Streptococcus pneumoniae is still a significant cause of infection among older adults and is associated with increased morbidity and mortality among this segment of the population. Changes occur with aging that affect all functions of the body, including the immune system.
Background

*S. pneumoniae* was first isolated and grown in 1881 by Louis Pasteur.1 Around the same time, it was found to be a major cause of pneumonia. In 1884, a Gram stain technique was used to differentiate *S. pneumoniae* from other microorganisms causing pneumonia. In 1902, Fred Neufeld, a German microbiologist, demonstrated pneumococcal bacterial capsule swelling (quelling) by treating the microorganism with type-specific anti-sera. In 1904, Neufeld and Rimpau demonstrated opsonization of *S. pneumoniae* using antipneumococcal antibodies. In 1913, Lister showed the development of type-specific antibodies against different strains of *S. pneumoniae*. These discoveries paved the way toward development of a pneumococcal vaccine in the early part of the 20th century.

Attempts to control pneumococcal infection by vaccination were undertaken initially in 1911, and the first pneumococcal vaccine was made from killed pneumococcal cells.2 In 1930, Thomas Francis Jr., showed capsular polysaccharide to be immunogenic in humans.1 Later on, purified polysaccharides from the capsule of the pneumococcal bacteria were used as a vaccine to induce immune response in the body. The discovery of penicillin and other effective antibiotics, however, diverted the attention of health care providers from the use of vaccine for some time.2 But during the last few decades, the way pneumococcal vaccine is developed and used has changed significantly, thanks to the better understanding of the human immune system and to advancement in technology. Currently, 2 different types of pneumococcal vaccines—polysaccharide and conjugate vaccines—are employed for the prevention of pneumococcal disease. Polysaccharide vaccines contain purified polysaccharides from the bacterial capsule as antigen,

Both innate and adaptive arms of the immune system are affected by aging. Older subjects are infected with *S. pneumoniae* more than young adults because of altered immune response and the presence of comorbidities. The dollar amounts we spend for the treatment of pneumococcal infection will be enormously high. There is no doubt that the discovery and use of antibiotics have revolutionized the way we provide care for bacterial infections in this modern era, but emerging antibiotic resistance poses a serious challenge for our health care system and the care of our older patients. Prevention is always a better strategy. The pneumococcal vaccine works in the aged, at least for the prevention of invasive pneumococcal diseases (IPDs). It prevents infection, saves money, and decreases hospitalization and duration of hospital stay. Most importantly, the pneumococcal vaccine decreases morbidity and mortality rates.
have shown that aging is associated with alterations in both innate and adaptive arms of the immune system.\textsuperscript{10,11} The presence of comorbidities such as smoking, diabetes mellitus, and chronic cardiopulmonary diseases makes older people more vulnerable to pneumococcal infection.\textsuperscript{5,6} Emerging antibiotic resistance, along with an increasing aging population in the nation, is another challenge our health care system faces while caring for older patients with pneumococcal infection.\textsuperscript{12}

Immunization is 1 of the most important public health measures toward preventing infection.\textsuperscript{13,14} Disease prevention with immunization is effective and less costly on the public and on our health care system than is antibiotic therapy and hospitalization as a means of eliminating or reducing the burden of infectious diseases for which a vaccine has been developed.

Figure 1. Incidence of IPD is higher among younger and those individuals who are aged $\geq 65$ years. Mortality from IPD is higher among those who are aged $\geq 65$ years than among younger individuals.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{Incidence of IPD is higher among younger and those individuals who are aged $\geq 65$ years. Mortality from IPD is higher among those who are aged $\geq 65$ years than among younger individuals.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{Incidence of IPD is higher among younger and those individuals who are aged $\geq 65$ years. Mortality from IPD is higher among those who are aged $\geq 65$ years than among younger individuals.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure3.png}
\caption{Incidence of IPD is higher among younger and those individuals who are aged $\geq 65$ years. Mortality from IPD is higher among those who are aged $\geq 65$ years than among younger individuals.}
\end{figure}

Epidemiological data

\textit{S. pneumoniae} is still a significant cause of infections among infants, younger children, and older adults. It is a major health care concern in the United States (Figure 1) and worldwide.\textsuperscript{3,4} It also affects the health of millions who have other chronic medical problems that put them at increased risk of being infected with this microorganism.\textsuperscript{5,6} Death from infection with \textit{S. pneumoniae}, particularly from IPD, is more common than that from any other vaccine-preventable disease in the United States.\textsuperscript{7} In the year 2011, an estimated 36,850 cases of and 4250 deaths from IPD occurred in the United States. More than half of these cases occurred in adults who had an indication for pneumococcal vaccine.\textsuperscript{8} According to the World Health Organization (WHO) estimates, pneumococcal infection causes approximately 1.7 million deaths annually in the world.\textsuperscript{4}

Streptococcal pneumonia infection is more common and more serious among older adults than among their younger adult counterparts.\textsuperscript{3,4} Care for pneumococcal infection in older adults is expensive and is a significant burden on our health care system. According to some estimates, in 2004 there were 242,000 hospitalizations for pneumococcal pneumonia, with a total of 1.4 million hospital days; 194,000 emergency department visits; and 374,000 outpatient visits among those who were aged 65 years or older. The direct cost for care of pneumococcal infection in this age group was $1.8 billion.\textsuperscript{9}

Reasons for greater vulnerability to pneumococcal infection among older adults are many. Age and comorbidities are some of the most important factors. Aging reduces physiologic reserve, functional capacity, and the capability of the body to fight infections. Studies while conjugate vaccines contain an additional immunogenic nonpneumococcal protein conjugated to individual pneumococcal polysaccharides to increase immunogenicity of the vaccine in children, as purified polysaccharides alone were found to be less immunogenic in children aged younger than 2 years.

Streptococcal pneumonia infection is more common and more serious among older adults than among their younger adult counterparts.
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An infection. This translocation of the microorganism in itself depends on many factors, including mucosal integrity, the patient’s medical and functional status, body immune response, and bacterial virulence. S. pneumoniae is an extracellular bacterium (stays outside the cell of the host) that can be cleared by the immune system at either the colonization or the infection site. Both innate and acquired immunity are used to clear the microorganism from the 2 sites. All components of the 2 arms of the immune system (including macrophages, neutrophils, humeral immunity, and T cell immunity) are involved in the process of clearing S. pneumoniae. Opsonophagocytosis is considered 1 of the most important mechanisms of phagocytic clearance of S. pneumoniae, both at the mucosal surfaces and within blood and tissues. There is, however, no evidence that the current pneumococcal vaccine can trigger a full immune response that incorporates all the above elements in clearing pneumococcal organisms from the body or site of infection.

Vaccines have been in use for more than 30 years for the prevention of streptococcal pneumonia infection.

(41%) than among those who had some college education. Pneumococcal vaccine has now been in use for the past 3 decades. Its use has been recommended by WHO, the Centers for Disease Control and Prevention (CDC), and other agencies in the United States. According to a CDC report, among adults aged 65 years and older, the incidence of IPD has decreased 33.9% between 1997 and 2008, from 62 to 41 new cases per 100,000 population, exceeding the Healthy People 2010 target of 42 per 100,000. At present, 1 of the objectives (Objective IID-4) of Healthy People 2020 is immunization with pneumococcal vaccine to further reduce the incidence of IPD.

Body immune response and vaccines’ efficacy

Both types of pneumococcal infections, invasive (pneumonia, bacteremia, meningitis) and noninvasive (sinusitis, otitis media, bronchitis), are preceded by nasopharyngeal colonization by the bacteria. The mode of transmission from person to person is via mucosal secretions and airborne droplets.

After colonizing the nasopharynx, the microorganism migrates to the potential site of infection. It is the translocation of the bacteria to the potential site of infection that initiates
At present, there are 2 types of pneumococcal vaccines licensed and marketed in the United States. PCV13 (pneumococcal conjugate vaccine) is a conjugate 13-valent vaccine that has been available in the United States since 2009. It contains antigenic capsular polysaccharides from 13 strains of *S. pneumoniae* that are responsible for most of the serious pneumococcal infections in children. These polysaccharides are conjugated with a protein to increase the vaccine’s immunogenicity in children. It is used as part of childhood vaccination in this country and worldwide (*Table 1*).

The other pneumococcal vaccine is PPV23 (pneumococcal polysaccharides vaccine), which is a 23-valent vaccine and has been available since 1983. It contains antigenic capsular polysaccharides from the 23 strains of *S. pneumoniae* that are responsible for most of the serious pneumococcal infections in adults. Its use is recommended in adults who are aged 65 years and older and in those who are younger (≥2-64 years old) who have a comorbid condition that puts them at increased risk of being infected with *S. pneumoniae* (*Table 1*). These vaccines induce formation of serotype-specific antibody in the body that could provide antibody-mediated protection against the offending organism.

Because IPD is associated with increased morbidity and mortality, the PCV13 and PPV23 vaccines are each designed with the intent to prevent IPD in both children and adults. Primary PCV13 (or its predecessors) has been used to prevent IPD and some of the noninvasive pneumococcal infections (otitis media) in children and adults with some chronic conditions (*Table 1*). Recent studies have shown that the incidence of IPD among older individuals has decreased in areas where pneumococcal conjugate vaccine has been introduced to younger children. This reduction is, however, more prominent among healthy older adults. It has been concluded that this decrease in the incidence of IPD among older adults is most probably secondary to a decrease

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### Table 1. Recommendations for PCV13 and PPV23

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Indication</th>
<th>Booster</th>
<th>Indication</th>
<th>Booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Children aged 2-71 mo*</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes^b</td>
</tr>
<tr>
<td>2. Children aged 6-18 y and adults aged 19-64 y with 1 or more chronic conditions</td>
<td>No</td>
<td>NA</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Chronic cardiovascular disease (including CHF and cardiomyopathies, but not HTN); COPD, emphysema, and asthma^c; diabetes mellitus, alcoholism, chronic liver disease (including cirrhosis), and smoking^d</td>
<td>No</td>
<td>NA</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Cerebrospinal fluid leaks, cochlear implants</td>
<td>Yes</td>
<td>1 dose</td>
<td>Yes</td>
<td>1 dose</td>
</tr>
<tr>
<td>Sickle cell disease and other hemoglobinopathies, congenital or acquired asplenia, congenital or acquired immunodeficiency, HIV, chronic renal failure, nephrotic syndrome, leukemia, lymphoma, Hodgkin disease, generalized malignancy, iatrogenic immunosuppression, solid organ transplant, and multiple myeloma</td>
<td>Yes</td>
<td>1 dose</td>
<td>Yes</td>
<td>1 dose</td>
</tr>
<tr>
<td>3. Adults aged 50-65 y with or without chronic conditions</td>
<td>Approved by FDA, but not recommended by ACIP^a</td>
<td>No</td>
<td>Approved by FDA, but not recommended by ACIP^a</td>
<td>—</td>
</tr>
<tr>
<td>4. Adults aged ≥65 y with or without chronic conditions</td>
<td>Approved by FDA, but not recommended by ACIP^a</td>
<td>No</td>
<td>Yes^e</td>
<td>1 dose</td>
</tr>
</tbody>
</table>

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*a* Childhood immunization schedule depends on the month started, vaccination status, and child’s condition.

*b* PPV23 booster dose should be given age ≥5 y after the first PPV23 dose and age ≥8 wk after the first PCV13 dose.

*c* Asthma and smoking are indications for PPV23 vaccination in age group 19-64 y.

*d* PCV13 should be given at least 1 y after PPV23 administration in adults.

*e* All adults aged ≥65 y should receive a dose of PPV23, regardless of previous history of vaccination with pneumococcal vaccine.

**Abbreviations:** ACIP, Advisory Committee on Immunization Practices; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; HTN, hypertension; IPD, invasive pneumococcal disease; NA, not applicable.

**Source:** Centers for Disease Control and Prevention. Available at: http://www.cdc.gov/vaccines/vpd-vac/pneumo/vac-PCV13-adults.htm

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administration of PPV23 and improved survival, decreased chance of respiratory failure or other complications, and decreased length of hospital stay among adult patients with community-acquired pneumonia who are aged 65 years and older.\textsuperscript{14,15,27} Still other studies cannot provide clear evidence to support vaccine efficacy to protect older individuals against noninvasive pneumococcal disease and pneumonia. Although the clinical effectiveness of PPV23 remains a topic of controversy, available data support the use of this vaccine to prevent IPD in older and high-risk groups.\textsuperscript{14,15,26,27} There is consensus among various organizations (WHO, CDC, and other health care organizations) with regard to the use of PPV23 in adults aged 65 years and older and in high-risk groups for prevention of IPD.\textsuperscript{15,27}

**Final notes**

Mortality from IPD is high among older adults. Approximately 1 of 10 older individuals with IPD dies of the disease.\textsuperscript{15,26} PPV23 vaccine is approximately 56% to 75% efficacious for the prevention of IPD caused by vaccine serotype \textit{S pneumoniae}.\textsuperscript{27,28} According to some studies, it also has a desirable effect on the severity of the disease and length of hospitalization.\textsuperscript{4} Data submitted to the FDA for the approval of PCV13 for those who are aged 50 years and older show a better antibody response in this age group. Consequently, a question arises: Is the conjugate vaccine better than the nonconjugate one in terms of clinical outcome? We do not have an answer to that question yet. Ongoing trials will help us answer that question. If the conjugate vaccine is found to be superior to the nonconjugate one, will it change the way pneumococcal vaccine is manufactured for older adults?

Although controversy exists, vaccination of older adults with PPV23, for now, is in the best interest of this age group, as recommended by ACIP and other health organizations, nationally and internationally. Mortality from IPD is high (10%) among this age group. We have supporting data that this age group benefits from immunization with pneumococcal vaccine.\textsuperscript{14,15,26,27}

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**Table 2. Adults reporting receiving pneumococcal vaccination, ever, in 2010 and 2011 compared with Healthy People 2020 objectives, %**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>2010</th>
<th>2011</th>
<th>Healthy People 2020, objective</th>
</tr>
</thead>
<tbody>
<tr>
<td>â‰¥65 y, healthy</td>
<td>59.7</td>
<td>62.3</td>
<td>90</td>
</tr>
<tr>
<td>19-64 y, high risk</td>
<td>18.5</td>
<td>20.1</td>
<td>60</td>
</tr>
<tr>
<td>&gt;18 y, long-term care or nursing home</td>
<td>NA</td>
<td>NA</td>
<td>90</td>
</tr>
</tbody>
</table>

**Sources:**


On the basis of the data available, the author believes that older-aged people would benefit from pneumococcal vaccination for prevention of IPD. According to CDC, ACIP, and WHO recommendations, adults who are aged 65 years and older should get vaccinated with PPV23 once if there is no contraindication, such as allergy (Table 1). No booster vaccination is recommended for persons aged 65 years and older. Individuals who are between ages 2 and 64 years and who have comorbid conditions that put them at increased risk for pneumococcal infections may get the PPV23 vaccine 1 to 2 times (Table 1). PCV13 has been approved by the FDA for people who are aged 50 years and older, but it has not yet been recommended by ACIP, for lack of supporting data of its clinical effectiveness; data do support its effectiveness in terms of antibody response (Table 1).

References


Abdul Elahi, MD, MPH, obtained his medical degree from Sindh Medical College, Karachi, Pakistan, in 1993. He completed his residency in internal medicine in 2004 and his fellowship in geriatrics in 2005 at Maimonides Medical Center, Brooklyn, NY. Since 2005, Dr Elahi has served as faculty at the Rowan University School of Osteopathic Medicine, in the New Jersey Institute of Successful Aging. He can be reached at elahiaw@rowan.edu.