This protocol applies to seasonal influenza only. For novel influenza viruses, refer to guidelines specific for those viruses.

1. Case Definition

1.1 Confirmed Case:
Influenza-like illness (ILI)* with laboratory confirmation of infection. Laboratory confirmation includes at least one of:
- Isolation of influenza virus by cell culture from an appropriate clinical specimen
- Detection of influenza virus nucleic acid by nucleic acid amplification test (NAAT)
- Demonstration of influenza virus antigen in an appropriate clinical specimen

1.2 Probable (Clinical) Case:
Influenza-like illness (ILI)* in a person in the absence of laboratory confirmation of infection (i.e., testing has not been performed) when the presence of influenza virus has been confirmed in the community.

1.3 Institutional Outbreak:
Two or more cases of ILI* (including at least one laboratory-confirmed case) occurring within a seven-day period in an institution. An institution includes but is not limited to hospitals, long-term care facilities for both adults and children (e.g., personal care homes, nursing homes, chronic care facilities) and correctional facilities (1, 2).

1.4 School Outbreak:
Greater than 10% absenteeism or absenteeism that is higher than the expected level for that school which is likely due to ILI*. School outbreaks are an indication of community transmission of influenza (2).

*Influenza-like illness (ILI) is characterized as: acute onset of respiratory illness with fever and cough and with one or more of the following:
- Sore throat
- Arthralgia (joint pain)
- Myalgia (muscular pain)
- Prostration (extreme exhaustion) that could be due to influenza virus

In children < 5 years of age, gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea) may be present. In patients < 5 years or ≥ 65 years old, fever may not be prominent. Note: Illness associated with novel influenza viruses may present with other symptoms (1).

2. Reporting Requirements

2.1 Laboratory:
- All positive influenza laboratory results must be faxed to Manitoba Health, Public Health Surveillance Unit (204-948-3044 secure fax).
- Clinical laboratories are required to submit isolate sub-cultures or primary specimen from individuals who tested positive for influenza virus to Cadham Provincial Laboratory (CPL) within seven days of report. Influenza specimens from suspected or confirmed outbreaks should be submitted directly to CPL.

2.2 Health Care Professional:
- The local public health unit should be notified by the facility health care professional (e.g., infection prevention and control practitioner) when the institutional outbreak definition is met. If urgent consultation is required outside of regular business hours, contact the on-call Medical Officer of Health at 204-788-8666. The Respiratory Outbreak Summary Report form should be completed for all institutional outbreaks by the facility health care professional and returned to the Public Health Surveillance Unit. CNPHI (Canadian Network for
Public Health Intelligence) users should login to CNPHI and enter data into the Respiratory Outbreak Summary. Non-CNPHI users may request the form by email: outbreak@gov.mb.ca.

- Adverse events following immunization should be reported by health care professional by completing and returning the form available at: http://www.gov.mb.ca/health/publichealth/cdc/docs/aefi_form.pdf.

3. Surveillance

- Information on hospitalized and deceased cases of influenza are collected weekly from the regional health authorities by Manitoba Health, Seniors and Active Living.
- Other important surveillance data within the province are also collected routinely during influenza season and throughout the year. This includes laboratory testing, characterization of circulating virus and antiviral susceptibility, ILI in the community that is medically attended (i.e., walk-in clinics and emergency room visits), outbreak investigation, antiviral dispensing and immunization coverage.
- Manitoba’s weekly and end of season influenza reports are available at: http://www.gov.mb.ca/health/publichealth/surveillance/reports.html.

4. Clinical Presentation/Natural History

Influenza is an acute viral infection of the respiratory tract characterized by fever, cough (usually dry), sore throat, arthralgia, myalgia and prostration (3). Other symptoms may include headache and coryza (3). Cough is often severe and can last two or more weeks. Fever and other symptoms when present, usually resolve in five to seven days (3). Influenza may be clinically indistinguishable from other viral respiratory diseases (e.g., rhinovirus) (3), and approximately 50% will not develop the classical symptoms described above (4).

A high rate of secondary complications, particularly otitis media and pneumonia occur in children with influenza infection (5). The most frequent complication of influenza is pneumonia, usually secondary bacterial pneumonia (4). Primary viral influenza pneumonia is an uncommon complication, but when it occurs, has a high fatality rate (4). Table 1 below lists people at higher risk of influenza-related complications or those more likely to require hospitalization (6). Most deaths associated with influenza in industrialized countries occur in individuals 65 years of age and older (7).

**Table 1: People at high risk of influenza-related complications or hospitalization.**

- Adults and children with the following chronic health conditions:
  - Cardiac or pulmonary disorders (including bronchopulmonary dysplasia, cystic fibrosis and asthma);
  - Diabetes mellitus and other metabolic diseases;
  - Cancer, immune compromising conditions (due to underlying disease, therapy or both);
  - Renal disease;
  - Anemia or hemoglobinopathy;
  - Neurologic or neurodevelopmental conditions. These include seizure disorders, febrile seizures and isolated developmental delay in children and neuromuscular, neurovascular, neurodegenerative,
neurodevelopmental conditions and seizure disorders in adults, but excludes migraines and neuropsychiatric conditions without neurological conditions;
- Morbid obesity (BMI ≥ 40).
- Children and adolescents (up to 18 years) undergoing treatment for long periods with acetylsalicylic acid, because of the potential increase of Reye’s syndrome associated with influenza (6).
- Individuals of any age who are residents of long-term care facilities (6).
- Individuals ≥ 65 years of age (6).
- All children less than 5 years of age (6).
- All pregnant women (especially those in the third trimester of pregnancy) (6, 8) and women up to four weeks postpartum regardless of how the pregnancy ended (8).
- First Nations, Métis and Inuit peoples (6).

5. Etiology
Three distinct types of seasonal influenza virus are recognized based on major antigenic differences: A, B and C (3-5). Influenza A viruses are divided into subtypes based on the expression of two surface glycoproteins; the hemagglutinin (H) and the neuraminidase (N). There are numerous H and N subtypes. Mutations in the genes encoding the H and N glycoproteins during replication result in the constant emergence of new strains of influenza A viruses (3). Both influenza A and B viruses can cause seasonal outbreaks of influenza (3); however, antigenic variation occurs more slowly in influenza B viruses. Influenza B generally causes milder disease than type A (4). Type C influenza is rarely reported as a cause of human illness and has not been associated with epidemics (4).

The nomenclature of influenza virus is described by the geographic site of isolation, the laboratory number, the year of isolation and virus subtype (subtype is for A viruses only). Examples are; A/New Caledonia/20/99(H1N1) and A/Brisbane/10/2007(H3N2) and B/Malaysia/2506/2004 (3).

6. Epidemiology
6.1 Reservoir and Source:
Humans are the only known host for influenza types B and C viruses (4). Influenza A may infect both humans and animals (4).

6.2 Transmission:
Person-to-person transmission through large respiratory droplets when infected persons cough or sneeze is believed to be the primary transmission route (3-4). Transmission may also occur through direct or indirect contact with respiratory secretions (e.g., touching surfaces contaminated with influenza virus and then touching the eyes, nose or mouth) (4). Individuals with asymptomatic infection can transmit virus to susceptible individuals (e.g., asymptomatic health care worker to patient and vice versa) (9, 10). Human influenza viruses may persist for hours on solid surfaces, particularly in lower temperatures and lower humidity (3).

6.3 Occurrence:
General:
Influenza infection causes pandemics, epidemics, localized outbreaks and sporadic disease. Pandemics occurred in 1889, 1918, 1957, 1968 and 2009. Influenza outbreaks occur annually in autumn and winter months in temperate regions resulting in three to five million cases of severe illness and 250,000 to 500,000 deaths globally (7). Attack rates in unvaccinated populations in epidemics are estimated to be 10% - 20% (5) but may be much higher in closed populations (3). Influenza attack rates are higher in children than in adults (5).
Influenza A(H1N1)pdm09 was the most common strain detected in Africa, the Americas, Asia, Europe and Oceania for most of the 2015/16 season (11). By the end of the 2015/16 season, influenza B virus predominated for most of the northern hemisphere (12).

In Canada, the flu season started later than usual for 2015/2016, initially with influenza A(H3N2) being the most common sub-type affecting Canadians (13, 21). Influenza activity peaked nationally in the second week of March 2016 (22). By the end of the season there were more cases of A(H1N1) identified than A (H3N2) (21). Cases of influenza B increased towards the end of the season (21). Hospitalizations, ICU admissions and deaths among the pediatric population were above expected levels based on the past several influenza seasons (21).

Manitoba:
- The 2015/16 season was delayed by two months compared to the three previous seasons. The activity started to increase in late January and peaked at the beginning of March 2016. Overall, the activity level this season was lower than the 2014/15 season, but higher than the 2012/13 and 2013/14 seasons.
- Influenza A was the dominant type in the 2015/16 season. Younger populations were more affected for the 2015/16 season as influenza A(H1N1) predominated, compared to the previous season where influenza A(H3N2) predominated. There were a total of 849 cases of influenza A and 222 cases of influenza B reported between September 1, 2015 and June 4, 2016.
- Between September 2015 and June 4, 2016, there were 17 laboratory-confirmed outbreaks of influenza A, two of influenza B, and one with both influenza A and B reported. Two outbreaks occurred in hospitals and the rest occurred in long-term care facilities.
- There were 22 influenza-associated deaths in the 2015/16 season: 19 with influenza A and 3 with influenza B. Of the patients who died, the majority were under the age of 65.

6.4 Incubation Period:
Usually two days but ranges from one to four days (3-4).

6.5 Host Susceptibility and Resistance:
Susceptibility depends upon natural or vaccine-induced levels of protective immunity in the population, the age and condition of the population (refer to Table 1 for risk factors), predisposing comorbidity, strain virulence and the extent of antigenic variation of new viruses (3).

6.6 Period of Communicability:
Adults can transmit influenza from the day before symptom onset until approximately five days after (4). Children can transmit influenza for 7-10 days after onset of illness or longer (3, 4). Immunocompromised individuals may shed virus for longer periods (3).

7. Laboratory Diagnosis
During influenza season, viral testing should be considered for individuals with ILI only if the results might influence clinical management, or were specifically requested as part of active formal surveillance systems.
7.1 Virus Detection:

Nucleic acid amplification testing (NAAT) is the primary test used to confirm infection. Infection may also be confirmed by isolation of influenza viruses by cell culture and/or by identification of viral antigens. When testing is indicated, specimens should be taken as close to onset of illness as possible, preferably within five days of onset (15). The Cadham Provincial Laboratory (CPL) respiratory virus specimen collection procedure is available at: http://www.gov.mb.ca/health/publichealth/cpl/docs/nasopharyngeal_collection.pdf. Other clinical laboratories may conduct some influenza testing so requirements may vary. Specimens destined for CPL should be transported with a cold pack (to maintain a temperature of approximately 4°C) and shipped as soon as possible. Type of testing performed and turnaround times for results will vary. For urgent testing, CPL should be contacted at 204-945-6953 or after hours at 204-945-6655 to make arrangements. If an unusual or highly virulent form of influenza is suspected, the lab and ultimately CPL should be notified prior to sample submission.

7.2 Serology:

Serologic testing is not recommended for detection and management of acute illness (15). Serology should only be done for retrospective epidemiological purposes and/or research purposes.

7.3 Specimen Submission:

An appropriately labeled requisition MUST accompany each specimen destined for CPL. Ensure that both the specimen and the requisition are clearly labeled with the specimen date, patient’s name and unique identifier such as PHIN or DOB.

7.4 Typing and Resistance Analysis:

CPL can determine whether a detected influenza virus is type A or B. Hemagglutinin antigen determination is also available, but may not be routinely performed (e.g., H1 or H3). Variant typing (e.g., Brisbane vs. Hong Kong) is currently conducted on a subset of positives in cooperation with the National Microbiology Lab (NML) in Winnipeg. Antiviral drug resistance testing is available after consultation with CPL at 204-945-6953.

8. Management and Control

8.1 Case Management:

Clinical judgment based on underlying conditions, disease severity and time since symptoms onset are important factors in treatment.

- Detailed antiviral recommendations for specific populations (e.g., children and youths, adults with renal impairment) are available from the Association of Medical Microbiology and Infectious Diseases Canada (AMMI) at: https://www.ammi.ca/?ID=5&Language=ENG and from the Canadian Paediatric Society at: http://www.cps.ca/documents/position/use-of-antiviral-drugs-for-influenza-paediatric-summary-2012-2013 and clinicians should review these as well as the respective product monographs before prescribing.

- As per the AMMI Guidelines, when indicated, treatment with antivirals should be initiated as rapidly as possible after onset of illness because the benefits of treatment are much greater with initiation at < 12 hours than at 48 hours (8). Antiviral therapy should be initiated even if the interval between illness onset and administration of antiviral medication exceeds 48 hours if the illness is: 1) severe enough to require hospitalization; 2) progressive, severe or complicated,
regardless of previous health status; 3) in an individual belonging to a group at high risk for severe disease (8). Refer to Table 1 for risk groups and Section 8.34 for information on oseltamivir.

- Clinicians should be familiar with local seasonal antiviral resistance patterns when prescribing antiviral therapy for treatment.
- Cases should be monitored for bacterial complications and antibiotics prescribed accordingly (3).
- Salicylates should not be given to children with probable or confirmed influenza because of the association with Reye’s syndrome (3).
- When an outbreak has not been declared in a long-term care facility, treatment of residents with oseltamivir is now covered through the Personal Care Home Drug Formulary.

8.2 Contact Management:
- Routine antiviral chemoprophylaxis of asymptomatic contacts is not recommended.
- Antiviral chemoprophylaxis may be considered in the setting of a defined significant exposure (e.g., household contact or health care associated exposure such as shared hospital accommodation) of an immunocompromised patient to a suspected or lab-confirmed case of influenza, in consultation with an expert (8).
- Refer to the AMMI guidelines for indications where early antiviral treatment is preferred to antiviral post-exposure prophylaxis.

8.3 Institutional Outbreak Management:
8.31 Pre-outbreak Planning:
- ILI surveillance processes should be in place.
- A facility outbreak management plan detailing roles, responsibilities and investigation, control and communication processes should be in place and reviewed regularly. Education of staff of this outbreak management plan should be conducted by the facility on an annual basis in preparation for the influenza season.
- It is recommended that all institutions have current physician standing orders for prompt initiation of influenza antiviral medications for patients/residents who develop symptoms or for whom prophylaxis is indicated.
- Patients/residents should be immunized (unless contraindicated) according to current Manitoba Health recommendations available at: http://www.gov.mb.ca/health/flu/index.html. Influenza immunization is a universal publicly-funded program in Manitoba.
- Health care workers (HCWs) should be immunized annually with influenza vaccine unless contraindicated. Other facility staff (e.g., food handlers, maintenance workers) should be offered immunization. Transmission of influenza between infected HCWs and their vulnerable patients/residents results in significant morbidity and mortality. Randomized controlled trials conducted in
geriatric long-term care settings have demonstrated that vaccination of HCWs is associated with substantial decreases in morbidity and mortality in the residents. Therefore, HCWs should consider annual influenza vaccination included in their responsibility to provide the highest standard of care. In the absence of contraindications, refusal of HCWs to be immunized against influenza implies failure in their duty of care to patients/residents (6). This recommendation is supported by the Canadian Nurses Association https://www.cna-ainc.ca/~media/cna/page-content/pdf-en/ps_influenza_immunization_for_rns_e.pdf?la=en.

- Facilities should have plans that address staff illness, including communicable respiratory illness.

8.32 Viral Testing during Outbreaks:

- If a patient/resident of an institution not known to have any cases of influenza develops ILI, a nasopharyngeal swab/aspirate should be collected immediately for rapid influenza testing (NAAT or antigen testing) as part of the initial investigation.
- No more than six persons who are ill with ILI should be swabbed at one time.
- Once influenza is established as the cause of the outbreak, nasopharyngeal swabs should continue to be collected from one or two apparent new cases (staff or residents) every three or four days to confirm the duration of the outbreak and monitor for antiviral treatment failure/resistance.
- Laboratory outbreak testing coordination and outbreak code assignment can be arranged through a Medical Officer of Health or by contacting the CPL Outbreak Coordinator at 204-945-7473. Refer also to the Outbreak Response Support section on page 12 of the CPL Guide to Services available at: http://www.gov.mb.ca/health/publichealth/cpl/documents.html.

8.33 Control:

Infection Prevention and Control during Institutional Outbreaks:

- Any unimmunized staff and patients/residents should be offered immunization unless contraindicated. This may not prevent illness during the current outbreak, but will provide protection against different strains should they circulate later in the season.
- For HCWs who are unimmunized, in accordance with Workplace Safety recommendations, a procedure/surgical mask should be worn consistently within the institution as additional protection for themselves and their patients/residents.
- Institutional staff with ILI should immediately notify Occupational Health or designate and/or Infection Prevention and Control for the facility/regional program in which they work and in consultation with them determine when it is appropriate to return to work.
- In order to protect vulnerable patients/residents in an outbreak it is reasonable to exclude from direct patient/resident care HCWs who develop confirmed or probable influenza. It may be reasonable to consider exclusion of unvaccinated HCWs who are not taking antiviral prophylaxis. Health care organizations should have policies in place to deal with this issue.
- Cohorting of ill patients/residents if appropriate (15, 16).
- Patients/residents with ILI should be placed on Droplet and Contact Precautions. Refer to Manitoba Health, Seniors and

- Group activities should be stopped, reduced or restricted to a given ward.
- New admissions should be cancelled if appropriate and feasible; if not possible, immunization and chemoprophylaxis should be provided to the new admissions (16).
- Visitors should be notified so those at high risk of complications from influenza may elect to cancel their visit.
- Visitors are required to wear a mask as per Droplet and Contact Precautions.
- Individual HCWs may be cohorted to work with patients/residents who are ill or with patients/residents who are well. If they work with both ill and well patients/residents, they should move from non-infected to infected patients/residents ensuring adherence to Routine Practices and Additional Precautions.
- Education of patients/residents, visitors and staff regarding respiratory hygiene and hand hygiene (3).

**Antiviral Treatment during Institutional Outbreaks:**

- All symptomatic patients/residents with laboratory-confirmed virus infection should be treated with an appropriate influenza antiviral medication (15).
- After one case of laboratory-confirmed influenza has been detected, all other symptomatic cases should be considered for treatment where appropriate (15).
- When an outbreak has been declared in an institution (refer to Section 1.3 for institutional outbreak definition), oseltamivir treatment is supplied to patients/residents through the provincial vaccine warehouse.

**Antiviral Chemoprophylaxis during Institutional Outbreaks:**

The facility Medical Director will determine if the institutional outbreak definition has been met. The decision may be reached in consultation with the regional Medical Officer of Health (MOH) and Infection Prevention and Control. Generally when an outbreak has been declared, unless contraindicated, antiviral chemoprophylaxis:

- Is recommended for all patients/residents, regardless of influenza vaccination history, who have not already been ill with ILI (15, 16).
- Should be considered for all unimmunized HCWs who provide care to persons at high risk of complications (15, 16, 17).
- Should be considered for HCWs, regardless of vaccination status during outbreaks with strains for which the current vaccine is not well matched (17).
- The responsibility for the prescribing and provision of chemoprophylaxis to HCWs resides with the institution and/or individual regional health authority.

When an outbreak has been declared in an institution, oseltamivir prophylaxis is supplied to patients/residents through the provincial vaccine warehouse.

**Ordering Antiviral:** In pre-outbreak settings, oseltamivir may be obtained through regular drug procurement channels and billed through the PCH Drug Formulary. Once an outbreak has been declared, oseltamivir (75 mg and 30 mg) can be ordered by the facility Medical Director, Infectious Diseases Specialist or the regional MOH through the provincial vaccine warehouse. Some regions may have pre-positioned stock in
their region in order to access stock sooner. The 30 mg capsule formulation has been added to accommodate reduced recommended dosages for adults with renal impairment. Call 204-948-1333 or 1-855-683-3306 to order. After hours, call 204-805-4096. Product will be shipped as boxes containing 10 capsules each of 75 mg or 30 mg capsules. Specify the number of boxes of 75 mg and/or 30 mg capsules required and the destination.

8.34 Information on Oseltamivir (Tamiflu®):

In 2014, oseltamivir was added to the Manitoba Pharmacare Program under the PCH (Personal Care Home) Drug Formulary. As a result, regional health authorities can access oseltamivir via two routes depending on the status of influenza as an outbreak. When one or more patients/residents with ILI require treatment with oseltamivir, and prior to the facility declaring an outbreak, the facility Medical Director can order and treat patients/residents without cost to the patient/resident. Oseltamivir also continues to be provided through Public Health at the time of an outbreak (i.e., two or more cases of ILI including at least one laboratory-confirmed case).

Asymptomatic adult patients/residents with creatinine clearance of > 60 mL/min should receive prophylaxis at 75 mg OD for 10 days or until the outbreak is determined to be over, whichever occurs first (8). If the outbreak is not over after 10 days, the local Medical Officer of Health should be consulted to see if prophylaxis should continue.

Recovered patients/residents with prior, laboratory-confirmed influenza A or B during the outbreak in question do not require treatment or prophylaxis.

Patients/residents or HCWs receiving chemoprophylaxis who develop ILI should be assessed and tested to determine the cause of their illness, which may be due to the current virus, another viral agent or an oseltamivir-resistant influenza virus (18). Expert consultation is suggested to address the cause, organize testing for neuraminidase inhibitor resistance, and to assess the possible need to switch to another neuraminidase inhibitor (18). To limit the potential transmission of antiviral drug-resistant influenza virus, measures should be taken to reduce the contact between ill persons taking antiviral drugs for treatment and other persons, including those receiving antiviral chemoprophylaxis (19). Pediatric dosing is available at https://www.ammi.ca/?ID=5&Language=ENG and http://www.cps.ca/documents/position/use-of-antiviral-drugs-for-influenza-pediatric-summary-2012-2013.

Consultation with Pediatric Infectious Diseases is recommended for antiviral treatment/prophylaxis of children < 1 year of age.

When considering use of influenza antiviral medications, clinicians must consider the patient/resident’s age, weight and renal function, presence of other medical conditions; indications for use (i.e., chemoprophylaxis or therapy) and the potential for interactions with other medications. Oseltamivir dosages may need to be modified based on the presence of renal disease or other comorbidities. Refer to product monograph and insert. Dosage recommendations for adults with renal impairment are available from the Association of Medical Microbiology and Infectious Diseases (AMMI) at: https://www.ammi.ca/?ID=5&Language=ENG.

The most common adverse events include headache, nausea, vomiting and abdominal pain.

8.4 Preventive Measures:

- Education of the public and HCWs regarding respiratory hygiene and hand hygiene (3).
• Encouraging the public to stay home when they have ILI.
• Encouraging visitors to follow facility/organization infection prevention and control procedures when visiting ill people.

9. Travel Considerations
Immunization with the most current available influenza vaccine should be considered for all individuals who wish to avoid influenza while travelling to areas where influenza is likely to be circulating. The effectiveness of influenza vaccine for travelers may vary, depending on differences between influenza strains encountered abroad and those included in the current vaccine available in Canada (20). Vaccines prepared specifically for use in the Southern Hemisphere are not available in Canada, and the extent to which recommended vaccine components for the Southern Hemisphere may overlap with those available in Canadian formulations will vary. A decision in favour or against re-vaccination (i.e., boosting) of travelers to the Southern Hemisphere between April and October if they had already been vaccinated in the preceding fall/winter with the Northern Hemisphere vaccine depends on individual risk assessment, the similarity or differences between the Northern and Southern hemisphere vaccines, and the availability of a reliable and safe vaccine at the traveller’s destination (6).

10. Additional Resources
Information for health professionals and the public is available on the Seasonal Flu website at: www.gov.mb.ca/health/flu/index.html.

National Advisory Committee on Immunization (NACI) current Statement on Seasonal Influenza Vaccine.

References


