The 5th International Vaccinology Workshop in Japan 2012
Vaccines as solutions for healthcare issues: Challenges and Expectations

International House of Japan
5-11-16 Roppongi, Minato-ku, Tokyo 106-0032
February 18-19, 2012
The Scientific Committee

• Stanley PLOTKIN
• Kazunobu OUCHI
• Takashi NAKANO
• Katsuhiko MIKOSHIBA
• Alain BOUCKENOOGHE
• Catherine DUTEL
• Daisuke TSUZUKI
• Teruya NAGAO
Dear participants,

It is our pleasure to welcome you to ‘The 5th International Vaccinology Workshop’ in Tokyo!

France and Japan have a history of excellent research in vaccine, immunity and infectious diseases and it is our great pleasure to provide opportunities for brilliant international and Japanese experts in this field to meet and exchange knowledge.

This series of Workshops was first organized in 2003, thanks to the wish of Prof. Hitoshi Kamiya.

He wanted to bring to Japan information on the development of new vaccines and the public health effect of both new and old vaccines.

In the 4th Tokyo Workshops many subjects were discussed which were of interest to both Japanese and foreign scientists. Those workshops were successful in stimulating new ideas and therefore the participants wished us to organize a 5th one.

This 5th workshop has been organized by Fondation Mérieux, under the aegis of the French Embassy in Japan, Association Pasteur Japan (affiliated with Institut Pasteur, Paris)

This year we will discuss vaccination for Pertussis, Nosocomial pathogens, Poliomyelitis vaccination and Travelers Vaccines.

We hope that all participants will enjoy the talks and discussions in a spirit of scientific communication and improvement in preventive medicine.

The Scientific Committee
Fondation Mérieux

Fondation Mérieux is an independent family foundation created in 1967 by Doctor Charles Mérieux with official charitable status by French government in 1976. This is a culmination of a family’s involvement in scientific research for over a century.

The headquarters of the Fondation are in the center of Lyon, in the building where Charles Mérieux first set up his laboratory in 1911.

Fondation Mérieux contributes impartially by promoting the transfer of knowledge and the sharing of scientific innovations and supporting research projects into communicable diseases and their prevention.

Fondation Mérieux focuses its expertise in clinical biology to further the fight against infectious diseases among vulnerable populations. It works directly with local actors to create and strengthen biology laboratories, and link them together via a network to allow them to develop their local capacities in the long term.

Fondation Mérieux helps to disseminate and increase awareness of scientific innovations throughout the world by holding training and conferences for the international public health community.

Association Pasteur Japon

Established in March 2005 with the initiative of Institut Pasteur, as a specified non-profit organization under the NPO law of 1998, Association Pasteur Japon is promoting, as a main activity, the exchange of researchers in the field of medical science between Japan and Institut Pasteur network and at the same time, the dissemination of most advanced medical information with the aim of contributing to the advancement of public health in Japan and throughout the world.

Up to now, Association Pasteur has sent more than 10 Japanese post-doctoral researchers to Institut Pasteur in Paris, co-funded by the French Ministry of Foreign and European Affairs.

For the success of the 5th International Vaccinology Workshop

The Embassy of France has the pleasure to support a welcome initiative by Fondation Mérieux: the organization of a workshop dedicated to infectious diseases. As in many aspects of medical research, international cooperation has become a key factor in the success of fighting infectious diseases. The resurgence of diseases that were thought to be almost eradicated and the appearance of new ones in countries that were so far pared makes it all the more essential to share resources and knowledge. We hope that this goal will be achieved through this seminar.

Dr Florence Rivière-Bourhis  
Counsellor for Science and Technology  
Embassy of France in Japan
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**Opening remarks**
09.00 - 09.50

**Opening session**
09.00 - 09.10

Dr Stanley PLOTKIN
Dr Kazunobu OUCHI
Dr Takashi NAKANO

**Dr Hitoshi KAMIYA Memorial Lecture**
09.10 - 09.50

**The Memorial of Dr Hitoshi Kamiya**

- Biography of Dr Hitoshi Kamiya
- Scientific lecture: Vaccines against Cytomegalovirus, a cause of many diseases

Dr Toshiaki I哈Ra
Dr Stanley PLOTKIN

**Session 1**
09.50 - 12.30

**Adult Pertussis. What should we do for pertussis in adolescent and adults in Japan?**
Chaired by Dr Okada, Dr Wirsing von König, Dr Kikuchi

**Global Pertussis Epidemiology**
09.50 - 10.20

Dr Carl-Heinz WIRSING VON KÖNING
# Scientific Programme

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### Session 2

**Vaccines against nosocomial pathogens.**

**Opportunity of vaccine against Nosocomial Pathogens.**

**Chaired by Dr Daum, Dr Bouckenooghe, Dr Kato, Dr Tateda, Dr Inamatsu**

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### Session 3: Japan Poliomyelitis Vaccination Update

How to manage the switch from OPV to IPV in the Immunization schedule?

Chaired by Dr Nakano, Dr Bakker, Dr Vidor, Dr Plotkin

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Chaired by Dr Kano, Dr Hamada, Dr Thisyakorn, Dr Ouchi, Dr Watanabe Dr Steffen

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Keynote lecture

The Memorial of Dr Hitoshi Kamiya
Dr Toshiaki IHaRA
Biography of Dr Hitoshi Kamiya

Dr Stanley PLOTKIN
Scientific lecture: Vaccines against Cytomegalovirus, a cause of many diseases
Session 1

Adult Pertussis.
What should we do for pertussis in adolescent and adults in Japan?
Global Pertussis Epidemiology

Carl-Heinz WIRSING VON KÖNIG
Institut für Hygiene und Labormedizin - HELIOS Klinikum Krefeld
Germany

Pertussis remains endemic worldwide, even in countries with sustained high vaccination coverage. Resurgence of pertussis in the post-vaccination era has been reported in many areas of the world. As a vaccine preventable disease, pertussis is notifiable in most countries. However, epidemiological data from various national surveillance systems can be contradictory and they may not reflect the true burden of diseases.

Newer data are available to describe the basics for pertussis epidemiology, and several surveillance systems are in place that can be compared in respect to their suitability for other countries. Depending on the information that surveillance systems are meant to provide, epidemiological tools are available ranging from seroprevalence studies, statutory notification systems, and sentinel surveillance studies towards a theoretical ideal surveillance methodology.

Pertussis epidemiology also needs standardized laboratory capabilities and greater harmonization of clinical definitions. Taken together this will lead to a more comprehensive surveillance and a better estimate of the real burden of pertussis infections worldwide.
Implementation of pertussis vaccine in adult in Japan: Why, Which vaccine and How

Hajime KAMIYA
National Institute of Infectious Diseases
Infectious Disease Surveillance Center - Japan

Pertussis is an acute respiratory infectious disease caused by a respiratory tract infection with *Bordetella pertussis*. *B. pertussis* is as highly contagious as measles virus and transmitted through direct contact with discharges from upper respiratory mucous membranes of infected persons or with droplet. Vaccination is most effective in pertussis prevention and control. Owing to widespread vaccination, pertussis cases in the world markedly decreased. In Japan, current diphtheria-tetanus-acellular pertussis (DTaP) combined vaccine containing purified antigen (the main principles are detoxified PT and FHA) was introduced in 1981 and then cases steadily decreased. However, recently, it has been shown that adolescents and adults become susceptible due to the waning of vaccine-acquired immunity and new strategy of control seems necessary.

In this session, I would like to present the current situation of adolescent and adult pertussis in Japan, point out some of the reasons why there are many pertussis among adults, and efforts and challenges of Japanese researchers to decrease this disease.
Options for protecting newborns against pertussis: cocoon strategy; maternal immunization; neonatal immunization

Peter McIntyre
National Centre for Immunisation Research and Surveillance, (NCIRS) Australia

As it was prior to the introduction of pertussis vaccine, the greatest risk of death and severe morbidity continues to be among infants, even in countries with long-standing high coverage of pertussis vaccines. In such countries, although the absolute numbers of infant deaths have fallen greatly, those that remain occur almost all occur before 2 months of age (when the first dose of vaccine is currently given) and hospitalisations from pertussis predominantly occur before the 3rd dose of pertussis vaccine at 6 months. Potential options to reduce or eliminate this severe morbidity include indirect (cocoon) protection of the infant through immunisation of close contacts and direct protection through maternal immunisation during pregnancy or immunisation of the infant soon after birth. Each of these approaches has limitations, evidence gaps and challenges in implementation.

The challenge in providing indirect protection by immunisation of close contacts lies in how extensive the “cocoon” needs to be (mother only, mother and father, or all adults in close contact including those outside the household). There is evidence that for the youngest infants, those at greatest risk of death, there is a disproportionate risk of transmission from the mother. Lack of success of the cocoon approach could be from insufficient breadth of the cocoon (from narrow recommendations, implementation difficulties or a wider circle of potential transmission than expected) or limited effectiveness of such vaccination in reducing transmission to the infant. Insufficient breadth of the cocoon might only be addressed by more general adult immunisation and its effectiveness requires high quality field studies; further data should arise soon from studies in the US and Australia. Recently, the relevant Australian expert committee judged cocoon immunisation insufficiently cost-effective for inclusion in the national immunisation program.

The challenge for direct protection strategies is lack of empiric evidence of effectiveness, despite both maternal and neonatal immunisation being identified as potential strategies and some early trials in the 1930s and 1940s.
For maternal immunisation, the theoretical basis seems sound, as high titre antibody titres are achieved in the mother and there is preferential transport of IgG to the baby in the last trimester of pregnancy, producing very high titres at birth. It is presumed that this would provide early protection but the degree to which infant response to pertussis-containing and other vaccines after birth would be affected is unknown, as is the proportion of women who would accept a recommendation to immunise in pregnancy and whether immunisation in pregnancy would need to be repeated. Following the recent ACIP recommendation, information on both these counts should be rapidly forthcoming.

Neonatal immunisation has been studied for a number of vaccines and is routine practice for Hepatitis B, BCG and in some settings OPV. It is under study for pneumococcal conjugate vaccine. For pertussis, work on neonatal immunisation was hampered for many years by early but flawed reports of “immune tolerance”. Neonatal immunisation has been studied again in the acellular era. Diphtheria-tetanus-pertussis vaccine was ineffective in a US trial but small trials of monovalent acellular pertussis vaccine in Italy, Germany and Australia have shown early infant responses and no evidence of tolerance. Over 400 babies have been recruited into a study of neonatal immunisation in Australia with a range of immunogenicity outcomes; first results should be available during 2012.

Severe morbidity, and especially death, in young infants from pertussis, a disease with long-standing immunisation in place, has a high public impact. Direct prevention strategies are most closely targeted to prevent severe morbidity in young infants. Success may require a combination of approaches, all of which have challenges to overcome in evidence for effectiveness, implementation and not least demonstration of cost-effectiveness in an environment of increasing competition for scarce public health resources.
Session 2

Vaccines against nosocomial pathogens.
Opportunity of vaccine against Nosocomial Pathogens.
Nosocomial infections: issues and challenge

Kazuhiro TATEDA
Department of Microbiology and Infectious Diseases - Toho University School of Medicine - Japan

Nosocomial infections are a serious concern in the world. Several organisms, such as MRSA, Pseudomonas aeruginosa and Clostridium difficile, are leading cause of these life-threatening infections. P. aeruginosa is a glucose-non-fermentative gram-negative rod, and frequent nosocomial organisms associated with hospital-acquired pneumonia, urinary tract infections and sepsis. Especially recent days, appearance and spreading of multiple-drug resistant P. aeruginosa (MDRP) have posed a new dilemma in the clinical setting. Since MDRP usually demonstrate resistance characteristics to a variety of antibiotics, including carbapenem, fluoroquinolone and amynoglicosides, there are only few compounds left for the treatment. Several investigators have tried to develop vaccine against P. aeruginosa infections or preventions, although we could not experienced clinical success in vaccine strategy against P. aeruginosa infections. In this presentation, the history and reviews of P. aeruginosa vaccine strategy will be summarized and several new approaches will be introduced. Especially, importance and impact of quorum-sensing systems and autoinducer molecules, such as homoserine lactone, as a vaccine target will be discussed.
Progress towards a vaccine against *Staphylococcus aureus*  

Robert S. DAUM  
University of Chicago - USA  

High attack rates and the ability of *Staphylococcus aureus* to develop resistance to all antibiotics in medical practice heightens the urgency for vaccine development. *S. aureus* causes many disease syndromes, including invasive disease, pneumonia, and skin and soft tissue infections. It remains unclear whether a single vaccine could protect against all of these. Vaccine composition is also challenging. Active immunization with conjugated types 5 and 8 capsular polysaccharides, an iron scavenging protein, *isdB*, and passive immunization against clumping factor A and lipoteichoic acid have all proven unsuccessful in clinical trials. Many experts advocate an approach using multiple antigens and have suggested that the right combination of antigens has not yet been identified. Others advocate that a successful vaccine will require antigens that work by multiple immunologic mechanisms. Targeting staphylococcal protein A and stimulating the T-helper 17 lymphocyte pathway have each received recent attention as alternative approaches to vaccination in addition to the more traditional identification of opsonophagocytic antibodies. Many questions remain as to how to successfully formulate a successful vaccine and to whom it should be deployed.
Clostridium difficile infections in Japan

Haru KATO
Department of Bacteriology II - National Institute of Infectious Diseases - Japan

*Clostridium difficile* is well known as an important cause of healthcare-associated infection. Specific strains have been documented to be endemic/epidemic, and patients infected with particular strains were more likely to develop severe disease, suggesting that strain differences play some role in the pathogenicity of this organism. PCR ribotype 027 has been reported to be responsible for multiple outbreaks and a major portion of the increase in *C. difficile* infection (CDI) rates in North America and Europe in the past decade. In Japan, outbreaks caused by 027 strain have not reported so far, while some sporadic CDI cases due to 027 strain have been found. The types found to be frequently endemic/epidemic in Japanese hospitals are PCR ribotypes smz, trf, 002, and 014, of which type trf strain is toxin A-negative, toxin B-positive (A⁻B⁺). Our experience with strain typing showed that two types of *C. difficile* (PCR ribotypes smz and trf) were found to be spreading in multiple hospitals. The emergence of CDI caused by A⁻B⁺ strains has been reported in Korea, Poland, and Ireland as well as in Japan. Fulminant colitis cases caused by A⁻B⁺ strain will be shown and discussed.
Nosocomial Diseases - Clostridium difficile: are we making progress?

Alain BOUCKENOOGHE
Sanofi Pasteur - Singapore

*Clostridium difficile* infection (CDI) is the most common cause of nosocomial infectious diarrhea in Europe and North America, and has also now spread to communities outside the hospital environment. In response to the increasing disease burden of *C. difficile*-associated diarrhoea, Sanofi Pasteur is currently undertaking the clinical development of a vaccine for primary disease prevention. The candidate is a toxoid vaccine, designed to stimulate immunity against exotoxins A and B, which are secreted by the *C. difficile* bacterium. These toxins are highly injurious to the human colon, causing enterocyte cell death, a marked acute inflammatory response and severe mucosal injury.

Results from Phase I studies in healthy adult (18-55 years) and elderly (≥65 years) volunteers have been encouraging. The candidate vaccine has been well tolerated and highly immunogenic against exotoxins A and B. A subsequent dose-ranging, Phase II study, with primary objectives to further describe the safety and immunogenicity of the candidate vaccine and also to record the occurrence of first-time CDI episodes, is now actively enrolling 650 participants. Data from this study will assist in Phase III development. Although still at an early stage, results with this vaccine are encouraging and support continued clinical development for the primary prevention of *C. difficile*-associated diarrhoea.
Session 3

Japan Poliomyelitis Vaccination Update.
How to manage the switch from OPV to IPV in the Immunization schedule?
Poliovirus Vaccines: Current Status in Japan

Hiroyuki SHIMIZU
WHO Global Specialized Polio Laboratory - National Institute of Infectious Diseases - Japan

In Japan, indigenous poliomyelitis was eliminated in the 1970s and the last type 1 poliovirus was isolated from an acute flaccid paralysis (AFP) case in Nagano Prefecture in 1980. No wild polioviruses have been isolated for nearly 20 years after the identification of a wild type 3 poliovirus from a non-AFP case in Shiga Prefecture in 1993. To reduce the inherent risk of OPV, vaccine-associated paralytic poliomyelitis (VAPP) and polio outbreaks due to circulating vaccine-derived polioviruses (cVDPVs), introduction of IPV (DPT-IPV and standalone IPV) to polio immunization in Japan is urgently needed and the development of IPV products is ongoing. Accordingly, further polio immunization strategies, including the immunization schedule using DPT-IPV and standalone IPV, interchangeability of different IPV products (Sabin-IPV and conventional IPV), intensified polio surveillance activities, and appropriate polio vaccine stockpile, should be developed to maintain polio-free status in Japan prior to the introduction of IPV.

The introduction of IPV products in the near future and serious public concerns about the remaining risk of VAPP due to routine OPV immunization in Japan have resulted in the apparent decline in routine OPV immunization rate in 2011. Although nationwide OPV coverage rate in autumn has not been reported yet, a survey by MOHLW indicated that the number of immunized children in early 2011 was 17.5% lower than that in 2010 (10.2-22.4% lower at different geographical areas). Some of the unimmunized children with OPV may be immunized with imported IPV mainly at the private sectors; however, the recent development of polio immunity gaps in some populations should be carefully monitored. In this regard, risk assessment and preparedness plan for the importation of wild polioviruses and emergence of cVDPV will be urgently needed for the transition period from OPV to IPV in Japan.
Sabin-IPV development for clinical studies and technology transfer to local manufacturers

Wilfried A.M. BAKKER
National Institute for Public Health and the Environment
Vaccinology Unit - The Netherlands

RIVM developed a production process for Sabin-inactivated polio vaccine (Sabin-IPV) based on the current large-scale Salk-IPV production technology. The use of attenuated Sabin instead of wild-type Salk polio strains provides additional safety during vaccine manufacturing. Further, it opens the opportunity for process improvements. In this way, a more affordable IPV is strived for.

For that, a lab-scale process was set-up based on historical Salk-IPV manufacturing data. Currently, both USP (cell and virus culture) and DSP (clarification, concentration, purification and inactivation) unit-operations approximate the large-scale. Using this model, a modified process was developed to generate Sabin-IPV for the currently ongoing phase I clinical trials. Next to that, technology transfer to local vaccine manufacturers has started. An update on these activities will be given.

In parallel, a research program is ongoing to further modernize and optimize the process, and reduce the cost per dose. In USP, increased cell densities, were realized. After subsequent virus culture and purification, this resulted in significantly increased product yields. Currently, the obtained results in both USP and DSP are being confirmed, and the operational ranges are being studied for future technology transfer purposes.

Clinical trials, up to phase II, using Sabin-IPV have been conducted by different institutes in several countries. A review of the results, and the current status in these Sabin-IPV clinical studies, will be given. In order to ultimately replace regular IPV, Sabin-IPV should show a comparable or better: (i) safety profile, and (ii) protection against wild-type poliovirus.
Anticipating issues for the next 2 years (OPV to IPV and DTP to DTP-IPV transition)

Takashi NAKANO
Kawasaki Medical School - Japan

The debut of OPV in Japan was brilliant. It was urgently imported to control the occurring huge outbreak of poliomyelitis, and distributed to all the Japanese children. Soon after the OPV mass vaccination campaign, polio was expelled from the country. This was an event two years ago than OPV approval in the United States (1963). However, the step in Japan was late afterwards while the overseas countries introduced IPV to evade VAPP which was the disadvantage impossible to avoid in OPV.

IPV is expected to be finally introduced in Japan approximately one year later. Candidates will be two kinds of IPV, Sabin-strain derived IPV (sIPV) and wild-strain derived IPV (wIPV). In addition, DPT-IPV combination vaccine and IPV alone product will be introduced. For OPV routine immunization schedule in Japan, less inoculation number of times (2 doses) has been used. It is supposed about IPV that the schedule of the global standards, that is, 4 doses for basic immunity during early childhood will be adopted. The DPT dose in Japan is four times in total. To avoid hyperimmunization of DPT, both DPT-IPV combination vaccine and IPV alone product will be administered to an infant who has been received one or more shots of DPT. As many people recently fear a risk of VAPP in Japan and put off OPV, the number of children with DPT immunization history without OPV is increasing. It is necessary to investigate interchangeability of sIPV and wIPV in advance, because DPT-sIPV product and wIPV alone product is expected to be introduced.

Many overseas countries using IPV carry out booster vaccination for the schoolchild period. As combination vaccine can increase the coverage, it is important to discuss whether we incorporate additional IPV shot in booster dose of DT routine schedule (11 and 12 years old). Naturally, it is the matter which we should examine in conjunction with the introduction of Tdap in Japan.
Session 4

Travelers vaccines. Vaccines as solutions for traveler’s risk.
Dengue clinical review

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Dengue infection, one of the most devastating mosquito-borne viral diseases in humans, is now a significant problem in many countries. The disease, caused by the four dengue virus serotypes, ranges from asymptomatic infection to undifferentiated fever, dengue fever (DF), and severe dengue hemorrhagic fever (DHF) with or without shock. DHF is characterized by fever, bleeding diathesis and a tendency to develop a potentially fatal shock syndrome. Dengue infection with organ impairment mainly involves central nervous system and liver.

Consistent hematological findings include vasculopathy, coagulopathy, and thrombocytopenia. Laboratory diagnosis includes virus isolation, serology, and detection of dengue ribonucleic acid. Successful treatment, which is mainly supportive, depends on early recognition of the disease and careful monitoring for shock. A severity-based revised dengue classification for medical interventions has been developed and validated in many countries. Prevention depends primarily on control of the mosquito vector. The feasibility of a dengue vaccine is high.
Dengue is the most important arbovirus infection, with over 50 million infections annually worldwide. Indeed, it is expanding and increasing, driven by unprecedented urban growth in the topics and subtropics, unprecedented international travel and failing public health infrastructure.

Although often described as a neglected tropical disease, many policy makers in dengue-endemic countries do not see it that way. Rather, it is because the mosquito vector, *Aedes aegypti*, is superbly adapted to live and survive in urban domestic environments that many well-intended control programs either fail or are not sustainable. New approaches to dengue control are necessary.

Although dengue vaccines have been under development for decades, several candidate vaccines have recently progressed in clinical trials in humans. This update will briefly review two live attenuated recombinant chimeric tetravalent vaccines that are in phase I trials to evaluate dose ranging, immune responses and safety in small numbers of vaccine recipients.

The update will also detail a live attenuated yellow fever-dengue chimeric tetravalent vaccine that is currently in two phase 3 trials, one in Latin America and the other in Southeast Asia. These trials aim to assess the efficacy of the vaccine, as well as to gather safety, immunogenicity data in large numbers of vaccine recipients, and to attempt to determine immunological correlates of protection. Enrolment (>10,000 2-14 year old children) into the Asian trial was completed at the end of 2011; enrolment (>20,000 9-16 year olds) into the Latin American trial will be complete in the very near future.
Recent trends on traveler’s vaccinations in Japan

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More than 16 million Japanese travelers go abroad every year. However, Japanese oversea travelers have not had enough information of foreign countries and immunization.

Our research revealed that many Japanese travelers have got sick due to vaccine preventable diseases (VPDs) such as cholera, typhoid fever, hepatitis A (HVA), and hepatitis B (HVB) and so on. In Asia, they have frequently got cholera in India and Philippine, typhoid fever in Nepal and India, HVA in Nepal and India, HVB in Thailand and Philippine, respectively. I am sure one of the reasons is that typhoid vaccine and meningococcal vaccine have not approved yet in Japan.

Thirty seven (14.6%) universities among 254 universities in Japan experienced vaccine preventable diseases among their dispatched staffs and students. Two hundred forty two (47.4%) companies among 511 companies in Japan experienced vaccine preventable diseases among their dispatched staffs. Only less Japanese travelers get good information from medical staff in clinics than travelers in western countries. Japanese travelers lived in western countries visit travel clinics more frequently than they lived in Japan.

In all, travel medicine in Japan is far behind to western contries. We hope travel vaccine lag should be over soon and Japanese travelers need more vaccines to prevent VPDs. We need more enlightenment to Japanese citizens and fill up vaccine centers and travel clinics.
Global standard in travel medicine: a risk management perspective

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Travel vaccines are an effective means to reduce the risk of infection, incapacitation, sequelae and death among travelers. First, it is essential to comply with vaccine requirements in the destination countries, mainly by immunizing against yellow fever. A travel health consultation is a welcome opportunity to deliver missing vaccine doses according to the national routine vaccination program, eg. offering protection against diphtheria, tetanus, pertussis, hepatitis B, measles, and human papillomavirus. For recommended specific travel vaccinations, priorities in the past were often determined by a simplistic approach basing on incidence rates. Severity must also be taken into account as permanent pathological conditions and death may result from vaccine preventable diseases.

Influenza among travelers has been demonstrated to occur with a monthly incidence rate of 1% in the tropics and subtropics; this rate may be higher during epidemics in winter. Outbreaks have been described particularly on cruise ships, where fatalities occurred. Hepatitis A, and particularly at some destinations typhoid fever, have a substantial incidence rate. With respect to sequelae or death a variety of neurological infections are a greater threat to travelers: Animal bites with potential risk of rabies transmission are usually reported by 0.2 to 0.4% of travelers per month; meningococcal disease, Japanese encephalitis, and the almost eradicated poliomyelitis are rare, but potentially devastating. In contrast, cholera and tuberculosis are lesser threats at least to short term travelers.

Professionals offering travel vaccines have a complex task; they must take into account the destination, duration of stay (also consider cumulative exposure), travel characteristics and legal obligations. Besides these environmental factors, also host factors play a role: Often the time span until departure and costs set limitations to an optimal protection, and immune deficiency, pregnancy or other conditions — lastly also the lack of vaccine supplies may necessitate specific decisions for a good risk management.
N. meningitidis is an important and devastating human pathogen, a leading cause of meningitis and septicemia, causing substantial morbidity and mortality worldwide. Despite appropriate treatment the fatality rate for invasive meningococcal disease (IMD) can be high, and about 20% of patients surviving IMD will suffer from significant sequelae. Historically, the epidemiology of IMD has been characterized by an endemic background with the occurrence of large epidemics and smaller outbreaks at irregular intervals. New epidemics or outbreaks cannot be excluded as it is impossible to reliably predict the epidemiology of IMD. The reported incidence of meningococcal disease varies widely and may represent an underestimation of true disease burden. The highest age-specific incidence of IMD is consistently observed in infants and children <5 years old. Although the capsular polysaccharide of most serogroups that cause disease are excellent vaccine antigens, the serogroup B polysaccharide is similar to that of human neural tissue and does not elicit adequate immune responses. While the effectiveness of polysaccharide vaccines to prevent IMD has been demonstrated in adults, immunological studies have shown that conjugate vaccines are more immunogenic in young children. The introduction of polysaccharide-conjugate vaccines from early childhood onwards and the development of protein based serogroup B vaccines to protect against IMD caused by serogroup ACWY or B are major advances in the control and potential elimination of this serious disease.

Keywords: Meningitis, Meningococcal disease, Meningococcal conjugate vaccines, meningococcal epidemiology