REVIEW ARTICLE

Pertussis: Not Only a Disease of Childhood

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SUMMARY

Introduction: Pertussis is not just a childhood disease, but a respiratory infection that causes persistent cough in all age groups, from newborns to the elderly.

Methods: The authors performed a selective literature search and reviewed national and international recommendations for treatment and vaccination.

Results: Pertussis is found principally in young unvaccinated infants, but school-age children, adolescents, and adults are also affected. Up to 1% of infants contract pertussis, and their respiratory symptoms are often accompanied by apnea. School-age children occasionally display the coughing spasms typical of the disease. Annually, 0.2% to 0.5% of all adolescents and adults are infected and suffer from prolonged, frequently non-paroxysmal coughing. Severe and fatal cases of pertussis occur mainly in newborns and infants, and 25% of affected adults experience complications. Bordetella DNA may be detected by polymerase chain reaction (PCR) for four weeks after symptom onset; except in infants, the sensitivity of this diagnostic technique is low. Although the diagnosis can be confirmed by serological tests, the methods are not well standardized. Treatment with a macrolide prevents the spread of infection, but generally does not alleviate the symptoms. Combination vaccines are the most effective means of prophylaxis.

Discussion: Pertussis is usually not included in the differential diagnosis of persistent respiratory symptoms. The considerable burden of disease could be reduced in adults and young infants by vaccinating adults with acellular combination vaccines. Dtsch Arztebl 2008; 105(37): 623–8
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Pertussis, also known as whooping cough, is a classical childhood disease. After a vaccine became available, the number of notified cases fell dramatically (1), leading to the removal of pertussis from the list of notifiable diseases in West Germany in 1963. In many industrialized nations, however, the number of pertussis notifications has increased substantially in recent years, especially among school-age children, adolescents, and adults – a trend that has also been observed in former East Germany (2). In the present study, we performed a systematic search of clinically relevant international literature and reviewed national and international recommendations for treatment and vaccination *(box 1)*.

Epidemiology and disease burden

Natural infection with the bacterium Bordetella pertussis confers only 3.5 to 12 years of protective immunity against reinfection (3, 4). Data on the duration of immunity are sparse, however, due to the practical difficulties of distinguishing between first infection and reinfection, and because the symptoms of pertussis can vary widely.

The protective effect induced by acellular vaccines is approximately 85% after three doses and lasts for at least five years (1, 3), after which a gradual decrease in immunity is observed. As a result, the incidence of pertussis can be expected to be high in school-age children, adolescents, and adults who do not receive booster vaccinations, even in settings where high vaccine coverage in young children has been achieved.

In many countries, the annual incidence of pertussis in adolescents and adults ranges from 0.18% to 0.51%, independently of vaccine coverage in childhood (5). In Germany, a study conducted in Rostock and Krefeld pointed to a frequency of 165 cases per 100 000 population per year (6). Whereas almost all birth cohorts since 1964 have been vaccinated in Rostock, vaccine coverage in Krefeld was low from the 1970s until around 1995. Nevertheless, there was no statistical difference in the incidence of pertussis among adults in the two cities, demonstrating that vaccination during infancy has no influence on the incidence of disease during adulthood.

Pertussis is endemic in Germany (2). Every three to four years, a wave of infections occurs, which at its peak shows an incidence that is three to four times as high as during the interepidemic periods. Due to different surveillance systems, the notification data in Europe show stark variations, ranging from <1 (Portugal) to 200 (Switzerland) registered cases per 100 000 inhabitants per year (7). In eastern Germany, the incidence of

BOX 1

Search Strategy

Data sources: PubMed, Cochrane Database, Robert Koch Institute databases, vaccination and treatment recommendations in Germany and the US

Publication dates: 1998-2008

Search terms: "pertussis" **and** "disease," "clinical," "complication," "hospitalisation," "death," "reinfection," "epidemiology," "newborn," "infant," "children," "adolescents," "adults," "culture," "PCR," "serology," "vaccination," "acellular," "cost"

Filter: The clinical relevance of the identified publications was evaluated based on their abstracts. Relevant review articles are cited whenever possible.

registered pertussis cases in 2006 ranged from 12 in Saxony to 68 in Mecklenburg-West Pomerania per 100 000 population per year (2). Infants under six months of age had the highest rate of hospitalization. Forty percent of cases registered with the Robert Koch Institute between the years 2002 and 2007 involved children under the age of one (2), and 63 of the 88 deaths due to pertussis between 1980 and 2006 occurred in this group (www.gbe-bund.de). Among newborns and young infants, pertussis is the most common infectious cause of death (8).

Complications associated with pertussis occur in approximately 25% of adults, and in approximately 40% of those over the age of 60 (9). Between 1% and 4% of adult cases require hospitalization (9). Mortality is rare.

Chain of infection

Because maternal antibodies do not reliably confer immunity to pertussis, newborns are susceptible to infection immediately after birth. The incubation period of pertussis can last from 7 to 28 days, and communicability is highest during the first two weeks of infection.

In infants, the source of infection cannot be indentified in 30% to 69% of cases (10–13). In cases in which the source of infection can be traced, half of the children have been infected by their parents – usually by the mother. Older siblings are another frequent source of infection even if they have been vaccinated, because often their immunity has waned in the absence of a booster vaccination. In one study, grandparents were the source of infection in 8% of cases, and other adult household members in 22% of cases (13). Although school-age children are infected primarily by their classmates, parents are also a source of infection. Adolescents are infected, for the most part, by friends and classmates.

Case definition and notification requirement

Pursuant to the Infection Prevention Act (Infektionsschutzgesetz; IfSG), pertussis is currently not included on the national list of notifiable diseases in Germany; there are, however, state-specific regulations in the eastern part of the country that do require notification. As specified in the pertussis case definition given in *box 2*, an infection can be confirmed directly by means of culture or through detection of bacterial nucleic acids with polymerase chain reaction (PCR). Serological confirmation of infection is currently defined as a single high pertussis-specific IgA titer or an increase in IgG antibody titers between two samples. In the revised case definition expected to become effective in early 2009, a single high IgG antibody titer, rather a than single high IgA antibody titer, is required to confirm the diagnosis.

Symptoms and complications

The symptoms of pertussis can vary widely, depending on age, individual immunity (first infection or reinfection), and time elapsed since previous pertussis infection or vaccination.

Newborns and young infants

Some newborns may not present with the coughing spasms typical of pertussis. Following an atypical onset, up to 90% of infants experience typical paroxysmal coughing (1).

Severe complications such as apnea, encephalopathy, and pneumonia are most common in this group. In a study of admissions to pediatric departments for pertussis complications, 75% of infants under the age of six months were diagnosed with pneumonia, 25% with apnea requiring respiratory support, 14% with seizures, and 5% with encephalopathy (14).

School-age children

This group of children, the majority of whom have been vaccinated, is more likely to display the typical symptoms of pertussis, including coughing spasms followed by the signature inspiratory "whoop" and vomiting. The principle complications in this group are pneumonia and otitis media.

Adolescents and adults

Approximately 10% to 20% of all adults with coughing that persists for more than seven days have pertussis (5). Adolescents and adults may present only with prolonged coughing (which in 70% to 90% of cases is paroxysmal in nature), but without other typical findings such as whooping or vomiting. The average duration of coughing ranges from 36 to 48 days.

In a quarter (23% to 28%) of adult patients, pertussis leads to complications such as (5, 9)

- weight loss
- seizures
- syncope
- pneumonia (approx. 10%)
- otitis media
- incontinence
- pneumothorax
- rib fracture
- hernia.

Complications occur in more than 40% of cases among individuals over the age of 60 (9).

Differential diagnosis

In addition to B. pertussis and B. parapertussis, a number of pathogens can cause pertussis-like symptoms (15), including adenoviruses, respiratory syncytial viruses (RSV), human parainfluenza viruses, influenza viruses, Mycoplasma pneumonia, and rhinoviruses. Infections with more than one pathogen are not uncommon, and dual infections with RSV and B. pertussis are frequent among infants.

Laboratory diagnosis

Laboratory diagnosis of pertussis is challenging. The bacteria can be identified directly by culture or by detection of bacterial nucleic acids through PCR (16). Nasopharyngeal secretions or deep nasopharyngeal swabs are appropriate specimens. In young unvaccinated infants, culture and PCR have a sensitivity of approximately 70% (16). The only appropriate method for diagnosing pertussis in school-age children, adolescents, and adults is PCR, which has a sensitivity of 10% to 30%. However, because the sensitivity of PCR decreases with the duration of coughing, it is unlikely to be useful after four weeks. In Germany, culture and PCR are reimbursed by the statutory health insurance (SHI) funds.

Diagnosing pertussis using commercial serological assays (ELISA) is also problematic, because IgG and IgA antibodies against pertussis toxin (PT) are detectable in most school-age children, adolescents, and adults. As a result, serological diagnosis must be based on a significant increase in antibody titer or on a single high antibody titer above an age-adjusted cutoff. An immune response to vaccination cannot be distinguished from an infection; it is also impossible to assess immunity to pertussis using serological methods. Commercially available assays use different antigens and interpretations. For practical purposes, the following approach is recommended:

- IgG anti-PT ≥ 100 ELISA units/mL (EU/mL) (relative to a US FDA reference preparation) is indicative of recent infection.
- IgG anti-PT < 40 EU/mL is not indicative of recent infection.
- IgG anti-PT = 40 EU/mL but < 100 EU/mL requires testing another sample or detecting antibodies against other antigens to confirm the specificity of the assay (15, 17).

Treatment

A Cochrane analysis of 11 randomized controlled studies on antibiotic treatment of pertussis showed that although antibiotics were effective in eliminating B. pertussis within seven days (three to five days for azithromycin), the antibiotics did not alter the clinical course of the illness.

Macrolides have been the mainstay of pertussis treatment for decades. Most recent studies have thus compared the different macrolides to one another. Although trimethoprim/sulfamethoxazole (TMP-SMZ) has been cited as an alternative for patients who cannot tolerate macrolides, its use has been evaluated only in one comparative study with tetracycline (18).

Randomized studies have demonstrated that there was no difference in outcome between 7-day and 14-day courses of treatment with erythromycin and treatment with the macrolides azithromycin or clarithromycin (18). Treatment with erythromycin is thus recommended for seven days, with azithromycin for three to five days, and with clarithromycin for seven days.

Only a few controlled studies on symptomatic interventions using salbutamol, diphenhydramine, or dexamethasone have been conducted to date, and the available evidence is insufficient to draw any conclusions about their effects (19).

Box 3 gives a summary of recommendations on antibiotic treatment (20, 21).

BOX 2

Robert Koch Institute Case Definition

Clinical presentation: indicative of pertussis if at least one of the following symptoms is present:

- Paroxysmal coughing
- Inspiratory stridor (i.e. whooping)
- Post-tussive vomiting
- Apnea, especially in infants

Laboratory confirmation: positive result for **at least one** of the following methods:

- Isolation of pathogen from nasopharyngeal swabs or secretions
- Detection of bacterial nucleic acid (e.g. PCR from nasopharyngeal swabs or secretions)
- Detection of IgA antibodies
- Detection of IgG/IgA antibodies (4-fold titer increase in two samples, e.g. ELISA)

To be reported to the appropriate state authorities:

Clinically confirmed cases:

Clinical presentation indicative of pertussis (except for apnea) if persists for more than 14 days

Clinically/epidemiologically confirmed cases:

Clinical presentation indicative of pertussis with no laboratory confirmation, but evidence of epidemiological linkage (incubation time approx. 7 to 20 days) **with** laboratory confirmation of infection

Clinical and laboratory confirmation:

Clinical presentation indicative of pertussis and laboratory confirmation

Source: www.rki.de/cln_91/nn_494670/DE/content/Infekt/EpidBull/Merkblaetter/Ratgeber_Mbl_Pertussis.html

BOX 3

Suggestions for Treatment and Antimicrobial Prophylaxis of Pertussis (20, 21)

Newborns
- Erythromycin 40 mg/kg BW per day in 3 to 4 doses for 7 (14) days
- 6 months and older: azithromycin 10 mg/kg BW once daily for 5 days

Children
- Azithromycin 10 mg/kg BW once daily for 3 days
- or: azithromycin 10 mg/kg BW once daily for 1 day and 5 mg/kg BW for an additional 4 days
- or: clarithromycin 15 mg/kg BW in 2 doses for 7 days

Adolescents
- Azithromycin 500 mg once daily for 3 days
- or: clarithromycin 2 × 500 mg daily for 7 days

Newborns and young infants

As a rule, newborns and young infants should still be a treated with erythromycin. For this group, erythromycin is available as a syrup and as an intravenous solution, and clarithromycin as a syrup. Azithromycin has been approved for children older than six months. US Centers for Disease Control (CDC) guidelines (20) and the 2006 Report of the Committee on Infectious Diseases (21) recommend azithromycin as the antibiotic of choice in newborns, because erythromycin treatment is associated with an increased risk of pyloric stenosis (20). However, pyloric stenosis has also been reported in association with the use of azithromycin (22).

Young and school-age children

Clarithromycin and azithromycin are as effective as erythromycin, but are better tolerated. Although there are data on the in vitro susceptibility of B. pertussis to roxithromycin, no clinical studies have been conducted to date (18).

Adolescents and adults

Macrolides are also the standard form of treatment in this group. Adverse events are less common under treatment with azithromycin or clarithromycin compared to erythromycin (18). To lessen the period of communicability, experts recommend initiating antibiotic treatment within four weeks of cough onset (20, 21).

Antibiotic prophylaxis

Because only two controlled studies have investigated antibiotic prophylaxis in pertussis contacts to date, there is insufficient evidence to determine the effectiveness of this approach (18). Based on its potential benefits, however, experts recommend antibiotic prophylaxis in households with young unvaccinated infants. Recommendations for the duration and dose of prophylaxis are similar to those for treatment (20, 21).

Costs of disease

Studies in the US and Germany have estimated direct costs per adult case to be € 104 (DE) or between $ 141 to $ 326 (US), and indirect costs to be € 434 (DE) or between $ 447 and $ 1232 (US) (6, 23).

Vaccination strategies

The currently approved acellular pertussis vaccines have demonstrated their efficacy in a range of randomized controlled studies in infants (1) and in a smaller, randomized controlled study in adolescents and adults (24). Because pertussis vaccines are not available as a single vaccine, the German Standing Vaccination Committee (Ständige Impfkommission, STIKO) always recommends combination vaccine products (25). Formulations with reduced concentrations of the pertussis antigenic components are available for immunization against tetanus, diphtheria, and pertussis (Tdap) and against tetanus, diphtheria, pertussis, and polio (Tdap-IPV); both are approved for adolescents and adults, as well as for children above the age of three (Tdap) or four (Tdap-IPV). The current STIKO recommendations are summarized in the *table*.

Primary immunization requires a series of four injections using combination vaccines with the full concentration of pertussis antigens. The first three injections should be administered at the end of the second, third, and fourth months after birth. In Germany, approximately 95% of children have completed this series by the age of two (data from 2003 to 2006) (e1).

Primary immunization needs to be initiated as early as possible to limit the period during which infants are vulnerable to infection. Even a single dose of vaccine can provide measurable protection against a severe course of disease (1). Primary immunization is completed by administering a fourth dose of the vaccine between 12 and 15 months after birth. In Germany, 85% of children aged two and 90% of children aged three to six have completed the four-dose series. Among older children, this percentage is lower, at 69.5% (26).

Booster vaccination is given to preschool-age children using a vaccine formulation with reduced concentrations of pertussis antigenic components (Tdap). STIKO has recommended this dose since January 2006 (25).

In adolescents (9 to 17 years), the reduced-antigen-content combination vaccine is also used for booster vaccination. The vaccination coverage in this age group is between 30% and 50%.

Routine booster vaccination for adults is currently under discussion in Germany; it has recently been recommended in Saxony, France, Austria, the United States, Canada, and Australia. The aim of booster vaccination in this group is to reduce disease burden in vaccinated individuals, to decrease the number of

infections among unvaccinated infants, and to achieve improved herd immunity. No studies of this approach have been conducted thus far. One model of adult vaccination in Germany showed that routine vaccination of German adults would be cost-effective (e2). Data on the duration of protection in adults after administration of the reduced-antigen-content combination vaccine are not yet available.

The current STIKO recommendation for adult booster vaccination is limited to the following groups:

- Women who are planning to become pregnant
- Persons working in the field of pediatrics, in preschools, or in daycare centers.
- Contact persons in households with infants (e.g. parents, grandparents, babysitters)

According to the German Regulation of Biological Substances Act (BioStoffV), employers must offer vaccination to employees who are at risk for exposure to the pathogen that causes pertussis. This is particularly relevant for nursing and medical staff working in pediatrics and obstetrics.

Everyday issues

Vaccination

Occasionally, school-age children and adolescents will have no record of being vaccinated against pertussis; in such cases, a catch-up vaccination is indicated. The only vaccines that have been approved for primary immunization are those with full pertussis antigen content, albeit only in children up to the age of six. Studies (e6) have shown that, in older children, a single dose of vaccine with reduced antigen content (Tdap or Tdap-IPV) induces a sufficient immune response in 90% of cases. There is no contraindication to vaccinate individuals without a history of pertussis vaccination. Indeed, due to the prevalence of B. pertussis, most cases are, in reality, booster immunizations.

In cases of infection in physician practices and hospitals, it is often recommended that healthcare personnel be vaccinated against pertussis. It is unclear, however, how long the interval should be between this and the last vaccination with tetanus and diphtheria toxoids. STIKO recommends an interval of five years, if possible; however, a Canadian and a French study (e4, e5) have shown that administering a Tdap vaccine 18 months, or even four weeks, after immunization with a dT vaccine did not lead to a significantly higher risk of adverse events. There is also no formal contraindication against administering the vaccine to individuals who have been immunized with tetanus or diphtheria toxoids less than five years previously.

Antibiotic treatment and prophylaxis

For adults who need antibiotic prophylaxis or treatment, azithromycin and clarithromycin are better tolerated than erythromycin. However, only erythromycin may be used in women who are pregnant or breastfeeding, and this only if clearly indicated.

The question of whether vaccinated, asymptomatic contacts should receive antibiotic prophylaxis should be addressed on a case-by-base basis. To break the chain of infection, chemoprophylaxis should be recommended to personnel working in high-risk areas (e.g. neonatal wards).

TABLE

Current STIKO Vaccination Recommendations (25)

Who?	When?	What with?
Primary immunization		
All newborns	Aged 2, 3, 4 months	Combination vaccination containing aP (i.e. for primary vaccination)
All infants	Aged 11–14 months	Combination vaccination containing aP (i.e. for primary vaccination)
Booster immunizations*:		
All children	Aged 4–5 years	Combination booster vaccine (Tdap)
All adolescents	Aged 8–16 years	Combination booster vaccine (Tdap-IPV)
Women planning to become pregnant	Before pregnancy	Combination booster vaccine (Tdap) (or, if indicated, Tdap-IPV)
Individuals with contact to newborns or infants	Preferably before birth	Combination booster vaccine (Tdap) (or, if indicated, Tdap-IPV)
Staff in nurseries, preschools, daycare centers	Preferably before commencing employment	Combination booster vaccine (Tdap) (or, if indicated, Tdap-IPV)
Staff in pediatric hospitals and postnatal wards	Preferably before commencing employment	Combination booster vaccine (Tdap) (or, if indicated, Tdap-IPV)
(All adults)	(Only in Saxony)	Combination booster vaccine (Tdap) (or, if indicated, Tdap-IPV)

* In cases where tetanus prophylaxis is indicated due to an injury, the need for pertussis immunization should be assessed and, if necessary, a combination vaccine should be used.

Employees in healthcare and public facilities

According to section 34, paragraph 1 of the IfSG, personnel in public facilities such as nurseries, daycare centers, and schools who are diagnosed with pertussis must be suspended from duty and may return to work no earlier than five days after antibiotic treatment has been initiated. Without antibiotic treatment, affected personnel must wait at least three weeks after symptom onset before resuming work (e6). Healthcare facilities should follow the same measures, even though the IfSG does not formally require that affected medical personnel be suspended from duty. Vaccination status should be assessed and updated; immunity, however, cannot be ascertained by serological testing.

Conflict of interest statement
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REFERENCES

1. Edwards KM, Decker MD: Pertussis Vaccine. In: Plotkin SA, Orenstein WA, Offitt P (eds): Vaccines. 5. Auflage. Philadelphia, PA, USA: Saunders 2008; 467–518.
2. Robert-Koch-Institut: Zur Situation bei ausgewählten Infektionskrankheiten in Deutschland: Keuchhusten-Erkrankungen in den neuen Bundesländern seit 2002. Epidemiol Bull 2007; 50: 475–81.
3. Wendelboe A, van Rie A, Salmaso S, Englund JE: Duration of Immunity against pertussis after natural infection or vaccination. Ped Inf Dis J 2005; 24: 58–62.
4. Versteegh FG, Schellekens JF, Nagelkerke AF, Roord JJ: Laboratory confirmed reinfection with Bordetella pertussis. Acta Paediatr 2002; 91: 95–7.
5. Wirsing von König CH, Halperin S, Riffelmann M, Guiso N: Pertussis of adults and infants. Lancet Infect Dis 2002; 2: 744–50.
6. Riffelmann M, Littmann M, Hülße C, O'Brien J, Wirsing von König CH: Pertussis bei Erwachsenen: Häufigkeit, Symptome und Kosten. Dtsch Med Wschr 2006, 131: 2829–34.
7. EUVAC-Net: Pertussis Surveillance, Final Report. www.ssi.dk/graphics/euvac/pdf/pertussis.pdf
8. Markov PV, Crowcroft NS: Modelling the unidentified mortality burden from thirteen infectious pathogenic microorganisms in infants. Epidemiol Infect 2007; 135: 17–26.
9. de Serres G, Shadmani R, Duval B et al.: Morbidity of pertussis in adolescents and adults. J Infect Dis 2000; 182: 174–9.
10. Crowcroft NS, Booy R, Harrison T et al.: Severe and unrecognised: pertussis in the UK. Arch Dis Child 2003; 88: 802–9.
11. Bisgard KM, Pascual FB, Ehresmann KR et al.: Infant pertussis: Who was the source? Ped Inf Dis J 2004; 23: 985–9.
12. Kowalzik F, Barbosa AP, Fernandes VR et al.: Prospective multinational study of pertussis infection in hospitalized infants and their household contacts. Ped Inf Dis J 2007, 26; 238–42.
13. Wendelboe AM, Njamkepo E, Bourillon A et al.: Transmission of Bordetella pertussis to young infants. Ped Inf Dis J 2007; 26: 293–9.
14. Herzig P, Hartmann D, Fischer D et al.: Pertussis complications in Germany – 3 years of hospital-based surveillance during the introduction of acellular vaccines. Infection 1998; 26: 227–31.
15. Mattoo S, Cherry JD: Molecular pathogenesis, epidemiology and clinical manifestations of respiratory infections due to Bordetella pertussis and other Bordetella subspecies. Clin Microbiol Rev 2005; 18: 326–82.
16. Riffelmann M, Caro, V, Guiso N, Wirsing von König CH, Consensus Group: Nucleic acid amplification tests for diagnosis of Bordetella infections. J Clin Microbiol 2005, 43: 4925–9.
17. Wendelboe AM, Van Rie A: Diagnosis of pertussis: a historical review and recent developments. Expert Rev Mol Diagn 2006; 6: 857–64.
18. Altunaiji S, Kukuruzovic R, Curtis N, Massie J: Antibiotics for whooping cough (pertussis). Cochrane Database of Systematic Reviews: Reviews 2007. Chichester, UK: John Wiley & Sons, Ltd 2007; DOI : 10 1002 /14651858 CD004404 pub3 2007.
19. Pillay V, Swingler G: Symptomatic treatment of the cough in whooping cough Cochrane Database of Systematic Reviews: Reviews 2008. Chichester, UK: John Wiley & Sons, Ltd 2008; DOI: 10.1002/14651858.CD003257
20. Tiwari T, Murphy TV, Moran JS: Recommended antimicrobial agents for the treatment and postexposure prophylaxis of pertussis. 2005 CDC guidelines. Morbidity and Mortality Weekly Reports 2005; 54: 1–16.
21. American Academy of Pediatrics: Pertussis. In: Pickering LK, Baker CJ, Long SS, McMillan JA (eds.): Red Book: 2006 Report of the Committee on Infectious Diseases. 27. Auflage. Elk Grove Village, IL, USA: American Academy of Pediatrics 2006; 498–526
22. Morrison W: Infantile hypertrophic pyloric stenosis in infants treated with azithromycin (report). Ped Inf Dis J 2007; 26: 186–8.
23. Lee GM, Lett S, Schauer S et al. for the Massachusetts Pertussis study group: Societal costs and morbidity of pertussis in adolescents and adults. Clin Infect Dis 2004; 39: 1572–80.
24. Ward JI, Cherry JD, Chang SJ et al.: Efficacy of an acellular pertussis vaccine among adolescents and adults. N Engl J Med 2005; 353: 1555–63.
25. Current STIKO recommendations: www.rki.de/stiko-empfehlungen

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E-REFERENCES

e1. Poethko-Müller C, Kuhnert T, Schlaud M: Durchimpfung und Determinanten des Impfstatus in Deutschland. Ergebnisse des Kinder- und Jugendgesundheitssurveys (KiGGS). Bundesgesundheitsbl 2007; 50: 851–62.

e2. Lee G, Riffelmann M, Wirsing von Koenig CH: Cost effectiveness of pertussis vaccination of adults in Germany. Vaccine 2008; 26: 3673–9.

e3. Knuf M, Zepp F, Meyer C, Grzegowski E, Wolter J, Riffelmann M, Wirsing von König CH: Immunogenicity of a single dose of reduced-antigen acellular pertussis vaccine in a non-vaccinated adolescent population. Vaccine 2006; 24: 2043–8.

e4: Halperin SA, Sweet L, Baxendale D et al.: How soon after a prior tetanus-diphtheria vaccination can one give adult formulation tetanus-diphtheria-acellular pertussis vaccine? Pediatr Infect Dis J 2006; 25: 195–200.

e5: Beytout J, Launay O, Dubray C et al.: REPEVAX can be safely administered as a booster one month after tetanus, diphtheria and poliomyelitis vaccination: an option for managing increasing incidence of Bordetella pertussis (whooping cough) infection. Poster P 1325, 18. European Congress of Clinnical Microbiology and Infections Diseases, Barcelona, 19. – 22. April 2008.

e6: Bekanntmachungen des Robert Koch-Instituts: Empfehlungen für die Wiederzulassung in Schulen und sonstigen Gemeinschaftseinrichtungen. Merkblatt für Ärzte, Leitungen von Gemeinschaftseinrichtungen und Gesundheitsämter. Bundesgesundheitsblatt 2001; 44: 830–43.