AMERICAN ACADEMY OF PEDIATRICS

Committee on Infectious Diseases

Policy Statement: Recommendations for the Prevention of Pneumococcal Infections, Including the Use of Pneumococcal Conjugate Vaccine (Prevnar), Pneumococcal Polysaccharide Vaccine, and Antibiotic Prophylaxis

ABSTRACT. Heptavalent pneumococcal conjugate vaccine (PCV7) is recommended for universal use in children 23 months and younger, to be given concurrently with other recommended childhood vaccines at 2, 4, 6, and 12 to 15 months of age. For children 7 to 23 months old who have not received previous doses of PCV7, administration of a reduced number of doses is recommended. Two doses of PCV7 are recommended for children 24 to 59 months old at high risk of invasive pneumococcal infection—including children with functional, anatomic, or congenital asplenia; infection with human immunodeficiency virus; and other predisposing conditions—who have not been immunized previously with PCV7. Recommendations have been made for use of 23-valent pneumococcal polysaccharide (23PS) vaccine in high-risk children to expand serotype coverage. High-risk children should be given vaccines at the earliest possible opportunity. Use of antibiotic prophylaxis in children younger than 5 years with functional or anatomic asplenia, including children with sickle cell disease, continues to be recommended. Children who have not experienced invasive pneumococcal infection and have received recommended pneumococcal immunizations may discontinue prophylaxis after 5 years of age.

The safety and efficacy of PCV7 and 23PS in children 24 months or older at moderate or lower risk of invasive pneumococcal infection remain under investigation. Current US Food and Drug Administration indications are for administration of PCV7 only to children younger than 24 months. Data are insufficient to recommend routine administration of PCV7 for children at moderate risk of pneumococcal invasive infection, including all children 24 to 35 months old, children 36 to 59 months old who attend out-of-home care, and children 36 to 59 months old who are of Native American (American Indian and Alaska Native) or African American descent. However, all children 24 to 59 months old, regardless of whether they are at low or moderate risk, may benefit from the administration of pneumococcal immunizations. Therefore, a single dose of PCV7 or 23PS vaccine may be given to children 24 months or older. The 23PS is an acceptable alternative to PCV7, although an enhanced immune response and probable reduction of nasopharyngeal carriage favor the use of PCV7 whenever possible.

ABBREVIATIONS. PCV7, heptavalent pneumococcal conjugate vaccine; 23PS, 23-valent pneumococcal polysaccharide; SCD, sickle cell disease; DTaP, diphtheria and tetanus toxoids and acellular pertussis; HbOC, *Haemophilus influenzae* type b conjugate vaccine; HIV, human immunodeficiency virus; AOM, acute otitis media.

The recommendations in this statement do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

The purpose of this report is to provide recommendations for use of the heptavalent pneumococcal conjugate vaccine (PCV7), Prevnar (Lederle Laboratories, Pearl River, NY; Wyeth-Ayerst Pharmaceuticals, Marietta, PA), and 23-valent pneumococcal polysaccharide (23PS) vaccines. In addition, recommendations for the continuing use of antibiotic prophylaxis in children with sickle cell disease (SCD) and asplenia will be given, and the use of antibiotics and vaccines in children who attend out-of-home care will be discussed. The American Academy of Pediatrics' Committee on Infectious Diseases provided recommendations for pneumococcal polysaccharide vaccines in 1985.[1] Revised recommendations and supporting data for the use of pneumococcal vaccines and antibiotic prophylaxis have been reviewed recently[2,3] and accompany these recommendations.

Initially, there may be delays in acquiring adequate supplies of PCV7 or providers may have logistic or resource constraints in administering pneumococcal vaccine. Data supporting the administration of PCV7 to healthy, moderate-risk or high-risk children older than 24 months are limited and confined to evaluations of safety and immunogenicity in small groups of children. For the purposes of the current recommendations, children at high risk are defined as those with annual rates of invasive pneumococcal infection of at least 150 cases per 100 000, whereas children at moderate risk have rates of at least 20 cases per 100 000. The administration of PCV7 is of highest priority for infants and toddlers 23 months and younger and children at high risk because of underlying disease. Currently, there are insufficient safety, efficacy, and immunogenicity data on which to base a recommendation for universal immunization of any children older than 24 months, other than those who are at high risk. The US Food and Drug Administration approved PCV7 (Prevnar) in February 2000 and has indicated PCV7 for use only in children younger than 24 months.

RECOMMENDED IMMUNIZATION OF ALL CHILDREN 23 MONTHS AND YOUNGER

The PCV7 vaccine is recommended for routine administration to all children 23 months and younger at 2, 4, 6, and 12 to 15 months (Table 1). Each

.5-mL dose of PCV7 should be administered intramuscularly. The initial 2-month dose should be given no earlier than 6 weeks of age. Infants of very low birth weight (≤1500 g) should be immunized at the time that they attain a chronological age of 6 to 8 weeks, regardless of their calculated gestational age. All doses of PCV7 may be administered concurrently with other childhood immunizations, including all diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccines, all *Haemophilus influenzae* type b conjugate vaccines, both hepatitis B vaccines, inactivated poliovirus vaccine, measles-mumps-rubella vaccine, and varicella vaccine, using a separate syringe for the injection of each vaccine and administering each vaccine at a different site.

All children 23 months and younger who have not received doses of PCV7 before 6 months of age should be given catch-up doses according to the schedules in Table 1. Children 7 to 11 months old who have not previously received doses of PCV7 should receive 2 doses at least 6 to 8 weeks apart, followed by a third dose at 12 to 15 months of age or at least 6 to 8 weeks after the second dose. Children 12 to 23 months old who were not previously immunized should receive 2 doses at least 6 to 8 weeks apart.

Infants should begin the PCV7 immunization series in conjunction with other required vaccines at the time of the first regularly scheduled health maintenance visit after at least 6 weeks of age. Children 23 months or younger who begin a catch-up PCV7 immunization series at 7 months or older should start at the time of their next clinic visit, including those visits not related to well-child care unless contraindicated (eg, moderate or severe febrile illness) (Evidence grade I).

RECOMMENDED IMMUNIZATION OF CHILDREN 24 TO 59 MONTHS OLD AT HIGH RISK OF INVASIVE PNEUMOCOCCAL DISEASE

The PCV7 vaccine is recommended for all children 24 to 59 months old who are at high risk for invasive pneumococcal infection (Table 2). High-risk children include children with SCD and other types of functional or anatomic asplenia, human immunodeficiency virus (HIV) infection, or primary immunodeficiency and children who are receiving immunosuppressive therapy. Children at high risk of pneumococcal disease experience rates of infection that are at least 150/100 000. The following schedules are recommended for those high-risk children who are 24 to 59 months of age and who may have received previous doses of 23PS vaccine or PCV7 (Table 3).

1. For high-risk children who have received 4 doses of PCV7, a dose of 23PS vaccine is recommended at 24 months of age, to be given at least 6 to 8 weeks after the last dose of PCV7.
2. For high-risk children who have received 1 to 3 doses of PCV7 before 24 months of age, a single additional dose of PCV7 should be given at least 6 to 8 weeks after the last dose of PCV7. This should then be followed by a dose of 23PS vaccine at least 6 to 8 weeks later. An additional dose of 23PS vaccine should be given no earlier than 3 to 5 years after the initial dose of 23PS vaccine.
3. For high-risk children 24 to 59 months old who have received only a single previous dose of 23PS vaccine, there are minimal data regarding the safety of subsequent doses of pneumococcal conjugate vaccines. However, 2 doses of PCV7 are recommended, to be given at an interval of 6 to 8 weeks. Administration of the PCV7 immunization series should begin no earlier than 6 to 8 weeks after the last dose of 23PS vaccine. An additional dose of 23PS vaccine is recommended 3 to 5 years after the first dose of 23PS vaccine.
4. For high-risk children 24 to 59 months old who have received no previous doses of either 23PS vaccine or PCV7, 2 doses of PCV7 are recommended, to be given at an interval of 6 to 8 weeks, followed by a single dose of 23PS vaccine no less than 6 to 8 weeks after the last dose of PCV7. An additional dose of 23PS vaccine is recommended 3 to 5 years after the last dose.

Minimal safety and immunogenicity data are available regarding the use of combined regimens of PCV7 and 23PS vaccine, and no data exist regarding the efficacy of these regimens for the prevention of pneumococcal disease. Currently available immunogenicity data suggest that PCV7 induces a primary immune response that will provide immune memory for the boosting of antibody to some serotypes contained within 23PS vaccine. Because 23PS vaccine provides a potentially expanded serotype coverage, its use is recommended for high-risk children. However, previous experience with pneumococcal polysaccharide vaccines has suggested that repeated doses of 23PS vaccine may be associated with an increased incidence of local reactions. Recommendations for the number of doses and the interval between doses of pneumococcal vaccines should be carefully observed (Table 3) (Evidence grade II-2, III).

TABLE 1. Recommended Schedule of Doses for PCV7, Including Primary Series and Catch-Up Immunizations, in Previously Unvaccinated Children*

Age at First Dose	Primary Series	Booster Dose†
2–6 mo	3 doses, 6–8 wk apart	1 dose at 12–15 mo of age
7–11 mo	2 doses, 6–8 wk apart	1 dose at 12–15 mo of age
12–23 mo	2 doses, 6–8 wk apart	
≥24 mo	1 dose	

* Recommendations for high-risk groups are given in Table 3.
† Booster doses to be given at least 6 to 8 weeks after the final dose of the primary series.

TABLE 2. Children at High Risk of Invasive Pneumococcal Infection

High risk (attack rate of invasive pneumococcal disease >150/100 000 cases/y)
1. SCD, congenital or acquired asplenia, or splenic dysfunction
2. Infection with HIV

Presumed high risk (attack rate not calculated)
1. Congenital immune deficiency: some B- (humoral) or T-lymphocyte deficiencies, complement deficiencies (particularly C1, C2, C3, and C4 deficiencies), or phagocytic disorders (excluding chronic granulomatous disease)
2. Chronic cardiac disease (particularly cyanotic congenital heart disease and cardiac failure)
3. Chronic pulmonary disease (including asthma treated with high-dose oral corticosteroid therapy)
4. Cerebrospinal fluid leaks
5. Chronic renal insufficiency, including nephrotic syndrome
6. Diseases associated with immunosuppressive therapy or radiation therapy (including malignant neoplasms, leukemias, lymphomas, and Hodgkin's disease) and solid organ transplantation*
7. Diabetes mellitus

Moderate risk (attack rate of invasive pneumococcal disease >20 cases/100 000/y)
1. All children 24–35 mo old
2. Children 36–59 mo old attending out-of-home care
3. Children 36–59 mo old who are of Native American (American Indian and Alaska Native) or African American descent

* Guidelines for the use of pneumococcal vaccines for children who have received bone marrow transplants are currently undergoing revision (Centers for Disease Control and Prevention, personal communication, 2000).

TABLE 3. Recommendations for Pneumococcal Immunization With PCV7 or 23PS Vaccine for Children at High Risk of Pneumococcal Disease, as Defined in Table 2*

Age	Previous Doses	Recommendations
≤23 mo	None	PCV7 as in Table 1
24–59 mo	4 doses of PCV7	1 dose of 23PS vaccine at 24 mo, at least 6–8 wk after last dose of PCV7 1 dose of 23PS vaccine, 3–5 y after the first dose of 23PS vaccine
24–59 mo	1–3 doses of PCV7	1 dose of PCV7 1 dose of 23PS vaccine, 6–8 wk after the last dose of PCV7 1 dose of 23PS vaccine, 3–5 y after the first dose of 23PS vaccine
24–59 mo	1 dose of 23PS	2 doses of PCV7, 6–8 wk apart, beginning at least 6–8 wk after last dose of 23PS vaccine 1 dose of 23PS vaccine, 3–5 y after the first dose of 23PS vaccine
24–59 mo	None	2 doses of PCV7 6–8 wk apart 1 dose of 23PS vaccine, 6–8 wk after the last dose of PCV7 1 dose of 23PS vaccine, 3–5 y after the first dose of 23PS vaccine

* Children with SCD, asplenia, HIV infection, and other high-risk factors.

IMMUNIZATION OF CHILDREN 24 TO 59 MONTHS OLD AT MODERATE RISK OF INVASIVE PNEUMOCOCCAL INFECTION

Currently available data are inadequate to recommend routine universal administration of PCV7 or 23PS vaccine to children >24 months of age at moderate risk for invasive pneumococcal disease. Children at moderate risk experience attack rates of a least 20/100 000 but generally have rates less than those of high-risk children. Children at moderate risk include: all children 24 to 35 months old; children 36 to 59 months old who attend out-of-home care (≥4 hours/week with at least 2 unrelated children); and children 36 to 59 months old who are of Native American (American Indian and Alaska Native) or African American descent. Other factors that may be considered when establishing priorities for possible elective immunization of children 24 to 59 months old with PCV7 or 23PS vaccine include social or economic disadvantage, residence in crowded or substandard housing, homelessness; chronic exposure to tobacco smoke; or a history of severe or recurrent otitis media within the year before immunization or previous tympanostomy tube placement. Children for whom PCV7 vaccine is elected should be given the vaccine in the schedule listed in Table 1. Alternatively, the 23PS vaccine can be given as a single dose for all children 2 years or older.

The relative merits of PCV7 and 23PS vaccine given as a single dose in children older than 2 years have not been subjected to rigorous prospective comparative studies of immunogenicity, safety, or efficacy. Conjugate vaccines initiate immunologic memory and provide an enhanced immune response in children 24 to 59 months old. In children older than 2 years, antibody responses after administration of PCV7 are quantitatively and qualitatively greater (eg, enhanced opsonization), compared with responses after administration of 23PS vaccine. Unlike PCV7 immune responses, young children fail to respond to some serotypes in the 23PS vaccine, including some serotypes included in the conjugate vaccine. Immune responses to all pneumococcal serotypes may not occur after injection of the 23PS vaccine until children are 5 or more years old. Further,

the duration of antibody responses is greater after administration of PCV7. Conjugate vaccines similar to PCV7 have reduced nasopharyngeal carriage of vaccine serotypes and may provide a secondary benefit by limiting spread of invasive serotypes among young children. A single dose of 23PS vaccine has been recommended since 1985 for children 2 years or older who are at risk of pneumococcal disease.[1,2] The 23PS vaccine provides potential protection against an expanded number of serotypes, and the cost of 23PS vaccine is considerably less than that of PCV7. Data regarding the efficacy of 23PS vaccine are conflicting, but 2 recent studies have suggested that 23PS vaccine may provide modest protection in children.

Therefore, either PCV7 or 23PS vaccine can be used for elective administration to children 24 to 59 months old. A single dose of each vaccine has been administered safely to children. Based on the considerations reviewed above, PCV7 is the preferred vaccine. However, until further data are available, 23PS vaccine is an acceptable alternative for children older than 2 years when economic or other barriers prohibit the use of PCV7. If PCV7 vaccine is used, a single dose of 23PS vaccine after administration of PCV7 should be considered, particularly in children of American Indian descent, to provide broadened pneumococcal coverage against serotypes not contained within PCV7. In recent studies, PCV7 has provided coverage for <50% of invasive serotypes in Native American children. The dose of 23PS vaccine should be given no earlier than 6 to 8 weeks after the last dose of PCV7 (Evidence grade III).

IMMUNIZATION OF HEALTHY CHILDREN 5 YEARS AND OLDER

Health care professionals also may elect immunization with PCV7 or 23PS vaccine for certain children 60 months or older. The risks for invasive pneumococcal disease are much lower for children 60 months or older. No efficacy data and limited safety and immunogenicity data are available on which to base a recommendation for the use of PCV7 in children 5 years and older. Studies of small numbers of children with SCD and HIV suggest that PCV7 is safe and immunogenic when administered to children up to 13 years old. Therefore, administration of a single dose of PCV7 to children of any age, particularly children at high risk for invasive pneumococcal infection, is not contraindicated. However, 23PS immunization also may be effective and immunogenic in older children at increased risk of invasive or severe respiratory tract infections caused by pneumococci. Therefore, immunization with a single dose of PCV7 or 23PS vaccine is acceptable. If both vaccines are used, then the administration of each should be separated by 6 to 8 weeks (Evidence grade III).

USE OF PNEUMOCOCCAL VACCINE IN CHILDREN WITH SEVERE OR RECURRENT OTITIS MEDIA

Pneumococcal polysaccharide vaccines have not reduced the incidence of acute otitis media (AOM) in children of any age and, therefore, 23PS vaccine is not recommended for the prevention of AOM. The PCV7 has provided a modest reduction (<10%) in the incidence of AOM in children with a history of recurrent AOM, as defined by at least 3 or more episodes in 6 months or 4 or more episodes in the year before the administration of the vaccine. However, PCV7 may be beneficial for children 24 to 59 months old who have not received pneumococcal vaccines previously and who have a history of recurrent AOM, or for children who have AOM complicated by placement of tympanostomy tubes (Evidence grade I).

CONTROL OF TRANSMISSION OF PNEUMOCOCCAL INFECTION AND INVASIVE DISEASE AMONG CHILDREN ATTENDING OUT-OF-HOME CARE

Rates of invasive pneumococcal infection among children attending out-of-home care are twofold to threefold higher than among other healthy children of the same age not enrolled in out-of-home care (defined as at least 4 hours per week in out-of-home care shared with at least 2 unrelated children). The 23PS immunization does not reduce nasopharyngeal carriage of pneumococci. Insufficient data are available regarding the efficacy of PCV7 in preventing or interrupting nasopharyngeal carriage or transmission of pneumococcal infection in out-of-home-care settings where one or more invasive pneumococcal infections have occurred. Current data suggest that there is approximately a 50% decrease in nasopharyngeal carriage of vaccine serotypes among children who receive pneumococcal conjugate vaccines, but there may be replacement of vaccine serotypes with nonvaccine serotypes. Therefore, until more data are available, routine immunization with PCV7 or 23PS vaccine is not recommended for children in out-of-home care, but the elective use of either vaccine is not contraindicated. In addition, available data are insufficient to recommend any antibiotic regimen for preventing or interrupting the carriage or transmission of pneumococcal infection in these settings (Evidence grade III).

GENERAL RECOMMENDATIONS FOR USE OF PNEUMOCOCCAL VACCINES

1. Either 23PS vaccine or PCV7 may be given concurrently with other vaccines. Either pneumococcal vaccine should be injected with a separate syringe in a separate site when administered with other vaccines. The concurrent administration of pneumococcal vaccines with measles-mumps-rubella vaccine, varicella vaccine, DTaP vaccine, inactivated poliovirus vaccine, oral poliovirus vaccine, *H influenzae* type b conjugate (HbOC) vaccine, or hepatitis B vaccine has not been shown to meaningfully impair the immune response to other vaccines or pneumococcal vaccines. Rates of local reactions after administration of PCV7 are comparable with those of HbOC, but fever and local reactions occur more often. Data are not available on the immunogenicity or adverse reactions with concurrent administration of *Haemophilus* protein conjugate vaccines other than HbOC (CRM_{197}). The PCV7 vaccine does not contain thimerosal (Evidence grade I).

2. When elective splenectomy is performed for any reason, scheduled immunization with PCV7 or 23PS vaccine should be performed at least 2 weeks before splenectomy. Immunization should precede the initiation of immune-compromising therapy by at least 2 weeks (Evidence grade III).
3. In general, pneumococcal vaccines should be deferred during pregnancy, because the effects on the fetus are unknown, and immunization during pregnancy poses a theoretical risk to the developing fetus. However, inactivated or killed vaccines, including other experimental and licensed polysaccharide vaccines such as group B streptococcal and 23PS vaccines, have been administered safely during pregnancy. A high risk of severe pneumococcal disease in a pregnant woman should be considered when making decisions regarding the need for pneumococcal immunization, and 23PS vaccine can be given during pregnancy. Household contacts of pregnant women may be given either vaccine (Evidence grade III).

USE OF ANTIBIOTIC PROPHYLAXIS IN CHILDREN WITH SCD AND FUNCTIONAL OR ANATOMIC ASPLENIA

Antibiotic prophylaxis is recommended for all children with SCD and functional or anatomic asplenia, regardless of whether they have received pneumococcal immunizations. Although the efficacy of penicillin prophylaxis in children with functional or anatomic asplenia other than SCD has not been studied, it is reasonable to use prophylaxis in the same regimen. Antibiotic prophylaxis should be begun before 2 months of age or as soon as SCD or asplenia occurs or is otherwise recognized or suggested by screening procedures. Oral administration of penicillin V potassium is recommended at a dosage of 125 mg twice a day until 3 years of age and at a dosage of 250 mg twice a day after 3 years of age. Children who have not experienced invasive pneumococcal infection and have received recommended pneumococcal immunizations may discontinue penicillin prophylaxis after 5 years of age (Evidence grade I).

PNEUMOCOCCAL IMMUNIZATION OF CHILDREN WITH A PAST HISTORY OF PNEUMOCOCCAL DISEASE

Children who have experienced invasive pneumococcal disease should receive all recommended doses of pneumococcal immunization (PCV7 or 23PS vaccine) appropriate for their age and underlying condition. The full series of scheduled doses should be completed even if the series is interrupted by an episode of invasive pneumococcal disease.

EVIDENCE GRADING

I. Evidence obtained from at least one properly randomized, controlled trial.
II-1. Evidence obtained from well-designed, controlled trials without randomization.
II-2. Evidence obtained from well-designed cohort or case–control analytic studies, preferably from >1 center or research group.
II-3. Evidence obtained from multiple time series with or without intervention. Dramatic results in uncontrolled experiments, such as the results of the introduction of penicillin treatment in the 1940s, could be regarded as this type of evidence.
III. Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

REFERENCES

1. American Academy of Pediatrics, Committee on Infectious Diseases. Recommendations for using pneumococcal vaccine in children. *Pediatrics*. 1985;75:1153–1158
2. Centers for Disease Control and Prevention. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR CDC Surveill Summ*. 1997;46(RR-8):1–24
3. American Academy of Pediatrics, Committee on Infectious Diseases. Technical report: prevention of pneumococcal infections, including the use of pneumococcal conjugate and polysaccharide vaccines and antibiotic prophylaxis. *Pediatrics*. 2000;106:367–376

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