

MEETING REPORT



ASVAC2019: 7th Asian Vaccine Conference

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ABSTRACT

The 7th Asian Vaccine Conference (ASVAC 2019) was held in Yangon, Myanmar from 13 to 15, September 2019. It brought together stakeholders in the field of vaccination to address challenges and issues relevant to clinical practice and immunization programs in the region. The conference themed “Immunization: sustaining health security in Asia”, included pre-conference workshops, a Vaccinology Masterclass, plenary lectures, symposia, and poster presentations. There were over 700 participants ~ 400 local and 300 international from 31 countries ~ and 55 international and local speakers from 19 countries. An Asian EPI managers’ meeting was also held on 11–12 September in Naypyidaw, the new capital of Myanmar, and was hosted by the Ministry of Health and Sports, Myanmar with support from World Health Organization, UNICEF and other partners. This inter-regional meeting aimed to strengthen the cooperation and collaboration of EPI Managers and others involved in implementing immunization programs in the region. The conference was organized by the Immunization Partners in Asia Pacific (IPAP) and hosted by Myanmar Pediatric Society and the Ministry of Health and Sports, Myanmar. Other partners included the Confederation of Meningitis Organization, Philippine Foundation of Vaccination, Pediatric Infection Disease Society of the Philippines, Asia Pacific Alliance for the Control of Influenza, PATH, ROTA Council, International Society of Tropical Pediatrics, Asian Society for Pediatric Infection Diseases and other partners. Previous conferences have been held in Siem Reap (2009), Manila (2010), Jakarta (2011), Cebu (2013), Hanoi (2015) and Singapore (2017). The 8th Asian Vaccine Conference will be held in Penang, Malaysia in 2021 to further IPAP’s vision of a world where no one suffers from a vaccine-preventable disease.

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Opening address by the ministry of health and sports, Myanmar

The Minister (H.E. Dr Myint Htwe) welcomed participants and voiced appreciation of the comprehensive conference program and lineup of expert speakers. He called on local participants to take full advantage of all sessions. The importance of vaccines and immunization programs emphasize that current teaching in the field of immunology needs to be strengthened and support should be given for local participants to attend relevant international courses. Local priority research areas related to vaccines should be identified and a range of efforts should be made to ensure Myanmar improves vaccination coverage. New research on heat-stable vaccines, reduced doses and improved schedules and better vaccines should be ongoing. Investments in vaccine-related research promises many potential future benefits. Myanmar needs to learn from the experiences of others and implement necessary actions. Despite limited financial and human resources, it is important to develop strategies to increase the effectiveness of vaccination programs. Policymakers within the Ministry should consider strategies for introducing new vaccines including addressing issues related to vaccine regulation, distribution, delivery, pricing, and financing. The minister

concluded by encouraging everyone to work together to increase vaccine coverage to the entire population to prevent the spread of preventable diseases in the world.

Plenary lectures

The Opening Plenary Lecture was on “Partnerships and Collaborations to advance the vaccine agenda: lessons from the rotavirus experience” by Roger Glass (Director Fogarty International Center, National Institutes of Health). By 1985 rotavirus was recognized as a priority disease in developing countries, and with vaccines in development, countries, including Myanmar, demonstrated significant disease burden using standardized WHO surveillance tools. This information has supported Myanmar’s decision to introduce a rotavirus vaccine in 2020 with GAVI support. However, many other countries in Asia have yet to include a rotavirus vaccine in their National Immunization Programmes (NIP) and we need to better understand the reasons why there has been this hesitancy to do so. Global partnerships, starting with the successful eradication of smallpox, have grown and matured through The Children’s Vaccine Initiative, Gavi, Bill and Melinda Gates Foundation

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and sourcing novel financing mechanisms. Much progress has been made to achieve the Decade of Vaccine's vision of world free of vaccine-preventable diseases, but much work is still to be done. New opportunities include scaling up birth dose of Hepatitis B vaccine, additional DPT boosters, greater use of oral cholera vaccines and post-exposure rabies vaccine, meningococcal conjugate vaccines, and the future promise of respiratory syncytial virus (RSV) vaccines. The value of vaccines is well established and the vaccine community has come together ~ from the largest global agencies and donors to regional, national, and local programs. However, anti-vaccine sentiment has grown and ongoing investment in research is essential to address such problems and make continued improvements to our vaccination programs.

Janet Englund (University of Washington) spoke on "*Maternal vaccination: for the woman, fetus and infant*". Neonates, with their immature immune systems, are particularly vulnerable to a range of infections. IgG antibodies that protect the mother can also transfer through the placenta to protect the infant. Factors that influence the effectiveness of maternal immunization include placental damage (malaria and HIV) and timing of vaccination (stage of gestation and timing of birth). Maternal vaccination to prevent tetanus is well established. WHO's initiative for Maternal and Neonatal Tetanus Elimination has made good progress but, as of January 2018, 15 countries have still to achieve elimination. Pertussis mortality is highest in the first month of life. Following an outbreak of pertussis in the United Kingdom, Tdap-IPV maternal vaccination was introduced in 2012. Vaccine effectiveness for pertussis was high at 3 months. WHO recommends influenza vaccines in pregnancy due to the high risk of severe disease and the safety of seasonal influenza vaccine throughout pregnancy. Clinical studies in Mali, Nepal, South Africa, and Bangladesh have shown a reduction in pneumonia and stunting in infants whose mothers received influenza vaccine. A pipeline of RSV vaccines and monoclonal antibodies are in development. Results from the Novavax RSV maternal immunization trial showed 39% efficacy for medically significant RSV lower respiratory tract infection. However, challenges remain with the development of RSV vaccines. A multivalent conjugate Group B Streptococcal vaccine was recently shown to be safe and immunogenic in a South African study. Since the threat of legal liability is a cause of concern for vaccine manufacturers, indemnification may be needed before companies will participate in the production and testing of maternal vaccines.

Stephen Chacko from WHO's South East Asian Region Office (SEARO) spoke on "*Reemerging Measles*". Global Vaccine Action Plan targets include measles elimination in two WHO regions and rubella in two regions by 2015 and the elimination of both measles and rubella in all regions by 2020. Although progress has been made these targets are OFF TRACK with only 43% members states having eliminated measles and 41% rubella by mid-2019. Measles mortality has fallen 80% since 2000 and vaccine coverage has increased (86% with one dose of a measles containing vaccine and 67% with two doses). However, there were still 20.7 million unvaccinated children in 2017 with the greatest numbers being in Nigeria, India, Pakistan, Indonesia, and Ethiopia.

Since late 2018 there have been increasing reports of measles cases including in Europe. Root causes for these outbreaks include hesitancy, inadequate health services, and programs and conflict. With its very high R_0 (12–18) measles can rapidly spread to pockets of unvaccinated populations. Vaccine efficacy is 99% with two doses of measles vaccine. Herd protection is usually possible with 95% coverage with two doses. Sub-optimal vaccination remains the cause of most measles cases and outbreaks and resurgence of measles are primarily due to failure to vaccinate. Pockets of under/unvaccinated populations pose a threat to the measles elimination targets and ongoing national, regional and global commitments are needed for success.

Ping Ing Lee (National Taiwan University Children's Hospital) speaking on "*Hepatitis vaccines*" noted that most deaths from hepatitis viral infections are late complications from Hepatitis B Virus (HBV) and Hepatitis C virus (HCV). Less commonly deaths result from fulminant hepatitis caused by HBV, Hepatitis A virus (HAV) and Hepatitis E virus (HEV). An estimated 1 million deaths occur annually from chronic complications (cancer and cirrhosis). WHO has a goal for hepatitis elimination by 2030 and this will require substantial reductions in both cases and deaths from HBV, HCV, and HEV. HAV is transmitted fecal-orally and improved hygiene has reduced infections and seroprevalence rates. Very effective HAV vaccines are available that have long-term protection and are recommended by WHO according to endemicity and cost-effectiveness. Highly effective vaccines are also available for HBV. HBV vaccination at birth can effectively prevent the perinatal transmission of HBV. Western Pacific and Africa have the highest rates of infection. Universal introduction of HBV in Taiwan has been highly successful in terms of reducing the prevalence of infection, fulminant infections and long-term complications. WHO recommends universal HBV vaccination with 3 doses. Transmission of HCV is similar to that of HBV, but vaccine development has been challenging. Control of HCV currently depends on the antiviral treatment that has >95% cure rate but at a significant financial cost. Hepatitis D virus infection will worsen outcomes for those patients already infected with HBV. HEV can result fulminant hepatitis and has a high case-fatality rate in pregnant women. A vaccine has been developed in China, but limited data is available and there are no recommendations for general use.

The Closing Plenary Lecture on "*Future trends in vaccinology*" by Kim Mulholland (Murdoch Children's Research Institute and London School of Hygiene and Tropical Medicine) provided a reflective and sometimes sobering overview of where we are in terms of under-introduced new vaccines, reemergence of measles, vaccine hesitancy and the role-played by industry in our failure to address issues of equity. Current Human Papilloma Virus (HPV) vaccines are all similarly effective at preventing cervical cancer but the high price and limited supply still prevent these vaccines reaching millions of women, particularly those in the poorest locations. Optimal age of HPV vaccination and a number of doses remains unanswered questions. Pneumococcal conjugate vaccines (PCV) remain expensive despite their availability for 20 years. Serotype replacement needs continuous monitoring although mechanisms to do so are not always in place. New

pneumococcal vaccines with greater valences are under development. The need for RSV vaccines are high and research and development is ongoing with a range of approaches including maternal and neonatal vaccination. Despite four WHO prequalified rotavirus vaccines national introductions have remained sub-optimal in Asia. Neonatal dosing schedules of rotavirus vaccine show promise. Dengue vaccines are in development from three main companies. The Philippine experience as presented in detail during the conference has had a devastating impact on vaccine confidence. Factors affecting confidence include the information available to medical staff, journalists, and the community. Quality national web sites and vigilant management of crises are important. The role of industry is often not appreciated but lack of trust of “Big pharma” and perceptions of the profit motive being behind some safety scares may play a role. An important question to consider is why most major phase 3 trials are now controlled by industry. Many of these trials are of poorer quality with too many sites, unnecessarily large costs and results that may not be trusted. The reemergence of measles should challenge us to understand better what is going on and why this is happening. To what extent is the decline in vaccine uptake a global phenomenon or confined to isolated groups. Why is there an apparent decline in the respect for science? And why is there so little research in the field? We need to ask better questions to understand who the unvaccinated are. We should research alternative measles schedules and new generation measles vaccines. We need to question the status quo which is clearly failing. Finally, Prof Mulholland tackled the global priority of equity. There should be universal access to life-saving vaccines. We need to ensure that poor, marginalized communities such as minorities, refugees and internally displaced children are not excluded from national programs. We should consider removing lifesaving vaccines from the private sector when these vaccines are not part of national programs. We should acknowledge that it is not right that vaccines can bring billions of dollars to shareholders but not be accessible to millions of children.

IPAP partner symposia

These 60–90-min sessions, were developed and organized in collaboration with IPAP partner organizations.

New opportunities for adolescent vaccination

Adolescence is an important window for vaccination against several important diseases. HPV is an important example where national preadolescent vaccination programmes through school-based or primary care services have demonstrated a substantial impact on HPV infections and CIN2+ amongst girls and women and anogenital warts in the population. Programs with multi-cohort vaccination and high coverage had a greater direct impact and herd effects. Evaluation of a pilot vaccination program in Mongolia after 5–6 years revealed very favorable vaccine effectiveness for HPV16 and HPV18 in the range of 75%–92% in both 3 and 1 dose study, triggering the government’s decision to re-start HPV vaccination in 2020. The findings were presented by Tsetsegsaikhan Batmunkh (National Cancer Council of Mongolia). The second presentation covered Pertussis vaccination in adolescence and pregnancy (Zulkifli Ismail, Secretary

General, Asia-Pacific Pediatric Association). There has been a worldwide resurgence of pertussis disease in recent decades. The very young and young adults are susceptible. Household contacts and adolescents with waning immunity are important sources of infection in infants. Strategies to contain the spread of Pertussis include a vaccine boost in adolescents, vaccination of close contacts of infants (known as cocooning) and also maternal immunization (data suggests this is more effective than cocooning in protecting infants against Pertussis) and vaccination of health-care workers. Pramod Jog (former Committee Member of the International Pediatric Association) presented on ‘*Optimal adolescent vaccination schedules – review of WHO guidelines*’. He highlighted that the changing disease epidemiology and waning immunity in adolescence may increase the susceptibility of this age group to many vaccine preventable infections. He suggested school as an alternate vaccination site and concurrent administration of vaccines for optimal utilization of resources. Emphasizing that every medical encounter is an opportunity to vaccinate, the health-care practitioner must listen, evaluate and address legitimate concerns the patient or caregiver may have regarding the vaccination. It is important to provide the actual context of information, refute misinformation, provide valid information and educate while making a clear recommendation on specific vaccines.

Dengue and vaccine safety

Edsel Salvana (National Institutes of Health, University of the Philippines Manila) powerfully demonstrated how poor science communication can have a devastating negative impact on the entire NIP. The Philippines were the first country in the world to use Dengvaxia® for mass vaccination. While the science seemed solid, a persistent safety signal led some prominent epidemiologists and dengue researchers to urge caution, especially for use in mass programs. The rapid introduction of this new vaccine may have been politically motivated prior to an election. Subsequence analysis of clinical trial efficacy data showed an increased risk of severe dengue in seronegative recipients. When Sanofi announced these results, pandemonium ensued with a political witch hunt unfounded with accusations of genocide leveled against former health officials and the former president. Scientifically unsound autopsies claimed to show evidence of viscerotropism and neurotropism from the vaccine. The ongoing media frenzy resulted in vaccine confidence plummeting and a resultant measles outbreak killing hundreds. Lessons learned include proper treatment of safety signals, clearer science communication of new findings, educating the public on scientific methods and risk/benefit, and the need to insulate public health programs from party political influence.

Anh Wartel (Head of Clinical Development and Regulatory, International Vaccine Institute) reviewed in further detail the epidemiology and global disease burden of dengue. About half of the world’s population are at risk of dengue and there are an estimated 390 million infections per year, of which 96 million are clinical. Death should be rare if proper medical care is provided in a timely manner. Vaccination should be considered as part of an integrated

prevention and control approach. Dengvaxia® is still the only licensed vaccine and only indicated for individuals living in endemic areas who have already been exposed to dengue in the past, covering the age from 9 years and above up to 45 years depending on the market authorizations. A pre-vaccination screening is therefore recommended for this vaccine, which has logistic and programmatic implications. Other dengue vaccine candidates are being developed by other manufacturers and two are in late stage development.

Kyaw Zin Wai, Myanmar provided updates on dengue diagnostic and management guidelines. The disease can be suspected by clinical signs and symptoms but these can be nonspecific. Definitive diagnosis requires virus isolation, viral RNA detection, antigen detection, antibodies detection, and combined Ag/Ab detection. Rapid bedside diagnostic tests are available. Treatment for dengue is supportive with appropriate judicious fluid resuscitation. There is no advantage of colloids over crystalloids but the latter may be preferred in severe shock. Blood products may be given with severe hemorrhage. Other treatment approaches are under clinical development.

Gagandeep Kang (Christian Medical College, Vellore and previous member of Global Advisory Committee on Vaccine Safety, GACVS) provided updates on “*Dengue vaccine safety guidelines*”. The explanatory hypothesis for severe dengue in vaccinated individuals is that seronegative vaccinated subjects experience a secondary-like infection, whereas seropositive individuals experience a tertiary-like infection. The Strategic Advisory Group of Experts (SAGE) on immunization in 2018 considered the potential benefits and harms of giving dengue vaccine with and without pre-vaccination individual screening. Although overall a mass vaccination program without screening in endemic settings would provide overall population benefit, the increased risk of severe disease to seronegative subjects is an example of the “trolley problem” i.e. harming some individuals to benefit a larger number of individuals. During a 5-year follow-up, approximately 5 additional hospitalized dengue cases, or 2 additional severe dengue cases, per 1000 vaccinees with no previous dengue infection (i.e. dengue naïve subjects) could occur following vaccination, compared with unvaccinated seronegative children. The GACVS recommends that there should be enhanced measures to reduce exposure to dengue infection among populations where the vaccine has already been administered and adherence to other disease preventive measures. Prompt medical care is necessary for everyone with dengue-like symptoms, and post-marketing surveillance should be continued. Clear communication is paramount, as even with individual level screening as recommended by SAGE, some truly seronegative individuals may be vaccinated due to a false positive test result and even in seropositive individuals efficacy against dengue is high, but not 100%.

Respiratory vaccines

Respiratory pathogens cause a significant proportion of morbidity and mortality across all ages. Influenza is a major player in this field and one infectious disease that will certainly cause another pandemic, as discussed by Prabda Praphasiri (CDC Bangkok) in his presentation on ‘*Scaling influenza vaccine uptake*’. He discussed the goals of the Partnership for

Influenza Vaccine Introduction (PIVI) in creating sustainable vaccination programs and building immunization infrastructure, capacity and vaccine delivery systems in low and middle-income countries. Seasonal influenza vaccination programs are a foundation for a pandemic response; although more countries have influenza vaccine programs today than in the previous decade, there are still significant gaps in implementation. PIVI is, therefore, working with country partners to develop and implement vaccine programs and collaborate with contributing partners for the supply and distribution of vaccines as well as support evaluation, provide technical guidance and assistance to achieve a sustainable plan for vaccination.

Kim Mulholland presented an update on PCV coverage across Asia. Unfortunately, Asia has been the slowest region in the world to introduce PCVs and the children who do not receive PCV are typically the ones at greatest risk of pneumonia and death. This gap is contributing to the increasing inequity in child health across many parts of Asia. In addition, many of the countries that have yet to introduce PCV into NIP are themselves the largest markets for private sales of PCVs. RSV has a large morbidity and mortality burden. Interventions under development include RSV maternal vaccine and monoclonal antibodies. Clint Pecenka’s (PATH) presentation on “*Estimating the impact and cost-effectiveness of RSV interventions on infant health*” noted that either intervention can potentially avert millions of RSV cases, hospitalizations and deaths across the world with a large proportion in Asia. The data suggests that a monoclonal antibody could be more impactful than a maternal vaccine due to higher expected coverage, efficacy and longer duration of protection. There is also some evidence suggesting a significant impact on all-cause lower respiratory tract infections, averting millions of severe cases, hospitalizations, and deaths. RSV interventions are likely to be cost-effective in most low- and middle-income countries. Influenza carries substantial economic burden compounded by the phenomena of antigenic shift and drift which can lead to epidemics and global pandemics. The routine seasonal influenza vaccines are moderately effective (approximately 60% in seasons with good antigenic match). The challenges in global surveillance, tight manufacturing schedules and limitations in surge capacity in times of global pandemic are major concerns that are yet to be resolved. The concept of a universal influenza vaccine in the form of a heterotypic vaccine is still at the proof-of-concept stage. John Tam (APACI) presented various novel concepts and potential for the development of a universal influenza vaccine.

Enteric vaccines

This session was in partnership with the ROTA Council. Umesh Parashar (US Center for Disease Control and Prevention) emphasized that without vaccination rotavirus is the leading cause of acute gastroenteritis in young children and great public health benefits have been documented with the use of the four currently available WHO prequalified rotavirus vaccines. Herd protection and reduced convulsions have been unexpected additional benefits. Injectable vaccines and other strategies may improve the efficacy of rotavirus

vaccines in low-income settings. More effort is needed to ensure that rotavirus vaccines are included in all NIPs. Norovirus is the other leading cause of acute gastroenteritis in all age groups and two candidate vaccines have shown moderate efficacy. Challenges include who to vaccinate and how to protect against multiple genotypes with viral evolution. Kathy Neuzil (University of Maryland School of Medicine) covered Typhoid Conjugate Vaccines (TCV). Although typhoid is preventable by improvements in hygiene and sanitation, it remains a major health threat to poor and marginalized communities, particularly in the face of emerging antibiotic resistance. Typhar TCV (Bharat Biotech) has been licensed in India and prequalified by the WHO. The Typhoid Vaccine Acceleration Consortium (TyVAC) is supporting TCV clinical trials in Nepal, Malawi, Bangladesh, and Burkina Faso and preliminary results show excellent safety and robust immunogenicity. An interim analysis in Nepal showed >80% efficacy against laboratory-confirmed disease. SAGE recommends a single dose of TCV from 6 months with catch up to 15 years in endemic settings. Clint Pecenka highlighted that, for both rotavirus and typhoid vaccines, decision makers ask whether the vaccines are both cost-effective and affordable. Cost-effectiveness thresholds ideally should be country-specific, but most countries have yet to develop their own thresholds. Economic evaluations of rotavirus vaccination were thus compared to a relatively stringent threshold of 0.5 GDP and were found to be cost-effective relative to this threshold in nearly all countries. Affordability is impacted by budget, vaccine prices, and delivery costs. Current median price of rotavirus vaccines for non-GAVI and non-PAHO middle-income countries is USD7.75 (3.57–67.63) per dose but this should fall with increased uptake of the two new WHO pre-qualified Indian vaccines. Six studies have shown that TCVs are likely cost-effective in high-incidence countries. The current price per dose is USD1.5 but there is little information on the situation in non-Gavi countries. In addition to these economic costs, it is also important to think of the opportunity costs provided by freeing up beds to treat other illnesses and reduced overcrowding.

Communication, AEFIs, and advocacy

Communication and advocacy have been a core focus of ASVAC conferences. As a parent-patient survivor member organization, CoMO has a strong interest in vaccine safety to maintain a positive and broad acceptance of vaccination as the most effective preventative strategy against meningitis. Bruce Langoulant described the goals and relevant activities and strategies of CoMO. He explained WHO's initiative to "Defeat Meningitis by 2030" and introduced the audience to the Meningitis Progress Tracker and steps to expand CoMO's activities in Asia.

Speaking about "*Delivering vaccines: equity and the power of communities*" Craig Burgess (John Snow Inc.) overviewed global trends in rising inequities in immunization coverage, reasons for these and potential ways forward. It is important to better understand the needs and barriers faced by certain communities – specifically those living in fragile circumstances such as the urban poor, remote rural locations, and

those facing stigma and discrimination. Implementation research can better inform budget and policy decisions when investing in strategies to reach those left behind. The Equity Reference Group on Immunization provide practical recommendations for countries and partners to take forward and Governments and donors to invest in. There is an urgent need to engage communities in the planning, budgeting, implementation, and monitoring of services so immunization programs are more acceptable, appropriate and sustainable. Strategies for increasing equity and immunization systems include Global Routine Immunization Strategy and Practices (GRISP), Reach Every District (RED) strategy and Reach Every Community (REC). In addition, local and national investments for supply chain enhancements, addressing missed opportunities and developing community partnerships could all further promote equity.

Aye Mya Chan Thar (Assistant Director of Myanmar's Expanded Programme on Immunization) covered "*Assessing and communicating Adverse Event Following Immunization (AEFI)*". AEFI can be defined as any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the use of vaccine. The adverse event may be any unfavorable or unintended sign, an abnormal laboratory finding, a symptom or a disease. WHO's cause-specific definitions of AEFI are: (1) vaccine product-related reaction; (2) vaccine quality defect-related reaction; (3) immunization error-related reaction; (4) immunization anxiety-related reaction; and (5) coincidental event. Serious AEFIs are those that lead to death; hospitalization; persistent or significant disability or incapacity; congenital anomaly/birth defect; or other life-threatening event. AEFI causality assessment is vital and a WHO worksheet is available which includes checklists and algorithms. Proactive risk management is extremely important and there should be close coordination between AEFI response and communications strategies. Experience with Myanmar's JE campaign was shared. Key communication strategies include: (1) media briefing; (2) two-way communication with parents through radio, social media and hotlines; and (3) public opinion monitoring.

Ranjan Kumar Pejaver's Immunize India Project has successfully targeted families via their mobile devices to track vaccination status and provide reminders for boosters and completion of schedules. This is an effective and modern way of providing a proactive service to help families complete their relevant vaccination courses providing optimal protection levels individually and for communities.

Neuro vaccines

Anthony Marfin (PATH) noted that 11 closely related flavivirus makes up the Japanese Encephalitis (JE) complex. There are at least 15 JE vaccines, of which three are WHO prequalified. The JE virus is distantly related to Yellow Fever, Zika, and Dengue. Although less than 1% of those infected with the JE virus experience encephalitis, encephalitis is associated with mortality (20–30%) and long-term neurological impairment (30–50%). Prior to vaccination programs there were 70,000 cases per year in endemic countries. It is important to remember that with this

zoonotic disease transmission continues in the absence of human cases. JE vaccines have generally been shown to be cost-effective and adding long-term social and health care costs for neurological sequelae may make vaccines cost-saving. JE incidence fell 78% in Nepal following vaccine introduction and acute encephalitis syndrome fell 59% suggestion under-diagnosis of JE. 13 of 24 JE endemic countries did not have vaccination programs in 2009 and by 2019 this has fallen to 5 countries. Boosters doses may be required but requirements may vary in different settings. Although considered a rural disease, JE may have urban transmission.

Xingli Xu on behalf of Qihan Li (Institute of Medical Biology, Chinese Academy of Medical Science) provided updates on the Enterovirus 71 inactivated human diploid cell vaccine. The research and development process was outlined, including the animal infection models and challenge tests. A Phase 3 study was conducted on 12,000 children (6–71 months) in 7 counties and good protection was demonstrated with no safety concerns. The vaccine is a C4 sub-genotype and cross-neutralization tests on other genotypes have been undertaken. In December 2015 the vaccine was approved by China Food and Drug Administration. A phase 4 study conducted in Xiangyang during 2016–2017 identified one infection in 40,724 vaccinated children and 29 infections in the approximately 100,000 unvaccinated children.

Vaccines to prevent brain damage in newborns and fetuses were reviewed by Hiroyuki Moriuchi (Nagasaki University). Congenital cytomegalovirus (CMV) disease burden varies but rates can be as high as 1–2%, resulting in mortality, long-term disability, and enormous economic burden. Despite a number of CMV vaccines in early development, challenges exist since maternal immunity is not completely protective. Zika virus is spread by mosquitoes, but also sexually and transplacentally. Infections during the first trimester can cause neurological damage in the fetus, including microcephaly. Asia is regarded as endemic for the Zika virus but circulating strains may be less pathogenic. However, preexisting dengue virus infection may increase the risk of serious Zika virus infection. Congenital rubella syndrome remains a threat in those countries where susceptible populations exist, such as Japan and Vietnam.

Terapong Tantawichien (Chulalongkorn University) concluded the session with an update on rabies vaccine guidelines. The key success of the substantial reduction of human rabies in Asia has been the increased accessibility to post-exposure prophylaxis (PEP) using an improved regimen of intradermal (ID) rabies vaccination, intensified follow-up of exposed patients, public education, mass dog vaccination and control of stray dogs. New WHO recommendations are for a shortened course of PEP. The maximum benefits of rabies immunoglobulin (RIG) are gained when it is administered directly into the wound. Two booster doses of rabies vaccine (ID or IM) are recommended on days 0 and 3 or a single booster vaccination (4 doses of 0.1-mL ID) for exposed pre-immunized individual. PEP can be simplified to two-site ID doses on days 0 and 7.

Panel discussions

National Vaccine Institute panel discussion ASEAN vaccine security and self-reliance (AVSSR)

The panel on ASEAN Vaccine Security and Self-Reliance (AVSSR) emphasized the importance of a regional effort to ensure vaccine security, the current updates on the successes, challenges, and opportunities of the AVSSR. Nakorn Prem Sri (Director of NVI, Thailand) began the session by addressing the historical background and objectives of AVSSR workshops that started in 2014. The aim of the workshops has been to increase regional collaboration and to achieve access and security of quality and safe vaccines. Stephane Guichard (Regional Advisor of WHO-SEARO) discussed the importance of regional collaboration and future opportunities. UNICEF supply division described various areas of vaccine procurement including price sharing, joint tendering or pooled-procurement, and its challenges, requirements, prerequisites, appropriate mechanisms, and benefits among the region. Thailand's Food and Drug Administration and its National Health Security Office (the national procurement agency) shared experiences on regulations and the impact on vaccine collaboration in the region, plus challenges and opportunities of harmonizing vaccine regulations. The National Health Security Office also shared details of the current vaccine procurement mechanism for Thailand's population, and the feasibility and challenges for regional pooled-procurement. Thailand is supporting this initiative for a regional pool-procurement mechanism and emergency stockpiling among ASEAN Member States through an appropriate platform or mechanisms in compliance within national laws and local context.

Vaccine hesitancy

Increasing and maintaining vaccination uptake is vital for vaccines to achieve their effectiveness and success in avoiding vaccine-preventable diseases. Vaccination is not only the most successful health intervention ever; it reduces inequalities in our societies and brings about significant social and economic returns that go beyond the individual and family and the society as a whole. There is, unfortunately, a very real and increasing resistance to vaccination around many parts of the world that is jeopardizing the progress and success of this very valuable health intervention. WHO has listed Vaccine Hesitancy as one of the 10 threats to global health in 2019. This session was designed to highlight this important problem by a panel of leaders in the region. The panel was moderated by Daniel Goh (National University of Singapore) and Zulkifli Ismail and with H.T. Wickramasinghe (Sri Lanka) and Saw Win (Myanmar) as panelists. Points discussed include: What is vaccine hesitancy? What are examples in the region? What is the impact around us? What are some factors, root causes, and reasons? What are some strategies to address the problem? The panel had a vibrant discussion with active participation from the audience, covering a good range of inputs from countries in the region. Key take-away points included:

- (1) Vaccine attitudes are a continuum, ranging from total acceptance to complete refusal. Vaccine-hesitant individuals (or families) are a heterogeneous group within the continuum.
- (2) Vaccine hesitancy is highly infectious; in this age of social media and mass communication (or miscommunication), erroneous information can be propagated very rapidly with dire consequences.
- (3) Strengthening vaccine programs is important to improve vaccine uptake. This includes building trust and confidence in vaccine effectiveness, reducing complacency in the impact of vaccine-preventable diseases, improving access and availability and affordability of appropriate vaccines. These would involve strengthening vaccination program coordination, building stakeholder relations, identify vulnerable populations, addressing concerns promptly and adequately through communications and dissemination of information.

The session drew a lot of interest and participation but unfortunately, the time allocated was rather short (30 min) to go into greater depth of discussion. It, however, highlighted the importance, interest, and awareness of vaccine hesitancy in the region and prompts the organizers to allocate more time in future ASVAC meetings dedicated to this important topic.

Meet the experts

ASVAC's final session tackled practical issues in a question and answer format following short presentations on "*Senescence and Vaccination*" (Shelley De la Vega, University of Manila); "*Immunisation in office practice boosting your memory cells priorities and practicalities*" (Pramod Jog); and "*Assessment and Capacity Building for School-Based Health Program Indonesia's experience*" (Sri Rezeki S. Hadinegoro, University of Indonesia). The session was moderated by Ye Myint Kyaw (University of Medicine 1, Yangon) and Lulu Bravo (University of Philippines Manila)

Asian EPI managers meeting: "Enhancing immunisation programmes: new opportunities and technical updates"

This workshop was held on 11–12 September, Naypyidaw, Myanmar. It was hosted by the Ministry of Health and Sports, Myanmar, and led by Htar Htar Linn (EPI manager) with support of WHO, UNICEF, ASVAC and other partners including PATH, the ROTA Council, PIVI and APACI. H.E. Dr Myint Htwe, Union Minister of Health and Sports, Myanmar opened the meeting. Jayantha Liyanage (WHO SEARO) reviewed the progress of the Decade of Vaccines (2011–2020). Although, only 3 of 5 targets of the Global Vaccine Action Plan have been met in the region much progress has been made. The Immunization Agenda 2030 has a global strategy to leave no one behind by linking to primary health care and universal health coverage agendas, expanding vaccinations across the life course, with better use of sub-national data and country-driven approaches to make

people the center of everything. This new vision and strategy will be endorsed at the World Health Assembly in 2020.

Three of the seven workshop sessions were vaccine-specific: influenza, rotavirus and HPV vaccines. John Tam over-viewed of influenza vaccines and noted how manufacturing capacity would be unable to match timing and volume in case of a global pandemic. Influenza vaccines are shown to be both effective and cost-effective in low- and middle-income countries. Prabda Praphasiri outlined the process of influenza vaccine policy development in low- and middle-income countries. Pandemic influenza is one of the top 10 global health threats and robust seasonal influenza vaccination programs are critical to a country's ability to respond quickly and effectively to a pandemic. Panome Sayamoungkhoun (EPI Manager, Laos PDR) and Ha Thi Cam Van (Ministry of Health, Vietnam) provided insights into country plans for scaling up influenza vaccination of health-care workers and other target groups. In the Rotavirus Vaccine session, Mathu Santosham (John Hopkins University), reviewed the significant impact that rotavirus vaccines have had, but noted that Asia has lagged in rotavirus vaccine introductions. Arup Deb Roy (John Snow Inc), shared India's impressive success of rolling out its two indigenous rotavirus vaccines to a birth cohort of over 26 million newborns. Best practices and lessons learned included evidence-based planning, effective implementation, and continuous monitoring. Kamran Mehedi (John Snow Inc) shared some of the challenges that Bangladesh has experienced regarding the planned introduction of the rotavirus vaccine. Theingi Win Myat reviewed Myanmar's rotavirus surveillance activities and plans for vaccine introduction in 2020. Finally, for the HPV vaccine session Kim Mulholland, opened by reviewing cervical cancer risk factors and burden and emphasized that the vaccine still remains out of reach of many girls and women due to very high prices and limited availability. Control of cervical cancer is achievable with an effective screening program, HPV vaccination and effective detection and treatment of cases. Tsetsegsaikhan Batmunkh reported how a pilot HPV vaccine introduction program had resulted in an anti-vaccine response and stopping of the program in Mongolia. Manjula Kariyawasm (Epidemiology Unit, Ministry of Health, Sri Lanka) shared decision-making and implementation experience of Sri-Lanka's school-based HPV vaccination program. Suchada Jiamsiri (Ministry of Public Health) shared Thailand's experiences with a pilot school-based program and subsequent problems with vaccine shortages.

The remaining four sessions covered a range of topics including programmatic updates: strengthening the supply chain and introduction of the new tool on Effective Vaccine Management Assessment (EVMA 2.0) (Chandrasegarar Solomon, UNICEF Regional Office Amman and Abu Obeida Eltayeb, Regional Office Bangkok); technical updates on diphtheria (Shalini Desai, WHO HQ); invasive bacterial disease (Kim Mulholland); Japanese Encephalitis and Typhoid (Anthony Marfin); challenges and opportunities with Acute Flaccid Paralysis surveillance (Sudhir Joshi, WHO), measles elimination (Jayantha Liyanage); responding to outbreaks of emerging vaccine-preventable disease (Sudhir Joshi and Jayantha Liyanage); Hepatitis B birth dose strategies (Khin

Pyone Kyi, NITAG, Myanmar); and communication strategies demonstrated with a role-play using the caregiver journey framework as a tool to better understand and develop strategies to promote vaccination demand (Dynes Michelle, CDC staff, UNICEF Bangkok).

Preconference workshops

South-East-Asia sub-regional “Vaccine Procurement Practitioners Exchange Forum” (VPPEF)

For its seventh edition, the VPPEF was jointly organized by UNICEF, the National Vaccine Institute (NVI) Thailand, the Learning Network for Countries in Transition (LNCT) and ASVAC. The themes of the VPPEF were aligned with the ASVAC, including the introduction of new vaccines to national immunization programs, with a focus on vaccine security to ensure the sustained, uninterrupted supply of affordable vaccines of assured quality. One important objective of the VPPEF is to build a community of practice on vaccine procurement at the sub-regional level. The content of the discussions and exchange between countries and partners were very rich, due in large part to the diversity in their vaccine procurement modalities (i.e. self-procuring, self-producing and procuring through UNICEF) and opportunities to share procurement practices and challenges. Country delegations from nine countries (Indonesia, Lao PDR, Mongolia, Myanmar, Papua New Guinea, Philippines, Thailand, Vietnam and Timor-Leste) shared experiences in the areas of vaccine decision-making to facilitate the sustained introductions of new vaccines to their Expanded Programme on Immunization, including the use of health economics and market intelligence in their decision-making, and regulatory considerations to source quality-assured vaccines. A key outcome of the VPPEF was countries' commitment to a series of actions to improve their procurement of vaccines aligned to their national health plans. To support this effort, discussions will continue online through the VPPN (Vaccine Procurement Practitioners Network) and LNCT and further leverage the cross-country collaboration through the sub-regional initiative such as the AVSSR led by the NVI of Thailand.

Pneumococcal disease prevention in the era of conjugate vaccines: what's new?

The Asian Strategic Alliance for the Prevention of Pneumococcal diseases (ASAP) is a group of clinicians dedicated to the prevention of pneumococcal diseases in the region. As part of its regular efforts to improve the understanding and prevention of pneumococcal diseases, it hosted a pre-conference symposium focusing on reviewing new developments in the area of pneumococcal disease prevention. The series of talks covered updates on the pneumococcal seroprevalence status and vaccine use, the changing disease burden and prevention strategies in adults as well as the role and use of PCV in at-risk populations. There were close to 100 attendees at this session with a fairly equal local and international delegate representation.

Workshop by Confederation of Meningitis Organizations (CoMO): help us make a difference to meningitis across Asia at ASVAC

CoMO has a wide representation of members across the world but the Asian region is under represented. The workshop promoted CoMO to participants by providing updates on the Eliminating Meningitis by 2030 project and a new Project Tracker tool to encourage more regional membership and closer relationships with Asian health leaders. Understanding the barriers in countries toward meningitis awareness and preventative action through vaccination is an ongoing mission and varies from country-to-country. Networking with, and identifying, new CoMO members who are typically parents and patient survivors who have engaged or wish to engage in local advocacy along with professional Friends of CoMO, who are typically health professionals with meningitis and/or are pro-vaccination, is the ongoing CoMO mission. At ASVAC 2019 in Myanmar, we met many interested doctors and pediatricians who would like to become Friends of CoMO and we will be establishing a Myanmar network of Friends. The Meningitis 2030 project of WHO and our Project Tracker will feature strongly in our work with the new network as it will with the other 75 CoMO members across 35 countries.

ASVAC 2019 Vaccinology Masterclass

The ASVAC Vaccinology Masterclass was one of the pre-conference events at the 2019 conference in Yangon. This is the second edition of the Masterclass and attracted over 172 attendees (117 locals and 55 international). The five-hour program was compacted to the Friday afternoon before the conference. The program opened with an overview of the history and impact of vaccination by Mathu Santhosham, followed by a review of basic vaccine immunology (including basic immune responses and the role of adjuvants, vaccine clinical development, diseases surveillance in vaccination strategies, concept of cross-protection and herd immunity) delivered by a panel of speakers. A session on communication strategies in vaccination, debunking the myths and addressing the anti-vaccine movement was delivered by Zulkifli Ismail of Malaysia who highlighted the *Immunise4Life* program aiming to instill vaccine confidence. A practical walk-through vaccines across the ages; from infancy to adolescence, in pregnancy and in the elderly brought us up to speed with the latest recommendations and concepts in disease prevention across the lifespan. A highlight of the Masterclass was the clinical case presentations and quiz. To end off the program, we took a glimpse into the future in the areas of vaccine technology and advances in delivery, brought to us by Philippe Buchy. The program was very well-received and will certainly be a regular feature at future ASVAC conferences.

Industry symposia

There were six industry symposia. Bharat Biotech's pre-conference evening symposium overviewed the company's vaccine portfolio and progress and in particular the inclusion of their rotavirus vaccine in India's NIP.

Takeda's lunch symposium on the first day covered details of dengue disease burden in Asia, the background to understanding the dengue immune response to infection and vaccination, as well as an update on Takeda's dengue tetravalent live attenuated vaccine candidate (TAK-003). Phase II studies showed that this vaccine elicits tetravalent neutralizing antibodies against DENV-1, 2, 3 and 4 in both seronegative and seropositive recipients for at least 2-years post-vaccination. There was a lower incidence of symptomatic dengue in TAK-003 vaccine vs. placebo recipients during the 18 months of febrile surveillance, and its safety profile was also considered acceptable.

GSK's evening symposium covered two topics: strategies to improve vaccine effectiveness through providing broad protection and new opportunities for maternal immunization, particularly focusing on the influenza vaccine.

The lunch symposium on the second day included presentations from Serum Institute of India outlining the company's vaccine portfolio and new vaccines in development. Their rotavirus vaccine has also been included in India's successful roll out rotavirus vaccines in the NIP. MSD focused on HPV vaccine and opportunities for disease control in Asia-Pacific Region, and AJ Vaccines presented updates of the immunogenicity and safety of their IPV-A1 vaccine, which is a stand-alone adjuvanted inactivated polio vaccine that has been evaluated in a Phase 3 trial in the Philippines.

Summary

High prices of vaccines are still preventing millions from being protected from vaccine-preventable diseases, but more puzzling and worrying is trying to understand why individuals and communities should choose not to protect

themselves. Although vaccine hesitancy was a topic of interest in ASVAC 2017 it was not yet of the level of concern as identified in ASVAC 2019. Many of the conference sessions touched on this important topic, either directly or tangentially. Participants were much better able to understand why vaccine hesitancy is listed by WHO as one of the top 10 threats to global health in 2019. Lack of equity and high vaccine prices was the other recurring conference theme that clearly needs to be addressed if we are to achieve the vision of Decade of Vaccines of ensuring that no-one dies of a vaccine-preventable disease. More needs to be done at many levels to improve equity, both within and between countries. The potential for pooled procurement of vaccines was discussed but regulatory, political and other hurdles remain. Equity should be high on the agenda whenever vaccines and immunizations are discussed, whether within households, within communities, within NITAGs, within Ministries of Health, within Ministries of Finance, within WHO, UNICEF and Gavi, and most important within boardrooms. More needs to be done to ensure that price is never the reason why someone cannot to be immunized with a life-saving vaccine.

Disclosure of potential conflicts of interest

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