Preventing Invasive Meningococcal Disease: Routine and Special Vaccination Recommendations

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Invasive meningococcal disease (IMD) is a sporadic, uncommon, life-threatening bacterial infection of the cerebrospinal fluid or the blood stream caused by Neisseria meningitidis (N. meningitidis). N. meningitidis is a leading cause of bacterial sepsis and meningitis in the United States (U.S.) and worldwide. Although disease incidence is at historic lows, nationally, the overall case fatality rate for IMD remains between 9% and 12%. Complications from IMD impact up to 20% of survivors and include permanent sequelae such as hearing loss, neurologic damage, and limb/digit loss. Meningococcal disease can also manifest as pneumonia and joint infection.

Meningococcal vaccination is routinely recommended for groups at increased risk for the disease to prevent meningococcal infection and its complications. The Advisory Committee on Immunization Practices (ACIP) recommends meningococcal vaccination for adolescents, persons with certain medical conditions, and persons with increased risk for exposure. In Los Angeles County (LAC), since April 2014, there is a local vaccination recommendation for men who have sex with men (MSM) at elevated risk for meningococcal disease. This article provides information on IMD, disease trends in LAC, vaccination recommendations, and resources.

**Background**
Humans are the only known reservoir for N. meningitidis. Transient nasopharyngeal carriage rates for N. meningitidis can be as high as 10% during the winter and early spring among asymptomatic individuals. The bacteria is transmitted by respiratory droplets or by direct contact with nose or throat secretions from persons colonized with the bacteria.

N. meningitidis is classified into serogroups determined by the chemical and antigenic structure of the bacterial polysaccharide capsule.

**Figure 1. Invasive Meningococcal Disease in LA County, 2010-2014**
Distribution of IMD Cases Since 2010: The most common serogroups are B, C, and Y, but serogroups W-135 and Z have been documented. B and Y cases have been declining since 1995.
To date, thirteen serogroups have been identified. Most human disease is caused by serogroups A, B, C, Y, and W-135. The distribution of the serogroups differs geographically with serogroups B, C, and Y being common in LAC and the U.S. [See Figure 1] In the Caribbean region, Latin America and Europe, serogroups B and C are the predominant serogroups, while serotypes A, X, and W are more common in Africa. Additionally, some serogroups are more common among certain age-groups. In the U.S., serogroup B causes 60% of the IMD that occurs in children through 59 months of age, while serogroups C, Y, and W cause 73% of the IMD among persons ≥11 years of age.

**Risk Factors for Invasive Meningococcal Disease**

Epidemiological studies have linked bacterial and host characteristics as well as environmental and behavioral factors to the risk of developing IMD. Encapsulated strains are more virulent than non-encapsulated strains. Host factors, such as complement pathway deficiencies and anatomic or functional asplenia including sickle cell anemia increase the risk for IMD. Recent epidemiologic studies support HIV-infection as an independent risk factor for IMD. Additionally, antecedent viral infections and chronic underlying illnesses may predispose to IMD.

Environmental and behavioral factors that are associated with an increased risk of developing IMD include: smoking (actively or passively), household crowding, travel to a country with increased exposure risk for IMD, or occupational exposure such as working in a laboratory that processes specimens for *N. meningitidis* testing. College freshmen living in dormitories appear to be at higher risk for meningococcal disease. In 2014, two outbreaks of serogroup B disease among students at two universities on opposite coasts of the U.S. were documented. Additionally, alcohol consumption and bar patronage has been found to be correlated with enhanced transmission of meningococcal disease during outbreaks.

**Invasive Meningococcal Disease Surveillance in Los Angeles County**

The incidence of IMD in LAC has declined over the last two decades, from 0.60 per 100,000 (1995-99) to 0.22 per 100,000 (2009-14). This follows declining national trends of IMD incidence, which dropped from 1.23 per 100,000 in 1995 to 0.18 per 100,000 in 2012. The overall case fatality rate for IMD in LAC since 1995 is 12.5% with 56 deaths occurring in the past 20 years. Despite the drop in IMD incidence, the case fatality rate has increased from 11% (1995-99) to 19.4% (2009-14) (unpublished data).

Since 1995 nearly all LAC IMD cases have been classified as sporadic (99%) with very few secondary cases occurring associated with clusters or outbreaks (1%). Two-thirds of documented clusters and outbreaks have been attributed to serogroup C disease and the remaining were serogroup B. The most recent clusters and outbreaks occurring since 2011 have all been attributed to serogroup C disease, including those associated with the homeless community and travel to Tijuana.

**Invasive Meningococcal Disease among Men Who Have Sex With Men**

In fall 2012, New York City (NYC) Department of Health and Mental Hygiene (DOHMH) reported an outbreak of serogroup C IMD cases among MSM from 2010-12. Soon after, in December 2012, LAC Department of Public Health (DPH) documented two male serogroup C IMD cases who identified themselves as MSM. In response, DPH initiated enhanced surveillance of IMD to document the incidence of IMD among MSM and to detect any epidemiologic linkages among MSM cases.
Since October 2012, DPH has collected the gender of sex partner for all cases of IMD to determine the proportion that are MSM and to evaluate commonalities between cases such as party attendance, use of social applications (apps) for dating, common bath houses, and linkage to travel to NYC. MSM cases had serogroup testing as well as pulse field gel electrophoresis (PFGE) analysis to identify any genetic linkages between LAC cases and NYC IMD MSM cases.

From October 2012 to December 2014, there were 35 IMD cases in LAC and 13 identified themselves as MSM. The median age of cases among MSM was 28 years [range: 21-50 years]. Among the 13 MSM cases, 4 cases were HIV-positive. There were 5 fatal cases in MSM and 2 were among HIV-positive MSM. Most cases were serogroup C. [See Figure 2]

Of ten serogroup C IMD MSM cases, two IMD cases had identical PFGE patterns to each and also had a PFGE pattern that been documented in the 2010-2012 NYC MSM IMD outbreak. DPH case investigations did not support any cluster or outbreak of IMD among MSM in LAC or a connection to the NYC outbreak. Though PFGE has been useful in augmenting and supporting common source exposures for food-borne and healthcare-related outbreaks, it has not been frequently used and remains challenging to interpret with respect to IMD investigations. PFGE results should always be interpreted in conjunction with the epidemiological case investigation.

Review of MSM IMD cases in LAC since October 2012 shows an increased risk of IMD among MSM. The incidence of IMD among MSM in LAC is estimated to be 2.39 cases per 100,000 population per year.13 [See Table 1] This is 9 times the rate in non-MSM adult males in LAC (0.26 cases per 100,000 per year) and 11 times the rate among all LAC adults (0.21 cases per 100,000 per year). The rate among MSM also is comparable to college freshmen and college dormitory residents, and about half the rate of college freshmen who live in dormitories, a group for whom the ACIP recommends meningococcal vaccination.5

Meningococcal Vaccines
Six meningococcal vaccines are licensed by the Food and Drug Administration to provide protection against meningococcal serogroups that cause disease in the U.S.5,14-17 [See Table 2]

Advisory Committee on Immunization Practices
Meningococcal Vaccination Recommendations
The ACIP recommends routine vaccination for adolescents aged 11 through 18 years and for persons at increased risk for meningococcal disease. [See Figure 3]

For adolescents, a dose of meningococcal quadrivalent conjugate vaccine (MenACWY) is routinely recommended for adolescents 11 through 12 years of age, with a follow-up booster dose at age 16 years.3 Adolescents who receive their first dose of meningococcal vaccine between 13 and 15 years of age should receive a booster dose at 16 through 18 years of age. If the first dose is received after the adolescent turns 16 years of age, a booster dose is not needed. Adolescents who are HIV positive should receive 2 doses at 11 or 12 years of age, separated by 2 months and a booster dose at 16 years of age.3

The ACIP recommends routine vaccination of persons aged ≥2 months at increased risk for meningococcal disease. This includes individuals ≥2 months of age with medical conditions such as anatomical or functional asplenia including sickle cell disease or persistent complement component deficiency. These persons at highest-risk for IMD should be routinely vaccinated with conjugate vaccine as early as 2 months of age, using any of the available conjugate vaccine products licensed for their age group. Follow-up booster doses are required as long as the increased-risk status exists.5

Vaccination is also recommended for:
• Individuals ≥2 months of age who are at risk during a community outbreak attributable to a vaccine-containing serogroup
• Under or unvaccinated first-year college students living in residence halls, military recruits, and microbiologists with occupational exposure.
• Individuals ≥9 months of age who travel to or reside in countries in which meningococcal disease is hyperendemic or epidemic.

Of note, because the meningococcal quadrivalent polysaccharide vaccine (MPSV4) is the only licensed product for persons 56 years of age and older, it should be used for persons of that age group who are at increased risk for IMD,

Table 1. Estimated Incidence of Invasive Meningococcal Disease by Population Group, October 2012-September 2014

<table>
<thead>
<tr>
<th>POPULATION</th>
<th>INCIDENCE (PER 100,000/YR.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAC non-MSM adults (≥18 yrs.)</td>
<td>0.21</td>
</tr>
<tr>
<td>LAC male non-MSM (≥18 yrs.)</td>
<td>0.26</td>
</tr>
<tr>
<td>LAC MSM (≥18 yrs.)</td>
<td>2.39</td>
</tr>
<tr>
<td>U.S. College freshmen</td>
<td>1.9</td>
</tr>
<tr>
<td>U.S. College freshmen living in dormitories</td>
<td>5.1</td>
</tr>
</tbody>
</table>

continued on page 4 >
### Table 2. Meningococcal Vaccines Licensed for Use in the United States

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Trade Name and Manufacturer</th>
<th>Licensure Year</th>
<th>Age Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningococcal Quadrivalent Polysaccharide Vaccine (MPSV4)</td>
<td>Menomune Sanofi Pasteur</td>
<td>1981</td>
<td>• FDA-approved for use in persons 2 years of age and older</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• Protects against serogroups A, C, W, and Y</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• Ideal for vaccination due to one-time exposure, such as for persons travelling to areas where meningococcal disease outbreaks frequently occur</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Only meningococcal vaccine licensed for use in persons 56 years of age and older</td>
</tr>
<tr>
<td>Meningococcal Quadrivalent Conjugate Vaccine (MenACWY-D)</td>
<td>Menactra Sanofi Pasteur</td>
<td>2005</td>
<td>• FDA-approved for use in persons 9 months through 55 years of age</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Routinely recommended for adolescents 11 through 12 years of age, with a follow-up booster dose at age 16 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Protects against serogroups A, C, W, and Y</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Conjugated to a protein that enables it to elicit immunologic memory</td>
</tr>
<tr>
<td>Meningococcal Quadrivalent Conjugate Vaccine (MenACWY-CRM)</td>
<td>Menevo Novartis Vaccines</td>
<td>2010</td>
<td>• FDA-approved for use in persons 2 months through 55 years of age</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Routinely recommended for adolescents 11 through 12 years of age, with a follow-up booster dose at age 16 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Protects against serogroups A, C, W, and Y</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Conjugated to a protein that enables it to elicit immunologic memory</td>
</tr>
<tr>
<td>Combination Haemophilus Influenzae Type b (Hb) and Bivalent Meningococcal Conjugate Vaccine (Hib-MenCY-TT)</td>
<td>Menhibrix GlaxoSmithKline</td>
<td>2012</td>
<td>• FDA-approved as a 4-dose series for children 6 weeks through 18 months of age</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Protects against Hib and meningococcal serogroups C and Y</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Conjugated to a tetanus toxoid protein to enhance immunogenicity against Hib and meningococcal components</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Does not provide immunity against tetanus</td>
</tr>
<tr>
<td>Meningococcal Serogroup B (Factor H Binding Protein)</td>
<td>Trumenba Pfizer, Inc.</td>
<td>2014</td>
<td>• FDA-approved for use in persons 10 years through 25 years of age</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Protects against serogroup B meningococcal disease</td>
</tr>
<tr>
<td>Meningococcal Group B Vaccine (Recombinant, Adsorbed)</td>
<td>Bexsero Novartis</td>
<td>2015</td>
<td>• FDA-approved for use in persons 10 years through 25 years of age</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Protects against serogroup B meningococcal disease</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• Two intramuscular doses should be given at least one month apart</td>
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</table>

**Figure 3. Meningococcal Vaccine Recommendations-ACIP and LA County DPH**

**ACIP recommends meningococcal vaccination for the following groups:**

- Routine vaccination of adolescents aged 11 through 18 years
- Routine vaccination of persons aged ≥2 months at increased risk for meningococcal disease including:
  - Individuals ≥2 months of age with medical conditions such as anatomical or functional asplenia including sickle cell disease or persistent complement component deficiency
  - Under or unvaccinated first-year college students living in residence halls, military recruits, and microbiologists with occupational exposure
  - Individuals ≥9 months of age who travel to or reside in countries in which meningococcal disease is hyperendemic or epidemic
  - Individuals ≥2 months of age who are at risk during a community outbreak attributable to a vaccine serogroup

**In addition to ACIP recommended groups, LAC DPH recommends routine meningococcal vaccination for:**

- HIV-infected gay/MSM
- Gay/MSM, regardless of HIV status, who regularly have close or intimate contact with multiple partners or who seek partners through the use of digital applications (“apps”), particularly those who share cigarettes/marijuana or use illegal drugs.
when only one dose of vaccine is required. In instances where persons of that age group have already received a prior dose of a conjugate meningococcal vaccine or where such persons will receive booster doses after age 55 years, the ACIP recommends off-label use of a conjugate meningococcal vaccine (MenACWY-D or MenACWY-CRM).3

Finally, the ACIP voted during their winter 2015 meeting to recommend the use of either of the two recently licensed meningococcal serogroup B vaccines (Trumenba and Bexsero) in persons at high risk for IMD. These vaccines are licensed for use in persons between 10 and 25 years of age, only. Official guidance regarding their use, including age indications, are expected to be published in an upcoming issue of Morbidity and Mortality Weekly Report.

LA County Department of Public Health Meningococcal Vaccine Recommendations for Men Who Have Sex with Men
In addition to ACIP recommended groups, DPH recommends meningococcal vaccination for MSM at increased risk for IMD. The vaccine should be offered to:

- All HIV-infected gay/MSM
- Gay/MSM, regardless of HIV status, who regularly have close or intimate contact with multiple partners or who seek partners through the use of digital applications (“apps”), particularly those who share cigarettes/marijuana or use illegal drugs. [See Figure 3]

DPH is providing meningococcal vaccine at no-cost for individuals who are uninsured or who have inadequate insurance coverage for vaccines.18 The California Department of Public Health supports the vaccine recommendation for HIV-positive MSM and MSM in risk groups for IMD and has made meningococcal conjugate vaccine for adults 19 years of age and older available through special Section 317 funding to local county public departments throughout California.19, 20 The NYC DOHMH recommends the vaccination of MSM at high risk for IMD as well.21

Invasive Meningococcal Disease Resources
The following resources are available from the DPH and other public health entities:

- Vaccine resources for health professionals: http://www.publichealth.lacounty.gov/ip/DiseaseSpecific/Meningococcal.htm
- Meningococcal disease for health professionals including a weekly disease count: http://publichealth.lacounty.gov/acd/Mening.htm
- “Stop Before You Swap” meningitis resources for MSM including disease and risk-reduction information as well as vaccination locations: http://publichealth.lacounty.gov/ip/DiseaseSpecific/dontswap.htm
- LAC DPH Health Update on Vaccination of High Risk MSM to Prevent IMD: http://publichealth.lacounty.gov/eprp/Health%20Alerts/Meningitis%20Prevention%20MSM%202015HAN-HealthUpdate_0215.pdf

Conclusion
While the incidence of invasive meningococcal disease in LAC has been declining, the disease remains a cause of significant concern. Case-fatality rates are as high as 12% and up to 20% of survivors will have permanent disease sequelae. Providers are strongly encouraged to routinely vaccinate adolescents, as well as other individuals who are at increased risk for infection and complications.

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REFERENCES
9. CDC Health Advisory. Meningococcal disease outbreak at Princeton University and a recent outbreak at the University of California, Santa Barbara (UCSB). Distributed via the CDC Health Alert Network. November 27, 2013, 10:30 ET (10:30 AM ET) CDCHAN-00357.
Overall, there have been over 23,500 cases of Ebola virus disease (EVD) in Guinea, Liberia and Sierra Leone, with over 9,500 reported deaths. Though markedly lower than the epidemic’s peak, new confirmed EVD cases continue to occur in the affected countries of West Africa. Many of the cases arise from unknown chains of transmission, primarily stemming from affected individuals unable or reluctant to seek treatment. Ongoing community engagement remains both a challenge and a priority.

While there have been no new cases of EVD in the U.S. for several months, investments to improve the nation’s level of preparedness continue. In the U.S., 55 hospitals are designated by the Centers for Disease Control and Prevention (CDC) as “Ebola Treatment Centers,” each capable of providing comprehensive care to people diagnosed with EVD. In California, eight hospitals have received this designation—two in LAC. Throughout the nation, federal, state and local public health and health care agencies are working with health care systems, facilities and providers to ensure a coordinated response when and if an EVD response is necessary. In LAC, the DPH took the lead in working closely with public and private hospitals to ensure that health care partners are well informed and ready to respond to a possible EVD case through issuing health care guidance via electronic messaging, conference calls, and in-person meetings.

In addition, DPH—together with the local Emergency Medical Services Agency—co-leads a multi-sector health care coalition to present issues and coordinate resources for health care partners, providers and facilities.

Through CDC supplemental funding to the Healthcare Preparedness Program, Public Health Emergency Preparedness Program, and Epidemiology and Lab Capacity Program, DPH and the Department of Health Services are working together to develop collaborative plans, training, exercises, and additional resources to maximize the momentum created in 2014 to further improve public health preparedness for Ebola and other pathogens that may threaten public health.

Visit the Department of Public Health’s Ebola Readiness page to find latest updates at: www.publichealth.lacounty.gov/media/ebola.htm
California is just recovering from a large measles outbreak that was triggered by an exposure of measles at the Disneyland Parks in December 2014. As of March 30, 2015, 28 LAC residents had been infected and more cases may occur among people who have had contact with persons in the initial wave of infections. Although the current outbreak may be coming toward its end, it’s important to remember that each year we have cases of measles in LAC, most of which are related to international travel.

Take advantage of recent public awareness regarding measles to strongly encourage vaccination for all unvaccinated patients and staff. Consider recalling patients who have not received recommended doses of measles-containing vaccines to the clinic for vaccination.

**Additional Recommendations**

To help protect patients and staff, health care providers are encouraged to take the following actions:

- Consider measles when evaluating any patient who has a fever and a rash that starts on the head and spreads down to the rest of the body (descending rash).
- IMMEDIATELY institute respiratory and airborne precautions for all persons with a measles-like rash and fever.
- Reduce exposures: schedule patients for the end of the day and have them enter via a separate entrance. Do not send patients to the Emergency Department (ED) unless they require hospitalization and contact the ED first.
- Obtain specimens for confirmation of diagnosis: blood for serology, and throat swab and urine specimen for PCR.
- IMMEDIATELY report suspect cases to the Los Angeles County Department of Public Health Morbidity Central Reporting Unit at (888) 397-3993. After 5 pm or on weekends, call: (213) 974-1234. Do not wait for laboratory confirmation.
  - Long Beach suspect cases can be reported to Long Beach Health and Human Services at (562) 570-4302 during business hours or (562) 435-6711 during non-business hours.
  - Pasadena suspect cases can be reported to the Pasadena Public Health Department at (626) 744-6043.
- Offer immunoglobulin to all high risk persons, including immunocompromised persons, within 6 days of exposure. Protect those who are not immunocompromised but are not immune to measles by vaccinating within 72 hours following exposure. Provide a list of exposed staff and patients to the Public Health Department.

**Resources**

The DPH has compiled a variety of educational resources to help clinicians and their staff promote vaccination, diagnose and report cases, and provide appropriate post-exposure prophylaxes.

- Visit the Los Angeles County Department of Public Health’s measles webpage at http://publichealth.lacounty.gov/media/measles/index.htm for outbreak updates and links to resources for providers, schools, and patients.
- Download measles alerts; posters; educational materials; and guidelines regarding measles vaccination, testing, diagnosis, and treatment at http://publichealth.lacounty.gov/ip/MeaslesOutbreakHCP.htm
- Watch the webinar, “Measles Update: A Primer for Health Care Providers.” The archive has been approved for AMA PRA Category 1 Credit. Topics include the presentation of measles and modified measles, laboratory testing, treatment, prophylaxis, reporting and strategies for prevention. http://publichealth.lacounty.gov/ip/MeaslesWebinar.htm
- Sign up for the Los Angeles Health Alert Network to receive updates regarding communicable disease outbreaks, immunizations, drug shortages and recalls, and other important public health issues. Join at http://publichealth.lacounty.gov/lahan/
Reportable Diseases & Conditions
Confidential Morbidity Report
Morbidity Unit (888) 397-3993
Acute Communicable Disease Control
(213) 240-7941
Sexually Transmitted Disease
Confidential Morbidity Report
(213) 744-3070
www.publichealth.lacounty.gov/dhsp/ReportCase.htm (web page)
Sexually Transmitted Disease
Confidential Morbidity Report
(213) 744-3070
www.publichealth.lacounty.gov/dhsp/ReportCase/STD_CMR.pdf (form)
Adult HIV/AIDS Case Report Form
For patients over 13 years of age
Division of HIV and STD Programs
(213) 351-8196
www.publichealth.lacounty.gov/dhsp/ReportCase.htm
Pediatric AIDS Surveillance Program
(213) 351-8153
Must first call program before reporting
www.publichealth.lacounty.gov/dhsp/ReportCase.htm
Tuberculosis Suspects & Cases
Confidential Morbidity Report
Tuberculosis Control (213) 745-0800
www.publichealth.lacounty.gov/tb/forms/cmrd.pdf
Lead Reporting
No reporting form. Reports are taken over the phone.
Lead Program (323) 869-7195
Animal Bite Report Form
Veterinary Public Health (877) 747-2243
www.publichealth.lacounty.gov/vet/biteintro.htm
Animal Diseases and Syndrome
Report Form
Veterinary Public Health (877) 747-2243
www.publichealth.lacounty.gov/vet/disintro.htm