



HPV vaccines

Many questions remain unanswered

BY NEIL ARYA, MD

Many Canadian provinces and American states are now struggling with issues of whether to offer mass inoculation of the human papillomavirus (HPV) vaccine. Questions revolve around the massive costs of such a program, its overall effectiveness and the desirability of this particular vaccine. There are a host of unanswered concerns, not the least of which is the vaccine's long-term efficacy, i.e. if a preteen vaccinated now will retain immunity in 10 years, when she will actually need the protection. Also, what about men and boys, and should the vaccine be recommended to all adults who ask for it?

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Off-label indications

Many physicians have asked about the following, but there are currently no research results:

- patients who've already had sex
- women over 26 who've never had sex
- men and boys who ask for vaccination

HPV and cancer

- HPV
 - transmitted by oral, vaginal and anal sex
 - causes vaginal, vulvar, penile and anal warts
 - > 100 known strains — only 1/3 affect genitalia
 - serotypes 6 and 11 — 90% of genital warts
 - types 16 and 18 — 70% of cervical cancers
 - type 16 — primarily implicated in HPV-induced head and neck squamous cell cancers
 - 31, 33, 35, 45, 58 — moderate-risk
 - vertical transmission — laryngeal papillomatosis in newborn, may be life-threatening, though not oncogenic
- oral sex with > 5 partners in lifetime — linked to HPV-associated throat cancer¹
- with Pap screening, cervical cancer death rates in Canada have declined from 11 per 100,000 in 1951 to 2.4 in 1995
- parts of Africa, Central and South America and Micronesia with fewer PAP smears have > 50 cases per 100,000, with 50% mortality
- vulnerable groups in Canada — Aboriginal and immigrant women and those with disabilities — less PAP screening accessible
- possible long-term immunity — up to 90% of infections clear on their own within 2 years
- grade 1 cervical intraepithelial neoplasia (CIN) — not precancerous
- 40% of CIN grade 2 regresses spontaneously
- as per American College of Gynecologists, only CIN grade 3 and adenocarcinoma in situ require therapy

Quadrivalent vaccine

- HPV types 6,11,16,18
- recombinant virus-like proteins — can't induce cancer, do trigger antibody response
- intramuscular injection — 3 shots at 0, 2 and 6 months
- total cost ≥ \$360
- administered in schools or doctors' offices
- reduces rate of anogenital and vaginal warts — 2.1 to 1.3 per 100 woman-years
- testing — as cervical cancer takes years to develop, dysplasia used as a marker
- efficacy significant up to grade 2 CIN
- recommended before first sexual intercourse and to women 14-26, even with previous Pap abnormalities or HPV infections
- programs targeted to girls ages 9-13
- research subjects — > 20,000 females of all ages
- few girls under 16 tested, short duration only

Disadvantages

- no evidence of protection against grade 3 CIN and adenocarcinoma in situ³
- no increased viral clearing in people already infected with HPV 16/18, so can't be used for treatment⁴
- not approved for pregnant women
- still requires routine Pap smears
- possible significant increase in Guillain-Barré syndrome (GBS), especially when co-administered with meningococcal vaccine

Bivalent vaccine

- approved in Australia and European Union
- serotypes 16, 18
- some cross-protection against strains 31 and 45 — 31 is quite prevalent in Inuit and other marginalized populations
- covers up to 70% of cervical cancers
- no protection against genital warts
- possibly more sustained immune response
- applicable to age range 15-55

Considerations

For both vaccines:

- length of immunity unknown — will boosters be needed and how often?
- long-term safety unknown
- reproductive effects need to be monitored
- possible epidemiologic shift
 - occurred with pneumococcal vaccine among Alaskan Aboriginal children
 - other high-risk oncogenic strains might fill ecologic vacuum^{3,5}
- safe sex precautions — possible laxity and sense of invulnerability, e.g. HIV with advent of antiretrovirals
- increased cervical cancer risk if women don't get boosters, if required, or Pap smears
- boys and men — should be vaccinated if HPV-linked anogenital warts and cancer are to be eliminated
- vaccine not tested in men
- to reduce cervical cancer, more strains must be included, i.e. for certain high-risk groups
- costs — BC Cancer Agency estimates that cost of vaccine is 7 times that of savings over 25 years; break-even point \$60 instead of \$360
- other targets to lower HPV-cancers
 - promotion of Pap smears and condoms
 - develop affordable HPV DNA testing
- ON, NS, NL and PEI now provide vaccine to Grades 7 and 8 girls

References:

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