THE JOURNAL OF FAMILY PRACTICE

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Your guide to the new pneumococcal vaccine for children

Since PCV7 (Prevnar) became available in 2000, rates of invasive pneumococcal disease have dropped sharply in the United States. Now, an expanded PCV13 vaccine that can prevent many of the remaining cases will replace PCV7.

A new, 13-valent pneumococcal conjugate vaccine (PCV13, Prevnar 13), from Wyeth Pharmaceuticals was licensed by the US Food and Drug Administration (FDA) in February for use in all children ages 6 weeks to 59 months. The new vaccine was licensed for the prevention of invasive pneumococcal disease (pneumonia, meningitis, and bacteremia) and otitis media.[1] PCV13 is meant to replace the 7-valent PCV7 (Prevnar), and will offer protection against a wider array of pneumococcal serotypes.[1]

Invasive pneumococcal disease in kids has diminished substantially

Soon after PCV7 was included in the routine child immunization schedule, the incidence of invasive pneumococcal disease (IPD) began to decline.[2-5] In 1 study, the annual rate of IPD among children younger than 5 years of age decreased from 98.7 cases/100,000 in 1998–1999 to 22.6 cases/100,000 in 2006-2007.[3] This decline was due to a decrease in the rate of disease caused by the 7 vaccine serotypes, from 81.9 cases/100,000 to 0.4 cases/100,000.

However, during that same time period, the rate of IPD caused by nonvaccine serotypes increased from 16.8 cases/100,000 population to 22.1 cases/100,000.[3] The percentage of IPD caused by nonvaccine serotypes rose from 20% to 90% among children younger than 5 years of age during that time period.[3]

Fewer cases in adults, as well

In addition to the decline of IPD in children, there has also been a decline in adults. In those older than age 65, the rate of IPD decreased from 60.1/100,000 to 38.2/100,000 between 1998 and 2007—most likely because routine use of the PCV7 vaccine in children has resulted in decreased carriage and transmission of infection from children to adults.[3] As in children, the decline was due to a decreasing incidence of infection from PCV7 vaccine serotypes, from 33.7 cases/100,000 to 3.3 cases/100,000. At the same time, the rate of disease caused by nonvaccine serotypes increased from 26.4 cases/100,000 to 34.9 cases/100,000.[3]

Nonvaccine serotypes still cause concern

While the overall decline in IPD has been a public health success, the increase in incidence of disease caused by nonvaccine serotypes has been cause for concern. According to an analysis of 2007 data from the Centers for Disease Control and Prevention (CDC)'s Active Bacterial Core surveillance, 64% of IPD cases in children younger than 5 years of age in 2006-2007 were caused by serotypes 1, 3, 5, 6A, 7F, and 19A.[6] Several of these replacement

TABLE 1

PCV13: Routine vaccination schedule

Age at first dose	Primary series*	Booster dose†
2-6 months	3 doses	1 dose, 12-15 months
7-11 months	2 doses	1 dose, 12-15 months
12-23 months	2 doses	None
24-59 months, healthy children	1 dose	None
24-71 months for children with certain chronic diseases or immunocompromising conditions (see **TABLE 3**).	2 doses	None

*Minimum interval between doses is 8 weeks, except for children vaccinated at <12 months for whom the minimum interval is 4 weeks. Minimum age for first dose is 6 weeks.

†Given at least 8 weeks after previous dose.

Source: CDC. *MMWR Morb Mortal Wkly Rep.* 2010.[1]

serotypes have high levels of resistance to penicillin and erythromycin. This trend is what led to the development of the PCV13, which adds these 6 to the 7 serotypes covered by Prevnar.

The dosing schedule is complicated

The recommended schedule for the older PCV7 vaccine has always been a challenge, because the number of doses depends on the age of the child when first vaccinated.[7,8] The introduction of PCV13 adds to the complexity, because many children will be in the midst of a PCV7 series when they make the transition to PCV13.

The Advisory Committee on Immunization Practices (ACIP) recommendations on how many doses of PCV13 a child should receive depend now on the age at which the first PCV vaccine was received (either PCV7 or PCV13), the number of doses of each received, and the presence or absence of high-risk medical conditions. These recommendations are summarized below and illustrated in **TABLE 1** and **TABLE 2**.

- **For a child who started PCV7 on time and is in mid series**, the recommendation is to simply finish the series with PCV13.
- **If a child has completed a series of PCV7**, the recommendation is to give him or her 1 dose of PCV13 up to age 59 months. (If the child has a chronic underlying medical condition, this age is extended to 71 months.[1])
- **Infants between the ages of 1 and 6 months** who have never received any PCV product should complete a series of PCV13 at 2, 4, 6, and 12 to 15 months—the same time line as the PCV7 series.
- **Children ages 7 to 59 months** who have not been vaccinated with PCV7 or PCV13 previously should receive 1 to 3 doses of PCV13, depending on their age at the time when vaccination begins and whether underlying medical conditions are present (**TABLE 3**).
- **Healthy children ages 24 to 59 months** without previous PCV vaccine should receive 1 dose of PCV13.
- **Children ages 24 to 71 months** without previous PCV vaccine who have a chronic medical condition that increases their risk for pneumococcal disease should receive 2 doses of PCV13, 8 weeks apart.[1]

Recommendations for children at higher risk

Provisional recommendations from ACIP advise that children 2 through 18 years of age at increased risk for invasive pneumococcal disease should also receive 23-valent pneumococcal polysaccharide vaccine (PPSV23). Ideally, the child should have received all of the recommended doses of PCV13 before the physician administers PPSV23, with a minimum interval of at least 8 weeks after the last dose of PCV13.

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PCV13 adds coverage for 6 additional serotypes that now cause a majority of the remaining cases of invasive disease.

TABLE 2

In transition: From PCV7 to PCV13

Infant series			Booster dose	Supplemental PCV13 dose
2 months	**4 months**	**6 months**	**≥12 months***	**14-59 months†**
PCV7	PCV13	PCV13	PCV13	None
PCV7	PCV7	PCV13	PCV13	None
PCV7	PCV7	PCV7	PCV13	None
PCV7	PCV7	PCV7	PCV7	PCV13

*No additional PCV13 doses are indicated for children ages 12-23 months who have received 2 or 3 doses of PCV before age 12 months and at least 1 dose of PCV13 at ≥12 months.

†For children with underlying medical conditions (see **TABLE 3**), a single supplemental PCV13 dose is recommended through age 71 months.

Source: CDC. *MMWR Morb Mortal Wkly Rep*. 2010.[1]

Dosing schedules depend on age, history of previous PCV7 immunization, and the presence of an underlying chronic disease or immunocompromising condition.

TABLE 3

Underlying conditions that place kids at risk for pneumococcal disease

Risk group	Condition
Immunocompetent children	Chronic heart disease* Chronic lung disease† Diabetes mellitus Cerebrospinal fluid leaks Cochlear implant
Children with functional or anatomic asplenia	Sickle cell disease and other hemoglobulinopathies Congenital or acquired asplenia or splenic dysfunction
Children with immunocompromising conditions	HIV infection Chronic renal failure and nephrotic syndrome Diseases associated with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, and Hodgkin's disease; or solid organ transplantation Congenital immunodeficiency‡

*Particularly cyanotic congenital heart disease and cardiac failure.

†Including asthma if treated with prolonged high-dose oral corticosteroids.

‡Includes B- (humoral) or T-lymphocyte deficiency; complement deficiencies, particularly C1, C2, C3, and C4 deficiency; and phagocytic disorders (excluding chronic granulomatous disease).

Source: CDC. *MMWR Morb Mortal Wkly Rep*. 2010.[1]

However, some children will have previously received PPSV23. They should also receive the recommended PCV13 doses. A second dose of PPSV23 is recommended 5 years after the first dose of PPSV23 for children who have sickle cell disease, or functional or anatomic asplenia, human immunodeficiency virus (HIV) infection, or other immunocompromising conditions. No more than 2 PPSV23 doses are recommended.[9]

The ACIP provisional recommendations also say that a single dose of PCV13 may be administered to children ages 6 to 18 years who are at increased risk for IPD because

of sickle cell disease, HIV infection or other immunocompromising condition, cochlear implant, or cerebrospinal fluid leaks, regardless of whether they have previously received PCV7 or PPSV23.[9] This, however, is an off-label recommendation.

The usual contraindications

PCV13 is contraindicated among individuals known to have a severe allergic reaction to any component of PCV13 or PCV7 or to any diphtheria toxoid-containing vaccine, because the pneumococcal antigens are conjugated to a diphtheria carrier protein.[1]

A useful vaccine, with its share of challenges

The pneumococcal conjugate vaccine combats infections such as pneumococcal pneumonia and meningitis, which are potentially serious—even though their incidence is relatively low.

The vaccine's high private-sector cost—reported by the manufacturer to the CDC as $435 for the full, 4-dose series of PCV13—can be a drawback for the family physician trying to keep a full array of vaccine products on hand.[10] Eligible low-income and uninsured children can receive free vaccine under the federal Vaccines for Children Program, and providers who choose to enroll in the program can access free vaccines and may charge for the expense of administering them.[11]

With this hurdle overcome, the remaining challenge for physicians will be to stay on top of the complicated dosing schedule. **JFP**

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