Cervical Cancer Prevention FACT SHEET

ACCP Alliance for Cervical Cancer Prevention

Risk Factors for Cervical Cancer: Evidence to Date

Human papillomavirus (HPV) infection has been established as the necessary, but not solely sufficient, cause of cervical cancer.[1] The vast majority of women infected with an oncogenic HPV type never develop cervical cancer, which suggests that additional factors acting in conjunction with HPV influence the risk of disease development. Cofactors such as parity, use of oral contraceptives, tobacco smoking, immunosuppression—particularly related to human immunodeficiency virus (HIV), infection with other sexually transmitted diseases, and poor nutrition all have been associated, to various extents, with the development of invasive cervical cancer. Their specific role in the development of cervical cancer remains unclear, however. Age of sexual debut, lifetime number of sexual partners, history of sexually transmitted infections, and other characteristics of sexual activity are linked to the likelihood of becoming infected with HPV and are not considered to be cofactors for the progression from HPV infection to cervical cancer.

The role of HPV infection

While there are more than 50 HPV types that infect the genital tract, 15 of them (types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82) have been identified as high-risk oncogenic types linked to cervical cancer. An analysis of pooled data from 11 case-control studies from nine countries (all but two of which were developing countries) involving 1,918 women with cervical cancer found that eight types—16, 18, 31, 33, 35, 45, 52, and 58—account for 95 percent of cervical cancers.[2] HPV 16, the most prevalent type, accounts for 50 to 60 percent of cervical cancer cases. HPV 18, the second most prevalent type, accounts for 10 to 12 percent.[3] There is variability in the high-risk HPV types most prevalent in different countries and regions.

HPV is one of the most common sexually transmitted infections. In the vast majority of cases, however, the infection clears or becomes undetectable within one to two years. For example, among a cohort of HPV-negative college women, 46 percent acquired an HPV infection within three years. After a median follow-up of 60 months, most of these HPV infections did not progress to cervical lesions.[4]

High parity: A cofactor

Pooled data from eight case-control studies on invasive cervical cancer and two studies on carcinoma *in situ* (CIS) from four continents suggest that, compared to women who had never given birth, those with three or four full-term pregnancies had 2.6 times the risk of developing cervical cancer; women with seven or more births had 3.8 times the risk.[5]

Other studies corroborate this positive relationship found between high parity and cervical cancer.[6,7] The physiologic reason for the association is unclear; possibilities include hormonal factors related to pregnancy or cervical trauma associated with delivery.

High parity *and* oral contraceptive use tied to cervical cancer: The WHO response

"Many cases of cervical cancer are preventable through appropriate screening practices. Where screening services are available, oral contraceptive users should use these services, as advised for other women. However, in many settings screening services are not available; often, pregnancy morbidity and mortality risks in these settings are high, and combined oral contraceptives are one of the few contraceptive methods widely available. Further, because parity appears to be a risk factor for cervical cancer, the use of oral contraceptives may reduce the risk of cervical cancer attributable to parity. Women should not be denied use of combined oral contraceptives simply because they are unable to access screening services. The risk of maternal mortality from non-use of contraception would likely far exceed any additional risk of cervical cancer for most women."[8]

Long-term use of oral contraceptives: A possible cofactor

Research suggests that there is a potential long-term relationship between prolonged use of oral contraceptives and development of cervical cancer. An analysis of pooled data from ten case-control studies of patients with invasive cervical cancer or CIS suggests that long-term use of oral contraceptives could increase the risk of cervical cancer by up to four-fold in women with HPV infection.[9]

Pending the results of several studies currently under way, WHO convened a meeting of experts that focused on cervical cancer, oral contraceptives, and parity. The group published recommendations against changing oral contraceptive prescribing practice or use.[8] (See sidebar, page 1.)

Other Cofactors

- Smoking appears to be strongly associated with the development of precancerous cervical lesions and cancer.[10,11] Smoking is among the most consistently identified environmental cofactors likely to influence the risk of cervical cancer; studies show at least a twofold risk for current smokers compared to non-smokers.[10,11,12]
- Women infected with HIV are more readily infected with high-risk HPV types and are more likely to develop precancerous lesions (and develop them more rapidly) than HIV-negative women in the same age category.[13,14,15] To date, the magnitude of elevated risk for cervical cancer among these women is unclear, however.
- Women who are co-infected with HPV and another sexually transmitted agent, such as *Chlamydia trachomatis* or herpes simplex virus-2 (HSV-2), are more likely to develop cervical cancer than are women who are not co-infected. One pooled analysis of seven case-control studies examining the effect of HSV-2 infection in the etiology of invasive cervical cancer found that among HPV DNA-positive women, HSV-2 was associated with about a three-fold increased risk of developing cervical cancer after adjustment for potential confounders.[16]
- Low socio-economic status (SES) is recognized as a risk factor for many health problems, including cervical cancer, particularly in low-resource settings. Women with low SES often have limited income, restricted access to health care services, poor nutrition, and a low level of awareness about health issues and preventive behavior. All of these factors can make them more vulnerable to illness and preventable diseases such as cervical cancer.[17]
- While some researchers have speculated that poor hygienic practices or conditions may increase risk of HPV infection or cervical cancer, there is no consistent evidence to support this assertion.[18,19]

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