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Travel medicine for the millennium: What your patients should know before they go

INTRODUCTION

It is estimated that more than 1 billion travelers worldwide journey by air and more than 50 million leave developed nations to visit underdeveloped countries.¹⁻³ Essentially, all travelers should seek or be given advice before extensive travel. Yet, despite the available information and resources, up to 70 percent of travelers report some health problem, and approximately 8 percent will require medical care or pharmacotherapy during their journey or after they return.^{2,4} Nurse practitioners seeking to become resourceful clinicians for their traveling patients require continual education and frequent updating in regard to the study and treatment of travel-related diseases. This review will examine clinical opportunities and responsibilities as they relate to pre- and post-travel illness prevention and treatment. It will further focus on the nurse practitioner's role in educating and caring for his or her patients in the area of travel medicine.

TABLE 1
Risk assessment list for travel

Travel-specific	Traveler-specific
Travel destination with specific travel itinerary.	Existing medical condition(s) and current status of each.
Type of travel (air, sea, car, etc.)	Current immunization status/pregnancy status.
Accommodations anticipated (hotels, hostels, outdoor camping, etc.)	Allergy history and adverse drug reaction history.
Length of stay	Current medication history and dosage regimens.
Travel type: Urban versus rural	
Anticipated activities (hiking, fresh-water activities such as swimming, altitude exposure, sexual activity, etc.)	
Guide-oriented versus off-tourist routes.	

PREPARATION: TRAVEL RISK ASSESSMENT

Health care providers should assess patients thoroughly to minimize the risk of travel-related injury and disease. This assessment should consider the traveler's health status and medical conditions and the details of the impending travel (see Table 1). It is important for the clinician to consider several issues:

1. A strong relationship with patient clientele is crucial so that an appropriate and timely

assessment and travel strategy can be designed. Last minute "assessments" and poor planning often result in a state of unpreparedness and associated unnecessary injury or illness. Nurse practitioners that have interactive and trusting relationships with their patients can initiate appropriate assessment and educate patients as necessary.

2. Nurse practitioners interested in providing this clinical service for their patients must understand the breadth and

By: Vincent J. Colucci, PharmD, BCPS

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Program Goal:
To improve the nurse practitioner's skills in assessing and prescribing prevention and treatment of travel-associated illness or injury.

Learning Objectives
Upon completion of this program, the clinician should be able to:
1. Perform a baseline assessment of a traveler's risk of illness or injury depending on his or her existing medical condition(s) and planned place of travel.
2. Assess and outline an immunization plan to

- bring patients up to date on routine adult vaccinations.
- 3. Identify and access various resources for immunization recommendations and site-specific disease state updates.
- 4. List, prescribe or recommend simple measures, including pharmacotherapy, to treat or prevent travel-related injury or illness.
- 5. Assist travelers in designing a site- and activity-specific checklist to minimize the risk of travel-associated injury or illness.

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TABLE 2
Personal precautions for travelers to developing countries.²

Illness or event	Precautions
Traveler's diarrhea	Avoid uncooked food (other than peeled fruits or vegetables), non-bottled beverages and unpasteurized dairy products. Eat well-cooked, hot foods. Do not eat food purchased from street vendors. Use bottled water for drinking, making ice cubes and brushing teeth. Wash hands with soap and water frequently, especially before each meal.
Respiratory infection	Avoid excessive outdoor activity in areas of heavy air pollution during hot or humid parts of the day. Consider tuberculin skin testing before and after travel.
Arthropod-borne illnesses (including malaria, dengue, yellow fever and Japanese encephalitis)	Minimize exposure of skin. Use repellents according to manufacturers' instructions (daytime use for dengue, nighttime use for malaria). For skin use 10 percent to 30 percent DEET-based products.* For clothes, consider treating with permethrin-based products. To prevent malaria, minimize outdoor evening and night activity. Consider use of an insecticide-treated mosquito net unless bedroom is protected against mosquitos and consider use of insecticide spray in bedroom at night. Regularly check for adherent ticks during rural activities.
Sexually transmitted diseases	Abstain from sex or use safe-sex precautions, including condoms, in all encounters. Avoid relations with commercial sex workers.
Accidents, trauma and injuries	Avoid nighttime driving in rural areas. Use seat belts and infant or child car seats if available. Avoid use of alcohol while driving or engaging in water sports. Use flotation devices or life jackets. Use helmets when riding bicycles. Avoid politically unstable areas. Avoid use of motorcycles and mopeds and overcrowded public transportation. Check rooms for exits and keep a flashlight handy.
Blood-borne infections (including hepatitis B, hepatitis C and human immunodeficiency virus)	Avoid skin-perforating procedures (acupuncture, piercing, tattooing, venipuncture) and sharing of razors. Avoid invasive medical or dental procedures. Avoid contact with blood or blood products. Consider carrying a sterile or disposable needle or syringe.
Altitude illness	Ascend slowly. Acclimate for at least two to three days at 2,500 to 3,000 meters before ascending higher, then allow approximately two days per 1,000 meters of altitude gained. If symptoms of altitude illness develop, stop ascent. If symptoms persist or worsen, descend immediately. Avoid excessive physical activity until acclimated. Minimize use of alcohol and drink plenty of fluids. Mountain climbers and other traveling at 3,500 to 5,000 meters may benefit from expert advice.
Bites or envenomations	Do not pet or feed animals (especially dogs and monkeys). Avoid direct contact with animals. Consider minimizing jogging or bicycling. Check bedding before use. Check shoes before wearing. Use covered footwear except on the beach; consider wearing reef shoes in the water. Avoid touching or handling marine creatures.
Freshwater- and seawater-	Avoid swimming or wading in nonchlorinated fresh water, especially if stagnant or slowly flowing. Eating predatory reef fish (barracuda, jackfish, grouper, snapper) may cause ciguatera poisoning. Scuba divers should have certification. Follow established timetables for flying after diving.
Heat-, humidity- and sun-related illnesses	Drink plenty of fluids, avoid dehydration and rest frequently. Avoid excessive physical activity. Wear light-colored, loose-fitting clothing. Wear sunscreen with a sun protection factor (SPF) of 15 to 40. Wear hat and sunglasses.
Transportation-associated illnesses	During the flight, to prevent barotrauma, chew or swallow during ascent and descent. For young children, feed or use a pacifier during ascent and descent. To prevent venothrombosis, avoid dehydration, minimize alcohol consumption and move around the cabin during prolonged flights. To prevent motion sickness, move to the center of the vehicle, fix eyes on still, distant objects and increase airflow across face. Consider use of prophylaxis. To prevent jet lag, melatonin and dietary modifications are of unproved benefit. The body clock normally resets one hour per day. Engage in activity in sunlight after arrival at destination.
General	Consider taking a medical kit containing thermometer, tweezers, bandages, sunscreen, insect repellent, topical antibiotic, an analgesic such as acetaminophen, an antimobility agent for diarrhea and other medications. Also consider taking a water purifier or tablets and disposable needle or syringe. Carry all medicines in prescription bottles. Carry list of medical conditions, allergies, medications, dosages and contact numbers. If there is a cardiac problem, carry copy of recent electrocardiogram. When undertaking high-risk or long-term travel, consider obtaining medical-evacuation insurance.

* DEET denotes N, N-diethyl-m-toluamide, now called N, N-diethyl-3-methylbenzamide.

depth of the practice of travel medicine, or “emporiatrics,” and stay well informed of current concepts, guidelines and resources.

3. The prevention and treatment of travel-related issues and injuries will require organization and appropriate resource dedication if sufficient service is to be rendered effectively. Nurse practitioners and their clinical co-workers must understand this and be willing to provide said resources and service, both as informational and direct patient care.

TABLE 3
Pharmacotherapy for traveler’s diarrhea

Drug	Dosage	Comment
Azithromycin	1000mg once or 500mg daily for three days	5mg/kg to 10mg/kg in children or pregnant women
Ciprofloxacin	500mg bid one to three days	Do not use in children or pregnant women; may interact with warfarin or theophylline
Levofloxacin	500m a day for one to three days	Do not use in children or pregnant women
Norfloxacin	400mg bid one to three days	Do not use in children or pregnant women
Ofloxacin	300mg bid one to three days	Do not use in children or pregnant women
Rifaximin	200mg tid for three days	For use in children younger than 12 year of age, do not use if febrile or blood in stool or infections caused by <i>C. jejuni</i>

INDIVIDUAL PRECAUTIONS AND GENERAL PREVENTABLE MEASURES

Travel may be associated with non-infectious risks and illness, many of which can be prevented or self-treated if appropriately educated (see Table 2).

High altitude sickness

Rapid ascension to altitudes higher than 8,000 feet (2,500 meters) can cause acute mountain sickness (AMS) in up to 25 percent of people. This usually manifests as headache, nausea/vomiting, light headedness and insomnia. Rarely, it can progress to pulmonary or cerebral edema, but this usually is associated with elevations greater than 17,000 feet (5,000 meters). The most effective measure to prevent AMS is by acclimating to altitude with two- to four-day stays at lower elevations (2,000-4,000-foot intervals) and then a graded ascent to higher altitudes at no more than 1,000 feet (approximately 300 meters) daily.⁵⁻⁸

Nurse practitioners can be instrumental in this type of education. Alternatively, preventive pharmacotherapy usually is with acetazolamide, a carbonic anhydrase inhibitor, taken at a dose of 125mg to 250mg twice daily (Diamox Sequels can be substituted at a dose of 500mg daily). This medication should start one to two days before ascent

and should be continued at the higher elevations for 48 hours or longer. Recommended pediatric dosage is 5mg/kg per day in two to three divided doses. Individuals who are pregnant or nursing mothers, have liver or kidney disease, diabetes, adrenal failure, allergies to sulfa or the compound itself should not take Acetazolamide. Blurred vision is a common side effect that usually disappears shortly after stopping the medication. Side effects such as tingling in the fingers and toes, taste alterations and frequent urination also can be common, and patients should be consulted to drink more fluids than normal to prevent dehydration and headaches. Other agents, such as dexamethasone and nifedipine, have been studied, but are reserved for expeditious mountaineering or acetazolamide intolerance.^{6,7} Mountaineering expeditions require expert advice and are beyond the scope of this review.

Venous thromboembolism

Recent evidence⁹⁻¹¹ has documented an increased risk of venous thromboembolism (VTE) with prolonged travel and immobilization in a car or airplane. This risk is increased in individuals with a history of VTE, obesity, malignancy or documented hypercoagulable states.⁹⁻¹¹ Risks can be minimized by intermittent stopping (e.g. vehicle travel), arising and

walking in the aisles during airplane travel, isometric exercises and wearing compression hosiery. Drinking sufficient fluids and avoiding caffeinated beverages and sympathomimetics also can mitigate risks. There is some data supporting prophylactic anticoagulants such as vitamin K antagonists or heparins for patients with a history of previous venous thrombosis and/or thrombophilia. Treatment can include a single dose of a low molecular weight heparin as prophylaxis to high-risk travelers to decrease the risk of VTE. However, since warfarin kinetics warrant initiating the drug five to seven days prior to travel, this method is impractical, has not been well-studied and is not advised. In addition, the anticoagulant response varies considerably from person to person and the anticoagulant efficacy cannot be predicted on the basis of units/kg given.

Jet lag

Travelers often will complain of insomnia, decreased sleep quality, irritability and headache when flying long distances crossing several longitudes and time zones. This is usually characterized as “jet lag” and often times has been more severe when traveling eastward.¹ Few treatment or prevention strategies have proven effective, however, some general advice can be helpful. Remaining well-hydrated, avoiding ethanol and pursuing activities in sunlight on arrival

may be effective. Immediate release melatonin, taken as a 2mg to 3mg dose starting on the first night of travel, and then continued

for up to five days after arrival, has been reported to assist in normalizing sleep cycles.¹² Studies, however, have been equivocal, per-

haps related to product variance and impurities. Melatonin has almost no side effects other than somnolence, but should not be co-administered with MAO-inhibitors or by individuals with auto-immune disorders. There is evidence that zolpidem 5-10mg (Ambien) taken on the first night after arrival and continued for three nights can be effective.¹ Due to its rapid onset of action, zolpidem should be administered immediately before going to bed. Although the next-day residual effects are minimal, zolpidem is a central nervous system depressant and patients should be cautioned on possible combined effects when taken with other CNS depressants and/or alcohol.

PATIENT SCENARIO 1

Problem

Two 23-year old college students enter your community setting for information regarding their plan to travel to Nicaragua for a six-month church mission. They will not be departing for another six weeks, but are beginning their preparations and information-gathering. They will be working in rural parts of the country for the majority of their stay. Both are currently healthy and do not relate any drug allergy history to you. Neither of the young men takes any prescription medications. Their main concerns are about malaria and traveler's diarrhea. Some church elders have told them they will need potent antimalarial drugs requiring long-term treatment and, in addition, they should use Pepto Bismol to prevent the diarrhea. What is a reasonable response?

Assessment

Malaria response: An initial educational response should be reasonably simple but also one of information exchange. They can be guided to Web-based resources such as www.cdc.gov/travel/diseases.htm#malaria, or the malarial information can be retrieved for them. They should be educated that Nicaragua is a chloroquine-sensitive area and that chloroquine phosphate is the agent that should be considered first choice. This will be dosed once weekly starting two weeks before they depart and should continue four weeks after they return. It is imperative to explain and emphasize this latter instruction, as latent malaria often is a problem. Personal protective measures should also be employed, such as purchasing and applying insecticides containing DEET of about 30 percent to 35 percent strength. It should be applied to exposed skin between dusk and dawn when the malaria mosquitoes are biting. This also can be applied to clothing and mosquito netting. Permethrins also could be used in conjunction with DEET products, particularly for the clothes and netting. Application may be necessary every three to four hours.

Traveler's diarrhea response: Precautions should be taken to prevent diarrhea. Boiling water is by far the most effective and reliable method to purify water for drinking purposes. Purchasing a good water filter may help, but will not eliminate viruses. Using iodine as a chemical disinfectant cannot reliably purify. Often, the diarrhea is self-limiting, however, with a long duration of stay other protective measures should be taken. Travelers should peel all their own uncooked fruit and vegetables and wash hands with soap and water frequently, especially before eating. If boiling water is inconvenient or unavailable, use bottled water for drinking or brushing teeth. Avoid unpasteurized dairy products. They should have an anti-motility agent, such as loperamide, and be given proper dosing instructions. Most travel medicine consultants do not recommend chemoprophylaxis, but suggest self-treatment (one to three days) with a fluoroquinolone or extended-spectrum macrolide like azithromycin. Therefore, a prescription can be written and filled in advance of their trip. They should begin treatment if they have persistent (more than three days) and moderate to severe diarrhea. They should be educated on rehydrating with purified water or electrolyte solutions to prevent dehydration or electrolyte imbalances.

This situation presents a great opportunity to establish a more in-depth assessment. Time should be scheduled for one or more return visits to more thoroughly review and assess travel plans, itineraries, risks and prevention strategies. The practitioner can then establish herself or himself as a resource and point-of-care provider. This can be achieved after the students return for follow-up assessments.

Motion sickness

Many travelers are plagued by motion sickness despite different methods of travel. Many agents have been tried, with only moderate effectiveness. The anticholinergic agent, scopolamine, administered either orally or transdermally as a patch, has been shown to decrease symptoms. Transdermal scopolamine is applied to the skin behind the ear six to eight hours before exposure and is changed every three days. Patients should be advised to wash their hands and avoid touching or contacting their eyes after handling the patch. Individuals with underlying disease states, such as irritable bowel syndrome, urinary complications and Alzheimer's disease, may experience exacerbations secondary to the anticholinergic effects. Oral phenothiazines with anticholinergic properties (e.g., chlorpromazine, prochlorperazine) can be helpful, but may be sedating and are generally less effective as prophylactic agents. OTC antihistamines

with anticholinergic properties, such as dimenhydrinate or meclizine, can be effective for milder symptoms. Ginger also has been anecdotally described as helpful, but studies are lacking.^{1,13} Anticholinergic agents should not be used in patients that are pregnant or in those that have, or had, glaucoma, an enlarged prostate or obstruction of the stomach or intestines. Side effects commonly experienced with the use of anticholinergics include blurred vision and dry mouth.

Travelers' diarrhea

The most common illness to afflict travelers is diarrhea. Incidence varies from 10 percent to 60 percent of travelers to developed countries. Despite many cases being self-limiting (average duration approximately four days), as many as 20 percent to 40 percent of people will have to delay travel or make significant

itinerary changes due to diarrhea.^{2,3}

Enterotoxigenic or enteroaggregative strains of *E. coli* and species of *Campylobacter*, *Shigella* and *Salmonella* account for the majority of identified. Viral and parasitic pathogens are less-commonly identified.^{1,2} Nurse practitioners can be instrumental in prevention and treatment of traveler's-associated diarrhea. An effective educational and counseling plan for travelers visiting areas of poor hygiene should include the avoidance of raw vegetables and fruit they have not peeled themselves, unpasteurized dairy products, cooked food not served steamy hot, ice and tap water. Additionally, instructions should be given regarding fluid replacement and oral rehydration in case of diarrhea, particularly for children, the elderly and patients who take diuretics daily. Antimicrobial prophylaxis for diarrhea is not commonly prescribed, but rather travelers should be instructed to initiate

self-treatment when diarrhea symptoms become distressing or persistent. Immunocompromised individuals (not including children or pregnant women) may benefit from prophylaxis such as ciprofloxacin 500mg, levofloxacin 500mg, ofloxacin 500mg or norfloxacin 400mg daily during travel and for two days after return. Taking two tablets of bismuth subsalicylate four times daily also can be effective, but less so. Other antimicrobial treatment options are listed in Table 3. Travelers also should carry an anti-motility agent, such as loperamide, (taken as a 4mg loading dose, then 2mg after each loose stool up to 16mg/day). Loperamide should be avoided or discontinued if fever, bloody diarrhea and/or constipation are present.

Insect bite protection

Barrier protection is the first appropriate step to mitigate insect bites. This includes

TABLE 4
Malaria chemoprophylaxis in adults and children

Drug	Adult dosage	Pediatric dosage
Chloroquine Phosphate (Aralen) for chloroquine sensitive areas	300mg base (500mg salt) once a week. Start one to two weeks before entering malarious area; continue for four weeks after leaving. Take with food.	5mg/kg (base)/8.3mg/kg (salt) up to adult dose; once per week as in adults.
Mefloquine HCL (Lariam) for chloroquine resistant areas	228mg base (250mg salt) once a week. Start one to two weeks before entering malarious area; continue for four weeks after leaving. Take with food.	Less than 9kg: 5mg/kg salt once a week. 10kg to 19kg: 1/4 tablet once a week. 20kg to 30kg: 1/2 tablet once a week. 31kg to 45kg: 3/4 tablet once a week. More than 46kg: one tablet once a week.
Doxycycline (Vibramycin and others)	100mg daily with food. Start one to two days before entering malarious area and continue for four weeks after leaving. Alternative to mefloquine. Can use in mefloquine resistance.	2mg/kg daily, up to adult dose. Start and stop use as with adult dose.
Atovaquone/proguanil (Malarone and Malarone Pediatric)	One 250mg/100mg tablet daily. Start one to two days before entering malarious area and continue for seven days after leaving.	11kg to 20kg: One peds tablet daily. 21kg to 30 kg: Two peds tablets daily. 31kg to 40 kg: Three peds tablets daily. More than 41kg: as adult. Start and stop use as with adult dose.
Primaquine phosphate	30mg base (26.3mg salt) once daily. Start one to two days before entering malarious area. Continue for seven days after leaving and take with food and 8 ounces of water. Can also be used for reducing relapses. Use 26.3mg tab once daily for 14 days after departing area.	0.5mg/kg (base)/d up to adult. Start and stop as with adult dose.

TABLE 5
Recommended Adult Immunization Schedule, by Vaccine and Age Group
UNITED STATES, OCTOBER 2005-SEPTEMBER 2006

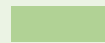
Vaccine ▼	Age group ►	19–49 years	50–64 years	> 65 years
Tetanus, diphtheria (Td) ^{1*}		1-dose booster every 10 yrs		
Measles, mumps, rubella (MMR) ^{2*}		1 or 2 doses	1 dose	
Varicella ^{3*}		2 doses (0, 4–8 wks)	2 doses (0, 4–8 wks)	
----- Vaccines below broken line a for selected populations -----				
Influenza ^{4*}		1 dose annually	1 dose annually	
Pneumococcal (polysaccharide) ^{5,6}		1-2 doses		1 dose
Hepatitis A ^{7*}		2 doses (0, 6–12 mos, or 0, 6–18 mos)		
Hepatitis B ^{8*}		3 doses (0, 1-2, 4-6 mos)		
Meningococcal ⁹		1 or more doses		

NOTE: These recommendations must be read along with the footnotes.

*Covered by the Vaccine Injury Compensation Program.



For all persons in this category who meet the age requirements and who lack evidence of immunity (e.g., lack documentation of vaccination or have no evidence of prior infection)



Recommended if some other risk factor is present (e.g., based on medical, occupational, lifestyle, or other indications)

This schedule indicates the recommended age groups and medical indications for routine administration of currently licensed vaccines for persons older than 19 years. Licensed combination vaccines may be used whenever any components of the combination are indicated and when the vaccine's other components are not contraindicated. For detailed recommendations, consult the manufacturers' package inserts and the complete statements from the ACIP (www.cdc.gov/nip/publications/acip-list.htm).

Report all clinically significant postvaccination reactions to the Vaccine Adverse Event Reporting System (VAERS). Reporting forms and instructions on filing a VAERS report are available by telephone, 800-822-7967, or from the VAERS Web site at www.vaers.hhs.gov.

Information on how to file a Vaccine Injury Compensation Program claim is available at www.hrsa.gov/osp/vicp or by telephone, 800-338-2382. To file a claim for vaccine injury, contact the U.S. Court of Federal Claims, 717 Madison Place, N.W., Washington D.C. 20005, telephone 202-357-6400.

Additional information about the vaccines listed above and contraindications for vaccination also is available at www.cdc.gov/nip or from the CDC-INFO Contact Center at 800-CDC-INFO (232-4636) in English and Spanish, 24 hours a day, 7 days a week.



light-colored clothing, long-sleeve shirts and pants, and covered shoes. Where available, travelers should sleep indoors, under cover or within insecticide-impregnated nets. Mosquitoes that transmit malaria are most active between dusk and dawn; those that transmit dengue fever are most active during daylight hours.

Repellents and insecticides: N,N-diethyl-m-toluamide (DEET) remains the most widely used topical insect repellent and remains very effective in repelling mosquitoes, chiggers, gnats and fleas. It can be applied to exposed skin and clothing. Most authorities suggest DEET concentrations of 30 percent to 35 percent. Higher concentrations protect longer but with no increased efficacy. A long acting military formulation (25 percent to

33 percent DEET Ultrathon) can protect for six to 12 hours.¹⁴ Another available formulation with a longer duration of protection is called Sawyer Controlled Release (DEET 20 percent). DEET should not be used in infants younger than 2 months, but its safety has been demonstrated in second and third pregnancy trimesters.¹ The American Academy of Pediatrics recommends concentrations not more than 30 percent in children and infants older than 2 months; The Centers for Disease Control and Prevention (CDC) extends the safe concentration up to 50 percent. Nurse practitioners should instruct patients that while DEET can decrease the effectiveness of sunscreens, the opposite has not been shown to be the case. Other possible agents to recommend include pi-

caridin 7 percent (Cutter Advanced), which has shown protectiveness up to four hours and permethrin (Duranon, Permanone). The latter is a reasonable recommendation as an insecticide and can be used on mosquito nets, clothing, tents and sleeping bags. It also is effective against ticks. Permethrin remains active through several washings and provides additional protection in combination with DEET.

Malaria

Malaria is a parasitic infection caused by one of four protozoan species of Plasmodium with *P. falciparum* and *P. vivax* being the most common. *P. falciparum* causes the most severe infection and can result in death.^{1,2,13} Female *Anopheles* mosquitoes

transmit the infection primarily during their nighttime feeding habits. The increase in travelers to developing countries and the growing resistance to drugs by the Plasmodium species increase the risk of contracting malaria. Other risk factors include the country of travel, the specific area within the country, time spent outdoors after sundown, the season and the altitude (transmission is rare above 6,000 feet). These elements of the planned trip should be thoroughly researched prior to travel or prior to initiation of drug prophylaxis. It is important to realize that no drug is 100 percent effective in the prevention of malaria and other risk-reducing measures should be invoked (any measure that reduces exposure to the night-biting *Anopheles* mosquito). See discussion under "insecticides." DEET-containing formulations should be applied to exposed skin between dusk and dawn. Concentrations of more than 30 percent usually are effective. Applications may be required as frequently as every three to four hours.

The use of antimalarial drugs and their potential adverse effects must be weighed against the risk of acquiring malaria. The drug of choice is chloroquine in areas where chloroquine resistance has not been described, although these areas are increasingly fewer. The current drug of choice for travelers traveling to chloroquine-resistant areas is mefloquine. Rarely, mefloquine has been associated with CNS toxicity, including neuropsychiatric reactions, psychosis, convulsions and other cognitive changes (reported incidence is approximately one in 200 users).¹ For those individuals unable to tolerate mefloquine or those who are traveling to areas with documented mefloquine resistance, doxycycline becomes the preferred agent. The usual precautions with prescribing doxycycline (gastrointestinal disturbances, photosensitivity and avoidance of multi-valent minerals) apply to the traveler as well. Agents for malaria, including dosing, are listed in Table 4.

Malaria during pregnancy may have severe and dire outcomes. For pregnant women traveling to endemic areas and cannot defer travel, chemoprophylaxis is imperative. Doxycycline and primaquine

PRACTICE POINTS

Practitioners interested in providing clinical services related to travel medicines for their patients must understand the breadth and depth of the practice of "emporiatrics" and stay well-informed of current concepts, guidelines and resources.

An effective educational and counseling plan for travelers visiting unindustrialized areas should include food avoidance recommendations, instructions regarding fluid replacement and oral re-hydration in case of diarrhea and the effective use of DEET and sunscreens.

Travel risk assessment provides an excellent opportunity for reviewing and updating recommended adult immunizations.

Alterations in immune responses may lead to clinically significant changes in the protective efficacy of certain vaccines.

Patients should be advised to obtain an ample supply of their medications from their pharmacy before they depart. Prescriptions should be written generically if they will require filling in another country, or arrangements to obtain refills via mail should be made in advance.

are contraindicated in pregnancy. Chloroquine is safe and mefloquine can be used if chloroquine-resistant areas are the destination. It is extremely important for nurse practitioners to convey or reiterate to their traveling patients that while malaria can be effectively treated early in its course, a delay in treatment can result in serious or even fatal outcomes. Travelers to malarious areas should seek medical attention if they become febrile either during or up to a year after their return (especially in the first two to three months after returning).

IMMUNIZATIONS

Recommended adult routine vaccinations

Travel risk assessment provides an excellent opportunity for reviewing and updating recommended adult immunizations. Currently, there are five vaccines routinely recommended by the United States Advisory Committee on Immunization Practices: tetanus-diphtheria-pertussis (Tdap), pneumococcal, influenza, varicella and measles-mumps-rubella (MMR), see Table 5. All adults should be up to date with these immunizations, especially those traveling to developing countries. Once updated on routine vaccines, others including hepatitis A and B, meningococcal and possibly herpes zoster and human papillomavirus may be war-

ranted depending on individual needs and travel destinations.

The practitioner should be aware that aging may be associated with alterations in immune responses and may lead to clinically significant changes in the protective efficacy of certain vaccines. There is a paucity of data in regard to this issue, however, any practitioner rendering care as it relates to travel medicine is advised to keep abreast of any new literature in this area.¹⁵

COMMON TRAVEL VACCINES

Hepatitis A vaccine

Despite the high incidence of infection, hepatitis A also is the most vaccine-preventable travel-related illness. A majority of hepatitis A cases occur in travelers to Mexico and Central America but exists wherever there is potential fecal contamination of food and water, including the United States. Those traveling off the usual tourist routes or backpackers should be immunized. The hepatitis A vaccine is indicated for most non-immunocompromised adults traveling to developing countries. The vaccination consists of a two-dose regimen for both adults and adolescents and the second dose can be given between six and 18 months after the initial dose (see Table 6). Two commercial products are available and cross-

TABLE 6
Some adult immunizations for travel

Illness	Vaccine	Dosage Schedule (non-immune person)	Booster
Cholera	Oral killed whole-cell recomb B Subunit vaccine (WC-rBS)	More than six years: two doses separated by one to six weeks. Two to six years: three doses separated by one to six weeks.	More than six years: two years.
Typhoid	Parenteral heat and acetone inactivated.	Two doses IM more than four weeks apart.	Three years
	Parenteral Vi capsular Polysaccharide (Typhim Vi)	25mcg (one dose) IM	Two years
	Oral live attenuated <i>S. typhimurium</i> TY21a (Vivotif Berna)	One capsule q 48 hours for four doses.	Two years
Yellow Fever	Live attenuated viral strain (YF-Vax)	One dose	10 years
Rabies	Human diploid cell vaccine greater than 2.5 IU rabies antigen (Imovax, RabAvert)	Pre-exposure: 1ml IM days 0, 7 and 28.	Two years or per sero-testing
Japanese encephalitis	Inactivated viral mouse brain-derived vaccine (JE-Vax)	1ml SC days 0, 7 and 30.	More than three years
Polio	Inactivated Polio vaccine (IPV) killed polio virus; trivalent.	One IM dose.	Six to 12 months
Meningococcal	Meningococcal quadrivalent Polysaccharide vaccine (Menomune)	One dose SC (0.5ml-50mcg each Ag)	Three to five years
	Conjugate quad-vaccine	One dose IM (0.5ml-4mcg each Ag)	Unknown

reactive. Both require two to four weeks to produce antibodies after the first inoculation, although it should be noted that the hepatitis A virus has a 28-day incubation period. Thus, a first dose is protective even if the exposure is within four weeks of immunization. Intramuscular immune globulin (fractionated immunoglobulins, mostly IgG) is an option for short-term protection, keeping in mind that it is a blood-borne product and is costly.^{2,15,16}

Hepatitis B vaccine

Vaccination against hepatitis B is recommended for travelers going to high-risk areas or if their plans include a long duration of stay or frequent returns. Any exposure to health care treatment, invasive procedures, cosmetic needles or unprotected sex warrants vaccination against hepatitis B. Two recombinant vaccines are available and interchangeable, i.e., a three-dose series started with one

vaccine may be completed with the other. The primary vaccination consists of three IM doses given at 0, one and six months and possibly a fourth dose at 12 months (Engerix-B). An interrupted hepatitis B vaccination series does not require starting the series over.^{2,15,16} A combination product for hepatitis A and B (Twinrix) containing the same antigenic components as the individual products is available for patients 18 years and older (three-dose series: 0, one and six months). At least two doses should be administered before travel. The combination product also can be used to complete the initial series if it was started with a monovalent product.^{2,15}

In April of 2007, the FDA approved an accelerated dosing schedule for Twinrix. This schedule consists of three doses given within three weeks, followed by a booster at 12 months. This accelerated dosing schedule provides an opportunity for travelers to obtain immunization in a relatively short pe-

riod of time and may be useful in increasing the rate of Hepatitis A and B immunization among travelers.

Cholera

Cholera risk is low with most trips unless work is planned in refugee camps or travelers are going to places where cholera is endemic. Unfortunately, the parenteral U.S. vaccine no longer is available; a European oral vaccine (Dukoral) is available in some countries and Canada.¹

Typhoid

Vaccination against typhoid should be targeted to those traveling to South Asia, North and West Africa, long-term travelers and those deviating from established tourist routes or itineraries. It also may be prudent to vaccinate immunocompromised patients and those with severe ischemic heart disease or mechani-

TABLE 7
Selected Web sites for the travel health care professional and traveler

Web site	Discription
www.cdc.gov	Centers for Disease Control and Prevention (CDC), Atlanta, GA 30333. See 'Travelers' Health' section. Online references: <i>Health Information for International Travel</i> , 1999-2000. Information also available at 877-FYI-TRIP (877-394-8747).
www.cdc.gov/nip	Central resource page of the National Immunization Program of the CDC. Includes vaccine recommendations for adults and children. Vaccination information sheets are available. (800) 232-2522.
www.cdc.gov/travel/index.htm	The CDC health information page for international travel.
www.cdc.gov/travel/yb/index.htm	The CDC listing of travel-related Web sites containing general travel advice, country-specific information (including malaria risk and anti-malarial recommendations). Yellow Book resource.
www.who.int/ith	The World Health Organization's Web site, containing general travel advice and anti-malarial recommendations.
www.state.gov	State department services including consular information, travel advisories, security and incident reports. Bureau of Public Affairs, U.S. Dept. of State, Washington, D.C., 20520. (202) 647-6575.
www.who.int/health-topics/idindex.htm	World Health Organization. Avenue Appia 20, 1211 Geneva 27 Switzerland. Includes maps of travel-related infectious diseases.
www.hc-sc.gc.ca	Health Canada Online research page. Search travel information. Canadian Laboratory Centre for Disease Control. Health Canada, A.L. 0913A, Ottawa, On KIA 0K9, Canada. (613) 957-2991.
www.astmh.org	American Society of Tropical Medicine and Hygiene, 60 Revere Dr., Suite 500, Northbrook, IL 60062. (847) 480-9592.
www.istm.org	Internation Society of Travel Medicine. P.O. Box 871089, Stone Mountain, GA 30087. (770) 736-7060.
www.fitfortravel.scot.nhs.uk/	Fit for Travel (Scotland). Advice for health care practitioners and the public.

cal heart prostheses, since they will have more complicated disease exacerbations should typhoid infection occur.¹⁵

Yellow fever

Yellow fever is a rare but potentially fatal viral infection transmitted by mosquitoes. It is endemic to certain areas of Latin America and sub-Saharan Africa. Updated CDC resources should be reviewed for country-specific and current recommendations (see Table 7). Nurse practitioners should advise patients entering areas requiring yellow fever vaccination that the immunization must occur 10 days prior to travelers' entry.¹ Furthermore, the administration of the vaccine must be at an approved World Health Organization (WHO) yellow fever vaccination center.¹ Approved centers can be obtained from local, state or national public health de-

partments. This vaccine is contraindicated in immunocompromised individuals or those with an allergy to eggs.

Rabies vaccine

Travelers to developing countries who will be exposed to direct animal contact and a high-risk bite should receive rabies vaccination as prophylaxis. Additionally, post-exposure prophylaxis including rabies immune globulin (RIG) may not be available in developing countries.

Japanese encephalitis

Another potentially fatal mosquito-borne viral illness is Japanese encephalitis. Those traveling to rural Asia near pig farms or rice paddies from May to October for extended stays (longer than four weeks) should receive the Japanese encephalitis vaccine. Three doses of vaccine are given,

with the second dose given seven days after the first and the third dose given 30 days after the first. The third dose should be given at least 10 days prior to travel. Children younger than 1 year of age should not receive the vaccine.

Meningococcal vaccine

Meningococcal vaccine is recommended in children older than 2 years of age and in adults traveling to endemic areas or to the sub-Saharan region of Africa from December to June. During the Hajj (annual pilgrimage to Mecca), Saudi Arabia requires a certificate of vaccination of pilgrims older than 6 months of age against meningococcal meningitis. Those working with refugees or living abroad in dormitories also should be immunized.

Polio vaccine

Adults not previously immunized

against the poliovirus should receive a primary series of inactivated polio vaccine if traveling to endemic regions (Nigeria, India, Pakistan and Afghanistan). Protection is required four weeks before leaving for the endemic area and requires a single dose of inactivated polio vaccine, but nurse practitioners should advise travelers that this only produces partial protection. Previously immunized adults who have never received a booster should receive one.

PRIMARY CARE PROVIDER ROLE

Primary care providers can play a crucial role as providers of health care and resource information in the field of travel medicine. However, it should be stressed that in order to provide appropriate care, the time and willingness to enhance one's skills in this area are extremely important. Practitioners specializing in travel medicine should have their time and schedules balanced to provide adequate time to schedule appointments for travel risk assessments, evaluations and recommendations. Having a resource library, both online¹⁷ and hard copy, is essential and, as mentioned earlier, updated CDC resources should be reviewed for country-specific and current recommendations (see Table 7). Establishing patient rapport is important and the travel assessment should be continued after the patient returns from travel.³ Patients should be informed about reporting febrile courses, diarrhea, malaise, dermatological or respiratory

PATIENT SCENARIO 2

Problem

Mary is a 28-year-old respiratory therapist who comes to your practice for advice. She states that next week she is traveling to the Caribbean Islands to visit a friend living there. She will be traveling for about 10 days. Her friend lives on a remote part of one of the islands. This is her first trip outside of the United States. She is worried about food poisoning. What should you tell her?

Assessment

Since it is unlikely Mary is a "vaccinated traveler," she is probably most at risk for hepatitis A and should at least be treated prophylactically for that. Travelers going anywhere other than Canada, Western Europe, Japan, Australia or New Zealand should receive the hepatitis A vaccine. The vaccination usually consists of two IM doses separated by six to 18 months, however, since Mary is leaving next week, giving only one dose will not ensure appropriate antibody levels are reached. Protective levels of the antibody usually require about two to four weeks. This is somewhat buffered in that the incubation period for hepatitis A is about four weeks. Nevertheless, to ensure protection, Mary should receive an IM dose of hepatitis A vaccine (IM) and immune globulin (Ig) 0.02ml/kg IM.

disorders that occur or present up to several months after they return home. Thus, primary care providers are in a unique position to assess and diagnose the traveling patient and provide comprehensive patient care. Finally, primary care providers should counsel patients on the danger of filling or refilling their prescription medications in foreign countries as some drugs with the same brand name as the U.S. product will contain different drugs.¹⁸ Patients should be advised to obtain an ample supply of their meds from their pharmacy before they depart, prescriptions should be written generically if they will require filling in another country, or arrangements to obtain refills via the mail should be made in advance.

CONCLUSION

Emporiatics has become a specialized field and nurse practitioners are uniquely positioned to become key resources. Maintaining the current state of health, educating about preventable travel-related disease and injury and assessing and prescribing for traveler needs are essential components for involved nurse practitioners. Nurse practitioners can be more easily accessible both in the traditional clinical setting and from the evolving retail health care center setting and may often be the first prescriber many travelers seek before leaving or upon returning. Evaluating and treating patients before departure and upon return plays a crucial role in preventing or mitigating travel-related illness or injury.

¹Anon. Advice for Travelers. Treatment Guidelines from The Medical Letter 2006;4:25-34. ²Ryan ET, Kain KC. Health Advice and Immunizations for Travelers. N Engl J Med 2000;342:1716-25. ³Ryan ET, Wilson ME, Kain KC. Illness after International Travel. N Engl J Med 2002 ;347 :505-16. ⁴Freedman DO, Weld LH, Kozarsky PE, Fisk T, Robins R, von Sonnenburg F, et al. Spectrum of Disease and Relation to Place of Exposure among Ill Returned Travelers. N Engl J Med 2006;354:119-30. ⁵Colucci VJ, Allington DR. Acute Mountain Sickness. US Pharmacist . July 2002;60-66. ⁶Colucci VJ, Allington DR. Hypothermia and Frostbite. US Pharmacist. Dec 2002;HS36-43. ⁷Anon. High Altitude Sickness. Med Letter Drugs Ther 1992;34:84-86. ⁸Canada Communicable Disease Report. Advisory Committee Statement (ACS) on High Altitude Illnesses. 1998;24(ACS-4). ⁹Martinelli I, Taioli E, Battaglioli T, Podda GM, Passamonti SM, Pedotti P, et al. Risk of Venous Thromboembolism After Air Travel. Arch Intern Med 2003;2771-74. ¹⁰Ferrari E, Chevallier T, Chapellier A, Baudouy M. Travel as a Risk Factor for Venous Thromboembolic Disease. CHEST 1999;115:440-44. ¹¹Hughes RJ, Hopkins RJ, Hill S, Weatherall M, Van de Water N, Nowitz M, et al. Frequency of venous thromboembolism in low to moderate risk long distance air travelers: the New Zealand Air Traveller's Thrombosis (NSATT) study. Lancet 2003;362:2039-44. ¹²Buscemi N. Efficacy and safety of exogenous melatonin for secondary sleep disorders and sleep disorders accompanying sleep restrictions: meta-analysis. BMJ 2006;332:332-385. ¹³Sorensen SJ, Frye CB. Travel Medicine. In: Pharmacotherapy Self-Assessment Program. 4th Ed. ACCP. Kansas City (MO): ACCP 2001. Book 4:143-65. ¹⁴Fradin MS, Day JF. Comparative efficacy of insect repellents against mosquito bites. N Engl J Med 2002;347:13-18. ¹⁵Leder K, Weller PF, Wilson ME. Travel Vaccines and Elderly Persons: Review of Vaccines Available in the United States. CID 2001;33:1553-66. ¹⁶Anon. Adult Immunizations. Treatment Guidelines from the Medical Letter. 2006;47(4): 47-54. ¹⁷Keystone JS, Kozarsky PE, Freedman DO. Internet and Computer-Based Resources for Travel Medicine Practitioners. CID 2001;32:757-65. ¹⁸Anon. A different drug, a different country, but the same brand name? Pharmacist's Letter/Prescriber's Letter 2005;21(4):210401.

Travel medicine for the millennium: What your patients need to know before they go

Learning Assessment

Successful completion of "Travel medicine for the millennium: What your patients need to know before they go," is accredited for 1.25 contact hours of credit. To obtain credit, answer the following questions and complete the evaluation online at www.retailclinician.com.

- 1. John is a 32-year-old living in the Washington, D.C., area. He comes to your practice asking for a recommendation for preventing altitude sickness. He is preparing for some backcountry skiing (above 9,000 feet) in Colorado in a week. Which one of the following pharmacotherapeutic regimens would you prescribe?**

 - Acetazolamide 500mg sustained-release tablet every 24 hours, starting 24 hours before ascent and continuing for two days at altitude.
 - Dexamethasone 4mg twice daily on first day of ascent, then once daily for seven days while above 8,000 feet.
 - Nifedipine 10mg daily starting two days before ascent, but then as needed for such symptoms as headache.
 - Acetazolamide 250mg TID one day before ascent, then once daily for seven days while above 8,000 feet.
- 2. Mrs. O'Brien is a 60-year-old woman who will be traveling to Ireland in two days. She is obese and has a history of DVT and pulmonary emboli. Which of the following is the most effective risk-reducing regimen for recurrent DVT for Mrs. O'Brien?**

 - Start warfarin 10mg daily.
 - Compression stockings, one SC dose of LMWH, arising and walking during the flight.
 - Avoiding caffeine.
 - Advise that she not go, she is at too large a risk for developing DVT.
- 3. Which of the following regimens is best for treatment of travelers' diarrhea in a 35-year-old man?**

 - Ciprofloxin 500mg BID for two days.
 - Norfloxin 400mg TID for four days.
 - Doxycycline 100mg daily for one week.
 - Rifampin 10 daily for one week.
- 4. To control illness-transmitting mosquitoes the concentration of N,N-diethyl-m-toluamide (DEET) most effective is:**

 - 8 percent
 - 95 percent
 - 60 percent
 - 30 percent to 35 percent
- 5. Which of the following agents could be used effectively on clothes and mosquito netting to minimize the risk of malaria transmission?**

 - picaridin
 - permethrin
 - DEET 8 percent
 - malathion
- 6. An individual intolerant of mefloquine could be treated effectively with:**

 - azithromycin
 - ciprofloxacin
 - doxycycline
 - desensitization to mefloquine
- 7. Patients entering countries requiring Yellow Fever vaccination must be advised that they must receive the vaccination:**

 - two days prior to entry.
 - 10 days prior to entry.
 - it is a post-exposure vaccine, thus they receive it after leaving the area.
 - upon arriving at their destination.
- 8. JS is a 38-year-old health care worker who has received two doses of Engerix-B, the last being about nine months ago. He is traveling to Central America to provide rural health care and will leave in about 12 weeks. He would like the hepatitis A vaccine as well. Your best advice would be:**

 - JS must start the hepatitis vaccination series over since it has been more than six months since his last dose.
 - JS can be treated with a combination vaccine (A and B), but must delay his trip for six months.
 - JS requires two different vaccination series.
 - JS can use a combination vaccine to complete his hepatitis B series and can travel with two doses of hepatitis A administered.
- 9. The dose of mefloquine for a 23kg child would be:**

 - 250mg mefloquine HCL given once a week starting one to two weeks before entering malarious area and continuing for four weeks after leaving.
 - 125mg mefloquine HCL given once a week starting one to two weeks before entering malarious area and continuing for two weeks after leaving.
 - 125mg mefloquine HCL given once a week starting one to two weeks before entering malarious area and continuing for four weeks after leaving.
 - Use doxycycline, mefloquine is contraindicated in children.
- 10. Which combination of agents would be most helpful in managing your patient's travelers' diarrhea?**

 - Oral rehydration solutions and loperamide.
 - Ciprofloxacin and iodine tablets.
 - Bismuth subsalicylate and norfloxacin.
 - Diphenoxylate/atropine and azithromycin.