

Vaccination for Meningococcus

Stephen C. Eppes, M.D.
duPont Hospital for Children
Jefferson Medical College

Disease Presentations

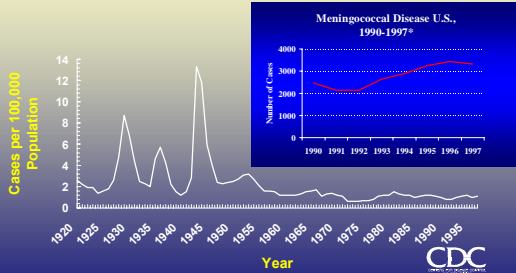
- Bacteremia without sepsis
- Meningococcemia without meningitis
- Meningitis with or without meningococcemia
- Pneumonia (adults)

Meningococcal Disease: Epidemiology

- Serogroups A, B, C, Y, and W135
- Africa: serogroup A predominates
- United States: serogroups B, C, and Y
- Recent increase in cases in adolescents and young adults
- Recent increase in cases due to serogroup Y
- Case-fatality rate 10-20%
- Sequelae in 10-20% (neurologic, limb loss)

Epidemiology

Meningococcal Disease United States, 1920-1997

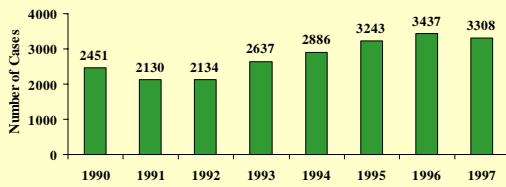


* CDC. Summary of notifiable diseases, United States 1997. *MMWR*, 46(54), November 20, 1998, 74.

Epidemiology

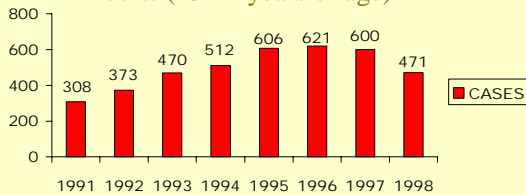
Meningococcal Disease United States, 1990-1997

Meningococcal Disease U.S., 1990-1997



* CDC. Summary of notifiable diseases, United States 1997. *MMWR*, 46(54), November 20, 1998, 74.

Cases of Meningococcal Disease in Young Adults (15-24 years of age)



Centers for Disease and Prevention. Summary of notifiable disease, United States, 1991. *MMWR*, 1992; 40(53):10.
Centers for Disease and Prevention. Summary of notifiable disease, United States, 1992. *MMWR*, 1993; 41(55):10.
Centers for Disease and Prevention. Summary of notifiable disease, United States, 1993. *MMWR*, 1994; 42(53):10-11.
Centers for Disease and Prevention. Summary of notifiable disease, United States, 1994. *MMWR*, 1995; 43(53):10.
Centers for Disease and Prevention. Summary of notifiable disease, United States, 1995. *MMWR*, 1996; 44(53):10.
Centers for Disease and Prevention. Summary of notifiable disease, United States, 1996. *MMWR*, 1997; 45(53):10.
Centers for Disease and Prevention. Summary of notifiable disease, United States, 1997. *MMWR*, 1998; 46(54):10,45,73.
Centers for Disease and Prevention. Summary of notifiable disease, United States, 1998. *MMWR*, 1999; 47(53):12.

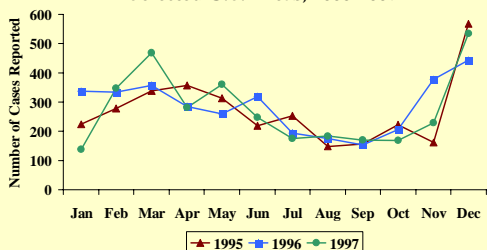
Year 2000: 2256 Cases Age Specific Numbers and Rates

< 1 year	259 cases	6.79 per 100,000
1-4 years	308	2.04
5-14	292	0.74
15-24	482	1.28
25-39	229	0.38
40-64	356	0.44
> 65	312	0.90

Epidemiology

Seasonal Variation in Meningococcal Disease

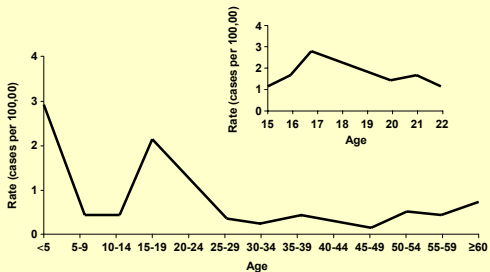
Selected U.S. Areas, 1995-1997



2 CDC. Summary of notifiable diseases, United States 1997. MMWR 46(53), November 20, 1998, 3.
3 CDC. Summary of notifiable diseases, United States 1996. MMWR 45(53), October 31, 1997, 3.
4 CDC. Summary of notifiable diseases, United States 1995. MMWR 44(53), October 25, 1996, 3.

Epidemiology

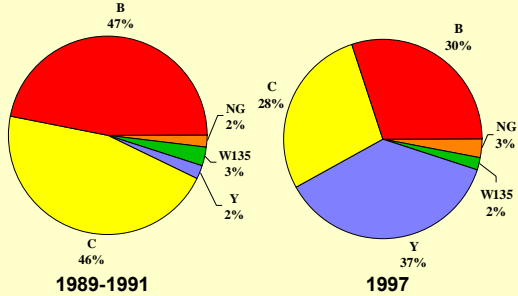
Average Annual Incidence of Meningococcal Disease by Age Group, Maryland, 1992-1997



1 Harrison LH, Dwyer DM, Maples CT, Billmann L. The risk of meningococcal infection in Maryland college students. JAMA. 1999;281(20):pg.1908. Copyright 1999, American Medical Association.

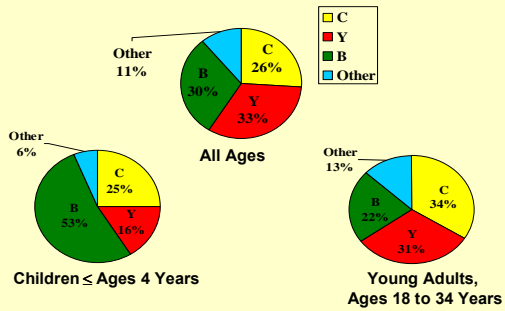
Epidemiology

Changing Serogroup Distribution in the U.S.



5 Martone et al. The Changing Epidemiology of Meningococcal Disease in the US With an Emphasis on College Health Issues, a publication of the National Foundation for Infectious Diseases, May 1999 pp. 4 fig 4.

Serogroup Distribution in the United States, in 1997



Centers for Disease Control and Prevention. Active Bacterial Core Surveillance (ABCS) Report. Emerging Infections Program Network. *Neisseria meningitidis*, 1997.

Disease Transmission

- Humans only known reservoir -- nasopharyngeal colonization
- Invasive disease occurs in newly infected
- Person to person
- Oral secretions / respiratory droplets

Meningococcal Disease: Risk Factors

- Overcrowding
- Smoking
- Immune deficiencies (hypo- or agammaglobulinemia, asplenia, terminal complement deficiencies)
- Viral URI (especially influenza)

Meningococcal Prophylaxis

- Close contacts (household, daycare, exposure to oral secretions)
- ASAP, ideally within 24 hours
- 3 agents, all 90-95% effective in reducing NP carriage on *N. meningitidis*
 - rifampin
 - ciprofloxacin
 - ceftriaxone (IM/IV)

Meningococcal Polysaccharide Vaccines

- October 1971 -- monovalent C vaccine used in US Army recruits
- 1975 -- FDA approves both group A and C vaccines
- 1976 -- FDA approves bivalent A/C vaccine
- In field studies, A and C vaccines provided 87-90% protection

U.S. Army Experience

- Through 1960's -- 30.1 cases per 100,000 each year
- Following initiation of vaccine in early 1970's -- 1.4 cases per 100,000 each year

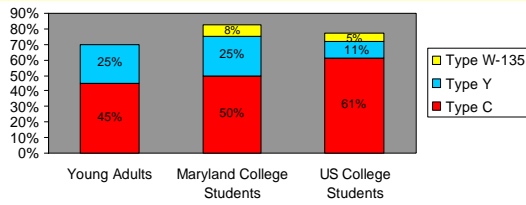
Menomune® - A/C/Y/W-135

- Polysaccharide vaccine licensed in 1981
- Indications:
 - military recruits
 - travelers to endemic countries
 - to arrest outbreaks and epidemics
 - healthcare workers*
 - recommendation for college students

Menomune® -- Adverse Effects

- Injection site pain/redness, mild, 4-56%
- Allergic reactions < 1:1,000,000 doses
- Serious inj. site reactions < 1:1,000,000
- Guillain-Barré < 1:1,000,000

Disease in Young Adults is Largely Preventable



- At least 70% of all cases of meningococcal disease in college students are vaccine preventable

Rosenstein NE, Perkins BA, Stephens DS, et al. The changing epidemiology of meningococcal disease in the United States, 1992-1996. *J Infect Dis* 1999; 180: 1894-1901.
Harrison LH, Dwyer DM, Maples CT, et al. Risk of meningococcal infection in college students. *JAMA*. 1999; 281: 1906-1910.
Froeschke JE. Meningococcal disease in college students. *Clin Infect Dis*. 1999; 29: 216-216.

Cases and Deaths Reported for Vaccine-Preventable Infectious Disease Among Young Adults (ages 15-24) in 1997

Disease	Measles	Mumps	Hepatitis A,B,C	Meningococcal disease
Cases	30	74	6923	600
Deaths	0	0	24*	89*

- *Deaths from viral hepatitis including Hepatitis B.
- +Deaths from meningococcal disease and meningitis.

Centers for Disease Control and Prevention. Summary of notifiable diseases, United States, 1997. *National Vital Statistics Reports*. 1999; 47 (19): 52-54.

Why Are College Students Special?

- College freshmen in dorms
new, crowded environment
new stresses and behaviors
potential exposures to meningococcal carriers
- Radiator heat, white race, and URI's are additional risk factors

Similarities Between Military Recruits and College Freshmen

- Age
- Geographic diversity
- Stress
- Living conditions - clusters
- Increase in carrier rates with new students/recruits

Residing on Campus as a Risk Factor

Source	Population	Comparison	Relative Risk
Harrison et al	College-aged students in Maryland	Dormitory vs. nondormitory	3.4
Froeschle	US college students	Dormitory vs. nondormitory	8.9 -22.9

- New data continue to show that college-aged students living on campus have significantly higher risk than those living in the community
- Other risk factors for meningococcal disease include: bar patronage, drinking alcohol and active or passive cigarette smoking

Harrison LH, Dwyer DM, Maples CT, et al. Risk of meningococcal infection in college students. *JAMA*. 1999; 281:1906-1910.
 Froeschle JE. Meningococcal disease in college students. *Clin Infect Dis*. 1999; 29:216-216.
 Inrey PB, Jackson LA, Ludwinski PH, et al. Outbreak of serogroup C meningococcal disease associated with campus bar patronage. *Am J Epidemiol*. 1996;143:624-630.
 Inrey PB, Jackson LA, Ludwinski PH, et al. Meningococcal carriage, alcohol consumption, and campus bar patronage in a serogroup C meningococcal disease outbreak. *J Clin Microbiol*. 1995;33(12):3133-3137.

Epidemiology

Average Annual Incidence of Meningococcal Infection, Maryland College Students, 1992-1997

Group	Total Cases	Population	Annual Incidence
4-year college	11	105,623	1.74
On-campus housing*	7	35,974	3.24
Off-campus housing	4	69,649	0.96
General population†	17	196,902	1.44

* $P=.05$ for comparison of annual incidence between on-campus vs. off-campus housing residents;
 † $P=.08$ for comparison of annual incidence between on-campus housing residents and the general population

† Students aged 18- to 22-years-old, excluding the 4-year college population

1 Harrison LH, Dwyer DM, Maples CT, Billmann L. The risk of meningococcal infection in Maryland college students. *JAMA*. 1999;281(20):pg1908.

Risk Factors for College Students

Bruce et al. JAMA 2001;286:688-693

- Case control study from 9/1/98 to 8/31/99; 231 colleges and 50 state health depts.
- 96 cases of meningococcal disease
- Freshmen in dormitories rate 5.1 / 100,000 (odds ratio 3.6 vs. other college students)
- Other risks: kissing, drinking, parties, movies, white race, radiator heat, school cafeteria, part time job, URI
- 68% had vaccine preventable serotypes

Meningococcal Vaccination for College Students

- 1997: American College Health Association recommends that students consider vaccination
- 1999: ACIP recommends information about disease and benefits of vaccination be provided to students and families; immunization should be available, especially for freshmen

AAP Recommendations for College Students

Pediatrics, Dec. 2000

- Entering freshman should be informed about benefits and limitations of vaccination
- Students should consider immunizations based on risk/benefits (higher in dorms)
- Vaccinate students who desire it (college health service)
- Not recommended for off-campus dwellers

Vaccinating Freshmen: Cost-Effectiveness

- Cost per case prevented would be \$671,000 to \$1,800,000 (AAP)
- Cost per death prevented would be between \$7 and \$20 million (AAP)
- Freshman in dormitories: Cost per life-year saved \$80,000-100,000 (assumes \$53.60 cost per dose, \$5 for admin., vaccine efficacy 87%, and 75% of deaths vaccine preventable)
- Not considered are family tragedy, public anxiety, or sequelae (e.g. loss of limbs)

Others for Whom Vaccination is Recommended MMWR 2000;49:1-10

- Asplenia
- Complement deficiencies
- Research, industrial, and clinical laboratory personnel with potential exposure
- Travelers to areas which are hyperendemic or epidemic

Menomune® -- Limitations

- No protection against serogroup B
- Not useful for children < 2 years of age
- Does not eliminate carriage
- Use in outbreaks helpful, but does not significantly impact total disease
- Duration of protection unknown; antibody levels decline in 2-3 years; revaccination recommended if risk factors persist

Conjugate Meningococcal Vaccines

- Conjugation to protein carrier
- Increased immunogenicity, including infants
- Immunological memory (T cells)
- Improved functional antibody

N. meningitidis Group C Vaccine Conjugated to CRM₁₉₇ Rennels et al. PIDJ, 2001

- 106 healthy US babies, immunized at 2, 4, 6 and 12-15 months, compared to Prevnar
- Moderate to severe local reactions $\leq 3.2\%$
- High titers of bactericidal antibody
- Conclusion: generally safe, good candidate vaccine for group C meningococcus

Meningococcal Serogroup C Conjugate Vaccine Ramsay et al., Lancet, 2001

- CRM₁₉₇ MCC vaccine used routinely in UK teenagers and toddlers since Nov. 1999
- Increased surveillance for group C disease
- Efficacy for teenagers: 97%
- Efficacy for toddlers: 92%

Tetravalent Conjugate A/C/Y/W-135 Vaccine

- Safe -- headache, malaise, and irritability were most common systemic AEs; injection site events common but usually mild
- Very immunogenic -- adults and toddlers
- Efficacy in disease prevention not yet demonstrated

Recent Publications of Interest

- **Meningococcal Disease**, Rosenstein NEJM 2001;344:1378
- **Risk Factors for Meningococcal Disease in College Students**, Bruce JAMA 2001;286:688
- **Invasive Meningococcal Disease in Adolescents and Young Adults**, Harrison JAMA 2001;286:694
- **Toward Control of Meningococcal Disease: Reducing Risk in College Students**, Wenger JAMA 2001;286:720
- **Prevention and Control of Meningococcal Disease**, (ACIP) MMWR 2000;49:1-10

Thank You

Questions?
