

Meningococcal Serogroup B Vaccines

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Meningococcal Bacteria



Neisseria Meningitides:

- Gram-negative diplococcus with at least 13 serogroups based on capsular type, and "strains".
- Serogroups A.B.C., Y, W-135 cause most infections

Droplet spread: Person to person





Meningococcal Infection



Asymptomatic carrier state (transient)

- Meningococcal bacteria in the nasopharynx
- No symptoms/Immunizing event
- 5 to 10% of the population





Infection (Rare)

- Damage or irritation to the mucosal lining of the nasopharynx allows encapsulated bacteria to enter the bloodstream and cause infection
- Incubation period 3 to 4 days (range 2 to 10 days)

Meningococcal Disease Risk Factors for Invasive Disease

- Organism
- Age
 - Infants younger than one year old
 - Adolescents and young adults 16 through 23 years old

Host factors

- Lack of a spleen or non-functioning spleen
- Medication: Eculizumab-affects immune system
- Lack of complement proteins (needed for immune function)
- Certain genetic factors

Environmental factors

- Viral infection (upper respiratory tract infection)
- Crowding (dorm, barracks)
- Active and passive smoking
- Occupational (microbiologists)
- Travel exposure









Meningococcal Disease



Meningococcemia (Blood stream)

- About 35-40%
- Rapid onset
- Fever
- Petechial or purpuric rash
- Hypotension
- Shock
- Multi-organ failure

Pneumonia

About 9%



Meningitis

- About 50%
- Rapid onset
- Fever
- Headache
- Stiff neck
- Photophobia
- Lethargic
- Nausea
- Vomiting
- Seizures

* Often <u>both</u> meningitis and blood infection

*Symptoms can vary and may come on suddenly and/or severely. Please contact your health care provider with questions

Meningococcal Disease







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Meningococcal Disease: Outcomes/Sequelae



- 10% to 15% case fatality rate
 - Higher in adolescents, in those with coma, hypotension, leukopenia, and thrombocytopenia and among those who do not have meningitis.
- 11% to 19% of survivors have long term effects:
 - Hearing loss
 - Neurologic disability
 - Digit or limb amputations
 - Skin scarring
 - May also experience subtle long-term neurologic deficits, such as impaired school performance, behavioral problems, and attention deficit disorder



Incidence by Serogroup and Vaccine Coverage, US 1993-2012



ABCs cases from 1993-2012 estimated to the U.S. population with 18% correction for under reporting[№] National Immunization Survey – Teen; 2006-2012⁶

Incidence of Meningococcal Disease by Age and Serogroup, US 2005-2012





Source: Courtesy of the Centers for Disease Control and Prevention. Data on File: National Notifiable Diseases Surveillance System with additional serogroup data provided by state and local health departments.

Meningococcal Disease: Incidence



Meningococcal Disease is <u>Rare</u>:

- Since the early 2000s, annual incidence rates have decreased
- Since 2005 only an estimated 800 to 1000 US cases have been reported annually
- In 2013, there were about 550 total US cases of meningococcal disease reported (160 seroB)
- The number of cases generally peaks each year in January and February

Meningococcal Disease: Post-exposure Prophylaxis



- Preventive antibiotic treatment (CIPRO 500) for <u>close contacts</u> of patients with meningococcal disease during the 7 days before onset of disease:
 - Exposure directly to a patient's oral secretions through close social contact, such as kissing or sharing of toothbrushes or eating utensils
 - Healthcare workers who intubate/suction/mouth to mouth resuscitation
 - Child care and preschool contacts
 - People who frequently slept in the same dwelling as the infected person within this 7 day period
 - For airline travel lasting more than 8 hours, passengers who are seated directly next to an infected person

Ideally should be initiated within 24 hours after the index patient is identified; prophylaxis given more than 2 weeks after exposure has little value.

Meningococcal Disease: Outbreak Control



Most cases of meningococcal disease are sporadic, with fewer than 5% associated with outbreaks <u>Outbreak Definition</u>

- Outbreaks can occur in communities, schools, colleges, prisons, military barracks, MSM communities, and other populations
- An outbreak occurs when there are multiple cases of the same serogroup and strain in a community or institution over a short period of time (3 months)
- Depending on the size of the institution and specific circumstances, having just two cases of the same serogroup may be considered an outbreak o ≥2 unrelated cases in organization with <5000 persons
 o ≥3 unrelated cases in organization with ≥5000 persons

Outbreak Control

- Making sure all close contacts of a patient receive antibiotics to prevent them from getting the disease; this is known as prophylaxis
- Vaccinating people identified as being at increased risk

Meningococcal Disease on U.S. College Campuses, 2013-2016

While this graph only includes college students, all young adults ages 16-21 years old are at increased risk of getting meningococcal disease.



- Of those who survived, it is not known how many suffer long-term complications. In general, as many as 20 percent of survivors live with permanent disabilities, such as brain damage, hearing loss, loss of kidney function or limb amputations.
- This data is <u>based on media reports</u> and cases reported directly to NMA. Additional cases that were not featured in the news may be missing. If you know of any cases not reported on this map, please contact NMA.

Meningococcal Disease: Outbreaks



Current Outbreaks (as of 10/10/16)

- Rutgers University-New Brunswick is experiencing an outbreak of serogroup B meningococcal disease and recommending that people at increased risk get vaccinated.
- Southern California is experiencing a community outbreak of meningococcal disease, primarily among adult gay and bisexual men. The California Department of Public Health (CDPH) recommends gay and bisexual men and people with HIV get the MenACWY vaccine

http://www.cdc.gov/meningococcal/outbreaks/

Cases and Outbreaks of Meningococcal Disease in Rhode Island 1993-2015





P.C. Outbreak and Response, Round 1



Mass MenB vaccination campaign

- Case 1: 19-year-old undergraduate
- Case 2: 20-year-old undergraduate (no links to case1)
- Novel strain type: ST9096
- 71 close contacts identified and given prophylaxis
- 2 cases in ~4,500 students
- Attack rate = 44 cases per 100,000 students
 - 489-fold higher than the national incidence in persons aged 17-22 years



Serogroup B meningococcal disease. Both Novel strain type ST9096

Meningococcal Serogroup B Vaccines



- MenB-FHbp (Trumenba[®], Pfizer) licensed on October 29, 2014. 2 factor H binding proteins. Schedule 0-2-6 months
- MenB-4C (Bexsero[®], Novartis) licensed on January 23, 2015. 3 recombinant proteins: NHBA/NadA, FHbp, OMV Schedule 0-1 month
- Licensed based on safety and immunogenicity studies...not effectiveness.
- No post licensure safety data and understanding of impact on carriage is limited
- No safety or effectiveness data for pregnant women

P.C. Mass Vaccination Campaign



Eligible students:

- all undergraduate students
- graduate students who:
 - live or work on campus OR
 - o are in an intimate relationship with an undergraduate OR
 - $\circ\,$ are asplenic or immunocompromised
- Students were directed to report to the vaccination clinic
 - If declined vaccination, required to sign opt-out form
- Vaccine offered at no cost to eligible participants
- Dose 1: Feb 2015
- Dose 2: April 2015
- Dose 3: September 2015



PC MenB Vaccination Coverage Rates



Mass MenB Vaccination Campaign, 2015

Trumenba Dose	Month	Eligible Students	Vaccination Coverage
1	February	3,745	94%
2	April	3,741	80%
3	September	4,087	77%

Serogroup Results by PCR





Associations with SeroB Meningococcal Carriage



Characteristic	Bivariate Prevalence Ratio ¹	p-value	Multivariable Prevalence Ratio ¹	p-value
Male	1.5 (1.3, 1.8)	<0.001	1.3 (1.1, 1.5)	<0.001
Recent upper respiratory symptoms ³	1.1 (1.0, 1.2)	0.064		
Smoke ²	1.5 (1.3, 1.7)	<0.001	1.3 (1.1, 1.5)	0.003
Second-hand smoke ²	1.2 (1.1, 1.4)	0.006	1.0 (0.8, 1.1)	0.610
Visit bars, clubs, parties ≥1x/wk	1.9 (1.6, 2.2)	<0.001	1.8 (1.5, 2.1)	<0.001
Recent antibiotic use ²	0.4 (0.3, 0.6)	<0.001	0.4 (0.3, 0.6)	<0.001

Prevalence ratios account for repeat participants using GEE methods; ²In the past 30 days; ³In the past 2 weeks

Meningococcal Disease: Vaccines



Trade Name	Type of Vaccine	Serogroups Included	Year	Approved Ages
Menomune	Polysaccharide	A, C, W, Y	1981	2 years and older
Menactra	Conjugate	A, C, W, Y	2005	9 months–55 years
Menveo	Conjugate	A, C, W, Y	2010	2 months–55 years
MenHibrix	Conjugate	C, Y and Hib	2012	6 weeks–18 months
Trumenba	Protein	В	Oct 2014	10–25 years
Bexsero	Protein	В	Jan 2015	10–25 years

ACIP Recommendations for MenB vaccines June 2015



Licensed for age group: 10-25

- Genetic deficiencies of Complement Deficiency: 10,000 fold risk or anyone taking a drug called eculizumab (also called Soliris[®])
- Functional or anatomic asplenia (40-70%mortality)
- Laboratorians who work with isolates (13/100,000 vs .18/100,000 for general population)
- During outbreaks (200 to 1400 fold increased risk)

Note: Not for travel, not for freshmen in dorms, not for military recruits, not for all adolescents (unlike polysaccharide quadrivalent vaccine)

ACIP Recommendations for MenB vaccines October 2015



For adolescents and young adults, ACIP recommends that a MenB vaccine series:

- May be administered to people 16 through 23 years of age
- With a preferred age of vaccination of <u>16 through 18 years</u>.
- Although several small MenB outbreaks have occurred on college campuses since 2013 (30 cases over 4 years), college students in general are not at higher risk of MenB then persons of the same age who are not college students.
- Consequently, ACIP does not routinely recommend MenB vaccination for college students. However, college students may choose to receive MenB vaccine to reduce their risk of serogroup B meningococcal disease.

http://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/mening.html

Men B Vaccine Information Statement



Risks of a vaccine reaction

More than half of the people who get serogroup B meningococcal vaccine have mild problems following vaccination. These reactions can last up to 3 to 7 days, and include:

- Soreness, redness, or swelling where the shot was given
- Tiredness or fatigue, fainting
- Headache
- Muscle or joint pain, shoulder pain
- Fever or chills
- Nausea or diarrhea

Rare: Anaphylaxis, neutropenia

Contraindications:

- Breast feeding/Pregnancy,
- prior severe vaccine reactions
- latex allergy (Bexero)

Meningococcal Vaccines Compared



	Men ACYW135	MenB
Licensed for ages	Menactra 9mo-55yrs MenVeo 2mo-55yrs	10yrs-25yrs
Schedule	11-12 yrs, booster at 16yrs Min interval 8weeks.	6-23, recommended at 16-18yrs, 2 doses Bexero, 3 doses Trumenba.
	Additional boosters every 5 yrs for continuous risk.	Min interval not spelled out No boosters even for risk groups
Effectiveness	85-90% effective Wanes in 5 yrs.	63-88% immunogenic in trials. 66% Princeton outbreak study. No data but suspect fairly rapid waning of immunity.
Effect on Carriage	Reduces carriage	Trumenba: No effect(PC study) Bexero: 18% reduction
Safety profile	Safe	Slightly more reactogenic
Strength of Reccomendation	Cat A: Recommended for risk groups	Cat A: Risk groups Cat B: 16-18 yr olds Permissive decision to be made between parent and physician

Meningococcal B Disease: Summary



- Meningococcal disease is rare
- Teens and young adults age 16-23 are at a higher risk for Men B disease. Meningococcal disease has a higher case fatality rate than many other bacterial infections and serious long term health effects for 10-15% of survivors.
- Two Men B vaccines are available in the United States
- The long term duration of immunity from Men B vaccines is unknown at this time
- College students may choose to receive Men B vaccine to reduce their risk of serogroup B meningococcal disease
- College Health Services should be prepared to respond to cases and outbreaks including mass vaccination efforts.



Questions?





Grading of Recommendations, Assessment, Development & Evaluation. GRADE



Men B vaccination strategies



Use of Serogroup B Meningococcal Vaccines in Adolescents and Young Adults: Recommendations of the Advisory Committee on Immunization Practices, 2015

Jessica R. MacNeil, MPH¹; Lorry Rubin, MD²; Temitope Folaranmi, MBChB^{1,3}; Ismael R. Ortega-Sanchez⁴; PhD; Manisha Patel, MD¹; Stacey W. Martin, MS¹

TABLE 2. Potential cases and deaths prevented and cost-effectiveness of different strategies for MenB vaccination of adolescents and young adults, including college students, by age — United States

Age at MenB series	Cases prevented	Deaths prevented	NNV* to prevent case	NNV to prevent death	Cost per QALY (million \$)
11 yrs	15	2	203,000	1,512,000	8.7
16 yrs	28	5	107,000	788,000	4.1
18 yrs	29	5	102,000	638,000	3.7
College student	9	1	368,000	2,297,000	9.4

Abbreviations: MenB = meningococcal B vaccine; NNV = number needed to vaccinate; QALY = quality-adjusted life years.

Sources: Unpublished data, ACIP meeting June 2015. Key model assumptions were presented at the June 2015 ACIP meeting. Methods described in Shepard CW, Ortega-Sanchez IR, Scott RD 2nd, Rosenstein NE. Cost-effectiveness of conjugate meningococcal vaccination strategies in the United States. Pediatrics 2005;115:1220–32.



Timeline of the meningococcal outbreak at Princeton University



IND, Investigational New Drug NJDOH, New Jersey Department of Health

Bexsero Immunity-Princeton University Outbreak



Canada/Australia Study*		
(11 through 17 years of		
age)		

United Kingdom Study[†] (18 through 24 years of age)



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

≥4-FOLD hSBA RESPONSE 1 MONTH POSTDOSE 2ª

Strain (antigen)	% (95% CI) N=298-299	% (95% CI) N=147-148⁰		
H44/76 (fHbp)	98 (95, 99)	78 (71, 85)		
5/99 (NadA)	99 (98, 100)	94 (89, 97)		
NZ98/254 (PorA P1.4)	39 (33, 44)	67 (58, 74)		
COMPOSITE hSBA RESPONSE ^d				
Time point	% (95% Cl) N=298-299	% (95% CI) N=136-186⁰		
Time point Baseline (prevaccination)	% (95% Cl) N=298-299 0	% (95% CI) N=136-186° 24 (18, 30)		
Time point Baseline (prevaccination) 1 month postdose 2	% (95% Cl) N=298-299 ⁹ 0 63 (57, 68)	% (95% CI) N=136-186° 24 (18, 30) 88 (82, 93)		

Immunogenicity of a Meningococcal B Vaccine during a University Outbreak

Nicole E. Basta, Ph.D., Adel A.F. Mahmoud, M.D., Ph.D., Julian Wolfson, Ph.D., Alexander Ploss, Ph.D., Brigitte L. Heller, B.S., Sarah Hanna, A.B., Peter Johnsen, M.D., Robin Izzo, M.S., Bryan T. Grenfell, D.Phil., Jamie Findlow, Ph.D., Xilian Bai, Ph.D., and Ray Borrow, Ph.D. N Engl J Med 2016; 375:220-228 | July 21, 2016 | DOI: 10.1056/NEJMoa1514866

- Sample of 607 Princeton students 4 months after vaccine campaign
- At least 18 years old
- 499 received both doses of vaccine on schedule and were tested
- · Tested blood antibody levels to vaccine and outbreak strains
- Vaccine strain (44/76 fHbp): 87-100% had immunity
- Outbreak strain: 66% (CI 61.8%-70.3%) had immunity

Mumps on Campus!

Sue Fitzgerald, RN, MHA, CIC Harvard University Health Services Internal Medicine / Infection Prevention

NECHA 2016



Overview and Objectives

- Clinical presentation of mumps infection
- Role of Immunizations
- Discuss Mumps outbreak in a unvaccinated vs. vaccinated population
- Describe management of Mumps in various college settings



What Causes Mumps?

• Virus- Paramyxoviridae family



How is Mumps transmitted?

Direct contact with infected saliva/ droplets



Mumps Facts

- ▶ Fever, headache, fatigue, facial pain -2 days
- Jaw pain / swelling caused by Parotitis 3-7 days
- RARE- endocarditis, testicular pain or swelling, oophoritis, pancreatitis, meningitis, encephalitis, miscarriage
- Infectious 2 days BEFORE symptoms of swelling
- Incubation is 12–25 days



What does Mumps Parotitis look like?









r like nothing at all.....





HARVARD UNIVERSITY Health Services

MMR Vaccine -Best Choice for now

- Measles-Mumps-Rubella
 - Single Mumps vaccine in 1967; MMR in 1971
 - (before vaccine= 186k cases/ year)
 - BUT: Mumps component is:
 - 78% effective after 1st immunization;
 - 88% effective after 2nd immunization
- Since vaccination programs began, 90% reduction in Mumps cases
 - (<2k cases documented)
- Sporadic outbreaks
 - 2006– colleges,
 - 2009– Orthodox community,
 - 2010's Mid-West, Canada (NHL)



http://www.cdc.gov/mumps/outbreaks.html

Number of mumps cases by year since 2010

Year	Cases
2010	2,612
2011	370
2012	229
2013	584
2014	1,223
2015*	1,057
2016**	1,786

*Cases as of January 2, 2016. Case count is preliminary and subject to change.

**Cases as of August 13, 2016. Case count is preliminary and subject to change.

Source: Morbidity and Mortality Weekly Report (MMWR), Notifiable Diseases and Mortality Tables



Vaccinated vs. Unvaccinated

<u>"Highly Vaccinated"</u>

- 99% Undergrads & 98% Grad students had 2 or 3 MMR's
- HUHS Health Care Workers
 - Immunized & titers required for MMR, Varicella and Hepatitis B
- Health Science (Medical, Dental School, "Special HSPH")
 - Immunized & titers
- <u>Unvaccinated:</u> 44 Undergrads & Graduate
 Students with Religious or Medical Exempt (some with titers)



Timeline for Mumps at Harvard

- 1 case of "atypical" Parotitis January 4^{th-} through Jan 15th, 2016 (? Index case)
 - Undergrad visited Minnesota over holiday break (12/19/15), later discovered had contact with Mumps case.
 - Serology= "Mumps Immunity" and swab when finally done (> 3 days later) = Negative PCR
 - Began unilateral, progressed 10 days later to bilateral parotitis
 - Given antibiotics some "doubted it could be mumps" because of serology and Negative PCR



Timeline for Mumps at Harvard

- From Feb 15th–Feb 24th
 - 20 cases of Parotitis (none 'seemingly' connected)
 - 12 had serology- "Showed Immunity" to Mumps High IGG and low IGM)
 - By Feb 21st per DPH had switched to Buccal swab for PCR-testing (6 positive Mumps, 1 Negative PCR)

month	cases	POS	NEG
Feb	24	6	5
Mar	57	16	31
April	52	27	25
May	52	13	31





Timeline of Cases







Department of Public Health

- Parotitis in "highly vaccinated population"
- Cambridge PHD and MA State DPH Epidemiologists reviewed cases and approved testing
- "Break through event", DPH consulted with CDC at beginning of outbreak
- Conference calls, daily updates of specimens sent and line lists faxed
- Joint communications through HUHS, DPH, PHD and Communications to University and local community
- Currently = Genetic Sequencing of Swabs for "Origin"



Management: Self-isolation vs Quarantine

- Infectious 2 days before swelling starts, through 5 days after onset (Rule of 6")
- Alternate housing Dorm "swing space" or driven home or to local non-risk relatives
- Graduate students remained in apartments (with additional support) or moved to alternate Graduate housing.
- Unvaccinated student (religious exemption) <u>quarantined</u> for 15 days after contact with Swab-Positive case per DPH



Alternate Housing and Academic Support

- Urgent Care provided student with snacks, OTC meds, thermometer and handouts for care.
- Transport to alternate housing by Van or HUPD
- Residential Dean:
 - coordinated room assignment & notified staff
 - Deans of Students / Instructors to provide academic support
 - Coaches / trainers of athletes





Alternate Housing and Academic Support

- Needed single room / private bathroom
- Cohort of swab positive cases ONLY when housing became "tight"
- Meals delivered by Dining Services or "runner"
- Twice Daily Nursing telephone "Wellness checks"





The Mumps Response Team

- Emergency Management HUPD
- Health Services
 Facilities
- Dining Services Transportation
- Environmental Health & Safety
- As needed:
 - Graduate School Deans of Students
 - Program leads (Commencement, Reunions)
 - Human Resources (Employees who were sick)
 - Securitas (contract security guards)



Mumps Daily Calls & Situation Report

- Daily or twice weekly call:
 - 1. Case counts, schools impacted, location of students in isolation
 - 2. Any new information from DPH
 - 3. Status of housing availability
 - 4. Any new procedures/policies we need to discuss
 - 5. Problem resolution
 - 6. Communication plan inside and outside Harvard
- Nightly Situation Report Email:
 - Brief update email sent to University Administrators, Deans and Department Heads, General Counsel, Emergency Management Team



Lessons Learned

- Much carried over from H1N1 experience:
 - Relocation, Coordination, Communication
- Transparency & Communication to Stakeholders was crucial:
 - Joint communications with DPH, Letters from Director and Provost,
 - Pre-enrollment, Reunion and Summer Programs
 - FAQ's and medical information to academic, administrative staff & students
- Contingency planning needed:
 - Bed capacity, Dining services over Spring Break when kitchens closed



Lessons Learned

- Limiting Social Exposure
 - Notice to students about "Party Behavior" (use disposable cups, not sharing food or beverages)
 - "If you are sharing saliva you are sharing Mumps!"
 - Most challenging to control!
- Athletics
 - Changed behaviors regarding beverages, no participation if ill.
 - Gym water fountains



Where We Are Now

- 2 cases in Summer School Students (June-July)
- 2 unrelated graduate students: 1 in August, 1 in September
- 50 day countdown for no new infections (2 incubation cycles)
- Challenges for alternate housing going forward
- Ongoing outbreaks in Arkansas, Ozarks, Midwest



Community and Public Health

Community:

- Health Services & University Emergency Management
- Cambridge Public Health Department
- Higher Education Partners Collaboration
- University & Public Health Workgroup
 - State Dept. of Public Health
 - Monitor local and national outbreaks
 - Collaborative work through State, CDC Epidemiologists
 - School of Public Health / DPH State Lab work together to perform genetic sequencing to identify

The Take-Away

- Vaccines are good but not perfect, but should be pursued!
- Don't assume it <u>can't</u> be mumps (or measles or varicella) — providers may not be familiar with presentation
- "Childhood diseases" can happen in adults, even when vaccinated and labs say "they are immune"
- It is a BIG effort to inform, educate & prevent spread of any infection
- Jury still out on a 3rd MMR as a Booster

Public Health and other school colleagues can be great allies!



THANK YOU!



