

## Mini Review

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# Pre-Travel Vaccinations and Malaria Prophylaxis for International Travelers

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## ABSTRACT

International travel has increased dramatically the past decades, potentially posing health risks at the level of traveler and the level of public health. Vaccine-preventable diseases and malaria constitute a non-negligible proportion of imported infectious diseases to developed countries. This is a short review of pre-travel advice regarding vaccination and malaria prophylaxis for international travelers to developing countries. Vaccination and malaria prophylaxis depend on a risk-benefit analysis, weighting the risk of the disease against the risk of possible side effects of the vaccine or antimalarial agent. Recommendations for vaccination and malaria prophylaxis are based on the epidemiological situation at destination, travel's (e.g., destination, purpose and duration of travel) and traveler's (e.g., demographics, medical history and past vaccinations) characteristics. Recommendations of vaccination and malaria prophylaxis should be based on selective and individualized risk assessment. Public health authorities should increase awareness of travelers and health professionals for travel related health issues in order to prevent travel-associated vaccine-preventable diseases and malaria and promote safety both for the traveler as well as for the community.

**KEY WORDS:** Pre-travel; Vaccination; Prophylaxis; Malaria; International traveler.

**ABBREVIATIONS:** MMR: Measles-Mumps-Rubella; VFRs: Visiting Friends and Relatives; YF: Yellow Fever; JE: Japanese Encephalitis.

## INTRODUCTION

International travel has increased dramatically the past decades. The number of international arrivals is expected to reach 1.6 billion by the year 2020, with a significant increase noted in tropical and subtropical areas.<sup>1</sup> International travels may pose health risks for the individual and contribute to the global spread of infectious diseases. Vaccine-preventable diseases constitute a non-negligible proportion of imported infectious diseases to developed countries.<sup>2,3</sup> GeoSentinel Surveillance Network data demonstrated that vaccine-preventable diseases accounted for 3% of febrile episodes among 6957 travelers who reported fever as a chief reason for seeking care after travel at a GeoSentinel clinic during 1997-2006.<sup>4</sup> In this GeoSentinel study, typhoid fever, hepatitis A, and influenza A were the most common vaccine-preventable diseases among febrile travelers after returning mainly from a travel to a tropical or subtropical area.<sup>4</sup>

Vaccinations are considered an important preventive measure of pre-travel preparation.<sup>5,6</sup> In addition, pre-travel vaccinations most probably constitute the most common reason international travelers seek consultation for prior to their departure.<sup>5,6</sup> Travel vaccines include a) routine vaccines which consist of vaccines incorporated in the national immunization programs, b) required vaccines which are necessary for entry into certain countries, and c) recommended vaccines whose recommendation depends on the risks of exposure at travel destination.

Malaria is endemic in over 100 tropical and subtropical countries worldwide, with an estimated annual global burden of 350-500 million infections and approximately 1 million

deaths, 90% of which occur in sub-Saharan Africa only.<sup>7-10</sup> The increasing international travel in association with the enormous influx of immigrants from malaria-endemic countries had a significant impact on imported malaria cases in developed countries the past decades.<sup>11-13</sup> Although the number of malaria cases has decreased significantly over the past years,<sup>9</sup> it is estimated that more than 10,000 international travelers who visit malaria-endemic areas acquire malaria every year; this figure may be higher due to under-reporting.<sup>12</sup> In most of these cases, anti-malaria prophylaxis either was not prescribed or the patient did not adhere to prophylaxis. Occasionally, incorrect anti-malaria prophylaxis is prescribed.<sup>14</sup>

Risk assessment should be individualized on the basis of the epidemiological situation at destination, travel characteristics (e.g., areas visited, purpose and duration of travel), and traveler's characteristics (e.g., age, medical and previous vaccination history).<sup>5,6</sup> In addition, pre-travel consultation provides a timely opportunity for updating routine vaccinations.<sup>5,6,15,16</sup> Travel medicine consultants should get updated information about the current epidemiology trends globally from public health authorities through internet, and be familiarized with the adverse events of vaccines and anti-malaria medications among others.

This is a short review of pre-travel advice in regards to vaccination and malaria prophylaxis for international travelers to developing countries. Different trends of pre-travel advice are taken under consideration.

### Pre-travel Vaccinations

Vaccinations are key parts of travel preparation for the reduction of the risk of vaccine-preventable diseases for the traveler as well as the risk of their international spread. GeoSentinel data demonstrated that 1.5% of 37,542 ill returned travelers presenting to a GeoSentinel site had vaccine-preventable infections; only 29% of those attended for pre-travel consultation which emphasizes the potentially lost opportunity for intervention, given the high efficacy of almost all vaccines.<sup>2</sup>

Travel provides an opportunity for travelers to update their routine immunizations, which are incorporated in their national immunization programs including tetanus-diphtheria vaccine, measles-mumps-rubella (MMR), poliomyelitis, meningococcal and influenza vaccines.

Travel vaccines include hepatitis A, typhoid fever, cholera, meningococcal, yellow fever, rabies and Japanese encephalitis vaccines. Although there is a 10-50 fold decrease of hepatitis A incidence in travelers the last few years, the relative risk for travelers remains significant,<sup>17,18</sup> and now-a-days hepatitis A remains one of the common vaccine-preventable diseases diagnosed among international travelers. Travelers, especially those visiting friends and relatives (VFRs), may also contribute to the importation of vaccine-preventable diseases in their countries of permanent residence and occasionally to the re-emer-

gence of the onset of epidemics of vaccine-preventable diseases. Such a notable example is hepatitis A. All susceptible people aged over 1 year traveling for any purpose, frequency, duration to countries with high or intermediate hepatitis A endemicity especially if they are traveling to rural areas should be vaccinated before departure (2 doses scheme).<sup>6,19,20</sup>

Typhoid fever which is hyper-endemic in the Indian subcontinent is a common diagnosis among ill returning travelers accounting for 47.6% of all vaccine-preventable disease cases.<sup>2</sup> Typhoid vaccination is recommended for travelers to developing countries according to the type of accommodation (local peoples' homes), duration of travel (longer duration of travel) and eating behaviour (adventurous eater).<sup>6,19,20</sup> The risk of cholera infection for most travelers is very low. It is indicated for humanitarian relief workers in disaster areas and refugee camps who may be at risk.<sup>19</sup>

Meningococcal vaccine is indicated for long-term travelers, and particularly for those living in close contact with the indigenous population and thus are at risk for meningococcal infection.<sup>6,19-21</sup> Haji pilgrims, travelers to sub-Saharan Africa, especially to the meningitis belt, as well as international university students are at increased risk for meningococcal disease and should be vaccinated accordingly before departure.

Yellow fever (YF) vaccination is recommended for the prevention of travelers to areas where there is a risk of the disease. Under International Health Regulations (IHR, 2005), any country may require a YF vaccination certificate for travelers coming from areas with risk of yellow fever transmission, even if travelers are on transit through the country. Only a small number of African countries require proof of YF vaccination from all arriving travelers.<sup>19</sup>

Rabies is not a common travel related infection however the disease has potentially long latency and a fatal outcome. Pre-exposure rabies vaccination is recommended to long-term travelers, particularly to children and to those involved in extensive outdoor activities in rural areas, namely bicycling, hiking, camping, and backpacking even if they travel for short duration.<sup>6,19,20</sup> Rabies vaccination is also recommended for specific occupations at risk (e.g., veterinarians).

The risk of Japanese encephalitis (JE) in persons from non-endemic countries traveling to Asia is considered low. However JE vaccination is indicated for travelers who stay for prolonged period of time in rural areas with active JEV transmission and expatriates.<sup>6,19,20,22</sup>

### Malaria Prophylaxis

Malaria prophylaxis recommendations depend on a risk-benefit analysis, weighting the risk of the disease against the risk of possible side effects of the drug.<sup>23,24</sup> There are only few evidence-based studies available regarding the risk of infection in trav-

elers.<sup>25-28</sup> Prescribing practices vary to a great extent between different countries. While in Europe “stand-by-medication” is used for many malaria-endemic areas without high endemicity, in the USA a stand-by-medication strategy is not established.<sup>29-31</sup>

Destination is considered the main risk factor in regards to the risk assessment of malaria acquisition.<sup>32-34</sup> According to the GeoSentinel surveillance network database, the risk for acquiring malaria per region visited was higher in sub-Saharan Africa followed by Oceania, South Asia, Central America, Southeast Asia and South America.<sup>35</sup> Analysis of malaria imported into eight European countries from the Indian subcontinent, led to a consensus statement by the TropNet group recommending that non-selective prescription of prophylaxis for visitors to India, Pakistan, Bangladesh, and Sri Lanka should be dropped.<sup>31</sup>

Travelers VFRs are at higher risk for acquisition of malaria compared to non-VFRs,<sup>35-38</sup> and according to GeoSentinel data that migrants VFRs were 4.5 times more likely to acquire malaria compared with tourist travelers, and this increase was even greater (8-fold) when travel destination was sub-Saharan Africa.<sup>39</sup> VFRs typically demonstrate travel and behavioural patterns which render them at high risk for malaria exposure. Contributing factors include lack of provision of pre-travel services which are rarely sought by VFRs and misconceptions about possession of life-long immunity against malaria which make them less likely to receive or adhere to malaria prophylaxis recommendations. In addition, VFRs may face difficulties in accessing health-care services due to economic, cultural, language, or legal issues.<sup>35-39</sup> Long-term travelers including expatriates are also at higher risk for acquisition of malaria due to longer exposure to areas where the disease is endemic and poor compliance to continuous malaria prophylaxis and personal protective measures.<sup>23,40</sup> Travel-medicine consultants should be familiar with malaria prophylaxis, and especially with their side effects and contra-indications. Advice about mosquito protection should be provided. Travelers should be aware of the signs and symptoms of malaria and issues of self-medication should be discussed, on the basis of travel and travelers characteristics. Lastly, travelers traveling to or returning from malaria endemic areas should be advised that they should seek immediate medical attention in case they develop fever. If this is the case, their travel history should be reported to their healthcare professionals and the diagnosis of malaria should be verified or excluded through accurate tests.

## CONCLUSION

Recommendations of vaccination and malaria prophylaxis should be based on selective and individualized risk assessment taking in consideration, not only the travel destination, but also the duration and purpose of travel, the area and specific place of stay, and the travelers activities. Public health authorities should increase awareness of travelers and health professionals for travel related health issues in order to prevent travel-associated vaccine-preventable diseases and malaria and promote safety both for the traveler as well as for the community.

## CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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