Update on the Epidemiology of Meningococcal Disease and Guidance for the Control of Meningococcal Disease Outbreaks in the U.S.

Sarah Meyer, MD MPH
Advisory Committee on Immunization Practices Meeting
February 22, 2017
Agenda

- Epidemiology of meningococcal disease and clusters/outbreaks in the United States
- Current guidance for the evaluation and management of meningococcal disease outbreaks
- Proposed updates to CDC meningococcal disease outbreak guidance
- Next steps
Meningococcal Disease Incidence – United States, 1996-2015

1.3 cases/100,000 population

MenACWY vaccine

0.12 cases/100,000 population

MenB vaccine

Year

Incidence per 100,000

Abbreviations: MenACWY = quadrivalent conjugate meningococcal vaccine against serogroups A, C, W, Y; MenB vaccines = serogroup B meningococcal vaccines

Source: 1996-2015 NNDSS Data

Source: National Notifiable Diseases Surveillance System (NNDSS) data with additional serogroup data from Active Bacterial Core surveillance (ABCs) and state health departments
Average Annual Incidence by Age-Group and Serogroup—United States, 2006-2015

Source: National Notifiable Diseases Surveillance System (NNDSS) data with additional serogroup data from Active Bacterial Core surveillance (ABCs) and state health departments
Clusters/Outbreaks of Meningococcal Disease in the U.S.

- Information on outbreak associated cases is collected through the National Notifiable Diseases Surveillance System (NNDSS), but reporting is likely incomplete.

- CDC conducted a retrospective review of all meningococcal disease cases from 2009-2013 to identify and characterize clusters/outbreaks.
  - Cluster: 2 cases of the same serogroup within 3 months
  - Outbreak: ≥ 3 cases of the same serogroup and attack rate (AR) of >10 cases/100,000 population within 3 months
  - Classified as organization (common affiliation other than shared geography) or community-based (no other affiliations besides shared geography)

- From 2009-2013, of the 3,683 cases reported to NNDSS, 195 (5.3%) were primary cases associated with 41 clusters.
## Summary of Clusters/Outbreaks* in the United States, 2009-2013

<table>
<thead>
<tr>
<th>Type</th>
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<td>2</td>
<td>22</td>
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* Excludes clusters from Texas as different criteria for defining clusters was used.
# MSM = Men who have sex with men
‡ Among clusters with known population size
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Serogroup Distribution of Organization-Based Cluster/Outbreak-Associated vs. Sporadic Meningococcal Disease Cases, 2009-2013

![Bar chart showing serogroup distribution](image-url)
## University Based Serogroup B Clusters/Outbreaks†, 2008–2016

<table>
<thead>
<tr>
<th>State of University Location</th>
<th>Outbreak Period</th>
<th>Cases (deaths)</th>
<th># Undergraduates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ohio</td>
<td>Jan 2008 – Nov 2010</td>
<td>13 (1)</td>
<td>24,000</td>
</tr>
<tr>
<td>Pennsylvania</td>
<td>Feb – Mar 2009</td>
<td>4</td>
<td>10,000</td>
</tr>
<tr>
<td>Pennsylvania</td>
<td>Nov 2011</td>
<td>2</td>
<td>5,000</td>
</tr>
<tr>
<td>New Jersey</td>
<td>Mar 2013 – Mar 2014</td>
<td>9 (1)</td>
<td>5,000</td>
</tr>
<tr>
<td>California</td>
<td>Nov 2013</td>
<td>4*</td>
<td>18,000</td>
</tr>
<tr>
<td>Rhode Island</td>
<td>Jan – Feb 2015</td>
<td>2</td>
<td>4,000</td>
</tr>
<tr>
<td>Oregon</td>
<td>Jan – May 2015</td>
<td>7 (1)</td>
<td>20,000</td>
</tr>
<tr>
<td>California</td>
<td>Jan – Feb 2016</td>
<td>2**</td>
<td>5,000</td>
</tr>
<tr>
<td>New Jersey</td>
<td>Mar – Apr 2016</td>
<td>2</td>
<td>35,000</td>
</tr>
<tr>
<td>Wisconsin</td>
<td>Oct 2016</td>
<td>3</td>
<td>30,000</td>
</tr>
<tr>
<td>Oregon</td>
<td>Nov 2016</td>
<td>2</td>
<td>25,000</td>
</tr>
</tbody>
</table>

*Where CDC consulted; †1 additional associated case identified after retrospective case review; **1 additional patient with inconclusive laboratory results

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**MenB Vaccination**
Serogroup C Meningococcal Disease Clusters/Outbreaks†
Among Men Who Have Sex With Men, 2010-2017

<table>
<thead>
<tr>
<th>Jurisdiction</th>
<th>Outbreak Period</th>
<th>Number of cases (deaths) among MSM</th>
</tr>
</thead>
<tbody>
<tr>
<td>New York City</td>
<td>Aug 2010 – Feb 2013</td>
<td>22 (7)</td>
</tr>
<tr>
<td>Los Angeles</td>
<td>Oct 2012 – Sep 2014</td>
<td>10 (4)</td>
</tr>
<tr>
<td>Chicago*</td>
<td>June 2015 – Sep 2016</td>
<td>11 (1)*</td>
</tr>
<tr>
<td>Southern California</td>
<td>Mar – Sep 2016</td>
<td>21 (2)</td>
</tr>
<tr>
<td>Miami</td>
<td>Sep 2016 – Jan 2017</td>
<td>3 (1)</td>
</tr>
</tbody>
</table>

Where CDC consulted; *Includes one case identified among a resident of a different state who had epi-links to Chicago
Summary: Epidemiology of Meningococcal Disease

- Rates of disease have declined from approximately 1 to 0.1 cases/100,000 population in the past 20 years.
  - Decline seen in all serogroups, including serogroup B.

- Each cluster/outbreak is unique with wide range in number of cases, population size and characteristics, and duration.
  - Creates challenges in applying guidance for the control of meningococcal disease outbreaks.

- In recent years, several serogroup B outbreaks in universities and serogroup C outbreaks among MSM populations have been reported.
Guidance for the Evaluation and Management of Meningococcal Disease Outbreaks:

Current Guidance and Proposed Updates
Guidance for Evaluation and Management of Meningococcal Disease Outbreaks in the U.S.

- **Published guidance**: Originally developed in 1997 and updated in 2013 in Appendix B of the ACIP “Prevention and Control of Meningococcal Disease” statement.

- **Interim guidance**: Developed in 2014 for the control of serogroup B outbreaks in organizational settings prior to licensure of MenB vaccines in the U.S.

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Key Components of Meningococcal Disease Outbreak Guidance

- Cases to be included in the case count for vaccine decision-making
- Population: organization- and community-based outbreaks
- Outbreak thresholds and the decision to vaccinate
- Defining the vaccination group
- Role of molecular genotyping
- Other control measures (e.g., mass chemoprophylaxis)
Updated Guidance for the Evaluation and Management of Meningococcal Disease Outbreaks

- Current guidance developed under different epidemiologic context and prior to the availability of conjugate MenACWY or MenB vaccines.

- Several recent outbreaks have identified challenges in managing outbreaks using the current guidance.

- State and local health departments expressed a need for updated guidance better adapted to the current situation.
Updated Guidance for the Evaluation and Management of Meningococcal Disease Outbreaks

- **Objective:** Update and harmonize guidance for the investigation and public health management of meningococcal disease outbreaks due to all serogroups.

- **Activities:**
  - Review of the literature to describe the use and impact of meningococcal vaccines in outbreak settings.
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- Role of molecular genotyping
- Other control measures (e.g., mass chemoprophylaxis)
- Serogroup B vaccine selection based on expected vaccine coverage against an outbreak strain
- Re-evaluation of outbreak status
Cases to Include for Vaccine Decision-Making and the Role of Molecular Genotyping
Current Guidance: Cases to Include for Vaccine Decision-Making and the Role of Genotyping

- Only primary cases of the same serogroup should be included in case count for vaccine decision-making, as primary cases indicate ongoing transmission:
  - Primary case: case that occurs in the absence of previous known close contact with another patient.
  - Co-primary or secondary case: case that occurs among close contacts of a primary case, with onset ≤24 hours (co-primary) or >24 hours (secondary) of the primary case.
Challenges: Cases to Include for Vaccine Decision-Making

- Determining whether cases had close contact may be challenging in some populations.
- Community versus public health perception of an outbreak: may create confusion and communication challenges when some cases “don’t count.”
Challenges: Role of Molecular Genotyping

- Serogroup alone may not be sufficient to determine whether cases are related.

- New tools for molecular typing: whole genome sequencing (WGS) provides highest resolution.
  - Role of WGS in confirming outbreaks becoming increasingly important, particularly with the availability of serogroup B vaccines.
  - However, there will continue to be cases in whom an isolate is not available.
Proposed Guidance: Cases to Include for Vaccine Decision-Making

- Removal of classification of cases as primary, co-primary, or secondary.
- Evidence of related/identical strains by WGS not required for inclusion of cases in the case count.
  - However, if sequencing demonstrates that a case is unrelated to others in the outbreak, this case should not be included.
- **Proposed guidance:** All cases of meningococcal disease of the same serogroup are included in the case count unless there is evidence of genetically distinct strains by whole genome sequencing.
Outbreak Thresholds and the Decision to Vaccinate
## Current Guidance: Outbreak Thresholds and the Decision to Vaccinate

<table>
<thead>
<tr>
<th>Guidance</th>
<th>Outbreak Threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Published</td>
<td><strong>3 cases with attack rate &gt; 10 cases/100,000 population in 3 months</strong></td>
</tr>
<tr>
<td>Interim</td>
<td><strong>2 cases in pop &lt;5,000 and ≥ 3 cases in pop ≥ 5,000 in 6 months (serogroup B organization-based outbreaks only)</strong></td>
</tr>
</tbody>
</table>
Challenges: Outbreak Thresholds and the Decision to Vaccinate

- Meningococcal outbreaks are not “one size fits all”; there is a need for flexibility to evaluate each outbreak on a case-by-case basis.

- The threshold of 10 cases/100,000 is ~100 times higher than U.S. national incidence; however, in the absence of data, difficult to define a more appropriate threshold.
  - Situations occur in which outbreak threshold not reached despite a clear need for intervention (i.e., 2016 serogroup C outbreak among MSM in California, with 21 cases and attack rate of ~6 cases/100,000.)

- Little tolerance for additional cases viewed as preventable.

- Attack rates are challenging to calculate in community outbreaks and outbreaks among special populations due to difficulty in defining the denominator.
Proposed Guidance: Outbreak Thresholds

- **Proposed guidance:** Each outbreak should be evaluated on a case-by-case basis to determine threshold for vaccination. In general:
  - Organization-based: 2-3 cases of meningococcal disease of the same serogroup within 3 months.
  - Community-based: Incidence of meningococcal disease of the same serogroup that is above expected in the affected community during a 3-month period.
Proposed Guidance: Decision to Vaccinate

- Considerations for vaccine decision-making:
  - Size of population
  - Ability to define a target group for vaccination
  - Whether ongoing transmission is likely or if cases likely represent a single transmission event (i.e., household contacts, roommate, boyfriend/girlfriend)
  - Feasibility of a vaccination campaign
  - Timing of potential vaccination in relation to cases
Serogroup B Vaccine Selection and Coverage of Outbreak Strain
Current guidance: MenB Vaccine Selection

- Current guidance: None (no MenB vaccines available at time of writing.)
Challenges: MenB Vaccine Selection

- Unlike conjugate MenACWY vaccines, MenB vaccines induce an immune response to subcapsular proteins, which vary by strain.

- While WGS can identify the presence of MenB vaccine antigens in the outbreak strain, it cannot determine expression of the antigens or expected coverage by MenB vaccines against a particular outbreak strain.

- There are challenges to conducting additional testing to determine coverage against the outbreak strain in real-time during an outbreak.
Proposed Guidance: MenB Vaccine Selection

- Proposed guidance:
  - Identification of MenB vaccine antigens by molecular characterization should not drive the choice of MenB vaccine (MenB-FHbp or MenB-4C) during an outbreak of meningococcal disease at this time.
  
  - No vaccine preference for outbreak control:
    - MenB-4C: 2-dose schedule
    - MenB-FHbp: 3-dose schedule
Re-evaluation of Outbreak Status
Current Guidance: Re-evaluation of Outbreak Status

- No current guidance on when to declare an outbreak as being “over.”
Challenges: Re-evaluation of Outbreak Status

- Meningococcal disease epidemiology is dynamic and unpredictable, with outbreak-associated cases sometimes reported months after the last known case.

- Public health officials need guidance on how long to continue vaccination and other public health interventions.
  - i.e., after vaccinating undergraduates at a university with MenB vaccine, do incoming freshman the following year need to be vaccinated?

- Prematurely declaring an outbreak as being “over” can erode public trust if further cases are identified.
Proposed Guidance: Re-evaluation of Outbreak Status

- Because of the unique epidemiology of meningococcal disease outbreaks, it is difficult to declare an outbreak as being “over.”

- **Proposed guidance:** For public health decision-making, after one year without any new reported cases, the risk of meningococcal disease likely returns to baseline.
Summary of Updated Guidance

- **Case count for vaccine decision-making:** All cases of meningococcal disease of the same serogroup are included unless there is evidence of genetically distinct strains by whole genome sequencing.

- **Outbreak threshold for vaccine decision-making:** Each outbreak should be assessed on a case-by-case basis, though in general:
  - Organization-based: 2-3 cases of the same serogroup within 3 months.
  - Community-based: Incidence of the same serogroup above expected in the affected community during a 3-month period.

- **MenB vaccine selection:** No preference between MenB vaccines during outbreaks.

- **Re-evaluation of outbreak status:** After one year without any new reported cases, the risk of meningococcal disease likely returns to baseline.
Next Steps

- Finalization of CDC guidance document for control of meningococcal disease outbreaks.
- Publication of updated guidance document on CDC website, to replace current guidance in Appendix B of ACIP’s “Prevention and Control of Meningococcal Disease” and the interim guidance for MenB outbreaks.
- Continued efforts to improve reporting and collection of epidemiologic data of meningococcal disease outbreaks.
Acknowledgements

State and local health departments

Subject Matter Experts
Alison Arwady  Cody Meissner  Elizabeth Briere
Carol Baker  Barbara Montana  Amanda Cohn
Stephanie Black  Jeffry Moore  Jonathan Duffy
Doug Campos-Outcalt  Paul Offit  Temitope Folaranmi
Paul Cieslak  Georges Peter  Stephen Hadlner
Susan Even  Anuja Rastogi  Susan Hariri
Mary Ferris  Lorry Rubin  Jessica MacNeil
Kathy Harriman  William Schaffner  Stacey Martin
Lee Harrison  David Stephens  Leonard Mayer
Mary Healy  Tina Tan  Lucy McNamara
Rachel Herlihy  Don Weiss  Sarah Meyer
Pete Johnson  Margaret Yacovone  Gina Mootrey
Sarah Kemble  Jane Zucker  Ismael Ortega-Sanchez
Lucia Lee  Alison Albert  John Otshudimea
Martin Luta  Amy Blain  Conrad Quinn
Paul McKinney  Virginia Bowen  Heidi Soeters
Xin Wang
Thank You

For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.