HPV Vaccine ? Only in Females? Think Again!

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Introduction

Human papillomaviruses (HPV) are one of the most common sexually transmitted infections in the world.\(^1,2\) In the U.S., there are 6.2 million new cases of HPV a year.\(^2\) More than a quarter of females between 14 and 59 years have HPV. The prevalence increases each year from age 14 to 24 years, reaching a prevalence of 44.8% in women between 20 and 24 years.\(^3\)

More than one hundred phenotypes of HPV exist. Phenotypes are classified by their carcinogenic potential, from high-risk to low-risk, that cause benign lesions like genital warts.\(^3\) Most HPV infections resolve within 2 years. Less than 10% of HPV infections persist. Those that persist are strongly associated with precancerous and cancerous lesions.

HPV types 6 and 11 cause 90% of genital warts.\(^2,4,5\) In the U.S. there are >500,000 new cases a year.\(^2,4\)

HPV types 16 and 18 cause 70% of cervical cancers.\(^2-6\) There are >12,000 newly diagnosed cases of cervical cancer and >4,000 deaths due to cervical cancer in the U.S. annually.\(^2,7\) There are half a million new cases of cervical cancer diagnosed and a quarter million associated deaths in the world yearly. Cervical cancer is one of the most common causes of female mortality.\(^1,3\)

Preventative HPV vaccination programs in young girls, 9-12 years is needed globally.\(^2,7\)
"Catch-up" vaccination for females between the ages of 13 to 26 years is also recommended by the U.S. Advisory Committee on Immunization Practices (ACIP). In British Columbia, girls in Grades 6 and 9 are offered the HPV vaccine free of charge.

**What are other complications of HPV?**

Infection with other phenotypes of HPV increases the risk for developing low-grade cervical dysplasia and vaginal, vulvar and all other cervical cancers in women. HPV infections predispose to anal cancer, penile cancer, oropharyngeal cancer and recurrent respiratory papillomatosis (a rare but potentially fatal disease). Ninety percent of vaginal cancers, 50% of penile cancers and 85% of anal cancers are associated with HPV infection. High-risk HPV phenotypes are present in 3.4% of women. Women with AIDS, or those taking an immunosuppressant, are more likely to have high-risk HPV infection and cervical cancer.

**Should HPV vaccine be given to men?**

At first, HPV vaccine was recommended for females - not males - even though HPV rates are the same in men and women. An anticipated "herd-immunity" from vaccinating females was thought to protect males. However, <50% of adolescent girls complete the 3-dose series in the U.S. and France. A vaccination rate of >75% is likely required to achieve herd-immunity, otherwise both sexes should be vaccinated.

Routine HPV vaccination is also required to protect males who have sex with males (MSM), a population that would not be protected if only females were vaccinated. One study reported that vaccination of boys and men with the quadrivalent vaccine was cost-effective in preventing HPV-related infections and cancer in males and their female sexual partners. In another study (n=4,065) of males aged 16 - 26 years, 85% of whom had sex only with women with the other 15% MSM, the HPV vaccine prevented persistent HPV infection in 86% of HPV-naive patients. As well, the quadrivalent vaccine prevents genital warts in 90% of men vaccinated prior to exposure to HPV types 6, 11, 16 and 18.

**New Indications for HPV Vaccine**

In 2009, the FDA approved the quadrivalent HPV vaccine for use in males and the ACIP agreed that it could be used in boys and men aged 9-26 years for the prevention of genital warts. In 2010, the FDA approved the quadrivalent HPV vaccine for the prevention of anal cancer and associated precancerous lesions (anal intraepithelial neoplasia grades 1, 2 and 3, related to HPV types 6, 11, 16 and 18) in males and females aged 9-26.

**Vaccination Rates**

Even though in North America, vaccination of young females with HPV vaccine is publicly
funded, the vaccination rate is still not optimal.\textsuperscript{5,9} Less than 1% of boys between 11 and 17 years and 15% on college campuses have been immunized against HPV in the U.S.\textsuperscript{10,11} Males are more motivated to get vaccinated to prevent HPV-related cancers than genital warts in their partners or themselves. In the U.S., the ACIP has announced that boys 11-12 years and males up to the age of 21 years should be vaccinated against HPV.\textsuperscript{7} B.C. does not have an HPV vaccination program for boys.\textsuperscript{8}

\textbf{Available HPV Vaccines}

The original HPV vaccine marketed in 2006 was a quadrivalent HPV vaccine (Gardasil\textsuperscript{®} by Merck), containing virus-like particles (VDL) 6, 11, 16 & 18.\textsuperscript{2,5} It is almost 100% effective in preventing infections from HPV types 6, 11, 16 & 18 for at least 5-7 years after vaccination and possibly longer.\textsuperscript{1,2,5} Antibody levels could remain high for 20 years.\textsuperscript{3} The quadrivalent vaccine is ineffective against pre-existing HPV infections and related lesions.\textsuperscript{5} The immune response to HPV vaccines is twice as great in 9-15 year-olds than in older groups.\textsuperscript{1}

A few years later, a bivalent vaccine (Cervarix\textsuperscript{TM} by GSK), effective against HPV types 16 and 18 was approved.\textsuperscript{2} The bivalent vaccine is not expected to decrease the incidence of genital warts, recurrent respiratory papillomatosis or low-grade cervical lesions associated with HPV types 6 and 11.\textsuperscript{4}

About 35 million doses of quadrivalent vaccine have been given in the U.S.; over 61 million doses worldwide.\textsuperscript{9} Only minor adverse effects have been reported (e.g. dizziness, headache, pyrexia, fainting and local reaction).\textsuperscript{1,2,9} The vaccine is the most expensive vaccine, costing almost $360 U.S. ($500 in Canada)\textsuperscript{12} for 3 doses given at 0, 1 or 2 and 6 months.\textsuperscript{1-3,7} However, it could save money because the cost of HPV-related diseases in the U.S. is estimated to be 4 billion dollars annually.

\textbf{Conclusion}

HPV rates are the same in men and women. Vaccination against HPV is effective in about 90% of subjects, if given before infection. All females and males should, therefore, be vaccinated before sexual contact.

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