



## New advances—and challenges— in cervical cancer screening

With their historic 1942 monograph on cytopathology, Papanicolaou and Trout sparked a revolution in the detection and treatment of cervical cancer. That document laid the foundation for the development and widespread use of the Papanicolaou (Pap) test for cervical cancer screening, which has reduced cervical cancer mortality by 70% in the United States. Few other major cancers have been so successfully constrained.

Now a second revolution is upon us, triggered by expanded use of liquid-based cytology and human papillomavirus (HPV) DNA tests. These tests came about largely due to new sampling techniques, as well as our clearer understanding of the central role HPV infection plays in the pathogenesis of cervical cancer. HPV is a family of more than 100 viruses, of which about 30 are sexually transmitted. About 13 of the HPV viruses are “high-risk” and associated with nearly all cervical cancers as well as some cases of vaginal, vulvar, and penile cancers.

### New screening guidelines

Most gynecologists recommend annual Pap tests for sexually active women of reproductive age, but some organizations have begun revising their screening guidelines. For example, the American Cancer Society recently updated its recommendations. While the previous guidelines allowed the provider and patient to decide what they wanted to do, the new guidelines, outlined below, are a bit more directive:

- Initiate Pap screening within 3 years of the start of sexual activity, but no later than age 21.

(The previous recommendation was no later than age 18.)

- Perform annual Pap testing up to age 30 if the traditional screening method is used, or biannual testing with liquid-based cytology.
- Screen the patient every 2 to 3 years after age 30, provided she has had 3 normal tests in a row.
- Testing may be unnecessary between the ages of 18 and 21, as well as in women over 70 with a history of normal smears.
- In special situations, such as cases of HIV or immunosuppression, annual testing remains the recommendation.

One of the organization’s goals was to reduce the cost of testing without compromising detection rates of high-grade cervical neoplasia and cancer.

### Combination test offers improved sensitivity

In April of this year, the US Food and Drug Administration approved the combination of liquid-based Pap and HPV DNA testing for all women after age 30. The reasoning? The conventional Pap test has a sensitivity of about 50%, while liquid-based cytology has a sensitivity of 70% to 80%. HPV DNA testing—first approved in March 2000 to help guide the approach to women with a Pap test demonstrating atypical squamous cells of unknown significance—has a sensitivity of 85% to 95%. By combining the liquid-based Pap and HPV DNA tests, the clinician can achieve a sensitivity close to 100%.

With this combined test, the interval between cervical screening exams could

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extend even further: Given the long transit time from HPV infection to cervical neoplasia, it is likely that once every 3 years would suffice.

### **A new challenge for gynecologists**

If the combined test takes hold, the practice of obstetrics and gynecology could be altered forever. Patients have been well educated that they need to return every year for a health examination, in part because of the need for an annual Pap test. With the trend toward lengthening the screening interval for various women, many patients may be inclined to skip their annual health examination altogether. In other words, if women believe they need a combined HPV and Pap test only every 3 years, they may be reluctant to see their gynecologist in the intervening period.

Thus, although the new recommendations make sense for cervical cancer detection and treatment, they don't convince women of the continued need for annual examinations. That challenge falls to us.

### **Another revolution on the horizon**

Many years in the future, a third revolution is likely—one that involves population-based vaccination for high-risk HPV subtypes. Such a strategy is sorely needed in countries where access to cervical cancer screening and treatment is extremely limited. Although the rate of cervical cancer has been markedly reduced in many developed nations, the disease remains pervasive in poorer countries. Effective polyvalent HPV vaccines will be especially valuable in these settings. In fact, this coming revolution should be one of the great advances in women's health worldwide and should forever change the practice of gynecology. ■



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