The Resurgence of Measles in the Twenty First Century

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Disclosures: None
On January 2, 2015:

- A 3 yo Riverside girl was admitted to Children’s Hospital of Orange County, differential diagnosis included measles
  - URI, fever, followed by a descending rash
  - No travel
  - Did recently go to Disneyland
  - History of MMR vaccination

- 8 month old sibling admitted to CHOC on January 5
- Both diagnosed with measles by PCR
By the end of the Day on January 5

• 11 yo Orange County Resident also PCR positive for measles
  – Recent travel to Disneyland
• 3 additional confirmed and 6 suspect cases of measles identified around state and country
• 9 in CA, 2 in UT
• All at Disneyland 12/17 or 12/18
California Measles Cases, December 2014 – April 17th, 2015

131 outbreak-associated measles cases in California

88% of outbreak cases in SoCal

Outside of CA:
AZ 7
UT 3
NE 2
WA 2
CO 1
OR 1
Mexico 1
Canada 159

Courtesy: Jennifer Zipprich, CDPH
By the end of the Day on January 5

• 3 year old confirmed to have disease
• 8 month old sibling also confirmed case
• 11 y.o. Orange County resident also PCR positive for measles
• California Department of Public Health reported 3 confirmed and 6 suspect cases of measles identified
  – 7 in CA, 2 in UT
• All at Disneyland 12/17 or 12/18
Measles in the United States
Measles Around the World

• Endemic measles eliminated in United States in 2000
• Virus continues to be endemic in many parts of the world
• France had a major outbreak in 2010-2012
• Philippines had major outbreak from 2013-2015
Measles Nationally

• From January 1 to May 29, 173 confirmed cases from 21 states
• 70% trace to Disneyland outbreak
• 136 cases in California—131 Disney-related
• On April 17, 2015, measles outbreak declared over in California
Measles Cases in the United States, 2007-2016

Number of Measles Cases

Adapted from CDC data
United States Measles Importations

• In 2014:
  – 23 outbreaks
  – 667 cases
  – 27 states
  – Many associated with importations from Philippines, which saw a large national outbreak in 2014

• 2015 Disneyland outbreak caused by B3 strain, which has been seen in Philippine outbreaks

• In 2013, 50% of importations came from Europe
  – France in particular was source
Age Distribution of 2015 California Measles Outbreak

- Highest incidence in < 1 yo
- Majority of cases in adults

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Total</th>
<th>Incidence per 100,000 population*</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>14</td>
<td>2.67</td>
<td>11%</td>
</tr>
<tr>
<td>1-4</td>
<td>21</td>
<td>1.05</td>
<td>16%</td>
</tr>
<tr>
<td>5-19</td>
<td>24</td>
<td>0.31</td>
<td>18%</td>
</tr>
<tr>
<td>20-29</td>
<td>30</td>
<td>0.54</td>
<td>23%</td>
</tr>
<tr>
<td>30-39</td>
<td>21</td>
<td>0.40</td>
<td>16%</td>
</tr>
<tr>
<td>40-49</td>
<td>10</td>
<td>0.19</td>
<td>8%</td>
</tr>
<tr>
<td>50-59</td>
<td>9</td>
<td>0.18</td>
<td>7%</td>
</tr>
<tr>
<td>60-69</td>
<td>1</td>
<td>0.03</td>
<td>1%</td>
</tr>
<tr>
<td>70+</td>
<td>1</td>
<td>0.03</td>
<td>1%</td>
</tr>
</tbody>
</table>

*Population denominator data from the Department of Finance have been standardized with 2010 Census data
Vaccination Status of 2015 California Measles Outbreak

Of 131 California cases:

- 82 (63%) had documented immunization status
- 57 (70%) of cases with documented status were unvaccinated
  - Majority not vaccinated due to personal belief
- 49 (37%) had no immunization status documented

Courtesy: Jennifer Zipprich, CDPH
Measles in Orange County, 2015

35 cases:
- 17 females
- 21 adults
- 14 children
- 5 hospitalized
- 22 cases in our County in first three months of 2014
Immunization Status of 57 Orange County Cases, 2014 and 2015

38 adults cases:
• 1 with no MMR
• 9 with 2 MMRs
• 1 with 1 MMRs
• 3 with evidence of seroimmunity
• 24 with uncertain immunization status

19 pediatric cases:
• 18 with no MMR
• One 15 month old with one MMR
• Two under one year of age
• 10 vaccine refusers
Measles Symptoms in 57 Orange County Cases, 2014 and 2015
Measles Prodrome

• 8-12 day incubation period
• Prodrome lasts for 2-4 days and consists of:
  – Fever
  – Cough
  – Coryza
  – Conjunctivitis
  – Koplik’s Spots
• Rash follows around day 14
Character of Measles Rash in Orange County Cases, 2014 and 2015

- 56 of 57 with rash
- All rashes involved face initially
- Starts on face, often top of forehead, sometimes behind ears
- Spreads downward
- Initially maculopapular, then becomes confluent
- Most prominent on the face
Symptoms of 57 Measles Cases, 2014-2015

- Fever: 93%
  - For those with temperature information, all but 1 reported a fever over 101°F (101.2 to 104.7)
- Cough: 72%
- Coryza: 66%
- Conjunctivitis: 49%
- Koplik Spots (N = 41): 22%
- Diarrhea: 10%
## Symptoms by Immunization Status, 2014 and 2015 OC Measles Cases

<table>
<thead>
<tr>
<th></th>
<th>Not vaccinated (n=20)</th>
<th>Vaccinated/serologic proof of immunity (n=12)</th>
<th>Unknown Vaccination Status (n=27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>100%</td>
<td>75%</td>
<td>92%</td>
</tr>
<tr>
<td>Cough</td>
<td>83%</td>
<td>42%</td>
<td>73%</td>
</tr>
<tr>
<td>Coryza</td>
<td>89%</td>
<td>25%</td>
<td>62%</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>72%</td>
<td>8%</td>
<td>42%</td>
</tr>
<tr>
<td>Koplik spots</td>
<td>38%</td>
<td>12%</td>
<td>0%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>11%</td>
<td>10%</td>
<td>8%</td>
</tr>
<tr>
<td>Rash duration</td>
<td>6 days (4-8d)</td>
<td>4.2 days (4-5d)</td>
<td>5 days (2-9d)</td>
</tr>
<tr>
<td>Hospitalized</td>
<td>20%</td>
<td>0%</td>
<td>19%</td>
</tr>
</tbody>
</table>

### Complications:
- One otitis media
- One pneumonia
Measles Testing
Measles Polymerase Chain Reaction (PCR) Testing

• Most sensitive and specific test for diagnosis
• Oropharyngeal PCR very sensitive in first three days after rash starts
  – Nasopharyngeal PCR may be a bit less sensitive
  – In many instances, this is only test we would order
• Urine testing also sensitive, especially useful days 4-9 after rash starts
Satellite Clinic Site

Outdoor clinic under a canopy
One medical assistant
One office technician
For safe testing of suspect cases who have already been assessed by a medical provider
Tests performed included:
Oropharyngeal PCRs
Serum IgM
### Measles Testing Results for 57 Measles Cases in 2014-15

<table>
<thead>
<tr>
<th></th>
<th>IgM</th>
<th>OP PCR</th>
<th>Urine PCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>35</td>
<td>47</td>
<td>20</td>
</tr>
<tr>
<td>Negative</td>
<td>13</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Not done</td>
<td>9</td>
<td>7</td>
<td>32</td>
</tr>
</tbody>
</table>

All 15 unvaccinated patients tested were IgM +

For 10 Vaccinated Patients:
- 5 IgM negative, 3 IgM positive, 2 Not Done
- All 9 tested were OP PCR positive
United States Measles Cases, 2015

42 of 45 went to a Disney Theme Park
Orange County Cases and Their Connections, 2015

- Disney visitors
- Disney staff
- Mall exposure
- Household
- Healthcare
- Work site
- Unknown

Dates:
- 12/30
- 1/7
- 1/14
- 1/21
- 1/28
- 2/4

A Same Day.

- 37y
- 70y
- 29y
- 21y
- 3y
- 45y
- 14y
- 34y
- 8y
- 11y
- 9m
- 13y
- 25y
- 43y
- 25y
- 23m
- 14m
- 36y
- 36y
- 19y
- 39y
- 22y
- 11y

https://www.cdc.gov/mmwr/mmwrhtml/mm6412a4.htm

Cited:


Measles Case Cluster without Known Exposure, Rash Onset Jan 18-Feb 4
Orange County 2015
2014 Measles Outbreak, Ohio, Confirmed Cases by Date of Rash Onset,
N=377

Data as of 7/15/2014
Source: Ohio Disease Reporting System
Measles Outbreak in Quebec, 2015

• Resulted from initial exposure of two families in Disneyland
• Cluster centered on group of families in community north of Montreal
• 20 families with 7-10 children each
• Resulted in 139 cases across Canada
Measles Cluster 2, Orange County, 2014

Initial cases:
- 28 yo M
- 18 yo Pt.
- 38 yo F
- 32 yo Nurse
- 41 yo M
- 45 yo M
- 21 yo F
- 45 yo Mom
- 25 yo sib

Secondary cases:
- 36 yo Nurse
Healthcare Facility Transmission, 2014 and 2015

• 57 cases
• 91 healthcare facility exposure events
• >3000 patients and staff exposed
• 10 total transmissions
• 7 healthcare workers
  – 1 additional healthcare worker developed disease-likely patient exposure, though no source identified
• 3 patients
Measles Follow Up of Exposed

- **Exposure**
  - Vaccination within 72h

- **Rash onset**
  - Time in days

- **Incubation periods**
  - Shortest
  - Longest

- **Exclusion from work**
  - d5-21 post exposure

- **IG within 6 days**
Immune Globulin

- Effective if given within 6 days of exposure
- Provides limited protection
- Both MMR and IG minimally effective for close contacts
- Immunization with live vaccines needs to be delayed 5 months after IG
- Dosage is 0.5mL/kg for measles exposures
- Expensive
- Limited supply
- OCPH targeted to high risk persons: infants, immune compromised
- IVIG given to exposed non-immune pregnant women
Measles Infection Control

• Airborne precautions necessary in clinical settings
• Facilities without negative pressure room can see patient:
  – Outside
  – At end of day
• N-95 masking recommended for healthcare workers
2014-2015 Healthcare Workers Developing Measles

Of 10 healthcare facility transmissions:

• 5 of 7 healthcare worker cases had evidence of immunity
• 5 of 7 healthcare worker cases had a history of face-to-face exposure to case of measles
• 1 was custodial worker who cleaned room after patient left
• 1 was healthcare worker who denied face to face exposure to patient
• 3 were patients in same waiting room at same time as cases:
  • 9 month old
  • 18 yo with history of two MMRs
  • 19 yo with unknown immunization history
# Healthcare Workers with Measles Clinical and Epidemiologic Features, 2014

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>Measles Immunity Prior to Exposure</th>
<th>Exposure</th>
<th>Illness Onset</th>
<th>Fever</th>
<th>Cough</th>
<th>Coryza</th>
<th>Rash</th>
<th>Days Considered infectious while asymptomatic</th>
<th>Days working during active symptoms</th>
<th>Number of patients exposed</th>
</tr>
</thead>
<tbody>
<tr>
<td>32</td>
<td>IgG⁺</td>
<td>3/3/2014</td>
<td>3/17/2014</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>3/18/14</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>36</td>
<td>IgG⁺</td>
<td>3/3/2014</td>
<td>3/14/2014</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>3/18/14</td>
<td>0</td>
<td>4</td>
<td>850</td>
</tr>
<tr>
<td>41</td>
<td>2 MMR</td>
<td>3/7/2014</td>
<td>3/18/2014</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>3/20/14</td>
<td>2</td>
<td>2</td>
<td>26</td>
</tr>
<tr>
<td>37</td>
<td>4 MMR IgG⁺</td>
<td>3/7/2014</td>
<td>3/16/2014</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>3/20/14</td>
<td>0</td>
<td>4</td>
<td>72</td>
</tr>
<tr>
<td>40</td>
<td>Unknown vaccine history, IgG equivocal</td>
<td>3/7/2014</td>
<td>3/19/2014</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>3/21/14</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Cost of Measles Containment in an Ambulatory Pediatric Clinic

- Cost assessment of follow up to one measles case in an outpatient pediatric setting
- 52 patients exposed
- 60 caretakers
- 10 employees
- 5 patients <6 months required IG
- 13 patients 6-11 months required MMR
- Overall cost $5655

Wendorf, et al. PIDJ, June, 2015
OCHCA Healthcare Facility Response, 2015

- Emphasize that facilities assure that exposed staff have evidence of immunity
- Exclude from days 5-21 exposed staff without proof of immunity
- Emphasize that staff with evidence of immunity still have a small risk of developing disease
- Facilities (in general) contacted low risk patients by phone or letter to inform them of exposure:
  - Over 1 year of age
  - Immunocompetent
  - Not pregnant
  - Not healthcare worker
- OCHCA’s response was predicated on a large outbreak
Number of Community Measles Exposures, 2015

• 1955 community contacts identified in total thus far
• 1858 were healthcare facility contacts
  – These are significant underestimations
  – Approximately 20-30% of identified contacts cannot be reached
• 828 contacts attempted by OCHCA
  – Majority of non-high risk healthcare contacts in 2015 contacted by the facility
  – Screened for evidence of immunity
  – Over 200 exposed “high risk” persons tested
    • 98% seroimmune
Up-to-Date Immunizations at Kindergarten Enrollment, Private and Public Schools Within Each School District, 2014-15

Percent Up-To-Date
- 76.9% - 85.1%
- 85.2% - 89.9%
- 90.0% - 96.9%
OCHCA Followed Up on High Risk Persons

• Under one year of age generally
  – Pediatric practices and area pediatric children’s hospital followed up with this group with their exposures

• Pregnant women

• Immunocompromised
  – Immune globulin or IVIG given to these groups

• Health care workers
Summary Points

• Measles disease was weighted toward unvaccinated cases
• Measles outbreak size will be affected by community immunization rates
• Breakthrough disease can occur in previously-vaccinated adults
• Healthcare providers who care for measles patients are at particular risk of disease, even if they are immunized
Measles Cases in the United States in 2016

- January 2 to July 22:
- 48 people from 13 states were reported to have measles
- No specific outbreaks reported by CDC
Acknowledgments

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  • Jennifer Zipprich, MPH
  • Kathleen Harriman
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  • Steve Klish, MPH