

CHILDHOOD IMMUNIZATION: WHAT'S ON THE HORIZON?

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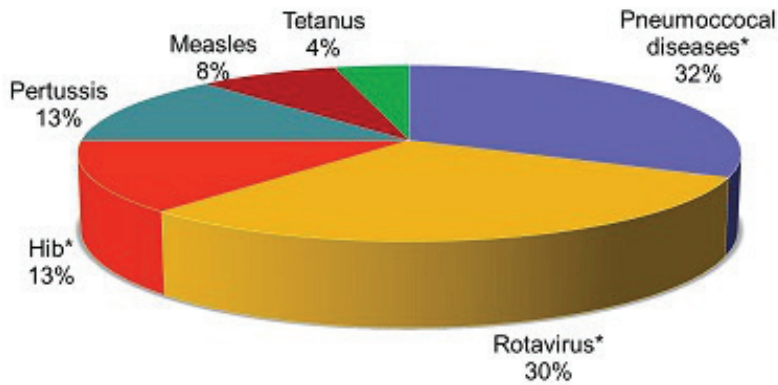
Immunization is the best form of prevention in children. Sadly, over one and a half million children under five years of age unnecessarily pass away annually, and among these deaths 17% are vaccine preventable. Influenzae B, Pneumococcal and rotavirus account for the top three causative agents (Fig 1). The pneumococcal conjugate and rotavirus vaccines, which could prevent the most significant 'killers,' namely pneumonia and diarrhea, have been introduced to ASEAN countries. The two new vaccines under development are the quadrivalent influenza vaccine, which replaces the trivalent form, and the long awaited dengue virus vaccine.

Myriads of diseases can result from pneumococci in the under-five year-old population, starting with meningitis being the most serious, followed by bacteremia, pneumonia, and otitis media. The incidence of invasive pneumococcal diseases (IPD) describes a U-shaped curve, where the vulnerable age groups are the two extreme ends, the under 5s and over 65s. Bacteremia, pneumonia, and meningitis in this order of incidence affect children; those under two years are most prone to infection. The world distribution of under five years death from pneumococcal disease before the vaccine introduction demonstrates that Thailand is among many other countries that has a death rate of 10-100

per 100,000, while in most of the African countries the incidence are as high as 300-500 per 100,000. Fortunately, there are tools to combat these invasive diseases.

Polysaccharide Pneumococcal Vaccine (PPV) was problematic, as it is immunogenic to those children over two years of age. For the last decade, there are two conjugated vaccines that deal with this issue, the ten valent (PCV-10) and thirteen-valent (PCV-13), with the combined effect covering up to 80% of all invasive pneumococcal forms (CDC, 2013). PCV immunization ought to begin from two months old with three-dose primary series and a booster dose at 12-18 months of age (3+1 strategy). If started later, then fewer doses are required.

Opportunity should not be missed to cover the most vulnerable group, however. Equally effective as an alternative, particularly in Europe, is the optional two-doses for primary series-plus-one booster dose (2+1 strategy) for healthy infants. The Finnish national program success is indicated by the IPD incidence dropping from 60/100,000 to 10, thereby vastly reducing the burden of diseases. As of 2012, 86 countries, representing 44% worldwide, have adopted the PCV immunization program (Fig 2) (Coller and Clements, 2011). For Africa with their high risk population, 20 countries receive their donated vaccines



Source: Black *et al*, 2010.

Fig1–The distribution of the common causes of childhood mortality.



Fig 2–The countries that implemented a pneumococcal conjugate vaccine in national program.

through Global Alliance for Vaccine and Immunization (GAVI). Only three countries in ASEAN however have come on board with the mass campaign, namely Singapore, the Philippines, and Lao PDR.

Rotavirus is the most common viral gastroenteritis in infant and children. Africa and ASEAN are the most affected by this disease (Gupta *et al*, 2012). The mortality

figure from rotavirus gastroenteritis varies within the ASEAN region, ranging from 2 up to 220 per 100,000 children under the age of five years (Kawai *et al*, 2012). Unsurprisingly, WHO endorses the implementation of rotavirus vaccine for all countries. This vaccine may be given simultaneously with DTP. None of the vaccines is without its risk; for rotavirus the literature to date sug-

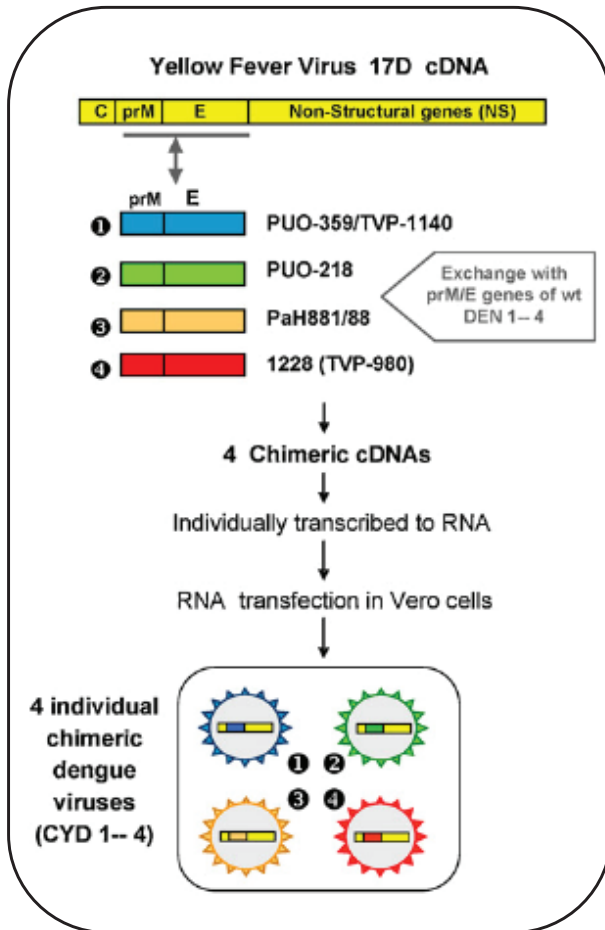


Fig 3—Diagram showing the structure of chimeriVax dengue vaccine based on yellow fever virus.

gests the incidence of intussusceptions to be small. For GAVI, this is a high priority work, aiming to administer the rotavirus vaccine to 50 million children by 2015.

Two types of the vaccine are currently available, the monovalent RV1 and pentavalent RV5, which can be administered as early as two months of age. Other forms are also available in China, Vietnam, and India on a restricted basis. For Thailand, a preliminary program was implemented in 2011, the results of which were promis-

ing, with under 10% with diarrhea as a mild side effect from almost 9,000 doses given. The Philippines has already introduced this vaccine into their program.

Concerning influenza, an epidemic can occur at any time. Coping with an outbreak is an ongoing challenge. Three kinds of influenza vaccines are marketed; inactivated vaccine given intramuscularly, inactivated vaccine given intradermally, and intranasal live attenuated vaccine. The trivalent inactivated form given intradermally, which resulted in better immunogenicity, should be given to the elderly and adults who respond poorly to the intramuscular form. The live attenuated quadrivalent vaccine is approved in the US but is not yet available in Thailand. The influenza vaccine is recommended to people at high risk of morbidity and mortality including pregnant women, children aged from 6 months to 5 years, adult older than 50 years, people with underlying diseases (chronic pulmonary, cardiovascular, renal, hepatic, neurological, hematologic, metabolic disorders), person

with immunosuppression, patient at risk of Reye syndrome (that is, children age <18 year with long-term use of aspirin), morbid obesity, body mass index ≥ 40 kg/m², and household contact with a high-risk population.

One publication compares the guidelines for giving influenza vaccine among five ASEAN countries (Rodgers and Klugman, 2011). Singapore and Thailand appear to have the most wide ranging coverage. However, the estimated number

of people who received influenza vaccine in Thailand is only 10%, while in the US, one-out-of-two people get the influenza vaccine seasonally. ASEAN should seriously consider increasing the coverage of influenza vaccine. Indonesia, Thailand, and Vietnam have developed in-country capacity for influenza vaccine production to prepare for the pandemic influenza.

Dengue affects almost half of the world's population, and those who live mainly in South America, Africa, and Asia. Three types of dengue vaccines have reached clinical trials, including live attenuated vaccine, DNA vaccine, and subunit vaccine (Sabchareon *et al*, 2012). Chimerivax live attenuated dengue vaccine is produced by using yellow fever virus vaccine (17 D strain) as a backbone and combined it with the envelope protein of dengue virus subtypes 1-4 (Fig 3). The vaccine was studied as a Phase II clinical trial in a randomized placebo control trial in Ratchaburi Province, Thailand. The 3-dose vaccine was given subcutaneously to about 4,000 children from ages 4 to 11-years old, using a 0-6-12 month schedule (Tate *et al*, 2012). The overall vaccine efficacy to prevent clinical dengue disease was 30.2% (95% CI: 13.4-56.6). The efficacy for each serotype is non-uniform, with poor efficacy for dengue virus subtypes-2. Phase III is ongoing, while other live-attenuated vaccines are being considered at the same time.

In conclusion, we expect to see more programs implemented for life-saving vaccines in this region, especially conjugated pneumococcal vaccine, rotavirus vaccine, and influenza vaccine. New vaccine development, especially dengue vaccine to reduce mortality among children in this region and worldwide, is underway.

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