

Meningococcal Disease and Vaccine Response In HIV-Infected Persons

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February 26, 2014

Acknowledgements

- ❑ **Don Weiss – New York City Department of Health and Mental Hygiene**
- ❑ **Active Bacterial Core surveillance (ABCs) Principal Investigators and Surveillance Officers**
- ❑ **Henry Wu**

Background

- ❑ **HIV is an established risk factor for several bacterial infections**
- ❑ **Current incidence of meningococcal disease and HIV infection in the United States has made evaluations of risk challenging**
- ❑ **HIV infection is not an indication for routine MenACWY vaccination in the current ACIP recommendations, however if a HIV-infected person is vaccinated they should receive a 2-dose primary series**

Meningococcal Disease in HIV-Infected Persons

- ❑ **Surveillance data from the 8-county metropolitan area of Atlanta from 1988 to 1993 found HIV-infected adults had a nearly 24-fold increased risk for meningococcal disease¹**
- ❑ **GERMS – South Africa study²**
 - 45% of 308 meningococcal disease patients were HIV-infected
 - Age adjusted RR 11.3 (95%CI 8.9-14.3)
 - Case-fatality ratio among HIV-infected cases was 20% vs. 11% among HIV-uninfected cases

¹Stephens 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

²Cohen 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. **4**

Evaluation of Risk for Meningococcal Disease Among Persons Infected With HIV – Active Bacterial Core surveillance (ABCs)

- ❑ **Chart review of HIV-infected meningococcal disease cases reported through ABCs from 2000-2008**
 - Incidence calculations limited to cases that met the CDC-AIDS surveillance case definition
- ❑ **32 HIV-infected cases reported during 2000-2008**
 - 25% serogroup B, 39% serogroup C, 29% serogroup Y
- ❑ **9 additional HIV-infected cases reported during 2009-2012**

HIV Related Clinical Data for Meningococcal Cases with HIV infection Obtained from Expanded Chart Reviews, All Ages (N=32)

| | N (%) |
|--|---------|
| Concurrent CD4 count available | 22 (69) |
| ≥500 cells/μL | 7 (32) |
| 200-499 cells/μL | 9 (41) |
| <200 cells/μL | 6 (27) |
| History of AIDS defining condition | 12 (38) |
| CDC AIDS surveillance case definition met | 18 (56) |
| Reported HAART use | |
| Currently taking at time of presentation | 16 (61) |
| Previous use | 7 (27) |
| Never use | 3 (12) |
| Currently taking opportunistic infection prophylaxis at the time of presentation | 6 (19) |

Increased Incidence of Meningococcal Disease in Persons Meeting the CDC-AIDS Case Definition, ABCS, 2000-2008

| | CDC-AIDS criteria met | | CDC-AIDS criteria not met | |
|-------|-----------------------|---------------------|---------------------------|---------------------|
| | Cases | Incidence (95% CI)* | Cases | Incidence (95% CI)* |
| Total | 17 | 3.48 (1.97-5.62) | 474 | 0.28 (0.25-0.30) |

*per 100,000 person years

RR = 12.6 (95%CI 7.9-20.2)

Evaluation of Risk for Meningococcal Disease Among Persons Infected With HIV – New York City

- ❑ **Match of meningococcal disease surveillance data from 2000-2011 to death and HIV registries in New York City**
 - Age-matched case-control analysis including a subset of HIV-infected cases with CD4 count and viral load measurements near the time of meningococcal disease
- ❑ **40 HIV infected cases reported during 2000-2011**
 - 33% serogroup C, 48% serogroup Y

Incidence of Meningococcal Disease in Persons Aged 15-64 Years, New York City, 2000-2011

| | HIV-infected (Incidence per 100,000) (n=40) | HIV-uninfected (Incidence per 100,000) (n=223) | Risk Ratio (95% CI) |
|-------------------------|--|---|--------------------------------|
| Incidence per 100,000 | 3.4 | 0.34 | 10.0 (7.2, 14.1) |
| Case Fatality Ratio (%) | 10 | 23 | |

Declining Risk of Meningococcal Disease Among Persons Aged 15-64 Years, New York City, 2000-2011

| Interval | HIV-infected (Incidence per 100,000) | HIV-uninfected (Incidence per 100,000) | Risk Ratio (95% CI) |
|---------------------|--|--|------------------------|
| 2000-2002 (n=78) | 4.7 | 0.41 | 11.4 (6.2-21.1) |
| 2003-2005 (n=69) | 4.2 | 0.35 | 11.8 (6.4-22.0) |
| 2006-2008 (n=71) | 3.3 | 0.36 | 8.9 (4.6-17.4) |
| 2009-2011 (n=45) | 1.9 | 0.23 | 8.2 (3.5-19.3) |

Incidence of Meningococcal Disease by Gender in Persons Aged 15-64 Years, New York City, 2000-2011

| Gender | HIV-infected (Incidence per 100,000) | HIV-uninfected (Incidence per 100,000) | Risk Ratio (95% CI) |
|--------|--|--|------------------------|
| Men | 3.6 | 0.29 | 12.2 (8.1, 18.5) |
| Women | 2.9 | 0.38 | 7.6 (4.0, 14.5) |

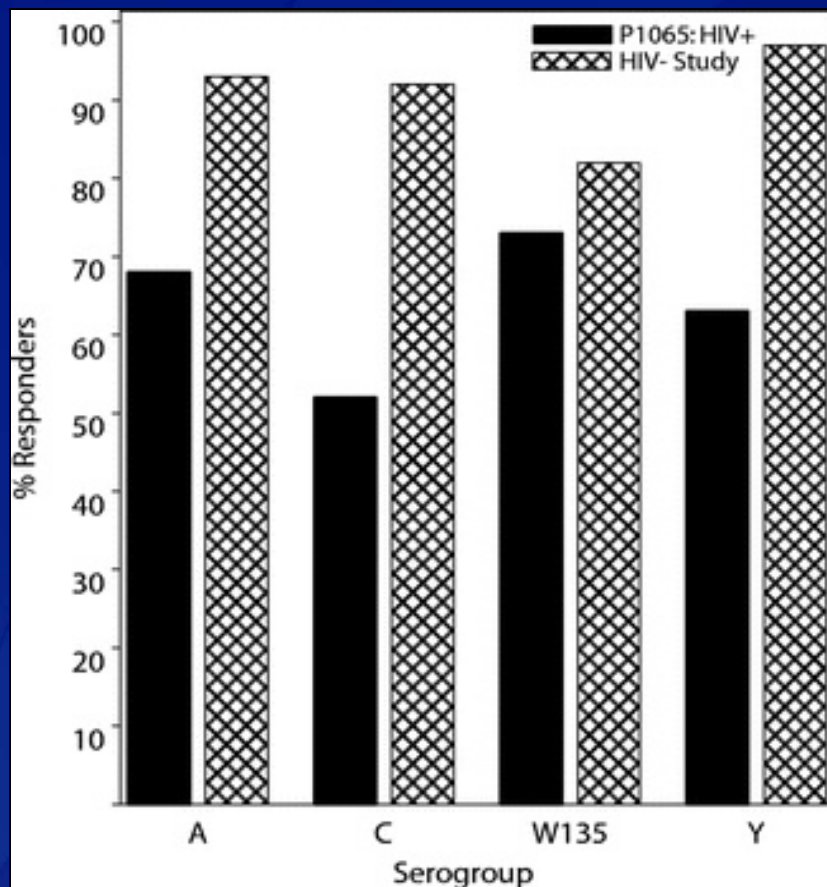
Increased Risk for Meningococcal Disease Among HIV-Infected Persons, New York City, 2005-2011

| | Case Patients with Meningococcal Disease and HIV (n) | Control Patients (HIV Only) (n) | Matched Odds Ratio (95% CI) |
|--------------------------------|--|---------------------------------|-----------------------------|
| CD4⁺ Count | | | |
| ≥0.200x10 ⁹ cells/L | 6 | 35 | Ref |
| <0.200x10 ⁹ cells/L | 10 | 13 | 5.3 (1.4-20.4) |
| HIV Viral Load | | | |
| 0-399 copies/mL | 4 | 24 | Ref |
| ≥400 copies/mL | 10 | 18 | 4.5 (0.9-22.2) |

Summary

- ❑ **Increased incidence of meningococcal disease in HIV-infected persons**
 - Among HIV-infected persons, low CD4 count or high viral load increases risk
- ❑ **Risk is declining along with meningococcal disease incidence in the United States**
- ❑ **Mixed data on case-fatality ratio**

Rates of Response (≥ 4 -Fold Increase in rSBA Titer) to a Single Dose of MenACWY-D at Week 4 by Serogroup in HIV-Infected and Healthy Adolescents



P1065 Study Population:

- 11 to 24 years of age
- 324 subjects enrolled
- 305 had entry and week 4 serology results

≥ 4 -fold increase in rSBA titer at week 4:

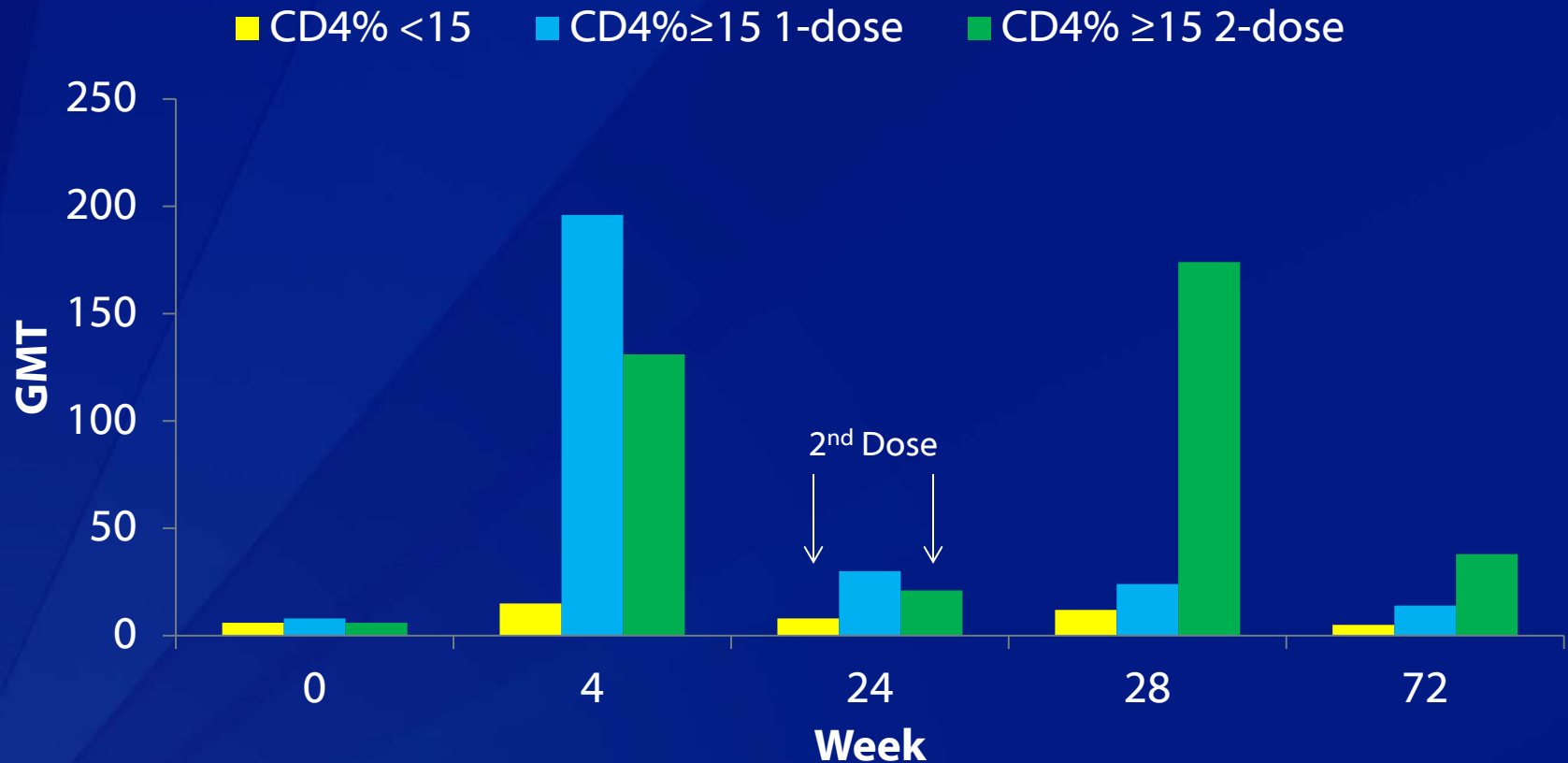
- Serogroup A: 68%
- Serogroup C: 52%
- Serogroup W: 73%
- Serogroup Y: 63%

Multivariable Logistic Regression Results for Immunogenicity Response to Serogroup C as Predicted by Clinical Characteristics

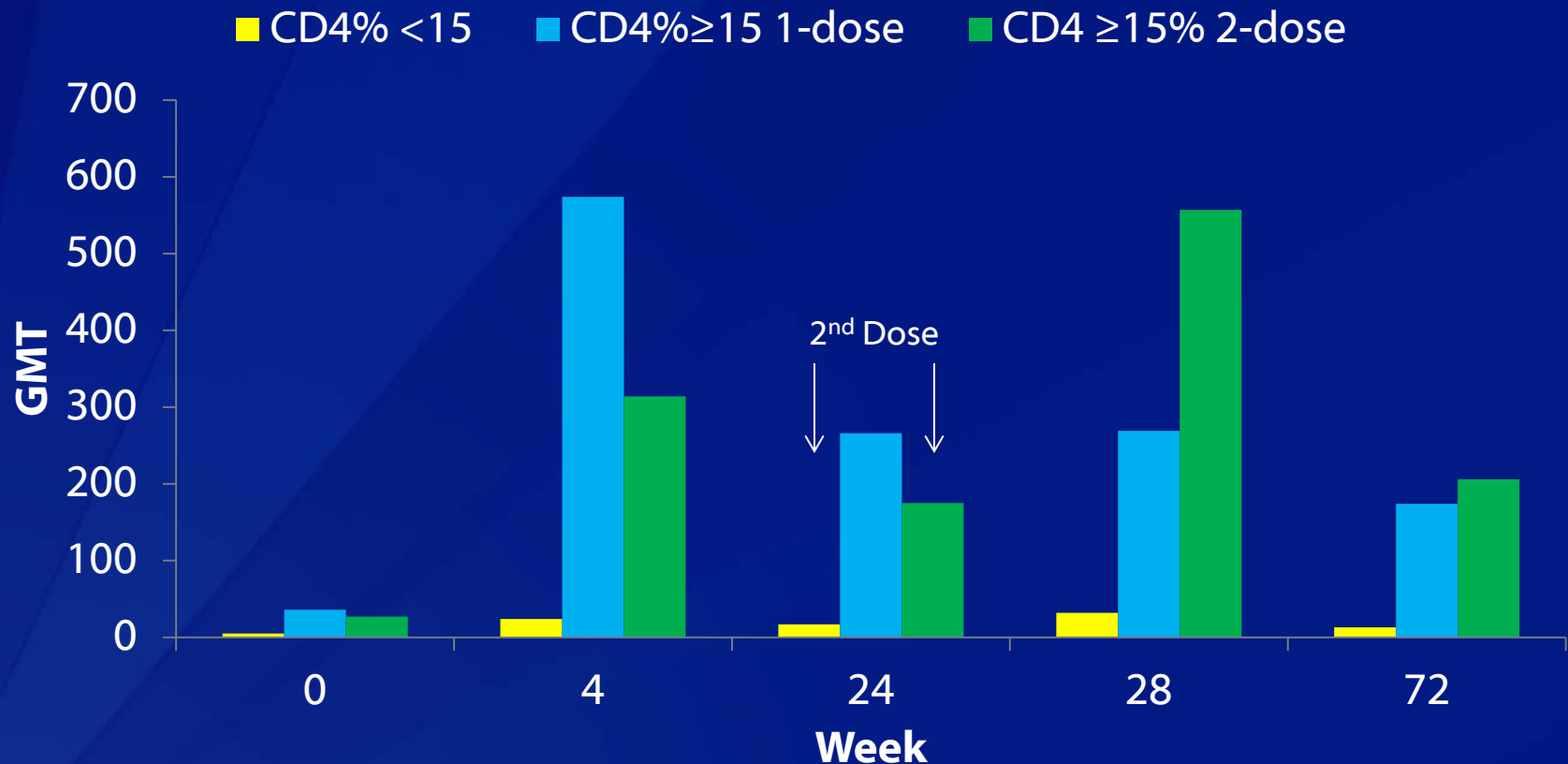
| Predictor | Adjusted Odds Ratio for Response | 95% CI | P value |
|-----------------------------|----------------------------------|--------------|---------|
| CD4 stratum | | | 0.003 |
| <15% | 0.14 | (0.04, 0.45) | |
| 15-<25% | 0.61 | (0.36, 1.04) | |
| ≥25% | 1.00 | Ref | |
| Viral load: (copies/mL) | | | 0.005 |
| <400 | 1.00 | Ref | |
| 400-10,000 | 0.62 | (0.33, 1.17) | |
| >10,000 | 0.33 | (0.17, 0.64) | |
| CDC Clinical Classification | | | <0.001 |
| Class N/A | 1.00 | Ref | |
| Class B/C | 0.38 | (0.23, 0.64) | |

Phase I/II, Open-Label Trial of Safety and Immunogenicity of Meningococcal (Groups A, C, Y, and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine in Human Immunodeficiency Virus-Infected Adolescents. *Pediatric Infectious Disease Journal*. 29(5):391-396, May 2010.

GMT rSBA Titers for Serogroup C for Subjects with Serology Data at Weeks 0, 4, 24, 28 and 72



GMT rSBA Titers for Serogroup Y for Subjects with Serology Data at Weeks 0, 4, 24, 28 and 72



Antibody Persistence in Subjects with CD4% ≥ 15 at Week 72 by Serogroup

| Serogroup | Group | % subjects with rSBA titer $\geq 1:128$ at Wk 72 | % subjects with rSBA titer $\geq 1:8$ at Wk 72 |
|-----------|--------|--|--|
| A | 1-dose | 57% | 59% |
| | 2-dose | 71% | 76% |
| C | 1-dose | 21% | 24% |
| | 2-dose | 35% | 49% |
| W | 1-dose | 60% | 69% |
| | 2-dose | 66% | 77% |
| Y | 1-dose | 63% | 80% |
| | 2-dose | 71% | 84% |

Summary

- ❑ **Seroresponse to MenACWY-D in HIV-infected adolescents suppressed compared to healthy adolescents**
 - 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

Conclusions

❑ **Modest increase in absolute risk of meningococcal disease among HIV-infected adults**

- Approximately 2-4 cases/100,000 persons, declining over time
- Comparison: Incidence of pneumococcal disease in adults with AIDS was 298 cases/100,000 in 2007 in the United States¹

❑ **Number of preventable cases low**

- Given current incidence of meningococcal disease and HIV infection in the US, the total number of meningococcal disease cases in HIV-infected persons is likely low
- Duration of protection from vaccine is short in HIV-infected persons

❑ **The Meningococcal Work Group does not propose changes to the current ACIP recommendations for HIV-infected persons at this time**

Rationale for No Changes to Recommendations

- ❑ Persons with HIV at lower risk compared to other recommended groups (e.g. microbiologists, complement component deficiencies, etc.), however, risk is lifelong and there would be a need for multiple boosters**
- ❑ We do not know if persons vaccinated when CD4 counts are high will be protected when CD4 counts decline**
- ❑ Cost-effectiveness analysis has not been done, but would likely not impact the Work Group's conclusions**

Thank you

National Center for Immunization & Respiratory Diseases
Meningitis and Vaccine Preventable Diseases Branch

