Immunization Update:
The Important Role of Vaccines

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Vaccines have played an important role in the health of our families since their introduction in North America > 40 years ago. Most adults of childbearing age are of the post vaccine era, often having never experienced these illnesses first hand. Without good knowledge of the effects of these diseases and potential sequelae, they cannot make good informed decisions about immunization. Counselling families on the importance of protecting themselves through vaccination requires up-to-date information on both the diseases we immunize against and the newest recommendations for vaccine administration.

Many new vaccines are now available for previously non-preventable illness such as meningococcal disease. Other vaccines that have been administered for longer periods of time are also undergoing re-evaluation and recommendations for most effective use in today's population are emerging.

Quadravalent meningococcal vaccines have recently been licensed for use in children and adults. Changes in disease epidemiology have also resulted in updates for the use of measles, mumps, rubella (MMR) vaccine and varicella vaccines. This update reviews disease epidemiology and current recommendations for vaccine administration of these three vaccines.

What is the quadravalent meningococcal vaccination?

Neisseria meningitidis is a bacterium that causes a variety of severe diseases. Meningitis is the most common presentation, comprising 75% of all infections. Meningococcemia, the most severe of the clinical disease states, comprises 20% of invasive meningococcal infection with the highest mortality (48%) and rate of permanent sequelae (50%). Organ specific infection is less common (5%) and can cause occult bacteremia, arthritis, myocarditis and pneumonia or infect any specific organ.

There are 18 serogroups of *N. Meningitidis*, 11 of which are known to cause meningococcal disease. Four are currently vaccine preventable—A, C, W-135 and Y. The burden of disease worldwide is mainly distributed between the four vaccine preventable serogroups and serogroup B, for which there is no currently licensed vaccine in Canada. Unlike pneumococcus, there is no cross protection between serogroups following vaccination.

Serogroups B and C comprise the bulk of disease in Canada and are the most common groups that infect children < 10-years-of-age. Serogroups Y and W 135 are seen with increased frequency in the adolescent and adult in Canada. Group A is uncommon in North America, although it is a significant cause of meningococcal disease in Asia

Table 1

Epidemiology of invasive meningococcal disease in Canada 1995-2004 by Serogroup[1]

Serogroup	Annual number of cases (range)	Average annual rate per 100,000 population	Median age (years)	Case fatality rate (%)
C	84 (47-182)	0.27	19	13
B	93 (65-129)	0.30	11	6
Y	28 (17-41)	0.09	45	7
W-135	9 (2-17)	0.03	19	8
A	0.5 (0-2)	0.002	41	0

and Africa. Peak rates of disease are under age one (9.2/100,000) and between ages 15 to 19 years (2/100,000).[1] These are, however, patterns only—individuals of any age no matter where they live are susceptible.

It is clear that this disease is rare, however potentially devastating, warranting appropriate preventative strategies such as immunization. Counselling families on their risk of invasive meningococcal disease should be done in a way that is meaningful to them. Statistics that health professionals commonly refer to, such as those in Table 1, can be confusing for families. Offering more tangible rates of infection and disease burden will help them make appropriate decisions about immunizing themselves and their families.

In Canada, four people will develop meningococcal infection each week, including:

- One child < 14-years-of-age
- One child 15- to 19-years-of-age
- Two adults

Meningococcal C-conjugate vaccine is administered to all children in Canada either in infancy or through catch-up programs at various ages in different provinces. Currently, Menactra® is the only quadravalent vaccine in Canada and is licensed for children more than two-years-of-age and adults. This vaccine offers coverage for serogroups A, Y, W-135 and C.

Recommendations on routine immunization with the quadravalent meningococcal vaccine differ amongst provinces and Canadian and American advisory bodies. The National Advisory Committee on Immunization (NACI) has not recommended routine immunization of all Canadian children (Table 2). It is important to recognize that they concluded that the vaccine was safe and effective; however, the burden of disease in Canadian children was felt to be too low to recommend routine vaccination of all children. This recommendation must be interpreted in light of administration of public health policy, not the care of the individual patient, where recommendations should be based on provision of the best healthcare available. The American Academy of Pediatrics has strongly recommended vaccination of all children, either at age 11, high school or post-secondary entry. Many provinces have made similar recommendations in their healthcare policy as well as many provincial pediatric societies. Again, it is important to remember that any serogroup can infect any age individual. The infrequency of the disease needs to be balanced by the significant morbidity and mortality when discussing the importance of quadravalent meningococcal vaccine with individual patients.

How do we manage the mumps virus and its outbreaks?

Mumps is typically a relatively benign illness. Subclinical infection is common. It is, however,

Table 2
Adapted ACIP MMR vaccination recommendations

Infants and children	Two doses measles, mumps and rubella (MMR): • First dose after first birthday • Second dose no sooner than 1 month after first and ideally at 15-18 months, but definitely prior to school entry
Secondary/post-secondary students	• Documented 2 doses of MMR or • Document serologic marker of immunity or • Serologically confirmed mumps infection or • Birth date prior to 1970
Healthcare workers	• Documented 2 doses of MMR or • Document serologic marker of immunity or • Serologically confirmed mumps infection or • Birth date prior to 1970 • Consider single dose MMR for those born prior to 1970
Military	• Documented two doses of MMR or • Document serologic marker of immunity or • Serologically confirmed mumps infection or • Birth date prior to 1970 • Consider single dose MMR for those born prior to 1970

ACIP: Advisory Committee on Immunization Practices

important to remember that serious complications and sequelae can occur. The most severe complication, meningoencephalitis, is rare but can result in mortality. Transient or permanent deafness is seen in 0.5 to 5/100,000 cases, orchitis in up to 50% and oophoritis in 5%. Orchitis and oophoritis are usually unilateral and therefore do not commonly result in sterility. Congenital anomalies are not described with infection during pregnancy, although infection in the first trimester is associated with increased rates of spontaneous abortion.[3]

Since the mumps vaccine was licensed in Canada in 1969 there have been sporadic outbreaks in all areas of the country. In the last decade, we have seen two large and four smaller outbreaks in Canada. The US and Britain have seen much larger outbreaks as well. The majority of subjects had received only one dose of the MMR vaccine (75%), although cases were seen (9%) in those with clear documentation of two doses of MMR as well.[3] However, the vaccine has been extremely successful at decreasing cases of mumps in our population. Prior to 1969 there were approximately 34,000 cases/annum reported in Canada. Following single dose MMR, the rates dropped dramatically to < 330 cases/annum and following a move to the two dose regimen < 80 cases/annum.

Vaccine effectiveness has been estimated by many studies to be approximately 64% after a single dose and > 88% after a second dose.[3] The reason for outbreaks of mumps is not known. It may be primary vaccine failure or waning immunity. Outbreaks have usually been observed in high-risk populations (*i.e.*, individuals with single dose vaccination in settings such as post-secondary education where respiratory spread occurs readily). Outbreaks have also been seen in communities that are undervaccinated with importation of the index case from international immigration from countries with no or poor vaccine coverage.

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Children in Canada who are ≤ 10-years-of-age should have received two doses of MMR. Timing of vaccine administration differs from province to province and as well in the US. The first dose is typically given at 12- to 15-months-of-age, a second at either 18 months or at age four to six. Time between doses should be a minimum of 28 days. Optimal timing of doses has not been established.

Recommendations for outbreak management have not yet been published by NACI. Recommendations typically are made locally. The Advisory Committee on Immunization Practices (ACIP) has made recommendations that are useful for the Canadian setting (Table 2). Their recommendations differ in terms of age groups due to earlier introduction of MMR into the US and the administration of the second dose of MMR at age four. Taking these changes into account, adapting ACIP strategy to Canadian outbreaks of mumps would involve:

- Ensure all children age one to 10 years have two documented doses MMR
- Second dose MMR to children 10 to 17 years who do not have:
  - Serologically documented-immunity or prior infection
- Second dose MMR to post-secondary students who do not have:
  - Serologically documented-immunity or prior infection
- Second dose MMR for healthcare workers who do not have:
  - Serologically documented-immunity or prior infection

Some provinces have broadened their approach to mumps prevention and have recommended routine vaccination of all individuals born after 1970 and prior to the initiation of the two dose MMR schedule, which occured circa 1996 in most provinces, unless there is documentation of prior infection with mumps virus.

Currently there seem to be contradictory recommendations from ACIP and Provincial Health Authorities with ACIP recommending vaccinating those born prior to 1970 who have not had mumps and Provincial Health Authorities recommending a second vaccine for all those born after 1970 and prior to the two dose MMR schedule. This is not truly conflicting as ACIP is recommending vaccinating non-immune individuals born prior to 1970 and Provincial Health Authorities are recommending that all individuals with only one MMR and without documented wild mumps virus infection have two doses of MMR.

What is the varicella vaccine breakthrough infection?

Varicella (chicken pox), prior to the vaccine era, was one of the most common diseases of childhood. While clinical illness is usually mild, more severe disease requiring hospitalization or even resulting in death is well described. Vaccine programs for varicella were introduced into North America beginning in 1995. Since this time, we have seen approximately 87% reduction in hospitalization rates and 66% reduction in varicella attributed deaths.[4]

Pre- and post-licensure trials estimate single dose vaccine efficacy at a range of 70% to 90% over study periods from four to 10 years. Efficacy in reducing secondary household attack rates, a more vigorous test of efficacy due to the intensity of exposure, were estimated at 79%. Efficacy in prevention of moderate to severe disease, defined by a variety of criteria including number of lesions, fever, hospitalization or complications, is approximately 95%.[5]

However, breakthrough infection is becoming increasingly more common. Breakthrough is defined as varicella infection occurring > 42 days after immunization. Breakthrough disease is typically much milder, with a shorter duration, papules which may not progress to vesicles and usually patients will have < 50 vesicles. However, breakthrough disease can also present similar to wild

Table 3

ACIP recommendations for two dose varicella vaccination

Children age 1-4 years:

- First dose at 12-15 months, second at age 4

Adolescents and adults without evidence of prior immunity*:

- Two doses 4-8 weeks apart

Individuals of any age with single dose history:

- Catch up everyone with single dose

Pregnancy:

- Screen for immunity and for nonimmune
- Give two doses 4-8 weeks apart after delivery

* ACIP criteria for varicella immunity include:
- 1 dose age 1-4 years old, 2 doses school age
- Serologically confirmed immunity
- Varicella disease confirmed by medical practitioner

virus infection in up to 25% of individuals and two breakthrough disease deaths have been reported in the US in immune competent individuals. Estimated rates of breakthrough infection are currently 15% per lifetime.[5]

Second dosing of the varicella vaccine has been suggested to decrease breakthrough rates and to decrease spread during an outbreak. Offering a second varicella vaccine has been shown in a variety of studies to decrease population breakthrough rates by 3.3 to 5 fold.[4-5] The second dose of vaccine should be offered no sooner than three months after primary vaccination in children < 12-years-of-age and between four to eight weeks following primary vaccination in all individuals > 12-years-of-age (Table 3).

In Canada, NACI has made no formal recommendation to date. However, in the US, ACIP has made clear recommendations, which many provinces in Canada have already adopted into their immunization strategies.

Recommendations differ from province to province however, most suggest administering varicella vaccine to all unimmunized children < 13-years-of-age. For those > 13-years-of-age, including adults, without a confirmed history of varicella, serology should be done to confirm immunity as most will be immune. Many individuals will have had varicella and not recall the illness or have had subclinical disease which is not uncommon.

For control of outbreaks, ACIP recommends offering a second dose to all at risk as long as criteria for spacing of vaccine in children < 12 years and > 12 years is met. They also suggest offering the vaccine even if it is late in the outbreak situation.

Take-home message

- Who is at risk for meningococcal disease?
  - Infants/children/adults of any age
- A second MMR should be considered for all individuals born after 1970 and prior to initiation of the two dose MMR schedule who have not had mumps infection
- Providing two doses of varicella vaccine significantly decreases rates of breakthrough infection

Conclusion

The role of providing up-to-date, evidence-based counsel to families regarding vaccination is challenging. We must take into account recommendations that are based on cost effectiveness for mass vaccination, on ideal patient care and disease prevention, as well as the growing number of vaccines now given to children and adults. Teaching families about the disease states and their potential serious complications, educating them about vaccines and changing recommendations, as well as understanding parental concerns about the number of vaccines now given, can help to ensure we protect our children and families to the best extent possible.

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For references, please contact **cme@sta.ca**