

# Meningococcal Disease and Meningococcal Vaccine

**August, 2016**

# ***Neisseria meningitidis***

- ❑ **Aerobic gram-negative bacteria**
- ❑ **At least 13 serogroups based polysaccharide capsule**
- ❑ **Most invasive disease caused by serogroups A, B, C, Y, and W**
- ❑ **Relative importance of serogroups depends on geographic location and other factors (e.g., age)**

# **Meningococcal Disease Pathogenesis**

- ❑ Organism colonizes nasopharynx**
- ❑ In some persons organism enters the bloodstream and causes infection at distant site**
- ❑ Antecedent URI may be a contributing factor**

# *Neisseria meningitidis*

## Clinical Features

- ❑ Incubation period 3-4 days (range 2-10 days)
- ❑ Abrupt onset of fever, meningeal symptoms, hypotension, and rash
- ❑ Fatality rate 10%-15%, up to 40% in meningococemia

# Meningococcal Meningitis

- ❑ **Most common presentation of invasive disease**
- ❑ **Results from hematogenous dissemination**
- ❑ **Clinical findings**
  - fever
  - headache
  - stiff neck

# Meningococemia

- ❑ Meningococemia
- ❑ Bloodstream infection
- ❑ May occur with or without meningitis
- ❑ Clinical findings
  - fever
  - petechial or purpuric rash
  - hypotension
  - shock
  - acute adrenal hemorrhage
  - Multi-organ failure

# Meningococcal Disease



# Meningococcal Disease



*N Engl J Med.* 2001;344:1372

# *Neisseria meningitidis*

## Risk Factors for Invasive Disease

### ❑ Host Factors

- Deficiencies in the terminal common complement pathways
- Functional or anatomic asplenia
- Chronic underlying disease
- Certain genetic factors (altered genes: mannose-binding lectin and tumor necrosis factor)

### ❑ Environmental factors

- Household crowding
- Active and passive smoking
- Antecedent viral infection

### ❑ Occupational (microbiologists)

# *Neisseria meningitidis*

## Risk Factors for Invasive Disease

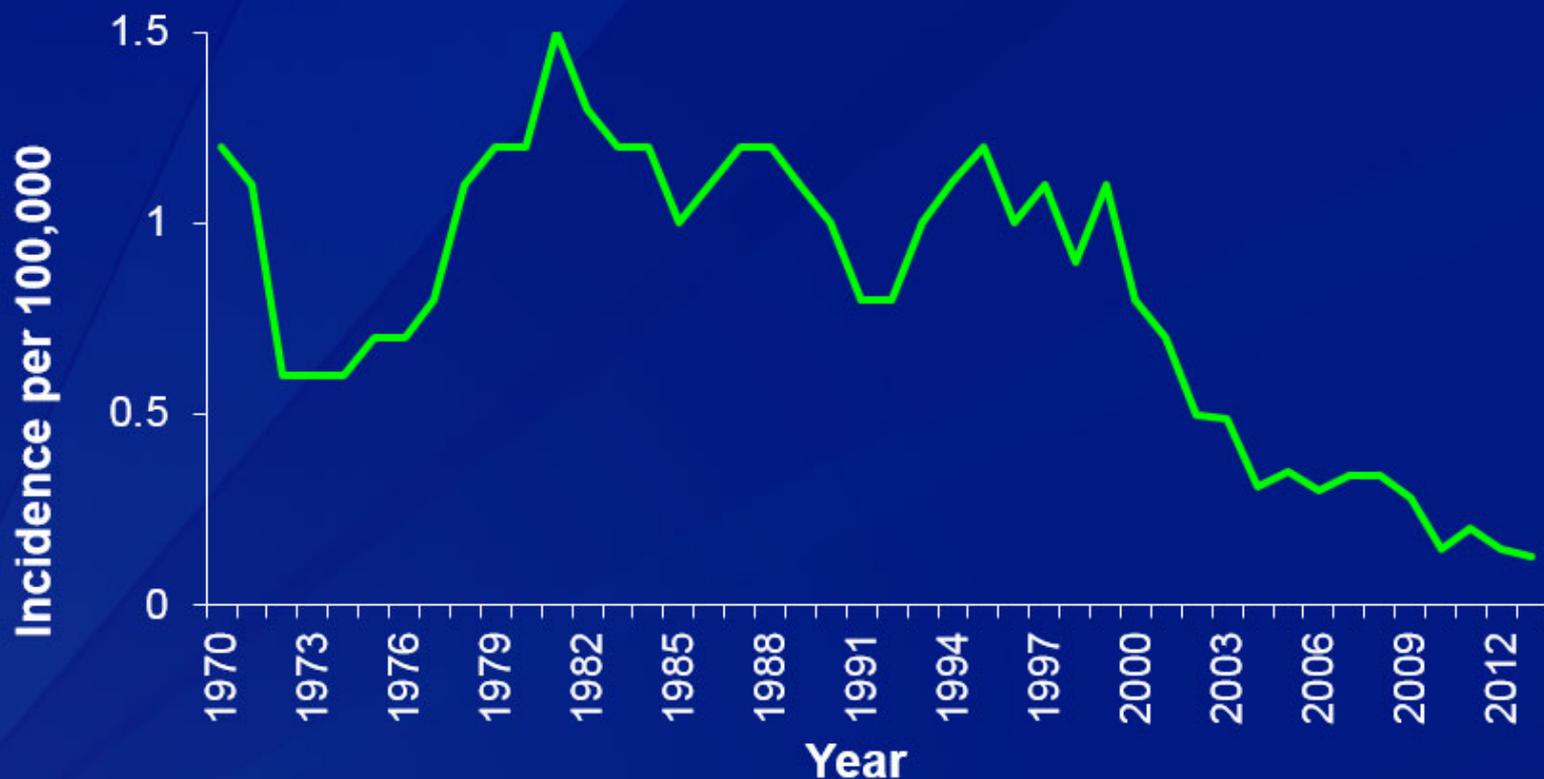
### □ College Students

- Studies in 1990s – overall incidence similar to or lower than their counterparts in general population\*
- Case control study of 50 cases and other studies in the 1990s#
  - First-year college students living in residence halls at higher risk

\*JAMA 1999;281:1906-10

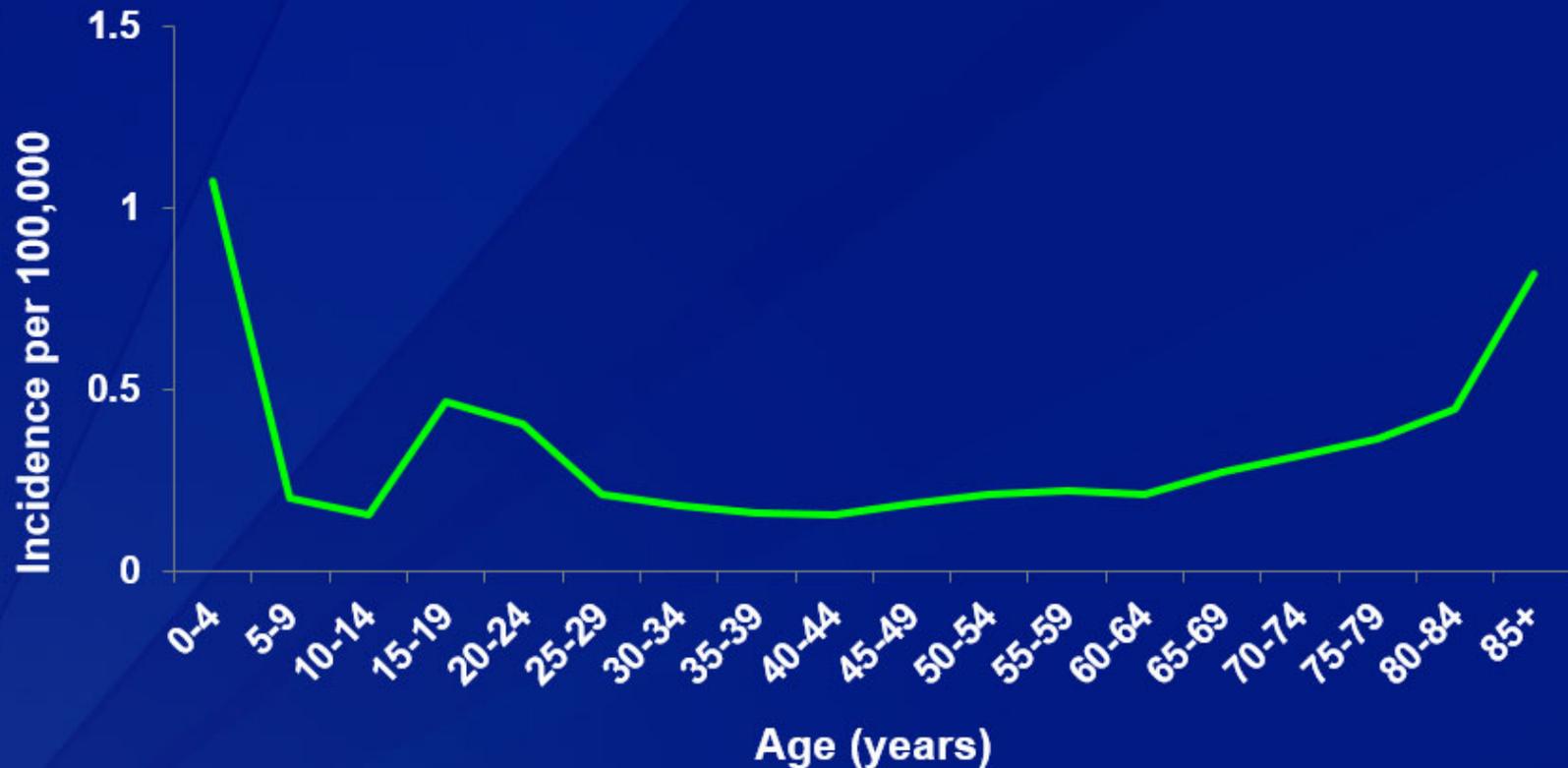
#Abstracts of the 39<sup>th</sup> Meeting of the IDSA. Philadelphia, PA: IDSA; 1999:276  
Epidemiol Infect 1999;122:351–7. Clin Infect Dis 1999;29:215–6.

# Meningococcal Disease Incidence, United States, 1970-2013



SOURCE: CDC. 1970-1996 National Notifiable Diseases Surveillance System, 1997-2013 Active Bacterial Core surveillance estimated to U.S. population

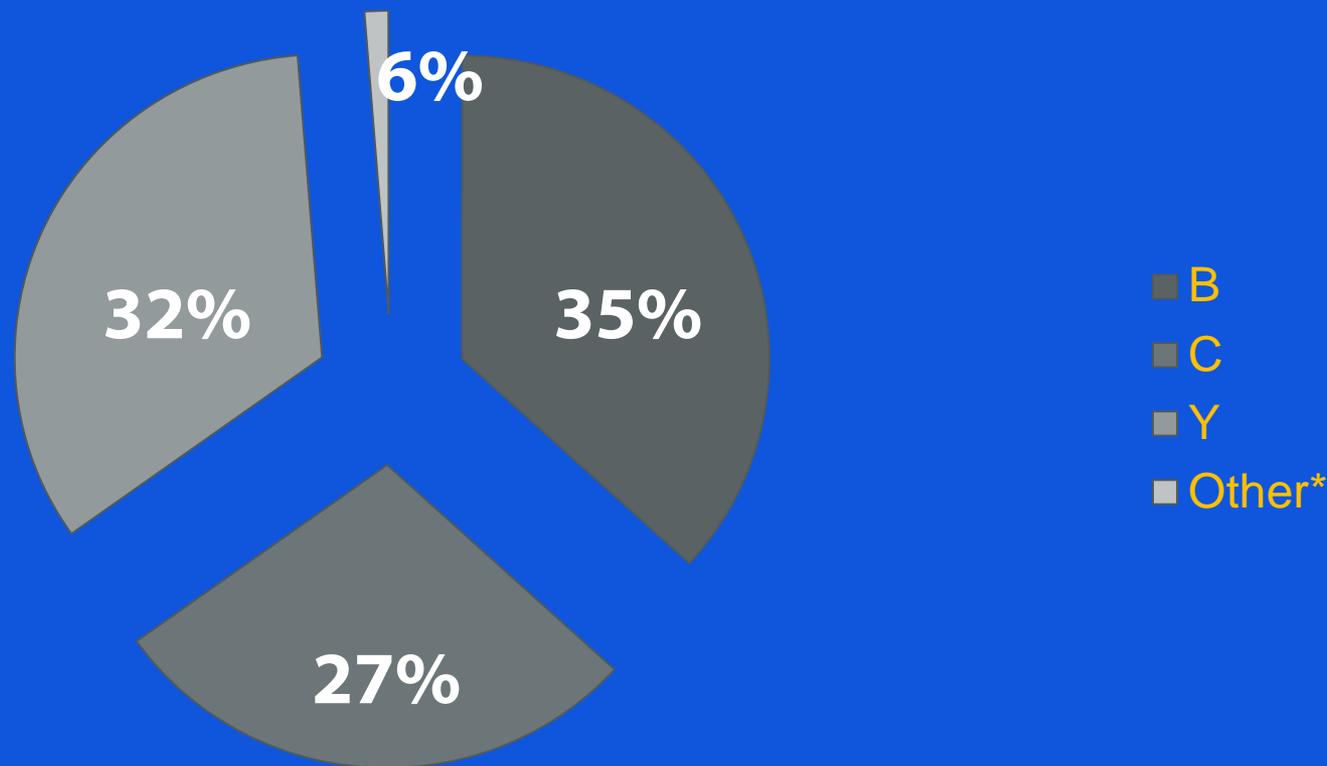
# Meningococcal Disease Incidence by Age, United States, 2005-2013



SOURCE: CDC. National Notifiable Diseases Surveillance System

# Meningococcal Disease Serotypes in the U.S., 2005-2011

Meningococcal Serotypes in the U.S.



\*Includes serogroup W135, nongroupable, and other serogroups.

MMWR, March 22, 2013; Recommendations and Reports / Vol. 62 / No. 2

# Meningococcal Outbreaks in the United States

- ❑ **Outbreaks account for 2%-3% of reported cases**
- ❑ **Most recent outbreaks caused by serogroup C and B**

# **MENINGOCOCCAL VACCINES**

# **Meningococcal Polysaccharide Vaccine (MPSV4)**

- ❑ Menomune (sanofi pasteur)**
- ❑ Quadrivalent polysaccharide vaccine (A, C, Y, W-135)**
- ❑ Administered by subcutaneous injection**
- ❑ 10-dose vial contains thimerosal as a preservative**
- ❑ Single-dose vial available**

# Polysaccharide Vaccines

- ❑ **Age-related immune response**
- ❑ **Not consistently immunogenic in children younger than 2 years**
- ❑ **Little or no booster response**
- ❑ **Antibody with less functional activity**
- ❑ **Response improved by conjugation to a protein antigen**

# MPSV4 Recommendations

- ❑ **Approved for persons 2 years of age and older**
- ❑ **Not recommended for routine vaccination of civilians**
- ❑ **Should be used only for persons at increased risk of *N. meningitidis* infection who are 56 years of age or older, expected to need meningococcal vaccine once**

# **Meningococcal Conjugate Vaccines**

- ❑ **Meningococcal polysaccharide conjugated to protein carrier**
- ❑ **Elicit both T- and B-cell immunity (T-cell dependent immunity)**
- ❑ **3 brands currently licensed in the United States**
  - Menactra (Sanofi Pasteur)
  - Menveo (Novartis)
  - MenHibrix (GlaxoSmithKline)

# **Menactra MenACWY Vaccine**

- ❑ Licensed by FDA in January 2005**
- ❑ Quadrivalent polysaccharide vaccine conjugated to diphtheria toxoid (MenACWY-D)**
- ❑ Approved for persons 9 months through 55 years of age**
- ❑ Intramuscular injection**
- ❑ Single dose vials**

# Menveo MenACWY Vaccine

- ❑ Licensed by FDA in February 2010
- ❑ Lyophilized serogroup A vaccine reconstituted with liquid containing serogroups C, Y, and W135 (MenACWY-CRM)
- ❑ May be used for any person 2 months through 55 years of age for whom MCV4 is indicated, including revaccination
- ❑ Intramuscular injection
- ❑ Single dose vials

# **(Hib-MenCY-TT) MenHibrix**

- ❑ **FDA licensed June 2012**
- ❑ **Combination vaccine for infants/ children 6 weeks through 18 months to prevent invasive disease from *N. meningitidis* C and Y and Hib.**
- ❑ **Lyophilized powder reconstituted with saline diluent**
- ❑ **Single dose administered as a 4-dose series at 2, 4, 6, and 12 - 1 months**
  - **1<sup>st</sup> dose may be given at 6 weeks**

# **Interchangeability of Conjugate Vaccine Brands**

- ❑ Limited data suggest that different conjugate vaccine products can be used interchangeably.**
- ❑ Whenever feasible, the same brand of vaccine should be used for all doses of the vaccination series**
- ❑ If vaccination providers do not know or have available the type of vaccine product previously administered, any product should be used to continue or complete the series**

# **Routine Adolescent MenACWY Vaccine Recommendations**

**Figure 1. Recommended Immunization schedule for persons aged 0 through 18 years – United States, 2016.**

**(FOR THOSE WHO FALL BEHIND OR START LATE, SEE THE CATCH-UP SCHEDULE [FIGURE 2]).**

These recommendations must be read with the footnotes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars in Figure 1. To determine minimum intervals between doses, see the catch-up schedule (Figure 2). School entry and adolescent vaccine age groups are shaded.

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19–23 mos	2–3 yrs	4–6 yrs	7–10 yrs	11–12 yrs	13–15 yrs	16–18 yrs
Hepatitis B <sup>1</sup> (HepB)	1 <sup>st</sup> dose	← 2 <sup>nd</sup> dose →			← 3 <sup>rd</sup> dose →											
Rotavirus <sup>2</sup> (RV) RV1 (2-dose series); RV5 (3-dose series)			1 <sup>st</sup> dose	2 <sup>nd</sup> dose	See footnote 2											
Diphtheria, tetanus, & acellular pertussis <sup>3</sup> (DTaP: <7 yrs)			1 <sup>st</sup> dose	2 <sup>nd</sup> dose	3 <sup>rd</sup> dose			← 4 <sup>th</sup> dose →				5 <sup>th</sup> dose				
Haemophilus influenzae type b <sup>4</sup> (Hib)			1 <sup>st</sup> dose	2 <sup>nd</sup> dose	See footnote 4		← 3 <sup>rd</sup> or 4 <sup>th</sup> dose → See footnote 4									
Pneumococcal conjugate <sup>5</sup> (PCV13)			1 <sup>st</sup> dose	2 <sup>nd</sup> dose	3 <sup>rd</sup> dose		← 4 <sup>th</sup> dose →									
Inactivated poliovirus <sup>6</sup> (IPV: <18 yrs)			1 <sup>st</sup> dose	2 <sup>nd</sup> dose	← 3 <sup>rd</sup> dose →							4 <sup>th</sup> dose				
Influenza <sup>7</sup> (IIV; LAIV)					Annual vaccination (IIV only) 1 or 2 doses						Annual vaccination (LAIV or IIV) 1 or 2 doses			Annual vaccination (LAIV or IIV) 1 dose only		
Measles, mumps, rubella <sup>8</sup> (MMR)					See footnote 8		← 1 <sup>st</sup> dose →					2 <sup>nd</sup> dose				
Varicella <sup>9</sup> (VAR)							← 1 <sup>st</sup> dose →					2 <sup>nd</sup> dose				
Hepatitis A <sup>10</sup> (HepA)							← 2-dose series, See footnote 10 →									
Meningococcal <sup>11</sup> (Hib-MenCY ≥ 6 weeks; MenACWY-D ≥ 9 mos; MenACWY-CRM ≥ 2 mos)				See footnote 11										1 <sup>st</sup> dose		Booster
Tetanus, diphtheria, & acellular pertussis <sup>12</sup> (Tdap: ≥ 7 yrs)														(Tdap)		
Human papillomavirus <sup>13</sup> (2vHPV: females only; 4vHPV, 9vHPV: males and females)														(3-dose series)		
Meningococcal B <sup>11</sup>														See footnote 11		
Pneumococcal polysaccharide <sup>5</sup> (PPSV23)												See footnote 5				

Range of recommended ages for all children
Range of recommended ages for catch-up immunization
Range of recommended ages for certain high-risk groups
Range of recommended ages for non-high-risk groups that may receive vaccine, subject to individual clinical decision making
No recommendation

This schedule includes recommendations in effect as of January 1, 2016. Any dose not administered at the recommended age should be administered at a subsequent visit, when indicated and feasible. The use of a combination vaccine generally is preferred over separate injections of its equivalent component vaccines. Vaccination providers should consult the relevant Advisory Committee on Immunization Practices (ACIP) statement for detailed recommendations, available online at <http://www.cdc.gov/vaccines/hcp/acip-recs/index.html>. Clinically significant adverse events that follow vaccination should be reported to the Vaccine Adverse Event Reporting System (VAERS) online (<http://www.vaers.hhs.gov>) or by telephone (800-822-7967). Suspected cases of vaccine-preventable diseases should be reported to the state or local health department. Additional information, including precautions and contraindications for vaccination, is available from CDC online (<http://www.cdc.gov/vaccines/recs/vac-admin/contraindications.htm>) or by telephone (800-CDC-INFO [800-232-4636]).

This schedule is approved by the Advisory Committee on Immunization Practices (<http://www.cdc.gov/vaccines/acip>), the American Academy of Pediatrics (<http://www.aap.org>), the American Academy of Family Physicians (<http://www.aafp.org>), and the American College of Obstetricians and Gynecologists (<http://www.acog.org>).

**NOTE: The above recommendations must be read along with the footnotes of this schedule.**

# MenACWY Recommendations\*

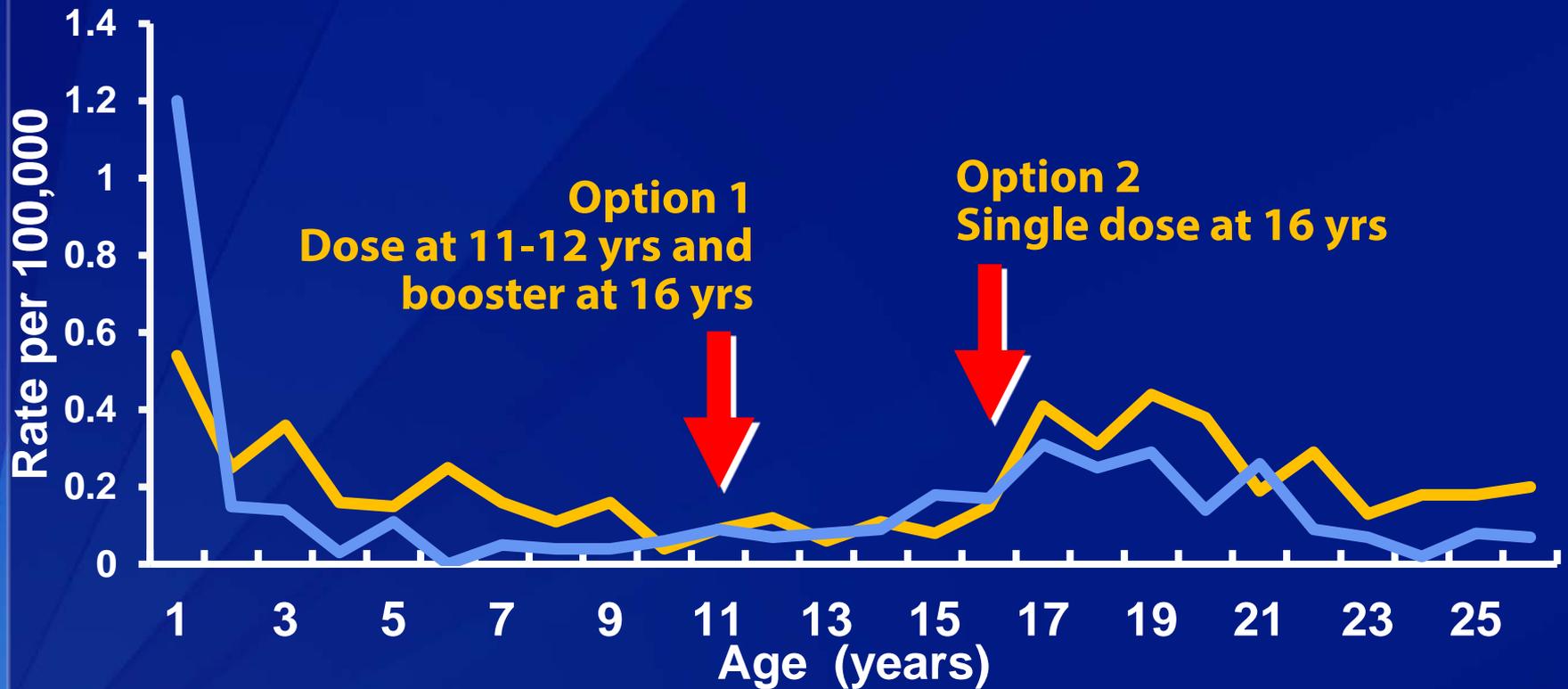
- ❑ Administer MenACWY at age 11 or 12 years with a **booster dose** at 16 years of age
- ❑ Administer 1 dose at age 13 through 15 years if not previously vaccinated
- ❑ For persons vaccinated at age 13 through 15 years, administer a one-time booster dose is recommended, preferably at or after 16 through 18 years of age
- ❑ The minimum interval between doses is 8 weeks

\*Off-label recommendation. *MMWR* 2013;62(RR-2):10-11

# **Meningococcal Conjugate (MenACWY) Revaccination**

- ❑ In its 2005 recommendations for MenACWY, ACIP made no recommendation about revaccination pending the availability of additional data**
- ❑ Serologic data are now available from the manufacturer that show significant decline in antibody 3-5 years after vaccination, although few breakthrough cases have been reported**

# Rates of Meningococcal Disease (C and Y) by Age, 1999-2008



Active Bacterial Core surveillance (ABCs), 1998-2008

# MenACWY Adolescent Vaccination Recommendations

- ❑ A booster dose is **not recommended** for healthy persons if the first dose is administered at or after 16 years of age
- ❑ A booster dose is **not recommended** for healthy persons after 21 years of age who are not at increased risk of exposure
  - A booster dose is not recommended for healthy persons 22 years of age and older even if the first dose was administered at 11-15 years of age

# **MenACWY Vaccine Recommendations for Persons at Increased Risk for Meningococcal Disease**

# High-risk Groups: Functional or Anatomic Asplenia\*

- ❑ **Younger than 19 months**
  - Infant series at 2, 4, 6, and 12-15 months with HibMenCY-TT or MenACWY-CRM
  
- ❑ **19-23 months who have not received a complete series**
  - 2-dose primary series of MenACWY-CRM 12 weeks\*\*
  
- ❑ **24 months or older who have not received a complete series**
  - 2-dose primary series of either MenACWY 8-12 weeks apart

\*Including sickle-cell disease

\*\* Doses valid if 8 weeks apart

# High-risk Groups: Persistent Complement Component Deficiency\*

## ❑ Children 2-18 months

- Infant series at 2, 4, 6, and 12-15 months with HibMenCY-TT or MenACWY-CRM; OR
- 2-dose primary series of MenACWY-D starting at 9 months at least 12 weeks apart\*\*

## ❑ 19-23 months without complete series of HibMenCY-TT or MenACWY

- 2-dose primary series of MenACWY starting at least 12 weeks apart\*\*

## ❑ 24 months or older who have not received a complete series of HibMenCY-TT or MenACWY

- 2-dose primary series of MenACWY starting at least 12 weeks apart\*\*

\* Including persons taking Soliris (eculizumab)

\*\* Doses valid if 8 weeks apart

# MenACWY Recommendations and HIV

- ❑ **June 2016 ACIP vote regarding HIV-infected persons**
- ❑ **Routine vaccination of HIV-infected persons  $\geq 2$  months**
- ❑ **Primary schedule depends on age**
  - **$< 2$  years: 4 doses Menveo or MenHibrix or 2 doses Menactra**
  - **$\geq 2$  years: 2 doses or Menveo**
- ❑ **Will require lifetime boosters**

# **Meningococcal Vaccine Recommendations for Persons 2 through 55 years at High Risk**

## **□ Persons who:**

- Are first-year college students aged  $\leq 21$  years living in residential housing**
- Travel to, or are residents of, countries where meningococcal disease is hyperendemic or epidemic**
- Are microbiologists routinely exposed to isolates of *Neisseria meningitidis***
- Military recruits**

## **□ Administer: 1 dose of MenACWY**

# Meningococcal Vaccine Use in Outbreaks

- ❑ **Both MenACWY, and MPSV4 recommended for use in control of outbreaks caused by A, C, W, and Y**
  
- ❑ **HibMenCY-TT may be used for age-appropriate persons in outbreaks specifically caused by C and Y**
  
- ❑ **Outbreak definition:**
  - **at least 3 confirmed or probable primary cases of the same serogroup**
  - **period of 3 months or less**
  - **primary attack rate of more than 10 cases per 100,000 population**

# Meningococcal Vaccine Booster Doses

- ❑ **Children who receive primary immunization and remain at increased risk should receive booster doses**
  - **if primary immunization complete by 7 years of age first booster should be 3 years after primary immunization and every 5 years thereafter if at continued risk**
  
- ❑ **If primary immunization complete on or after 7 years of age**
  - **first booster should be 5 years after primary immunization and every 5 years thereafter if at continued risk**

# MenACWY Revaccination Recommendations

- ❑ Other high-risk persons recommended for boosters:
  - Microbiologists with prolonged exposure to *Neisseria meningitidis*
  - Frequent travelers to or persons living in areas with high rates of meningococcal disease (see next slide)
- ❑ Revaccinate **every 5 years** as long as the person remains at increased risk
  - MenACWY for persons 2 through 55 years of age
  - MenACWY for persons 56 years and older also (off-label recommendation) if repeated vaccination anticipated

\*Off-label recommendation. *MMWR* 2013;62(RR-2):10-11

# International Travelers and Revaccination\*

- ❑ **International travelers should receive a booster dose of MenACWY if the last dose was administered 5 or more years previously**
  - Vaccination in the 3 years before the date of travel is required by the government of Saudi Arabia for all travelers to Mecca during the annual Hajj

\*CDC Travelers Health website at <http://www.cdc.gov/travel>

# Meningococcal Vaccines

## Adverse Reactions

	<b>MPSV</b>	<b>MenACWY</b>
Local reactions for 1-2 days	4%-48%	11%-59%
Low-grade fever	3%	5%-17%
Systemic reactions (headache, malaise, fatigue)	3%-60%	4%-54%

# **MenB Vaccine Recommendations**

# Meningococcal B Vaccines

<b>Product Name/ACIP abbreviation</b>	<b>FDA Age Indications</b>	<b>Dosage/Route/Schedule</b>
Trumenba <sup>®</sup> MenB-FHbp	10 through 25 years of age	<ul style="list-style-type: none"><li>• 3 doses – 0.5 mL each</li><li>• IM injection</li><li>• 0-, 1-2-, and 6-month</li></ul>
Bexsero <sup>®</sup> MenB-4C	10 through 25 years of age	<ul style="list-style-type: none"><li>• 2 doses – 0.5 mL each</li><li>• IM injection</li><li>• 0, 1–6 month</li></ul>

# ACIP MenB Recommendations

- ❑ MenB should be administered as either a 2-dose series of MenB-4C or a 3-dose series of MenB-FHbp
- ❑ The same vaccine product should be used for all doses
- ❑ MenB-4C and MenB-FHbp may be administered concomitantly with other vaccines indicated for this age, but at a different anatomic site, if feasible
- ❑ No product preference to be stated

# Meningococcal B Recommendations

- ❑ Recommendation for use in individuals  $\geq 10$  years of age at increased risk of disease
- ❑ Recommendation for use in adolescents and young adults not at increased risk for disease

# ACIP MenB Recommendations

- ❑ **Certain persons aged  $\geq 10$  years\* who are at increased risk for meningococcal disease should receive MenB vaccine. These persons include:**
  - **Persons with persistent complement component deficiencies**
  - **Persons with anatomic or functional asplenia\*\***
  - **Microbiologists routinely exposed to isolates of *Neisseria meningitides***
  - **Persons identified as at increased risk because of a serogroup B meningococcal disease outbreak**

\*ACIP off-label recommendation

\*\*Including sickle cell disease

[www.cdc.gov/mmwr/preview/mmwrhtml/mm6422a3.htm?s\\_cid=mm6422a3\\_w](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6422a3.htm?s_cid=mm6422a3_w)

# ACIP MenB Recommendations

- ❑ **Certain other groups included in MenACWY (MCV4) recommendations for persons at increased risk, are not in this recommendation**
- ❑ **MenB – NOT currently recommended for:**
  - **Children aged 2 months – 9 years of age**
  - **Persons who travel to or reside in countries where meningococcal disease is hyperendemic or epidemic because risk is generally not caused by serogroup B**
  - **Routine use in first-year college students living in residence halls, military recruits, or all adolescents**

# MenB for Adolescents and Young Adults

- ❑ A MenB vaccine series *may* be administered to adolescents and young adults aged 16–23 years to provide short-term protection against most strains of serogroup B meningococcal disease\*
- ❑ The preferred age for MenB vaccination is 16–18 years

\* Permissive recommendation (Category B)

MMWR October 23, 2015 / 64(41);1171-6

# **Meningococcal Vaccine**

## **Contraindications and Precautions**

- ❑ Severe allergic reaction to vaccine component or following prior dose**
  
- ❑ Moderate or severe acute illness**



# Meningococcal Resources

- ❑ **ACIP's Meningococcal Recommendations web page**  
[www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/mening.html](http://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/mening.html)
- ❑ **CDC's Meningococcal Infection web page**  
[www.cdc.gov/meningococcal/index.html](http://www.cdc.gov/meningococcal/index.html)
- ❑ **CDC's Meningococcal Vaccination web page**  
[www.cdc.gov/vaccines/vpd-vac/mening/default.htm](http://www.cdc.gov/vaccines/vpd-vac/mening/default.htm)
- ❑ **Immunization Action Coalition Meningococcal web page**  
[www.immunize.org/meningococcal/](http://www.immunize.org/meningococcal/)
- ❑ **Children's Hospital of Philadelphia Vaccine Education Center Meningococcal web page**  
[www.chop.edu/service/vaccine-education-center/a-look-at-each-vaccine/meningococcus-vaccine.html](http://www.chop.edu/service/vaccine-education-center/a-look-at-each-vaccine/meningococcus-vaccine.html)