Cervical Cancer Prevention

New Guidelines in the United States and New Opportunities for Low- and Middle-Income Countries

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KEYWORDS

• Cervical cancer prevention • Consensus conference • Cancer prevention
• Low- and middle-income countries

KEY POINTS

- New cervical guidelines in the United States focus on reducing unnecessary testing and bringing diagnostic terminology into line with current understanding of the natural history of human papillomavirus (HPV) disease.
- Implementation of new cervical screening and management guidelines will likely decrease the number of young women requiring colposcopy.
- As colposcopists see fewer cases, and as increasing immunization decreases the impact of HPV-16, the diagnostic skills of colposcopists will be challenged.
- In resource-poor countries, newer non–cytology-based tests offer the possibility of significantly reducing the burden of cervical cancer.

The events of the past 18 months may well signal a watershed for cervical cancer screening in the United States and also in low-resource countries. The changes wrought perhaps do not compare with 2006, when the first human papillomavirus (HPV) DNA vaccine was approved, but all of us will be practicing differently as a result of recent events.

March 2012 saw the publication of the recommendations of the November 2011 Consensus Conference sponsored jointly by American Cancer Society (ACS), the American Society for Colposcopy and Cervical Pathology (ASCCP), and the American Society for Clinical Pathology (ASCP).[1] These professional organizations for the first time recommended the use of cotesting, that is, screening with cytology and HPV testing, as preferable to screening with cytology alone in women aged 30 to 65 years. The US Preventive Services Task Force, in a coordinated release of publications, also

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recommended cotesting, but gave it equal weight to cytology.[2] Several months later the American College of Obstetricians and Gynecologists (ACOG), in its updated Practice Bulletin on cervical cancer screening, endorsed the ACS/ASCCP/ASCP recommendations.[3] Based on European and American studies, these professional organizations recommended screening intervals of 3 years for those women screened with cytology alone and 5 years when cotesting is used. Metaphorically speaking, this is the last nail in the coffin of the annual Papanicolaou (Pap) test. ACOG, while recognizing that annual cervical cytology screening in the United States population has the potential to lead to more harms than benefits, has reminded its members of the potential benefits of routine gynecologic visits independent of the Pap test.[4]

Also in March the ASCCP, in collaboration with the College of American Pathologists (CAP), convened the Lower Anogenital Squamous Terminology (LAST) Standardization Project consensus conference. Its purpose was to harmonize the nomenclature of HPV-associated squamous intraepithelial lesions across multiple tissues of the lower anogenital tract. Their recommendations were published in July 2012.[5] These recommendations will not have as much direct impact on clinicians as the new screening guidelines, but they will change the way biopsies of squamous tissues of the cervix, vulva, vagina, perianus, penis, and anus are interpreted and reported. These guidelines move from the accustomed 3-tiered nomenclature, intraepithelial neoplasia (-IN) grades 1, 2, and 3, to a 2-tiered terminology of low-grade or high-grade squamous intraepithelial lesion (LSIL, HSIL), similar to cytology. It has long been recognized that CIN 2 is a poorly reproducible diagnosis. The LAST guidelines recommend the use of the immunostain p16 to increase the reliability of determining which should be called LSIL and which HSIL. This recommendation has been controversial, especially as it relates to the potential for overuse of p16 and its impact on the management of young women with HSIL on biopsy.[6] Although there are no long-term studies evaluating the natural history of lesions that are morphologically called CIN 2, but are p16 negative, classification of equivocal high-grade lesions based on p16 staining has been shown to correlate well with interpretation on adjudicated histology review.[7] The LAST nomenclature will necessitate greater clinical skill in managing young women with HSIL on biopsy. The ASCCP Consensus Guidelines since 2006 have allowed for conservative management of CIN 2 and CIN 3, but have recommended treatment at a diagnostic threshold of CIN 3.[8] In the case of a diagnosis of HSIL not otherwise specified, young women can still be managed conservatively with semiannual cytology and colposcopy, so long as the transformation zone remains fully visualized, and the lesion is not large with widespread HSIL or becomes clinically more severe in appearance during the observation period.[6]

The first ASCCP Consensus Conference on the management of women with abnormal cytology and histology took place in 2001. Its recommendations[9] were updated in 2006 based on studies published in the intervening years.[8,10] In September 2012, relying largely on data from the extensive Kaiser Permanente of Northern California (KPNC) database, the management guidelines were again updated.[11] These new recommendations built on the previous ASCCP guidelines, but recognized that cervical cancer screening results will now include the outcomes of HPV tests for most women aged 30 years and older. The KPNC group has used cotesting and has maintained its database of outcomes since 2003.[11]

Primary prevention of HPV-related cancers is being adopted in many countries around the world. Australia and Great Britain, for example, have incorporated HPV vaccines in national immunization programs, and report that greater than 72% and 84% of 12- to 13-year-old girls, respectively, have received all 3 doses of vaccine. Mexico and Rwanda have also recently started a national HPV immunization program.