

Influenza (Seasonal)

Including Pandemic (H1N1) 2009

Case Definition

Confirmed Case

Clinical illness^[1] 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.

^[1] 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, or 65 years of age and older, fever may not be prominent.

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 influenza.

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, long-term care facilities (LTCF) and prisons.

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

Reporting Requirements

1. Physicians/Health Practitioners and others

Physicians, health practitioners and others listed in Section 22 of the *Public Health Act* shall notify the Alberta Health Services (AHS) Zone Medical Officer of Health (MOH) or designate in the prescribed form by mail, fax or electronic transfer within 48 hours (two days) about the following:

- all hospitalized (i.e., inpatient admission) confirmed cases of influenza.

2. Laboratories

The Provincial Laboratory for Public Health shall report all positive laboratory results by mail, fax or electronic transfer within 48 hours (two days) to the:

- Chief Medical Officer of Health (CMOH) or designate,
- MOH (or designate) and
- attending/ordering physician.

3. Alberta Health Services

Completion of a case report form is required at a minimum, for the first 100 hospitalized influenza cases in the 2010–2011 influenza season and thereafter will be determined on a yearly basis.

- The MOH (or designate) shall forward the initial *Alberta Provincial Hospitalized Influenza and Severe Respiratory Illness (SRI) Report Form* of all hospitalized confirmed influenza cases to the CMOH (or designate) within 48 hours (two days) of notification and the final report within two weeks of discharge from hospital.
- For out-of-zone reports within the province, the MOH (or designate) first notified shall notify the MOH (or designate) where the case resides by mail, fax or electronic transfer and fax a copy of the positive laboratory report within 48 hours (two days).
- For out-of-province and out-of-country reports, the following information should be forwarded to the CMOH (or designate) by phone, fax or electronic transfer within 48 hours (two days) including:
 - name,
 - date of birth,
 - out-of-province health care number,
 - out-of-province address and phone number,
 - attending physician (locally and out-of-province) and
 - positive laboratory report (faxed).

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 type A (subtype H1N1) virus began to circulate in humans. It is a triple reassortment swine influenza A virus containing genes originating from avian, human and swine. The hemagglutinin, nucleoprotein and non-structural genes are derived from classical swine 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 pandemic H1N1 2009 (pH1N1) 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

The symptoms of influenza can range from non-febrile upper-respiratory tract illness to severe or fatal pneumonia. Initially, the most commonly reported symptoms include acute onset of cough, fever, headache, sore throat, coryza, chills, myalgia and prostration.(1) A severe cough can last two or more weeks while fever and other symptoms resolve within five to seven days.

Otitis media, nausea and vomiting are more common in children.(3) Influenza can worsen underlying conditions such as congestive heart failure or chronic obstructive pulmonary disease (COPD) in older adults.(1)

Outbreaks of influenza are associated with excess morbidity and mortality, characterized by higher than normal rates of pneumonia and influenza-related hospitalizations and deaths.(4)

Diagnosis

Diagnosis of influenza is made through a variety of molecular assays for detection and confirmation including direct fluorescent antigen (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 person 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 and there are assays available that can differentiate between the different subtypes of influenza A (e.g., H3 or H1 or pH1N1).

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.

Epidemiology

Reservoir

Humans. Influenza A viruses can also circulate in birds, pigs, horses, ferrets, seals and other animals.(1;4) Seasonal influenza is usually not a zoonotic disease, although there can be exceptions.(1) Influenza B viruses only circulate in humans.(4) A third subtype of influenza virus exists, type C influenza which is associated with sporadic cases and minor localized outbreaks does not cause nearly the significant burden of disease that influenza A and B does.

Transmission

Seasonal influenza is transmitted from person to person primarily via large droplet particles and droplet nuclei (i.e., aerosol) that are generated when the infected person coughs or sneezes.(3) These large droplets can settle on the mucosal surfaces of the upper respiratory tract of susceptible people who are within three feet of the infected person. 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 one to two days and on soft surfaces (cloth, tissues and paper) for eight to 12 hours.(5) However, the virus can only **infect** a person for up to eight hours on hard surfaces and only a few minutes on soft surfaces.

Incubation Period

The incubation period for seasonal influenza is one to four days.(1;6) Pandemic (H1N1) 2009 influenza appears to have a longer incubation period; median four days, range one to seven days.(7)

Period of Communicability

Infected persons 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 three to five days after onset.(3) Individuals who are elderly, severely ill or children may shed virus for longer periods, up to 14 days.(4;8) Individuals who are immunocompromised may shed the virus for weeks or months.(9-12)

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.(4;13)

Attack rates tend to be highest in young children while over 90% of influenza deaths occur in individuals 65 and older;(4) however, influenza-related deaths can occur in any age group.

The following individuals are at higher risk for complications related to seasonal influenza (including pH1N1) and may be more likely to require hospitalization:(14)

- healthy pregnant women (the risk of influenza-related hospitalization increases with increasing length of gestation; e.g., it is higher in the 3rd than the 2nd 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,
 - chronic 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) and
 - morbid obesity (BMI \geq 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
- adolescents < 19 years receiving long-term acetylsalicylic acid (ASA) therapy.

Occurrence

Worldwide

Seasonal 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.(15)

While pH1N1 is now included with seasonal influenza, it initially began in the early spring of 2009 as clusters of severe respiratory illness in Mexico and mild illness in the southwestern 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.(16) 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.(14) According to the World Health Organization (WHO), over 18,400 persons died between April 2009 and August 2010 as a result of pH1N1.(17)

Canada

Each year seasonal influenza causes outbreaks during the fall and winter months. The annual incidence of seasonal influenza varies depending on the strain that circulates and the susceptibility of the population it affects. It is estimated that up to 8000 people, mostly individuals over the age of 65, die from influenza-related complications such as pneumonia every year.(18)

The first case of pH1N1 in Canada was reported by Nova Scotia on April 26, 2009. While most illnesses caused by the pH1N1 virus were self-limiting, a number of severe outcomes were reported. Hospitalization rates were highest for children under age five years; 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.(14)

For up-to-date national influenza surveillance information refer to the [FluWatch weekly reports](#).

Alberta

In Alberta, seasonal influenza results in an average of 1500 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.

On April 27, 2009 the first case of pH1N1 2009 was reported in Alberta. During the 2009–2010 influenza season 5193 cases of influenza were reported in Alberta, including 476 hospitalizations and 71 deaths.

Refer to the [Influenza Surveillance in Alberta](#) website for up-to-date surveillance information.

Key Investigation & Control

Management of Cases

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

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

- reported to Alberta Health and Wellness (AHW) by completing the *Alberta Provincial Hospitalized Influenza and Severe Respiratory Illness (SRI) Report Form*.

Non-Hospitalized cases:

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

Daycares, Preschools and Schools:

- Schools with > 10% absenteeism should report to the local public health zone for further investigation.
- School closure as a measure to mitigate the spread of seasonal influenza is not currently recommended. Consideration for school closure will require consultation between the CMOH, local MOH and the affected school authority.

Treatment of Cases

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 Regimes 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 on the AHW website: [Influenza Surveillance in Alberta](#)
- See [Oseltamivir \(Tamiflu®\)](#) Product Monograph.(19)
- See [Zanamivir \(Relenza®\)](#) Product Monograph.(20)
- See [Amantadine \(Symmetrel®\)](#) Product Monograph.

Management of Contacts

- Post-exposure prophylaxis of contacts is generally not recommended. Antivirals are usually recommended for treatment only.
- 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

Respiratory outbreaks require immediate notification to the MOH (or designate), who in turn will notify CMOH (or designate). Outbreaks of respiratory illness where influenza is the identified/suspect causative organism should be managed in a similar fashion to any respiratory outbreak and reported to AHW using the *Alberta Outbreak Reporting Form (AORF)*. Refer to the [Outbreak Surveillance Definitions](#)

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

- A facility is deemed a closed facility when it has a fixed residential population with limited turnover.
- Triggers for outbreak investigation include:
 - one confirmed case of influenza within the facility, i.e., unit or floor within seven days or
 - two or more cases of ILI, one of which can be a staff member with known contact with resident/patient case, in one geographic area within a seven day period or
 - more than one geographic area of the facility reporting a case of ILI.
- 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.

Preventive Health Measures

- Provide general and ongoing education to the public regarding seasonal influenza.
- All Albertans over the age of six months are now eligible to receive annual influenza vaccine under the provincially funded program. Protective antibody levels are generally achieved by two weeks following immunization.(14)
- Pneumococcal vaccine may be useful in preventing secondary bacterial infections in populations at high risk for influenza-related complications.

Resources

Alberta Health and Wellness website
www.health.alberta.ca/health-info/influenza.html

Alberta Health Services website
<http://www.albertahealthservices.ca/1828.asp>

Annex 1: Antiviral Regimes for Influenza (21;22) (Based on current sensitivity testing)

OSELTAMIVIR (TAMIFLU®)		
Age/Weight	Treatment	Prophylaxis recommended dose for at least 10 days**▲
Age 1 – 12 years*	15 kg or less:	30 mg twice daily x 5 days
	16 to 23 kg:	45 mg twice daily x 5 days
	24 to 40 kg:	60 mg twice daily x 5 days
	40 kg or greater:	75 mg twice daily x 5 days
Age ≥ 13 years (including pregnant and nursing women) no Renal Impairment		75 mg twice daily x 5 days
Age ≥ 13 years with Renal Impairment		Creatinine Clearance (CrCl) 10–30 mL/min: • Reduce to 75 mg once daily x 5 days CrCl 10–30 mL/min: • 75 mg every other day or 30 mg of suspension daily
* Oseltamivir is not approved for use in children less than one 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.(23) ** For the control of outbreaks in closed facilities prophylaxis is recommended for a minimum of 14 days and up to 1 week after most recent case identified.(8) ▲ Viral shedding may continue for up to 14 days in children and elderly after the onset of influenza illness. Therefore, if the index case is a child or an elderly person, preventive therapy may continue for up to 14 days.(18)		
ZANAMIVIR (RELENZA®)		
Age/Weight	Treatment	Prophylaxis
Age ≥ 7 years (including pregnant and nursing women)	<ul style="list-style-type: none"> 10 mg (2 inhalations) twice daily for 5 days started within 48 hours of onset of symptoms. 	In a household setting: <ul style="list-style-type: none"> 10 mg 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: <ul style="list-style-type: none"> 10 mg once daily x 28 days No data on effectiveness when initiated more than 5 days after outbreak identified in community.
Renal/Hepatic Impairment	As systemic exposure is limited after inhalation (4–17%), adjustments in renal insufficiency or hepatic impairment may not be required, but studies are lacking.	
AMANTADINE		
Age	Treatment	
Age 1 to 9 years	5 mg/kg once daily, or divided, twice daily, total daily dose not to exceed 150 mg	
Age ≥ 10 years and ≤ 64 years (including pregnant and nursing women)	200 mg once daily, or divided twice daily†§	
Age ≥ 65 years	100 mg once daily‡	
With Renal Impairment		
Creatinine clearance (mL/min/1.73m ²)	Dosage for those 10 to 64 years	Dosage for those ≥ 65 years
> 80 mL/min	100 mg twice daily	100 mg once daily
60–79 mL/min	Alternating daily doses of 200 mg and 100 mg	Alternating daily doses of 100 mg and 50 mg
40–59 mL/min	100 mg once daily	100 mg every 2 days
30–39 mL/min	200 mg twice weekly	100 mg twice weekly
20–29 mL/min	100 mg three times/week	50 mg three times/week
10–19 mL/min	Alternating weekly doses of 200 mg and 100 mg	Alternating weekly doses of 100 mg and 50 mg

† Reduction of dosage to 100 mg/day is recommended for people with a seizure disorder, because they may be at risk of more frequent seizures when the dosage is 200 mg/day.

§ For children who are > 10 years of age but who weigh < 40 kg a dosage of 5 mg/kg daily is advised regardless of age.

‡ The reduced dosage is recommended to minimize the risk of toxic effects, because renal function generally declines with age and because side effects have been reported more frequently in the elderly.

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