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Vaccine-Preventable Infectious Respiratory Diseases in the Elderly

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1. Introduction

Many infections occur more frequently in the elderly and are often associated with morbidity and mortality. Pneumonia, particularly due to *Streptococcus pnuemoniae*, is the most frequent cause of death in geriatric patients. After suffering influenza, there is a problem in that the elderly tend to get pneumonia as an influenza-related disease. Therefore, annual immunization against influenza and pneumococcal vaccines at the age of 65 years are recommended for all adults who are 65 years old and older [(1)]. In this review, we address whether the protective efficacy of the influenza vaccine and 23-valent pneumococcal polysaccharide vaccine (PPV23) in the elderly with and without chronic obstructive pulmonary disease can be shown among recent epidemiological studies.

2. Important

Routine annual influenza vaccination is recommended for all persons aged 6 months and above [(1,2).] The elderly are considered a high risk group, because the risks for complications, hospitalizations, and deaths are higher among adults aged 65 years and older, in spite of rates of infection from seasonal influenza being highest among children. It should be considered that the elderly with poor physical and nutritional status tended to respond poorly to the influenza vaccination.

In addition to annual influenza vaccination, all persons should be vaccinated with PPV23 at age 65 years to prevent invasive pulmonary diseases in all-cause pneumonia or mortality [(3)]. Even though it is said the immune response of the elderly is likely to be declined, almost all persons older than 65 years indicate antibody elevations above clinical effective response after vaccination of influenza and/or PPV23. The introduction of the 7-valent pneumococcal conjugate vaccine (PCV7) in children may alter the vaccine-preventable disease burden in older adults and, correspondingly, the potential magnitude of the benefit of PPV23[(4)].

3. Information

3.1 Influenza

The elderly have been considered the priority group for influenza vaccination, but their influenza vaccine-induced antibodies were believed to decline more rapidly than young

adults. Song et al. evaluated long-term immunogenicity of the influenza vaccine among the elderly [5]. Serum hemagglutinin inhibition (HAI) titers were determined at pre- and post-vaccination periods. Of the 1,018 subjects, 716 (70.3%) were followed up during a 12-month period. Seroprotection rates at 4 weeks post-vaccination ranged from 70.1% to 90.3% depending on the age group and influenza vaccine virus strain. At 6 months post-vaccination, seroprotection rates for all three strains had declined significantly in adults 65 years old or older ($P<0.01$) as compared to young adults.

Hara et al. also assessed the immune response and serum nutritional status of 153 elderly residents of nursing homes (mean age 84.4 years) to the influenza vaccine [6]. Post-vaccination of HAI titers to A/H1N1 and B were low compared to young adults. However, seroconversion rates, which indicated greater than or equal to a fourfold rise for A/H1N1 and A/H3N2, were unexpectedly high among the elderly. Among all subjects, lower age and higher serum concentrations of total protein, albumin, Vitamin E and folate were associated with an intact immune response, e.g., post-vaccination HAI titers showed greater than 40 for at least one vaccine strain. In an age-adjusted analysis limited to the elderly, only Vitamin E showed a significant association with the immune response. These results suggested that Vitamin E may play an important role in maintaining the immune response, especially among the elderly.

The other publication by Sagawa et al. has considered physical and nutritional factors [7]. Pre- and post-vaccination HAI titers were determined for 203 individuals aged 65 years or older residing in a nursing home. For the assessment of physical and nutritional status, information was retrieved from care records. The immune response to the vaccination was assessed as good in 122 subjects based on a fourfold rise or more in HAI titer after vaccination for at least one of three vaccine strains. In a univariate logistic regression analysis with poor versus good immune response, factors found to be significantly associated with a poor immune response were disability, a combination of body mass index (BMI) less than 18.5 and body weight loss in 6 months or 5% or more, mid-upper-arm circumference of less than 80%, arm muscle circumference of less than 80% and total protein of less than 6.5 g/dL (Table 1). Physical and nutritional indicators might be useful in identifying individuals who are unlikely to have a good immune response to the influenza vaccination. In a multivariate analysis, the association remained significant for a low level of daily activities and a combination of BMI less than 18.5 and body weight loss in 6 months of 5% or more. Elderly individuals with poor physical and nutritional status tended to respond poorly to the influenza vaccination compared to elderly with good status. A low level of daily activities and a combination of being underweight and having had recent body weight loss are good indicators of a poor immune response.

According to the review by Skowronski DM[8], seroprotection rates of 70%-100% were maintained not just at 4 months but also at 5 months and even at >6 months, for the A/H3N2 and A/H1N1 vaccine components. Seroprotection rates appeared less consistent for the B vaccine component, throughout the postimmunization period. Seroconversion appears to vary substantially and inversely with preimmunization titers but not with age. The historic concern that the influenza vaccine-induced antibody response in the elderly declines more rapidly and below seroprotective levels within 4 months of immunization should be reconsidered.

3.2 Pneumococcal pneumonia

Bacteremic pneumonia is the most common cause of invasive pneumococcal disease (IPD), accounting for 90% of all cases [9]. There are over 90 different serotypes of *S. pneumoniae,* some are highly invasive whereas others rarely cause disease. Although there is variation in the serotype distribution between age groups and across different geographical populations, mortality associated with pneumococcal pneumonia in adults has remained unchanged at 25% of all pneumonia deaths over the past 40 years [10].

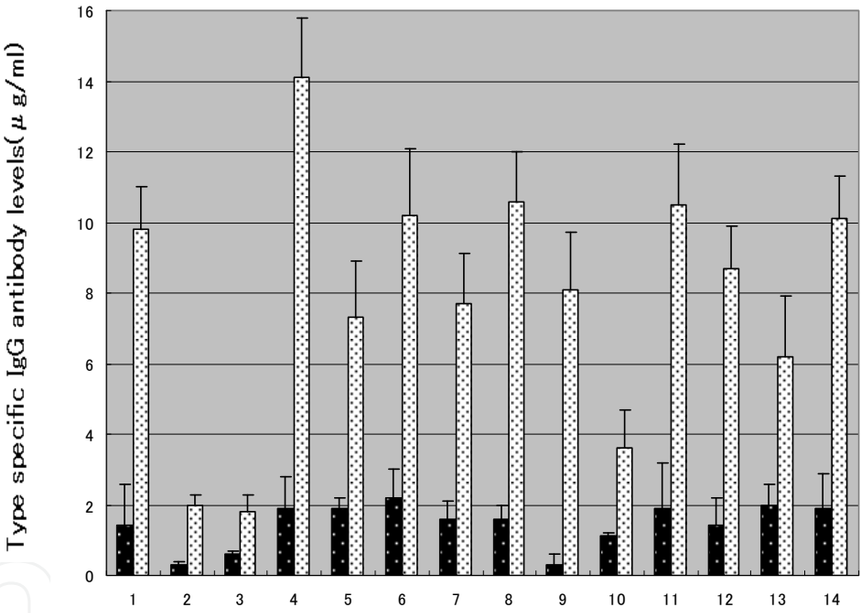
Variable			Crude	
	n	(%)	OR	95% CI
Male	44	21.7	0.95	0.48–1.87
Age ≥89 years	93	45.8	1.19	0.68–2.10
Disability	178	88.0	0.25	0.07–0.69
BMI <18.5	92	45.3	0.70	0.40–1.23
Bodyweight loss in 6 months ≥5%	35	17.2	0.81	0.45–1.46
BMI <18.5 and bodyweight loss in 6 months ≥5%	23	11.3	0.46	0.24–0.88
AC <80%	33	15.8	0.45	0.21–0.97
TSF <80%	104	51.2	0.88	0.50–1.55
AMC <80%	21	10.3	0.37	0.14–0.92
Diabetes	33	16.3	0.57	0.27–1.20
Pulmonary disease	15	7.4	1.33	0.45–4.40
Total protein <6.5 g/dL	63	31.0	0.52	0.29–0.95
Albumin <3.4 g/dL	52	25.6	0.74	0.36–1.53
Zinc <54 μg/dL	54	26.6	1.03	0.58–1.83
HDL cholesterol <43 mg/dL	52	25.6	1.08	0.57–2.09
LDL cholesterol >156 mg/dL	52	25.6	0.65	0.37–1.15

Mean ± standard deviation. AC, mid-upper-arm circumference; AMC, mid-upper-arm muscle circumference; BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TSF, triceps skinfold thickness.

Table 1. Odds ratios (OR) with 95% confidence intervals (CI) of a good immune response for each subgroup [7]

Since 1997, the Advisory Committee on Immunization Practices (ACIP) has recommended to prevent IPD, i.e., bacteremia, meningitis or infection of other normally sterile sites through use of the PPV23 among all adults aged above 65 years and those adults aged 19-64 years with underlying medical conditions that put them at greater risk for serious pneumococcal infection [11]. The updated recommendations [3] in 2010 include the following changes from 1997 ACIP recommendations: 1) the indications for which PPV23 vaccination is recommended include smoking [12] and asthma [13,14], and 2) routine use of PPV23 is no longer recommended for Alaska natives or American Indians aged below 65 years unless they have medical or other indications for PPV23 [15].

It has been reported that the antibody concentration level rose more than 1μg/ml (so-called protective level for vaccine-related pneumonia) referring to one muscle (or subcutaneous) injection of PPV23 among almost all of the elderly subjects [16]. As the antibody levels among 14 serotypes can be commercially measured as showing in Figure 1, some several serotypes showed a level of more than 1μg/ml even before vaccination in among the elderly.



Type-specific IgG antibody levels to Streptococcus polysaccharide
Note: All types illustrated significantly ($p<0.05$) except type 3 and 4.

Fig. 1. The concentration of the type-specific IgG antibodies before and after PPV23 vaccination among elderly (mean±SE) (Before vaccination After vaccination) [16]

The Cochrane Collaboration supports the use of PPV23 to prevents invasive pulmonary diseases in all-cause pneumonia or mortality [17] by prospective, randomized controlled trials (RCTs) or quasi-randomised trials that compared PPV23 with placebo, control vaccines, or no intervention. The studies included participants at elevated risk of pneumococcal disease due to older adults aged 50 to 85 years with previous hospital admission for community-acquired pneumonia in Sweden [18] and community-based older adults in Finland [19].Ten

studies involving 35,483 participants were included for outcome as IPD all causes with 15 events in the vaccinated group and 60 events in the control group, even though a subgroup analysis for the elderly was not performed. PPV23 reduced overall risk for IPD with was a pooled estimated odds ratio (OR) of 0.26 (95% confident interval (CI) 0.15 to 1.46; random-effects model). PPV23 was shown to be effective against all-cause pneumonia with a pooled estimated OR of 0.71 (95% CI 0.52 to 0.97) by a random-effects model. There was no evidence of protective efficacy against all-cause mortality, with a pooled estimated OR of 0.87 (95% CI 0.69 to 1.10; random-effects model). Enen though this meta-analysis has failed to demonstrate evidence for pneumococcal polysaccharide vaccination effectiveness against mortality (all cause or pneumococcal related), it demonstrates strong evidence of protection against IPD, with a correlate of efficacy from the RCTs of 74% (95% CI 56% to 85%) as shown in Fig 2.

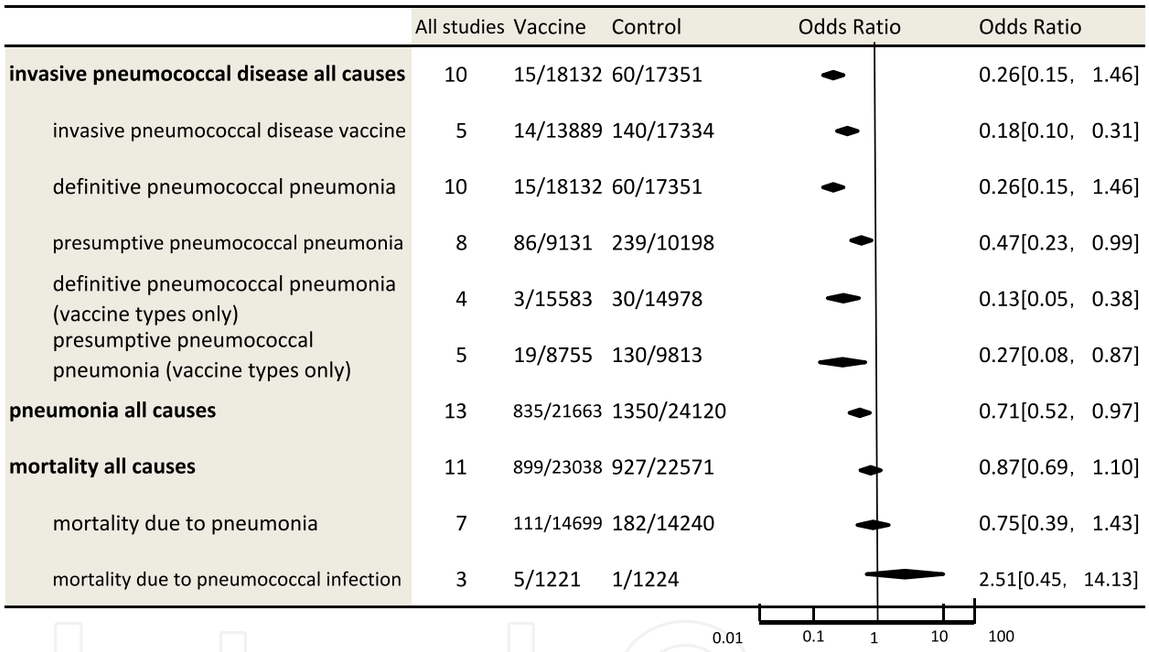


Fig. 2. Odds ratios (OR) with 95% confidence intervals (CI) of Comparison of RCTs of vaccination versus placebo for PPV23 vaccination (modified from article 17)

Observational studies have suggested effectiveness estimates ranging from approximately 50% to 80% for prevention of IPD among immunocompetent older adults and adults with various underlying illnesses, supporting the recommendations for using PPV23 to prevent IPD [20], although the effectiveness has not been demonstrated among immunocompromised persons or very old persons. A recent meta-analysis of 15 RCTs and seven non-randomized observational studies of PPV23 efficacy and effectiveness suggested an overall efficacy of 74% against IPD (CI = 56%-85%), based on pooled results of 10 of the RCTs [21]. Analysis of the results from the seven observational studies yielded a pooled vaccine effectiveness estimate of 52% (CI = 39%--63%). In contrast, a recent meta-analysis that included six RCTs estimated the combined PPV23 efficacy against pneumococcal bacteremia at only 10%, with a very wide CI (CI = -77%--54%) [13].

Regarding revaccination, ACIP recommendations for revaccination with PPV23 among the adult patient groups at greatest risk for IPD (i.e., persons with functional or anatomic asplenia and persons with immunocompromising conditions) remain unchanged. ACIP does not recommend routine revaccination for most persons for whom PPV23 is indicated. A second dose of PPV23 is recommended 5 years after the first dose for persons aged 19--64 years with functional or anatomic asplenia and for persons with immunocompromising conditions. ACIP does not recommend multiple revaccinations because of uncertainty regarding clinical benefit and safety.

It is said the changing epidemiology of IPD following the introduction of the 7-valent pneumococcal conjugate vaccine (PCV7) in children has altered the vaccine-preventable disease burden in older adults and, correspondingly, the potential magnitude of the benefit of PPV23 [22]. Finally, newer vaccines, such as PCV7 [23,24] or those employing serotype-independent antigens, offer the potential to provide clinical protection against pneumococcal infection in the growing population of older adults in the 21st century. In summary, the decrease in rates of pneumonia [25] and IPD among young children after the introduction of PCV7 indicates that eliciting protective immunity against invasive and non-invasive pneumococcal infections by vaccination is a realistic goal. The unconjugated polysaccharide vaccine has reduced the risk of IPD among older adults, and protein-conjugated vaccines have provided substantial direct benefits to children and indirect benefits to adults. Future opportunities to further reduce the risk of pneumococcal infections in adults will depend on advances in our understanding of the mechanisms of protective responses to *S. pneumoniae* in the systemic and, particularly, in the respiratory mucosal compartments.

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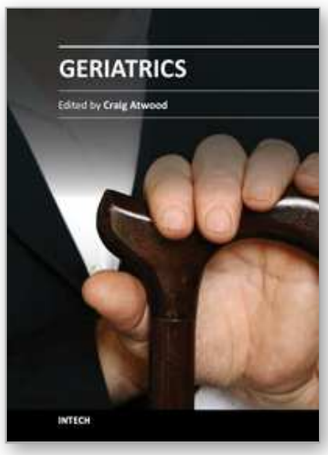

Geriatrics

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With the baby boomer generation reaching 65 years of age, attention in the medical field is turning to how best to meet the needs of this rapidly approaching, large population of geriatric individuals. Geriatric healthcare by nature is multi-dimensional, involving medical, educational, social, cultural, religious and economic factors. The chapters in this book illustrate the complex interplay of these factors in the development, management and treatment of geriatric patients, and begin by examining sarcopenia, cognitive decline and dysphagia as important factors involved in frailty syndrome. This is followed by strategies to increase healthspan and lifespan, such as exercise, nutrition and immunization, as well as how physical, psychological and socio-cultural changes impact learning in the elderly. The final chapters of the book examine end of life issues for geriatric patients, including effective advocacy by patients and families for responsive care, attitudes toward autonomy and legal instruments, and the cost effectiveness of new health care technologies and services.

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