

# **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  $\geq 96\%$
- 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  $\geq 1$  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  $\geq 7$  years)
  - Prevention of influenza (aged  $\geq 5$  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

Virus	Oseltamivir	Zanamivir	Adamantanes
2009 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 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 rimantidine 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)