

High-Risk Human Papillomavirus and Cervical Cancer

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Human papillomavirus (HPV) is the most common sexually transmitted anogenital tract infection in the United States with 20 million current infections and 6.2 million new cases each year. It is estimated that at least 50% of sexually active people will become infected at some point in their lives.¹ Most cases of cervical HPV infection are transient, clearing within two years without treatment and manifesting no long-term consequences.² There are more than 100 distinct types of HPV, of which approximately 20 can cause cervical cancer (so-called high-risk types (hrHPV)).³ HPV is also associated with less common types of cancers including oral, vulvar, vaginal, penile, anal, and oropharyngeal. HPV can also be transmitted from mother to child causing respiratory papillomatosis.⁴ Most HPV anogenital infections are transient; though in a small percentage of cases, portions of the genome of hrHPV can persist, integrate into the host cellular genome, and initiate oncogenic events in regulatory and DNA repair mechanisms that may lead to carcinogenesis. Although regular screening through Papanicolaou tests account for a sharp decline in the morbidity and mortality associated with cervical cancer, more than 11,070 women were newly diagnosed with cervical cancer in the United States in 2008, and approximately 3,870 women die from the disease annually.⁵ The majority of such cases occur due to lack of adequate screening, but a minority have been associated with false negative tests (due to sampling, screening, or interpretive errors). Because the presence of hrHPV is a necessary condition for the development of cervical cancer and testing for the identification of hrHPV DNA in cervical specimens is a highly sensitive procedure, the addition of this test to the cervical cancer screening process has proven to be an effective tool for both primary screening and cost-effective triage of patients.

The United States Food and Drug Administration (FDA) has approved hrHPV testing for the triage of women with equivocal Papanicolaou tests (atypical squamous cells of undetermined significance) and for primary screening in conjunction with the Papanicolaou test in women over the age of 30 years. The American Society for Colposcopy and Cervical Pathology has developed additional guidelines for hrHPV testing in patient management post-treatment as well as for triaging postmenopausal women with low-grade squamous intraepithelial lesions on cytology.⁶ The addition of hrHPV testing can have an additive effect to the standard cytology method, thereby increasing the chance of catching treatable cervical precancers early, improving prognosis, eliminating unnecessary procedures, and hence decreasing medical costs.

In June of 2006, the FDA approved the first human papillomavirus vaccine directed against hrHPV types 16 and 18 (the two most common cancer associated types) and low-risk HPV types 6 and 11 (the two most commonly associated with external genital condylomas). The FDA approved a second vaccine against types 16 and 18 only in 2009. The CDC's Advisory Committee on Immunization Practices recommended routine HPV vaccination of 11- to 12-year-old girls with a "catch-up" vaccination for females 13 to 26 years of age. This primary prevention tool could significantly reduce the incidence of cervical cancer, as clinical studies have shown

near complete efficacy in the prevention of high-grade dysplasias associated with the covered hrHPV types.⁷ With the implementation of the vaccine, health care providers now can educate parents and teens about the benefits of vaccination. The vaccine is administered in three doses on a schedule of 0, 2, and 6 months, and most insurance companies will cover some or all of the cost.⁸

In summary, hrHPV infection is a known risk factor for the development of cervical cancer. Identification of patients with this infection and the exclusion of patients not having the virus have allowed us to effectively manage patients with improved prognosis, thereby decreasing the incidence of advanced disease and decreasing the need for unnecessary procedures and their associated medical costs. In addition, widespread implementation of the new HPV vaccine should further decrease the incidence of high-grade precancerous lesions in younger generations, making cervical cancer an even less common health issue in the future.

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