

The HPV Vaccine in Men



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HPV is a DNA virus which is transmitted by direct contact of skin or mucosal surfaces. There are > 100 HPV genotypes. Approximately 40 HPV genotypes cause anogenital infection. Anogenital HPV genotypes are categorized as either low-risk genotypes, meaning that they have little or no oncogenic potential, or as high-risk genotypes, meaning that they are recognized as oncogenic. Anogenital HPV infection is the most prevalent of all STIs with a cumulative incidence exceeding 50% of the population.

Of the low-risk anogenital HPV genotypes, the two most important are HPV 6 and 11, which together are responsible for > 90% of cases of anogenital warts in both men and women. Among high-risk anogenital HPV genotypes, HPV 16 and 18, in that order, are the most important, because collectively they cause about 70% of cases of cervical carcinoma. Oncogenic HPV genotypes are responsible for about 90% of cases of anal, 40% of cases of vulvovaginal, 40% of cases of penile and 35% of cases of oropharyngeal carcinoma, with HPV 16 and 18 being the two dominant genotypes.¹

In July 2006, Health Canada approved the HPV vaccine, a quadrivalent HPV vaccine containing genotypes HPV 6, 11, 16 and 18. Presently, the HPV vaccine is officially

approved only for females in Canada and the US, specifically for females 9- to 26-years-old, based principally on data from two large phase III studies called Females United To Unilaterally Reduce Endo/Ectocervical Disease (FUTURE I and FUTURE II).^{2,3} More recently, the FUTURE III study demonstrated that the HPV vaccine is also effective in females 25- to 45-years-old.⁴

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Why consider HPV immunization in males?

Women were the initial focus of HPV vaccine clinical trials, because women bear a higher burden of HPV disease than men. However, women do not bear a higher burden of HPV infection. Studies among male university students show

very high rates of genital HPV infection,⁵ at least as high as demonstrated in women. As in women, increasing numbers of lifetime sexual partners and smoking are risk factors for anogenital HPV infection in men.^{5,6} A recent study from British Columbia showed that the incidence of genital warts was slightly higher among men than among women.⁷ Many health professionals are unaware that 32% of all HPV-related cancers occur in men.¹ These cancers are mainly:

- anal,
- penile,
- scrotal and
- oropharyngeal.

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Immunogenicity and efficacy of the HPV vaccine in males

Block, *et al* showed that anti-HPV titres against the four vaccine serogroups were at least as high in 10- to 15-year-old males as in 10- to 15-year-old females and 16- to 23-year-old females.⁸ In a study of 4,065 men 16- to 26-years-old,



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98.9%, 99.2%, 98.8% and 97.4% of subjects who received three doses of the HPV vaccine seroconverted to HPV 6, 11, 16 and 18, respectively.⁹ In the same cohort of patients, vaccine efficacy against any HPV 6/11/16/18 related external genital lesions was 90.4% and vaccine efficacy against HPV 6/11/16/18 persistent infection was 85.6%.¹⁰ In a separate study of men who have sex with men (MSM), vaccine efficacy against HPV 6/11/16/18 related external genital lesions was 79.0% and efficacy against persistent HPV 6/11/16/18 infection was 94.4%.¹¹ In this MSM cohort, 96.5%, 97.4%, 94.2% and 89.5% of subjects seroconverted for HPV 6, 11, 16 and 18, respectively, at month seven.¹¹

Discussion

HPV is the most prevalent of all STIs, infecting > 50% of men and women. While limiting the numbers of sexual partners and using condoms are helpful strategies to prevent STIs, these are of limited efficacy in the HPV infection given the exceedingly high prevalence of anogenital HPV infection. The HPV vaccine is an important advance in the prevention of anogenital HPV infection.


Although the HPV vaccine is currently officially approved only for women in Canada and the US, the notion of trying to prevent an STI by immunizing only one gender is irrational. No other vaccine licensed in Canada is recommended for just one gender, nor are there biological reasons to believe that vaccine efficacy will differ by gender. The HPV vaccine elicits similar immunogenicity in males and females and efficacy is also extremely high in males,

with the caveat that the duration of follow-up is considerably shorter in men, because male studies were initiated years later than the female studies.

There are two reasons to immunize males for HPV. The first is to prevent morbidity, mortality and healthcare costs related to HPV disease in males. However, the second reason is to protect women from HPV disease by engendering herd immunity. It is clear that heterosexual women acquire anogenital HPV infection from their male sexual partners with the risk of this occurring with a first sexual partner of about 30% at one year and 40% at two years.¹²

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The folly of immunizing one gender because of greater disease burden is illustrated by what happened with rubella vaccine some 20 years ago. Because of the serious problem of congenital rubella syndrome, there was an initial emphasis in immunizing only females for rubella. While this strategy had some efficacy, cases of congenital rubella syndrome did not diminish substantially until it was recognized that both males and females needed to be immunized in order to engender herd immunity to prevent rubella outbreaks that could affect susceptible women of childbearing age. This experience reminds me of one of the popular sayings: “Those who fail to learn from history

are doomed to repeat it.” Immunizing only females for HPV infection is a mistake. It is inconsistent with the principles of vaccination for common diseases which recommend immunization of the entire population, preferably at a young age for maximal benefit. It is time that both females and males be immunized against HPV in order to achieve significant reductions of HPV-related morbidity, mortality and healthcare costs. 

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