2013 statement on human papillomavirus DNA test utilization

Diane Davis Davey, MD, Diane Davis Davey, MD, Ritu Nayar, MD

February 2014—The Cytopathology Education and Technology Consortium in 2009 issued a statement on human papillomavirus DNA test utilization that was published in multiple journals.1 This statement was a concise summary of the clinical indications for high-risk or oncogenic HPV testing based on guidelines of the American Society for Colposcopy and Cervical Pathology and the American Cancer Society published from 2002 through 2007.2,3 These organizations have since published newer consensus guidelines addressing HPV testing,4,5 and the previous summary no longer reflects current screening and management guidelines.

High-risk HPV testing has proven utility in cervical cancer screening and management. The 2012 screening guidelines endorsed by the ACS, ASCCP, and American Society for Clinical Pathology state that combined cervical cytology and HPV testing is now the preferred strategy for women age 30 and older. The 2012 ASCCP guidelines for management of abnormal cervical cancer screening tests and cancer precursors use co-testing extensively as a sensitive and efficient way to manage and follow these women. Inappropriate or too frequent screening, including HPV testing, can lead to increased costs without proven benefit and may cause patient harm by overtreatment. The following educational statement is intended to improve adherence to current guidelines, thereby improving the health care of women. The American Congress of Obstetricians and Gynecologists affirms these recommendations, and the U.S. Preventive Services Task Force says co-testing is acceptable.6,7

1. High-risk (oncogenic) HPV DNA testing is appropriate in the following circumstances.

   1.1 Routine cervical cancer screening in conjunction with cervical cytology (co-testing) for women ages 30–65 years. (For women ages 30–65 with cytology reported as absent or insufficient endocervical/transformation zone component, early repeat cytology is not indicated and co-testing is preferred.)

   1.1.1 For women whose cytology and HPV results are both negative, repeat both tests only after a five-year interval (applies only to routine screening; for women with negative co-tests following previous abnormal cytology, see below).
**Fig. 1.** Cell color indicates if HPV testing (or co-testing) is preferred (green), acceptable but not preferred (yellow), or not appropriate (red). Numbers in table cells refer to the text outline. Appropriate uses of human papillomavirus testing and co-testing (Papanicolaou test with HPV) are shown (A) in routine screening and triage, (B) as surveillance after abnormal Pap/HPV-positive (+) findings without colposcopy, (C) after colposcopy, and (D) after treatment. UNSAT indicates an unsatisfactory Pap test; ASC-US, atypical squamous cells of undetermined significance; LSIL, low-grade squamous intraepithelial lesion; ASC-H, atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion; AGC, atypical glandular cells; HSIL, high-grade squamous intraepithelial lesion; NILM, negative for intraepithelial lesion or malignancy; -, negative; CIN, cervical intraepithelial neoplasia. (a): For AGC results, HPV testing is not recommended as a triage tool; however, a negative HPV test may be helpful in suggesting endometrial versus endocervical origin. Co-testing is recommended at 12 and 24 months post-colposcopy. (b): For women 30 and older who are both cytology and HPV negative, repeat both tests only after a five-year interval. (c): For women 30 and older, HPV testing is preferred as a co-test, with repeat co-testing at one year if HPV is negative. HPV testing may be ordered as a triage for LSIL in postmenopausal patients. (d): NILM/HPV+: Repeat both tests in one year (or perform HPV genotyping). Colposcopy is recommended if HPV positive on repeat regardless of cytology result.

<table>
<thead>
<tr>
<th>Age</th>
<th>Routine Screening</th>
<th>Triage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>UNSAT</td>
<td>ASC-US</td>
</tr>
<tr>
<td>21-24</td>
<td>2.1</td>
<td>2.5</td>
</tr>
<tr>
<td>25-29</td>
<td>2.1</td>
<td>2.5</td>
</tr>
<tr>
<td>30+</td>
<td>2.1</td>
<td>2.5</td>
</tr>
</tbody>
</table>

For women whose cytology results are negative and HPV test is positive, repeat both tests in one year or do HPV 16/18 genotyping; women with HPV 16/18 positive results are referred for colposcopy.

Initial triage management of women 25 years and older with a cytology result of atypical squamous cells of undetermined significance (ASC-US). Triage management is acceptable for women ages 21-24, but repeat cytology at 12
months is preferred.

1.3 Follow-up co-testing of women 25 years and older with preceding HPV negative ASC-US at three years per ASCCP management guidelines5,8 or at five years according to 2012 ACS/ASCCP/ASCP screening guidelines.(4)

1.4 Initial triage management of women ages 30 years and older with low-grade squamous intraepithelial lesion (LSIL), generally when performed as part of a screening co-test. In postmenopausal patients, HPV testing may be ordered as a triage for LSIL. If the HPV result is negative in either age group, repeat co-testing at 12 months is recommended.

1.5 Post-colposcopy co-testing, at 12 months, for women 25 years and older, with either no lesion or cervical intraepithelial neoplasia (CIN) 1 and with a preceding “lesser” cytology result (ASC-US, LSIL, negative cytology with HPV 16+ or 18+ or persistent HPV infection).

1.6 Post-colposcopy co-testing of women 25 years and older at 12 and 24 months, in those with no lesion or CIN 1 when the preceding cytology result was a high-grade squamous intraepithelial lesion (HSIL), or atypical squamous cells, cannot exclude HSIL (ASC-H).

1.7 Post-colposcopy co-testing of women 21 years and older at 12 and 24 months, in those with no lesion or CIN 1 on colposcopy and preceding cytology result of atypical glandular cells, not otherwise specified (AGC, NOS).

1.8 Follow-up co-testing of women 30 years and older at three years following previous negative co-test results with various preceding cytology abnormalities and no evidence of a high-grade lesion on colposcopy. An example is a woman with LSIL, CIN 1 on biopsy and negative co-test at 12 months; see 2012 ASCCP algorithms for more detail.(5)

1.9 Post-treatment co-testing surveillance of women 25 years and older at 12 and 24 months (and then three years later) with treated CIN 2 and 3. See 2012 ASCCP algorithms for details on women ages 21-24.(5)

2. High-risk (oncogenic) HPV testing is generally not appropriate in the following situations:

2.1 Routine cervical cancer screening in women younger than 30 years.

2.2 Routine cervical cancer screening with co-testing more often than every five years when previous co-test results were negative (and no prior abnormality).

2.3 Initial triage or management of women younger than 25 years with any cytologic abnormality (HPV triage is acceptable for ASC-US, but repeat cytology is preferred).

2.4 Initial triage or management of women younger than 30 years with LSIL.

2.5 Initial triage or management of a woman any age with unsatisfactory cytology, ASC-H, HSIL, or atypical glandular cells of any type.

3. Repeat high-risk HPV testing should generally not be done before 12 months.

4. There is currently no evidence-based guideline recommending HPV genotyping as a management tool in women with abnormal cytology results such as ASC-US.

5. Testing for low-risk (non-oncogenic) HPV types has no role in cervical cancer screening, or in the triage, management, or followup of women with abnormal cytology results.

The intent of this summary is to facilitate provider education and to encourage the appropriate use of HPV testing. Clinical judgment should always be used when applying a guideline to an individual patient because it is impossible to develop guidelines that will apply to all situations.

References


3. Wright TC, Massad LS, Dunton CJ, Spitzer M, Wilkinson EJ, Solomon D, for the 2006 American Society for Colposcopy and Cervical Pathology-sponsored Consensus Conference. 2006 consensus guidelines for the...


---

**Dr. Davey, Dr. Goulart, and Dr. Nayar wrote the preceding statement on behalf of the Cytopathology Education and Technology Consortium. CETC member organizations include the CAP, American Society of Cytopathology, American Society for Clinical Pathology, American Society of Cytopathology, International Academy of Cytology, and Papanicolaou Society of Cytopathology. The authors thank Teresa Darragh, MD, Debbie Saslow, PhD, Mark Schiffman, MD, MPH, Diane Solomon, MD, and Mark Stoler, MD, for their review of the manuscript.**

Dr. Davey is assistant dean of graduate medical education and a professor of pathology, Department of Clinical Sciences, University of Central Florida College of Medicine and Orlando Veterans Affairs Medical Center, Orlando, Fla. Dr. Goulart is director of cytopathology services, New England Pathology Associates, PC, and LifePath Partners, LLC, Mercy Medical Center, Springfield, Mass. Dr. Nayar is a professor of pathology, Department of Pathology, Northwestern University Feinberg School of Medicine, Chicago, and director of the Cytopathology Division, Northwestern Medicine. Direct correspondence to her at r-nayar@northwestern.edu.