Alberta

Public Health Disease Management Guidelines

Influenza – Seasonal

Ministry of Health, Government of Alberta

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Influenza, Seasonal Public Health Disease Management Guideline

https://open.alberta.ca/publications/influenza

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Health and Wellness Promotion Branch

Public Health and Compliance Branch

Alberta Health

Case Definition

Confirmed Case

Clinical illness[(A)] with laboratory confirmation of infection:

- Detection of influenza RNA

OR

- Demonstration of influenza virus antigen in an appropriate clinical specimen

OR

- Significant rise (e.g., fourfold or greater) in influenza IgG titre between acute and convalescent sera

OR

- Isolation of influenza virus from an appropriate clinical specimen.

Outbreak Surveillance Definitions

Schools: Greater than 10% absenteeism OR absenteeism that is 10% higher than baseline levels determined by schools or surveillance region which is likely due to ILI.

Hospitals and Residential Institutions: Two or more cases of ILI within a seven-day period, including at least one laboratory-confirmed case. Institutional outbreaks should be reported by the fastest means possible (FMP). Residential institutions include, but are not limited to, facility living, home living/supportive living, and correctional facilities.

Other: Two or more cases of ILI within a seven-day period, including at least one laboratory-confirmed case; i.e., workplace, closed communities.

[(A)] Clinical illness defined as influenza-like illness (ILI) is characterized as follows: acute onset of respiratory illness with fever and cough and with one or more of the following:

- sore throat
- arthralgia
- myalgia
- prostration that could be due to influenza virus.

In children under five years of age, gastrointestinal symptoms may also be present. In patients under five years of age, or 65 years of age and older, fever may not be prominent.

Reporting Requirements

1. Physicians, Health Practitioners and others

Physicians, health practitioners and others shall notify the Medical Officer of Health (MOH) (or designate) of the zone, of all confirmed cases in the prescribed form by mail, fax or electronic transfer within 48 hours (two business days).

2. Laboratories

All laboratories shall report all positive laboratory results by mail, fax or electronic transfer within 48 hours (two days) to the:

- by FMP to the MOH (or designate) of the zone, and
- by mail, fax or electronic transfer within 48 hours (two business days) to the Chief Medical Officer of Health (CMOH) (or designate).

3. Alberta Health Services and First Nations Inuit Health Branch

- The MOH (or designate) of the zone where the case currently resides shall forward the initial *Hospitalized Seasonal Influenza Report* of all hospitalized confirmed influenza cases (including deaths) to the CMOH (or designate) within two weeks of notification and the final report within two weeks of discharge from hospital or resolution of the influenza case status.
- For out-of-province and out-of-country reports, the following information should be forwarded to the CMOH (or designate) by FMP:
  - name,
  - date of birth,
  - out-of-province health care number,
  - out-of-province address and phone number,
  - positive laboratory report, and
  - other relevant clinical / epidemiological information.

Epidemiology

Etiology

Influenza viruses belong to the *Orthomyxoviridae* family and are classified into three distinct types: influenza A, B and C. The majority of seasonal influenza epidemics are caused by influenza A and B viruses. Influenza A is further subtyped based on the 16 different hemagglutinin and nine different neuraminidase surface glycoproteins. Currently, H1N1 and H3N2 are the most common influenza A subtypes circulating among humans.[1]

In 2009, a novel influenza A virus (subtype H1N1), later renamed A(H1N1)pdm09, began to circulate in humans. It is a triple reassortment swine influenza A virus containing genes originating from avian, human and swine viruses. The hemagglutinin, nucleoprotein and non-structural genes are derived from classical swine virus of North American lineage. The neuraminidase and matrix genes are from Eurasian swine lineage, the polymerase genes PA and PB2, are from avian North American lineage and the PB1 polymerase gene is from an H3N2 human seasonal strain.[2] Since the end of the pandemic, the A(H1N1)pdm09 strain is now considered part of the circulating seasonal strains of influenza.

Influenza B viruses have diverged into two antigenically distinct lineages, namely Yamagata and Victoria.[3]

Clinical Presentation

Influenza typically begins with an abrupt onset of fever, chills, headache, prostration, myalgia and dry cough.[1] These symptoms are commonly followed by sore throat, nasal congestion and rhinitis.[4] The cough can last two weeks or more with the fever and other symptoms resolving in 5 – 7 days in uncomplicated cases. [1]

The onset of influenza in children is similar to adults although calf muscle myalgia, cervical adenopathy and fever may be particularly prominent.[5] Gastrointestinal (GI) involvement (nausea, vomiting and diarrhea) have been reported in children with influenza but GI involvement in adults is uncommon.[1]

Complications from influenza infection include primary influenza viral pneumonia, bacterial pneumonia (e.g., *Streptococcus pneumoniae* and *S. pyogenes*), exacerbation of chronic pulmonary conditions, sinusitis, otitis media, febrile seizures, encephalitis, myositis and death.[1] Reye syndrome has also been associated with influenza infections in children.[4] It is typically seen in children who have been given aspirin to treat fever from influenza.

Outbreaks of influenza are often associated with excess morbidity and mortality, and characterized by higher than normal rates of pneumonia and influenza-related hospitalizations and deaths.[5]

Reservoir

Humans. Influenza A viruses can also circulate in birds, pigs, horses, ferrets, seals and other animals. Influenza is usually not a zoonotic disease, although there can be exceptions.[1] Influenza B viruses only circulate in humans.[5] A third subtype of influenza virus exists, type C influenza, which is associated with sporadic cases and minor localized outbreaks. It does not cause nearly the significant burden of disease that influenza A and B does.

Transmission

Influenza is transmitted from person-to-person primarily via large droplet particles and droplet nuclei (i.e., aerosol) that are generated when the infected individual coughs or sneezes.[3] These large droplets can settle on the mucosal surfaces of the upper respiratory tract of susceptible people who are within two feet of the infected individual. Indirect transmission may also occur such as when touching surfaces contaminated with influenza virus and then touching the eyes or nose.

The virus can survive on hard surfaces (door handles, telephones, computer keyboards, light switches, countertops, etc.) for 1 – 2 days and on soft surfaces (cloth, tissues and paper) for 8 – 12 hours.[6] The virus can only **infect** an individual for up to eight hours on hard surfaces and only a few minutes on soft surfaces.

Incubation Period

The incubation period for influenza is generally 1 – 4 days with an average of 2 days.[1,4]

Period of Communicability

Infected individuals can shed the virus from the day before symptoms begin and are considered to be infectious up to seven days after illness onset. The amount of virus an individual sheds however is presumed to decrease substantially by 3 – 5 days after onset.[3] Individuals who are elderly, severely ill or children may shed virus for longer periods, up to 14 days.[5,7] Individuals who are immunocompromised may shed the virus for weeks or months.[8-11]

Host Susceptibility

Susceptibility is universal but also may depend on previous exposure providing cross-protection to new strains.[3] Influenza A is typically associated with greater morbidity and mortality than influenza B and typically affects the elderly, whereas influenza B is more often seen in young children. As well, H3N2-like viruses tend to be associated with more severe illness than H1N1-like or H1N2-like viruses.[5,12]

Attack rates tend to be highest in young children, while over 90% of influenza deaths occur in individuals 65 and older; however, influenza-related deaths can occur in any age group.[5]

The following individuals are at higher risk for complications related to influenza (including A(H1N1)pdm09) and may be more likely to require hospitalization:[13]

- healthy pregnant women; the risk of influenza-related hospitalization increases with increasing length of gestation; (i.e., it is higher in the third trimester than the second trimester) including the initial six weeks post partum,
- healthy children < five years (especially children < two years),
- adults ≥ 65 years,
- adults (including pregnant women) and children with the following chronic health conditions:
    - cardiac disorders (including hypertension that requires regular medical follow-up or treatment),
    - pulmonary disorders (including asthma, COPD, bronchopulmonary dysplasia and cystic fibrosis),
    - diabetes mellitus and other metabolic diseases,
    - renal disease,
    - chronic hepatic disease,
    - anemia or hemoglobinopathy,
    - conditions (including neurological) that compromise the ability to clear airway secretions and are associated with an increased risk of aspiration,
    - immunodeficiency or immunosuppressing conditions (including cancer) due to underlying disease and/or therapy and
    - morbid obesity (BMI ≥ 40 as chronic lung problems linked to extreme and morbid obesity, may increase an individual's risk),
- aboriginal populations,
- people of any age who are residents of nursing homes and other chronic care facilities and
- children and adolescents receiving long-term acetylsalicylic acid (ASA) therapy.

Incidence

General

Influenza occurs in annual epidemics of varying severity depending on the strain circulating. Between three and five million severe cases, and 250,000 to 500,000 deaths occur each year worldwide.[14]

While A(H1N1)pdm09 is now considered to be a seasonal strain of influenza, it initially began in the early spring of 2009 as clusters of severe respiratory illness in Mexico and mild illness in the south western United States (California and Texas). The spread of the virus rapidly evolved into a worldwide occurrence and was declared as the first influenza pandemic of the 21st century, based on the level of spread, not severity.[15] There were two waves of the pandemic. The severity of the pandemic was considered mild to moderate, with the overwhelming majority of patients experiencing mild symptoms and recovering fully without the need for hospitalization or medical care.[13] According to the World Health Organization (WHO), over 18,400 individuals died between April 2009 and August 2010 as a result of A(H1N1)pdm09.[16]

Canada

Each year, influenza causes outbreaks in Canada during the fall and winter months. The annual incidence of influenza varies depending on the strain that circulates and the

susceptibility of the population it affects. It is estimated that up to 20,000 hospitalizations occur in a given year related to influenza. Between 4,000 to 8,000 Canadians, mostly seniors, may die from pneumonia related to influenza and others may die from other serious complications of influenza.[13]

The first case of A(H1N1)pdm09 in Canada was reported by Nova Scotia on April 26, 2009. While most illnesses caused by the A(H1N1)pdm09 virus were self-limiting, a number of severe outcomes were reported. Hospitalization rates were highest for children under five years of age; however, the highest mortality rate occurred in adults aged 45 and older. Having at least one underlying medical condition, being pregnant or of Aboriginal status significantly increased the risk of hospitalization for ICU admission and death.[13]

For up-to-date national influenza surveillance information refer to the FluWatch national surveillance.

Alberta

In Alberta, influenza results in an average of 1,500 cases each year, including up to 500 hospitalizations and upwards of 30 deaths although the true incidence is likely under reported based on estimates provided by the Public Health Agency of Canada. Since the 2009 pandemic, season influenza cases and deaths have returned to pre-pandemic levels.

On April 27, 2009 the first case of A(H1N1)pdm09 was reported in Alberta. During the 2009–2010 influenza season 5,193 cases of influenza were reported in Alberta, including 476 hospitalizations and 71 deaths.

Public Health Management

Diagnosis

Diagnosis of influenza is made through a variety of molecular assays for detection and confirmation including direct fluorescent antibody (DFA) and molecular testing (e.g., polymerase chain reaction [PCR]).

DFA detects influenza A & B, respiratory syncytial virus (RSV) and the parainfluenza viruses in nasopharyngeal swabs and aspirates. When positive, a DFA result is definitive for that agent; however, a negative result does not necessarily rule out disease and could mean the sample was collected incorrectly, collected too late in illness or that this individual has cross-immunity (i.e., immunity from a previous exposure to another influenza strain). DFA tests positive for influenza A cannot determine which subtype of influenza A is present in the sample.
PCR is useful in that it is, by orders of magnitude, significantly more sensitive than DFA at detecting influenza. Assays that can differentiate between the different subtypes of influenza A (e.g., H3 or H1 or A(H1N1)pdm09) are available.

Although molecular testing is more sensitive than DFA, the turnaround time for DFA is much shorter and remains a valuable tool in early influenza diagnosis.

Key Investigation

Hospitalized cases (as defined under reporting requirements) are required to be:

- reported to Alberta Health by completing the *Hospitalized Seasonal Influenza Report* form.

Non-Hospitalized cases:

- are under laboratory surveillance only. No report form is required.

Daycares, Preschools and Schools:

- Schools with greater than 10% absenteeism OR absenteeism that is 10% higher than baseline levels determined by schools or surveillance region which is likely due to ILI should report to the local public health zone for further investigation.
- School closure as a measure to mitigate the spread of influenza is not currently recommended. Consideration for school closure will require consultation between the CMOH, local MOH and the affected school authority.

Management of a Case

- Individuals with symptoms of influenza should be told to self-isolate and monitor themselves for worsening symptoms.

Treatment of a Case

Treatment with antivirals is NOT generally indicated for mild to moderate illness unless the individual is at high risk for influenza-related complications. Treatment should be considered for severe cases. (See Host Susceptibility)

- See *Annex 1: Antiviral Regimens for Influenza* for dosing and schedules. Prescribing should be based on recent testing for antiviral resistance. Antiviral susceptibilities and resistance information can be obtained weekly and reports are available via FluWatch national surveillance.
- See Oseltamivir (Tamiflu®) Product Monograph.[17]
- See Zanamivir (Relenza®) Product Monograph.[18]

Management of Contacts

- Post-exposure prophylaxis of contacts is generally not recommended. Antivirals are usually recommended for treatment only, generally in those individuals at high risk for influenza-related complications.
- Provide targeted education to contacts of cases through public messaging including disease information and preventive measures.
- Household contacts should be instructed to:
  - continue their normal activities but self-isolate if they develop symptoms of ILI.
  - practice proper respiratory etiquette (e.g., cough into a sleeve).

- clean hands with soap and water frequently. Use alcohol-based hand gels (containing at least 60% alcohol) when soap and water are not available or when hands are not visibly dirty.
- ensure regular cleaning of high-touch objects and surfaces.

Outbreak Management
Outbreaks of ILI require immediate notification to the MOH (or designate), who in turn will notify the CMOH (or designate). All outbreaks should be reported to Alberta Health using the *Alberta Outbreak Reporting Form (AORF)*. Refer to the Outbreak Surveillance Definitions. ILI outbreaks should be managed as per direction from the local MOH.

Special Considerations for Outbreaks in Closed Facilities (including residential institutions and correctional facilities)

- A facility is deemed a closed facility when it has a fixed residential population with limited turnover.
- The MOH will determine the need and extent of outbreak control measures, use of antivirals for treatment and/or prophylaxis and the need for restrictions on admissions and transfers to and from the facility.
  - See *Annex 1: Antiviral Regimens for Influenza* for dosing and schedules. Prescribing should be based on recent testing for antiviral resistance. Antiviral susceptibilities and resistance information can be obtained weekly and reports are available via FluWatch national surveillance.

Preventive Measures

- Provide general and ongoing education to the public regarding influenza.
- All Albertans six months of age and older are eligible to receive annual influenza vaccine under the provincially funded program. Protective antibody levels are generally achieved two weeks following immunization.[19]
- Pneumococcal vaccine may be useful in preventing secondary bacterial infections in populations at high risk for influenza-related complications.

Resources

- Alberta Health website: https://www.alberta.ca/influenza-the-flu.aspx
- Alberta Health Services website: www.albertahealthservices.ca/influenza.asp

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ANNEX A: Antiviral Regimens for Influenza

(Based on current sensitivity testing)

OSELTAMIVIR (TAMIFLU®)			
Age/Weight		**Prophylaxis** (recommended dose for at least 10 days[▲])	**Treatment** (for 5 days)
Age 1–12 years*	15 kg or less:	30 mg once daily	30 mg twice daily
	>15 – 23 kg:	45 mg once daily	45 mg twice daily
	>23 – 40 kg:	60 mg once daily	60 mg twice daily
	>40 kg:	75 mg once daily	75 mg twice daily
Age ≥ 13 years (including pregnant[◆] and nursing women[⌘]) no Renal Impairment		75 mg once daily	75 mg twice daily
Adults with Renal Impairment		Creatinine Clearance (CrCl) less than 10 mL/min (and not on dialysis) • No data*	CrCl less than 10 mL/min (and not on dialysis) • Single 75 mg dose for the duration of the illness
		CrCl 10–30 mL/min: • 30 mg every other day for 10 days.	Creatinine Clearance (CrCl) 10–30 mL/min: • 30 mg once daily
		CrCl 31–60 mL/min: • 30 mg once daily for 10 days.	Creatinine Clearance (CrCl) 31–60 mL/min: • 30 mg twice daily
Adults Undergoing Haemodialysis*		Consult attending physician. Reference documents can be found at: www.ammi.ca/guidelines, or by accessing the Tamiflu product monograph at www.rochecanada.com	Consult attending physician. Reference documents can be found at: www.ammi.ca/guidelines, or by accessing the Tamiflu product monograph at www.rochecanada.com
Adults Undergoing Peritoneal Dialysis		• For adult patients on continuous ambulatory peritoneal dialysis (CAPD) an initial dose of 30 mg of oseltamivir administered prior to the start of dialysis followed by further 30 mg doses administered every 7 days, for a period of 10–14 days, is recommended.	• For adult patients on CAPD, a single 30 mg dose of oseltamivir administered prior to the start of dialysis is recommended.

* *Oseltamivir is not approved for use in children less than one year of age as it has not been evaluated adequately. It had been previously approved for off-label use in this age group by the Public Health Agency of Canada during the 2009 pandemic only.*

▲ *For the control of outbreaks in closed facilities, prophylaxis is recommended for a minimum of 10 days and up to 10 days after most recent case identified.*

◆ *Oseltamivir should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Oseltamivir in standard doses is recommended for treatment of pregnant women with influenza based on the extensive safe use of oseltamivir to treat pregnant women during the pandemic. The decision to use oseltamivir should be made in consultation with the woman's attending physician. Immunization is recommended for pregnant women, and is preferable to prophylaxis.*

⌘ *Limited data demonstrated that oseltamivir and the active metabolite were detected in breast milk; however the levels were low, which would result in a subtherapeutic dose to the infant. Considering this information and the pathogenicity of the circulating influenza virus strain, administration of oseltamivir may be considered where the potential benefit to the lactating mother justifies the risk to the nursing infant.*

* *Consult attending physician/Infectious Disease physician regarding treatment and/or prophylaxis recommendations.*

ZANAMIVIR (RELENZA®)		
Age/Weight	**Prophylaxis**	**Treatment**
Age ≥ 7 years (including pregnant[♥] and nursing women[♣]) **Excluding individuals with severe underlying airway disease or severe asthma[♦]**	In a household setting: • 10 mg (2 inhalations) once daily x 10 days. • No data on effectiveness when initiated more than 1.5 days after onset of signs or symptoms in index case. In a community outbreak setting: • 10 mg once daily x 28 days No data on effectiveness when initiated more than 5 days after outbreak identified in community.	10 mg twice daily for 5 days started within 48 hours of onset of symptoms.

♥ *Zanamivir, should not be used in pregnancy, especially during the first trimester, unless the possible benefit to the patient outweighs any possible risk to the fetus.*

♣ *Nursing mothers should be instructed that it is not known whether zanamivir is excreted in human milk, caution should be exercised when zanamivir is administered to a nursing mother.*

♦ *Zanamivir is not generally recommended for treatment in patients with severe underlying airway disease and asthma because of the risk of serious adverse events and because the efficacy has not been demonstrated in this population.*

ANNEX B: Guideline Revision History

Revision Date	Document Section	Description of Revision
August 2019	General	• Updated guideline template and hyperlinks. No change to case definition or guideline references. • Added Annex D: Guideline Revisions
	Reporting Requirements	• Added “(including deaths)” for clarity.