Human Papillomavirus Testing, Vaccination, and Gynecologic Screening

Fight or Flight?

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The implementation of cervical cancer screening programs beginning in the 1950s is largely credited with a more than 70% reduction in cervical cancer deaths in the United States. In the decades since the introduction of these programs, the annual or biennial Papanicolaou (Pap) test has gained widespread acceptance by patients and clinicians as part of required preventive health care for women. However, advances in knowledge of the pathogenesis of cervical neoplasia have resulted in more advanced and accurate testing modalities related to human papillomavirus (HPV) testing and, most recently, in the development of vaccines for the prevention of infection by the most common oncogenic types of HPV. The integration of these testing modalities and vaccines into patient care will have profound effects on the current and future practice of gynecologic cytopathology. Although the exact scope of these effects is not yet fully understood, the primary result, regardless of the technology, will most likely be a significant reduction in the number of Pap tests performed annually in the United States. Cytopathology professionals need to prepare for the outcomes of this evolution in cervical cancer prevention and patient management.

In 2002 and 2003, the American Cancer Society, the American College of Obstetrics and Gynecology, and the US Preventive Services Task Force each published revised guidelines for cervical cancer screening related to the onset, cessation, and frequency of Pap test screening. Although there is some variation among these guidelines, they can be summarized as follows:

1. Screening should begin 3 years after the onset of sexual activity or by the age of 21 years, whichever occurs first.
2. Cessation of screening can occur at the age of 65 or 70 years with documentation of 3 negative Pap test results within the preceding 10 years.
3. Screening should occur every 2 to 3 years; for women 30 years and older who have dual screening with the Pap test and HPV testing, a screening interval of 3 years is appropriate if the results of both tests are negative.
4. Screening is not recommended for women after hysterectomy, except in patients who had the procedure because of cervical neoplasia.

Even without new technologies, simple adherence to the current recommended screening guidelines would cause a decrease in Pap test volumes when compared with annual screening. Solomon et al. used data from multiple National Health Interview Surveys and the US Census Bureau to estimate Pap test volumes in the United States over time. They then analyzed those data and concluded that adherence to these guidelines with biennial Pap test screening for women 18 to 29 years old and triennial Pap test screening with high-risk HPV testing for women 30 years or older has the potential to reduce the total screening Pap test volume by half by 2010. Data analysis in an article by Eltoum and Roberson showed similar findings, with the conclusion that despite expected increases in the population of women eligible for Pap test screening, the total number of Pap tests performed will decline significantly.

The ASCUS-LSIL [atypical squamous cells of undetermined significance–low-grade squamous intraepithelial lesion] Triage Study (ALTS) trial data published in 2003 provided evidence of the clinical usefulness of high-risk HPV testing to triage equivocal Pap test results (atypical squamous cells of undetermined significance [ASCUS]) in lieu of immediate colposcopy or repeated Pap tests at specified intervals as management tools. Four years later, sales estimates of the Food and Drug Administration–approved Hybrid Capture II
HPV test (Digene, Gaithersburg, MD) suggest that 85% of ASCUS cases are currently triaged by high-risk HPV testing. The excellent negative predictive value of combined testing in ASCUS/HPV-negative cases eliminates the need for short-interval repeated Pap tests, which further reduces Pap test volumes. We are definitely seeing this trend in our laboratory at the University of Virginia Health System, Charlottesville.

However, achievement of these reductions is obviously dependent on the willingness of practicing clinicians and patients to adopt these recommendations. Adoption and compliance are not foregone conclusions. Many physicians raise concerns about changing the ingrained annual Pap test and physical examination that are mainstays of women’s preventive health care. If women are told they no longer need annual cervical cancer screening, will they still feel compelled to visit their physicians for other health monitoring? In addition, inappropriate use of HPV testing by not following recommended guidelines has the potential to add significantly to the cost of women’s health care. The duration of protection provided by the vaccines is not known.

The recent introduction of prophylactic HPV vaccines has the greatest potential to transform the practice of gynecologic cytology. The current vaccines completely protect against the most common oncogenic HPV virus types, HPV-16 and HPV-18, in unexposed adolescents and women. Because these viral types are associated with the development of approximately 70% of cervical cancers, full compliance with vaccination recommendations has enormous potential to reduce the incidence of cervical cancer by that amount. A second generation of vaccines that covers additional oncogenic types, which cause up to 90% of cervical cancer worldwide, is under development.

Although the full effects of cancer prevention with HPV vaccines and the shrinking role of cervical cancer screening will most likely not be seen for decades, there will be a significant impact on the frequency of abnormal test results much sooner because significant fractions of almost all abnormal Bethesda reporting categories are due to HPV-6, HPV-11, HPV-16, and HPV-18. Furthermore, other factors will influence the impact of vaccines. They include the following:

1. Controversy about mandatory vaccination for adolescent girls may slow implementation of vaccination programs. Despite strong advertising campaigns by vaccine manufacturers and political pressure in state legislatures, societal and cultural opposition remains.
2. Adolescents currently being vaccinated will not reach the “cervical cancer risk” age of 30 years or older for at least a decade.
3. Vaccines are not completely effective in women with established infections.
4. Currently available vaccines are not effective against HPV types responsible for 30% of cervical cancers.
5. The duration of protection provided by the vaccines is not known.

Until these issues are resolved, women will still need to be screened regardless of their vaccination status. How they will be screened—with HPV testing, by Pap test screening, or a combination—is yet to be determined. The likely focus on HPV testing as a primary screening tool would further reduce Pap test volumes for the laboratory because HPV testing is more sensitive and more predictive of outcome. For a thorough and thoughtful analysis into the possible effects of HPV vaccines on cytology and HPV testing, readers are referred to a recent article by Schiffman. The article includes discussion of scientific background on HPV and cervical cancer, HPV vaccines, and the potential effects of the vaccines on current screening programs.

The evidence is inescapable that a reduction of Pap test volumes will occur. How large the reductions will be and how soon they will occur are the only remaining questions. It is also clear that these shrinking volumes will have profound implications for the future operations of cytology laboratories and for cytotecnology training programs. Looking forward, managing these changes is the greatest challenge for cytology laboratory directors and managers and allied health educators in the next decades.

The article by Eltoum and Roberson in last month’s issue of the Journal provides insight into the potential impact of these new technologies on the cytology labor market. The authors used their previously published data on potential reductions in Pap test volumes to assess how the current and future cytotecnology workforce will be affected. Their conclusions, although not surprising, raise serious challenges for laboratory professionals practicing gynecologic cytology. Some of the challenges are as follows:

1. Adherence to the recommended screening guidelines will offset any potential Pap test volume increases owing to enlarging patient populations eligible for screening and will dramatically decrease the number of Pap tests performed annually.
2. Expansion of HPV testing and HPV vaccines will further reduce Pap test volumes in the coming decades.
3. Reduction in Pap test volumes will lead to reduction in the demand for cytotecnologists in the workplace.
4. Practicing cytotechnologists and cytology educators will have to adapt to these changing market forces to meet the demands of evolving laboratory practice. Despite reductions in the number of cytotechnology programs during the past decade and only a 76% occupancy rate for these programs, estimates of the number of cytotechnologists entering the workforce, if current rates continue, compared with historical separation rates, suggest an annual net growth of 1.6% per year. The vacancy rate for cytotechnologist positions, currently about 3%, has been declining since its peak in the early 1990s, a trend that is likely to continue. This is confirmed by the ASCP Board of Registry’s 2006 Annual Survey of Medical Laboratory Science Programs that indicates only 65% of cytotechnology students answering the survey got work in a laboratory, as compared with 97% to 100% for histotechnicians/histotechnologists, 89% for medical technologists, and 98% for pathologists’ assistants. Another factor in this equation is the aging of the cytotechnology workforce, which has the potential to accelerate historical separation rates and provide more balance to the number of cytotechnologists entering the workforce. Other technologies such as automated screening will also influence cytotechnology workforce needs.

The basic market forces of supply and demand are in action. As the volume of Pap tests decreases and the application of Pap testing changes, cytology practitioners (as cytotechnologists or by another name) will be required to focus on nongynecologic and fine-needle aspiration cytology and the expansion of molecular pathology. The workforce may be smaller but will require higher skill levels and additional training. This is the challenge for cytology practice in the coming decades. Some of these changes are already affecting many cytology laboratories; others will become more evident in the years to come. Laboratory directors, managers, and cytology educators face a balancing act in providing and retaining sufficient quality, skilled cytology practitioners to meet the current needs of the health care system while preparing the practitioners to shift their focus to nongynecologic cytology and molecular pathology as Pap test volumes shrink. The future is indeed challenging. We, as cytology practitioners, can choose to adapt and fight to establish a new role in the evolving process of cervical cancer prevention, or we can flee and leave the field to others.

References

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