Considerations for Use of MenACWY Vaccines In HIV-Infected Persons

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Background

- **HIV is an established risk factor for several bacterial infections**
- **A growing body of evidence supports an increased risk for meningococcal disease among HIV-infected persons**
- **ACIP does not currently include HIV-infected persons in the recommendations for routine vaccination of persons at increased risk of meningococcal disease**
  - If a HIV-infected person aged ≥2 years is vaccinated they should receive a 2 dose primary series

February 2016 ACIP Meeting

- **Reviewed available evidence for**
  - Increased risk of meningococcal disease among HIV-infected persons
  - MenACWY vaccine response in HIV-infected persons
  - Programmatic and other considerations

Growing Body of Evidence of Increased Risk Among HIV-Infected Persons

Years	Site	Population	# Cases	Risk
1996-1999	Atlanta[1]	18–45 years	132	24-fold increased risk
2003-2007	South Africa[2]	All ages	504	11-fold increased risk
2000-2008	U.S. – ABCs[3]	25–64 years	491	13-fold increased risk
2000-2011	U.S. – NYC[4]	15–64 years	265	10-fold increased risk
2011-2013	England[5]	All ages	2353	5-fold increased risk

[1]Stephens DS, Hajjeh RA, Baughman WS, Harvey RC, Wenger JD, Farley MM. Sporadic meningococcal disease in adults: results of a 5-year population-based study. Ann Intern Med. 1995: 123:937-40

[2]Cohen C, Singh E, Wu HM, Martin S, de Gouveia L, Klugman KP, et al; Group for Enteric Respiratory and Meningeal Disease Surveillance in South Africa (GERMS-SA). Increased incidence of meningococcal disease in HIV-infected individuals associated with higher case-fatality ratios in South Africa. AIDS. 2010; 24:1351-60.

[3]Harris CM et al. Meningococcal Disease in Patients with HIV Infection-A Review of Cases Reported Through Active Surveillance in the United States, 2000-2008. *Manuscript Under Preparation.*

[4]Miller L, Arakaki L, Ramautar A, Bodach S, Braustein S, et al. Elevated Risk for Invasive Meningococcal Disease Among Persons with HIV. Ann Intern Med. 2014; 160:30-38.

[5]Simmons RD. et al. Risk of invasive meningococcal disease in children and adults with HIV in England: a population-based cohort study. BMC Med. 2015; 13: 297.

Summary of Evidence of Increased Risk Presented in February 2016

- **Increased risk of meningococcal disease in HIV-infected persons**
  - Among HIV-infected persons, low CD4 count or high viral load further increases risk
  - Similar increase in risk for both males and females
  - Overall, risk declining along with meningococcal disease incidence in the United States
- **Meningococcal disease in HIV-infected persons primarily due to serogroups C, W, and Y**
- **Mixed data on case-fatality ratio**
  - More recent studies show a lower CFR in HIV-infected persons

Summary of MenACWY Response Data Presented in February 2015

- **Seroresponse to MenACWY-D conjugate vaccine in HIV-infected adolescents suppressed compared to healthy adolescents and HIV-infected 2- to 10-year-olds**
  - Low CD4 count or high viral load suppresses response further
- **Immune response to MenACWY-D wanes rapidly**
  - Boost response seen to second dose, however duration of protection still an issue

Siberry GK, et al. Phase I/II, open-label trial of safety and immunogenicity of meningococcal polysaccharide diphtheria toxoid conjugate vaccine in human immunodeficiency virus-infected adolescents. PIDJI. 2010;29(5):391-396.

Lujan-Zilbermann J, et al. Immunogenicity and safety of 1 vs 2 doses of quadrivalent meningococcal conjugate vaccine in youth infected with HIV. J Pediatr. 2012;161(4):676-681 e672.

Siberry GK, et al. Safety and immunogenicity of quadrivalent meningococcal conjugate vaccine in 2- to 10-year-old HIV-infected children. PIDJ. 2012;31(1):47-52.

Programmatic Considerations

- **Approximately 1 million persons living with HIV in the U.S.[1]**
  - 40,000 new HIV infections each year[1]
- **About 50% of persons diagnosed with HIV receive regular HIV care[2]**
  - Of those retained in care, 89% are prescribed antiretroviral therapy and 77% achieve viral suppression[2]
- **For HIV-infected persons in care:**
  - HIV clinics may administer other vaccines recommended for HIV-infected persons
  - May be more likely to have CD4 counts and viral loads favorable for immunogenicity

[1] Centers for Disease Control and Prevention. *HIV Surveillance Report, 2014*. http://www.cdc.gov/hiv/library/reports/surveillance
[2] http://www.cdc.gov/hiv/prevention/programs/pwp/linkage.html

Meningococcal Disease Among HIV-Infected Men Who Have Sex With Men (MSM)

- **Risk for meningococcal disease in MSM was discussed in detail during February's ACIP meeting**
- **Of meningococcal disease cases among MSM for whom HIV status is known, the majority (59%) are HIV-infected**
  - Makes disentangling the relative contribution of HIV and MSM status to the increase in risk challenging in MSM populations
- **Vaccinating HIV-infected persons offers an opportunity to also potentially impact meningococcal disease risk among MSM**

Summary

- **A growing body of evidence demonstrates an increased risk of meningococcal disease among HIV-infected persons**
  - Between 5- to 24-fold increased risk for meningococcal disease in HIV-infected persons
  - In HIV-infected persons, risk primarily due to serogroups C, W, and Y
- **Suboptimal vaccine response and programmatic challenges may limit the impact of vaccination on disease burden in HIV-infected persons**
- **HIV-infected persons represent a relatively small, defined population who receive care in a specialized medical setting**

Work Group Considerations

- **Current consideration is for MenACWY conjugate vaccine only, not serogroup B meningococcal vaccine**
  - In HIV-infected persons, risk primarily due to serogroups C, W, and Y
  - No safety or immunogenicity data is available for use of serogroup B meningococcal vaccines in HIV-infected persons
- **Increased risk from HIV-infection is life long, therefore regular booster doses would be recommended for HIV-infected persons**
  - Current booster recommendations: 3 years if age <7 years at previous dose and 5 years if age ≥7 years at previous dose

Work Group Discussion

- **Strong support for including HIV-infected persons in groups at increased risk of meningococcal disease**
  - Evidence of increased risk of meningococcal disease
  - Benefit to targeted group
  - Recognition of suboptimal vaccine response and duration of protection
- **Differing opinions on Work Group about the age at which to begin vaccination of HIV-infected persons (i.e., 2 months or 11 years of age)**
  - Majority of Work Group members support vaccinating HIV-infected persons aged ≥2 months

Including HIV-Infected Children 2 months–10 Years In Recommendation

- **Pros:**
  - Harmonizes with current ACIP recommendations for use of MenACWY vaccine in persons with functional/anatomic asplenia or complement component deficiencies
  - Small number of HIV-infected children in U.S. (not a burdensome or expensive recommendation)
  - Biologically it is unlikely that increased risk of meningococcal disease in HIV-infected persons differs for children and adults
  - hSBA titers following 1 or 2 doses of MenACWY vaccine in HIV-infected children aged 2-10 years is higher than in HIV-infected adolescents 11-24 years of age

Including HIV-Infected Children 2 months–10 Years In Recommendation

- **Cons:**
  - Depending upon timing of doses, may not fully harmonize with ACIP/AAPs recommendations for use of MenACWY vaccines at age 11-12 years
  - Would require multiple doses (primary series + boosters) over the child's lifetime
  - Limited data to document burden of disease in HIV-infected children in U.S.

Policy Options

- **Human Immunodeficiency Virus (HIV)-infected persons aged ≥2 months should routinely receive MenACWY vaccine* (Category A)**

  OR

- **Human Immunodeficiency Virus (HIV)-infected persons aged ≥11 years should routinely receive MenACWY vaccine** (Category A)**

*Includes MenACWY-D (Menactra®), MenACWY-CRM (Menveo®), and Hib-MenCY-TT (MenHibrix®)
**Includes MenACWY-D (Menactra®) and MenACWY-CRM (Menveo®)

Guidance for Use of MenACWY for HIV-Infected Persons

- **Persons aged ≥2 years with HIV who have not been previously vaccinated should receive a two dose primary series of MenACWY (0, 2 months)**
  - Multi-dose schedule for children aged <2 years
- **Persons with HIV who have been previously vaccinated with one dose of MenACWY should receive a second dose at the earliest opportunity*, and then continue to receive boosters at the appropriate interval**
  - Current booster recommendations: 3 years if age <7 years at previous dose and 5 years if age ≥7 years at previous dose

*8 week minimum interval between doses