

# Clinical management of human infection with pandemic (H1N1) 2009

## Introduction

The majority of illnesses caused by pandemic (H1N1) 2009 virus infection have been self-limited mild-to-moderate uncomplicated disease, severe complications including fatal outcomes have been reported.

The pandemic (H1N1) 2009 influenza virus differs in its pathogenicity from seasonal influenza in two key aspects.

- 1- The majority of human population has little or no pre-existing immunity to the virus, infection has been in a wider age range.
- 2- The virus can infect the lower respiratory tract and cause rapidly progressive pneumonia especially in children and young to middle-aged adults.

The incubation period appears to be approximately 2-3 days, but could range up to 7 days; the infective period starts one before symptoms and continue up to 7 days after symptoms.

The epidemiology of pandemic (H1N1) 2009 virus infection shows a **wide clinical spectrum of disease** ranging from non-febrile, mild upper respiratory tract illness, febrile influenza like illness (ILI) to severe or even fatal complications, including rapidly progressive pneumonia. The most commonly reported symptoms have included cough, fever, sore throat, muscle aches, malaise, and headache. Some patients have experienced gastrointestinal symptoms (nausea, vomiting, and/or diarrhea).

### **Uncomplicated influenza:**

- Patients may present with some or all of these symptoms: fever, cough, sore throat, rhinorrhea, headache, muscle pain, and malaise, but no shortness of breath and no dyspnoea.

Gastrointestinal illness may also be present, such as diarrhoea and/or vomiting, especially in children, but without evidence of dehydration.

### **Complicated or severe influenza:**

- Presenting clinical (e.g. shortness of breath/dyspnoea, tachypnea, hypoxia) and/or radiological signs of lower respiratory tract disease (e.g. pneumonia), central nervous system (CNS) involvement (e.g. encephalopathy, encephalitis), severe dehydration, or presenting with secondary complications, such as renal failure, multiorgan failure and septic shock. Other complications can include rhabdomyolysis and myocarditis.
- Exacerbation of underlying chronic disease including asthma, COPD, chronic hepatic, renal failure, diabetes, or other cardiovascular conditions.

- Any other condition or clinical presentation requiring hospital admission for clinical management.
- Any of the signs of disease progression.

**Risk factors for severe disease:**

- Infants and young children, in particular <2 years
- Pregnant women
- Persons of any age with chronic pulmonary disease (e.g. asthma, COPD)
- Persons of any age with chronic cardiac disease (e.g. congestive cardiac failure)
- Persons with metabolic disorders (e.g. diabetes)
- Persons with chronic renal disease, chronic hepatic disease, certain neurological conditions (including neuromuscular, neurocognitive, and seizure disorders), hemoglobinopathies, or immunosuppression, whether due to primary immunosuppressive conditions, such as HIV infection, or secondary conditions, such as immunosuppressive medication or malignancy
- Children receiving chronic aspirin therapy
- Persons aged 65 years and older

**Signs and symptoms of progressive disease**

Patients who present initially with uncomplicated influenza may progress to more severe disease. Progression can be rapid (i.e. within 24 hours). The following are some of the indicators of progression, which would necessitate an urgent review of patient management:

- Symptoms and signs suggesting oxygen impairment or cardiopulmonary insufficiency:
  - Shortness of breath (with activity or at rest), difficulty in breathing, turning blue, bloody or coloured sputum, chest pain, and low blood pressure;
  - In children, fast or laboured breathing and Hypoxia, as indicated by pulse oximetry.
- Symptoms and signs suggesting CNS complications:
  - Altered mental status, unconsciousness, drowsiness, or difficult to awaken and recurring or persistent convulsions (seizures), confusion, severe weakness, or paralysis.
- Evidence of sustained virus replication or invasive secondary bacterial infection based on laboratory testing or clinical signs (e.g. persistent high fever and other symptoms beyond 3 days).
- Severe dehydration, manifested as decreased activity, dizziness, decreased urine output, and lethargy.

**Diagnosis:**

1. Rapid test (negative result can not rule out H1N1 infection).
2. Real time Reverse transcriptase polymerase chain reaction (RT-PCR), which is a confirmatory test for H1N1.

**Under no circumstances should influenza diagnostic testing delay initiation of infection control practices or antiviral treatment, if pandemic (H1N1) 2009 disease is suspected clinically and epidemiologically.**

**General treatment considerations:**

Most people with pandemic (H1N1) 2009 virus infection have had self-limiting uncomplicated illness. Supportive care can be provided as needed, such as antipyretics (e.g. paracetamol ) for fever or pain and fluid rehydration. Salicylates (such as aspirin and aspirin-containing products) should NOT be used in children and young adults (aged <18 years) because of the risk of Reye's syndrome

Pregnant women, especially those with co-morbidities, are at increased risk for complications from influenza virus infection which may be associated with an increased risk of adverse pregnancy outcomes, such as spontaneous abortion, preterm birth, and fetal distress. Consequently, pregnant women with suspected or confirmed pandemic (H1N1) 2009 virus infection warrant closer observation and early antiviral treatment, non-steroidal anti-inflammatory drugs (NSAIDs), including aspirin, are associated with fetal risks and maternal bleeding and are, therefore, contraindicated in pregnancy

**Some specific recommendations:**

- Patients with flu-like symptoms should be directed to a designated waiting area and given instruction and educational materials regarding respiratory hygiene and cough etiquette to cover mouth and nose with a tissue when coughing or sneezing, discard tissue in a bin with a lid, and then clean hands. Patients who can tolerate it should wear a medical or surgical mask, which should also be worn during patient transport and transfer.
- Patient should be evaluated, respiratory rate should be recorded for 1 full minute, as well as oxygen saturation when available. Senior care staff should be notified and consulted if respiratory rate is high or oxygen saturation is under 90%. History should document flu-like symptoms, date of onset, travel, exposure to persons with flu-like symptoms, and comorbid conditions, and alternative or additional diagnoses should be considered.
- Specialized diagnostic tests, such as reverse transcriptase polymerase chain reaction, may be indicated. When taking respiratory samples, healthcare personnel should wear a medical or surgical mask, eye protection, and gloves. Specimens should be correctly labeled and sent with biohazard precautions in compliance with local regulations. Suspected cases of H1N1 infection should be reported to the local authorities.
- When the patient arrives at the isolation room, restricted entry and infection control signs should be posted. When available, dedicated patient equipment

should be provided. Patients should be separated by at least 1 meter (3.3 feet). The local hospital protocol should be implemented for frequent linen and surface cleaning.

- Before a healthcare staff member or visitor enters an isolation room or cohort, they should put on a medical or surgical mask and clean their hands by hand rubbing with an alcohol-based hand rub formulation or by hand washing with soap and water.
- Before any exposure to a patient with known or suspected H1N1 influenza infection, healthcare staff should put medical or surgical mask and clean their hands. When there is risk for exposure to body fluids or splashes, eye protection, gown, and gloves should also be worn. Personal or dedicated patient equipment should be cleaned and disinfected. Between patients, staff should change their gloves and clean their hands.
- When aerosol-generating procedures, such as intubation, bronchoscopy, cardiopulmonary resuscitation, or suctioning are being performed, only those staff essential to the procedure should be allowed access. The procedure should be done in an adequately ventilated room. A gown, particulate respirator (if available; e.g., certified N95), eye protection, and gloves should be worn.
- Before a healthcare staff member or visitor leaves an isolation room or cohort, they should remove their gloves, gown, mask, eye protection, and any other personal protective equipment and discard disposable supplies according to hospital protocol. Hands should be cleaned and dedicated patient equipment and personal equipment used by the patient should be cleaned and disinfected. Viral-contaminated waste should be disposed of as clinical waste.
- Alternative or additional diagnoses should be considered in patients with known or suspected H1N1 infection.
- Supportive treatment for patients with H1N1 infection should be similar to that for any influenza patient. Supplemental oxygen should be given as needed to maintain oxygen saturation above 90%, as well as to patients with increased respiratory rate if monitoring oxygen saturation is not feasible. For patients younger than 18 years, paracetamol or acetaminophen is recommended as an antipyretic. Patients with evidence of pneumonia or secondary bacterial infection should receive appropriate antibiotics. Use of the antiviral drugs oseltamivir or zanamivir should be considered after weighing contraindications and potential drug interactions.
- Before a patient with a confirmed or suspected case of H1N1 influenza infection is discharged from hospital, the patient and/or caregiver should be educated and given materials regarding respiratory hygiene and cough etiquette and counseled regarding home isolation, infection control, and limiting social contact. Patient contact information should be recorded.
- After discharge, dedicated patient equipment should be discarded or cleaned and disinfected according to the hospital protocol, linen should be changed and laundered without shaking, surfaces should be cleaned according to the hospital per local protocol, and viral-contaminated waste should be disposed of as clinical waste.

## Recommendations for Antiviral Treatment of H1N1

For patients with confirmed or strongly suspected infection with influenza pandemic (H1N1) 2009, specific recommendations regarding use of antivirals for treatment of pandemic (H1N1) 2009 influenza virus infection are as follows:

- Oseltamivir (Tamiflu) should be prescribed in 75mg twice daily for five days, treatment should be started as soon as possible, for patients with severe or progressive clinical illness depending on clinical response, higher doses of up to 150 mg twice daily and longer duration of treatment may be indicated. This recommendation is intended for all patient groups, including pregnant women, neonates, and children younger than 5 years of age.
- Antiviral treatment is not required in patients not in at-risk groups who have uncomplicated illness caused by confirmed or strongly suspected influenza virus infection. Patients considered to be at risk are infants and children younger than 5 years of age; adults older than 65 years of age; nursing home residents; pregnant women; patients with chronic comorbid disease including cardiovascular, respiratory, or liver disease and diabetes; and immunosuppressed patients because of malignancy, HIV infection, or other diseases.
- Oseltamivir treatment should be started as soon as possible after the onset of illness in patients in at-risk groups who have uncomplicated illness caused by influenza virus infection.

Mothers who are breast feeding may continue breastfeeding while ill and receiving oseltamivir or zanamivir.

### Oseltamivir

The following tables describe the doses of Tamiflu for children:

15 kg or less	30 mg orally twice a day for 5 days
15-23 kg	45 mg orally twice a day for 5 days
24-40 kg	60 mg orally twice a day for 5 days
>40 kg	75 mg orally twice a day for 5 days

>3 months to 12 months	3 mg/kg twice daily
>1 month to 3 months	2.5 mg/kg twice daily
0 to 1 month*	2 mg/kg twice daily

## **Zanamivir**

Zanamivir is indicated for treatment of influenza in adults and children (>5 years). The recommended dose for treatment of adults and children from the age of 5 years (based on data from studies in typical uncomplicated influenza) is two inhalations (2 x 5mg) twice daily for 5 days

### **Side effects:**

#### **Oseltamivir**

Nausea and vomiting the most frequent side effects and more common among children, which may be less severe if oseltamivir is taken with food. However self-injury and delirium have been reported in some people on oseltamivir in Japan.

#### **Zanamivir**

Is generally not recommended for those who have chronic lung diseases such as asthma and chronic obstructive pulmonary diseases. It may cause decrease respiratory function and bronchospasm, less frequent side effects include diarrhea, nausea sinusitis, nasal infection, bronchitis, headache and dizziness.

### **Chemoprophylaxis:**

Post exposure chemoprophylaxis in healthy individual (antiviral agents) is discouraged for prevention of illness based in potential exposure in community for both adult and children.

Specific recommendations regarding the use of antiviral for chemoprophylaxis of pandemic (H1N1) 2009 influenza virus infection are as follows:

- When risk for human-to-human transmission of influenza is high and the probability of complications of infection is high, either because of the influenza strain or because of the baseline risk of the exposed group, use of oseltamivir may be considered as postexposure chemoprophylaxis for the affected community or group, for individuals in at-risk groups.
- Individuals at-risk groups or healthcare personnel need not be offered antiviral chemoprophylaxis if the likelihood of complications of infection is low.

### **Infection control**

Infection control Standard plus Droplet Precautions.

Critical majors:

1. Avoid crowding patients together, promote distance between patients
2. Perform hand hygiene (frequent hand washing and using antiseptic solution)
3. Protect mucosa of mouth and nose especially during aerosol-generating procedures, use a particulate respirator (N95, FFP2 or equivalent), eye protection, gowns, gloves, and an adequately ventilated room, which can be naturally or mechanically ventilated.

**Note: this information was adopted from WHO and CDC guidelines for management of H1N1**

