

ST03 Emerging Considerations in Travel Medicine: Japanese Encephalitis (JE) and Meningococcal Disease**ST03.1 Introduction: Emerging Risks to Travelers – Selected Neurological Infections**

R. Steffen, University of Zurich, Division of Communicable Diseases, Zurich, Switzerland

International travel has changed over the last few years. While regions such as Europe began to stagnate in terms of international tourist arrivals in 2008, other regions continued to grow; the Middle East (+11.3%), Africa (+4.6%), and South and Southeast Asia (+4%) all recorded overall growth in 2008.¹

With the widening destination list for international travelers, we should be prepared to advise our travelers on diseases we may not have considered a major risk before. This symposium will focus on two such diseases – Japanese Encephalitis (JE) and meningococcal disease.

JE is the most important viral encephalitis in Asia, with 30–50,000 cases per year, causing 10–15,000 deaths. Up to half of survivors of JE are left with significant neurological sequelae. JE is enzootic across a wide region of Asia and is transmitted by mosquitoes and maintained in an enzootic cycle involving pigs and wild animals. Humans are incidentally affected. Travelers visiting the enzootic area are at risk from JE, as demonstrated by a growing body of case-study evidence of JE in travelers without ‘classical’ exposure to rice paddies. Measures to reduce JE in humans involving methods targeting pigs or mosquitoes have had mixed results and are associated with substantial costs; therefore, human vaccination provides the best protection.

Meningococcal disease, caused by *Neisseria meningitidis*, occurs at rates of 1–5 cases per 100,000 in developed countries. It is associated with a case-fatality ratio of ~10%, and significant long-term sequelae in up to 19% of survivors. Symptoms can progress rapidly, often leading to death within 24–48 hours. Sporadic outbreaks occur worldwide, but large outbreaks occur regularly in the sub-Saharan ‘meningitis belt’ and occurred at the Hajj pilgrimage to Mecca before the introduction of vaccination requirements. During outbreaks, rates of disease far exceed the norm, sometimes as high 100–800 per 100,000. Travelers visiting these areas are at increased risk of developing disease or becoming a carrier, thus creating a risk of transporting the disease to their home country.

Data from clinical trials of two new vaccines against these diseases will be presented – IXIARO®, a Vero-cell-derived JE vaccine, and MenACWY-CRM197, an investigational, quadrivalent, conjugate vaccine with the potential to protect all age groups against serogroups A, C, W-135 and Y.

Reference:

1. World Tourism Organization (UNWTO). UNWTO world tourism barometer (excerpt). 2009.

ST03.2 Meningococcal Disease - Vaccine Strategies for Travelers

A. Wilder-Smith, National University of Singapore, Singapore, Singapore

With increasing travel and tourism worldwide, travelers are choosing to visit less traditional destinations. Routine vaccinations in a traveler's home country often cannot ensure protection at such destinations. Therefore, there is a need for better awareness of infectious diseases and vaccinations. Diseases that are commonly associated with travel include cholera, hepatitis A, rabies, typhoid fever, and yellow fever. However, meningococcal disease is often neglected in travel vaccine recommendations, despite the high case-fatality rates and variable global incidence of the disease. As such, meningococcal disease awareness among travelers is low. Meningococcal disease strikes rapidly and can be fatal within 24 hours, even when the best healthcare is available. In addition, the time frame within which clinical diagnosis and treatment can occur is narrow, which is particularly relevant for travelers who may not be able to obtain timely and accurate diagnosis and treatment in foreign countries and remote regions.

New vaccines to prevent meningococcal disease have been licensed in recent years. Quadrivalent meningococcal conjugate vaccines offer the broadest, most durable, and most effective protection. However, these vaccines are not yet available in all regions and so current vaccination strategies are suboptimal. It is therefore timely to discuss vaccine strategies: current indications for meningococcal vaccination in travelers, high risk groups, differences between the newer conjugate meningococcal vaccines and the older polysaccharide vaccines and new available data.

ST03.3 Japanese Encephalitis – Devastating Outcomes and Shifting Opinions

T. Jelinek, Berlin Center for Travel and Tropical Medicine, Berlin, Germany

Japanese Encephalitis (JE) is the most important viral encephalitis in Asia. JE has devastating consequences: approximately one in three patients with symptomatic JE die and another one in three are left with significant neurological sequelae. The World Health Organization estimates that JE was the cause of 13,900 deaths in 2002, and resulted in nearly 700,000 disability-adjusted life years.¹

There is currently no specific treatment for JE, and personal protective measures do not provide sufficient protection against JE virus-infected mosquitoes. As a result, vaccination is the best protection against JE for travelers.

Current guidelines on the vaccination of travelers against JE were largely designed to minimize exposure to the only JE vaccine available at the time (a mouse-brain-derived vaccine which was associated with rare, serious adverse events). As a result, few travelers to Asia have historically been vaccinated. However, the possibility of infection with JE virus can often not be ruled out when traveling to endemic areas. In addition, symptomatic infection can have serious clinical implications for the traveler concerned. A number of case studies will be presented that illustrate these points.

With the launch of IXIARO® (Intercell/Novartis Vaccines), a new, Vero-cell-derived JE vaccine, we have an opportunity to reassess our attitudes towards vaccination of travelers against JE. Opinion is changing, with many travel medicine experts now believing a broader set of recommendations regarding which travelers should receive vaccination against JE is appropriate.

Reference

1. World Health Organization. Causes of death 2002. <http://www.who.int/research/en/>. 2004.

ST03.4 IXIARO® – a New Vaccine Against Japanese Encephalitis for Travelers

E.C. Jong, University of Washington, Seattle, USA

Japanese Encephalitis (JE) is the most important viral encephalitis in Asia and is an unpredictable threat to travelers visiting the region. IXIARO® (Intercell AG and Novartis Vaccines and Diagnostics Inc.) is a new, Vero-cell-derived JE vaccine. The clinical profile of IXIARO will be reviewed in this presentation.

IXIARO is an inactivated JE vaccine based on virus strain SA14-14-2 cultured in Vero cells. It is adjuvanted with aluminium hydroxide.¹ It contains neither stabilizers nor preservatives and is presented in a pre-filled syringe.¹ IXIARO is administered as a two-dose schedule with doses on days 0 and 28.¹ IXIARO is indicated for the active immunization against JE of adults.¹

In clinical trials, IXIARO has been shown to be highly immunogenic after two doses, resulting in seroconversion of 98% (n=352/361) of subjects by day 56.² The second dose of IXIARO has been shown to result in a rapid increase in protective antibodies, resulting in a seroconversion rate of >97% seven days after this dose.³ Follow-up studies have demonstrated good persistence of immunity, with 95% (n=172/181) of subjects retaining protective antibody titers 6 months after immunization, and 83% (n=151/181) after 1 year.⁴

In the pivotal safety trial, IXIARO has demonstrated good tolerability, with a similar profile to placebo.⁵ Subsequent studies have confirmed the safety and tolerability profile of IXIARO. Importantly, several thousand subjects have now been vaccinated with IXIARO and no allergic reactions have been observed.⁵ IXIARO may be administered at the same time as a hepatitis A vaccine (Havrix 1440®; GlaxoSmithKline), with no detrimental effects on the immunogenicity or tolerability of either vaccine.⁶

References

1. Novartis Vaccines. IXIARO Summary of Product Characteristics. 2009.
2. Tauber E et al. *Lancet* 2007; 370: 1847-53.
3. Dubischar-Kastner K et al. Abstracts of the 57th American Society for Tropical Medicine and Hygiene annual meeting, New Orleans, LA, USA, December 7-11 2008; Abstract 908.
4. Schuller E et al. *Vaccine* 2008; 26: 4382-6.
5. Tauber E et al. *J Infect Dis* 2008; 198: 493-9.
6. Lehner C et al. Abstracts of the 56th American Society of Tropical Medicine and Hygiene Annual Meeting 2007; Abstract 122.