

Spotlight on Health

Cervical Cancer Screening

The introduction of the Pap test to screen for cervical cancer has dramatically reduced the number of deaths from the disease. This test has been the gold standard for cervical cancer screening for many decades. Since the discovery that the human papillomavirus (HPV) causes the majority of cervical cancer cases, DNA- and mRNA-based HPV tests have also become available. They are now used to complement the Pap test.

In this newsletter, we'll review screening options for cervical cancer and look at the benefits of co-testing (a Pap test *plus* an HPV test). We'll also review how co-testing coincides in with cervical cancer screening guidelines.

Cervical Cancer Screening Saves Lives

Cervical cancer used to be the number 1 cause of cancer death in women. But the use of the Pap test to screen for cervical cancer has significantly decreased the number of women who develop cervical cancer and those who die from the disease.¹ The Pap test detects abnormal precancerous cells (CIN, cervical intraepithelial neoplasia). Screening for cervical cancer with the Pap test is very effective because, in most cases, precancerous cells take years to undergo malignant transformation.

In contrast to Pap testing, HPV testing detects the presence of the HPV virus. The presence of high-risk HPV genotypes markedly increases the risk of cervical cancer.² Early HPV tests were DNA-based; they looked for the presence of HPV DNA. Subsequently, E6 and E7 oncoproteins were identified, and E6/E7 mRNA HPV testing was introduced.³ The cervical cancer screening test, HPV mRNA E6/E7, detects for the presence and activity of HPV infection.³ Testing for HPV mRNA has similar sensitivity for detecting CIN as DNA testing. However, it has significantly greater specificity, which can reduce the false-positive rate.²⁻⁴

Benefits of Co-testing

Co-testing means performing a Pap test plus an HPV test. Co-testing every 5 years has several benefits compared with Pap testing alone every 3 years⁵:

- Increased sensitivity for grade 3 CIN (CIN3)
- Lower subsequent risk of CIN3 or higher (CIN3+) and cancer following a negative HPV result
- Increased detection of cervical adenocarcinoma

Co-testing also improves the detection of adenocarcinoma of the cervix relative to Pap testing alone.⁶ This is important, as the incidence of adenocarcinoma has been increasing.⁷

The benefits of co-testing were shown in a 2015 study that looked at data in 3 ways: single Pap result, single HPV result, and co-test result.⁶

Co-testing was the most sensitive of the 3 for detecting precancer (CIN3+):

- Pap only: 91% sensitivity
- HPV only: 94% sensitivity
- Co-testing: 99% sensitivity



Risk Factors for Cervical Cancer¹⁰

- Smoking
- HIV infection
- Some immunosuppressive medications
- Past or present sexually transmitted infection (chlamydia)
- Diet low in fruits and vegetables
- Being overweight
- Long-term use of oral contraceptives
- Never having used an intrauterine birth control device
- 3 or more full-term pregnancies
- Age younger than 17 at first full-term pregnancy
- Family history of cervical cancer

Co-testing also missed the fewest cases of cancer. Of the cervical cancers detected in the study:

- 5.5% were co-test negative
- 12.2% were Pap-only negative
- 18.6% were HPV-only negative

Screening Guidelines Include Co-testing

The most recent American College of Obstetricians and Gynecologists (ACOG) cervical cancer screening guidelines reiterate that co-testing is preferred to screen women 30 to 65 years of age.⁵

ACOG 2016 Cervical Cancer Screening Guidelines⁵

Age (years)	Recommended Screening
<21	No screening
21 to 29	Pap test every 3 years
30 to 65	Pap test + HPV co-testing every 5 years (preferred) or Pap test every 3 years
>65	No screening (if low cancer risk) ^a

^a 3 consecutive negative Pap tests or 2 consecutive negative co-tests within the last 10 years, with the most recent test within the past 5 years.

How the Laboratory Can Help

Quest Diagnostics offers a selection of tests for cervical cancer screening. ThinPrep[®] and SurePath[™] liquid-based cytology assays are available. Liquid-based cytology is more effective at detecting CIN and adenocarcinoma of the cervix than a conventional Pap smear.⁸ ThinPrep is preferred due to superior specimen stability, and offers more time to conduct additional tests such as for HPV.⁹ HPV E6/E7 mRNA testing, co-testing, and HPV genotyping are also available. Information about these tests can be found on the Quest Diagnostics [Test Center](#).

Quest also offers panels that combine cervical cancer screening with screening for certain common sexually transmitted infections (STIs). More information on these tests can be found at QuestDiagnostics.com/SMARTcodes.

References

1. Cervical cancer statistics. Centers for Disease Control and Prevention website. <http://www.cdc.gov/cancer/cervical/statistics/>. Updated June 7, 2017. Accessed February 2, 2018.
2. Monsonego J, Hudgens MG, Zerai L, et al. Evaluation of oncogenic human papillomavirus RNA and DNA tests with liquid-based cytology in primary cervical cancer screening: the FASE study. *Int J Cancer*. 2011;129:691-701.
3. Szarewski A, Ambroisine L, Cadman L, et al. Comparison of predictors for high-grade cervical intraepithelial neoplasia in women with abnormal smears. *Cancer Epidemiol Biomarkers Prev*. 2008;17:3033-3042.
4. Aptima [package insert]. San Diego, CA: Hologic, Inc; 2015.
5. The American College of Obstetricians and Gynecologists. Practice bulletin no. 168: cervical cancer screening and prevention. *Obstet Gynecol*. 2016;128:e111-e130.
6. Blatt AJ, Kennedy R, Luff RD, et al. Comparison of cervical cancer screening results among 256,648 women in multiple clinical practices. *Cancer Cytopathol*. 2015;123:282-288.
7. Castanon A, Landy R, Sasieni PD. Is cervical screening preventing adenocarcinoma and adenosquamous carcinoma of the cervix? *Int J Cancer*. 2011;139:1040-1045.
8. Haghighi F, Ghanbarzadeh N, Ataee M, et al. A comparison of liquid-based cytology with conventional Papanicolaou smears in cervical dysplasia diagnosis. *Adv Biomed Res*. 2016;5:162.
9. ThinPrep 2000 System [package insert]. Marlborough, MA: Hologic, Inc; 2017.
10. What are the risk factors for cervical cancer? American Cancer Society website. <https://www.cancer.org/cancer/cervical-cancer/causes-risks-prevention/risk-factors.html>. Accessed February 2, 2018.

QuestDiagnostics.com

Quest Diagnostics Incorporated and its subsidiaries (Quest) complies with applicable federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. ATTENTION: If you speak **English**, language assistance services, free of charge, are available to you. Call 1.844.698.1022. ATENCIÓN: Si habla **español** (Spanish), tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 1.844.698.1022. 注意：如果您使用繁體中文 (Chinese)，您可以免費獲得語言援助服務。請致電 1.844.698.1022。

Quest, Quest Diagnostics, any associated logos, and all associated Quest Diagnostics registered or unregistered trademarks are the property of Quest Diagnostics. All third-party marks—® and ™—are the property of their respective owners. © 2018 Quest Diagnostics Incorporated. All rights reserved. SH7502 3/2018