Cervical cancer awareness and HPV prevention in Canada

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Cervical cancer is the second most common cancer in women worldwide and human papillomavirus (HPV) is implicated in more than 99% of these cancers. The virus is also responsible for anal and vaginal warts, anal cancer, and cancer of the vulva and penis. In Canada, HPV prevalence estimates vary depending on populations studied, ranging from 20% to 60%, with dire warnings that our Canadian data underestimate the problem.

In 2006, Gardasil—a quadrivalent recombinant vaccine—was introduced to the Canadian pharmaceutical market to prevent HPV. A second vaccine, Cervarix, is expected to be approved in Canada in 2007. These vaccines have the potential to change the demographics of cervical cancer and its prevention and treatment in Canada and internationally.

This is an opportune moment to review what we know about HPV and to consider the future of cervical screening and cervical cancer prevention.

Just the facts

- Human papillomavirus is a sexually transmitted infection. Transmission occurs through contact with infected genital skin, mucous membranes, or bodily fluids from a partner with overt or subclinical infection.
- The predominant HPV risk factor is the number of sexual partners in one's lifetime. There is no doubt that this infection and cervical cancer are sexually transmitted by infected partners.
- There are more than 100 HPV types (DNA viruses), 40 of which have been found in the cervicovaginal area.
- There are high-risk types (oncogenic HPV-16 and HPV-18) and low-risk, non–cancer-causing types, including those responsible for common genital warts (HPV-6 and HPV-11).
- Human papillomavirus infections of the genital tract might be clinical (condyloma acuminatum, or genital warts) but most are subclinical and can only be diagnosed cytologically (Papanicolaou test) or virologically (DNA detection).
- Most HPV infections are transient (three fourths of low-risk HPV types resolve between an initial and a subsequent assessment).
- The median HPV DNA duration is 8 months.
- The lifetime risk of being diagnosed with cervical cancer is 0.78% and the lifetime risk of dying from cervical cancer is 0.26%.
- Every week in Ontario approximately 10 women are diagnosed with cervical cancer and 3 women die from cervical cancer.

Screening for HPV

Human papillomavirus infection is the main reason we do Pap testing, repeat Pap testing, and colposcopy. Routine, serial Pap screening resulted in reducing cervical cancer mortality by 50% in the past 30 years. Smear cytology has a sensitivity of 70% to 80% and liquid-based cytology has a sensitivity of 85% to 95%, based on current disease prevalence; liquid-based cytology is, therefore, the preferred tool. Various parts of Canada have distinct guidelines for the use of Pap testing and varying availability and indications for newer technologies of HPV-DNA testing. This will clearly change after vaccination takes effect.

Prevention

What is the best HPV preventive strategy for our female and male patients? With the development and evaluation of many other prevention strategies, including

Preventing HPV

MODE OF PREVENTION	EFFICACY
Sexual abstinence or long-term monogamy	Not reliable.
Latex condom use	Does not protect against oral, digital, or perineal transmission.
Immunization	• Gardasil quadrivalent HPV recombinant vaccine was released by Merck in 2006. • Gardasil covers HPV-6 and HPV-11, which cause 90% of genital warts, and HPV-16 and HPV-18, which cause cervical and anal cancer. • Cervarix (from GlaxoSmithKline) will likely be approved later in 2007. It is a vaccine that protects against oncogenic HPV-16 and HPV-18. It is formulated with AS04, an adjuvant that boosts the immune system response to HPV strains for a longer period. It will not cover strains causing genital warts.

Immunization against HPV	
American resources	• Centers for Disease Control and Prevention offers *HPV Vaccine Questions and Answers*, available from **http://www.cdc.gov/std/hpv.**
Canadian resources	• National Advisory Committee on Immunization (NACI) is a national committee of recognized experts in the fields of pediatrics, infectious diseases, immunology, medical microbiology, internal medicine, and public health. Recommendations from NACI on vaccine use in Canada are published every 4 years in the Canadian Immunization Guide. Publications are available from **http://www.phac-aspc.gc.ca/naci-ccni/is-si/index.html**. • The Society of Obstetricians and Gynaecologists of Canada (SOGC) convened a consensus working group made up of representatives from 6 national specialty societies to develop guidelines on HPV prevention that were published in early 2007. Publications are available from **http://www.sogc.org/guidelines**. • The SOGC has also launched a website with educational materials on HPV, available from **http://www.hpvinfo.ca**.
Who should be vaccinated?	• The current pharmaceutical guideline for HPV vaccines is to immunize 9-year-old girls before their first sexual contacts and other girls and women up to the age of 26.
Sexually active women	• Women who were sexually active before immunization might be infected by HPV, but not necessarily by types 6, 11, 16, or 18. Immunization is, therefore, still a good strategy to prevent cervical and anal cancer.
Gardasil indications and use	Gardasil is indicated for prevention of the following diseases caused by HPV types 6, 11, 16, and 18: • Cervical cancer • Genital warts (condylomata acuminata) and for the following precancerous or dysplastic lesions: • Cervical adenocarcinoma in situ • Cervical intraepithelial neoplasia grade 2 and grade 3 • Vulvar intraepithelial neoplasia grade 2 and grade 3 • Vaginal intraepithelial neoplasia grade 2 and grade 3 • Cervical intraepithelial neoplasia grade 1
Gardasil contraindications and precautions	• Gardasil is not intended to be used for treatment of active genital warts, cervical cancer, cervical intraepithelial neoplasia, vulvar intraepithelial neoplasia, or vaginal intraepithelial neoplasia. • This vaccine will not protect against diseases that are not caused by HPV. • The vaccine is not shown to protect against diseases due to HPV types other than 6, 11, 16, and 18. • As with all injectable vaccines, appropriate medical treatment should always be readily available in case of rare anaphylactic reactions following administration of the vaccine. • The decision to administer or delay vaccination because of a current or recent febrile illness depends largely on the severity of the symptoms and their origin. Low-grade fever itself and mild upper respiratory infection are not generally contraindications to vaccination. • Patients with impaired immune responsiveness, whether due to the use of immunosuppressive therapy, a genetic defect, human immunodeficiency virus (HIV) infection, or other causes, can have reduced antibody response to active immunization. • As with other intramuscular injections, Gardasil should not be given to individuals with bleeding disorders, such as hemophilia or thrombocytopenia, or to persons receiving anticoagulant therapy unless the potential benefits clearly outweigh the risk of administration.
Information for the patient, parent, or guardian	• The health care provider should inform the patient, parent, or guardian that vaccination does not substitute for routine cervical cancer screening. • Gardasil is not recommended for use in pregnancy. • Note: Women who receive Gardasil should continue to undergo cervical cancer screening according to usual standard of care.
Practical information	• Gardasil is given as 3 injections over 6 months (0, 2, and 6 mo). • Gardasil requires strict cold-chain protocol for storage and transportation. • The HPV vaccine series is not currently a reimbursable cost.

hepatitis B vaccines, we have learned that universal, sex-neutral vaccination induces herd immunity thereby significantly reducing transmission of disease.[3]

Should we not vaccinate men as well as women? Given how this disease is spread, we could significantly reduce a woman's risk of cervical cancer through immunizing all adolescents. We made a similar public health decision years ago in immunizing all children to prevent mumps orchitis. We also eradicated polio from most communities. Vaccinating only girls against HPV could be considered akin to vaccinating against *Escherichia coli* to prevent diarrhea without cleaning the water supply. We might do just that sometimes when we are desperate or when we feel the job is too big or simply beyond our capacity. Is that how we are approaching eradicating cervical cancer?

Human papillomavirus disease is not without a significant burden for men—it causes anogenital warts in many men and anogenital cancer in some. Anogenital

warts carry a serious psychological burden. Anogenital cancer, however, is a significant health risk, which is imposed particularly on that subgroup of higher-risk men (and women).

The main argument against immunizing male patients at this time is that studies of HPV vaccine safety and efficacy have been conducted only with female patients. This is a lesson in sex-based analysis: incidence and prevalence of disease, clinical diagnosis, risk factors, treatment efficacy, and disease progression are inevitably influenced by biological sex differences and socially/culturally shaped gender differences. Too often, the male patient is used as the sex/gender-neutral norm in medical research. In HPV vaccine research, ironically, studies focused on women. The studies should have included both men and women. Indeed, attention to sex and gender should be an integral component of all medical research, including pharmaceutical research.

How will a successful HPV strategy affect long-term health system costs? No baseline data in Canada show the true annual costs of cervical screening with the huge amount of money and physician-power that is now spent on cytology, colposcopy, and follow-up of abnormal Pap results. The experts, however, have no doubt that this vaccine signals a great change in thinking about cancer prevention. Researchers have noted that it would be useful to compare costs of improving the effectiveness and coverage of cervical screening versus combining immunization and screening.[2] Researchers have also noted that national registries are the way to go if we want to understand the cost and the disease burden and if we really want to effect change.

There will be short-term costs for long-term gain: we are immunizing 9-year-old girls today for a disease to which they will not be exposed until they are sexually active, perhaps 10 years later. After exposure to HPV, it can then take an additional 20 years for the disease process to develop into cervical cancer. We also have to bear in mind that new technologies for prevention, screening, and treatment are certain to develop in the next 30 years. It is clearly challenging to calculate the cost of immunization and screening today relative to the potential burden of disease 30 years from now.

What are potential barriers to immunization?

- Vaccines for HPV are expensive, at a cost of $400 for the series of 3 injections. The federal budget, announced March 2007, includes $300 million over 3 years for a national vaccine program.
- Women who are new immigrants to Canada, aboriginal women, women with low literacy skills, and women who live in poverty are seldom or never screened with Pap tests. How likely is it that they or other marginalized populations will be able to afford or access the HPV vaccine?
- Coverage is a problem (even with worldwide support, coverage for standard childhood vaccines is only 74% in developed countries and as low as 30% in developing countries).[3] Newer models of care with preventive care bonuses might improve vaccine coverage.
- Recognizing and countering the stigma attached to HPV as a sexually transmitted illness will be important. The virus is endemic and is spread by "life" rather than by "sex." Immunization against HPV does not promote free sex; the vaccine merely protects women and men from specific genital warts and cancers. Safer-sex education remains an important component of primary health care.
- Physician and patient lack of knowledge, awareness, or support of the vaccine could be an obstacle. Again, consistent advisory body support and statements from medical associations will help the front-line physicians to convey to their patients (and their patients' parents) the importance of immunizing all children to protect them before they become sexually active women and men. Acceptability will depend on this clear message.
- It is unclear whether the vaccine is beneficial for those who are already infected with oncogenic HPV.

Participate in HPV prevention strategies

Without a doubt, there is much to debate in setting national strategies to address the burden of HPV disease. Family physicians have the privilege—indeed, the responsibility—to engage in the process of developing and implementing an HPV prevention strategy for Canada.

How might one participate? Join working groups to provide a primary care perspective in the development of national HPV guidelines.

Family physicians were invited to attend the Canadian Human Papillomavirus Vaccine Research Priorities Workshop that was held in Quebec city in November 2005. The workshop report is available through the Public Health Agency of Canada.[1]

On November 28, 2006, the Society of Obstetricians and Gynaecologists of Canada (SOGC), the Health Leadership Institute of the DeGroote School of Business, McMaster University, medical experts—including family physicians—patient advocates, cancer survivors, public health officials, and media met in Montreal to consult on key public health opportunities and challenges:

- incorporating new and emerging technologies into prevention programs across Canada;
- educating stakeholders about the disease and the virus (HPV) that causes it; and
- reaching underserved women.

One point raised in this conference is that we very often find ourselves with new technologies that are ahead of policies. This is most certainly true of family medicine. Primary care reform and technological innovations have changed our ability to track such preventive

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services as immunizations and Pap testing. As family physicians, we have a great deal to contribute to the discussion of how to create central registries and how to achieve each of these 3 goals, and we need to do everything in our power to be at the table for these kinds of discussions.

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Bulletin Board

Under pressure

One in 4 people in health care settings across Canada has a pressure ulcer at any given time, yet around 70% of pressure ulcers are preventable. The Canadian Association of Wound Care (CAWC), a non-profit organization of health care professionals, industry participants, patients, and caregivers, has developed a series of on-line resources to improve prevention and treatment of pressure ulcers. These resources include recommendations on prevention and treatment of pressure ulcers in diabetes, venous insufficiency, and palliative care, as well as a look at the latest research. See **www.cawc.ne**t to access the wound-care resources.

Active for life

It is well known that exercise is beneficial for health. As physicians, we encourage our patients to engage in regular physical activity. But how active are they? A recent survey by The Alberta Centre for Active Living (**www.centre4activeliving.ca**) found that more than 60% of all Albertans were physically active enough to achieve health benefits; this percentage was slightly higher than in the previous survey in 2005. The survey revealed changes in the percentage of sufficiently active people.

- It decreases with age.
- It is higher among people with more education.
- It is higher among people with the highest annual household incomes.
- It is higher among people who have never married or who are separated.

How should we encourage the other 40% to exercise? For tips, see Health Canada's Healthy Living Unit at **www.phac-aspc.gc.ca/pau-uap/fitness/**.

Food banks

More than 820 000 Canadians use one of the 650 food banks in Canada each month. About 40% of food bank users are children. The unpredictable nature of donations to food banks makes it challenging to meet recipients' nutritional needs. A recent study compared the contents of 30 food hampers with food recommended in Canadian guidelines at a large urban food bank in southwestern Ontario. Although the hampers were intended to supply 3 days' worth of food per person, 99% of hampers did not. They contained 1.6 days' worth of energy per person. Most food groups (fruit and vegetables, meats and alternatives, and dairy products) were below recommended levels in the hampers, as were numerous vitamins and minerals. Grains and cereals met the lower range of *Canada's Food Guide* recommendations. Energy from fat and protein scarcely met the minimums recommended.

Many Canadians are under the impression that food banks are able to provide sufficiently for people in need. There is a growing body of evidence that this perception is erroneous. The authors recommend encouraging more perishable food donations and improved storage facilities at food banks; however, this recommendation does not address the larger issue of poverty in Canada.

Source: Irwin JD, Ng VK, Rush TJ, Nguyen C, He M. Can food banks sustain nutrient requirements? A case study in southwestern Ontario. *Can J Public Health* 2007;98(1):17-20.

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