grouping with options more dependent on HPV correlations in the over 30 year olds and more conservative in women 21 to 24. For women over 30 with LSIL cytology and no HPV test or positive HPV test, colposcopy is recommended. However, the conservative option of co-testing at one year without colposcopy is preferred in women with HPV-negative LSIL. In women 21 to 24 with LSIL, followup cytology at one year is recommended. Colposcopy as an option is limited to women with ASC-H, HSIL, or AGC at one year or ASC-US + at two years.

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Post-biopsy management options. The recommendation changes post-biopsy are dependent on whether the colpo-histologic findings are preceded by lesser or greater abnormalities and require correlation for the algorithmic followup. When biopsy-proven LSIL (CIN 1) is preceded by a lesser abnormality such as ASC-US or LSIL, management is conservative with co-testing at one-year intervals. Women with biopsy-proven LSIL (CIN 1) preceded by ASC-H or HSIL cytology may have alternative tracks, including co-testing at one and two years or a diagnostic excisional procedure.

Women with LSIL (CIN 1) on endocervical sampling are managed according to the guidelines for CIN 1 and should not be considered as a “positive” ECC. Repeat endocervical sampling is recommended in one year. In this context only abnormal strips in the ECC which constitute findings of HSIL (CIN 2/3) or atypical endocervical glandular

epithelium would require a diagnostic excisional procedure.

More conservative management options are again recommended for younger women, even those with biopsy-proven HSIL (CIN 2/3). Here, treatment and observation are acceptable when colposcopy is adequate. Observation in this group is more frequent, at six-month intervals.

Essential changes from prior management guidelines are summarized in Box 1 of the published official ASCCP guidelines update4,5 and the reader is referred there for further study and review of the algorithm charts.

Only time will tell how successful the guidelines will be in balancing simplicity with precision in management. Although recommendations for more conservative management in younger women and in women with lower-grade lesions seem logical, the intricacies of the new algorithms with respect to index cytology, HPV status, age, and colposcopic correlation may be difficult to tease apart in advising patients and planning management. Widely differing intervals for followup among age groups and categories may lead to confusion, with some women being followed too frequently and others too late. Computerized algorithmic strategies may be helpful.

Interpretation of the new management guidelines may also be hampered by the failure to incorporate the new LAST recommendations. The guidelines do not fully embrace the LAST classification, and this raises the question whether the management guidelines will need to be rewritten to align more completely with the new histologic terminology. The disconnect may be a source of confusion to practitioners and pathologists.

Concern has also been expressed about how the extended screening intervals and variable followup intervals will affect the patient's return for routine screening and for followup of abnormal findings. Further complicating followup will be how physicians and practice groups manage the recall of women as their ages and status evolve over time. Great care will have to be taken and educational effort made to ensure that women understand the new call-back intervals with regard to cervical cancer screening and management of abnormal findings.n

References

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