Charting the Course to Prevention of Important Bacterial Infections

Pertussis Disease:
On the Rise in Adolescents and Adults

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

Pertussis disease, commonly thought to be exclusively an infant and toddler disease, is in fact a significant problem among adolescents and adults in the United States. In 2002, 28% of the total reported pertussis cases occurred in adolescents (10–19 years) and 24% occurred in adults (≥20 years). Even these statistics undervalue the overall significance of the disease, considering an estimated 25% of protracted cough illness in adolescents and adults is pertussis disease and an estimated 12% of cases are actually reported nationwide. Waning protection from childhood vaccines plays a large role in the rising rates of adolescent and adult pertussis disease. Booster immunization was hindered in the past by the age-dependent increase in adverse reactions to the available whole-cell vaccines. However, new acellular vaccines, which contain purified pertussis toxoid and key bacterial outer-membrane proteins, are effective and better tolerated than the whole-cell forms.

Healthcare providers should be aware of adolescent and adult pertussis disease for a number of reasons. First, although typically the disease is less severe in these older populations than in infants, it is not without risk, and complications of the disease can include pneumonia, seizures, and encephalopathy. Second, adolescents and adults are thought to serve as the primary reservoir of *Bordetella pertussis* for transmission to infants and young children, the groups most susceptible to severe disease. Finally, the economic impact of the disease can be high. Thus, a number of academic studies argue that pertussis booster immunization may be warranted in adolescents.

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Learning Objectives

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

- Understand the etiology, diagnosis, and treatment of pertussis disease
- Describe recent US epidemiological trends showing the increasing prevalence of adolescent and adult disease
- Recognize the importance of waning vaccine coverage in adolescents and adults

Needs Assessment

Recent epidemiological studies indicate that pertussis disease is a significant problem in adolescents and adults, but misconceptions about the disease in these populations persist. This CE home study audiotape program has been created to increase healthcare provider awareness of pertussis disease in the United States.

We hope that by listening to this audiotape and reading the information presented in this booklet, healthcare providers will be better informed about the incidence, diagnosis, severity, treatment options, and prevention of pertussis disease.

Who Should Participate

This program is intended for healthcare providers who may treat pertussis 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.

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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 Greenberg discloses that he receives grant/research support from Aventis, GlaxoSmithKline, and Wyeth, is a consultant for Aventis and GlaxoSmithKline, and is on the speakers bureau for Aventis, GlaxoSmithKline, and Wyeth. He states that the activity includes discussion of investigative or off-label uses of products.

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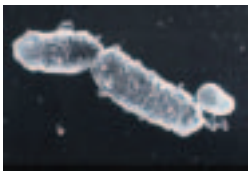
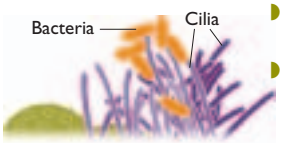
Pertussis Disease

Bordetella pertussis[1]



- Aerobic gram-negative bacillus
- Infects only humans
- Produces an array of toxins, most notably pertussis toxin
- Undergoes antigenic modulation and phase variation

B pertussis Adheres to Ciliated Epithelial Cells in the Respiratory Tract

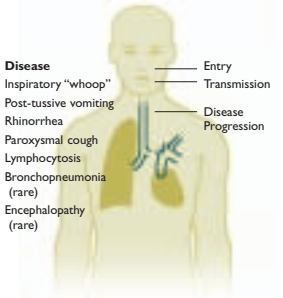


- Transmitted by respiratory droplets
- Bacteria multiply on mucous membranes of the respiratory tract

B pertussis Case Definitions

- The two most widely used definitions for pertussis disease are:
  - CDC Surveillance Case Definition: 14 days or more of coughing with paroxysms, inspiratory whooping, or post-tussive vomiting
  - WHO Definition of Classical Pertussis (whooping cough): 21 days or more of paroxysmal cough with laboratory confirmation in adolescents and adults

Pathogenesis, Signs, and Symptoms[2]

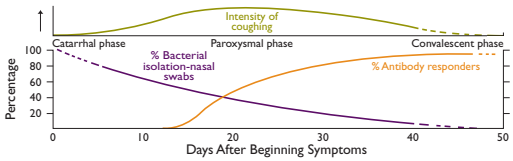


- Although rare, the most common complication of pertussis infection, and the cause of most pertussis-related deaths, is secondary bacterial pneumonia
- Serious neurologic complications may occur, such as encephalopathy and seizures, and are most likely the result of hypoxia consequent to paroxysmal cough

B pertussis Phases of Disease Progression

Phase	Characteristics of a Typical Case
Catarrhal	Week 0–1: Coryza, mild fever, non-productive cough
Paroxysmal	Week 1–6: Paroxysmal cough, inspiratory "whoop," post-tussive vomiting, pneumonia, and possible seizures
Convalescent	Week 6–12: Paroxysmal cough

Time Course of Clinical Symptoms, Success of Cultures, and Development of Antibodies[2]



Pertussis-Related Hospitalizations, Complications, and Deaths, by Age Group — US, 1997–2000[3]

Age group	No. with pertussis	Hospitalized (%)	Complications: Pneumonia* (%)	Complications: Seizures (%)	Complications: Encephalopathy (%)	Deaths (%)
<6 mo	7203	63.1	11.8	1.4	0.2	0.8
6–11 mo	1073	28.1	8.6	0.7	0.1	0.1
1–4 y	3137	10.3	5.4	1.2	0.01	<0.1
5–9 y	2756	3.1	2.5	0.5	—	0.1
10–19 y	8273	2.1	1.9	0.3	0.1	—
≥20 y	5745	3.5	2.6	0.6	0.1	<0.1
Total	**28,187**†	**20.0**	**5.2**	**0.8**‡	**0.1**	**0.2**

* Radiographically confirmed.
† Excludes 92 (0.3%) persons of unknown age with pertussis.
‡ Excludes one person of unknown age with seizures.

References

1. Courtesy of Philippe Gounon, Institut Pasteur, Paris.
2. Available at: www.md.huji.ac.il/microbiology/book/ch031.htm. Accessed August 2003.
3. CDC. *MMWR*. 2002;51:73.

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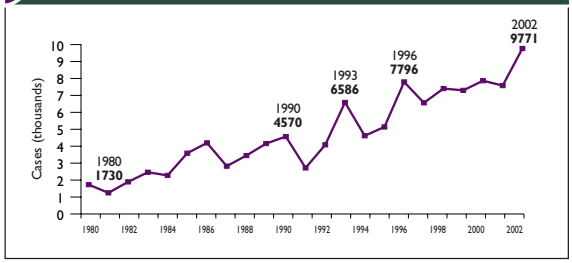
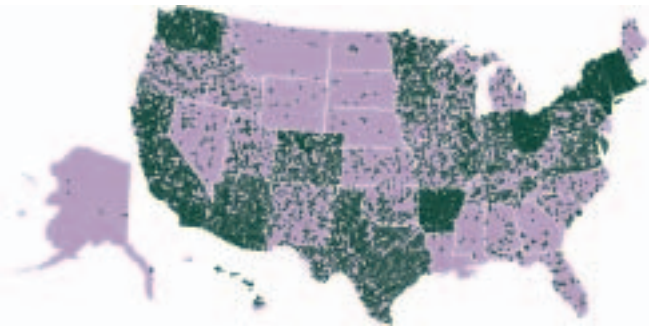
US Epidemiology

Pertussis Is on the Rise Again in the US[1–5]



Mid-1940s	→	Whole-cell DTP vaccine introduced
1970	→	>99% reduction in incidence
1976	→	Pertussis disease at all-time low
1980–2002	→	5.6-fold increase in reported incidence despite unchanged immunization rates

Reported Pertussis Cases in 2002*[6]
Each Dot Represents One Case

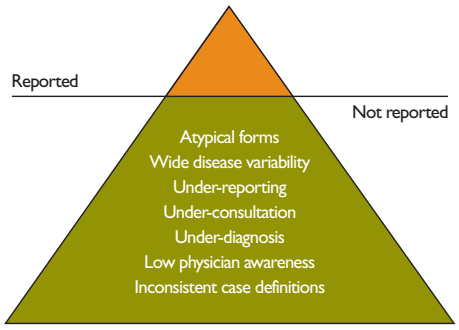


- Sharp demarcation at state borders illustrates inconsistent reporting
- A recent evaluation of California, where there is a high incidence of pertussis disease, estimated that only 64% to 77% of hospitalized cases are reported[7]

*The total number of cases and incidence rate for each state represents provisional numbers, which may change as states report more cases for 2002.

Reported Cases of Pertussis Are the Tip of the Iceberg

- Nationwide, an estimated 12% of pertussis cases are actually reported[8]
- Under-reporting may be greatest among adolescents and adults[8]



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3. CDC. *MMWR*. 2000;50:1175.
4. CDC. *MMWR*. 2002;51:723.
5. CDC. *MMWR*. 2003;52:747.
6. Bacterial Vaccine Preventable Diseases Branch, National Immunization Program, CDC. 2002.
7. McCoy et al. Immunization Program, LA Co Dept of Health Svcs, 1999.
8. Güriş et al. *Clin Infect Dis*. 1999;28:1230.

Pertussis Disease:
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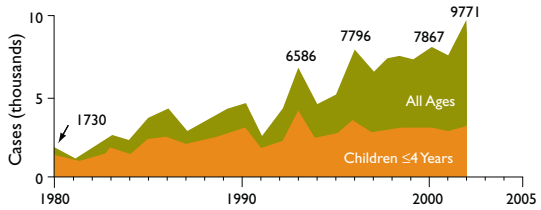
Increased Pertussis Disease in Adolescents and Adults

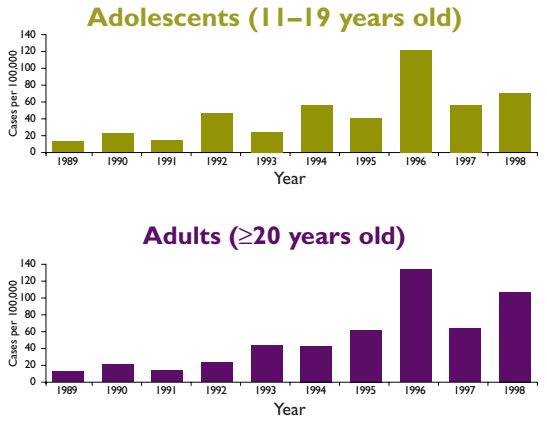
Increased Incidence of Pertussis Cases[1,2]



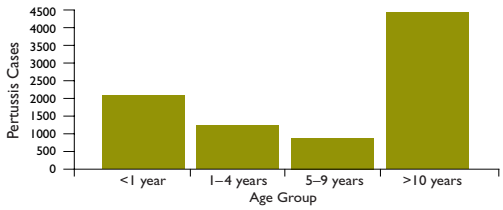
- In 1980, the overwhelming majority of the 1730 reported cases of pertussis disease occurred in children aged ≤4 years
- By 2002, the total number of reported cases had increased by 5.6 fold, primarily due to the dramatic increase in the incidence of pertussis disease in older children and adults†

†Based on CDC data from years 1980–2001 and most recent provisional data for 2002.

Pertussis Cases Reported in Massachusetts, 1989–1998[4]



2002 Reported Pertussis Cases by Age[2]



- ≥53% of reported pertussis cases were among persons 10 years of age or older

- Diagnosing pertussis disease in adolescents and adults is challenging because clinical presentation is more diverse than in infant disease[3]
- Advances in diagnostic tools have allowed pertussis diagnosis to be confirmed more readily in cases of persistent cough[4]

Complications Resulting From *B pertussis* Infection[5]

- Complications are more common in adults than adolescents (28% vs 16%)
- Pneumonia occurs in 2% of patients <30 years old and 5% to 9% of older patients
- Urinary incontinence occurs in 34% of women >50 years of age
- Neurologic sequelae include seizures and encephalopathy
- Other complications associated with pertussis disease in adults include otitis media, cervical lymphadenopathy, aspiration, unilateral acute hearing loss, rib fracture, inguinal hernia, lumbar pain, and weight loss

References

1. CDC. *MMWR*. 2002;51:73.
2. CDC. *Pertussis Surveillance Report*. 2003.
3. Wright. *South Med J*. 1998;91:702.
4. Yih et al. *J Infect Dis*. 2000;182:1409.
5. De Serres et al. *J Infect Dis*. 2000;182:174.

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Diagnosis and Treatment

Clinical Presentation of Pertussis Disease Is Different in Adolescents/Adults vs Infants

	Infants	Adolescents/Adults
Disease severity	Frequently severe	Frequently mild; however, pertussis disease may account for 21% to 26% of coughs lasting ≥7 days[1,2]
Immunologic status of infected patients	Incompletely immunized or unimmunized	Previously vaccinated with waning immunity
Mean days to full recovery[2]*	75	Adolescents, 74 Adults, 93
Patients with complications[3]†		
Hospitalization	63.1%	2.7%
Pneumonia	11.8%	2.2%
Seizures	1.4%	0.4%
Deaths	0.8%	<0.1%

*Infants were <1 year; adolescents, 10 to 20 years; adults, ≥21 years.
†Infants were <6 months; adolescents/adults ≥ 10 years.

Diagnosis[4,5]

Confirmed case

- Nasopharyngeal aspirate or Dacron™ swab for *B pertussis* growth on Regan Lowe or Bordet-Gengou medium
- Diagnosis confirmed with isolation of *B pertussis* or positive polymerase chain reaction (PCR) test

Clinical case

- Acute cough illness lasting ≥14 days with paroxysms, inspiratory "whooping," or post-tussive vomiting without other apparent cause

Treatment[5,6]

- A 14-day course of erythromycin is the classic treatment, however, common and serious side effects make compliance difficult; therefore a 5-day course of azithromycin is used more frequently‡
- In the event of allergy to macrolides, an alternative is trimethoprim-sulfamethoxazole

‡Discusses off-label use not currently approved by the FDA.

- In cases of persistent cough, a diagnosis of pertussis disease may be confirmed by several available tools

Diagnostic Tools

Most frequently used: PCR
Reference diagnostic tool: Bacterial culture
Other: IgG titer to pertussis toxin (ELISA)
Direct fluorescent antibody test (DFA)

References
1. Edwards et al. In: Plotkin et al, eds. *Vaccines*. 1999:293.
2. Strebel. *Infect Med*.1996;13(suppl):33.
3. Lee et al. *Arch Fam Med*. 2000;9:989.
4. CDC. *MMWR*. 2002;51:73.
5. CDC. *Guidelines for the Control of Pertussis Outbreaks*. 2000.
6. Halperin et al. *Pediatrics*. 1997;100:65.

Pertussis Disease:
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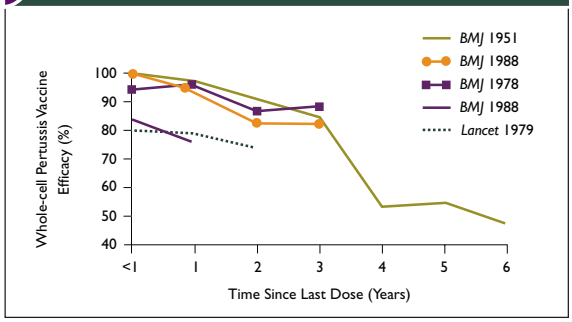
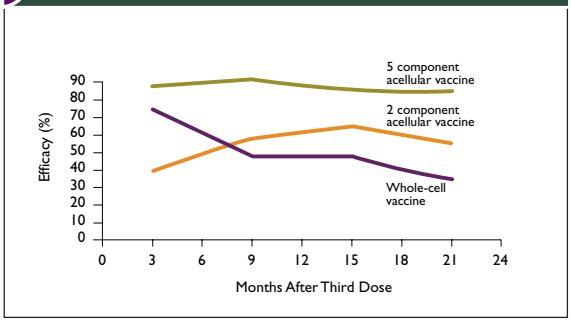
Waning Pertussis Immunity

Pertussis Immunity Wanes Over Time[1–5]



Vaccine Efficacy in Stockholm, 1992[6]

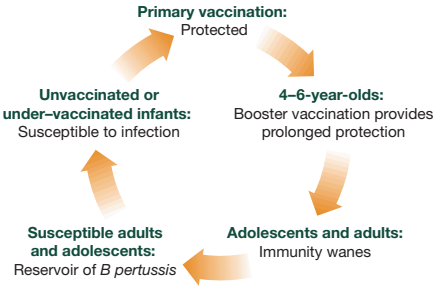


Outbreaks Occurring in Adolescents and Adults Due to Waning Immunity

JAMA 1998	Finland; 153 cases confirmed by PCR or culture
MMWR 2003	Illinois, US; 21 cases of adults ≥20 years of age
J Infect Dis 1994	Finland; Attack rate was 2535/100,000 in 7–15-year-olds and 248/100,000 for those >15 years old
JAMA 1996	California, US; Attack rate was 176/100,000 in adults
Acta Paediatr Jpn 1995	Japan; 7/38 11- and 12-year-olds (6 additional cases in 5 homes from contact)
Pediatr Infect Dis J 2003	Canada; reported increased incidence 9–15-fold in adolescents and 23-fold in adults
Emerg Infect Dis 1997	Netherlands; 1-year, 9-fold change in incidence
N Engl J Med 1994	Ohio, US; 1993 Cincinnati outbreak of which 11% were adults

- Today's adults were immunized with whole-cell vaccine as infants and young children
- New CDC data indicate that pertussis disease incidence in adults increased 400% from 1990–2001[7]

Cycle of Pertussis Susceptibility in Vaccinated Populations[8]



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1. Blennow et al. *BMJ*. 1988;296:1570.
2. Church. *Lancet*. 1979;2:188.
3. Jenkinson. *BMJ*. 1978;2:577-578.
4. Jenkinson. *BMJ*. 1988;296:612.
5. Medical Research Council [Britain]. *BMJ*. 1951:4721.
6. Gustafsson et al. *N Engl J Med*. 1996;334:349.
7. CDC. 2002; unpublished results.
8. Adapted from von König et al. *Lancet Infect Dis*. 2002;2:774.

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Rationale for Vaccinating Adolescents and Adults

B Pertussis Reservoirs

Healthcare Providers
The annual incidence of pertussis disease in healthcare workers (around 2.5%) is higher than the incidence of the most common diseases for which they are vaccinated[1]

Adults/Parents
Approximately 25% of persistent cough illness ≥14 days in adults is pertussis disease[2]

Adolescents/Siblings
In Massachusetts from 1989–1998, the incidence of adolescent pertussis disease increased 10 fold. Adolescents serve as the primary reservoir in school outbreaks[3]

Elderly
In the Netherlands, the attack rate for pertussis disease in elderly persons, age 55–94 years, was an average 53%, from one study of an outbreak in 1999. The elderly may be at considerable risk of mortality from pertussis disease[4]

Adolescents and Adults Are Primary Sources for Infant Transmission

Healthcare Providers
Most hospital outbreaks of pertussis disease involve transmission from healthcare workers to pediatric patients[5]

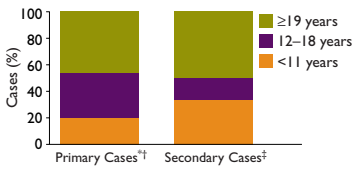
Adults/Parents
In Chicago, young mothers with a cough >7 days were shown to be a significant source of pertussis disease transmission to their young infants[6]

Most at Risk

Grandparents
In 15% of families, an adult patient was identified as the source of infection for other household members. Fifteen percent of these adults were grandparents or great-grandparents of an affected child[7]

Adolescents/Siblings
For 27% of infants hospitalized with pertussis disease in London between 1998 and 2000, an older, fully-vaccinated sibling was the source of infection[8]

The Source of Secondary Pertussis Cases Within a Household Is Likely to Be an Older Family Member[9]



*Household member with the earliest date of onset of illness. Also includes co-primary cases who had onset within 6 days of primary illness and second-primary cases, when >28 days had elapsed since household illness onset.

†6 of 8 primary cases <6 months old acquired infection from adults outside the home.

‡All non-primary cases in household.

Mortality From Infant Pertussis Disease

- During 1980–1998, the average annual incidence of reported pertussis cases and deaths among US infants increased 50%[10]
  - Increase was primarily among infants <4 months of age
- 17 infants died of pertussis in 2000[11]
  - All had onset at <4 months of age
- In 2002, 22 pertussis deaths were reported to the CDC[12]
  - 21 were 12 weeks or younger
  - One was <21 weeks

References

1. Wright et al. *Infect Control Hosp Epidemiol.* 1999;20:120.
2. Wright. *South Med J.* 1998;91:702.
3. Yih et al. *J Infect Dis.* 2000;182:1409.
4. Mertens et al. *Eur J Clin Microb Infect Dis.* 1999;18:242.
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9. Biellik et al. *J Infect Dis.* 1988;157:1134.
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12. Tiwari. CDC. February 2003.

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Prevention

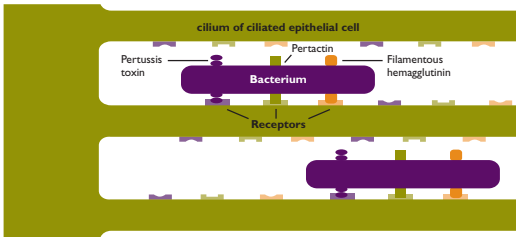
Whole-Cell Vaccines[1]

- Good efficacy
- May induce unwanted reactogenicity
- Poor tolerability with repeated use
  - Injection site reactions (pain, redness, and swelling)
  - Drowsiness and fever

Acellular Vaccines[1]

- Efficacy comparable to whole-cell vaccines
- Less reactogenic (low-dose formulations of diphtheria toxoid and pertussis antigens)
- Strong antibody responses to all 5 vaccine components
- Improved tolerability
  - Fewer and milder injection site reactions
  - Lower incidence of drowsiness and fever

Acellular Pertussis Vaccine Components[2]



Pertussis toxoid
Inactivated pertussis toxin

Filamentous hemagglutinin
Cell wall component and adhesin

Fimbrial agglutinogens 2+3
Bacterial appendages involved in attachment

Pertactin
Outer-membrane protein and adhesin

Options for Overcoming Pertussis Disease

- Reduce pertussis disease morbidity in adolescents and adults
  - Active booster vaccination[3]
  - Appropriate antibiotic prophylaxis
- Increase nationwide surveillance
  - Track disease transmission and associated outbreaks[4]
- Better educate patients and practitioners
- Improve diagnostic methods

Adopted Strategies for Adolescents and Adults[5]

Strategy	Recommended in
Universal routine vaccination of all adults	Austria
Universal vaccination of adolescents	France, Germany, Canada
Vaccination of pediatric healthcare workers	European Union
Vaccination of family contacts of newborns	Expected in Germany, 2003
Vaccination of child care workers	European Union

References

1. Keitel. *Clin Infect Dis*. 1999;28:s118.
2. Halperin. *Pediatr Infect Dis J*. 2000;19:276.
3. Halperin. *Can J Infect Dis*. 2001;12:74.
4. CDC. *MMWR*. 2002;51:73.
5. von König et al. *Lancet Infect Dis*. 2002;2:774.

Pertussis Disease:
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Summary

- Incidence of pertussis in adolescents and adults has been rising since 1976[1]
- Adolescent and adult cases can be severe[2]
- Symptoms in adolescents and adults are atypical and pertussis disease is often undiagnosed and consequently under-reported[3]
- When left untreated, adolescents and adults can transmit *B pertussis* to infants and young children, who are at greater risk for severe complications, including death[4]
- Acellular pertussis multicomponent vaccines (TdaP) proposed for booster immunization of adolescents and adults have:
  - Documented immunogenicity
  - Documented tolerability
- Practitioners and patients need to be educated about
  - Rising rates of pertussis disease in the United States
  - Recognition of pertussis disease symptoms in adolescents and adults
  - Use of vaccination as a preventative strategy in all age groups

Goal is to provide protection from pertussis disease across all age groups and consequently reduce pertussis disease incidence in the United States

References

1. CDC. *MMWR*. 1997;46:71.
2. De Serres et al. *J Infect Dis*. 2000;182:174.
3. Güriş et al. *Clin Infect Dis*. 1999;28:1230.
4. Crowcroft et al. *Arch Dis Child*. 2003;88:802.

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: Pertussis 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. ***Bordetella pertussis* is highly contagious because**
   - **a.** It is a blood-borne infection
   - **b.** It spreads easily through the body, eg, to the brain and lymph nodes
   - **c.** Bacteria in the respiratory tract become airborne in tiny droplets
   - **d.** Bacteria are viable for long periods outside the human body

2. **Serious complications of pertussis disease include all of the following *except***
   - **a.** Pneumonia
   - **b.** Arthritis
   - **c.** Seizures
   - **d.** Encephalopathy

3. **Pertussis incidence in the United States in 2002 is**
   - **a.** As high as in the pre-vaccine era
   - **b.** Reduced from the pre-vaccine era, but rising
   - **c.** As low as in 1976 (>99% reduced from the pre-vaccine era)
   - **d.** Easy to monitor, due to well-established reporting and diagnostic practices

4. **Which of the following tests would NOT aid a diagnosis of pertussis disease in an adult with protracted cough illness?**
   - **a.** Culture of bacteria from a nasopharyngeal swab
   - **b.** Polymerase chain reaction to identify bacterial DNA
   - **c.** Serological identification of bacterial antigens
   - **d.** Assessment of cytokine levels in the blood

5. **After the last pertussis booster vaccination at 4–6 years of age, how long does protection from pertussis disease last?**
   - **a.** Pertussis immunity is nearly undetectable after about 12 years
   - **b.** Protection lasts upwards of 20 years
   - **c.** Recipients of whole-cell pertussis vaccine may be protected longer than recipients of acellular vaccine
   - **d.** Protection lasts a lifetime

6. **The steady rise in pertussis disease incidence in the last two decades reflects**
   - **a.** Larger increase in adolescent and adult cases than in infant and pediatric cases
   - **b.** Waning immunity, with the half-life for vaccine efficacy being 5–6 years after the last vaccine dose
   - **c.** The impact of adolescents and adults as *B pertussis* reservoirs
   - **d.** All of the above

7. **Transmission of *B pertussis* from adolescents and adults to infants is of greater concern than the reverse type of transmission because**
   - **a.** Infant-to-adult transmission occurs only to immunocompromised adults
   - **b.** *B pertussis* can be more virulent after residing in an adult host
   - **c.** Infants, because of absent or incomplete vaccination, are susceptible to severe disease with potentially fatal complications
   - **d.** Although infants and adults suffer similar pertussis disease morbidity, infants may additionally experience growth retardation

8. **Which statement is *false?* Acellular pertussis vaccine is generally preferred over whole-cell vaccine for adolescents and adults because**
   - **a.** It is associated with fewer injection site reactions
   - **b.** It elicits strong antibody responses to selected *B pertussis* components that are key for infection
   - **c.** It may provide longer-lasting immunity
   - **d.** Its efficacy is approximately twice that of whole-cell vaccine

9. **The combination diphtheria-tetanus-acellular pertussis vaccines for adolescents and adults contain**
   - **a.** High doses of all vaccine antigens
   - **b.** Low-dose diphtheria toxoid and high-dose tetanus toxoid
   - **c.** Low-dose tetanus toxoid and high-dose pertussis toxoid
   - **d.** Low-dose diphtheria toxoid and low-dose pertussis toxoid

10. **Which of the following strategies would be predicted to lower pertussis disease incidence in the United States?**
    - **a.** Educate physicians and the public about pertussis disease symptoms across all age groups
    - **b.** Make diagnostic tools, especially the polymerase chain reaction, more widely available
    - **c.** Give booster vaccination to adolescents and adults
    - **d.** All of the above

Program Evaluation (AANP Program #0403155)

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:					
– Understand the etiology, diagnosis, and treatment of pertussis disease	1	2	3	4	5
– Describe recent US epidemiological trends showing the increasing prevalence of adolescent and adult disease	1	2	3	4	5
– Recognize the importance of waning vaccine coverage in adolescents and adults	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**	**6.**	**a**	**b**	**c**	**d**
2.	**a**	**b**	**c**	**d**	**7.**	**a**	**b**	**c**	**d**
3.	**a**	**b**	**c**	**d**	**8.**	**a**	**b**	**c**	**d**
4.	**a**	**b**	**c**	**d**	**9.**	**a**	**b**	**c**	**d**
5.	**a**	**b**	**c**	**d**	**10.**	**a**	**b**	**c**	**d**

Name _____ Degree _____

Phone _____ Fax _____ e-mail _____

Institution/Affiliation _____ SS# _____

Mailing Address _____

City _____ State _____ Zip _____

Signature _____

Pertussis Disease PM