

MEETING REPORT



ASVAC2017: 6th Asian Vaccine Conference

Daniel Yam Thiam Goh^a, Lulu Bravo^b, and E. Anthony S. Nelson^{ib c}

^aDepartment of Paediatrics, National University of Singapore, Singapore; ^bDepartment of Paediatrics, University of the Philippines, Manila, Philippines; ^cDepartment of Paediatrics, The Chinese University of Hong Kong, Hong Kong, People's Republic of China

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Introduction

The 6th Asian Vaccine Conference organized by Immunisation Partners in Asia Pacific (IPAP) followed meetings in Siem Reap (2009), Manila (2010), Jakarta (2011), Cebu (2013), Hanoi (2015). Envisioning a world where no person shall suffer from a vaccine preventable disease, IPAP through its partner organisations, provided a focused program around the theme “#YOLO: Let #VaccinesProtect You:” consisting of pre-conference workshops on rotavirus and dengue; a vaccinology masterclass; 6 plenary lectures; 7 partner symposia and 2 industry symposia. There were 371 delegates from 27 countries.

ROTA council advocacy workshop

The Rotavirus Organization of Technical Allies (ROTA) Council's technical pre-conference session “*Building the Investment Case for Rotavirus Vaccines through Evidence*” was led by Mathu Santosham (ROTA Council chair; Johns Hopkins University) and attended by over 40 scientific investigators, pediatric leaders, and EPI managers from 15 primarily lower-middle income Asian countries. Tony Nelson's (The Chinese University of Hong Kong) overview of diarrheal and rotavirus disease and Daniel Payne's (Centers for Disease Control and Prevention, United States) summary of vaccine impact, highlighted substantial declines in rotavirus deaths and hospitalizations following vaccine introductions, and emphasized the systemic nature of rotavirus infections. Megan Carey (Bill and Melinda Gates Foundation) reviewed the 2 WHO prequalified vaccines and their national introduction in over 80 countries and Zulkipli Ismail (Secretary-General of the Asia Pacific Pediatric Association) raised challenges for rotavirus vaccine introduction in middle-income countries. Lulu Bravo (University of the Philippines; Pediatric Infectious Disease Society of the Philippines) moderated a discussion on evidence gaps in countries considering rotavirus vaccine introduction. Participants highlighted the need for additional evidence on the influence of diarrheal disease on malnutrition, potential impact of rotavirus vaccines on stunting and shared lessons learned from introduction deliberations and stalled rollouts. The session concluded with presentations from Helen Saxenian (Results for Development) on sustainable immunization financing mechanisms and Lois

Privor-Dumm (International Vaccine Access Center, Johns Hopkins University) on evidence-based advocacy.

Dengue vaccination masterclass

The world's first dengue vaccine was licensed in December 2015. It is the culmination of over 2 decades of scientific innovation and collaboration in the field of dengue research. As part of the continued effort to strengthen the healthcare practitioners' understanding of the use of vaccination as part of an integrated approach in dengue control, Sanofi Pasteur hosted the first Regional Dengue Masterclass inviting approximately 50 healthcare professionals from 6 Asian countries where the vaccine is registered (Singapore, Philippines, Thailand, Indonesia, Cambodia and Malaysia) and where Dengue is endemic and a major public health concern. Daniel Goh (National University of Singapore) reviewed dengue disease epidemiology, and Punnee Pitisuttithum (Mahidol University) and Maria Rosario Capeding (Research Institute for Tropical Medicine, Philippines) provided key clinical data from the efficacy studies and safety profile including the long-term safety follow-up data and immunobridging studies. Salvacion Gatchalian (Pediatric Infectious Diseases Society of the Philippines) walked the audience through the frequently asked questions on the clinical research pathway, benefit/risk evaluation and the dengue vaccine clinical research as a whole. The panel discussion with all the speakers and Jaime Santos (Pediatrician, Philippine Children's Medical Center) included practical aspects of dengue vaccination (e.g., potential associated events linked to the YF-17D backbone in the vaccine construct, side effects, overall safety profile, dengue diagnostics, vaccine efficacy by dengue serological status, and a potential increased risk of severe dengue).

ASVAC vaccinology masterclass 2017

213 participants participated in 5 hours of brief, focused and succinct presentations by a panel of experts covering a wide range of topics including basic vaccine immunology, impact of vaccination on disease epidemiology, myths and facts about vaccination and vaccine hesitancy, vaccines through the ages, as well as a quiz on clinical cases. The session opened with

CONTACT E. Anthony S. Nelson ✉ tony-nelson@cuhk.edu.hk Department of Paediatrics, Lui Che Woo 6/F Clinical Sciences Building, Prince of Wales Hospital, Shatin, Hong Kong Special Administrative Region, PR China.

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highlights on the immunology of how vaccines work. The effects of adjuvants, the role of combination vaccines, safety and monitoring in vaccine development, and concepts in health economics were covered. This was followed by a brief walk through the history of vaccines, its impact in medical advancement and ethics in vaccination. Next were the myths and facts in vaccination contributing to vaccine hesitancy, covering areas such as antigen overload, toxins in vaccines, autism, and religion. Vaccination through the ages reviewed specific vaccines and schedules from infancy to the elderly, and the role of vaccination in pregnancy. An interactive quiz on clinical cases put the knowledge into practical application. Jerome Kim, (Director, International Vaccine Institute, South Korea) concluded the Masterclass with a presentation covering the important aspects of funding for research and development and the future pipeline of vaccines, taking the audience through a glimpse into the future of vaccination.

Plenary lectures

Yoshihiro Takashima (Medical Officer, Expanded Program on Immunization, World Health Organization (WHO) Regional Office for the Western Pacific) opened the conference speaking to “Global Vaccine Action Plan (GVAP): Monitoring Progress - Addressing Issues.” He highlighted that only one (introduction of new vaccines) of the 6 GVAP targets (a world free of polio; elimination of maternal and neonatal tetanus, measles and rubella; and coverage of DPT3 of 90% overall and 80% in every district) have so far been met globally. Reasons for low and sometimes falling coverage include conflict. In the Western Pacific region there is a new strategy for measles and rubella elimination and there has been good progress with Hepatitis B control.

Charung Muangchana’s (National Vaccine Institute, Thailand) lecture on “Who is Responsible for Lack of Vaccines?” addressed issues of vaccine security. Recent shortages of traditional EPI vaccines and unaffordable new vaccines emphasizes the need for improved vaccine security in the Asian region. In the event of a new pandemic there are real concerns about whether Asia would receive vaccines in a timely manner. The Association of South East Asian Nations (ASEAN) clearly requires a new strategy to ensure regional vaccine security.

James Molton (National University Hospital, Singapore) reviewed “Vaccines for Travellers.” Travel Medicine has an increasing following in the Asia Pacific region more so because of the constant presence and recognition of disease outbreaks brought about by both natural and man-made disasters. Other factors contributing to this awareness are the rapid industrialization, urbanization and more sophisticated technology for surveillance. The importance of studying epidemiology of diseases, risk to travelers, and the impact of vaccines on these diseases was highlighted. Childhood immunization should always be maintained at the highest level and should be constantly be reviewed particularly when traveling. Waning immunity is recognized for many vaccines (including Diphtheria, Pertussis, Tetanus, Measles, Mumps, Rubella, Hepatitis A) and needs to be better understood. International guidelines for other travel vaccines such as for Yellow Fever, Meningococcal and Polio are regularly being updated. Improving the science of travel

medicine and encouraging pre-travel consultations could reduce the spread of communicable and vaccine-preventable diseases.

Polio Eradication is a priority global goal and the final plenary session of the first day concluded with Ananda Bandyopadhyay (Bill & Melinda Gates Foundation) giving updates on Polio Eradication and low dose injectable polio vaccine (IPV). Emmanuel Vidor (Sanofi Pasteur, France) provided a manufacturer’s perspective of the “Challenges in the Polio Endgame, through and beyond Eradication Certification.” The session concluded with Eriq Tayag (Department of Health, Philippines) providing a Ministry of Health perspective. Currently, only 3 countries (Pakistan, Afghanistan and Nigeria) still report polio due to wild poliovirus. There is optimism that a polio-free world can be achieved and certified by 2020 (the first goal of the Decade of Vaccines). The long-term goal of sustaining a world free of all types of polioviruses also requires replacement of all oral polio vaccine (OPV) with IPV for routine immunization. New low-dose adjuvanted injectable polio vaccines could be one of the options facilitating the transition from OPV to IPV by addressing supply and cost constraints. The cooperation of all countries to end polio is essential, especially critical for those in conflict areas. The demand for IPV is high and this presents challenges to manufacturers, including adequate production of quality controlled products which should be equitably distributed. Governments and ministries of health for their part are willing to implement all the recommendations and strategies. However, many countries are looking for the funding and need to seek assistance both from national and international agencies to achieve and sustain the goal of polio eradication.

Kim Mulholland (London School of Hygiene and Tropical Medicine) tackled the challenges of “Choosing and Prioritizing Vaccine for the National Immunisation Programme (NIP).” The lecture explored the many factors that go into the decision making process for the inclusion of a particular vaccine into a NIP. As countries adopt more evidence-based approaches, it cannot be denied that industry could also play an influential role in the choice of vaccines to include in the NIP. Asia in general is lagging behind Africa in the introduction of new vaccines such as *Haemophilus influenzae* type B (HiB) and pneumococcal conjugate vaccine (PCV); in part because of the lack of reliable disease burden data. There are doubts raised about “ambiguous vaccine trial results” with anti-vaccine disinformation and campaigns adding to the barriers for immunization. When the high cost of the vaccine is considered, public health burden becomes the bigger issue so that affordability takes center stage and the clamour to reduce the price of the vaccines become the main driver for its introduction. Human papilloma virus (HPV) vaccine and rotavirus vaccine introductions present other features that are unique in some countries which are unable to put them in the NIP despite evidence of cost-effectiveness and health economic benefits.

William Hausdorff (independent consultant, Belgium) gave the final plenary lecture on “How can vaccines help achieve a *Grand Convergence* in global health by 2035” taking inspiration from the 1993 World Bank Report: Investing in Health, and the recent Lancet Commission report on “Global health 2035: a world converging in one generation.” The concept of “*Grand Convergence*” was illustrated with a graph demonstrating the

narrowing of gaps in child survival between high, low and middle income countries. It is argued that “with proper investment” these mortality rates could converge to a very low level in all countries within the next 20 y. Crucial to achieving this will be appropriately valuing health, to strengthen the economic case for investment. Two main strategies for how vaccines can help this process were outlined: first, extending the coverage of existing vaccines to maximise their utility, and second developing new vaccines. However, deciding which vaccines to prioritise can be problematic, and traditionally, the real world priorities have not matched those of the academic and research communities. New tools, such as the Strategic Multi-Attribute Ranking Tool (SMART), allow for a transparent assessment of the complex and varied drivers of vaccine priorities to facilitate considered decision-making by National Immunisation Technical Advisory Groups. Harvard economist David Bloom has argued that governments massively undervalue vaccines and that traditional cost-effectiveness models miss many elements which have an economic benefit: the “insurance” value of vaccines, the avoidance of antimicrobial resistance, promoting cognitive development and school attendance in children, reductions in inequality and resilience against the disruptive effects of outbreaks, as well as the economic value of additional life years. Investing in health, and vaccines in particular, makes great economic and humanitarian sense. The scientific vaccine community needs to persuasively make the economic case for immunisation, and these messages should be prominently and persistently highlighted.

IPAP partner symposia

These 90 minute sessions, were developed and organized in collaboration with IPAP partner organisations.

Emerging diseases and future directions

In collaboration with Asian Society for Pediatric Infectious Diseases (ASPID), the session covered pneumococcal disease (Ping-Ing Lee, National Taiwan University Children’s Hospital), norovirus (October Sessions, Duke-NUS Medical School, Singapore), Enterovirus 71 (EV71) (Gang Liu, Beijing Children’s Hospital) and Zika (Pornthep Chanthavanich, Asia Pacific Travel Health Society). With more countries putting PCV in their national immunization programs or using PCV more widely within the private sector, surveillance of pneumococcal diseases needs to be standardized, with reporting of severe pneumococcal disease and monitoring serotype replacement. In Asia the use of PCV in NIPs is limited, despite pneumonia remaining a major killer of children. Wider use of PCV in the region would promote well-being, reduce antimicrobial use and potentially antibiotic resistance. Other diseases that cause considerable morbidity such as norovirus are not yet vaccine preventable. Studies underway provide hope that norovirus may also be classified as a vaccine-preventable disease in the not too distant future. EV71 is now a vaccine preventable disease in China and vaccines for Zika are being developed. With increasing travel and the threats of both natural and man-made disasters, there is a need for better and greater protection against these emerging diseases.

Adolescent vaccination and school-based immunization

This session, in collaboration with the International Society of Tropical Pediatrics (ISTP), covered vaccines for HPV (Saidatul Norbaya Buang, Ministry of Health, Malaysia), dengue (Tikki Pang, National University of Singapore), pertussis (Leong Hoe Nam, Mount Elizabeth Novena Hospital, Singapore) and tetanus (Tony Nelson) in adolescence. Adolescent vaccination offers new opportunities and challenges. Malaysia has achieved high coverage of HPV vaccination of girls with a school-based program. Despite concerns about religious perception, HPV introduction has been very successful in Malaysia by presenting it as an anti-cervical cancer vaccine, in a setting where school enrolments of girls are >90%. Good communication to the public and health staff was essential for the success of this introduction. Dengue vaccine is licensed for the adolescent age group and with adolescents being physically active and mobile between different environments (indoor, outdoor), they are potentially at greater risk of dengue infection. The February 2017 WHO tetanus position paper revises scheduling to recommend the 6th tetanus vaccine dose (3rd booster dose) at 9–15 y which provides new opportunities for its inclusion in school-based schedules. These new tetanus schedules aim to achieve maternal and neonatal tetanus elimination and broader tetanus control. Countries are encouraged to use combined DT/Td vaccines rather than tetanus toxoid only containing vaccines. Improved vaccination documentation will prevent too frequent doses and improved surveillance can identify immunity gaps. Despite these opportunities, school-based vaccination programmes present challenges in terms of access, administration and funding.

Influenza vaccination for all?

The Asia Pacific Alliance for the Control of Influenza (APACI) developed a comprehensive session that reviewed influenza vaccination policy in Asia-Pacific region (John Tam, Polytechnic University, Hong Kong), universal seasonal influenza vaccination recommendation in the US and evidence to support influenza vaccination for children (Joe Bresee, Centers for Disease Control and Prevention, United States) and maternal immunization for protection for mothers and newborns (Anahita Chauhan, Saifee Hospital, India). Joe Bresee reviewed the value of risk-based strategies for influenza vaccination policies in most countries, focusing on WHO’s SAGE recommendations for vaccinating 5 key target groups: young children, pregnant women, health care workers, elderly persons and persons with underlying chronic diseases. He summarized the evidence for focusing vaccination programs on prevention of influenza among young children, highlighting the high rates of hospitalizations as well as compelling data on the value of vaccination in preventing the most severe outcomes, and on reducing costs and social impacts of the disease.

Rotavirus vaccines: Opportunities and challenges

The ROTA Council’s symposium on “Rotavirus Vaccines: Opportunities and Challenges” kicked off the last day of ASVAC 2017. Daniel Payne highlighted global vaccine impact, especially the rapid, substantial reductions in rotavirus deaths, hospitalization, and treatment-associated costs in countries routinely using vaccines. Mathu Santosham noted the lag in vaccine introductions in Asia, highlighting barriers including

declining diarrhea mortality and a lack of understanding of the health, economic, and societal consequences of rotavirus. Rakesh Kumar (United Nations Development Programme, India) shared the status of the Bharat vaccine and Indian rotavirus vaccine introduction, which has reached about 9% of India's birth cohort to date. He cited as key challenges training, cold chain expansion, high wastage rates, and complications of a phased rollout in a mixed public-private system. Carl Kirkwood (Bill and Melinda Gates Foundation) provided an update on the product landscape, including 2 nationally licensed Indian vaccines that may soon be prequalified by WHO for use globally, particularly in Gavi-eligible countries, and several new vaccine candidates in development. Frédéric Debellut (PATH, Switzerland) shared results of cost-effectiveness studies, highlighting that rotavirus vaccines continue to be a good investment even in low mortality settings and countries not eligible for Gavi support.

Cholera

Namseon Beck (International Vaccine Institute) began the IVI symposium on Cholera by noting that effective cholera prevention and control relies on comprehensive WASH interventions and vaccination. The Oral Cholera Vaccines (OCV) have good safety profiles with protection efficacy of more than 60% and herd immunity lasting more than 3 y. However during the cholera epidemics in Haiti there was limited experience in using OCVs in outbreaks, which was further challenged by limited vaccine supply (Ralph Ternier, Partners in Health, United States). Through the technical support and strategic investment by IVI, 2 OCVs are now prequalified by the WHO in increasing quantities. The surveillance program in Africa (Africhol) proves OCV campaigns should target highly endemic areas involving entire population to halt cholera transmission, which requires understanding of the target groups, their behavior and living conditions to reach them. Dominique Legros (WHO, Switzerland) reported that in 2013, WHO established an OCV stockpile for outbreak control and emergencies. As of 2017, almost 8 million doses have been deployed for 40 mass campaigns in 14 countries. Implementing OCV campaigns proved feasible and well accepted in a variety of settings. Martin Mengel (Agence de Médecine Préventive, France) emphasized that further work should go into the demonstration of vaccine impact, documenting and improving delivery costs as well as the timeliness of the response. Innovative strategies for OCV delivery should be further explored in an effort to simplify the implementation and reduce the overall cost.

Patient groups as partners in vaccine advocacy

Advocacy has been a core value of ASVAC conferences and partnering with the Confederation of Meningitis Organisations (COMO) and the International Vaccine Access Center, John Hopkins University, 4 speakers shared their expertise: Christopher Head (President, COMO); Zulkifli Ismail, Lois Privor-Dumm and Naveen Thacker (President, Asia Pacific Pediatric Association). This session highlighted successful examples of advocacy from the region and the role of Patient Groups. Elements of that success included a recognition of many stakeholders and their role in change. Despite the presence of many competing priorities, advocates must be able to outline a common vision and leverage opportunities to speak about how

vaccines contribute to the priorities of others. Evidence is at the heart of successful advocacy, but clearly not enough ~ knowing how to communicate to various audiences, including policy makers, the public, finance ministers, journalists, medical professionals and experts is crucial and providing a story that helps connect people to the reason why change is needed is essential. Patients' experience has been shown to be valuable as part of advocacy process in other regions but that this is less evident in Asia Pacific. Use of social media has also shown to be effective in addressing the changing ways in which parents and others process information. Speaking about the broader value of vaccines in terms of what is important for the target audience can also help engage stakeholders. Addressing vaccine hesitancy requires a tailored approach to ensure potential concerns are appropriately understood and addressed often in a direct fashion that engages other trusted stakeholders. Additional training and working together with advocates, partners, infectious disease experts and medical professionals can help to harness the power of advocacy to achieve sustainable change.

Meet the experts: FAQs in vaccination

ASVAC's final symposium tackled practical issues in a question and answer format following short presentations on surveillance and adverse events following immunisation (AEFI) (H.T. Wickramasinghe, Asiri group of Hospitals, Colombo, Sri Lanka); vaccine scheduling and administration (Iqbal Ahmad Memon, Sir Syed College of Medical Sciences for Girls, Faculty Agha Khan University of Health Sciences); aging and vaccines (Shelley Ann F. De la Vega, National Institutes of Health, Philippines); and vaccines for immunocompromised patients (Anne Goh, Singapore Paediatric Society). Surveillance of AEFI is an integral component of the process of ensuring safety of vaccines and should include the timely communication of the results of investigations of AEFI. Scheduling and administration of vaccines were highlighted including the age when the vaccine is most effective, number of doses and availability of combination vaccine. The issue of immunosenescence has important implications for the aging population and consideration and further study is needed to see how vaccines can be made more effective for this population. For the immunocompromised host, consideration is needed for the most appropriate vaccines to be given and to constantly determine the right timing for these vaccines.

Industry symposia

GSK lunch symposium: The value of vaccination

This 90 minute session over lunch, in the format of a conversation between presenters, began with the developments in DTP-based vaccines (Lee Bee Wah, Mount Elizabeth Medical Centre, Singapore and Jan Dolhain, GSK Vaccines). Highlights include the increasing disease burden and the need for improved vaccine updates. Next was the discussion on 'Characteristics of an Ideal Vaccine: Do Rotavirus Vaccines Fit?' (Gyneth Bibera and Sanjoy Datta, GSK Vaccines). Rotavirus vaccination has been shown to be efficacious for the prevention of severe rotavirus gastroenteritis in large-scale clinical trials in both developed and less developed settings. The next session on influenza vaccines (Philippe Buchy, Michael Nissen, and Anar Andani, GSK

Vaccines) highlighted the estimated 1 billion influenza infections that occur worldwide every year, with approximately 300,000 to 500,000 deaths annually. The median proportion of the 2 lineages of influenza B viruses detected during influenza seasons is estimated at 22.6%, and the quadrivalent influenza vaccine can significantly overcome vaccine mismatch when the most prevalent circulating lineage is not the one included in the trivalent vaccine. 'Overall impact of Pneumococcal Conjugate Vaccines: What really matters' (William Hausdorff and Bruce Mungall, GSK Vaccines). A GSK analysis of publicly available data indicates that irrespective of which country, or which vaccine has been used, there are similar reductions in vaccine type and overall invasive pneumococcal disease (IPD) in young children, but the magnitude of the increases in replacement disease are slightly more variable. In older adults (> 50yrs), in contrast, there appears to be considerable setting-specific variability in whether decreases in vaccine-type IPD translate into an overall herd IPD impact, or whether non-vaccine type replacement essentially fills in the gap.

Sanofi lunch symposium: Recent advances in dengue vaccination

Stakeholders from public/private donors and health organizations, vaccine manufacturers, policy makers to healthcare professionals highlighted the need to strengthen the understanding in using the dengue vaccine as part of an integrated approach in dengue control. Dengue is a major public health concern in Asian endemic countries. Results from the 3 efficacy studies, and the safety profile of the dengue vaccine including the long-term safety data, were presented by investigators of the clinical studies (Punnee Pitisuttithum and Maria Rosario Capeding). Salvacion Gatchalian and Anne Goh chaired a panel discussion with vaccinators (Jaime Santos, Punnee Pitisuttithum, and Maria Rosario Capeding) that took the audience through the frequently asked questions on the clinical data (e.g., adverse reactions, efficacy, safety profile), benefit/risk evaluation, and the use of the dengue vaccine.

Post-conference roundtable: Pneumococcal conjugate vaccines - Potential, challenges & value in Asia countries

The last day of the 6th ASVAC ended with a roundtable discussion chaired by Kim Mulholland and William Hausdorff, and attended by key opinion leaders from 10 Asian countries and 5 vaccine manufacturers. This was supported by an educational grant from GSK but

independently organized by the Asian Strategic Alliance for Pneumococcal disease prevention (ASAP). The aim was to discuss potential and perceived barriers to introduction of pneumococcal conjugate vaccines in the region. Despite the diversity between, and within, each country in the Asian region, there were a few generalizable factors including: (1) availability of local disease burden, serotyping and cost-effectiveness data; (2) strong advocacy from local medical fraternity with help from within the national administration/government; (3) political will with financial capability to ensure sustainability of the vaccine in the national program; (4) vaccine cost and its transparency; and (5) the need for a regional pooled vaccine purchasing mechanism to negotiate vaccine price. Among the main barriers identified was a lack of serotype surveillance data pre- and post-vaccine introduction. A common voice is needed to advocate for vaccination for the whole region and each country that had been successful in introducing the vaccine should help in this process. A regional pooled vaccine purchasing mechanism would be a major step forward.

Summary

Vaccines are a major tool in our armamentarium against infectious diseases across the world; they are the single entity that has had most impact in medical advancement in past decades and is a field that is constantly evolving and developing. Forums, such as the Asian Vaccine Conference, that bring together thought leaders from various areas in vaccinology, are opportunities to share knowledge of the latest updates in a concise and interactive format. The 6th Asian Vaccine Conference in Singapore saw participation from across the region and beyond of health professionals in the public and private sectors, policy makers, researchers, scientists, industry and vaccine manufacturers. The meeting helped establish networks for vaccine advocacy and communication and enabled significant interaction and exchange of ideas to improve the understanding and practice of vaccinology across the region.

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ORCID

E. Anthony S. Nelson  <http://orcid.org/0000-0002-2521-3403>