

The Intersection Between HPV and HIV Infections: Is There an Increased Susceptibility to HIV Acquisition in HPV-Infected Women?

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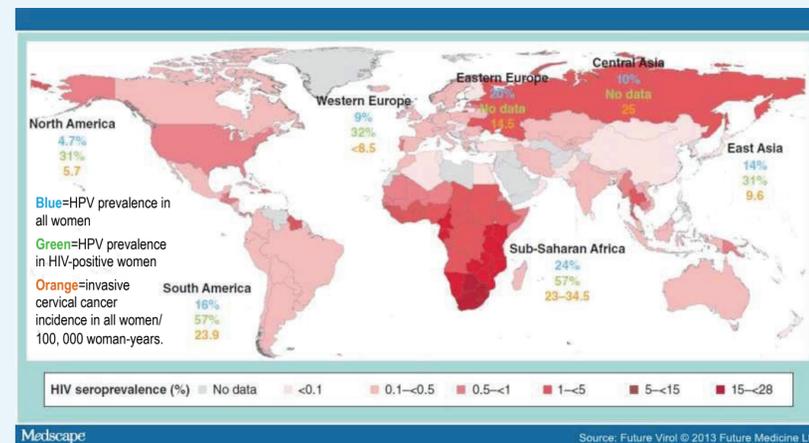
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INTRODUCTION

It has been well documented that HIV infection is associated with HPV infection and the progression to cervical carcinoma. Since the spread of HIV/AIDS epidemic, HPV-related cervical carcinoma had such a high prevalence in HIV-infected individuals that it became established as an AIDS-defining illness. Cervical cancer is the most common AIDS-related malignancy, and the sixth most common presenting AIDS-defining illness in women.¹ Additionally, HIV infection leads to a 5-fold increase in multiple new HPV infections within 6 weeks of seroconversion.² Not only does HIV impact acquisition of HPV at molecular and cellular levels, HIV and HPV viruses interact in complex ways such that each enhances the acquisition and amplification of the other.

EPIDEMIOLOGIC IMPACT OF CO-INFECTION

-HPV infection and ICC incidence rates show highest prevalence in regions where HIV infection is most prevalent
 -85% of the world's cervical cancer burden is in developing countries, with a large proportion in sub-Saharan Africa where rates are as high as 34.5/100,000 women



HPV infection prevalence in the cervix and invasive cervical cancer incidence according to WHO HIV seroprevalence distribution in 2010. (3)

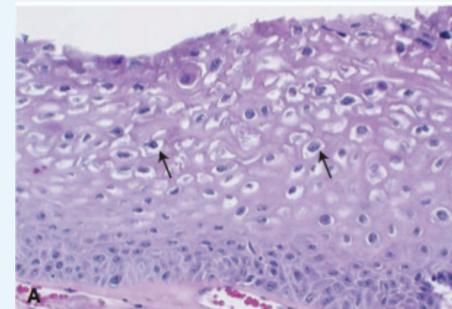
-There is a shift in HPV genotype distribution in some countries highly endemic for HIV in sub-Saharan Africa
 -One study found that the distribution of HR HPV genotypes found in ICC samples of 38 countries is different according to the extent of HIV infection within those countries
 -Although HPV type 16 remained the most common genotype found in ICC in all of the countries, in countries with higher HIV seroprevalence types 16 and 45 were found relatively less frequently and type 18 more frequently⁴
 -HIV infected women with HSIL showed a higher proportion of infection with non-16 genotypes such as 11, 18, 33, 51, 52, 53, 58, 61, and with multiple HPV types⁵

HPV FAVORS HIV ACQUISITION

-Risk of acquiring HIV is doubled when infection by HPV of any genotype is present prior to HIV exposure
 -Risk of acquiring HIV is increased if infected with two or more genotypes of HPV concurrently³
 -Significantly increased HIV risk when type-specific HPV was non-persistent
 -Infection with HPV genotypes covered by the 9-valent vaccine associated with more than 2.5 times increased risk for HIV acquisition versus 2 times increased risk with genotypes covered by the quadrivalent vaccine
 -Up to 37% of HIV infections in women in sub-Saharan Africa were attributable to infection with prevalent HPV of any genotype²

POSSIBLE MECHANISMS

-HPV is a DNA virus with a tropism for squamous epithelium⁶
 -HR HPV genotypes produce E6 and E7 proteins
 -E7 down-regulates E-cadherin, potentially increasing permeability of the genital lining to HIV²
 -HPV-infected tissue has demonstrated a reduced density and altered morphology of Langerhans' cells within the lining of the genital tract, reducing protection from HIV²



-The host immune response to HPV is mediated by T-lymphocytes
 Recruitment of primary target cells for HIV to the genital mucosa to eliminate the HPV infection
 -Loss of HPV detection can happen just before detection of HIV acquisition³
 -HPV non-persistence, which is likely to be associated with a T-lymphocyte influx, was shown to be associated with HIV acquisition when persistent infection was not²
 -Women with HPV-associated cervical dysplasia have demonstrated elevated levels of cytokine IL-1 β , which activates a promoter region in the HIV genome²

OTHER CONTRIBUTING FACTORS

-Similar behavioral risk factors for acquisition of HPV and HIV infections, including lack of condom use, multiple sexual partners, and high-risk sexual partners
 -Age at infection often earlier for HPV than HIV³
 -There is a need for prevention before sexual debut to have meaningful impact, because HIV infected individuals may already harbor HPV infection, reducing efficacy of ICC prevention through vaccination of HIV+ individuals

PROPOSED PREVENTION STRATEGIES

-While a *direct* causative relationship between HPV and HIV acquisition has not been established, the association may be capitalized on as a point of intervention and prevention, especially in areas in which *both* HPV and HIV infections are endemic.
 -Due to the high cervical cancer burden in these dual-endemic areas, there is no question that a HPV vaccination program will have profound implications on improving outcomes for women in reducing incidence of HPV-related cervical cancer.
 -It should also be considered for the potential implications in reducing the spread of HIV and its associated morbidity and mortality.
 -However, because of the variation in HPV subtypes causing high grade cervical intraepithelial lesions and cervical carcinoma in these locations, utilization of the currently available vaccine may not be sufficient to significantly impact the spread of HPV, and therefore potential spread of HIV, in susceptible populations.



CONCLUSION

An vigorous vaccine program of the multivalent vaccine currently in clinical trials, covering HPV genotypes 6, 11, 16, 18, 31, 33, 45, 52, and 58,⁴ needs to be implemented and studied in endemic areas in order to determine the impact that HPV prevention may have on reducing the spread of HIV in those Populations.

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