

Clinical Guidance for Novel H1N1 Influenza and Seasonal Influenza

Healthcare Briefings

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Outline

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

Clinical Assessment

Clinical Assessment

- Cannot distinguish between seasonal influenza, novel 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 novel 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

Diagnostic Testing

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

Sensitivity of RIDTs

- Low to moderate sensitivity for both seasonal and novel influenza compared to culture or PCR
- 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 (e.g., patient has severe symptoms or is at high risk for complications)

Other Influenza Diagnostic Tests

- Immunofluorescence (DFA or IFA)
- PCR
- Culture
- All are more sensitive than rapid tests
- Usually only available through commercial diagnostic laboratories
- Results are usually not immediately available to guide clinical decisions

Novel Influenza A (H1N1) Testing – Private Labs

- Requires PCR testing
- Available at selected commercial and hospital labs approved by the NYSDOH Clinical Evaluation Laboratory Program (CLEP)
- Focus Laboratories (a reference lab for Quest) is currently the only commercial lab approved by CLEP to conduct novel H1N1 testing on NYS residents

Novel Influenza A (H1N1) Testing – Public Health Labs

- Novel 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

Diagnostic Testing in Patients with Suspected Influenza

- *Patients hospitalized with severe symptoms – providers may 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

Antiviral Medications, Treatment and Prophylaxis

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 exposure)
- Side effects
 - Wheezing, and breathing problems
- Not recommended for persons with chronic respiratory disease



Antiviral Treatment - Indications

- Recommended for
 - Patients hospitalized with suspected or confirmed influenza (severe illness)
 - Patients with mild or severe influenza who are at high risk for influenza complications
- Treatment should be started empirically and should not await laboratory confirmation

Conditions that Place People at High-Risk for Flu Complications

- Children <5 years
- Persons with underlying medical conditions:
 - Chronic lung disease, including asthma
 - Chronic heart, kidney, or liver disease
 - Neurologic or neuromuscular disorders
 - Metabolic disorders, including diabetes
 - Hematologic disorders
 - Immunosuppression
- Pregnant women
- Persons <19 yo on long-term aspirin therapy
- Adults ≥65 years

Antiviral Treatment - Timing

- Treatment should be started as early as possible
- 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
 - Consider prescriptions for selected patients that can be filled after telephone consultation

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 novel 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 (novel H1N1, seasonal H1N1, seasonal H3N2) are circulating in the area
- Surveillance information posted on Health Commerce System
- 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

Virus	Oseltamivir	Zanamivir	Adamantanes
Novel H1N1	Sensitive*	Sensitive	Resistant
Seasonal H1N1	Resistant	Sensitive	Sensitive
Seasonal H3N2	Sensitive	Sensitive	Resistant
Seasonal B	Sensitive	Sensitive	Resistant

*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 novel H1N1, or seasonal H1N1, or seasonal H3N2
 - Base treatment on surveillance data
 - If novel 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 novel 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 Issues

- 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.

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 novel 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 regional and state influenza activity on a regular basis
- Initiate early, empiric treatment for persons with severe illness and/or persons with high risk conditions
- Understand limitations of diagnostic testing
- Advise people with mild illness NOT to go to the ED
- Can consider prophylaxis for exposed high-risk individuals