

Annex 5. Clinical Guidelines

Person responsible: Medical Epidemiology

Back-up: Medical Epidemiology

Rationale:

Healthcare providers play an essential role in the detection of an initial case of novel or pandemic influenza in a community. Early identification and isolation of cases may help slow the spread of influenza within a community. Clinical awareness of novel or pandemic influenza disease can also benefit the individual patient, as rapid diagnosis and initiation of treatment can avert potentially severe complications. However, detection is complicated by the lack of specific clinical findings and commercially available laboratory tests to rapidly distinguish novel or pandemic influenza from seasonal influenza. In addition, neither the clinical characteristics of a novel or pandemic influenza virus strain nor the groups at highest risk for complications can necessarily be defined beforehand. Therefore, clinicians face significant challenges in: 1) quickly identifying and triaging cases, 2) containing the spread of infection, 3) beginning an efficient and comprehensive workup, 4) initiating antiviral and other supportive therapy, and 5) anticipating clinical complications.

Clinical management of patients during pandemic influenza will follow many of the same principles of patient care as in cases of interpandemic seasonal strains of influenza. Specifically, health care workers need to know: 1) signs and symptoms of influenza-like illness, 2) the strains that are circulating in their community, 3) the appropriate tests to diagnose influenza, 4) the appropriate infection control precautions, 5) how to select the correct antiviral medication, 6) the side effects of antiviral medications, and 7) how to prescribe antivirals for prophylaxis.

Additional difficulties that will be faced in a pandemic include: 1) differentiating seasonal strains of influenza from pandemic strains, 2) deciding which antivirals would be most appropriate to use, and 3) determining which populations would benefit most from antiviral treatment when limited supplies are available.

Overview:

Annex 5 provides clinical guidelines for the initial screening, assessment, and management of patients with suspected novel influenza during the Maine Interpandemic Period, and for patients with suspected pandemic influenza during the Maine Pandemic Alert and Pandemic Periods. The Appendices include information on the clinical presentation and complications of seasonal influenza, the clinical features of infection due to previous pandemic influenza viruses, and the management of patients with community-acquired pneumonia or secondary bacterial pneumonia during a pandemic. The guidance is current as of December 2011, and is subject to change as experience is gained.

During the Maine Interpandemic Period, early recognition of illness caused by a novel influenza A virus strain will rely on a combination of clinical and epidemiologic features. During the

Maine Pandemic Period (in a setting of high community prevalence), diagnosis will likely be more clinically oriented because the likelihood will be high that any severe febrile respiratory illness is pandemic influenza. During periods in which no human infections with a novel influenza A virus strain have occurred anywhere in the world (Maine Inter-Pandemic Period: Pre-Pandemic), or when sporadic cases of animal-to-human transmission or rare instances of limited human-to-human transmission of a novel influenza A virus strain have occurred in the world (Maine Inter-Pandemic Period: Level I), the likelihood of novel influenza A virus infection is very low in a returned traveler from an affected area who has severe respiratory disease or influenza-like illness. Since human influenza A and B viruses circulate worldwide among humans year-round, the possibility of infection with human influenza viruses is much higher and should be considered. Once localized person-to-person transmission of a novel influenza A virus strain has been confirmed (Maine Inter-Pandemic Period: Level II), the potential for novel influenza A virus infection will be higher in an ill person who has a strong epidemiologic link to the affected area (Box 1).

Maine Benchmark	Definition	Activities
Maine Inter-Pandemic Period		
Pre-pandemic	No new influenza virus subtypes have been detected in humans. An influenza virus subtype that has caused human infection may be present in animals, or a circulating animal influenza poses a substantial risk of human disease.	Awareness: Mitigation and preparedness activities
Level I	Human infection(s) with a new subtype, but no human-to-human spread, or at most, rare instances of spread to a close contact.	
Level II	Confirmed human outbreak overseas	
Maine Pandemic Alert Period		
Level III	Widespread human outbreaks in multiple locations overseas	On Standby: Heightened preparedness activities
Level IV	First human case in North America	
Maine Pandemic Period		
Level V	First human case(s) in Maine, or in close geographic proximity to Maine	Activate: Response activities
Level VI	Increases and sustained transmission throughout the State of Maine	
Maine Post Pandemic Recovery Period		
Level VII Post-Pandemic Recovery Phase	Indices of influenza activity have returned to pre-pandemic levels.	Recovery activities

This Annex is designed to serve as a guide for clinicians, with the understanding that the management of influenza is based primarily on sound clinical judgment regarding the individual patient as well as an assessment of locally available resources, such as rapid diagnostics, antiviral drugs, and hospital beds. Early antiviral therapy shortens the duration of illness due to seasonal

influenza and would be expected to have similar effects on illness due to novel or pandemic influenza viruses (see **Annex 7: Antiviral Drug Distribution and Use**).¹

Clinical management must also address supportive care and management of influenza-related complications.

Other Annexes that cover topics of potential interest to clinicians:

Annex 1. Pandemic Influenza Surveillance

Annex 2. Laboratory Diagnostics

Annex 3. Healthcare Planning

Annex 4. Infection Control

Annex 6. Vaccine Distribution and Use

Annex 7. Antiviral Drug Distribution and Use

The Maine CDC will assess the clinical guidance released by federal partners on an ongoing basis during a pandemic and will align state guidelines accordingly. These guidelines will encompass the following based on Maine Response Levels:

Clinical Guidelines for the Maine Interpandemic Period

- Criteria for evaluation of patients with possible novel influenza
 - Clinical criteria
 - Epidemiologic criteria
 - Travel risks
 - Occupational risks
- Initial management of patients who meet the criteria for novel influenza
- Management of patients who test positive for novel influenza
- Management of patients who test positive for seasonal influenza
- Management of patients who test negative for novel influenza

Clinical Guidelines for the Maine Pandemic Alert and Pandemic Period

- Criteria for evaluation of patients with possible pandemic influenza
 - Clinical criteria
 - Epidemiologic criteria
- Initial management of patients who meet the criteria for pandemic influenza
- Clinical management of pandemic influenza patients

Annex 5. Clinical Guidelines

Maine Inter-Pandemic Period

Mitigation and Preparedness Rapid Detection and Containment ME Level 0, I, II

During the Maine Interpandemic Period, the primary goal is to quickly identify and contain cases of novel influenza. To limit the need to evaluate an overwhelming number of patients, the screening criteria should be specific, relying on a combination of clinical and epidemiologic features. Febrile respiratory illnesses are one of the most common indications for medical evaluation, particularly during the winter. Nonetheless, during the Maine Interpandemic Period, human cases of novel influenza are expected to be quite rare, and laboratory diagnosis will most likely be sought for those with severe respiratory illness, such as pneumonia. The main features of case detection and clinical management during the Maine Interpandemic Period are outlined in Figure 1.

A. Criteria for evaluation of patients with possible novel influenza: During the Maine Interpandemic Period, human infections with novel influenza A viruses will be an uncommon cause of influenza-like illness; therefore, both clinical and epidemiologic criteria should be met. The criteria will be updated when needed as more data are collected.

1. Clinical criteria:

- a. Any suspected cases of human infection with a novel influenza virus must first meet the criteria for influenza-like illness (ILI):
 - i. Temperature of $>38^{\circ}\text{C}$, *and*
 - ii. Cough, sore throat or dyspnea (since lower respiratory tract involvement might result in dyspnea (shortness of breath), dyspnea should be considered as an additional criterion).
 - iii. Therefore, the full clinical criteria are: **fever plus one of the following: sore throat, cough or dyspnea**
- b. Pandemic influenza virus strains can vary in severity and might present with different clinical syndromes than previous pandemics (see Appendix 1 and Appendix 2). In such a situation, the clinical criteria will be modified accordingly by federal CDC and posted at www.cdc.gov/flu. Maine CDC will keep abreast of any changes in clinical criteria and make

any necessary modifications to state clinical guidance.

- c. Given the large number of influenza-like illnesses that clinicians encounter during a typical flu season, **laboratory evaluation** for novel influenza A viruses during the Maine Interpandemic Period is recommended only for:
- i. Hospitalized patients with severe ILI, including pneumonia, who meet the epidemiologic criteria (see below), *or*
 - ii. Non-hospitalized patients with ILI **and** with strong epidemiologic suspicion of novel influenza virus exposure (e.g., direct contact with ill poultry or swine in an affected area, or close contact with a known or suspected human case of novel influenza.). (Annex 2: Laboratory Diagnostics)
 - iii. Recommendations for the evaluation of patients with respiratory illnesses are provided in Box 2. Exceptions to the current clinical criteria are provided in Box 3.

2. **Epidemiologic criteria:** Epidemiologic criteria for evaluation of patients with possible novel influenza focus on the risk of exposure to a novel influenza virus with pandemic potential. Although the incubation period for seasonal influenza ranges from 1 to 4 days, the incubation periods for novel types of influenza are currently unknown and might be longer. Therefore, the maximum interval between potential exposure and symptom onset is set conservatively at 10 days.

Exposure risks—Exposure risks fall into two categories: travel and occupational.

a. Travel risks

Persons have a travel risk if they have:

- recently visited or lived in an where a human case of novel influenza has been confirmed, **and**
- either had direct contact with an animal reservoir known to harbor novel influenza, **or**
- had close contact with a person with confirmed or suspected novel influenza. Updated listings of areas affected by current/recent novel strains are provided on the websites of the OIE (http://www.oie.int/eng/en_index.htm), WHO (www.who.int/en/), and CDC (www.cdc.gov/flu/).

Clinicians should recognize that human influenza viruses circulate worldwide and year-round. Therefore, during the Maine Interpandemic Period, human influenza virus infection can be a cause of ILI among returned travelers at any time of the year, including during the summer in the United States.

b. Occupational risks

The level of occupational risk for infection with a novel influenza strain depends in part on whether or not jobs require

close proximity to people potentially infected with the pandemic influenza virus, or whether they are required to have either repeated or extended contact with known or suspected sources of pandemic influenza virus such as coworkers, the general public, outpatients, school children or other such individuals or groups. Information on limiting occupational risk is provided on the Occupational Safety Administration website at: http://www.osha.gov/Publications/influenza_pandemic.html#difference.

B. Initial management of patients who meet the criteria for novel influenza: When a patient meets **both the clinical and epidemiologic criteria** for a suspected case of novel influenza, healthcare personnel should initiate the following activities:

- 1. Implement infection control precautions** for novel influenza, including Respiratory Hygiene/Cough Etiquette.
 - a. Implement Droplet Precautions for a minimum of 14 days, unless there is full resolution of illness or another etiology has been identified before that period has elapsed.
 - b. Healthcare personnel should wear surgical or procedure masks on entering a patient's room, as per Droplet Precautions. They should also wear gloves and gowns, when indicated for Standard Precautions (see Annex 4).
 - c. Patients should be admitted to a single-patient room, and patient movement and transport within the hospital should be limited to medically necessary purposes (see also Annex 4, Infection Control).
- 2. Notify Maine CDC.** Report each patient who meets the clinical and epidemiologic criteria for a suspected case of novel influenza to Maine CDC by calling 1-800-821-5821 as soon as possible to facilitate initiation of public health measures (see **Annex 1, Surveillance**). Designate one person as a point of contact to update Maine CDC on the patient's clinical status.
- 3. Obtain clinical specimens for novel influenza A virus testing and notify Maine CDC to arrange testing.** Testing will be directed by public health authorities (see Annex 2, Laboratory Diagnostics for more details).
 - a. Since the optimal specimens for detecting novel influenza A virus infections are currently unknown, if feasible, **all** of the following respiratory specimens should be collected for novel influenza A virus testing:
 - i. Nasopharyngeal swab
 - ii. Nasal swab, wash, or aspirate
 - iii. Throat swab; and

- iv. Tracheal aspirate (for intubated patients).
 - b. Store specimens at 4°C in viral transport media until transported or shipped for testing.
 - c. Acute (within 7 days of illness onset) and convalescent serum specimens (2–3 weeks after the acute specimen and at least 3 weeks after illness onset) should be obtained and refrigerated at 4°C or frozen at minus 20–80°C. Serological testing for novel influenza virus infection can be performed only at CDC.
4. Clinicians should immediately notify Maine CDC of their intention to ship clinical specimens from suspected cases of human infection with avian influenza, to ensure that the specimens are handled under proper biocontainment conditions (see Annex 2).
5. **Novel influenza can be confirmed by RT-PCR or virus isolation from tissue cell culture with subtyping.** RT-PCR for testing of novel influenza viruses cannot be performed by a hospital laboratory and is available only at state public health laboratories (HETL) and CDC. **Viral culture of specimens from suspected novel influenza cases should be attempted only in laboratories that meet the biocontainment conditions for BSL-3 with enhancements or higher.**
6. **Rapid influenza diagnostic tests and immunofluorescence** (indirect fluorescent antibody staining [IFA] or direct fluorescent antibody staining [DFA]) may be used to detect seasonal influenza, but **should not be used to confirm or exclude novel influenza during the Maine Interpandemic Period.**
- a. Rapid influenza tests have relatively low sensitivity for detecting seasonal influenza (Uyeki, 2003), and their ability to detect novel influenza subtypes is unknown. Sensitivity will likely be higher in specimens collected within two days of illness onset, in children, and when tested in clinical laboratories that perform a high volume of testing. Such tests can identify influenza A viruses but cannot distinguish between human infection with seasonal and novel influenza A viruses.
 - b. Because rapid influenza tests can result in both false negatives and false positives, these tests should be interpreted with caution, and RT-PCR testing for influenza should be performed. Further information on rapid diagnostic testing is provided in **Annex 2.**
7. Acute and convalescent serum samples and other available clinical specimens (respiratory, blood, and stool) should be saved and refrigerated or frozen for additional testing until a specific diagnosis is made.

- 8. Evaluate alternative diagnoses.** An alternative diagnosis should be based only on laboratory tests with high positive-predictive value (e.g., blood culture, viral culture, PCR, *Legionella* urinary antigen, pleural fluid culture, transthoracic aspirate culture). If an alternate etiology is identified, the possibility of co-infection with a novel influenza virus may still be considered if there is a strong epidemiologic link to exposure to novel influenza.

- 9. Decide on inpatient or outpatient management.** The decision to hospitalize a suspected novel influenza case will be based on the physician’s clinical assessment and assessment of risk and whether adequate precautions can be taken at home to prevent the potential spread of infection. Patients cared for at home should be separated from other household members as much as possible. All household members should carefully follow recommendations for hand hygiene and infection control (See **Annex 4** “Care of Pandemic Influenza Patients in the Home” p. 17-18).

- 10. Initiate antiviral treatment** as soon as possible, even if laboratory results are not yet available. Clinical trials have shown that these drugs can decrease the illness due to seasonal influenza duration by several days when they are initiated within 48 hours of illness onset. During the Maine Interpandemic Period, available virus isolates from any case of novel influenza will be tested for resistance to the currently licensed antiviral medications. See **Annex 7** for current antiviral information and treatment strategies.

- 11. Assist public health officials with the identification of potentially exposed contacts.** In general, persons in close contact with the case-patient at any time beginning one day before the onset of illness are considered at risk. Close contacts might include household and social contacts, family members, workplace or school contacts, fellow travelers, and/or healthcare providers (see **Annex 8** and **Annex 9**).

C. Management of patients who test positive for novel influenza

- a. If a patient is confirmed to have an infection with a novel influenza virus:
 - i. Continue antiviral treatment
 - ii. Maintain isolation and infection control precautions
 - iii. Isolate patients with novel influenza from seasonal influenza patients

D. Management of patients who test positive for seasonal influenza

Many suspected novel influenza cases may be found to have seasonal human influenza, particularly during the winter season. It

should be recognized that **human influenza viruses circulate among people worldwide, including during non-seasonal influenza activity in the United States.**

For patients with confirmed seasonal influenza:

- a. Maintain Standard and Droplet Precautions
- b. Continue antiviral treatment for a full treatment course (e.g., 5 days)

E. Management of patients who test negative for novel influenza

1. The sensitivity of the currently available tests for detecting novel influenza viruses is unknown, and false-negative test results may occur. Therefore, if test results are negative but the clinical and epidemiologic suspicion remains high, continuing antiviral treatment and isolation procedures should be considered. Test results might be negative for influenza viruses for several reasons:
 - a. Some patients might have an alternate etiology to explain their illness. The general work-up for febrile respiratory illnesses described below should evaluate the most common alternate causes.
 - b. A certain number of truly infected cases might also test falsely negative, due to specimen collection conditions, to viral shedding that is not detectable, or to sensitivity of the test.
2. Interpretation of negative testing results should be tailored to the individual patient in consultation with hospital infection control and infectious disease specialists, as well Maine CDC and federal CDC.
3. In hospitalized patients who test negative for novel influenza but have no alternate diagnosis established, novel-influenza-directed management should be continued if clinical suspicion is high and there is a strong epidemiologic link to exposure to novel influenza.
4. When influenza tests are negative and an alternative diagnosis is established, isolation precautions and antiviral drug therapy for novel influenza may be discontinued based on clinician's assessment, particularly in the absence of a strong epidemiologic link, if the alternative diagnosis is made using a test with a high positive-predictive value, and if the clinical manifestations are explained by the alternative diagnosis.

Maine Pandemic Alert and Pandemic Periods

ME Levels III, IV, V, IV

During the Maine Pandemic Alert and Pandemic Periods, the primary goal of rapid detection is to appropriately identify and triage cases of pandemic influenza. During these periods, outpatient clinics and emergency departments might be overwhelmed with suspected cases, restricting the time and laboratory resources available for evaluation. In addition, if the pandemic influenza virus exhibits transmission characteristics similar to those of seasonal influenza viruses, illnesses will likely spread throughout the community too rapidly to allow the identification of obvious exposures or contacts. Evaluation will therefore focus predominantly on clinical and basic laboratory findings, with less emphasis on laboratory diagnostic testing (which may be in short supply) and epidemiologic criteria. Nevertheless, clinicians in communities without pandemic influenza activity might consider asking patients about recent travel from a community with pandemic influenza activity or close contact with a suspected or confirmed pandemic influenza case. The main features of clinical management during the Pandemic Period are outlined in Figure 2.

A. Criteria for evaluation of patients with possible pandemic influenza

1. Clinical criteria:

- a. Suspected cases of pandemic influenza virus infection must first meet the criteria for influenza-like illness (ILI):
 - i. Temperature of $>38^{\circ}\text{C}$, *and*
 - ii. Cough, sore throat or dyspnea (since lower respiratory tract involvement might result in dyspnea (shortness of breath), dyspnea should be considered as an additional criterion).
 - iii. Therefore, the full clinical criteria are: **fever plus one of the following: sore throat, cough or dyspnea**
- b. Pandemic influenza virus strains can vary in severity and might present with different clinical syndromes than previous pandemics (see Appendix 1 and Appendix 2). In such a situation, the clinical criteria will be modified accordingly by federal CDC and posted at www.cdc.gov/flu. Maine CDC will keep abreast of any changes in clinical criteria and make any necessary modifications to state clinical guidance.

Recommendations for general evaluation of patients with influenza-like illness are provided in Box 2. Exceptions to the

clinical criteria are provided in Box 3.

2. Epidemiologic criteria

During the Maine Pandemic Alert and Pandemic Periods, an exposure history will be marginally useful for clinical management when disease is widespread in a community. In addition, there will be a relatively high likelihood that any case of ILI during that time period will be pandemic influenza. Once pandemic influenza has arrived in a particular locality, clinical criteria will be sufficient for classifying the patient as a suspected pandemic influenza case.

B. Initial management of patients who meet the criteria for pandemic influenza

When a patient meets the criteria for a suspected case of pandemic influenza, healthcare personnel should initiate the following activities:

1. **Follow Maine CDC recommendations on reporting** for patients who meet the criteria for pandemic influenza. See **Annex 1** for guidance on case reporting during the Pandemic Alert and Pandemic Periods.
2. **If the patient is hospitalized, implement infection control precautions for pandemic influenza**, including Respiratory Hygiene/Cough Etiquette (**Annex 4, Box 1**). Place the patient on Droplet Precautions for a minimum of **5 days** from the onset of symptoms. Healthcare personnel should wear surgical or procedure masks on entering a patient's room, as per Droplet Precautions, as well as gloves and gowns when indicated, as per Standard Precautions (**Annex 4, Box 1**). Once a pandemic is underway, hospital admission of patients should be limited to those with severe complications who cannot be cared for outside the hospital setting. Patients should be admitted to either a single-patient room or an area designated for cohorting of patients with influenza. Patient movement and transport outside the isolation area should be limited to medically necessary purposes (**Annex 4, Box 1**).
3. **Obtain clinical specimens** for general evaluation, as clinically indicated (see Box 2). Once pandemic influenza has arrived in a community, influenza testing will likely not be needed for most patients. Laboratory testing in conjunction with Maine CDC will likely be performed in a subset of pandemic influenza cases, however, as part of ongoing virologic surveillance to monitor the antigenic evolution of the strains for vaccine strain selection purposes (see **Annex 1**). At the beginning or end of a pandemic outbreak in a community, diagnostic testing might aid cohorting decisions, but may be optional in the setting of high local prevalence. Influenza diagnostic testing should be considered before initiating treatment with antivirals (see **Annex 7**). Guidelines for pandemic influenza virus testing are provided in **Annex 2**.

As with seasonal influenza, RT-PCR and virus isolation from tissue culture will be the most accurate methods for diagnosing pandemic influenza. Generally, specimens should include combined nasopharyngeal aspirates or nasal swabs, and throat swabs, stored at 4°C in viral transport media. During the Maine Pandemic Alert and Pandemic Periods, BSL-2 conditions should be sufficient for viral culture of clinical specimens from suspected pandemic influenza patients.

Rapid diagnostic tests for influenza and immunofluorescence may be helpful for initial clinical management, including cohorting and treatment (see above). However, rapid influenza tests have relatively low sensitivity for detecting seasonal influenza, and their ability to detect pandemic influenza viruses is unknown. Sensitivity will likely be higher in specimens collected within two days of illness onset, in children, and when tested at clinical laboratories that perform a high volume of testing. Because during a pandemic a negative rapid test may be a false negative, test results need to be interpreted within the overall clinical context. For example, it may not be optimal to withhold antiviral treatment from a seriously ill high risk patient on the basis of a negative test; however, in a setting of limited antiviral drug availability, treatment decisions in less high risk situations could be based on test results. The risk of a false-negative test also must be taken into account in making cohorting decisions. Rapid diagnostic testing should not preclude more reliable testing, if available. Further information on rapid diagnostic testing can be found in **Annex 2**.

4. **Decide on inpatient or outpatient management.** The decision to hospitalize a suspected pandemic influenza case will be based on the physician's clinical assessment of the patient as well as the availability of hospital beds and personnel. Guidelines on cohorting and infection control for admitted patients can be found in **Annex 3** and **Annex 4**.

An unstable patient will be considered a high priority for admission, but patients with high-risk conditions (see Appendix 1) might also warrant special attention, such as observation or close follow-up, even if disease is mild. On the other hand, home management with follow-up might be appropriate for well-appearing young children with fever alone. See **Annex 7** for inpatient and outpatient treatment strategies.

Patients cared for at home should be separated from other household members as much as possible. All household members should carefully follow recommendations for hand hygiene, and tissues used by the ill patient should be placed in a bag and disposed with other household waste (**Annex 4, Box 1**). Infection within the household may be minimized if a primary caregiver is designated; ideally, someone who does not have an underlying condition that places them at increased risk of severe influenza disease. Although no studies have assessed the use of masks at home to decrease the spread of infection, using a surgical or procedure mask by the patient or caregiver during interactions may be of benefit. Separation of eating utensils for use by a patient with influenza is not necessary, as long as they are washed with warm water and soap (**Annex 4, Box 1**).

C. Clinical management of pandemic influenza patients

See **Annex 7** for current antiviral information and treatment strategies.³ In addition to use of antivirals, clinical management of severe influenza should address supportive care and the rapid identification and treatment of secondary complications. Ribavirin and immunomodulatory therapies, such as steroids, are not approved by the FDA for treatment of severe influenza of any type and are purely investigational at this time. These agents frequently have severe adverse effects, such as bone marrow and hepatic toxicity, while the benefits of these therapies are unknown. During the Maine Pandemic Alert and Pandemic Periods, Maine CDC and federal CDC may request virus isolates from persons who fail treatment or antiviral prophylaxis, as these strains may more likely be drug resistant. In addition, randomly collected isolates will be tested for resistance to establish nationwide rates (see **Annex 1**).

Children aged <18 years with suspected or confirmed pandemic influenza should not be treated with aspirin or other salicylate-containing products because of an increased risk of Reye syndrome (characterized by acute encephalopathy and liver failure) in this age group.

The major clinical presentations and complications related to seasonal human influenza occur more commonly in persons with certain underlying medical conditions, such as chronic respiratory or cardiovascular disease and extremes of age, and are described in Appendix 1. Limited data are available on risk factors and complications related to infection with novel influenza viruses, and these may change as individual strains evolve. A summary of the clinical presentations and complications associated with recent pandemic influenza viruses is included in Appendix 2. In particular, post-influenza community-acquired pneumonia will likely be a commonly encountered complication, and clinicians will need to be aware of recommended methods for diagnosis and treatment. Guidance on the management of influenza-related pneumonia is presented in Appendix 3.

Maine Post Pandemic Recovery

**Recovery Activities
ME Level VII**

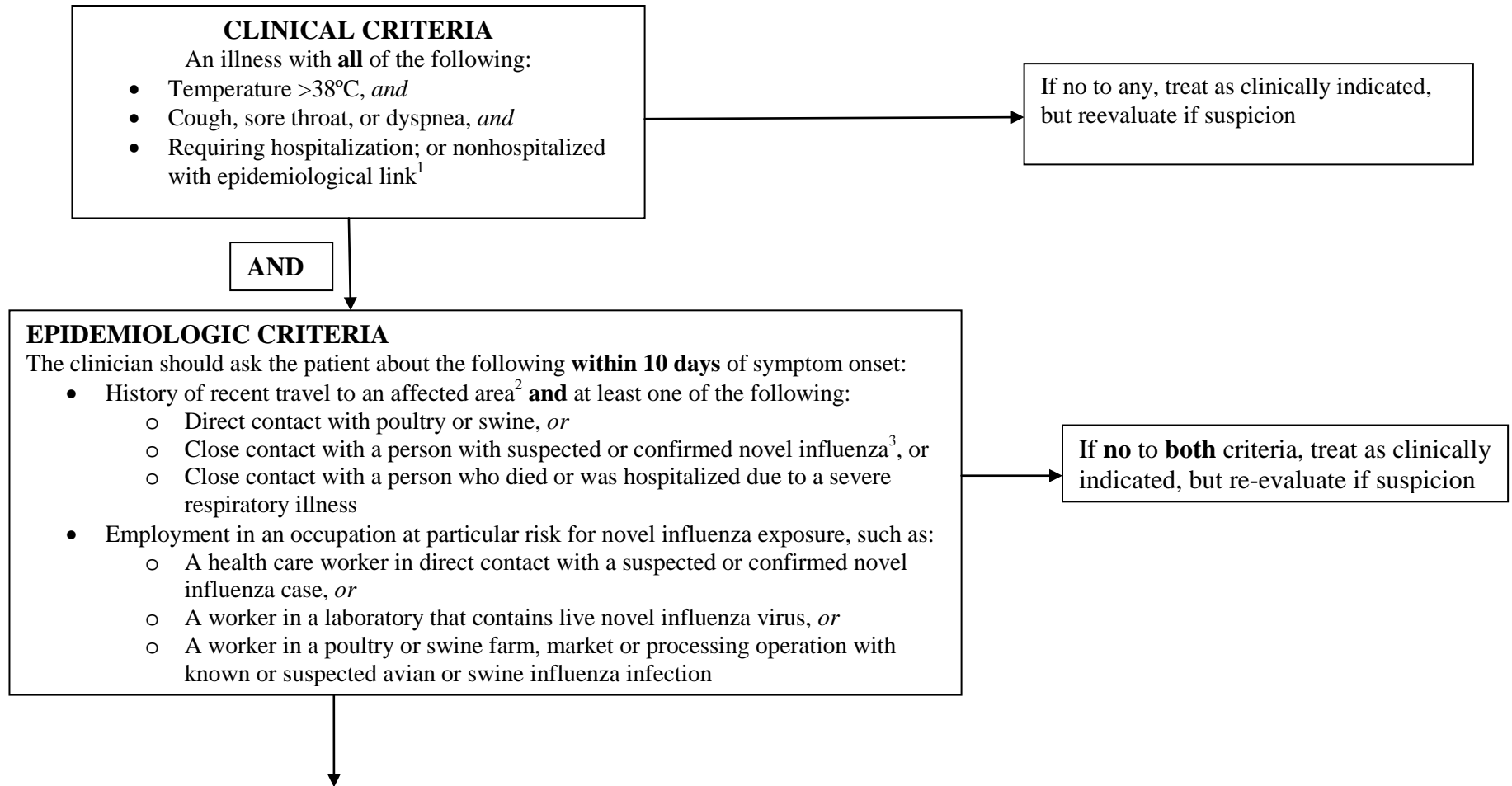
1. Return to Maine Interpandemic Period activities
2. Re-evaluate effectiveness and feasibility of clinical guidelines and update/modify as necessary
3. Provide feedback to providers regarding effectiveness and timeliness of clinical response, emphasizing lessons learned and areas for improvement

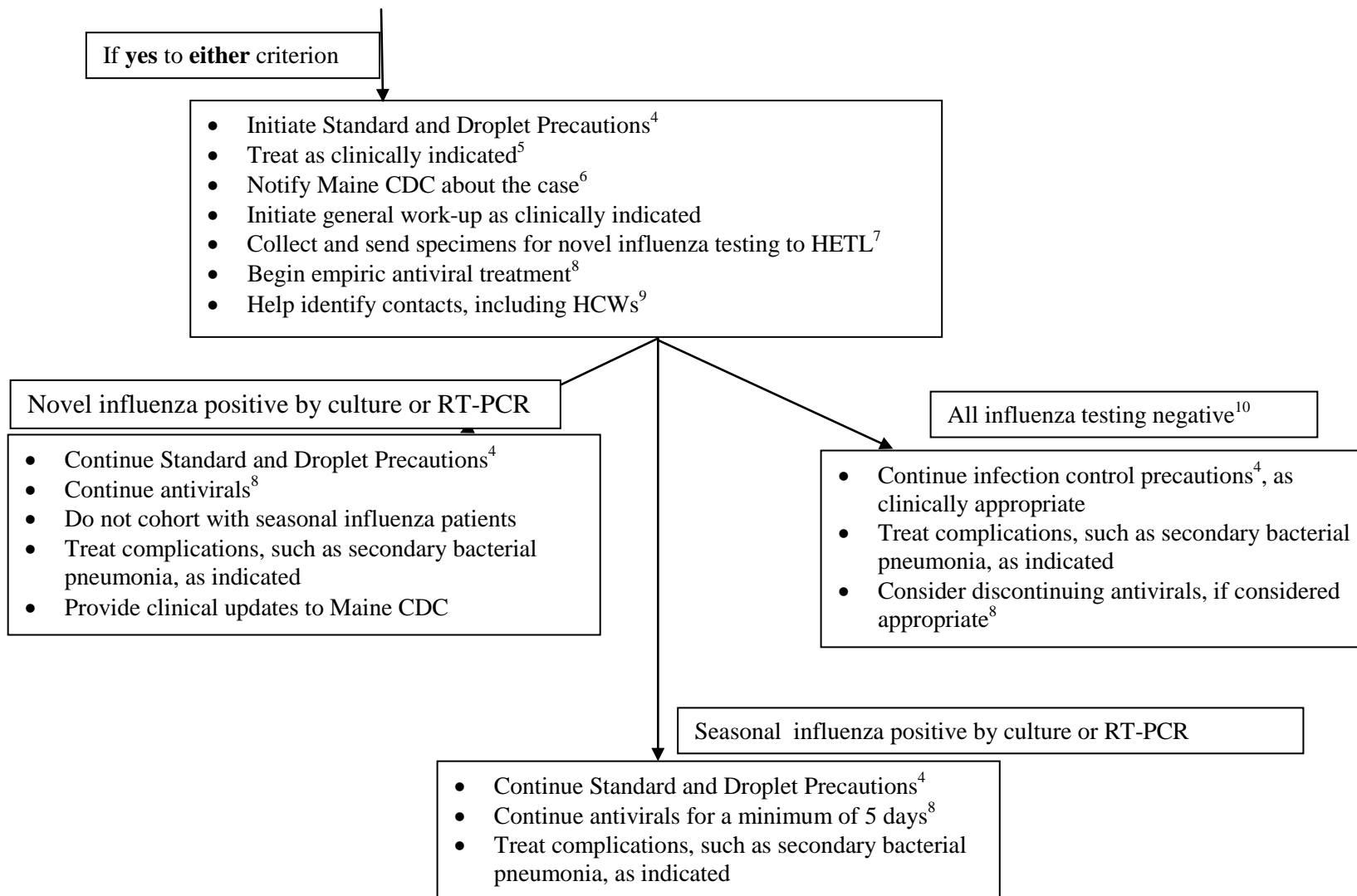
Annex 5. Clinical Guidelines Summary Matrix

Service / Function: Clinical Guidance	Maine Inter-Pandemic Period: Awareness Mitigation/ Preparedness ME Level 0, I, II	Maine Pandemic Alert Period: Standby Heightened Preparedness ME Levels III, IV	Maine Pandemic Period: Activate Response Plan Response ME Levels V, VI	Maine Post Pandemic Recovery Period Recovery ME Level VII
Provider education	Provide up to date information to providers regarding identification of suspect cases of novel influenza including clinical and epidemiologic criteria →	→	→	→
Facilitate investigation of suspected novel influenza cases	→	→	→	
Provide or facilitate laboratory testing	→	→	→	
Provide updated information on optimal treatment/ management strategies		→	→	
Rapid detection to appropriately identify and triage cases of pandemic influenza		→	→	
Containment and control		Encourage appropriate infection control precautions →	→	
Evaluate effectiveness of clinical guidelines and make necessary modifications	→	→	→	→

Figure 1. Case Detection and Clinical Management During the Maine Interpandemic Period

Situation: No human cases of novel influenza are present in the community. Human cases might be present in another country or another region of the United States.

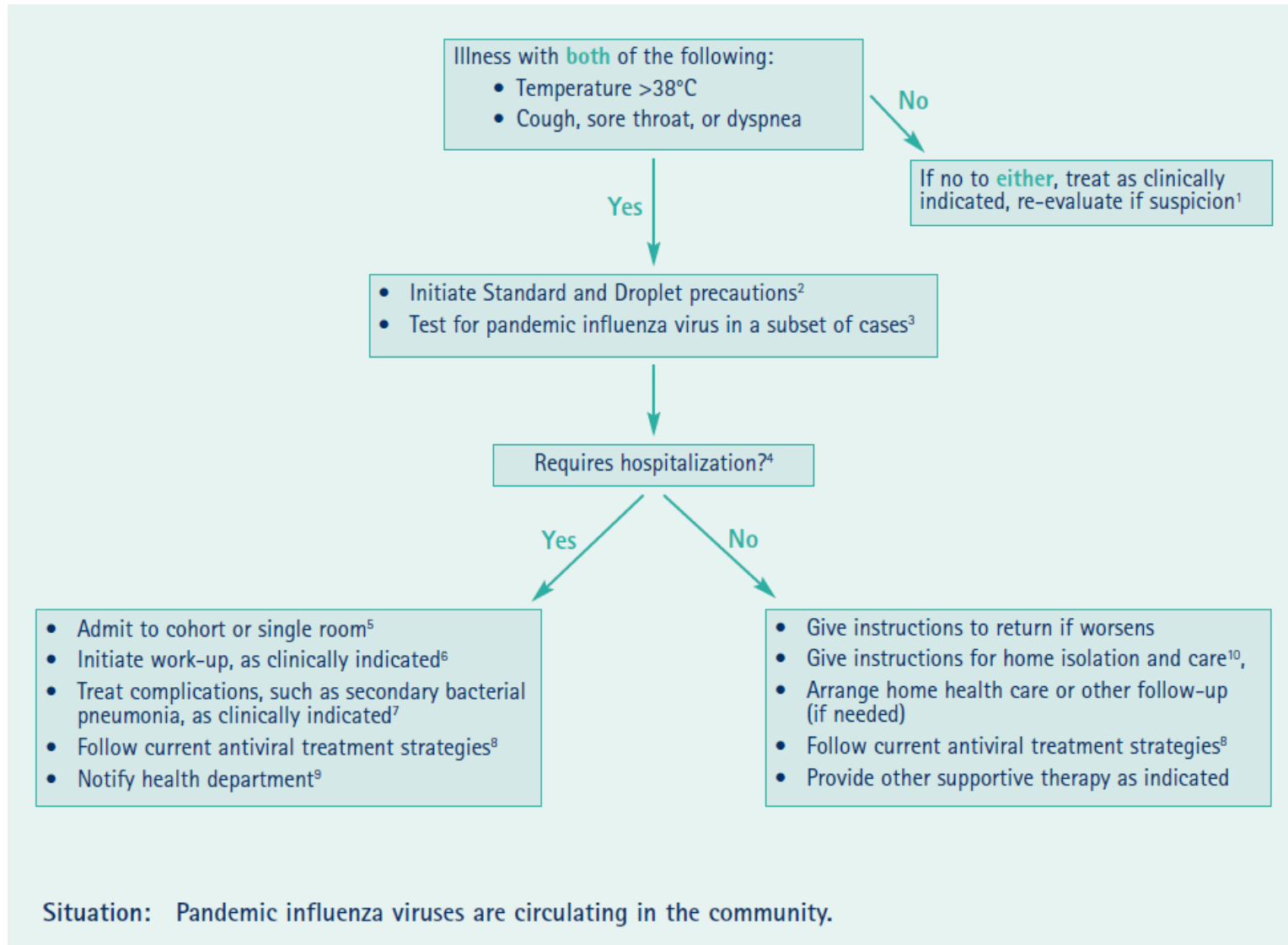




Footnotes to Figure 1:

1. Further evaluation and diagnostic testing should also be considered for outpatients with strong epidemiologic risk factors and mild or moderate illness. (See Box 2).
2. Updated listings of areas affected by current/recent novel strains are provided on the websites of the OIE (http://www.oie.int/eng/en_index.htm), WHO (www.who.int/en/), and CDC (www.cdc.gov/flu/).
3. Close contact includes direct physical contact, or approach within 3 feet (1 meter) of a person with suspected or confirmed novel influenza.
4. Standard and Droplet Precautions should be used when caring for patients with novel influenza or seasonal influenza (Annex 4).
5. Hospitalization should be based on all clinical factors, including the potential for infectiousness and the ability to practice adequate infection control. If hospitalization is not clinically warranted, and treatment and infection control is feasible in the home, the patient may be managed as an outpatient. The patient and his or her household should be provided with information on infection control procedures to follow in the home (Annex 4). The patient and close contacts should be monitored for illness by local public health department staff.
6. Guidance on how to report suspected cases of novel influenza is provided in Annex 1.
7. Guidelines for novel influenza virus testing can be found in Annex 2. All of the following respiratory specimens should be collected for novel influenza A virus testing: nasopharyngeal swab, wash or aspirate; throat swab; and tracheal aspirate (if intubated), stored at 4° C in viral transport media; and acute and convalescent serum samples.
8. Strategies for the use of antiviral drugs are provided in Annex 7.
9. Guidelines for the management of contacts in a healthcare setting are provided in Annex 3.
10. Given the unknown sensitivity of tests for novel influenza viruses, interpretation of negative results should be tailored to the individual patient in consultation with Maine CDC. Novel influenza directed management may need to be continued, depending on the strength of clinical and epidemiologic suspicion. Antiviral therapy and isolation precautions for novel influenza may be discontinued on the basis of an alternative diagnosis. The following criteria may be considered for this evaluation:
 - a. Absence of strong epidemiologic link to known cases of novel influenza
 - b. Alternative diagnosis confirmed using a test with a high positive-predictive value
 - c. Clinical manifestations explained by the alternative diagnosis

Figure 2. Case Detection and Clinical Management in the Maine Pandemic Alert and Pandemic Periods



Footnotes to Figure 2:

1. Antiviral therapy and isolation precautions for pandemic influenza should be discontinued on the basis of an alternative diagnosis only when both of the following criteria are met:
 - a. Alternative diagnosis confirmed using a test with a high positive-predictive value, and
 - b. Clinical manifestations entirely explained by the alternative diagnosis
2. Standard and Droplet Precautions should be used when caring for patients with novel influenza or seasonal influenza (Annex 4).
3. Guidance on laboratory testing during the Maine Pandemic Alert and Pandemic Periods can be found in Annex 2. Generally, specimens should include respiratory samples (e.g., nasopharyngeal wash/aspirate; nasopharyngeal, nasal or oropharyngeal swabs, or tracheal aspirates [if intubated]) stored at 4° C in viral transport media
4. The decision to hospitalize should be based on a clinical assessment of the patient and the availability of hospital beds and personnel.
5. Guidelines on cohorting can be found in Annex 4. Laboratory confirmation of influenza infection is recommended when possible before cohorting patients.
6. The general work-up should be guided by clinical indications (See Box 2).
7. Guidance on the evaluation and treatment of community acquired pneumonia and suspected post-influenza community-acquired bacterial pneumonia are provided in Appendix 3.
8. Strategies for the use of antiviral drugs are provided in Annex 7.
9. Guidance on the reporting of pandemic influenza cases is provided in Annex 1.
10. Patients with mild disease should be provided with standardized instructions on home management of fever and dehydration, pain relief, and recognition of deterioration in status. Patients should also receive information on infection control measures to follow at home (Annex 4).

Box 1. Risk of Novel Influenza in Persons with Severe Respiratory Disease or Influenza-Like Illness During the Interpandemic and Pandemic Alert Periods

Clinicians should recognize that human influenza A and B viruses and other respiratory viruses circulate year-round among people throughout the world. Seasonal human influenza A and B community outbreaks occur in temperate climates of the northern and southern hemisphere, and human influenza activity may occur year-round in subtropical and tropical regions. Outbreaks of human influenza can occur among travelers during any time of the year, including periods of low influenza activity in the United States (e.g., summer).

Maine Inter-Pandemic Period: ME Level 0

A novel influenza A virus has been detected in animals but not in humans. **During these phases, the risk of human infection with a novel influenza A virus strain is extremely low. The risk of human infection with human influenza viruses or other viruses is much higher in persons living in or traveling to affected areas.**

Maine Inter-Pandemic Period: ME Level I

A novel influenza A virus has been detected in humans through sporadic animal-to-human transmission in an affected area (e.g., direct contact with infected poultry), and few cases of limited, local human-to-human transmission have occurred (small clusters of cases). **During these phases, the risk of human infection with a novel influenza A virus strain is very low. The risk of human infection with human influenza viruses or other viruses is much higher in persons living in or traveling to affected areas.**

Maine Inter-Pandemic Period: ME Level II

A novel influenza A virus has been detected in humans in larger clusters in an affected area, suggesting that the virus is becoming better adapted to spread among people. **During this period, the risk of human infection with a novel influenza A virus strain is higher, depending on specific exposures, in persons living in or traveling to affected areas. Human infection with human influenza viruses or other viruses will occur and should still be considered.**

Box 2. Clinical Evaluation of Patients with Influenza-Like Illness During the Interpandemic and Pandemic Alert Periods

- Patients who require hospitalization for an influenza-like illness for which a definitive alternative diagnosis is not immediately apparent* should be questioned about: 1) travel to an area affected by novel influenza A outbreaks in animals (e.g., poultry or swine), 2) direct contact with animals potentially infected with novel influenza subtypes, 3) close contact with persons who have suspected or confirmed novel influenza, or 4) occupational exposure to novel influenza viruses (such as through agricultural, health care, or laboratory activities).
- Patients may be screened on admission for recent seasonal influenza vaccination and pneumococcal vaccination. Those without a history of immunization should receive these vaccines before discharge, if indicated.
- Patients meeting the epidemiologic criteria for possible infection with a novel strain of influenza should undergo a routine diagnostic work-up, guided by clinical indications. Appropriate personal protective equipment should be used when evaluating patients with suspected novel influenza, including during collection of specimens.**
- Diagnostic testing for a novel influenza A virus should be initiated as follows:
 - Collect all of the following specimens: nasopharyngeal swab, nasal swab, wash or aspirate, throat swab, and tracheal aspirate (if intubated), and place into viral transport media and refrigerate at 4° C until specimens can be transported for testing.
 - Immediately contact Maine CDC at 1-800-821-5821 to report the suspected case and to arrange novel influenza testing by RT-PCR.
- Depending on the clinical presentation and the patient's underlying health status, other initial diagnostic testing might include:
 - Pulse oximetry
 - Chest radiograph
 - Complete blood count (CBC) with differential
 - Blood cultures
 - Sputum (in adults), tracheal aspirate, and pleural effusion aspirate (if an effusion is present) Gram stain and culture
 - Antibiotic susceptibility testing (encouraged for all bacterial isolates)
 - Multivalent immunofluorescent antibody testing or PCR of nasopharyngeal aspirates or swabs for common viral respiratory pathogens, such as influenza A and B, adenovirus, parainfluenza viruses, and respiratory syncytial virus, particularly in children
 - In adults with radiographic evidence of pneumonia, *Legionella* and pneumococcal urinary antigen testing
 - If clinicians have access to rapid and reliable testing (e.g., PCR) for *M. pneumoniae* and *C. pneumoniae*, adults and children <5 years with radiographic pneumonia should be tested
 - Comprehensive serum chemistry panel, if metabolic derangement or other end-organ involvement, such as liver or renal failure, is suspected

*Further evaluation and diagnostic testing should also be considered for outpatients with strong epidemiologic risk factors and mild or moderate illness (see Box 3).

**Healthcare personnel should wear surgical or procedure masks on entering a patient's room (Droplet Precautions), as well as gloves and gowns, when indicated (Standard Precautions) (see Annex 4).

Box 3. Special Situations and Exceptions to the Clinical Criteria

Persons with a high risk of exposure – For persons with a high risk of exposure to a novel influenza virus (e.g., agricultural workers from an affected area,* caregiver of a patient with laboratory-confirmed novel influenza, employee in a laboratory that works with live novel influenza viruses), epidemiologic evidence might be enough to initiate further measures, even if clinical criteria are not fully met. In these persons, early signs and symptoms – such as rhinorrhea, conjunctivitis, chills, rigors, myalgia, headache and diarrhea – in addition to cough or sore throat, may be used to fulfill the clinical criteria for evaluation.

High-risk groups with atypical symptoms – Young children, elderly patients, patients in long-term care facilities, and persons with underlying chronic illnesses might not have typical influenza-like symptoms, such as fever. When such patients have a strong epidemiologic risk factor, novel influenza should be considered with almost any change in health status, even in the absence of typical clinical features. Conjunctivitis has been reported in patients with influenza A (H7N7) and (H7N3) infections. In young children, gastrointestinal manifestations such as vomiting and diarrhea might be present. Infants may present with fever or apnea alone, without other respiratory symptoms, and should be evaluated if there is an otherwise increased suspicion of novel influenza.

*Updated lists of affected areas are provided at the websites of the OIE (http://www.oie.int/eng/en_index.htm), WHO (www.who.int/en/), and federal CDC (www.cdc.gov/flu/).

Appendix to Annex 5

The following Appendices elaborate on the clinical guidelines:

- I. Clinical Presentation and Complications of Seasonal Influenza
- II. Clinical Presentation and Complications of Illness Associated with Previous
Pandemic Influenza Viruses
- III. Guidelines for Management of Community-Acquired Pneumonia, Including Post-
Influenza Community-Acquired Pneumonia

Appendix 1. Clinical Presentation and Complications of Seasonal Influenza

Although often quite characteristic, the clinical picture of seasonal influenza can be indistinguishable from illness caused by other respiratory infections. The frequent use of non-specific terms such as "flu" and "influenza-like illness" makes the clinical diagnosis of influenza even more indefinite. Even when the diagnosis of influenza is confirmed, management can be challenging, as influenza virus infection can result in subclinical infection, mild illness, uncomplicated influenza, or exacerbation of underlying chronic conditions to fulminant deterioration, and can result in a wide variety of complications.

This appendix provides a brief description of the common presentations and complications of seasonal human influenza. Novel and pandemic influenza viruses might, however, cause quite different clinical syndromes than seasonal influenza. For instance, seasonal influenza-related complications more commonly affect those at the extremes of age, whereas previous pandemics resulted in disproportionate morbidity and mortality in young and previously healthy adults. It will be essential to describe and disseminate the clinical features of novel or pandemic influenza cases as soon as they are identified. Appendix 2 includes a brief clinical summary of illnesses associated with previous influenza pandemics and with avian influenza A (H5N1) virus in humans.

Presentation

- A typical case of uncomplicated seasonal influenza begins abruptly and is manifested by systemic symptoms such as fever, chills, myalgias, anorexia, headache, and extreme fatigue. Fever typically lasts 2–3 days and usually reaches 38–40°C, but can be higher (particularly in children).
- Respiratory tract symptoms such as nonproductive cough, sore throat, and upper respiratory congestion occur at the same time, although these may be overshadowed by systemic complaints.
- Physical examination typically reveals fever, weakness, mild inflammation of the upper respiratory tract, and rare crackles on lung examination, but none of these findings is specific for influenza.
- In uncomplicated illness, major symptoms typically resolve after a limited number of days, but cough, weakness, and malaise can persist for up to 2 weeks.
- In the elderly and in infants, the presenting signs can include respiratory symptoms with or without fever, fever only, anorexia only, lassitude, or altered mental status. In children, fevers are often higher than in adults and can lead to febrile seizures. Gastrointestinal manifestations (e.g., vomiting, abdominal pain, diarrhea) occur more frequently in children. Fever or apnea without other respiratory symptoms might be the only manifestations in young children, particularly in neonates.

Influenza is difficult to distinguish from illnesses caused by other respiratory pathogens on the basis of symptoms alone. Fever and cough, particularly in combination, are modestly predictive of influenza in unvaccinated adults, as is the combination of fever, cough, headache, and

pharyngitis in children. Other constitutional signs and symptoms, such as chills, rigors, diaphoresis, and myalgias, are also suggestive. The positive predictive value of any clinical definition is strongly dependent on the level of influenza activity and the presence of other respiratory pathogens in the community.

Routine laboratory findings

No routine laboratory test results are specific for influenza. Leukocyte counts are variable, although thrombocytopenia and severe leukopenia have been described in fulminant cases. Leukocytosis of >15,000 cells/ml should raise suspicion for a secondary bacterial process. Comprehensive laboratory testing might reveal other influenza-related complications (see below).

Differential diagnosis

The fever and respiratory manifestations of seasonal influenza are not specific and can occur with several other pathogens, including respiratory syncytial virus (RSV), parainfluenza viruses, adenoviruses, human metapneumovirus, rhinoviruses, coronaviruses, and *Mycoplasma pneumoniae*. In contrast to influenza viruses, most of these pathogens do not usually cause severe disease, particularly in previously healthy adults. RSV and parainfluenza viruses can, however, lead to severe respiratory illness in young children and the elderly and should be considered in the differential diagnosis if circulating in the community. Even if an alternate etiology is determined, viral or bacterial co-infections can still be a possibility.

The tendency for influenza to occur in community epidemics and to affect persons of all ages can sometimes allow the clinician to diagnose seasonal influenza with reasonable certainty in the absence of laboratory testing. Nevertheless, a definitive diagnosis requires laboratory testing. Rapid influenza diagnostic tests and immunofluorescence testing using a panel of respiratory pathogens have become increasingly available for aiding clinical management of patients with suspected influenza. Instruction for submitting specimens for influenza testing at the Maine CDC Health and Environmental Testing Laboratory (HETL) can be found at http://www.maine.gov/dhhs/etl/micro/submitting_samples.htm. Further information on diagnostic testing for influenza can be found at <http://www.cdc.gov/flu/professionals/diagnosis/>.

Complications

Groups at risk for complications of influenza

The following groups are currently recognized by the Advisory Committee on Immunization Practices (ACIP) to be at higher risk for complications of seasonal influenza (e.g., hospitalization; death) compared to healthy older children and younger adults (CDC, MMWR, 2010):

- Children younger than 5 years, but especially those < 2 years
- Adults aged 50 years and older
- Women who are or will be pregnant during the influenza season
- Adults and children who have chronic pulmonary (including asthma) or cardiovascular (except isolated hypertension), renal, hepatic, neurological, hematologic, or metabolic disorders (including diabetes mellitus)

- Persons who have immunosuppression (including immunosuppression caused by medications or by HIV)
- Children and adolescents (aged 6 months--18 years) who are receiving long-term aspirin therapy and who might be at risk for experiencing Reye syndrome after influenza virus infection
- Residents of nursing homes and other long-term--care facilities
- American Indians/Alaska Natives
- Persons who are morbidly obese (BMI \geq 40)

Types of influenza complications

Exacerbations of underlying chronic diseases are the most common serious complications of influenza. Complications are frequently related to underlying respiratory disease, such as chronic obstructive pulmonary disease (COPD). In some cases, typical influenza symptoms might be brief or minimal compared to the exacerbation of the underlying disease, particularly in the elderly.

Secondary bacterial pneumonia, another common complication, is characterized by an initial improvement in influenza symptoms over the first few days followed by a return of fever, along with a productive cough and pleuritic chest pain. Findings include lobar consolidation on chest x-ray and, in adults, sputum smears positive for leukocytes and bacteria. The most commonly isolated pathogens are *Streptococcus pneumoniae*, *Staphylococcus aureus*, group A *Streptococcus*, and *Haemophilus influenzae*.

Influenza virus infection can also result in a primary viral pneumonia. A prominent feature of previous influenza pandemics, primary influenza viral pneumonia is currently a relatively rare outcome of seasonal influenza in adults. In contrast, children with pneumonia are more likely to have a viral etiology, including influenza, than a bacterial cause. Primary influenza pneumonia usually begins abruptly, with rapid progression to severe pulmonary disease within 1–4 days. Physical and radiologic findings are consistent with diffuse interstitial and/or alveolar disease, including bilateral inspiratory crackles on auscultation and diffuse pulmonary infiltrates on chest radiographs. Hypoxia and hemoptysis indicate a poor prognosis, and recovery can take up to 1–2 weeks. Mixed viral-bacterial pneumonia is slightly more common than primary viral pneumonia, and, although mixed pneumonia may have a slower progression, the two are often indistinguishable. Bacterial pathogens in mixed infections are similar to those found in secondary bacterial pneumonias.

Bronchiolitis due to influenza is more common in children, with a clinical picture similar to that of RSV or parainfluenza virus infections. Influenza is a cause of croup (laryngotracheobronchitis) in children, and, although influenza viruses are a less common etiology than other respiratory viruses, the illness can be more severe. Children with influenza can also develop otitis media, due to either direct viral infection or secondary bacterial involvement. Similarly, bacterial sinusitis can develop in older children and adults with influenza.

Seasonal influenza can cause a range of cardiovascular complications, most commonly as an exacerbation of an underlying condition such as congestive heart failure. Pregnant women and children with congenital heart defects can also experience worsening cardiac function during an

influenza illness. Cardiac inflammation, such as myocarditis and pericarditis, can be found occasionally, although clinical manifestations are rare. Available reports suggest that myocarditis might have occurred more frequently during pandemic years. Influenza virus is not typically identified in heart tissue, suggesting that the host inflammatory response might play a role. Although influenza has been associated in rare instances with sudden death possibly due to cardiac arrhythmia, this outcome has been difficult to investigate.

Gastrointestinal involvement is uncommon with seasonal influenza, although more commonly reported in children. Manifestations can include vomiting and diarrhea, sometimes leading to significant dehydration. Transient hepatic inflammation can occur in rare circumstances.

Myositis related to influenza is another complication more commonly found in children, although more frequently associated with influenza B. Involvement may be limited to pain and weakness of the lower extremities but can progress to rhabdomyolysis and renal failure in some cases.

Among the neurologic complications associated with seasonal influenza, uncomplicated self-limited febrile seizures are the most common, usually occurring in younger children with high fever. Influenza-associated encephalopathy, characterized by an acute alteration in mental status within the first few days of fever onset, is a recently recognized complication of influenza in children. Most reports of influenza-associated encephalopathy have been in Japanese children, but the condition has been reported sporadically in other countries, including the United States. The syndrome can include seizures, neurologic deficits, obtundation, and coma. While most children recover completely, some cases can result in permanent sequelae or death. This condition might be due to an abnormal host inflammatory response without viral infection of the central nervous system. Guillain-Barre syndrome and transverse myelitis have been reported to occur in very rare instances after influenza, but no definite etiologic relationship has been established.

Reye syndrome is another serious neurologic complication associated with influenza. It is characterized by an acute encephalopathy combined with hepatic failure in the absence of inflammation in either the brain or the liver. Hepatic involvement includes fatty infiltration, hypoglycemia, and hyperammonemia, whereas neurologic manifestations include cerebral edema, delirium, coma, and respiratory arrest. Reye syndrome was found to be associated with the use of aspirin in children; its incidence has decreased dramatically since the 1980s after aspirin use was discouraged in children.

Seasonal influenza can be associated with systemic complications, such as sepsis and shock. Sepsis caused by invasive coinfection with *Staphylococcus aureus*, including methicillin-resistant *S. aureus* (MRSA), or other bacteria, such as *Neisseria meningitidis* has been reported. Toxic shock syndrome without bacterial co-infection has also been reported.

Appendix 2. Clinical Presentation and Complications of Illness Associated with Previous Pandemic Influenza Viruses

Human infections with different avian influenza A viruses have emerged and caused mild to severe illness in recent years, including H9N2, H7N7, H7N3, and H7N2.

Illnesses associated with previous pandemic viruses

Since most people do not have previous immunity to novel influenza A viruses, an influenza pandemic results in an increased rate of severe disease in a majority of age groups. Nevertheless, the pandemics of the past century demonstrated significant variability in terms of morbidity. The 1918–19 pandemic was particularly notable in affecting young, healthy adults with severe illness. A significant proportion of patients developed fulminant disease, accompanied by a striking perioral cyanosis, leading to death within a few days. Postmortem examinations in these patients frequently revealed denuding tracheobronchitis, pulmonary hemorrhage, or pulmonary edema. Others survived the initial illness, only to die of a secondary bacterial pneumonia, usually due to *Streptococcus pneumoniae*, *Staphylococcus aureus*, group A *Streptococcus*, or *Haemophilus influenzae*.

The clinical features of the subsequent pandemics of 1957–58 and 1968–69 were also typical of influenza-like illness, including fever, chills, headache, sore throat, malaise, cough, and coryza, but were milder compared to the 1918–19 pandemic. On a population level, the impact of influenza in 1957–58 was only one-tenth that observed in 1918–19, and the excess death rate in 1968–69 was only half that observed during 1957–58. However, death rates were elevated among the chronically ill and the elderly, and the occurrence of severe complications, such as primary viral pneumonia, was notably increased in healthy young adults during the 1957–58 pandemic, particularly in pregnant women. The 2009 H1N1 pandemic affected between 43 to 89 million people in 74 countries. Between 8,870 and 18,300 deaths were related to H1N1 (WHO website, 7/2012). This pandemic disproportionately affected children, pregnant women, and those with underlying conditions.

Implications for the next pandemic

The characteristic clinical features of the next influenza pandemic cannot be predicted. It is reasonable to assume that most affected persons will have the typical features of influenza (e.g., fever, respiratory symptoms, myalgia, malaise). However, past pandemics have varied considerably with regard to severity and associated complications. Even as the next pandemic begins and spreads, the characteristic features might change, particularly if successive waves occur over several months. Given this potential for a dynamic clinical picture, it will be important for clinicians and public health partners to work together to disseminate updated and authoritative information to the healthcare community on a regular basis.

Appendix 3. Guidelines for Management of Community-Acquired Pneumonia, Including Post-Influenza Community-Acquired Pneumonia

Rationale

Post-influenza bacterial community-acquired pneumonia will likely be a common complication during the next pandemic and might affect approximately 10% of persons with pandemic influenza, based on data from previous influenza pandemics. Assuming that pandemic influenza will affect about 15%–35% of the U.S. population, approximately 4.4 to 10.2 million cases of post-influenza bacterial community-acquired pneumonia could occur.

Post-influenza bacterial community-acquired pneumonia often presents as a return of fever, along with a productive cough and pleuritic chest pain, after an initial improvement in influenza symptoms over the first few days. Findings include lobar consolidation on chest x-ray and, in adults, sputum smear positive for leukocytes and bacteria. As with other bacterial infections, leukocytosis with increased immature forms may be present, but this finding is neither sensitive nor specific. The most common etiologies of post-influenza bacterial pneumonia are *Streptococcus pneumoniae*, *Staphylococcus aureus*, group A *Streptococcus*, and *Haemophilus influenzae*. Primary viral pneumonia, with abrupt onset and rapid progression, is more common than bacterial pneumonia in children, yet rare in adults. Physical and radiologic findings in viral pneumonia are consistent with interstitial and/or alveolar disease and include bilateral inspiratory crackles and diffuse infiltrates. Mixed viral-bacterial pneumonia is slightly more common than primary viral pneumonia, but they are often indistinguishable. Bacterial pathogens in mixed infections are similar to those found in secondary bacterial pneumonias. Droplet and Standard Precautions are currently recommended for community-acquired pneumonia of bacterial etiology (ref CDC, 2004).

Treatment of community-acquired pneumonia, including post-influenza bacterial community-acquired pneumonia will pose challenges for clinicians during a pandemic. Secondary bacterial pneumonia following influenza virus infection will be difficult to distinguish from community-acquired pneumonia that is not preceded by influenza. Current guidelines for the treatment of adult community-acquired pneumonia (CAP) during the Interpandemic Period de-emphasize the use of diagnostic testing for pathogen-directed treatment and favor empiric therapy with safe and effective broad-spectrum antibacterials, especially extended-spectrum macrolides and fluoroquinolones. However, these antibacterials will likely be in short supply during a pandemic.

Guidance for the management of community-associated pneumonia in adults (ref Mandell) and children (ref. Bradley) are included as attachments to this Appendix.

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