Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

8 Protection of Travelers

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More than 1.1 billion people, including an estimated 60 million children, travel internationally each year.[1–3] Up to 8% of travelers to developing countries seek medical care while abroad or on returning home.[4] Although travel can expose children to some risks, the benefits are many. A careful pretravel evaluation to provide appropriate guidance and preparation is critical to protect pediatric travelers and their families and allow them to enjoy their time abroad.

PREPARATION FOR TRAVEL

General Advice

A pretravel evaluation should be performed at least 6 to 10 weeks before travel. The entire itinerary for the trip should be reviewed, including destinations, time and duration of travel, types of accommodation, activities, and potential exposure to insects and animals. The evaluation also should review the medical and immunization history of the child to ensure that appropriate advice is given regarding preventive measures, including necessary vaccines. This evaluation can be accomplished by providing a form for parents to complete and bring to the initial pretravel assessment visit. Particular attention should be given to children of immigrants who are returning to their home countries to visit friends and relatives (VFR) because these children have been shown to be at increased risk for many infectious diseases.[1,5,6] Many excellent resources, most of which are accessible online, provide pretravel advice for pediatricians (Box 8.1).

Travel health guidance should be provided regarding safety issues and infectious diseases.[7–9] Motor vehicle crashes are the most common cause of death among travelers; therefore, particular attention must be given to use of seat belts and car seats as recommended according to the age and size of the child.[10] Car seats may not be readily available at the destination and should accompany the family. Other injury concerns for children include drowning, falls from unprotected balconies or windows, and electrical injuries from unprotected outlets. Children and adolescents who participate in extreme sports and outdoor activities while traveling also should be informed of the potential risks. A parent traveling alone with children should have notarized documentation authorizing him or her to travel with the children.

Advice regarding food and water precautions and insect avoidance should be reviewed thoroughly. Skin protection is an important topic and includes both the risk of serious sunburn and the avoidance of infectious diseases. For sunblock, 30 is the minimum sun protection factor (SPF) recommended for children. Sunblock should be applied 30 minutes before exposure and always before insect repellent is applied where both are needed. Adolescent travelers should be counseled regarding safer sex practices and risks of body piercing and tattooing in less developed countries. Freshwater exposure of any kind should be avoided in areas that are endemic for schistosomiasis or where *Leptospira* species can contaminate the water. Exposure to infected stool of animals or humans can result in several types of parasitic infection either directly (e.g., hookworm) or through fecal-oral exposure (e.g., *Toxocara* spp.). Shoes provide more protection than sandals for children exposed to contaminated environments. Animal bites can result in injury, bacterial infection at the site, or rabies; therefore, children should be cautioned to avoid unknown animals while traveling. Because disposable diapers may

BOX 8.1 Resources and Additional Information for Travelers

- World Health Organization (WHO). International Travel and Health, print version updated biannually, online version updated regularly:www.who.int/ith/
- WHO vaccine summaries: http://www.who.int/immunization/monitoring_surveillance/en/
- Centers for Disease Control and Prevention (CDC). Health Information for International Travel, updated approximately every 2 years (The Yellow Book, Atlanta, GA: US Department of Health and Human Services): http://wwwnc.cdc.gov/travel/page/yellowbook-home-2014
- CDC travel information section: www.cdc.gov/travel/
- CDC *Morbidity and Mortality Weekly Report* (MMWR Morb Mortal Wkly Rep): http://www.cdc.gov/mmwr/
- CDC *Emerging Infectious Diseases Journal:* http://wwwnc.cdc.gov/eid/
- CDC Malaria Hotline: 770-488-7788
- CDC Travelers' Health Automated Information Line (toll-free): 877-FYI-TRIP
- GIDEON (Global Infectious Diseases and EpidemiOlogy Network): www.gideononline.com/
- Pickering LK, Baker CJ, Kimberlin DW, Long SS (eds). Red Book: 2012 Report of the Committee on Infectious Diseases, 29th ed. Elk Grove Village, IL, American Academy of Pediatrics, 2009 (888-227-1770 Publications); new edition published every 3 years
- Pan American Health Organization, the regional office of the WHO: www.paho.org/
- Immunization Action Coalition: http://www.immunize.org/resources/manufact_vax.asp
- United States State Department Hotline for American Travelers: 202-647-5225
- United States State Department: http://travel.state.gov/content/travel/english.html
- International Association for Medical Assistance to Travellers: www.iamat.org
- Program for Monitoring Emerging Diseases (Pro-MED-mail): www.promedmail.org
- Committee to Advise on Tropical Medicine and Travel (CATMAT): http://www.phac-aspc.gc.ca/tmp-pmv/catmat-ccmtmv/index-eng.php
- Travax (NHS National Services Scotland): www.travax.scot.nhs.uk/
- United States: American Society for Tropical Medicine and Hygiene travel health: www.astmh.org
- International Society for Travel Medicine: www.istm.org
- United Kingdom (TravelHealth): www.travelhealth.co.uk/diseases/travelclinics.htm
- Canada Public Health Agency: www.travelhealth.gc.ca

BOX 8.2 Pediatric Travel Medical Kit

NONPRESCRIPTION ITEMS

- Personal information card: name, birth date, chronic medical conditions, regular medications, allergies, blood type, vaccination record, emergency contact information
- First aid supplies: bandages, adhesive tape, gauze, antiseptic cleaning solution, commercial suture or syringe kit (with letter from physician)
- Thermometer
- Analgesics or antipyretics: acetaminophen, ibuprofen
- Skin care products: sunscreen (sun protection factor [SPF] ≥30), barrier ointment/cream, topical corticosteroid cream, disinfectant solution (e.g., chlorhexidine)
- Antihistamine (e.g., diphenhydramine)
- Insect repellent (diethyltoluamide [DEET]), insecticide (permethrin)
- Water purification system
- Oral rehydration packets
- Antimotility agent (e.g., loperamide) if older child (≥2 years)
- Extra pair of prescription glasses

PRESCRIPTION ITEMS

- Currently prescribed medications
- Antimalarial prophylaxis
- Antibiotic for severe travelers' diarrhea (see text)
- Topical antibacterial ointment or cream
- Topical antifungal ointment or cream
- Topical ophthalmic and otic antibiotic solution

not be available in some countries, parents should be aware that cloth diapers must be ironed after washing to kill eggs and larvae deposited on clothing by the tumbu fly, the vector of myiasis, in parts of Africa.

A travel medical kit should be assembled before travel and carried with the family at all times (Box 8.2). As at home, medications should be stored in childproof containers out of reach of children. A discussion of travel health insurance and what to do in the event of illness should be included in the evaluation. In addition, written material summarizing the pretravel advice can be helpful for families.

TABLE 8.1 Acceleration of Routine Vaccine Schedule for Travel[a]

Vaccine	Earliest Age for First Dose	Minimum Interval Between Doses
Combined hepatitis A and B[b]	1 yr	1 wk, 2 wk between second and third doses (booster after 1 yr)
Hepatitis A	1 yr	6 months[c]
DTaP	6 wk	4 wk, 6 mo between third and fourth doses
IPV	6 wk	4 wk
OPV	Birth	4 wk
Hib (conjugate)	6 wk	4 wk (booster after 12 months of age)
Hepatitis B	Birth	4 wk, 8 wk between second and third doses (third dose should be given ≥16 weeks after first dose)
PCV13	6 wk	4 wk, 8 wk between third and fourth doses (after 12 mo of age)
Measles	6 mo followed by MMR at 12 mo and at 4 to 6 yr of age	4 wk
MMR	12 mo	4 wk
Rotavirus[d]	6 wk	4 wk
Varicella	12 mo	4 wk if ≥13 yr of age 3 mo if <13 yr of age

[a]Regular immunization schedule should be reinstituted on return from the endemic area.
[b]Combined hepatitis A and B accelerated schedule is an off-label use for children.
[c]Hepatitis A booster does not need to be given as an accelerated schedule because the seroconversion rate following the first dose is high. The second dose can be given any time after 6 months to induce long-lasting immunity.
[d]For rotavirus vaccine, the maximum age for the first dose is 14 wk and 6 days, and the maximum age for the last dose is 8 months and 0 days.
DTaP, diphtheria and tetanus toxoids and acellular pertussis; Hib, *Haemophilus influenzae* type b; IPV, inactivated poliovirus vaccine; MMR, measles, mumps, rubella; OPV, oral poliovirus vaccine; PCV13, 13-valent pneumococcal conjugate vaccine.

Immunizations Overview

Although immunization rates have been increasing in the United States, significant numbers of children are underimmunized.[11] Many countries with low immunization rates have ongoing transmission of vaccine-preventable illnesses that rarely are seen in North America. Consequently, children who travel must have up-to-date immunization coverage to minimize their risk of contracting vaccine-preventable diseases. Country-specific vaccine-preventable disease statistics and immunization schedules can be found on the World Health Organization (WHO) website, and a listing of international vaccine names also is available online.[12,13]

Travel vaccines are divided into the categories of routine, required, and recommended. *Required* travel vaccines are needed by travelers to cross international borders according to health regulations at the destination. Proof of yellow fever vaccination may be required for entry into or travel from countries where yellow fever is endemic. Vaccinations against meningococcus, influenza virus, and polio virus are required for travelers to the Hajj in Saudi Arabia.[14] *Recommended* travel vaccines include vaccines that should be considered according to the risk of infection during travel.

During the pretravel evaluation, some children may need to receive vaccines in the routine childhood and adolescent immunization schedule administered in an accelerated manner to complete their primary series, catch up with vaccinations, or complete the recommended pretravel vaccine series before departure (Table 8.1).[15–17] The routine or catch-up schedule for immunizations should be continued when the child returns.

Two or more inactivated vaccines or an inactivated and a live vaccine can be administered simultaneously or at any interval. In general, 2 parenterally administered live vaccines should be administered either simultaneously or at least 28 days apart.[18] Caution must be used when scheduling live vaccine administration following immune globulin (IG) administration because decreased immunogenicity of the vaccines can result.[16] This is particularly true of measles and varicella vaccines. Measles- and varicella-containing vaccines should be deferred from 3 to 11 months after IG administration depending on the indication and dose of IG required (see Chapter 5). Although the effect of IG administration on the immunogenicity of varicella vaccine is unknown, the current recommendation is to use the same guidelines for varicella vaccine and IG as are used for measles-containing vaccines.[19] IG administration does not interfere with the immune response to yellow fever vaccine, oral poliovirus vaccine (OPV), rotavirus vaccines, or any inactivated vaccines. IG should not be given <14 days after administration of a live vaccine.

Routine Immunizations

Most North American vaccine-preventable diseases are endemic globally; therefore, a child's routine vaccination schedule should be brought up to date before travel.[15] In particular, the primary series of vaccines, including at least 3 doses of diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine, should be administered by standard or accelerated schedules (see Table 8.1). The tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) adolescent preparation vaccine should be used as the adolescent booster beginning at 11 years of age.[20] People 7 through 10 years of age who are not fully immunized against pertussis should receive a single dose of Tdap. Tdap can be administered regardless of the interval since the last tetanus- and diphtheria-containing vaccine.

Underimmunized children <6 years of age also should receive the conjugate *Haemophilus influenzae* type b (Hib) vaccine before travel.

Although global poliomyelitis eradication had been targeted for 2005, poliomyelitis remains endemic in 3 countries: Afghanistan, Nigeria, and Pakistan.[21] OPV, although widely used in the WHO Expanded Programme on Immunization-Plus (EPI-PLUS), is not available in the US. An accelerated schedule for inactivated poliovirus vaccine (IPV) should be initiated if required, with the first dose given at 6 weeks of age and subsequent doses given at least 4 weeks apart.[15] If a child is traveling in the first few weeks of life and OPV is available, vaccination with OPV can be initiated at birth, with subsequent doses at 4-week intervals.[17] A booster dose of IPV should be given at 4 to 6 years of age and at least 6 months following the previous dose.

Approximately 400 children die of measles every day; children <1 year of age have the highest risk of severe disease.[22] Suboptimal immunization rates raise the risk of transmission within the US, as evidenced by the 2015 outbreak linked to undervaccinated children at a California amusement park.[23] Moreover, the risk of subacute sclerosing panencephalitis is related to acquisition of measles virus at a young age. Maternal antibodies generally protect infants for <6 months. Children between 6 and 12 months of age who are traveling to countries where measles is endemic (including all countries where measles vaccination is not universal) should receive 1 dose of measles, mumps, rubella (MMR) vaccine before travel. Only doses given at or after 12 months of age count as part of the routine US immunization schedule. Children >12 months of age should receive 2 doses of MMR given at least 28 days apart before travel.

Hepatitis B is part of the routine immunization schedule in the US.[24] Children who have not completed their routine hepatitis B series should receive hepatitis B vaccine before travel to highly endemic areas. The hepatitis B series can be accelerated with doses given at 0, 1, and 2 months, followed by a fourth dose at 12 months. A hyperaccelerated schedule of 0, 7, and 21 days with a fourth dose at 12 months can be used if necessary. Although this schedule is not licensed by the US Food and Drug Administration, it is used widely in travel clinics. A 2-dose schedule of adult Recombivax HB (Merck, Whitehouse Station, NJ) at 0 and 4 to 6 months is licensed in the US for adolescents 11 through 15 years of age.[24]

Hepatitis A vaccine, recommended universally for US children, should be given as a 2-dose schedule beginning at 12 to 24 months of age with the second dose 6 months later.[25] Children who have not received the hepatitis A vaccine series should be vaccinated before travel to developing countries. Most hepatitis A cases imported into the US by travelers are related to travel to Mexico and Central America.[25] Although hepatitis A generally causes asymptomatic or mild infection in young children, such children can shed the virus for prolonged periods. Consequently, vaccination of young travelers is recommended to protect both the recipient and any contacts. Children from birth to <12 months of age who are at high risk of exposure to hepatitis A can be given 0.02 mL/kg of IG intramuscularly as passive hepatitis A prophylaxis.[25] For travel lasting longer than 3 months, a larger dose of 0.06 mL/kg should be used.

Twinrix (GlaxoSmithKline, Philadelphia) is a combined hepatitis A and B vaccine that is licensed for people ≥18 years of age.[17,24] Twinrix-Junior is not licensed in the US but is available widely in Europe and Canada for children 1 through 15 years of age. These vaccines are given in a 3-dose schedule at 0, 1, and 6 months. For last-minute travel they can be accelerated in a schedule of 0, 7, and 21 days with a booster given at 1 year.[26] In Canada and parts of Europe, 2 *adult* doses of the vaccine administered 6 months apart have been approved for children 1 through 15 years of age.[27,28]

Varicella vaccine is recommended for all susceptible children and is given in the US for children from 12 months through 12 years of age. For children <13 years of age, a second dose should be given 3 months after the first. For adolescents 13 years of age and older, 2 doses are required with an interval of at least 4 weeks between doses.[19]

The 13-valent pneumococcal conjugate vaccine (PCV13) is part of the routine childhood immunization schedule and should be given as a 4-dose series at 2, 4, 6, and 12 through 15 months of age, although the schedule can be accelerated (see Chapter 123).[29]

Two quadrivalent conjugate meningococcal vaccines for serogroups A/C/Y/W-135 (MCV) are licensed in the US for children. Menactra (Sanofi Pasteur, Swiftwater, Pa) is licensed as a 2-dose series between the ages of 9 and 23 months, whereas Menveo (GlaxoSmithKline) is licensed as a 4-dose series starting at 2 months of age. Both vaccines are recommended for persons at increased risk of meningococcal disease, including travelers to countries with hyperendemic or epidemic meningococcal disease.[30] In addition, MCV is recommended routinely for use in all children 11 to 12 years of age, with a booster dose at 16 years of age. Administer 1 dose at 13 through 18 years of age if the patient is not previously vaccinated (see Chapter 125).[31] As of January 2015, 2 novel vaccines for serogroup B have been approved in the US for persons 10 to 25 years of age in response to an outbreak in university students.[32] Bexero (GlaxoSmithKline) has been approved for use in Canada for children 2 months of age and older.[33] However, this vaccine is generally not recommended for travel unless someone is traveling to an area with an ongoing outbreak of serogroup B meningococcal disease.

Influenza vaccine is recommended for all people without medical contraindications 6 months of age and older.[34] The influenza season occurs from April to September in the southern hemisphere and year-round in the tropics. Influenza outbreaks have occurred on cruise ships and organized group tours in any latitude and season.[35]

Rotavirus vaccine is recommended for all US children starting at 2 months of age in a 2- or 3-dose schedule depending on which of the 2 licensed vaccines is used.[36] Rotavirus vaccine can be given in an accelerated dosing schedule, if needed (see Table 8.1).

Two human papillomavirus (HPV) vaccines are licensed in the US and Canada and are recommended for use in all girls at 11 to 12 years of age.[37] HPV4 vaccine is recommended for boys and girls at 11 to 12 years of age. HPV vaccines in children are administered in a 2- or 3-dose schedule, the second and third dose 2 and 6 months after the first dose or a single 6-month dose. The first dose can be given as early as 9 years of age.

Required and Recommended Vaccines for Travel

Table 8.2 provides details regarding travel vaccines recommended for children.

Cholera Vaccine

The risk of cholera is low for travelers. Cholera vaccines are not available in the US. However, they are licensed in some countries: WC/rBS (Dukoral, SBL Vaccines, Solna, Sweden) and 2 closely related bivalent cholera vaccines Shanchol (Shantha Biotec, Hyderabad, India) and mORCVAX (Vabiotech Vietnam).[38] Dukoral is licensed for children ≥2 years of age. Cholera vaccine is not required for entry into any country. The WHO recommends use of cholera vaccine only for travelers at high risk such as emergency or relief workers who plan to work in refugee camps or as healthcare personnel in endemic areas.[39]

Typhoid Vaccine

Typhoid vaccine is recommended for pediatric travelers to the Indian subcontinent and other developing countries in Central and South America, the Caribbean, Africa, and Asia.[40] Children are particularly at risk of developing typhoid and of becoming chronic carriers. Two vaccines are available for prevention of typhoid: a live, attenuated oral vaccine (Ty21a), which can be used in children ≥6 years of age; and a purified Vi capsular polysaccharide vaccine that is delivered intramuscularly to children ≥2 years of age. The efficacy of both vaccines is approximately 50% to 70%; receipt of the vaccine does not eliminate the need for food and water precautions.[41–43] If exposure continues, revaccination is recommended every 2 years for the polysaccharide vaccine and every 5 years for the oral Ty21a vaccine.

The Ty21a vaccine is available only in capsules in the US, thus limiting usefulness in younger children. The Ty21a vaccine must be refrigerated and taken with cool liquids approximately 1 hour before eating. The Ty21a vaccine should not be taken concurrently with the antimalarial proguanil, and antibiotics should not be used from the day before the first capsule until 7 days after completing the vaccine course. Clinical trials of a Vi conjugate vaccine demonstrating safety, efficacy, and immunogenicity in infants and children are ongoing.[44–46]

Yellow Fever Vaccine

Yellow fever vaccine is a live, attenuated vaccine that may be required or recommended for travel to central South America and sub-Saharan

TABLE 8.2 Schedule and Dosing for Travel Vaccines

Vaccine	Schedule	Minimum Age	Dose (mL)	Route	Booster Dose
BCG (live, attenuated)	1 dose	Birth	<1 yr: 0.05 mL ≥1 yr: 0.1 mL	Intradermal preferred but subcutaneous acceptable	None
Hepatitis A/B, combined (inactivated/recombinant)	3 doses: 0, 1, and 6 mo	1 yr	0.5 mL	Intramuscular	None
Meningococcal A/C/Y/W-135 (conjugated polysaccharide)	2–6 mo = 4 doses: 0, 2, 4, 12 mo 7–23 mo = 2 doses: 0, 3 mo >23 mo = 1 dose	2 mo	0.5 mL	Intramuscular	<7 yr: 3 yr ≥7 yr: 5 yr
Rabies (inactivated cell culture)	3 doses: 0, 7, 21 or 28 days	Birth	1.0 mL	Intramuscular	Consider at 2 yr if high-risk
Typhoid, Ty21a (live, attenuated)	4 doses: alternate days	6 yr	1 capsule	Oral	5 yr
Typhoid, Vi (capsular polysaccharide)	1 dose	2 yr	0.5 mL	Intramuscular	2 yr
Yellow fever (live, attenuated)	1 dose	9 mo	0.5 mL	Subcutaneous	10 yr
Japanese encephalitis (inactivated cell culture)	2 doses: 0 and 28 days	2 mo	<3 yr = 0.25 mL ≥3 yr = 0.5 mL	Intramuscular	1 yr

BCG, bacille Calmette-Guérin.

Africa. Some countries in Africa require an international certificate of vaccination (or a physician's waiver letter) against yellow fever for all entering travelers; other countries may require evidence of vaccination for travelers coming from or traveling through endemic areas. The vaccine is recommended for all children ≥9 months of age traveling to endemic areas. A single dose of yellow fever vaccine confers lifelong immunity; therefore, boosters are not required for protection. However, a booster may be required every 10 years by some countries.[47] Risks and benefits of yellow fever vaccination and likelihood of infection must be considered carefully in pregnant women and in people who are immunocompromised.[48] Yellow fever vaccine contains egg protein; therefore, people with previous anaphylaxis in response to eggs should not receive the vaccine. The vaccine is only available in the US from providers certified by state health departments.[49]

A yellow fever vaccine–associated encephalitis syndrome has been reported in young infants at a rate of 0.5 to 4 per 1000 infants vaccinated.[17] Neurologic symptoms occur 7 to 21 days after immunization; disease is related to reversion of vaccine virus to wild-type neurotropic virus. Consequently, the vaccine is contraindicated in infants <6 months of age. For infants 6 to 9 months of age who cannot avoid travel to a yellow fever–endemic area, consultation with an expert in the field is recommended. Yellow fever vaccine–associated viscerotropic disease, a severe systemic illness that can result in fatal organ failure, rarely has been reported.

Rabies Vaccine

Rabies is highly endemic in Africa, Asia (particularly India, China, and Indonesia), and parts of Latin America, but the risk to travelers is low. Preexposure rabies immunization is recommended for travelers with an occupational risk of exposure, for people planning extended stays in endemic areas where medical care is limited, and for outdoor travelers.[50] However, studies suggest that animal bites often occur during short-term travel.[51] Given that children are more likely to interact with animals and not report an animal bite, rabies preexposure vaccination should be considered for children traveling to endemic countries for at least 1 month.[52] The preexposure vaccine is 3 doses of 1.0 mL each given intramuscularly at 0, 7, and 21 or 28 days.[50] The series can be administered using either of the 2 licensed vaccines in the US: human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV). If a vaccinated child is bitten or sustains a skin-penetrating scratch by a potentially rabid animal, the wound must be washed thoroughly, and 2 additional doses must be completed as soon as possible (given 3 days apart); rabies IG is not required.[53] Without preexposure immunization, rabies IG and 4 doses of an approved vaccine (given over 14 days) are required; however, rabies IG is often not available in many developing countries.[53]

Japanese Encephalitis Virus Vaccine

Japanese encephalitis, an arboviral infection transmitted by night-biting *Culex* mosquitoes, is endemic in rural areas of Asia, although occasional epidemics occur in periurban areas. In temperate regions, transmission occurs from April to November, but disease occurs year-round in tropical and subtropical areas. The disease is uncommon in travelers.[54] Although most cases are subclinical, half of patients with clinical disease have persistent neurologic abnormalities, and the case fatality rate is 20% to 30%.[54] The vaccine is recommended for all travelers who are traveling in endemic areas for at least 1 month. Vaccination also should be considered for shorter-term travelers with increased risk of Japanese encephalitis virus exposure. One Japanese encephalitis vaccine (JE-VC [IXIARO], Valneva Austria, Vienna, Austria, distributed by Intercell USA, Gaithersburg, Md) is licensed in the US for people ≥2 months of age.[54] Two doses of JE-VC are administered 1 month apart. For adults at ongoing risk of exposure, a booster dose of JE-VC is recommended at 1 to 2 years after the primary series.[54] For children, the duration of immunity is unknown.

Meningococcal Vaccine

Five serogroups of *Neisseria meningitidis* (A, B, C, Y, and W135) are responsible for most meningococcal disease. The epidemiology of serogroups responsible for disease is changing worldwide; B, C, and Y are most prevalent in the US, whereas A, C, and W135 cause most epidemic disease in sub-Saharan Africa. The incidence in the US is 0.3 cases in 100,000, and in sub-Saharan Africa it can be as high as 800 cases in 100,000 annually.[30,32]

Meningococcal vaccine is required for travelers to the Hajj and also is recommended for people traveling to the "meningitis belt" in equatorial Africa during the dry season from December to June, where serogroup A accounts for 85% of all cases. One of the quadrivalent conjugate vaccines for serogroups A/C/Y/W-135 (MCV4) can be given to children beginning at 2 months of age. Children who received the conjugate or polysaccharide meningococcal vaccine before 7 years of age should be revaccinated within 3 years if they remain at risk.[31] Novel serogroup B meningococcal vaccines have been approved for use in the US[32] and Canada.[33]

Tickborne Encephalitis Virus Vaccine

Tickborne encephalitis virus is transmitted by *Ixodes ricinus* ticks in the forests of central and eastern Europe during the summer months.[55] Two vaccines are licensed in Europe for use in children ≥1 year of age (FSME-IMMUN, Baxter Vaccine, Vienna, Austria; and Encepur, Novartis, Germany. According to CDC's *Yellow Book*, neither is licensed in the US.[3,43]

Bacille Calmette-Guérin Vaccine

Bacille Calmette-Guérin (BCG) vaccine is part of the routine vaccination schedule in many developing countries where tuberculosis (TB) is highly endemic. BCG does not prevent TB infection but has been shown to decrease the incidence of severe TB disease such as miliary TB and TB meningitis. Vaccination with BCG is generally not recommended in the US; however, it can be considered in selected children after consultation with a TB expert. In addition, children who do not receive BCG and who have traveled to a country with a high TB burden should have a tuberculin skin test before and 3 months after returning from travel.[56]

MALARIA

Malaria is caused by infection with *Plasmodium* species, most commonly through the bite of an infected female *Anopheles* mosquito. Malaria is a leading cause of death among children <5 years of age worldwide, and it causes approximately 200 million infections and more than 500,000 deaths each year.[57] Young children, pregnant women, and people who previously have not been exposed to malaria have the highest risk of severe disease. Although malaria is endemic throughout the tropics, the highest risk for malaria infection in travelers occurs in sub-Saharan Africa, Papua New Guinea, the Solomon Islands, and Vanuatu.[52,58] No vaccine is available for prevention of malaria infection in travelers; therefore, families traveling with children must be provided with advice regarding personal protective measures and malaria chemoprophylaxis if they are traveling to endemic areas.

Chemoprophylaxis

The type of chemoprophylaxis recommended depends on the likelihood of drug resistance, potential adverse reactions, cost, and convenience. In addition, characteristics of the individual traveler, including age, ability to swallow tablets, and any specific contraindications, are relevant.[59] Breast-feeding infants require prophylaxis because antimalarial drugs do not reach high enough levels in human milk. Several medications are recommended for prevention of malaria in children: chloroquine, mefloquine, doxycycline, and atovaquone/proguanil.[59,60] Chloroquine is inexpensive and well tolerated, but it is of limited efficacy because of resistance to *Plasmodium falciparum* in all regions except parts of the Caribbean and Central America. Atovaquone/proguanil is typically the best tolerated, but it is the most expensive. It is approved for children >5 kg and comes as pediatric tablets. Mefloquine is safe for use in pregnancy and neonates and has the convenience of weekly dosing. Adult tablets need to be broken and compounded into a liquid. Neuropsychiatric side effects limit its tolerability, and increasing resistance is reported in Southeast Asia.[60] Doxycycline is contraindicated in children <9 years of age because of dental staining. Primaquine is recommended as a primary agent in areas with a high incidence of *Plasmodium vivax,* such as Central America, and as a second-line agent in other areas when other antimalarial drugs cannot be used (see Chapter 271).[61] Chloroquine should be initiated 1 to 2 weeks before travel and preferably 4 weeks before travel for mefloquine; doxycycline, atovaquone/proguanil, and primaquine can be started 1 day before exposure. Most chemoprophylactic agents must be continued for 4 weeks after departure from malaria-endemic areas except for atovaquone/proguanil and primaquine, which must be continued for only 1 week after exposure. However, in an atovaquone/proguanil prophylaxis study in 485 Israeli subjects, 87% discontinued the drug 1 day after travel; no cases of malaria occurred, suggesting a shorter duration after travel can be adequate.[62] Updated guidelines from national organizations such as the Centers for Disease Control and Prevention (CDC) and the Committee to Advise on Tropical Medicine and Travel (CATMAT) can be found online (see Box 8.1).

Protective Measures

Because no malaria chemoprophylaxis is 100% effective, personal protective measures, such as barrier and chemical protection and exposure avoidance, should be used to minimize risk of contact with mosquitoes. These protective measures also can decrease the risk of other vector-borne diseases, such as dengue and other arboviruses.

Because *Anopheles* species mosquitoes that transmit malaria bite from dusk to dawn, children must have adequate protection during these hours. The *Culex* species mosquitoes that transmit Japanese encephalitis virus also bite primarily between dusk and dawn, whereas the *Aedes* species mosquitoes that transmit dengue, chikungunya, and yellow fever viruses bite primarily during the day. When a risk of insect exposure exists, children should be dressed in light-colored clothing that covers their arms and legs. Other measures to avoid insect bites include staying in air-conditioned or well-screened accommodation or using insecticide-treated bed nets.

Chemical protection provides additional defense against insect-borne diseases. The safest and best studied is *N,N*-diethyl-meta-toluamide (DEET).[59] Although adverse reactions, such as encephalopathy and rashes, have been described with excessive or prolonged use of high concentrations of DEET in children, this compound is considered safe when used appropriately according to product label instructions (Box 8.3).[58,63] The concentration of DEET correlates with the duration of protection; therefore, products with lower concentrations must be reapplied. DEET is recommended by the American Academy of Pediatrics in concentrations up to 30% for children as young as 2 months of age; in standard preparations, this concentration provides 4 to 6 hours of protection.[64] Non–DEET-containing repellents such as picaridin, IR3535, and oil of lemon eucalyptus appear to be safe and well tolerated but must be reapplied more frequently.[61] Oil of lemon eucalyptus is not recommended in children <3 years of age.

Permethrin (a safe chrysanthemum derivative) is a contact insecticide that can be used for treatment of bed nets and clothing.[60] Permethrin-treated fabric has a duration of efficacy between 2 weeks and 6 months depending on the method of treatment. The best chemical protection against mosquito bites is use of a combination of permethrin-treated clothing and an effective insecticide on exposed skin.

TRAVELERS' DIARRHEA

Travelers' diarrhea is one of the most common illnesses among travelers, and it affects 22% to 39% of children who travel.[65,66] Both the incidence and the severity of travelers' diarrhea are age dependent, with the highest rates, longest duration, and greatest severity occurring in infants and children younger than 3 years of age.[67,68] Children's stools normally can be quite variable; consequently, travelers' diarrhea is defined as a twofold or greater increase in the frequency of unformed stools, lasting at least 2 to 3 days. The infectious causes of travelers' diarrhea in children and adults predominantly are bacterial and include enterotoxigenic *Escherichia coli* (ETEC), which is the most common cause, enteroaggregative *E. coli* (EAEC), *Salmonella, Campylobacter, Shigella,* enteropathogenic *E. coli* (EPEC), and, rarely, shigatoxin-producing *E. coli* (STE). Viral and parasitic infections are less common causes of pediatric travelers' diarrhea, although rotavirus, *Cryptosporidium parvum, Giardia lamblia,* and *Entamoeba histolytica* also account for a small proportion of diarrhea cases in young travelers. Studies show that 15% or more of cases of travelers' diarrhea may be caused by norovirus.[69,70]

The risk of developing travelers' diarrhea depends on the travel destination, with rates as high as 73% among children traveling to North Africa and 61% among children visiting India.[67] Travel to Southeast Asia, Latin America, and other African countries has been associated with

BOX 8.3 Precautions for Use of Diethyltoluamide

- Use repellents containing ≥30% DEET only.
- Apply sparingly to exposed skin.
- Apply only to intact skin.
- Apply to face by wiping; avoid eyes and mouth; do not spray directly on face.
- Wash off with soap and water when coming indoors.
- Do not inhale or ingest repellent.
- Do not apply on hands or other areas that are likely to come in contact with the eyes or mouth.
- Do not allow children younger than 10 years of age to apply DEET themselves. Apply to your own hands and then apply to the child.
- Do not use on children less than 2 months of age.

DEET, diethyltoluamide.

rates of approximately 40%. Although travelers' diarrhea generally is a self-limited infection, it can cause significant morbidity, particularly if it results in moderate to severe dehydration. Parents must be counseled regarding the symptoms and signs of dehydration, as well as the approach to oral rehydration and when to seek medical attention.[71]

Preventive Measures

Because no vaccines are licensed in the US for prevention of travelers' diarrhea in children, counseling regarding food and water precautions is the most important preventive measure. Vaccines are in development in preclinical and clinical phases against ETEC, *Shigella* spp., and *Campylobacter jejuni*. A cholera vaccine that also provides short-term protection against ETEC is licensed in Canada and Europe for children ≥2 years of age.[72]

General rules regarding food and water precautions when traveling apply to both children and adults; however, young children are more likely to explore the environment with their hands and mouths, thus creating opportunities for infection and increasing their risk of diarrhea.[52] Frequent handwashing with soap and water is critical, particularly before eating, although alcohol-based handwashes can be used when water is not available.

Children must be reminded to use safe water sources for all drinking, tooth brushing, and food preparation. Safe water sources include bottled water from a trusted source or water that has been boiled, chemically treated, or filtered. Combination chemical and filter pumps can provide the best protection because filters vary in the size of microbes that are removed.[73] Water should be boiled for at least 1 minute at altitudes <2000 m and 3 minutes at >2000 m.[56] Carbonated drinks also are considered safe for drinking, but water used to make ice can be contaminated. For infants, breastfeeding is the safest form of nutrition. In addition to its many health benefits, breastfeeding does not require a source of clean water, unlike the use of formula, both in its preparation and in the cleaning of bottles.

The selection and preparation of foods are important during travel to minimize the risk of travelers' diarrhea. Although the advice to "boil it, cook it, peel it, or forget it" frequently is given, this often is not practical to follow. If possible, only steaming-hot, freshly made food should be consumed. Families traveling with children should have a ready supply of snacks and avoid buying food from street vendors (Box 8.4).

Additional food and water precautions can decrease risk of other infectious diseases while traveling. These include avoidance of unpasteurized dairy products to eliminate the risk of brucellosis and other bacterial infections. Raw or undercooked meat and fish should not be consumed because of the risk of parasitic infections. Avoiding undercooked seafood can decrease the risk of hepatitis A. In developing countries, raw vegetables and fruit that cannot be self-peeled should be avoided.

Chemoprophylaxis for travelers' diarrhea generally is not advised in children.[67] However, short-term prophylaxis (<3 weeks) could be considered for children with increased susceptibility to travelers' diarrhea, such as children with achlorhydria or children in whom travelers' diarrhea could have significant medical consequences (e.g., children with chronic renal failure, congestive heart failure, diabetes mellitus, or inflammatory bowel disease).[74]

BOX 8.4 Prevention of Travelers' Diarrhea in Children

DO

- Eat only thoroughly cooked food served hot.
- Peel fruit.
- Drink only bottled, carbonated, boiled, chemically treated, or filtered water.
- Prepare all beverages and ice cubes with boiled or bottled water.
- Wash hands before eating or preparing foods.
- Continue breastfeeding throughout travel period.

DO NOT

- Eat raw vegetables or unpeeled fruit.
- Eat raw seafood or shellfish or undercooked meat.
- Eat food from street vendors.
- Drink tap water
- Consume milk or dairy products unless labeled as pasteurized or irradiated.

Treatment

Treatment of travelers' diarrhea in children must include close attention to hydration status, and parents should be counseled regarding early signs of dehydration. Oral rehydration therapy using a homemade or commercially prepared oral rehydration solution (ORS) can be used to prevent dehydration associated with diarrheal disease. Commercial ORS should be used to treat mild to moderate dehydration; severe dehydration can require intravenous fluid resuscitation.[75,76] ORS packets should be part of a family's travel medical kit. Locally made preparations can be used early in therapy, although they differ in composition from the reduced-osmolarity ORS recommended by the WHO (Table 8.3).[75] For infants, breastfeeding should be continued, along with oral rehydration and solid food intake, although foods high in simple sugars should be avoided because the increased osmotic load can worsen fluid losses.

Loperamide generally is used in combination with antibiotics for treatment of travelers' diarrhea in adults; however, the role of loperamide in pediatric travelers' diarrhea remains controversial, even though this drug is licensed for use in children ≥2 years of age. Although loperamide has been shown to decrease the duration and severity of acute diarrhea in children, it has been associated with significant side effects in children and is not recommended for children <3 years of age.[76–78] Zinc supplementation has been associated with improved outcomes in diarrheal disease in children in developing countries, but zinc supplementation is not recommended in treatment of travelers' diarrhea.[76]

Empiric treatment with antimicrobial agents can be considered in pediatric travelers' diarrhea. However, treatment should be confined to moderate to severe diarrhea, given data that show a marked increased carriage of extended spectrum β-lactamase (ESBL)–producing Enterobacteriaceae with antibiotic use.[79] Azithromycin often is used as the first choice for treatment of pediatric travelers' diarrhea, especially in areas with a high prevalence of fluoroquinolone-resistant *Campylobacter* species (e.g., South and Southeast Asia), because the drug is given once a day and has a known safety profile in children. A dose of 10 mg/kg once daily for 3 days (maximum dose of 500 mg) is appropriate.[67] In adults, a single dose of antibiotic has been shown to be as effective as 3 days of treatment; therefore, in children a full 3-day course may not be necessary.[80,81]

Fluoroquinolones for 1 to 3 days are the drug of choice for adults with travelers' diarrhea that is moderate to severe, persistent (>3 days), or associated with fever or bloody stools. Although concerns exist regarding the potential for development of arthropathy and antimicrobial resistance with fluoroquinolone use in children, the US Food and Drug Administration has approved ciprofloxacin for anthrax and as a second-line agent for the treatment of urinary tract infections in children from 1 through 17 years of age.[82] Therefore, fluoroquinolones could be considered safe in children for the short course required for travelers' diarrhea. A 1- to 3-day course of ciprofloxacin at a dose of 30 mg/kg/day divided twice daily with a maximum dose of 500 mg twice daily is recommended for children with moderate to severe or bloody diarrhea.[67]

Rifaximin (Xifaxan), a nonabsorbed rifamycin derivative, has been approved in the US for treatment and prevention of travelers' diarrhea for people ≥12 years of age.[83] A liquid preparation is available in some

TABLE 8.3 Formulation of Oral Rehydration Solution

World Health Organization	Home Formula
NaCl 2.6 g/L (75 mmol/L sodium)	6 level teaspoons sugar
KCl 1.5 g/L (20 mmol/L potassium)	1/2 teaspoon salt
Trisodium citrate, dihydrate 2.9 g/L (10 mmol/L citrate)	1 L water
Glucose, anhydrous 13.5 g/L (75 mmol/L glucose)	A splash of lemon juice (for taste)

KCl, potassium chloride; NaCl, sodium chloride; $NaHCO_3$, sodium bicarbonate.

countries for pediatric use. The drug is indicated for the management of noninvasive diarrheas such as those seen in ETEC infection, cholera, or EAEC infection when fever and bloody diarrhea are absent.

If travelers' diarrhea does not respond to a course of antimicrobial therapy, medical attention should be sought to investigate other possible causes of the diarrhea. Postinfectious irritable bowel syndrome is well recognized in adults as well as in children.

EMERGING INFECTIOUS DISEASES

Several infectious agents, such as Ebola virus, severe acute respiratory syndrome (SARS) and Middle Eastern respiratory syndrome (MERS) coronaviruses, chikungunya virus, Zika virus, the H5N1 strain of avian influenza virus, and the pandemic (H1N1) 2009 influenza virus have emerged as potentially widespread health threats. Given the constantly changing epidemiology of infectious diseases, pediatricians who advise families regarding travel health must keep informed of the current status of emerging infectious diseases that can pose a threat to the traveler. Several websites provide up-to-date information regarding such infections, including those of the WHO and the CDC (see Box 8.1).

IMMUNOCOMPROMISED TRAVELERS

Children with immunodeficiencies require special consideration at their pretravel evaluation because of increased risk of travel-related illness.[84] Most patients with an altered immune system, particularly people with decreased T-lymphocyte immunity, should not receive live vaccines because of risk of developing clinical illness from the vaccine strain.[84] IPV should be given instead of OPV to all members in the family of an immunocompromised person, and Vi typhoid vaccine should be administered instead of the Ty21a vaccine to an immunocompromised child, although the patient is not at risk if family members receive the live oral vaccine.[16,85] However, MMR, varicella, and yellow fever vaccines should be considered for human immunodeficiency virus (HIV)–seropositive children who are not severely immunocompromised (see Chapters 205 and 227). Killed or subunit vaccines can be administered to children with altered immunity, although responses to the vaccines can be diminished.[85] Asplenic patients may respond poorly to polysaccharide vaccines in particular. Patients with certain B-lymphocyte deficiencies, such as X-linked agammaglobulinemia and common variable immunodeficiency, should avoid OPV, vaccinia, and live bacterial vaccines, although other patients with humoral immunodeficiencies, including selective immunoglobulin (Ig) A and IgG subclass deficiency, must avoid only OPV; other live vaccines can be considered.

Some travel-associated illnesses can be more severe in immunocompromised travelers. Asplenic travelers are at greater risk of severe babesiosis and malaria, and organ and stem cell transplant recipients are more likely to develop bacteremia associated with gastroenteritis from *Salmonella* or *Campylobacter* spp.[86] HIV-seropositive travelers with low $CD4^+$ lymphocyte counts must be particularly conscious of risk factors associated with opportunistic infections such as *Toxoplasma gondii, Cystoisospora* (previously *Isospora*) *belli, Salmonella* spp., and *C. parvum,*[86] and therefore they must be particularly cautious regarding food, water, and animal exposures. In addition, because of the risk of disseminated strongyloidiasis in immunocompromised hosts, closed footwear should be encouraged strongly in such travelers.

RETURN FROM TRAVEL

Routine posttravel screening generally is not required for asymptomatic, short-term travelers, although screening can be considered for long-term travelers, expatriates, adventure travelers, and people who have experienced significant illness while traveling.[4] If posttravel screening is indicated, the tests required should be determined by the potential exposures associated with the travel itinerary and any symptoms, if present.

Children who develop fever after travel should seek immediate medical attention, and parents must inform physicians caring for them of their travel itinerary. This is particularly critical if the itinerary has included a malaria-endemic area given that chemoprophylaxis cannot prevent all cases of malaria. Because malaria can manifest with nonspecific symptoms in children, any symptoms of fever, rigors, headache, malaise, abdominal pain, vomiting, diarrhea, poor feeding, or cough following travel to an endemic country should be evaluated promptly by a physician.[52,87]

Travel-related illness has been shown to be highly dependent on itinerary. In a report of disease and relation to place of exposure among ill returned travelers, significant regional differences in proportionate morbidity were reported.[4] Typhoid fever was seen most frequently in travelers returning from South Asia. Malaria was the most frequent cause of febrile illness among travelers returning from sub-Saharan Africa, whereas dengue was a more frequent cause of fever in most other areas. Rickettsial infections, primarily tickborne spotted fever, occur more frequently than malaria or dengue among travelers returning from South Africa.[4]

All references are available online at www.expertconsult.com.

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