

From Livingstone to ecotourism

What's new in travel medicine?

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abstract

OBJECTIVE To review recent developments in the field of travel medicine and to outline the knowledge and resources family physicians need for providing health advice to travelers headed for tropical or developing countries.

QUALITY OF EVIDENCE Personal files; references from review articles and from a recent textbook of travel medicine; current guidelines on pretravel advice; and a review of the 1996 to 1999 MEDLINE database using "travel medicine" as a term and subject heading, "trave(l)lers' diarrhea" as a text word and subject heading, "immunization + travel," and "malaria + chemo prevention" were used as information sources. Priority was given to randomized controlled trials and recommendations of expert or national bodies.

MAIN MESSAGE Some elements of travel medicine, such as malaria chemoprophylaxis, have become more complex. Some valuable new preventive measures, such as hepatitis A vaccine, treated bed nets, and antimalarial drugs, have become available. Some health risks, such as cholera, have been overemphasized in the past, whereas others, such as tuberculosis and sexually transmitted diseases, have been underemphasized. Information sources relevant for providing travel health advice have improved and expanded. Canadian evidence-based guidelines addressing most important travel health issues are now available.

CONCLUSIONS Travel medicine is a rapidly evolving field. Physicians intending to provide health advice to travelers to high-risk parts of the world should be well prepared and have access to good, up-to-date information.

résumé

OBJECTIF Examiner les faits nouveaux dans le domaine de la médecine des voyages et faire valoir les connaissances et les ressources requises par les médecins de famille pour donner des conseils en matière de santé aux voyageurs qui se rendent dans des pays tropicaux ou en développement.

QUALITÉ DES DONNÉES Les sources d'information comportaient des dossiers personnels; de références d'articles de revue et d'un récent manuel sur la médecine des voyages; les guides de pratique actuels sur les conseils préalables au voyage; et une recension de la base de données MEDLINE, de 1996 à 1999, à l'aide des termes en anglais «médecine des voyages» comme terme et rubrique sujet, «diarrhée des voyage(ur)s» comme mot dans le texte et rubrique sujet, «immunisation + voyage», et «paludisme + chimioprévention». La priorité a été accordée aux essais aléatoires contrôlés et aux recommandations d'experts ou d'organismes nationaux.

PRINCIPAL MESSAGE Certains éléments de la médecine des voyages, comme la chimioprophylaxie contre le paludisme, deviennent de plus en plus complexes. Certaines nouvelles mesures de prévention utiles, comme le vaccin contre l'hépatite A, les moustiquaires de lit traités et les antipaludéens, sont maintenant disponibles. Certains risques pour la santé, comme le choléra, ont été exagérés par le passé, tandis que d'autres, comme la tuberculose et les maladies transmises sexuellement, n'ont pas fait l'objet de suffisamment d'attention. Les sources de renseignements sur les conseils de santé à prodiguer avant les voyages sont meilleures et plus nombreuses. Des lignes directrices canadiennes fondées sur des données probantes sont maintenant disponibles.

CONCLUSIONS La médecine des voyages est un domaine en évolution rapide. Les médecins qui ont l'intention de prodiguer des conseils de santé aux voyageurs à destination de régions du monde à risque élevé devraient être bien préparés et avoir accès à de l'information fiable et à jour.

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The art of successful travel consists in carrying as few impediments as possible but always taking your wits with you.

—Dr David Livingstone¹

Livingstone might be thought of as the father of travel medicine. He was the original “high-risk” traveler, his expeditions long preceding those of the most adventurous modern cross-Africa truck trekkers or Himalayan mountain bikers. He almost certainly had the only available travel vaccine, smallpox. He boiled his water, believing in advance of the discovery of intestinal pathogens that bad water was responsible for his recurrent diarrhea. He also depended on quinine during his African explorations.

Previous British expeditions in Africa had suffered losses of between 36% and 100% of their European members over periods of just a few months. Using quinine for prophylaxis and presumptive therapy, Livingstone lost “only” 17% of the European members of his party during 5 years of African exploration.¹

Travel medicine has changed, not only since Livingstone’s time but in the past decade, into an established area of clinical knowledge and practice and a field of scientific investigation. An International Society of Travel Medicine complete with journal has been established, and training and accreditation are evolving.

Quality of evidence

Cohort and retrospective studies of returned travelers have greatly increased our understanding of the frequency of adverse health events and the relative importance of specific travel-acquired conditions. Estimates of malaria risk are largely based on local epidemiologic information, the quality of which varies widely. Evidence for the efficacy of the newer antimalarial agents and vaccines is largely from randomized controlled clinical trials. Evidence on the risk of many specific travel-associated illnesses, such as sexually transmitted diseases (STDs) and tuberculosis, comes from small studies of returned travelers and from epidemiologic studies of disease rates in the countries in which they traveled. Good evidence from clinical trials supports empiric therapy for travelers’ diarrhea.

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This article focuses on advice and preventive measures before travel and does not attempt to address the health problems of returned travelers. Several important developments in travel medicine are summarized in **Table 1**.



Who seeks travel health advice and where?

Seeking and providing travel health advice are often hit-or-miss affairs. The travel industry—airlines and travel agents—has not taken consistently effective measures to identify itineraries during which travelers could run health risks or to direct travelers to appropriate sources of advice. Some have been reluctant to “frighten” travelers with talk of risks and exotic diseases. Fortunately, this attitude appears to be changing.

Immigrants from tropical countries returning to visit their homelands are an important group of travelers who might be less likely to seek travel health advice but who might be at increased risk for some travel-acquired illnesses.² Travelers commonly receive conflicting information and recommendations from their friends and family, from the destination country’s embassy in Canada, from the press (particularly regarding the antimalarial drug, mefloquine), from local people in the destination country, and from other travelers, and should be advised to expect this. Even when travelers do consult a physician or travel clinic before departure, the quality of the advice they receive can vary considerably.³

Table 1. New developments in travel medicine

More Canadians traveling to "exotic" destinations
More scientific knowledge about travel risks and interventions
New problems, such as development of chloroquine-resistant malaria
Better solutions, such as hepatitis A vaccine and treated bed nets
Better information, including Web-based resources

What health risks are associated with travel?

Health risks do not exist only in exotic or tropical destinations. Travelers can be exposed to Lyme disease in endemic areas of the United States or tick-borne encephalitis in parts of Europe. Travelers to the former Soviet Union risk the diseases of poverty or failure of the public health system, such as hepatitis A, diphtheria, and multidrug-resistant tuberculosis.

Diarrhea. It is said that travel broadens the mind and loosens the bowels. Diarrheal illness is the most common travel-specific health problem, although risk varies with destination and travel style. Diarrhea is not usually serious, but it is frequently distressing and disruptive of travel activities. Many organisms can cause diarrhea in travelers, but most acute infections are bacterial.

Hepatitis A. Previously underestimated as a travel health risk, hepatitis A ranks high in both frequency and severity among health problems experienced by short-term travelers.⁴ Hepatitis was also found to be the single most serious health problem among American missionaries in Africa, and serologic studies in these long-stay travelers demonstrated that infection with hepatitis A was almost inevitable if they stayed long enough in the field.^{5,6} Hepatitis A can be disabling for weeks to months and has a relatively high mortality rate, particularly in older adults. Risk of hepatitis A is not limited to adventurous destinations but can be encountered in popular vacation spots, such as Mexico and the Caribbean.

Malaria. Among the infectious diseases encountered by travelers, malaria carries the greatest risk of death, particularly for travelers to sub-Saharan Africa. Increasing numbers of Canadians, now more than 1000 annually, are returning from the tropics with malaria, and there have been several malaria deaths in recent years.^{7,8} Diagnosis and appropriate management are often suboptimal or delayed in Canada.⁹

Typhoid fever and cholera. Typhoid fever is substantially less common than malaria but remains a concern for travelers to high-risk destinations. Cholera is very rare among most travelers. Greater than usual indiscretion is required to catch it because the infectious dose is high, and it is treatable with access to basic medical care.

Dengue fever, hepatitis B, Japanese B encephalitis, meningococcal disease, rabies. Dengue fever, an unpleasant, but usually self-limiting viral illness transmitted by a day-biting mosquito, has made a dramatic resurgence and is now relatively common in the Caribbean and other common tourist destinations.¹⁰ No vaccine is currently available. Hepatitis B is highly endemic in many developing countries and can be acquired not only by sexual contact, but also by close contact with children. Japanese B encephalitis is rarely seen in travelers, but when it occurs, it carries a high risk of death or permanent neurologic sequelae. Recurrent epidemics of meningococcal disease occur across the Sahel belt of Africa, and sporadic epidemics sometimes occur in other developing regions. Rabies is occasionally reported in travelers.¹¹ Rates of dog rabies are very high in countries, such as India, Thailand, and some parts of Latin America; at least 15 000 people are thought to contract rabies in India annually.

Sexually transmitted diseases. In the tropics, STDs include particularly unpleasant conditions, such as chancroid, and are likely to be drug resistant. In many developing countries, human immunodeficiency virus is highly prevalent, particularly among commercial sex workers (90% in one group of prostitutes in Kenya). Heterosexual transmission rates appear to be much higher than in North America, perhaps due to coexistent STDs. Human immunodeficiency virus is by no means a theoretical risk of travel—I have cared for several Canadians who acquired HIV infection heterosexually while working or traveling in high-prevalence countries.

Tuberculosis. Tuberculosis has probably been underestimated as a risk of travel and work overseas.¹² Depending on the circumstances of living or traveling, travelers can assume the local risk of tuberculosis exposure, which can be up to 3% per year and is probably much higher among health workers.

Heart disease, accidents. Overall, the most common cause of death among Canadians overseas, as in Canadians at home, is heart disease. Another important noninfectious risk of travel is motor vehicle accidents, the most common cause of death among American Peace Corps volunteers. Physical violence, usually civil rather than military or political, can be a risk in developing countries.

Rare, exotic diseases. Travelers are generally at low risk of most of the more exotic tropical diseases, but they might have read about them and express concerns. American trypanosomiasis (Chagas' disease) has never, as far as I can determine, been described in a returned traveler, though it is seen in immigrants from countries where it is endemic. Leprosy is extraordinarily uncommon in returned travelers.¹³ African sleeping sickness was found in only 13 American travelers over 17 years.

Intestinal helminths might be a concern for Canadian volunteers living in rural villages who are exposed to local conditions for long periods, but are otherwise uncommon. Several cases of neurologic diseases due to schistosomiasis have been recorded,¹⁴ and a case of cerebral cysticercosis was recently described in a traveler from Italy to Latin America 2 years after return.¹⁵ In general, however, these are all examples of exceptions that prove the rule: while some of these conditions are important health problems for immigrants from countries where these diseases are endemic, they are very rare in Canadian travelers to those countries.

Interventions

The initial, central element of travel health advice is individualized assessment (**Table 2**). **Table 3** gives food and water precautions that are heeded by travelers to widely varying degrees and that have variable effects¹⁶ on preventing diarrhea. Food hygiene, particularly restaurant standards, might be an important factor in risk of diarrhea and is often outside travelers' control.

Because travelers' diarrhea is far from being wholly preventable in high-risk environments, it is particularly important to provide travelers with the information and tools to manage it. Travelers should be advised about maintaining hydration. The symptoms of mild, self-limited diarrheal episodes can be managed with loperamide. Adult travelers other than those at very low risk could be given prescriptions for a 1- to 3-day course of a quinolone for severe, acute episodes of diarrhea.

Table 2. Individualized assessment of travelers

Itinerary: consider such detail as region of travel within a destination country, rural or urban travel, and duration of travel

Travel style: backpack or five-star

Personal characteristics and special problems: allergies, pregnancy, children, diabetes, and other conditions

Specific activities and exposures: occupational or recreational

Table 3. Food and water precautions

DO	DON'T
Drink tea or coffee	Use ice
Drink carbonated drinks	Eat salad
Eat cooked food piping hot	Patronize roadside food vendors
Eat fruit you peel yourself	Drink unpasteurized milk
Purify water*	
• Bring to a rolling boil (altitude-dependent formulas not necessary)	
• Add iodine	
• Use filters and purifiers	

*Bottled water is unreliable in some countries.

Vaccination

Preparing for travel presents a good opportunity to update routine Canadian vaccinations. Diphtheria, tetanus, and measles are not limited to the tropics, but exposure is more common in low-income countries.¹⁷ Do not forget influenza, and remember that the season is reversed south of the equator.¹⁸

Hepatitis A vaccine should be offered to travelers going anywhere outside North America, western Europe, Australia, New Zealand, and Japan and is a first priority for "high-risk" travelers. There is little if any place remaining for use of immune globulin for travelers. Hepatitis B vaccine has perhaps been underemphasized in travel advice, particularly for long-stay travelers and those who might be sexually active with local partners or work with children. A combined hepatitis A and B vaccine is now available.

Detailed information on the indications for specific travel vaccines (**Table 4**¹⁸⁻²⁵) can be found in travel health information resources (**Table 5**²⁶).

Table 4. Travel vaccines

UPDATING CANADIAN VACCINES

Diphtheria and tetanus

Measles

Polio ("old world" only)

Influenza with or without pneumococcal¹⁸

TRAVEL OUTSIDE "WESTERN" COUNTRIES AND JAPAN

Hepatitis A

Typhoid for high-risk travelers¹⁹

LEGALLY REQUIRED (FOR TRAVEL TO SPECIFIC PARTS OF AFRICA AND SOUTH AMERICA)

Yellow fever

GEOGRAPHICALLY DETERMINED

Japanese B encephalitis (South and Southeast Asia)²⁰Meningococcal (African Sahel and epidemics)²¹

Tick-borne encephalitis (central Europe)

DEPENDING ON PLANNED ACTIVITIES

Rabies²²

Hepatitis B

Bacillus Calmette-Guérin or pretravel and post-travel
Mantoux tests^{23,24}

RARELY REQUIRED

Cholera²⁵**Malaria prevention**

Avoiding mosquitoes remains the first element of malaria prevention. The *Anopheles* mosquito conveniently confines its biting to the hours between dusk and dawn. Impregnating bed nets with permethrin has been shown to markedly increase their protective efficacy, and treated nets have reduced malaria incidence and mortality according to studies in the tropics.²⁷ It is reasonable to assume they will also work for travelers. Every traveler to malaria-endemic areas should be strongly encouraged to get one.

Diethyltoluamide (DEET) remains highly effective. It is extraordinarily safe, although a few episodes of neurologic events have been attributed to it among literally billions of applications.^{28,29} Travelers are advised, therefore, not to use high-concentration formulations and to avoid unnecessary body surface area or lengthy exposure in children.

Malaria chemoprophylaxis is perhaps the most challenging area of travel medicine, and access to up-to-date, detailed information and expert recommendations is critical.^{30,31} Some travelers to tropical

countries will be at little or no risk of malaria and should not receive chemoprophylaxis at all.

The regions of the world where chloroquine is still reliably effective are few and shrinking. The combination of chloroquine and proguanil appears to be clearly inferior to mefloquine, which remains the drug of choice for most travelers to malaria-endemic areas.³² It is associated with rare (≤ 1 in 10000) serious neuropsychiatric problems and more common, troublesome, but not dangerous, adverse effects such as nausea, sleep disturbance, vivid dreams, and mood alteration. These effects have received a great deal of press—it has been suggested that the most serious adverse effect of mefloquine is its tendency to cause hysteria in journalists who have never taken the drug!

In several studies involving more than 2000 subjects given mefloquine, the drop-out rate was in the 1% to 3% range, indicating that most people tolerate mefloquine readily. A "loading dose" strategy might help identify those who have problems with mefloquine before they leave Canada. Former concerns about use with β -blockers or calcium channel blockers, long-term use, and use for infants have largely been allayed by experience. Current guidelines³¹ support use of mefloquine during pregnancy, particularly after the first trimester, but a recent study from Thailand³³ suggests a possible association between maternal mefloquine use and adverse fetal outcomes. On the other hand, malaria is especially dangerous for pregnant women and their fetuses. Hence, travelers should be cautioned that visiting malaria-endemic areas during pregnancy or with small children is risky.

Doxycycline is the usual second-choice chemoprophylactic for chloroquine-resistant areas. Its efficacy appears to approach that of mefloquine when adherence is assured.³⁴ In practice, the requirement for daily dosing often compromises adherence. Practical problems include gastrointestinal upset, vaginal candidiasis, and rarely, photosensitivity. It is not recommended for pregnant women or children 8 years of age or younger. In the American forces in Somalia, where both mefloquine and doxycycline were used, more adverse events were observed among troops using doxycycline.³⁵

Several promising developments include a combination of atovaquone and proguanil (Malarone), which is approved in Canada for *treatment* of malaria. It is highly effective for drug-resistant malaria and might be effective for prophylaxis if taken daily.^{36,37} Primaquine, the drug long used to eradicate the

latent liver stage of *Plasmodium vivax* and *ovale*, has recently been found to be effective prophylaxis against *P falciparum*.³⁸ Theoretically, it should have the unique advantage that it could be discontinued shortly after leaving the endemic area, unlike standard malaria prevention agents that must be continued for 4 additional weeks. Primaquine can cause severe hemolysis in people with some forms of glucose-6-phosphate dehydrogenase (G6PD) deficiency, however, so most travelers must be tested for this red-cell abnormality before using primaquine. The role of these two prophylactic medications in travelers is not yet clear.

Some travelers prefer the idea of treating malaria when it occurs rather than taking prophylactic medication for a prolonged period. Problems with this strategy include the impossibility of accurate clinical diagnosis of malaria even by experts, much less by sick lay travelers, and the frequent difficulty of gaining rapid access to reliable diagnosis and therapy in unfamiliar countries. In practice, travelers who have used a self-treatment strategy seem to have used it poorly.³⁹ Availability of accurate "dipstick" tests for malaria could make this strategy more feasible, and atovaquone-proguanil appears to be an attractive candidate for self-treatment. This approach cannot be widely recommended at present because lay travelers have problems with accurate interpretation of currently available tests.⁴⁰

Travelers should be advised to inform physicians of their travel to malaria-endemic areas if and when they present with any unexplained febrile illness within a year of their return.

Miscellaneous risks

Travelers should be routinely advised about the high risk of STDs and HIV in many tropical or low-income countries. Extra attention to travelers who are young, unaccompanied, planning a long stay, or who have a history of STD risk, appears reasonable.⁴⁰ Risk of tuberculosis should be addressed, either by before-and-after travel skin testing or consideration of bacillus Calmette-Guérin vaccine, particularly for travelers planning long-term stays and those working in health disciplines.^{19,20}

Information on prevention and management of problems, such as jet lag⁴² and altitude sickness,⁴³ is available in the Committee to Advise on Tropical Medicine and Travel's (CATMAT) guidelines. There are also guidelines for advising travelers with pre-existing problems, such as cardiac or pulmonary disease, diabetes, and HIV.⁴⁴⁻⁴⁷

Table 5. Travel health information resources

RESOURCE	DESCRIPTION
Centres for Disease Control and Prevention (CDC)	<i>Yellow Book</i> : Health information for international travel www.cdc.gov/travel/travel.html
World Health Organization (WHO)	<i>Yellow Book</i> : International travel and health www.who.int
Committee to Advise on Tropical Medicine and Travel (CATMAT)	<i>International Travel Health Information: Guidelines for Health Professionals</i> (binder format available): CATMAT statements and guidelines, including malaria recommendations www.hc-sc.gc.ca/hpb/lcdc/osh/reccom_e.html#catmat
Laboratory Centre for Disease Control (LCDC)	Fax link 1-613-941-3900, 24-hr service providing travel health information for travelers and travel health professionals www.hc-sc.gc.ca/hpb/lcdc/osh/tmp_e.html Regularly updated information, including international outbreak and health hazard information and a list of clinics providing travel health services in Canada
Journal	<i>Journal of Travel Medicine</i>
Books	<i>Don't Drink the Water</i> (new edition imminent) <i>Canadian Immunization Guide Textbook of Travel Medicine and Health</i> (DuPont & Steffen)
Society	International Society of Travel Medicine, PO Box 15060, Atlanta, GA 30333-0060 USA
Other electronic resources	Freedman DO. Keeping current. Travel medicine resources available on the Internet. ²⁶

Cost-effectiveness

The cost-effectiveness of travel health advice varies with the anticipated level of exposure to health risks and across the spectrum of specific interventions. One analysis determined that typhoid and hepatitis A vaccines were not cost-effective, but that malaria prophylaxis was highly cost-effective for travelers to areas where it is endemic.⁴⁸ The case for cost-effectiveness might be of immediate practical relevance because travel health advice is no longer covered by health care insurance in some provinces.

Key points

- Most family physicians are unable to keep up with constantly changing recommendations for foreign travelers and need access to resources that are routinely updated. This article lists several accurate, reliable websites that provide that information.
- Several new preventive measures are now available: hepatitis A vaccine, treated bed nets, and new antimalarial drugs.
- Malaria chemoprophylaxis is becoming increasingly complex and requires detailed information about travel itinerary, current medical problems, and the spectrum of medications available.
- In the past, some risks, such as cholera, have been overemphasized while others, such as hepatitis, tuberculosis, motor vehicle accidents, and sexually transmitted diseases, have been underemphasized.

Points de repère

- La majorité des médecins de famille ne sont pas en mesure de se tenir au fait des recommandations constamment renouvelées à prodiguer aux personnes qui voyagent à l'étranger. Ils doivent avoir accès à des ressources systématiquement mises à jour. Le présent article donne la liste de quelques sites Web fiables et exacts qui fournissent ces renseignements.
- Il existe maintenant de nouvelles mesures préventives: le vaccin contre l'hépatite A, des moustiquaires de lit traitées et de nouveaux médicaments antipaludéens.
- La chimioprophylaxie contre le paludisme devient de plus en plus complexe et exige des renseignements détaillés sur l'itinéraire du voyage, les problèmes de santé actuels et l'éventail des médicaments disponibles.
- Par le passé, certains risques comme le choléra ont été exagérés, tandis que d'autres comme l'hépatite, la tuberculose, les accidents de la route et les maladies transmises sexuellement n'ont pas reçu l'attention nécessaire.

Conclusion

Travel medicine is an evolving and rewarding field. Physicians or nurses planning to provide travel health advice to high-risk travelers should acquire training and experience in the area and use one or more current, comprehensive reference sources. ♣

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