

Pneumococcal Vaccination in Thailand: A Reappraisal of Adopting US Recommendations for Thai Health Problems

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Commercially available pneumococcal vaccine (Pneumovax[®] 23), manufactured by Merck is now available in Thailand. This vaccine has been widely utilized in the United States since 1983 with two very good reasons. Firstly, the incidence of invasive pneumococcal disease in the USA is high (3,000 cases of meningitis and 50,000 cases of bacteremia annually) and the vaccine is safe and proved to be cost-effective because it decreases the incidence of pneumococcal bacteremic disease by 56 to 81 percent. Secondly, strains of penicillin-resistant *Streptococcus pneumoniae* (PRSP), becoming increasingly common in the USA makes the vaccine even more desirable.

The US Advisory Committee on Immunization Practices (ACIP)¹ recommends vaccination to all persons in the following groups:

- a) Person aged ≥ 65 years.
- b) Immunocompromised persons aged ≥ 2 years who are at increased risk for illness and death with pneumococcal disease because of chronic illness such as diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), chronic congestive heart failure (CHF), alcoholism and liver cirrhosis.
- c) Persons aged ≥ 2 years with functional or anatomic asplenia.
- d) Persons aged ≥ 2 years living in environment in which the risk for disease is high.
- e) Immunocompromised persons aged ≥ 2 years such as those who have HIV, leukemia, lymphoma, Hodgkin disease, multiple myeloma, chronic renal failure, nephrotic syndrome, organ or bone marrow transplantation, persons receiving immunosuppressive

chemotherapy and long-term systemic corticosteroids.

Before we embrace the US recommendation regarding pneumococcal vaccination, we have to look at our prevalence of pneumococcal bacteremic disease in Thailand. Since we do not have the surveillance study of invasive pneumococcal disease in Thailand, we can not be certain of the definite prevalence of pneumococcal bacteremic disease. Nevertheless we are quite certain that it is uncommon compared to that of the Western countries. We have to rely on the incidence of invasive pneumococcal disease in various hospitals in Thailand. Our own data from Vichaiyut Hospital, a 130-bed private hospital which serves many elderly with chronic illnesses such as diabetes mellitus, chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF) and liver cirrhosis and also many immunocompromised patients, support our impression. Out of average 8,000 annual admissions, we only had three bacteremic pneumococcal pneumonia and no pneumococcal meningitis in the last five years. In fact we have not seen a single case of pneumococcal bacteremic disease in the last two years. The incidence of pneumococcal bacteremia in our hospital was 0.075 per 1,000 hospital admissions per year. All of our bacteremic *S. pneumoniae* were penicillin-sensitive. These three patients survived with appropriate treatment. All of them were older than 65 years and one had diabetes mellitus. One may argue that patients of middle and higher socio-economic status have low incidence of pneumococcal bacteremic disease. Let us look at the data from

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Bamrasnaradura Hospital, a 300-bed referral hospital for full-blown AIDS patients of lower socioeconomic status with average 14,500 annual admissions. The incidence of pneumococcal bacteremia and meningitis in the last seven months was practically zero.²

The prevalence of pneumococcal bacteremia and meningitis in Siriraj Hospital, a 2,600-bed primary and tertiary referral hospital in Bangkok was also low.³ Out of 60,000 annual admissions, only 115 pneumococcal bacteremic patients and 19 pneumococcal meningitis patients were seen during 1992-1998. Of these, 19 patients were younger than two years. The incidence of invasive pneumococcal disease in Siriraj Hospital was about 0.4 per 1,000 hospital admissions per year. The major risk factors in this series were alcoholism, diabetes mellitus, nephrotic syndrome, corticosteroid use and old age. Available data from Chiang Mai University Hospital, a 1,800-bed hospital with average yearly admission of 45,000 patients suggested that the incidence of invasive pneumococcal disease in the north was 2.5 times higher than Siriraj Hospital in Bangkok. One hundred and one pneumococcal bacteremic diseases were seen in adults during 1995-1997 and 48 invasive pneumococcal diseases, including bacteremia, meningitis and empyema, were seen in children during 1994-1997.⁴ The annual incidence of invasive pneumococcal disease in Chiang Mai University Hospital was about one per 1,000 hospital admissions per year. A surveillance study in South Carolina, USA showed the incidences of pneumococcal bacteremia among infants, young adults and persons ≥ 70 years of age to be 160, 5 and 70 cases per 100,000 population respectively.⁵ We do not have the exact explanation why invasive pneumococcal disease in Thailand is not as common as in the Western countries. In the USA, studies have shown that the rate of pneumococcal bacteremia depends on race.⁵ The annual incidence of pneumococcal bacteremia for the blacks (29 per 100,000 population) was higher than that for whites (11.6 per 100,000 population). Besides the difference in the climate and home environment, one can speculate that the Thais are fortunate to have genes which allow the body to mount effective natural polysaccharide antibody against *S. pneumoniae* at a young age.⁶ We are still waiting for the study of serotypes that caused the invasive pneumococcal infection in

Thailand to see whether these serotypes are represented in this 23 pneumococcal polysaccharide vaccine.

Penicillin-resistant *S. pneumoniae* (PRSP) is becoming more common in Thailand as in other countries because of over-utilization of antibiotics. The incidence of intermediate and high-level resistant PRSP ranged from 15-69 percent. More importantly, the incidence of high-level resistant PRSP is still increasing.⁴ However, the clinical significance of PRSP pneumonia without bacteremia or meningitis is uncertain. There was no significant difference in the mortality rate between patients with penicillin-susceptible and patients with penicillin-resistant pneumococcal pneumonia.⁷ The precise incidence of pneumococcal pneumonia in Thailand is difficult to ascertain because routine sputum cultures are insufficiently specific and sensitive. It is very important to realize that pneumococcal vaccine is not effective in protecting non-bacteremic pneumococcal pneumonia or common upper respiratory disease (e.g. sinusitis or acute otitis media). This vaccine is not indicated in children aged less than 2 years because the antibody response to the polysaccharide antigens is poor in this age group.

Based on the low incidence of invasive pneumococcal bacteremic disease in Thailand and the high cost of pneumococcal vaccine (about 900 baht per dose), we believe at present it is not cost-effective in recommending this vaccine to all immunocompetent persons older than 65 years and all HIV patients. This vaccination should be optional and reserved for a selected population i.e. those with very high risk or multiple risk factors such as splenectomized patients, alcoholism with chronic liver disease, systemic lupus erythematosus with nephrotic syndrome, diabetic elderly with COPD or CHF. We should continue surveillance of prevalence of pneumococcal bacteremic disease and adopt the US recommendation when the prevalence is rising to a significant level.

Utilization of pneumococcal vaccination is one of the example why the recommendation in one country may not be appropriate for the others because of the difference in the prevalence of the disease. Another good example that also fits this scenario is the recommendation from the Ministry of Public Health on primary prophylaxis for *Mycobacterium avium* complex (MAC) and cryptococcosis in AIDS

patients.⁸ Even though we have made a proposal on this issue⁹, the Thai guidelines continue to recommend primary prophylaxis for MAC when CD₄ cell count below 75 cells/ μ L but advise against primary prophylaxis for cryptococcal infection citing the reason that it is not cost-effective and does not prolong life. Obviously this Thai guidelines follow the US recommendation¹⁰ and totally disregard the difference in the prevalence of the diseases.

In our experience, we have not seen a single case of MAC infection in our AIDS and non-AIDS patients in the last 8 years at Vichaiyut Hospital despite our looking actively for it. Most of atypical mycobacteria isolates from both AIDS and non AIDS patients turned out to be *Mycobacterium chelonae*. In the meantime we have seen many cases of cryptococcal meningitis in our AIDS patients. We do not believe in the theory that lack of diagnostic capability may be largely responsible for the apparently low prevalence of MAC infection in Thailand. Disease caused by MAC in AIDS patients in sub-Saharan Africa is also uncommon. It was postulated that BCG vaccination and natural TB infection might confer protection against MAC. Although disseminated MAC with bacteremia has been reported in Thai AIDS patients,¹¹ MAC infection usually occurred after TB, PCP pneumonia or cryptococcal meningitis. By the time Thai AIDS patients develop MAC infection, they already are in the preterminal state. One can say that they die with MAC rather than die of MAC. It is a totally different story with cryptococcal infection. It comes early in AIDS patients and it is very common in Thailand. The prevalence of cryptococcal infection is at least five times of that of American counterpart. Nowadays Thai AIDS patients usually survive their PCP pneumonia and tuberculosis but many of them die from cryptococcal meningitis. If we were to follow the Thai guidelines by giving clarithromycin or azithromycin as primary prophylaxis for MAC, AIDS patients would have succumbed to cryptococcal meningitis long before they developed MAC infection. We did call for a double-blind placebo controlled trial of effectiveness of fluconazole as primary prophylaxis for cryptococcal infection in Thai AIDS patients with CD₄ cell count below 100 cells/ μ L to settle this dispute two years ago. The cost of fluconazole has declined a lot since then because the generic form is now available in Thailand.

We are happy to hear that the study on cost-effectiveness of primary prophylaxis for cryptococcal infection will be carried out soon at Bamrasnaradura Hospital.¹² In fact, a well-designed multicenter clinical trial should be performed so that more solid and useful data will be obtained to resolve this controversy.

In summary, it is necessary that we have accurate data on the epidemiology of all diseases in Thailand. Before any organization or public authority adopts the Western guidelines, it is of utmost importance to consider the difference in the epidemiology of the diseases and if possible, to conduct our own study regarding the cost effectiveness. Otherwise, we might give our patients a disservice and waste a large sum of money in especially this hard time of economic crisis.

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