Immunization in Canada: a 6-year update

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Introduction

In the six years since the publication in this journal of "Immunization in Canada: a success to build on," immunization programs in Canada have changed substantially. In this commentary, we will review the current status of immunization programs in Canada, highlighting vaccines newly introduced into Canada's publicly funded programs. We will also describe immunization committees recently established in Canada and the role they play in Canada's vaccine program decision-making process. Finally, we will briefly review new vaccines that may soon be available in Canada.

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In 2003, there was universal, publicly funded immunization against nine diseases in Canada (diphtheria, tetanus, pertussis, polio, *Haemophilus influenzae* type b, hepatitis B, measles, mumps, and rubella).[1] Despite the National Advisory Committee on Immunization's (NACI) recommendations for immunization of infants against varicella, *Neisseria meningitidis* type C (meningococcal C conjugate vaccine), *Streptococcus pneumoniae* (pneumococcal conjugate vaccine), and against pertussis in adolescents, there were no publicly funded programs set-up at the time. Since 2003, new vaccines have been added to Canada's list of universal, publicly funded programs. As well, NACI has released updates and statements on the recommended immunization schedules for certain diseases that were previously publicly funded in 2003.

In 2003, NACI was the committee that provided recommendations on the use of vaccines in Canada.[2] Although NACI's role is to make national recommendations on vaccine use, the decision to implement a new vaccine into publicly funded immunization programs as well as the purchasing of the vaccine is the responsibility of the provinces and territories. Decision-making structures for each province/territory varied greatly and in part led to lack of standardization and inconsistencies in the immunization programs and schedules across Canada.[3]

Current epidemiology and vaccine programs in Canada

Since 2003, seven vaccines have been added to Canada's universal, publicly funded immunization program: 1) varicella vaccine, 2) pneumococcal conjugate vaccine, 3) influenza vaccine for young children and pregnant women, 4) Human papillomavirus (HPV) vaccine, 5) meningococcal C conjugate vaccine (MenC), 6) Quadrivalent meningococcal conjugate vaccine (Men ACYW), and 7) adolescent and adult formulation tetanus, diphtheria, and acellular pertussis vaccine (Tdap).[4]

The varicella-zoster virus (VZV) is a DNA virus; primary infection with VZV causes chickenpox. VZV can establish a latent infection in the sensory ganglia, from where it can be reactivated in later years as zoster (shingles).[2] In 2002, NACI recommended varicella vaccine for all children at 12 months of age.[1] In 2003, less than half the provinces/territories provided the vaccine as part of their publicly funded program. Since 2007, all provinces and territories have provided universal, publicly funded vaccinations against varicella for all children ages 12–18 months, and half of the provinces and territories have catch-up programs.[4] Outbreak studies done in the United States showed that there was an overall vaccine effectiveness of 70%–90% in preventing varicella disease of any severity, and 95% protection against severe varicella for 7 to 10 years after immunization.[5]

Since 2003, the pneumococcal conjugate vaccine has been incorporated into the publicly funded immunization programs for all provinces and territories. Based on NACI's recommendations, infants in all of the provinces and territories, except Quebec, are immunized at 2, 4, 6, and 12–18 months of age.[6] In Quebec infants are immunized at 2, 4, and 12 months of age.[4] In Alberta, the first province to implement universal pneumococcal conjugate vaccine, surveillance in the Calgary region showed a large decline in the occurrence of invasive pneumococcal disease (IPD) among children <2 years of age. When compared with the combined rate between 1998 and 2001, the rate in 2004 decreased by 81.6% to 11.7 cases of infection per 100,000 for all serotypes, by 92.6% to 3.9 cases for the seven serotypes included in the vaccine and by 93.4% to 3.9 cases for these vaccine serotypes and related serotypes within the same serogroups.[7] In 2004–2005, investigators of the Canadian Immunization Monitoring Program, Active (IMPACT) undertook active, population-based surveillance for invasive pneumococcal infections in Greater Vancouver (473,000 children) and demonstrated a rapid and substantial decrease in incidence rates of infection for children 6–23 months old with routine infant vaccination. Disease rates for 6–23 month olds decreased 84.6% (92.5% for vaccine serotypes), further confirming the effectiveness of the pneumococcal vaccination program.[8]

Several changes have been made to the immunization schedule for influenza within Canada since 2002 to provide publicly funded vaccine for additional groups at increased risk of complications from influenza. Throughout Canada, there is now universal public funding for influenza vaccine for all children aged 6–23 months.[6] Influenza vaccine is now recommended for all pregnant women, regardless of their stage of pregnancy.[6] In Ontario, there is universal public funding for influenza vaccine for people of all ages. In April of 2009, a significant shift in the influenza virus led to emergence of a novel H1N1 strain of swine origin and the World Health Organization declaring

an influenza pandemic.[9] A nationwide program of H1N1 vaccination for all Canadians was implemented in late October 2009.

One of the biggest successes in Canadian immunization and immunization programs in the last six years has been the implementation of a universal vaccination program against HPV. HPV is one of the most common sexually transmitted viruses, comprising at least 40 types that are able to infect the genital tract. Almost all cervical cancers are the result of HPV infections;[10] the overall prevalence of HPV (any type) in Canada ranges from 10.8% to 29.0%. The most recent Canadian data show that the highest prevalence (26.9%) of HPV is in women <20 years of age. Subtypes 16 and 18 are the most prevalent (16.7%), although prevalence does vary with age, region, and ethnicity.[11] The incidence of cervical cancer has greatly declined since the integration of regular PAP smears, yet cervical cancer is still estimated to be the second most common malignancy in women. In 2005, it was estimated that approximately one million women had cervical cancer, with over 250,000 deaths attributed to the disease.[12] For each new case of invasive cancer found by cytology in Western countries, there are approximately 50 to 100 other cases of precursor lesions that require follow-up or management.[13]

The recommendations for the use of the first licensed HPV vaccine (Gardasil®, Merck) were published by NACI in February 2007. A second vaccine (Cervarix™, GlaxoSmithKline) will soon be available. Because HPV is a sexually transmitted infection, the primary age group targeted for the immunization is girls aged 9 to 13, before they become sexually active.[6] Gardasil® is a quadrivalent vaccine administered on a separate three-dose schedule of 0.5 mL per injection, at 0, 2, and 6 months. Once administered, the vaccine prevents against infection with HPV 16 and 18, as well as HPV 6 and 11. The former are two common high-risk types of HPV that cause 70% of cervical cancer cases. The latter are two lower risk types that are rarely associated with cervical cancer, but are the major causes of genital warts.[10] Clinical studies have been performed with the quadrivalent vaccine to measure its immunogencity and efficacy. During Phase II and Phase III trials, the efficacy against cervical cancer and the prevention of HPV-16 and HPV-18-related cervical cancer surrogates (cervical intraepithelial neoplasia [CIN] 2, CIN3 or adenoma in situ [AIS]) was 100% (95% CI: 93% to 100%) and 99% (95% CI: 93% to 100%). In the combined data set from the Phase II and Phase III studies, efficacy against external genital lesions, vulvar intraepithelial neoplasia, and vaginal intraepithelial neoplasia related to HPV-6, -11, -16, or -18, including warts, was 99% (95% CI: 95% to 100%) in the per protocol efficacy and 95% in the modified intention to treat analysis (95% CI: 90% to 98%).[14] Cervarix is a bivalent HPV 16 and 18 vaccine. Clinical trial results were similar to the quadrivalent vaccine, with 90%–100% efficacy against the development of high-grade cervical lesions associated with HPV 16 and 18 for periods of up to 5.5 years. One month following the administration of the third dose, nearly all participants (>99%) had developed antibodies against the types of HPV contained in the vaccine. Further surveillance has showed that aside from the prevention of lesions caused by HPV 16 and 18, the bivalent vaccine is also 35% to 60% effective in preventing infections caused by types 31 and 45, which are responsible for 8%–10% of cervical cancers.[15] As of May 2009, Cervarix™ was under review by Health Canada, and Gardasil® is used for HPV vaccination programs across Canada.[15]

In 2006, $300 million was allocated by the federal government for implementation of HPV programs across Canada.[16] Currently, all the provinces and territories within Canada offer universal public funding for immunization against HPV, except for Nunavut which has announced a program that will be starting in the winter of 2009.[4] HPV vaccine has only been integrated into the universal, publicly funded immunization programs across Canada as of 2009, so there is little information on the long-term effectiveness of the vaccine. Studies are still in progress testing the long-term efficacy, and its effectiveness in decreasing the occurrence of HPV and cervical cancer.

Since 2001, NACI has recommended meningococcal C conjugate vaccine for children <1 year of age, children from 1–4 years of age, adolescents, and young adults.[1] However, full implementation of a universal, publicly funded vaccine program with meningococcal C conjugate vaccine did not occur across Canada until 2007. In more recent years, there has been a significant decline in occurrence of serogroup C invasive meningococcal disease (IMD). IMPACT's 12 centres, located in children's hospitals in eight different provinces, conducted active population-based surveillance for hospital admissions

in all ages related to *Neisseria meningitidis* from January 2002 to December 2007. Incidence rates of Group C invasive disease decreased six-fold in provinces that were first to establish universal infant immunization. Rates decreased in both children and adults suggesting an effect of herd immunity.[17] In 2006, a quadrivalent meningococcal A, C, Y, W135 conjugate vaccine (Menactra®, Sanofi Pasteur) was approved for use in Canada. The incidence of serogroup Y IMD has remained relatively stable across time in Canada, with a slightly higher median age, due to more cases in the >65 age group. The remaining two serogroups, A and W135, protected against in the quadrivalent vaccine remain rare in Canada.[18] In May 2007, NACI recommended the use of the quadrivalent meningococcal vaccine for immunization of persons 2–55 years in the following high-risk groups: persons with anatomic or functional asplenia; persons who have complement, properdin, or factor D deficiencies; travelers when meningococcal vaccine is indicated, including pilgrims to the Hajj in Mecca; research, industrial, and clinical laboratory personnel who are routinely exposed to N. meningitidis; and military recruits. Presently, although all provinces have implemented publicly funded immunization programs with the meningococcal C conjugate vaccine, only three provinces have funded use of the quadrivalent vaccine. In New Brunswick and PEI, the quadrivalent conjugate meningococcal vaccine is used as part of each province's catch-up program in grade 9. In Ontario, quadrivalent meningococcal vaccine is used in accordance with NACI's recommendations for individuals 2–55 years of age who fall under the high-risk category.[4] There are no data yet on the efficacy of the MenACYW vaccine.

Pertussis, or whooping cough, is a highly contagious infection of the respiratory tract, caused by *Bordetella pertussis*. Since the introduction of pertussis vaccination, the number of reported cases has drastically declined, from 160 cases per 100,000 in the mid-20th century to <20 cases per 100,000 in the 1980s. The infection is most severe in infants, though it can affect individuals of any age. In the last decade, the number of adolescents and adults with pertussis has steadily increased. The proportion of pertussis cases in adolescents and adults ≥15 years of age has increased from 9.6% in 1995 to 16.4%, 21.2%, and 31.3% in 1998, 2001, and 2004 respectively. This increased incidence may be due in part to better detection and reporting of cases of pertussis. Active surveillance for pertussis in Canada has documented pertussis infection in 10–20% of adolescents and adults with a non-improving cough illness lasting 7 or more days.[2] For many years, the immunization schedule against pertussis has consisted of a primary series at 2, 4, and 6 months of age, and booster doses at 18 months and 4–6 years. Immunization for adolescents and adults against pertussis was not included in the schedules, despite the increases in occurrence. In 2002, NACI recommended that all adolescents should receive a single booster dose of the adolescent/adult formulation of the Tdap vaccine, as well as adults who have not previously received a dose.[1] As of 2008, all provinces and territories had implemented a publicly funded, adolescent immunization program against pertussis.[4]

The Canadian Immunization Committee (CIC)

The National Immunization Strategy was approved in 2003, with $45 million from the Canadian federal government. One year later, in 2004, the Canadian Immunization Committee (CIC) was established.[19] CIC is a federal/provincial/territorial body that provides leadership in immunization by giving advice and recommendations on implementation of the National Immunization Strategy (NIS) and issues affecting immunization. The committee comprises a senior representative, often the Chief Medical Officer of Health, from each province/territory. Although NACI produces statements on its recommendations for immunizations, it is up to the individual provinces and territories as to what vaccine programs they choose to implement and fund. Each jurisdiction decides which products will be purchased and which will be offered free of charge to certain target groups. The goal of the CIC is to aid individual provinces and territories in this decision-making process. In order to best assist the provinces, the CIC performs a thorough cost-analysis, and utilizes an analytical framework created by Erickson and De Wals.[20] The framework was developed to allow comprehensive and systematic evaluation of all factors that should be considered before making decisions regarding the pertinence of new immunization programs. Before its use within the Canadian immunization programs, the framework had been used to structure reports on control programs against communicable diseases in Quebec. The first step in adapting and developing the framework to the Canadian immunization structure was to contact key scientific and public health experts involved in the planning

Table 1 *Criteria and key questions outlined in the Erickson–De Wals framework for assessing Canadian immunization programs.*

Criteria	*Key Questions*
1 Burden of disease	Does the burden of disease justify a control program?
2 Vaccine characteristics	Do the characteristics of the vaccine permit implementation of an effective and safe immunization program?
3 Immunization strategy	Is there an immunization strategy which allows goals of the control program as well as sanitary and operational objectives to be attained?
4 Cost-effectiveness	Is it possible to obtain funding for the program and are cost-effectiveness indicies comparable to those of other health care interventions?
5 Acceptability	Does a high level of demand or acceptability exist for the immunization program?
6 Feasibility	Is program implementation feasible given existing resources?
7 Ability to evaluate	Can the various aspects of the program be evaluated?
8 Research questions	Have important research questions affecting implementation of the program been adequately addressed?
9 Equity	Is the program equitable in terms of accessibility of the vaccine for all target groups?
10 Ethical considerations	Have ethical considerations regarding implementation of the immunization program been adequately addressed?
11 Legal considerations	Have legal concerns regarding implementation of the immunization program been adequately addressed?
12 Conformity of programs	Does the planned program conform to those planned or implemented elsewhere (other regions, countries)?
13 Political considerations	Will the proposed program be free of controversy and/or produce some immediate political benefit?

of immunization programs across Canada. These specialists were asked their views on what factors have been of most importance when making recent decisions regarding publicly funded immunization programs. After repeated questionnaires and analysis of responses, a list was generated of a framework that outlined 58 criteria classified into 13 categories, all directly pertinent to the implementation of new vaccine programs (Table 1) that were shown to increase the reliability in decision-making.[20] It is hoped that the formation of the Canadian Immunization Committee will bring homogeneity and equity to immunization programs across Canada.[3]

The link between the CIC & NACI

The first step in the process of introducing a new vaccine in Canada is its regulatory approval by the Biologics and Genetic Therapies Directorate (BGTD) of Health Canada. In order for a vaccine to be authorized for use in Canada it must undergo multiple preclinical studies and clinical trials that measure its safety and efficacy. After extensive review of all supporting data the vaccine may be approved for sale. The BGTD conducts prerelease testing on every lot of vaccine and monitors subsequent safety in use, in collaboration with the Public Health Agency of Canada (PHAC) and the vaccine manufacturer.[21] After the vaccine is approved for use, NACI reviews and summarizes the studies, evaluating the level and quality of the evidence, and makes a recommendation regarding the use of the vaccine. The CIC performs a cost-analysis and characterizes the factors associated with a universal program according to the Erickson–De Wals framework. Using NACI's recommendations and the CIC analysis, each province and territory then decides whether or not to fund the vaccine and utilize it in their immunization programs.

Vaccines of the future

With the continuing success of vaccinations and immunization programs, it can be predicted with confidence that

the addition of additional vaccines to routine schedules is on the horizon. Currently, there are two safe and effective vaccines against rotavirus gastroenteritis (RGE) (RotaTeq®, Merck; Rotarix™, GlaxoSmithKline) that are approved for use in Canada. Rotavirus (RV) is one of the leading causes of severe diarrhea among infants and young children.[22] Despite limited Canadian data, RV appears to have a high prevalence among Canadian children <5 years of age (1/62 to 1/312 children hospitalized for rotavirus infection). Based on the observed vaccine efficacy in clinical trials that were performed, implementation of universal immunization of all Canadian infants could be expected to prevent as many as 56,000 cases of RGE, 33,000 physician visits, 15,000 emergency department visits and 5,000 hospitalizations annually.[23] The significant protection against RGE is sustained through two years after vaccination.[24] NACI has released a limited statement on the rotavirus vaccine. CIC has not yet made a statement regarding the rotavirus vaccine and there are no universal programs in Canada. In the United States, universal rotavirus vaccine programs have been implemented and have resulted in a significant reduction in hospitalizations related to rotavirus infection.[23]

Due to the high success of the varicella vaccine in children, a vaccine to prevent zosters/shingles (varicella for the elderly) has been approved for use in Canada (Zostavax™, Merck). The risk of having at least one reactivation to herpes zoster is 15% to 20%, which means there are likely a significant number of cases occurring each year in Canada.[6] Zoster vaccine has been widely implemented in the United States but is not yet widely available for use in Canada.

Two combination vaccines for measles, mumps, rubella, and varicella will soon be available in Canada. MMRV was licensed in 2006 in the United States, and quickly recommended for routine use in children. The MMRV combination vaccine is currently not available in Canada.[2]

A 9-valent pneumococcal conjugate vaccine (Synflorix™, GlaxoSmithKline) is available in Canada and may replace the 7-valent pneumococcal vaccine (Prevnar®, Wyeth) in some jurisdictions. A 13-valent pneumococcal conjugate vaccine (Wyeth) will soon replace their 7 valent vaccine. A quadrivalent Men ACYW conjugate vaccine that can be administered to infants is under development as well as a meningococcal B vaccine.

Conclusion

With the undeniable past success of vaccine and immunization programs, it is important for the public and, in particular, health care workers to keep themselves up to date and informed. The public must be reassured about the safety, effectiveness, and benefits of immunization. Primary care practitioners must be knowledgeable advocates for the individual and population benefits of immunization as a lifelong investment into Canada's future. With the constantly changing field of vaccinology in Canada, undoubtedly another update will be needed in the next 4–5 years.

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New – Practitioner Guide for the Management of Whiplash-Associated Disorder in Adults

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The chiropractic clinical practice guideline, *Management of Whiplash-Associated Disorder in Adult*s, is now available on the Canadian Chiropractic Association website. Both the full Guideline as published in the journal WORK (Issue 35, 2010), and the easy reference Practice Guide for practitioners are posted on the website. To locate the Guideline and the Practice Guide visit www.chiropracticcanada.ca, click on About Us on the top navigation bar, then choose Clinical Practice Guidelines from the left navigation bar.

The development of chiropractic clinical practice guidelines is a joint initiative of the Canadian Chiropractic Association and the Canadian Federation of Chiropractic Regulatory and Educational Accrediting Boards.

Management of Whiplash-Associated Disorder in Adults complements the clinical practice guideline *Treatment of Adult Neck Pain Not Due to Whiplash*. A guideline on management of headache is currently in progress and is expected to be published in 2011.