Meningococcal Disease and Vaccines

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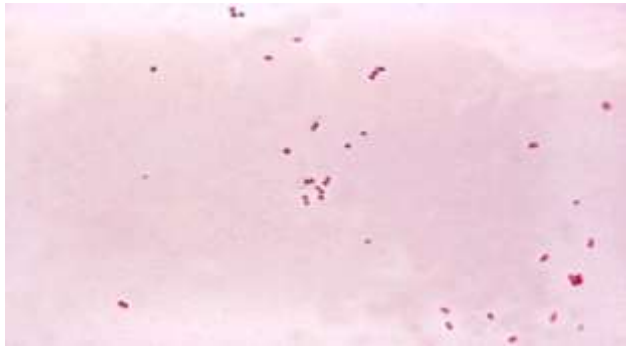
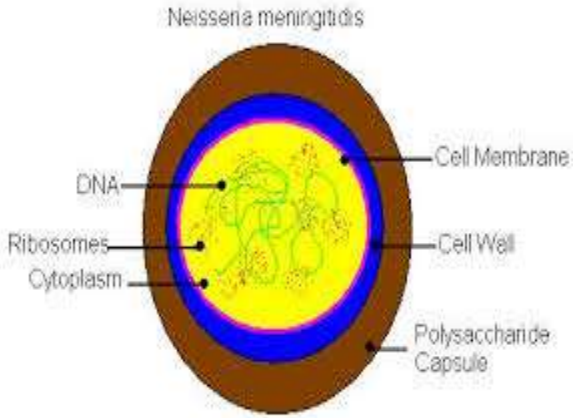
Objectives

- Discuss *Neisseria meningitidis* (meningococcus) and its associated diseases
- Review meningococcal ACWY vaccines
- Review meningococcal B vaccines

Neisseria meningitidis (Meningococcus)

- Bacteria (gram-negative diplococcus)
- The polysaccharide capsule and the proteins that project out from the cell wall are important antigens





AAP. 2015 Red Book Online Visual Library. Meningococcal Infections.
http://dg743.wordpress.com/2008/02/17/structure-and-anatomy

Meningococcal Disease

- Severe disease that progresses rapidly
- Sepsis (meningococcemia)
- Meningitis
- Focal disease (pneumonia and arthritis)
- Case-fatality rate for meningococcal disease is 10% to 15% and is somewhat higher in adolescents

From: **Meningococcal Infections**

Red Book®, 2012

Figure Legend:

A 2-year-old white male with acute meningococcemia with septic shock and purpura fulminans.
Courtesy of George Nankervis, MD

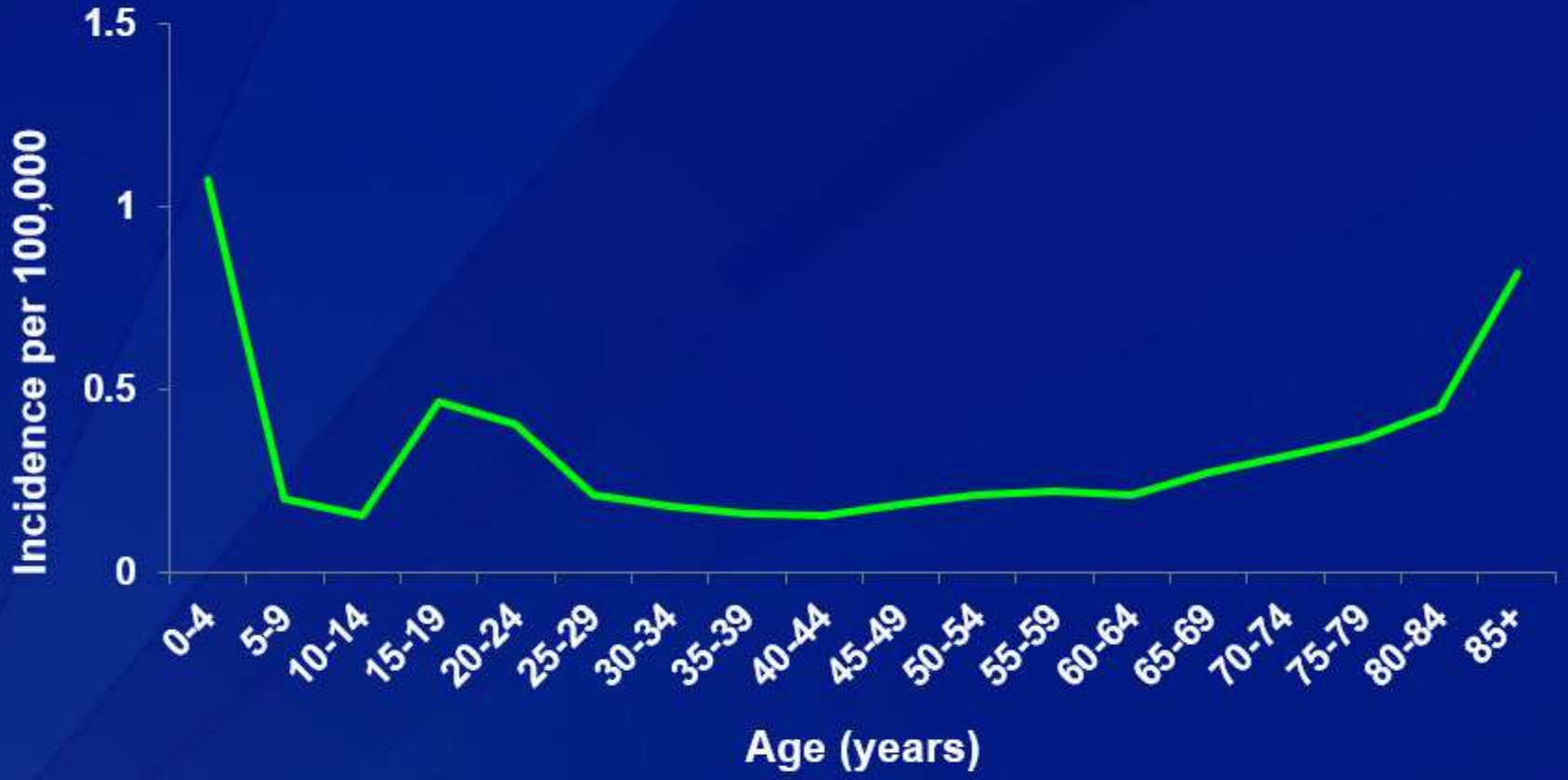
Risk Factors for Meningococcal Disease

- Persons who have problems with the function of their spleen or the complement proteins
- HIV infection with one of the above indications
- Family members of an infected person
- Smoking, including passive exposure to smoke
- Recent upper respiratory infection
- Crowding
- College students (living in residence halls)

Prevention of Meningococcal Disease

- Given the severe manifestations of meningococcal disease, prevention of disease is an important public health goal.
- For another bacterial cause of meningitis (*Haemophilus influenzae* type b or Hib), a vaccine has been the most important strategy in preventing disease.
- Since Hib vaccination was added to the infant schedule, Hib disease has decreased over 99% (from over 20,000 to less than 20 cases per year).

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



SOURCE: CDC. National Notifiable Diseases Surveillance System

Different Types of *Neisseria meningitidis*

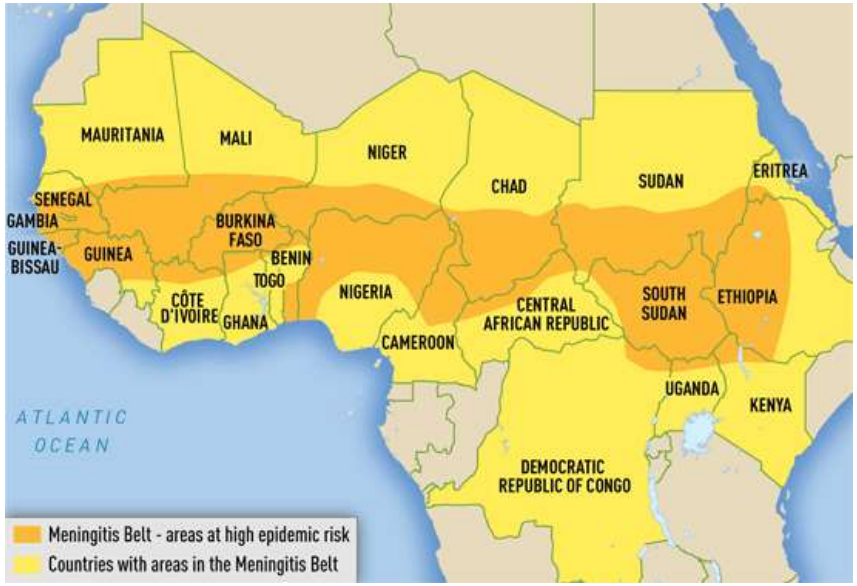
- Meningococci are classified into different serogroups based on the composition of their polysaccharide capsule.
- Thirteen different serogroups have been described.
- Some meningococci do not have a capsule and are referred to as nontypable.
- Almost all severe meningococcal disease is caused by serogroups A, B, C, Y, and W.

Different Types of *Neisseria meningitidis*

- Protection acquired through infection and disease is serogroup-specific. Individuals who survive meningococcal disease due to serogroup B make an immune response that is specific to serogroup B. They are still susceptible to disease from the other serogroups.

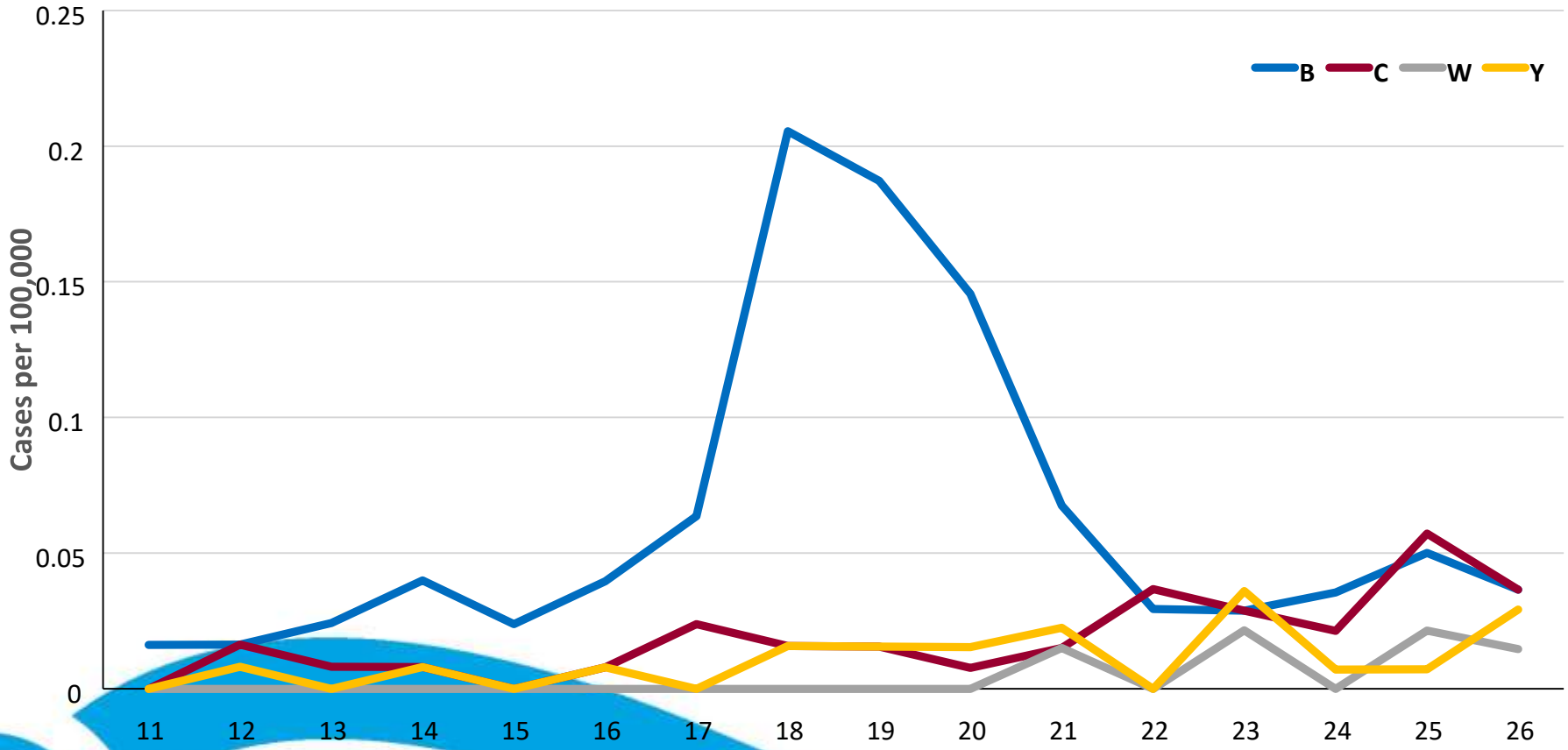
Neisseria meningitidis Serogroup A

- Serogroup A meningococcal disease is associated with epidemics in sub-Saharan Africa
- Rare in the United States
- Travelers need protection



CDC. Yellow Book. Travelers' Health. Meningococcal Disease.

Incidence of Meningococcal Disease Among Adolescents and Young Adults by Serogroup, 2014-2016



Source: CDC. Unknown serogroup and other serogroups excluded.

Designing An "Ideal" Meningococcal Vaccine

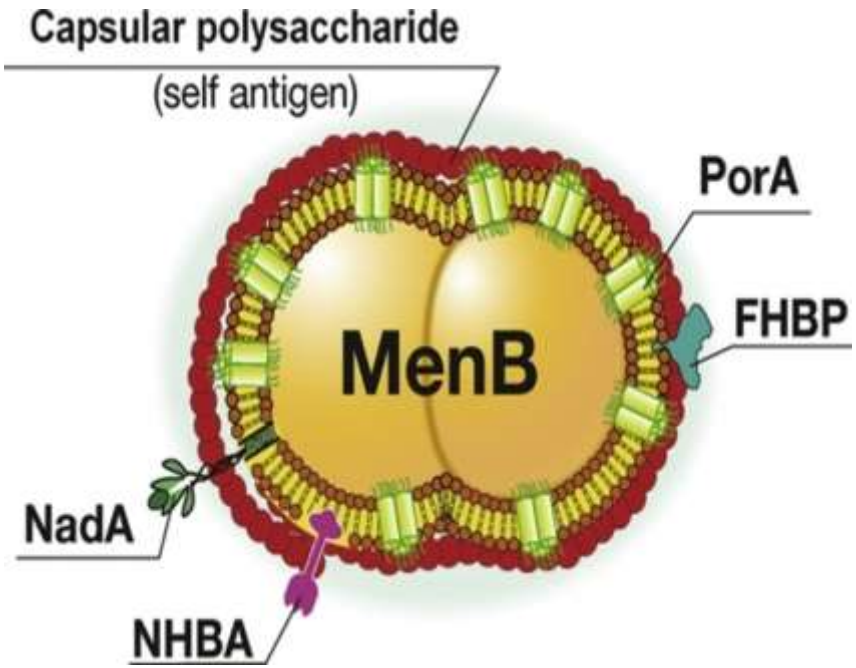
- Covers all the types that usually cause invasive disease: A, B, C, W, and Y
- Offers protection to those in the age groups with the highest incidence:
  - Young infants
  - Adolescents and young adults
  - Elderly
- Will likely need to include antigens based on the polysaccharide capsule and/or the outer membrane proteins because they are the major antigenic determinants

Designing An "Ideal" Meningococcal Vaccine

- Remembering that young children do not make good immune responses to polysaccharide antigens, a protein conjugate may need to be added to the capsular polysaccharide to improve the immune response (similar to the pneumococcal polysaccharide-protein conjugate vaccine)

Meningococcal Vaccines

- Meningococcal ACWY polysaccharide-protein conjugate vaccines were prepared, and studied.
- Meningococcal ACWY vaccines were safe and produced good immune responses.
- However, when the B part was added, the immune response was poor.



F1000 Med Rep. 2011;3:16.

Meningococcal ACWY Vaccines

- Men-ACWY-CRM vaccine
- Men-ACWY-D vaccine
- Both are administered intramuscularly
- Either can be administered as part of the recommended schedule for adolescents.
- Adolescent Recommendation:
  - Two doses of the same formulation
  - First dose at 11-12 years
  - Second dose at 16 years

Additional Caveats about Men-ACWY Vaccines

- Adolescents who receive their first dose at age 13 through 15 years should receive a booster dose at age 16 through 18 years.
- Adolescents who receive a first dose of Men-ACWY vaccine after their 16th birthday do not need a booster dose unless they become at increased risk for meningococcal disease.
- Men-ACWY vaccine is the one referenced in the Ohio meningococcal laws.

Ohio Meningococcal Laws

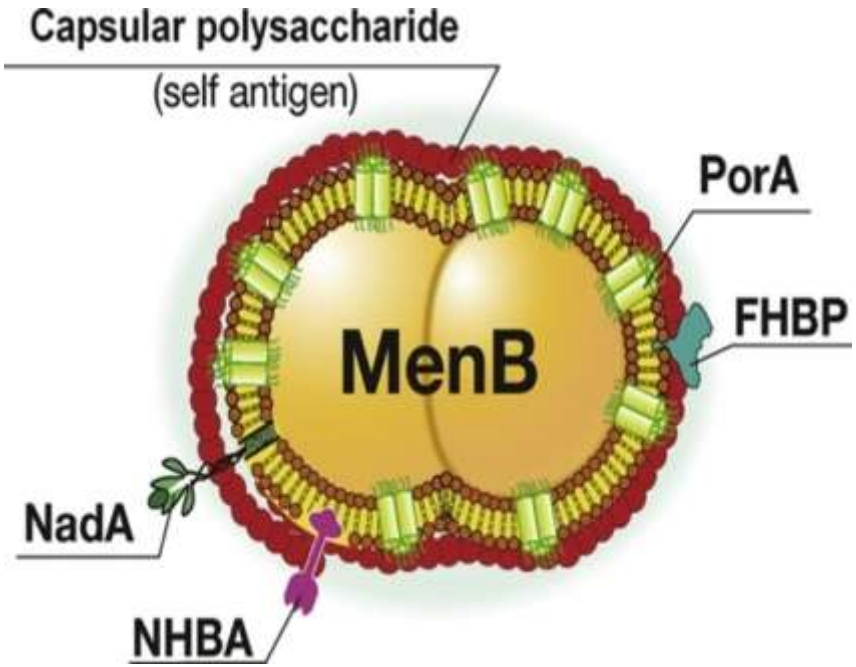
- Mandate that started with the 2016-2017 school year
- Requires students to be immunized against meningococcal ACWY disease
  - One dose of Men-ACWY vaccine required before 7th grade
  - Second dose of Men-ACWY vaccine required before 12th grade
  - If the first dose was given after the 16th birthday, then a second dose is not required
- Legislation allows for medical and personal exemptions

Colleges and Meningococcal ACWY Vaccines

- Legislation passed in Ohio in 2005 requires college students to disclose their Men-ACWY vaccination status to the college
- The law does not require vaccination
- The law does not require the college to provide or pay for the vaccine
- Some colleges have their own requirements for incoming first-year students living in residence halls or for all incoming students

Meningococcal B Vaccines

- Polysaccharide capsule is similar to a self antigen so it is poor at inducing immune responses
- Focused on using the outer membrane proteins as antigens



F1000 Med Rep. 2011;3:16.

Meningococcal Serogroup B Vaccines

- Two vaccines have been approved by the FDA to protect against *Neisseria meningitidis* serogroup B disease
- Both are only licensed for use in persons 10 to 25 years of age
- One vaccine is Men-B-4c (has four components from the outer membrane derived from different strains)
- The other vaccine is Men-B-FHbp (contains FHBP proteins from both of the FHBP subfamily types)
- The CDC has not indicated a preference between the two Men-B vaccines

Meningococcal Serogroup B Vaccine

- A routine adolescent Men-B vaccine recommendation would be expected to prevent 15 to 29 cases and 2 to 5 deaths per year, assuming all eligible persons were immunized.
- Currently, it is not cost-effective to immunize all adolescents against meningococcal serogroup B disease.
- Therefore, the Advisory Committee on Immunization Practices (ACIP) of the CDC has developed two categories of recommendations for Men-B vaccines.

Men-B Vaccine Category A Recommendation

- Category A recommendation: Recommended. Give the vaccine unless there is a contraindication or precaution
- Other adolescent vaccines (Tdap, HPV, Men-ACWY, and influenza) have a Category A recommendation.
- Men-B vaccine has a Category A recommendation only for individuals 10 to 25 years of age :
  - With complement protein deficiencies
  - With problems with function of the spleen
  - Who are at risk during an outbreak of meningococcal B disease (The CDC defines outbreaks and those at risk.)
  - Microbiologists who routinely work with *Neisseria meningitidis*

Men-B Vaccine Category B Recommendation

- Category B recommendation: Permissive. Adolescents, their parents, and young adults can decide on an individual basis.
- Either Men-B vaccine can be used (no preference)
- Based on currently available information, Men-B vaccines are safe and effective.
- The preferred age of Men-B vaccine receipt is 16 to 18 years but they are licensed up to age 25 years.
- This permissive recommendation is based on the facts that meningococcal serogroup B disease is rare, the vaccines are expensive, and currently, it is not cost-effective to recommend them for all adolescents.

Men-B Vaccine Category B Recommendation

- Both types of Men-B vaccine are covered by Vaccines for Children (up to 18 years of age).
- Private insurance carriers vary in their coverage of Men-B vaccines so the family should check about coverage before administration.
- Colleges can decide on an individual basis as to whether they recommend Men-B vaccines for first-year students who will be living in residence halls or other entering students.

Men-B Vaccine Category B Recommendation

- College students should check with the student health department at their college regarding vaccine recommendations.
- The manufacturers of Men-B vaccines are advertising directly to the lay public so health care providers need to be prepared to address their questions.

Other Men-B Vaccine Considerations

- The two Men-B vaccines (Men-B-4C and Men-B-FHbp) are NOT interchangeable.
- The same type of vaccine should be used for all doses.
- Minimum intervals have not been defined. Use the schedule.
- Men-B vaccines can be administered at the same time as other vaccines in a separate syringe and at a separate site.

Men-B-4C Vaccine

- Two doses
- First dose at day 0
- Second dose ≥ 1 month later
- Contraindication: Severe allergic reaction to a previous dose of Men-B vaccine or any of its components
- Adverse events reported in clinical trials
  - Severe pain at injection site: 20%-29%
  - Muscle pain (severe): 12%-13%
  - Use of antipyretic medication: Not measured

Men-B-FHbp Vaccine

- Two or three doses
- Two dose schedule: 0 and ≥ 6 months
- Three dose schedule: 0, 1-2 months, and ≥ 6 months
- The two-dose schedule should not be used for individuals at high risk of meningococcal serogroup B disease (those in the Category A recommendation groups).
- Contraindication: Severe allergic reaction to a previous dose of Men-B vaccine or any of its components
- Adverse events reported in clinical trials
  - Severe pain at injection site: 5%-8%
  - Muscle pain (severe): 1%-3%
  - Use of antipyretic medication: 17%-28%

Adoption of Men-B Vaccine Recommendations

- E-mail and Internet survey from October 2016 to December 2016
- Nationally representative sample of pediatricians and family practice physicians
- Discussion of Men-B vaccine
- Decision to recommend Men-B vaccine
- Delivery of Men-B vaccine

Kempe A, et al. *Pediatrics*. 2018;142(3):e20180344

Results

- Response rate was 72% (660 of 916)
- Discussion of Men-B vaccine during routine visits
  - Pediatricians: 51%
  - Family practice physicians: 31%
- Among those who discussed often or always, 91% recommended Men-B vaccine
- Among those who never or rarely discussed, only 11% recommended Men-B vaccine
- Currently administer the Men-B vaccine
  - Pediatricians: 73%
  - Family practice physicians: 41%

Results

- Factors that increased the likelihood of recommendation:
  - Men-B disease outbreaks (89%)
  - Disease incidence (62%)
  - Effectiveness (52%)
  - Safety (48%)

- Factors that decreased the likelihood of recommendation:
  - Category B recommendation (45%)
  - Lack of knowledge about the Men-B vaccine

Conclusions

- Meningococcal disease has a high case-fatality rate in adolescents and young adults
- Men-ACWY vaccines are recommended for all adolescents.
- Men-B vaccines are permissive for healthy persons 10 to 25 years of age. They are required for those who are at high risk of invasive Men-B disease.
- Physicians have gaps in knowledge about Men-B disease and vaccines and this is the major driver in their decision to discuss these vaccines.