

Influenza (H1N1) 2009 Key issues for case management

Background

- The clinical spectrum of influenza A (H1N1) 2009 virus infection can vary from asymptomatic infection to moderate disease to serious complicated illness that may include exacerbation of other underlying conditions, severe viral pneumonia with multi-organ failure, and invasive bacterial co-infection.
- The incubation period appears to be approximately 2 to 3 days, but could range up to 7 days.
- Patients who present initially with uncomplicated influenza may progress to more severe disease.
- In severe cases, patients generally begin to deteriorate around 3 to 5 days after symptom onset.
- Deterioration may be rapid, with many patients progressing to respiratory failure within 24 hours, requiring immediate admission to an intensive care unit. Upon admission, many patients need immediate respiratory support with mechanical ventilation. However, some patients do not respond well to conventional respiratory support, further complicating management.

Case description: possible scenarios

Uncomplicated influenza

- Influenza-like illness symptoms: fever, cough, sore throat, rhinorrhea, headache, muscle pain, malaise, but no shortness of breath, no dyspnoea.
- Gastrointestinal illness such as diarrhoea and/or vomiting, especially in children, but without evidence of dehydration.

Signs and symptoms of progressive disease

- Symptoms and signs suggesting cardiopulmonary insufficiency: shortness of breath, difficulty in breathing, hemoptysis or coloured sputum, chest pain and hypotension. In children fast or laboured breathing may indicate progressive disease. Hypoxia as indicated by pulse oximetry.
- Symptoms and signs suggesting central nervous system (CNS) complications: altered mental status, unconscious, drowsiness, or difficult to awaken; recurring or persistent convulsions (seizures), severe weakness or paralysis.
- Evidence of sustained virus replication or invasive secondary bacterial infection is based on laboratory testing or clinical signs (e.g. persistent high fever and other symptoms beyond three days, sepsis, rapid deterioration).
- Severe dehydration: decreased activity, dizziness, decreased urine output, lethargy.

Complicated or severe influenza

- May be indicated by shortness of breath, dyspnoea, tachypnea, hypoxia, cyanosis, CNS findings, radiological signs of pneumonia, severe dehydration or presenting secondary complications such as renal failure, multi-organ failure, septic shock.
- Exacerbation of underlying chronic disease, including asthma, chronic obstructive pulmonary disease, chronic hepatic or renal failure, diabetes or other cardiovascular conditions can cause severe complications.

High Risk Groups for Complications:

- Influenza virus infection in any patient can result in severe or complicated illness, and approximately 1/3 of very severe influenza cases have no known underlying risk factors.
- However persons at higher risk of complications of Influenza A (H1N1) 2009 virus infections also include pregnant women, infants and young children in particular <2 years, persons aged 65 years and older, persons with chronic pulmonary disease (e.g. asthma, COPD), persons with chronic cardiac disease (e.g. congestive cardiac failure), persons with metabolic disorders (e.g. diabetes), persons with chronic renal disease, chronic hepatic disease, chronic neurological impairment, hemoglobinopathies, or who are immunocompromised or under immunosuppression, children receiving chronic aspirin therapy and persons who are obese or morbidly obese.

Diagnosis:

- On an individual patient basis, uncomplicated influenza can be diagnosed based on signs and symptoms when influenza viruses are known to be circulating in a community.
- Laboratory diagnostic testing, when available, should be prioritized for patients in whom confirmation of influenza virus infection may affect clinical management, including patients considered at-risk and/or those with complicated or progressive respiratory illness, or hospitalized patients.
- Rapid influenza diagnostic tests can produce quick result in 15 minutes or less, however false negative results are common. Negative results from rapid tests cannot guide treatment and Infection Control decisions.

Overall recommendations:

- All patients should be instructed to return for follow-up, should they develop any signs or symptoms of progressive disease or fail to improve within 72 hours of the onset of symptoms.
- In patients with progressive or complicated illness provide continuous monitoring of vital signs (e.g. temperature, blood pressure, pulse, respiratory rate, level of conscious, clinical signs of dehydration or shock) and oxygen saturation (pulse oximetry or blood gas analyses).
- Initial treatment decisions should be based on clinical presentation and epidemiological data and under no circumstances should treatment be delayed pending laboratory confirmation.

Infection control

- Appropriate infection control measures (Standard plus Droplet Precautions) should be adhered to at all times.
- Whenever performing high-risk aerosol-generating procedures (e.g. bronchoscopy, or any procedure involving aspiration of the respiratory tract) use a particulate respirator (N95, FFP2 or equivalent), eye protection, gowns, gloves, and carry out the procedure in a well ventilated room (> 12 air changes per hour).
- Isolation precautions for hospitalized patients with influenza symptoms should be continued for 7 days after onset of illness or 24 hours after the resolution of fever and respiratory symptoms, whichever is longer, while a patient is in a health-care facility.

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Non-steroidal anti-inflammatory drugs (NSAIDs), including aspirin

- Paracetamol (acetaminophen) may be given orally or by suppository.
- Avoid administration of salicylates (aspirin and aspirin-containing products) in children and young adults (< 18 years old) due to the risk of Reye's syndrome.

Antibiotic treatment

- Antibiotic chemoprophylaxis should not be used.
- Primary viral pneumonia is the most common finding in severe cases and a frequent cause of death.
- Secondary bacterial infections have been found in approximately 30% of fatal cases.
- When pneumonia is present, bacteria frequently reported include *Haemophilus influenzae*, Group A *Streptococcus* (*Streptococcus pyogenes*) and *Staphylococcus aureus* (which may include MSSA and MRSA). Empirical treatment with broad-spectrum antibiotics that will cover these pathogens is appropriate in the setting of severe H1N1 (2009) influenza causing respiratory or multi-organ failure.

Corticosteroids

- Corticosteroids should not be used routinely for treatment of influenza A (H1N1) 2009 virus infection.
- Low doses of corticosteroids may be considered for patients in septic shock who require vasopressors and have suspected adrenal insufficiency.
- Prolonged use of or high dose corticosteroids can result in serious adverse events in influenza virus-infected patients, including opportunistic infection and possibly prolonged viral replication.

Antiviral drug therapy

- Patients in high risk groups with uncomplicated illness, should be treated with oseltamivir or zanamivir.
- Do not use amantadine or rimantadine due to widespread resistance to these drugs among circulating influenza A viruses.
- The conventional oseltamivir dose is 75mg twice per day (bid) for 5 days. In order to ensure aggressive antiviral treatment and therapeutic levels clinicians may consider the use of higher doses up to 150 mg bid and longer duration of treatment.
- Oseltamivir treatment of hospitalized patients with suspected influenza should be undertaken empirically. Start treatment as soon as possible as the benefits are greatest as close to illness onset as possible. **Do not delay initiation of oseltamivir treatment while waiting for influenza testing results.**
- Immunosuppressed persons may demonstrate prolonged viral replication (weeks to months) and are at increased risk of developing oseltamivir resistant virus infections with oseltamivir treatment.
- Oseltamivir resistance remains low, but clinicians can consider the emergence of oseltamivir resistance in a treated patient who has not improved after 5 days or is worsening.

Oseltamivir dosage recommendations:

Infants less than 1 year of age:	Persons older than 1 year of age:
– 0 to 1 month, 2 mg/kg bid	– 15kg or less, 30 mg orally bid for 5 days
– >1 to 3 months, 2.5 mg/kg bid	– 15-23kg, 45 mg orally bid for 5 days
– >3 to 12 months, 3 mg/kg bid	– 24-40kg, 60 mg orally bid for 5 days
	– >40kg, 75 mg orally bid for 5 days

Notes on oseltamivir treatment:

- Treatment should be started within 48h of symptoms onset, but it may also be used at any stage of active disease
- If creatinine clearance <30 ml/min reduction in dose of oseltamivir should be considered.
- In patients with severe or progressive illness not responding to normal treatment regimens, higher doses of oseltamivir and longer duration of treatment may be appropriate.
- Oseltamivir or zanamivir might be used as post exposure chemoprophylaxis for exposed individuals in known risk groups.
- For exposed persons where the likelihood of complications of infection is low, antiviral chemoprophylaxis need not be offered.
- Pregnant women and children aged less than 1 year with uncomplicated illness due to influenza virus infection should not be treated with amantadine or rimantadine.

Fluid therapy and vasopressors

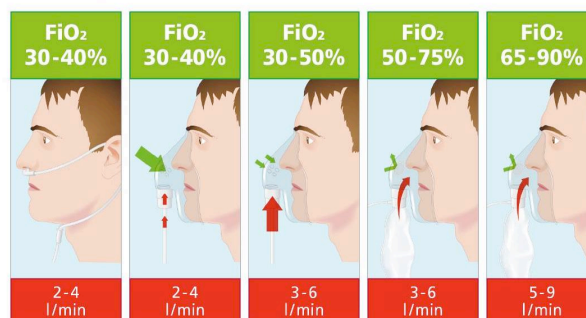
- A conservative fluid strategy expansion should be undertaken as over-hydration seems to worsen outcome

Oxygen therapy

- Maintain oxygen saturation above 90%. When an oxygen saturation monitor is not available, provide oxygen if respiratory rate is elevated at rates indicated below:

Age	Respiratory rate
<2 months	≥60/minute
2–11 months	≥50/minute
1–5 years	≥40/minute
>5–12 years	≥30/minute
≥13 years	≥20/minute

- Consider to increase to 92–95% in some clinical situations, for example during pregnancy.
- When treating severe hypoxaemia with an oxygen mask, the mask should be equipped with an oxygen reservoir bag and high-flow of oxygen should be used (up to 10-15 l/min in adults) to ensure sufficiently high inspired oxygen concentration.



Advanced respiratory support

- Lung protective mechanical ventilation strategies should be used.
- Early intubation seems to improve outcomes; current experience of intensive therapy unit staff suggests using noninvasive ventilation as an interim measure may worsen outcomes.
- Standard ventilation strategies (high positive end-expiratory pressure [PEEP], High Frequency Oscillation [HFO]) may cause alveolar over-distension or worsen oxygenation/haemodynamics.
- High sedative therapy may be needed to suppress ventilatory drive, anxiety, and delirium – requirement for neuromuscular blockade is common.