PNEUMOCOCCAL DISEASE PREVENTION IN THE ERA OF CONJUGATE VACCINES: WHAT'S NEW?

Getting more vaccines to more people
ASIAN VACCINE CONFERENCE

Asap
Asian Strategic Alliance for Pneumococcal disease prevention

INTRODUCTION

Asian Strategic Alliance for Pneumococcal Disease Prevention (ASAP) is a working group formed by healthcare professionals to highlight the burden of pneumococcal disease and to foster collaboration in fight against pneumococcal disease in Asia. Continuing with its educational outreach activities, ASAP held another symposium titled "Pneumococcal Disease Prevention In The Era Of Conjugate Vaccines: What's New?" at the 7th Asian Vaccine Conference (ASVAC 2019) in Myanmar from 13-15 September 2019. Prof. Zulfikli Ismail, Clinical Professor from KPJ Healthcare University College Malaysia and A/Prof. Daniel Goh, Senior Pediatrician from National University Hospital Singapore chaired the symposium.

THE OBJECTIVES OF THE SYMPOSIUM WERE TO:

- Emphasize the pneumococcal disease burden in adults and its clinical and economic implications
- Provide update on recommendations for pneumococcal vaccination in high-risk groups of individuals with co-morbidities and immunosuppressive conditions
- Highlight the pneumococcal serotype prevalence and immunogenicity of currently available pneumococcal vaccines in Asia

PROGRAMME:

Talk 1: Pneumococcal Disease Burden And Prevention Strategies In Adults
Prof. Sri Rezeki S Hadinegoro
Department of Child Health Medical Faculty
University of Indonesia, Indonesia

Talk 2: Update on Pneumococcal Serotype Prevalence and Vaccine Use
Dr. Maria Rosario Z. Capeding
Head of Department of Microbiology
Research Institute for Tropical Medicine, Philippines

Talk 3: Pneumococcal Vaccine In Special At-Risk Groups
Dr. H.T Wickramasinghe
President of Sri Lanka College of Paediatricians, Sri Lanka

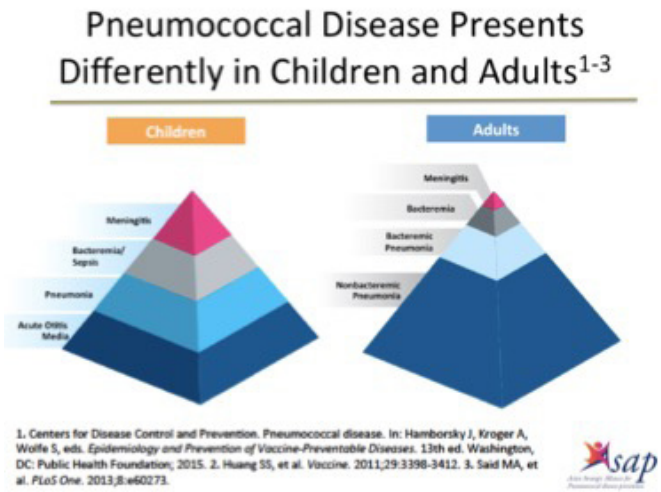
KEY TAKE-HOME MESSAGES

1. Community acquired pneumonia (CAP) is a major cause of morbidity and mortality in adults across the world, with streptococcus pneumoniae being the most common infecting pathogen.
2. The burden of pneumococcal disease in adults is underestimated. For every case of bacteremic pneumococcal pneumonia, there are at least 3 additional cases of non-bacteremic pneumococcal pneumonia in adults.
3. Comorbidities and immunosuppressive conditions increase the risk of pneumococcal disease, leading to increased hospitalization, increased emergency room visits and longer ICU stays further increasing the health care cost and resource utilization.
4. With the increasing ageing population and increasing risk of co-morbidities, the population at risk of pneumococcal disease is expected to increase, highlighting the need for robust disease prevention strategies.
5. The Centres for Disease Control and Prevention (CDC) recommend inclusion of pneumococcal vaccination in childhood immunization programmes, in adults above 65 years of age and in children and adults 19 through 64 years old who have certain medical conditions or who smoke.
6. Introduction of pneumococcal vaccination has led to significant decline in burden of pneumococcal disease in some countries across the world. Both pneumococcal conjugate vaccines (10-valent pneumococcal conjugate vaccine; PCV10 and 13-valent pneumococcal conjugate vaccine; PCV13) have demonstrated comparable immunogenicity and impact on reducing incidence of invasive pneumococcal disease (IPD), pneumonia and nasopharyngeal carriage.
7. 23valent pneumococcal polysaccharide vaccine (PPSV23) provides reasonable immunity for both IPD and CAP, but the immunity fades off after 5 years, justifying revaccination. Combination of PCV13 and PPSV23 has shown slightly better results than PPSV23 alone in HIV-infected individuals.
8. Surveillance data on serotype distribution in Asia is limited. Strengthening of existing surveillance systems, setup of new surveillance sites, improved delivery of healthcare, and improved political will and financial assistance are needed to enhance vaccine uptake and to evaluate the impact of vaccination in Asian countries.

PNEUMOCOCCAL DISEASE BURDEN AND PREVENTION STRATEGIES IN ADULTS

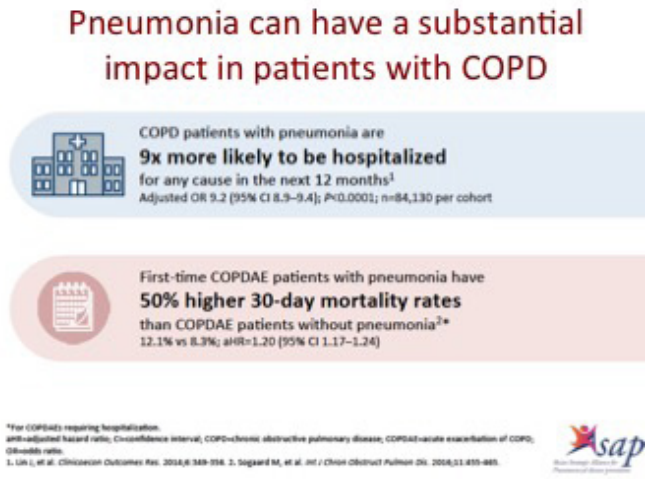
Prof. Sri Rezeki S Hadinegoro from Department of Child Health Medical Faculty, University of Indonesia highlighted the increased risk of pneumococcal diseases in adults with chronic and immunosuppressive conditions. The clinical and economic implications of increasing pneumococcal disease burden with the increasing prevalence of chronic conditions in ageing population were discussed.

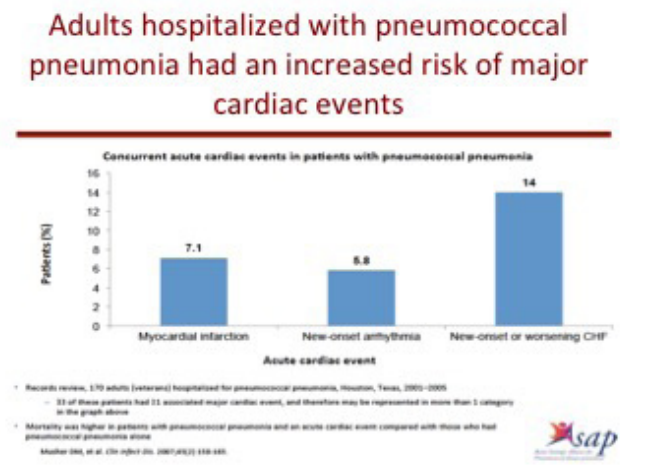
Community acquired pneumonia is a major cause of morbidity and mortality in adults across the world, with streptococcus pneumoniae being the most common infecting pathogen.[1] The prevalence of streptococcus pneumonia in community-acquired pneumonia (CAP) is estimated to be 27.3% in developed countries across the world1 and 29.2% in Asia[2]. Unlike that in children, the global burden of pneumococcal disease in adults is not well established. The incidence of bacteremic or invasive pneumococcal disease (IPD) in adults is commonly reported, but the incidence of non-bacteremic pneumococcal pneumonia is under documented, thus underestimating the actual burden of pneumococcal disease in adults. It is estimated that for every case of bacteremic pneumococcal pneumonia, there are at least 3 additional cases of non-bacteremic pneumococcal pneumonia in adults.[1]



Though the risk of infection with S.pneumonia is highest in youngest (less than 2 years) and oldest age (more than 65 years) groups[3], adults with chronic and immunosuppressive conditions are also at an increased risk of developing pneumococcal disease. There is an increased risk of infection in individuals with co-morbid conditions such as chronic lung disease, chronic liver disease, cardiovascular disease, chronic renal function, diabetes mellitus, and decreased immune function.[4-6] CAP imposes a significant burden on older adults as it worsens the underlying comorbid conditions, impacts daily activities and productivity and requires caregiver assistance.[7] Poor outcomes have been documented even in well functioning elderly patients hospitalized for pneumococcal pneumonia.[8]

Chronic obstructive pulmonary disease (COPD) patients with pneumonia are nine times more likely to be hospitalized and four times more likely to have an emergency room visit during a 12-month follow-up period.[9] Adults hospitalized with pneumococcal pneumonia are also at an increased risk of acute cardiac event, such as myocardial infarction, serious arrhythmia, or new or worsening congestive heart failure.[10] In addition, mortality rates in hospitalized patients with pneumococcal pneumonia are also higher in elderly patients and in those with underlying disease.[11] Furthermore, longer stays and higher mortality rates have also been documented in CAP patients admitted to intensive care unit compared to ward patients.[12]





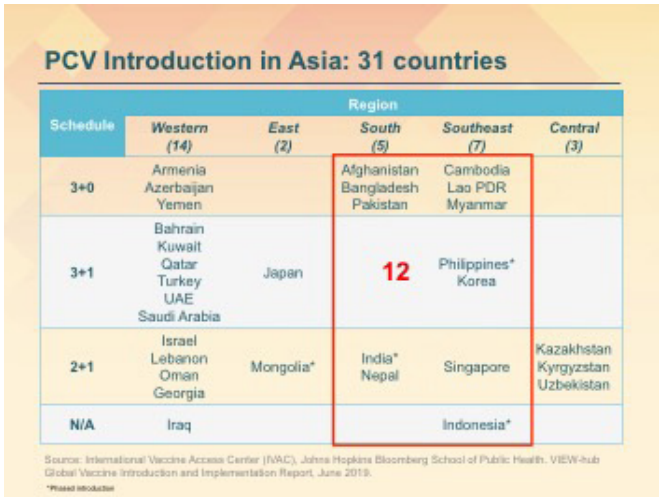
The increased hospitalization and increased emergency room visits due to pneumococcal pneumonia increase the health care cost and resource utilization leading to a significant economic burden.[9] With the increasing ageing population and increasing prevalence of chronic illnesses, the clinical and economic burden of pneumococcal pneumonia is expected to increase even further highlighting the need for prevention of pneumococcal pneumonia in adults. Two vaccines are currently available for pneumococcal vaccination in adults; the 23-valent pneumococcal polysaccharide vaccine (PPV23) and the 13-valent pneumococcal protein-conjugate vaccine (PCV13). The Community-Acquired Pneumonia Immunization Trial in Adults (CAPITA) has showed that PCV13 is effective in preventing vaccine-type pneumococcal, bacteremic, and nonbacteremic community-acquired pneumonia and vaccine-type invasive pneumococcal disease in adults 65 years of age or older.[13] The Centres for Disease Control and Prevention (CDC) recommends pneumococcal vaccination for all adults 65 years or older, and for adults 19 through 64 years old who have certain medical conditions or who smoke.[14]

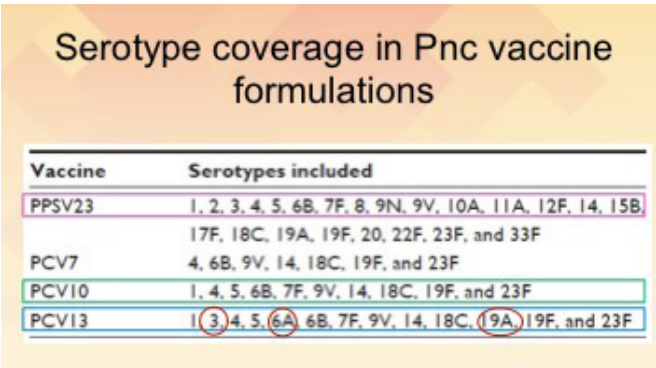
UPDATE ON PNEUMOCOCCAL SEROTYPE PREVALENCE AND VACCINE USE

Dr. Maria Rosario Z. Capeding, Head of Department of Microbiology at the Research Institute for Tropical Medicine in Philippines presented an update on the role of pneumococcal vaccination in reducing the disease burden and also focused on importance of pneumococcal vaccination in Asia. The limitations in vaccine implementation and disease surveillance in Asia were discussed. The need for strengthening of existing surveillance systems, and political and financial support for successful vaccine implementation in Asia was emphasized.

Introduction of pneumococcal vaccination has led to significant decline in incidence of IPD among children and adults. After introduction of pneumococcal vaccines in children in United States ((PCV7 in 2000 and PCV13 in 2010), IPD decreased from 100 cases per 100,000 people in 1998 to 9 cases per 100,000 in 2015. IPD caused by the 13 serotypes covered by PCV13 decreased from 91 cases per 100,000 people to 2 cases per 100,000 people from 1998 to 2015.[15] United States introduced PCV13 in 2012 for use among adults 19 years or older with immune-compromising conditions and in 2014 for all adults 65 years or older.[15] Following which, IPD caused by 13 serotypes included in PCV13 in adults 19-64 years old reduced from 11 cases per 100,000 to 2 cases per 100,000 people from 1998 to 2015.[15] Furthermore, IPD caused by the 13 serotypes included in PCV13 in adults 65 or older decreased from 44 cases per 100,000 in 1998 to 5 cases per 100,000 people in 2015. IPD caused by the serotypes covered by PPSV 23 decreased from 51 cases per 100,000 in 1998 to 13 cases per 100,000 in 2015 in adults 65 or older.[15]

According to June 2019 data, 145 countries have introduced PCV into their National Immunization Programs, 15 countries have plans to do so while no decision has been made by 34 countries.[16] Though PCV has now been introduced in 31 Asian countries, there is limited surveillance on serotype distribution in Asia due to a variety of factors ranging from challenges in determining disease burden, lack of well performing surveillance sites, difficulty in vaccine delivery and lack of baseline data and capacity for post-vaccination impact evaluation.[17] However, serotype prevalence data from India, Nepal, Bangladesh and Sri Lanka demonstrates that PCV10 covers approximately 70% and PCV13 covers approximately 74% of the serotypes that cause IPD.17 This data is certainly encouraging for Asian countries introducing PCV in their immunization schedules. Nevertheless, in order to evaluate the impact of vaccination, experts have identified the need for strengthening of existing surveillance systems, setup of new surveillance sites, improved political will and financial assistance in Asian countries.[17]





WHO 2019 Position Paper on pneumococcal conjugate vaccines in infants and children under 5 years of age recommends worldwide inclusion of PCVs in childhood immunization programmes.[18] WHO recommends a 3-dose schedule either as 2p+1 or as 3p+0, starting at 6 weeks of age.[18] The 2p+1 schedule has potential benefit over 3p+1 as higher antibody levels are induced in the 2nd year of life. The recommended interval between 2 primary doses in 2p+1 schedule is ≥8 weeks with a booster dose at 9-18 months of age.[18]

Both PCV10 and PCV13 induce comparable immunogenicity and no differences between higher-valent PCVs on overall disease burden have been demonstrated. [18-20] According to the WHO 2019 position statement both PCV10 and PCV13 have comparable immunogenicity and impact on IPD, pneumonia and nasopharyngeal carriage due to shared vaccine serotypes.[18] According to the WHO Strategic Advisory Group of Experts on Immunization (SAGE) 2017 review there is no evidence of different net impact on overall disease burden between PCV10 and PCV13.[19] However, additional benefit of PCV13 in settings where disease due to serotype 19A or serotype 6C is significant is acknowledged.[18,19] In addition, Pan American Health Organization (PAHO): 2016 systematic review on the impact and effectiveness of PCV also demonstrates significant impact of both PCV10 and PCV13, with no evidence of the superiority of one vaccine over the other on pneumonia, IPD or meningitis hospitalization reduction in children under 5 years old.[20]

PNEUMOCOCCAL VACCINE IN SPECIAL AT-RISK GROUPS

Dr. H.T Wickramasinghe, Consultant Pediatrician and President of Sri Lanka College of Paediatricians presented a talk on importance of pneumococcal disease prevention and vaccine recommendations in high-risk groups. The risk of pneumococcal infection is highest in children below 2 years of age and in elderly people more than 65 years of age[4]. In addition, adults aged 19–64 years with chronic and immunosuppressive conditions are also at an increased risk of developing pneumococcal disease. High-risk group includes individuals with co-morbid conditions such as chronic lung disease, chronic liver disease, cardiovascular disease, chronic renal function, diabetes mellitus, and decreased immune function.[5-7] Since pneumococcal disease is more severe in high-risk individuals[21], vaccination to protect these individuals is important.

CLASSIFICATION OF HIGH-RISK GROUPS

Group A: Immuno-compromised

1. Sickle cell disease
2. Splenectomy and functional asplenia
3. Immune deficiency syndromes, Congenital and acquired (Humoral, cellular, complement and phagocytic abnormalities)
4. Malignancies
5. Immuno-suppressive therapy
6. Organ/BM transplant
7. Chronic renal failure and Nephrotic syndrome

Group B

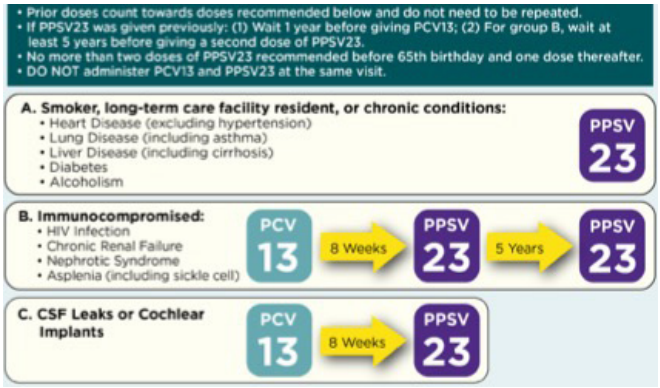
1. Cerebrospinal fluid Leak
2. Cochlear Implants

Group C: Chronic Disabilities

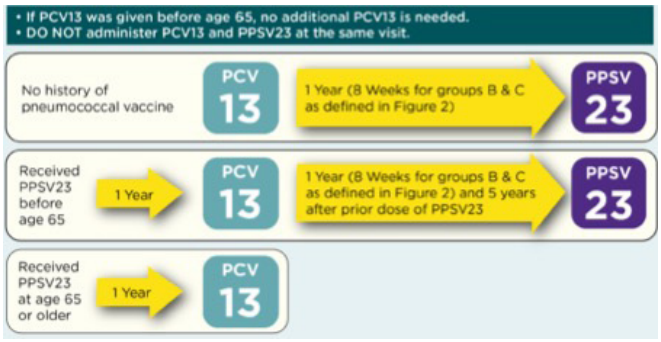
1. Congenital Heart diseases, congestive cardiac failure, Cardiomyopathy
2. Chronic Respiratory Diseases, E.g. Asthma. COPD
3. Chronic Liver diseases
4. Diabetes
5. Alcoholism
6. Smoking

CDC recommends pneumococcal vaccination for adults above 65 years of age14 and for adults 19 through 64 years old who have certain medical conditions or who smoke.[14] Two pneumococcal vaccines are recommended for adults: PCV13, 13-valent pneumococcal conjugate vaccine and PPSV23, 23-valent pneumococcal polysaccharide vaccine.

CDC recommendations on pneumococcal vaccination for people 2-64 years of age



CDC recommendations on pneumococcal vaccination for people >65 years of age



Effectiveness of 23valent pneumococcal polysaccharide (PPSV23) vaccine against invasive disease has been demonstrated in people aged ≥65 years.[22] The vaccine efficacy of PPSV23 has also been proven in preventing IPD and CAP in individuals over the age of 50.[23]Furthermore, protective effect of PPSV23 against pneumococcal and all-cause CAP for 5 years is documented.[24] PPSV23 provides reasonable immunity for both IPD and CAP, however the immunity fades off after 5 years, thus justifying revaccination. Furthermore, though the results of PPSV23 efficacy in HIV positive patients[25] and solid organ transplant patients26 are not encouraging; combination of PCV13 and PPSV23 has shown slightly better results than PPSV23 alone in HIV-infected individuals.[27]

Talking about the future of pneumococcal vaccines, Dr. Wickramasinghe discussed a mouse model study, which showed that increase in density of pneumococci in the nasopharynx is associated with the transition of the organism from commensal to pathogen; and vaccination with histidine triad protein D (PhtD), an S. pneumoniae adhesin vaccine candidate, can prevent pneumococcal density from reaching a pathogenic threshold.[28] The way to the future could thus be a pneumococcal protein vaccine to prevent conversion of commensal pneumococci to a pathogenic form, and a conjugate pneumococcal vaccine to cover all the virulent strains of pneumococci so that the non-vaccine type serotypes will prevail to colonize the nasal cavity.

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