#### CONNECTICUT MEDICAL ASSISTANCE PROGRAM DEPARTMENT OF SOCIAL SERVICES

#### & ACENTRA HEALTH QUARTERLY NEWSLETTER



Connecticut Department of Social Services Making a Difference





#### **Protection Against Pneumococcal Disease**

The bacteria Streptococcus pneumoniae (S.pneumoniae) is a gram-positive anaerobe and a common colonizer of the upper respiratory tract. Up to 65% of children in the United States (US) carry S.pneumoniae and < 10% of adults are carriers.<sup>1,2</sup> Infection is spread predominantly via respiratory droplets and nasal secretions from infected or carrier individuals. Aspirated bacteria can cause noninvasive disease or more serious invasive pneumococcal disease (IPD) - Image 1.2 Sinusitis and otitis media are examples of



noninvasive disease whereas IPD occurs in normally sterile sites. 2,3 Examples of IPD include pneumonia, bacteremia, meningitis, osteomyelitis, and septic arthritis.<sup>2,3</sup> Otitis media and pneumonia are the most common forms of *S.pneumoniae* infection in children and adults, respectively.4 S.pneumoniae is the leading cause of bacterial pneumonia in both children and adults in the US and worldwide and is also a leading cause of bacteremia and meningitis.1,3,5,6,7 Mortality rates from invasive disease caused by S.pneumoniae range from 5-35% based on manifestation, patient age, and comorbid conditions.7 The World Health Organization (WHO) recently named S.pneumoniae as one of the top four priority pathogens for antimicrobial resistance. There is a need to focus on increasing antimicrobial coverage through antibiotic treatment and prevention through vaccination and coverage of pathogenic serotypes.8

There are more than 100 different serotypes, or strains, of S.pneumoniae, and they are differentiated by their capsular polysaccharide structure (CPS). CPS covers or coats the outside of the pneumocontributing factor to the virulence and survival of S.pneumoniae, assisting the bacteria with host colonization and evading the human immune system.8 Only a handful of serotypes cause disease and vary based on age group and geographic location.6,9 For example serotypes 22F and 33F cause the worst illness in children and carry the highest rates of morbidity and antibiotic resistance.<sup>6</sup> Serotype 3 is also problematic in children and continues to be a cause of residual disease.<sup>6</sup>

Serotype 4 is a geographic example which occurs at higher rates in the western US (Alaska, Colorado, Navajo Nation, New Mexico, and Oregon).

While antibiotics are the gold standard for treatment of S.pneumoniae infection, vaccines prevent illness. As a natural immune defense, humans develop antibodies to pneumococcal CPS which is what helped scientists develop vaccines against S.pneumoniae.6,9 Vaccines are used primarily in the young and old, and in patients with risk factors for IPD (Box 1).10,11 There are two categories of pneumococcal vaccines: pneumococcal conjugate vaccines (PCVs) and pneumococcal polysaccharide vaccines (PPSVs). The first vaccine was made available in 1977, PCV14, a conjugate vaccine that covered 14 serotypes of the bacteria.<sup>6</sup> A second vaccine was made available in 1983, PPSV23, a polysaccharide vaccine that is still used today and covers 23 serotypes of the bacteria.<sup>6</sup> Since then, other PCVs have been developed, covering a range of serotypes. Today there are 4 vaccines on the market, three PCVs and one PPSV.<sup>11</sup>

# coccal bacteria and is the most important **Pneumococcal conjugate vaccines** contributing factor to the virulence and **(PCVs)**

PCV15
PCV20
PCV21

Pneumococcal polysaccharide vaccine (PPSV)

PPSV23

The difference between conjugate vaccines and the polysaccharide vaccine is how they create immunity. PPSVs create

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### Box 1.<sup>10,11</sup>

Risk factors for IPD/higher morbidity include older age and chronic medical conditions such as coronary artery disease (CAD), diabetes, malignancy, lung, and kidney disorders.<sup>2</sup> A complete list of risk factors according to the CDC include: Alcoholism: cerebrospinal fluid leak; chronic heart, liver, or lung disease; chronic renal failure; cigarette smoking; cochlear implant; congenital or acquired asplenia; diabetes mellitus; generalized malignancy; HIV; Hodgkin disease; immunodeficiency; iatrogenic immunosuppression; leukemia, lymphoma, or multiple myeloma; nephrotic syndrome; solid organ transplant; or sickle cell disease or other hemoglobinopathies. These are certain risk factors for people aged 19-49 to support the vaccination with PCV21 or PCV20.<sup>4</sup> Other risk factors include: obesity, homelessness, and people who work as welders.

Risk factors for IPD in infants and children include sickle cell disease, HIV, preterm birth.

immunity by producing a T-cell response, without creating B-cell memory.<sup>3,6,8,12</sup>This leads to an ineffective immune response in infants, antibody decline, and loss of protection about 5 years after vaccination in adults.12 Therefore PPSV23 is only recommended for use in adults.13 PCVs produce both a T-cell response and B-cell memory via CPS conjugation to a non-toxic carrier protein leading to an effective immune response in infants and children, and longer lasting immunity in adults.<sup>3,6,8,12</sup> It should be noted that PCV vaccines are contraindicated in patients who are allergic to the diphtheria toxoid due to the conjugation of PCV vaccines to CRM197, a nontoxic genetically altered diphtheria toxin.<sup>10</sup>

The Centers for Disease Control (CDC) recommend pneumococcal vaccination for children < 5 years of age, adults  $\geq$  50 years of age, and adults aged 19-49 with certain risk factors (Box 1).<sup>11</sup>

For children younger than 5 years of age, the CDC recommends administration of a 4-dose PCV series (PCV15 or PCV20), one dose at each of the following ages: 2 months, 4 months, 6 months, 12 through 15 months.<sup>11</sup>

In October 2024, the Advisory Committee on Immunization Practices (ACIP) released a new recommendation for older adults. The previous guidance recommended that patients  $\geq$  65 years of age receive a single dose of a pneumococcal conjugate vaccine (PCV), with recommendations for patients aged 19-64 years of age with risk factors. It is now recommended that all patients  $\geq 50$ **years of age** receive a single dose of a pneumococcal conjugate vaccine (PCV21 or PCV20) regardless of risk factors with recommendations for patients aged 19-49 years of age with risk factors.<sup>10</sup> The decision to lower the recommended age for vaccination was twofold - to increase widespread vaccination rates among 50-64-year-olds, and to decrease disease and mortality rates.<sup>10</sup> Approximately 30-50% of people aged 50-64 have one or more risk factors for developing IPD, however, only 37% are vaccinated compared to 70% of people ≥65 years of age who are vaccinated.<sup>10</sup> PCV21 and PCV20 are considered first line options in adults because more than half of IPD cases in recent years are caused by serotypes covered by those formulations.<sup>10</sup> If an adult patient received PCV15 in the past, vaccination with PPSV23 should be administered to provide full coverage.

When considering the best pneumococcal vaccine option, the CDC has created a

questionnaire to assist patients and health care providers to select the best option. <u>https://www2a.cdc.gov/vaccines/</u> <u>m/pneumo/pneumo.html</u>

Also listed below are caveats associated with the four different vaccines on the market.

#### PCV15 – Vaxneuvance<sup>14,15</sup>

Vaxneuvance is a 15 valent conjugate vaccine approved for use in pediatric and adult patients to prevent invasive disease caused by S.pneumoniae serotypes listed in Image 2.10 For children younger than 5 years of age, the CDC recommends administration of a 4-dose PCV series, with either PCV15 or PCV20. If the series was started with a lower valency vaccine, PCV15 can be used to complete the series. For adults, PCV15 can be administered first, followed by PPSV23 for full coverage, however this option is not considered first line. PCV15 covers all serotypes contained in the lower valency PCV13 with the addition of 22F and 33F, two serotypes that cause severe illness in children. PCV15 has enhanced immunogenicity against serotype 3 and provides coverage in geographic areas where  $\geq$ 30% of pneumococcal disease is caused by serotype 4. Serotype 4 is more common in the western US, occurring more frequently in people < 65 years of age who have a chronic condition such as homelessness, cigarette smoking, injection drug use, chronic lung disease, and/



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#### PCV20 - Prevnar 2010,16

Prevnar 20 is a 20 valent pneumococcal conjugate vaccine approved for use in pediatric and adult patients to prevent invasive disease caused by S.pneumoniae serotypes listed in Image 2.10 PCV20 covers all serotypes contained in the lower valency PCV13 with the addition of 8, 10A, 11A, 12F, 15B, 22F, and 33F. For children younger than 5 years of age, the CDC recommends administration of a 4-dose PCV series, with either PCV15 or PCV20. If the series was started with a lower valency vaccine, PCV20 can be used to complete the series. For adults, first line pneumococcal vaccination is a single dose of either PCV21 or PCV 20. PCV20 is preferred over PCV21 in adults who reside in geographic areas where  $\geq 30\%$  of pneumococcal disease is caused by serotype 4 (western US), especially those who have a chronic condition such as homelessness, cigarette smoking, injection drug use, chronic lung disease, and/or alcoholism.6 Prevnar 20 protects against specific serotypes that cause about 60% of IPD.

#### PCV21 – Capvaxive<sup>10,17</sup>

Capvaxive is a 21 valent pneumococcal conjugate vaccine approved for use in adult patients to prevent invasive disease caused by serotypes listed in Image 2.10 Recently brought to market this vaccine covers the most pneumococcal strains compared to all other PCVs. While it does contain 10 of the same serotypes contained in PCV20, there are 11 additional serotypes, 8 of which are exclusive to PCV21, protecting against specific serotypes that cause 80% of IPD cases. A single dose of PCV21, or PCV20, is the first line recommendation for vaccinating against pneumococcal disease in all adults.

#### PPSV23 – Pneumovax 23<sup>18</sup>

Pneumovax 23 is a 23 valent polysaccharide vaccine approved for use in adults to prevent pneumococcal disease caused by serotypes listed in Image 2.10 PPSV23 should be used in adults who previously received vaccination with PCV15 to obtain full coverage.<sup>10</sup> PPSV23 is not recommended for use in children < 2 years of age due to inability to create immunologic memory.8

Vaccines are an important tool in preventing infectious disease. When infants and children are vaccinated against pneumococcal disease, they create indirect protection for the community while providing direct protection for themselves.<sup>10</sup> Up to 65% of children in the US are carriers of S.pneumoniae making pediatric vaccination important for controlling community spread. Vaccinating adults is also important, especially those with risk factors for severe disease and patients who are  $\geq$  50 years of age because the risk of complications and mortality associated with IPD increases with age. When counseling patients about pneumococcal vaccination, health care providers should address topics that impact vaccine acceptance such as age, gender, racial disparities, socioeconomic status, education, income, and health insurance status.10,19 Vaccine utilization and acceptance are crucial for protecting individual patients and entire communities against preventable disease.

Dagan R, Danino D, Weinberger DM. The Pneumococcus-Respiratory Virus Connection—Unexpected Lessons From the COVID-19 Pandem-ic. JAMA Netw Open. 2022;5(6):e2218966.
 Weiser JN, Ferreira DM, Paton JC. Streptococcus pneumoniae: trans-

mission, colonization and invasion. Nat Rev Microbiol. 2018 Jun;16 (6):355–367.

Kobayashi M, Pilishvili T, Farrar JL, et al. Pneumococcal vaccine for adults aged  $\geq$  19 years: recommendations of the advisory committee on immunization practices – United States, 2023. *MMWR Morb Mortal Wkly Rep.* 2023;72(3):1–40.

## 4. <u>https://www.cdc.gov/pneumococcal/hcp/clinical-signs/</u> index.html#:~:text=The%20incubation%20period%20of%

20pneumococcal.Cough%20productive%20of%20mucopurulent% 20sputum 5, GBD 2016 Lower Respiratory Infections Collaborators. Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory infections in 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Infect Dis.* 2018;18(11):1191-210.

2018;18(11):1191-210.
6. Chapman TJ, Olarte L, Dbaibo G, et al. PCV15, a pneumococcal conjugate vaccine, for the prevention of invasive pneumococcal disease in infants and children. *Expert Rev Vaccines*. 2024;23(1):137-147.
7. Martens P, Worm SW, Lundgren B, et al. Serotype-specific mortality from invasive Streptococcus pneumoniae disease revisited. *BMC Infect* DV: 2004 Inter 204:201.

Marking Markovski and State Streamonia Cascas Forsica. Birle Infect Dis. 2004 Jun 30;4:21.
 Micoli F, Romano MR, Carboni F, et al. *Glycoconjugate Journal*. 2023;40:135-148.
 Akkoyunlu M. State of pneumococcal vaccine immunity. *Human*

 Akkoyunlu M. State of pneumococcal vaccine immunity. *ruman Vaccines & Immunohergentics*, 2024; 20(1): 1-6.
 Kobayashi M, Leidner AJ, Gierke R, et al. Expanded recommendations for use of pneumococcal conjugate vaccines among adults aged ≥ 50 years. Recommendations of the advisory committee on immunization practices – United States, 2024. *MMWR Morb Mortal Wkly Rep.* 2025;74 (1):1-8.

https://www.cdc.gov/pneumococcal/hcp/vaccine-recommendations/

1. Index.html 12. Nakashima K, Fukushima W. Strategies for pneumococcal vaccination in older adults in the coming era. *Human Vaccines & Immunotherapeutics*. 2024; 20(1).

13. Golos M, Eliakim-Raz N, Stern A, et al. Conjugated pneumococcal vaccine versus polysaccharide pneumococcal vaccine for prevention of pneumonia and invasive pneumococcal disease in immunocompetent and immunocompromised adults and children. Cochrane Database Syst Rev. 2019 Feb 20:2019(2):CD012306

2019 Feb 20;2019(2):CD012306. 14. Kobayashi M, Farrar JL, Gierke R, et al. Pneumococcal conjugate vaccine among U.S. children: updated recommendations of the advisory committee on immunization practices – United States, 2022. MMWR Morb Mortal Wkly Rep. 2022;71(37):1174–1181. 15. Vaxneuvance [package insert]. Rahway, NJ: Merck Sharp & Dohme LLC; May 2024.

16. Prevnar 20 [package insert]. Philadelphia, PA: Wyeth Pharm. LLC;

April 2023.

April 2023.
17. Capvaxive [package insert]. Rahway, NJ: Merck Sharp & Dohme LLC; June 2024.
18. Pneumovax 23 [package insert]. Rahway, NJ: Merck Sharp & Dohme

Hormonovak 25 (package insert), Kairway, 10. Welck binap & Boline LLC; April 2023.
 Chitaree W, Buawangpong N, Yotruangsri T, et al. J Primary Care & Community Health. 2024;15: 1–10.

20. Prepare to Give More Adults a Pneumococcal Vaccine, Pharmacist's Letter December 2024

https://www.cdc.gov/acip/meetings/presentation-slides-october-23-24-2024.html

22. Kobayashi M, Leidner AJ, Gierke R, et al. Use of 21-valent pneumo-Kodydain W, Jeduier AB, Oreke K, et al. Ose of 219 which pheambo-coccal conjugate vaccine among U.S. adults: updated recommendations of the advisory committee on immunization practices – United States, 2024. MMWR Morb Mortal Wkly Rep. 2024;73(36):793–798.

## Image 2 Serotypes\*,<sup>†</sup> included in pneumococcal vaccines currently recommended for adults — United States, 2024

Included in vaccine	Not included in vaccine
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	Serotype																															
Vaccine	1	3	4	5	6A	6B	7F	9V	14	18C	19A	19F	23F	22F	33F	8	10A	11A	12F	15B	2	9N	17F	20	15A	15C	16F	23A	23B	24F	31	35B
PCV21																																
PPSV23																																
PCV20																																$\square$
PCV15																																

Abbreviations: PCV = pneumococcal conjugate vaccine; PCV15 = 15-valent PCV; PCV20 = 20-valent PCV; PCV21 = 21-valent PCV; PSV23 = 23-valent pneumococcal polysaccharide vaccine.

\* PCV21 is approved for the prevention of invasive pneumococcal disease caused by serotype 15B based upon prespecified criteria for the proportion of participants with fourfold or more rise in opsonophagocytic activity responses. https://www.fda.gov/media/179426/download?attachment

<sup>†</sup> PCV21 contains serotype 20A.