"Ills, Pills, Shots, & More...."

TRAVEL MEDICINE

A COMPREHENSIVE APPROACH

MEDICAL GRAND ROUNDS

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The hazards of travel have been recognized by the soldier, the missionary and the trader for centuries. The concept of quarantine was first implemented in 1377, when the authorities in Venice noted that there was a problem with regular outbreaks of plague affecting the city's inhabitants which occurred shortly after the arrival of ships from the East. As a result, Venice and Rhodes introduced the first regulations governing the arrival of ships whereby the ships were detained at a distance- complete with passengers, cargo and crew- for 40 days *(quaranto giorni),* before being allowed to proceed to their final destination [1].

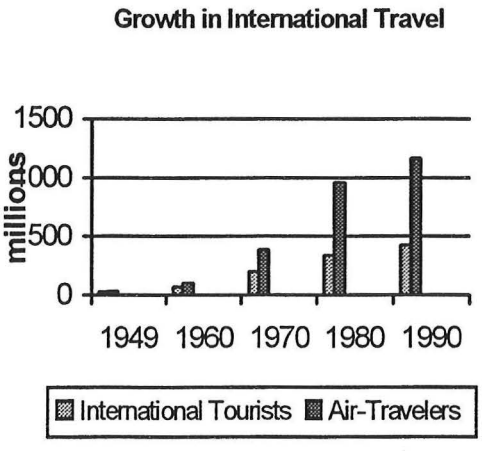
Health hazards were noted in later times, such as the ill-fated Darien Expedition of the 1690s when some 2000 Scots died as a result of appalling local conditions where malaria and yellow fever were rife. By the 19th century the continent of Africa posed the greatest threat; for example, the missionaries Mungo Park, David Livingstone, and Mary Slessor all died in Africa, succumbing respectively to trauma (drowned while under attack by hostile natives), dysentery with internal hemorrhage, and 'exhaustion'.

A study of 1427 Scottish Presbyterian missionaries who worked abroad between 1873 and 1929 revealed that 25% had to return prematurely due to personal or family illness, and further 11% died in service. In addition, it was noted that more were affected by adverse health among those appointed in the earlier years, when less was known about tropical diseases; and that the problems were more severe for those appointed to the most climatically rigorous areas, such as West Africa. Interestingly, missionaries with a medical background experienced fewer problems, probably because of their knowledge of illness and its prevention [2].

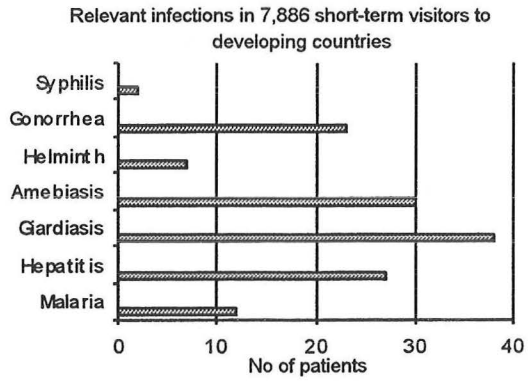
Travelers can of course also be responsible for spreading infection. The last epidemic of cholera in England and Wales occurred in 1866. It was brought by emigrants passing from Hull and Grimsby to Liverpool on their way to America. A severe epidemic with 2122 deaths occurred in Liverpool and the disease subsequently spread to London, Portsmouth, Chester and elsewhere.

TRAVEL EPIDEMIOLOGY

As international travel continues to grow, the goal of travel medicine evolved to promote travelers' health beyond tropical medicine and parasitology, to include other disciplines such as psychiatry, high altitude pathophysiology, and behavioral sciences. Steffen, et al, reported on health problems in 10,524 Swiss tourists after travel to developing countries.



Fifteen per cent of the travelers reported health problems, 8% consulted a physician, and 3% were unable to return to work for an average of 15 days. The incidence of infection per month abroad was as follows: giardiasis, 7/1,000; amebiasis, 4/1,000; hepatitis, 4/1,000; gonorrhea, 3/1,000; and helminthiases malaria, or syphilis, < 1/1,000. There were no cases of typhoid fever or cholera [3].



Studies indicate that less than 50% of travelers to the developing world consult a physician prior to travel. It is likely that far fewer visit a specialized travel clinic. Hill et al examined the demographic profile, past medical and immunization history, itinerary, and reason for travel of 2,445 travelers to the developing world seen at a travel medicine service. A chronic medical condition was reported by 27% of all travelers. Four per cent of all travelers were intolerant to sulfonamides, and 9% had contraindications to mefloquine use for malaria prophylaxis. Many travelers were due to receive the primary series or updating of routinely recommended immunizations: 43% for tetanus/diphtheria, 55% of those born after 1956 for measles, and 70% for poliovirus if their travel itinerary included a poliomyelitis risk. Most travel (71%) was for vacation, 13% for teaching or study, 11% for business, and 5% for missionary activities. The median travel duration was 21 days. Fifty two per cent of all travel was to ten countries in East Africa, the Indian subcontinent, the Far East, and South America [4].

TRAVEL MEDICINE CONSULTATION

PRETRAVEL OFFICE VISIT

The goals of pretravel office visits are:

- To detect medical problems that may emerge during travel.
- To give indicated immunizations: travelers should be seen at least one month prior to travel to allow for immunization/booster administration. Records of immunization should be appropriately completed to avoid any ambiguity at border crossing.
- To answer questions and to educate patients regarding precautions related to diet, insect protection, and behavior.
- To instruct patients in the use of certain medications such as malaria prophylaxis and antidiarrheal agents.
- Travelers should be encouraged to take care of any unattended medical problems (dental, eye, ENT complaints) that might erupt into more significant problems and threaten travel plans. Travelers should carry, in their carry-on luggage or on their person, extra-supplies of prescription medications and eyeglasses.

Health advice to travelers should take into account a variety of factors including:

- Travel destinations and their indigenous health problems.
- Required vaccinations as condition of entry.
- Mode of travel and type of accommodation.
- The duration of travel.
- Routine immunizations history.
- Special requirements for extended travel or for close contacts with indigenous populations.
- Modifying factors such as seasonal risks, altitude, and urban versus rural exposure.
- The patient's medical history, especially chronic problems that might disrupt foreign travel.

SPECIAL CONSIDERATIONS

PULMONARY DISEASES

Commercial aircrafts normally cruise around 35,000 ft. Cabin pressure is kept at levels equivalent to those occurring at altitudes of 6,000-8,000 ft. This will reduce the PaO_2, of a healthy individual, from 98 mm Hg at sea level to less than 60 mm Hg [5].

"COPD" is the second most common diagnosis in patients requiring emergency room evaluation for symptoms occurring after air flight [6]. **The clinical significance of cabin altitude related hypoxemia in patients with chronic pulmonary disease is not fully known.** Swartz, et al, demonstrated a reduction in PaO_2 to approximately 30-40 mm Hg in 13 patients with COPD flown to altitudes as high as 8,000 ft in an un-pressurized aircraft; none developed clinical symptoms [7]. Dillard, et al, reported on 100 patients with COPD who were followed prospectively for a 28 month period. Of the 44 patients who traveled by commercial air carriers, only 12 (27%) consulted their physician prior to travel. Eight patients (18.2%) developed symptoms during travel, including dyspnea, chest pain, edema, wheezing, and cyanosis. Two patients developed multiple symptoms requiring in-flight oxygen supplementation for relief [8]. A more recent study by Kramer, et al, documented the safety of prolonged air travel in patients with advanced lung disease flown to medical centers remote from Israel for lung transplantation or pulmonary thromboendartrectomy [9]. Gong, et al, demonstrated that the best single predictor of PaO_2 for the resting individual at various altitudes was their sea level value of measured PaO_2. Most individuals with an arterial PaO_2 of 77 mm Hg, at sea level, will have an $PaO_2 > 55$ mm Hg, at 8,000 ft.

Current recommendations suggest measuring the FEV_1 and PaO_2 within 2 weeks before the flight to predict in-flight PaO_2 for patients with COPD. Pulmonary function should be optimized to maintain the best FEV_1 possible by continuing bronchodilator and corticosteroid therapy before and during flights. When concerned about the ability of any patient to tolerate lowered cabin pressures, physicians may request supplemental oxygen for their patients. Such requests should be made to the airline at least 48-72 hours in advance, and normally a fee is charged by the airline. Passengers are

not usually permitted to use their own oxygen apparatus and oxygen is not provided during transit in the airport. Travelers should request non-smoking seats on international flights in order to avoid elevated carboxyhemoglobin levels. Since most cabins are maintained at 8%-12% humidity, patients should be encouraged to maintain adequate hydration to avoid problems with thick secretions. An extra supply of inhalers should be kept in the carry-on luggage for treatment of exacerbations.

The above recommendations also apply to patients who are planning for mountain travel and trekking. Patients with primary pulmonary hypertension and those with sleep apnea syndrome do not tolerate high altitude well. If such travel cannot be avoided, therapy with a calcium channel blocker and supplemental oxygen might benefit patients with primary pulmonary hypertension. Acetazolamide and supplemental oxygen are advised for patients with sleep apnea.

Early empiric antibiotic therapy of upper respiratory infections (otitis, sinusitis) may be advisable, particularly in patients with chronic pulmonary disease. Prophylactic topical or systemic decongestants and instructions regarding middle ear ventilation are the best aids in avoiding barotrauma. Patients with acute sinusitis or otitis media should be discouraged from flying.

The risk of ***M. tuberculosis*** **transmission on an aircraft** does not appear to be greater than in other confined places. Persons known to have infectious tuberculosis should avoid commercial carriers or travel by private transportation. Patients with infectious tuberculosis should have, at least, three negative sputum smear examinations for AFB prior to air travel. In March 1995, The CDC summarized six investigations of possible transmission of *M. tuberculosis* on aircraft and provided guidance for notifying passengers and flight crews in the event of exposure to tuberculosis during travel on commercial aircraft. When making the decision regarding possible exposure notification, the following should be considered: the flight duration, the infectiousness of the index patient, and proximity to the index patient [10].

CARDIAC DISEASES

Cardiovascular events including myocardial infarctions and cerebrovascular events are among the leading causes of death among US travelers. A study of international air travel form 1977-1984 showed that the major cause of in-flight death was unexpected cardiac events (56%) [11]. Another study analyzed US civilian death occurring abroad during 1975 and 1984. Except for travel to Mexico, cardiovascular disease was the leading cause of death among both male and female travelers [12].

Contraindications to air travel include recent myocardial infarction (within 6 weeks), decompensated CHF, uncontrolled arrhythmias, recent CVA (within 2 weeks), uncontrolled severe hypertension, and recent DVT (within 6 weeks). Patients should carry on their person, not in checked-in luggage, a summarized medical history, copy of

a recent EKG, and a supply of medications. Airlines should be contacted to provide supplemental oxygen during flights above 22,500 ft in patients with chronic heart disease.

Automatic implantable cardiac devices and pacemakers are not considered contraindications to flight and are not affected by metal detectors used in airport security. Pacemaker wearers should carry copies of EKGs performed both with and without pacemakers activation. Electronic telephone checks of pacer function cannot be transmitted via international satellites.

There are no controlled studies concerning the risk to people with known cardiac disease of venturing to high altitude. **Patients with severe angina and marginally controlled CHF should avoid altitude.** Hypertensives may find their pressures elevated at altitude. Following a low salt diet, getting increased rest during the first few days at altitude, and using clonidine, prazosin, Ca channel blockers, or ACE inhibitors may be effective.

DEEP VENOUS THROMBOSIS AND PULMONARY EMBOLISM

With the onset of frequent intercontinental air travel, an increasing number of cases of deep venous thrombosis (DVT) and pulmonary embolism were observed during, or within 48 hours after, a long distance flight. Sarvesaran demonstrated that pulmonary embolism was the second leading cause (18%) of in-flight or post-flight death at London-Heathrow Airport between 1979 and 1983 [13].

The "Economy Class Syndrome" is being more recognized recently [14]. This syndrome is attributed to sitting constrained in a cramped position, which may be the initiating factor for the development of DVT. Immobility,. shifts of body fluids, orthostatic stress, and compression of the popliteal vein at the edge of the seat may be contributing factors leading to DVT [15]. Most of the published cases of "Economy Class Syndrome" have been people with obesity, smokers, those on oral contraceptives, or those who had other risk factors for thrombosis [16,17,18].

Patients at increased risk for DVT and pulmonary embolism include those with a previous history of venous disease or trauma; those with cardiac disease, venous stasis, or dehydration; and pregnant women. Such patients should avoid the inside or middle seating and should obtain bulkhead seats if possible in order to maximize leg room. They should use support hose, take frequent walks, do isometric calf exercises, remain well hydrated, and avoid excessive alcohol. Prophylactic low-dose heparin or aspirin should be considered.

Patients on chronic anticoagulation therapy should be able to travel without risk of complications. However, factors frequently associated with travel may also affect anticoagulation therapy: degree of physical activity, change in alcohol intake and food habits, compliance with medications, gastrointestinal disturbances affecting drug

absorption, antibiotic use, and febrile illness. Providing the patient with a card containing all the necessary information about the medical conditions for which anticoagulation is advised and recommended therapeutic range, may help facilitate appropriate contact with health care personnel when traveling [19].

DIABETES MELLITUS

Insulin adjustment is not recommended for north-south travel and is only needed for east-west travel if the traveler crosses more than six time zones [20,21].

Recommendations for insulin-adjustment when flying across time -zones	
Eastbound	Day of departure: usual dose First morning of destination (local time): use 2/3 usual dose Test glucose level 10 h after A.M. dose: give the remaining 1/3 dose if glucose > 240 mg/dL
Westbound	Day of departure: usual dose Test glucose level 18 h after the A.M. dose: give 1/3 usual A.M. dose if glucose > 240 mg/dL, followed by a snack or meal Morning of destination (local time): usual dose

Recommendations for Travelers with Diabetes

1. Advice needs to be individualized, simple, and given by expert personnel.
2. Travelers with diabetes on insulin or oral therapy should inform the airline beforehand of their diabetes and its treatment, in case of unexpected hypoglycemia.
3. Requests for in-flight "diabetic diets" are not to be advised as they may be very variable. Some form of carbohydrate should always be carried by the traveler.
4. Frequent self-monitoring of blood glucose during travel is recommended.
5. In planning an insulin regimen, essential informations include: local time of departure, flight duration, and local time of arrival.
6. The time of the usual meal and insulin before departure and after arrival should be agreed, and the time between these injections calculated. If this time is in excess of about 15 h, then additional in-flight insulin with food may be needed.
7. For frequent time-zone travelers, multiple injections may be considered; care with intermediate-acting insulin is needed during travel.
8. Unexpected delays may occur necessitating extra food and insulin doses.
9. Encourage patients to carry medications, syringes, needles, and snacks with them in carry-on luggage or on their person.
10. The Diabetes Alert Card, written in several languages is available from the American Diabetes Association. Identification for patients should include a bracelet or necklace with their names and a doctor's letter containing the diagnosis.
11. Supplies should include:

- Sufficient insulin for the entire trip and a prescription to replace any lost supplies with the same brand and potency of insulin
- A supplemental bottle of regular insulin for emergency use
- U-100 disposable syringes and needles for the entire trip with a physician's note indicating the need for these items
- Blood glucose testing strips and lancets

EPILEPSY

In-flight epileptic seizures are rare. Most major airlines have polices regarding passengers with epilepsy, but the policies vary widely, and in some cases they are counterproductive. A recent survey showed that most airlines recommend dose modification of anti-epileptic medications prior to air travel. Some airlines offer training to their crew in different types of epilepsy and appropriate first-aid measures. Only 57% of the airlines include diazepam in their emergency medical kit [22].

Recommendations for Travelers with Epilepsy

- In-flight seizures seldom have any impact on the normal operations of airlines.
- It is inappropriate for patients to alter established treatment regimens before travel.
- Patients should be permitted to travel without need of supervision.
- Forewarning airlines is necessary for those individuals whose seizures are severe or frequent. Such passengers should carry their regular medication during air travel, make themselves known to the cabin crew, and discuss before takeoff their wishes in the event of a seizure. This might eliminate the need for unnecessary diversions and unscheduled landings in the case of those individuals traveling alone who suffer an in-flight seizure.
- Materials used to train cabin crews should be reviewed by experts in epilepsy.
- International bodies governing civil air travel should have uniform policies regarding epileptic passengers, contents of medical kits, review of first aid manuals, and whether or not only a physician may administer medications. Laws in some countries prohibit the carrying of diazepam in aircraft medical kits.

SEXUALLY TRANSMITTED DISEASES

Sexually transmitted diseases have always been associated with travel. In the UK, during 1976, 14% of cases of early syphilis and 3% of cases of gonorrhea were contracted abroad [23]. In Sweden 32% of the new cases of syphilis reported in 1986 were acquired abroad [24]. By 1991, 44% of gonorrhea in heterosexual men in Victoria-Australia was acquired abroad: 68% of these infections were acquired from commercial sex workers (CSW) [25].

According to the British Communicable Disease Surveillance Center, the increase in reports of heterosexually acquired HIV infection is more rapid than the increase in any other exposure category, and more than 70% of heterosexually acquired HIV infections are contracted while traveling abroad [26]. Hawkes, et al, demonstrated that 18.6% of international travelers attending the Hospital for Tropical Diseases, London, reported having sex with at least one new partner during their most recent trip, and half of these admitted to more than one new partner [27]. The prevalence of HIV in this group was 2.2%, similar to that found among Belgian and Dutch expatriates living in Africa [28,29]. Gills, et al, reported the results of a postal survey of 577 adults, aged 10-40 years, selected from the register of a general practice in Nottingham, to measure the prevalence of risky sexual behavior. Of the 354 patients who traveled abroad in the previous 12 months, 5% had had sex with a new partner, while abroad, without the use of condoms [30]. Similar results were reported in a survey of young tourists in a youth hostel in Copenhagen [31].

Little attention has been paid to educating travelers about the risk of unsafe sex. Success of such counseling has been well documented. A total of 338 American Peace Corps volunteers who served in Zaire between 1985-1988 received intensive training and counseling before being posted, and no seroconversions to HIV or HBV were observed [32].

The global pandemic of AIDS would not have occurred without modern international travel. It is worthwhile talking about sexual risks with anyone who intends to travel, and inquiring about sexual behavior of people who have returned. A history of other behaviors such as high alcohol consumption or drug use may help identify risk-takers. Tourists visiting a vacation town in the UK demonstrated a considerable interaction between sexual promiscuity, high alcohol consumption, and use of recreational

drugs. Many tourists perceived these behaviors as important parts of what makes up a "good vacation" [33].

Data suggest an alarmingly high prevalence of HIV among some CSW, with a rise from 7% to 15% within 6 months in a one city in northeastern Thailand [34]. Among men who attended an STD clinic in Melbourne-Australia who had had sex in Southeast Asia within the preceding three months, 60% had sexual contact with CSWs [35]. **There are a number of commonly held myths about sex-workers that need to be discussed and exposed as false during pre-travel consultation visit** [36]**:**

1. **Certificates:** the most important myth is that a health certificate provided by a CSW can demonstrate freedom from STDs. Such documents are completely misleading and can be easily falsified. The risk of transmission of infection is not related to the most recent check-up. It is related to the infections that the most recent partners have transmitted.
2. **Assessing risk by appearance:** if a potential sex partner looks fit and healthy, he/she is unlikely to be infected. Some tourists believe that they can select a prostitute who poses a lower risk for HIV because he/she is young, or less attractive and may therefore have had fewer partners. This is , of course, untrue.
3. **Condoms:** while the risk of transmission of STDs is minimized by consistent condom use, it is not entirely eliminated. Buying condoms before departure ensures that safer sex is at least an option. There may be an added protection from buying condoms that conform to known US safety standards.
4. **Other means of preventing STD:** there is no place for the prescription of prophylactic treatment for bacterial STDs. This practice may also contribute to the development of antibiotic resistance. Requests of such treatment indicate that the person is likely to put themselves and future partners at risk of STD.
5. **The magical check-up:** in some of the larger metropolitan STD clinics returned travelers sit waiting for the magical check-up that would guarantee freedom from infection before returning to their regular partners. If only that were possible.

Advice to prevent exposure to and infection with HIV while traveling

To protect yourself against HIV infection

- Do not have penetrative sex except with your usual partner. Casual sexual intercourse is very risky. People can be infectious even though they may not be aware of it, even if they look and feel well.
- If you do have sex with a new partner, always use a condom. Condoms are the most effective, currently available, protection against HIV/AIDS and other STDs. Pack an adequate supply of condoms, if you think you may need them when traveling, as they might not be easily available or of good quality in some countries. Inspect expiration date.
- If you drink or use recreational drugs, remember that both drugs and alcohol can make it easier to forget about "safer sex".
- Do not inject non-prescribed drugs. If you do, use new injection equipment and never share.
- Do not have a tattoo, acupuncture, or ear piercing, unless you can be sure that the equipment is sterile.
- Only have emergency medical or dental treatment while traveling. If you need a blood transfusion, try to ensure that it is absolutely necessary and that HIV-screened blood is being used. If you are going to an area where the availability of sterile needles and syringes for medical treatment is in doubt, consider taking a special medical kit with you.

HIV Infected Patients

Preparing HIV infected individuals for international travel represents a special challenge. Restrictions on crossing international borders, special vaccination requirements, accessibility to health care overseas, and susceptibility to infections present at the destination should be considered.

At least fifty countries, particularly in the Middle East and Eastern Europe, currently restrict the entry of travelers with HIV. These regulations apply mostly to students, workers, and others applying for long-term entry permits, although in a few countries visitors staying for short periods (2 weeks) are required to be tested. Some countries insist on HIV testing after arrival and will not accept the results of testing done elsewhere [37].

As the number of CD4 lymphocytes falls, the risk of HIV symptoms and opportunistic infections increases and , at the same time, the ability to respond to immunizations declines. It is ideal, therefore, to immunize HIV patients at the earliest opportunity. Live viral vaccines may be given to asymptomatic HIV-infected patients with normal CD4 counts if they are at risk for the disease but should be avoided in patients with AIDS or low CD4 counts. If a specific vaccine (e.g. yellow fever) is required for entry into a country, a medical exemption to immunization may be given. However, in high-risk situations a live vaccine may still be indicated. Other means of protection against infections, such as the use of insect repellents and very strict food and water precautions, should always be vigorously employed. If the health risks cannot be reduced to acceptable levels, alterations in the travel plan may be necessary [38].

Enteric pathogens pose the greatest threat to HIV-infected travelers. There are no data to suggest that travelers' diarrhea, most commonly caused by enterotoxigenic *Escherichia coli*, is more common in this group of patients. *Salmonella, Shigella, Campylobacter, Cryptosporidium,* and *Isospora* infections are associated with more severe and persistent diarrheal illness in HIV-infected hosts. Because of the increased risk of infection and morbidity from bacterial pathogens, continuous antibiotic prophylaxis for travelers' diarrhea should be considered for the HIV-infected travelers. HIV-infected travelers to tropical countries should be warned about the hazards of water, ice, etc. and may want to take their own portable water filter with them for prolonged visits.

The risk for **lower respiratory infections** is increased by prior viral respiratory infections, especially influenza. Therefore, annual influenza vaccination is recommended for HIV-infected patients. Tuberculosis is a low risk to the short-term traveler but the risk increases with the duration of travel. BCG vaccination is not recommended because of concerns about dissemination, however, isoniazid prophylaxis may be considered for long-term travelers to countries with a high prevalence of tuberculosis (e.g. in sub-Saharan Africa).

Several **vector-borne diseases** may be associated with more severe course in HIV-infected individuals. Recent reports describe visceral leishmaniasis and Chaga's disease as new opportunistic infections in AIDS patients. Theoretically, babesiosis and yellow fever are likely to be more severe in an immunosuppressed host. There is nothing to suggest that HIV infection increases the risk or severity of malaria, so routine prophylaxis should be advised [39,40].

USE OF VACCINES/IMMUNOGLOBULINS IN HIV-INFECTED PATIENTS
IMMUNOLOGIC PROPHYLAXIS
1. Hepatitis B vaccine
2. Pneumococcal vaccine
3. Hemophilus influenzae B vaccine
4. Influenza vaccine
5. Td
6. MMR if patient not immunized
7. Hepatitis A vaccine
THE FOLLOWING LIVE VACCINES ARE CONTRAINDICATED:
1. BCG
2. Oral polio vaccine (OPV)
3. Oral typhoid vaccine
4. Yellow fever vaccine
5. Varicella zoster vaccine
THE FOLLOWING INACTIVATED VACCINES CAN BE USED IF INDICATED:
1. Polio vaccine (iPV)
2. Typhoid (ViCPS)
3. Rabies
4. Meningococcal meningitis vaccine
THE FOLLOWING IMMUNE GLOBULINS ARE RECOMMENDED AS INDICATED:
1. IG is recommended for exposure to hepatitis A or travel to HAV-endemic areas. It is also recommended for symptomatic patients exposed to measles regardless of immunization status.
2. VZIG is recommended for susceptible patients after significant exposure to varicella.
3. TIG is recommended for those with serious wounds and < 3 doses of tetanus toxoid or booster >10 years
4. HBIG recommended within 72 hr after exposure to HBV (if not already immune)
5. HRIG for post-exposure prophylaxis

ASPLENISM

Ideally all asplenic patients should be vaccinated against *S. pneumoniae, H. influenzae*, and *N. meningitidis* whether or not they are traveling. In general, the response to these vaccines in asplenics is suboptimal; however this response may be partially protective. As there may be doubts about the quality and quantity of the antibody response, travelers to less developed countries may consider oral penicillin prophylaxis at least for the duration of the trip. There are no vaccines for babesiosis or malaria. Asplenic patients should avoid tick and mosquito bites and take the currently recommended malaria prophylaxis.

JET LAG

Jet lag is a constellation of physical and psychological symptoms associated with rapid crossing of multiple time zones. These symptoms are secondary to disturbance of the physiologic circadian rhythm and sleep cycle. **Symptoms of jet lag are common with time zone changes of more than 5 hours.** While nearly all travelers will experience some symptoms with large time zone shifts, there is considerable individual variation in severity and time to recovery. The time to re-establishment of circadian equilibrium is generally greater with eastward than westward flights. Sleep deprivation, difficulty sleeping, and a delay in cycling the sleep pattern to match that of the destination occur, resulting in fatigue and associated symptoms. Mood disturbance, anorexia, and gastrointestinal symptoms are common. Jet lag can adversely affect athletic performance and manual and cognitive skills.

Travelers crossing multiple time zones by air should be advised of the likely occurrence of jet lag and its implications. Travelers should consider that they may wish to plan important physical or intellectual activities, such as competitive sports or critical negotiations, for 48 hours or more after arrival in a new time zone. Travelers should also be encouraged to be well-rested and not sleep deprived at the commencement of a trans-meridian journey. The traveler who intends to stay in a new time zone for other than a very short period of time should attempt immediately on arrival to adjust his/her cycle of sleeping, eating and activity to that of the destination. **Short-acting benzodiazepines** may be used to facilitate sleep for the first night or few nights in a new time zone. Travelers should be aware of benzodiazepines' potential effect on cognitive and manual skills. Travelers can be advised that **exposure to bright light**, particularly outdoor daylight, at the destination may speed readjustment of the circadian rhythm and could reduce symptoms of jet lag. Three small randomized controlled studies in air travelers, each using a somewhat different regimen of **melatonin** administration, found small and inconsistent reduction in jet lag symptoms [41].

MOTION SICKNESS

Motion sickness is a normal response to perception of motion where there is sensory conflict about body motion perceived by different receptors (visual, vestibular, and body proprioceptor). The incidence of motion sickness ranges from less than 1% on a large aircraft to almost 100% on a rough sea voyage under evacuation conditions. Boat travel is most likely to cause motion sickness, followed by travel by air, car, and train.

Several measures have been recommended to minimize motion sickness, however, these are based on reported anecdotal experience (see table).

The Following May Be Recommended To Minimize/Prevent Motion Sickness

1. **Minimize exposure:**
- be located in the middle of the plane or boat where movement is least – be in a semi-recumbent position whenever possible
- minimize head and body movements.
2. **Restrict visual activity:** – fix vision on the horizon or some other stable external object
- avoid fixation on a moving object
- avoid reading
- close eyes, if below deck or in an enclosed cabin.
3. **Improve ventilation and remove noxious stimuli.**
4. **Reduce the magnitude of the motion stimulus:** – avoid or minimize acceleration and deceleration
5. **Engage in distracting activity:**
- be in control of the vehicle
- perform mental activity.

Recommended dietary manipulations include decreasing large oral intakes, taking frequent small feedings, and avoiding alcohol.

Several medications are available for the prevention of motion sickness. There is no one standard approach that is ideal for everyone in all circumstances. **Oral regimens** must be taken prior to the exposure, both to allow absorption and to attain adequate levels. Regimens are usually considerably less effective once symptoms of motion sickness have begun. With the onset of symptoms, absorption becomes less effective, and with vomiting, becomes close to impossible. Once severe manifestations have begun, rectal suppositories may still be an option if intramuscular injections are not possible.

Regimens Available For The Prevention Of Motion Sickness				
Drug	**Oral dose (mg)**	**Interval to be effective (hrs)**	**Dose frequency (hrs)**	**Use in pregnancy**
Cinnarizine	30	2-5	6-8	?No
Cyclizine	50	1-2	4-6	?No
Dimenhydrinate	50-100	1-2	4-6	?No
Meclizine	25-50	2	6-24	?No
Promethazine	25	1.5-2	4-6	Yes
Scopolamine patch	patch	8	72	No

For treatment of established symptoms, options are more limited. Once vomiting has commenced, no oral regimen is likely to be effective. Intramuscular promethazine (25 mg to 50 mg) appears to be the most effective means of managing already developed severe motion sickness, but most travelers will not be able to administer intramuscular injections. Rectal suppositories are available with dimenhydrinate. Several preparations can be dissolved in the mouth, but their effectiveness in the presence of vomiting may be significantly compromised. If the exposure is likely to be prolonged, a scopolamine patch can also be applied, but this will not provide immediate benefit. Compounds like caffeine alone do not appear effective, but may counteract some of the drowsiness seen with common agents like the antihistamines. **Acupressure,** using a commercially available product applying pressure at a point above the wrist, has not been shown to be effective.

Adverse reactions to medications used for motion sickness: motion sickness itself may contribute to some of the symptoms attributed to the medications, but drowsiness is common with all except those that include sympathomimetic agents. Symptoms are usually dose-related and it may be possible to strike a balance between efficacy and adverse reactions (e.g., in most individuals scopolamine 0.3 mg will produce significant protection with minimal side effects) [42].

ACCIDENTS

Accidents account for about 25% of deaths among US travelers abroad [43,44]. Travelers should be strongly urged to:

- Wear safety belts in all vehicles
- Avoid drinking and driving or riding with drivers who seem "under the influence"
- Avoid night time driving whenever possible
- Avoid riding motorbikes and motorcycles
- Avoid low class transportation in mountain terrain

OTHER MEDICAL CONDITIONS

Gas expansion can cause pain and perforation of the eardrum if the Eustachian tubes are blocked (e.g. by infection). The expansion of gas introduced during recent medical procedures (e.g. colonoscopy) or surgery can cause pain and may stretch suture lines risking perforation of a hollow viscus or bleeding. Undetected pneumothorax may progress to tension pneumothorax.

People should not fly after **eye surgery** involving intraocular injection of gas until an ophthalmologist has confirmed complete resorption of the gas. The patient with a residual intraocular gas volume of 0.6 ml, approximately 10% of the volume of the eye, can compensate for the decreases in cabin pressure as the airplane ascends without a symptomatic rise in intraocular pressure. Larger volumes may be accommodated in aircrafts that decompress to less than 8,000 ft or that take off from altitudes above sea level. The patient with residual intraocular gas who experiences pain or dimness of vision in an ascending airplane can obtain relief if the cabin altitude is decreased by 2,000 ft. This will require a modest adjustment in the altitude of the airplane [45,46]. **Patients with diabetic retinopathy** may develop worsening retinal ischemia and hypoxia after prolonged air travel. Aggravation of laser-treated diabetic cystoid macular edema after prolonged flight has been reported [47].

IMMUNIZATIONS

Immunizations for international travel are an integral part of vacation preparation. Immunization recommendations should take into account travel destination and duration, style of accommodation, and planned activities. Traveler's age, immunization history, allergies, and underlying medical conditions should also be considered.

In general, several vaccines can be administered simultaneously, at different injection sites, without an adverse effect on protective efficacy. Inactivated vaccines can be given simultaneously or at different times with other inactivated or live virus vaccines without interfering with the immune response. Exception are the yellow fever and cholera vaccines, which should be given on the same day or at least 3 weeks apart. If possible, live virus vaccines should be given on the same day or at least 30 days apart. Tuberculin (PPD) skin testing should be performed on the same day as live virus vaccines are being given, or 4-6 weeks afterwards, because some live virus vaccines may impair the response to the PPD skin test. Attenuated live virus vaccines are generally contraindicated in pregnant and nursing women, young infants, and immunosuppressed persons.

Vaccines can be grouped into three categories: **required** (yellow fever), **recommended** (hepatitis A, hepatitis B, Japanese encephalitis, typhoid, meningococcus, plague, rabies, and BCG), and **routine** (diphtheria, tetanus, MMR, poliovirus, influenza, and pneumococcus) [48,49,50].

REQUIRED VACCINES

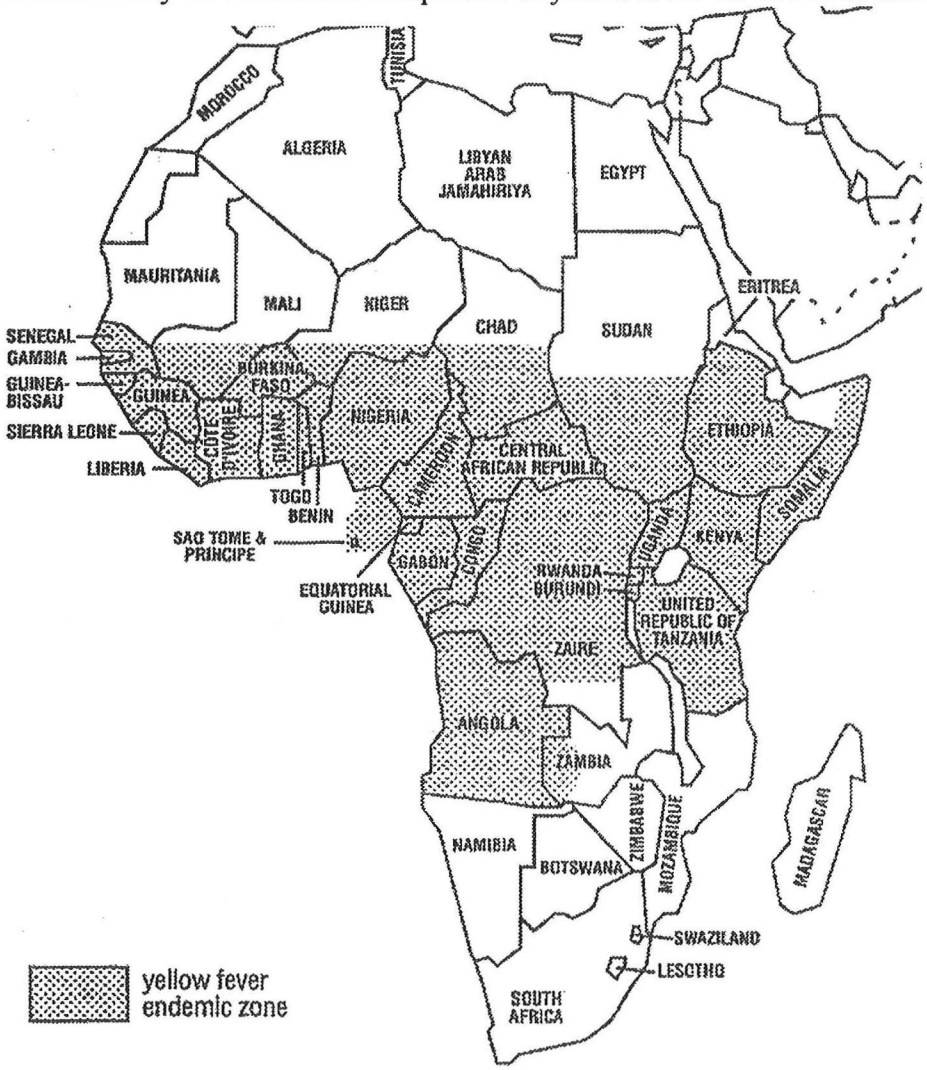
YELLOW FEVER VACCINE

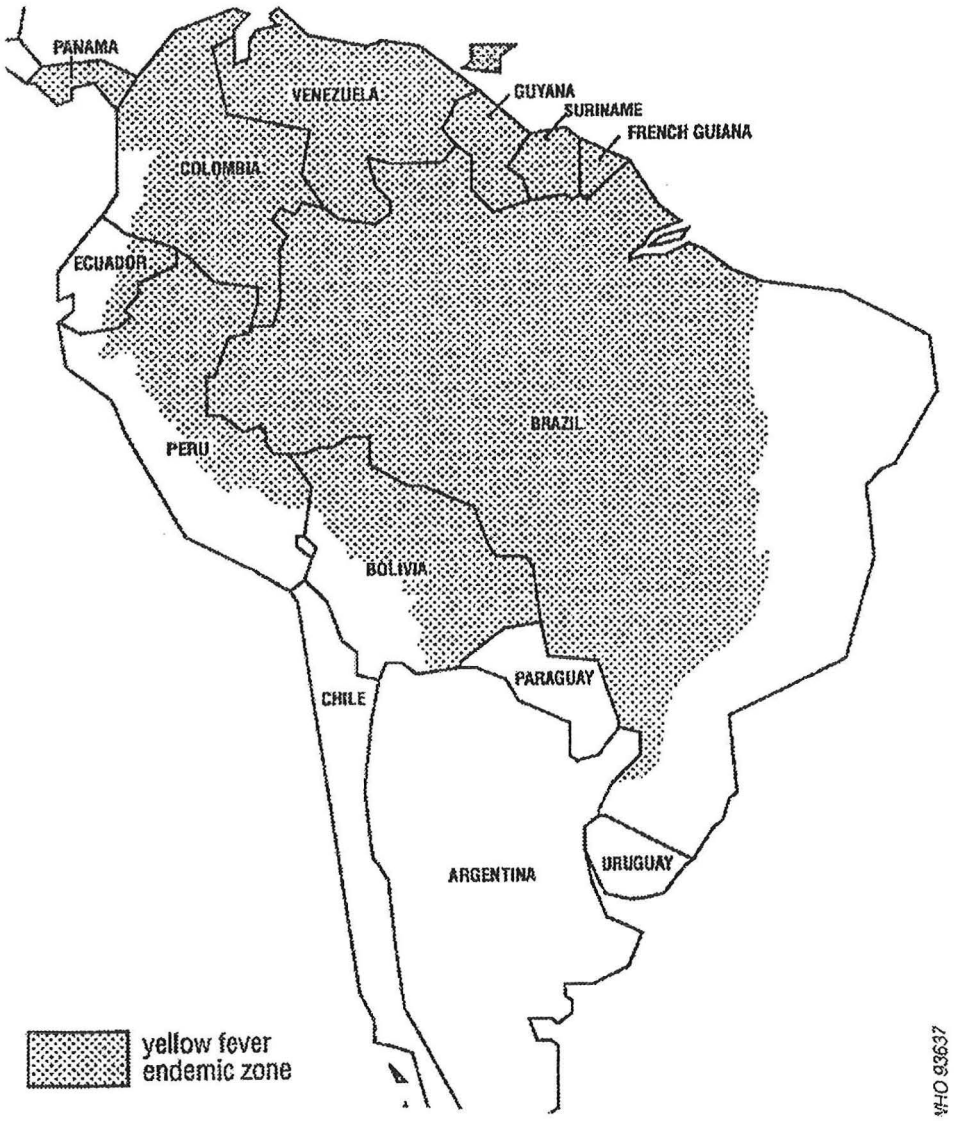
Since the 1980s, yellow fever has re-emerged across Africa and in Southeast Asia. The total of 18,735 cases and 4,522 deaths reported from 1987 to 1991 represent the greatest amount of yellow fever activity reported to the World Health Organization (WHO) for any 5-year period since 1948 [51]. Yellow fever continues to pose risks for international travelers to parts of South America and Africa.

Yellow fever, a viral disease transmitted by the mosquito *Aedes aegypti*, is very rare in travelers. However, most countries have regulations and requirements for yellow fever vaccination that must be met prior to entering the country. General precautions to avoid mosquito bites including the use of insect repellent, protective clothing, and mosquito netting should be followed.

Yellow fever vaccine, a live-attenuated virus vaccine, confers long-lived immunity (10 years or more) after a single dose. The vaccine is well tolerated; fewer than 5% of vaccinees develop mild headache, muscle pain, or other minor symptoms 5 to 10 days after vaccination. A booster dose is recommended every 10 years.

Yellow fever vaccine should never be administered to infants <6 months old due to a risk of developing viral encephalitis. In most cases, vaccination should be deferred until 9 to 12 months of age, unless the risk of yellow fever infection outweighs the risk of vaccine side effects. The vaccine is also contraindicated in pregnant women, persons with allergy to eggs, and in immunosuppressed individuals. Patients with asymptomatic HIV infection may be vaccinated if exposure to yellow fever cannot be avoided.





CHOLERA VACCINE

Cholera is an acute intestinal infection caused by *Vibrio cholerae* O-1 or O-139. The infection is often mild and self-limited or subclinical. Persons with severe cases respond dramatically to simple fluid- and electrolyte-replacement therapy and oral antibiotic therapy with tetracycline or a fluoroquinolone, if necessary. Infection is acquired primarily by ingesting contaminated water or food; person-to-person transmission is rare. **Currently no country or territory requires vaccination as a condition for entry.** However, local authorities may continue to require documentation of vaccination against cholera; in such cases, a single dose of vaccine is sufficient to satisfy local requirements. **The risk of cholera to U. S. travelers is so low that it is questionable whether vaccination is of benefit.** Travelers to cholera-infected areas are advised to avoid eating uncooked food, especially fish and shellfish, and to peel fruits themselves. Carbonated bottled water and carbonated soft drinks are usually safe.

Currently available vaccines are only about 50% effective in reducing clinical illness from *Vibrio cholerae* O1 infection for 3-6 months after vaccination, with the greatest protection for the first 2 months. Illness caused by the recently discovered *Vibrio cholerae* O-139 is probably unaffected by currently available vaccines. The complete primary series (two doses of 0.5 mL, each give SQ or IM at least 1-4 weeks apart) is suggested only for special high-risk groups who work and live in highly endemic areas under less than adequate sanitary conditions. Vaccination often results in 1-2 days of pain, erythema, and induration at the site of injection, which may be accompanied by fever, malaise, and headache.

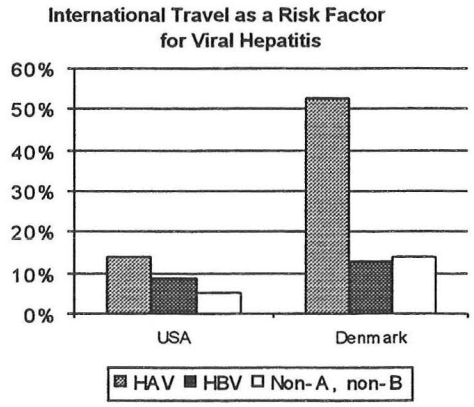
Oral vaccines for cholera have been developed. Studies have shown that they are safe and immunogenic (up to 90% seroconversion after a single dose). A reduction in the occurrence of enterotoxigenic *E. coli*-associated diarrhea was noted as a secondary outcome in the population vaccinated with whole-cell cholera vaccine. Currently there are no recommendations for the use of oral cholera vaccines as they are still under consideration for licensure [52,53].

RECOMMENDED VACCINES

HEPATITIS B VACCINE

The prevalence of the carrier state of HBsAg is low in North America and western Europe, but in Southeast Asia, China, Africa, Central and South America, and the Middle East, 8%-15% of the population may be chronically infected.

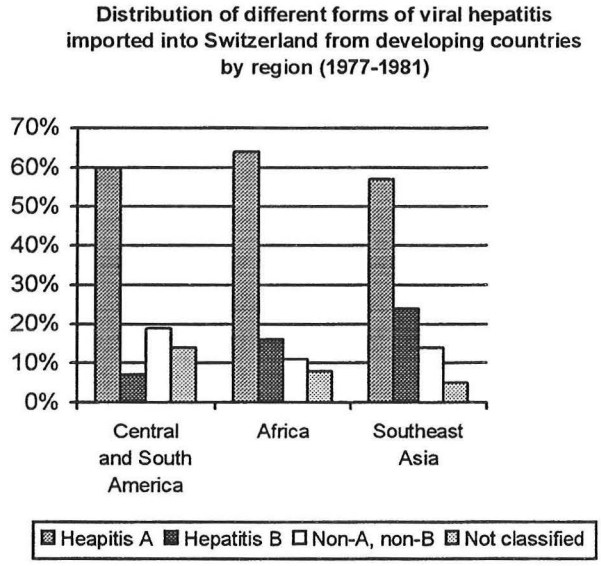
Hepatitis B has not been regarded as a disease of travelers. Relatively little data on the epidemiology of HBV in travelers exist. Studies in the US and Denmark identified international travel as an associated risk factor in 9% and 13%, respectively, of the reported cases of HBV [54,55]. Professionals working in developing countries may be at high risk of hepatitis B. In a study of 219 French agricultural community and medical volunteers working in Africa, 10.3% developed HBV infection during an 18-30 months period [56]. Another study of expatriate married men working in Southeast Asia for UNOCAL UK Ltd. showed a seroconversion rate of 9% within 2 years, with field workers converting more often than office employees [57].



Hepatitis B vaccine contains a recombinant, yeast derived, hepatitis B surface antigen and is protective in 90% of the recipients. Ideally, hepatitis B vaccination of travelers should begin at least 6 months before travel to allow for completion of the full

vaccine series. High-risk travelers including personnel performing medical duties, those providing disaster relief in the developing world, long-term missionaries and foreign aid volunteers, and short-term visitors to highly endemic areas who are likely to engage in high-risk behaviors, such as IVDU with needle sharing, tattooing, acupuncture and casual, non-protected sexual encounters, should be vaccinated.

HEPATITIS A VACCINE



European and North American travelers born after World War II have a very low prevalence of anti-HAV [58]. Low anti-HAV prevalence rates were also found in US Navy and Marine Corps personnel [59]. **Symptomatic hepatitis A is the most common serious illness among adult travelers** [60]. In unprotected travelers, hepatitis A has been estimated to occur 100 times more frequently than typhoid fever and 1,000 times more often than cholera [61]. In 1995, an estimated 25 million US travelers visited developing regions where HAV is endemic [62]. The risk of symptomatic hepatitis A for a one-month journey to an endemic area is estimated to be as high as one in 300 unimmunized travelers staying in high-quality accommodations. The risk is six-fold higher for adventurous travelers who live and eat off the beaten track. Infection is spread via the fecal-oral route with contaminated water, food, inadequately cooked or raw shellfish, serving as frequent sources [63].

Promoting hygiene in the kitchens of tourist settings, to developed world standards, should lower the incidence of HAV infections as suggested by the finding that on some Nile River cruise ships the weekly incidence rate of travelers' diarrhea falls to a low of 15% when the owners inspect the galleys, whereas in weeks when there are no inspection this rate is 70-90%. Avoiding risky food, observing the old rule **"boil it, cook it, peel it, or forget it"** may be impractical especially for business travelers who often have to accept food offered by their hosts [64].

Until recently, HAV prevention was mainly achieved by passive immunization using **anti-HAV immunoglobulin (IG)**, prepared from pooled plasma collected from healthy adult donors. Administration of anti-HAV-IG before or within two weeks of travel provides protection against clinical disease in 70-90% of subjects. The duration of protection is dose-dependent and relatively short; even a high dose of IG provides protection against the clinical disease for no more than 4-6 months. Occasional shortages

in HAV-IG supplies, in addition to the need for repeated immunizations, inconvenience, expense, and discomfort may have led to poor compliance.

The recent approval by the US Food and Drug Administration of two **inactivated HAV vaccines (Havrix® and Vaqta®)** represents a remarkable improvement in immunoprophylaxis. An initial dose of the vaccine followed by a booster dose given at 6-12 months is recommended for adults. **Pre-exposure protective efficacy rate is 95%-100%.** The duration of immunity to infection after vaccination is not known with certainty. However, vaccine-induced immunity is likely to be prolonged and may exceed 10 years. Whether booster doses are required thereafter remains to be determined. The vaccine is well tolerated with soreness at the injection site being the most frequent side effect. For travelers to endemic areas who leave within too short a period to be certain of immune status, simultaneous administration of HAV-IG and HAV vaccine, at separate deltoid sites, may be appropriate. **HAV vaccination for travelers was reported to be more cost-effective than passive immunization with IG.** For some adult travelers who are likely to have had hepatitis A in the past (i.e., persons older than 40 years of age, persons born in parts of the world with intermediate or high levels of hepatitis A, or persons with clotting disorders), screening for HAV antibodies before travel may be useful to determine susceptibility and eliminate unnecessary vaccination or IG prophylaxis [65,66,67].

JAPANESE ENCEPHALITIS VACCINE

Japanese encephalitis is the leading cause of viral encephalitis in Asia. Infection is transmitted primarily by *Culex tritaeniorhyncus* mosquito. The disease occurs primarily in China, Korea, the Indian sub-continent, and the southeast Asian countries of Myanamar, Thailand, Cambodia, Laos, Vietnam, Malaysia, Indonesia and the Philippines. Japanese encephalitis also may occur with a lower frequency in Japan, Taiwan, Singapore, Hong Kong, and eastern Russia. In all areas, **Japanese encephalitis is primarily a rural disease.**

Transmission is usually seasonal, following the prevalence of mosquitoes. In China, Korea and other temperate areas, the transmission season extends through the summer and fall. In other subtropical and tropical regions, risk is associated with the rainy season, which varies with each country. **The chance that a traveler to Asia will develop Japanese encephalitis is probably very small**. The majority of infected persons develop mild to no symptoms, however, among persons who develop encephalitis (1:200), morbidity and mortality are in excess of 60%. Infection in pregnant women during the first and second trimester has been associated with miscarriages. **The vaccine is recommended only for long-term travelers in rural areas**, except under special circumstances such as a known outbreak of Japanese encephalitis. Older persons (> 55 years old) may be at higher risk for disease after infection and should be carefully considered for vaccination if they travel in areas of risk.

Studies have shown that a three-dose (1.0 mL) subcutaneous series (days 0, 7, and 30) is required to develop adequate immunity. A short course of vaccine can be given on days 0, 7 and 14, but this schedule may be less effective. **Serious allergic side effects** from the vaccine have been reported from up to 0.1% of vaccinees. These side effects can be delayed for several days after vaccination and consist of urticaria, angioedema, itching without rash, joint swelling, erythema multiforme, or erythema nodosum. Persons who have multiple allergies, especially to bee stings and various drugs, appear to be at higher risk for side effects and probably should not be vaccinated except under strict medical supervision. Mild local and systemic side effects have been reported in 20% of vaccinees. A booster dose may be required two years after the primary vaccination series if the traveler is still at risk of exposure [68,69].

The vaccine should not be administered to the following persons unless the benefit of the vaccine clearly outweighs the risk: patients with acute or active infections; chronic hepatic, cardiac, or renal disorders; those with malignancies; history of multiple allergies or hypersensitivity to components of the vaccine; and pregnancy.

RABIES VACCINE

Rabies vaccination is not a requirement for entry into any country. However, travelers to countries with endemic rabies should be warned about the risk of acquiring rabies outside the US. Rabies is common in most of the developing world, and occurs in both urban and rural settings. In the US during the period 1980-1992, 10 travelers developed rabies acquired outside of the country. Dogs are the main reservoir of the disease in many developing countries, but other animals may also be infected.

Preexposure vaccination for rabies is recommended for persons (limit use to those with greater risk of animal exposure: veterinarians, farm workers, and spelunkers, or children too young to understand their need to avoid animals or to report a traumatic contact) living in or visiting (for more than 30 days) countries with endemic dog rabies. These areas include most countries in Central and South America, the Indian subcontinent, Southeast Asia, and most of Africa. Most island countries in the Caribbean and Oceania are free of rabies. **Preexposure vaccination greatly simplifies, but does not eliminate, the need for post-exposure treatment.**

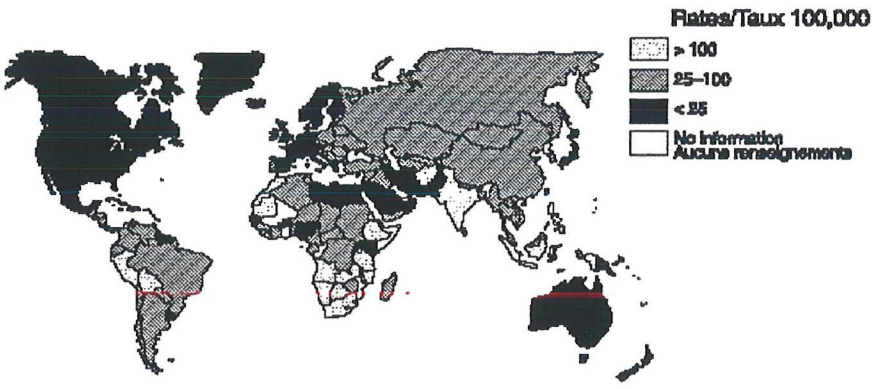
For international travelers, three 0.1 ml intradermal or three 1.0 ml intramuscular vaccinations are given over a 21 day period. Risk of vaccination is estimated to be minor and serious reactions are rare. Persons who will also be taking mefloquine or chloroquine for malaria prevention should complete their three-dose intradermal rabies vaccinations before these medications are begun as they may interfere with the antibody response to rabies vaccine. Otherwise, the intramuscular dose/route should be used [70,71].

TICKBORNE ENCEPHALITIS

Tickborne encephalitis, also known as spring-summer encephalitis, occurs in Scandinavia, Western and Central Europe and the former Soviet Union. Risk of acquiring the disease is greatest from April through August when the tick vector is most active. Human infections follow bites of infected *Ixodes ricinus* ticks, usually in persons who visit or work in forests, fields or pastures. Infection also may be acquired by consuming unpasteurized dairy products from infected cows, goats, or sheep. Otherwise, the risk to travelers is low.

Although effective vaccines may be obtained in Europe, available data do not support a recommendation for its routine use in US travelers. Travelers are advised to minimize exposure to tick bites and to avoid the consumption of unpasteurized dairy products.

BACILLE CALMETTE-GUERIN (BCG)



Approximately one-third of the world's population is infected with *Mycobacterium tuberculosis* and is at risk for developing the disease. International travel to an area of endemic transmission for tuberculosis may be a risk factor for acquiring a new infection.

Due to the mode of transmission of tuberculosis, it can be assumed that certain travelers may be at risk. Travel in an area of high endemicity; prolonged duration of exposure; and activities which intensify exposure, such as health-care work, refugee-care work, and back packing may be significant in determining acquisition of a new infection.

BCG vaccine is not recommended for most travelers. Travelers who anticipate possible prolonged exposure to tuberculosis should have a tuberculin skin test before leaving. If the reaction is negative, they should have a repeat test after returning to the US [72].

TYPHOID FEVER VACCINE

Salmonella typhi is transmitted by contaminated food or water and is prevalent in many developing countries of Latin America, Africa, and Asia. The major sources of imported cases between 1985 and 1994 were people coming from Mexico and the Indian subcontinent. The case fatality rate during this time was 0.5%.

Currently available vaccines have been shown to protect 70% - 90% of recipients. Therefore, even vaccinated travelers should be cautious in selecting their food and water. **The oral vaccine** consists of four capsules containing live attenuated bacteria. They are taken every other day for 7 days. The entire four doses should be repeated every 5 years if the person is at continued risk. Reactions are rare and include nausea, vomiting, abdominal cramps, diarrhea, and skin rash. The oral vaccine must be kept refrigerated and should be administered only with cool liquids. Co-administration with oral antibiotics is contraindicated. This vaccine is not recommended for immunosuppressed persons. **The new injectable (ViCPS) vaccine** consists of 1 shot. A booster dose given every 2 years provides continued protection for repeated exposure. Reactions are rarer than with the old, killed injectable typhoid vaccine, and include discomfort at the site of injection for 1-2 days, fever, and headache [73,74,75,76].

MENINGOCOCCAL VACCINE

Meningococcal infection is a severe, often fatal, disease. The areas of the world where meningococcal meningitis is traditionally endemic include regions of sub-Saharan Africa **(The Meningitis Belt)**. Disease occurrence in these areas is seasonal and can greatly exceed that found in other parts of the world.

The following persons should be considered for vaccination: adolescents and children traveling to an area of epidemic meningococcal activity; health care workers and individuals working in field epidemiology, research, international aid, or refugee camps in areas of epidemic meningococcal activity; persons working or living in the "traditional" endemic meningococcal areas of the world; persons who will be involved in activities that the local health authority or government would consider to represent a risk for acquiring meningococcal disease; flight attendants and cabin crews, military or intelligence personnel who travel extensively and unpredictably; persons making contact with people in rural parts of endemic areas; and pilgrims to Mecca for the annual Hajj or 'Umra (Saudi Arabia requires evidence of vaccination against meningococcus disease for these persons).

Vaccination is not recommended for people making short-term business or holiday trips to areas of heightened meningococcal activity who will have little contact with or exposure to local populations in crowded conditions [77].

PLAGUE

Plague continues to be enzootic in rural rodent populations in several continents with occasional outbreaks among commensal rodents in villages and small towns. Urban outbreaks are rare and limited. Wild rodent plague poses a real, though limited, risk to humans. When infection spreads to domestic or peridomestic rodents in urban or populated areas, humans are at markedly increased risk of exposure. Wild rodent plague exists in the western third of the United States, in widely scattered areas of South America, in northcentral, eastern and southern Africa, Madagascar, Iranian Kurdistan, along the frontier between Yemen and Saudi Arabia, central and southeast Asia, and portions of the Russian Federation.

Vaccination against plague is not required by any country as a condition for entry. Furthermore, the efficacy of the vaccine in humans has not been demonstrated in a controlled trial. Vaccination might be considered for persons who will have direct contact with wild or commensal rodents or other animals in plague-epizootic areas and for persons who will reside or work in plague-enzootic rural areas where avoidance of rodents and fleas is difficult. **Vaccination is rarely indicated for travelers to countries reporting cases, particularly if their travel is limited to urban areas with modern hotel accommodations.** Travelers who genuinely may be at risk for acquiring plague should consider chemoprophylaxis with tetracycline 500 mg. q.i.d. during periods of exposure in an active epizootic or epidemic area.

ROUTINE VACCINES

DIPHTHERIA/TETANUS TOXOIDS

Diphtheria remains a serious disease throughout much of the world. Most cases occur in unimmunized or inadequately immunized persons. In particular, **large outbreaks of diphtheria are currently occurring throughout the former Soviet Union**. Tetanus is a global health problem. The disease occurs almost exclusively in persons who are unimmunized, inadequately immunized, or whose immunization history is unknown. A booster dose of Td vaccine given to adults at 10-year intervals throughout life is recommended to maintain immunity.

Measles-Mumps-Rubella (MMR)

The risk of measles exposure during world travel is high and many recently reported cases of measles occurred in US citizens exposed abroad or were owing to exposure to an imported case. Serologic testing for immunity is recommended for travelers born after 1956 who have not had a diagnosis of measles in the past or who are

uncertain of their immune status. A dose of measles vaccine is recommended for people in that age group if there is insufficient time before departure for testing.

POLIOVIRUS VACCINE

In a recent survey of 233 American travelers, 12% were found to be lacking antibodies to polioviruses. All travelers in this survey who had received polio vaccination within the previous 5 years had protective antibodies. Only 84% of those who had received a polio booster >5 years earlier had protective antibodies [78]. Travelers to countries where poliomyelitis is epidemic or endemic are considered to be at increased risk of poliomyelitis and should be fully immunized. In general, travelers to developing countries should be considered to be at increased risk of exposure to wild poliovirus. A primary series consists of either three doses of trivalent oral poliovirus vaccine (OPV) or enhanced potency inactivated polio vaccine (eIPV). Persons who have previously received a primary series may need additional doses of a polio vaccine before traveling to areas with an increased risk of exposure to wild poliovirus.

For unvaccinated adults or adults whose immunization status is unknown and who are traveling to countries in which the risk of exposure to wild poliovirus is increased, primary immunization with eIPV is recommended whenever this is feasible. eIPV is preferred because the risk of vaccine associated-paralysis following OPV is slightly higher in adults than in children [79].

INFLUENZA VACCINE

Influenza vaccination has not been recommended for people traveling abroad other than for those for whom it is normally recommended. However, traveling and travelers may represent an important combination of exposure to the virus and risk for influenza. In one study, "flu" symptoms were second only to gastrointestinal upset in passengers and crew on commercial air flights to the Russian Far East [80]. Although the rate of influenza symptoms in this study was no greater than for the general population in the US, the economic burden of disease due to disrupted travel, business, and vacation plans would be at least as great as in the non-traveler.

The influenza season is usually from November to March in the northern hemispheres, and is reversed in the southern hemisphere (May to October). In the tropics, the virus can be isolated year around, and epidemics of disease can occur at various times of the year, including the summer months. The influenza vaccine is distributed early in the fall and is formulated annually based on new influenza virus strains predicted to arrive in North America. Due to the reversed seasonality of influenza in the southern hemisphere, the North American formulated vaccine may not be a perfect match for those strains being transmitted in the south but will likely provide protection against some if not all of them.

An important aspect of influenza infection while traveling is the risk that the strain of the virus will not yet have been included in current vaccines, therefore, vaccinated persons may not be fully protected. Recommendations have been made to identify "high-risk" individuals who are proposing to travel abroad so that they and their eligible close contacts may be offered vaccination or post-influenza A exposure preventive therapy with amantadine or rimantadine.

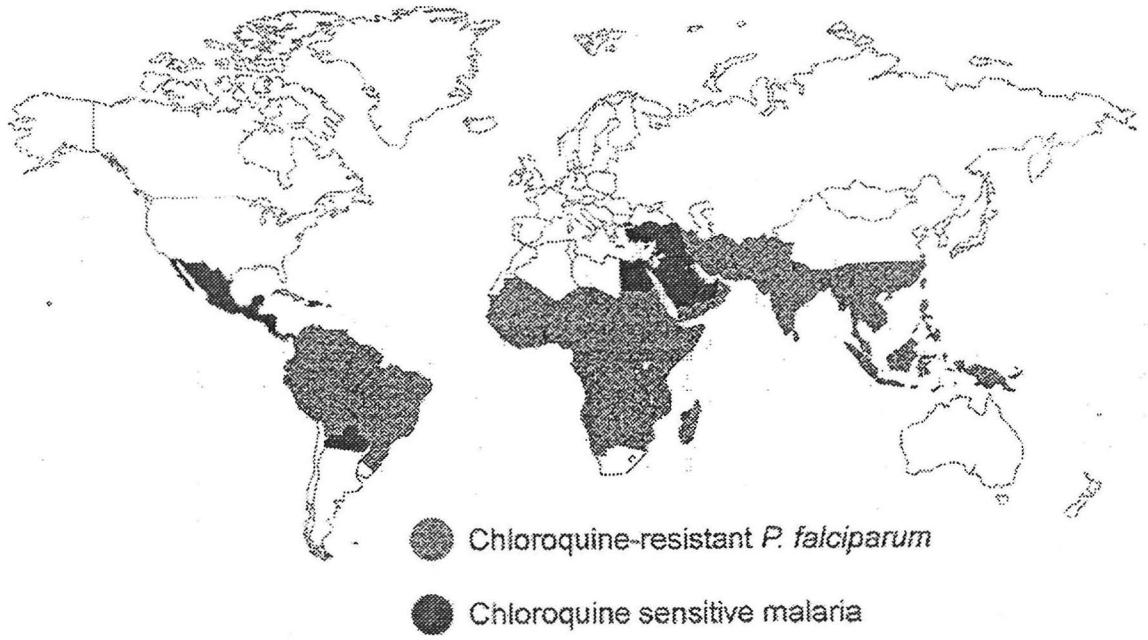
Routine, primary immunization against influenza, for the susceptible general population, should follow the annual recommendations of Advisory Committee on Immunization Practices (ACIP) based on the predictions for endemic and epidemic influenza strains regardless of the intention to travel. Pre-departure influenza immunization should be considered for anyone leaving the US during the local influenza transmission season and for those who will be exposed during the influenza transmission season at the destination. This may require a special effort to stock influenza vaccine outside of the fall months when it is usually used in the US. If the available influenza vaccine in the US does not include the strains of virus being transmitted where and when the traveler will be at risk, obtaining the appropriate vaccine, if available and if it can be safely administered, should be considered at the destination [81].

PNEUMOCOCCAL VACCINE

Pneumococcal vaccine, a 23-valent vaccine of pneumococcal polysaccharide, is recommended for all individuals over the age of 65 years and for special groups of patients whose health places them at special risk from complications of pneumonia. These patients include those with chronic pulmonary diseases, ischemic heart disease, diabetes mellitus, alcoholism, renal failure, transplanted organs, immunosuppression, splenectomy, and functional asplenia.

Pneumococcal vaccine should be given as a single intramuscular or subcutaneous dose (0.5 mL). The duration of immunity is unknown, but revaccination is not routinely recommended for adults with a normal immune system. Revaccination at 6 years after the first dose should be considered for those with the highest risk of rapid decline in antibody levels, as in patients with chronic renal failure, nephrotic syndrome, or transplant recipients.

MALARIA



Among every million travelers to endemic areas, there will be 2,000-5,000 cases of imported malaria, 80-90% caused by *Plasmodium falciparum* (1600-4000 cases); of those cases 0.5%-1% (8-40 cases) will die [82].

Malaria transmission occurs in most of sub-Saharan Africa, in large areas of the Middle East, Southern Asia, Southeast Asia, Oceania, Central and South Africa, Haiti, and the Dominican Republic. The risk of transmission is increased in rural areas but is diminished at altitudes above which the *Anopheles* mosquito does not breed. Transmission is dependent upon the duration of exposure to the mosquitoes and activity during exposure. Travel to urban areas of Southeast Asia, Central and South America is considered to entail minimal risk, although urban travel in the other malaria-endemic zones may be associated with significant risk of infection.

All travelers to malaria-endemic zones should be advised to use **personal protective measures** to reduce the risk of insect bites. These include: remaining in well-screened areas, using air conditioning, sleeping under mosquito netting, wearing clothing that reduces the amount of exposed skin, and the using an insect repellent on exposed skin. Insect repellents containing N,N diethylmetatoluamide (DEET) are the most effective. Household insect sprays and mosquito netting treated with permethrin should also be used.

Currently there are no available antimalarials that guarantee complete protection against malaria. Symptoms due to malaria may occur as early as one week after first exposure, and as late as several years after leaving a malaria zone regardless of whether chemosuppression has been used. Several factors need to be assessed when selecting a chemosuppressive regimen before travel. The itinerary should be reviewed in detail to highlight known areas of malaria transmission; the specific activities (rural travel,

night-time exposure, unscreened accommodations) of the individual in the malaria zone; and health factors (age, pregnancy, previous splenectomy, or chronic illness) that might increase the severity of malaria [83].

Chloroquine is recommended for travel to areas where chloroquine resistance has not been reported. Except for its bitter taste, chloroquine is usually very well tolerated. Dark-skinned persons may experience generalized itchiness, which is not indicative of drug allergy. Chloroquine is taken once weekly, beginning one week prior to entering a malaria zone, continuing during the period of exposure, and for four weeks after leaving the malarious area. Chloroquine is safe for pregnant women and young children, but overdoses are frequently fatal.

In chloroquine-sensitive malarious areas, when chloroquine cannot be taken, **proguanil** in a single daily dose may be taken, beginning one week prior to exposure, once every day during the period of exposure, and once daily for four weeks after leaving the malarious area. Proguanil is not known to cause harm to the developing fetus and is safe for infants and young children. Proguanil resistance may occur independently of chloroquine resistance.

Mefloquine is the drug of choice for most travelers to regions with chloroquine-resistant *P. falciparum.* In chemosuppressive doses, mefloquine is well tolerated. Adverse effects are similar in frequency and severity to those reported with weekly chloroquine use. The most frequent (25%) side effects from mefloquine are nausea, strange dreams, dizziness, mood changes, insomnia, headache, and diarrhea. Only about 1% of mefloquine users have to discontinue prophylaxis because of adverse effects. Severe neuropsychiatric reactions (psychosis, seizures) are infrequent with prophylactic doses. In treatment doses, however, neuropsychiatric reactions are reported to be 10 to 60 times more frequent.

Resistance to mefloquine was first described in Thailand in 1982. At present, however, resistance to mefloquine is not a significant problem except in rural wooded regions of Thailand bordering Myanmar (Burma) and Cambodia. Doxycycline should be used for malaria chemosuppression in these regions. Mefloquine may still be used for chemosuppression in other areas of Southeast Asia.

Mefloquine is contraindicated in patients with a seizure disorder or history of serious psychiatric illness. Precautions for the use of mefloquine include pregnancy (especially first trimester) and children < 15 kg, occupations or activities in which vertigo may be life-threatening such as airline pilots, concurrent use of chloroquine or quinine-like drugs including halofantrine, and underlying cardiac conduction disturbances. Insufficient mefloquine is excreted in breast milk to protect a nursing infant.

Mefloquine is taken once weekly, beginning 1 to 2 weeks prior to entering a malaria zone, continuing during the period of exposure, and then once weekly for 4 weeks after leaving the malarious area. For travelers who have less than 1 week before

departure, consideration may be given to the use of a loading dose of mefloquine. Limited data suggest that mefloquine taken once daily for 3 days before travel followed by once weekly is a well tolerated and effective way to achieve therapeutic blood levels rapidly. There is no evidence that toxic metabolites of mefloquine accumulate, and long-term use of mefloquine (> 1 year) by Peace Corps volunteers in Africa has not been associated with additional adverse effects. It is recommended, therefore, that the use of mefloquine not be arbitrarily restricted to six months in long-term travelers who are at risk of acquiring malaria in mefloquine-sensitive areas [84].

For persons unable to take mefloquine, doxycycline could be taken prophylactically, or less optimally chloroquine plus proguanil, with the provision of Fansidar (sulfadoxine-pyrimethamine) for presumptive self-treatment when disease occur [85].

For areas with chloroquine sensitive *P. falciparum*	
• Chloroquine phosphate	• 300 mg po qwk
• Hydroxychloroquine sulfate	• 400 mg po qwk
For areas with chloroquine resistant *P. falciparum*	
• Mefloquine	• 250 mg po qwk
• Doxycycline	• 100 mg po qd
• Proguanil	• 200 mg po qd (+) chloroquine weekly
For terminal prophylaxis after exposure to *P. vivax* or *P. ovale*	
• Primaquine	• 15 mg base po qd for 14 d.
For presumptive therapy	
• Fansidar	• 3 tablets po as a single dose

TRAVELERS' DIARRHEA

Travelers' diarrhea is expected to occur annually in approximately 11 million people traveling from industrialized countries to the developing world. Thirty percent of them will be confined to bed, and an additional 40% will suffer from severe limitation of their activities. A number of risk factors have been associated with travelers' diarrhea, including geographic destination, season and mode of travel, standard of accommodation, and length of travel [86,87,88,89].

Travelers' diarrhea is caused by food- or waterborne pathogens transmitted via the fecal-oral route. The most typical presentation is the abrupt onset of watery or loose stools which may be accompanied by cramps, nausea, vomiting (15%), fever and/or blood in stools (22%). Onset is usually early in the trip, often by the third day, with a second peak after ten days [90,91].

Bacteria are thought to cause 80% of cases of travelers' diarrhea. **The most common isolates from patients have been *E. coli*, particularly enterotoxigenic strains, and *Shigella* species.** A variety of other organisms have been implicated, including *Campylobacter* spp., salmonellae, vibrios, *Aeromonas*, and *Plesiomonas*. The most common protozoan agent is *G. lamblia*. *Cryptosporidia* and cyclospora are unusual causes, and *Entamoeba histolytica* is rare. Viruses, notably Norwalk agent and rotavirus, also cause travelers' diarrhea [92,93].

Travelers should exercise caution in the **selection and preparation of food and dairy products.** Produce should be freshly peeled or freshly cooked. Food obtained from street vendors who lack both adequate sanitary facilities or behavior for themselves and refrigeration for perishable food is most risky. In cholera-endemic countries, particularly those in South America bordering the Pacific Ocean, seafood and undercooked fish are dangerous.

Travelers to destinations with high-risk for diarrhea must ensure that they have a **safe supply of water for drinking and for brushing their teeth.** Commercially bottled water and carbonated beverages are generally but not universally safe. Beer is free of enteric pathogens. Ice cubes may represent frozen packages of enteric pathogens and must be considered contaminated. Water may be treated by heat, filtration, or with chemicals. Boiling water for one minute is an effective way of killing all enteric pathogens. Tea or coffee prepared from boiling water and served hot are safe. Filters that work according to particle size are effective in removing bacteria and parasites but not viruses. Chemical treatment with iodine is effective against all three types of pathogens. Chlorine is effective against most pathogens but is relatively ineffective against *Giardia* cysts. The efficacy of chlorine is diminished by particulate matter and by cold water temperatures.

Diarrhea must be treated at least with **fluid replacement**. The standard fluid management of diarrhea is oral rehydration solution standardized by the WHO. Fluids should be consumed at a rate to allay thirst and maintain a pale urine color. Intravenous fluids are best avoided in developing world areas, but may be occasionally lifesaving. **Bismuth subsalicylate** antagonizes the action of heat-labile toxin produced by *V. cholerae* and certain *E. coli*. It is slow to act, and frequent doses are required. If the liquid form is to be used a large volume of it must be carried by the traveler.

Loperamide (Imodium AD®) may be used alone to treat mild diarrhea in adults and older children. Antimotility agents have been used in the management of diarrhea. **Diphenoxylate** has been associated with toxic megacolon in patients with bacillary dysentery and is not recommended.

Published studies have indicated that trimethoprim-sulfamethoxazole (TMP/SMX), trimethoprim alone, or a quinolone is more effective than a placebo (63). A 3-day course of an antibiotic is conventional. Recent studies have shown similar efficacy of a single, large dose of TMP/SMX or of a quinolone. Single dose therapy with quinolones has been associated with a 40% failure rate in infections caused by *Shigella dysenteriae* as well as relapse of *Campylobacter* infections.

Antibiotics may be used to prevent diarrhea in highly selected short-term (up to 3 weeks) travelers. Although TMP/SMX and quinolones have been shown to be effective in reducing the risk of diarrhea in short-term healthy travelers (64) they are not recommended for most. The reasons are several. First, only a minority of such short-term travelers will develop diarrhea; second, increased antibiotic use will increase the

incidence of adverse reactions and may encourage the development of bacterial resistance; and finally, presumptive therapy is highly effective in those travelers who do get sick.

Preventive therapy may be considered for travelers under the following circumstances: 1) important trip, where even a brief illness cannot be tolerated, 2) increased susceptibility to diarrhea because of achlorhydria, prior gastrectomy, or poor experience in previous trips, 3) immunosuppression predisposing to systemic dissemination of enteric pathogens, 4) chronic renal failure, CHF, severe angina, insulin dependent diabetes mellitus, or inflammatory bowel disease for whom severe complications of diarrhea might result [94,95,96].

SCHISTOSOMIASIS

Approximately, 200 million persons are infected with schistosomiasis worldwide. Travelers to endemic areas of the Caribbean, South America, Africa, and Asia are at risk. Schistosomiasis is most prevalent in Brazil, Puerto Rico, St. Lucia, Egypt, most of sub-Saharan Africa, southern China, the Philippines, and Southeast Asia. Those at greatest risk are travelers who engage in wading, bathing, or swimming in fresh water in rural areas where poor sanitation and appropriate snail hosts are present. Even brief exposures to contaminated water can result in infection [97].

Since there is no practical way for the traveler to distinguish infested from non-infested water, fresh water swimming in rural areas of endemic countries should be avoided. In such areas heating bathing water to 122°F for 5 minutes or treating it with iodine or chlorine will make the water safe. If these measures are not feasible, allowing bathing water to stand for 3 days is advisable. Swimming in adequately chlorinated swimming pools is virtually always safe, even in endemic countries. At this time there are no available drugs which are known to be consistently effective as prophylaxis.

DENGUE FEVER

Dengue fever is an acute febrile illness, associated with myalgias, arthralgias, headache, and skin rash. It is caused by one of four serotypes of the dengue virus and is transmitted by *Aedes aegypti* mosquito. The disease is distributed throughout the tropical and subtropical areas and has been reported in over 100 countries worldwide.

While the disease is often mild and self-limiting, it may present in a severe form associated with hemorrhagic complications, shock, and, in some cases, death. **Dengue hemorrhagic fever (DHF)** is more common in people less than 15 years of age and in people having their second infection.

Although dengue fever has been reported in some international travelers, in general there is a low risk of DHF in tourists returning to the developed world. All travelers to areas endemic for dengue fever are advised to use personal insect protective

measures to reduce the risk of day-biting mosquitoes. There are currently no vaccines for preventing the acquisition of dengue fever.

BASIC SOURCES OF INFORMATION ON TRAVEL MEDICINE

- "Health Information for International Travel"-**The Yellow Book**: published annually by the US Department of Health and Human Services; is available through the Superintendent of Documents (US Government Printing Office, Washington DC 20402, telephone 202-783-3238).
- "Guide for Adult Immunization"-**The Green Book**: published by the American College of Physicians (800-523-1546).
- **The Travel Medicine Advisor**: published by the American Health Consultants (800-688-2421), updated periodically; a newsletter (The Travel Medicine Advisor Update) is included in the cost of the text.
- The International association for Medical Advice to Travelers (**IAMAT**, 417 Center Street, Lewiston, NY 14092).
- **The US State Department** Hotline (202-647-5225)
- **World Wide Web (WWW) Resources**:
    - Infectious Diseases Link (http://www.idlinks.com)
    - American Society of Tropical Medicine and Hygiene (http://www.astmh.org)
    - **CDC Travel Information** (http://www.cdc.gov)
    - **C.I.A. World Factbook** (http://www.odci.gov/cia/publications/95 fact/index)
    - **U.S. State Department Travel Warnings** (http://www.state.gov)
    - MedWeb Infectious Diseases (http://www.gen.emory.edu/medweb/medweb.id.htm)
    - **World Health Organization** (http://www.who.ch\wer\issues.htm)
    - American Society for Microbiology (http://www.asmusa.org)
    - Global Health Network (http://www.pitt.edu/home/ghnet/)
    - Texas Department of Health (http://www.tdh.state.tx.us)
    - The Hot Zone (http://www.visi.com/~chris/hotzone/)
    - Emerging Infectious Diseases (http://www.cdc.gov/ncidod/eid/eid.htm)
    - **Canada Communicable Disease Report** (http://hpbl.hwc.ca:8300/)

Countries for which an official yellow fever certificate of vaccination issued within the previous 10 years is mandatory are:

Benin	Gabon	Paraguay (required on departure if going to an infected country and/or coming from endemic areas)
Burkina Faso	Ghana	Rwanda
Cameroon	Liberia	Sâo Tome & Principe
Central African Republic	Mali	Togo
Chad (recommended)	Mauritania (for a stay of more than 2 weeks)	Zaire
Colombia (recommended)	Niger	
Congo	Panama (recommended if going toProvince of Darién)	
Côte d'Ivoire		
French Guiana		

Countries requiring yellow fever vaccination certificate from travelers who have had a stop-over in yellow fever endemic country

Afghanistan	Ethiopia	Malaysia	St. Kitts and Nevis
Albania	Fiji	Maldives	St. Lucia
Algeria	French Polynesia	Malta	St. Vincent & Grenadines
American Samoa	Gambia	Martinique	Samoa
Angola	Greece	Mauritius	Saudi Arabia
Antigua & Barbuda	Grenada	Mexico	Senegal
Australia	Guadeloupe	Mozambique	Seychelles
Bahamas	Guatemala	Myanmar-Burma	Sierra Leone
Bangladesh	Guinea	Namibia	Singapore
Barbados	Guinea-Bissau	Nauru	Solomon Islands
Belize	Guyana	Nepal	Somalia
Benin	Haiti	Netherlands Antilles	South Africa
Bhutan	Honduras	New Caledonia & Dependencies	Sri Lanka
Bolivia	India	Nicaragua	Sudan
Brazil	Indonesia	Nigeria	Suriname
Brunei Darussalam	Iran (Islamic Republic of)	Niue	Swaziland
Burundi	Iraq	Oman	Syrian Arab Republic
Cambodia	Jamaica	Pakistan	Tanzania, United Republic of
Cape Verde	Jordan	Papua New Guinea	Thailand
China	Kenya	Paraguay	Tonga
Christmas Islan (Australia)	Kiribati	Peru	Trinidad & Tobago
Djibouti	Laos	Philippines	Tunisia
Dominica	Lebanon	Pitcairn	Turkmenistan
Ecuador	Lesotho	Portugal - from infected areas and going to Azores or Madeira	Uganda
Egypt	Libyan Arab Jamahiriya	St. Helena	* Viet Nam
El Salvador	Madagascar (including transit)		Yemen
Equatorial Guinea	Malawi		Zimbabwe
Eritrea			

COUNTRIES INFECTED WITH YELLOW FEVER - As of 8/16 /1996.

AFRICA **Angola:**Provinces Bengo, Luanda. **Cameroon**: Northern Province. **Gabon:** Ogooué-Invindo Province. **Gambia:** Upper River Division. **Ghana:** Upper West Region. **Guinea:** Siguiri Region. **Liberia:** Counties Bassa, Bomi, Bong, Sinoe. **Nigeria:** States Anambra, Bauchi, Bendel, Benue, Cross River, Imo, Kaduna, Kwara, Lagos, Niger, Ogun, Ondo, Oyo, Plateau. **Sierra Leone** :*Eastern Province*. **Sudan**: South of 12° North & **Zaire**: North of 10°South

SOUTH AMERICA **Bolivia**: Departments Beni, Cochabamba, La Paz, Santa Cruz. **Brazil**: Territories Amapá, States Amazonas, Maranhaõ, Pará. **Colombia:** Departments Antioguia, Boyaca, Cesar, Choco, Cundinamarca, Norte de Santander, Santander, Vichada. Intendencias Arauca, Caquetá, Casanare, Cucuta, Guaviare, Meta, Putumayo. **Ecuador:** Provinces Morona-Santiago, Napo, Pastaza, Sucumbios, Zamora-Chinchipe. **Peru**: Departments Amazonas, Ancash, Ayacucho, Cusco, Huanuco, Junin, Loreto, Madre de Dios, Pasco, Puno, San Martin, Ucayali.

CHOLERA - WORLD SITUATION

As of week ending **August 16, 1996** cholera cases are being reported from:

AFRICA	Mali	AMERICAS	Peru	MID-EAST
Angola	Mauritania	Argentina	Suriname	Iraq
Benin	Mozambique	Belize	Venezuela	
Burkina Faso	Niger	Bolivia	ASIA	
Burundi	Nigeria	Brazil	Afghanistan	
Cameroon	Rwanda	Columbia	Bhutan	
Cape Verde	SaoTome &Principe	Costa Rica	India	
Chad	Senegal	Ecuador	Laos	
Côte d'Ivoire	Sierra Leone	El Salvador	Mongolia	
Djibouti	Somalia	French Guiana	Myanmar	
Ghana	Swaziland	Guatemala	Nepal	
Guinea	Tanzania	Guyana	Philippines	
Guinea-Bissau	Togo	Honduras	Vietnam	
Kenya	Uganda	Mexico	EUROPE	
Liberia	Zaire	Nicaragua	Moldova	
Malawi	Zambia	Panama	Ukraine	

Malaria Risk by Geographic Areas in Countries with Endemic Malaria

Country	Areas of risk within country	Recommended Regimen(s)
Afghanistan	All	Mefloquine
Algeria	Sahara region	None
Angola	All	Mefloquine
Argentina	Rural areas near Bolivian border	Chloroquine
Azerbaijan	Southern border areas	Chloroquine
Bangladesh	All, except no risk in city of Dhaka	Mefloquine
Belize	Rural areas, except no risk in Belize District	Chloroquine
Benin	All	Mefloquine
Bhutan	Rural areas in districts bordering India	Mefloquine
Bolivia	Rural areas only, except no risk in Oruro Department and Province of Ingavi, Los Andes, Omasuyos, Pacajes, Southern and Central Potosi Department	Mefloquine
Botswana	Northern part of country (North of 21° South)	Mefloquine
Brazil	Rural areas of Acre, Amazonas, Goias, Maranhao, Mato Grosso and Para States; and territories of Amapa, Rondonia, Roraima and urban areas of Amazon, River Basin	Mefloquine
Burkina Fasa	All	Mefloquine
Burma: see Myanmar		
Burundi	All	Mefloquine
Cambodia	All, no risk in Phnom Penh Doxycycline on Western borders	Mefloquine
Cameroon	All	Mefloquine
Central African Republic	All	Mefloquine
Ceylon: see Sri Lanka		
Chad	All	Mefloquine
China	Rural areas only in Anui, Fujian, Guangdong, Guangxi, Guizhou, Hebel, Henan, Hubei, Hunan, Jiangsu, Jiangxi, Liaoning, Shanxi, Shandong, Sichuan, Yunnan, Xignjiang and Zhejiang Provinces/autonomous regions	Chloroquine (Mefloquine for southern provinces bordering Myanmar, Laos and Vietnam)
Colombia	In general, rural areas only, no risk in Bogota and vicinity	Mefloquine
Comoros	All	Mefloquine
Congo	All	Mefloquine
Costa Rica	None in central highlands Limited risk in rural areas of Alajuela, Guanacaste, Limon and Puntarenas Provinces	Chloroquine
Cote d'Ivoire (formerly Ivory Coast)	All	Mefloquine
Dijbouti	All	Mefloquine

Malaria Risk by Geographic Areas in Countries with Endemic Malaria

Country	Areas of risk within country	Recommended Regimen(s)
Dominican Republic	All rural areas. Highest risk is areas bordering Haiti. No risk in tourist areas.	Chloroquine
Ecuador	All areas in provinces of Esmeraldas, Guayas, Manabi, El Oro. Rural areas in provinces of Los Rios, Morona, Santiago, Napo, Pastaza, Zamora, Chinchipe and Pinchincha. (No risk in Quito and vicinity, the central highland tourist areas or the Galapalgos Islands). Chloroquine resistance in Guaquil	Mefloquine
Egypt	Rural areas of Nile Delta, El Faiyum, the oases and part of Southern (upper) Egypt. (No risk in main tourist areas including cruises.)	Choroquine
El Salvador	Rural areas only	Chloroquine
Equatorial Guinea	All	Mefloquine
Eritrea	All, except above 2,000 metres	Mefloquine
Ethiopia	All, no risk in Addis Ababa and above 2,000 metres	Mefloquine
French Guiana	All	Mefloquine
Gabon	All	Mefloquine
Gambia	All	Mefloquine
Ghana	All	Mefloquine
Guatemala	Rural areas only, except no risk in central highlands	Chloroquine
Guinea	All	Mefloquine
Guinea-Bissau	All	Mefloquine
Guyana	Rural areas in Rupununi and North West Regions	Mefloquine
Haiti	All	Chloroquine
Honduras	Rural areas only	Chloroquine
India	All areas, including Delhi and Bombay, except no risk in Himechel, Pradesh, Jammu, Kashmir and Sikkim	Mefloquine
Indonesia	In general, rural areas only, except high risk in all areas of Irian Jaya. No risk in Jakarta or resort areas of Java or Bali.	Mefloquine
Iran, Islamic Republic of	Rural areas only in the provinces of Sistan-Baluchestan and Hormozgan, the southern parts of Fars, Kohgiluych-Boyar, Lorestan and Chahar Mahai-Bakhtiani and the north of Khuzestan	Mefloquine
Iraq	All areas in northern region; Duhok, Erbil, Kirkuk, Ninawa and Sulaimanya province	Chloroquine
Ivory Coast: see Cote d'Ivoire		
Kenya	All except city of Nairobi and above 2,500 metres	Mefloquine
Lao People's Domestic Republic	All areas, except no risk in city of Vientiane	Mefloquine
Liberia	All	Mefloquine
Libyan Arab Janahiriya	Limited risk in two small foci in Southwest of country	None
Madagascar	All, highest in coastal areas	Mefloquine

Malaria Risk by Geographic Areas in Countries with Endemic Malaria

Country	Areas of risk within country	Recommended Regimen(s)
Malawi	All	Mefloquine
Malaysia	In general, rural areas only, but throughout Sabah (NE Borneo). Otherwise, none in urban and coastal areas	Mefloquine
Mali	All	Mefloquine
Mauritania	All areas, except no risk in the northern areas of Dakhlet-Nouadhibou, Inchiri, Adrar and Tiris-Zemour	Mefloquine
Mauritius	Rural areas only, except no risk on Rodgrigues	Chloroquine
Mayotte	All	Mefloquine
Mexico	Rural areas only No risk in resort areas	Chloroquine
Morocco	Very limited risk in rural areas of coastal provinces	None
Mozambique	All	Mefloquine
Myanmar (formerly Burma)	Rural areas, doxycycline for Thai borders	Mefloquine
Namibia	All areas of Ovamboland and Caprivi Strip	Mefloquine
Nepal	Rural areas in Terai District and hill districts below 1,200 metres. No risk in Kathmandu.	Mefloquine
Panama	Rural areas, west of Canal Rural areas, east of Canal	Chloroquine Mefloquine
Papua New Guinea	All	Mefloquine
New Hebrides: see Vanuatu		
Nicaragua	In general, rural areas only; however, risk exists in outskirts of towns of Chinandega, Leon, Granada, Managua, Nandiame and Tipitapa	Chloroquine
Niger	All	Mefloquine
Nigeria	All	Mefloquine
Oman	All	Mefloquine
Pakistan	All, areas below 2,000 metres.	Mefloquine
Paraguay	In general, only rural areas bordering Brazil	Chloroquine
Peru	In general, all rural areas, except no risk in Lima and vicinity and coastal area of Southern Lima	Chloroquine Mefloquine for borders with Brazil
Philippines	Rural areas only, except no risk in Manila and province of Bohol, Catanduanes, Cebu and Leyte Rural areas of Luzon, Basilan, Mindoro, Palawan, Mindanao and Sulu-Archipelago	Chloroquine Mefloquine
Rwanda	All	Mefloquine
Sao Tome and Principe	All	Mefloquine
Saudi Arabia	All areas except the Eastern, Northern and Central provinces, the high altitude areas of Asir province, and the urban areas of Jeddah, Mecca, Medina and Taif	Chloroquine

Malaria Risk by Geographic Areas in Countries with Endemic Malaria

Country	Areas of risk within country	Recommended Regimen(s)
Senegal	All	Mefloquine
Sierra Leone	All	Mefloquine
Solomon Islands	All	Mefloquine
Somalia	All areas	Mefloquine
South Africa	Rural areas (including game parks) in the north, east, and western low altitude areas of Transvaal and in Natal coast	Mefloquine
Sri Lanka (formerly Ceylon)	All areas except Colombo	Mefloquine
Sudan	All	Mefloquine
Suriname	Rural areas only, except no risk in Paramaribo district and coastal areas north of 5° North	Mefloquine
Swaziland	All lowland areas	Mefloquine
Syrian Arab Republic	Rural areas only except no risk in districts of Damascus, Deir-es-zor and Sweida	Chloroquine
Tajikistan	In southern border areas	Chloroquine
Tanzania, United Republic of	All	Mefloquine
Thailand	Rural border areas only, no risk in Bangkok or beach resort areas. Mefloquine resistance. Doxycycline recommended on borders with Myanmar and Cambodia for overnight exposure	Doxycycline
Togo	All	Mefloquine
Turkey	Cukorova/Amikova areas and southeast Anatolia	Chloroquine
Uganda	All	Mefloquine
United Arab Emirates	All, except no risk in cities of Dubai, Sharjahg Ajmain, Umm at Qaiwan, and Emirate of Abu Dhabi	Chloroquine
Vanuatu (formerly New Hebrides)	All, except no risk on Fortuna Island	Mefloquine
Venezuela	Rural areas of all border states; Apure, Bolivar, Barinas Merida, Tachira and Zulia states	Mefloquine
Viet Nam	Rural areas only, no risk in Red & Mekong Deltas	Mefloquine
Yemen	All, except no risk in Aden & airport areas	Mefloquine
Yemen, Democratic	All	Mefloquine
Zaire	All	Mefloquine
Zambia	All	Mefloquine
Zimbabwe	All, except no risk in cities of Harare and Bulawayo	Mefloquine

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