Vaccination against human papillomavirus

My primary concern about the commentary on human papillomavirus (HPV) vaccine Gardasil by Abby Lippman and colleagues[1] is that the full burden of disease prevented by Gardasil is overlooked. Clinical trials have shown that the quadrivalent HPV vaccine is 96%–100% effective at preventing infections from the HPV types that cause the most diseases: types 6, 11, 16 and 18. These HPV types are responsible for more than 90% of genital warts, about 70% of cervical and anogenital cancers and high-grade precancers, and 35%–50% of low-grade cervical, vaginal and vulvar lesions. All 4 types cause abnormal Papanicolaou smear results. Recent data on cross-protection have shown that Gardasil offers additional protection against 10 cancer-causing HPV types not included in the vaccine.[2]

HPV infections annually lead to about 400 000 abnormal Pap smear results, 85 000 consultations because of genital warts and 36 000 new cases of genital warts, as well as 1400 cervical cancer diagnoses and 400 cervical cancer deaths.[3] HPV is also linked to other cancers in both men and women, such as cancers of the penis, anus, vagina and vulva, as well as loss of female fertility. Moreover, HPV in the oral cavity is associated with an increased risk of laryngeal papillomatosis[4] and head and neck cancers.[5]

Regarding the efficacy of Pap smear testing at preventing cervical cancer, according to a 1998 surveillance report published by the Public Health Agency of Canada, about 40% of cervical cancer cases were found in women screened within the previous 3 years.[6] Pap smear testing is also woefully inadequate for those women most likely to develop cervical cancer, namely, those who are poor, poorly educated or marginalized.

Despite incredible advances in communication over the last 20 years and a vast improvement in Pap smear screening programs, our ability to further reduce the incidence and prevalence of cervical cancer has stalled. The incidence and prevalence of genital warts in Canada have also been on the rise over the past 20 years, which seems to indicate that current preventive measures are insufficient. Immunization with the quadrivalent HPV vaccine, coupled with proper education, continued Pap smear testing and ongoing post-vaccination surveillance, is the new standard of care in Canada.

James A. Mansi PhD
Director
Medical & Scientific Affairs for Vaccines
Merck Frosst Canada
Kirkland, Que.

Competing interests: James Mansi is an employee and stockholder of Merck Frosst Canada.

REFERENCES

1. Lippman A, Melnychuk R, Shimmin C, et al. Human papillomavirus, vaccines and women's health: questions and cautions. *CMAJ* 2007;177:484-7.
2. Brown D. HPV type 6/11/16/18 vaccine: first analysis of cross-protection against persistent infection, cervical intraepithelial neoplasia (CIN), and adenocarcinoma in situ (AIS) caused by oncogenic HPV types in addition to 16/18. Presented at the 47th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy; 2007 Sep 17–20; Chicago (IL).
3. Brisson M. The health and economic burden of HPV infection, genital warts, cervical dysplasia and cervical cancer in Canada [presentation]. Presented at the 7th Canadian Immunization Conference; 2006 Dec 3; Winnipeg (MB). Available: www.phac-aspc.gc.ca/cnic-ccni/2006/pres/_pdf-sun-dim-dec03/4-Hall-B-Viral-Diseases-and-Vaccines/Brisson_BOI-HPV_Imm-Conference-2006.pdf (accessed 2007 Oct 26).
4. Lee JH, Smith RJ. Recurrent respiratory papillomatosis: pathogenesis to treatment review. *Curr Opin Otolaryngol Head Neck Surg* 2005;13:354-9.
5. Smith EM, Ritchie JM, Summersgill KF, et al. Human papillomavirus in oral exfoliated cells and risk of head and neck cancer. *J Natl Cancer Inst* 2004; 96:449-55.
6. Public Health Agency of Canada. *Cervical cancer screening in Canada: 1998 surveillance report.* Ottawa: Health Canada; 2002. Available: www.phac-aspc.gc.ca/publicat/ccsic-dccuac/index.html (accessed 2007 Oct 26).

DOI:10.1503/cmaj.1070118

We disagree with many of Abby Lippman and colleagues' arguments against HPV vaccination.[1] The quantity and quality of the scientific evidence in support of HPV vaccines and new technologies for cervical cancer screening, such as HPV testing, are just as good as, if not better than, those anchoring other strategies for cancer prevention. As with most new vaccines, cost is a concern. With time, competition and economies of scale make vaccination policies more affordable. A paradigm change in cervical cancer screening using HPV-testing technology is likely to occur in synergy with vaccination and will help to improve cost-effectiveness.[2] There are lessons to be learned, but adjustments in policies can be made as the new science emerges.

Seemingly cautious arguments that we do not know enough about HPV vaccination of girls and women are irrelevant and untenable. The vaccines have been thoroughly tested in young women aged 15–25 years at risk of HPV exposure and proven to be safe and efficacious; immunobridging studies indicate that the immune response in adolescents is stronger than in young and old adults; and to be of maximal benefit, vaccination programs must focus on pre-exposure prophylaxis. The argument about herd immunity is not yet one that we can use. Eventually, phase IV trials may lead to policy revisions, and vaccination of boys and men could become a complementary prevention strategy.

The argument that cervical cancer will not develop in most women infected with oncogenic HPVs ignores basic cancer epidemiology. Most smokers will not develop lung cancer, yet we consider smoking cessation the foremost cancer prevention paradigm. More importantly, lung cancer can develop in people who have never smoked, but an infection with an oncogenic HPV type is a necessary precursor for cervical cancer. Incidentally, safe sex is practically an oxymoron in the prevention of HPV infection; condom use is not protective.[3]

Finally, we disagree with the argument that there is no Canadian cervical cancer epidemic to justify urgency. Cervical cancer rates have declined in Canada, but the enormous costs and morbidity resulting from screening and managing precursor lesions are seldom appreciated. By analogy, Canadian childhood cancer mortality (180 deaths of children aged 0–19 years in 2007[4]) has declined, but not fast enough.