The 2016 Massachusetts Mumps Outbreak: Understanding Why Mumps Spread Among Vaccinated Individuals
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Director, Division of Epidemiology and Immunization
Massachusetts Department of Public Health
Thursday, December 13, 2018, 12:00-1:00 p.m.
• No conflicts to report
Mumps

- Paramyxovirus
- Incubation period 12-25 days (usually 16-18)
- Respiratory droplet spread
- Infectious 2 days before until 5 days after parotid swelling
Clinical Findings

- Nonspecific prodrome: low-grade fever (3-4 d), myalgia, anorexia, malaise, and headache
- Parotid swelling one (25%) or both sides
- May be mild URI or asymptomatic
- Many other causes of parotitis
Complications

- Prevaccine era 10% of aseptic meningitis
- Prevaccine common cause of sensorineural deafness
- Orchitis (3-10% adolescent and adult males)
- Oophoritis and mastitis in females <1%
- Pancreatitis, encephalitis, myocarditis, arthritis

- All complications much rarer in vaccinated individuals
Mumps vaccine
Jeryl Lynn Hilleman with her sister, Kirsten, in 1966 as a doctor gave her the mumps vaccine developed by their father. New York Times
Mumps vaccine

- Live attenuated vaccine component of MMR
- ACIP 12-15 months and 4-6 years
  - MMRV
- Mumps 2-dose effectiveness approx 88% (31–95%)
- Single dose is about 78% (range: 49%–92%) effective
Number of Reported Mumps Cases, United States – 1968 - 2017

Source: National Notifiable Diseases Surveillance System (passive surveillance); 2017 data as of October 7, 2017. Presented by Dr. Mona Marin, CDC, ACIP Meeting 10-25-17
Mumps incidence is on the rise

Source: MMWR, Notifiable Diseases and Mortality Tables
In recent years outbreaks largely confined to universities and other close contact settings, including teams, clubs, schools, other work places, prisons and the Marshallese community.

- Median age 21
- Half of the outbreaks had <10 cases; half of the outbreaks occurred in colleges/universities
- A small number of outbreaks (13%) with $\geq$50 cases accounted for 83% of all outbreak related cases
- Current 2-dose schedule sufficient for control in general population
- But not in intense exposure settings with increased force of infection

Source: National Notifiable Disease Surveillance System (passive surveillance); 2017 data as of October 7, 2017.
CDC. MMWR 2018;67(1):33.
Presented by Dr. Mona Marin, CDC, ACIP Meeting 10-25-17
Mumps
Background

• MA experienced an increase in reported mumps cases in 2016 & 2017.
  • 11 cases were reported in 2014 and 2015, 364 in 2016 & 2017.
Mumps outbreak in Massachusetts

*The Boston Globe* reported cases at:

- Harvard University
- University of Massachusetts Boston
- Boston University
- Tufts University
- Bentley University
- Endicott College

Source: data.cdc.gov/NNDSS
Methods

• Information for cases reported from 1/1/2014-6/30/2017 was collected via the Massachusetts Virtual Epidemiologic Network (MAVEN) surveillance system
• Sequencing libraries were constructed from 200 PCR-positive specimens from MA, as well as 59 PCR-positive specimens from other US jurisdictions
• Whole genome nucleotide sequencing was performed
• Phylogenies were reconstructed and annotated using MAVEN data.
  • Epidemiologic links
  • Institutional association
## Results

<table>
<thead>
<tr>
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<th>Cases in Study n=198</th>
<th>All Cases n=375</th>
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<tbody>
<tr>
<td><strong>Race</strong></td>
<td>Asian (7.57%)</td>
<td>Asian (8.00%)</td>
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<tr>
<td></td>
<td>Black/African American (6.57%)</td>
<td>Black/African American (5.60%)</td>
</tr>
<tr>
<td></td>
<td>White (65.66*)%</td>
<td>White (60.53%)</td>
</tr>
<tr>
<td></td>
<td>Other (9.60%)</td>
<td>Other (8.80%)</td>
</tr>
<tr>
<td></td>
<td>Unknown (10.60%)</td>
<td>Unknown (17.06%)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>Male (49.49%)</td>
<td>Male (49.33%)</td>
</tr>
<tr>
<td></td>
<td>Female (50.51%)</td>
<td>Female (50.67%)</td>
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<tr>
<td><strong>Vaccination Status</strong></td>
<td>1 MMR (2.53%)</td>
<td>1 MMR (4.53%)</td>
</tr>
<tr>
<td></td>
<td>2 MMR (64.65%)</td>
<td>2 MMR (64.27%)</td>
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<tr>
<td></td>
<td>Unvaccinated (5.56%)</td>
<td>Unvaccinated (4.53%)</td>
</tr>
<tr>
<td></td>
<td>Unknown (27.27%)</td>
<td>Unknown (26.67%)</td>
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<tr>
<td><strong>Age Group</strong></td>
<td>&lt;5 yrs (0%)</td>
<td>&lt;5 yrs (1.87%)</td>
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<tr>
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<td>5-9 yrs (0%)</td>
<td>5-9 yrs (1.07%)</td>
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<td>10-14 yrs (0.51%)</td>
<td>10-14 yrs (0.27%)</td>
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<td>15-19 yrs (23.23%)</td>
<td>15-19 yrs (21.87%)</td>
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<td>20-24 yrs (48.48%)</td>
<td>20-24 yrs (42.40%)</td>
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<td>25-29 yrs (11.62%)</td>
<td>25-29 yrs (12.27%)</td>
</tr>
<tr>
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<td>≥ 30 yrs (16.16%)</td>
<td>≥ 30 yrs (20.27%)</td>
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</tbody>
</table>
Results

Mumps Cases by Week
1/1/2016-6/30/2017, Massachusetts

- Total Cases
- Study Cases

Number of Reported Cases

Week End Date

1/1/2016 to 6/30/2017
Harvard-affiliated

Community-affiliated
Results
Summary

- SH sequence data to trace global spread

- Whole genome sequences reveal ongoing transmission in the United States

- Genomic data reveals multiple co-circulating lineages in Massachusetts

- Combining genomic and epidemiological data gives the most complete picture of transmission within it
Co-circulating mumps lineages at multiple geographic scales


doi: https://doi.org/10.1101/343897

This article is a preprint and has not been peer-reviewed [what does this mean?]

Abstract

Despite widespread vaccination, eleven thousand mumps cases were reported in the United States (US) in 2016-17, including hundreds in Massachusetts, primarily in college settings. We generated 203 whole genome mumps virus (MuV) sequences from Massachusetts and 15 other states to understand the dynamics of mumps spread locally and nationally, as well as to search for variants potentially related to vaccination. We observed multiple MuV lineages circulating within Massachusetts.
Mumps in Massachusetts 2016 - 2017

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</tr>
</thead>
<tbody>
<tr>
<td>Mumps</td>
<td>7</td>
<td>15</td>
<td>9</td>
<td>4</td>
<td>6</td>
<td>71</td>
<td>5</td>
<td>6</td>
<td>258</td>
<td>191</td>
<td>8</td>
</tr>
</tbody>
</table>

*includes confirmed and probable to better reflect the burden of disease. 2017 data are preliminary and subject to change.

Confirmed and Probable Mumps Cases by Cluster Type - MA 2016-2017 (N=449)

2016: 258 cases*
2017: 191 cases*
Why outbreaks in college?

- Close prolonged contact
- 12+ years since last MMR
- Waning immunity?
- Viral changes?
Waning immunity to mumps

Lewnard & Grad, Sci Trans Med 2018
Mumps outbreaks have been increasing in recent years

- In part due to **waning immunity of the 2 dose series** in the settings of an increased force of infection (close, prolonged contact). 2 dose vaccine effectiveness: 88% (range of 31-95%). 2 dose schedule sufficient for control in general population.

- Data limited and insufficient at this time to fully characterize the impact of MMR3 on reducing the size or duration of an outbreak. Studies are ongoing.

- Data do support use of a third dose of a mumps-containing vaccine for **improving an individual’s** protection against mumps disease and its complications during an outbreak.

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**Recommendation of the Advisory Committee on Immunization Practices for Use of a Third Dose of Mumps Virus–Containing Vaccine in Persons at Increased Risk for Mumps During an Outbreak**

Mona Marin, MD  •  Marcel Marois, MD  •  Kelly L. Moore, MD  •  Minh Do, MD

A substantial increase in the number of mumps outbreaks and outbreak-associated cases has occurred in the United States since late 2014. To address this public health problem, the Advisory Committee on Immunization Practices (ACIP) reviewed available evidence and determined that a third dose of mumps–containing (MMR) vaccine is safe and effective at preventing mumps. During October 2017 meeting, ACIP recommended a third dose of a mumps vaccine (vaccines) for persons previously vaccinated with 2 doses who are identified by public health authorities as being part of a group or population at increased risk for acquiring mumps because of an outbreak. The purpose of the recommendation is to improve protection of persons in outbreaks who have mumps disease and transmission-based. Despite this recommendation, mumps outbreaks continued to be reported throughout the United States, particularly in settings where persons have close, prolonged contact (e.g., schools and close living communities). To assist state and local health departments in responding to mumps outbreaks, CDC issued guidance on use of a third dose of MMR vaccine in the 2017 Morbidity and Mortality Weekly Report for the Surveillance of Vaccine Preventable Diseases. The guidance was based on limited, anecdotal provided activities for health departments operating within the context of a third dose in specifically identified target populations. Additional evidence on effectiveness and safety for third dose of MMR vaccine recently became available and was presented to ACIP during 2017. This report summarizes the evidence concluded by ACIP on the benefits of a third dose of a mumps

CDC. MMWR 2018;67(1):33.

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Adult Immunization Conference 2018
MMR 3rd dose -- U Iowa
Cardemil et al. NEJM 2017
A Third Dose:

- CDC reviewed three studies regarding the use of a 3rd dose.
- All studies reported lower attack rates among persons who received the third dose during the outbreak compared with persons who had received 2 doses before the outbreak.
- Incremental vaccine effectiveness of 2 doses vs. 3 doses ranged from 61% to 88%, with one estimate statistically significant at 78.1% VE (CI = 60.9 - 87.8%).
- This study also found students who had received MMR2 ≥13 years prior had a 9-fold increased risk.

- Appears safe

- Duration of protection is unknown
  - Limited immunologic evidence suggest antibody titers decline within 1 year after the 3rd dose.

- 3rd dose should be deployed strategically in certain outbreaks as determined by public health authorities

CDC. MMWR 2018;67(1):33.
Persons previously vaccinated with 2 doses of a mumps virus–containing vaccine who are identified by public health authorities as being part of a group or population at increased risk for acquiring mumps in certain outbreak settings should receive a 3rd dose of a mumps virus–containing vaccine to improve an individual’s protection against mumps disease and related complications.

Factors to be considered:

- Size of target population
- Mumps incidence/number of cases
- MMR3 vaccine coverage needed to impact the outbreak
- Timing of MMR3 vaccination
- Social networks
- Intensity and duration of close contact

Call MDPH Division of Epidemiology and Immunization at 617-983-6800 for consultation.

Discussion

• Genetic similarity of viral genome sequences from mumps cases in Massachusetts and other jurisdictions suggests mumps virus may be widely circulating in the United States, not confined to sporadic outbreaks.
• Within Massachusetts, the data suggest transmission occurred both between institutions and into the community.
• Our observation that genetic distance is a good predictor of epidemiologic linkage indicates that whole-genome data can be used to infer linkage between cases not identified by traditional epidemiological methods, showing the power of WGS to inform public health investigations and interventions.
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