A Week in the Life of a Travel Clinic

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In a typical week in Travel Health Services (THS), our travel clinic in Syracuse, N.Y., we counseled and immunized 21 travelers. It was the usual diverse, intelligent, vital group of people: a 45-year-old mother with her 12- and 15-year-old daughters who were preparing to meet her husband in Virginia and travel by air to Nairobi, Kenya, overland to Kampaala, Uganda, and then by air to Mozambique; a 54-year-old man with a serious and progressive disabling neurologic disorder who was traveling first to Brazil and later to Thailand, Australia, and Europe—he was racing the clock before his advancing disability precluded travel; a 64-year-old woman embarking on a 2-week pilgrimage in Morocco, from Tangier to Fes to Meknes to Marrakech to Tarfaya, seeking the roots of her ancient Jewish family; a 65-year-old man who was traveling but wanted only his annual flu shot; a 59-year-old businessman who was leaving in 6 days for Bombay, Delhi, and Bhusawal in India and then on to Dhaka, Bangladesh—as we see all too often, he had not allowed adequate time for effective immunization; a 47-year-old man leaving for Quito, Ecuador, his base for high-peak technical climbing; a 63-year-old woman anticipating a 2-week high-elevation visit to La Paz, Bolivia, and Machu Picchu, Peru, taking with her a history of frequent premature heartbeats; a 41-year-old businessman, 6 weeks postsplenectomy, leaving in 4 days for the Pacific Rim—he was sent on his way with immune globulin, extensive counseling, and a plan for a posttrip immunization program (because of his splenectomy); a 46-year-old woman with a history of asthma, heading for a mission retreat in El Salvador, who received hepatitis A, influenza, and oral typhoid vaccines—3 h later, she called back with an acute asthma attack and hives, which responded readily to treatment; a 37-year-old businessman departing in 18 days for Bombay and Surat in India, the latter being the site of the recent “epidemic” of plague; a China-born couple in their late 50s returning home and desiring protection against “liver failure”, with the sketchiest understanding of hepatitis viruses; a resident physician, his wife, and their 5-month-old daughter, preparing for a 2-month visit to Zambia, where he was to work in the mission hospital where he was born to missionary parents 28 years ago; a 34-year-old businesswoman off to the Pacific Rim; two daughters, age 4 months and 4 years, of a lady born in India returning home to her birth city of Bombay for 1 month; and a 59-year-old woman also attending the mission retreat in El Salvador.

During this week at THS, we encountered the usual wide spectrum of demographics, travel experience, reasons for traveling, and itineraries. With just 21 travelers, the destinations included all continents except Antarctica. People were traveling for business, professional, and altruistic reasons and for pure touring pleasure. THS draws from an area of about 1,000,000 population; metropolitan Syracuse is the largest urban area at less than 500,000 persons. Given the region’s farming and small-enterprise economic base, we have been somewhat surprised at the amount and diversity of travel abroad.

In fact, central New York appears to reflect the national and international scene. Around our shrinking globe, 500 million travelers cross national boundaries each year, including 40 million Americans. One concomitant of this massive movement is exposure to potential pathogens on an unprecedented scale. Perhaps even more worrisome is the increasing potential
for the ready introduction, via air travel, of pathogens unknown to, or long disappeared from, a given geographical area (138). Even as we close in on polio eradication, we face an expanding distribution of malaria, dengue, diphtheria, and many other infections. Nearly 30 pathogenic microbes and/or infectious diseases have been described only in the past two decades, and another 20 have reemerged as threats to our health (91).

Travel medicine, with its integration of microbiology, infectious diseases, tropical medicine, epidemiology, and public health, holds considerable attraction for a wide spectrum of professionals with interests in human interaction with other species. In this review, I will try to convey the scope of travel medicine, without exhaustively examining the vectors, all possible infectious entities, detailed epidemiology of the diseases, or the nuances of therapy. I will address the risks that travelers face, the structure of systems available to prepare travelers, and the nature of the resources available to help travelers with their preparation.

**TRAVEL RISKS, RISK-BENEFIT, AND COST-BENEFIT**

The death rate of Americans traveling overseas is less than 5 per 100,000. The majority of deaths are due to cardiovascular and other preexisting medical disease and injuries. Fatal injuries largely involve motor vehicle accidents or drownings. Even homicides and suicides outnumber deaths due to infectious diseases: 2.9 versus 1% of overseas deaths (54). However, while little can be done systematically to prevent the noninfectious deaths, many if not most of the infection-related deaths are preventable. Two excellent examples are malaria, which can be avoided with conscientious use of personal protection measures, including insect repellents, and chemoprophylaxis; and hepatitis A, for which we now have two highly effective vaccines.

The incidence of nonfatal illness, compared with fatalities, is remarkably high: 45 to 75% (110, 113). Traveler’s diarrhea leads the list, with a 30 to 60% incidence in trips of 4 weeks or more to a developing country (113). As with most travel risks, prevention reduces the odds: strict adherence to food and water precautions, backed up by the judicious use of an appropriate antibiotic for treatment, can drastically reduce the misery caused by traveler’s diarrhea.

Vaccines are available for use against many of the infectious agents encountered while traveling (Table 1). There is, however, considerable debate about the cost-effectiveness of immunizations for travel (39, 139). It has been calculated that for nonimmune adults traveling to northern Thailand, it costs about $9 million to prevent one case of rabies, $6 million to prevent a death due to hepatitis A, and $4 million to prevent a case of Japanese encephalitis (39, 140). Behrens and Roberts have calculated the cost of averting one case of hepatitis A or typhoid fever with vaccine to be about $300,000 (5). Although such calculations are not exact, their order of magnitude justifies the assertion that all travel vaccines are probably cost-ineffective (5). Indeed, the failure of most health insurance plans to pay for travel immunizations is a tacit acceptance of this cost-ineffectiveness argument. As Dawood points out, however, such analyses look at the cost to society, not to the individual (39). It should be noted that the standard of cost-effectiveness as the sole determinant of services is not applied this strictly to most areas of American medicine. Medical insurance plans in many developed countries currently pay for pretravel health care.

### TABLE 1. Vaccines most frequently used in travel medicine

<table>
<thead>
<tr>
<th>Vaccine type</th>
<th>Disease</th>
<th>Vaccine brand name</th>
<th>Manufacturer and/or distributor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live</td>
<td>Measles</td>
<td>Attenuvax</td>
<td>Merck</td>
</tr>
<tr>
<td></td>
<td>Measles, mumps, rubella</td>
<td>MMR</td>
<td>Merck</td>
</tr>
<tr>
<td></td>
<td>Mumps</td>
<td>Mumpsvax</td>
<td>Merck</td>
</tr>
<tr>
<td></td>
<td>Polio</td>
<td>Orimune (oral)</td>
<td>Lederle</td>
</tr>
<tr>
<td></td>
<td>Rubella</td>
<td>Meruvax</td>
<td>Merck</td>
</tr>
<tr>
<td></td>
<td>Typhoid fever</td>
<td>Vivotif-Berna (oral)</td>
<td>Berna</td>
</tr>
<tr>
<td></td>
<td>Varicella</td>
<td>Varivax</td>
<td>Merck</td>
</tr>
<tr>
<td></td>
<td>Yellow fever</td>
<td>YF-Vax</td>
<td>Connaught</td>
</tr>
<tr>
<td>Inactivated</td>
<td>Cholera</td>
<td>Cholera vaccine</td>
<td>Wyeth</td>
</tr>
<tr>
<td></td>
<td>Hepatitis A</td>
<td>Havrix</td>
<td>SmithKline Beecham</td>
</tr>
<tr>
<td></td>
<td>Hepatitis A</td>
<td>VAQTA</td>
<td>Merck</td>
</tr>
<tr>
<td></td>
<td>Hepatitis B</td>
<td>Engerix-B</td>
<td>SmithKline Beecham</td>
</tr>
<tr>
<td></td>
<td>Hepatitis B</td>
<td>Recombivax HB</td>
<td>Merck</td>
</tr>
<tr>
<td></td>
<td>H. influenza type B</td>
<td>HibTITER</td>
<td>Lederle</td>
</tr>
<tr>
<td></td>
<td>Influenza A and B</td>
<td>Fluzone°</td>
<td>Connaught</td>
</tr>
<tr>
<td></td>
<td>Japanese encephalitis</td>
<td>JE-Vax</td>
<td>Connaught</td>
</tr>
<tr>
<td></td>
<td>N. meningitidis</td>
<td>Menomune</td>
<td>Connaught</td>
</tr>
<tr>
<td></td>
<td>Polio</td>
<td>IPOL (injectable)</td>
<td>Connaught</td>
</tr>
<tr>
<td></td>
<td>Rabies</td>
<td>Imovax ID (intradermal)</td>
<td>Connaught</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Imovax (intramuscular)</td>
<td>Connaught</td>
</tr>
<tr>
<td></td>
<td>S. pneumoniae</td>
<td>Pneumovax 23</td>
<td>Merck</td>
</tr>
<tr>
<td></td>
<td>S. pneumoniae</td>
<td>Pnu-Immune 23</td>
<td>Lederle</td>
</tr>
<tr>
<td></td>
<td>Tetanus, diphtheria</td>
<td>Toxoids, absorbed</td>
<td>Connaught</td>
</tr>
<tr>
<td></td>
<td>Typhoid fever</td>
<td>Typhoid vaccine</td>
<td>Wyeth</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Typhim Vi</td>
<td>Connaught</td>
</tr>
<tr>
<td>Immune globulin</td>
<td>Various</td>
<td>Gamma IgG</td>
<td>Armour</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Immune globulin (human)</td>
<td>Michigan Department of Public Health</td>
</tr>
</tbody>
</table>

° Including intramuscular immune globulin preparations.

b Brand used by THS; many other preparations are available.
Through the eyes of the traveler, however, each trip is a unique, exciting, and important event, usually representing considerable expenditure. Disruption of the experience by malaria, hepatitis, or typhoid fever is calamitous, even if the outcome is not fatal. Coping with serious illness away from one’s comfortable support systems can be terrifying. Dawood puts it very nicely: “Ultimately, travel is about enjoyment. As a traveler, I place a high value upon peace of mind, which is a factor that is almost impossible to take account of in terms of a cost-benefit analysis” (39). For many travelers, the addition of $100 to $300 to the cost of the trip is worth this peace of mind.

If we lean toward this individual risk-benefit position, several important caveats must be carefully considered. First, no vaccine is 100% effective: a sufficiently intense inoculum or length of exposure can overcome the vaccine-induced protection. Immunization against fecal-oral pathogens causing diseases such as polio, hepatitis A, typhoid fever, or cholera does not give one license to sample heedlessly the profferings of street vendors—one of the surest ways to become infected.

Second, no vaccine is completely safe. Most vaccines are associated with a small but finite percentage of adverse reactions: local reactions, including sore arms and induration, and systemic reactions with fever, myalgia, and malaise. Most vaccines have been associated rarely with more severe reactions, usually of an immunologic nature. Most notorious, possibly, is Japanese encephalitis vaccine, which has a local and systemic reaction rate of 20%, including a 0.1 to 1.0% rate of generalized urticaria and anaphylaxis occurring up to 10 days after the immunization. Clearly, such a vaccine must be used judiciously, with considerable constraint.

Third, not all trips or all travelers are the same. The octogenarian circumnavigating the globe on a luxury liner, disembarking for only a few hours at high noon, and eating and drinking nothing ashore is at minimal risk. To be sure, even this person risks diseases spread by the fecal-oral route because locally purchased foods prepared in the ship’s galley may spread enterotoxigenic Escherichia coli with ease. The businessman hopscotching from one five-star hotel to another along the Pacific Rim, drinking only gin and tonic without ice and bottled beer, is at virtually no risk. At the other end of the spectrum, intrepid trekkers in Nepal, many days by foot from medical care, are at substantial risk for hepatitis A, hepatitis E, enteric bacterial and protozoal infections (e.g. typhoid fever and infections by enterotoxigenic E. coli and Cyclospora), polio, tetanus, diphtheria, measles, and rabies. Unprotected sexual activity adds the very real possibility of hepatitis B, sexually transmitted diseases, and human immunodeficiency virus (HIV) infection.

Adequate and accurate knowledge about preventing the acquisition of disease is without doubt the traveler’s most effective weapon. Careless or ignorant behaviors can overwhelm the best insect repellents, the most carefully chosen chemoprophylaxis, and the most appropriate vaccines.

**SOURCES AND QUALITY OF PRETRAVEL MEDICAL ADVICE**

Until rather recently, the chief sources of pretravel medical advice and immunizations were the traveler’s primary-care physician or a governmental health department (in the United States, usually the county health department). These providers depended heavily, often exclusively, on the U.S. bible for travel: *Health Information for International Travel*, better known as the “Yellow Book” (26). The 1970s and 1980s saw a great increase in the number of Americans traveling abroad, including 15 million to destinations in less developed countries. These travelers faced increased exposure to poor sanitation systems, lower hygienic standards of food preparation and distribution, and decreased access to the style and sophistication of medical attention expected in the United States. The ranks of the tourists were swelled by the burgeoning cadre of businessmen as the global economy expanded.

Numerous studies have illuminated the inadequacies of the traditional dispensers of travel information. For example, in a survey conducted by the Centers for Disease Control and Prevention (CDC), 1,062 primary-care physicians were polled. Of the 548 respondents, 196 (36%) said that they gave pretravel advice. When these 196 practitioners were presented with three travel scenarios, one physician (0.5%) gave appropriate advice in all three scenarios, 40% gave no correct advice, and 22% had no opinion (79)! In another survey, only 1% of German and 11% of Swiss general practitioners reported correct recommendations on immunizations and malaria prophylaxis (55). A 1994 survey of representatives of 42 public health departments in Canada demonstrated that even such experienced travel advice providers as these had areas of weakness, giving correct advice about meningococcal disease and malaria only half the time (80). Travel advice from embassies was in accord with that from the CDC only 38% of the time, according to one recent study. Egregious misadvice was encountered; e.g., spokespersons for countries with endemic yellow fever failed to mention that yellow fever immunization was required for entry (118)! As to the use of travel agents as a source of travel health information, one study in England found that only 24% of the agents mentioned the risk of malaria to travelers to sub-Saharan Africa (7).

The evident need for greater scope, consistency, and knowledge in pretravel health care has been met by the emergence over the past 10 to 15 years of travel medicine as a new medical discipline. Practitioners of this specialty have coalesced into the International Society of Travel Medicine (ISTM), with another major focus in the American Committee on Clinical Tropical Medicine and Travelers’ Health (ACCTMTH) of the
American Society of Tropical Medicine and Hygiene (ASTMH) (Table 2).

Do specialists in travel medicine perform better at giving travel advice than other health practitioners? This has not yet been firmly demonstrated, although at least one study has found that travelers obtaining pretravel advice in a travel medicine specialty clinic reported a significantly lower rate of trip-related illness (22%) than did travelers without such advice (48%) (110). The question is further complicated by the lack of definition about just what credentials, experience, and services are essential to merit designating oneself as a travel medicine specialist. In a milestone study addressing this thorny issue, the finding by Keystone et al. that up to 75% of spokespersons for World Health Organization (WHO)-designated yellow fever centers gave erroneous or inappropriate travel advice is of great concern (70). It should be noted, however, that a substantial portion of WHO-designated yellow fever centers would not be considered travel medicine clinics by current standards.

**TRAVEL MEDICINE CLINICS**

**Current Status of Travel Clinics**

Traditionally in the United States, pretravel immunizations and travel medicine advice were provided by county health departments. While many such venues still provide expert travel advice, governmental units increasingly are bulking at “subsidizing” travelers. In such situations, the necessary expertise for high-quality advice may erode with progressively constrained budgets. Presently, only 8% of clinics associated with members of the ISTM are affiliated with public health entities (57).

In view of the above trends, and recognizing the increasing volume and rapidity of international travel, the discipline of travel medicine has emerged over the past two decades. A recently published survey of travel clinics staffed by members of ISTM provides the first systematic assessment of travel clinics worldwide (57). Of 341 travel clinics identified, 213 (62%) were in the United States; 107 (31%) were in Europe, the United Kingdom, Ireland, Australia, or New Zealand; and 21 (6%) were in other countries. Seventy-five (47%) (110) of 160 are open 2 days or less. Clearly, given the volumes reported, some travel clinics are integrated into other types of clinical practice, and the ability of their professionals to focus on remaining up to date in travel medicine could be limited (57).

Virtually all the travel clinics are physician directed, but the dispensing of advice is widely shared with nurses. Worldwide, in only 16% of the clinics did a nurse alone provide travel advice; in the United States, the number was 22%. The median consultation time was 30 min. Telephone consultations, the bête noire of a profitable travel clinic (for financial and medical/legal reasons), are provided by these clinics to physicians 89% of the time and to the public 66% of the time. Sixteen percent of the clinics charged for such telephone consultation (57).

The postgraduate training of the physicians also varied a great deal, with some striking regional differences. Overall, 63% were trained in infectious diseases and/or tropical medicine. Other preparation included general medicine or family practice (16%), internal medicine (17%), emergency medicine (11%), occupational medicine (7%), and public health or preventive medicine (6%). However, in Canada, 54% were generalists; in the United States, 52% were trained in infectious diseases; and in Europe and the United Kingdom, the majority were trained in tropical medicine (70 and 59%, respectively) (57).

Perhaps the most surprising result of the survey was that 37% of the travel clinics sold travel-related items to their clientele: e.g., insect repellents, mosquito nets, and sunscreens. Many travel clinics, ours included, find this activity distasteful, although in smaller locales in temperate climates, some items may be hard to find on the shelves of local merchants year round (57).

**Lists of U.S. and International Travel Clinics**

Not infrequently, travelers—especially students or businesspersons—must begin preparation for a trip in one city and complete it in another, in the United States or overseas. Lists of U.S. and international travel clinics are available from several sources (Table 3).

**Overview of a Representative Travel Clinic**

Metropolitan Syracuse, with a population of less than 500,000, is the largest urban area in the middle of a sparsely populated central New York region totaling roughly 1,000,000 persons. The region’s economic base is farming and light industry. THS was established in March 1994, when the county travel clinic was closed as an economy measure. Travel advice and immunizations had been heavily subsidized at the country
travel clinic, which was well regarded by its patients. THS is the only private, for-profit travel medicine practice in the region. However, the health departments of several adjacent counties provide pretravel immunizations to their citizens.

THS is based in a seven-member infectious-disease group, with the intensive involvement of three infectious-disease physicians, working with a dedicated Registered Nurse. We are currently making the transition to a combined physician-nurse practitioner model for cost containment reasons without sacrificing the quality of consultation. Strong emphasis is given to the medical history of each patient and to providing both verbal and written advice on key matters. The practice is sited in the University Hill area of Syracuse, within walking distance of three universities and three hospitals and six blocks from the center of the city, with ready access (two blocks) to the interstate highway network.

The reasons why THS patients travel reflect the largely non-commercial nature of the region: tourism, 58%; business, 20%; religious or philanthropic, 11%; educational (student or educator), 11%. Africa is the most common destination (27%); 23% of patients go to Central or South America, 22% go to Asia, 13% go to the Indian subcontinent, and 15% go elsewhere.

Initially, county health departments were the major source of referrals to THS, but this has shifted toward referrals from primary-care physicians and former patients as our services have become better known. In our attempt to reach the potential traveler, mailings with brochures have been sent to all primary-care physicians, county health departments, travel agencies, manufacturers and exporters, colleges, universities, and high schools in central New York.

THS providers use a wide variety of sources in an intensive effort to remain current in travel advice (see the sections on information sources and the Internet, below).

A TYPICAL TRAVEL CLINIC VISIT

Patient History

The patient history in a travel clinic must be comprehensive yet focused. The goal is to elicit as efficiently as possible the information that may guide the travel medicine practitioner in providing optimal advice about a specific patient’s planned trip.

The past medical history includes questions regarding each organ system. The history of coronary artery disease in a person contemplating trekking in Nepal warrants a more in-depth discussion of altitude and exertion, oxygenation and hypoxemia, and air rescue services. A person with ulcerative colitis perhaps could tolerate the oral typhoid vaccine but may elect to receive the injectable vaccine, if only to avoid the difficult questions that arise if an exacerbation of the colitis occurs on day 3 of the oral vaccine series. A history of a reaction to a prior shot allows today’s injections to be given with the patient reclining on the examination table, to avoid that head-bashing faint. Questions about neuropsychiatric problems, in an effort to remain current in travel advice (see the sections on special population, below).

A detailed immunization history is obtained, using (if available) the traveler’s old International Certificates of Vaccination—the Yellow Card which a travel clinic provides to each traveler. Getting patients to remember to bring in the details of their immunization history has proven very difficult. In the office visit, patients’ memories are pushed to be sure about their most recent tetanus-diphtheria (Td) immunization (Td every 10 years is recommended). Frequently, there is uncertainty whether an individual has received the tetanus immunization alone or whether Td was administered; we often place a telephone call to the patient’s physician during the interview to be sure of the facts. Given the resurgence of diphtheria in the former Soviet Union countries and its ongoing presence in developing countries, a diphtheria booster is now more important than ever.

The traveler’s detailed itinerary is crucial if travel health advice is to be accurate. For example, a traveler proceeding from South Africa to Guinea-Bissau would not have to show evidence of yellow fever immunization to gain entrance (although the traveler should have the vaccine if traveling outside major urban areas), while a traveler in the opposite direction could be quarantined for 6 days upon arrival in South Africa without yellow fever certification. A more common example would be the round-the-world cruise with 20 to 40 ports of call; only one, or a few, of these ports present a malaria risk, greatly affecting the calculation of the timing of malaria chemoprophylaxis. Some restrictions are temporary, such as the plague “epidemic” in India in 1995, when it was not possible to progress from India to certain other countries (most notably Pakistan).

The itinerary is more broadly important, as well. Malaria prophylaxis would not be necessary for travelers to Beijing but would be essential in parts of southern China. A businessman staying in the five-star hotels of Bangkok would not need to consider Japanese encephalitis vaccine, whereas the anthropologist in northern Thailand’s farms and mountains would be well advised to consider this protection against the most deadly encephalitic agent in Asia. Virtually no tourist should consider receiving the present injectable cholera vaccine, but it would make considerable sense for a relief worker in a refugee camp in Zaire to receive it.

Patient Education

Educating the patient is the most important and yet the most difficult task of the travel clinic visit. There are serious time constraints, and the verbal portion of the educational effort must be kept within limits without sacrificing quality. In our clinic, we try to optimize the face-to-face opportunity by obtaining all the demographic and itinerary information prior to
the clinic visit. The physician then obtains the medical history, recommends appropriate immunization, and makes the most crucial educational points—which vary from case to case. In addition, upon arrival in our office, the traveler is handed a packet of printed material. Some of this information is general: guidelines for international travel; a list of companies that provide air ambulance services; correct use of insect repellents; guidelines for international travel; a list of companies that provide air ambulance services; correct use of insect repellents; risks from food and drink including traveler’s diarrhea, hepatitis A, hepatitis B, and typhoid fever; vaccine recommendations for Td, measles, mumps, rubella (MMR), and varicella; and HIV testing requirements for entry into foreign countries (40). Depending on the itinerary, numerous other information sheets will be placed in the packet, including those about malaria, schistosomiasis, Japanese encephalitis, rabies, dengue, altitude sickness. In fact, there is so much information that would seem useful if transmitted and retained that overload is a distinct threat. In addition to the above, we provide even more information about certain situations: jet lag (113); motion sickness (117); the “Economy Class syndrome” (known in England during World War II as the bomb shelter syndrome), i.e., the occurrence of a massive pulmonary embolus upon arising from a prolonged sitting position (76); Sun exposure (97); and high-altitude illness (9).

The known vaccine-vaccine and vaccine-drug interactions are taken into account by the provider before making final recommendations, as are the known adverse effects of the common vaccines (Table 4). Each patient is informed (verbally and in the printed material) of the possible adverse effects of the vaccines administered and of the medication prescribed. Frequent limitations to our recommending the vaccine of choice include insufficient time before departure (hepatitis A vaccine, oral typhoid vaccine, any vaccine that will not yield protective antibody before the possible exposure), the need for immune globulin (affects the use of MMR and varicella vaccines), and the use of antibiotics that cannot be discontinued (e.g., oral typhoid vaccine, a live attenuated strain of Salmonella typhi, cannot be taken with antibiotics). The medications prescribed most frequently in our travel clinic are antibiotics. These include ciprofloxacin (Cipro) or trimethoprim-sulfamethoxazole (Bactrim, Septra) for empirical treatment of traveler’s diarrhea and mefloquine (Lariam), chloroquine (Aralen), or doxycycline (generic) for malaria prophylaxis. We also prescribe acetazolamide for altitude sickness prophylaxis and recommend loperamide (Imodium), a nonprescription medication, as the antimotility, antidiarrheal agent of choice. In practice, the most common limitations in prescribing a drug of choice are allergies, history of depression or seizures (predictive of problems in tolerating mefloquine), history of drug intolerance (e.g., severe photosensitivity with doxycycline). The traveler is informed of the more common side effects.

**“Negotiation” of Immunizations**

The final decision about which vaccines will be administered is very much a matter of negotiation between the provider and the patient. The patient’s basic tendency to be a “risk taker” or “risk avoider” is an intrinsic part of the mix. Presented with the same information on the risks and the potential effects of illness for any given traveler, one person wants everything possible and another only what is required by law (i.e., yellow fever or meningococcal vaccine in certain countries). Factored into this, often explicitly, is the cost. Vaccines and expert consultation are expensive. To some travelers (risk avoiders), the price is of little importance relative to the peace of mind they gain knowing that they have done all that is reasonable. Some-

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Interaction with</th>
<th>Precaution</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMR</td>
<td>Immune globulin</td>
<td>Give these vaccines at least 2 weeks before or 3 to 5 months after immune globulin.</td>
<td></td>
</tr>
<tr>
<td>OTV</td>
<td>Antibiotics</td>
<td>Administer at least 3 days after antibiotic therapy is completed. Do not take antibiotics for at least 10 days after the OTV course is completed.</td>
<td></td>
</tr>
<tr>
<td>OTV</td>
<td>Mefloquine</td>
<td>Allow at least 24 h between a dose of OTV and mefloquine.</td>
<td></td>
</tr>
<tr>
<td>OTV</td>
<td>OPV</td>
<td>Give OPV 7 to 10 days before or 10 to 14 days after OTV.</td>
<td></td>
</tr>
<tr>
<td>Rabies (HDCV)</td>
<td>Antimalarial agents (chloroquine, mefloquine)</td>
<td>End the rabies vaccine series at least 30 days before starting chloroquine treatment. Use the intramuscular rabies vaccine if the 30-day interval is not possible.</td>
<td></td>
</tr>
<tr>
<td>Live virus vaccines (MMR, OPV, yellow fever, varicella)</td>
<td>Other live virus vaccines</td>
<td>Give live virus vaccines on the same day, or separate the doses by at least 1 month.</td>
<td></td>
</tr>
<tr>
<td>Live virus vaccines (MMR, OPV, yellow fever, varicella)</td>
<td>Tuberculin skin test (PPD)</td>
<td>Do the PPD test on the same day the live virus vaccine is given, or wait for 4 to 6 weeks. The live virus vaccines can impair the response to the PPD.</td>
<td></td>
</tr>
<tr>
<td>Varicella vaccine</td>
<td>Immune globulin</td>
<td>Avoid immune globulin for 5 months before, and 2 months after the varicella vaccine.</td>
<td></td>
</tr>
<tr>
<td>Varicella vaccine</td>
<td>Salicylates</td>
<td>Avoid the use of salicylates for 6 weeks after varicella immunization to prevent Reye syndrome.</td>
<td></td>
</tr>
<tr>
<td>Yellow fever vaccine</td>
<td>Cholera vaccine</td>
<td>Give the two vaccines on the same day or at least 3 weeks apart.</td>
<td></td>
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</tbody>
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*Abbreviations: OTV, oral typhoid vaccine; OPV, oral polio vaccine; PPD, purified protein derivative.*
times such persons have to be talked out of wanting cholera vaccine, for example, or Japanese encephalitis vaccine. The risk takers are much more likely to select one or two vaccines, usually hepatitis A and Td update, and not feel troubled about skipping the others.

PREVENTION OF DISEASES WITH EFFECTIVE VACCINE OR CHEMOPROPHYLAXIS

The hoary maxim “An ounce of prevention is worth a pound of cure” could well have been coined for travelers considering the health risks of travel, for whom this “ounce” can take the form of behavior modification, chemoprophylaxis, vaccines, or a combination thereof. Among the nearly innumerable possibilities are about 30 infectious agents, or groups of agents, that the traveler is most likely to encounter. Fortunately, we have good vaccines or workable chemoprophylactic regimens for many of these infectious agents faced by travelers. There is a danger in regarding such diseases as being different from the diseases without effective interventions, in that the traveler may lose sight of the fact that food and water precautions are still vital and that protective measures against mosquitoes and other insects are extremely important. No vaccine or chemoprophylactic regimen is 100% effective. A sufficiently heavy inoculum of S. typhi may overwhelm the vaccine-induced immunity, and an attack by large numbers of mosquitoes infected with malaria organisms can overpower the mefloquine prophylaxis.

Diseases Associated with Contaminated Food and Water

Hepatitis A. In the United States, hepatitis A is endemic at a very low prevalence, with sporadic outbreaks, when the incidence rises dramatically. For example, in Syracuse’s home county, Onondaga, there are fewer than 15 cases of hepatitis A annually, for an approximate incidence of 3 per 100,000. Elsewhere in the United States, however, there have been at least 14 reported outbreaks since 1994, with the incidence of infection as high as 500 per 100,000 (104). The patterns in Canada, Western Europe, Australia, and New Zealand are similar. Hepatitis A is generally a benign disease, and is mistakenly thought by some to be entirely so. However, of the estimated 143,000 patients with hepatitis A in the United States each year, 11,400 are hospitalized and 80 die of fulminating hepatitis (85). Children younger than 2 years are likely to be asymptomatic; older children and adults may have no symptoms but usually show typical findings of hepatitis: loss of appetite, nausea, fever and chills, jaundice, dark urine, light-colored stools, abdominal pain, malaise, and fatigue.

In developing countries, however, hepatitis A is highly endemic and presents perhaps the quantitatively greatest risk to the traveler from the developed world. The risk of contracting hepatitis A on a visit to India, for example, is 1,800 times greater than in the typical U.S. city (85). The modern history of cholera began with the first pandemic (1817 to 1823), involving the Middle East, the Near East, southern Asia, and Japan. The fifth and sixth pandemics were certainly caused by the Vibrio cholerae O1 classical biotype, which probably also caused the first four (74).

The present pandemic, the seventh, which began in 1961 and continues to the present on six continents, is caused by the El Tor biotype of V. cholerae. A notable difference in the response to this pandemic was the readiness of clinicians treating the disease to use WHO oral rehydration salts solution, which greatly reduced the mortality rate in some areas of the world. The appearance of V. cholerae O139 Bengal strain in 1992 may well herald the onset of the eighth pandemic (74).

The power of cholera lies in the precipitous onset of voluminous diarrhea, which, if untreated with oral or intravenous fluid replacement, kills the patient rapidly. Cholera flourishes in crowded, impoverished areas, but when it is epidemic, it crosses social and national boundaries. Tourists are at extremely low risk in areas of endemic infection, with imported cholera rates ranging from 0.2 per 100,000 (United States) to 13.0 per 100,000 (Japan, where it is sedulously looked for in returning travelers) (142). Recently, six passengers of a cruise ship in Southeast Asia were diagnosed with V. cholerae O139 Bengal, traced to their eating yellow rice at a Bangkok buffet restaurant (12). In 1992, more than 100 passengers on a Buenos Aires to Lima to Los Angeles flight were infected with V. cholerae O1. The reported morbidity and mortality due to the health providers’ failure to use appropriate oral and intravenous rehydration techniques demonstrated a lack of readiness of the U.S. health care system to handle such emergencies (8).

Given the present very low risk of cholera for the Western traveler and the poor performance characteristics of the presently available killed, whole-cell cholera vaccine (including total lack of protection against V. cholerae O139), immunization is not widely recommended. Moreover, considerable comfort can be gained from the knowledge that a single 1.0-g dose of ciprofloxacin (the most commonly prescribed antibiotic for traveler’s diarrhea), is effective in the treatment of cholera (72). Several high-efficacy oral cholera vaccines are under study at present, and one is available in Europe. There are certain known risk factors that must be taken into account should such a vaccine become available for use in the United States. These include high gastric pH from surgery, use of H2 blockers (e.g., cimetidine) or sodium pump inhibitors (e.g., omeprazole), and blood group antigen O. Normally, the low gastric pH decreases the viability of ingested vibrios, reducing the inoculum size and thus lessening the likelihood of clinical products are available in the United States: Havrix (SmithKline Beecham Pharmaceuticals) and VAQTA (Merck & Co., Inc.). Both vaccines are highly effective, and both are available in two-dose series for adults and children. The second dose is given 6 months (VAQTA) or 6 to 12 months (Havrix) after the first and provides an essentially 100% protective titer. Mild pain, tenderness, and swelling at the immunization site are the only side effects usually seen with Havrix (the vaccine we use at THS). Postmarketing reports of other adverse events are widely varied and are often not clearly linked to the vaccine.

At THS, we recommend that anyone traveling anywhere but northern Europe, Canada, Australia, and New Zealand receive hepatitis A vaccine. It seems likely that this vaccine will become a routine childhood immunization in the United States at some point.

Cholera. Few diseases have had the global impact of cholera or have provoked such terror. The disease has likely been around for millennia, initially in endemic form and later, since the 17th century, as epidemics. The modern history of cholera begins with the first pandemic (1817 to 1823), involving the Middle East, the Near East, southern Asia, and Japan. The fifth and sixth pandemics were certainly caused by the Vibrio cholerae O1 classical biotype, which probably also caused the first four (74). The present pandemic, the seventh, which began in 1961 and continues to the present on six continents, is caused by the El Tor biotype of V. cholerae. A notable difference in the response to this pandemic was the readiness of clinicians treating the disease to use WHO oral rehydration salts solution, which greatly reduced the mortality rate in some areas of the world. The appearance of V. cholerae O139 Bengal strain in 1992 may well herald the onset of the eighth pandemic (74).

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Typhoid fever. Typhoid fever, an intestinal and systemic febrile illness caused by *S. typhi*, is often not accompanied by diarrhea and is contracted from contaminated food and water. The incidence of the disease has steadily declined in the United States for several decades. Now, the majority of cases of typhoid fever seen in the United States are in individuals who have traveled to other countries. In addition to *S. typhi*, the traveler may encounter numerous etiologic agents of enteric fever, including other *Salmonella* spp.

Strict adherence to food and water precautions serves to protect most travelers against typhoid. When only the whole-cell vaccine with its adverse effects of high fevers, malaise, and severe pain and swelling injection site was available, many people elected to rely on careful intake of food and water instead. Two highly effective vaccines with very few side effects are now available: typhoid vaccine live oral Ty21a (Vivotif Berna Vaccine; Berna Products Corp.) and typhoid Vi polysaccharide vaccine (Typhim Vi; Connaught Laboratories, Inc.). Both vaccines have a low incidence of adverse reactions, which include low-grade fever, headache, and abdominal discomfort with the Ty21a and low-grade fever, headache, and redness and swelling at the injection site with the ViCPS (21).

With the increasing prevalence of antibiotic-resistant *S. typhi* around the world, the appeal of typhoid vaccination is increasing. In our clinic, we recommend it most frequently for travelers to certain parts of South America, Africa, and the Indian subcontinent, including Nepal.

Polio. For Americans under the age of 40 years, polio is a historical curiosity. The inactivated (IPV) and then the oral (OPV) trivalent polio vaccines eliminated polio in the United States now is rare and is related to the live oral vaccine itself. The ACIP recently issued their first new guidelines since 1987 for the primary polio vaccination series. There are three acceptable options: IPV followed by OPV; OPV alone; or IPV alone (1a, 31).

A poliomyelitis eradication program was initiated by the WHO in 1988. Great progress has been made toward eradication, but polio is extant in sub-Saharan Africa and Southeast Asia, including the Indian subcontinent (24). A single booster for adults traveling to these areas is recommended (26). We have discovered in our travel clinic that many adults have not had their primary polio vaccine series. For such people, we immediately begin a primary series and vigorously stress food and water precautions.

Diseases Associated with Insect Vectors

Malaria. (i) Epidemiology and clinical picture. After decades of combat, malaria continues to win its wars around the globe. It is estimated that between 300 and 500 million people are infected worldwide by one or more of the four *Plasmodium* species: *P. falciparum*, *P. vivax*, *P. malariae*, and *P. ovale* (103). About seven million Americans travel to malarious areas each year (94), bringing back nearly half of the approximately 1,000 cases seen annually in the United States. Most other cases are in citizens of other countries diagnosed in the United States. In 1992, there were seven deaths in the United States, a nearly 1% fatality rate (25). Moreover, several cases of malaria acquired in the United States, all thought to have been introduced to a receptive microenvironment by persons traveling from other countries, have been reported in recent years (13).

Fever (‘jungle fever’) is the hallmark of malaria. In malarious areas, fever is often assumed to be malaria until proven otherwise by diagnostic efforts (often not attempted due to lack of available medical resources) or treatment failure (much more common). In addition to fever, other common symptoms include headaches, night sweats, insomnia, and aching muscles and joints; abdominal pain and diarrhea are less common but not rare (62). Malaria due to *P. falciparum* may progress to more serious, often fatal, disease such as cerebral malaria.

(ii) Personal protection measures. By far the most important factor in avoiding malaria is to prevent mosquito bites. Several personal protection measures used alone have a positive effect, and combinations are additive: (i) use a repellent incorporating 30 to 50% N,N-diethylmethyltoluamide (DEET) on the exposed skin (27); (ii) wear permethrin-soaked or sprayed clothing (123); (iii) sleep under mosquito netting, preferably permethrin sprayed or soaked (33); and (iv) spray living and sleeping quarters with a product containing a pyrethroid (26). The warnings on the labels of these products should be scrupulously adhered to, particularly regarding the use on children, in whom serious neurologic events have occurred (26).

(iii) Chemoprophylaxis. To prevent malaria, a few basic guidelines should be remembered: (i) an effective antimalarial regimen is still possible for the vast majority of travelers; (ii) 100% compliance is a must; and (iii) even if the prescribed medication is taken faithfully, malaria can be contracted by the bites of a sufficient number of malaria-infected mosquitoes or in areas where drug-resistant mosquitoes are endemic. Thus, personal protection measures are often crucial.

While numerous malarial chemotherapeutic regimens are used (often inappropriate ones, unfortunately), travelers from the United States usually are prescribed one of four: (i) chloroquine (Aralen), 500 mg orally once weekly, for areas where *P. falciparum* is still susceptible, e.g., the Caribbean, Central America, Egypt, and most of China; (ii) mefloquine (Lariam), 250 mg orally once weekly, for areas with chloroquine-resistant but mefloquine-susceptible malaria, e.g., Amazonia, sub-Saharan Africa, the Indian subcontinent, and much of southeast Asia; (iii) doxycycline, 100 mg orally once daily, for areas with mefloquine-resistant malaria, e.g., the Thailand-Burma border area, Papua New Guinea, Irian Jaya, and Mozambique (82); and (iv) a combination of prophyllaxis with chloroquine, 500 mg orally once weekly, and self-treatment with a single dose of pyrimethamine-sulfadoxine (Fansidar) if the traveler contracts malaria. Chloroquine is effective against susceptible malarial strains, particularly *P. vivax*, even in areas of resistant *P. falciparum* strains, and thus gives partial protection (26, 145).

Additional useful agents include primaquine, proguanil (Paludrin; used with chloroquine [abroad only]), and possibly azithromycin (Zithromax) (3). Even assuming an appropriate regimen, 100% compliance is essential; less than that can dramatically increase the risk of acquiring malaria (51, 99).

All prophylactic regimens should begin prior to entering a malarious area, to assess the traveler’s tolerance of the medication and to ensure adequate levels in tissue at the time of first exposure. A lead time of 1 to 2 weeks is recommended for chloroquine and mefloquine and 1 to 2 days is recommended for doxycycline. After leaving a malarious area, the traveler should continue to take the antimalarial medication for 4 weeks. This allows ample time for emergence of the parasites (*P. falciparum* being of the greatest concern) from liver cells into the bloodstream, where the antimalarial medication kills them (113, 125).

(iv) The mefloquine flap. Mefloquine, better known among travelers by its brand name, Lariam, is the most commonly prescribed antimalarial drug now that chloroquine resistance has spread worldwide. Its efficacy has been well established, and in large studies the side effects have been shown to differ...
little, quantitatively, from those of chloroquine or chloroquine plus proguanil (78, 125). Over the past year, there has been increasing attention in the media to the side effects of mefloquine, stemming from negative, even hostile, attitudes about the drug in some travelers. The concern among travelers blossomed in the United States with the recent publication of a Condé Nast Traveler article: “Are these pills safe? Controversy over antimalarial drug” (38). Most readers of that article did not get past the title to the author’s bottom line: “Undoubtedly I would still choose Lariam [mefloquine]” (38). In the travel clinic, we now see travelers refusing mefloquine, choosing implicitly the risk of malaria in order to avoid a drug that they perceive to have unacceptably serious risks.

What are the facts? Controlled trials show little if any difference between the incidence of adverse events with chloroquine and with mefloquine: 5 to 20% (122). Other studies show a consistently somewhat higher incidence of neuropsychiatric symptoms with mefloquine: headache, vertigo, dizziness, excitement, sleeping problems, depression, anxiety, and dissociation from reality (38, 60, 122). The incidence of these adverse effects is probably about 5%; indeed, over 80% of travelers taking mefloquine in some studies report no side effects of any type (60). The incidence of serious mefloquine-associated adverse effects on the central nervous system is probably 1:20,000 to 1:10,000 (71), similar to that of chloroquine, which is 1:13,600 (125).

Prospective, controlled studies are needed, and they should take into account the possibility that the explanation for the reported variability of serious side effects lies in the host’s neuropsychiatric status, including the use of substances such as ethanol. Witter recently reported a case in which alcohol use with mefloquine clearly led to paranoid delusions, auditory and visual hallucinations, depression, and suicidal ideation (141). The increased risk of toxic psychosis with mefloquine in persons with a history of depression and of seizures in persons with a seizure disorder is well known. Although we ask each traveler about such history, the accuracy of the responses may be questioned in an unknown percentage of cases. If this information is generalized to other travelers, especially if it is generalized to the use of other mind-altering substances, an explanation may be at hand. To date, adverse-effect studies have not addressed well the issue of neuropsychiatric history and have not addressed at all the issue of alcohol and other substance use.

In the meantime, in our travel clinic we try hard to get an accurate history of depression or other psychiatric illness or seizures. Each person prescribed mefloquine is warned not to drink any alcohol for 12 h before and 24 h after taking the weekly dose of mefloquine. Faced with this hardship, several patients have elected to take doxycycline instead. Ironically, doxycycline has as poor a compliance record in its use as an antimalarial drug as does mefloquine (106). Further, we tell our patients that there is one thing worse than the side effects of mefloquine, and that is malaria!

(v) Rapid diagnosis. Some postulate that the availability of accurate rapid diagnosis of malaria, followed by prompt treatment, would bypass the issue of adverse effects of the present chemoprophylaxis drugs. Although this remains to be demonstrated, rapid tests have been developed and are being investigated (48). Whether a net decrease in toxic events would be achieved by trading larger-volume, lower-dosage prophylactic treatment for lower-volume, higher-dosage malaria therapy is uncertain (71).

(vi) Malaria vaccine. Hopes for an effective malaria vaccine have been raised in recent years by the widely tested—and now discredited—candidate vaccine Spf66 (102). While no effective vaccine is yet available for clinical use, an experimental recombinant circumsporozoite protein vaccine was recently shown to prevent disease in six of seven malaria-naive volunteers challenged with P. falciparum sporozoites (86, 126).

Japanese encephalitis virus infection. The flavivirus Japanese encephalitis virus (yellow fever and dengue viruses are also flaviviruses) is the most common cause of epidemic viral encephalitis in the world (58). The virus is endemic in Southeast Asia and the Indian subcontinent (19, 26) and is carried by Culex mosquitoes, which find the rice paddies of the region ideal breeding ground. Domestic pigs, which are typically a part of that agrarian scene, play an important amplifying role. Serologic data demonstrate nearly complete infection of the indigenous population by adulthood. Obviously, travelers planning any length of stay in such areas would be at risk. However, only 11 U.S. residents and 13 other Western travelers have had documented Japanese encephalitis virus infection, a rate calculated to be less than 1 per 10⁶ annually. For a traveler staying 1 month or longer in the area of endemic infection, the risk of infection would be that of the indigenous population: 1 per 1,000 per month (19).

Judging by the seroprevalence, the majority of Japanese encephalitis virus infections are asymptomatic. The recognized syndrome includes fever, chills, malaise, headache, and nausea and vomiting, followed by signs of encephalitis. The inactivated Biken strain vaccine, licensed in the United States and distributed by Connaught Laboratories, Inc. (JE-VAX), is 91% effective. Japanese encephalitis vaccine has gained quite a reputation for adverse effects. About 20% of the vaccinees experience sore, red, swollen injection sites, with about half that number reporting systemic side effects of fever, headache, malaise, rash, chills, dizziness, myalgia, nausea and vomiting, and abdominal pain (19). Beginning in 1989, a new pattern of adverse effects was seen, first reported from Australia: urticaria and/or angioedema of the extremities, face, and oropharynx. The onset of the reaction averaged 12 h following the first dose, with reactions occurring up to 10 days after subsequent dosages. The reactions may be associated with certain vaccine lots, but this is not yet clear. Since the vaccine has been released in the United States, the incidence of facial edema and generalized urticaria have been 0.1 and 1.0%, respectively (130).

Not everyone going to Asia should receive the vaccine. Because Japanese encephalitis virus transmission patterns differ widely with rainfall and other factors, immunizing travelers for a specific “transmission season” is not reliable. Persons who are going to be in areas of endemicity for Japanese encephalitis for 1 month or more should receive the primary vaccine series and should be urged to use personal protection measures against mosquitoes (19).

Yellow fever. Unlike other vaccines that are used at the discretion of the traveler, yellow fever vaccine is unique because many countries stipulate its use in travelers crossing their borders. In addition to the requirements established by these countries, the CDC advises travelers outside urban areas in South American and African yellow fever-endemic zones to be immunized as well, even in countries that do not currently report the presence of the disease (26).

The mosquito vectors for yellow fever virus are Haemagogus spp. in the jungle and Aedes aegypti in urban areas (urban transmission is usually seen only in epidemic situations). Clinically, the disease ranges from asymptomatic, to a febrile illness similar to dengue fever, to severe hemorrhagic illness with fulminant hepatitis and renal failure. Yellow fever vaccine is a live attenuated strain (17D) of the virus, which produces nearly 100% immunity. The duration of vaccine protection is officially
recognized by the WHO as being 10 years. Thus, countries that regulate the vaccine require an International Certificate of Vaccination (the Yellow Card, provided by every travel clinic) completed, signed, dated (within 10 years), and stamped with an approved Yellow Fever Vaccination Center’s “official” stamp.

Serious reactions to yellow fever vaccine are rare. Mild headaches, myalgia, and slight fevers are seen in 2 to 5% of vaccinees 5 to 10 days after the immunization. This time interval distinguishes yellow fever vaccine from most others, for which reactions, if seen, occur very soon after the time of immunization (Japanese encephalitis vaccine is another notable exception). Yellow fever vaccine should not be used in infants under 4 months (British recommendations are under 1 year); in the first trimester of pregnancy, and, unless life saving, not at all in pregnancy; or in immunocompromised persons (26). However, in a study of 44 HIV-infected persons with CD4 cell counts above 200/mm³, yellow fever vaccine was well tolerated, with no decrease in CD4 cell counts or increase in circulating p24 antigen levels but with only a 35% seroconversion rate (50).

Tick-borne encephalitis virus infection. The flavivirus tick-borne encephalitis virus is transmitted by a small hard tick, usually Ixodes ricinus, and usually from April through August in forested areas of central and eastern Europe. The infection rate for tourists is very low, based on U.S. military data of 0.9 case per 1,000 human months (66). The clinical spectrum of disease ranges from asymptomatic to fatal, with about a 1 to 2% fatality rate (77). The primary immunization series takes 6 months. Because the vaccine is not available in the United States, American travelers are largely dependent on personal protection measures, especially DEET-containing repellents.

Diseases Associated with Environmental or Animal Contacts

Tetanus and diphtheria. While only tetanus involves environmental (soil) contact, for adults tetanus and diphtheria are inextricably intertwined, since all booster injections use the combined vaccine, Td. The effectiveness of tetanus and diphtheria childhood immunizations is attested by the low incidence of each in the United States: 50 to 65 cases per year of tetanus, and fewer than 5 cases of diphtheria (46). Most of these cases of tetanus and diphtheria are in adults who have never had a complete primary immunization series. The additional failure to receive the recommended Td booster every 10 years results in the status quo: more than half of American adults do not have protective levels of antibody. It is recommended that an adult who has not completed a primary series should do so when that fact is discovered. As to further boosters, the CDC recommends routine Td boosters every 10 years (16), while the American College of Physicians advocates a single booster at age 50 years (1). The recommended interval for a Td booster drops from 10 to 5 years if a contaminated wound is being treated. A person with such a wound should also receive human tetanus immune globulin if the previous Td was given more than 5 years earlier (10).

Whichever practice of routine Td immunization the traveler and the provider choose, preparing for travel is a good time to update Td immunizations. In our travel clinic, we advocate the Td booster every 10 years for overseas travelers. A challenge faced daily in a travel clinic is the frequent situation of the patient remembering a “tetanus shot” following a wound but with no idea whether it was tetanus alone or Td. In our area, most emergency departments have used Td for several years, but this has not been a uniform practice. This is of particular importance because of the surge of diphtheria in different parts of the world, particularly in the newly independent states of the former Soviet Union (53).

Rabies. In the United States, nearly 30,000 residents receive rabies vaccine each year, either as postexposure prophylaxis or because of occupations that bring them into contact with animals (46). The most common use of the vaccine is in the postexposure situation, often in conjunction with rabies immune globulin (RIG). The present vaccines, human diploid cell rabies vaccine and rabies vaccine adsorbed, are quite effective as preexposure prophylaxis and are recommended for use by anyone planning to live for more than 1 month in several regions where rabies is highly endemic, e.g., parts of Mexico, India, Nepal, Philippines, Vietnam, and several others (26).

Following a rabid bite, good wound cleansing and debride-ment with prompt use of RIG is essential to help ensure survival. Even with such care, prophylactic failure and death can occur (135). In our travel clinic, we discuss the issues with travelers to areas of rabies endemcity, paying particular attention to the traveler’s access to high quality postbite care. We see this issue most frequently for trekkers in Nepal and some adventure travelers to remote areas of South America and less frequently in others. Vaccine recipients occasionally describe local reactions of pain, redness, swelling or itching at the injection site, headache, nausea, abdominal pain, myalgias, and dizziness. However, the type of reactions that make us wary of recommending the vaccine are immune complex-like symp-toms that occur in about 6% of vaccines: urticaria, pruritus, and malaise. Once begun for good reason, the entire series should be completed. Chloroquine phosphate and possibly structurally related antimalarial drugs such as mefloquine (although there are no data regarding mefloquine) may interfere with the antibody response to rabies vaccine administration (26).

Diseases Associated with Person-to-Person Transmission

Hepatitis B. Hepatitis B virus (HBV) is a major health problem worldwide, including in the United States. It is estimated that 1 to 1.25 million U.S. citizens are chronically infected with HBV, and many of these are potentially infectious to others. Approximately 4,000 to 5,000 persons die each year from HBV-related chronic liver disease. Infected infants are most likely to progress to chronic HBV disease. After the perinatal period, most HBV transmission is through exchange of blood or blood-derived fluids in health care workers, blood transfusion, illicit injecting drug use, acupuncture, and tattooing and through sexual activity. In less developed areas however, the extremely high prevalence of HBV infection (≥10%) forces the conclusion that other person-to-person exposures must play a role (26, 133).

Hepatitis B immunization is now part of the routine immunization recommendations in the United States; it is targeted at neonates, preschool children, and young adolescents as part of a public health campaign to eliminate the transmission of HBV in the United States. Eventually, therefore, primary HBV immunization for travelers will be less of an issue. Meanwhile, immunization can be considered by all, since any traveler may be at risk for postransfusion blood transfusion with unscreened blood in a less developed country. The vaccine is recommended for short-term travelers (<6 months) who predictably may have direct contact with blood (e.g., health care workers) or may have sexual contact in an area of high prevalence and for long-term residents (>6 months) with potential high-risk exposure or who will live in rural areas and/or have prolonged, daily physical contact with local populations (26).
The two recombinant HBV vaccines available in the United States (Recombivax HB [Merck & Co.] and Engerix-B [Smith-Kline Beecham Pharmaceuticals]) are highly effective (80 to 95%, and virtually 100% if protective antibody is demonstrated), with negligible adverse effects. They are both licensed for and are routinely given intramuscularly as a three-dose series at intervals of 0, 1, and 6 months or 0, 1, and 2 months. Engerix-B is also licensed as a four-dose regimen given at 0, 1, 2, and 12 months. None of these regimens is ideal for the many travelers who allow too little time for immunizations before travel. With Engerix-B, 3-week and 4-week schedules of HBV vaccine administration are highly effective in producing protective immunity: >90 to 100% when a 12-month booster dose is added (11, 81). In our travel clinic, we now routinely use a 0-, 7-, and 21-day and 12-month regimen.

Intradermal immunization with HBV vaccine is not recommended at this time because of inadequate antibody responses, despite some attractive features of vaccine cost and ease of administration (17). The question of reimmunization is not fully resolved, because there is some evidence that protection outlasts antibody titers; the CDC does not recommend routine antibody testing or booster vaccine, except in hemodialysis patients (26). We advise the patient of this, but we also advise at least those few at higher risk that it may be reasonable to assess titers and reimmunize (probably a single dose) if the titer falls below 10 mIU/ml, the level proven to be associated with protection, until more data are forthcoming.

Influenza. Influenza vaccine has traditionally been recommended for anyone over 5 months of age who is at increased risk for complications of influenza, and for health care workers and others with close contact with the high-risk group. Indications have now been broadened to include anyone, including completely healthy people, who want to reduce the chance of contracting influenza (28). Indeed, immunization against influenza is both clinically beneficial and cost-effective in young healthy workers, with significantly fewer sick days and physician office visits (100). Influenza virus is endemic in tropical regions, and an influenza booster is frequently in order for the traveler, even when the flu season has not yet begun at home. Unfortunately, influenza vaccine production and distribution is seasonal, and the travel clinic may not be stocked in July. Moreover, each season’s formulation reflects the predicted strains, which may not be applicable to all countries.

Measles, mumps, and rubella. Following the surge of cases of measles, mumps, and rubella in the late 1980s, epidemiologic and serologic investigation led to the new, strong recommendations that anyone born since 1956 should receive measles vaccine alone to the defined group at risk who will travel in the near future.

Meningococcal disease. Most infections due to Neisseria meningitidis in the United States are sporadic and are caused by serogroup B, although outbreaks of serogroup C have recently been reported (61). In sub-Saharan Africa from December to June and in northern India and Nepal, there are regular epidemics of serogroup A and occasionally serogroup C meningococcal disease. A meningococcal polysaccharide vaccine, groups A, C, Y and W-135 combined (Menomune A/C/Y/W-135 [Connaught]) provides excellent protection for 2 years and is recommended for persons living in or traveling to the high-risk regions. In addition, because of an outbreak during the Haj a few years ago, Saudi Arabia requires certification of immunization for pilgrims to Mecca. We have learned directly from returned travelers that meningococcal vaccine is being required much more broadly by Saudi Arabia than is advertised.

Pertussis. The story of pertussis (whooping cough) immunization policies and practices has been stormy in recent decades. The significant protective effect of whole-cell vaccines has been abandoned in some quarters because of fears (on an inconclusive basis) of consequent neurologic damage to children. Acellular pertussis vaccines which can be used for part or all of a child’s pertussis immunization series have now been developed (30). The issue of the need for adult boosters now must be addressed, because a considerable incidence of pertussis is still seen each year in adults (2).

Pneumococcal disease. There are about 40,000 deaths due to invasive pneumococcal disease in the United States each year. In part because of conflicting efficacy data, pneumococcal vaccine has never been implemented as widely as public health experts would hope, even though full implementation of the 23-valent vaccine would prevent half of the cases of pneumococcal invasive disease each year (46). We take advantage of the pretravel clinic visit to assess the traveler’s risk factors (the major one being age of 65 years or older) and advise that pneumococcal vaccine be administered if it is indicated.

Varicella. Chickenpox can be a serious disease in children, and the new varicella vaccine (Varivax [Merck & Co.]) was developed primarily for them. However, in susceptible adolescents and particularly in adults, the disease is much worse, with a significant incidence of sometimes fatal pneumonia. The vaccine is highly effective, and although there are some questions about the long-term (decades) effect on the vaccine recipients’ susceptibility to varicella and their subsequent incidence of shingles, the vaccine is recommended for many groups of adults. Health care workers form the major group, but overseas travelers who face greater exposure than at home comprise another sizable group. Eligible adults should receive two 0.5-ml doses subcutaneously at 0 and 4 to 8 weeks (47). Many practitioners who see few children are reluctant to stock the vaccine because it must be shipped and stored frozen at a constant temperature that the average office refrigerator freezing compartment may not sustain. Travel clinics usually stock it, and it may be wise for the traveler to inquire about the storage conditions.

PREVENTION OF DISEASES WITH NO EFFECTIVE VACCINE OR CHEMOPROPHYLAXIS

For a considerable number of infectious agents faced by the traveler, there is neither an effective vaccine nor recommended chemoprophylaxis. For these encounters, travelers’ only defense is modification of their behavior to avoid contaminated
Diseases Associated with Contaminated Food and Water

Traveler’s diarrhea. One topic commonly emerges in any group of reminiscing travelers: their most memorable bout of traveler’s diarrhea. Like influenza, once you have endured the agonies of real traveler’s diarrhea, written descriptions—no matter how articulate—pale. Traveler’s diarrhea afflicts roughly half of all travelers to less developed countries but can occur in a visitor to any country. Curiously, there is not agreement as to who owns the disease: one traveler, i.e., “traveler’s” diarrhea (41, 65), or many, i.e., “travelers”’ diarrhea (113, 116).

There is not even consistency within the same group of authors (41, 116).

(i) Pathogens. The pathogens of traveler’s diarrhea (Table 5) are spread by fecal-oral mechanisms. Water and foods are contaminated by lack of sanitary disposal of feces; crops may be fertilized with human waste, leaving bacteria on the produce; and poor personal hygiene can lead to contamination of both food and water during the preparation of meals. Viruses may be spread more readily via contaminated water than via food (41).

Traveler’s diarrhea is caused by bacterial enteric pathogens in 40 to 60% of patients (41, 83). The 40% or so of cases of traveler’s diarrhea in which a bacterial pathogen is not demonstrated may be due to viruses or to as yet undescribed bacterial pathogens or parasites (42). Traveler’s diarrhea is most common in the first several days of exposure and is highly correlated with dietary indiscretions. Diarrhea decreases dramatically in frequency with prolonged residence in an area, even given continued lack of rigid adherence to food and water precautions—a fact that may reflect the development of immunity to the pathogens (44).

Other than Giardia (e.g., in Russia), parasites are a minor cause of traveler’s diarrhea. However, over the past decade, a newly discovered coccidian parasite, Cyclospora cayetanensis, has emerged as a significant cause of traveler’s diarrhea, especially in Nepal (29). Cyclospora-induced diarrhea usually strikes with an incubation period of 1 week, whereas the average for bacterial traveler’s diarrhea is shorter at 4.1 days (68). A recent outbreak in the United States was traced to the ingestion of raspberries imported from Guatemala (29, 32). This creates the ironic possibility of a visitor to the United States from Costa Rica developing diarrhea due to C. cayetanensis in New York City from indulging in fresh raspberries grown in Guatemala!

(ii) Disease syndrome. The hallmark of traveler’s diarrhea is the occurrence of several loose to watery stools accompanied by abdominal pain and cramps. It is often accompanied by malaise and decreased appetite; however, fever, vomiting, and bloody stools (which defines dysentery) occur in only 10 to 20% of cases. Untreated, the disease lasts from 3 to 5 days, with about 20% of the sufferers forced to bed rest (41).

(iii) Treatment. While it is likely that absolute adherence to the travel adage of “Cook it, boil it, peel it, or forget it” would prevent most cases of traveler’s diarrhea, this maxim often becomes theoretical as one faces the difficulty in implementing such sage advice in the real world of international travel (84).

The reality is that each trip is such an investment for that traveler that we must take advantage of the clearly established efficacy of antibiotics in our approach to traveler’s diarrhea. Given that premise, we know that antibiotics can be effectively used in two ways: prophylactically or as empirical therapy when the traveler’s diarrhea syndrome develops.

There is substantial consensus that widespread use of prophylaxis, either antibiotics or bismuth subsalicylate, is not warranted. The arguments against antibiotic prophylaxis include side effects, both allergic (e.g., skin rash) and nonallergic (e.g., photosensitization, diarrhea due to disruption of the normal gut flora by the antibiotic); possible selection of resistant bacteria in the traveler; development of Clostridium difficile colitis; unnecessary cost; encouragement of a less careful attitude about food and water precautions (41); and the contribution of travelers’ antibiotics to antibiotic resistance in the host country.

The last concern must be weighed against the current extensive use of antibiotics for agricultural and human medicinal purposes in such countries already (43). The arguments against bismuth subsalicylate (e.g., Pepto-Bismol) prophylaxis are less persuasive. However, in our experience, it is the rare traveler who will commit to the requisite two large pink tablets four times daily, particularly when the alternating pink-and-black tongue begins, the taste of food is affected, and the sticky black stools appear.

It is generally agreed that a more appropriate approach to traveler’s diarrhea is to treat it quickly when it appears. The basic options are to replace fluids only; replace fluids and use a motility inhibitor such as loperamide (Imodium) or diphenoxylate HCl (Lomotil); replace fluids and use bismuth subsalicylate and loperamide; or replace fluids, use loperamide, and take antibiotics. The last option is by far the most popular

### TABLE 5. Etiology of traveler’s diarrhea

<table>
<thead>
<tr>
<th>Organism</th>
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<tbody>
<tr>
<td>Invasive bacteria</td>
</tr>
<tr>
<td>Aeromonas hydrophila</td>
</tr>
<tr>
<td>Campylobacter jejuni</td>
</tr>
<tr>
<td>Clostridium perfringens type A</td>
</tr>
<tr>
<td>Escherichia coli, enteroinvasive</td>
</tr>
<tr>
<td>Escherichia coli O157:H7</td>
</tr>
<tr>
<td>Plesiomonas shigelloides</td>
</tr>
<tr>
<td>Salmonella species</td>
</tr>
<tr>
<td>Shigella species</td>
</tr>
<tr>
<td>Vibrio vulnificus</td>
</tr>
<tr>
<td>Yersinia enterocolitica</td>
</tr>
<tr>
<td>Noninvasive bacteria</td>
</tr>
<tr>
<td>Clostridium botulinum</td>
</tr>
<tr>
<td>Clostridium difficile</td>
</tr>
<tr>
<td>Escherichia coli, enterotoxigenic</td>
</tr>
<tr>
<td>Vibrio cholerae (O1, O139)</td>
</tr>
<tr>
<td>Vibrio fluvialis</td>
</tr>
<tr>
<td>Vibrio parahaemolyticus</td>
</tr>
<tr>
<td>Viruses</td>
</tr>
<tr>
<td>HAV</td>
</tr>
<tr>
<td>HEV</td>
</tr>
<tr>
<td>Norwalk agent</td>
</tr>
<tr>
<td>Rotavirus</td>
</tr>
<tr>
<td>Parasites</td>
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<tr>
<td>Balantidium coli</td>
</tr>
<tr>
<td>Blastocystis hominis</td>
</tr>
<tr>
<td>Cryptosporidium parvum</td>
</tr>
<tr>
<td>Cyclospora cayetanensis</td>
</tr>
<tr>
<td>Dientamoeba fragilis</td>
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<tr>
<td>Entamoeba histolytica</td>
</tr>
<tr>
<td>Giardia lamblia</td>
</tr>
<tr>
<td>Isospora belli</td>
</tr>
<tr>
<td>Strongyloides stercolaris</td>
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<tr>
<td>Trichinella spiralis</td>
</tr>
</tbody>
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food, dirty water, a variety of stinging and biting insects, certain environmental hazards, and sexually transmitted diseases.
today. The antibiotic class of choice at the moment is the fluoroquinolones. While ciprofloxacin has been used in most studies, there is little reason to select one fluoroquinolone over another: ciprofloxacin, norfloxacin, or ofloxacin. The most cost-effective dose of ciprofloxacin has not been established. The reported dosages studied range from a single 500-mg tablet to 500 mg twice daily for 3 days (105, 114). We recommend that the traveler take one 500-mg ciprofloxacin tablet when the onset of traveler’s diarrhea is first perceived (not waiting for full-blown symptoms), along with loperamide to help control the diarrhea. The ciprofloxacin should be discontinued when the diarrhea stops. Rarely are more than three or four doses needed.

Despite the consensus against prophylaxis, there are occasional situations when prophylactic antibiotics may reasonably be used: severe underlying health problems, an extremely important trip (e.g., diplomatic, high-level business), unwillingness or inability to adhere to food and water precautions, and perhaps decreased gastric acid production secondary to surgery or chronic medication.

There are some problems with antibiotic treatment of traveler’s diarrhea, however. Presently, C. cayetanensis does not respond to the fluoroquinolones and trimethoprim-sulfamethoxazole must be used. More important is the appearance of resistant enteric pathogens, especially Campylobacter spp., with resistance not only to the fluoroquinolones but now to azithromycin (73, 112).

(iv) Counseling. In addition to our best advice on the selection of safe foods and avoidance of contaminated water, the special challenges presented by children, infants, and pregnancy require the attention of the travel health provider. These issues are covered well elsewhere (41, 65, 95, 113; see also the section on special populations of travelers, below). A few critical points will suffice here. Infants and children seriously dehydrate more readily than do adults, and so replacement of water and salts is often critical. Ciprofloxacin and related fluoroquinolones should not be used in persons under age 18 and three or four doses needed.

(v) Vaccine. The emerging specter of enterotoxigenic E. coli (ETEC), the cause of more than half of the cases of traveler’s diarrhea) resistant to antibiotics makes urgent the development of effective vaccines. Clinical trials of vaccines against ETEC, Shigella spp., and V. cholerae (which can cause traveler’s diarrhea in addition to its classical dramatic cholera syndrome with profuse, acutely dehydrating diarrhea) are under way (127). In fact, one oral cholera vaccine under trial has shown 50% efficacy cross-protection against ETEC. This protection is probably related to humoral and cell-mediated immunity responses to the RBS subunit (rBS) antigen, since the heat-labile enterotoxin of ETEC is structurally, functionally, and antigenically similar to the V. cholerae toxin BS (116).

Hepatitis E. Five hepatitis viruses (A, B, C, D, and E) are well characterized, and more are emerging, with hepatitis G virus (HGV) and hepatitis GB virus C (HGBV-C) being the most fully explored (59). Hepatitis E virus (HEV) is more important than HAV in some developing countries of Asia, Africa, and the Middle East. It is particularly dangerous for pregnant women, with fatality rates of up to 20%. An HEV vaccine composed of a 55-kDa viral core protein was shown to be highly protective in monkeys (131); no human trials have yet been reported. It is hoped that a combined HAV and HEV vaccine will become available for travelers.

Transmissible spongiform encephalopathy—mad cow disease. Quite recently, the possibility that a priori disease of cattle can be transferred to humans through the ingestion of beef created an uproar in Europe (27, 37). The occurrence of a variant form of Creutzfeldt-Jakob disease and its linkage to bovine spongiform encephalopathy is a startling development, whose importance is unfolding. The programs of cattle destruction in the United Kingdom may have reduced the risk, but diagnostic tests for cattle and humans are urgently needed. Rationally or not, many Europeans are avoiding beef (35, 136). The questions are not sufficiently researched to allow confident advice to the traveler.

Other parasitic diseases. Innumerable other parasites are associated with food and water—far too many to chronicle here. When traveling, one is well advised to eat only well-done meats (including fish), foods too hot to eat immediately when they are served, or fruits and vegetables washed and peeled by the traveler.

Diseases Associated with Insect Vectors

A large number of viruses and parasites are transmitted to humans via mosquitoes, ticks, mites, flies, and other insects. A brief discussion of a selected few will help emphasize the importance of behavior modification in the prevention of these diseases: there is no effective treatment and no vaccine.

Dengue. Dengue is a mosquito-borne viral disease characterized by headache and fever of sudden onset, rash, joint pain, aching muscles, and nausea and vomiting. All U.S. cases in recent history have been imported, although the transmission vector, A. aegypti is now present year-round in the U.S. Gulf coast. More important than the above syndrome, usually referred to as dengue or dengue fever, is the syndrome of dengue hemorrhagic fever, usually associated with repeat dengue infections: fever, thrombocytopenia, hypoalbuminemia, pleural effusions, and peritoneal effusions. With the progression to hypotension, the prognosis worsens and the name “dengue shock syndrome” is applied. Dengue is increasing in South America, Central America and the Caribbean and is now affecting tourists. Trials of a vaccine containing all four strains of dengue are under way, but for now, avoidance of mosquito bites is the only defense against the disease (111).

Venezuelan equine encephalitis. Venezuelan equine encephalitis occurs in epidemics in northern South America, most recently in Colombia in 1995. The epidemics, prompted by heavy rains, involve horses, humans, and mosquitoes. Between epidemics, the disease survives most probably via a small-rodent/mosquito enzootic cycle. In the recent epidemic, over 45,000 people were infected, 4% of whom developed neurologic symptoms. Death or permanent neurologic damage is frequent in those with encephalopathy (22, 23). The epidemic may be aborted with an equine vaccine, but there is no human vaccine. Tourists rarely go to the affected areas; if they do, avoidance of mosquito bites is the only defense against the disease.

Chagas’ disease. Chagas’ disease, caused by Trypanosoma cruzi, which is transmitted by blood-sucking reduvid bug (“kissing bugs”), is a major parasitic disease in South and Central America, with a range extending up into Texas. Because tourists are rarely housed in the thatched-roofed huts where the vectors largely live, stealing out at night to bite the victim, it is a rare disease of foreigners. Avoidance is the only defense, for until very recently there was no effective treat-
ment. Recently a new triazole, dubbed D0870, has allowed cures in experimental animals (132).

**Ebola fever.** Although much is known about the virus (actually viruses, since four distinct strains are now recognized) that causes Ebola fever and although an insect vector and animal host is postulated as an enzootic cycle, neither is clearly identified. Ebola virus has been contracted by a human performing an autopsy on an infected chimpanzee and has been linked to red colobus monkeys and bats (4, 88). While no tourists have been infected, travelers should avoid areas of endemic infection and stay away from primates.

Other diseases due to insect borne-pathogens. Numerous other pathogens are insect borne, and no effective chemoprophylaxis is available for them (18). These are of substantial importance to residents, including some expatriates, but are quite rare in tourists. Examples include mosquito-borne diseases such as filariasis, Chikungunya fever, Ross River virus, and Rift Valley fever; fly-borne disease such as leishmaniasis (sand fly), onchocerciasis (black flies), African trypanosomiasis (tsetse fly), and bartonellosis (Oroya fever; sand fly); tick-borne diseases such as relapsing fever and Congo-Crimean hemorrhagic fever; and gnat- or midge-borne diseases including Oropouche virus disease.

Diseases Associated with Environmental Contact

Several diseases are contracted through contact with infectious forms in the soil or water. Two examples, schistosomiasis and plague, illustrate this type of infection hazard.

**Schistosomiasis.** Schistosomiasis (bilharzia) is an infectious disease that is contracted most frequently by people swimming in freshwater contaminated with the parasite; one cannot tell by looking at a body of water if it is contaminated. Maps of schistosome distribution are notoriously inaccurate and optimistic, as the venue of schistosomes’ life cycle expands steadily. The local populace is often ill informed, and much denial enters into certain local beliefs (by the expatriates at least) such as “There are no schistosomes in Lake Malawi.” The reality is that Lake Malawi, a large, beautiful lake—so seductive on a hot day—is full of schistosomes in its shallower areas (108). Even brief exposures to contaminated water during washing or washing can result in infection. Salt water is safe, however.

A recent report of 62 patients with schistosomiasis in a German clinic highlights the importance of knowing about this ubiquitous disease. Of these patients, 95% were exposed in Africa, most prominently in West Africa, i.e., the Volta River (24%), Niger (21%), and the Congo River (5%), but also in Lake Victoria and other bodies of water in East Africa (11%), the Zambezi River (14%), and Lake Malawi (11%) (63).

After exposure to freshwater containing schistosomal cercariae, the swimmer often experiences an intense itching with or without a papular rash. (A related avian parasite is present in U.S. lakes, causing “swimmer’s itch” but not producing systemic disease.) From 2 to 10 weeks later, the exposed person may experience a serum sickness-like febrile illness, known as Katayama fever, with chills, organomegaly, weight loss, headache, anorexia, nausea and vomiting, diarrhea, myalgias and arthralgias, and dry cough. Years to decades later, chronic schistosomiasis becomes recognizable with inflammation and fibrosis of the involved organs, particularly the liver and urinary bladder (36).

Preventative advice to the traveler includes the following: (i) don’t walk barefoot in the tropics; (ii) don’t swim in freshwater in areas of possible schistosome infestation; (iii) if inadvertently exposed to possibly schistosome-infested water, towel all exposed parts of the body vigorously to reduce penetration of the cercariae into the skin; (iv) use chlorinated water for washing; (v) don’t use water that you wouldn’t drink for toothbrushing, cleansing an ostomy tube, etc. Any returning traveler who gives a history of likely exposure, especially if cercarial dermatitis or Katayama fever is described, should have an evaluation that includes looking for eggs in the stool or urine and serology (a good enzyme-linked immunosorbent assay is available) (56). The disease is treatable (praziquantel), and recovery is good unless organ fibrosis is too extensive (36, 63).

**Plague.** Plague, bacterial disease caused by *Yersinia pestis*, is transmitted by rodents, especially rats, and their infected fleas. It occurs in either the bubonic or pneumonic form, the untreated mortality rate is over 50%, and the pneumonic form is quite contagious. The distribution of *Y. pestis* is virtually worldwide, but the risk to the usual traveler is negligible. Even in Vietnam, the only country with a WHO plague warning, the risk is basically to those who will be working closely with the soil, e.g., agronomists, forest workers, and anthropologists. The current vaccine has a dark reputation for side effects and is not available in the United States. Travelers who perceive themselves at risk should consider tetracycline or doxycycline prophylaxis. Plague was most recently brought to world attention by the alleged epidemic in Surat, India. While little plague was documented, the reaction of the international community ranged from observing and interviewing travelers arriving from India to closing borders to India (e.g. Pakistan), with resultant disruption of commerce (14).

**Sexually Transmitted Diseases**

A surprising number of travelers engage in casual, often unprotected, sex while traveling abroad, with resultant significant morbidity. The risk of contracting HIV is so well known that it will not be discussed here. Suffice it to say, unprotected sex overseas has never been more risky. The best defense is to abstain from casual sex. At the very least, condoms should be used consistently.

**SPECIAL POPULATIONS OF TRAVELERS**

Most of the travelers we see in our travel clinic are in basically good health; adequate pretravel advice involves mainly considerations of their itinerary and its attendant risks rather than their medical problems. However, several subsets of travelers have risks that are potentially exacerbated by their underlying physical conditions, such as diabetes and pregnancy, or by the extreme conditions of their proposed activity, e.g., high-altitude trekking or climbing. I will briefly consider here a few such groups, but not others who engage in activities such as SCUBA diving, white-water rafting, and wilderness alpine skiing. As a broad resource for the travel medicine provider caring for these special populations, the book by Jong and McMullen is unsurpassed (64). For the lay traveler, Rose’s book is written with less medical jargon (113).

**Pregnant Women**

An unexamined belief that a pregnant woman can do anything she would do if not pregnant flies in the face of reality, given the risks and rigors of some touring experiences in the less developed parts of the world. The travel medicine practitioner is prepared to help with the plans, preparation, and education necessary. Here, I will outline the major areas of concern; the traveling mother-to-be must consult closely with...
both her obstetrician and travel medicine provider, who in turn should be talking with each other.

The basic tenet is that the pregnant woman should not travel if there is any hint of an obstetrical problem or if expert care is not assuredly available in the host country. The potential problems begin with getting there. Aircraft fly at about 37,000 feet and are pressurized to about 8,000 feet. However, the observed maternal increased heart rate, decreased blood oxygen, and increased respiratory rate have no important effects on the vital signs of the fetus (98). The issue of cosmic radiation is more problematic, and pregnant women are advised to fly less than 50 h per month. At its most intense, i.e., during flights at high altitudes during solar flares, cosmic radiation is far higher per hour than the radiation delivered in a chest X-ray (98). For perspective, chest X-rays are never performed on a pregnant woman without shielding the fetus.

Extensive data on the safety of vaccines in pregnancy are available for very few vaccines (26, 87, 113). MMR is contraindicated. Yellow fever vaccine is contraindicated unless exposure to yellow fever virus is unavoidable. Most other vaccines are thought to be relatively safe, at least if the risk of the disease is truly significant. Rabies vaccine and RIG have been shown to be safe in one study of 190 pregnant Thai women (34).

Malaria prophylaxis is another matter. Chloroquine, which is no longer reliable prophylaxis in much of the world, has been shown by vast, if not controlled, experience to be safe in pregnancy. Mefloquine, on the other hand, has not been shown to be safe in the first half of pregnancy, and the claims for safety in the second half have been challenged (101, 134). Doxycycline, the usual backup for mefloquine, is sure to cause marred teeth in the exposed fetus. The pregnant woman, at least in the first half of pregnancy, might seriously question whether the trip is worth the risks of the malaria medication. In advising the intended traveler who is pregnant, we work especially closely with the obstetrician.

Infants and Children

A total of 1.5 million children under the age of 16 years travel abroad annually (96). The approach of a travel clinic for children is basically the same as for adults, with some important variations on the themes. Routine immunizations should be up to date, and the routine of administration might need to be altered to accommodate the timing of the absence from the country. Particular attention should be given to the adequacy of diphtheria, tetanus, pertussis (DTP) immunization. Travel-related vaccine considerations unique to the child should be discussed with the travel clinic personnel (109). The hygienic practices of toddlers that contribute to gastrointestinal infections in U.S. day care centers will ensure traveler’s diarrhea (90), which tends to be worse in children than adults. Children dehydrate and become ill more quickly. Families should travel prepared with oral rehydration solution salts for reconstitution in clean water for the ill child (90). Failure to equalize pressure on either side of the tympanic membranes can cause severe pain, and careful attention must be given to the ears of children with a history of such problems. The use of nasal sprays, decongestants, and perhaps steroid sprays should be considered. Administering malaria medication to a young child is a challenge remembered by parents for a long time. Moreover, mefloquine is approved only for children weighing over 15 kg. In practice, mefloquine is given to infants as small as 5 kg, but its safety for them has not been shown. Chloroquine suspension is available overseas, which is helpful in the areas of chloroquine-susceptible malaria (90). Protection against insects requires the same personal protection measures as for adults but is more difficult to accomplish for children: netting, covering clothing, and low-concentration DEET repellents.

The Diabetic Traveler

The prepared diabetic can travel with relative ease. The issues are well presented elsewhere in the detail that the problem merits (49, 67, 92). A major issue is the adjustment of insulin dosage as one travels east or west across multiple time zones; avoidance of hypoglycemia is the major immediate goal. Several publications specific to the needs of the diabetic traveler are available (92).

The Immunocompromised Traveler

Although the recent focus has been on HIV-infected travelers (69), travel clinics are increasingly being visited by patients on chronic glucocorticosteroid therapy, splenectomized patients, patients with chronic renal failure, and patients with bone marrow or solid organ transplants on steroids, cyclosporine, and other immunosuppressive drugs (20, 121). Most other immunocompromised states are associated with acute or chronic illness, and, in our experience, travel abroad by these persons seems to be rare.

Severely immunocompromised, non-HIV-infected persons. In practice, the group of severely immunocompromised, non-HIV-infected persons consists largely of patients on acute or chronic steroid therapy at dosages higher than those used for physiologic replacement. In general, live vaccines (measles, mumps, rubella, oral polio, oral typhoid, oral cholera, and Mycobacterium bovis BCG) should not be given to these patients. When possible, immunizations should be concluded at least 2 weeks before the initiation of the steroid treatment; in practice, starting the steroid treatment is rarely an elective decision, and such forethought is simply not possible. Since travelers may be at increased risk of exposure to measles, mumps, rubella, varicella, tetanus, and hepatitis A, patients for whom travel is unavoidable might well benefit from the antibodies to these agents contained in immune globulin. The recommended dosage is 0.05 ml/kg of body weight intramuscularly (maximum dose, 15 ml) (20). Careful and thorough education is important here, as is the assurance of good medical care in the host countries.

HIV-infected persons. Early in HIV disease, when the CD4+ cell counts are still high, HIV-positive patients may respond adequately to vaccines and do not demonstrate clinically increased susceptibility to bacterial and viral pathogens. As HIV progresses, the patient’s immune system becomes increasingly dysfunctional; the incidence and seriousness of pneumococcal, H. influenzae, and perhaps other bacterial infections increase; viral infections, such as those caused by herpes simplex virus, cytomegalovirus, and perhaps adenovirus and enterovirus, become chronically expressed; and the patient’s response to vaccine antigens becomes predictably poorer (115). HIV-positive patients do travel considerably, and careful education on the risks of contaminated food and water are particularly important.

Despite the weak response to many antigens, the CDC recommendation has been that although live vaccines should be avoided (MMR being the exception, if truly indicated), pneumococcal, Td, hepatitis B (for the seronegative), and possibly H. influenzae type b vaccines are appropriate. By extension, killed vaccines, such as injectable polio, meningococcal, and others, would not be contraindicated, although their effec-

The Prepared Diabetic can travel with relative ease. The issues are well presented elsewhere in the detail that the problem merits (49, 67, 92). A major issue is the adjustment of insulin dosage as one travels east or west across multiple time zones; avoidance of hypoglycemia is the major immediate goal. Several publications specific to the needs of the diabetic traveler are available (92).
tiveness is always in question in patients with HIV disease (20).

The current dilemma, however, is that there is recent evidence that certain immunizations stimulate the replication of HIV (119, 124). The boost in circulating levels of HIV RNA is short-lived, and confirmation of the effect in HIV-infected patients who are taking combination antiretroviral therapy is needed. In the meantime, HIV-positive travelers need to be aware of the data, and immunizations need to be most carefully balanced against the patient's risk.

Immunosuppressed travelers at risk for specific infections.

Persons with renal failure, diabetes, alcoholic cirrhosis, or asplenia may be at increased risk for certain diseases. In particular, pneumococcal, H. influenzae, and perhaps meningococcal vaccines are recommended. Immune response may well be impaired, and increased dosage, or repeat administration of vaccine, should be considered. Unfortunately, serologic measurement of the antibody response to administered antigens is not readily available. Examples of the special needs of these patients include recommendation for a pneumococcal vaccine booster at 6 years (although this is probably not indicated for patients with normal immune systems) (20) and prearrangement of dialysis care for patients with chronic renal failure.

The Elderly Traveler

Twelve percent of Americans aged 75 years or older travel overseas, and the response of travel medicine to their needs has been well reviewed (93). The key elements of travel preparation for the elderly are essentially the same as for younger travelers, with some extra emphases. For example, all travelers are warned about the lower PO2 in an airplane (which, per se, is rarely a health problem at any age) and the negative effects of alcohol, antihistamines, tranquilizers, sleeping pills, anti-motion-sickness drugs, etc.; but by combining these, the effects could be problematic for one with early dementia, for example. Other issues such as extremes of climate, age-associated decrease in sensory, motor, and perceptual skills, visual alterations, and motion-limiting spinal osteoarthritis all bring physiological reality to the aging traveler. Two good, readable sources are available for elderly travelers who wish to get detailed suggestions on enhancing the quality of their trip (75, 93).

As to immunizations in the elderly, 40% of persons in their sixties do not have protective levels of tetanus antitoxin. Similarly, as many as 84% of persons in that age group do not have protective serum levels of diphtheria antitoxin. It seems especially prudent to continue to apply to the elderly the general recommendation of the CDC that Td boosters be given every 10 years.

Travelers to High Altitudes

Acute mountain sickness (AMS) occurs in 84% of travelers who fly directly from Kathmandu (1,300 m) to Shyangboche (3,740 m) and sleep that night at 3,860 m—the most extreme short-interval acclimatization data available (89). Most altitudes achieved are less dramatic, but AMS, high-altitude pulmonary edema, and high-altitude cerebral edema can all occur at much more modest elevations. The issues of acclimatization and precautions should be carefully investigated by the traveler using sources such as the excellent chapter by Bezruchka (9).

In our travel medicine practice, we see few true adventure travelers, but we do advise quite a number of tourists going to La Paz, Bolivia, or Machu Picchu, Peru, and other high-eleva-

<table>
<thead>
<tr>
<th>Source of assistance</th>
<th>Contacting the source</th>
</tr>
</thead>
<tbody>
<tr>
<td>International Association for Medical Assistance to Travellers (IAMAT)</td>
<td>417 Center St., Lewiston, NY 14092, (716) 754-4883</td>
</tr>
<tr>
<td>American Citizens Services (ACS), domestic</td>
<td>(202) 647-5225</td>
</tr>
<tr>
<td>American Citizens Services (ACS), abroad</td>
<td>U.S. embassies, consulates, and consular agencies</td>
</tr>
</tbody>
</table>

Healthy Care While Abroad

When serious illness or injury strikes the traveler abroad, the result is often a nightmare. As with all other aspects of travel, preparation is the key to coping with such personal disasters. An excellent, detailed source for information about this issue is available (113). At a minimum, the traveler should give advanced thought to insurance coverage, to finding a doctor while abroad, and to air medical evacuation.

Insurance

Important factors to consider with regard to insurance include determining in advance, and in writing to avoid misunderstanding, exactly what your regular health insurance policies will cover; purchasing first-coverage or supplemental insurance if your policy has gaps (remember that Medicare does not cover health care expenses outside the United States, other than some limited situations in Canada and Mexico); being prepared to pay for health care and get reimbursed by insurance later; and considering the purchase of Travel Insurance with Assistance (113).

Finding a Doctor Overseas

Prior to travel. Contribute to the International Association for Medical Assistance to Travellers prior to your trip, and request their booklet which lists hospitals and doctors abroad (Table 6). All the physicians listed speak English and have agreed to abide by a modest standard fee schedule.

While abroad. There are several ways to locate a doctor while abroad. Any American can call upon the American Citizens Services, a State Department agency that operates in all U.S. embassies, consulates, and part-time consular agencies around the globe (Table 6) (15). If you purchased travel insurance with assistance, call the company’s 24-h assistance number. Some credit cards, particularly gold or platinum, have 24-h assistance telephone numbers; inquire into this before leaving the United States. Solicit personal recommendations...
from embassy employees, missionaries, and U.S. or Canadian employees of international companies.

**Air Medical Evacuation**

Most air evacuations from a foreign country to home are accomplished on regularly scheduled commercial flights. However, when the situation requires it, a chartered aircraft is essential. This process can cost upward of $100,000. The traveler should be sure that insurance purchased for a trip would cover such a contingency. There are more than 20 air ambulance companies, mostly based in the North America and Europe, but with others on each continent (113).

**INFORMATION SOURCES: PRINT, TELEPHONE, FAX, AND SUBSCRIPTION SOFTWARE**

The amount of information readily available to the traveler and to the travel medicine practitioner is substantial and seems to be growing geometrically. The following assortment of reference works, periodicals, and a few other information resources have proven to be particularly helpful to us, first in organizing THS and then in our day-to-day counseling of travelers. More detailed lists of information sources may be found in some of the reference works.

**Reference Works**

A list of reference works is given in Table 7.

In the manual by Jong and McMullen (64), the 14 chapters of Section One cover all the bases with regard to risks, preparedness, immunizations, water quality, malaria, etc. The following sections are more clinically oriented and discuss fever, diarrhea, skin lesions, sexually transmitted diseases, and worms, each with several disease-specific chapters or detailed groups of diseases. The writing is geared to the travel medicine provider and is thorough without excess taxonomy, epidemiology, and parasitology. The appendix is an excellent, complete, well-organized list of information resources. Overall, it is highly useful to the travel health provider.

Rose (113) provides 17 chapters addressing most areas of travel health concern, including trip preparation, jet lag, travelers’ diarrhea, malaria, and emergency medical transport; this is followed by a 200-page section, World Medical Guide, which has a concise disease risk summary for 11 geographic regions, followed by one to three pages on each country in that region: embassy telephone number, time zone in relation to Greenwich mean time, entry requirements, and brief information on telephone, electricity, tourism office, American Express, embassy and consulate addresses, doctors, and hospitals. The major section of each country piece is a Health Advisory, which discusses concisely the specific risks in that country. Rose’s book is geared to the sophisticated traveler but is a good quick reference in the clinic for the travel health provider, as well. The book is published annually.

Updated and published annually, the scope of the book by Thompson (128) is more narrow than that of the previous two, being focused on all aspects of both routine and special (i.e., travel) vaccines. Following a most authoritative presentation of each vaccine is a chapter on special situations for travelers, including pregnancy and HIV. Unique to this book is Section 5, Other Standards and Guidelines, which addresses vaccine issues such as storage and handling, infection control, record-keeping, misconceptions concerning contraindications to vaccination, adverse events, and sample letters (for physicians to send with the traveler confirming HIV negativity, the need for certain medicines, syringes, etc.). The final section, a directory of resources and publications, manufacturers and distributors, and products, is an invaluable resource. A nice touch is the initial two pages, New in 1996, which immediately orients the regular user to the latest information.

In the guide by Wilson (137), the encyclopedic section on the distribution of infections, particularly the part which addresses each country individually, is a constant help to the practitioner of travel medicine. The section on diseases is an accurate, concise summary of all aspects of an incredible number of tropical diseases. I use it as a reference all the time. The appendices comprise an imaginative, unique 33 pages which include a glossary, in which you can find, for example, what all those countries in Africa were called when you were in school; a listing of diseases by incubation period; vectors; drugs for parasitic infections; and resources.

The authoritative work by Plotkin and Mortimer (107) is the main reference in our travel clinic for in-depth consideration of the fundamentals of vaccines. The book provides a definitive discussion of virtually all vaccines.

Good atlases (52, 129) are essential in travel medicine, and we keep one in the clinic wherever the physician or nurse practitioner travel specialist is working on recommendations.

### Table 7. Reference works

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Title (reference)</th>
<th>Yr of publication</th>
<th>Publisher</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO</td>
<td>International Travel and Health, Vaccination Requirements, and Health Advice, 1995 (144)</td>
<td>1995</td>
<td>World Health Organization Publications Center U.S., 49 Health Organization Publications Center</td>
</tr>
</tbody>
</table>

Updated and published annually, the scope of the book by Thompson (128) is more narrow than that of the previous two, being focused on all aspects of both routine and special (i.e., travel) vaccines. Following a most authoritative presentation of each vaccine is a chapter on special situations for travelers, including pregnancy and HIV. Unique to this book is Section 5, Other Standards and Guidelines, which addresses vaccine issues such as storage and handling, infection control, record-keeping, misconceptions concerning contraindications to vaccination, adverse events, and sample letters (for physicians to send with the traveler confirming HIV negativity, the need for certain medicines, syringes, etc.). The final section, a directory of resources and publications, manufacturers and distributors, and products, is an invaluable resource. A nice touch is the initial two pages, New in 1996, which immediately orients the regular user to the latest information.

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Good atlases (52, 129) are essential in travel medicine, and we keep one in the clinic wherever the physician or nurse practitioner travel specialist is working on recommendations.
before the patient’s clinic visit. The Times atlas is superb (129), if a bit ponderous; it is complete, current, and well indexed. In the travel clinic we use the Hammond Atlas (52), which is well-indexed, easier to read than the Times atlas, and physically more manageable for use when obtaining more detail of the planned itinerary from a traveler in the clinic. A CD-ROM atlas with the detail of these two print atlases that is indexed as well or better is badly needed.

Two annual publications (26, 144) of the CDC and the WHO present both the basic epidemiologic information accrued by these organizations and the derivative policy and recommendations. While the aura of “official” is comforting, for rapidly evolving clinical situations such as the use of hepatitis A and oral typhoid vaccines, the clinician will need more for rapidly evolving clinical situations such as the use of hepatitis A and oral typhoid vaccines, the clinician will need more current information. For malaria and yellow fever, however, these sources are absolutely invaluable to the travel medicine practice (Table 7).

The CDC, WHO, and U.S. State Department publish several periodicals and offer facsimile services which are an invaluable help to the travel medicine practitioner (Table 8). The weekly Morbidity and Mortality Weekly Report (MMWR), published by the CDC, is the best source for timely information on developing immunization issues, emerging infectious diseases, and epidemiology. In Recommendations and Reports (MMWR) the CDC irregularly issues definitive recommendations on a wide variety of immunization issues, including reports from the Advisory Committee on Immunization Practices. As a timely update to the Yellow Book, the CDC issues a biweekly Summary of Health Information for International Travel (“Blue Card”) with the most current information from WHO regarding countries with a risk of cholera, yellow fever, and plague. Via its FAX Information Service, the CDC also makes available regional-, country-, and disease-specific information sheets. These sheets are concisely and thoughtfully written and are an excellent basic resource. However, sometimes clinical practice progresses faster than the updating of these recommendations. The Weekly Epidemiological Record is the definitive WHO publication of the global epidemiology of a wide spectrum of diseases.

Three excellent irregularly published sheets from the Consular Information Program of the U.S. State Department are of considerable help in preparing travelers for destinations experiencing terrorism, civil unrest, warfare, natural disasters, or political instability (Table 8). Consular information sheets are available for every country of the world and provide detailed factual information of use to the traveler, including addresses, immigration issues, health conditions, minor political disturbances, and local dress code customs. Travel warnings are issued as needed and constitute specific recommendations for action regarding some current hot spot; e.g., all Americans should leave Rwanda, and why. Public announcements concerning travel are issued as needed to disseminate information quickly about serious situations such as bomb threats to airlines, weapons shipments, violence by terrorists, coups, and anniversary dates of terrorist events.

### Periodicals, Bulletins, Directives, and Monographs

The number of items that could be listed in this section is expanding rapidly. Most are of frequent use to the travel medicine provider, while some are helpful primarily for patient education efforts. The publications used regularly in our THS practice are listed with accession information and a brief commentary on each in Table 9.

### Computer Software-Based Services

I am aware of three computer software-based travel medicine services (Table 10), but I do not find any of them to be the definitive answer to running a travel clinic. In practice, we frequently wish to present the information in a somewhat different way, or the computer service’s format is not sufficiently friendly to the reader, or the updates are not as current as the traveler needs. I suspect that it is difficult to produce and update such a product profitably. While it is a promising medium, its potential is not yet realized.

### INTERNET: WWW, FTP, AND E-MAIL

Access to information via the Internet has increased explosively in just the past year and promises to continue to do so. Internet access, particularly the World Wide Web (WWW), is rapidly becoming the norm for the dissemination of travel information of all types. The sources are of two basic types: those which provide easier (and free) access to the tradi-
TABLE 9. Travel medicine resources: periodicals, bulletins, directives, and monographs

<table>
<thead>
<tr>
<th>Resource</th>
<th>Publication information</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Journal of Travel Medicine</td>
<td>International Society of Travel Medicine (ISTM); Decker Periodicals, Hamilton, Ont., Canada.</td>
<td>This journal is rapidly becoming the major publication for clinical research on issues of importance to travel medicine. Further, the abstracts and the selected bibliography section in each issue allow the travel medicine provider rapid access to an extensive amount of information published in other journals.</td>
</tr>
<tr>
<td>Travel Medicine NewsShare</td>
<td>ISTM, circulation limited to members. For membership information: ISTM, P.O. Box 871089, Stone Mountain, GA 30087-0028.</td>
<td>This newsletter is valuable to the travel medicine practitioner not only for currency in ISTM activities but also for providing otherwise unpublished helpful bits of information from members around the world.</td>
</tr>
<tr>
<td>Journal of the American Society</td>
<td>American Society of Tropical Medicine and Hygiene (ASTMH), 60 Revere Dr., Suite 500, Northbrook, IL 60062.</td>
<td>Authoritative journal which emphasizes research in the pathophysiology and epidemiology of tropical diseases.</td>
</tr>
<tr>
<td>of Tropical Medicine and Hygiene</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tropical Medicine and Hygiene</td>
<td>ASTMH, circulation limited to members. For membership information, ASTMH, 64343 First St. NW, Washington, DC 20015.</td>
<td>Available to members of ASTMH, this newsletter has considerable late-breaking information concerning travel medicine and provides updated information on electronic access sources.</td>
</tr>
<tr>
<td>News</td>
<td></td>
<td></td>
</tr>
<tr>
<td>The Travel Medicine Advisor</td>
<td>American Health Consultants, 3525 Piedmont Rd. NE, Six Piedmont Center, Suite 400, Atlanta, GA 30305.</td>
<td>Initial subscription includes a large, loose-leaf binder with several valuable sections, including information sheets for individual countries, which may be used in patient education (some of these are outdated with respect to immunizations for polio and hepatitis A). The bimonthly update material includes revised binder inserts and a newsletter, Travel Medicine Advisor Update, which provides abstracts of highly relevant current articles, with expert travel medicine commentary. These products have constituted a core element of our travel medicine practice.</td>
</tr>
<tr>
<td>Emerging Infectious Diseases</td>
<td>National Center for Infectious Diseases, CDC, 1600 Clifton Rd., Mailstop C-12, Atlanta, GA 30333.</td>
<td>This newly established journal delivers what its title promises: examination of all aspects of new and rejuvenated pathogens. It is also available free of charge on the Internet.</td>
</tr>
<tr>
<td>Traveling Healthy</td>
<td>Traveling Healthy, Inc., 108-48 70th Rd., Forest Hills, NY 11375.</td>
<td>Geared toward the sophisticated and motivated traveler, this eight-page subscription newsletter focuses on one or two topics each month and delivers a thorough, practical analysis with detailed advice for the traveler. Each issue also includes smaller articles and news items. This newsletter is particularly helpful for patient education purposes.</td>
</tr>
<tr>
<td>The Journal of Infectious Diseases [JID]; Clinical Infectious Diseases [CID]</td>
<td>Infectious Diseases Society of America. University of Chicago Press, 5720 South Woodlawn Ave., Chicago, IL 60637.</td>
<td>Two peer-reviewed journals with excellent original research (JID) and clinical research and reviews (CID). Both are invaluable to the travel medicine practitioner.</td>
</tr>
<tr>
<td>World Malaria Risk Chart</td>
<td>IAMAT, 40 Regal Rd., Guelph, Ontario N1K 1B5, Canada; phone (519) 836-0102; Fax (519) 836-3412. Also, 417 Center St., Lewiston, NY 14092; phone (716) 754-4883.</td>
<td>This annually revised chart and numerous others such as climatic conditions around the world are unique resources. A donation is requested when ordering IAMAT’s products. IAMAT materials are regularly of great use in our travel medicine practice.</td>
</tr>
<tr>
<td>Health Hints for the Tropics</td>
<td>ASTMH, Editor, Martin S. Wolfe. Distributed by ASTMH, 60 Revere Dr., Suite 500, Northbrook, IL 60062.</td>
<td>This slender monograph is a useful, concise source of advice for the traveler.</td>
</tr>
</tbody>
</table>
Despite the myriad possible risks faced by travelers to developing countries, the vast majority return with no lasting illness. The most common affliction experienced by the returned traveler is diarrhea and malaise, which is responding slowly with empirical antibiotic therapy, perhaps because it was not bacterial in etiology. Our travel clinic has reservations about the practice of screening all returned travelers for eosinophilia, intestinal parasites, and tuberculosis (143). Rather, we advise our patients to seek immediate attention if they have a febrile illness with or without significant diarrhea, and we evaluate them promptly for malaria, typhoid and other enteric fevers, hepatitis, and amoebiasis. If other signs and symptoms such as mild diarrhea, malaise, and low-grade temperature elevations persist longer than 1 week to 10 days, we initiate an appropriate workup. We believe that this approach is both cost-effective and clinically prudent, as long as the patient is educated in the approach and has assured access to the travel specialist.

### CONCLUDING REMARKS

Travel medicine is an emerging discipline given birth by the burgeoning travel habits of world citizens. As travelers face current and emerging infections and other risks in their travels, pretravel health expertise is increasingly perceived as essential to a safe trip. As a discipline, travel medicine is young but rapidly defining itself. Travel medicine practitioners not only deliver informed care but also are taking responsibility for

### TABLE 10. Computer software-based services

<table>
<thead>
<tr>
<th>Software</th>
<th>Accession information</th>
</tr>
</thead>
<tbody>
<tr>
<td>CATIS</td>
<td>Department of Family and Community Medicine, ES g-438A, 200 Elizabeth St., Toronto, Ontario M5G 2C4, Canada.</td>
</tr>
<tr>
<td>Travax</td>
<td>Travel Health Information Services, Shoreland Medical Marketing, 10625 W. North Ave., Milwaukee, WI 53226; (608) 831-2331 (phone); (414) 774-4060 (fax).</td>
</tr>
<tr>
<td>Travel Care</td>
<td>Care Ware, Inc., 9555 Poole St., La Jolla, CA 92037; (619) 455-1484 (phone); (619) 455-5429 (fax).</td>
</tr>
</tbody>
</table>

ftp.cdc.gov. Type anonymous for the “user id.” Give your Internet e-mail address in response to the prompt for the password. Select subdirectory Pub, then subdirectory Travel.

### TABLE 11. Internet government sponsored travel information services

<table>
<thead>
<tr>
<th>Organization and service</th>
<th>World Wide Web</th>
<th>E-mail</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDC homepage</td>
<td><a href="http://www.cdc.gov/">http://www.cdc.gov/</a></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDC MMWR</td>
<td><a href="http://www.cdc.gov/travel/travel.html">http://www.cdc.gov/travel/travel.html</a></td>
<td>MMWR.<a href="mailto:lists@list.cdc.gov">lists@list.cdc.gov</a></td>
<td>Body of e-mail should read &quot;subscribe mmwr-tox&quot;</td>
</tr>
<tr>
<td>CDC Traveler’s Health menu</td>
<td><a href="http://www.cdc.gov/travel/travel.html">http://www.cdc.gov/travel/travel.html</a></td>
<td></td>
<td>Text of the “Yellow Book”—Health Information for International Travel</td>
</tr>
<tr>
<td>CDC Emerging Infectious Diseases</td>
<td><a href="http://www.cdc.gov/ncidod/EID.htm">http://www.cdc.gov/ncidod/EID.htm</a></td>
<td></td>
<td>Text of the journal Emerging Infectious Diseases see Table 9</td>
</tr>
<tr>
<td>U.S. State Department (Consular information sheets, travel warnings, public announcements)</td>
<td><a href="http://travel.state.gov">http://travel.state.gov</a></td>
<td>&lt;travel-advisories <a href="mailto:REQUEST@stolaf.edu">REQUEST@stolaf.edu</a>&gt;</td>
<td></td>
</tr>
<tr>
<td>WHO homepage</td>
<td><a href="http://www.who.ch">http://www.who.ch</a></td>
<td></td>
<td>At homepage, choose Travelers’ Health menu</td>
</tr>
<tr>
<td>WHO disease news</td>
<td><a href="http://www.who.ch/programmes/emc/news.htm">http://www.who.ch/programmes/emc/news.htm</a></td>
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</tr>
<tr>
<td>WHO General public information</td>
<td><a href="mailto:info@who.ch">info@who.ch</a></td>
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<td>Statistical information</td>
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<td>Library</td>
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<tr>
<td>Staff E-mail addresses</td>
<td><a href="mailto:whoem-mail@who.ch">whoem-mail@who.ch</a></td>
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</table>

### TABLE 12. University travel-related World Wide Web sites

<table>
<thead>
<tr>
<th>University</th>
<th>World Wide Web address</th>
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</thead>
<tbody>
<tr>
<td>Emory University</td>
<td><a href="http://www.cc.emory.edu/twhsc/emweb.medweb.id.html">http://www.cc.emory.edu/twhsc/emweb.medweb.id.html</a></td>
</tr>
<tr>
<td>Travel Medicine Service</td>
<td><a href="http://www.gen.emory.edu/travelmed.html">http://www.gen.emory.edu/travelmed.html</a></td>
</tr>
<tr>
<td>Tropical Medicine Service</td>
<td><a href="http://www.gen.emory.edu/travel.medweb.tropmed.html">http://www.gen.emory.edu/travel.medweb.tropmed.html</a></td>
</tr>
<tr>
<td>Stanford University Travel</td>
<td><a href="http://www-eland.stanford.edu/medicineservice/links.html">http://www-eland.stanford.edu/medicineservice/links.html</a></td>
</tr>
<tr>
<td>Tulane University, Virology</td>
<td><a href="http://www.tulane.edu/~vmms/tropicalweb.htm">http://www.tulane.edu/~vmms/tropicalweb.htm</a></td>
</tr>
<tr>
<td>University of Virginia, Traveler’s Clinic</td>
<td><a href="http://www.med.virginia.edu/medicine/travel.htm">http://www.med.virginia.edu/medicine/travel.htm</a></td>
</tr>
<tr>
<td>University of Washington, Medical College of Wisconsin, International Travellers Clinic</td>
<td><a href="http://www.intmed.mcu.edu/travel.html">http://www.intmed.mcu.edu/travel.html</a></td>
</tr>
<tr>
<td>University of Wisconsin, Virology</td>
<td><a href="http://www.bokklabs.wisc.edu/900/EIINet">http://www.bokklabs.wisc.edu/900/EIINet</a></td>
</tr>
<tr>
<td>Yale Emerging Infections Information Network</td>
<td><a href="http://who.int/healthinfo/ternology/termlinks.html">http://who.int/healthinfo/ternology/termlinks.html</a></td>
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</tbody>
</table>
TABLE 13. Other travel-related World Wide Web sites and e-mail addresses

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researching the myriad practical questions facing travelers and the process of assisting travelers effectively. With time, it is likely that practice guidelines that will assist both the provider and the traveler will emerge.

ACKNOWLEDGMENTS

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REFERENCES

20. Department of State. 1996. Human immunodeficiency virus (HIV) testing requirements for entry into foreign countries. Bureau of Consular Affairs, Public Affairs and Policy Coordination Staff, Department of State, Washington, D.C.


