Chapter 11: The HPV Vaccines, Liquid Based Cytology and HPV Testing

On completion of this section, the learner will be able to describe the following:
1. The Human Papillomavirus (HPV) Vaccine
2. Liquid Based Cytology
3. HPV Testing

The HPV Vaccines\textsuperscript{1,2}

Three HPV vaccines have been approved for use in Canada:

<table>
<thead>
<tr>
<th>Vaccine type</th>
<th>HPV types covered</th>
<th>Protects against:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervarix</td>
<td>16, 18</td>
<td>Over 70% of cervical cancers</td>
</tr>
<tr>
<td>Gardasil-4*</td>
<td>6, 11, 16, 18</td>
<td>Over 70% of cervical cancers and 90% of genital warts</td>
</tr>
<tr>
<td>Gardasil-9**</td>
<td>6, 11, 16, 18, 31, 33, 45, 52, 58</td>
<td>90% of cervical cancers and 90% of genital warts</td>
</tr>
</tbody>
</table>

* Gardasil-4 is no longer available (2018).
** Gardasil-9 has been used in the Public – Health program since 2018

Recommendations

Although the Pap Test Learning Module for Healthcare Providers focuses on secondary prevention of cervical cancer, it is important to emphasize the importance of primary prevention of cervical cancer with HPV vaccination. Although HPV vaccines were studied using cervical dysplasia as study endpoints, there are other disease sites that benefit from these vaccines (Fig 1).

The single biggest determinant of a parent’s decision to vaccinate their child is a strong recommendation from a healthcare provider. Studies from other countries with higher uptake of vaccination in school-based programs show that the more knowledgeable the vaccinators, the greater the uptake rate.
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The Manitoba Immunization Program determines its criteria from National Advisory Committee on Immunization (NACI), Provincial Experts, provincial statistics and risk, the medical literature and available funding.
The Manitoba HPV Immunization Program
In the 2008-2009 school year, Manitoba Health introduced a vaccine program for grade 6 girls. In 2016, Manitoba Health added grade 6 boys to the Manitoba HPV Immunization Program. The program is voluntary opt-in program, and is administered by public health nurses. It is important to monitor this website.

Manitoba’s Immunization Program: Vaccines Offered Free-of Charge (Eligibility Criteria for Publicly-Funded Vaccines, 2018)

Vaccines listed here are provided free-of-charge to individuals who are registered with Manitoba Health, Seniors and Active Living (MHSAL) and for those who are part-way through an immunization series started in another province or territory as part of a publicly-funded program (pending product availability). MHSAL covers all costs associated with administering a publicly-funded vaccine (e.g. physician fees).

Individuals who do not receive a publicly-funded vaccine when it is first recommended are eligible to receive the vaccine at a later time (unless otherwise stated). This is commonly referred to as, ‘once eligible, always eligible.’

- Healthy females born on or after January 1, 1997 and healthy males born on or after January 1, 2002 are eligible to receive the HPV vaccine, routinely provided as part of the grade 6 school-based immunization program.
- For healthy females and males 11 to less than 15 years of age, 2 doses are recommended. For those who are 15 years of age and older, a 3-dose schedule is recommended, unless the first dose of vaccine was administered before the age of 15.
- Individuals with at least one of the following high-risk criteria are eligible to receive up to 3 doses:
  - Immunocompetent HIV-infected males 9-26 years of age and females 9-45 years of age.
  - Males 9-26 years of age and females 9-45 years of age who have congenital immune deficiencies (B cell deficient, T cell mixed defects, phagocytic and neutrophil disorders, complement deficiency) or acquired immune deficiencies (pre-solid organ transplant or post-solid organ transplants, hematopoietic stem cell transplant recipients, as per
CancerCare Manitoba Blood and Marrow Transplant (BMT) Immunization Schedule.

- Males ≤ 18 years of age who are, or who have ever been, incarcerated.
- Individuals who are currently, or who have previously been, diagnosed with recurrent respiratory papillomatosis.
- Males 9-26 years of age who identify as gay or bisexual
- Transgender males and transgender females 9-26 years of age.
- Females 9-45 years of age who have a newly diagnosed high-grade cervical histopathology result.
- Males 9-26 years of age and females 9-45 years of age who are victims of sexual assault.
- Patients currently under the care of a haematologist or oncologist from CancerCare Manitoba (CCMB) who have the following conditions and have been provided a CCMB directed Immunization Schedule:
  1. Malignant neoplasms (solid tissue and haematological) including leukemia and lymphoma, or clonal blood disorder, and who will receive or have completed immunosuppressive therapy including chemotherapy or radiation therapy, or
  2. Hypo- or asplenic (Sickle Cell Disease, etc.)

For minimum intervals between doses of HPV vaccine, please see the Canadian Immunization Guide

cancercare.mb.ca/screening PAP TEST LEARNING MODULE FOR HEALTH CARE PROVIDERS CHAPTER 11 PAGE 4
Opportunistic HPV Vaccination: An Expanded Vision

There are several incorrect and unfounded Myths about HPV vaccinations:

1. **MYTH:** Women who have the HPV vaccine do not need to get a Pap test.

   **FACT:** The HPV vaccine does not protect against all the types of HPV that cause cervical cancer. Women still need Pap tests regularly even if they have been vaccinated against HPV.

2. **MYTH:** The vaccine can give you the virus and cause cancer.

   **FACT:** The vaccine does not contain a live or killed virus. The vaccine contains a virus like particles of different types of the human papilloma virus. When you take the vaccine, your body makes antibodies which fight the real virus if you’re ever exposed to it.

3. **MYTH:** The HPV vaccine is only recommended for women up to 26.

   **FACT:** The HPV vaccines were studied using study parameters between the ages of 9 to 26. Other studies have demonstrated that there is no upper age that individuals stop receiving benefits of this vaccine.
4. **MYTH:** There is no benefit to administering the HPV vaccine to individuals treated for cervical dysplasia.

**FACT:** Studies show that females who have already been treated for cervical dysplasia may also benefit from receiving the vaccine. It is unlikely they would have been exposed to all HPV types covered in the vaccines. It would also potentially benefit them from HPV disease in other disease sites.

**Dosage and Schedule**
The vaccine is given in 2 or 3 separate doses of 0.5 mL as follows:
- Gardasil: 0, 2 and 6 month intervals.

They are administered intramuscularly in the deltoid or anterolateral upper thigh.

**Vaccine Efficacy**
The HPV vaccines are most effective when given to females before they start having sexual contact. If received before exposure to the HPV types covered in the vaccines, it will be almost 100% effective in preventing infection from the HPV types that the vaccine provides protection against. Studies show that females who have already been sexually active may also benefit from receiving the vaccine as it is unlikely they would have been exposed to all HPV types covered in the vaccines. Studies are ongoing to determine if a booster is required to enhance the duration of protection.

**Safety**
The vaccines are safe. Health Canada has approved the vaccines based on a scientific review of their quality, safety and effectiveness. As with all vaccines, side effects may occur including rare adverse events, e.g. allergic reactions, nausea, dizziness. The most common side effects are soreness, pain and swelling at the injection site.

Vaccine safety is consistently being monitored in Canada and other jurisdictions.
What is in the vaccine?
The HPV vaccines contain proteins that act like the HPV virus. The body starts making antibodies and white blood cells to fight against these virus-like particles. This builds up immunity to the HPV virus. There is no active virus in the vaccines. Nor are there any antibiotics or preservatives, such as mercury or thimerosal.

Pap Tests and the HPV Vaccine
All three vaccines have demonstrated to be very effective in preventing HPV infection. There are, however, other HPV types not covered in the vaccines that can cause cervical cancer. Women who receive the HPV vaccine therefore, still need to have regular Pap tests as recommended by their provincial cervical cancer screening program.

Liquid Based Cytology
With Liquid Based Cytology (LBC), a sample of cells is taken from the cervix using a broom-like device. The cervical sample is deposited in a liquid medium and sent to the laboratory for examination.

It is accepted there are marginal increases in sensitivity and decreases in specificity offers no clinical performance advantage for detection of high-grade precancerous lesions. The decision by laboratories to incorporate LBC is based on a cost-effectiveness analysis, practicality to laboratories and cytotechnologists and the ability to also serve as a platform for molecular testing for HPV Testing, Gonorrhea, Chlamydia and trichomonas.

Publications from the *Netherlands National Cervical Cancer Screening* what LBC platform is used has clinical significance.

Because LBC removes most artifacts and other obscuring elements; the frequency of unsatisfactory results is reduced. LBC also allows for automated cytology reading and provides the foundation to perform HPV testing.
HPV Testing\textsuperscript{2,8}

HPV testing is molecular DNA testing for the detection of oncogenic HPV types that can cause cervical cancer and its precursors. HPV testing can be applied in the following settings:

i. Primary screening for high-risk HPV types alone or in combination with cytology

ii. Triage of women with equivocal cytological results (HPV reflex testing), or

iii. Follow-up of women treated for precancerous neoplastic lesions to determine success or failure of treatment (test of cure).

The benefits of HPV testing have been well demonstrated and include:

- Compared with the Pap test, HPV testing is much more sensitive to detect high-grade precancerous lesions.
- HPV testing is better at detecting cervical adenocarcinoma
- HPV testing allows for a longer screening interval and earlier cessation of screening
- HPV testing is more attractive as vaccinated cohorts reach screening age to monitor vaccine efficacy and determine if a HPV vaccine booster is required
- HPV testing provides the opportunity to facilitate self-sampling for unscreened populations

Commercially available tests are constantly evolving and approved by Health Canada.

HPV tests can be distinguished by:

1. Their detecting either HPV DNA or RHA
2. What high-risk HPV genotypes are detected
3. Threshold of HPV copies before a test becomes positive

Currently, HPV testing is not offered routinely in Manitoba.
CancerCare Manitoba Screening Program Resources

National Advisory Committee on Immunization

Manitoba Health
1. What are the nine HPV types that Gardasil-9 protects against when administered prior to sexual activity?
2. Who are the HPV vaccines recommended for? Who is it not recommended for?
3. What are the benefits to using liquid based cytology?
4. Describe the three ways that HPV testing can be used.

References


