

Assessment and Counseling of International Travelers: A Guide for Practicing Physicians

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ABSTRACT

Because of globalization, there has been a significant increase in international travel. Thorough planning and ample preparation time is essential, especially for persons traveling to unfamiliar countries. Pre-travel healthcare counseling may reduce the risk of acquiring preventable illnesses abroad and should be encouraged. This article reviews the general approach to pre-travel planning, and provide physicians with a guide for counseling international travelers on infectious and non-infectious hazards and its' prevention, including immunization, chemoprophylaxis, non-vaccine preventable diseases such as traveler's diarrhea, high altitude illness, malaria, and air travel-related illnesses. (*J Infect Dis Antimicrob Agents* 2005;22:133-49.)

INTRODUCTION

Because of the modern trend in increasing globalization, people around the world now travel from their country to foreign lands for a variety of reasons, including vacation, business, study, and training. The duration of their stay obviously varies, depending on the nature of their venture.

The top ten international travel destinations in 2004 collected by World Tourism Organization (WTO) are France, Spain, United States, China, Italy, United Kingdom, Hong Kong, Mexico, Germany, and Austria.

Many old infectious diseases have been re-emerging in the past few years. Since 2003, there were outbreaks of Polio in several African countries, and new emerging infectious diseases such as Severe Acute Respiratory Syndrome (SARS) and Avian influenza A (H5N1) which have caused outbreaks in Southeast Asia and instilled a global scare of an epidemic. Dengue and dengue hemorrhagic fever (DHF) has expanded rapidly and now includes most tropical countries of Asia, the South Pacific, the Caribbean, South and Central America and Africa. West Nile fever is now prevalent

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throughout North America. However, malaria still remains the most common cause of fever in travelers.

With more elderly people traveling, non-infectious conditions such as cardiovascular events are also on the increase. Crime, motor vehicle accidents and drowning still occur frequently in developing countries. These incidents are among the top causes of tourist casualties. Thorough planning and ample preparation time is essential, especially for persons traveling to unfamiliar countries. Falling ill in an unfamiliar country may have dire consequences for any traveler. Seeking pre-travel healthcare advice may reduce the risk of acquiring preventable illnesses abroad.

General approach to a pre-travel preparation

Travelers should be advised to see a physician at least 2 months before traveling. Depending on the travel destination and risk assessments, individualized prevention strategies may be devised and vaccination administered if needed.

Travelers should be asked to provide essential information pertaining to anticipated destination, duration of stay, type of accommodations, contact numbers, type of activities, before visiting a physician. If they are an adventurous traveler, they are likely to need protective vaccination for food-borne diseases or insect-transmitted diseases. Travelers should be advised to check their health insurance status while abroad. This may be of even greater importance for elderly and chronically ill persons. If there is doubt that their insurance will provide travel coverage, they should take out special travel health insurance for the duration of their stay abroad. Some countries now require that tourists have evidence of health insurance when applying for a visa. Travel to remote and developing regions with inadequate health care facilities brings up the need for special insurance.

These policies cover potentially expensive air medical evacuation to the nearest treatment facilities for a catastrophic illnesses and/or injuries. Several international medical assistance companies can provide such coverage relatively inexpensively. All of the pertinent information should be given to the traveler as a resource, with clear instructions and contact numbers should the returning traveler become ill. Table 1 shows a general approach to a pre-travel assessment office visit.

Immunization and chemoprophylaxis

Vaccine and chemoprophylaxis preventable diseases

Some diseases, such as food-borne diseases (typhoid, hepatitis A, etc.), blood- or body fluid- borne diseases (hepatitis B), and vector-borne diseases (yellow fever, Japanese encephalitis) are vaccine preventable. Others diseases, such as rabies can be prevented effectively with post-exposure prophylaxis when given appropriately and in a timely fashion. Malaria and leptospirosis may be prevented by chemoprophylaxis.

Vaccines can be divided into three groups.

1. Routine vaccines
2. Vaccines required for certain destinations before entering
3. Recommended vaccines for persons with risk of exposure

1. Routine immunizations

Certain vaccines are routinely administered to the general population as mandated by national immunization programs, such as diphtheria, tetanus, measles, mumps, etc. Review of the immunization record offers the opportunity to update or complete vaccination schedules

for inadequately immunized travelers or those with waning immunity. Persons born in the United States before 1957 or any time in developing countries, they are considered immune to measles. (Table 2)

2. Vaccines required for certain destinations before entering

The only vaccine that may require proof of receipt before entering into certain countries is yellow fever

Table 1. A general approach to a pre-travel office visit.

Review information and assess risk	age A list of all medical conditions including pregnancy, allergy and medications including over the counter medications and vaccination history Purpose of the trip and exact/detailed itinerary to assess seasonal diseases and risks of exposure, i.e., urban or rural area, type of accommodation, expected activities
Provide medical advice/vaccine/chemoprophylaxis	Update routine vaccine profile Administer vaccine needed for certain destinations Administer recommended vaccines based on destination and risks of exposure Offer malaria chemoprophylaxis if risk for malaria exist- provide the best suited chemoprophylaxis and educate patient on personal protection against mosquitoes Educate on sexual transmitted diseases, blood/body fluid-borne diseases, and traveler's diarrhea
Provide advice on non-infectious precautions	High altitude illness, crime avoidance, diving and swimming Safety, health insurance (includes international coverage), and how to contact family members
General information	Traveler's embassy location in that area Traveler's contact number and how to contact family members.

Table adapted from the reference 20.

Table 2. Immunization and chemoprophylaxis.

Routine vaccine	Required vaccines for certain destinations before entering	Recommended vaccines for persons with risks of exposure
Tetanus-diphtheria	Yellow fever	Hepatitis A
Pertussis	Meningococcal*	Typhoid
Varicella-zoster		Rabies
Polio		Meningococcal
Influenza		Japanese B encephalitis
Pneumococcus		Tick-borne encephalitis
Hepatitis B		Cholera
<i>Haemophilus influenzae</i> type B		
Measles, mumps, Rubella		

*The tetravalent vaccine (A, C, Y, W-135) is required by Saudi Arabia for Hajj and Umrah pilgrims

vaccine because of increasing cases including fatal cases in unvaccinated travelers¹⁻³ and the potential of introduction of yellow fever to a new country where the mosquito vector is present. Yellow fever is a viral hemorrhagic fever caused by Flaviviridae and transmitted by daytime-biting mosquitoes, *Haemagogus* spp. in South America and *Aedes* spp. in Africa. It has caused large epidemics in Africa and the Americas. Clinical features vary from subclinical infection, abortive, nonspecific febrile illness without jaundice, or life-threatening disease with fever, jaundice, renal failure, hemorrhage, shock⁴⁻⁵, myocardial injury, and central nervous system dysfunction.⁶ Rare adverse effects of this vaccine are vaccine-related neurotropic disease (YEL-AND)⁷⁻⁸ and viscerotropic disease (YEL-AVD).⁹

The vaccine should not be administered to pregnant women (category C) and immunosuppressed persons due to concerns about live attenuated virus vaccines.¹⁰ On the contrary, asymptomatic HIV-infected patients with CD4 counts above 200/ μ L should be immunized because one study showed a good serological response without adverse events.¹¹ Letters of waiver may be obtained for those traveling to areas where the risk of disease is low yet vaccination is an international travel requirement, but may pose a health risk to the traveler. Trips may have to be canceled if the risk is significant in persons who cannot receive vaccine. In addition to immunization, general protection such as mosquito net and N, N.-diethyl-3-methylbenzamide (DEET) should be encouraged. Countries that require yellow fever vaccine are listed at <http://www.cdc.gov/travel/diseases.htm#yellow> and <http://www.who.int/ith>.

3. Recommended vaccines for persons with risk of exposure

Vaccines are recommended to persons based on exposure risk. For example, hepatitis A, polio, typhoid

fever, cholera should be given to travelers with potential exposure to food and beverage in areas with poor hygiene and sanitation. Vaccines are also recommended for travelers with risk of exposure during certain activities such as rabies and tick-borne encephalitis for outdoor travelers in endemic areas, *Neisseria meningitidis* in a congregate settings, and hepatitis B from new sexual partner, etc. Healthcare workers are at particular risk for occupational acquisition of hepatitis B.

Routine immunizations

Dosage and schedule of routine immunizations can be found in standard textbooks. This article will review only travel-related vaccines in adults.

Hepatitis B vaccine

It is recommended for all non-vaccinated travelers especially high risk groups such as health care workers, travelers who anticipate having a new sexual partner during stay, or with prolonged stays in aboriginal or native communities, and travelers from low-incidence area to endemic area. Travelers should be advised regarding body fluid and blood precaution and safe sex as well.

Polio vaccine

Everyone should receive a completed primary series and then a one-time booster with enhanced-potency inactivated polio vaccine (eIPV) for at-risk travelers. Oral polio vaccine was discontinued in the USA because of the rare vaccine-associated paralytic poliomyelitis.

Influenza vaccine

Influenza has a worldwide distribution. Outbreaks usually occur in November-March in the northern hemisphere and April-September in the southern hemisphere. Because of rapid mutation and the seasonal differences, vaccine in one hemisphere might not be effective in another. Therefore, vaccination should be

arranged promptly at the destination for travelers who travel across the hemisphere. It is also recommended for the elderly, healthcare workers, persons with respiratory and cardiac diseases, diabetes mellitus, and immunosuppressive condition.

Recommended vaccine for persons with risks of exposure

Physician should check for the latest occurrences of vaccine preventable disease to help making decision in difficult situations. Physician should provide traveler of possible side effects of each vaccine.

Hepatitis A vaccine

It is indicated for travelers whose destination is outside of the United States, Canada, Japan, Australia, New Zealand, Scandinavian countries, and developed countries in Europe. Immunoglobulin administration concomitant with vaccine is rarely used for pre-exposure because of the high rates of developing immunity from vaccine alone unless travel to endemic area occurs within less than 2 weeks after vaccination.¹² Serum antibody test may be beneficial for people from endemic areas, those who had a history of hepatitis, or those who were born before 1945. The first dose should be given at least 4 weeks prior to travel. If using combination vaccine for hepatitis A and B (Twinrix), at least two doses should be given prior to travel because of lower concentration of antigen in this form compared to pure hepatitis A vaccine. Combined hepatitis A and B vaccine makes immunization easier but it is not available in Thailand.

Typhoid vaccine

A typhoid vaccine is recommended for persons traveling to developing countries, especially the Indian subcontinent and parts of tropical South America, who plan to stay > 1 month and who may exposed to poor

sanitation. Vaccines are commercially available in two forms: parenteral capsular polysaccharide (Vi), and live attenuated oral vaccine (Ty 21a). Neither gives 100 percent protective efficacy or is protective against paratyphoid. The protective efficacy of the parenteral type (Vi) ranged only from 53 percent to 72 percent.¹³ Moreover, an optimal antibody response may be overwhelmed by a large oral inoculum. Nevertheless, physicians should offer this vaccine to travelers for some protection because of the emergence of multidrug-resistant strains including fluoroquinolone-resistant strains. It is very important that travelers take extra precautions related to food and water consumption in endemic areas. Antibacterials may impair the development of immunity of oral vaccine if given concomitantly. Another form of vaccine which is not commercially available is the modified Vi vaccine conjugated to nontoxic recombinant *Pseudomonas aeruginosa* exotoxin A (rEPA). It was shown to have more than 90 percent efficacy in children two to five years old.¹⁴⁻¹⁵

Rabies

Rabies is transmitted through mammal bites, a dog bite being the most common in developing countries. Pre-exposure immunization should be considered for those who travel to endemic areas for one month or more, for a high-risk person over a short period, or for persons who travelling to areas where access to healthcare facilities with rabies vaccination capabilities is expected to be greater than 24 hours. Post-exposure immunization with vaccine and immunoglobulin with copious wound cleaning can be given to non-immunized travellers if bitten in an endemic area. Hypersensitivity occurs more commonly with vaccines prepared from non-human sources than with human diploid-cell vaccine. Transverse myelitis, neuropathy, or encephalopathy

have been associated with the use of animal brain-tissue vaccines. Examples of these include Semple and suckling mouse brain products which are still in use in South America, Viet Nam, Bangladesh, Nepal, Pakistan and parts of India and Africa. The antibody response to intradermal human diploid-cell rabies can be lowered by chloroquine if being used concomitantly. Serology can be checked after immunization for persons who require long term protection such as laboratory persons working with rabies virus and veterinarians.

Meningococcal vaccine

It is recommended for travelers to high-risk areas, congregate places, and for first-year university students in USA. It is required for Mecca and Umrah pilgrims. Both bivalent (A, C) and quadrivalent vaccines (A, C, Y W135) do not cover serogroup B which is more common in the United States.

Japanese encephalitis vaccine

Japanese encephalitis (JE), transmitted by the *Culex* spp. mosquito, is the most important cause of epidemic arbovirus encephalitis in Asia. Vaccine is recommended for prolong-stayed travelers (>one month) in endemic areas particularly in rice or pig farms, or persons involve in high-risk activities, i.e., camping, bicycling, field work, etc. It takes up to one month to develop full seroprotection. Travelers should be observed for 30 minutes after vaccination for any adverse reactions and may travel 10 days after receiving the last dose. Serious vaccine-related side effects have been more frequently since the early 1980's and the late 1990's.¹⁶ The risk for JE short-term travelers is 1 case per million travelers per year and for travelers in rural areas in high risk season is 1 case per 5,000 to 1 case per 20,000 travelers per week.¹⁷ However, in recent post-marketing data review in the

US showed no serious neurological complications.¹⁸

Tick-borne encephalitis vaccine

Tick-borne encephalitis is a viral meningoencephalitis transmitted by *Ixodes* ticks in spring and summer, and sometimes by unpasteurized dairy products in endemic areas. Endemic areas are in the forest of East and Central Europe, and Siberia. Travelers should use general precautions including using protective clothes, repellants, and insecticide.

Cholera vaccine

Sanitary precaution including avoidance of contaminated food and drink is the most important measure to prevent disease. However, it is recommended for persons at high risk such as health workers in refugee situations or emergency relief.

Special conditions: immunocompromised persons and pregnancy

Maternal-fetal related contraindications can complicate the pre-travel immunization. Obstetrician should be consulted with any questions. Live vaccines should not be given in pregnancy and killed vaccine should be delayed to until the second trimester. Pregnant women should be advised to postpone travel until postpartum, especially for travel to the countries that require yellow fever vaccine.

Physicians should ask about HIV risk factors. All vaccines can be used in HIV-infected persons¹⁹ with CD4 count > 500/mm³ and travelers who take prednisone < 20 mg/day for > 2 weeks. However, yellow vaccine should not be given to any HIV-infected persons especially if only to follow regular requirements. Live virus vaccines should be given after 1 month of discontinuing immunosuppressive agents and after 3 months after last chemotherapy in remission stage of hematologic malignancies.²⁰

Malaria

Malaria is a preventable mosquito-transmitted disease with a global distribution. Infection may occur in the setting of absolute compliance to prophylaxis due to the emergence of resistance in many areas. The most severe form is caused by *Plasmodium falciparum* which accounts to 80 percent of cases in travelers to Africa where the highest rate of transmission is in the South of Sahara.

Anopheles spp. is the mosquito vector for malaria and is active during the night time in contrast to *Aedes* spp., which transmits Dengue and yellow fever during the daytime. Travelers should be informed of the risk, the incubation period, and the main symptoms. Pre-travel preparation includes chemoprophylaxis, counseling on the use of repellents, dress in long sleeves and trousers, and using screens and netting (impregnated with permethrin-containing sprays if possible). *N,N*-diethyl-3-methylbenzamide (DEET)-based products provide complete protection for the longest duration. Higher concentrations of DEET provide even longer-lasting protection. A 23.8 percent concentration has a mean complete-protection time of 301.5 minutes²¹; therefore, it is safe to use a concentration of 20-35 percent. Permethrin or another insecticide, deltamethrin may be available in some countries but not in Thailand.

In Thailand, risk is limited to evening or nighttime exposure in rural forest/jungle areas infrequently visited by travelers: primarily border regions with Laos, Myanmar, and Cambodia. The risk is highest in the provinces of Chiang Mai (not in the city), Mae Hong Son, Tak, Kanchanaburi, Ratchaburi, Chanthaburi, Trat, Prachuap Khiri Khan, and Sa Kaeo, and lower in most provinces in the south except Surat Thani and Yala. There is no risk in the interior of Thailand nor in the cities and main tourist resorts (Bangkok, Chiang Mai, Chiang Rai, gulf islands, Pattaya, Phuket Island, Ko Samui, etc.). Chemoprophylaxis for this area includes

doxycycline or atovaquone/proguanil (Malarone). Primaquine may be used in special circumstances (not in G6PD deficiency person). (www.travax.com). In Thailand, Mefloquine remains an option for special situations even with resistance near the borders with Cambodia and Myanmar. Doxycycline is an additional treatment option, although not 100 percent effective. Unfortunately, Malarone is not available in Thailand. Either atovaquone/proguanil or doxycycline or mefloquine (or primaquine in special circumstances) are options for a trip to Myanmar (not Thailand/Myanmar border), Cambodia (not Thailand/Cambodia border), the Philippines, Indonesia, East Timor, Laos, Malaysia, and Vietnam.

Chloroquine-resistant areas are found in the Indian Subcontinent, Hainan and Yunnan provinces of China, the Philippines, and Africa regions except North Africa.

There is no malaria risk in the United States, Canada, and Western Europe. Regional malaria information can be obtained at <http://www.cdc.gov/travel/regionalmalaria/index.htm>

A new drug that was developed but not yet available is Tafenoquine, a synthetic analogue of primaquine.²²

Pregnant women should not travel to the endemic area but if it is avoidable, chloroquine and mefloquine can be used even though, there is not a lot of data supporting safety of mefloquine especially in the first trimester (category C). Table 4 shows antimalarial chemoprophylaxis.

Non-vaccine preventable diseases

Non-vaccine preventable infectious disease

Traveler's diarrhea

It is common in travelers who travel to developing countries especially in the first two weeks. It is usually self-limited but severe dehydration can complicate this condition. The classic form is defined as passage of

Table 3. Travel-related Immunization in adults.

Vaccine, type	Initial dosage/booster	Contraindication	Adverse effect	Use in pregnancy	Use in HIV infection	Available in Thailand
Routine						
Hepatitis B ^a inactivated, recombinant DNA	4 weeks before travel IM, volume varies with manufacturer Standard: day 0, 1 month, 6-12 months Booster: none Accelerated: day 0, 1 month, 2 months Booster: 6-12 months Hyper-accelerated: day 0, 10, 21 Booster: 12 months ⁴³	Adverse reaction to previous dose.	Local reaction	Yes	Yes	Engerix-B, Euvax-B, H-B-Vax II, Heberbiovac HB, Hepavax-Ge
Influenza Inactivated and Live virus	2 weeks before travel Inactivated: 1 dose, SC or IM Live vaccine: Age 9-49 years: 0.5 ml, intranasal Booster: annually	Hypersensitivity to previous dose or egg Live vaccine: Age 5-17 years who takes aspirin	Local reactions Fever Malaise	Yes, but should wait until after first trimester	Yes	Agrippal (inactivated), Fluarix, Vaxigrip (inactivated, split virion)
Pneumococcal polysaccharide	1 dose of 0.5 mL of the 23-valent vaccine, SC or IM Booster: after 5 years for high-risk persons	Adverse reaction to previous dose	Mild local reactions, Arthus-like reaction with booster doses	Yes	Yes	Pneumo 23, Pneumovax 23 (23-valent)
Polio OPV (oral polio vaccine): live attenuated virus eIPV (Enhanced-potency inactivated virus)	4 weeks before travel OPV at 6, 10, 14 weeks of age (plus a dose at birth in endemic countries) eIPV at 2, 4, and 12-18 months. Booster-single dose SC or IM of eIPV if adequate childhood vaccination	None	Very rarely vaccine- associated paralytic poliomyelitis (VAPP) OPV was discontinued in the USA because of VAPP.	Yes	Should receive eIPV	Polio Sabin
Varicella-zoster Live-attenuated virus-Oka strain	SC, 0.5 ml Age < 13 years: 1 dose Adult: 2 doses- 0, 4-8 weeks Booster-none	Reaction to previous dose Cellular immune deficiency Active untreated tuberculosis	Rashes at the injection site and varicella-like rashes elsewhere ⁴⁴	No	Not in symptomatic HIV infection	Okavax, Varilrix

Vaccine, type	Initial dosage/booster	Contraindication	Adverse effect	Use in pregnancy	Use in HIV infection	Available in Thailand
Required vaccine						
Yellow vaccine Live-attenuate 17D virus	≥10 days before travel Adults and children 9 months- 0.5 ml SC Booster: Every 10 years, monitor closely in the elderly	Egg allergy Hypersensitivity to previous dose Immunocompromised persons	Rare: vaccine-related neurologic and viscerotropic disease	Yes, but only at high risk	Probably If CD4 ≥200 cells/mm ³	Not available
Recommended vaccine for persons with risks of exposure						
Cholera Live and killed attenuated	3 weeks before travel (killed vaccine), 1 week (live vaccine) 2 doses, orally -1 week apart (killed vaccine), 1 week live vaccine Booster- none	Hypersensitivity to previous dose For live vaccine, no antibiotics one week before and after immunization.	Mild local and systemic reactions	No	No	Not available
Hepatitis A Inactivated virus	4 weeks before travel 2 doses: 0, 6-24 months, IM Booster: may not be necessary	Hypersensitivity to previous dose	Local reactions	Yes, but only at high risk	Yes	Avaxim, Havrix, VAQTA
Typhoid -Live attenuated Ty 21a strain - Vi capsular polysaccharide (Vi CPS)	One week prior to travel -Vi CPS: single dose of 0.5 mL, deep SC or IM Booster: every 2-3 years -Live Ty21a vaccine- enteric-coated capsules: 1 capsule 4 doses orally at 2-day intervals Booster: every 5 years	Avoid proguanil, mefloquine, and antibiotics 1 week before (12 hours in the USA) and after given Ty21a vaccine No Vi CPS for <2 years old	None significant Oral form has fewer side effects than parenteral form.	Should be avoided because the safety is unknown	Yes (killed vaccine) Unknown (live vaccine), should avoid	Vivotif (a live Ty 21a vaccine), Typhim Vi (Vi CPS)
Meningococcal Purified bacterial capsular polysaccharide	2 weeks before travel 1 dose of 0.5 ml deep SC or IM Booster: may be given after 3-5 years.	Severe reaction to previous dose	Mild local reaction Fever (rare)	Yes	Yes	Meningococcal A+C (groups A and C)

Vaccine, type	Initial dosage/booster	Contraindication	Adverse effect	Use in pregnancy	Use in HIV infection	Available in Thailand
Rabies Cell-cultured or embryonated egg vaccine	1 ml IM or 0.1 ml ID on day 0, 7, and 21-28 Booster: depends on exposure risk ID route is less immunogenic than IM route but also is cost-saving.	Severe reaction to previous dose	Hypersensitivity Anaphylaxis Neuroparalytic reactions	Yes	Yes	TRCS-Verorab
Japanese encephalitis Inactivated virus	At least 2 doses before travel Adults: 3 doses of 1 mL on day 0, 7 to 14, and 28 to 30 (day 0, 7, 14 in USA if time limited) or 2 doses given 7-4 days apart ^b Children < 3 years of age: may be given 3 doses of 0.5 mL Booster after 1 year then every 3 years	Hypersensitivity to vaccine components esp. gelatin, neomycin	Hypersensitivity reactions Neurological complications Occur mainly in travelers from non-endemic areas ^{16-17,45-47}	Should be avoided but may consider in high-risk travelers	Unknown, should avoid	JE-Vaccine (Beijing strain)
Tick-borne encephalitis Killed vaccine	Second dose 2 weeks before departure 2 doses IM 4-12 weeks apart Booster: 9-12 months after 2 nd dose	Sensitivity to thiomersal (vaccine preservative) Adverse reaction to previous dose	Local reactions Fever (rare)	Should be avoided but may consider in high-risk travelers	Unknown, should avoid	Not available

Abbreviations: SC = subcutaneous, IM = intramuscular, ID = intradermal

a. The second dose should be given at least 2 weeks before departure.

b. suggested to provide short-term immunity but is effective in only 80 percent of recipients.

Table adapted from references.⁴⁸⁻⁴⁹

Table 4. Antimalarial chemoprophylaxis.

Drug	Duration and Dosage	Contraindication	Pregnancy/ breast-feeding	Region that can be used	Availability in Thailand
Atovaquone-Proguanil combination pill (A/P) (Malarone)	Begin 1-2 days prior to travel and continue for 1 week after travel Adult 250 mg A/100 mg P 1 tablet once daily Pediatric 62.5 mg A/25 mg P 11-20 kg: 1 tablet once daily 21-30 kg: 2 tablets once daily 31-40 kg: 3 tablets once daily >40 kg: adult dose	Hypersensitivity to atovaquone or proguanil Creatinine clearance <30 ml/min Children weighing less than 11 kilograms (25 pounds)	No data for atovaquone but not recommended in women who breastfeed infants weighing <11 kg	Areas with chloroquine- or mefloquine-resistant <i>P. falciparum</i> The South Pacific Africa regions except North Africa Hainan and Yunnan provinces of China Indian Subcontinent ^a Darié n Province and San Blas Province in Panama Tropical South America (except Paraguay)	No
Chloroquine	Begin 1 week prior to travel (1 day prior for daily dose) and continue for 4 weeks after travel Adult (chloroquine base) 300 mg once weekly or 100 mg daily for 6 days each week	Hypersensitivity to chloroquine Epilepsy Psoriasis	Safe	Areas with chloroquine-sensitive <i>P. falciparum</i> <i>Caribbean</i> East Asia except Hainan and Yunnan provinces of China Eastern Europe and the NIS ^b Mexico and Central America ^c Middle East ^d , Argentina, Paraguay	Yes (but should not be used because of resistance)
Chloroquine/proguanil combination	Begin 1 day prior to travel and continue for 4 weeks after travel This tablet is not for persons of <50 kg. >50 kg: 100 mg chloroquine base plus proguanil 200 mg once daily	Hypersensitivity to chloroquine or proguanil Liver/kidney insufficiency Epilepsy Psoriasis	Safe	Same as chloroquine	No
Doxycycline	Begin 1 week prior to travel and continue for 4 weeks after travel Adult 100 mg tablet once daily Pediatric (>8 years old) 1.5 mg salt/kg once daily (do not exceed 100 mg)	Hypersensitivity to tetracycline Liver disease Children < 8 years old	Contraindicated in pregnancy but may be used during breastfeeding	Areas with chloroquine- or mefloquine-resistant <i>P. falciparum</i> The South Pacific Africa regions except North Africa Hainan and Yunnan provinces of China Indian Subcontinent Darié n Province and San Blas Province in Panama Tropical South America (except Paraguay)	Yes

Drug	Duration and Dosage	Contraindication	Pregnancy/ breast-feeding	Region that can be used	Availability in Thailand
Mefloquine (250 mg tablet)*	Begin 2-3 weeks prior to travel and continue for 4 weeks after travel Weekly dosage Adult 1 tablet Pediatric 5-12 kg (3-23 months): 1/4 tablet 13-16 kg (2-3 years): 1/3 tablet 17-24 kg (4-7 years): 1/2 tablet 25-35 kg (8-10 years): 3/4 tablet 36 to 50 kg (11-13 years): 1 tablet	Hypersensitivity to mefloquine Psychiatric or convulsive disorder History of severe neuropsychiatric disease Concomitant halofantrine treatment Treatment with mefloquine in previous 4 weeks.	Safe (Category C)	Areas with chloroquine-resistant <i>P. falciparum</i> The South Pacific Africa regions except North Africa Hainan and Yunnan provinces of China Indian Subcontinent Darié n Province and San Blas Province in Panama Tropical South America (except Paraguay)	Yes (Mephaquin, Mequin)
Primaquine Used in special circumstances For presumptive anti-relapse therapy (terminal prophylaxis) of <i>P. vivax</i> and <i>P. ovale</i>	Begin 1-2 days prior to travel and continue for a week in special circumstances and 2 weeks for terminal prophylaxis after return Adult 52.6 mg salt (30 mg base primaquine) once daily Pediatric 0.6 mg/kg base (1.0 mg/kg salt) up to adult dose, once daily	G6PD Deficiency (testing is required)	Contraindicated in pregnancy. Test infants for G6PD level before given primaquine in women who breastfeed.	The South Pacific Africa regions except North Africa Hainan and Yunnan provinces of China Indian Subcontinent Darié n Province and San Blas Province in Panama Tropical South America (except Paraguay)	Yes
Hydroxychloro- quine sulfate	Begin 1-2 weeks prior to travel and continue for 4 weeks after travel Adult 400 mg once weekly Pediatric 6.5 mg/kg (up to a maximum of 400 mg) once weekly	Hypersensitivity to hydroxychloroquine Presence of retinal or visual field changes attributable to any 4-aminoquinoline compound Long-term therapy in children	Safe	An alternative to chloroquine for prophylaxis only in areas with chloroquine-sensitive <i>P. falciparum</i>	Yes (Plaquenil)

Table adapted from reference.^{48,50}

a. Indian Subcontinent countries are Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan, Sri Lanka

b. NIS = the Newly Independent States of the Former Soviet Union (in Armenia, Azerbaijan, Georgia, Kyrgyzstan, Tajikistan, Turkmenistan, and Uzbekistan)

c. In Mexico, Belize, Guatemala, El Salvador, Nicaragua, Honduras, Costa Rica, and the Bocas Del Toro Province of Panama

d. Except in Iran, Saudi Arabia, Yemen, and Musandam Province in Oman

e. Not recommended in people who need fine coordination and spatial discrimination, i.e., pilots, machine operators

three or more unformed stools in 24 hours accompanied by with one of these symptoms: nausea, vomiting, abdominal cramps or pain, fever, blood in stools.²³ The most common etiologic agent is enterotoxigenic *Escherichia coli* but another emerging agent is enteroaggressive *E. coli*. Other pathogens include *Salmonella*, *Shigella*, *Campylobacter*, *Aeromonas hydrophila*, *Plesiomonas shigelloides* which account for 5 percent to 15 percent of cases. Protozoa such as *Entamoeba histolytica*, *Cryptosporidium parvum*, and *Giardia lamblia* cause diarrhea in less than 5 percent cases. Antibiotic- or antimalarial-associated diarrhea due to *Clostridium difficile* is also rare. Norovirus and rotavirus are the rare causes, but recently, outbreaks of noroviruses on cruise ships has been increasing.²⁴ There is an increased risk of infection in persons who take proton-pump inhibitors, who have achlorhydria, and young adults (20-29 years old) in view of the often adventurous behavior in this age group. In the absence of blood or pus in the stool, supportive treatment with antimotility agents is recommended. If diarrhea does not improve within 3-6 hours, empirical antibiotics using fluoroquinolone or azithromycin should be considered.²⁵⁻²⁶ Antibiotics should also be considered in persons with advanced HIV disease, persons with underlying medical problem that may be affected by diarrhea, and persons on an important agenda for less than a week who cannot afford to be sick. Rifaximin, a nonabsorbable rifamycin, is FDA-approved for traveler's diarrhea caused by noninvasive strain *E. coli* but not for bloody diarrhea or febrile diarrhea. It might not be effective against *Campylobacter* or *Shigella*.²⁷⁻²⁸ However, it is not available in Thailand.

Diseases associated with water exposure

Travelers anticipating water exposure activities who travel to endemic areas should be advised of the risks for acquisition of schistosomiasis. Leptospirosis

can also be transmitted through contaminated fresh water in developing countries. Prophylaxis with doxycycline 200 mg weekly may be given to high risk travelers who anticipate extensive water related activity.

Parasites

There are several parasitic infections depending on geographic areas and exposure risk. Travelers should be advised to avoid uncooked meat (*Taenia* spp.-beef and pork; *Gnathostoma*-fish or poultry), soil-contaminated food (roundworms), and walking barefoot (*Necator* and *Ancylostoma*) in tropical countries. Other conditions are swimmer's itch (*Schistosoma*), Seabather's eruption (larvae). Loiasis (*Loa loa*- deer fly bite) is endemic in Africa.

SARS and avian Influenza

Travelers should be advised to avoid traveling to the endemic area with potential SARS outbreaks and to avoid poultry contact in regions with avian influenza. If the trip is unavoidable, physicians should instruct travelers to observe for possible signs and symptoms and seek medical advice. Post-exposure prophylaxis with Oseltamivir may be considered for H5N1 infections.

Tuberculosis

For long-term travelers from developed countries to developing countries or persons who work in healthcare facilities, baseline tuberculin test and annual re-testing are recommended.

Snake bites

The important venomous snakes in Thailand are in Family Viperidae (vipers) and Elapidae (cobra, king cobra, kraits, and sea snakes). Snakes are active at night and in warm weather. In Southeast Asia snakebites usually occur as occupational exposures,

often in farmers, snake handlers, and fishermen. Most incidents happen when snakes are startled by being disturbed in the dark or undergrowth with bare feet or intentionally/unintentionally handled. Snake bites may also occur indoors when snakes search for their prey. Travelers should be advised to wear boots and long pants, especially at night, avoid sleeping on the floor, and refrain from harassing snakes.

Initial management includes: moving the victim out of the snake territory, cleaning the wound, immobilizing the affected part and reassuring the traveler. Restrictions of blood flow to the affected area, such as using a tourniquet or making an incision of the bite site, are not recommended.²⁹ If travelers' eyes are exposed to venom, copious rinsing of the eyes with water should be performed immediately. The traveler should be transferred to the nearest hospital as soon as possible. Snake identification is helpful, especially when antivenom is needed, but collecting the snake should only be done when it poses little danger. Clinical symptoms depend on types of venom. Treatment includes supportive measures and antivenom therapies.

Antivenom is purified immunoglobulin from horse serum or plasma. Monovalent and polyvalent antivenom therapies are available for specific or different species of snakes, consecutively. Antivenom use requires a clinical judgment for each individual and may be justified if benefits exceed risks because of adverse reaction(s), cost, and intermittent limitations in supplies. Generally, it is indicated in travelers with an evidence of systemic envenomation and/or severe local envenomation evidenced by local tissue destruction. Signs of systemic envenomation include: hemostatic abnormalities, evidence of neurotoxic reactions, cardiovascular abnormalities, acute renal failure, hemoglobinuria, myoglobinuria, and supporting laboratory evidence of systemic envenomation.²⁹ Reactions to antivenom are

common ranging from acute allergic reactions (i.e. anaphylactic/anaphylactoid reactions), pyrogenic (endotoxin) reactions to delayed serum sickness.

There is no absolute contraindication in administration of antivenom. However, physicians should be very careful in persons with a history of reaction to horse or sheep serum and/or a history of atopic diseases, especially severe asthma. In such cases, antivenom should be given only with signs of systemic envenomation; in addition, premedication with antihistamine, epinephrine, or corticosteroids may also be considered. Unfortunately, antivenom is not available for all types of snakes, such as sea snakes and some species of coral snake. In Thailand, the Queen Saovabha Institute is a major manufacturer of antivenom products.

Snakes' oral flora contain wide varieties of aerobes and anaerobes, especially enteric Gram-negative rods, anaerobes, and some Gram-positive organisms. Infection caused by *Aeromonas* spp. is rare but was reported.³⁰⁻³¹ A prophylactic antibiotic is useful in bite wounds from some snake species, such as Malayan pit vipers.³² Penicillin or erythromycin and a single dose of gentamicin³² or ceftriaxone are options but broad spectrum antibiotics covering gram-negative rods and anaerobes should also be considered for wounds contaminated with unsterilized blades or knives and in necrotic wounds.

Guidelines for the clinical management of snake bites in the Southeast Asian region is available at http://w3.whosea.org/LinkFiles/SDE_mgmt_snake-bite.pdf.

Non-infectious conditions

Air travel-related illnesses

Air-travelers are at risk for developing "economy class syndrome"³³⁻³⁴ or air travel-related deep vein thromboembolism and "economy class stroke syndrome".³⁵ Long-haul flight is the major risk factor

(more common in > 12 hours flight and rarely occurs in < 4 hours flight)³⁶⁻³⁷ but the risk is very low in travelers without preexisting risk factors. However, both conditions are not limited to only economy class passenger³⁸ and can occur with a long travel by other means of transportation. A single dose of low-molecular weight heparin showed a significant reduction of thrombosis in high-risk air-travelers.³⁹ Travelers are also at risk for other diseases because passengers and cargo aircraft may be vectors of disease such as tuberculosis, avian influenza, SARS, malaria, etc.⁴⁰

High altitude illness

This is a preventable syndrome caused by hypobaric hypoxia whereby the body cannot acclimatize to high altitudes. There are three major syndromes due to capillary leakage in the brain or lungs: acute mountain sickness (AMS), high-altitude cerebral edema (HACE), and high-altitude pulmonary edema (HAPE).⁴¹⁻⁴² The morbidity and mortality are high. Travelers who travel to a high-altitude must be able to recognize symptoms and know proper preventative measures for high-altitude illness. It occurs in travelers with a rapid ascent to altitudes of 8,000 feet (2,500 m) or more and the risk increases with increasing altitude. Acetazolamide can be used for prophylaxis; 125 mg-250 mg twice daily starting 1 day before ascent to altitudes above 3,000 metres, and first 2 days at the high altitude.⁴² Dexamethasone is an alternative.⁴² Recommended treatments for AMS and HACE include hyperbaric oxygen chamber, dexamethasone, and acetazolamide. Treatment of HAPE involves hyperbaric chamber with nifedipine and/or dexamethasone.⁴²

Drowning

Traveler should be instructed to be aware of the possibility in both fresh and sea water. Travelers should obtain information from local people for any risks.

Medical equipment and basic medical information

Travelers should carry a basic medical kit contains first-aid supplies including a thermometer, primary care physician card or a contact number and an insurance card. Recent EKG is necessary for a patient with cardiac problems.

Crime

Information can be obtained from local police officers or from media but travelers should be vigilant at all times.

Other

Travelers should check with the insurance company regarding international travel coverage. Most national plans do not include international coverage. Travelers should inform someone in their country of origin regarding the trip and how to contact travelers if possible.

Follow-up after return

Travelers should be advised to seek medical attention after return if they develop any illnesses. Travel history maybe helpful to diagnose a specific disease.

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