Prevention is the new Treatment - Vaccine Updates

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CSHP Ontario Branch Annual Education Conference
November 2018

Disclosures

- Presenter Disclosure
 - I have no current or past relationships with commercial entities
 - I have received no speaker's fee for this learning activity
- Commercial Support Disclosure
 - This program has received no financial or in-kind support from any commercial or other organization

Learning Objectives

- To describe the epidemiology of influenza and invasive meningococcal disease (IMD)
- To review select vaccines for influenza and IMD available
- To discuss updates in vaccine related guidelines and resources

Influenza - Background

- Respiratory infection caused by influenza A or B viruses
- Influenza A viruses:
 - Classified into subtypes based on two surface proteins haemagglutinin (HA) and neuraminidase (NA)
 - 3 subtypes of HA (H1, H2, H3) and 2 of NA (N1, N2) cause widespread disease
- Influenza B viruses:
 - 2 lineages B/Yamagata and B/Victoria

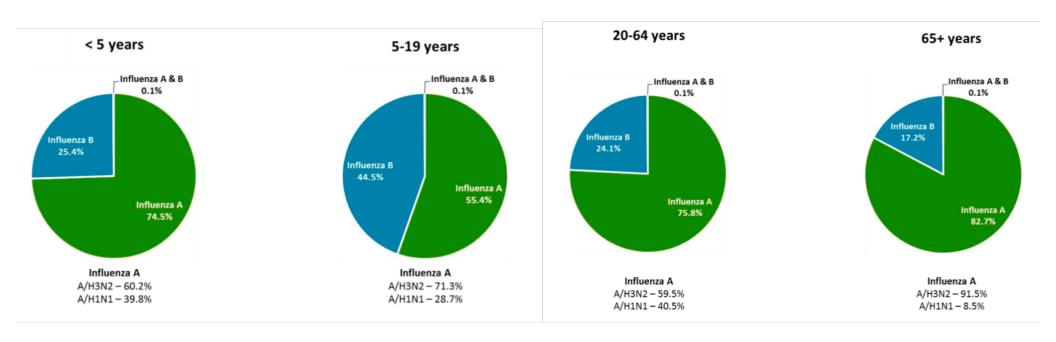
Influenza - Background

- Individuals at high risk of complications or hospitalizations:
 - Those with chronic medical conditions
 - Residents of nursing home or chronic care facilities
 - Adults ≥ 65 years old
 - Children 6 to 59 months of age
 - All pregnant women
- Serious influenza-related complications:
 - Pneumonia (viral or secondary bacterial)
 - Worsening of underlying medical conditions

Influenza - Epidemiology

- 10-20% of Canadian population contract influenza annually
 - Highest infection rates in children aged 5-9 years
- Morbidity and mortality highest in children <2 years, adults >65 years, and patients with underlying medical conditions
 - Canada: ~3,500 deaths annually
 - Ontario: annual averages of 272 deaths and over 620,000 health care utilization episodes

Influenza - Epidemiology



Influenza - Epidemiology

- 2012 Public Health Agency of Canada Survey Report:
 - Influenza immunization rate remained unchanged since 2001
 - General population: ~37%
 - Adults >65 years: ~65%
 - Adults 18-64 years with chronic medical conditions: ~38%
- 2017 Public Health Agency of Canada Impact Study:
 - Pharmacist expanded scope resulted in 5% vaccine uptake (95% CI 1.02-1.08)

Publicly Funded Influenza Vaccines – 2018/19

Vaccine Products	Quadrivalent Inactivated Vaccines (QIVs) Quadrivalent Live Attenuated Influenza Vaccine (Q-LAIV)		High-Dose Trivalent Inactivated Vaccines (High-Dose TIV)		
Viral Strains	A/H3N2, A/H1N1			A/H3N2, A/H1N1	
Contained	B/Yamagata, B/Victoria			B/Victoria	
	(15 mcg per antigen for QIVs)			(60 mcg per antigen)	
	(10 fluorescent focus units of each strain for Q-LAIV)				
Brand Name	FluLaval® Tetra	Fluzone® Quadrivalent	FluMist® Quadrivalent	Fluzone® High-Dose	
Dosage	1 dose (0.5 mL)*	1 dose (0.5 mL)*	1 dose (0.2 mL total, 0.1 mL in each nostril)*	1 dose (0.5 mL)	
Administration	Intramuscular	Intramuscular	Intranasal spray	Intramuscular	
Age Indications	≥6 months	≥6 months	2 to 59 years	≥65 years	
Formats	Multi-dose vials	Multi-dose vials Prefilled syringes	Prefilled sprayers	Prefilled syringes	

^{*2} doses required in the current season, given 4 weeks apart in children less than 9 years old receiving influenza vaccine for the very first time.

Publicly Funded Influenza Vaccines – 2018/19

Funding Eligibility by Age Group					
Age Group	Quadrivalent Inactivated Vaccines (QIVs)	Quadrivalent Live Attenuated Influenza Vaccine (Q-LAIV)	High-Dose Trivalent Inactivated Vaccines (High-Dose TIV)		
6 to 23 months	✓				
2 to 17 years	✓	✓			
17 to 64 years	✓				
65 years and older	✓		✓		

MF59-Adjuvanted Trivalent Inactivated Influenza (TIV) Vaccine – Fluad®/ Fluad Pediatric®

- Not publicly funded for the 2018/19 influenza season
- MF59: oil-in-water emulsion to help stimulate immune response

Viral Strains Contained	A/H3N2, A/H1N1 B/Victoria (15 mcg per antigen)		
Brand Name	Fluad [®]	Fluad Pediatric®	
Dosage	1 dose (0.5 mL)	1 dose (0.25 mL)*	
Administration	Intramuscular	Intramuscular	
Age Indications	≥65 years	6 months to 2 years	
Formats	Prefilled syringe	Prefilled syringe	

^{*2} doses required in the current season, given 4 weeks apart in children less than 9 years old receiving influenza vaccine for the very first time.

National Advisory Committee on Immunization (NACI) Guideline Update

- Fluzone® High-Dose (High-Dose TIV):
 - Provides superior protection compared to standard-dose TIV in adults ≥ 65 years
 - No evidence identified comparing high-dose vaccines to the MF59-adjuvanted standard-dose TIV vaccine
- Fluad® (MF59-Adjuvanted standard-dose TIV vaccine):
 - May be effective at reducing hospitalization and influenza complications in adults ≥ 65 years compared to those unvaccinated
 - Insufficient evidence comparing to unadjuvanted TIV subunit vaccines

National Advisory Committee on Immunization (NACI) Guideline Update

 Insufficient evidence comparing subunit to split virus standard-dose vaccines in terms of vaccine effectiveness and immunogenicity in older adults

Brand Name	Influvac®	Fluviral®	Agriflu®	Fluad® (Adult and Peds)	Fluzone® High-Dose	FluMist® Quadrivalent	FluLaval® Tetra	Fluzone® Quadrivalent
Vaccine Product	TIV	TIV	TIV	TIV	TIV	Live attenuated	QIV	QIV
Vaccine Type	Subunit	Split	Subunit	Subunit	Split	Live attenuated	Split	Split

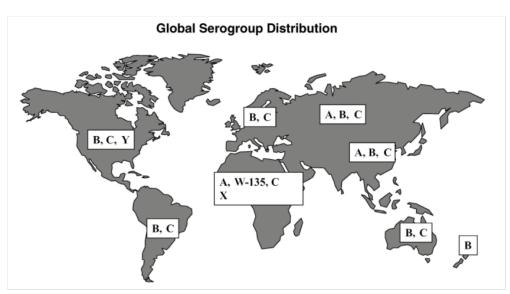
Meningococcus – Background

- Neisseria meningitidis
 - Gram-negative diplococcus
 - At least 13 different serogroups
 - 5 associated with invasive meningococcal disease (IMD): A, B, C, W-135, and Y
 - Transmitted through droplets of respiratory or throat secretions

Meningococcus – Background

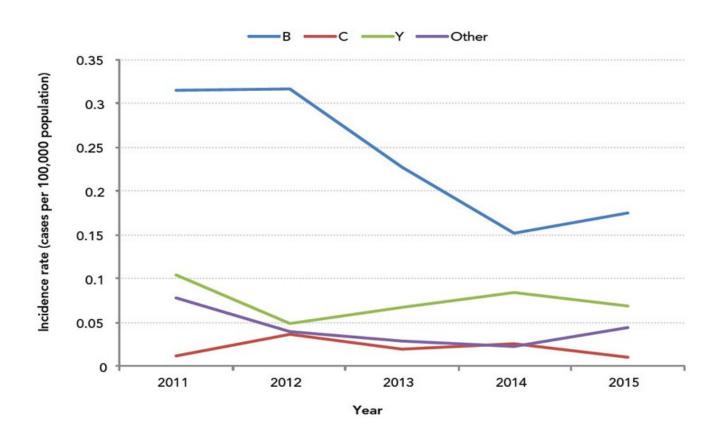
- Individuals at high risk of IMD:
 - Children <5 years of age
 - Asplenia
 - Immunocompromised
 - Travelers to endemic areas
 - Certain occupations (e.g. military personnel, research or lab personnel)
- Long-term sequelae:
 - Hearing loss
 - Neurologic disabilities

Meningococcus – Epidemiology



- Estimated 500,000 cases of IMD annually worldwide
- Highest rates in infants and adolescents

Meningococcus – Epidemiology



Multicomponent Meningococcal B Vaccine – Bexsero® (4CMenB)

Bacterial Components	NadA (Neisserial adhesion A) NHBA (Neisseria Heparin Binding Antigen) fHbp (factor H Binding Protein) PorA P1.4 (main antigen of Outer Membrane Vesicles)		
Dosage	0.5 mL per dose *Number of doses and intervals are age specific		
Administration	Intramuscular		
Age Indications	2 months to 25 years		
Formats	Prefilled syringes		
Publicly Funding Eligibility (High Risk Vaccine Program) • 2 months to 17 years of age • Eligible for 2 to 4 doses	 Acquired complement deficiencies (e.g., receiving eculizumab) Asplenia (functional or anatomic) Cochlear implant recipients (pre/post implant) Complement, properdin, factor D or primary antibody deficiencies HIV 		

Canadian Immunization Guide Update

- Bexsero® age indication for children aged 2 months to 11 months updated
- Pending updates:
 - Bexsero® dosage for children aged 2 months to 11 months
 - NACI statement on another meningococcal group B vaccine Trumenba™
- Bexsero® Product Monograph:
 - 2 to 5 months: 4 doses total
 - 2, 4, and 6 months of age, followed by the fourth dose (booster) between 12 and 23 months of age
 - 2, 3, and 4 months of age, followed by the fourth dose (booster) between 12 and 23 months of age
 - 6 to 11 months: 3 doses total, at least 2 months between doses
 - Third dose is given between 12 and 23 months of age (at least 2 months after second dose)

Canadian Immunization Guide Update

- Immunization Guide:
 - Travelers 2 to 11 months of age: 2 or 3 doses given 8 weeks apart (with another dose between 12-23 months of age at least 8 weeks from previous dose)
 - Post-exposure and outbreak control:
 - 2 to less than 6 months:
 - Unvaccinated: 1 dose immediately exposure, then 2 more doses with at least a 4 week interval
 - Previously vaccinated: 1 dose immediately exposure
 - 6 months to less than 11 years:
 - Unvaccinated: 1 dose immediately exposure, then 1 more dose with at least a 8 week interval
 - Previously vaccinated: 1 dose immediately exposure
 - High risk individuals from medical conditions 2 to 11 months of age: 2 or 3 doses given 8 weeks apart (with another dose between 12-23 months of age)

Meningococcal group B vaccine – Trumenba™

Bacterial Components	Bivalent: two recombinant lipoprotein (rLP2086) antigens from fHbp (factor H Binding Protein) subfamilies A and B fHBP variants A05 (subfamily A) and B01 (subfamily B).
Dosage	0.5 mL per dose Routine immunization: 2 doses total, administered 6 months apart Individuals at increased risk of invasive meningococcal disease: 3 doses total; 2 doses, administered at least 1 month apart, followed by a third dose at least 4 months after the second dose
Administration	Intramuscular
Age Indications	10 to 25 years
Formats	Prefilled syringes
Publicly Funding Eligibility	Not publicly funded in Ontario

Not interchangeable with Bexsero®. Need to complete the series with the same vaccine.

References

- 1. Public Health Agency of Canada National Advisory Committee on Immunization (NACI). Statement on Seasonal Influenza Vaccine for 2014-2015. Retrieved on Oct 8, 2018. URL: http://publications.gc.ca/collections/collection 2014/aspc-phac/HP40-114-2014-eng.pdf
- 2. Public Health Agency of Canada National Advisory Committee on Immunization (NACI). Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2018–2019. Retrieved on Oct 8, 2018. URL: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-statement-seasonal-influenza-vaccine-2018-2019.html
- 3. Kwong JC, Crowcroft NS, Campitelli MA, Ratnasingham S, Daneman N, Deeks SL, Manuel DG. Ontario Burden of Infectious Disease Study Advisory Group; Ontario Burden of Infectious Disease Study (ONBOIDS): An OAHPP/ICES Report. Toronto: Ontario Agency for Health Protection and Promotion, Institute for Clinical Evaluative Sciences; 2010.
- 4. Public Health Ontario. Influenza Vaccines available for Children and Older Adults for the 2018-19 Influenza Season. Retrieved on Oct 8, 2018. URL: https://www.publichealthontario.ca/en/eRepository/influenza-vaccines-2018-19-season.pdf
- 5. Buchan SA, Rosella LC, Finkelstein M, Juurlink D, Isenor J, Marra F, et al. Impact of pharmacist administration of influenza vaccines on uptake in Canada. CMAJ. 2017;189(4):E146-E152
- 6. Ministry of Health and Long-Term Care. Universal Influenza Immunization Program (UIIP). Retrieved on Oct 8, 2018. URL: http://www.health.gov.on.ca/en/pro/programs/publichealth/flu/uiip/
- 7. Seqirus Canada Inc. Product Monograph FLUAD Pediatric® and FLUAD®. Retrieved on Oct 8, 2018. URL: https://www.seqirus.ca/docs/627/59/2017%2018%20Fluad%20Product%20Monograph,0.pdf
- 8. DiazGranados CA, Dunning AJ, Kimmel M, Kirby D, Treanor J, Collins A, et al. Efficacy of High-Dose versus Standard-Dose Influenza Vaccine in Older Adults. NEJM. 2014;37(17):635-645
- 9. Public Health Agency of Canada National Advisory Committee on Immunization (NACI). Literature Review Update on the Efficacy and Effectiveness of High-Dose (Fluzone® High-Dose) and MF59-Adjuvanted (Fluad®) Trivalent Inactivated Influenza Vaccines in Adults 65 Years of Age and Older. Retrieved on Oct 8, 2018. URL: https://www.canada.ca/en/public-health/services/publications/healthy-living/executive-summary-literature-review-update-efficacy-effectiveness-fluzone-high-dose-fluad-trivalent-inactivated-influenza-vaccines-adults-65-older.html

References

- 1. Public Health Agency of Canada National Advisory Committee on Immunization (NACI). NACI Literature Review on the Comparative Effectiveness and Immunogenicity of Subunit and Split Virus Inactivated Influenza Vaccines in Adults 65 Years of Age and Older. Retrieved on Oct 8, 2018. URL:

 https://www.canada.ca/en/public-health/services/publications/healthy-living/literature-review-comparative-effectiveness-immunogenicity-subunit-split-virus-inactivated-influenza-vaccines-adults-65-vears-older.html
- 2. World Health Organization. Meningococcal meningitis. Retrieved on Oct 8, 2018. URL: http://www.who.int/news-room/fact-sheets/detail/meningococcal-meningitis
- 3. Rouphael NG, Stephens DS. Neisseria meningitidis: biology, microbiology, and epidemiology. Methods Mol Biol. 2012;799:1-20
- 4. Public Health Agency of Canada. Vaccine Preventable Disease: Surveillance Report to December 31, 2015. Retrieved on Oct 8, 2018. URL: https://www.canada.ca/en/public-health/services/publications/healthy-living/vaccine-preventable-disease-surveillance-report-december-31-2015.html
- 5. GlaxoSmithKline Inc. Product Monograph Bexsero®. Retrieved on Oct 8, 2018. URL: https://ca.gsk.com/media/1212390/bexsero.pdf
- 6. Ministry of Health and Long-Term Care. Publicly Funded Immunization Schedules for Ontario December 2016. Retrieved on Oct 8, 2018. URL: http://www.health.gov.on.ca/en/pro/programs/immunization/docs/immunization schedule.pdf
- 7. Public Health Agency of Canada Meningococcal Vaccine: Canadian Immunization Guide. Retrieved on Oct 8, 2018. URL: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-13-meningococcal-vaccine.html
- 8. Pfizer Canada Inc. Product Monograph Trumenba™. Retrieved on Oct 8, 2018. URL: https://www.pfizer.ca/sites/g/files/g10041266/f/201710/Trumenba PM 195550 05-Oct-2017 E.pdf