

HPV Testing and Cervical Cancer Screening

An abundance of data has implicated the human papillomavirus (HPV) as a necessary etiologic agent in the development of cervical carcinoma. Several dozen HPV types have been isolated from the human genital tract. Each viral type appears to have a relatively defined oncogenic potential. “High risk” or “oncogenic” types such as HPV16 and 18 are consistently identified in high-grade carcinoma precursors and carcinomas. “Low risk” types like HPV6 and 11 are associated with low-grade abnormalities such as exophytic condyloma and sub-clinical infections. To complicate matters, oncogenic HPV types are also often present as self-limited or sub-clinical infections in women with low-grade lesions or no lesions. Chronic, type-specific infection by oncogenic HPV appears to be necessary for the development of high-grade disease.

The most studied application for HPV testing has been as a means of “triaging” women with mild cytologic abnormalities in Pap tests, particularly *atypical squamous cells of undetermined significance* (ASCUS). ASCUS is a clinical and diagnostic dilemma. Nationwide, approximately two million women receive cytologic diagnoses of ASCUS, representing approximately 5% of Pap test reports. The substantial majority of ASCUS reflects benign conditions such as nonspecific reactive changes and self-limited HPV infections. However, ASCUS includes many women significant with underlying disease. The majority of women with biopsy-confirmed, high-grade squamous intraepithelial lesions (HSIL) have preceding cytologic diagnoses of ASCUS. The clinical management of patients with ASCUS is controversial and problematic. Currently available strategies include repeat Pap testing and immediate referral to colposcopy, but these approaches have substantial limitations and costs. Testing for oncogenic HPV types offers a promising, highly sensitive means for identifying the women with ASCUS who have underlying high-grade disease.

HPV ASSAY

HPV testing is performed at Central Pennsylvania Alliance Laboratory (CPAL) using the Digene Hybrid Capture II HPV assay. This tests for a broad panel of HPV types with high to intermediate oncogenic potential (HPV 16, 18, 31,33, 35, 39, 45, 51, 52, 56, 58, 59 and 68) but does not distinguish among the types in the group.

SPECIMEN REQUIREMENTS

The availability of the liquid-based Pap test has streamlined the incorporation of HPV testing into clinical management, eliminating the need for collection of a separate specimen or a second office visit to collect a specimen. The specimen is collected in the same way as a regular liquid-based Pap test, utilizing a spatula and endocervical brush and rinsing the material into the ThinPrep Preservcvt vial. HPV testing can be performed on residual material in the specimen after cytologic examination. Acetic acid is one potential interference, and washing the cervix with acetic acid must be avoided if an HPV test is desired.

ORDERING AND REPORTING

The cytopathology requisition provides the following checkboxes: Pap test only, HPV test if the Pap is ASCUS or AGUS, HPV regardless of Pap interpretation, and HPV only. For HPV only, the specimen is collected in the ThinPrep Preservcvt vial. **It is important**

to order the HPV testing at initial requisition. The specimen may outdate or be discarded if the HPV is requested after the Pap is reported. In cases with both Pap and HPV ordered, the results will be provided as an integrated report. The HPV results will be listed as “Detected” or “Not Detected”. A comment will include some risk assessment based on the combined Pap and HPV results. Because the HPV result is the primary means for risk stratification in these cases, the ASCUS will not be morphologically subclassified (e.g. favor reactive or favor SIL). In rare ASCUS cases, which are extremely suspicious for high-grade SIL or carcinoma, the HPV test will be deferred and immediate coloscopy will be recommended on the basis of the cytologic appearance. Integrated results will be available approximately one week later than a routine Pap test interpretation.

For additional information, please contact the Cytopathology department at (717) 851-5001 or CPAL at (717) 851-1416.

References:

1. Kinney W, Manos M, Hurly, Ransley J. Where’s the high-grade cervical neoplasia? The importance of minimally abnormal Papanicolaou diagnoses. *Obstet. Gynecol.* 1998. 91:973-976.
2. Solomon D, Schiffman M, Tarone R. Comparison of three management strategies for patients with atypical squamous cells of undetermined significance: Baseline results from a randomized trial. *J natl. Cancer Inst.* 2001. 93:293-299.
3. Sherman M, Schiffman M, Cox J. Effects of age and human papilloma viral load on colposcopy triage: Data from the randomized atypical squamous cells of undetermined significance/low-grade squamous intraepithelial lesion triage study (ALTS). *J Natl. Cancer Inst.* 2002. 94:102-107.