Etiologic Investigation of Sporadic Cases of Parotitis

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Disclaimer: The findings and conclusions in this presentation are those of the author and do not necessarily represent the views of the Centers for Disease Control and Prevention
Overview

• Background and epidemiology of mumps
• Challenges with sporadic cases of parotitis
• Project objectives
• Methods
• Findings
• Assessing a mumps diagnosis
• Summary and conclusions
Mumps

• Acute, viral illness that can present with
  – **Parotitis** (60-70%)
  – Other salivary gland swelling
  – Orchitis (in post-pubertal males)
  – Aseptic meningitis
  – Non-specific respiratory symptoms
  – Asymptomatic (~30%)

• **Transmission**
  – Respiratory droplet
  – Direct contact (saliva)

• **Only known cause of epidemic parotitis**
Mumps Vaccine

• The United States uses the Jeryl Lynn mumps vaccine strain

• Effectiveness
  – 1 dose ~78% (49-92%)
  – 2 doses ~88% (66-95%)

• Coverage during 2011 in the U.S.
  – 1 dose, 19-35 month-olds: ~92%
  – 2 doses, 13-17 year-olds: ~91%

1 MMWR 2013; 62(RR4):1-34
2 MMWR 2012; 61:689-96
3 MMWR 2012; 61:671-7
Mumps in the United States, 1967-2013

Reported Number of Mumps Cases

1967 Mumps VaccineLicensed
1977 1st Dose ACIP Recommendation
1989 2nd Dose ACIP Recommendation
1986-91 Resurgence
2006 2009-10 Outbreak Outbreak

Year
Laboratory Criteria for Mumps Diagnosis*

• Detection of mumps IgM antibody, or

• Demonstration of specific mumps antibody response in the absence of recent vaccination: either a 4-fold increase in mumps IgG titer as measured by a quantitative assay or a seroconversion from negative to positive using a serologic assay of paired acute and convalescent serum specimens, or

• Detection of mumps RNA (using RT-PCR), or

• Isolation of mumps virus in culture

*CSTE Position Statement 09-ID-50
Recent Laboratory Positivity Rates

- **2006 Midwest U.S. outbreak** – low proportion of cases were able to be laboratory-confirmed using IgM, RT-PCR, and viral isolation
  - IgM: 6/47 (13%)
  - RT-PCR and/or viral isolation: 12/39 (31%)

- **Fall 2006 UVA outbreak**
  - IgM: 6/47 (13%)
  - RT-PCR and/or viral isolation: 12/39 (31%)

- **2009-10 Northeast U.S. outbreak**
  - IgM: 550/1563 (35%)
  - RT-PCR: 373/530 (68%)
  - Viral isolation: 283/443 (64%)

- **2009-10 Guam outbreak**
  - IgM: 60/309 (19%)
  - RT-PCR: 28/34 (82%)
  - Viral isolation: 14/34 (41%)

Previously Infected or Vaccinated Individuals

• May not mount an IgM response
• May not have a 4-fold rise in IgG titer
• May already be IgG-positive on initial blood draw
• May have a viral load below the assay detection level

➤ Cannot rule-out a suspected mumps case based only on a negative lab test result
“Outbreaks” of Mumps-like Illness

- **Maine (throughout the state)**
  - September 2007 – February 2008
  - 102 cases, 97 had parotitis
  - Very few were epi-linked
  - 29/83 (35%) were IgM+
  - 1*/61 (2%) was RT-PCR+

- **Nevada (throughout greater Las Vegas)**
  - December 2007 – May 2008
  - 35 cases, all had parotitis or jaw swelling
  - 2 were epi-linked
  - 1/22 (5%) was IgM+
  - 0/7 were RT-PCR+

*Confirmed exposure to mumps in Africa*
Challenges with Sporadic Cases of Parotitis

- Are sporadic cases of parotitis really mumps?
- Cannot rule-out a suspected mumps case based solely on a negative lab result, especially in a previously vaccinated individual
- Non-mumps causes of parotitis exist on a non-epidemic scale
- Mumps cases require a large amount of resources to investigate and respond to
Objectives

- Assist state health departments in determining the etiology of sporadic cases of parotitis (suspected mumps)
- End fewer investigations of sporadic cases of parotitis with ambiguous findings
- Characterize the profile of viruses and epidemiologic features associated with sporadic cases of parotitis
Surveillance Population

• Sites
  – Arizona, California, Kansas, Michigan, North Carolina, Philadelphia, Tennessee, and Washington State

• Duration
  – 2009-2011
Case-patient Inclusion Criteria

• Must have parotitis

• Must be sporadic
  – Not epi-linked to 2 or more other cases of parotitis
  – Not epi-linked to a laboratory-confirmed mumps case
  – No recent travel to an area known to be experiencing high mumps activity
Procedures – State/Local

• Standard mumps case investigation performed
  – Relevant information collected
    ▪ Demographic
    ▪ Clinical
    ▪ Epidemiologic
    ▪ Vaccination
  – Specimens collected
    ▪ Serum
    ▪ Buccal swab
    ▪ Oropharyngeal swab
Procedures – CDC

• Nucleic acids extracted from swab specimens
• Presence of viral nucleic acids was tested for using PCR methods
  – Mumps virus (MuV)
  – Enteroviruses (EV), including human parechovirus (HPeV)
  – Human herpesvirus 6A & 6B (HHV-6A & HHV-6B)
  – Epstein-Barr virus (EBV)
  – Human parainfluenza virus 1-3 (HPIV 1-3)
  – Adenoviruses (AdV)
  – Human bocavirus (HBoV)
Findings*

- 101 patients
- Median patient age: 19 years (range: 0.3 – 76 years)
- Sex: 46% female
- Vaccination documented for 65/101 patients
  - 0 Doses: 18%
  - 1 Dose: 20%
  - 2 Doses: 62%
- Number of patients from each jurisdiction
  - AZ (6), CA (4), KS (13), MI (33), NC (15), PHL (10), TN (1), WA (19)

*Barskey et al. J Infect Dis in press.*
## Viruses Detected

<table>
<thead>
<tr>
<th>Virus</th>
<th>Number positive (n)</th>
<th>Percent positive (n/101)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epstein-Barr virus (EBV)</td>
<td>23</td>
<td>23%</td>
</tr>
<tr>
<td>Human herpesvirus 6B (HHV-6B)</td>
<td>10</td>
<td>10%</td>
</tr>
<tr>
<td>Human parainfluenza virus 2 (HPIV-2)</td>
<td>3</td>
<td>3%</td>
</tr>
<tr>
<td>Human parainfluenza virus 3 (HPIV-3)</td>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td>Human bocavirus (HBoV)</td>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td>Mumps (MuV)</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Enteroviruses (EV)</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Human parechovirus (HPeV)</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Human herpesvirus 6A (HHV-6A)</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Human parainfluenza virus 1 (HPIV-1)</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Adenoviruses (AdV)</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>38</strong></td>
<td><strong>38%</strong></td>
</tr>
</tbody>
</table>
Viral Detection by Age Group

No. of Cases

Age Group (years)

0-4 5-9 10-17 18-24 25-39 40+

EBV HHV-6B HPIV-2 HPIV-3 HBoV
Figure 2: Viral Detection by Onset Month

- **EBV**
- **HHV-6B**
- **HPIV-2**
- **HPIV-3**
- **HBoV**
Timing of Swab Collection

Figure 1

- No virus detected
- Virus detected

No. of Cases

Days Post Parotitis Onset

0 1 2 3 4 5 6 7 8 9 10 11 12
# Mumps IgM Results

<table>
<thead>
<tr>
<th>Assay</th>
<th>No Virus Detected</th>
<th>Virus Detected</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number Mumps IgM Positive (%)</td>
<td>Number Mumps IgM Positive (%)</td>
<td>Number Mumps IgM Positive (%)</td>
</tr>
<tr>
<td>EIA</td>
<td>3/27 (11%)</td>
<td>3/17 (18%)</td>
<td>6/44 (14%)</td>
</tr>
<tr>
<td>IFA</td>
<td>1/2 (50%)</td>
<td>2/3 (67%)</td>
<td>3/5 (60%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>2/15 (13%)</td>
<td>1/6 (17%)</td>
<td>3/21 (14%)</td>
</tr>
<tr>
<td>Total</td>
<td>6/44 (14%)</td>
<td>6/26 (23%)</td>
<td>12/70 (17%)</td>
</tr>
</tbody>
</table>
### Mumps Vaccination History of Patients*

<table>
<thead>
<tr>
<th>Doses</th>
<th>No Virus Detected n = 35</th>
<th>Virus Detected n = 30</th>
<th>Total n = 65</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>0</td>
<td>6 (17%)</td>
<td>6 (20%)</td>
<td>12 (18%)</td>
</tr>
<tr>
<td>1</td>
<td>9 (26%)</td>
<td>4 (13%)</td>
<td>13 (20%)</td>
</tr>
<tr>
<td>2</td>
<td>20 (57%)</td>
<td>20 (67%)</td>
<td>40 (62%)</td>
</tr>
</tbody>
</table>

*Where vaccination history was documented
Considerations When Assessing a Mumps Diagnosis in a Sporadic Case of Parotitis

- Mumps RT-PCR and culture results
- Laboratory results for other agents
- Mumps IgM test results
- Patient vaccination history
- Timing of specimen collection
- Time of year
Summary and Conclusions

- Mumps virus was not detected among any sporadic cases of parotitis
- A non-mumps virus was detected in 38% of sporadic cases of parotitis
  - Most were EBV
- Mumps vaccine effectiveness and coverage estimates within the U.S. are high
- Sporadic cases of parotitis within the U.S. may have a lower likelihood of being mumps
- Until more reliable methods for ruling-out a mumps etiology are developed, sporadic cases of parotitis should be treated as if they were mumps
Limitations

• Passive surveillance system
• Small numbers and convenience sample, so results might not be generalizable
• Obtaining specimens within 2 days of parotitis onset not always possible
• No control group, so causation should not be assumed
• Other infectious etiologies for parotitis exist, but were not tested for (e.g., HIV, cat scratch disease, and influenza)
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