PedsCases Podcast Scripts

This is a text version of a podcast from Pedscases.com on "CPS Meningococcal Vaccination" These podcasts are designed to give medical students an overview of key topics in pediatrics. The audio versions are accessible on iTunes or at www.pedcases.com/podcasts.

CPS Meningococcal Vaccination

Developed by Dr. Sarah Johnson and Dr. Joan Robinson for PedsCases.com.
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Introduction:

Hello everyone, my name is Dr. Sarah Johnson, a first year paediatrics resident at the Stollery Children's Hospital at the University of Alberta in Edmonton. This podcast was produced by PedsCases and the Canadian Pediatric Society (CPS), and will be summarizing the new CPS update statement on invasive meningococcal vaccinations for Canadian children and youth, with some background information on invasive meningococcal infections. This podcast was created under the guidance of Dr. Joan Robinson, a paediatric infectious diseases specialist and associate professor at the University of Alberta. She is the lead author of this CPS statement.

Learning Objectives

Today we will review:
1. The clinical presentation and epidemiology of *Neisseria meningitidis* in Canada;
2. The current vaccination schedule and guidelines for vaccination; and
3. How to identify children and adolescents who may need extra vaccinations.

Clinical Case

How about we start with a clinical case? You are a fourth year medical student on your community paediatrics rotation. A mother and her three children, ages 12 years, 2 years, and 1 month come in for check-ups. The family is going to visit relatives in Nigeria in several months and the children have received all their routine vaccinations. However, the mother says that she is worried about meningitis and was wondering if there were any extra shots her children could get to receive extra protection.

Clinical Presentation and Epidemiology

Neisseria meningiditis is a gram negative diploccocus that should be taken seriously as a pathogen, as it is responsible for causing invasive meningococcal disease, or IMD, which can lead to meningitis or sepsis. The incidence of IMD in Canada is currently 0.55

cases per 100 000 people per year, in other words between 154 and 229 cases per year across the country. The incidence is much higher in other countries, especially those in sub-Saharan Africa. Despite being relatively rare in Canada, infections with *Neisseria menigitidis* are important not to miss as IMD progresses rapidly. Even in children that develop IMD in countries with advanced health care, there is a 5% mortality rate, with 20% of survivors having long-term sequelae.

An infection with *N. meningiditis* starts out fairly innocently when a person becomes colonized with it in their nasopharynx. Most people that carry this bug may just have mild upper respiratory symptoms or be asymptomatic. However, for the small subset of people who develop IMD secondary to carriage of *N. meningitides*, it only takes a few days to develop symptoms. IMD most commonly causes septic shock or meningitis, but can also present as septic arthritis, pneumonia, pericarditis or occult bacteremia.

Patients with IMD are all bacteremic so they will be febrile. They will likely also have some combination of headache, loss of appetite, nausea, vomiting, myalgias or respiratory symptoms. In other words, it is a good idea to often keep IMD on your differential, due to the non-specific initial presenting symptoms. Most patients with IMD develop a rash within a few hours of onset of the fever. The classic petechial rash starts off as small lesions 1-2 mm in diameter that may be present on the soft palate, or the palpebral conjunctiva. Because the rash is subtle at first, you should examine every febrile child from head-to-toe, looking for any petechiae, or spots that do not blanche or disappear when you press on them. The petechiae soon coalesce into larger bruise-like non-blancheable lesions or echymoses. Within hours, patients can progress to septic shock and death. Therefore, in every febrile child, you should assess for signs of shock such as vital sign changes, cool extremities, leg pain, and pallor or mottling. For more details of normal ranges for pediatric vital signs by age group, please refer to the “Pediatrics Vitals Sign Reference Chart” available at www.pedscases.com.

If the bacteria crosses the blood brain barrier, the child will develop meningitis. Children with IMD and meningitis are thought to have a slightly better prognosis than children with IMD who do not have meningitis as they survived long enough to develop meningitis. The classic triad of fever, neck stiffness, and altered mental status that occur in cases of meningitis are not always present in children, and the younger the child, the higher your index of suspicion should be.

In Canada, IMD is most commonly caused by serogroups B and C, with the remainder of infections caused by serogroups, Y, and W. IMD tends to strike in a bimodal distribution, with infants and young adults suffering from the largest burden of disease. Serogroup B peaks in children younger than 5, and disease caused by serogroup C tends to occur in adolescents. Serogroup C has been responsible for the highest case-mortality. The immunization program in Canada has been an important factor leading to the decreasing incidence of infections from serogroup C IMD, without an increase in infections from the other serogroups.

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Vaccination Schedule

Currently all Canadian provinces and territories offer vaccination for the meningococcal conjugate strain C at age 12 months, as children respond better at this age than in the first year of life. British Columbia, Alberta, Yukon and the Northwest Territories offer extra doses at 2 or 4 months to protect younger children. However, the number needed to vaccinate to prevent one case is very large. Since a single vaccine at 12 months does not confer life-time immunity, a second vaccine is recommended for adolescents, before the second peak in burden of disease. Across Canada, adolescents are offered a Men-C-C booster or a quadrivalent meningococcal conjugate vaccination. This quadrivalent conjugate covers for serogroups A, C, Y, and W and is known as Men-C-ACYW. The reason conjugated vaccinations are used is because the polysaccharide capsule on *N. meningitidis* is not very immunogenic, and needs to be bound to proteins, such as tetanus or diphtheria toxoid, to induce a stronger immunogenic response. The only serious side effect of the meningitidis vaccination is anaphylaxis, which is a very rare event.

You are probably wondering about serogroup B. We mentioned that serogroups B and C cause most IMD in Canada, but you may have noticed that there is no coverage against serogroup B in either the infant or the quadrivalent adolescent vaccinations. This is because the polysaccharide capsule of serogroup B is similar to existing glycoproteins in the human body and therefore even when conjugated, vaccines have been poorly immunogenic. A vaccine targeting non-polysaccharide surface antigens is licensed for use in Canada and is called 4CMenB. It is used routinely in the UK and has been shown to be effective in infants. However, it is not routinely used in Canada as our incidence of serogroup B is much lower than in the UK, it takes 3 doses to protect an infant, and we think that immunity wanes within a few years. Currently, this vaccine is only recommended under special circumstances.

Recommendations for Meningococcal Vaccines for Children at Higher Risk

While many cases of IMD can be prevented with the routine schedule, there are individuals who require additional vaccinations due to certain risk factors. The updated CPS statement delves into these risk factors and outlines when the meningitis B vaccination should be used for children in Canada.

Children are at increased risk of IMD due to either an immunocompromised state, or because they are more likely than other children to be exposed, typically because of travel. Patients who require additional meningococcal vaccinations due to their immunocompromised state include those with HIV, asplenia, or functional asplenia (for example secondary to sickle cell anemia). Further, patients with immunodeficiencies such as properdin, factor D, complement deficiencies, primary antibody deficiencies, or patients with secondary complement deficiency from eculizumab (which is used for atypical HUS or for paroxysmal nocturnal haemoglobinuria) will need additional vaccinations.

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Patients with underlying medical conditions that result in an immunocompromised state will need to receive the Men-C-ACYW (the quadrivalent vaccine) and the 4CMenB vaccination as soon as possible assuming that they are at least two months old. These two vaccinations can be given along the same schedule. Patients will need two to three doses of both these vaccines, with each dose at least 8 weeks apart once their diagnosis is made, even if they have already had their Men-C-C vaccination. If the vaccines are given before they are 12 months of age, they will need booster doses at 12-23 months after their last dose was given. They will also need further boosters every 3 to 5 years until they turn 7, continuing every 5 years after that. This is because the immunity to the Men-B vaccination wanes very quickly. Children do not need to get the routine Men-C-C at 12 months if they already received Men-C-ACYW.

The group of immunocompromised patients who differ from this schedule are those children with transplants. These patients should get their routine meningococcal vaccines, but ideally should have their vaccines given pre-solid organ transplant, or post-hematopoietic stem cell transplant. The schedule is fairly detailed, can be confusing, and will likely change over time, therefore we recommend that you discuss each case with Public Health or an Infectious Disease Specialist.

Potential exposure to *N. meningiditis* is increased in some laboratory workers, military personnel, close contacts of a case of IMD, or travelers to endemic areas such as sub-Saharan Africa or Hajj pilgrims. For laboratory personnel and military personnel, one dose of Men-C-ACYW and 4CMenB should be given in addition to the routine schedule. For travellers to high risk areas (typically sub-Saharan Africa), the Men-C-ACYW should be provided. One dose should be given to anyone older than 23 months, two doses if between 12-23 months, and two or three doses if less than one year old. Doses should ideally be given eight weeks apart, but can be given four weeks apart if there is not enough time to space them out further before travel. Children need Men-C-ACYW to protect them against serogroups A, Y and W even if they have received their Men-C-C, but do not need to get their Men-C-C vaccination if they have had Men-C-ACYW. In the rare situation where they are going to an area where there is an ongoing serogroup B outbreak with a strain that is thought to be vaccine preventable, they might be eligible for the 4CMenB vaccine.

When a patient has been exposed to a case of IMD, contact your local Medical Officer of Health as soon as possible for advice

Case Review

And now, back to our case. Having just listened to this podcast you enthusiastically congratulate the mother on her interest in protecting her children via vaccination. You tell her that yes, we do have vaccines that can help prevent one of the causes of meningitis and that since they are going to Sub-Saharan Africa they should be eligible. Her 12 year old and 2 year old will need one dose of the Men-C-ACYW, but her 1 month

old will need two to three doses, starting when they are 2 months of age. The multiple doses for the baby should be given 8 weeks apart if there is time, but can be given as close together as 4 weeks if necessary. You encourage her to attend a travel clinic where more information can be obtained about other vaccinations and prophylaxis the family may need.

Learning Objectives

This brings us to the end of our PedsCases podcast on the updated CPS statement on invasive meningococcal vaccinations for Canadian children and youth. Today we have reviewed:
1. The clinical presentation and epidemiology of Neisseria meningitidis in Canada;
2. The current vaccination schedule and guidelines for vaccination; and
3. How to identify children and adolescents who may need extra vaccinations.

To conclude, let's summarize the most important take home points:

- Invasive meningococcal disease, while rare in Canada, can cause significant mortality and morbidity.
- Clinicians should suspect IMD in an infant or young adult with fever and systemic symptoms. A high index of suspicion is needed.
- Vaccinations for Neisseria *meningitis* serogroup C are given at 12 months and the quadrivalent vaccine covering serogroups A, C, Y, and W is given in adolescence with some variations between provinces.
- In patients who are immunosuppressed or at increased risk of exposure, additional doses of the quadrivalent vaccine and the 4CMenB vaccine may be needed.

We hope that this PedsCases podcast has been helpful. Thanks for listening!

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