Influenza
Diagnostic Options: Issues and Concerns
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Overview

- Options for influenza diagnosis
- Impact of flu prevalence on diagnosis
- Use of clinical symptoms in hospitalized children and adults
Diagnostic options

- Rapid tests and clinical symptoms
  - Moderate sensitivity and specificity
  - Differ by season, age, timing, and illness severity
  - Interpretation depends on influenza prevalence
- Culture
  - Old “gold standard”
  - Slow
- RT-PCR
  - High sensitivity and specificity
  - 1.6x culture for influenza (children)*
  - New “gold standard”
  - Potential for rapid turn-around

*Weinberg GA et al JID 2004
Effect of Influenza Prevalence on Predictive Value of Diagnostic Tests

Results from the CDC-Funded New Vaccine Surveillance Network (NVSN)
The New Vaccine Surveillance Network (NVSN)

Population-based ARI Surveillance
140,000 children <5 years
Surveillance Activities

Children <5 years of age
Residents of Surveillance Counties
Acute Respiratory Infection or Fever
Nasal/throat swab
Parental interview/chart review

Inpatient
- Hospitals with >95% of county hospitalizations for children
- Viral culture and RT-PCR
- Incidence of influenza

Outpatient
- Selected ED and outpatient clinics
- PCR only
- Proportion with influenza
Pneumonia and Influenza Mortality for 122 U.S. Cities
Week Ending 05/22/2004
Rapid tests in clinical practice

- 2797 hospitalized children enrolled and tested for influenza by culture & RT-PCR
  - 160 (6%) influenza positive
- 270 children (9.7%) also had a rapid test for influenza performed by hospital lab
- 41/270 (15%) flu+ by culture/RT-PCR

  - Sensitivity 63% (95% CI: 47%-78%)
  - Specificity 97% (95% CI: 94%-99%)

Grijalva et al, CID 2006
Predictive values for Influenza clinical rapid tests
NVSN Outpatient Surveillance 2002 - 2004

Positive Predictive values. 2002-2003 season
Negative Predictive values. 2002-2003 season
Predictive values for Influenza clinical rapid tests
NVSN Outpatient Surveillance 2002 - 2004

Positive Predictive values. 2002-2003 season

Negative Predictive values. 2002-2003 season

Positive Predictive values. 2003-2004 season

Negative Predictive values. 2003-2004 season
Clinical Symptoms in Patients Hospitalized with Influenza
Clinical Symptoms
Hospitalized patients

• Aged <5 years
  - New Vaccine Surveillance Network (CDC)
    • Population based hospital surveillance children in 3 US counties

• Aged 50+
  - NIH (Nashville, TN)
  - MedImmune (Knoxville, TN)
    • 2 hospitals in each county 2006–2007
    • Coverage 30-35% county population
% Discharge Diagnoses in Children <5 years with Confirmed Influenza 2000–2004

<table>
<thead>
<tr>
<th>Discharge Diagnosis</th>
<th>&lt;6 mos (n=79)</th>
<th>6-23 mos (n=49)</th>
<th>2-4 years (n=32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>28</td>
<td>24</td>
<td>34</td>
</tr>
<tr>
<td>Bronchiolitis</td>
<td>25</td>
<td>20</td>
<td>3</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>5</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>Asthma</td>
<td>1</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Seizure</td>
<td>0</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Viral Illness</td>
<td>22</td>
<td>6</td>
<td>28</td>
</tr>
<tr>
<td>Fever/Sepsis</td>
<td>19</td>
<td>10</td>
<td>3</td>
</tr>
</tbody>
</table>

Rapid antigen testing
Adults Hospitalized during Influenza Season

<table>
<thead>
<tr>
<th></th>
<th>Knox (N=367)</th>
<th>Davidson (N=190)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid Flu test performed</td>
<td>78 (21%)</td>
<td>46 (24%)</td>
</tr>
</tbody>
</table>
Conclusion 1

- Operating characteristics of clinical diagnosis and rapid tests
  - Vary by age, time of presentation, and possibly severity
  - May need “recalibration” each season
  - Very dependent on disease prevalence
    - Difficult to determine in real time
Conclusion 2

- Use of tests with moderate sensitivity and specificity in epidemic or pandemic requires
  - Rapid determination of “test(s)” of choice and operating characteristics by age group
  - Real-time estimates of disease prevalence
  - Thresholds for treatment/isolation/other measures
Conclusion 3

• Widespread availability of rapid tests with high sensitivity and specificity would greatly enhance clinical and public health decision-making