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Review

The epidemiology of human papillomavirus infections

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Abstract

Infection with oncogenic human papillomavirus (HPV) types is a necessary cause of cervical cancer, the second most frequently occurring cancer in women worldwide. Rates of acquisition of HPV are high, particularly among sexually active young adults. Reported estimates of incident HPV infection among initially negative women have reached as high as 60% over a 5-year follow-up period. In this article, we review the epidemiology of HPV infection. In addition to estimates of disease frequency, we highlight risk factors for HPV infection, including the number of lifetime sex partners, which is the most salient risk factor. We discuss significant issues surrounding the natural history of HPV infection, including viral persistence versus clearance, immune response, development of lesions and development of cancer. Finally, we discuss strategies for preventing HPV infection.

Keywords: Human papillomavirus (HPV); Sexually transmitted infection (STI); Cervical cancer; Epidemiology; Natural history

Contents

Abbreviations: HPV, human papillomavirus; HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion; VLP, virus-like particle

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1. Introduction

Human papillomaviruses (HPV) cause warts and have been well-established as the sexually transmitted agents that cause most invasive cervical cancers and their associated precancerous lesions (IARC, 1995). HPV is a very common infection, though most infected individuals eliminate evidence of the virus without ever developing clinically recognized manifestations. Thus, very few HPV-infected individuals progress to invasive cervical cancer. A well-established factor that partially explains differential cervical cancer risk is HPV type. Over 40 HPV types infect the human anogenital tract (zur Hausen, 1996). Based on pooled data from 11 case-control studies of the association between cervical cancer and HPV infection from multiple countries (Munoz et al., 2003), 15 HPV types have been classified as high-risk for development of cervical cancer, 3 have been classified as probable high-risk, 12 have been classified as low risk and 3 are considered to have undetermined risk (Table 1).

2. Prevalence

Estimates of the population prevalence of HPV infection among women around the world range from 2% to 44% (Bosch and de Sanjose, 2003). The wide variation in estimates is largely explained by differences in the age range of the populations studied and the sensitivity of the DNA assay used for detection of HPV infection. Overall, these DNA-based studies, combined with measurements of type-specific antibodies against HPV capsid antigens, have shown that most (>50%) sexually active women have been infected by one or more genital HPV types at some point in time.

In a Planned Parenthood population in the United States with mean age of 25 years, the prevalence of high-risk HPV infection was 27.4% (Kulasingam et al., 2002). Similar prevalence estimates have been found among female university students in the U.S. and Canada (Ho et al., 1998; Richardson et al., 2003). A recent study in Scotland showed the prevalence of PCR-detected HPV DNA in women with a mean age of 36.6 years attending routine cervical cancer screening to be approximately 20.5% for all HPVs and 15.7% for HR-HPVs (Cuschieri et al., 2004a).

HPV 16, which is one of the more common types among cytologically normal women, is also the most common type among cervical cancer cases (Franco et al., 1999; Ho et al., 1998; Liaw et al., 1999; Munoz et al., 2003; Richardson et al., 2003; Schiffman, 1992; Woodman et al., 2001). The prevalence of type-specific HPV infections among HPV-infected population-based controls from the International Agency for Research on Cancer (IARC) cervical cancer study and from a U.S. Planned Parenthood population is shown in Table 2.

Table 1
Classification of HPV types by cervical oncogenicity[a]

Risk classification	HPV types
High-risk	16, 18, 31, 33, 35 39, 45, 51, 52, 56 58, 59, 68, 73, 82
Probable high-risk	26, 53, 66
Low risk	6, 11, 40, 42, 43, 44 54, 61, 70, 72, 81, CP6108
Undetermined risk	34, 57, 83

[a] Data from Munoz et al. (2003).

2.1. Age

The prevalence of HPV infection is highest among young women and appears to drop off with increasing age (Schiffman, 1992). Using data from multiple international studies, the median oncogenic HPV prevalence among all women was 15.1%, while the median oncogenic HPV prevalence among women age 30 and older was 9.2% (Bosch and de Sanjose, 2003). Since most HPV infections occur soon after initiation of sexual activity and are transient, women over age 30 who are HPV positive include those who are persistent carriers as well as those with new infections. While most studies indicate a decrease in HPV prevalence with age, a handful of studies conducted in several different international regions have shown a peak prevalence of HPV infection in women below age 25, a decrease among women aged 35–54 and a second peak after age 55 (Herrero et