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Travelers' Health: Yellow Book

Health Information for International Travel, 2005-2006

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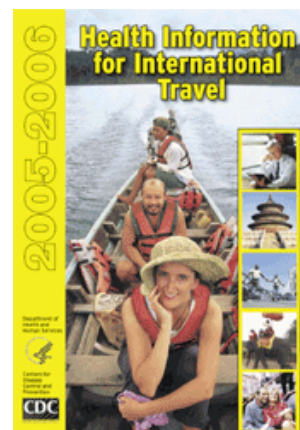
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Yellow Book: Health Information for International Travel, 2005-2006

Yellow Fever Vaccine Requirements and Information on Malaria Risk and Prophylaxis, by Country Table

Country	Yellow Fever		Malaria		
	Country Requirements ¹	CDC Recommendations ²	Area of Risk	Chloroquine Resistance	Recommendations for Prophylaxis ³
China	If traveling from an endemic zone	None	Travelers to cities and popular tourist areas, including Yangtze River cruises, are not at risk and do not need to take chemoprophylaxis. Rural areas only of the	Confirmed in the provinces of Hainan and Yunnan. Other provinces do not have chloroquine-resistant	Atovaquone/proguanil; doxycycline; or mefloquine in Hainan and Yunnan; Chloroquine in all other areas.

The Yellow Book is published every 2 years by CDC as a reference for those who advise international travelers of health risks. The Yellow Book is written primarily for health care providers, although others might find it useful.

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Country	Yellow Fever		Area of Risk	Malaria	Recommended Prophylaxis	Travelers' Health Automated Information Line TOLL FREE: 877-FYI-TRIP toll free information about ordering the Yellow Book and International Certificates of Vaccination and recorded messages on travel-related health topics) VIA EMAIL: Contact Us Form
	Country Requirements ¹	CDC Recommendations ²		Chloroquine Resistance		
			following provinces: Hainan, Yunnan, Fujian, Guangdong, Guangxi, Guizhou, Sichuan, Tibet (in the Zangbo River valley only), Anhui, Hubei, Hunan, Jiangsu, Jiangxi, and Shandong. In provinces with risk, transmission exists in rural communities <1,500m only during warm weather: north of latitude 33°N, July-November; between latitude 25°N and 33°N, May-December. South of latitude 25°N, transmission occurs year-round.	malaria.		

¹Yellow fever vaccine entry requirements are necessary for travelers to comply with in order to enter the country. In general, these are in place to prevent importation and transmission of yellow fever virus. Countries requiring yellow fever vaccination for entry adhere to the regulations put forth by WHO as stated in the International Health Regulations. Some countries require vaccination for travelers coming from an endemic zone. "Traveling from an endemic zone" is defined as transit through an endemic zone in the previous 6 days.

²The information in the section on yellow fever vaccine recommendations is advice given by CDC to prevent yellow fever infections among travelers.

³Please note, the U.S. Advisory Committee for Immunization Practices recommends avoiding vaccination in infants <9 months of age; travel of infants <9 months of age to countries in the yellow fever endemic zone or to countries experiencing a yellow fever epidemic should be postponed or avoided, whenever possible. If travel is unavoidable, medical waivers may be considered for infants <9 months of age to meet the entry requirements of these countries.

Geographic Distribution of Potential Health Hazards to Travelers

East Asia

Risk of infection is highly variable in the region. Access to clean water and good sanitary facilities are limited in many rural areas, especially in China and Mongolia. Respiratory infections (etiology often undefined) are common in travelers to the region. Chronic and latent infections in immigrants (and long-term residents) include tuberculosis, complications from chronic hepatitis B (and also hepatitis C) infection, schistosomiasis, paragonimiasis, and strongyloidiasis.

Vector-borne infections: Malaria is found in focal areas of China and North and South Korea. Japanese encephalitis (JE) is found in wide areas of China and Japan and focally in Korea. Transmission of malaria and JE is seasonal in many areas. Reported infections in travelers are rare. Other vector-borne infections include dengue, which has caused outbreaks in mainland China, Hong Kong, and Taiwan; spotted fever caused by *R. sibirica* (China, Mongolia); murine typhus; Oriental spotted fever caused by *R. japonica* (Japan); rickettsialpox (Korea); scrub typhus (especially in China, Korea, and Japan); tick-borne encephalitis (in forested regions northeastern China and in South Korea); visceral and cutaneous leishmaniasis (in rural China); lymphatic filariasis (in focal coastal areas of China and South Korea); and Crimean-Congo hemorrhagic fever* (in western China).

Food- and water-borne infections: Risk of diarrhea is highly variable within the region. Diarrhea in travelers may be caused by bacteria, viruses, and parasites. Risk of hepatitis A is high in some areas (excluding Japan), especially in rural areas of China and Mongolia. Outbreaks of hepatitis E have been reported in China. Cases of cholera were reported from China in 2002-2003. Sporadic cases of anisakiasis

are reported from Korea and Japan. Brucellosis is found, especially in sheep-raising regions of China and Mongolia. Paragonimiasis is endemic in China and still occurs in Korea. Clonorchiasis is found in local populations in China, Japan, Korea, and Taiwan, but risk to usual traveler is low.

Airborne and person-to-person transmission: The estimated annual incidence of tuberculosis per 100,000 population is 100-300 in China, Mongolia, and North Korea and 50-100 in Japan and South Korea. High rates of multiple drug-resistant tuberculosis are found in parts of China (about 10% in new patients). Outbreaks of SARS occurred in mainland China, Hong Kong, and Taiwan in 2003. Measles remains endemic in the region, and infection has occurred in adopted children from China and in travelers to the region. In tropical areas, influenza may occur during all months of the year.

Sexually transmitted and blood-borne infections: The prevalence of HIV in adults is low (0.1%-1%) in most of the region, but a much higher prevalence is found in focal areas in southern China. Hepatitis B is highly endemic among adults in region, excluding Japan. Prevalence of chronic infection exceeds 8% in many areas. Prevalence of hepatitis C is 10% or higher in Mongolia; 2.5%-9.9% in mainland China and Taiwan, and 1%-2.4% in the rest of the region. A high prevalence of HTLV-I is found focally in the southern islands of Japan.

Zoonotic infections: Rabies is widespread in China (not Hong Kong) and Mongolia. Avian influenza has been transmitted to humans in Hong Kong and China. To date, the virus has caused high mortality in humans but has not been readily transmissible from person to person. Highly pathogenic H5N1 has also been found in bird populations in Japan, and South Korea. Cases of human plague* are reported most years from China and Mongolia. Hantaviruses causing hemorrhagic fever with renal syndrome are a major health threat in China and the Republic of Korea, primarily affecting residents of rural areas in late fall and early winter. Risk to the usual traveler is low. Anthrax* is enzootic in China and Mongolia, and sporadic infection is reported in the rest of the region. Tularemia* occurs in China and Japan and is found especially in northern parts of region. Echinococcosis* is endemic in rural areas of China and Mongolia.

Schistosomiasis (*S. japonicum*) is present in focal areas in China, especially in the Yangtze River basin. Leptospirosis* is a risk, especially in tropical areas of China and South Korea. Cutaneous larva migrans is common in warm coastal areas. Cases of histoplasmosis have been reported.

Other risks for travelers include injury from motor vehicle accidents and venomous snake bites. Screening of blood before transfusion is inadequate in many hospitals in the region.

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Prevention of Specific Infectious Diseases

Amebiasis

Description

Amebiasis is caused by the protozoan parasite *Entamoeba histolytica*. Infection is acquired by the fecal-oral route, either by person-to-person contact or indirectly by eating or drinking fecally contaminated food or water.

Occurrence

Amebiasis occurs worldwide, especially in regions with poor sanitation. *E. histolytica* antibody prevalence rates (reflecting past or recent infection), commonly range from 6% to 25% in developing countries, but may exceed 50% in some communities.

Risk for Travelers

For travelers to developing countries, risk for infection is highest for those who live in or visit rural areas, spend time in backcountry areas, or eat or drink in settings of poor sanitation.

Clinical Presentation

The incubation period is commonly 2-4 weeks but ranges from a few days to years. The clinical spectrum of intestinal amebiasis ranges from asymptomatic infection to fulminant colitis and peritonitis. The parasite initially infects the colon, but it occasionally may spread to other organs, most commonly the liver (amebic liver abscess). In persons infected with *E. histolytica* who are symptomatic, the most common symptom is diarrhea. The diarrhea can worsen to painful, bloody bowel movements, with or without fever (amebic dysentery). *Entamoeba dispar*, a nonpathogenic amoeba that also inhabits the colon, cannot be distinguished from the pathogen *E. histolytica* by routine microscopy; however, an enzyme immunoassay kit for distinguishing the two organisms in fresh stool specimens is commercially but not widely available. Similarly, polymerase chain reaction (PCR)-based diagnostic tests have been developed but are not widely available.

Prevention

No vaccine is available. Travelers to developing countries should be advised to follow the precautions detailed in the section Risks from Food and Water in Chapter 2 and avoid sexual practices that may lead to fecal-oral transmission.

Treatment

Travelers may be advised to consult with an infectious disease specialist to ensure proper diagnosis and treatment. Iodoquinol or paromomycin are the drugs of choice for asymptomatic but proven *E. histolytica* infections. For mild or moderate to severe intestinal disease and extraintestinal disease (e.g., hepatic abscess), treatment with metronidazole or tinidazole should be immediately followed by treatment with paromomycin or iodoquinol. *E. dispar* infection does not require treatment.

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Prevention of Specific Infectious Diseases

Giardiasis

Description

Giardiasis is a diarrheal illness caused by the protozoan *Giardia intestinalis*, which lives in the intestines of persons and animals and is passed in their feces. Transmission occurs from ingestion of fecally contaminated food or drinking water, swallowing recreational water, from exposure to fecally contaminated environmental surfaces, and from person to person by the fecal-oral route.

Occurrence

Giardiasis occurs worldwide.

Risk for Travelers

Risk of infection increases with duration of travel and is highest for those who live in or visit rural areas, trek in backcountry areas, or frequently eat, drink, or swim in areas that have poor sanitation and inadequate drinking water treatment facilities.

Clinical Presentation

Symptoms, which occur approximately 1-2 weeks after ingestion of the parasite, include diarrhea, abdominal cramps, bloating, fatigue, weight loss, flatulence, anorexia, or nausea, in various combinations. Symptoms usually last >5 days and can become chronic, resulting in malabsorption. Fever and vomiting are uncommon.

Prevention

No vaccine is available, and there is no known chemoprophylaxis. To prevent infection, travelers to disease-endemic areas should be advised to follow the precautions included in the section Risks from Food and Water.

Treatment

Several effective antimicrobial drugs (e.g., tinidazole, metronidazole, quinacrine, albendazole, nitazoxanide) are now available. Treatment recommendations are available in textbooks on internal medicine and infectious diseases; consultation with a travel or tropical medicine specialist can also be sought.

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Prevention of Specific Infectious Diseases

Hepatitis, Viral, Type A

Description

Hepatitis A is a viral infection of the liver caused by hepatitis A virus (HAV). HAV infection may be asymptomatic or its clinical manifestations may range in severity from a mild illness lasting 1-2 weeks to a severely disabling disease lasting several months. Clinical manifestations of hepatitis A often include fever, malaise, anorexia, nausea, and abdominal discomfort, followed within a few days by jaundice.

Occurrence

HAV is shed in the feces of persons with HAV infection. Transmission can occur through direct person-to-person contact; through exposure to contaminated water, ice, or shellfish harvested from sewage-contaminated water; or from fruits, vegetables, or other foods that are eaten uncooked and that were contaminated during harvesting or subsequent handling.

HAV infection is common (high or intermediate endemicity) throughout the developing world, where infections most frequently are acquired during early childhood and usually are asymptomatic or mild. In developed countries, HAV infection is less common (low endemicity), but communitywide outbreaks still occur in some areas of the United States. Map 4-4 indicates the seroprevalence of antibody to HAV (total anti-HAV) as measured in selected cross-sectional studies among each country's residents.

Risk for Travelers

Hepatitis A is the most common vaccine-preventable infection acquired during travel. The risk for acquiring HAV infection for U.S. residents traveling abroad varies with living conditions, length of stay, and the incidence of HAV infection in the area visited. Travelers to North America (except Mexico), Japan, Australia, New Zealand, and developed countries in Europe are at no greater risk for infection than in the United States. For travelers to other countries, risk for infection increases with duration of travel and is highest for those who live in or visit rural areas, trek in back-country areas, or frequently eat or drink in settings of poor sanitation. Nevertheless, many cases of travel-related hepatitis A occur in travelers to developing countries with "standard" tourist itineraries, accommodations, and food consumption behaviors.

Clinical Presentation

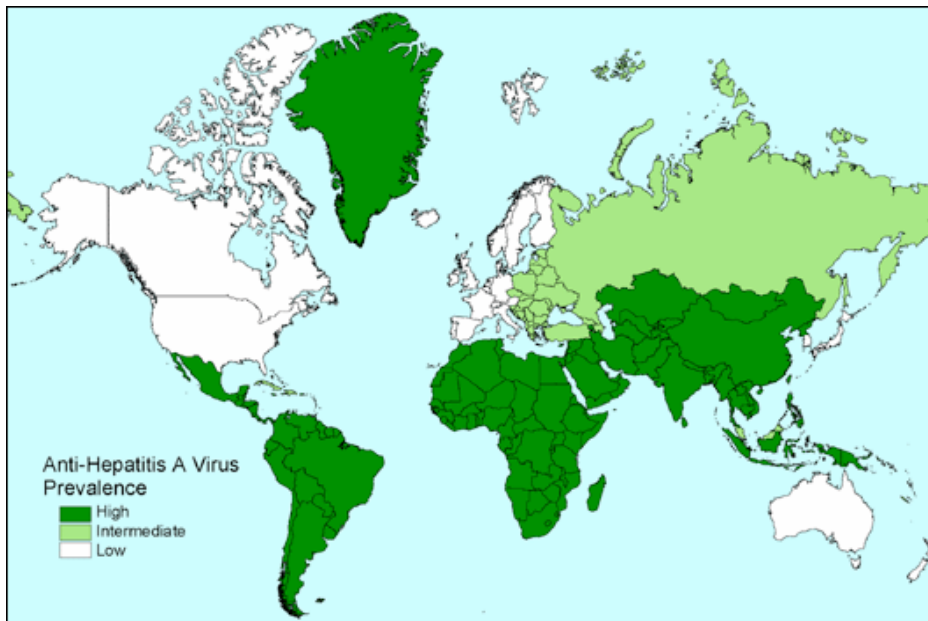
The incubation period for hepatitis A averages 28 days (range 15-50 days). Hepatitis A typically has an abrupt onset of symptoms that can include fever, malaise, anorexia, nausea, abdominal discomfort, dark urine, and jaundice. The likelihood of having symptoms with HAV infection is related to the infected person's age. In children <6 years old, most (70%) infections are asymptomatic; if illness does occur its duration is usually <2 months. No chronic or long-term infection is associated with hepatitis A, but 10% of infected persons will have prolonged or relapsing symptoms over a 6- to 9-month period. The overall case-fatality rate among cases reported to CDC is 0.3%; however, the rate is 1.8% among adults >50 years of age.

Prevention

Note: [Updated childhood and adolescent immunization schedule \(January 12, 2006\)](#)

Hepatitis A vaccine, immune globulin (IG), or both, are recommended for all susceptible persons traveling to or working in countries with an intermediate or high endemicity of HAV infection. Health-care providers should administer hepatitis A vaccination for persons traveling for any purpose, frequency or duration to countries that have high or intermediate endemicity of HAV infection. In addition, health-care providers should be alert to opportunities to provide vaccination for all travelers whose plans might include travel at some time in the future to an area of high or intermediate endemicity, including those whose current medical evaluation is for travel to an area where hepatitis A vaccination is not currently recommended.

Map 4-4. Geographic distribution of Hepatitis A prevalence, 2005



Vaccine and Immune Globulin

Two monovalent hepatitis A vaccines are currently licensed in the United States for persons 1 year of age or older ([Updated April 24, 2006](#)): HAVRIX, manufactured by GlaxoSmithKline ([Table 4-4](#)), and VAQTA (manufactured by Merck & Co., Inc.) ([Table 4-5](#)). Both vaccines are made of inactivated hepatitis A virus adsorbed to aluminum hydroxide as an adjuvant. HAVRIX is prepared with 2-phenoxyethanol as a preservative, while VAQTA is formulated without a preservative. All hepatitis A vaccines should be administered intramuscularly in the deltoid muscle.

Table 4-4. Licensed schedule for HAVRIX¹

Age group (Yrs)	Dose (EL.U.) ²	Volume	No. of doses	Schedule (Months)
1-18 (Updated April 24, 2006)	720	0.5 mL	2	0, 6 to 12
≥ 19	1,440	1.0 mL	2	0, 6 to 12

¹Hepatitis A vaccine, inactivated, GlaxoSmithKline

²EL.U. = enzyme-linked immunosorbent assay (ELISA) units

Table 4-5. Licensed schedule for VAQTA¹

Age group (Yrs)	Dose (EL.U.) ²	Volume	No. of doses	Schedule (Months)
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1-18 (Updated April 24, 2006)	25 units	0.5 mL	2	0, 6 to 18
≥ 19	50 units	1.0 mL	2	0, 6 to 18

¹Hepatitis A vaccine, inactivated, Merck & Co., Inc.

TWINRIX, manufactured by GlaxoSmithKline, is a combined hepatitis A and hepatitis B vaccine licensed for persons >18 years of age, containing 720 EL.U. of hepatitis A antigen (50% of the HAVRIX adult dose) and 20 µg of recombinant hepatitis B surface antigen protein (the same as the ENGERIX-B adult dose) (Table 4-6). Primary immunization consists of three doses, given on a 0-, 1-, and 6-month schedule, the same schedule as that commonly used for monovalent hepatitis B vaccine. TWINRIX contains aluminum phosphate and aluminum hydroxide as adjuvant and 2-phenoxyethanol as a preservative.

Table 4-6. Licensed schedule for TWINRIX¹

Age group (Yrs)	Hepatitis A dose/Hepatitis B dose	Volume	No. of doses	Schedule (Months)
≥ 18	720 EL.U. ² / 20 µg	1.0 mL	3	0, 1 6 months

¹Combined hepatitis A and hepatitis B vaccine, GlaxoSmithKline

²EL.U. = enzyme-linked immunosorbent assay (ELISA) units

The first dose of hepatitis A vaccine should be administered as soon as travel to countries with high or intermediate endemicity is considered. One month after receiving the first dose of monovalent hepatitis A vaccine, 94%-100% of adults and children will have protective concentrations of antibody. The final dose in the hepatitis A vaccine series is necessary to promote long-term protection. The immunogenicity of TWINRIX is equivalent to that of the monovalent hepatitis vaccines when tested after completion of the licensed schedule.

Many persons will have a detectable antibody to hepatitis A virus (anti-HAV) response to the monovalent vaccine by 2 weeks after the first vaccine dose. The proportion of persons who develop a detectable antibody response at 2 weeks may be lower when smaller vaccine dosages are used, such as with the use of TWINRIX. Travelers who receive hepatitis A vaccine <2 weeks before traveling to an endemic area and who do not receive immune globulin either by choice or because of lack of availability likely will be at lower risk of infection than those who do not receive hepatitis A vaccine or IG. In the case of travel within 4 weeks of vaccine administration, a dose of immune globulin (0.02 mL/kg) may be given alone or in addition to hepatitis A vaccine, at a different site, for optimal protection. In the case of unavailability or refusal of immune globulin, administration of hepatitis A vaccine alone for this group is recommended, but they should be informed that they are not optimally protected from acquiring hepatitis A in the immediate future (i.e., the subsequent 2-4 weeks).

Although vaccination of an immune traveler is not contraindicated and does not increase the risk of adverse effects, screening for total anti-HAV before travel can be useful in some circumstances to determine susceptibility and eliminate unnecessary vaccination or IG prophylaxis of immune travelers. Such serologic screening for susceptibility might be indicated for adult travelers who are likely to have had prior HAV infection if the cost of screening (laboratory and office visit) is less than the cost of vaccination or IG prophylaxis and if testing will not delay vaccination and interfere with timely receipt of vaccine or IG before travel. Such travelers may include those >40 years of age and those born in areas of the world with intermediate or high endemicity. Postvaccination testing for serologic response is not indicated.

Using the vaccines according to the licensed schedules is preferable. However, an interrupted series does not need to be restarted. Given their similar immunogenicity, a series that has been started with one brand of monovalent vaccine (i.e., HAVRIX or VAQTA) may be completed with the other brand. Hepatitis A vaccine may be administered at the same time as IG or other commonly used vaccines for travelers, at different injection sites.

In adults and children who have completed the vaccine series, anti-HAV has been shown to persist for at least 5-10 years after vaccination. Results of mathematical models indicate that after completion of the vaccination series, anti-HAV will likely persist for 20 years or more. For children and adults who complete the primary series, booster doses of vaccine are not recommended. Serologic testing to assess antibody levels after vaccination is not indicated.

Travelers who are <2 years of age, are allergic to a vaccine component, or otherwise elect not to receive vaccine should receive a single dose of IG (0.02 mL/kg), which provides effective protection against HAV infection for up to 3 months (Table 4-7). Those who do not receive vaccination and plan to travel for >3 months should receive an IG dose of 0.06 mL/kg, which must be repeated if the duration of travel is >5 months.

Table 4-7. Immune globulin for protection against viral Hepatitis A

Length of stay	Body weight		Dose volume (mL) ¹	Comments
	Lb	Kg		
<3 months	<50	<23	0.5	Dose volume depends on body weight and length of stay.
	50-100	23-45	1.0	
	>100	>45	2.0	
3-5 months	<22	<10	0.5	
	22-49	10-22	1.0	
	50-100	23-45	2.5	
	>100	>45	5.0	

¹For intramuscular injection

Adverse Reactions

Among adults, the most frequently reported side effects occurring 3-5 days after a vaccine dose are tenderness or pain at the injection site (53%-56%) or headache (14%-16%). Among children, the most common side effects reported are pain or tenderness at the injection site (15%-19%), feeding problems (8% in one study), or headache (4% in one study). No serious adverse events in children or adults that could be definitively attributed to the vaccine or increases in serious adverse events among vaccinated persons compared with baseline rates have been identified.

Immune globulin for intramuscular administration prepared in the United States has few side effects (primarily soreness at the injection site) and has never been shown to transmit infectious agents (hepatitis B virus, hepatitis C virus [HCV], or HIV). Since December 1994, all IG products commercially available in the United States have had to undergo a viral inactivation procedure or be negative for HCV RNA before release.

Precautions and Contraindications

These vaccines should not be administered to travelers with a history of hypersensitivity to any vaccine component. HAVRIX or TWINRIX should not be administered to travelers with a history of hypersensitivity reactions to the preservative 2-phenoxyethanol. TWINRIX should not be administered to persons with a history of hypersensitivity to yeast. Because hepatitis A vaccine consists of inactivated virus and hepatitis B vaccine consists of a recombinant protein, no special precautions need to be taken for vaccination of immunocompromised travelers.

Pregnancy

The safety of hepatitis A vaccine for pregnant women has not been determined. However, because hepatitis A vaccine is produced from inactivated HAV, the theoretical risk to either the pregnant woman or the developing fetus is thought to be very low. The risk of vaccination should be weighed against the risk of hepatitis A in women travelers who might be at high risk for exposure to HAV. Pregnancy is not a contraindication to using IG.

Other Prevention Tips

Boiling or cooking food and beverage items for at least 1 minute to 185°F (85°C) inactivates HAV. Foods and beverages heated to this temperature and for this length of time cannot serve as vehicles for HAV infection unless they become contaminated after heating. Adequate chlorination of water as recommended in the United States will inactivate HAV. Travelers should be advised that, to minimize their risk of hepatitis A and other enteric diseases in developing countries, they should avoid potentially contaminated water or

food. Travelers should also be advised to avoid drinking beverages (with or without ice) of unknown purity, eating uncooked shellfish, and eating uncooked fruits or vegetables that are not peeled or prepared by the traveler personally. (See Chapter 2, Risks from Food and Drink.)

Treatment

No specific treatment is available for persons with hepatitis A. Treatment is supportive.

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Prevention of Specific Infectious Diseases

Hepatitis, Viral, Type B

Description

Hepatitis B is caused by the hepatitis B virus (HBV). The clinical manifestations of HBV infection range in severity from no symptoms to fulminant hepatitis. Signs and symptoms of hepatitis B may include fever, malaise, anorexia, nausea, and abdominal discomfort, followed within a few days by jaundice.

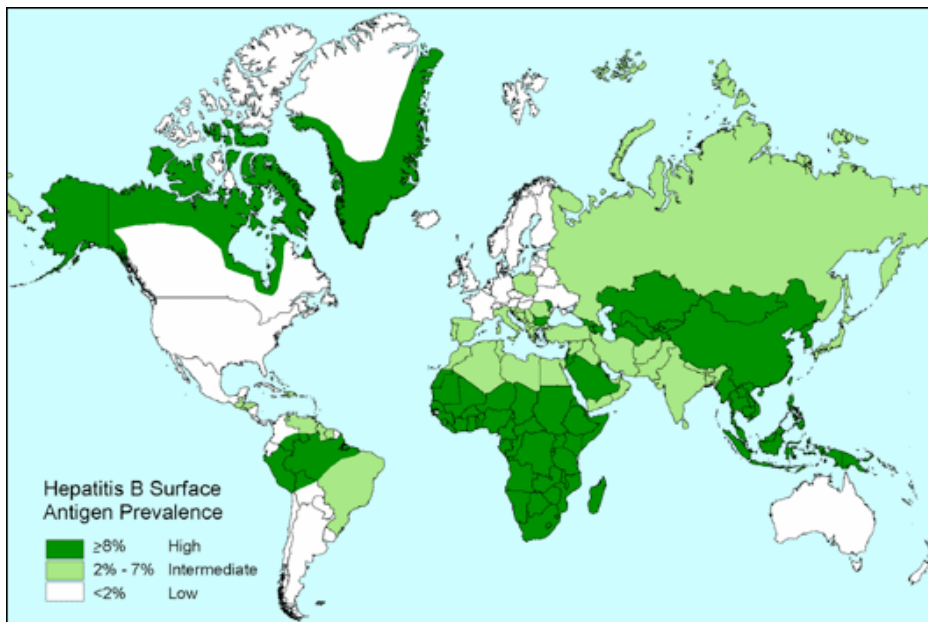
Occurrence

HBV is transmitted through activities that involve contact with blood or blood-derived fluids. Such activities can include unprotected sex with an HBV-infected partner; shared needles used for injection of illegal drugs; work in health-care fields (medical, dental, laboratory, or other) that entails direct exposure to human blood; receiving blood transfusions that have not been screened for HBV; or having dental, medical, or cosmetic (e.g., tattooing or body piercing) procedures with needles or other equipment that are

contaminated with HBV. In addition, open skin lesions, such as those due to impetigo, scabies, or scratched insect bites, can play a role in HBV transmission if direct exposure to wound exudates from HBV-infected persons occurs.

The prevalence of chronic HBV infection is low (<2%) in the general population in Northern and Western Europe, North America, Australia, New Zealand, Mexico, and Southern South America (Map 4-5). In the United States and many other developed countries, children and adolescents are routinely vaccinated against hepatitis B. The highest incidence of disease is in younger adults, and most HBV infections are acquired through unprotected sex with HBV-infected partners or through shared needles used for injection drug use. The prevalence of chronic HBV infection is intermediate (2%-7%) in South Central and Southwest Asia, Israel, Japan, Eastern and Southern Europe, Russia, most areas surrounding the Amazon River basin, Honduras, and Guatemala. The prevalence of chronic HBV infection is high (>8%) in all socioeconomic groups in certain areas: all of Africa; Southeast Asia, including China, Korea, Indonesia, and the Philippines; the Middle East, except Israel; South and Western Pacific islands; the interior Amazon River basin; and certain parts of the Caribbean (Haiti and the Dominican Republic).

Map 4-5. Geographic distribution of Hepatitis B prevalence, 2005



Risk for Travelers

The risk of HBV infection for international travelers is generally low, except for certain travelers in countries where the prevalence of chronic HBV infection is high or intermediate. Factors to consider in assessing risk include 1) the prevalence of chronic HBV infection in the local population, 2) the extent of direct contact with blood or secretions, or of sexual contact with potentially infected persons, and 3) the duration of travel. Modes of HBV transmission in areas with high or intermediate prevalence of chronic HBV infection that are important for travelers to consider are contaminated injection and other equipment used for health care-related procedures and blood transfusions from unscreened donors. However, unprotected sex and sharing illegal drug injection equipment are also risks for HBV infection in these areas.

Clinical Presentation

The incubation period of hepatitis B averages 120 days (range 45-160 days). Constitutional symptoms such as malaise and anorexia may precede jaundice by 1-2 weeks. Clinical symptoms and signs include nausea, vomiting, abdominal pain, and jaundice. Skin rashes, joint pains, and arthritis may occur. The case-fatality rate is approximately 1%. Acute HBV infection causes chronic (long-term) infection in 30%-90% of persons infected as infants or children and in 6%-10% of adolescents and adults. Chronic infection can lead to chronic liver disease, liver scarring (cirrhosis), and liver cancer.

Prevention

Vaccine

Hepatitis B vaccination should be administered to all unvaccinated persons traveling to areas with intermediate to high levels of endemic HBV transmission (i.e., with hepatitis B surface antigen [HBsAg] prevalence >2%) who will have close contact with the local populations. In particular, travelers who will have sex contact or will have daily physical contact with the local population; or who are likely to seek medical, dental, or other treatment in local facilities; or any combination of these activities during their stay should be advised to receive the vaccine.

Hepatitis B vaccination is currently recommended for all United States residents who work in health-care fields (medical, dental, laboratory, or other) that involve potential exposure to human blood. All unvaccinated United States children and adolescents (<19 years old) should receive hepatitis B vaccine. In addition, unvaccinated persons who have indications for hepatitis B vaccination independent of travel should be vaccinated, such as men who have sex with men, injection drug users, and heterosexuals who have recently had a sexually transmitted disease or have had more than one partner in the previous 6 months.

As part of the pre-travel education process, all travelers should be given information about the risks of hepatitis B and other bloodborne pathogens from contaminated medical equipment, injection drug use, or sexual activity, and informed of prevention measures (see below), including hepatitis B vaccination, that can be used to prevent transmission of HBV. Persons who might engage in practices that might put them at risk for HBV infection during travel should receive hepatitis B vaccination if previously unvaccinated. It is reasonable for physicians to consider their ability to accurately assess these potential risks, particularly among travelers to areas with intermediate or high levels of endemic HBV transmission, when considering if hepatitis B vaccine should be offered.

Two monovalent hepatitis B vaccines are currently licensed in the United States: Recombivax HB, manufactured Merck and Co., Inc., and Engerix B, manufactured by GlaxoSmithKline. These vaccines are produced through recombinant DNA technology by baker's yeast into which the gene for HBsAg has been inserted. The usual schedule of primary vaccination consists of three intramuscular doses of vaccine. The recommended dose varies by product and the recipient's age (Table 4-8). The vaccine is usually administered as a three-dose series on a 0, 1, and 6 month schedule. The second dose should be given 1 month after the first dose; the third dose should be given at least 2 months after the second dose and at least 4 months after the first dose. Alternatively, the vaccine produced by GlaxoSmithKline is also approved for administration on a four-dose schedule at 0, 1, 2, and 12 months. There is also a two-dose schedule for a vaccine produced by Merck & Co., Inc., which has been licensed for children and adolescents 11-15 years of age. Using the two-dose schedule, the adult dose of Recombivax-HB is administered, with the second dose given 4-6 months after the first dose. An interrupted hepatitis B vaccine series does not need to be restarted. A three-dose series that has been started with one brand of vaccine may be completed with the other brand.

Twinrix, manufactured by GlaxoSmithKline, is a combined hepatitis A and hepatitis B vaccine licensed for persons 18 years of age or more. Primary immunization consists of three doses, given on a 0-, 1-, and 6-month schedule, the same schedule as that used for single-antigen hepatitis B vaccine (Table 4-6). Twinrix consists of inactivated hepatitis A virus and recombinant HBsAg protein, with aluminum phosphate and aluminum hydroxide as adjuvant and 2-phenoxyethanol as a preservative.

Individual clinicians may choose to use an accelerated schedule (for either the hepatitis B vaccine or Twinrix) (i.e., doses at days 0, 7, and 21) for travelers who will depart before an approved vaccination schedule can be completed. The FDA has not approved accelerated schedules that involve vaccination at more than one time during a single month for hepatitis B vaccines currently licensed in the United States. Persons who receive a vaccination on an accelerated schedule that is not FDA approved should also receive a booster dose at one year after the start of the series to promote long-term immunity.

Table 4-8. Recommended doses of currently licensed Hepatitis B vaccines¹

Group	Dose	
	Recombivax-HB ^{1,2}	Engerix-B ¹
All infants (regardless of mother's HBsAg status), children, adolescents, and adults, birth through 19 years	5 µg	10 µg
Adults ≥ 20 years of age	10 µg	20 µg
Dialysis patients and other immunocompromised persons	40 µg ³	40 µg ⁴

¹Both vaccines are routinely administered in a three-dose series. Engerix-B also has been licensed for a four-dose series administered at 0, 1, 2, and 12 months.

²Recombivax-HB is now approved in a two-dose schedule for 11- to 15-year-olds (see "Preventive Measures").

³Special formulation (40 µg in 1.0 mL)

⁴Two 1.0 mL doses given at one site, in a four-dose schedule at 0, 1, 2, 6 months

Ideally, vaccination should begin at least 6 months before travel so the full vaccine series can be completed before departure. Because some protection is provided by one or two doses, the vaccine series should be initiated, if indicated, even if it cannot be completed before departure. Optimal protection, however, is not conferred until after the final vaccine dose. There is no interference between hepatitis B vaccine and other simultaneously administered vaccine(s) or with IG. The optimum site of injection in adults is the deltoid muscle. Long-term studies of healthy adults and children indicate that immunologic memory remains intact for at least 15 years and confers protection against chronic HBV infection, even though hepatitis B surface antibody (anti-HBs) levels can become low or decline below detectable levels. For children and adults whose immune status is normal, booster doses of vaccine are not recommended. Serologic testing to assess antibody levels is not necessary for most vaccinees. (See Vaccine Recommendations for Infants and Children, for a discussion of the hepatitis B immunization schedule for infants who will be traveling.)

Adverse Reactions

Hepatitis B vaccines have been shown to be very safe for persons of all ages. Pain at the injection site (3%-29%) and elevated temperature >37.7°C (>99.9°F) (1%-6%) are the most frequently reported side effects among vaccine recipients. In placebo-controlled studies, these side effects were reported no more frequently among persons receiving hepatitis B vaccine than among those receiving placebo. Among children receiving both hepatitis B vaccine and diphtheria-tetanus-pertussis (DTP) vaccine, these mild side effects have been observed no more frequently than among children receiving DTP vaccine alone. For hepatitis A vaccine (a component of the combination hepatitis A/hepatitis B vaccine Twinrix), the most frequently reported adverse reactions occurring within 3-5 days were soreness or pain at the injection site (56% among adults and 8% among children) and headache (14% among adults and 4% among children). No serious adverse events among children or adults that could be definitively attributed to hepatitis A vaccine or increases in serious adverse events among vaccinated persons compared with baseline rates have been identified.

Precautions and Contraindications

These vaccines should not be administered to persons with a history of hypersensitivity to any vaccine component, including yeast. The vaccine contains a recombinant protein (HBsAg) that is noninfectious. Limited data indicate that there is no apparent risk of adverse events to the developing fetus when hepatitis B vaccine is administered to pregnant women. HBV infection affecting a pregnant woman can result in serious disease for the mother and chronic infection for the newborn. Neither pregnancy nor lactation should be considered a contraindication for vaccination.

Behavioral preventive measures are similar to those for HIV infection and AIDS. When seeking medical or dental care, travelers should be advised to be alert to the use of medical, surgical, and dental equipment that has not been adequately sterilized or disinfected, reuse of contaminated equipment, and unsafe injecting practices (e.g., reuse of disposable needles and syringes). HBV and other bloodborne pathogens can be transmitted if tools are not sterile or if the tattoo artist or piercer does not follow other proper infection-control procedures (e.g., washing hands, using latex gloves, and cleaning and disinfecting surfaces and instruments). Travelers should be advised to consider the health risks if they are considering getting a tattoo or body piercing in areas where adequate sterilization or disinfection procedures might not be available or practiced. (See Seeking health care abroad.)

Treatment

No specific treatment is available for acute illness caused by hepatitis B. Antiviral drugs are approved for the treatment of chronic hepatitis B.

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- Anthony Fiore and Beth Bell

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Prevention of Specific Infectious Diseases

Influenza

Description

Influenza is caused by infection with either influenza A or B viruses. Influenza A viruses are further classified into subtypes on the basis of two surface proteins: hemagglutinin (H) and neuraminidase (N). Both influenza A and B viruses undergo continual minor antigenic change (i.e., drift), but influenza B viruses evolve more slowly and are not divided into subtypes. Influenza A (H1N1), A (H1N2), A (H3N2), and influenza B viruses currently circulate globally.

Occurrence

In the Northern Hemisphere, seasonal epidemics of influenza generally occur during the winter months on an annual or near annual basis and are responsible for approximately 36,000 deaths in the United States each year. Influenza virus infections cause disease in all age groups. Rates of infection are highest among infants, children, and adolescents, but rates of serious morbidity and mortality are highest among persons ≥ 65 years of age and persons of any age who have medical conditions that place them at high risk for complications from influenza (e.g., chronic cardiopulmonary disease). Children aged <2 years have rates of influenza-related hospitalization that are as high as those in the elderly. The emergence of a novel human influenza A virus could lead to a global pandemic, during which rates of morbidity and mortality from influenza-related complications could increase dramatically.

Risk for Travelers

The risk for exposure to influenza during international travel depends on the time of year and destination. In the tropics, influenza can occur throughout the year, while in the temperate regions of the Southern Hemisphere most activity occurs from April through September. In temperate climates, travelers can also be exposed to influenza during the summer, especially when traveling as part of large tourist groups with travelers from areas of the world where influenza viruses are circulating. Influenza vaccine should be recommended before travel for persons at high risk for complications of influenza if 1) influenza vaccine was not received during the preceding fall or winter, 2) travel is planned to the tropics, 3) travel is planned with large groups of tourists at any time of year, or 4) travel is planned to the Southern Hemisphere from April through September. In North America, travel-related influenza vaccination should take place by spring when possible, because influenza vaccine may not be available during the summer. Travelers at high risk for influenza-related complications who plan summer travel should consult with their physicians to discuss the symptoms and risks of influenza before embarking.

Clinical Presentation

Uncomplicated influenza illness is characterized by the abrupt onset of constitutional and respiratory signs and symptoms (e.g., fever, myalgia, headache, malaise, nonproductive cough, sore throat, and rhinitis). Among children, otitis media, nausea, and vomiting are also commonly reported with influenza illness. Respiratory illness caused by influenza is difficult to distinguish from illness caused by other respiratory pathogens on the basis of symptoms alone, and laboratory testing can aid in diagnosis. Influenza illness typically resolves relatively quickly for most persons, although cough and malaise can persist for >2 weeks. Influenza can exacerbate chronic conditions (e.g., pulmonary or cardiac disease), leading to secondary infections and severe complications. Influenza-related deaths can result from pneumonia as well as from exacerbations of cardiopulmonary conditions and other chronic diseases.

Prevention

Vaccines

Annual vaccination of persons at high risk for complications before the influenza season is the most effective measure for preventing influenza and associated complications. Two types of influenza vaccine are currently available for use in the United States: inactivated vaccine, administered by intramuscular injection, and live, attenuated influenza vaccine (LAIV), administered by nasal spray. LAIV is approved for use only in healthy persons 5-49 years of age. Annual influenza vaccination is recommended for the following groups who are at high risk for complications from influenza:

- Persons ≥ 50 years of age.
- Residents of nursing homes and other chronic-care facilities that house people of any age who have chronic medical conditions.
- Anyone ≥ 6 months of age who has a chronic disorder of the pulmonary or cardiovascular system, including asthma.
- Anyone ≥ 6 months of age who has required regular medical follow-up or hospitalization during the preceding year because of a chronic metabolic disease (including diabetes mellitus), renal dysfunction, hemoglobinopathy, or immunosuppression (including immunosuppression caused by medications and HIV).
- Anyone 6 months to 18 years of age who is receiving long-term aspirin therapy and might be at risk

for developing Reye syndrome after influenza.

- Women who will be pregnant during the influenza season.
- Children aged 6-23 months.
- Health-care workers and others (including household members) in close contact with persons at high risk for developing influenza-related complications.

Dosing, Timing, and Route of Vaccination

For persons at high risk for complications from influenza, annual vaccination is recommended because vaccine-derived immunity declines during the year and because the vaccine strains are continually updated to reflect ongoing antigenic changes among circulating influenza viruses. Dosage recommendations differ according to age group and type of vaccine used. For inactivated vaccine, two doses administered at least 1 month apart are required for previously unvaccinated infants and children <9 years of age. For previously unvaccinated children aged 5-8 years receiving LAIV, two doses are administered at least 6 weeks apart. For situations in which a child receives two different vaccine types, 4 weeks should separate doses if inactivated vaccine is used first, and 6 weeks should separate doses if LAIV is used first. In adults, studies have indicated little or no improvement in antibody response when a second dose of inactivated vaccine is administered during the same season; therefore, a booster is not recommended. For inactivated vaccine, infants and young children should be vaccinated in the anterolateral aspect of the thigh; all other recipients should be vaccinated in the deltoid muscle. LAIV is administered by nasal spray.

The target groups for influenza and pneumococcal vaccination overlap considerably. For travelers at high risk who have not previously been vaccinated with pneumococcal vaccine, health-care providers should strongly consider administering pneumococcal and influenza vaccines concurrently. Both vaccines can be administered at the same time at different sites without increasing side effects. Infants and children can receive influenza vaccine at the same time they receive other routine vaccinations.

Composition of the Vaccines

Both influenza vaccines contain three strains of inactivated influenza viruses. Viruses in inactivated vaccines are killed, while those in LAIV are live. These live viruses are attenuated and do not cause disease. The viruses used in both vaccines are representative of viruses likely to circulate in the upcoming season, and usually one or more vaccine strains are updated annually. Because the vaccine is grown in hen eggs, the vaccine may contain small amounts of egg protein. Influenza vaccine distributed in the United States may also contain thimerosal, a mercury-containing preservative. The package insert should be consulted regarding the use of other compounds to inactivate the viruses or limit bacterial contamination.

Adverse Reactions

Inactivated Vaccine

The most frequent side effect of vaccination with inactivated vaccine is soreness at the vaccination site that lasts up to 2 days. These local reactions generally are mild and rarely interfere with the ability to conduct usual daily activities. Fever, malaise, myalgia, and other systemic symptoms can occur following vaccination and most often affect people who have had no previous exposure to the influenza virus antigens in the vaccine (e.g., young children). These reactions begin 6 to 12 hours after vaccination and can persist for 1 to 2 days.

LAIV

The most frequent side effects of vaccination with LAIV include nasal congestion, headache, fever, vomiting, abdominal pain, and myalgia. These symptoms are associated more often with the first dose and are self-limited. There may be an increase in asthma or reactive airway disease in children aged <5 years, and LAIV is not approved for use among children in this age group.

Other Reactions

Allergic

Immediate reactions (e.g., hives, angioedema, allergic asthma, and systemic anaphylaxis) rarely occur after influenza vaccination. These reactions probably result from hypersensitivity to some vaccine component; most reactions likely are caused by residual egg protein and occur among people who have severe egg allergy. People who have developed hives, have had swelling of the lips or tongue, or have experienced acute respiratory distress or collapse after eating eggs should consult a physician for

appropriate evaluation to determine if vaccine should be administered. People who have documented immune globulin E (IgE)-mediated hypersensitivity to eggs, including those who have had occupational asthma or other allergic responses due to exposure to egg protein, may also be at increased risk for reactions from influenza vaccine, and similar consultation should be advised. Protocols have been published for safely administering influenza vaccine to people with egg allergies.

Guillain-Barré Syndrome (GBS)

Investigations to date indicate no substantial increase in GBS associated with influenza vaccines (other than the "swine flu" vaccine of 1976). A study of the 1992-93 and 1993-94 influenza seasons estimated a risk of GBS of slightly more than 1 case per million people vaccinated. The potential benefits of influenza vaccination in preventing serious illness, hospitalization, and death greatly outweigh the possible risks for developing vaccine-associated GBS.

Precautions and Contraindications

Pregnancy

Many experts consider influenza vaccination with inactivated vaccine safe during any stage of pregnancy. A study of influenza vaccination of more than 2,000 pregnant women demonstrated no adverse fetal effects associated with influenza vaccine. Influenza vaccine does not affect the safety of mothers who are breastfeeding or their infants. Breastfeeding does not adversely affect immune response and is not a contraindication for vaccination.

Persons Infected with HIV

Information is limited on the frequency and severity of influenza illness or the benefits of influenza vaccination among HIV-infected persons. On the basis of a risk-modeling study, the risk for influenza-related death among persons with AIDS appears higher than among those without AIDS. In addition, symptoms of influenza might be prolonged and the risk for complications from influenza increased for certain HIV-infected persons. HIV-infected persons who have minimal AIDS-related symptoms and high CD4+ T-lymphocyte cell counts can develop protective influenza antibody titers from influenza vaccine, and vaccination has been shown to prevent influenza in this group. However, influenza vaccine might not induce protective antibody titers in people who have advanced HIV disease and low CD4+ T-lymphocyte cell counts; a second dose of vaccine does not improve the immune response in these persons. Deterioration of CD4+ T-lymphocyte cell counts and progression of HIV disease have not been demonstrated among HIV-infected people who receive the vaccine. The effect of antiretroviral therapy on potential increases in HIV ribonucleic acid (RNA) levels following either natural influenza infection or influenza vaccine is unknown. Because influenza can result in serious illness and complications and because influenza vaccination can result in the production of protective antibody titers, vaccination will benefit many HIV-infected persons, including HIV-infected pregnant women.

Antiviral Medications

Influenza-specific antiviral drugs for chemoprophylaxis of influenza are important adjuncts to vaccine. The four currently licensed U.S. antiviral agents are amantadine, rimantadine, zanamivir, and oseltamivir. Amantadine and rimantadine are active against influenza A viruses but not influenza B viruses. Both drugs are approved by the U.S. Food and Drug Administration for the prophylaxis of influenza A virus infections. Oseltamivir has activity against both influenza A and B viruses and has been approved for prophylaxis. Amantadine and rimantadine are approved for prophylaxis in persons aged ≥ 1 year, and oseltamivir is approved for prophylaxis in persons aged ≥ 13 years.

Treatment

Amantadine and rimantadine are approved by the U.S. Food and Drug Administration for the treatment of influenza A virus infections. Zanamivir and oseltamivir are currently approved for treatment of both influenza A and B virus infections. These four drugs differ in dosing, approved age groups for use, side effects, and cost. The package inserts should be consulted for more information.

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Prevention of Specific Infectious Diseases

Rabies

Description

Rabies is an acute, fatal encephalomyelitis caused by neurotropic viruses in the family Rhabdoviridae, genus Lyssavirus. It is almost always transmitted by an animal bite that inoculates the virus into wounds. Very rarely, rabies has been transmitted by exposures other than bites that introduce the virus into open wounds or mucous membranes. All mammals are believed to be susceptible, but reservoirs are carnivores and bats. Although dogs are the main reservoir in developing countries, the epidemiology of the disease differs sufficiently from one region or country to another to warrant the medical evaluation of all mammal bites.

Occurrence

Rabies is found on all continents except Antarctica. In certain areas of the world, canine rabies remains highly endemic, including (but not limited to) parts of Afghanistan, Bangladesh, Brazil, Bolivia, China, Colombia, Ecuador, El Salvador, Guatemala, Haiti, India, Indonesia, Mexico, Myanmar (Burma), Nepal, Pakistan, Peru, the Philippines, Sri Lanka, Thailand, Vietnam, and Yemen. The disease is also found in dogs in many of the other countries of Africa, Asia, and Central and South America, except as noted in Table 4-14, which lists countries that have reported no cases of rabies during the most recent period for which information is available (formerly referred to as "rabies-free countries").

Additional information can be obtained from the World Health Organization (<http://www.who.int/GlobalAtlas/DataQuery/browse.asp?catID=01150000000&lev=3>), the Pan American Health Organization, local health authorities of the country, the embassy, or the local consulate's office in the United States. Lists are provided only as a guide, because status can change suddenly as a result of disease re-introduction.

Table 4-14. Countries and political units reporting no indigenous cases of rabies during 2003¹

Region	Countries
Africa	Cape Verde, Libya, Mauritius, Réunion, São Tome and Príncipe, and Seychelles

Americas	North: Bermuda, St. Pierre and Miquelon Caribbean: Antigua and Barbuda, Aruba, Bahamas, Barbados, Cayman Islands, Dominica, Guadeloupe, Jamaica, Martinique, Montserrat, Netherlands Antilles, Saint Kitts (Saint Christopher) and Nevis, Saint Lucia, Saint Martin, Saint Vincent and Grenadines, Turks and Caicos, and Virgin Islands (UK and US) South: Uruguay
Asia	Armenia, Cyprus, Hong Kong, Japan, Kuwait, Lebanon, Malaysia (Sabah), Qatar, and Singapore
Europe	Belgium, Denmark ² , Finland, France ² , Gibraltar, Greece, Iceland, Ireland, Isle of Man, Italy, Luxemburg, Malta, Netherlands ² , Norway (mainland), Portugal, Spain ² (except Ceuta/Melilla), Sweden, Switzerland, and United Kingdom ²
Oceania ³	Australia ² , Cook Islands, Fiji, French Polynesia, Guam, Hawaii, Kiribati, Micronesia, New Caledonia, New Zealand, Palau, Papua New Guinea, Samoa, and Vanuatu

¹Bat rabies may exist in some areas that are reportedly free of rabies in other animals.

²Bat lyssaviruses are known to exist in these areas that are reportedly free of rabies in other animals.

³Most of Pacific Oceania is reportedly rabies-free.

Risk for Travelers

Travelers to rabies-endemic countries should be warned about the risk of acquiring rabies, although rabies vaccination is not a requirement for entry into any country. Travelers with extensive unprotected outdoor exposure in rural areas, such as might be experienced while bicycling, camping, hiking, or engaging in certain occupational activities, might be at high risk even if their trip is brief. Casual exposure to cave air is not a concern, but cavers should be warned not to handle bats.

Clinical Description

The disease progresses from a nonspecific prodromal phase to paresis or paralysis; spasms of swallowing muscles can be stimulated by the sight, sound, or perception of water (hydrophobia); delirium and convulsions can develop, followed by coma and death.

Prevention

Preexposure vaccination with human diploid cell rabies vaccine (HDCV), purified chick embryo cell (PCEC) vaccine, or rabies vaccine adsorbed (RVA) may be recommended for international travelers based on the local incidence of rabies in the country to be visited, the availability of appropriate antirabies biologicals, and the intended activity and duration of stay of the traveler. Preexposure vaccination may be recommended for veterinarians, animal handlers, field biologists, spelunkers, missionaries, and certain laboratory workers. Table 4-15 provides criteria for preexposure vaccination. Preexposure vaccination does not eliminate the need for additional medical attention after a rabies exposure but simplifies postexposure prophylaxis in populations at risk by eliminating the need for rabies immune globulin (RIG) and by decreasing the number of doses of vaccine required. Preexposure vaccination is of particular importance for travelers at risk of exposure to rabies in countries where biologicals are in short supply and locally available rabies vaccines might carry a high risk of adverse reactions. Preexposure vaccination may also provide some degree of protection when there is an unapparent or unrecognized exposure to rabies and when postexposure prophylaxis might be delayed.

Table 4-15. Criteria for preexposure immunization for rabies

Risk Category	Nature of Risk	Typical Populations	Preexposure regimen
Continuous	Virus present continuously, often in high concentrations Specific exposures	Rabies research laboratory workers ¹ , rabies biologics production workers	Primary course: Serologic testing every 6 months; booster vaccination if antibody titer is below

	likely to go unrecognized		acceptable level ²
Frequent	Exposure usually episodic with source recognized, but exposure might also be unrecognized Bite, nonbite, or aerosol exposure possible	Rabies diagnostic laboratory workers ¹ , cavers, veterinarians and staff, and animal control and wildlife workers in rabies-epizootic areas	Primary course: Serologic testing every 2 years; booster vaccination if antibody titer is below acceptable level ²
Infrequent (greater than general population)	Exposure nearly always episodic with source recognized Bite or nonbite exposure	Veterinarians, animal control and wildlife workers in areas with low rabies rates; veterinary students; and travelers visiting areas where rabies is enzootic and immediate access to appropriate medical care, including biologics, is limited.	Primary course: No serologic testing or booster vaccination
Rare (general population)	Exposure always episodic, with source recognized Bite or nonbite exposure	U.S. population at large, including individuals in rabies-epizootic areas	No preexposure immunization necessary.

¹Judgment of relative risk and extra monitoring of vaccination status of laboratory workers is the responsibility of the laboratory supervisor (see U.S. Department of Health and Human Service's Biosafety in Microbiological and Biomedical Laboratories, 1999).

²Preexposure booster immunization consists of one dose of human diploid cell [rabies] vaccine (HDCV), purified chick embryo cell (PCEC) vaccine, or rabies vaccine adsorbed (RVA), 1.0 mL dose, intramuscular (IM) (deltoid area). Minimum acceptable antibody level is complete virus neutralization at a 1:5 serum dilution by the rapid fluorescent focus inhibition test. A booster dose should be administered if titer falls below this level.

Purified equine rabies immune globulin (ERIG) has been used effectively in some developing countries where human rabies immune globulin (RIG) might not have been available. If necessary, such heterologous product is preferable to no RIG administration in human rabies postexposure prophylaxis. The incidence of adverse reactions after the use of these products has been low (0.8%-6.0%), and most of those that occurred were minor. However, such products are neither evaluated by U.S. standards nor regulated by the U.S. Food and Drug Administration, and their use cannot be unequivocally recommended at this time. In addition, unpurified antirabies serum of equine origin might still be used in some countries where neither human RIG nor ERIG are available. The use of this antirabies serum is associated with higher rates of serious adverse reactions, including anaphylaxis.

Travelers should be advised that any animal bite or scratch should receive prompt local treatment by thorough cleansing of the wound with copious amounts of soap and water and a povidone-iodine solution if available; this local treatment will substantially reduce the risk of rabies. Travelers who might have been exposed to rabies should be advised to always contact local health authorities immediately for advice about postexposure prophylaxis and should also contact their personal physician or state health department as soon as possible thereafter.

Tables 4-16 and 4-17 provide information on preexposure and postexposure prophylaxis. Routine serologic testing is not necessary for travelers who receive the recommended preexposure or postexposure regimen with HDCV, PCEC, or RVA vaccines. Exposed travelers previously vaccinated with vaccines other than those produced by cell culture should receive the complete postexposure regimen unless they have developed a laboratory-confirmed antibody response to the primary vaccination. Serologic testing is still recommended for travelers whose immune response might be diminished by drug therapy or by diseases. Rabies preexposure prophylaxis may not be indicated for travelers to the countries in Table 4-14, and postexposure prophylaxis is rarely necessary after exposures to terrestrial animals in these countries.

Table 4-16. Preexposure immunization for rabies¹

Vaccine	Dose (mL)	No. of Doses	Schedule (days)	Route
HDCV	1.0	3	0, 7, 21 or 28	Intramuscular
PCEC	1.0	3	0, 7, 21 or 28	Intramuscular
RVA	1.0	3	0, 7, 21 or 28	Intramuscular

HDCV, human diploid cell vaccine; PCEC, purified chick embryo cell; RVA, rabies vaccine adsorbed.

¹Patients who are immunosuppressed by disease or medications should postpone preexposure vaccinations and consider avoiding activities for which rabies preexposure prophylaxis is indicated. When this course is not possible, immunosuppressed persons who are at risk for rabies should have their antibody titers checked after vaccination. Thus, preexposure immunization of immunosuppressed travelers is not recommended.

Table 4-17. Postexposure immunization for rabies¹

Immunization Status	Vaccine / Product	Dose	No. of doses	Schedule (days)	Route
Not previously immunized	RIG <i>plus</i>	20 IU/kg body weight	1	0	Infiltrated at bite site (if possible); remainder intramuscular.
	HDCV or PCEC or RVA	1.0 mL	5	0, 3, 7, 14, 28	Intramuscular
Previously immunized ^{2, 3}	HDCV PCEC RVA ³	1.0 mL	2	0, 3	Intramuscular

RIG, rabies immune globulin; HDCV, human diploid cell (rabies) vaccine; PCEC, purified chick embryo cell; RVA, rabies vaccine adsorbed.

¹All postexposure prophylaxis should begin with immediate thorough cleansing of all wounds with soap and water.

²Preexposure immunization with HDCV, PCEC, or RVA; prior postexposure prophylaxis with HDCV, PCEC, or RVA; or persons previously immunized with any other type of rabies vaccine and a documented history of positive antibody response to the prior vaccination.

³RIG should not be administered.

Adverse Reactions

Travelers should be advised that they may experience local reactions, such as pain, erythema, and swelling or itching at the injection site, or mild systemic reactions, such as headache, nausea, abdominal pain, muscle aches, and dizziness. Approximately 6% of persons receiving booster vaccinations with HDCV can experience an immune complex-like reaction characterized by urticaria, pruritus, and malaise. Once initiated, rabies postexposure prophylaxis should not be interrupted or discontinued because of local or mild systemic reactions to rabies vaccine.

Precautions and Contraindications

Pregnancy

Pregnancy is not a contraindication to postexposure prophylaxis.

Age

In infants and children, the dose of HDCV, PCEC, or RVA for preexposure or postexposure prophylaxis is the same as that recommended for adults. The dose of RIG for postexposure prophylaxis is based on body weight (Table 4-17).

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Prevention of Specific Infectious Diseases

Travelers' Diarrhea

Description

Travelers' diarrhea (TD) is a clinical syndrome resulting from microbial contamination of ingested food and water; it occurs during or shortly after travel, most commonly affecting persons traveling from an area of more highly developed hygiene and sanitation infrastructure to a less developed one. Thus, TD is defined more by circumstances of acquisition than by a specific microbial agent. In fact, there is considerable diversity in etiologic agents, which include bacteria, parasites, or viruses. A similar but less common syndrome is toxic gastroenteritis, caused by ingestion of pre-formed toxins. In this syndrome, vomiting may predominate, and symptoms usually resolve within 12-18 hours.

Pathogen isolation rates among TD studies vary from 30% to 60%. Most cases in which no pathogen is identified respond to antibiotics, suggesting that most of these are bacterial in origin.

Bacterial Enteric Pathogens

Bacteria are the most common cause of TD. In studies of etiologic agents at various destinations, bacteria are responsible for approximately 85% of TD cases, parasites about 10%, and viruses 5%.

Enterotoxigenic *Escherichia coli* (ETEC)

The most common cause of TD worldwide is ETEC. Ingestion of a large inoculum of this organism is necessary to produce disease. These high inoculums occur when there is a breakdown in sanitation, which

is often the case in developing countries where ETEC infections are common. ETEC typically produces a watery diarrhea associated with cramps. Fever may be low or absent.

Enteroaggregative *E. coli* (EAEC)

EAEC are increasingly recognized as a cause of TD and may be responsible for up to 25% of cases. EAEC resemble ETEC in clinical presentation and response to antibiotics.

Campylobacter jejuni

Campylobacter jejuni is a common cause of diarrhea in developed countries but is many times more prevalent in developing countries. The risk of acquiring infection with *Campylobacter* appears to vary by destination, with travel to Asia posing a higher risk in most studies. *Campylobacter* infections may be associated with bloody diarrhea as well as fever.

***Salmonella* spp.**

Although nontyphoidal *Salmonella* infections are frequently associated with foodborne outbreaks in industrialized countries, they are an infrequent cause of TD worldwide.

***Shigella* spp.**

The low infectious dose of this organism makes it one of the more commonly reported bacteria associated with TD. *Shigella* may cause a bloody diarrhea with constitutional symptoms and fever.

***Vibrio* spp.**

Diarrhea caused by *Vibrio parahaemolyticus* and non-O-group 1 *Vibrio cholerae* may be associated with eating raw or partially cooked seafood. *Vibrio cholerae* O-group 1 has in general been a rare cause of TD, but recent reports suggest this organism may be associated with the typical TD clinical picture in Western travelers to developing countries.

Other Bacteria

Other organisms that have been isolated from patients with TD include *Aeromonas hydrophila*, *Plesiomonas shigelloides*, and *Yersinia enterocolitica*.

Parasitic Enteric Pathogens

Parasitic protozoan pathogens account for about 10% of cases of TD and usually present with a more insidious onset. Travelers often complain of persistent symptoms, and the likelihood of recovery of a parasite rather than bacteria from stool specimens increases proportionately with duration of symptoms. The most common organisms in this category include *Giardia intestinalis*, *Cryptosporidium parvum*, *Cyclospora cayatanensis*, *Entamoeba histolytica*, and *Dientamoeba fragilis*.

Viral Enteric Pathogens

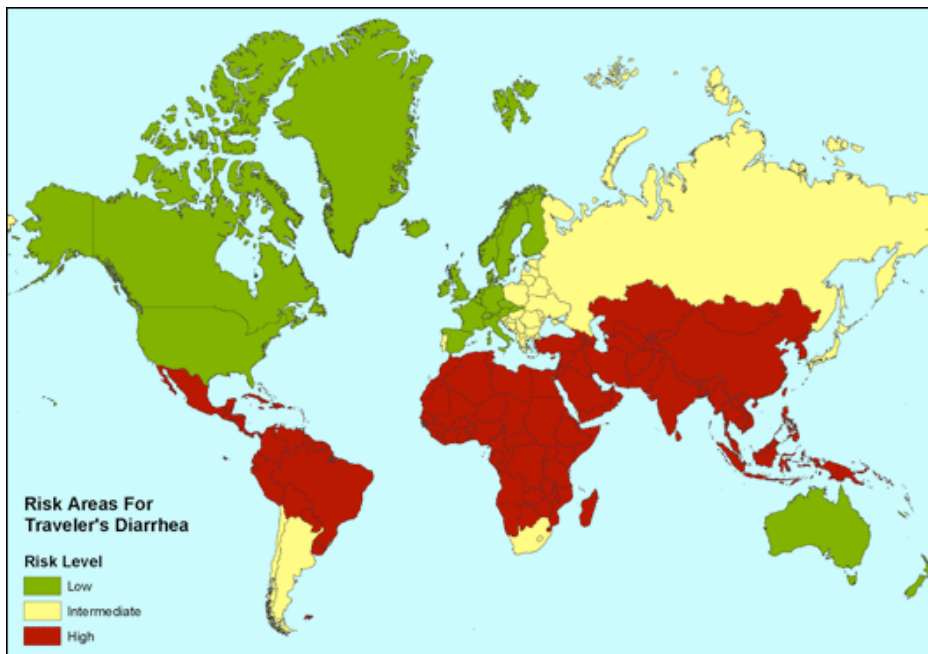
The contribution of viruses to the burden of TD appears to be quite small, although they can cause substantial morbidity from gastroenteritis, with primarily nausea and vomiting. Sporadic viral infections account for 5%-10% of cases of TD. Enteric viruses such as rotavirus and norovirus, which infect children in developing countries, may also infect travelers to developing countries. Outbreaks of norovirus have been reported on cruise ships. In such outbreaks, a high percentage of susceptible people are likely to become ill.

Occurrence

The most important determinant of risk is travel destination, and there are regional differences in both the risk and etiology of diarrhea. The world map is generally divided into three grades of risk: high, intermediate, and low. (See map 4-11). Low-risk countries include the USA, Canada, Australia, New Zealand, Japan, and countries in Northern and Western Europe. Intermediate-risk countries include those in Eastern Europe, South Africa, and some of the Caribbean islands. High-risk areas include most of Asia, the Middle East, Africa, and Central and South America. Some destinations that were previously considered high risk have now been classified as low or intermediate risk, including parts of Southern Europe and some of the Caribbean islands. On average, 30%-50% of travelers to high-risk areas will

develop TD during a 1- to 2-week stay. Based on the annual figure of 50 million travelers to developing countries, this estimate translates to approximately 50,000 cases of TD each day. In more temperate regions, there may be seasonal variations in diarrhea risk. In South Asia, for example, during the hot months preceding the monsoon, much higher TD attack rates are commonly reported.

Map 4-11. Areas of risk for travelers' diarrhea



Risk for Travelers

Travelers' diarrhea occurs equally in males and females and is more common in young adults than in older people. In short-term travelers, bouts of TD do not appear to protect against future attacks, and more than one episode of TD may occur during a single trip.

Clinical Presentation

Definitions of TD that rely on rigid criteria for frequency of loose stools in a 24-hour period are commonly used in clinical research studies but are not relevant to the clinical syndrome as it affects travelers.

Travelers' diarrhea is characterized by the fairly abrupt onset of loose, watery or semi-formed stools associated with abdominal cramps and rectal urgency. Symptoms may be preceded by a prodrome of gaseousness and abdominal cramping and additional symptoms may be associated, such as nausea, bloating, and fever. Vomiting may occur in up to 15% of those affected. Travelers' diarrhea is generally self-limited and lasts 3-4 days even without treatment, but persistent symptoms may occur in a small percentage of travelers. Postinfectious sequelae have been described, including reactive arthritis, Guillain-Barré syndrome, and postinfectious irritable bowel syndrome (PI-IBS). PI-IBS may occur in up to 3% of persons who contracted travelers' diarrhea.

Prevention

For travelers to high-risk areas, several approaches may be recommended, which can minimize but never completely eliminate the risk of TD. These include 1) instruction regarding food and beverage selection, 2) use of agents other than antimicrobial drugs for prophylaxis, and 3) use of prophylactic antibiotics.

Care in selecting food and beverages for consumption may minimize the risk for acquiring TD. Travelers should be advised to eat foods that are freshly cooked and served piping hot and to avoid water and beverages diluted with water (reconstituted fruit juices, ice, milk) and foods washed in water, such as salads. Other risky foods include raw or undercooked meat and seafood and raw fruits and vegetables.

Safe beverages include those that are bottled and sealed or carbonated. Boiled beverages and those appropriately treated with iodine or chlorine might also be safely consumed. Studies of TD risk at high-risk destinations show that consumption of food or beverages from street vendors poses a particularly high risk, and some studies suggest certain food items such as reheated prepared foods or buffet items are also high risk.

Although food and water precautions continue to be recommended, travelers may have difficulty following this advice. Furthermore, many of the factors that ensure food safety are out of the traveler's control.

The primary agent other than antimicrobial drugs studied for prevention of TD is bismuth subsalicylate (BSS), which is the active ingredient in Pepto-Bismol. Studies from Mexico have shown this agent (taken as either 2 oz of liquid or two chewable tablets four times per day) to reduce the incidence of TD from 40% to 14%. BSS commonly causes blackening of the tongue and stool and may cause nausea, constipation, and rarely tinnitus. BSS should be avoided by travelers with aspirin allergy, renal insufficiency, and gout and by those taking anticoagulants, probenecid, or methotrexate. In travelers taking aspirin or salicylates for other reasons, the use of BSS may result in salicylate toxicity. Caution should be used in administering BSS to children with viral infections, such as chickenpox or influenza, because of the risk of Reye syndrome. BSS is not recommended for children <3 years of age. Studies have not established the safety of BSS use for periods of greater than 3 weeks.

The use of probiotics, such as *Lactobacillus* GG and *Saccharomyces boulardii*, has been studied in the prevention of TD in limited numbers of subjects. Results are inconclusive.

Travelers should be cautioned that other nonantimicrobial agents, such as enterovioform and related halogenated hydroxyquinoline derivatives, are sometimes available to travelers at their destination. These substances are not useful in preventing TD, may cause serious neurologic adverse events, and should never be used for prophylaxis.

Prophylactic antibiotics have been demonstrated to be quite effective in the prevention of TD. Controlled studies have shown that diarrhea attack rates are reduced from 40% to 4% by the use of antibiotics. The ideal antibiotic is one to which the pathogenic bacteria are sensitive, which has changed over the past few decades as resistance patterns have evolved. Agents such as TMP-SMX and doxycycline are no longer considered effective antimicrobials against enteric bacterial pathogens. The fluoroquinolones have been the most popular and effective antibiotics for the prophylaxis and treatment of bacterial TD pathogens, but increasing resistance to these agents, initially among *Campylobacter* species and now among other TD pathogens, may limit their benefit in the future. A newly approved nonabsorbable antibiotic, rifaximin, is being investigated for its potential use in TD prophylaxis. Prophylactic antibiotics should not be recommended for most travelers. In addition to affording no protection against nonbacterial pathogens, they may also give the traveler a false sense of security, leading to neglect of the food and water precautions that might protect against other enteric diseases. In addition, the use of antibiotics may be associated with allergic or adverse reactions in a certain percentage of travelers, an unnecessary occurrence, as early self-treatment with antibiotics for established TD is quite effective.

Prophylactic antibiotics may be considered for short-term travelers who are high-risk hosts (such as those who are immunosuppressed) or are taking critical trips during which even a short bout of diarrhea could impact the purpose of their trip.

Treatment

Antibiotics are the principal element in the treatment of TD. Adjunctive agents used for symptomatic control may also be recommended.

Antibiotics

As bacterial causes of TD far outnumber other microbial etiologies, empiric treatment with an antibiotic directed at enteric bacterial pathogens remains the best therapy for TD. The benefit of treatment of TD with antibiotics has been proven in a number of studies. The effectiveness of a particular antimicrobial depends on the etiologic agent and its antibiotic sensitivity. Both as empiric therapy or for treatment of a specific bacterial pathogen, first-line antibiotics include those of the fluoroquinolone class, such as ciprofloxacin or levofloxacin. Increasing microbial resistance to the fluoroquinolones, especially among *Campylobacter* isolates, may limit their usefulness in some destinations such as Thailand and Nepal. An alternative to the fluoroquinolones in this situation is azithromycin. Rifaximin has been approved for the treatment of TD

caused by noninvasive strains of *E. coli*.

The standard treatment regimens consist of 3 days of antibiotic, although when treatment is initiated promptly shorter courses, including single-dose therapy, may reduce the duration of the illness to a few hours.

Nonspecific Agents

Bismuth subsalicylate (Pepto-Bismol), taken as 1 oz of liquid or two chewable tablets every 30 minutes for eight doses, has been shown to decrease stool frequency and shorten the duration of illness in several placebo-controlled studies. This agent has both antisecretory and antimicrobial properties. BSS should be used with caution in travelers on aspirin therapy or anticoagulants or those who have renal insufficiency. In addition, BSS should be avoided in children with viral infections, such as varicella or influenza, because of the risk of Reye syndrome.

Other nonspecific agents, such as kaolin pectin, activated charcoal, and probiotics, have had a limited role in the treatment of TD.

Antimotility Agents

Antimotility agents provide symptomatic relief and serve as useful adjuncts to antibiotic therapy in TD. Synthetic opiates, such as loperamide and diphenoxylate, can reduce bowel movement frequency and enable travelers to resume their activities while awaiting the effects of antibiotics. Loperamide appears to have antisecretory properties as well. These agents should not be used by travelers in diarrheal illness associated with high fever or blood in the stool, rather they should seek medical attention. Loperamide and diphenoxylate are not recommended for children <2 years of age. (Updated November 22, 2006)

Oral Rehydration Therapy

Fluid and electrolytes are lost in cases of TD, and replenishment is important, especially in young children or adults with chronic medical illness. In adult travelers who are otherwise healthy, severe dehydration resulting from TD is unusual unless vomiting is present. Nonetheless, replacement of fluid losses remains an important adjunct to other therapy. Travelers should remember to use only beverages that are sealed or carbonated. For more severe fluid loss, replacement is best accomplished with oral rehydration solutions (ORS), such as World Health Organization ORS solutions, which are widely available at stores and pharmacies in most developing countries. (See Table 4-19 for details.) ORS is prepared by adding one packet to the appropriate volume of boiled or treated water. Once prepared, solutions should be consumed or discarded within 12 hours (24 hours if refrigerated).

Table 4-19. Composition of WHO Oral Rehydration Solution (ORS) for diarrheal illness

Ingredient	Amount	Measurement
Sodium chloride	3.5 g/L	½ tsp
Potassium chloride	1.5 g/L	1¼ tsp
Glucose	20.0 g/L	2 tbsp
Trisodium citrate (or sodium bicarbonate)	2.9 g/L (or 2.5 g/L)	½ tsp
Water	1,000g	1 liter

Treatment of Protozoan Etiologies

The most common parasitic cause of TD is *Giardia intestinalis*, and treatment options include metronidazole, tinidazole, and nitazoxanide. Although cryptosporidiosis is usually a self-limited illness in immunocompetent persons, nitazoxanide can be considered as a treatment option. Cyclosporiasis is treated with TMP-SMX. Treatment of amebiasis is with metronidazole or tinidazole, followed by treatment with a luminal agent such as iodoquinol or paromomycin.

Treatment for Children

Children who accompany their parents on trips to high-risk destinations may be expected to have TD as well. There is no reason to withhold antibiotics from children who contract TD. In older children and teenagers, treatment recommendations for TD follow those for adults, with possible adjustments in dose of

medication. Macrolides such as azithromycin are considered first-line antibiotic therapy in children, although some experts are using short-course fluoroquinolone therapy with caution for travelers <18 years of age. Rifaximin is approved for use starting at age 12.

Infants and younger children are at higher risk for developing dehydration from TD, which is best prevented by the early use of ORS solutions. Breastfed infants should continue to nurse on demand, and bottle-fed infants should be offered full strength lactose-free or -reduced formula. Older infants and children should continue their regular diets during the illness.

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- Bradley A. Connor

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Prevention of Specific Infectious Diseases

Tuberculosis

Description

Mycobacterium tuberculosis is a rod-shaped bacterium that can cause disseminated disease but is most frequently associated with pulmonary infections. The bacilli are transmitted by the airborne route and, depending on host factors, may lead to latent tuberculosis infection (sometimes abbreviated LTBI) or

tuberculosis disease (TB). Both conditions can usually be treated successfully with medications.

Occurrence

In many other countries, tuberculosis is much more common than in the United States, and it is an increasingly serious public health problem.

Risk for Travelers

To become infected, a person usually has to spend a relatively long time in a closed environment where the air was contaminated by a person with untreated tuberculosis who was coughing and who had numerous *M. tuberculosis* organisms (or tubercle bacilli) in secretions from the lungs or voice box (larynx). Infection is generally transmitted through the air; therefore, there is virtually no danger of its being spread by dishes, linens, and items that are touched, or by most food products. However, it can be transmitted through unpasteurized milk or milk products obtained from infected cattle.

Travelers who anticipate possible prolonged exposure to tuberculosis (e.g., those who could be expected to come in contact routinely with hospital, prison, or homeless shelter populations) should be advised to have a tuberculin skin test before leaving the United States. If the reaction is negative, they should have a repeat test approximately 12 weeks after returning. Because persons with HIV infection are more likely to have an impaired response to the tuberculin skin test, travelers who are HIV positive should be advised to inform their physicians about their HIV infection status. Except for travelers with impaired immunity, travelers who already have a positive tuberculin reaction are unlikely to be reinfected.

Travelers who anticipate repeated travel with possible prolonged exposure or an extended stay over a period of years in an endemic country should be advised to have two-step baseline testing and, if the reaction is negative, annual screening, including a tuberculin skin test.

CDC and state and local health departments have published the results of six investigations of possible tuberculosis transmission on commercial aircraft. In these six instances, a passenger or a member of a flight crew traveled on commercial airplanes while infectious with tuberculosis. In all six instances, the airlines were unaware that the passengers or crew members were infected with tuberculosis. In two of the instances, CDC concluded that tuberculosis was probably transmitted to others on the airplane. The findings suggested that the risk of tuberculosis transmission from an infectious person to others on an airplane was greater on long flights (8 hours or more). The risk of exposure to tuberculosis was higher for passengers and flight crew members sitting or working near an infectious person because they might inhale droplets containing *M. tuberculosis* bacteria.

Based on these studies and findings, WHO issued recommendations to prevent the transmission of tuberculosis in aircraft and to guide potential investigations. The risk of tuberculosis transmission on an airplane does not appear to be greater than in any other enclosed space. To prevent the possibility of exposure to tuberculosis on airplanes, CDC and WHO recommend that persons known to have infectious tuberculosis travel by private transportation (that is, not by commercial airplanes or other commercial carriers), if travel is required. CDC and WHO have issued guidelines for notifying passengers who might have been exposed to tuberculosis aboard airplanes. Passengers concerned about possible exposure to tuberculosis should be advised to see their primary health-care provider for a tuberculosis skin test.

Prevention

Vaccine

Based on WHO recommendations, the Bacille Calmette-Guérin (BCG) vaccine is used in most developing countries to reduce the severe consequences of tuberculosis in infants and children. However, BCG vaccine has variable efficacy in preventing the adult forms of tuberculosis and interferes with testing for latent tuberculosis infection. Therefore, it is not routinely recommended for use in the United States.

Other

Travelers should be advised to avoid exposure to known tuberculosis patients in crowded environments (e.g., hospitals, prisons, or homeless shelters). Travelers who will be working in hospitals or health-care settings where tuberculosis patients are likely to be encountered should be advised to consult infection

control or occupational health experts about procedures for obtaining personal respiratory protective devices (e.g., N-95 respirators), along with appropriate fitting and training. Additionally, tuberculosis patients should be educated and trained to cover coughs and sneezes with their hands or tissues to reduce spread. Otherwise, no specific preventive measures can be taken or are routinely recommended for travelers.

Treatment

Persons who are infected or who become infected with *M. tuberculosis* can be treated to prevent progression to tuberculosis disease. Updated American Thoracic Society (ATS)/CDC recommendations for treatment of latent tuberculosis infection recommend 9 months of isoniazid as the preferred treatment and suggest that 4 months of rifampin is a reasonable alternative. Travelers who suspect that they have been exposed to tuberculosis should be advised to inform their physicians of the possible exposure and receive appropriate medical evaluation. CDC and ATS have published updated guidelines for targeted tuberculin skin testing and treatment of latent tuberculosis infection. Recent data from the WHO suggest that resistance is relatively common in some parts of the world. Travelers who have tuberculin skin test conversion associated with international travel should consult experts in infectious diseases or pulmonary medicine.

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- Michael Iademarco

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Prevention of Specific Infectious Diseases

Typhoid Fever

Description

Typhoid fever is an acute, life-threatening febrile illness caused by the bacterium *Salmonella enterica* Typhi.

Occurrence

An estimated 22 million cases of typhoid fever and 200,000 related deaths occur worldwide each year. Approximately 400 cases of typhoid fever, mostly among travelers, are reported to the Centers for Disease Control and Prevention each year.

Risk for Travelers

Typhoid vaccination is not required for international travel, but CDC recommends it for travelers to areas where there is a recognized risk of exposure to *S. Typhi*. Risk is greatest for travelers to the Indian Subcontinent and other developing countries in Asia, Africa, the Caribbean, and Central and South America. Travelers who are visiting relatives or friends and who may be less likely to eat only safe foods (cooked and served hot) and beverages (carbonated beverages or those made from water that has been boiled) are at greater risk. Vaccination is particularly recommended for those who will be traveling in smaller cities, villages, and rural areas off the usual tourist itineraries, where food and beverage choices may be more limited. Travelers have acquired typhoid fever even during brief visits of <1 week to countries where the disease is endemic. While immunization is recommended, travelers should be cautioned that none of the available typhoid vaccines is 100% effective, nor do they provide cross protection against other common causes of gastrointestinal infections. Typhoid vaccination is not a substitute for careful selection of food and drink.

Clinical Presentation

The hallmark of typhoid infection is persistent, high fevers. Other common symptoms and signs include headache, malaise, anorexia, splenomegaly, and relative bradycardia. Many mild and atypical infections occur.

Prevention

Vaccine

Two typhoid vaccines are currently available for use in the United States: an oral live, attenuated vaccine (Vivotif Berna vaccine, manufactured from the Ty21a strain of *S. Typhi* by the Swiss Serum and Vaccine Institute) and a Vi capsular polysaccharide vaccine (ViCPS) (Typhim Vi, manufactured by Aventis Pasteur) for intramuscular use. Both vaccines have been shown to protect 50%-80% of recipients. The intramuscular heat-phenol-inactivated vaccine (manufactured by Wyeth-Ayerst) has been discontinued. Table 4-20 provides information on vaccine dosage and administration. The time required for primary vaccination differs for the two vaccines, as do the lower age limits for use in children.

Primary vaccination with oral Ty21a vaccine consists of a total of four capsules, one taken every other day. The capsules should be kept refrigerated (not frozen), and all four doses must be taken to achieve maximum efficacy. Each capsule should be taken with cool liquid no warmer than 37°C (98.6°F), approximately 1 hour before a meal. This regimen should be completed 1 week before potential exposure. The vaccine manufacturer recommends that Ty21a not be administered to infants or children <6 years of age.

Primary vaccination with ViCPS consists of one 0.5 mL (25 µg) dose administered intramuscularly. One dose of this vaccine should be given at least 2 weeks before expected exposure. The manufacturer does not recommend the vaccine for infants <2 years of age. (See "[Vaccine Recommendations for Infants and Children](#)," "Typhoid Vaccine," for a discussion of typhoid immunization for infants who will be traveling.) Current recommendations for revaccination with either vaccine are provided in Table 4-20.

Adverse Reactions

Information on adverse reactions is presented in Table 4-21. Information is not available on the safety of these vaccines when they are used during pregnancy; it is prudent on theoretical grounds to avoid vaccinating pregnant women. (See Chapter 9.) Live, attenuated Ty21a vaccine should not be given to immunocompromised travelers, including those infected with HIV. The intramuscular vaccine presents theoretically safer alternatives for this group. The only contraindication to vaccination with ViCPS vaccine is a history of severe local or systemic reactions after a previous dose. Neither of the available vaccines should be given to travelers with an acute febrile illness.

Table 4-20. Dosage and schedule for typhoid fever vaccination

Vaccination	Age (yrs)	Dose/mode of administration	No. of doses	Dosing interval	Boosting interval
with cool liquid no warmer than 37°C (98.6°F)					

Table 4-21. Common adverse reactions to typhoid fever vaccines

Vaccine	Reactions		
	Fever	Headache	Local reactions
Ty21a ¹	0%-5%	0%-5%	Not applicable
Vi Capsular polysaccharide	0%-1%	16%-20%	7% erythema or induration \leq 1cm

¹The side effects of Ty21a are rare and mainly consist of abdominal discomfort, nausea, vomiting, and rash or urticaria.

Precautions and Contraindications

Theoretical concerns have been raised about the immunogenicity of live, attenuated Ty21a vaccine in persons concurrently receiving antibiotics, immune globulin, or viral vaccines. The growth of the live Ty21a strain is inhibited *in vitro* by various antibacterial agents. Vaccination with Ty21a should be delayed for >24 hours after the administration of any antibacterial agent. Available data do not suggest that simultaneous administration of oral polio or yellow fever vaccine decreases the immunogenicity of Ty21a. If typhoid vaccination is warranted, it should not be delayed because of administration of viral vaccines. Simultaneous administration of Ty21a and immune globulin does not appear to pose a problem.

Other Prevention

See Risks From Food and Water.

Treatment

Specific antimicrobial therapy shortens the clinical course of typhoid fever and reduces the risk of death. Persons who are potentially exposed to *S. Typhi* and who develop symptoms of typhoid fever should seek appropriate medical care. Antimicrobial therapy should be guided by local data on antimicrobial sensitivity.

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- Steve Luby and Eric Mintz

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Pre- and Post-travel General Health Recommendations

Planning for Healthy Travel

International travelers can take a number of simple steps to avoid potential health problems before and during travel. International travelers should contact their physicians, local health departments, or private or public agencies that advise international travelers at least 4 to 6 weeks before departure to schedule an appointment to receive current health information on the countries they plan to visit, obtain vaccinations and prophylactic medications as indicated, and address any special needs.

It is wisest for persons to postpone travel if they are not feeling well, particularly if they have febrile illnesses. By delaying travel, persons who are ill avoid potential emergencies and are courteous toward other travelers who may not wish to be exposed to someone with a transmissible illness. Trip cancellation insurance is available from a variety of sources.

Handwashing is one of the most important practices in preventing illness from infections while traveling. Travelers should wash their hands often with soap and water or an alcohol-based hand rub to remove potentially infectious materials from the skin and help prevent disease transmission.

New risks to international travelers may arise that are not detailed in this book. These new risks may result from unanticipated outbreaks of infectious diseases in an international travel destination or emerging infectious diseases.

Emerging infectious diseases are diseases of infectious origin the incidence of which in humans has increased within the past two decades or threatens to increase in the near future. Many factors or combinations of factors can contribute to disease emergence and outbreaks. New infectious diseases can emerge from genetic changes in existing organisms; known diseases can spread to new geographic areas and populations; and previously unknown diseases can appear in humans living or working in changing ecologic conditions that increase their exposure to insect vectors, animal reservoirs, or environmental sources of novel pathogens. A good example is the emergence of the [severe acute respiratory syndrome \(SARS\)](#). SARS is a viral respiratory illness caused by a coronavirus (SARS-CoV). SARS was recognized as a global threat in March 2003, after first appearing in Southern China in November 2002. Over the next few months, the illness spread to more than two dozen countries in North America, South America, Europe, and Asia. Although the 2003 global outbreak was contained, person-to-person transmission of SARS-CoV may recur. Although there is no evidence that direct contact with civets or other wild animals from live-food markets has led to cases of SARS, viruses very similar to SARS-CoV have been found in these animals. In addition, some persons working with these animals have evidence of infection with SARS-CoV or a very similar virus.

Reemergence can occur because of the development of antimicrobial resistance in existing infections (e.g., gonorrhea, malaria, and pneumococcal disease) or breakdowns in public health measures for previously controlled infections (e.g., cholera, tuberculosis, and pertussis).

Travelers should be aware of the occurrence of any disease outbreaks in their international destinations. Current travel notices on diseases of international concern are posted on the Travelers' Health home page on the CDC website at www.cdc.gov/travel/.

CDC issues different types of notices for international travelers. As of May 20, 2004, these definitions were refined to make the announcements more easily understood by travelers, health-care providers, and the general public. Each type of notice describes the level of risk for the traveler and recommended preventive measures. Guidance is posted on the CDC Travelers' Health website as outbreaks occur, in four levels:

In The News, the lowest level of notice, will provide information about sporadic cases of disease or an occurrence of a disease of public health significance affecting a traveler or

travel destination. The risk for an individual traveler does not differ from the usual risk in that area.

Outbreak Notice provides information about a disease outbreak in a limited geographic area or setting. The risk to travelers is defined and limited, and the notice will remind travelers about standard or enhanced travel recommendations, such as vaccination.

Travel Health Precaution provides specific information to travelers about a disease outbreak of greater scope and over a larger geographic area so they can take measures to reduce the risk of infection. The precaution also provides guidance to travelers about what to do if they become ill while in the area. CDC does not recommend against travel to a specific area but may recommend limiting exposure to a defined setting, such as poultry farms or health-care settings.

Travel Health Warning recommends against nonessential travel to an area because a disease of public health concern is expanding outside the areas or populations that were initially affected. The purpose of a travel warning is to reduce the volume of traffic to affected areas, thus limiting the risk of spreading the disease to unaffected areas.

A complete description of the definitions and criteria for issuing and removing travel notices can also be found at www.cdc.gov/travel/outbreaks.htm.

Table 2-1. Travel notice definitions

Type of Notice/ Level of Concern	Scope ¹	Risk for Travelers ²	Preventive Measures	Example of Notice	Example of Recommended Measures
In the News	Reports of sporadic cases	No increased risk over baseline for travelers observing standard recommendations	Keeping travelers informed and reinforcing standard prevention recommendations	Report of cases of dengue in Mexico, 2001	Reinforced standard recommendations for protection against insect bites
Outbreak Notice	Outbreak in limited geographic area or setting	Increased but definable and limited to specific settings	Reminders about standard and enhanced recommendations for the region	Outbreak of yellow fever in a state in Brazil in 2003	Reinforced enhanced recommendations, such as vaccination
Travel Health Precaution	Outbreak of greater scope affecting a larger geographic area	Increased in some settings, along with risk for spread to other areas	Specific precautions to reduce risk during the stay, and what to do before and after travel ³	Outbreak of avian influenza among poultry and humans in several countries in Southeast Asia in early 2004	Recommended specific precautions including avoiding areas with live poultry, such as live animal markets and poultry farms; ensuring poultry and eggs are thoroughly cooked; monitoring health
Travel Health Warning	Evidence that outbreak is expanding outside the area or populations initially affected	Increased because of evidence of transmission outside defined settings and/or inadequate containment measures	In addition to the specific precautions cited above, postpone nonessential travel ³	SARS outbreak in Asia in 2003	Recommended travelers to postpone nonessential travel because of level of risk

¹The term "scope" incorporates the size, magnitude, and rapidity of spread of an outbreak.

²Risk for travelers is dependent on patterns of transmission, as well as severity of illness.

³Preventive measures other than the standard advice for the region may be recommended depending on the circumstances (e.g., travelers may be requested to monitor their health for a certain period after their return, or arriving passengers may be screened at ports of entry).

-Patricia M. Simone

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Pre- and Post-travel General Health Recommendations

Risks from Food and Water

Contaminated food and drink are common sources for the introduction of infection into the body. Among the more common infections that travelers can acquire from contaminated food and drink are *Escherichia coli* infections, shigellosis or bacillary dysentery, [giardiasis](#), [cryptosporidiosis](#), [noroviruses](#), and [hepatitis A](#). Other less common infectious disease risks for travelers include [typhoid fever](#) and other salmonelloses, [cholera](#), rotavirus infections, and a variety of protozoan and helminthic parasites (other than those that cause giardiasis and cryptosporidiosis). Many infectious diseases transmitted in food and water can also be acquired directly through the fecal-oral route.

Food

To avoid illness, travelers should be advised to select food with care. All raw food is subject to contamination. Particularly in areas where hygiene and sanitation are inadequate, the traveler should be advised to avoid salads, uncooked vegetables, and unpasteurized milk and milk products such as cheese, and to eat only food that has been cooked and is still hot or fruit that has been washed in clean water and then peeled by the traveler personally. Undercooked and raw meat, fish, and shellfish can carry various intestinal pathogens. Cooked food that has been allowed to stand for several hours at ambient temperature can provide a fertile medium for bacterial growth and should be thoroughly reheated before serving. Consumption of food and beverages obtained from street vendors has been associated with an increased risk of illness.

The easiest way to guarantee a safe food source for an infant <6 months of age is to have the infant breastfeed. If the infant has already been weaned from the breast, formula prepared from commercial powder and boiled water is the safest and most practical food.

Cholera cases have occurred in people who ate crab brought back from Latin America by travelers. Travelers should be advised not to bring perishable seafood with them when they return to the United States from high-risk areas. Moreover, travelers may assume incorrectly that food and water aboard commercial aircraft are safe. Food and water may be obtained in the country of departure, where items may be contaminated.

Water

Swimming

A variety of infections (e.g., skin, ear, eye, respiratory, neurologic, and diarrheal infections) have been linked to wading or swimming in the ocean, freshwater lakes and rivers, and swimming pools, particularly if the swimmer's head is submerged. Water may be contaminated by other people and from sewage, animal wastes, and wastewater run-off. Diarrhea and other serious waterborne infections can be spread when disease-causing organisms from human or animal feces are introduced into the water. Travelers who swim should be advised to avoid beaches that may be contaminated with human sewage or dog feces.

Accidentally swallowing small amounts of fecally contaminated water can cause illness. Travelers should be warned to try to avoid swallowing water while engaging in aquatic activities. Generally, for infectious

disease prevention, pools that contain chlorinated water can be considered safe places to swim if the disinfectant levels and pH are properly maintained. However, some organisms (e.g., *Cryptosporidium*, *Giardia*, hepatitis A, and Norovirus) have moderate to very high resistance to chlorine levels commonly found in chlorinated swimming pools, so travelers also should avoid swallowing chlorinated swimming pool water. All travelers who have [diarrhea](#) should refrain from swimming to avoid contaminating recreational water.

Travelers should be advised to avoid swimming or wading with open cuts or abrasions that might serve as entry points for pathogens. In certain areas, fatal primary amebic meningoencephalitis has occurred after swimming in warm freshwater lakes or rivers, thermally polluted areas around industrial complexes, and hot springs, so travelers should avoid submerging the head and should wear nose plugs when entering untreated water to prevent water getting up the nose. Travelers should also be advised to avoid wading or swimming in freshwater streams, canals, and lakes in schistosomiasis-endemic areas of the Caribbean, South America, Africa, and Asia (see [Map 4-10, Geographic distribution of schistosomiasis](#)), or in bodies of water that may be contaminated with urine from animals infected with [Leptospira](#).

Drinking

Water that has been adequately chlorinated according to the minimum recommended water treatment standards used in the United States will afford substantial protection against viral and bacterial waterborne diseases. However, chlorine treatment alone, as used in the routine disinfection of water, may not kill some enteric viruses and the parasitic organisms that cause [giardiasis](#), [amebiasis](#), and [cryptosporidiosis](#). In areas where chlorinated tap water is not available or where hygiene and sanitation are poor, travelers should be advised that only the following may be safe to drink:

- Beverages, such as tea and coffee, made with boiled water.
- Canned or bottled beverages, including water, carbonated mineral water, and soft drinks.
- Beer and wine.

Where water might be contaminated, travelers should be advised that ice should also be considered contaminated and should not be used in beverages. If ice has been in contact with containers used for drinking, travelers should be advised to clean the containers thoroughly, preferably with soap and hot water, after the ice has been discarded.

It is safer to drink a beverage directly from the can or bottle than from a questionable container. However, water on the outside of beverage cans or bottles may also be contaminated. Therefore, travelers should be advised to dry wet cans or bottles before they are opened and to wipe clean surfaces with which the mouth will have direct contact. Where water may be contaminated, travelers should be advised to avoid brushing their teeth with tap water.

Treatment of Drinking Water

Travelers should be advised of the following methods for treating water to make it safe for drinking and other purposes.

Boiling

Boiling is by far the most reliable method to make water of uncertain purity safe for drinking. Water should be brought to a vigorous rolling boil for 1 minute and allowed to cool to room temperature; ice should not be added. This procedure will kill bacterial and parasitic causes of diarrhea at all altitudes and viruses at low altitudes. To kill viruses at altitudes >2,000 m (6,562 ft), water should be boiled for 3 minutes or chemical disinfection should be used after the water has boiled for 1 minute. Adding a pinch of salt to each quart or pouring the water several times from one clean container to another will improve the taste.

Chemical Disinfection

Chemical disinfection with iodine is an alternative method of water treatment when it is not feasible to boil water. However, this method cannot be relied on to kill *Cryptosporidium*. Two well-tested methods for disinfection with iodine are the use of tincture of iodine ([Table 2-2](#)) and tetraglycine hydroperiodide tablets (e.g., Globaline, Potable-Aqua, or Coghlan's). These tablets are available from pharmacies and sporting goods stores. The manufacturer's instructions should be followed. If water is cloudy, the number of tablets used should be doubled; if water is extremely cold (<5°C; <41°F), an attempt should be made to warm the water, and the recommended contact time should be increased to achieve reliable disinfection. Cloudy

water should be strained through a clean cloth into a container to remove any sediment or floating matter, and then the water should be boiled or treated with iodine. Iodine treatment of water is intended for short-term use only. When the only water available is iodine treated, it should be used for only a few weeks.

Table 2-2. Treatment of water with tincture of iodine

Tincture of iodine	Drops ¹ to be added per quart or liter	
	Clear water	Cold or cloudy water ²
2%	5	10

¹One drop = 0.05 mL. Water must stand for a minimum of 30 minutes before it is safe to use.

²Very turbid or cold water can require prolonged contact time; if possible, such water should be allowed to stand several hours before use. To ensure that *Cryptosporidium* is killed, water must stand for 15 hours before drinking.

Chlorine, in various forms, can also be used for chemical disinfection. However, its germicidal activity varies greatly with the pH, temperature, and organic content of the water to be purified; therefore, it can produce less consistent levels of disinfection in many types of water.

Water Filters

Portable filters currently on the market will provide various degrees of protection against microbes. Reverse-osmosis filters provide protection against viruses, bacteria, and protozoa, but they are expensive and larger than most filters used by backpackers, and the small pores on this type of filter are rapidly plugged by muddy or cloudy water. In addition, the membranes in some filters can be damaged by chlorine in water. Microstrainer filters with pore sizes in the 0.1- to 0.3- μ m range can remove bacteria and protozoa from drinking water, but they do not remove viruses. To kill viruses, travelers using microstrainer filters should be advised to disinfect the water with iodine or chlorine after filtration, as described previously. Some filtration kits come with an additional filter effective against viruses. Filters with iodine-impregnated resins are most effective against bacteria, and the iodine will kill some viruses; however, the contact time with the iodine in the filter is too short to kill the protozoa *Cryptosporidium* and, in cold water, *Giardia*.

Filters that are designed to remove *Cryptosporidium* and *Giardia* carry one of the four messages below—verbatim—on the package label.

- Reverse osmosis
- Absolute pore size of ≤ 1 micron
- Tested and certified by NSF International (formerly the National Sanitation Foundation) Standard 53 or NSF Standard 58 for cyst removal
- Tested and certified by NSF Standard 53 or NSF Standard 58 for cyst reduction

Filters may not be designed to remove *Cryptosporidium* and *Giardia* if they are labeled only with these words:

- *Nominal* pore size of ≤ 1 micron
- One-micron filter
- Effective against *Giardia*
- Effective against parasites
- Carbon filter
- Water purifier
- Environmental Protection Agency (EPA)-approved (Caution: EPA does not approve or test filters.)
- EPA-registered (Caution: EPA does not register filters for *Cryptosporidium* removal)
- Activated carbon
- Removes chlorine
- Ultraviolet light

- Pentiodide resins
- Water softener

Filters collect organisms from water. Anyone changing cartridges should wash hands afterwards. Filters may not remove *Cryptosporidium* as well as boiling does, because even good brands of filters may sometimes have manufacturing flaws that allow small numbers of organisms to pass through the filter. In addition, poor filter maintenance or failure to replace filter cartridges as recommended by the manufacturer can cause a filter to fail.

A travelers' guide to buying water filters for preventing cryptosporidiosis and giardiasis can be found at URL: www.cdc.gov/ncidod/dpd/parasites/cryptosporidiosis/factsht_crypto_prevent_water.htm. These two organisms are either highly (*Cryptosporidium*) or moderately (*Giardia*) resistant to chlorine; so conventional halogen disinfection may be ineffective. Boiling water or filtration can be used as an alternative to chemical disinfection.

Proper selection, operation, care, and maintenance of water filters are essential to producing safe water. The manufacturers' instructions should be followed. NSF International, an independent testing company, tests and certifies water filters for their ability to remove protozoa, but not for their ability to remove bacteria or viruses. Few published scientific reports have evaluated the efficacy of specific brands or models of filters against bacteria and viruses in water. Until such information becomes available, CDC cannot identify which specific brands or models of filters are most likely to remove bacteria and viruses. To find out if a particular filter is certified to remove cryptosporidia, contact NSF International by calling 1-877-867-3435; by fax to 313-769-0109; or by writing to 789 North Dixboro Road, P.O. Box 130140, Ann Arbor, Michigan 48113-0140; or online at <http://www.NSF.org/certified/DWTU/>. Under "Reduction claims for drinking water treatment units—health effects," check the box in front of the words "Cyst Reduction."

As a last resort, if no source of safe drinking water is available or can be obtained, tap water that is uncomfortably hot to touch might be safer than cold tap water; however, proper disinfection, filtering, or boiling is still advised.

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Pre- and Post-travel General Health Recommendations

Travelers' Health Kit

The purpose of a Travel Kit is twofold: to allow the traveler to take care of minor health problems as they

occur and to treat exacerbations of pre-existing medical conditions. A variety of health kits is available commercially and may even be purchased over the internet (see below); however, similar kits can be assembled at home. The specific contents of the health kit are based on destination, duration of travel, type of travel, and the traveler's pre-existing medical conditions. Basic items that should be included are listed below. See also [Chapter 8: International Travel with Infants and Young Children](#) and [Chapter 9: Advising Travelers with Specific Needs](#) for additional suggestions that may be useful in planning the contents of the kit.

New security measures were implemented on August 10, 2006, regarding what passengers may carry onto the airplane. Up-to-date information may be obtained at the [Transportation Security Administration's Website](#).

Medications

- Personal prescription medications (copies of all prescriptions, including the generic names for medications, and a note from the prescribing physician on letterhead stationary for controlled substances and injectable medications should be carried)
- Antimalarial medications, if applicable
- Antidiarrheal medication (e.g., bismuth subsalicylate, loperamide)
- Antibiotic for self-treatment of moderate to severe diarrhea
- Antihistamine
- Decongestant, alone or in combination with antihistamine
- Antimotion sickness medication
- Acetaminophen, aspirin, ibuprofen, or other medication for pain or fever
- Mild laxative
- Cough suppressant/expectorant
- Throat lozenges
- Antacid
- Antifungal and antibacterial ointments or creams
- 1% hydrocortisone cream
- Epinephrine auto-injector (e.g., EpiPen), especially if history of severe allergic reaction. Also available in smaller-dose package for children.

Other Important Items

- Insect repellent containing DEET (up to 50%)
- Sunscreen (preferably SPF 15 or greater)
- Aloe gel for sunburns
- Digital thermometer
- Oral rehydration solution packets
- Basic first-aid items (adhesive bandages, gauze, ace wrap, antiseptic, tweezers, scissors, cotton-tipped applicators)
- Antibacterial hand wipes or alcohol-based hand sanitizer
- Moleskin for blisters
- Lubricating eye drops (e.g., Natural Tears)
- First Aid Quick Reference card

Other items that may be useful in certain circumstances

- Mild sedative (e.g., zolpidem) or other sleep aid
- Anti-anxiety medication
- High-altitude preventive medication

- Water purification tablets
- Commercial suture/syringe kits (to be used by local health-care provider. These items will also require a letter from the prescribing physician on letterhead stationary)
- Latex condoms
- Address and phone numbers of area hospitals or clinics

Commercial medical kits are available for a wide range of circumstances, from basic first aid to advanced emergency life support. Many outdoor sporting goods stores sell their own basic first aid kits. For more adventurous travelers, a number of companies produce advanced medical kits and will even customize kits based on specific travel needs. In addition, specialty kits are available for managing diabetes, dealing with dental emergencies, and handling aquatic environments. If travelers choose to purchase a health kit rather than assemble their own, they should be certain to review the contents of the kit carefully to ensure that it has everything needed; supplementation with additional items for comfort may be necessary.

Below is a list of websites supplying a wide range of medical kits. There are many suppliers, and this list is not meant to be all inclusive.

- Adventure Medical Kits: www.adventuremedicalkits.com
- Chinook Medical Gear: www.chinookmed.com
- Harris International Health Care: www.safetravel.com
- Travel Medicine, Inc.: www.travmed.com
- Wilderness Medicine Outfitters: www.wildernessmedicine.com

A final reminder: a health kit is useful only if it is available. It should be carried with the traveler at all times, e.g., in carry-on baggage and on excursions. All medications, especially prescription medications, should be stored in carry-on baggage, in their original containers with clear labels. With heightened airline security, sharp objects will have to remain in checked luggage.

- Deborah Nicolls, Tamara Fisk, Phyllis Kozarsky

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Non-Infectious Risks During Travel

Jet Lag

The term "jet lag" is used to describe the symptoms that result from a difference between the internal clock and the external environment when a traveler crosses several time zones rapidly. Physiologic rhythms that are innately synchronized with the day-night cycle have to be reset to match the new time zone. Although incompletely understood, these rhythms include diurnal variation in body temperature and cortisol secretion. The major known mediator of the internal clock is melatonin, which is secreted by the pineal gland and induces sleepiness. Daylight suppresses melatonin secretion; meals and other factors also influence secretion.

Symptoms of jet lag are temporary and include excessive daytime sleepiness, nighttime insomnia, decreased performance, headache, general malaise, and gastrointestinal symptoms. Individual responses to crossing time zones and ability to adapt to the new time zone vary. Increasing age, crossing more time zones, or traveling eastward generally increase the time required for adaptation. Eastward travel is associated with difficulty in falling asleep at the new bedtime and difficulty arising in the morning, while westward travel is associated with early evening sleepiness and predawn awakening.

A variety of nonpharmacologic therapies have been used to attenuate the symptoms of jet lag. In principle, efforts to adjust light exposure, activity, and meal times to the new schedule as soon as possible after arrival promote more rapid resetting of the internal clock. Outside daylight, even on cloudy days, is more intense than interior lighting. Light masks and light boxes are available for purchase and at some hotels. Persons traveling eastward should seek bright light in the morning, while those traveling westward should seek bright light in the afternoon. In general, the more time spent outdoors in the first several days following travel, the faster the adjustment to the new time zone. The Argonne diet, which alternates high- and low-calorie days before departure, is often cited but has not been formally studied. The main benefit of this diet may be the inclusion of high-protein breakfasts, which increase levels of tyrosine and thus epinephrine and dopamine, promoting alertness, and high-carbohydrate dinners, which increase serotonin and melatonin, promoting evening sleepiness.

Over-the-counter and prescription medications have been used to promote sleep on long trips or at the new bedtime after arrival. Melatonin is available in the United States as an herbal supplement, although it is regulated in Canada and prohibited in some European countries. Since it is not under FDA regulation, rigorous studies of safety or standardization of doses are not available. However, melatonin seems to be safe and well tolerated, and doses of 0.5-5 mg promoted sleep and decreased jet lag in travelers crossing five or more time zones. Five-mg doses promoted more rapid sleep than lower doses; doses >5 mg had no additional benefit. Slow-release forms were not effective. Melatonin should be taken at the target bedtime, beginning 3-4 days before departure if possible. Zolpidem, a prescription nonaddictive sedative, has been shown to promote sleep in a small group of travelers; its effect on the internal clock is not known. Benzodiazepines may have a direct effect on neurons mediating the internal clock, as well as a hypnotic effect. Short-acting drugs in this class, such as temazepam, should be used to minimize oversedation the next day.

Agents that promote alertness, such as caffeine, and prescription medications, such as amphetamines and pemoline, may interfere with normal sleep and often have adverse effects and potential for dependence. One small study suggests that NADH (nicotinamide adenine dinucleotide), available as a nutritional supplement, may improve performance on the first post-arrival day; more data regarding its efficacy and safety are needed.

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- Tamara Fisk

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Non-Infectious Risks During Travel

Motion Sickness

Motion sickness, a common problem in travelers by automobile, train, air, and particularly sea, usually causes mild to moderate discomfort but in severe cases can be incapacitating. It affects up to half of children traveling in automobiles or airplanes and almost 100% of boat passengers in very rough seas. Motion sickness is more common in women, especially during pregnancy or menstruation, children age 2-12, and in persons who have migraine headaches, but little is known about individual susceptibility. Sensation of head position and movement is generated in the semicircular canals (angular acceleration or rotation) and otolith organs (vertical acceleration) in the inner ears and carried to the central nervous system via cranial nerve VIII. The signs and symptoms of motion sickness occur when sensory information about the body's position in or movement through space is contradictory or contrary to prior experience. Resulting signs and symptoms include dizziness, nausea, vomiting, pallor, and cold sweats.

Travelers who are susceptible to motion sickness can minimize symptoms by choosing seats with the smoothest ride (front seat of a car, forward cars of a train, and the seats over the wings in an airplane), focusing on distant objects rather than trying to read or look at something inside the vehicle, minimizing head movement, and if necessary lying supine.

Medications that may ameliorate symptoms of motion sickness include scopolamine (available in both patch and oral form), oral meclizine, dimenhydrinate, diphenhydramine, and promethazine ([Table 6-1](#)). Choice of medication is based on trip duration, underlying medical conditions, and concerns about sedation. Scopolamine patches are appropriate for longer voyages and should be applied 4 hours before departure and changed every 3 days if needed. Oral scopolamine is effective for 6-8 hours and can be used for short journeys or for the interval between application of the patch and onset of effectiveness. Other oral medications are efficacious for several hours and can also be used for shorter journeys. Oral medications should be started 1 hour before departure. All these medications can impair alertness and must be used with caution by persons operating vehicles or heavy machinery. This effect is additive with alcohol and is least severe with scopolamine. In addition, because these drugs all have anticholinergic properties, they should be avoided in travelers with narrow-angle glaucoma, pyloric obstruction, or prostatic hypertrophy and should be used with caution in those with asthma and cardiovascular disease. Side effects include dry mouth, blurred vision (especially for persons with hyperopia), and bradycardia. Promethazine primarily decreases nausea and has been combined with ephedrine (25-50 mg) to decrease sedation. Only dimenhydrinate and diphenhydramine are recommended for use in children. They may cause paradoxical excitation and should not be used in children <2 years of age.

Nonpharmacologic methods for motion sickness may benefit some persons but have not been proven consistently effective. High levels of ginger have been helpful in some persons. Pressure on the P6 acupuncture point of the wrist provides relief of nausea in pregnancy and after chemotherapy, but evidence for efficacy in motion sickness is contradictory.

Table 6-1. Dosages of anti-motion sickness medications

Medication	Dose	Contraindications	Adverse effects	Comments
Scopolamine	Patch: change every 72 hours. Apply to hairless area behind ear. Oral: 0.4-0.8 mg every 6-8 hrs	Gastrointestinal or bladder neck obstruction (e.g., prostatic hypertrophy), liver or kidney disease, risk for narrow-angle glaucoma	Dry mouth, bradycardia, blurred vision (especially in hyperopic persons), decreased memory for new information, decreased attention and alertness	Useful for longer journeys. Do not touch eyes after applying patch. Contraindicated in children.
Dimenhydrinate	Adult: 25-50 mg up to 4 times per day Children: 1.25 mg/kg, up to 25 mg. Can be	Use with caution in persons with asthma, cardiac arrhythmias, pyloric or bladder neck obstruction, narrow-angle glaucoma.	Drowsiness, thickened respiratory secretions, dry mouth, blurred vision, paradoxical excitation in children	

	repeated every 6 hrs			
Diphenhydramine	Adult: 25-50 mg up to 4 times per day Children: 1 mg/kg, up to 25 mg	As for dimenhydrinate	As for dimenhydrinate	
Promethazine	Adult: 25-50 mg up to 4 times per day	As for dimenhydrinate	As for dimenhydrinate; hypotension, abnormal movements	May be combined with ephedrine to help maintain alertness. Primarily controls nausea. Not recommended for children.
Mecizine	25-50 mg daily	Asthma, narrow-angle glaucoma, bladder neck obstruction	Drowsiness, dry mouth, occasional blurred vision	Not recommended for children.

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Non-Infectious Risks During Travel

Sunburn

Description

Sunlight, exposed skin, and time are all that are needed for sunburn. Sunlight consists of infrared, visible and ultraviolet light, and ultraviolet light consists of UVA, UVB and UVC rays. The UVA rays cause tanning and wrinkling, while UVB rays cause sunburn, aging, wrinkling, and skin cancer. UVC rays do not cause any health effects because they do not reach the earth's surface. Despite these hazards, sun exposure has benefits. UV radiation helps make vitamin D, a key factor for good calcium absorption. However, travelers should be aware of the risks of overexposure to these harmful UV rays.

Occurrence

Exposure to sunlight is influenced by geography, climate, and time of day and year. Countries near the equator and at higher elevation receive more UV rays. Sunlight exposure is highest during the summer and

from 10:00 a.m. to 4:00 p.m. Outdoor activities, whether snow skiing or spending the day at the beach, can increase the chances of getting sunburned. Snow and light-colored sand reflect UV light and increase sunburn risks. In these situations, UV rays may reach exposed skin from above and below. Even on cloudy days UV radiation reaches the earth.

Many drugs increase sensitivity to sunlight and the risk of getting sunburn. Some common ones include thiazides, diuretics, tetracycline, doxycycline, sulfa antibiotics, and nonsteroidal anti-inflammatory drugs, such as ibuprofen.

Clinical Presentation

Unlike a thermal burn, sunburn is not immediately apparent. Symptoms usually start about 4 hours after sun exposure, worsen in 24-36 hours, and resolve in 3-5 days. In mild sunburn, the skin becomes red, warm, and tender. More serious burns are painful, and the skin becomes swollen and may blister. When a large area is burned, headache, fever, nausea, and fatigue may develop. The pain from sunburn is worse 6-48 hours after sun exposure. Skin peeling usually begins 3-8 days after exposure. Severe sunburns can be serious in babies, small children, and older adults. Years of overexposure to the sun may lead to premature wrinkling, aging of the skin, age spots, and skin cancer.

In addition to the skin, eyes can get burned from sun exposure. Sunburned eyes become red, dry, painful, and feel gritty. Chronic exposure to sunlight may cause pterygium (tissue growth that leads to blindness), cataracts, and perhaps macular degeneration, a leading cause of blindness.

Prevention

Several steps can be taken to reduce the risk for sunburn. Dermatologists recommend using a full-spectrum sunscreen that blocks or absorbs all UV rays. Sunscreen comes in creams, gels, lotions, and wax sticks. While the type of sunscreen is a matter of personal choice, travelers may want to choose a water-resistant product that will not be easily removed by sweating or swimming. Sunscreens should be used regularly, even on cloudy days, because most of the UV rays pass through the clouds. Sunscreens can be applied under makeup. Although some cosmetic products contain sunscreens, their sun protection factor (SPF) is usually not high enough to be very protective.

Effective sunscreens should have an SPF of at least 15. SPF refers to the amount of time that persons will be protected from a burn. An SPF of 15 will allow a person to stay out in the sun 15 times longer than they normally would be able to stay without burning. The SPF rating applies only to UVB radiation. While the SPF number represents the most protection under the best conditions, sunscreen performance is affected by wind, humidity, perspiration, and proper application. Sunscreens should be liberally applied (at least one ounce) at least 20 minutes before going out in the sun. Special attention should be given to covering the ears, scalp, lips, neck, tops of feet, and backs of hands. Sunscreens should be reapplied at least every 2 hours and after every time a person gets out of the water or perspires. Some sunscreens may also lose efficacy when applied with insect repellents, necessitating more frequent application when the two products are used together.

Another effective way to prevent sunburn is by wearing appropriate clothing. Dark clothing with a tight weave is more protective than light-colored, loosely woven clothing. High-SPF clothing has been developed to provide more protection for patients with photosensitive skin or a history of skin cancer. This type of clothing contains colorless compounds, fluorescent brighteners, or specially treated resins that absorb UV and often provides an SPF of 30 or higher. Travelers should also wear wide-brimmed hats and sunglasses with almost 100% UV protection and with side panels to prevent excessive sun exposure to the eyes.

The UV index, which indicates how much ultraviolet light exposure will occur, can be found in the weather section of most large daily newspapers, in some television weather forecasts, and on the Internet. The UV index ranges from 1 (low) to 11 or higher (extremely high). Travelers are advised to take extra precautions to prevent sunburn when the UV index is higher.

Treatment

There is no quick cure for minor sunburn. Symptomatic treatment can be initiated with aspirin,

acetaminophen, or ibuprofen to relieve pain and headache and reduce fever. (Children and teenagers should generally not be given aspirin because of the danger of Reye syndrome.) Drinking plenty of water helps to replace fluid losses. Cool baths or the gentle application of cool wet cloths on the burned area may also provide some comfort. Travelers with sunburns should avoid further exposure until the burn has resolved. Additional symptomatic relief can be achieved through the application of a topical moisturizing cream, aloe, or 1% hydrocortisone cream. A low-dose (0.5%-1%) hydrocortisone cream can be helpful in reducing the burning sensation and swelling and speeding up healing.

If blistering occurs, lightly bandage or cover the area with gauze to prevent infection. The blisters should not be broken, as this will slow the healing process and increase the risk of infection. When the blisters break and the skin peels, dried fragments may be removed and an antiseptic ointment or hydrocortisone cream may be applied.

Indications for medical attention include severe sunburns (covering >15% of the body), dehydration, high fever, or extreme pain.

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Non-Infectious Risks During Travel

Altitude Illness

Travelers whose itineraries will take them above an altitude of 1,829-2,438m (6,000-8,000ft) should be aware of the risk of altitude illness. Travelers are exposed to higher altitudes in a number of ways: by flying into a high-altitude city, by driving to a high-altitude destination, or by hiking or climbing in high mountains. Examples of high-altitude cities with airports are Cuzco, Peru (3,000m; 11,000ft); La Paz, Bolivia (3,444m; 11,300ft); and Lhasa, Tibet (3,749m; 12,500ft).

Travelers vary considerably in their susceptibility to altitude illness, and no screening tests are available to predict someone's risk for altitude illness. Susceptibility to altitude illness appears to be inherent in some way and is not affected by training or physical fitness. How a traveler has responded in the past to exposure to high altitude is the most reliable guide for future trips but is not infallible.

Travelers with underlying medical conditions, such as congestive heart failure, myocardial ischemia (angina), sickle cell disease, or any form of pulmonary insufficiency, should be advised to consult a doctor familiar with high-altitude illness before undertaking such travel. The risk of new ischemic heart disease in previously healthy travelers does not appear to be increased at high altitudes.

Most people do not have visual problems at high altitude. However, at very high altitudes some persons who had incisional radial keratotomy (a procedure widely performed from the late 1970s to the early 1990s) may develop acute farsightedness. The laser surgery for vision correction that replaced radial

keratotomy (e.g., Lasik and other procedures) is not associated with visual disturbances at high altitudes.

Altitude illness is the result of traveling to a higher altitude faster than the body can adapt to that new altitude. Fluid leakage from blood vessels appears to be the main cause of symptoms. Altitude illness is divided into three syndromes: acute mountain sickness (AMS), high-altitude cerebral edema (HACE), and high-altitude pulmonary edema (HAPE). AMS is the most common form of altitude illness and, while it can occur at altitudes as low as 1,219-1,829m (4,000-6,000ft), most often it occurs in abrupt ascents to >2,743m (>9,000ft). The symptoms resemble those of an alcohol hangover: headache, fatigue, loss of appetite, nausea, and, occasionally, vomiting. The onset of AMS is delayed, usually beginning 6-12 hours after arrival at a higher altitude, but occasionally \geq 24 hours after ascent.

HACE is considered a severe progression of AMS. In addition to the AMS symptoms, lethargy becomes profound, confusion can manifest, and ataxia will be demonstrated during the tandem gait test. A traveler who fails the tandem gait test has HACE by definition, and immediate descent is mandatory.

HAPE can occur by itself or in conjunction with HACE. The initial symptoms are increased breathlessness with exertion, and eventually increased breathlessness at rest. The diagnosis can usually be made when breathlessness fails to resolve after several minutes of rest. At this point, it is critical to descend to a lower altitude. HAPE can be more rapidly fatal than HACE.

Determining an itinerary that will avoid any occurrence of altitude illness is difficult because of variations in individual susceptibility, as well as in starting points and terrain. The main point of instructing travelers about altitude illness is not to prevent any possibility of altitude illness, but to prevent death from altitude illness. The onset of symptoms and clinical course are sufficiently slow and predictable that there is no reason for someone to die from altitude illness unless trapped by weather or geography in a situation in which descent is impossible. The three rules that travelers should be made aware of to prevent death from altitude illness are:

- Learn the early symptoms of altitude illness and be willing to admit that you have them.
- Never ascend to sleep at a higher altitude when experiencing any of the symptoms of altitude illness, no matter how minor they seem.
- Descend if the symptoms become worse while resting at the same altitude.

Studies have shown that travelers who are on organized group treks to high-altitude locations are more likely to die of altitude illness than travelers who are by themselves. This is most likely the result of group pressure (whether perceived or real) and a fixed itinerary. The most important aspect of preventing severe altitude illness is to refrain from further ascent until all symptoms of altitude illness have disappeared.

Children are as susceptible to altitude illness as adults, and young children who cannot talk can show very nonspecific symptoms, such as loss of appetite and irritability. There are no studies or case reports of harm to a fetus if the mother travels briefly to high altitude during pregnancy. However, most authorities recommend that pregnant women stay below 3,658m (12,000ft) if possible.

Three medications have been shown to be useful in the prevention and treatment of altitude illness. Acetazolamide (Diamox) can prevent AMS when taken before ascent and can speed recovery if taken after symptoms have developed. The drug appears to work by acidifying the blood, which causes an increase in respiration and thus aids in acclimatization. An effective dose that minimizes the common side effects of increased urination, along with paresthesias of the fingers and toes, is 125mg every 12 hours, beginning the day of ascent. However, most clinical trials have been done with higher doses of 250mg two or three times a day. Allergic reactions to acetazolamide are extremely rare, but the drug is related to sulfonamides and should not be used by sulfa-allergic persons, unless a trial dose is taken in a safe environment before travel.

Dexamethasone has been shown to be effective in the prevention and treatment of AMS and HACE. The drug prevents or improves symptoms, but there is no evidence that it aids acclimatization. Thus, there is a risk of a sudden onset or worsening of symptoms if the traveler stops taking the drug while ascending. It is preferable for the traveler to use acetazolamide to prevent AMS while ascending and to reserve the use of dexamethasone to treat symptoms while trying to descend. The adult dosage is 4mg every 6 hours.

HAPE is always associated with increased pulmonary artery pressure. Drugs that can selectively lower pulmonary artery pressure have been shown to be of benefit in preventing and treating HAPE. Nifedipine

has been shown to prevent and ameliorate HAPE in persons who are particularly susceptible to HAPE. The adult dosage is 10-20mg every 8 hours. Sildenafil citrate (Viagra) can also selectively lower pulmonary artery pressure, with less effect on systemic blood pressure. Preliminary studies suggest that this class of drug may prove useful in prevention and treatment of HAPE.

Newer medications have recently been tried to help prevent AMS and HAPE. When taken before ascent, ginkgo biloba, an herbal remedy, was shown to reduce the symptoms of AMS in adults in two small trials. Ginkgo has not yet been compared with acetazolamide, although a study is planned. Inhaled salmeterol (a beta-adrenergic agonist) was demonstrated to help prevent HAPE in a small group of climbers who had previously shown susceptibility to HAPE. Whether salmeterol will prove beneficial in a more general population remains to be seen. The mechanism of action of salmeterol suggests that it could be of benefit in treating already established HAPE, but there are no studies yet to confirm this. Salmeterol was chosen for prophylactic studies because of a longer duration of action. The less expensive albuterol may also be effective, but no studies utilizing this drug at altitude have been done.

For trekking groups and expeditions going into remote high-altitude areas, where descent to a lower altitude could be problematic, a pressurization bag (the Gamow bag) can prove extremely beneficial. Persons with altitude illness can be zipped into the bag, and a foot pump can increase the pressure inside the bag by 2 lbs. per in², mimicking a descent of 1,500-1,800m (5,000-6,000ft), depending on the starting altitude. The total packed weight of the bag and pump is approximately 6.5kg.

For most travelers, the best way to avoid altitude illness is to plan a gradual ascent, with extra rest days at intermediate altitudes. If ascent must be rapid, acetazolamide may be used prophylactically, and dexamethasone and pulmonary artery pressure-lowering drugs, such as nifedipine or sildenafil, may be carried for emergencies.

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Introduction

Text updated: September 30, 2005

Introduction

The [Division of Global Migration and Quarantine](#) (formerly the Division of Quarantine), National Center for Infectious Diseases, Centers for Disease Control and Prevention (CDC), is pleased to present the

2005-2006 edition of *Health Information for International Travel*. The Yellow Book has been written, edited, published, compiled, and disseminated for over a quarter of a century. First published as a small pamphlet with sets of recommendations for the prevention of illnesses such as smallpox, the Yellow Book has become a trusted reference for travelers worldwide. In recent years, it has been written biennially, and it remains the standard set of recommendations for health maintenance and prevention of illness among US travelers. It is written primarily for health-care providers, including physicians, nurses, and pharmacists, although the public will find the book an excellent resource as well. The travel industry, multinational corporations, missionary and volunteer organizations, and families who vacation abroad can all find a wealth of information within this text. Although this information is also provided on CDC's Travelers' Health website (www.cdc.gov/travel), many readers find that this handy text is user-friendly enough to have on their shelves in their offices or at home.

The increase in global travel and the recognition of the specialty of Travel Medicine have resulted in a growing body of knowledge in the field, and an accompanying increase in research and evidence-based guidelines. The reader will immediately note that this is the first edition in which important references have been listed at the end of each section. This new feature will enable readers to quickly find additional and supporting data for the recommendations made.

This edition has been completely revised and updated. The contents have been reorganized, as have many of the chapters. Vaccine requirements have been clarified, and the maps have been improved. The "yellow pages" ([Chapter 5](#)) remain a quick reference for areas of the world where yellow fever vaccine is required or recommended and where malaria chemoprophylaxis is recommended. Sections that have been enhanced substantially include those covering [immunosuppressed travelers](#), [disabled travelers](#), [cruise ship travel](#), and [children who travel](#). New sections have been added on [air travel](#), [norovirus infection](#), [SARS](#), and [legionellosis](#). Although the authors of most sections are subject-matter experts at CDC, travel health experts from outside the agency have also made substantial contributions.

A new partnership between CDC and Elsevier publishing house to produce the Yellow Book was launched with this edition. Elsevier, publishers of numerous authoritative texts on infectious diseases and travel medicine, will collaborate with CDC to bring the Yellow Book to the public, institutions involved in health and travel, and to an even greater number of health-care providers, especially those who occasionally counsel travelers but have not had any formal training in travel medicine.

Other Sources of Travel Health Information from CDC

- "Yellow Book" online: The online version of the "Yellow Book" may be found on the CDC Internet website at www.cdc.gov/travel/yb/index.htm. It is searchable by destination country, disease, vaccination, type of traveler (e.g., pregnant or special needs), or other topics. The "Yellow Book" may also be accessed through the travelers' health home page.
- Travelers' Health home page: The CDC Travelers' Health home page, (www.cdc.gov/travel) is an important way of accessing the most current travel health information. It contains information about outbreaks and links to information about specific diseases, emergency preparedness and response, cruise ship sanitation, air travel health recommendations, emerging infections, vaccine requirements and recommendations, and medications for prevention and treatment of common travel-related problems. In addition, there are valuable links to other websites, such as the World Health Organization, the Pan American Health Organization, and the U.S. State Department, as well as state and local health departments.
- Travelers' Health Fax Information: CDC has discontinued the Travelers' Health voice-fax service (888-232-3299) as part of an agency-wide consolidation of consumer information services.
- Travelers' Health Electronic Mail: E-mail queries, comments, and suggestions for Travelers' Health, including comments about this book, may be made through a link from the Travelers' Health home page. Urgent health questions from the public should be directed to a health-care provider, and those from health-care providers should be directed to the local or state health department, or to a medical center with a specialist in travel or tropical medicine (see [Additional Sources of Travel Health Information](#)).
- Malaria Information: CDC's Malaria Branch has published a brochure, which may be accessed

and downloaded from the Travelers' Health website. In addition, specific malaria prevention and case management questions can be addressed to the CDC's Malaria Branch Telephone Hotline at 770-488-7788 during business hours. After hours and on weekends, a Malaria Branch clinician may be reached by calling 770-488-7100.

- Yellow Fever Vaccine Registry: In an effort to assist health-care providers and the public in locating a site for yellow fever vaccination and a proof-of-vaccine certificate, a registry of licensed yellow fever vaccine sites in the 50 states and U.S. territories has been added to the Travelers' Health website and is linked to the home page.
- National Immunization Program (NIP): CDC's vaccine program provides information on their website (www.cdc.gov/nip) about vaccines, their recommended schedules in adults and children, and adverse events.

Additional Sources of Travel Health Information

- The International Society of Travel Medicine (ISTM): The ISTM website, (www.istm.org) contains a list of travel health clinics both in the United States and worldwide. The ISTM primarily focuses on pre-travel health education and migration medicine.
- The American Society of Tropical Medicine and Hygiene (ASTM&H): The ASTM&H website (www.astmh.org) includes a directory of clinicians, primarily within the United States, who specialize in clinical tropical medicine and travelers' health. These health-care providers are available for evaluation of returning travelers who are ill.
- The World Health Organization (WHO): The WHO website (www.who.int) provides global health information and links to various other international sites. It also includes WHO's online travel health information, entitled International Travel and Health. In some instances, travel health recommendations from the WHO may vary from CDC guidelines. Variability in access to different vaccines and drugs, as well as some differences in expert opinion regarding the prevention of illness may contribute to the occasional differences.
- The Pan American Health Organization (PAHO): PAHO is a regional office of WHO. For travelers visiting other countries in the Western Hemisphere, the PAHO website (www.paho.org) includes information about outbreaks, disease trends, some country-specific health statistics, and disease control efforts in the Americas.
- The United States Department of State: This website (www.state.gov/travel) is very valuable for both travelers and those living abroad. It contains information about safety and security throughout the world, US consulate information, a list of companies that specialize in travel insurance and medical evacuation, and issues public announcements and travel warnings when there is a threat to the security of travelers. The U.S. Department of State also has a new secure online travel registration site <https://travelregistration.state.gov/ibrs/> for American citizens to record information about their trip abroad so that the Department of State can provide assistance in the case of an emergency.
- U.S. Central Intelligence Agency (CIA): The CIA website, (www.odci.gov/cia/publications; select World Factbook) contains useful information for travelers.

In addition to those listed above, a number of commercial travel health information resources may be accessed through health-care providers who subscribe to them. Many are quite useful and have excellent information.

The WHO International Health Regulations (IHR)

The purpose of the WHO IHR is to ensure maximum security against the international spread of diseases, with minimum interference with world traffic. Its origins date back to the mid-19th century when cholera epidemics spread throughout Europe. Epidemics were catalysts for intensive multilateral cooperation in public health. In 1948, the WHO constitution came into being, and the first International Sanitary Regulations were adopted in 1951. These were renamed the International Health Regulations in 1969; they

were modified in 1973 and 1981 and revised in May 2005. (Updated November 1, 2005) The IHR (2005) broaden the scope of the 1969 Regulations to cover existing, new, and re-emerging diseases, including emergencies caused by non-infectious disease agents. As a member state of the WHO, the United States adheres to the IHR and participates in their development.

The IHR were originally intended to help monitor and control six serious infectious diseases: [cholera](#), [plague](#), [yellow fever](#), [smallpox](#), relapsing fever and typhus. Today, only cholera, plague and yellow fever are notifiable diseases. The IHR (2005) additionally require States to notify WHO of all events that may constitute a public health emergency of international concern. For the purposes of the IHR, the incubation periods of the quarantinable diseases are 5 days for cholera, 6 days for plague, and 6 days for yellow fever.

Most immunizations are not required under the IHR but may be recommended to protect the health of the traveler. However, an International Certificate of Vaccination against yellow fever is required by some countries as a condition for entry ([Chapter 5](#)). Because some countries require vaccination against yellow fever only if travelers arrive from a country where the disease is present, current information must be taken into consideration in determining whether vaccinations are required. Although this text includes the most up-to-date information regarding these requirements at publication, the Travelers' Health website may be accessed for additional information.

Pre-Travel Health Measures

Although the information in this book can guide the health-care provider and public toward more healthy and safe travel, a risk assessment of every traveler should be performed. To determine the best health advice, it is not adequate to merely know the destination country. Numerous other factors help determine the risk of illness: the entire itinerary; the destination city, town, or village; the style of travel; the length of stay; and the season of travel. The underlying health of the traveler is equally important: medical problems, previous vaccinations, adverse events, current prescription and over-the-counter medications, previous travel, immune problems, and pregnancy issues are just some of these. Thus, travel health advice needs to be tailored both to the individual and to the itinerary. Many primary-care practitioners are comfortable in giving some pre-travel health advice and are encouraged to learn the basics; for the more complicated travel itineraries or for the traveler with multiple medical problems, it is advisable to refer to a travel health specialist.

In general, the risk of becoming ill during international travel depends on the region of the world visited, as well as the many factors listed above. Travelers to developing countries are at greater risk than those who travel to developed countries (e.g., Canada, Australia, New Zealand, Japan, and Western Europe) where the risk to the health of the traveler is no greater than that incurred in the United States. Travelers visiting urban tourist areas and staying in first-class accommodations may have a lower risk for exposure to infectious diseases. Consequently, additional vaccines and protective measures may be recommended for the more adventuresome travelers. Additionally, children, the elderly, pregnant women, and immunocompromised travelers may be particularly vulnerable to certain problems while traveling and may require more specialized counseling.

Health-care providers have available to them a number of vaccinations for protection of travelers. In addition, providers should take the opportunity, while giving advice to travelers, to update them on routine vaccinations as needed, such as diphtheria/tetanus and measles. Other vaccines that may be recommended include [pertussis](#), [poliomyelitis](#), [hepatitis A](#), [hepatitis B](#), [varicella](#), [Japanese B encephalitis](#), [meningococcal meningitis](#), [rabies](#), and [typhoid](#). For diseases for which no vaccines are available, specific preventive behaviors or medications that may be helpful are detailed in this book. Chapters are also included that address the specific needs of potentially high-risk travelers.

International travelers should contact health-care providers who provide pre-travel health advice at least 4-6 weeks before departure for current health information and to obtain vaccinations and prophylactic medications. Being a responsible traveler means taking care of oneself as well as being sensitive to the cultural variability and fragility of the environment in a world that has been made smaller by our ability to travel from one end of the globe to the other in a matter of hours. The goal of CDC's travel health information is to better enable individuals to enjoy their international travels safely.

- Stefanie Steele and Phyllis Kozarsky

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Introduction

General Recommendations for Vaccination and Immunoprophylaxis

Recommendations for immunization are developed by the Advisory Committee on Immunization Practices (ACIP), and these guidelines assist CDC in its role in the ongoing education of health-care providers and the public. To achieve optimal levels of protection against vaccine-preventable diseases, the recommendations are based on scientific evidence of benefits and risks, and, where there are little or no data, on expert opinion. The recommendations include information on general immunization issues and the use of specific vaccines. When these recommendations are issued or revised, they are published in the *Morbidity and Mortality Weekly Report* (www.cdc.gov/mmwr).

Vaccinations against [diphtheria](#), [tetanus](#), [pertussis](#), [measles](#), [mumps](#), [rubella](#), [varicella](#), [poliomyelitis](#), [hepatitis B](#), [Haemophilus influenzae type b](#), and [pneumococcal invasive disease](#) are routinely administered in the United States, usually in childhood. If travelers do not have a history of adequate protection against these diseases, immunizations appropriate to their age and previous immunization status should be obtained, whether or not international travel is planned. The fact that a person is seeing a travel health provider or a primary provider for immunizations for travel should be a signal to take the opportunity and vaccinate where there are gaps in routine coverage.

The childhood vaccination schedule changes annually, and recommendations for adolescents and adults change often. Vaccine providers should obtain the most current schedules from the National Immunization Program website, <http://www.cdc.gov/nip/>. The text and Tables [1-1](#), [1-2](#), [4-1](#) through [4-8](#), [4-12](#) through [4-17](#), [4-20](#) through [4-23](#), [8-2](#) through [8-4](#), [9-1](#), and [9-4](#), of this publication present recommendations for the use, number of doses, dose intervals, adverse reactions, precautions, and contraindications of vaccines and toxoids that may be indicated for travelers. For specific vaccines and toxoids, additional details on background, adverse reactions, precautions, and contraindications are found in the respective ACIP statements.

Spacing of Immunobiologics

Simultaneous Administration

All commonly used vaccines can safely and effectively be given simultaneously (that is, on the same day) without impairing antibody responses or increasing rates of adverse reactions. This knowledge is particularly helpful for international travelers for whom exposure to several infectious diseases might be imminent.

In general, inactivated vaccines may be administered simultaneously at separate sites. However, when vaccines commonly associated with local or systemic reactions are given simultaneously, reactions can be accentuated.

Simultaneous administration of acellular pertussis (DTaP); inactivated poliovirus (IPV); *Haemophilus influenzae* type b (Hib); measles, mumps, and rubella (MMR); varicella; pneumococcal conjugate; and hepatitis B vaccines is encouraged for persons who are the recommended age to receive these vaccines and for whom no contraindications exist.

[Yellow fever](#) vaccine may be administered simultaneously with all other currently available vaccines.

Limited data suggest that the immunogenicity and safety of Japanese encephalitis (JE) vaccine are not compromised by simultaneous administration with DTaP or whole-cell pertussis (DTP) vaccine. No data exist on the effect of concurrent administration of other vaccines, drugs (e.g., chloroquine or mefloquine), or biologicals on the safety and immunogenicity of JE vaccine.

Inactivated vaccines generally do not interfere with the immune response to other inactivated or live-virus vaccines. An inactivated vaccine may be given either simultaneously or at any time before or after a different inactivated vaccine or a live-virus vaccine.

The immune response to an injected live-virus vaccine (e.g., MMR, varicella, or yellow fever) might be impaired if administered within 28 days of another live virus vaccine. Whenever possible, injected live-virus vaccines administered on different days should be given at least 28 days apart. If two injected live-virus vaccines are not administered on the same day but <28 days apart, the second vaccine should be readministered at least 4 weeks later.

Live-virus vaccines can interfere with a person's response to tuberculin testing. Tuberculin testing, if otherwise indicated, can be done either on the day that live-virus vaccines are administered or 4-6 weeks later.

Missed Doses and Boosters

Persons will often forget to return for a follow-up dose of vaccine or booster at the specified time. It is unnecessary in these cases to restart the interrupted series or to add any extra doses. This is true for all vaccines except for the oral typhoid vaccine. Most products require periodic booster doses to maintain protection (See [Table 1-1](#)).

Table 1-1. Revaccination (booster) schedules

Vaccine	Recommendation
Cholera	No longer available in U.S.
Japanese encephalitis	Full duration of protection unknown. Neutralizing antibodies may persist at least 2 years after primary immunization
Hepatitis A (HAV)	Booster not recommended for adults and children who complete primary series (2 doses)
Hepatitis B (HBV)	Booster doses of vaccine are not recommended for adults and children who completed primary series according to routine schedule. ¹ Booster is recommended at least 6 months after the start of the accelerated schedule.
Influenza	1 annual dose
Measles, Mumps, Rubella (MMR)	1 dose if measles, mumps, or rubella vaccination history is unreliable and person did not have these illnesses; 2 doses for persons with occupational or other indications
Meningococcal Quadrivalent A,C, Y, W-135	Full duration of protection is unknown; immunity may persist at least 3 years in adults
Pneumococcal (polysaccharide)	One-time revaccination 5 years after original dose for persons > 65 years of age (if original dose was given before age 65) or who have immunosuppressive conditions.
Polio (IPV)	For adults who have completed primary series, a single lifetime booster
Rabies Preexposure vaccine	No serologic testing or boosters recommended for travelers. For persons in higher risk groups, such as rabies laboratory workers, serologic testing and booster doses are recommended. See Table 4-15.
Tetanus/diphtheria (Td)	Booster every 10 years
Typhoid Oral	Booster every 5 years
Typhoid IM	Booster every 2 years
Varicella	Booster not recommended after completion of primary series.

Yellow fever	Booster every 10 years. Note that there are age-related risks for severe adverse reactions.
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¹ Booster dosing may be appropriate for certain populations, such as hemodialysis patients

Immune Globulin Preparations

When MMR and varicella vaccines are given with immune globulin (IG, also called immune serum globulin and immunoglobulin) preparations, antibody response can be diminished. IG preparations do not interfere with the immune response to yellow fever vaccine. The duration of inhibition of MMR and varicella vaccines is related to the dose of IG. Administration of MMR or its components and of varicella vaccines should be delayed 3-11 months after IG administration ([Table 1-2](#)).

Table 1-2. Recommended intervals between administration of antibody-containing products and measles-containing vaccine or varicella vaccine¹

Indication	Dose	Recommended interval before measles or varicella vaccination
Tetanus (TIG)	250 units (10 mg IgG/kg) IM ²	3 months
<i>Hepatitis A (IG), duration of international travel</i>		
< 3-month stay	0.02 mL/kg (3.3 mg IgG/kg) IM	At least 5 months for varicella At least 3 months for measles
> 3-month stay	0.06 mL/kg (10 mg IgG/kg) IM	At least 5 months for varicella At least 3 months for measles
Hepatitis B prophylaxis (HBIG)	0.06 mL/kg (10 mg IgG/kg) IM	At least 3 months
Rabies prophylaxis (HRIG)	20 IU/kg (22 mg IgG/kg) IM	At least 3 months
Varicella prophylaxis (VZIG)	125 units/10 kg (20-40 mg IgG/kg) IM (maximum 625 units)	At least 5 months
<i>Measles prophylaxis (IG)</i>		
Immunocompetent contact	0.25 mL/kg (40 mg IgG/kg) IM	3 - 5 months
Immunocompromised contact	0.50 mL/kg (80 mg IgG/kg) IM	6 months
<i>Blood transfusion</i>		
Red blood cells (RBCs), washed	10 mL/kg negligible IgG/kg) IV	None
RBCs, adenine-saline added	10 mL/kg (10 mg IgG/kg) IV	At least 5 months for varicella At least 3 months for measles
Packed RBCs (Hct 65%) ³	10 mL/kg (60 mg IgG/kg) IV	At least 5 months for varicella At least 5 months for measles
Plasma/platelet products	10 mL/kg (160 mg IgG/kg) IV	At least 5 months for varicella At least 7 months for measles
Cytomegalovirus prophylaxis (CMV IGIV)	variable	At least 3 months
Respiratory syncytial virus (RSV) monoclonal antibody (Synagis) ⁴	15 mg/kg IM	No data (or unknown)
RSV prophylaxis (RSV IGIV)	750 mg/kg	9 months
<i>Intravenous immune globulin (IVIG)</i>		

Replacement therapy	300-400 mg/kg IV	8 months
Immune thrombocytopenic purpura (ITP)	400 mg/kg IV	8 months
ITP	1 gm/kg IV	10 months
ITP or Kawasaki disease	1.6 gm/kg IV - 2 gm	11 months

This table is adapted from the AAP Committee on Infectious Diseases. Recommended timing of routine measles immunization for children who have recently received immune globulin preparations. Pediatrics. 1994.

¹This table is not intended for determining the correct indications and dosage for the use of IG preparations. Unvaccinated people may not be fully protected against measles during the entire recommended interval, and additional doses of IG or measles vaccine may be indicated after measles exposure. Concentrations of measles antibody in an IG preparation can vary by manufacturer's lot. For example, fourfold or greater variation in the amount of measles antibody titers has been demonstrated in different IG preparations. Rates of antibody clearance after receipt of an immune globulin preparation can also vary. Recommended intervals are extrapolated from an estimated half-life of 30 days for passively acquired antibody and an observed interference with the immune response to measles vaccine for 5 months after a dose of 80 mg IgG/kg.

²IG, immune globulin; IM, intramuscular; IV, intravenous

³Assumes a serum IgG concentration of 16 mg/mL.

⁴Contains only antibody to respiratory syncytial virus.

IG administration may become necessary for another indication after MMR or its individual components or varicella vaccines have been given. In such a situation, the IG may interfere with the immune response to the MMR or varicella vaccines. Vaccine virus replication and stimulation of immunity usually occur 2-3 weeks after vaccination. If the interval between administration of one of these vaccines and the subsequent administration of an IG preparation is 14 days or more, the vaccine need not be readministered. If the interval is <14 days, the vaccine should be readministered after the interval shown in [Table 1-2](#), unless serologic testing indicates that antibodies have been produced. If administration of IG becomes necessary, MMR or its components or varicella vaccines can be administered simultaneously with IG, with the recognition that vaccine-induced immunity can be compromised. The vaccine should be administered in a body site different from that chosen for the IG injection. Vaccination should be repeated after the interval noted in [Table 1-2](#), unless serologic testing indicates antibodies have been produced.

When IG is given with the first dose of hepatitis A vaccine (HAV), the proportion of recipients who develop protective levels of antibody is not affected, but antibody concentrations are lower. Because the final concentrations of anti-HAV are many times higher than those considered protective, this reduced immunogenicity is not expected to be clinically important. IG preparations interact minimally with other inactivated vaccines and toxoids. Therefore, other inactivated vaccines may be given simultaneously or at any time interval after or before an antibody-containing blood product is used. However, such vaccines should be administered at different sites from the IG (not from each other).

Vaccination of Persons with Acute Illnesses

Every opportunity should be taken to provide appropriate vaccinations. The decision to delay vaccination because of a current or recent acute illness depends on the severity of the symptoms and their cause. Although a moderate or severe acute illness is sufficient reason to postpone vaccination, minor illnesses (such as diarrhea, mild upper respiratory infection with or without low-grade fever, or other low-grade febrile illness) are not contraindications to vaccination. Antimicrobial therapy is not a contraindication to vaccination, except with oral typhoid vaccine (Ty21a). People with moderate or severe acute illness with or without fever should be vaccinated as soon as the condition has improved. This precaution is to avoid superimposing adverse effects from the vaccine on underlying illness or mistakenly attributing a manifestation of underlying illness to the vaccine.

Routine physical examinations or temperature measurements are not prerequisites for vaccinating anyone who appears to be in good health. Asking if a person is ill, postponing a vaccination for someone with moderate or severe acute illness, and vaccinating someone without contraindications are appropriate procedures in immunization programs.

Vaccination Scheduling for Last-Minute

Travelers

In general, as noted above under "Simultaneous Administration," most vaccine products can be given during one visit for those anticipating imminent travel. Unless the vaccines given are boosters of those typically given during childhood, every vaccine has a time period necessary for the host to develop sufficient antibodies, and this period of time may vary depending on the vaccine. This information is found in the Food and Drug Administration (FDA) drug information insert that accompanies each product.

Some vaccines require more than one dose for best protection. The use of multiple reduced doses or doses given at less than minimum intervals can lessen the antibody response. Because some travelers visit their health-care providers without ample time for administration of the several vaccine doses recommended for optimal protection against certain diseases, studies have been performed and others are ongoing to determine whether accelerated scheduling is adequate. This concern is primarily the case for hepatitis B vaccine or the combined hepatitis A and B vaccine (See [Chapter 4](#)). With imminent travel, a clinician may opt to accelerate these vaccine schedules, with the understanding that such administration has not been FDA approved and thus not endorsed by CDC. However, many travel medicine experts are using shortened schedules, feeling that they may provide better protection than the administration of just one dose of vaccine before travel. It is unclear what level of protection any given traveler will have if a full series of vaccination is not completed when more than one dose is recommended.

Hypersensitivity to Vaccine Components

Vaccine components can cause allergic reactions in some recipients. These reactions can be local or systemic and can include anaphylaxis or anaphylactic-like responses. The vaccine components responsible can include the vaccine antigen, animal proteins, antibiotics, preservatives (e.g., thimerosal), or stabilizers (e.g., gelatin). The most common animal protein allergen is egg protein in vaccines prepared by using embryonated chicken eggs (influenza and yellow fever vaccines). Generally, people who can eat eggs or egg products safely may receive these vaccines, while people with histories of anaphylactic allergy (e.g., hives, swelling of the mouth and throat, difficulty breathing, hypotension, or shock) to eggs or egg proteins ordinarily should not. Screening people by asking whether they can eat eggs without adverse effects is a reasonable way to identify those who might be at risk from receiving yellow fever and influenza vaccines. Recent studies have indicated that other components in vaccines in addition to egg proteins (e.g., gelatin) may cause allergic reactions, including anaphylaxis in rare instances. Protocols have been developed for testing and vaccinating people with anaphylactic reactions to egg ingestion.

Some vaccines contain preservatives or trace amounts of antibiotics to which people might be allergic. Those administering the vaccine(s) should carefully review the information provided in the package insert before deciding if the rare person with such an allergy should receive the vaccine(s). Thimerosal in trace quantities may be found in the meningococcal polysaccharide vaccine (groups A, C, Y, and W-125 combined) and the Japanese encephalitis vaccines, as well as in a few others. For a listing of preservatives used and the vaccines in which they are found, see www.fda.gov/cber/vaccine/thimerosal.htm. No currently recommended vaccine contains penicillin or penicillin derivatives. Some vaccines (e.g., MMR and its individual component vaccines, IPV, varicella, rabies) contain trace amounts of neomycin or other antibiotics; the amount is less than would normally be used for the skin test to determine hypersensitivity. However, people who have experienced anaphylactic reactions to the antibiotic generally should not receive these vaccines. Most often, neomycin allergy is a contact dermatitis—a manifestation of a delayed-type (cell-mediated) immune response—rather than anaphylaxis. A history of delayed-type reactions to neomycin is not a contraindication to receiving these vaccines.

Reporting Adverse Events Following Immunization

Modern vaccines are extremely safe and effective. Benefits and risks are associated with the use of all immunobiologics—no vaccine is completely effective or completely free of side effects. Adverse events following immunization have been reported with all vaccines, ranging from frequent, minor, local reactions to extremely rare, severe, systemic illness such as that associated with yellow fever vaccine. Information on side effects and adverse events following specific vaccines and toxoids are discussed in detail in each ACIP statement. Health-care providers are required by law to report selected adverse events occurring after vaccination with tetanus vaccine in any combination, pertussis in any combination, measles and

rubella alone or in any combination, OPV, IPV, hepatitis B, varicella, *Haemophilus influenzae* type b (conjugate), pneumococcal conjugate, and yellow fever vaccines. Reportable events are generally those requiring the recipient to seek medical attention and are stated on the Vaccine Adverse Events Reporting System (VAERS) web site (www.vaers.org/reportable.htm). VAERS is a cooperative program for vaccine safety of the CDC and the FDA. Information about vaccine safety and reporting may be found on their homepage at www.vaers.org.

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- Phyllis Kozarsky, Paul Arguin, and Stefanie Steele

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