

Human papillomavirus

HPV OFTEN RECOGNIZED AS A NECESSARY FACTOR FOR THE DEVELOPMENT OF CERVICAL CANCER

FOR TECHNICAL INFORMATION, CONTACT:

■ Martha Bale, M.S., MT(ASCP)
Group Manager
Infectious Diseases
(801) 583-2787 x2236
(800) 242-2787 x2236

■ Rick Aldeen, M.B.A., M(ASCP)
Technical Supervisor
Microbial Antigen Detection
(801) 583-2787 x2726
(800) 242-2787 x2726

FOR SCIENTIFIC AND CLINICAL INFORMATION, CONTACT:

■ Gail L. Woods, M.D.
Medical Director
Infectious Diseases
(801) 583-2787 x2337
(800) 242-2787 x2337

■ Cathy A. Petti, M.D.
Medical Director,
Infectious Diseases
(801) 583-2787 x3174
(800) 242-2787 x3174

ARUP Laboratories
500 Chipeta Way
Salt Lake City, UT 84108
(800) 242-2787
(801) 583-2787
Reorder Number: 1417.04
www.aruplab.com
February 2004

Introduction

Over 100 genotypes of HPV have been identified based on DNA sequence heterology. Of the types described, a specific group, termed high-risk genital HPV types (especially 16, 18, 31, 45, and 58, but also 33, 35, 39, 51, 52, 56, 59, 68, 73, 82), are recognized as a necessary factor for the development of cervical cancer. However, most women infected with high-risk genital HPV, especially women <30 years of age, do not develop cervical cancer; their immune response effectively clears the infection over the course of several months. Specific factors that determine which HPV infections persist and develop into squamous intraepithelial lesions currently are unknown. Cigarette smoking is a possible cofactor, and in some women, compromise of the immune system appears to be involved.

Clinical Significance

Cervical screening with the Papanicolaou test (Pap smear) has been the mainstay of cervical cancer prevention for several decades. Of the approximately 50 million women in the United States who undergo cytologic screening annually, about 7% (3.5 million) have an abnormality that requires further evaluation. In 2002, consensus guidelines for management of women with cervical cytological abnormalities were published (Wright, et al., 2002). Recommendations for managing the group of women with atypical squamous cells of undetermined significance (ASC-US) include repeat Pap smear, colposcopy, or DNA testing for high-risk HPV genotypes. If liquid-based cytology is used or co-collection for HPV DNA testing is possible, reflex HPV DNA testing is preferred.

Appropriate Use of Test

Analysis of data from a large (>23,000 women) natural history study of HPV infection showed that the negative predictive value of combined HPV testing (using the Hybrid Capture 2 [HC2] HPV DNA test, Digene Corp., Gaithersburg, MD) and cytologic screening was 99% for development of cervical intraepithelial neoplasia (CIN3, a precursor to cervical cancer) or cancer (Sherman, 2003). In March 2003, the FDA approved the HC2 HPV DNA test to be used for screening, in conjunction with the Pap smear, of women over age 30

years for HPV infection. In August 2003, the American College of Obstetrics and Gynecology issued updated clinical management guidelines for obstetrician-gynecologists. These revised guidelines state that the combination of Pap smear and HPV DNA screening is appropriate for women aged ≥ 30 years; and if results are negative on both tests, women should be rescreened no more often than every 3 years.

Laboratory Diagnosis and Methodology

Currently, the HC2 HPV DNA test is the only commercial FDA-approved molecular test for detection of genital HPV in women. Of the liquid-based cytologic media available, only the Cytoc ThinPrep® Pap Test™ PreservCyt® Solution is FDA-cleared for testing with the HC2 HPV DNA test. Using liquid-based media for HC2 testing can be problematic. Not infrequently, the volume of liquid-based medium remaining after processing for cytological testing is insufficient to test for HPV with the HC2 assay. Minimum volumes for HC2 HPV testing are 4 mL for PreservCyt® and 2 mL for SurePath™ AutoCyte; if a lesser volume is submitted, the sample will be rejected. Additionally, there are problems with reproducibility for specimens with low-positive HPV results (Chapin, et al., 2003). If HPV testing is being used for primary screening, a positive HPV result from a liquid Pap medium with a normal Pap smear may merit confirmatory HPV testing of a sample collected in Digene Standard Transport Medium to rule out a false positive HPV result. For these reasons, co-collection using both a liquid-based cytology solution **and** the HPV standard transport medium is preferred. SurePath™ AutoCyte specimens will carry the ARUP compliance statement B (in-house validation).

The FDA recently approved changes to the Digene HPV HC2 assay that include repeat testing of samples that initially yield low-positive results. Instituting these changes should considerably reduce the number of equivocal results reported. However, if the sample volume received is insufficient for all required repeat testing, it will not be possible to resolve the HPV status without testing a new sample, preferably collected in the Digene Standard Transport Medium. When HPV status cannot be determined due to insufficient sample volume, a result of indeterminate will be reported.

REFERENCES

- ACOG Practice Bulletin. Clinical management guidelines for obstetrician-gynecologists. Number 45, August 2003.
- Chapin K, et al. Reproducibility of low-positive HPV results using the Digene Hybrid Capture II assay. Abstracts of the American Society of Cytopathology, Scientific Session of the 51st Annual Scientific Meeting, November 2003.
- Sherman ME et al. Baseline cytology, human papillomavirus testing, and risk for cervical neoplasia: a 10-year cohort analysis. *J Natl Cancer Inst* 2003; 95:46-52.
- Stoler MH. Human papillomavirus biology and cervical neoplasia: implications for diagnostic criteria and testing. *Arch Pathol Lab Med* 2003; 127:935-9.
- Wright TC et al. 2001 consensus guidelines for the management of women with cervical cytological abnormalities. *JAMA* 2002;287:2120-9.

Test Highlights

0065999 Human Papillomavirus (HPV) DNA Probe, High Risk Only HPV-HI

For test information, please see the ARUP User's Guide.

RELATED TEST

0060049 Human Papillomavirus (HPV) DNA Probe, High- & Low-Risk Groups HPV HL

MEDICARE COVERAGE OF LABORATORY TESTING

Please remember when ordering laboratory tests that are billed to Medicare/Medicaid, or other federally-funded programs, the following requirements apply:

1. Only tests that are medically necessary for the diagnosis or treatment of the patient should be ordered. Medicare does not pay for screening tests, except for certain specifically approved procedures, and may not pay for non-FDA approved tests or for those tests considered experimental.
2. If there is reason to believe that Medicare will not pay for a test, the patient should be informed. The patient should then sign an Advance Beneficiary Notice (ABN) to indicate that he or she is responsible for the cost of the test if Medicare denies payment.
3. Effective January 1, 1998, the ordering physician must provide an ICD-9 diagnosis code or narrative description, if required by the local fiscal intermediary or carrier.
4. Organ- or disease-related panels should be billed only when all components of the panel are medically necessary.
5. Both ARUP- and client-customized panels should be billed to Medicare only when every component of the customized panel is medically necessary.
6. Medicare National Limitation Amounts for CPT codes are available through CMS or its intermediaries. Medicaid reimbursement will be equal or less than the amount of Medicare reimbursement.

The CPT codes for the tests profiled in this test bulletin are in the "Test Highlights" section. The codes reflect ARUP's interpretation of CPT coding requirements, based upon AMA guidelines. CPT codes are provided only as guidance to assist you in billing. ARUP strongly recommends that clients reconfirm CPT code information with their local intermediary or carrier. CPT coding is the sole responsibility of the billing party. Also, if you have further questions regarding the appropriate use of any test, please contact ARUP's Client Services Department.

The regulations described above are only guidelines. Additional procedures may be required by your local intermediary or carrier.