Clinical Guidance for 2009 H1N1 Influenza and Seasonal Influenza

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Outline

- Clinical assessment
- Diagnostic testing
- Antiviral medications
  - Treatment
  - Prophylaxis
  - Resistance
- Other treatment and patient management issues
Clinical Assessment

Cannot distinguish between seasonal influenza, 2009 H1N1 influenza and infections with other respiratory viruses based solely on patient’s clinical presentation.

Initial patient management decisions need to be based on:

- Current levels of seasonal and novel influenza activity in the community
- Results of any influenza diagnostic tests, if performed
- Severity of patient’s illness
- Presence of any underlying conditions (including young/old age and pregnancy) that places the patient at higher risk for complications
Consider Influenza

Consider 2009 H1N1 or seasonal influenza in the differential diagnosis of any person presenting with an unexplained acute febrile respiratory illness, including:

- Influenza-like illness (ILI) – fever greater than or equal to 100F with cough or sore throat
- Pneumonia and fever
- Acute respiratory distress syndrome and fever (ARDS)
- Respiratory distress and fever

May be atypical presentations, such as presenting without a fever
Rapid Influenza Diagnostic Tests (RIDTs)

- Also called rapid antigen testing or EIA testing
- Can provide results within 30 minutes or less
- May provide some information to guide initial clinical decisions
- Cannot distinguish subtypes

RIDTs can either:

- Detect and distinguish between influenza A and B viruses,
- Detect both influenza A and B viruses but not distinguish between them, or
- Detect only influenza A viruses
RIDTs: Sensitivity and Specificity

- Low to moderate sensitivity (range 10-70%) for 2009 H1N1 influenza virus compared to culture or PCR
- High specificity (>95%)
- False negatives occur - A negative rapid result does not rule out influenza virus infection
- If clinical suspicion of influenza is high in a patient who tests negative by RIDT (or if RIDT is not offered), early empiric treatment should be administered, if treatment is appropriate
Direct Immunofluorescence Assays (DFAs)

- Widely available
- Variable sensitivity (range 47-93%) for 2009 H1N1 virus
- High specificity >= 96%
- DFAs detect and distinguish between influenza A and B viruses but do not distinguish among different influenza A subtypes
- Similar to RIDTs, a negative DFA test does not rule out influenza virus infection
Nucleic Acid Amplification Tests

- Includes rRT-PCR (real-time reverse transcriptase polymerase chain reaction)
- Most sensitive and specific of the influenza diagnostic tests, but false negatives can still occur
- Available through commercial and hospital diagnostic laboratories
- Results are usually not immediately available to guide clinical decisions
- Not all assays can differentiate 2009 H1N1 influenza virus from other influenza A viruses
2009 H1N1 Influenza Testing – Private Labs

- Requires specific PCR testing

- Available at several commercial and hospital labs approved by the NYSDOH Clinical Laboratory Evaluation Program (CLEP)
2009 H1N1 Influenza Testing – Public Health Labs

- 2009 H1N1 testing also conducted at public health laboratories (Wadsworth Center and selected county health departments)

- Focus of public health testing for the 2009-2010 influenza season will be on surveillance

- Will not be routinely available to providers and facilities for primary testing (will be available for special circumstances on a case-by-case basis e.g., antiviral susceptibility testing)
Diagnostic Testing in Patients with Suspected Influenza

- *Patients hospitalized with severe symptoms* – providers should consider commercially available influenza testing (rapid tests, DFA, IFA, PCR)

- *High-risk patients with milder symptoms* – may also consider commercial testing

- *Patients with milder symptoms who are not at high-risk* – influenza testing *usually not indicated* as results will not influence treatment decisions
Why Test for Influenza?

Test *if* it will influence clinical management:

- Clarify an unclear or unusual clinical presentation
- Impact decisions about other diagnostic testing, especially in a patient with severe symptoms
- Reinforce antiviral treatment decisions and infection control practices
- Reinforce antiviral prophylaxis decisions, especially in sensitive situations
- *May* guide selection of antivirals (e.g., + influenza B RIDT)
- Impact antibiotic treatment decisions

Test as needed/requested for public health surveillance
Influenza Antiviral Medications

- Two classes
  - Adamantanes
    - Rimatadine and amantadine
  - Neuraminidase inhibitors
    - Oseltamivir and zanamivir

- Used for both prevention and for treatment
Adamantanes

- **Amantadine**
  - Common dose-related minor CNS effects (e.g., insomnia); less common severe CNS effects (psychosis, seizure); GI effects (anorexia, nausea)
  - Adjust dose for decreased renal function

- **Rimantadine**
  - Approved by the FDA for treatment among adults, although some specialists use in children
  - CNS effects less common; GI effects
  - Adjust dose for decreased renal function
Oseltamivir (Tamiflu)

Available as a capsule or suspension administered by mouth

Approved in the U.S. for treatment or prevention of influenza in persons aged ≥1 year
- Emergency Use Authorization (EUA) for children <1 year
- Treatment: twice a day for 5 days
- Prevention: once a day for 10 days after exposure

Pediatric dosage depends on weight and age

Side effects: nausea, vomiting in some persons

Reports of delirium in pediatric patients (adolescents, most reports from Japan). Warning added to label in 2007

Adjust dose for decreased renal function
Zanamivir (Relenza)

- Orally inhaled powder – administered by mouth via special device

- Approved in the U.S. for
  - Treatment of influenza (aged ≥7 years)
  - Prevention of influenza (aged ≥5 years)

- Treatment dosage: two puffs in the morning and two at night for 5 days (5 days)

- Prevention dosage: 2 puffs once a day (typically for 10 days after last exposure)

- Side effects
  - Wheezing, and breathing problems

- Not recommended for persons with chronic respiratory disease
Antiviral Treatment - Indications

Recommended for:

- Hospitalized patients with suspected or confirmed influenza
- Patients with suspected or confirmed influenza who are severely ill or showing evidence of rapid clinical deterioration (regardless of previous health or age)

Should be considered for:

- Outpatients who are at higher risk for influenza complications (*next slide*)
- Clinical judgment should be used in deciding whether outpatients with risk factors require treatment
Conditions that Place People at High-Risk for Flu Complications

- Children <5 years old but esp. children <2 years old
- Persons with underlying medical conditions:
  - Chronic lung disease, including asthma
  - Chronic heart, kidney, or liver disease
  - Neurologic or neuromuscular disorders (e.g., cognitive dysfunction, spinal cord injuries, seizure disorders)
  - Metabolic disorders, including diabetes
  - Hematologic disorders
  - Immunosuppression
- Pregnant women
- Persons <19 yo on long-term aspirin therapy
- Adults ≥65 years old
Young Children – Revised Antiviral Recommendations

Children younger than 2 years old
- Hospitalization rate 2.5 times higher than the rates for children 2-4 years old
- “Generally recommended” for antiviral treatment

Children 2 – 4 years old
- More likely to require hospitalizations or urgent medical care for influenza than older children but risk is much lower than the risk for children less than 2 years old
- “Do not necessarily require antiviral treatment” if there is not a high risk condition and illness is not severe
- Providers should use clinical judgment
Antiviral Treatment - Timing

- Treatment should be started as early as possible and should **not** await laboratory confirmation.

- Treatment after 48 hours may have little benefit.
  - Exception: Those severely ill, high-risk conditions, pregnancy.

Steps to reduce delays in treatment:
- Inform high risk persons of signs of influenza and need for early treatment.
- Ensure rapid access to telephone consultation and clinical evaluation.
- Consider empiric treatment based on telephone contact if hospitalization not indicated.
Antiviral Treatment – Duration and Dosage

- Duration of treatment is 5 days
  - Hospitalized patients with severe illness might require longer treatment courses

- Dosage is same for seasonal and 2009 H1N1 influenza
  - Some experts recommend increased doses for some severely ill patients, but no data on effectiveness
Patients with Milder Illness

- Treatment generally not recommended for persons who are not at high risk or do not have severe illness

- Do **not** advise patients to go to the ED

- Office visits may not be necessary
  - Screen by phone
  - Prescribe antiviral medications (if indicated)
  - Provide symptomatic treatment recommendations
  - Advise to call if symptoms worsen
  - Advise to stay home until 24 hours after fever ends
Choice of Antiviral Medication

Providers need to review regional and state virus surveillance data weekly during the influenza season to determine which types (influenza A or B) and subtypes of influenza A viruses (2009 H1N1, seasonal H1N1, seasonal H3N2) are circulating in the area.

Surveillance information posted on Health Commerce System and NYSDOH web site.

Surveillance data, in conjunction with any rapid testing results, will help guide the choice of empiric treatment or prophylaxis.
### Expected Antiviral Resistance Patterns
#### United States
#### 2009-2010 Influenza Season

<table>
<thead>
<tr>
<th>Virus</th>
<th>Oseltamivir</th>
<th>Zanamivir</th>
<th>Adamantanes</th>
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</thead>
<tbody>
<tr>
<td>2009 H1N1</td>
<td>Sensitive*</td>
<td>Sensitive</td>
<td>Resistant</td>
</tr>
<tr>
<td>Seasonal H1N1</td>
<td>Resistant</td>
<td>Sensitive</td>
<td>Sensitive</td>
</tr>
<tr>
<td>Seasonal H3N2</td>
<td>Sensitive</td>
<td>Sensitive</td>
<td>Resistant</td>
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<tr>
<td>Seasonal B</td>
<td>Sensitive</td>
<td>Sensitive</td>
<td>Resistant</td>
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*Sporadic cases of oseltamivir-resistant novel H1N1 have been reported. Reports are rare and CDC continues to recommend oseltamivir for treatment and prophylaxis of novel H1N1.*
Choice of Antiviral Medication – Positive RIDT Results

Positive for influenza B: treat with oseltamivir or zanamivir (no preference)

Positive for influenza A: could be 2009 H1N1, or seasonal H1N1, or seasonal H3N2

- Base treatment on surveillance data
- If 2009 H1N1 or seasonal H3N2 likely, treat with oseltamivir or zanamivir
- If seasonal H1N1 is also circulating, treat with zanamivir OR combination oseltamivir and rimantidine (or use amantadine instead of rimantadine but more adverse effects)
Choice of Antiviral Medication – RIDT Negative or Not Done

- Cannot rule out influenza

- Use clinical symptoms, severity, and underlying disease to decide if treatment is appropriate

- Base choice of antiviral on surveillance data
  - If 2009 H1N1, seasonal H3N2 or influenza B likely, treat with oseltamivir or zanamivir
  - If seasonal H1N1 is also circulating, treat with zanamivir OR combination oseltamivir and rimantadine (or use amantadine instead of rimantadine but more adverse effects)
Antiviral Post-Exposure Prophylaxis (PEP)

- Can be considered for **high-risk persons** who had **close contact** with a person with influenza
  - Contact during ill person’s infectious period (defined as 1 day prior to onset until 24 after fever ends)
- Initiate PEP as soon as possible
  - Generally not recommended if more than 48 hours after last contact with an infectious person
- Duration: 10 days following last exposure
- Alternative to PEP: emphasis on early treatment
Choice of Antiviral Medication – Post-Exposure Prophylaxis

Persons who are candidates for post-exposure chemoprophylaxis should be provided with medications most likely to be effective against the influenza strain that is the cause of the close contact’s illness, if known.

Similar considerations as for treatment:

- Providers should be aware of regional and state surveillance data
- Base choice on antiviral susceptibility pattern
PEP and Outbreak Control

- Important infection control measure in long-term care facilities for seasonal influenza

- Can also be considered in other closed settings where persons at higher risk are housed

- Other settings (e.g., schools, camps, workplaces) – not recommended to offer PEP to all persons potentially exposed
  - Can consider PEP for those persons at high risk
  - Educate healthy persons about signs/symptoms of flu and to seek medical care if symptoms are severe
Other Treatment Considerations

- **Fevers in pregnant women** – Treat promptly with acetaminophen because maternal hyperthermia has been associated with various adverse fetal and neonatal outcomes.

- **Bacterial community-acquired pneumonia** – Influenza predisposes individuals to secondary bacterial infections. Consider possibility of co-infection and treat accordingly with antibiotics.
Pediatric Considerations

- **Aspirin or aspirin-containing products** – (e.g., bismuth subsalicylate – Pepto Bismol) should not be administered to any confirmed or suspected ill case of influenza aged 18 years old and younger due to risk of Reye syndrome.

- **Over-the-counter (OTC) cold medications** – children younger than 4 years of age should not be given OTC medications without first speaking with a health care provider.
Other Patient Management Issues

- All medical facilities and offices should strictly adhere to infection control recommendations for influenza.

- Patients, especially those who are at high risk for influenza complications, should be vaccinated with seasonal influenza vaccine as soon as it is available.

- Patients should be vaccinated with 2009 H1N1 vaccine according to the priority groups and recommendations established by the Centers for Disease Control’s (CDC) Advisory Committee on Immunization Practices (ACIP).

- Patients who have existing indications for pneumococcal vaccination should be vaccinated according to current ACIP recommendations.
Other Things to Do

Educate your patients
- How to reduce their risk of influenza
- How to care for someone who is ill at home
- Stay home when sick (until 24 hours after fever resolves)
- When to call their health care provider

Make a plan for your office / facility
- Communications / Staff education
- Triage
- Surge capacity and employee absenteeism
- Occupational health / employee vaccination
- Supplies

Stay informed - check websites frequently
Summary of Key Points for Clinical Management

- Review regularly regional and state influenza activity
- Initiate early, empiric treatment for persons with severe illness and persons with high-risk conditions
- Understand limitations of diagnostic testing
- Advise people with mild illness NOT to go to the ED
- For exposed high-risk individuals, consider chemoprophylaxis or counsel patient on early treatment (if symptoms develop)