Current Mumps Vaccination Recommendations and Epidemiology in the United States

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Outline

- Overview: mumps disease and transmission
- Mumps vaccine and vaccination recommendations in the United States
- Mumps epidemiology in the United States
- Topics for Work Group discussion
Mumps Disease

- Acute, viral illness that classically presents with parotitis (60%-70%)
- Other presentations
  - Other salivary gland swelling (10%)
  - Non-specific respiratory symptoms/asymptomatic infection (30%)

<table>
<thead>
<tr>
<th>Complications</th>
<th>Unvaccinated (%)*</th>
<th>Vaccine era (%)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orchitis‡</td>
<td>up to 30%</td>
<td>3-11</td>
</tr>
<tr>
<td>Mastitis‡</td>
<td>up to 30%</td>
<td>≤1</td>
</tr>
<tr>
<td>Hearing loss</td>
<td>4</td>
<td>≤1</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>4</td>
<td>≤0.1</td>
</tr>
<tr>
<td>Aseptic meningitis</td>
<td>1-15</td>
<td>0.2-0.5</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>0.03-0.5</td>
<td>0-0.3</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>5.5</td>
<td>&lt;1-2</td>
</tr>
</tbody>
</table>

*McLean HQ et al. MMWR 2013; †Data from US outbreak investigations 2006-2015; ‡Assessed in postpubertal male/female patients
Mumps Transmission

- Person-to-person direct contact with infected droplets or saliva or by inhalation of infectious respiratory droplets
- Requires close contact for spread
  - Infectiousness is less than measles and varicella\(^1\)
- Infectious period: 2 days before to 5 days after parotitis onset
- Can occur from persons with non-specific respiratory symptoms and asymptomatic infection
- Incubation period: 16-18 days (range 12-25 days)
- Infectiousness before symptoms, transmission from persons with asymptomatic/non-specific presentation contribute to prolongation of transmission/outbreaks

\(^1\)Hope Simpson RE. *The Lancet* 1952 (secondary attack rate in households among those age <15 years: measles-76%, varicella-61%, mumps 31%)
Mumps Vaccine in the United States

- Single antigen vaccine licensed in 1967
- Currently available as combination vaccines (Merck & Co., Inc.)
  - Measles, mumps, rubella (MMR) licensed in 1971
  - Measles, mumps, rubella, varicella (MMRV) licensed in 2005

Composition
- Live, attenuated mumps strain
- Jerryl Lynn strain, Genotype A

Effectiveness estimates (MMR)\(^1\)
- 1 dose: \(~77\% (49\%-91\%)\)^2
- 2 doses: \(~88\% (66\%-95\%)\)^2

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2 Ranges indicate results of individual studies and not confidence intervals
Mumps Vaccination Recommendations in the United States

- 1977*: 1 dose recommended for all children at any age after 12 months

- 1989: a second dose of measles vaccine recommended for improved measles control
  - Both doses of measles vaccine should be given as combined MMR, stating that “mumps revaccination is particularly important”
  - Effectively, this delivered a second dose of mumps vaccine

- 2006: formal recommendation for 2 doses of a live mumps virus-containing vaccine
  - School-aged children (grades K-12)
  - Adults in high risk groups
    - Healthcare facility personnel
    - International travelers
    - Students at post-high school educational institutions

Prior to 1977, mumps vaccine was not recommended for routine use: “may be considered for use in children approaching puberty, adolescents and adults, especially males” (1967), “may be used at any age from 12 months”, “vaccine is of particular value in children approaching puberty, adolescents and adults, especially males” (1968, 1972).

Reported Mumps Cases, United States, Vaccine Era, 1968-2016

Source: National Notifiable Diseases Surveillance System (cases, passive surveillance); National Immunization Survey (NIS) (1st dose coverage 19-35 year olds), National Health Interview Survey & NIS-Teen (2nd dose coverage); 2016 case data is preliminary (Feb 9, 2017) and subject to change.
Reported Mumps Cases, United States, Vaccine Era, 1968-2016

Source: National Notifiable Diseases Surveillance System (passive surveillance); 2016 data is preliminary (Feb 9, 2017) and subject to change.
Midwest Outbreak - 2006

- 6,584 cases, geographically focused (85% in Midwest)
- First large outbreak attributable to 2-dose vaccine-failure
- Incidence was highest among young adults aged 18-24 years
  - Most were college students
    - 2 dose MMR coverage in affected colleges: 90%-99%
    - Most had received the second dose >10 years previously
    - Dormitory living, freshman class status, time since 2^{nd} dose (≥10 years) were risk factors
- Standard control measures (e.g., isolation and vaccine catch-up campaigns) were implemented

Outbreaks in Northeast U.S. & Guam - 2009-2010

- Northeast: 3,502 cases\(^1\)
  - 97% of cases in Orthodox Jewish community
  - Adolescent (age 13-17 years) males the most affected group
    - 89% had 2 doses of MMR vaccine
  - Unique schools and large households; prolonged, intense exposures likely overcame protection afforded by the vaccine
- Guam: 505 cases\(^2\)
  - Highest attack rate
    - School-aged children (aged 9-14 years), 96% two-dose vaccinated
    - Ethnic minorities with higher household densities
- 3\(^{rd}\) MMR vaccine dose was used for outbreak control

Mumps Cases and Outbreaks, United States, July 2010-December 2016

- Increase in the number of reported cases and outbreaks
  - Genotype G virus

- 2010 through 2015: 23 outbreaks with ≥20 cases reported in 18 states
  - 22 (96%) occurred in close contact settings (18 in universities)
  - Highest incidence in the 18-25 years age group
    - Median age 19-23 years in 16 outbreaks
  - In half of university outbreaks >85% of case-patients had documented 2 MMR doses
  - Spread outside affected setting was minimal (3)

Mumps Cases and Incidence Rates by Year, 2010-Nov 2016

Source: National Notifiable Diseases Surveillance System (cases, passive surveillance); 2016 data is preliminary (Feb 9, 2017) and subject to change; Clemmons N, CDC, personal communication Feb 2017 (outbreaks)
Factors that May Contribute to the Increasing Number of Mumps Outbreaks (1)

- **Vaccine effectiveness**
  - 1 dose: ~77% (49%-91%)
  - 2 doses: ~88% (66%-95%)

- **Waning of vaccine-induced immunity**
  - Serologic studies suggest waning: seropositivity and neutralizing antibody titers decline over time\(^1\)\(^-\)\(^5\),
    - No established correlates of protection, implications of declining titer uncertain\(^3\)
    - Cellular immunity declines less than seropositivity over time (if at all)\(^6\)
  - Epidemiologic studies suggest waning: decreased vaccine effectiveness\(^7\) and increased odds of disease with time since vaccination\(^8\),\(^9\), evidence still limited
  - Waning of immunity does not explain the general geographical focal nature and that the oldest vaccinated cohorts not always most affected

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Factors that May Contribute to the Increasing Number of Mumps Outbreaks (2)

- **Force of infection**
  - Outbreaks in settings with high population density and contact rates that facilitate transmission (e.g., college campuses, close knit communities)

- **Vaccine-induced immunity less effective against other strains?**
  - No evidence to date, sera from vaccinated children neutralized diverse mumps strains\(^1,2\)
  - Antigenic differences among mumps virus strains detected\(^1-3\)
    - Lower antibody levels against non-vaccine strains
    - Might become more important with increasing time since vaccination

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Age-specific Vaccine Effectiveness Estimates\(^1\) for 1 and 2 Doses of MMR Vaccine*, UK, 2004-2005 Outbreak

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1st Dose
Overall 88%
Trend P<.001 for both curves

2nd Dose
Overall 95%

Herd Immunity Threshold\(^2\)

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*MMR vaccine contains either Jeryl Lynn strain or RIT 4385 strain (derived from the Jeryl Lynn strain)
Levels and Trend over Time of Vaccine-Induced Neutralizing Antibody

- Antibody induced by vaccination effectively neutralized genotype G virus, for all study subjects at each time point tested
- Geometric mean titers to genotype G strain were lower than those to Jeryl Lynn
- Antibody titers decreased over time
- Clinical significance of the findings cannot be conclusively ascertained

Table 1. Geometric mean titers (GMTs) of serum neutralizing antibody against the Jeryl Lynn and USA06-Iowa-G viruses.

<table>
<thead>
<tr>
<th>Virus</th>
<th>2-5 years after MMR1</th>
<th>1 month after MMR2</th>
<th>10 years after MMR2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jeryl Lynn</td>
<td>107.9 (83.6–139.2)</td>
<td>280.5 (212.1–371.0)</td>
<td>94.8 (73.2–122.9)</td>
</tr>
<tr>
<td>USA06-Iowa-G</td>
<td>56.2 (46.8–67.6)</td>
<td>110.4 (90.3–135.0)</td>
<td>56.6 (47.3–67.5)</td>
</tr>
</tbody>
</table>

Note: Data are the GMT (95% confidence interval). Titers were measured before administration of 2 doses of the measles, mumps, and rubella (MMR) vaccine (MMR2) (given 2-5 years after administration of 1 dose of the MMR vaccine [MMR1]) and at 1 month and 10 years thereafter.
A 3rd Dose of MMR Vaccine in Northeast & Guam Outbreaks, 2009-2010

- Northeast/Orange County, New York: 81% of eligible students vaccinated with a 3rd dose\(^1\)
- Guam: 33% of eligible students vaccinated with a 3rd dose\(^2\)

- Attack rates declined after the 3rd MMR dose in both school-based studies, but
  - In Guam, statistical significance could not be established due to the small number of cases recorded
  - In both studies, late timing of 3rd dose campaigns
    - The possibility of the declines being unrelated to the intervention could not be excluded

ACIP Statement Regarding a 3rd MMR Dose

- 2012: Data are insufficient to recommend for or against the use of a 3rd dose of MMR vaccine for mumps outbreak control
  - CDC issued guidance for consideration for use of a 3rd dose in specifically identified target populations along with criteria for public health departments to consider for decision making
    - Settings with >90% 2-dose vaccination coverage
    - Intense exposure settings such as schools and correctional facilities, and high attack rates (>5 per 1,000)
    - Ongoing transmission (>2 weeks)

Mumps Neutralizing Antibody in Young Adults After a 3rd Dose of MMR

- Very few subjects had titers negative (0.8%) or low (5.8%) before the 3rd dose
- Compared with pre-3rd dose (baseline), geometric mean titers were modestly but significantly higher one month and one year after the 3rd MMR dose
  - 104.1 (baseline) vs 159.2 (1 month); (P<0.0001)
  - 104.1 (baseline) vs 125.9 (1 year); (P<0.01)
- Minimal shifts in mumps titers from baseline to 1 month and 1 year

Fiebelkorn AP et al. Open Forum Infect Dis 2014
Neutralizing antibody to Jeryl Lynn strain; Seronegative: titer <1:8; low titer: between 1:8 and <1:16

![Graph](https://via.placeholder.com/150)
Summary

- Use of the mumps vaccine reduced disease levels ~99% versus pre-vaccine era in the United States
- Since 2006, mumps outbreaks have occurred in highly 2-dose vaccinated populations
- Current 2-dose schedule is sufficient for mumps control in the general population, but outbreaks can occur in well vaccinated populations in specific settings
- Intense exposure settings and waning immunity appear to be risk factors for secondary vaccine failure
- The benefit of a 3rd MMR dose still needs to be assessed
Topics for Work Group Discussion

- Review available evidence for risk factors for mumps among 2 dose MMR vaccine recipients
  - Protection against currently circulating mumps virus genotypes in the United States
- Review available evidence on benefit provided by the 3rd MMR dose
  - Additional benefit?
  - Short vs. long term
  - More epidemiologic and laboratory data forthcoming
- Policy options for prevention and control of mumps outbreaks in the United States
  - Programmatic implications and cost analysis of various policy options for a 3rd dose MMR to prevent or control mumps outbreaks
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