Pediatric Influenza:
what you need to know about testing, treatment & prophylaxis

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Buncombe County Dept. of Health & Human Services
January 8, 2014
Learning Objectives

• Understand the basic epidemiology of pediatric influenza and influenza-associated pediatric deaths
• Identify signs/symptoms of pediatric influenza
• Understand the use and limitations of influenza testing
• Understand the use of antiviral medications for the treatment and prevention of pediatric influenza
UPDATE ON CURRENT FLU SEASON

Make Small CHOICES, expect BIG things.
Influenza-Like Illness Surveillance in North Carolina, 2013-2014
Hospital Emergency Department Visits (NC DETECT) and
Outpatient Provider Visits (ILINet)

% ILI

Week Ending Date

2013-14 ED NC DETECT
2013-14 ILINet

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Courtesy of Anita Valiani, NC DHHS
INFLUENZA SURVEILLANCE, NC 2011-2013
Influenza-Like Illness in ILINet Outpatient Visits, as of December 28, 2013

Week Ending Date

%ILI

Note: Week ending displayed is for 2013-2014 influenza season. Flu seasons for previous years may have different week ending dates, but these only vary by a few days.

Courtesy of Anita Valiani, NC DHHS
Number of Influenza Tests Ordered and Number of Positive Results (A and B) by Week

For Mission Health System

Make Small CHOICES, expect BIG things.

Courtesy of Dr. David Buhner, PHE
PHE Surveillance: Positive Respiratory Virus Test Results by Week

Data source: NC DETECT

Make Small CHOICES, expect BIG things.

Courtesy of Anita Valiani, NC DHHS
Influenza Positive Tests Reported to CDC, National Summary, 2013-14 Season,
weeks ending Dec 08, 2013 - Dec 28, 2013
Reported by: U.S. WHO/NREVSS Collaborating Laboratories

Make Small CHOICES, expect BIG things.
Influenza Positive Tests Reported by the N.C. State Laboratory of Public Health (SLPH) by Week Ending Date

#Positive Specimens

Week Ending Date

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<td>25</td>
<td>30</td>
<td>25</td>
<td>20</td>
<td>15</td>
<td>10</td>
<td>5</td>
<td>2</td>
<td>1</td>
<td>0</td>
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</tr>
</tbody>
</table>

% Positive†

† Percent of submitted specimens for any influenza

Courtesy of Anita Valiani, NC DHHS

Make Small CHOICES, expect BIG things.
EPIDEMIOLOGY OF PEDIATRIC INFLUENZA
The Toll of Pediatric Influenza

• Average # of children < 5 years of age hospitalized each year for influenza complications = 20,000

• Influenza-associated death
  – Death resulting from a clinically compatible illness confirmed to be influenza through testing
  – No period of complete recovery between illness & death

*Physicians must report this to local health dept.*
Season | Total Deaths | Influenza A | Influenza B | Influenza A/B Not Distinguished | Influenza A & B
--- | --- | --- | --- | --- | ---
2009-10 | 282 | 279 | 2 | 1 | 0
2010-11 | 123 | 77 | 46 | 0 | 0
2011-12 | 35 | 25 | 9 | 1 | 0
2012-13 | 171 | 80 | 88 | 1 | 2
<table>
<thead>
<tr>
<th>Season</th>
<th>Total Deaths</th>
<th>Influenza A</th>
<th>Influenza B</th>
<th>Influenza A &amp; B</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013-14*</td>
<td>6</td>
<td>5</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

*As of Dec. 28, 2013; None in NC

http://gis.cdc.gov/GRASP/Fluview/PedFluDeath.html
Laboratory Confirmed Influenza-Associated Deaths Reported in North Carolina, by Age Group*

*As of Dec. 28, 2013

No. of Reported Deaths

<table>
<thead>
<tr>
<th>Age Group (Years)</th>
<th>0-4</th>
<th>5-17</th>
<th>18-24</th>
<th>25-49</th>
<th>50-64</th>
<th>65+</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>5</td>
<td>1</td>
</tr>
</tbody>
</table>

Courtesy of Anita Valiani, NC DHHS

Make Small CHOICES, expect BIG things.
Characteristics of Influenza-Associated Pediatric Deaths
Age Group Breakdown by Season

- 0-5 mo
- 6-23 mo
- 2-4 yr
- 5-11 yr
- 12-17 yr
- insufficient Data

Make Small CHOICES, expect BIG things.
http://gis.cdc.gov/GRASP/Fluview/Ped FluDeath.html

Make Small CHOICES, expect BIG things.
Who is at higher risk for complications from influenza?

- Children < 5 yo, but especially <2 yo
- Chronic lung diseases (e.g., asthma, CF)
- Chronic heart diseases (except HTN only)
- Chronic kidney disorders
- Chronic liver disorders
- Chronic blood disorders (e.g., sickle cell disease)
- Chronic metabolic disorders (e.g., diabetes, inherited metabolic disorders)
- Persons w/ immunosuppression (e.g., HIV, cancer, chronic steroids)
- Persons who are morbidly obese
- Persons < 19 yo on long-term aspirin therapy
- American Indians/Alaskan Natives
- Pregnant or post-partum (within 2 wks after delivery)
- Residents of chronic-care facilities

Make Small CHOICES, expect BIG things.
Characteristics of Influenza-Associated Pediatric Deaths
Percent of Deaths with Specified Medical Condition

- Neurologic Disorder
- Chromosomal Abnormality / Genetic Syndrome
- Cardiac Disease
- Immune Suppression
- Endocrine Disorder
- Mitochondrial Disorder
- Renal Disease
- Obesity
- Pregnant
- Other
- Pulmonary Disease
- Insufficient Data

http://gis.cdc.gov/GRASP/Fluview/PedFluDeath.html

Make Small CHOICES, expect BIG things.
Signs/Symptoms of Influenza

- **Abrupt** onset of
  - **Fever** (commonly 100 to 102°F lasting 3-4 days)
  - **Chills**
  - **Myalgia** (often severe)
  - **Headache**
  - **Fatigue/weakness** (often extreme exhaustion)
  - **Non-productive cough**
  - **Sore throat**
  - **Sneezing and/or nasal congestion**
  - **Nausea, vomiting, otitis media** also seen in children
  - **Young children** less likely to have typical influenza symptoms (like fever & cough)
Basic Epidemiology of Influenza

• **Incubation period:** 1-4 days

• **Contagious period:**
  - Adults from 1 day before symptoms start and for 5-10 days after illness begins
  - Children may be contagious several days before illness starts and for 10+ days after illness begins

• **Illness course:** 3-7 days if uncomplicated
  - Cough, malaise can last > 2 wks
Influenza Complications

- Influenza viral pneumonia
- Exacerbation of underlying medical conditions
- Secondary bacterial pneumonia, sinusitis, otitis media
- Co-infections with other viral or bacterial pathogens
- Respiratory failure
- Death
How distinguish flu from other respiratory pathogens?

- Difficult based only on signs/symptoms
- PPV of acute onset of cough & fever in areas with confirmed influenza virus circulation for lab-confirmed influenza infection

<table>
<thead>
<tr>
<th>Population</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generally healthy older adolescents &amp; adults</td>
<td>79-88%</td>
</tr>
<tr>
<td>Children 5-12 years old</td>
<td>71-83%</td>
</tr>
<tr>
<td>Children &lt; 5 years old</td>
<td>64%</td>
</tr>
</tbody>
</table>

From [http://www.cdc.gov/flu/professionals/acip/clinical.htm](http://www.cdc.gov/flu/professionals/acip/clinical.htm)
Bottom-line for who to suspect of having influenza

• The diagnosis of influenza illness should be considered in any patient with respiratory symptoms OR fever during flu season.

• Influenza surveillance information and diagnostic testing can help clinical judgment.
TESTING FOR INFLUENZA
Diagnostic Testing for Flu

1. Tests do **NOT** need to be performed on all patients with s/sx of flu
   - Once flu activity documented in community (especially during periods of peak activity), a clinical dx can be made for outpatients
   - Tests are most useful when they are likely to give results that will help with dx and tx decisions

2. Samples should be collected within the first 4 days of illness

3. Follow manufacturer’s instructions for testing

Make Small CHOICES, expect BIG things.
Figure 1: Guide for considering influenza virus diagnostic tests for individual patients when influenza viruses are circulating in the community

Does the patient have clinical signs and symptoms compatible with influenza?

YES

Will the results of influenza virus testing:

- change clinical care of the patient (especially for hospitalized patients and those with high risk conditions)
  or
- influence clinical practice for other patients

*Initiation of antiviral treatment, if clinically indicated, should not be delayed pending results of testing.

YES

Consider influenza virus testing.
(See Table 1 below for review of influenza virus testing methods; and Table 2 below for review of available RIDTs).

NO

Influenza virus testing probably not indicated.

NO

Influenza virus testing probably not indicated.

YES

Interpret influenza test results.
(See Figure 3 below for RIDTs).


Make Small CHOICES, expect BIG things.
## Diagnostic Testing for Influenza

<table>
<thead>
<tr>
<th>Test method</th>
<th>Potential Uses</th>
<th>Test Time</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Viral Culture</strong></td>
<td>Often for surveillance purposes (for virus strain ID, sub-typing, assessment for antiviral resistance, etc.) or confirmatory testing</td>
<td>3-10 days</td>
</tr>
<tr>
<td><img src="image" alt="star" /></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Rapid Influenza Diagnostic Tests</strong></td>
<td>Commonly for outpatient testing; can determine type</td>
<td>&lt; 15 minutes</td>
</tr>
<tr>
<td><strong>RT-PCR</strong></td>
<td>Used in-house at Mission; able to subtype; preferred for those w/exposure to animals/suspected to have novel influenza infection</td>
<td>1-6 hrs <em>(longer if specimen has to be sent to outside lab)</em></td>
</tr>
<tr>
<td><img src="image" alt="star" /></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Immunofluorescence</strong> (Direct or Indirect Antibody Staining)</td>
<td>Used for Mission’s in-house “Viral Respiratory Panel” which tests for Influenza A &amp; B, RSV, adenovirus, parainfluenzae types 1-3</td>
<td>1-4 hrs</td>
</tr>
</tbody>
</table>
Rapid Influenza Diagnostic Tests (RIDTs)

• Immunoassays that ID influenza A and B antigens in respiratory specimen
  – Some can distinguish between types A & B
• Qualitative (+/-)
• Results within 15 minutes
• Sensitivity 40-70%
• Specificity >90%
Use of RIDTs in Clinical Decision-making

False negative results more common than false positive results, especially during peak flu activity.

- Negative results do NOT rule out influenza infection in someone with symptoms suggestive of flu.
- Do NOT withhold antiviral tx from patients with suspected flu, even if negative RIDT.

False + results can also occur, especially during times when flu activity is low.
Factors That Influence RIDT Accuracy

1. Clinical s/sx of influenza
2. Prevalence of influenza activity in population tested
3. Time from illness onset to specimen collection
4. Type of specimen collected
5. Accuracy of test vs. “gold standard”
   • Sensitivity & specificity
Figure 3: Algorithm to assist in the interpretation of RIDT results and clinical decision-making during periods when influenza viruses are circulating in the community\(^1\)

**RIDT POSITIVE for one of the following:**
- Influenza A
- Influenza B
- Influenza A and B (A/B)

**RIDT NEGATIVE for one or more of the following:**
- Influenza A
- Influenza B
- Influenza A and B (A/B)

**Interpretation:**
- *Influenza virus infection likely\(^1,2\)*

**Actions:**
- Initiate antiviral treatment for influenza if clinically indicated.
- Consider additional influenza virus testing to confirm RIDT results, for subtyping of influenza A virus, to distinguish between influenza A and B viruses, or for more specific analyses, if indicated.
- Consider additional diagnostic testing for other pathogens and/or empiric antibiotic therapy for bacterial co-infection, if indicated.\(^3\)

**Interpretation:**
- *Cannot rule out Influenza virus infection\(^1,2\)*

**Actions:**
- Use clinical signs, symptoms, history, examination, information on local influenza activity in the community to decide if antiviral treatment is indicated.
- Do not use negative RIDT results exclusively for clinical decision-making, or for public health decisions, including identifying influenza outbreaks, or for decisions on infection control measures.
- Consider additional influenza testing if indicated. Consider additional diagnostic testing and/or empiric antibiotic therapy for bacterial infection if indicated.\(^3\)

When to Consider Further Influenza Testing beyond RIDT

• Negative RIDT when high community flu activity & laboratory-confirmed influenza dx is desired

• + RIDT when low community flu activity & a false + is a possibility

• Recent close exposure to pigs, poultry or other animals & novel influenza A infection is possible
Hospitalized Patients

1. Test for flu if suspect flu
   – Immunofluorescence, RT-PCR or viral culture

2. Start empiric antiviral tx ASAP
   Ø Do NOT wait for test results
   Ø Do NOT stop antiviral tx if negative RIDT

3. Implement infection control measures upon admission
   (again, even if negative RIDT)

4. Consider testing specimens from different respiratory sites (e.g., upper & lower respiratory tract) and/or on > 1 day

Make Small CHOICES, expect BIG things.
ANTIVIRALS FOR TREATMENT & PROPHYLAXIS
## Antivirals Recommended for Treatment & Chemoprophylaxis of Influenza A & B

<table>
<thead>
<tr>
<th>Antiviral</th>
<th>Use</th>
<th>FDA Approved for Ages</th>
<th>Not Recommended for Use in</th>
<th>Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oseltamivir (oral suspension or capsules)</td>
<td>Treatment</td>
<td>≥ 2 wks</td>
<td>n/a</td>
<td>Nausea, vomiting <em>(may be less severe if taken w/ food)</em></td>
</tr>
<tr>
<td></td>
<td>Chemo-prophylaxis</td>
<td>≥ 1 yr</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>Zanamivir (inhaled powder)</td>
<td>Treatment</td>
<td>≥ 7 yrs</td>
<td>People w/ underlying respiratory disease (e.g., asthma)</td>
<td>Diarrhea, nausea, sinusitis, nasal s/sxs, cough, headache, dizziness, ENT infections; <strong>Allergic reactions:</strong> oropharyngeal or facial edema</td>
</tr>
<tr>
<td></td>
<td>Chemo-prophylaxis</td>
<td>≥ 5 yrs</td>
<td></td>
<td></td>
</tr>
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</table>

When to Give Influenza Antivirals

➢ ASAP for anyone with **suspected or confirmed** influenza who:
  • is hospitalized;
  • has severe, complicated or progressive illness; OR
  • is at higher risk for severe illness/complications

➢ **Ideally** start tx within 48 hrs of illness onset
  • May still be beneficial when started after 48 hours
Antiviral Treatment of Patients NOT at High-Risk

• Antiviral tx can be considered for suspected or confirmed influenza in previously healthy, symptomatic outpatients not at high risk
  – Use clinical judgment
  – If tx can be initiated within 48 hours of illness onset
Key Messages on Treatment with Antivirals

- Focus use on those with severe illness or who are at higher risk for severe disease
- Do NOT wait on test results
- Start ASAP after illness onset
- Do NOT withhold antiviral tx from patients with suspected flu, even if negative RIDT.
- H/o influenza vaccination does NOT rule out influenza infection – give antivirals if indicated
Benefits of Influenza Antiviral Treatment

• Treatment with antivirals may:
  ➢ Shorten duration of fever & other symptoms
  ➢ Reduce risk of complications from flu
  ➢ Shorten duration of hospitalization

• Clinical benefit is greatest when antivirals started within 48 hrs of illness onset
## Recommended Dosage & Duration of TREATMENT for Influenza Antivirals

<table>
<thead>
<tr>
<th>Antiviral</th>
<th>Dose</th>
<th>Duration of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oseltamivir</strong></td>
<td>If &lt; 1 yr old: 3 mg/kg/dose BID (FDA-approved if ≥ 2 wks old; requires a different dispenser than what is co-packaged with medicine)</td>
<td>•Recommended for 5 days.</td>
</tr>
<tr>
<td></td>
<td>If &gt;1 yr old &amp; weigh &lt; 15 kg: 30 mg BID</td>
<td>•Longer treatment courses can be considered for patients who remain severely ill after 5 days of treatment.</td>
</tr>
<tr>
<td></td>
<td>If &gt;1 yr old &amp; weigh &gt; 15-23 kg: 45 mg BID</td>
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<td></td>
<td>If &gt;1 yr old &amp; weigh &gt; 23-40 kg: 60 mg BID</td>
<td></td>
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<tr>
<td></td>
<td>If &gt;1 yr old &amp; weigh &gt; 40 kg: 75 mg BID</td>
<td></td>
</tr>
<tr>
<td><strong>Zanamivir</strong></td>
<td>If ≥ 7 yr old: 10 mg (2 inhalations) BID (Not FDA-approved for use in children younger than 7 years of age)</td>
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</tbody>
</table>

Chemoprophylaxis for Influenza

1. Annual influenza vaccination
2. Antiviral medications
   • 70-90% effective at preventing flu
   • NOT recommended if > 48 hrs since last exposure
   • CDC does NOT recommend widespread or routine use of antivirals for chemoprophylaxis
   • Need to seek medical care if develop s/sxs of influenza

**Alternative = close monitoring/early initiation of antiviral tx**

Make Small CHOICES, expect BIG things.
Recommendations for Antiviral Chemoprophylaxis of Children

• To control outbreaks among high-risk children in institutional settings
• High-risk children who are close contacts of suspected or confirmed cases (regardless of vaccination status)
• High-risk children for whom vaccination is contraindicated or during 2 wks after vaccination (during outbreak)
### Recommended Dosage of Influenza Antivirals for CHEMOPROPHYLAXIS in Children

<table>
<thead>
<tr>
<th>Antiviral</th>
<th>Dose</th>
<th>Duration</th>
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</thead>
<tbody>
<tr>
<td>Oseltamivir</td>
<td>If &lt; 3 months of age, use not recommended unless situation judged critical. (<strong>Not FDA-approved</strong>)</td>
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<tr>
<td></td>
<td>If ≥ 3 months of age &amp; &lt; 1 year old: 3 mg/kg/dose once daily (<strong>Not FDA-approved</strong>)</td>
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<tr>
<td></td>
<td>If ≥ 1 year old &amp; weigh &lt; 15 kg: 30 mg daily</td>
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<td></td>
<td>If ≥ 1 year old &amp; weigh &gt; 15 – 23 kg: 45 mg daily</td>
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<td></td>
<td>If ≥ 1 year old &amp; weigh &gt; 23 – 40 kg: 60 mg daily</td>
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<tr>
<td></td>
<td>If ≥ 1 year old &amp; weigh &gt; 40 kg: 75 mg daily</td>
<td></td>
</tr>
<tr>
<td>Zanamivir</td>
<td>If ≥ 5 years old: 10 mg (2 inhalations) once daily</td>
<td></td>
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<tr>
<td></td>
<td>(Not FDA-approved for use in children younger than 5 years old)</td>
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</tbody>
</table>

- Recommended to be continued until 7 days after last exposure
  (CDC has additional guidance if outbreak in long-term care facility or hospital)

Taken from table at [http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm](http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm)
BE A HERO!

COVER YOUR COUGH
WASH YOUR HANDS
STAY HOME IF YOU’RE SICK
GET A FLU SHOT

TAKE THESE SIMPLE STEPS TO PROTECT YOU AND YOUR FAMILY

A message from BUNCOMBE COUNTY HEALTH & HUMAN SERVICES

Make Small CHOICES, expect BIG things.
Resources

- CDC – Information for Health Professionals
- NC Division of Public Health – Flu info for providers
  - http://www.flu.nc.gov/providers/
  - http://pediatrics.aappublications.org/content/early/2013/08/28/peds.2013-2377
- The Joint Commission – videos demonstrating specimen collection
  - http://www.youtube.com/watch?v=hXohAo1d6tk
- The Joint Commission -- Strategies for Improving Rapid Influenza Testing in Ambulatory Settings (CE available)
- Buncombe County Health and Human Services – flu posters in English/Spanish/Russian
  - http://buncombecounty.org/flu

Make Small CHOICES, expect BIG things.