

Following a multidisciplinary consensus conference held in Bethesda, Maryland in September 2006, the American Society for Colposcopy and Cervical Pathology (ASCCP) will issue a revision of the 2001 Guidelines for the Management of Cytological Abnormalities and Cervical Intraepithelial Neoplasia with publication anticipated by mid-summer 2007.¹ NPWH was among the nearly 30 national and international medical organizations and Federal agencies represented at the conference. The new ASCCP consensus guidelines reflect evidence-based advances in our understanding of the natural history of human papilloma virus (HPV), its influence on the development of cervical dysplasia and cancer, and the role of Pap tests with a liquid based sample. The guidelines also address the use of HPV DNA testing along with the Pap for primary screening of women 30 and older. This document provides a preliminary summation of the guidelines and the endorsement of NPWH.

Worldwide, HPV is the most common sexually transmitted infection (STI).² Most women will become infected at some point during their lifetime. The majority of women will clear HPV within 24 months with a median time to clearance of 8-9 months. Persistent high risk HPV (most commonly type 16 or 18) is the causative factor for cervical dysplasia and cervical cancer. The peak age for HPV infection occurs in the mid 20's while the peak incidence of cervical cancer is between the ages of 40-55. In the United States, cervical cancer is now a relatively rare occurrence occurring only when high risk types of HPV persist and are not cleared by a natural immune response.

HPV DNA Testing

Currently, only one testing method (Digene® HPV Test* using Hybrid Capture® 2 (hc2) technology) is FDA approved for screening of the 13 clinically-relevant high risk HPV types.³ This test does not screen for low-risk HPV types, none of which are utilized in management algorithms. Screening for low-risk HPV types is not recommended. The test may be performed using the liquid based cytology sample or co-collected in a separate tube by sampling the endocervical canal after the Pap sample is taken.

ASC-US Reflex HPV DNA Testing - Appropriate for Women of all Ages

An option for management of an ASC-US Pap (atypical squamous cells of undetermined significance) is reflex HPV DNA testing to determine whether HPV is present and if referral for colposcopy is indicated. It is appropriate to test women of all ages with ASC-US (borderline or equivocal) Pap results for HPV. Liquid based Pap samples can be tested immediately for HPV if there is an ASC-US result obviating the need for a return visit. Women with an ASC-US Pap who test positive for HPV should be advised to have colposcopy. Those who screen negative for HPV should be advised to have a Pap repeated in one year.

Primary Screening of Women 30 and older by Pap and HPV DNA Testing

NPWH strongly supports the ASCCP, American Cancer Society (ACS) and American College of Obstetricians and Gynecologists (ACOG) recommendations that women 30 and older may have expanded screening by having both a Pap and an HPV DNA test.^{1,4,5}

HPV screening can be performed at the same time as Pap screening with the combined results determining the timing of the next screen or need to perform colposcopy. The Pap has been reported to have sensitivity for identifying cervical intraepithelial neoplasia (CIN) as low as 50% in conventional Pap tests and improves to an accuracy of between 75% and 85% in liquid based tests. The HPV test is reported in studies to have greater than 99% sensitivity in detecting the presence of HPV.⁶⁻⁹ The combination of both tests improves the accuracy of screening by identifying women who have high risk HPV and require more diligent follow-up even when their Pap is negative. Women who have negative results on both tests have virtually no risk of disease and may safely widen their screening interval.

The routine use of HPV testing in women who are under 30 is not recommended as the prevalence of HPV is high and most infections or mild cellular abnormalities will be cleared by an immune response. The positive predictive value for disease on the cervix in a young woman with a positive HPV test and a negative Pap is low. Women 30 and older who are positive for high risk HPV are more likely have persistent infection which is the objective risk factor for cervical cancer. They may have disease on their cervix which could be missed by the Pap alone.

HPV testing in primary screening of women 30 and older is covered by many insurers.¹⁰ It is recommended that all women > 30 years be offered the opportunity for having both tests with the understanding that they may be responsible for an out of pocket cost if it is not covered.

Summary of Recommendations

- *Women who have negative Pap and HPV DNA tests results have little or no risk of disease on the cervix for many years and do not require repeat screening for 3 years.*

However, annual well-woman examinations and pelvic examination are still recommended.

- *Women who have a negative Pap and positive HPV results require repeat testing in 6 to 12 months. If, at 6-12 months, the HPV test is still positive even if the Pap is negative, colposcopy should be performed. Any neoplastic change that is found by colposcopy will be followed or treated according the ASCCP guidelines for management of women with cervical intra epithelial neoplasia.*
- *If any Pap is abnormal, the woman should be managed according to published guidelines regardless of HPV status.*

The increased sensitivity of the combined Pap and HPV DNA testing will identify women at risk for development of cervical dysplasia and cancer over time.

Patient Education

Women of all ages will need to be informed of the essential facts regarding HPV and risk of cervical cancer:

- Cervical cancer is preventable and caused by high risk types of HPV
- Most women will have HPV at some point
- The virus is usually cleared by an immune response
- Persistent HPV infection by high risk types is the factor that increases the risk for cervical cancer
- Infection by HPV is common but cervical cancer is rare

- When an HPV test is positive, it does not mean that the virus is new or that a partner has been unfaithful
- HPV can persist in the cells for decades

Essential facts regarding HPV testing

- The HPV test determines whether a woman has HPV in the cervical cells
- There is no treatment for HPV at this time
- The Pap looks for changes of cells caused by HPV
- The Pap and HPV test provide information that guides follow-up

If reflex HPV DNA testing is planned as a triage of an ASC-US Pap test, women need to be informed at the time of screening that the test will be performed if the immediate Pap is read as a borderline abnormal.

Informed Consent

NPWH recommends that women be informed that they will be tested for HPV if their Pap result is abnormal or if they are over 30 years old.. Counseling includes a brief rationale about the importance of HPV testing for identifying cervical cancer as well as an explanation about what the results mean. Many women and couples do not realize that a positive HPV result may be reflective of an infection that was acquired many years before.

Screening of Women Who Have Received the HPV Vaccine

It is not anticipated that the new guidelines will reflect any changes with regard to women who have received the HPV vaccine. *NPWH strongly recommends that health care professionals continue to screen all women according to guidelines regardless of whether they have received the vaccine.*

Future Recommendations

Anticipated changes/updates to the ASCCP Bethesda 2001 guidelines are expected to reflect a less aggressive treatment approach particularly for women under 20.

The Winter Issue of *Women's Health Care: A Practical Journal for Nurse Practitioners* will be dedicated to the new HPV vaccine, HPV DNA testing and other advances in cervical testing as well as detailed guidelines for the management of cervical screening results.

References

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⁷ Solomon D., et al. Comparison of Three Management Strategies for Patients with Atypical Squamous Cells of Undetermined Significance: Baseline Results from a Randomized Trial, *J. Nat Cancer Inst.* 2001; 93:293–299.

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⁹ Petry K., et al. Inclusion of HPV testing in routine cervical cancer screening for women above 29 years in Germany: results for 8466 patients, *British Journal of Cancer*,2003;88:1570–1577.

¹⁰ Digene® HPV Test*(DNAwithPap® Pap - Region by Region Insurance Coverage and Reimbursement. Availbale at: http://www.digene.com/labs/labs_reimburse_03.html Accessed December 18, 2006.

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