Charting the Course to Prevention of Important Bacterial Infections

Meningococcal Disease:
Examining Risk

A CE Audio Home Study Program

This program has been approved for 1.0 contact hour of continuing education (which includes 0.4 hours of pharmacology) by the American Academy of Nurse Practitioners.

Supported by an unrestricted educational grant from Aventis Pasteur.

Overview

Meningococcal disease is an extremely serious bacterial infection. Most commonly presenting as either meningococcal meningitis or meningococcemia, its fatality rate is high (10%), and many survivors (11%–19%) are permanently disabled with neuropathies or limb or hearing loss. The disease is caused by the gram-negative diplococcus *Neisseria meningitidis*, which is typically carried asymptomatically in the nasopharynx of up to 10% of healthy individuals. Clinically relevant strains of *N meningitidis* comprise 5 immunological serogroups: A, B, C, Y, and W-135.

In the United States, several important changes in the epidemiology of meningococcal infection have recently occurred. First, with the advent of conjugate vaccines against *Haemophilus influenzae* and *Streptococcus pneumoniae, N meningitidis* is now the most significant pathogen for bacterial meningitis. Second, the serogroup distribution of *N meningitidis* is changing, which may affect future prevention strategies. Third, although once most common in infants and young children, meningococcal disease now shows a significant incidence peak in adolescents and young adults as well. The Advisory Committee on Immunization Practices (ACIP) recommends that undergraduate college students, particularly freshmen who live or plan to live in dormitories or residence halls, consider getting a meningococcal vaccine. Currently available meningococcal vaccines are 85% to 100% effective against serogroups A, C, Y, and W-135, but physicians should be aware that they do not protect against serogroup B, which causes up to 40% of reported cases, mainly in infants. Moreover, vaccines available today are formulated from bacterial polysaccharides, which are ineffective in young children and fail to elicit long-term immunological memory in adolescents and adults. When available in the United States, quadrivalent meningococcal conjugate vaccines will protect against serogroups A, C, Y, and W-135, and are expected to have long-lasting immune memory.

Learning Objectives

After listening to the audiotape and reviewing the booklet, participants should be able to:

- Describe the changing etiology and complications of meningococcal disease
- Understand changing epidemiologic trends in the United States, and how *N meningitidis* is now the most common cause of bacterial meningitis for toddlers, adolescents, and adults
- Describe future prevention strategies

Needs Assessment

The danger of meningococcal disease is well known among physicians, but the importance of recent epidemiological trends is less appreciated. This CE home study audiotape program has been created to increase other healthcare provider awareness of these trends.

We hope that by listening to this audiotape and reading the information presented in this booklet, healthcare providers will better understand how to optimize prevention strategies to avoid this disease.

Who Should Participate

This program is intended for healthcare providers who may treat meningococcal disease.

CE Credit

This program has been approved for 1.0 contact hour of continuing education (which includes 0.4 hours of pharmacology) by the American Academy of Nurse Practitioners.

Release date: June 12, 2004
Expiration date: June 30, 2005

CE credit cannot be awarded after the expiration date.

Faculty

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Disclosure

Disclosure is requested when faculty members are confirmed. This educational activity may include discussion of an unlabeled use or an investigative use not yet approved for a commercial product. Therefore, it is incumbent on individuals participating in this activity to be aware of these factors in interpreting its contents and evaluating its recommendations. Every effort has been made to encourage faculty to disclose any commercial relationships or personal benefits that may be associated with their participation in this program. The following indicates the faculty and nature of their commercial relationships.

Dr Harrison has disclosed that he receives grant/research support from, is a consultant for, and is on the speakers bureau for Aventis Pasteur. He states that the activity does not include discussion of investigative or off-label uses of products.

Meningococcal Disease

Meningococcal Disease
- Meningitis and meningococcemia (can occur alone or in combination)
- 10% overall fatality rate
- 11%–19% survivors disabled (neuropathy, limb loss, hearing loss)
- 0.9–1.5 cases/100,000/year (2500–3000 cases/year)

Meningitis
- Fever and headache (flu-like symptoms)
- Meningismus (pain due to irritation of meninges)
- Altered mental status
- Seizures

3%–10% fatality rate

***Neisseria meningitidis*[1]**

Meningococcemia
- Rash
- Vascular damage
- Disseminated intravascular coagulation
- Tissue damage
- Shock

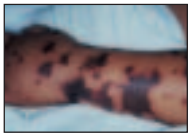
20%–40% fatality rate

- Gram-negative aerobic diplococcus
- Typically carried asymptomatically in the nasopharynx
- Transmitted via aerosol, secretions, person-to-person contact
- In nonepidemic periods, approximately 10% of healthy individuals are colonized
- May penetrate the mucosa to the bloodstream, leading to systemic meningococcal disease

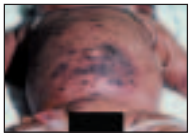
Distinguishing Early Meningococcal Disease From Other Acute Systemic Infections Can Be Difficult

Bacteriologic culture	Important, but sensitivity may be low
Antigen testing of urine/serum	Variable sensitivity and specificity
Polymerase Chain Reaction (PCR)	Currently being evaluated, but not widely available
Petechial or purpuric rash	Most valuable diagnostic tools outside of cerebral spinal fluid collection and laboratory analysis

Petechial/purpuric rash[2]



Meningococcemia[2]



Skin gangrene[2]

In the United Kingdom, the National Health Service successfully implemented a mass educational campaign that included simple ways to recognize signs and symptoms of meningococcal disease

Glass test[3]

- If the rash appears through the glass with pressure, or if meningococcal infection is otherwise suspected, action should be taken immediately

References
1. Available at: www.sanger.ac.uk/Projects/N_meningitidis. Accessed August 2003. Reprinted with permission.
2. Courtesy of R Rudoy, MD, Honolulu, Hawaii
3. Available at www.doh.gov.uk/cmo/progress/meningitis/menin2.htm. Accessed August 2003. Reprinted with permission.

Meningococcal Disease:
Examining Risk

US Epidemiology

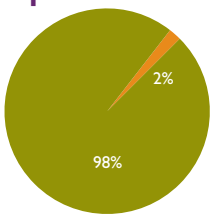
1990
Introduction of *H influenzae* type B (Hib) conjugate vaccine

1995

2000
Introduction of *S pneumoniae* conjugate vaccine

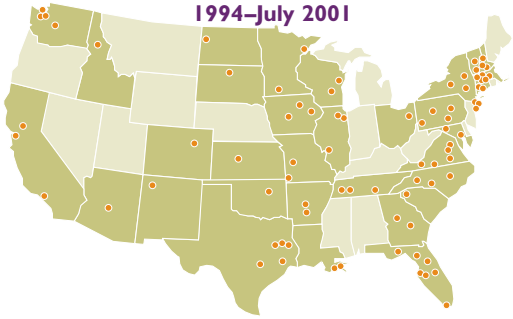
2001
N meningitidis **is now the most significant pathogen in the US for bacterial meningitis in all age groups**

Reported Cases

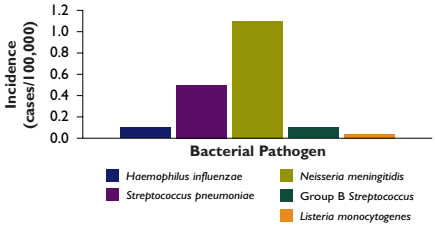


Outbreaks
Isolated (sporadic) cases

Meningococcal Disease Outbreaks in the United States[1]
1994–July 2001

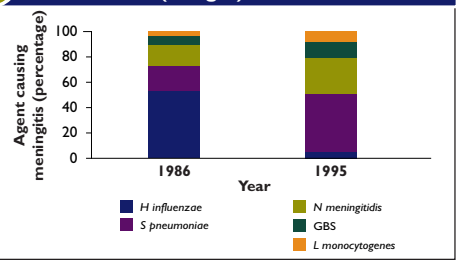


Major Causes of Bacterial Meningitis in 1995 (2–29-year-olds)[2]



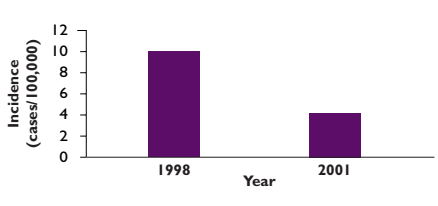
- *N meningitidis* is the most common cause of bacterial meningitis in the US for toddlers, adolescents, and young adults

Pathogenic Bacteria Causing Meningitis 1986 vs 1995 (all ages)[2]



- 94% ⬇ in % of bacterial meningitis cases caused by *H influenzae* after introduction of Hib conjugate vaccine (all ages, including infants)

Pneumococcal Meningitis in Patients 1998 vs 2001 (< 5 years old)[3]



- 59% ⬇ in % of bacterial meningitis cases caused by *S pneumoniae* after use of a pneumococcal conjugate vaccine

References
1. Centers for Disease Control and Prevention (CDC). Atlanta, Georgia.
2. Schuchat et al. *N Engl J Med.* 1997;337:970.
3. Whitney et al. *N Engl J Med.* 2003;348:1737.

Meningococcal Disease:
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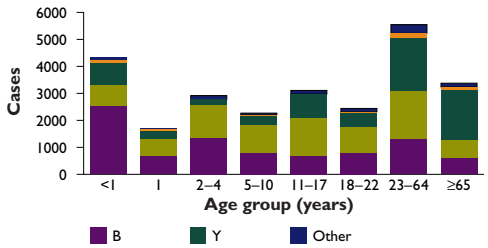
Serogroups

N meningitidis is classified into serogroups according to capsular polysaccharides

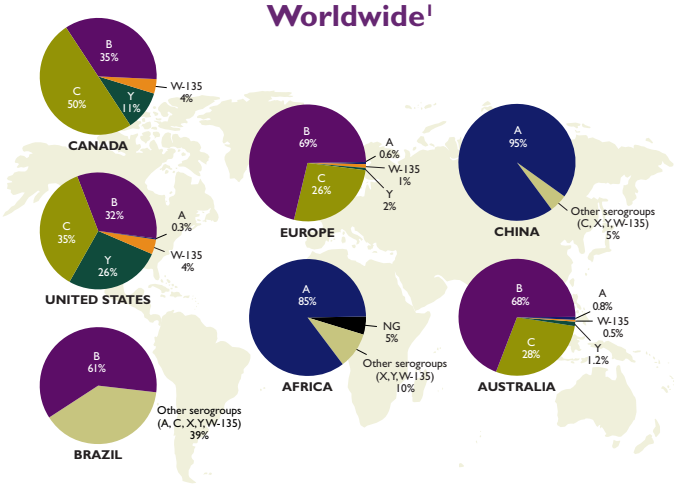
Clinically Significant Meningococcal Serogroups	
A	Leading cause of epidemic meningitis worldwide Rare in the US
B	Major cause of endemic disease in the US Occasional outbreaks (Oregon)
C	Major cause of endemic disease in the US Multiple outbreaks in schools/community
Y	Associated with pneumonia Increasing in the US
W-135	Small percentage of infections Recently caused the first known outbreak

- Serogroups A, B, C, Y, and W-135 cause ≥ 95% of meningococcal disease worldwide
- US healthcare providers need to be concerned with all 5 serogroups: A (for travelers), B (no vaccine available), C, Y, and W-135

Number of Cases of Meningococcal Disease in the US by Serogroup and Age, 1990–1997[1]

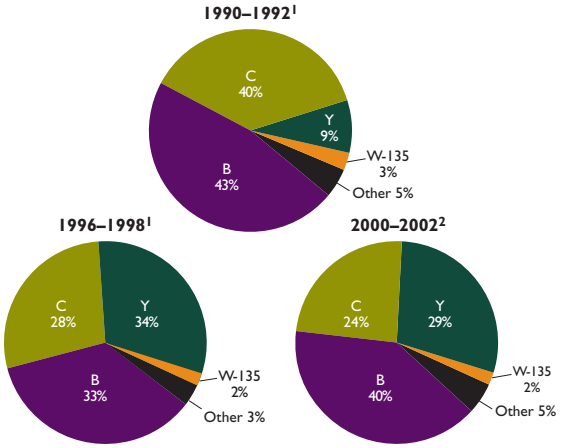


Meningococcal Epidemiology Worldwide[1]



NG=nongroupable

Recent Changes in Meningococcal Serogroup Distribution in the United States



References

1. Centers for Disease Control and Prevention (CDC). Atlanta, Georgia.
2. Active Bacterial Core Surveillance, CDC. Atlanta, Georgia.

College Students

Freshmen living in dormitories are substantially more likely to acquire meningococcal disease than are college students in general

Rates of Meningococcal Disease in College Students, September 1, 1998 to August 31, 1999[1]

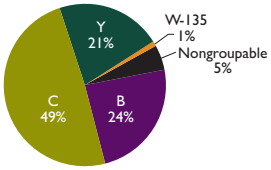
	Number of Cases	Population	Rates per 100,000 Population
All 18–23-year-olds	304	22,070,535	1.4
College students	96	14,897,268	0.6
Undergraduates	93	12,771,228	0.7
Freshmen	44	2,285,001	1.9
Dormitory residents	48	2,085,618	2.3
Freshmen living in dormitories	**30**	**591,587**	**5.1**

Disease in College Students Was Associated With:[2,3]

- Tobacco use
- Binge drinking
- Upper respiratory tract infections
- Immunosuppression
- Complement deficiency

Meningococcal Serogroup Distribution Among US Undergraduates[4]

September 1998–August 1999



Vaccination Guidelines for College Freshmen (Quadrivalent (ACYW-135) Polysaccharide Vaccine)

CDC Advisory Committee on Immunization Practices (ACIP)[4]

- *"Providers of medical care to incoming and current college freshmen, particularly those who plan to or already live in dormitories and residence halls, should, during routine medical care, inform these students and their parents about meningococcal disease and the benefits of vaccination."*

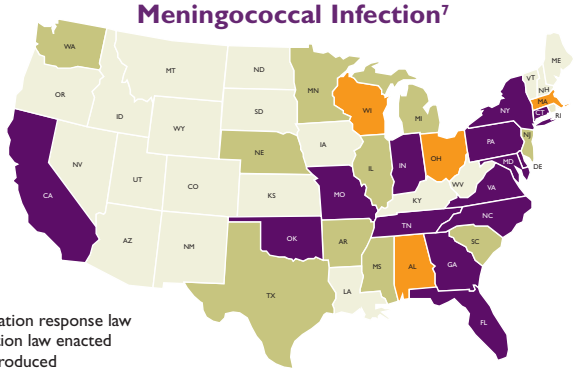
American Academy of Pediatrics[5]

- *"Students entering college, especially those who will be living in dormitories, and their parents should be informed during routine prematriculation medical visits about the increased risk of meningococcal disease…*
- *"Students should consider immunization in view of the risk of disease and potential benefits of immunization."*

American College Health Association[6]

- *"College freshmen living in dormitories are at modestly increased risk for disease and may wish to consider vaccination."*

State Legislation in Favor of Vaccinating College Students Against Meningococcal Infection[7]



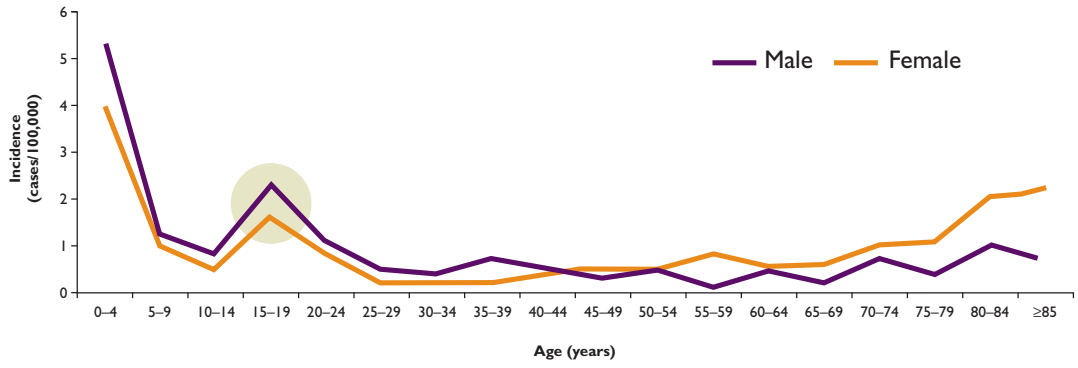
References

1. Bruce et al. *JAMA*. 2001;286:688.
2. Harrison et al. *JAMA*. 2001;286:694.
3. Rosenstein et al. *N Engl J Med*. 2001;344:1378.
4. CDC. *MMWR*. 2000;49(RR-07):1.
5. Available at: www.aap.org/policy/re0035.html. Accessed August 2003.
6. Available at: www.acha.org. Accessed August 2003.
7. Available at: www.nmaus.org/legislation/index.htm. Accessed August 2003.

Adolescents

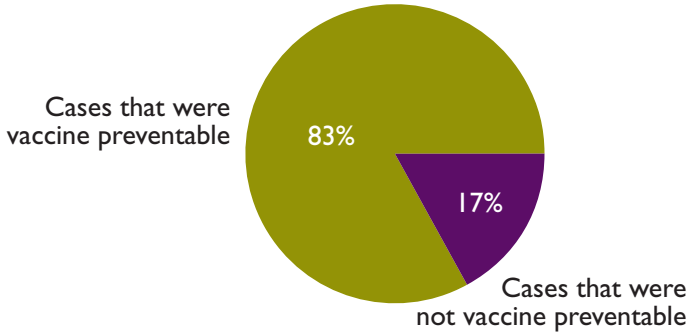
A peak in incidence of meningococcal disease occurs in adolescents

Race-Adjusted Rates of Meningococcal Disease, 1992–1996 (California, Georgia, Maryland, Tennessee, Connecticut, Minnesota, and Oregon)[1]



Meningococcal Disease Among 15–24-Year-Olds in Maryland[2]

- During 1996–1997, 15–24-year-olds accounted for 29.2% of all meningococcal infection
- Tobacco smoking was common among adolescents with meningococcal infection



References
1. Rosenstein et al. *J Infect Dis*. 1999;180:1894.
2. Harrison et al. *JAMA*. 2001;286:694.

Prevention: Quadrivalent (ACYW-135) Polysaccharide Vaccine

Advantages

- Provides protection against 4 of the 5 most common serogroups (A, C, Y, and W-135)
- Very favorable safety profile
- Proven efficacy and immunogenicity in older children and adults

Disadvantages

- Immunity lasts <5 years (no induction of immune memory)
- Unable to prime immune system
- Little effect on carriage rates
- Lacks serogroup B component
- Lack of efficacy in young children

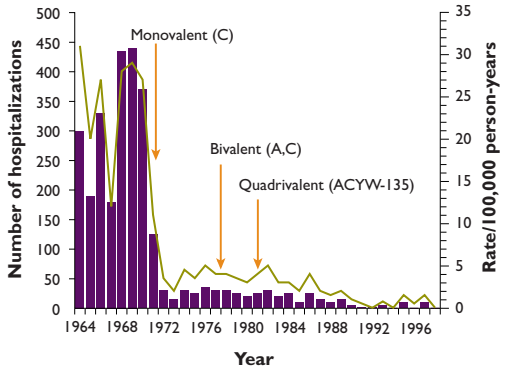
Current Usage

- Military
- College students
- Travelers
- Persons with certain chronic medical conditions, including those who are immunocompromised

A significant portion of meningococcal disease cases in US children and adolescents is caused by serogroups included in the ACYW-135 quadrivalent vaccine

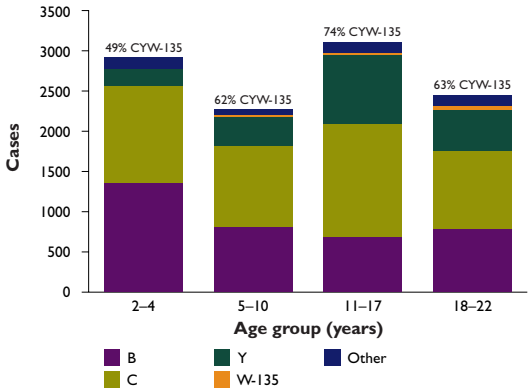
Meningococcal polysaccharide vaccine: Prevention in military populations

Meningococcal Disease Hospitalizations, Frequencies, and Rates: US Army, 1964–1998[1]



Bars indicate hospitalization frequencies; line indicates rates.

Cases of Meningococcal Disease by Serogroup in Children and Adolescents in the US, 1990–1997[2]



References
1. DeFraites. *MSMR*. 2000;6:2.
2. Centers for Disease Control and Prevention (CDC). Atlanta, Georgia.

Prevention: Conjugate Vaccine

Meningococcal C Conjugate Vaccine: The UK Experience

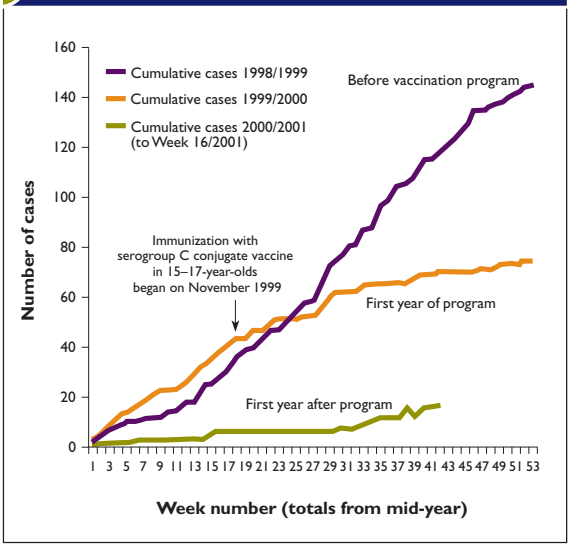
Advantages

- Immunization at 2 months–20 years has reduced meningococcal disease rates by 81% in the United Kingdom
- T-dependent immune response produces memory
- May increase duration of protection because of memory induction
- Herd immunity demonstrated in unvaccinated populations
- Carriage reduction demonstrated in adolescent population
- Boosting effect following a dose of polysaccharide or conjugate vaccine

Disadvantages

- Not available in the United States
- Currently available vaccines are monovalent (serogroup C)
- Ineffective against other serogroups (ie, lacks serogroup B component)

Serogroup C Meningococcal Disease in the UK[1]



- Adolescent cases of meningococcal disease caused by serogroup C ↓ 85% in the United Kingdom after implementing a vaccination program with conjugate meningococcal C vaccine[2]
- Unvaccinated children 1–17 years of age exhibited a 60% reduction in disease (herd immunity)[2]

References
1. Burrow et al. ICCAC. 2001.
2. Miller et al. *Vaccine*. 2001; 20:S58-S67.

Prevention: Future Strategies

When available in the United States, quadrivalent conjugate vaccines will offer greater serogroup protection than monovalent conjugate vaccines

Total Meningococcal Disease/Deaths and Percent Reduction From Unvaccinated Baseline 10 Years After Specific Vaccination Strategy With C & Y Conjugate Vaccine[1]

Vaccination Strategy	Disease Remaining	Percent Reduction	Deaths Remaining	Percent Reduction
No vaccination/baseline	1621		130	
Infant	1175	28	97	25
Toddler	1239	24	98	25
Adolescent	1284	21	84	35
College	1565	3	122	6
Infant + Adolescent + College	814	50	47	64
Toddler + Adolescent + College	878	46	48	63

Future Role of a Quadrivalent Meningococcal Conjugate Vaccine in the United States

- The use of a quadrivalent meningococcal conjugate vaccine is expected to provide the same highly effective protection as the UK monovalent meningococcal conjugate vaccine, but with expanded serogroup coverage
- Individuals vaccinated with quadrivalent meningococcal conjugate vaccine will have protection against the A, C, Y, and W-135 serogroups and are expected to have lasting immune memory
- Similar to the success of Hib and pneumococcal conjugate vaccines, a quadrivalent meningococcal conjugate vaccine is expected to dramatically reduce the incidence of meningococcal disease and its sequelae

References

1. Lingappa et al. *Vaccine*. 2001;19:4566.

Instructions for Receiving CE Credit

The following examination (page 13) provides the opportunity to assess your knowledge and understanding of the material presented in the audiotape and booklet.

To obtain 1.0 AANP contact hour, you must:

Complete the following CE Posttest by circling the correct responses on the answer sheet on Page 14.

- Answer the program evaluation questions
- Provide the requested personal information
- Mail or fax the Answer Sheet/Evaluation to the address below by June 30, 2005

Center for Bio-Medical Communication, Inc.
433 Hackensack Avenue, 9th Floor
Hackensack, NJ 07601
Attn: Meninge Posttest (AANP)
Fax: 201-342-7555

Tests will be graded, and in approximately 6 weeks after receipt, a CE statement of credit will be sent to each participant who achieves a score of 70% or greater.

Expiration date: June 30, 2005

CE Posttest

1. The overall fatality rate of meningococcal disease is
- a. 5%
- b. 10%
- c. 18%
- d. 25%
- e. 50%

2. The major etiologic agent causing bacterial meningitis in the United States today is
- a. *Neisseria gonorrhea*
- b. *Haemophilus influenzae*
- c. *Neisseria meningitidis*
- d. *Streptococcus pneumoniae*
- e. *Listeria monocytogenes*

3. Nearly half of all meningococcal disease cases in college students in the United States are caused by serogroup
- a. A
- b. B
- c. C
- d. Y
- e. W-135

4. Who is most likely to contract meningococcal disease?
- a. All 18–23-year-olds
- b. College freshmen
- c. Dormitory residents
- d. Freshmen living in dormitories
- e. Undergraduates

5. In which population have recent studies described a new peak incidence of meningococcal infections?
- a. Young children
- b. Adolescents
- c. Elderly people
- d. Frail elderly
- e. None of the above

6. The vast majority of cases of meningococcal disease in adolescents 15–24 years old were
- a. In Oregon
- b. Vaccine preventable
- c. In smokers
- d. In high school dropouts
- e. In hospitals

7. In addition to the need to vaccinate adolescents at risk of meningococcal disease, _____ have been protected with quadrivalent vaccines.
- a. Military personnel
- b. Immunocompromised patients
- c. College students
- d. Travelers
- e. All of the above

8. Most major serogroups infecting persons in the United States are covered in available vaccines.

True _____
False _____

9. Conjugate vaccines provide a boosting effect after doses of either polysaccharide or conjugate meningococcal vaccines.

True _____
False _____

10. Conjugate vaccines have which of the following advantages over polysaccharide vaccines?
- a. Reduces carriage rates
- b. Better immune memory
- c. Elicits herd immunity in unvaccinated populations
- d. Can be given to infants
- e. All of the above

Program Evaluation (AANP Program #0403156)

Please evaluate this CE Audio Home Study Program using the following scale:

1 = poor 2 = fair 3 = average 4 = good 5 = excellent

1. How successfully did this program meet each of its stated learning objectives?
After listening to the audiotape and reviewing the booklet, participants should be able to:

– Describe the changing etiology and complications of meningococcal disease	1	2	3	4	5
– Understand changing epidemiologic trends in the United States, and how *N meningitidis* is now the most common cause of bacterial meningitis for toddlers, adolescents, and adults	1	2	3	4	5
– Describe future prevention strategies	1	2	3	4	5
2. How would you rate the clinical usefulness of this program?	1	2	3	4	5
3. How well did this learning format work with your learning style?	1	2	3	4	5
4. Overall, how satisfied were you with this activity?	1	2	3	4	5
5. Accredited CE programs must be "free from commercial bias for or against any product." In this regard, how would you rate this program?	1	2	3	4	5

6. Do you expect to make any changes in your practice or attitudes as a result of this activity? ❒ **Yes** ❒ **No**

If yes, please explain _____

_____

7. Suggestions for future audiotape programs _____

_____

8. How long did it take you to complete this learning activity? _____

CE Posttest Answer Sheet

1.	a	b	c	d	e	**6.**	a	b	c	d	e
2.	a	b	c	d	e	**7.**	a	b	c	d	e
3.	a	b	c	d	e	**8.**	True	False			
4.	a	b	c	d	e	**9.**	True	False			
5.	a	b	c	d	e	**10.**	a	b	c	d	e

Name _____ Degree _____

Phone _____ Fax _____ e-mail _____

Institution/Affiliation _____ SS# _____

Mailing Address _____

City _____ State _____ Zip _____

Signature _____

Meningococcal Disease PM