Recommendations of advisory committee on immunization practices (ACIP) of USA on anti-pneumococcal vaccination

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Streptococcus pneumoniae is a gram-positive, alpha-hemolytic bacterium, first isolated in 1881 and identified as a causing agent of pneumonia by the late 1880s. Today, it still is a major cause of pneumonia, as well as otitis media and invasive pneumococcal disease, including meningitis, osteomyelitis and bacteremia.

The overall rate of community-acquired pneumonia (CAP) in adults is approximately 5.16 to 6.11 cases per 1000 persons per year; the rate of CAP increases with increasing age[1]. In 2004, pneumonia, along with influenza, was the leading cause of death among infectious diseases in the USA and the eighth cause of overall mortality, accounting for 2,3% of all deaths[2]. Despite the development of effective antimicrobial drugs, *S. Pneumoniae* remains the most common pathogen responsible for community-acquired pneumonia[3,4], with pneumococcal pneumonia mortality rates ranging from 10 to 20% and even exceeding 50% in high-risk groups[5]. While the emergence of multiple antibiotic-resistant pneumococci poses a great challenge to the scientific community, studies focusing on the prevention of the disease led to novel vaccine products and updated antipneumococcal vaccination strategies.

Currently, pneumococcal vaccination is available as a 23-valent pneumococcal polysaccharide vaccine (PPSV23) and a 13-valent pneumococcal conjugate vaccine (PCV13) that replaced an earlier 7-valent vaccine (PCV7).

Although, its efficacy in reducing streptococcal pneumonia has not been well established[6,7], PPSV 23 has been shown to protect against invasive pneumococcal disease[8]. It includes 23 purified capsular polysaccharide antigens (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), of which 12 are included in PCV13. According to **advisory committee on immunization practices** (ACIP) PPSV 23 vaccination is indicated for[9]:

1) All persons aged 65 or older(*)
2) Cigarette smokers
3) Nursing home or long term care facilities residents
4) Adults younger than 65 with:
   a) Chronic lung disease (COPD, asthma)
   b) Chronic cardiovascular diseases

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c) Diabetes mellitus
d) Chronic renal failure(•)
e) Nephrotic syndrome(•)
f) Chronic liver disease (including cirrhosis)
g) Alcoholism
h) Cochlear implants
i) Cerebrospinal fluid leaks
j) Immunocompromising conditions(•)
k) Functional or anatomic asplenia(•)

(*) Vaccination recommended even in the case of previous vaccination for any indication, and should be administered no less than 5 years after the previous dose
(•) Revaccination recommended 5 years after the first dose

PCV13, a 13-valent conjugate pneumococcal vaccine, approved in 2010 by the FDA for use in children replacing PVC7 and including six additional antigens, was approved by FDA in the end of 2011 for prevention of pneumonia and streptococcal invasive disease for adults 50 years of age or older[10]. The approval was granted under the Accelerated Approval Pathway, which allows the agency to approve products for serious or life-threatening conditions based on early evidence of their effectiveness that is reasonable to predict a positive clinical outcome. Accelerated approval was based on randomized, multicenter immunogenicity studies conducted in the United States and Europe that compared antibody responses to PCV13 with antibody responses to PPSV23 and was granted, provided that the manufacturing company would conduct further clinical trials in order to verify the anticipated benefit. Currently, a large scale clinical trial in 85,000 in individuals aged 65 years and older is under way in the Netherlands to estimate the clinical benefit of PCV13 in preventing pneumococcal pneumonia[11]. Despite, PCV13 having already been licensed by the FDA for use among adults aged 50 years or older, current **US Advisory Committee on Immunization Practices (ACIP) guidelines** recommend vaccination with PCV13, in addition to PPSV23, for adults aged 19 or older with[9]:

1. Immunocompromising conditions (Including chronic renal failure and nephrotic syndrome)
2. Functional or anatomic asplenia
3. Cochlear implants
4. Cerebrospinal fluid leaks

Individuals meeting the criteria above should receive both vaccinations as described below:

- Individuals with no previous vaccination with PCV13 or PPSV23 should receive a single dose of PCV13, followed by a dose of PPSV23 at least 2 months later
- Individuals having received one or more PPSV23 doses, should be given a single PCV13 dose, at least one year after the last PPSV23 dose.
- Patients requiring additional doses of PPSV23, should be revaccinated with PPSV23 at least 2 months after PCV13 and no sooner than 5 years after the last PPSV23 dose.

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