REVIEW

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Pneumococcal Vaccine and Patients with Pulmonary Diseases

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ABSTRACT

Chronic pulmonary diseases are chronic diseases that affect the airways and lung parenchyma. Examples of common chronic pulmonary diseases include asthma, bronchiectasis, chronic obstructive lung disease, lung fibrosis, sarcoidosis, pulmonary hypertension, and cor pulmonale. Pulmonary infection is considered a significant cause of mortality in patients with chronic pulmonary diseases. *Streptococcus pneumoniae* is the leading isolated bacteria from adult patients with community-acquired pneumonia, the most common pulmonary infection. Vaccination against *S. pneumoniae* can reduce the risk of mortality, especially from more serious infections in both immunocompetent and immunocompromised patients. Patients with chronic pulmonary diseases who take steroids or immunomodulating therapy (eg, methotrexate, anti-tumor necrosis factor inhibitors), or who have concurrent sickle cell disease or other hemoglobinopathies, primary immunodeficiency disorders, human immunodeficiency virus infection/acquired immunodeficiency syndrome, nephrotic syndrome, and hematologic or solid malignancies should be vaccinated with both 13-valent pneumococcal conjugate vaccine and the pneumococcal polysaccharide vaccine 23-valent.
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KEYWORDS: Invasive pneumococcal disease; Pneumococcal; Pneumonia; Pulmonary; *Streptococcus pneumoniae*; Vaccination

Pneumococcal disease describes many infectious processes caused by *Streptococcus pneumoniae*, including meningitis, pneumonia, bacteremia, bronchitis, sinusitis, and otitis media. Pneumonia is the most common presentation of pneumococcal disease in adults. In the United States, pneumococcal pneumonia is responsible for 30% of adult community-acquired pneumonia cases and 400,000 hospitalizations annually.[1] Pneumococcal pneumonia represents a common complication of many disease processes.

Chronic pulmonary diseases, as mainly defined by asthma, bronchiectasis, chronic obstructive lung disease, interstitial lung disease, sarcoidosis, pulmonary hypertension, and cor pulmonale, represent the third leading cause of death and account for more than 140,000 deaths in 2011.[2] Pneumococcal pneumonia is a frequent complication in patients with chronic pulmonary disease. Mortality is a frequent outcome in these cases, regardless of whether the patients have developed invasive disease.[3] For this reason, the management of pneumonia exists as a major contribution to the economic burden of chronic respiratory diseases. The cost of pneumonia treatment for Medicare beneficiaries alone was reported in excess of $13 billion in 2008.[4]

STREPTOCOCCUS PNEUMONIAE SEROTYPES

S. pneumoniae is classified on the basis of the presence of capsular polysaccharides on the organism. More than 90 different serotypes of *S. pneumonia* have been identified.[5] Each organism has been classified into 46 distinctive subgroups based on immunologic similarities.[6] Although invasive pneumococcal disease may occur with all serotypes, approximately 60% of cases are caused by the same 23 serotypes.[7,8] Furthermore, certain serotypes seem to be more commonly isolated from specific organ systems. For instance, serotypes 1 and 3 are isolated more frequently in

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pneumonia, and serotypes 6, 10, and 23 are isolated in meningitis regularly.[9,10] Regional variations also exist in *S. pneumoniae* serotype disease cause. A recently published meta-analysis showed that isolated serotypes from young children with invasive pneumococcal disease varied significantly in respect to geography. In addition, serotype 14 was the most common isolate from all over the world, and serotypes 1, 5, 6A, 6B, 14, 19F, and 23F were isolated in 50% of individuals.[11,12]

CLINICAL SIGNIFICANCE

- Immunocompromised patients have a poor response to pneumococcal polysaccharide vaccine 23-valent.
- 13-Valent pneumococcal conjugate vaccine is a safe and effective strategy to prevent invasive pneumococcal disease.
- Patients with chronic pulmonary diseases who take steroids or immunomodulating therapy or who have some certain risk factors should be vaccinated with both 13-valent pneumococcal conjugate vaccine and the pneumococcal polysaccharide vaccine 23-valent.

PNEUMOCOCCAL DISEASE

Pneumococcal disease can manifest in numerous body systems. Although *S. pneumoniae* is the leading isolated bacteria from adult patients with community-acquired pneumonia globally, pneumococcal disease can present in many other forms.[13-15]

Acute otitis media is one of the most commonly diagnosed diseases in children aged less than 5 years in the United States.[16] *S. pneumoniae* is the most common bacterial cause of acute otitis media.[17] *S. pneumoniae* is the leading bacterial cause of meningitis, and the mortality rate is especially high.[18] Prompt antibiotic therapy is indicated for pneumococcal infection. However, increasing drug-resistant strains and lack of development of new antibiotics are main concerns in the battle against these bacterial infections.[12]

Generally, pneumococcal disease is categorized as invasive or noninvasive pneumococcal disease. Invasive pneumococcal disease is defined as a serious condition with major organ involvement or bacteremia, in which *S. pneumoniae* isolates from normally sterile biofluids, such as blood, cerebrospinal fluids, pleural fluid, and peritoneal fluid. The case fatality of invasive pneumococcal disease is reported to be at least 10%. However, it is higher in elderly and immunocompromised patients.[19] An estimated 5000 adults died of invasive *S. pneumoniae* infections nationwide in 2009.[20] Noninvasive pneumococcal disease addresses less serious conditions, such as otitis media and nonbacteremic pneumococcal pneumonia.[21,22]

CONDITIONS PREDISPOSING TO PNEUMOCOCCAL DISEASE

Pneumococcal infection is common in patients with immunocompromising conditions,[23] central nervous system and spleen anatomic abnormalities,[24] hemoglobinopathies,[25] chronic pulmonary diseases,[26] heart failure,[27] and chronic kidney disease[28]; in patients who are smokers[29]; and in elderly patients.[30] Patients who have a low antibody level and ineffective serum opsonizing against *S. pneumonia* also are at a higher risk.[31]

PNEUMOCOCCAL VACCINES

Pneumococcal vaccination targeting common serotypes is the current recommended standard of prevention. Pneumococcal vaccines work by stimulating the humoral immune system that facilitates anticapsular antibody. The first large trial assessing the efficacy of pneumococcal vaccine goes back to 1911 in South Africa.[32] The first advanced pneumococcal vaccine was approved in the US by the Food and Drug Administration (FDA) in 1977. This vaccine included coverage of 14 serotypes. Invasive pneumococcal disease in immunocompetent children and adults has been declining after the introduction of pneumococcal vaccines in the United States. The rate of the disease declined 32% in the 20- to 39-year-old group, 8% for the 40- to 64-year-old group, and 18% for the ≥65 years group.[33] Although vaccines are the only current proven method for acquired pneumococcal resistance, emerging research indicates that cell-mediated immunity may also be achieved by CD4+ T cells regardless of antibody status or capsular type as observed in laboratory mice.[34]

PNEUMOCOCCAL POLYSACCHARIDE VACCINE 23-VALENT VACCINE

In 1983, additional serotypes were added to the original pneumococcal vaccine to form the pneumococcal polysaccharide vaccine 23-valent.[35] Pneumococcal polysaccharide vaccine 23-valent covers serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, and 33F (**Table 1**).[36,37]

In a study evaluating pneumococcal polysaccharide vaccine 23-valent against invasive pneumococcal disease, Butler et al[38] demonstrated an efficacy of 75% for the immunocompetent elderly (aged >65 years), 84% for patients with diabetes mellitus, 77% for patients with anatomic asplenia, and 65% for patients with chronic pulmonary disease.[38] The Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices recommended pneumococcal polysaccharide vaccine 23-valent immunization for all individuals who are in significant risk of invasive pneumococcal disease, such as patients with diabetes mellitus, chronic respiratory diseases (eg, chronic obstructive lung disease, asthma, and bronchiectasis), congestive heart failure, chronic renal failure, and chronic liver disease.[20] **Table 2** shows the current