Meningococcal Disease and Meningococcal Vaccines
Neisseria meningitidis

- Aerobic gram-negative bacteria
- At least 12 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
Meningococcal Meningitis

- Results from hematogenous dissemination

- Findings
  - Fever
  - Headache
  - Stiff neck

- Fatality rate: 10-15%
Meningococcemia

- Bloodstream infection
- May occur with or without meningitis

Clinical findings
- Fever
- Gastrointestinal symptoms
- Petechial or purpuric rash
- Hypotension
- Shock
- Acute adrenal hemorrhage
- Multi-organ failure

Fatality rate: up to 40%
Meningococcal Disease
Meningococcal Disease

Neisseria meningitidis
Risk Factors for Invasive Disease

- **Host Factors**
  - Deficiencies in the terminal common complement pathways
  - Taking eculizumab (Soliris)
  - Functional or anatomic asplenia
  - HIV

- **Environmental factors**
  - Household crowding
  - Active and passive smoking
  - Antecedent viral infection

- Occupational (microbiologists)
Meningococcal Disease Incidence – United States, 1996–2015

1.3 cases/100,000 population

0.12 cases/100,000 population

Year

Incidence per 100,000

Abbreviations: MenACWY = quadrivalent meningococcal conjugate vaccine; MenB vaccine = serogroup B meningococcal vaccines

Source: 1996-2015 NNDSS Data

Source: National Notifiable Diseases Surveillance System (NNDSS) data with additional serogroup data from Active Bacterial Core surveillance (ABCs) and state health departments
Meningococcal Disease by Serogroup, All Ages – United States, 2006-2015

Source: National Notifiable Diseases Surveillance System (NNDSS) data with additional serogroup data from Active Bacterial Core surveillance (ABCs) and state health departments
Excludes 20% with unknown serogroup
Meningococcal Vaccines
# Serogroup A, C, W, Y meningococcal vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Abbreviation</th>
<th>Type</th>
<th>Manufacturer</th>
<th>Serogroups</th>
<th>Approved ages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menactra®</td>
<td>MenACWY-D</td>
<td>Conjugate – Diphtheria toxoid</td>
<td>Sanofi Pasteur</td>
<td>A, C, W, Y</td>
<td>9 months—55 years</td>
</tr>
<tr>
<td>Menveo®</td>
<td>MenACWY-CRM</td>
<td>Conjugate-CRM\textsubscript{197}</td>
<td>GSK</td>
<td>A, C, W, Y</td>
<td>2 months—55 years</td>
</tr>
<tr>
<td>Trumenba®</td>
<td>MenB-FHbp</td>
<td>Protein</td>
<td>Pfizer</td>
<td>B</td>
<td>10—25 years</td>
</tr>
<tr>
<td>Bexsero®</td>
<td>MenB-4C</td>
<td>Protein</td>
<td>GSK</td>
<td>B</td>
<td>10—25 years</td>
</tr>
</tbody>
</table>
Meningococcal Conjugate Vaccines

- Meningococcal polysaccharide conjugated to protein carrier

- Elicit both T- and B-cell immunity (T-cell dependent immunity)

- 2 brands currently licensed and available in the United States
  - Menactra (Sanofi Pasteur)
  - Menveo (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 W (MenACWY-CRM)

- May be used for any person 2 months through 55 years of age for whom MenACWY is indicated, including revaccination

- Intramuscular injection

- Single dose vials
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.
Meningococcal Polysaccharide Vaccine (MPSV4)

- Menomune

- The manufacturer has discontinued production and supply of Menomune in the United States

- Last remaining lots expired September 2017
Updated Guidance for Use of Meningococcal Vaccines in Persons Aged ≥56 Years

- Meningococcal vaccines that are licensed for use in persons aged ≥56 years are not currently available in the United States.

- Persons aged ≥56 years who are recommended meningococcal vaccination because they are at increased risk for meningococcal disease should receive MenACWY conjugate vaccine.
  - This includes, meningococcal vaccine-naïve persons aged ≥56 years who anticipate requiring only a single dose of meningococcal vaccine (e.g., travelers and persons at risk as a risk of a community outbreak).
  - And persons who were vaccinated previously with MenACWY conjugate vaccine and are recommended for revaccination or for whom multiple doses are anticipated (e.g., person with asplenia, HIV, and microbiologists).
Routine Adolescent MenACWY Vaccine Recommendations
Figure 1. Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger—United States, 2018.

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 in gray.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Birth 1 mo 2 mo 4 mos 6 mos 9 mos 12 mos 15 mos 18 mos 10-23 mos 2-3 yrs 4-6 yrs 7-10 yrs 11-12 yrs 13-14 yrs 15 yrs 16 yrs</th>
<th>1-18 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B (HepB)</td>
<td>1st dose 2nd dose 3rd dose</td>
<td>1st dose</td>
</tr>
<tr>
<td>Rotavirus (RV) (2-dose series; RV5 3-dose series)</td>
<td>1st dose 2nd dose 3rd dose</td>
<td>1st dose</td>
</tr>
<tr>
<td>Diphtheria, tetanus, &amp; acellular pertussis (DtaP&lt;n yr)</td>
<td>1st dose 2nd dose 3rd dose</td>
<td>1st dose</td>
</tr>
<tr>
<td>Haemophilus influenza type b (HiB)</td>
<td>1st dose 2nd dose 3rd dose</td>
<td>1st dose</td>
</tr>
<tr>
<td>Pneumococcal conjugate (PCV13)</td>
<td>1st dose 2nd dose 3rd dose</td>
<td>1st dose</td>
</tr>
<tr>
<td>Inactivated polioivirus (IPV-&lt;18 yrs)</td>
<td>1st dose 2nd dose 3rd dose</td>
<td>1st dose</td>
</tr>
<tr>
<td>Influenza (IV)</td>
<td>Annual vaccination (IV) 1 or 2 doses</td>
<td>Annual vaccination (IV) 1 dose only</td>
</tr>
<tr>
<td>Measles, mumps, rubella (MMR)</td>
<td>See footnote 8</td>
<td>1st dose</td>
</tr>
<tr>
<td>Varicella (VAR)</td>
<td>1st dose</td>
<td>2nd dose</td>
</tr>
<tr>
<td>Hepatitis A (HepA)</td>
<td>2-dose series See footnote 10</td>
<td></td>
</tr>
<tr>
<td>Meningococcal (MenACWY-D 25-10, MenACWY-21)</td>
<td>See footnote 11</td>
<td>1st dose</td>
</tr>
<tr>
<td>Tetanus, diphtheria, &amp; acellular pertussis (Tdap&gt;2 yrs)</td>
<td>See footnote 14</td>
<td>1st dose</td>
</tr>
<tr>
<td>Human papillomavirus (HPV)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningococcal B (Meningococcal B)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumococcal polysaccharide (PPSV23)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Range of recommended ages for all children
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

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.
MenACWY Vaccine Recommendations for Persons at Increased Risk for Meningococcal Disease
Groups at Increased Risk

- **Younger than 2 years of age**
  - Functional or anatomic asplenia (including use of eculizumab (Soliris))
    - Menveo only
      - First dose before 7 months of age – four doses at 2, 4, 6, and 12 months
      - First dose on or after 7 months of age – 2 doses, 2\textsuperscript{nd} dose 12 weeks after the first dose, and after 1 year of age
  
  - HIV-infection
    - Menveo only
      - First dose before 7 months of age – four doses at 2, 4, 6, and 12 months
      - First dose on or after 7 months of age – 2 doses, 2\textsuperscript{nd} dose 12 weeks after the first dose and after 1 year of age

- Complement component deficiency
  - Younger than nine months of age
    - Menveo only
      - First dose before 7 months of age – four doses at 2, 4, 6, and 12 months
      - First dose on or after 7 months of age – 2 doses, 2\textsuperscript{nd} dose 12 weeks after the first dose and after 1 year of age
  
  - Nine months of age or older
    - Menactra or Menveo – 2 doses, 2\textsuperscript{nd} dose 12 weeks after the first dose and after 1 year of age
    - Menactra should be administered before DTaP or simultaneous with DTaP
Groups at Increased Risk

**2 years of age or older**

- Functional or anatomic asplenia
  Menactra or Menveo
  Menactra must NOT be administered simultaneously with PCV13
  Menactra should be administered before DTaP or simultaneous with DTaP

- HIV-infection
  Menactra or Menveo
  Menactra must NOT be administered simultaneously with PCV13
  Menactra should be administered before DTaP or simultaneous with DTaP

- Complement component deficiency
  Menactra or Menveo
  Menactra should be administered before DTaP or simultaneous with DTaP
# Meningococcal Vaccines Adverse Events

<table>
<thead>
<tr>
<th></th>
<th>MenACWY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local reactions</td>
<td>11%-59%</td>
</tr>
<tr>
<td>for 1-2 days</td>
<td></td>
</tr>
<tr>
<td>Low-grade fever</td>
<td>5%-17%</td>
</tr>
<tr>
<td>Systemic reactions</td>
<td>4%-54%</td>
</tr>
<tr>
<td>(headache, malaise, fatigue)</td>
<td></td>
</tr>
</tbody>
</table>

MenB Vaccine Recommendations
## Meningococcal B Vaccines

<table>
<thead>
<tr>
<th>Product Name/ACIP abbreviation</th>
<th>FDA Age Indications</th>
<th>Dosage/Route/Schedule</th>
</tr>
</thead>
</table>
| Trumenba ® MenB-FHbp          | 10 through 25 years of age | • 2-3 doses – 0.5 mL each  
• IM injection  
• 0, 1-2, and 6-month; OR  
• 0, 6 month |
| Bexsero® MenB-4C              | 10 through 25 years of age | • 2 doses – 0.5 mL each  
• IM injection  
• 0, 1–6 month |
ACIP MenB Recommendations

- MenB should be administered as either a 2-dose series of MenB-4C or a 3-dose or 2-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 adolescents and young adults not at increased risk for disease

- Recommendation for use in individuals ≥10 years of age at increased risk of disease
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

* Recommendation (Category B)
MMWR October 23, 2015 / 64(41);1171-6
ACIP MenB Recommendations

- Certain persons aged ≥10 years* who are at increased risk for meningococcal disease should receive MenB vaccine. These persons include:
  - Persons with persistent complement component deficiencies (including those taking eculizumab)
  - 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
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
  - HIV-infected people

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6422a3.htm?s_cid=mm6422a3_w
Use of 2- and 3-Dose Schedules of MenB-FHbp (Trumenba)
Meningococcal Serogroup B Vaccine

- For persons at increased risk for meningococcal disease and for use during serogroup B outbreaks, 3 doses of MenB-FHbp should be administered at 0, 1-2, 6 months

- When given to healthy adolescents who are not at increased risk for meningococcal disease, 2 doses of MenB-FHbp should be administered at 0 and 6 months
Meningococcal Vaccine
Contraindications and Precautions

- Severe allergic reaction to vaccine component or following prior dose

- Moderate or severe acute illness
Serogroup B meningococcal disease outbreaks on college campuses‡, 2013–2018

<table>
<thead>
<tr>
<th>State of University</th>
<th>Year started</th>
<th>Cases (deaths)</th>
<th>Undergraduate population</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Jersey</td>
<td>2013</td>
<td>9 (1)</td>
<td>5,000</td>
</tr>
<tr>
<td>California</td>
<td>2013</td>
<td>4*</td>
<td>19,000</td>
</tr>
<tr>
<td>Rhode Island</td>
<td>2015</td>
<td>2</td>
<td>4,000</td>
</tr>
<tr>
<td>Oregon</td>
<td>2015</td>
<td>7 (1)</td>
<td>20,000</td>
</tr>
<tr>
<td>California</td>
<td>2016</td>
<td>2**</td>
<td>5,000</td>
</tr>
<tr>
<td>New Jersey</td>
<td>2016</td>
<td>2</td>
<td>35,000</td>
</tr>
<tr>
<td>Wisconsin</td>
<td>2016</td>
<td>3</td>
<td>30,000</td>
</tr>
<tr>
<td>Oregon</td>
<td>2016</td>
<td>5</td>
<td>25,000</td>
</tr>
<tr>
<td>Massachusetts</td>
<td>2017</td>
<td>3</td>
<td>30,000</td>
</tr>
<tr>
<td>Pennsylvania</td>
<td>2017</td>
<td>2</td>
<td>3,600</td>
</tr>
</tbody>
</table>

During 2014–2016, 31.7% of serogroup B cases in college students were outbreak-related.

*Where CDC consulted; *1 additional associated case identified after retrospective case review; **1 additional patient with inconclusive laboratory results.
Meningococcal Vaccine Use in Outbreaks

- MenACWY recommended for use in control of outbreaks caused by A, B, C, W, and Y

- Outbreak definition:
  - Community-based
    - Increase in incidence above expected in a 3 month period
  - Organization-based
    - 2-3 cases in an organization in a 3 month period

Meningococcal Resources

- ACIP’s Meningococcal Recommendations web page
  www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/mening.html
- CDC’s Meningococcal Infection web page
  www.cdc.gov/meningococcal/index.html
- CDC’s Meningococcal Vaccination web page
  www.cdc.gov/vaccines/vpd-vac/mening/default.htm
- Immunization Action Coalition Meningococcal web page
  www.immunize.org/meningococcal/
- Children’s Hospital of Philadelphia Vaccine Education Center Meningococcal web page
  http://www.chop.edu/centers-programs/vaccine-education-center/vaccine-details/meningococcal-vaccine