Outbreaks of Serogroup B Meningococcal Disease on University Campuses – 2013

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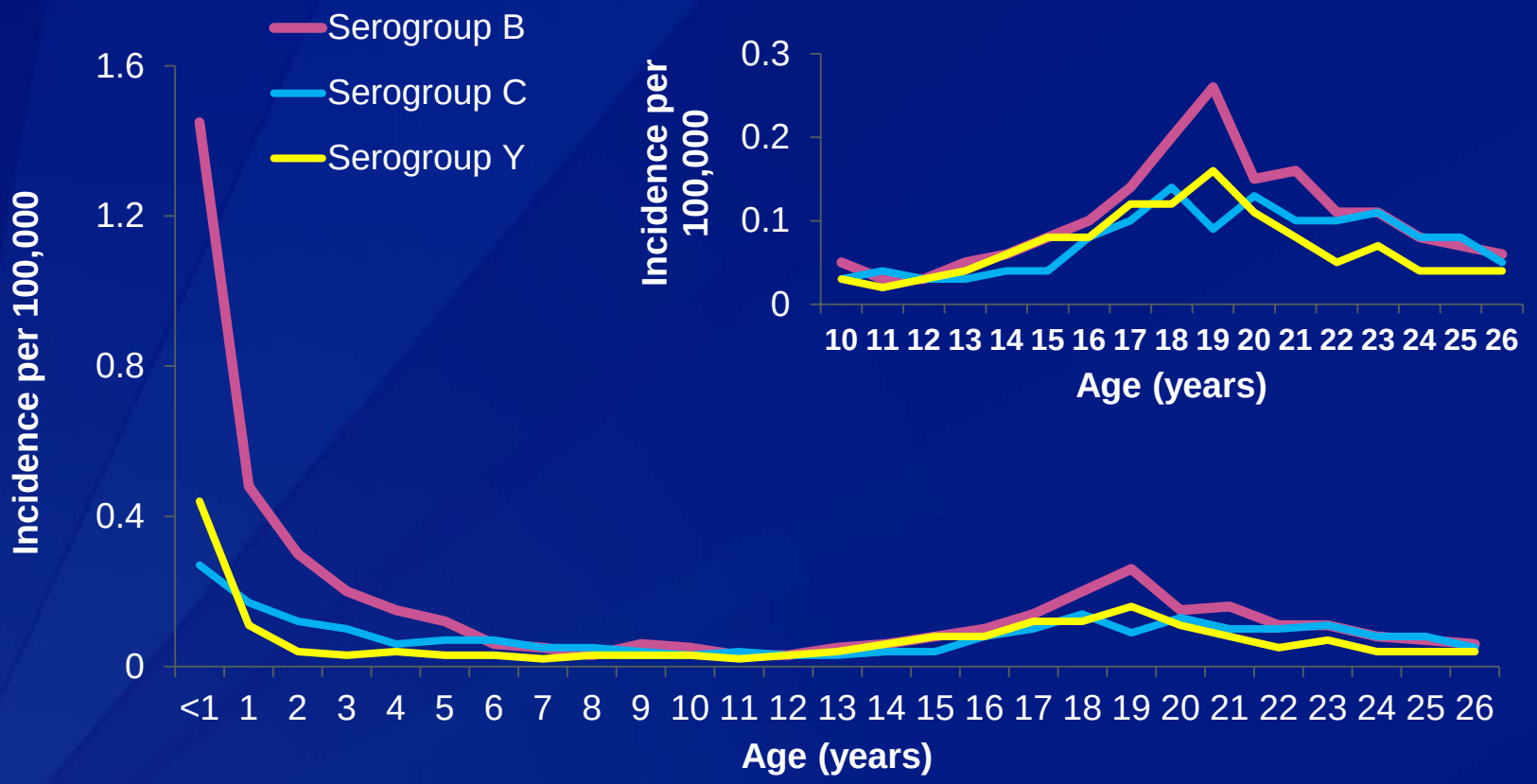
Incidence in All Serogroups, United States, 1993-2012*

*Source: ABCs cases from 1993 2012 estimated to the U.S. population with 18% correction for under reporting

Incidence of Meningococcal Disease by Age and Serogroup, United States, 2005-2012*



*Source: National Notifiable Diseases Surveillance System (NNDSS) with additional serogroup data provided by state and local health departments

Recent School Based Serogroup B Clusters/Outbreaks*

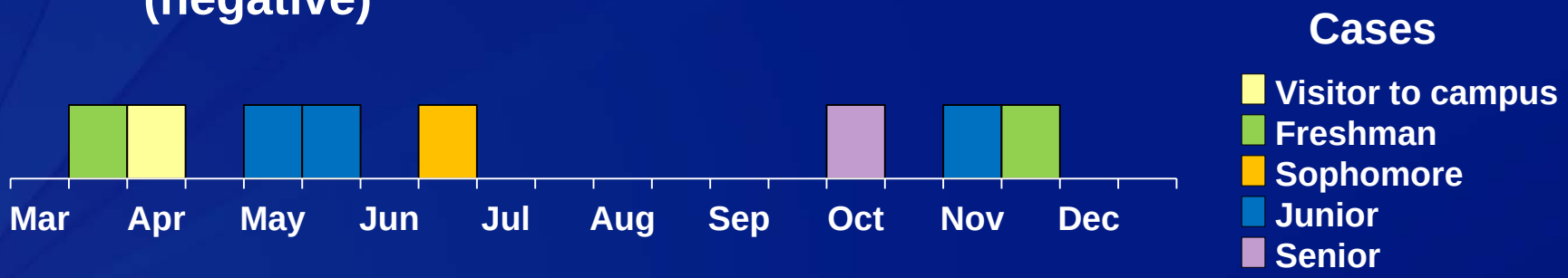
University	Outbreak Period	Number of cases
University 1	Feb – March 2009	4
University 2	Nov 2011	2
University 3	Jan 2008 – Nov 2010	13
Princeton University	March – Nov 2013	8
University of California—Santa Barbara	Nov 2013	4

CDC defines institutional meningococcal outbreaks as 3 cases (sometimes 2 cases) in a 3 month period comprising an attack rate of ≥10/100,000

*Where CDC consulted

Princeton University, NJ

- Eight cases of MenB among Princeton University students or persons with links to Princeton University from March – November 2013
  - Attack rate 134/100,000 among undergraduates
  - No fatalities; 2 cases with sequelae (neurocognitive deficit, hearing loss)
- Laboratory testing
  - All 7 strains identical: ST 409 (CC41/44/lineage3), PFGE 429, PorA (P1.5-1,2.2) , fHBP (1.276), NHBA (p0002) and *NadA* (negative)



No licensed MenB vaccine in US

- **Pfizer: MenB vaccine currently in development**
- **Novartis: Bexsero®, Recombinant MenB+OMV NZ (rMenB) Vaccine**
  - Recently licensed in Europe, Australia and Canada
    - Effectiveness inferred from immunogenicity
      - 2 dose series, with immune response after 1 dose
    - Safety in adolescents and adults (n=1584)
      - Headache, nausea, severe injection site pain, swelling erythema, malaise, myalgia and arthralgia reported in ≥10%
      - No serious adverse events reported
    - Contains 4 antigenic components (fHBP, NHBA, *NadA*, PorA)
  - Princeton isolates expressed two of the four antigens (fHBP and NHBA) in sufficient quantities to suggest protection with rMenB
    - Outbreak strain killed by a pooled post-immunization serum

Procurement of rMenB

- **Initial proposal to FDA to explore the use of rMenB in outbreak settings under an expanded access Investigational New Drug (IND) Protocol – August 2013**
- **Testing of isolates by Novartis for vaccine antigen matching – September – November 2013**
- **Epidemiologic investigation – October 2013**
- **Submission of IND protocol – November 2013**
  - Safety monitoring plan
  - Consents, vaccine information sheets, data collection instruments
- **CDC Institutional Review Board approval and FDA Safe-to-Proceed letter issued – November 2013**
- **Contractual agreements finalized between CDC, Novartis and Princeton University – December 2013**

Recommended Population for Vaccination – Princeton University

Groups	Number of People
Entire undergraduate student	5,214
Graduate students who live in undergraduate or graduate dormitories	541
Students, faculty, and staff with medical conditions at increased risk for meningococcal disease and spouses/parents living with undergraduates in dorms	17
Total	5,772

Vaccination Coverage – Princeton University

- **Dose 1 Clinics**
  - *December 9 – 12, 2014
  - January 15 – 16, 2014
  - February 17 – 20, 2014
- **Dose 2 Clinics**
  - January 15 – 16, 2014
  - *February 17 – 20, 2014

	Dose 1 N (%)	Dose 2 N (%)
Undergraduate Students	5035 (97)	4384 (89)
Graduate Students	421 (78)	316 (78)
Faculty/Staff/Other	15 (65)	9 (75)
TOTAL	5471 (95)	4709 (88)

Safety Follow-Up

- **Mandatory reporting of all serious adverse events (SAEs) to FDA**
  - Include death, a life-threatening adverse event (AE), hospitalizations, substantial disruption in the ability to conduct normal life functions, or a congenital anomaly/birth defect
- **To date, rate of SAEs reported is 2.0/1,000 vaccinees following the first dose and 0.2 /1,000 vaccinees following the second dose**
  - No SAEs have been determined to be causally related to rMenB
- **No concerning patterns among other types of AEs reported**

Serogroup B Meningococcal Disease in University of California- Santa Barbara (UCSB) Undergraduate Students (N=4*)

*Additional associated case identified on review of serogroup B cases with connections to UCSB during 2011-2013

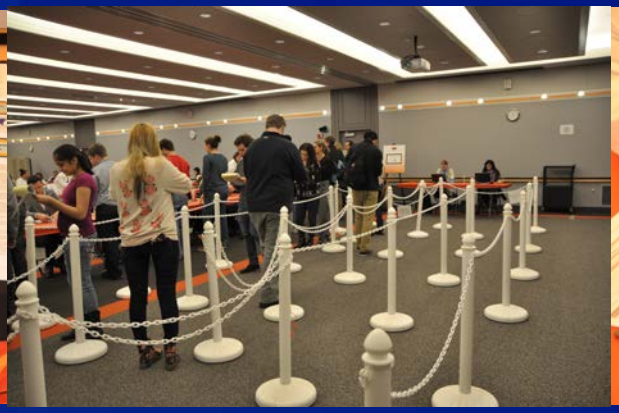
- **All cases in undergraduates (aged 18-22 years); no epi-links**
  - 4 recovered, 1 case with sequelae (bilateral foot amputation)
- **Attack rate of 21.1/100,000 (among UCSB 17-22 year olds)**
  - 234-fold higher than incidence rate for 17-22 year olds in general US population
- **All cases ST-32; PorA (P1.7,16-20), fHBP (1.1), NHBA (p0005), *NadA* (1.1); PFGE 467 and 468**
  - Different PFGE pattern compared to Princeton isolates
  - Outbreak strain killed by a pooled post-immunization serum

UCSB Vaccination Campaign

- CDC-sponsored expanded access IND approved by FDA for use in UCSB outbreak
- Target populations: All undergraduates, graduate students/faculty living in dormitories, and others with high-risk conditions (asplenia, complement component deficiency)
  - Estimate ~20,000 persons eligible for vaccination
- First dose campaign: February 24-March 7, 2014
  - Second dose in April 2014
- Safety surveillance plan in collaboration with UCSB and CDC

Challenges

- IND preparation process must address specifics of the outbreak
- Safety follow-up requirements
- Logistics of vaccine procurement and implementation


Meningococcal Outbreak Work Group

- **Ad hoc work group comprised of ACIP Meningococcal Work Group members, ACIP members, state pubic health officials, college health professionals, university administration, insurance industry, and CDC**
- **Objectives:**
  - Review available data on the recent epidemiology of meningococcal disease and outbreaks
  - Consider options for updating the current meningococcal disease outbreak guidelines
  - Develop guidance for use of meningococcal vaccines (both licensed and unlicensed) in an outbreak setting

Summary

- Vaccination now possible in response to MenB outbreaks
- Implementation of an unlicensed vaccine requires coordinated efforts between the institution, state and local health departments, manufacturer, FDA, and CDC
- ACIP outbreak workgroup developing guidance for management of MenB outbreaks
- Interim guidance to be presented at June ACIP

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- **Novartis**
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  - Meningitis and Vaccine Preventable Diseases Branch, DBD
  - Regulatory Affairs
  - Immunization Safety Office