Position Statement

Update on invasive meningococcal vaccination for Canadian children and youth

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Abstract

Invasive meningococcal disease (IMD) is serious, often resulting in fulminant sepsis or meningitis. IMD in Canada is primarily attributable to serogroups B and C. There are routine programs for serogroup C vaccine at 12 months of age, with some jurisdictions routinely providing additional earlier doses. Adolescents routinely receive a booster dose of serogroup C vaccine or of a quadrivalent (serogroups A, C, W and Y) vaccine. Serogroup B vaccines are not recommended for routine use pending further data on the efficacy and duration of protection from the available vaccine. However, children at increased risk for IMD should start immunization for serogroups B and C as soon as possible, assuming that they are at least 2 months of age.

Keywords: IMD; Meningitis; Sepsis; Vaccine

The present statement replaces three previous Canadian Paediatric Society (CPS) statements on meningococcal vaccines (1–3), supplements a previous CPS statement on meningococcal B vaccine (4) and updates the current epidemiology of invasive meningococcal disease (IMD) in Canada.

Five serogroups (A, B, C, Y and W, based on the polysaccharide capsule) cause virtually all IMD in Canada, with serogroups B and C predominating. Serogroup B disease has a peak incidence in children younger than 5 years of age and now accounts for over 70% of cases in this age group and over one-half of cases in all age groups (5,6). Serogroup C disease often occurs in outbreaks with a peak incidence in adolescents, and is associated with the highest case fatality rate (6). Since the introduction of routine conjugated meningococcal C (Men-C-C) immunization programs for infants, there has been a substantial decrease in meningococcal serogroup C incidence in all age groups, with no evidence of replacement by other meningococcal serogroups (5).

CLINICAL PRESENTATION

Neisseria meningitidis is a Gram-negative diplococcus. Asymptomatic nasopharyngeal carriage that persists for days to months is common. A very small percentage of carriers develop IMD, usually within a few days of acquiring carriage. IMD most commonly manifests as septic shock, meningitis or both, but can present as sepsis, pneumonia, septic arthritis, pericarditis or occult bacteremia. The Canadian Enhanced Meningococcal Surveillance System detected 154 to 229 cases of IMD annually from 2006 through 2011, for an incidence of 0.55 cases/100,000 population/year (5). Immunization Monitoring Program ACTive (IMPACT) provided surveillance data for over one-half of the Canadian population from 2002 through 2011 and detected 868 cases (449 adults; 419 children) of which 157 (18%) had sequelae apparent at discharge and 73 died (4% case fatality rate in children and 12% in adults) (6). As expected due to overlapping years and populations, the serogroup distribution in the two surveillance programs was similar: B (55% to 57%), C (12% to 19%), Y (17%), W (5%) and other/unknown (4% to 9%) (5,6). Although the disease burden of IMD in Canada is lower than for other invasive bacterial infections, including pneumococcal disease, meningococcal disease remains of great concern to both physicians and parents due to the characteristic rapid evolution of disease, sometimes leading to death or loss of limbs or digits.
CURRENT VACCINES

Table 1 shows the vaccines currently available in Canada. In 2001, Men-C-C vaccines became available and are currently routinely offered at 12 months of age in all Canadian jurisdictions. As of 2017, additional doses at 2 or 4 months of age are offered in Alberta, British Columbia, Yukon and the Northwest Territories to protect younger children and potentially to confer longer lasting immunity (7).

There are three quadrivalent conjugated vaccines (Men-C-ACYW) licensed in Canada for serogroups A, C, Y, and W. Menactra (Men-C-ACYW-DT; Sanofi-Pasteur) is conjugated to diphtheria toxoid protein, Menveo (Men-C-ACYW-CRM; Novartis Vaccines and Diagnostics Inc.) is conjugated to CRM<sub>197</sub> protein, and Nimenrix (Men-C-ACYW-TT; Pfizer Canada Inc.) is conjugated to tetanus toxoid protein. Adolescent programs with a single dose of either Men-C-C or Men-C-ACYW are in place in every jurisdiction in Canada. Children at high risk of IMD because of underlying medical conditions or exposure (as soon as the high risk condition is recognized) and require a minimum of two doses (8). Men-C-ACYW-CRM was immunogenic in children 2 months to 2 years of age in studies in the UK, Latin American and the USA (9) and is currently the recommended product in Canada for children in this age group at high risk of IMD. Men-C-ACYW-DT (10) and Men-C-ACYW-TT (11) were immunogenic in studies starting at 9 months of age, but the data in younger children are limited. All Men-C-ACYW vaccines are thought to be less immunogenic for serogroup C than Men-C-C (12), so there are currently no plans to replace Men-C-C with Men-C-ACYW for the routine infant program. Given the rarity of disease from serogroups A, Y and W, routinely providing both vaccines to infants is not recommended. Serious adverse events from Men-C-C or Men-C-ACYW are limited to anaphylaxis, which occurs very rarely.

Conjugate meningococcal vaccines induce strong antibody responses and prime the immune system to yield memory responses. Universal vaccination programs also reduce disease by decreasing carriage and conferring herd immunity. However, meningococcal disease has an incubation period as short as 2 days. Therefore, it is possible that an anamnestic response cannot be relied upon to prevent disease and that circulating antibodies are needed at all times for protection. Antibody titres to Men-C-C and Men-C-ACYW wane within a few years (12). Thus, lifetime protection (or even protection through late adolescence) may not be achieved with infant immunization followed by a single adolescent dose. Two adolescent doses are recommended in the USA. However, given the low incidence of IMD in older adolescents in Canada, only a single adolescent dose is currently advised.

The challenge in developing a vaccine for serogroup B is that the polysaccharide capsule of serogroup B is poorly immunogenic.

### Table 1. Meningococcal vaccines available in Canada

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Indications</th>
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<tbody>
<tr>
<td>Conjugated meningococcal C (Men-C-C)</td>
<td>Routinely offered at 12 months of age with earlier doses in Alberta, British Columbia, Yukon and the Northwest Territories (as of 2017)    Can omit 12 month dose if already received minimum one dose of Men-C-ACYW-CRM (because they are at high risk for IMD or travelled to a high-risk country) and are expected to receive a second dose within 8 weeks</td>
</tr>
<tr>
<td>Quadrivalent conjugated vaccines (Men-C-ACYW)</td>
<td>Used for the adolescent booster in Manitoba, Quebec and Nunavut (as of 2017) Used for the adolescent booster in all provinces and territories, except Manitoba, Quebec and Nunavut (as of 2017) Two or three doses recommended starting at 2 months of age for children at high risk of IMD, with a booster dose at 12–23 months, every 3–5 years until 7 years of age, and every 5 years thereafter Recommended for individuals ≥2 months of age travelling to countries with a high risk of invasive meningococcal disease (two or three doses if &lt;12 months old, two doses if 12–23 months, one dose if ≥24 months) Men-C-ACYW-CRM is currently recommended over the other two available brands (Men-C-ACYW-DT and Men-ACYW-TT) for children &lt;2 years of age</td>
</tr>
<tr>
<td>Meningococcal B vaccine (4CMenB)</td>
<td>Two or three doses recommended starting at 2 months of age for children at high risk of IMD, with a booster dose at 12–23 months, every 3–5 years until 7 years of age, and every 5 years thereafter</td>
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</table>

IMD Invasive meningococcal disease
Table 2. Patients at increased risk for invasive meningococcal disease

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<thead>
<tr>
<th>Risk increased because of underlying medical conditions</th>
<th>Patients at increased risk for invasive meningococcal disease</th>
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<tbody>
<tr>
<td>Asplenia or functional asplenia, including those with sickle</td>
<td><strong>•</strong> All adolescents should be offered one booster dose with Men-</td>
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<tr>
<td>cell anemia</td>
<td>C-C or Men-C-ACYW as per provincial or territorial programs.</td>
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<tr>
<td>Properdin, factor D or complement deficiency (including those</td>
<td><strong>•</strong> Children at increased risk for invasive meningococcal disease (IMD) because of underlying medical conditions (Table 2) should begin Men-C-ACYW and 4CMenB immunization at the time of diagnosis of this condition, assuming that they are at least 2 months of age and even if they have already received Men-C-C. They require two or three doses of both Men-C-ACYW and 4CMenB, administered a minimum 8 weeks apart (with the exception that 4CMenB doses can be given 4 weeks apart if the child is at least 11 years old). A 12- to 23-month booster dose of both vaccines is required when the initial doses were administered in the first year of life. Children at increased risk for IMD who have received Men-C-ACYW do not need to receive the routine dose of Men-C-C at 12 months of age. The preferred Men-C-ACYW vaccine before 2 years of age is Men-C-ACYW-CRM. See <a href="http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-meni-eng.php">www.phac-aspc.gc.ca/publicat/cig-gci/p04-meni-eng.php</a> for further details.</td>
</tr>
<tr>
<td>primary antibody deficiency</td>
<td><strong>•</strong> Transplant recipients should receive routine meningococcal immunizations. However, immunizations should be given pretransplant for solid organ recipients even if they have not yet reached the age when they are typically given, and repeated post-transplant for hematopoietic stem cell transplant recipients.</td>
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<tr>
<td>HIV</td>
<td><strong>•</strong> Travellers 2 months of age or older to areas where the meningococcal infection risk is high (Table 1) should receive Men-C-ACYW (two or three doses if &lt;12 months of age, two doses if 12 to 23 months of age, and one dose if older) even if they already received one or more doses of Men-C-C. Doses should be given 8 weeks apart but can be given 4 weeks apart if travel is imminent. Children do not need to receive the routine dose of Men-C-C at 12 months of age if they have already received minimum one dose of Men-C-ACYW-CRM and are expected to receive the second dose within 8 weeks. 4CMenB is recommended only in the rare situation of travel to an area with an ongoing serogroup B outbreak with a strain that is predicted to be vaccine-preventable.</td>
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<tr>
<td>Risk increased because of the potential for exposure</td>
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<tr>
<td>Laboratory workers who work with meningococcus</td>
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<tr>
<td>Military personnel living in close quarters</td>
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<tr>
<td>Travellers to endemic areas (currently, travellers to sub-Saharan Africa and <em>Hajj</em> pilgrims)</td>
<td></td>
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<tr>
<td>Close contacts of a case of IMD</td>
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**IMD Invasive meningococcal disease Information from ref. (15).**

However, a vaccine targeting nonpolysaccharide surface antigens (4CMenB – Bexsero; Novartis Vaccines and Diagnostics Inc.) was licensed in Canada in 2013. As outlined in a previous CPS statement, the efficacy of this vaccine is uncertain and it is not currently recommended for routine use (4). Three doses appear to be required in infants. Therefore, the 20% of cases that occur in the first 6 months of life might not be prevented by adding the vaccine to the routine schedule at 2, 4 and 6 months of age (4,13). Titres to some vaccine components wane significantly over a period as short as 12 months after a primary series but are readily boosted by an additional dose (14,15), indicating that frequent boosters may be required for this vaccine.

Since serogroup trends and immunization strategies differ between Canada and other countries, it will be critical to continue Canadian surveillance programs. IMPACT continues to actively monitor IMD at select hospitals, while the Enhanced Meningococcal Surveillance System monitors all IMD infections in Canada. Health care professionals who administer vaccines should report possible adverse events to public health authorities and to the Public Health Agency of Canada, at [www.phac-aspc.gc.ca/im/aefi-form-eng.php](http://www.phac-aspc.gc.ca/im/aefi-form-eng.php).

Strategies to protect the Canadian population against meningococcal infection will continue to evolve as serogroups shift, newer and better vaccines become available, and more is learned about the persistence of protective antibodies after immunization.

**RECOMMENDATIONS**

In view of the safety, immunogenicity and effectiveness of meningococcal vaccines, as well as the severity of some *Neisseria meningitidis* infections and public concern about the risk of severe meningococcal disease, the Canadian Paediatric Society recommends the following:

- All children in Canada should be immunized with one dose of Men-C-C at 12 months of age. Children may receive additional Men-C-C immunizations at an earlier age if recommended by provincial or territorial vaccine programs (7).
• Laboratory personnel who work with meningococcus and military personnel living in close quarters should receive one dose of both Men-C-ACYW and 4CMenB. Boosters are recommended every 5 years.

• For children with underlying medical conditions that increase their risk of IMD (Table 2), or ongoing travel, boosters of Men-C-ACYW are recommended every 3 to 5 years until 7 years of age, and every 5 years thereafter (8). Pending specific recommendations, boosters of 4CMenB should be given according to the same schedule.

• People who are eligible for chemoprophylaxis following exposure to a case of IMD should all receive immunization, if the strain is vaccine-preventable. A booster dose may be indicated even when the contact has previously been fully immunized. Such situations should be discussed urgently with the local Medical Officer of Health.

• Widespread immunization may be indicated during an IMD outbreak.

References

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