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Advice for Travelers

Patients planning to travel to other countries often ask for information about appropriate vaccines and prevention of diarrhea and malaria. More detailed advice for travelers is available from the Centers for Disease Control and Prevention (CDC) at www.cdc.gov/travel. Guidelines are also available from the Infectious Diseases Society of America (IDSA).¹

VACCINES

Common travel vaccines are listed in Table 2 on page 47. In addition to travel-specific vaccines, all travelers (including children) should be up to date on routine immunizations. Guidelines for routine adult immunization are available in a separate issue.² Immunocompromised or pregnant patients generally should not receive live virus vaccines, such as those for measles and yellow fever, although in some situations the benefit might outweigh the risk.³

HEPATITIS A — Hepatitis A vaccine, which is now part of routine childhood immunization in the US, is recommended for all unvaccinated travelers going to countries with intermediate or high hepatitis A endemicity (see Table 1 for low-risk areas).⁴ The two hepatitis A vaccines available in the US, Havrix and Vaqta, are usually administered in two IM doses. Patients who receive a first dose of one vaccine will respond to a second dose of the other.

Antibodies reach protective levels 2-4 weeks after the first dose. Even when exposure to the disease occurs sooner than 4 weeks after vaccination, the traveler is usually protected because of the relatively long incubation period (average 28 days) of hepatitis A. Second doses given up to 8 years after the first dose have produced protective antibody levels.⁵

For adults >40 years old, immunosuppressed patients and those with chronic liver disease or other chronic medical conditions who will be traveling to an endemic area in <2 weeks, a 0.02 mL/kg IM dose of immune globulin should be given in addition to the initial dose of vaccine. The same dose should be given to children <1 year of age and to travelers who elect not to receive the vaccine if they will be traveling for <3 months; a dose of 0.06 mL/kg IM should be given for travel lasting 3 months or longer. For travel durations of >5 months, the dose should be repeated.⁶

HEPATITIS B — Hepatitis B vaccine, which is now part of routine childhood immunization in the US, is recommended for all travel-specific vaccines, all travelers (including children) should be up to date on routine immunizations. Guidelines for routine adult immunization are available in a separate issue.² Immune compromised or pregnant patients generally should not receive live virus vaccines, such as those for measles and yellow fever, although in some situations the benefit might outweigh the risk.³

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HEPATITIS B — Hepatitis B vaccine, which is now part of routine childhood immunization in the US, is recommended for all travelers going to intermediate- or high-risk areas (see Table 1 for low-risk areas). In addition, travelers who may engage in behaviors that can increase the risk of transmission, such as injection drug use, unprotected sexual contact with new partners, dental treatment, skin perforation practices (tattoos, acupuncture, ear piercing) or medical tourism involving

<table>
<thead>
<tr>
<th>Table 1. Low-Risk Areas For Hepatitis A &amp; B*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis A¹</td>
</tr>
<tr>
<td>Asia Pacific (includes Japan, Australia, Singapore)</td>
</tr>
<tr>
<td>South Korea, Singapore</td>
</tr>
<tr>
<td>East Asia (includes China, Philippines, Vietnam)</td>
</tr>
<tr>
<td>Southeast Asia (includes Indonesia, Malaysia)</td>
</tr>
<tr>
<td>Australasia (includes Australia, New Zealand)</td>
</tr>
<tr>
<td>Caribbean</td>
</tr>
<tr>
<td>Europe</td>
</tr>
<tr>
<td>North America</td>
</tr>
<tr>
<td>Panama</td>
</tr>
<tr>
<td>United States³</td>
</tr>
<tr>
<td>Western Europe⁴</td>
</tr>
</tbody>
</table>

¹ All other areas are intermediate to high risk; vaccine is indicated.
² Regions with a low (<2%) prevalence of hepatitis B surface antigen (wwwnc.cdc.gov/travel/page/diseases/htm).
³ Risk is intermediate in Alaska natives and is high in indigenous populations of northern Canada.
⁴ Risk is intermediate in Greece, Portugal and Spain.

¹ Regions with a low or very low level of hepatitis A endemicity (KH Jacobsen and ST Wiersma. Vaccine 2010; 28:6653.
² Countries with a low (<2%) prevalence of hepatitis B surface antigen (wwwnc.cdc.gov/travel/page/diseases/htm).
³ Risk is intermediate in Alaska natives and is high in indigenous populations of northern Canada.
⁴ Risk is intermediate in Greece, Portugal and Spain.

[Table 1. Low-Risk Areas For Hepatitis A & B*]
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invasive medical treatment (injections, stitching), should, regardless of destination, be immunized against hepatitis B.

Two hepatitis B vaccines are available in the US: Engerix-B and Recombivax-HB. A 3-dose series started with one vaccine may be completed with the other. An interrupted series can be completed without being restarted.

HEPATITIS A/B — A combination vaccine (Twinrix) containing the same antigenic components as pediatric Havrix and Engerix-B is available for patients ≥18 years old. The combination vaccine can be used to complete an immunization series started with monovalent hepatitis A and B vaccines. Twinrix Junior is available outside the US for children 1-15 years old.

INFLUENZA — Influenza may be a risk in the tropics year-round and in temperate areas of the Southern Hemisphere from April to September. Outbreaks have occurred on cruise ships and on organized group tours in any latitude or season.7 Seasonal influenza vaccine directed against strains in the Northern Hemisphere is sometimes available in the US until the end of June; the US Advisory Committee on Immunization Practices (ACIP) recommends that persons for whom seasonal influenza vaccine is indicated8 consider being vaccinated before travel to the Southern Hemisphere during influenza season or to the tropics at any season, or when traveling in a group with persons from the Southern Hemisphere during their influenza season (April-September). In some years, the vaccine strains are the same in both hemispheres. If the vaccine strains are different, high-risk patients from the Northern Hemisphere who travel to the Southern Hemisphere during that region’s influenza season could also consider being immunized on arrival because the vaccine active against strains in the Southern Hemisphere is rarely available in the Northern Hemisphere. Seasonal influenza vaccines are prepared in eggs; hypersensitivity reactions could occur.

There is no commercial vaccine available for pathogenic strains of avian influenza (H5N1, H7N2, H9N2, H7N3, H7N7), but an inactivated vaccine against avian H5N1 is FDA-approved and is included in the US Strategic National Stockpile.

JAPANESE ENCEPHALITIS — Japanese encephalitis is an uncommon but potentially fatal mosquito-borne viral disease that occurs in rural Asia, especially near pig farms and rice paddies. It is usually seasonal (May-October), but may occur year-round in tropical regions. The attack rate in travelers has been very low.10 Vaccination is recommended for travelers who expect a long stay (≥1 month) in endemic areas or heavy exposure to mosquitoes (such as adventure travelers) during the transmission season. Vaccination should also be considered for travelers spending <1 month in endemic areas during the transmission season if they will be sleeping without air conditioning, screens or bed nets, or spending considerable time outside in rural or agricultural areas, especially in the evening or at night.11 Some Medical Letter reviewers suggest that, given the rarity of the disease in US residents, compulsive use of insect repellents and judicious avoidance of exposure to mosquitoes between dusk and dawn might be reasonable alternatives to vaccination for short-term travelers.

Two vaccines are FDA-approved in the United States. Ixiaro, a Vero cell culture-derived formulation, is administered in two doses 28 days apart.12,13 JE-Vax, a mouse-brain preparation, is the only one approved for use in children, but it is no longer available. According to the CDC, physicians may choose to use Ixiaro off-label in children.14 One study found that Ixiaro administered at half the adult dose was safe and induced a good immune response in children 1-3 years old.15 The adult dose is under investigation for use in children ≥3 years old. Vaccines are available for pediatric use in Asia.

MEASLES — Travel continues to be a cause of measles cases and outbreaks in the US.16,17 The measles vaccine is no longer available in a monovalent formulation. It is available as an attenuated live-virus vaccine in combination with mumps and rubella (MMR). Adults born in or after 1957 (1970 in Canada) and healthcare workers of any age who have not received 2 doses of live measles vaccine (not the killed vaccine that was commonly used between 1963 and 1968) after their first birthday and do not have a physician-documented history of infection or laboratory evidence of immunity should receive two doses of MMR vaccine, separated by at least 28 days.

Previously unvaccinated children ≥12 months old should receive 2 doses of MMR vaccine at least 28 days apart before traveling outside the US. Children 6-11 months old should receive 1 dose before traveling, but will still need two more doses for routine immunization, one at ≥12 months and another at least 28 days later.

MENINGOCOCCAL — Meningococcal vaccine is recommended for travelers going anywhere in the
### Table 2. Some Vaccines for Travel

<table>
<thead>
<tr>
<th>Vaccines</th>
<th>Adult Dose</th>
<th>Pediatric Age/Dose</th>
<th>Standard Primary Schedule</th>
<th>Duration of Protection</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatitis A</strong>&lt;br&gt;Havrix (GSK)&lt;br&gt;Vaqta (Merck)</td>
<td>1 mL IM (1440 EU)&lt;br&gt;1 mL IM (50 U)</td>
<td>1-18 yrs: 0.5 mL IM (720 EU)&lt;br&gt;1-18 yrs: 0.5 mL IM (25 U)</td>
<td>0 and 6-12 mos&lt;br&gt;0 and 6-18 mos</td>
<td>Probably lifelong after completion of primary series¹</td>
</tr>
<tr>
<td><strong>Hepatitis B</strong>&lt;br&gt;Engerix-B (GSK)&lt;br&gt;Recombivax-HB (Merck)</td>
<td>1 mL IM (20 mcg)&lt;br&gt;1 mL IM (10 mcg)</td>
<td>Birth-19 yrs: 0.5 mL IM (10 mcg)&lt;br&gt;Birth-19 yrs: 0.5 mL IM (5 mcg)</td>
<td>0, 1 and 6 mos²,³&lt;br&gt;0, 1 and 6 mos³,⁴</td>
<td>Probably lifelong after completion of primary series</td>
</tr>
<tr>
<td><strong>Hepatitis A/B</strong>&lt;br&gt;Twinrix (GSK)</td>
<td>1 mL IM (720 EU/20 mcg)</td>
<td>Not approved for &lt;18 yrs</td>
<td>0, 1 and 6 mos (alternative: 0, 7 and 21-30 days)</td>
<td>Booster recommended at 12 mos with accelerated schedule; otherwise probably lifelong after completion of primary series</td>
</tr>
<tr>
<td><strong>Japanese encephalitis</strong>&lt;br&gt;Ixiaro (Novartis)</td>
<td>0.5 mL IM</td>
<td>Not approved for &lt;17 yrs⁵</td>
<td>0, 28 days</td>
<td>A single booster &gt;1 yr after completion of primary series if ongoing risk⁶</td>
</tr>
<tr>
<td><strong>Meningococcal</strong>&lt;br&gt;Menomune (Sanofi Pasteur)</td>
<td>0.5 mL SC&lt;br&gt;(50 mcg of each antigen)</td>
<td>≥2 yrs: 0.5 mL SC&lt;br&gt;(50 mcg of each antigen)</td>
<td>Single dose</td>
<td>Repeat every 5 yrs⁷ with Menactra or Menveo if ongoing risk</td>
</tr>
<tr>
<td></td>
<td>0.5 mL IM (10 mcg serogroup A, 5 mcg serogroup C, Y, W135)</td>
<td>≥2 yrs: 0.5 mL IM (10 mcg serogroup A, 5 mcg serogroup C, Y, W135)</td>
<td>≥2-55 yrs:&lt;br&gt;single dose⁸</td>
<td>Repeat every 5 yrs⁷ if ongoing risk</td>
</tr>
<tr>
<td></td>
<td>0.5 mL IM (4 mcg of each antigen)</td>
<td>&lt;9 mos: 0.5 mL¹ IM&lt;br&gt;4 mcg of each antigen</td>
<td>9-23 mos: 0, 3 mos&lt;br&gt;≥2-55 yrs:&lt;br&gt;single dose</td>
<td>Repeat every 5 yrs⁷ if ongoing risk</td>
</tr>
<tr>
<td><strong>Rabies</strong>&lt;br&gt;Imovax (Sanofi Pasteur)</td>
<td>1 mL IM&lt;br&gt;(≥2.5 IU of rabies antigen)</td>
<td>Birth: 1 mL IM (≥2.5 IU of rabies antigen)</td>
<td>0, 7 and 21&lt;br&gt;or 28 days⁹</td>
<td>Routine boosters not necessary; for those engaging in frequent high-risk activities (cavers, veterinarians, laboratory workers), serologic testing is recommended every 2 yrs with booster doses if low levels¹⁰</td>
</tr>
<tr>
<td></td>
<td>1 mL IM&lt;br&gt;(≥2.5 IU of rabies antigen)</td>
<td>Birth: 1 mL IM&lt;br&gt;(≥2.5 IU of rabies antigen)</td>
<td>0, 7 and 21&lt;br&gt;or 28 days⁹</td>
<td></td>
</tr>
<tr>
<td><strong>Typhoid</strong>&lt;br&gt;Vivotif (Crucell/Berna)</td>
<td>1 cap PO (contains 2-6x10⁹ viable CFU of S. Typhi Ty21a)</td>
<td>≥6 yrs: 1 cap PO (contains 2-6x10⁹ viable CFU of S. Typhi Ty21a)</td>
<td>1 cap every other day x 4 doses</td>
<td>Repeat every 5 yrs if ongoing risk</td>
</tr>
<tr>
<td></td>
<td>0.5 mL IM&lt;br&gt;(25 mcg)</td>
<td>≥2 yrs: 0.5 mL IM (25 mcg)</td>
<td>Single dose</td>
<td>Repeat every 2 yrs (3 yrs in Canada) if ongoing risk</td>
</tr>
<tr>
<td><strong>Yellow Fever</strong>&lt;br&gt;YF-Vax (Sanofi Pasteur)</td>
<td>0.5 mL SC&lt;br&gt;(4.74 log₁₀ plaque forming units of 17D204 attenuated YF virus)</td>
<td>≥9 mos: 0.5 mL SC (4.74 log₁₀ plaque forming units of 17D204 attenuated YF virus)</td>
<td>Single dose</td>
<td>Booster dose every 10 yrs if ongoing risk</td>
</tr>
</tbody>
</table>

¹ Protection likely lasts at least 12 months after a single dose.
² An alternate schedule is 3 doses given at 0, 1 and 2 months, followed by a fourth dose at 12 months.
³ An accelerated schedule of 0, 7 and 14 days followed by a booster dose at 6 months has been used, but is not FDA-approved.
⁴ An alternate schedule for adolescents 11-15 years old is 0 and 4-6 months.
⁵ One study found that Ixiaro administered at half the adult dose was safe and induced a good immune response in children >3 years old (A Kaltenböck et al. Vaccine 2010; 28:834). The adult dose is under investigation for use in children >3 years old.
⁶ Adults previously vaccinated with JE Vax should receive a primary series of Ixiaro (MMWR Morb Mortal Wkly Rep 2011; 60:661).
⁷ Repeat after three years for children vaccinated at <7 years of age.
⁸ For children 2-5 years old at continued high risk, a second dose may be administered 2 months after the first.
⁹ Regimens for pre-exposure prophylaxis. If a previously vaccinated traveler is exposed to a potentially rabid animal, post-exposure prophylaxis with 2 additional vaccine doses separated by 3 days should be initiated as soon as possible.
¹⁰ Minimal acceptable antibody level is complete virus neutralization at a 1:5 serum dilution by the rapid fluorescent focus inhibition test.
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“meningitis belt” (semi-arid areas of sub-Saharan Africa extending from Senegal and Guinea eastward to Ethiopia) from December to June and should also be considered for areas where epidemics of *Neisseria meningitidis* are occurring, particularly for travelers who will have prolonged contact with the local population, such as those living in a dormitory, military institution or refugee camp, or working in a healthcare setting. Saudi Arabia requires a certificate of immunization for pilgrims during Hajj or Umrah.

Three quadrivalent vaccines are available against *N. meningitidis* serogroups A, C, Y and W-135. *Menomune*, which contains meningococcal capsular polysaccharides, is approved for all persons ≥2 years old. *Menactra and Menveo*, which contain capsular polysaccharides conjugated to diphtheria toxoid, are approved for children ≥9 months old (*Menactra*) or ≥2 years old (*Menveo*) and for adults ≤55 years old and are preferred for use in this age group, but *Menomune* is an acceptable alternative. None of the vaccines provide protection against serogroup B, which does not have an immunogenic polysaccharide capsule. Group B infections are rare in sub-Saharan Africa.

**POLIO** — Adults who have not previously been immunized against polio should receive a primary series (2 doses 4-8 weeks apart; third dose 6-12 months after the second) of inactivated polio vaccine (IPV) if traveling to areas where polio is still endemic (Nigeria, Pakistan, Afghanistan) or to areas with documented outbreaks or circulating vaccine-derived strains (see Table 3).

Previously unimmunized children should receive a 4-dose primary series of IPV; the minimum interval between doses is 4 weeks. A child who receives 4 doses before age 4 should be given a 5th dose.

If protection is needed within 4 weeks, a single dose of IPV is recommended, but provides only partial protection. Adult travelers to risk areas who have previously completed a primary series and have never had a booster should receive a single booster dose of IPV.

**RABIES** — Rabies is highly endemic in parts of Africa, Asia (particularly India and Bali, Indonesia), and Central and South America, but the risk to travelers is generally low. Pre-exposure immunization against rabies is recommended for travelers with an occupational risk of exposure, for those (especially children) visiting endemic areas where immediate access to medical treatment, particularly rabies immune globulin, tends to be limited, and for outdoor-adventure travelers. The 2 vaccines available in the US (*Imovax, RabAvert*) are similar.

After a bite or scratch from a potentially rabid animal, patients who received pre-exposure prophylaxis should promptly receive 2 additional doses of vaccine. Without pre-exposure immunization, the ACIP recommends human rabies immune globulin (HRIG) and is now recommending 4 doses of vaccine (over 14 days) instead of 5 doses (over 28 days). Immunosuppressed patients should still receive 5 doses of vaccine. The reduced vaccine dosing schedule may not be included in the manufacturer’s prescribing information. According to the CDC, cell culture rabies vaccines available outside the US are acceptable alternatives to FDA-approved vaccines; neural tissue vaccines have high rates of serious adverse effects. HRIG is a blood product, and its purity and potency may be less reliable, if it is available at all, in developing countries. Purified equine rabies immune globulin is available in some countries in Asia and has been used effectively, with a low incidence of adverse reactions.

**TETANUS, DIPHTHERIA AND PERTUSSIS** —

Previously unimmunized children should receive 3 or (preferably) 4 doses of pediatric diphtheria, tetanus and acellular pertussis vaccine (DTaP) before travel. An accelerated schedule can be used beginning at age 6 weeks, with the second and third doses given 4 weeks after the previous dose. The fourth dose is given 6 months after the third; the child must be at least 12 months old.

Adults with an uncertain history of primary vaccination should receive 3 doses of a tetanus and diphtheria toxoid vaccine. The first 2 doses should be administered at least 4 weeks apart and the third 6-12 months after the second. One of the 3 doses (preferably the first) should contain protein components of acellular pertussis combined with diphtheria and tetanus toxoids (Tdap) to also provide protection against pertussis. Two Tdap vaccines (*Adacel, Boostrix*) are available for adults. The ACIP recently recommended Tdap for use in adults ≥65 years old. DTaP contains larger amounts of diphtheria

Table 3. Countries with a Risk of Polio

<table>
<thead>
<tr>
<th>Country</th>
<th>Region</th>
</tr>
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<tbody>
<tr>
<td>Afghanistan</td>
<td>Equatorial Guinea</td>
</tr>
<tr>
<td>Angola</td>
<td>Eritrea</td>
</tr>
<tr>
<td>Benin</td>
<td>Ethiopia</td>
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<tr>
<td>Burkina Faso</td>
<td>Gabon</td>
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<tr>
<td>Burundi</td>
<td>Gambia</td>
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<tr>
<td>Cameroon</td>
<td>Ghana</td>
</tr>
<tr>
<td>Central African</td>
<td>Guinea</td>
</tr>
<tr>
<td>Republic</td>
<td>Guinea-Bissau</td>
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<tr>
<td>Chad</td>
<td>Iran</td>
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<tr>
<td>China</td>
<td>Kazakhstan</td>
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<tr>
<td>Congo</td>
<td>Kenya</td>
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<tr>
<td>Côte d’Ivoire</td>
<td>Kyrgyzstan</td>
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<tr>
<td>Democratic</td>
<td>Liberia</td>
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<tr>
<td>Republic of the</td>
<td>Mali</td>
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<tr>
<td>Congo</td>
<td>Mauritania</td>
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<tr>
<td>Djibouti</td>
<td>Namibia</td>
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</table>

and pertussis antigens than Tdap and is not licensed for use in adults.

Inactivated adsorbed (aluminum-salt-precipitated) tetanus and diphtheria toxoid (Td) has been the standard booster vaccine for adults. A booster dose of Td is recommended every 10 years. All persons ≥11 years old who have completed a primary childhood series and have not yet received Tdap should receive a single dose of Tdap. Tdap can be given regardless of interval since the last Td to provide pertussis protection before travel.

**TYPHOID** — Typhoid vaccine is recommended for travelers going to areas where there is an increased risk of typhoid fever, including southern Asia, East and Southeast Asia, Central and South America, the Caribbean and Africa, especially if they will be visiting friends or relatives or traveling outside routine tourist destinations.27,28

A live attenuated oral vaccine (Vivotif) is available for adults and children ≥6 years old. It is taken every other day as a single capsule (at least 1 hour before eating) for a total of 4 capsules, beginning no later than 2 weeks before departure; it protects for about 5 years. The capsules must be refrigerated. Antibiotics should be avoided for at least 72 hours before administration of the first capsule.

A purified capsular polysaccharide parenteral vaccine (Typhim Vi) for adults and children ≥2 years old is given at least 2 weeks before departure. A combined hepatitis A/typhoid vaccine (Vivaxim – SanofiPasteur) is available in Canada.

**YELLOW FEVER** — Yellow fever vaccine (YF-Vax), a single-dose attenuated live virus vaccine prepared in eggs, should be given at least 10 days before travel to endemic areas, which include tropical South America and sub-Saharan Africa. The parenteral vaccine previously licensed in the US is no longer available. Oral, whole-cell killed vaccines are available outside the US. Dukoral (Crucell, The Netherlands), licensed in many European countries and in Canada, is administered in 2 doses 1-6 weeks apart (3 doses in children 2-6 years old). Shanchol (Shantha Biotechnics, India) and ORC-Vax (Vabiotech, Vietnam) are administered in 2 doses 2 weeks apart to persons >1 year old.

**TICK-BORNE ENCEPHALITIS (TBE)** — TBE occurs in temperate areas of Europe and Asia; the risk area extends from eastern France to northern Japan, and from northern Russia to Albania.37,38 The risk of infection is greatest from April to November. Humans acquire the disease through the bite of a tick or, rarely, from eating unpasteurized dairy (mostly goat) products. Immunization is recommended only for travelers who will spend extensive time outdoors in rural areas.

No TBE vaccine is approved in the US, but two safe and effective vaccines are available in Europe (Encepur – Novartis; FSME-Immun – Baxter AG). The yellow fever vaccine is contraindicated in travelers who have a malignant neoplasm, symptomatic HIV infection, a CD4 count <200 cells/mm³, a thymus disorder associated with abnormal immune-cell function, or an egg allergy and in those who are immunocompromised. Yellow fever vaccine-associated viscerotropic disease, a severe systemic illness that can cause fatal organ failure, has been reported rarely. It has occurred only in first-time recipients. Vaccine-associated neurologic disease (encephalitis, Guillain-Barré, Bell’s palsy) has also occurred.31 The rates of these diseases are increased in infants and travelers >60 years old.32 Caution is advised for travelers ≥60 years old who are receiving the vaccine for the first time and for those with asymptomatic HIV infection and moderate immune suppression (CD4 counts 200-499 cells/mm³). A small case series study found a significant increase in relapse rates among travelers with multiple sclerosis who received yellow fever vaccine.33 There have been case reports of vaccine-associated neurologic disease in breast-fed infants of recently vaccinated women.34 The vaccine should be avoided if possible in infants <9 months old; it is contraindicated in infants <6 months old.

**OTHER VACCINES**

**CHOLERA** — The risk of cholera in tourists is very low. Vaccination is currently not recommended for routine use in travelers, but should be considered for those who plan to work in refugee camps, in outbreak settings, or as healthcare providers in endemic areas.35 The parenteral vaccine previously licensed in the US is no longer available. Oral, whole-cell killed vaccines are available outside the US. Dukoral (Crucell, The Netherlands), licensed in many European countries and in Canada, is administered in 2 doses 1-6 weeks apart (3 doses in children 2-6 years old). Shanchol (Shantha Biotechnics, India) and ORC-Vax (Vabiotech, Vietnam) are administered in 2 doses 2 weeks apart to persons >1 year old.

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adult formulation of FSME-Immun is also licensed in Canada. Both vaccines are usually given in 3 doses over 6-15 months, but Encepur can be given over 3 weeks (0, 7 and 21 days). Two TBE vaccines are available in Russia, but their safety and efficacy are unclear.

A booster dose should be given 3 years after completion of a standard primary series and 12-18 months after use of the accelerated schedule of Encepur. Subsequent boosters are given after 5 years for patients <50 years old and after 3 years for those ≥50 years old.

**TRAVELERS’ DIARRHEA**

The most common cause of travelers’ diarrhea, usually a self-limited illness lasting several days, is infection with noninvasive enterotoxigenic (ETEC) or enteroaggregative (EAEC) strains of *Escherichia coli*. Infections with *Campylobacter*, *Shigella*, *Salmonella*, *Aeromonas*, *Plesiomonas*, viruses and parasites are less common. In recent years, norovirus has become a more frequent cause of diarrhea in travelers; according to one study, norovirus infection was detected in 15.7% of returning international travelers with diarrhea. If diarrhea persists >3 days, is moderate to severe or is associated with high fever or bloody stools, self-treatment when symptoms are distressing or persistent.

**Treatment** – For mild diarrhea, loperamide (*Imodium*, and others), an over-the-counter synthetic opioid (4-mg loading dose, then 2 mg orally after each loose stool to a maximum of 16 mg/d for adults), often relieves symptoms in <24 hours, but some patients complain of constipation after use. Loperamide is approved for use in children >2 years old. It can be used with an appropriate antibiotic to shorten the duration of illness.

If diarrhea persists >3 days, is moderate to severe or is associated with high fever or bloody stools, self-treatment for 1-3 days (Table 4) with a fluoroquinolone is usually recommended. Azithromycin is an alternative and is the drug of choice for areas to which a high prevalence of fluoroquinolone-resistant *Campylobacter*, such as South and Southeast Asia. Azithromycin can be used in pregnant women and children (10 mg/kg/d x 3d), and in patients who do not respond to a fluoroquinolone within 48 hours.

Rifaximin, a non-absorbed oral antibiotic derived from rifampin, is approved for treatment of travelers’ diarrhea caused by noninvasive strains of *E. coli* in travelers ≥12 years of age. In clinical trials in patients with diarrhea mostly caused by *E. coli*, it has been similar in efficacy to ciprofloxacin, with fewer adverse effects. It should not be used for invasive infections associated with fever or blood in the stool or those caused by *C. jejuni*, *Salmonella*, *Shigella* or other invasive pathogens, or during pregnancy.

Packets of oral rehydration salts (*Ceralyte, ORS, and others*) mixed in potable water can prevent and treat dehydration, particularly in children and the elderly. They are available from suppliers of travel-related products and some pharmacies in the US, and from pharmacies overseas.

**Prophylaxis** – Medical Letter reviewers generally do not prescribe antibiotic prophylaxis for travelers’ diarrhea, but rather instruct the patient to begin self-treatment when symptoms are distressing or persistent. Some travelers, however, such as immunocompromised patients or those with time-dependent activities who cannot risk the temporary incapacitation associated with diarrhea, might benefit from prophylaxis. In such patients, ciprofloxacin 500 mg, levofloxacin 500 mg, ofloxacin 300 mg or norfloxacin 400 mg can be given once daily during travel and for 2 days after return and are generally well tolerated. According to some Medical Letter reviewers, azithromycin 250 mg once daily can also be used. In short (2-week) studies among travelers to Mexico and US military personnel in Turkey, rifaximin (200-1100 mg/d) was effective in preventing travelers’ diarrhea. Bismuth subsalicylate (*Pepto-Bismol, and others*) can prevent diarrhea in travelers who take 2 tablets 4 times a day for the duration of travel, but it is less effective than antibiotics and is not recommended for children <3 years old.

**MALARIA**

No drug is 100% effective for prevention of malaria; travelers should be told to use protective measures against mosquito bites in addition to medication.

---

**Table 4. Antimicrobial Drugs for Treatment of Travelers’ Diarrhea**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azithromycin</td>
<td>1000 mg once or 500 mg once/d x 1-3d</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>500 mg bid x 1-3d</td>
</tr>
<tr>
<td>Ofloxacin – generic</td>
<td>300 mg bid x 1-3d</td>
</tr>
<tr>
<td>Norfloxacin – Noroxin (Merck)</td>
<td>400 mg bid x 1-3d</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>500 mg once/d x 1-3d</td>
</tr>
<tr>
<td>Cipro (Bayer)*</td>
<td>500 mg bid x 1-3d</td>
</tr>
<tr>
<td>Cipro XR*</td>
<td>1000 mg once/d x 1-3d</td>
</tr>
<tr>
<td>Rifaximin – Xifaxan (Salix)</td>
<td>200 mg tid x 3d</td>
</tr>
</tbody>
</table>

*Also available generically

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[67x429]Children tend to have more severe illness and are more frequent cause of diarrhea in travelers; according to one study, norovirus infection was detected in 15.7% of returning international travelers with diarrhea. In recent years, norovirus has become a **TRAVELERS’ DIARRHEA**

The most common cause of travelers’ diarrhea, usually a self-limited illness lasting several days, is infection with noninvasive enterotoxigenic (ETEC) or enteroaggregative (EAEC) strains of *Escherichia coli*. Infections with *Campylobacter*, *Shigella*, *Salmonella*, *Aeromonas*, *Plesiomonas*, viruses and parasites are less common. In recent years, norovirus has become a more frequent cause of diarrhea in travelers; according to one study, norovirus infection was detected in 15.7% of returning international travelers with diarrhea. If diarrhea persists >3 days, is moderate to severe or is associated with high fever or bloody stools, self-treatment when symptoms are distressing or persistent.

**Treatment** – For mild diarrhea, loperamide (*Imodium*, and others), an over-the-counter synthetic opioid (4-mg loading dose, then 2 mg orally after each loose stool to a maximum of 16 mg/d for adults), often relieves symptoms in <24 hours, but some patients complain of constipation after use. Loperamide is approved for use in children >2 years old. It can be used with an appropriate antibiotic to shorten the duration of illness.

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**Prophylaxis** – Medical Letter reviewers generally do not prescribe antibiotic prophylaxis for travelers’ diarrhea, but rather instruct the patient to begin self-treatment when symptoms are distressing or persistent. Some travelers, however, such as immunocompromised patients or those with time-dependent activities who cannot risk the temporary incapacitation associated with diarrhea, might benefit from prophylaxis. In such patients, ciprofloxacin 500 mg, levofloxacin 500 mg, ofloxacin 300 mg or norfloxacin 400 mg can be given once daily during travel and for 2 days after return and are generally well tolerated. According to some Medical Letter reviewers, azithromycin 250 mg once daily can also be used. In short (2-week) studies among travelers to Mexico and US military personnel in Turkey, rifaximin (200-1100 mg/d) was effective in preventing travelers’ diarrhea. Bismuth subsalicylate (*Pepto-Bismol, and others*) can prevent diarrhea in travelers who take 2 tablets 4 times a day for the duration of travel, but it is less effective than antibiotics and is not recommended for children <3 years old.

**MALARIA**

No drug is 100% effective for prevention of malaria; travelers should be told to use protective measures against mosquito bites in addition to medication.
Countries with a risk of malaria are listed in Table 5. Some countries with endemic malaria transmission may not have malaria in the most frequently visited major cities and rural tourist resorts. Travelers to malarious areas should be reminded to seek medical attention if they have fever either during their trip or up to a year (especially during the first 2 months) after they return. Travelers to developing countries, where counterfeit and poor quality drugs are common, should preferably buy antimalarials before travel.

CHLOROQUINE-SENSITIVE MALARIA — Chloroquine is the drug of choice for prevention of malaria in the few areas that still have chloroquine-sensitive malaria (see Table 5, footnotes 4 and 5). Patients who cannot tolerate chloroquine should take atovaquone/proguanil, doxycycline, mefloquine or, in some circumstances, primaquine in the same doses used for chloroquine-resistant malaria (see Table 6).

CHLOROQUINE-RESISTANT MALARIA — Three drugs of choice with similar efficacy, listed with their dosages in Table 6, are available in the US for prevention of chloroquine-resistant malaria.

A fixed-dose combination of atovaquone and proguanil taken once daily is generally the best tolerated prophylactic, but it can cause headache, insomnia, GI disturbances and mouth ulcers, and it is expensive. Single case reports of Stevens-Johnson syndrome and hepatitis have been published. Atovaquone/proguanil should not be given to patients with severe renal impairment (CrCl <30 mL/min). There have been isolated case reports of treatment-related resistance to atovaquone/proguanil in Plasmodium falciparum in Africa, but acquisition of resistant disease in travelers appears to be rare. The protective efficacy of atovaquone/proguanil against *P. vivax* is variable, ranging from 84% in Indonesian New Guinea to 100% in Colombia. Some Medical Letter reviewers prefer other drugs for travel to areas where *P. vivax* predominates.

Mefloquine has the advantage of once-a-week dosing, but is contraindicated in patients with a history of any psychiatric disorder (including severe anxiety and depression), and also in those with a history of seizures or cardiac conduction abnormalities. Dizziness, headache, insomnia and disturbing dreams are the most common CNS adverse effects. Adverse effects in children are similar to those in adults, but the drug appears to be better tolerated in children, with a low incidence of CNS effects. If a patient develops psychological or behavioral abnormalities such as depression, restlessness or confusion while taking mefloquine, another drug should be substituted. Halofantrine (not available in the US) should not be taken together with mefloquine, or within 15 weeks of the last dose of mefloquine, due to potentially fatal prolongation of the QT interval; caution is also required when using quinine, quinidine or chloroquine to treat patients who have taken mefloquine prophylaxis.

Doxycycline, which frequently causes GI disturbances and can cause photosensitivity and vaginitis, offers an inexpensive once-daily alternative. Doxycycline should not be taken concurrently with antacids, oral iron or bismuth salts (including Pepto-Bismol).

<table>
<thead>
<tr>
<th>Table 5. Countries with a Risk of Malaria¹</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AFRICA</strong></td>
</tr>
<tr>
<td>Angola</td>
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<tr>
<td>Benin</td>
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<tr>
<td>Botswana²</td>
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<tr>
<td>Burkina Faso</td>
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<tr>
<td>Burundi</td>
</tr>
<tr>
<td>Cameroon</td>
</tr>
<tr>
<td>Cape Verde³</td>
</tr>
<tr>
<td>Central African</td>
</tr>
<tr>
<td>Republic</td>
</tr>
<tr>
<td>Chad</td>
</tr>
<tr>
<td>Comoros</td>
</tr>
<tr>
<td>Congo</td>
</tr>
<tr>
<td>Côte d’Ivoire</td>
</tr>
<tr>
<td>Democratic</td>
</tr>
<tr>
<td>Republic of the Congo</td>
</tr>
<tr>
<td>Djibouti</td>
</tr>
<tr>
<td><strong>AMERICAS</strong></td>
</tr>
<tr>
<td>Argentina²,³</td>
</tr>
<tr>
<td>Belize²,³</td>
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<tr>
<td>Bolivia²</td>
</tr>
<tr>
<td>Brazil</td>
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<tr>
<td>Colombia²</td>
</tr>
<tr>
<td>Costa Rica²,³</td>
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<tr>
<td>Dominican</td>
</tr>
<tr>
<td>Republic²,³</td>
</tr>
<tr>
<td>Ecuador²</td>
</tr>
<tr>
<td><strong>ASIA</strong></td>
</tr>
<tr>
<td>Afghanistan</td>
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<tr>
<td>Azerbaijan²,³</td>
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<tr>
<td>Bangladesh²</td>
</tr>
<tr>
<td>Bhutan³</td>
</tr>
<tr>
<td>Cambodia²,³</td>
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<tr>
<td>China²,³</td>
</tr>
<tr>
<td>Georgia²,³</td>
</tr>
<tr>
<td>India</td>
</tr>
<tr>
<td>Indonesia²</td>
</tr>
<tr>
<td><strong>OCEANIA</strong></td>
</tr>
<tr>
<td>Papua New Guinea</td>
</tr>
</tbody>
</table>

¹. Only includes countries for which prophylaxis is recommended. Regional variation in risk may exist within a country. Updated detailed information is available at www.cdc.gov/malaria/map and medical personnel can call the CDC Malaria Hotline at 770-488-7788.

². No malaria in major urban areas.

³. Limited to island of São Tiago.

⁴. Chloroquine is the drug of choice for prophylaxis.

⁵. Chloroquine is recommended in Anhui, Guizhou, Henan and Hubei provinces.

⁶. Mefloquine resistance has been reported along the borders between Cambodia, China, Laos, Myanmar and Thailand (Laos-Myanmar, Laos-Thailand, China-Myanmar, etc.) and in southern Vietnam. In these areas atovaquone/proguanil or doxycycline is recommended.
A fourth drug, primaquine phosphate, can also be used for prophylaxis, especially in areas where *P. vivax* is the predominant species, but in other areas it should be reserved for travelers unable to take any other drug; it is somewhat less effective than the alternatives against *P. falciparum*. Several studies however, have shown that daily primaquine can provide effective prophylaxis against chloroquine-resistant *P. falciparum* and *P. vivax*. In addition to primary prophylaxis, some experts also prescribe primaquine for “terminal prophylaxis” after departure from areas where *P. vivax* and *P. ovale* are endemic (see Table 6, footnote 3).

Primaquine can cause hemolytic anemia in patients with glucose-6-phosphate dehydrogenase (G-6-PD) deficiency, which is most common in African, Asian, and Mediterranean peoples. Travelers should be screened for G-6-PD deficiency before being treated with this drug. Primaquine should be taken with food to reduce GI effects.

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### Table 6. Drugs of Choice for Prevention of Malaria

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult Dosage</th>
<th>Pediatric Dosage</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All <em>Plasmodium</em> species in chloroquine-sensitive areas</strong>&lt;sup&gt;2,3&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chloroquine phosphate&lt;sup&gt;4,5&lt;/sup&gt;</td>
<td>500 mg (300 mg base) PO once/wk</td>
<td>5 mg/kg base (300 mg max) PO once/wk</td>
<td>Start: 1-2 wks before travel</td>
</tr>
<tr>
<td>(Aralen, and others)</td>
<td></td>
<td></td>
<td>Stop: 4 wks after leaving malarious zone</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All <em>Plasmodium</em> species in chloroquine-resistant areas&lt;sup&gt;2,3&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atovaquone/proguanil&lt;sup&gt;6&lt;/sup&gt;</td>
<td>1 adult tablet PO daily</td>
<td>≤9 kg: ½ peds tab/d</td>
<td>Start: 1-2d before travel</td>
</tr>
<tr>
<td>(Malarone, Malarone Pediatric, and others)</td>
<td></td>
<td>10-19 kg: ¾ peds tab/d</td>
<td>Stop: 1 wk after leaving malarious zone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20-30 kg: ½ tab once/wk</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;40 kg: 1 adult tab/d</td>
<td></td>
</tr>
<tr>
<td>Doxycycline&lt;sup&gt;7&lt;/sup&gt;</td>
<td>100 mg PO daily</td>
<td>≥8 yrs: 2 mg/kg/d PO, up to 100 mg/d</td>
<td>Stop: 1-2d before travel</td>
</tr>
<tr>
<td>(Vibramycin, and others)</td>
<td></td>
<td></td>
<td>Stop: 4 wks after leaving malarious zone</td>
</tr>
<tr>
<td>Mefloquine&lt;sup&gt;8,9&lt;/sup&gt;</td>
<td>250 mg PO once/wk</td>
<td>≤9 kg: 5 mg/kg salt once/wk</td>
<td>Start: ≥2 wks before travel</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10-19 kg: ¾ tabs once/wk</td>
<td>Stop: 4 wks after leaving malarious zone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20-30 kg: ½ tab once/wk</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;45 kg: 1 tab once/wk</td>
<td></td>
</tr>
<tr>
<td>Alternative:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primaquine phosphate&lt;sup&gt;11,12&lt;/sup&gt;</td>
<td>30 mg base PO daily</td>
<td>0.5 mg/kg base PO daily</td>
<td>Start: 1-2d before travel</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Stop: 1 wk after leaving malarious zone</td>
</tr>
</tbody>
</table>

1. No drug guarantees protection against malaria. Travelers should be advised to seek medical attention if fever develops after they return. Insect repellents, insecticide-impregnated bed nets and proper clothing are important adjuncts for malaria prophylaxis.
2. Chloroquine-resistant *P. falciparum* occurs in all malarious areas except Central America (resistance occurs in Panama east of the Canal Zone), Mexico, Haiti, the Dominican Republic, Paraguay, northern Argentina, North and South Korea, Georgia, most of rural China and some countries in the Middle East (chloroquine resistance has been reported in Yemen, Saudi Arabia and Iran). *P. vivax* with decreased susceptibility to chloroquine is a significant problem in Papua New Guinea and Indonesia. There are also a few reports of resistance from Myanmar, India, the Solomon Islands, Vanuatu, Guyana, Brazil, Colombia and Peru (JK Baird et al, Curr Infect Dis Rep 2007; 9:39). Chloroquine-resistant *P. malariae* has been reported from Sumatra, Indonesia (JD Maguire et al, Lancet 2002; 360:58).
3. Primames is given for prevention of relapse after infection with *P. vivax* or *P. ovale*. In addition to primary prophylaxis, some experts also prescribe primaquine phosphate 30 mg base/d (0.5 mg base/kg/d for children) for 14 days after departure from areas where these species are endemic (Presumptive Anti-Relapse Therapy [PART], “terminal prophylaxis”). Since this is not always effective as prophylaxis (E Schwartz et al, N Engl J Med 2003; 349:1510), others prefer to rely on surveillance to detect cases when they occur, particularly when exposure was limited or doubtful. See also footnote 11.
4. Alternatives for patients who are unable to take chloroquine include atovaquone/proguanil, mefloquine, doxycycline or primaquine dosed as for chloroquine-resistant areas.
5. Chloroquine should be taken with food to decrease gastrointestinal adverse effects. If chloroquine phosphate is not available, hydroxychloroquine sulfate is as effective; 400 mg of hydroxychloroquine sulfate is equivalent to 500 mg of chloroquine phosphate.
6. Atovaquone/proguanil is available as a fixed-dose combination tablet: adult tablets (Malarone, and others; 250 mg atovaquone/100 mg proguanil) and pediatric tablets (Malarone Pediatric, and others; 62.5 mg atovaquone/25 mg proguanil). To enhance absorption and reduce nausea and vomiting, it should be taken with food or a milky drink. The drug should not be given to patients with severe renal impairment (creatinine clearance <30 mL/min).
7. Doxycycline should be taken with adequate water to avoid esophageal irritation. It can be taken with food to minimize gastrointestinal adverse effects. It is contraindicated in children <8 years old.
8. In the US, a 250-mg tablet of mefloquine contains 228 mg mefloquine base. Outside the US, each 275-mg tablet contains 250 mg base. Mefloquine can be given to patients taking β-blockers if they do not have an underlying arrhythmia; it should not be used in patients with conduction abnormalities. Mefloquine should not be taken on an empty stomach; it should be taken with at least 8 oz. of water.
9. Most adverse events occur within 3 doses. Some Medical Letter reviewers favor starting mefloquine 3-4 weeks prior to travel and monitoring the patient for adverse events; this allows time to change to an alternative regimen if mefloquine is not tolerated.
10. For pediatric doses <½ tablet, it is advisable to have a pharmacist crush the tablet, estimate doses by weighing, and package them in gelatin capsules. There is no data for use in children <5 kg, but based on dosages in other weight groups, a dose of 5 mg/kg can be used.
11. Patients should be screened for G-6-PD deficiency before treatment with primaquine. It should be taken with food to minimize nausea and abdominal pain.
12. Not FDA-approved for this indication.
MEFLOQUINE-RESISTANT MALARIA — Doxycycline or atovaquone/proguanil is recommended for prophylaxis against mefloquine-resistant malaria, which occurs in the malarious areas of Thailand, in the areas of Myanmar and Cambodia that border on Thailand, in the border areas between Myanmar and China, and Laos and Myanmar, and in southern Vietnam.

PREGNANCY — Malaria in pregnancy is particularly serious for both mother and fetus; prophylaxis is indicated if travel cannot be avoided. Chloroquine has been used extensively and safely for prophylaxis of chloroquine-sensitive malaria during pregnancy. Mefloquine is now classified as category B (no evidence of risk in humans) for use during pregnancy. It has been reported to be safe for prophylactic use during any trimester of pregnancy. The safety of atovaquone/proguanil in pregnancy has not been established, and its use is not recommended. However, case series that included women who were treated with the combination in all trimesters of pregnancy have not identified major birth defects, and proguanil alone has been used in pregnancy without evidence of toxicity. Doxycycline and primaquine are contraindicated in pregnancy.

PREVENTION OF INSECT BITES

To minimize insect bites, travelers should wear light-colored, long-sleeved shirts, pants, and socks and covered shoes. They should sleep in air conditioned or screened areas and use insecticide-impregnated bed nets. Mosquitoes that transmit malaria are most active between dusk and dawn; those that transmit dengue fever bite during the day, particularly during early morning and late afternoon.

DEET — The most effective topical insect repellent is N, N-diethyl-m-toluamide (DEET). Applied on exposed skin, DEET repels mosquitoes, as well as ticks, chiggers, fleas, gnats and some flies. DEET is available in formulations of 5-100% even though increasing the concentration above 50% does not seem to improve efficacy. Medical Letter reviewers prefer concentrations of 20-35%. A long-acting polymer-based DEET formulation originally developed for the US Armed Forces (US Army Extended Duration Topical Insect and Arthropod Repellent – EDTIAR) containing 25-33% DEET (Ultraguard) protects for 6-12 hours. Microencapsulated and liposome-based sustained-release formulations containing 20% DEET (Sawyer Premium Controlled Release) and 30% DEET (Sawyer Ultra 30 Liposome Controlled Release), respectively, are also available and are claimed to provide protection for up to 11 hours. According to the CDC, DEET is probably safe in children and infants >2 months old; the American Academy of Pediatrics recommends use of formulations containing no more than 30%. One study found that applying DEET regularly during the second and third trimesters of pregnancy did not result in any adverse effects on the fetus. DEET has been shown to decrease the effectiveness of sunscreens when it is applied after the sunscreen; nevertheless, sunscreen should be applied first because it may increase the absorption of DEET when DEET is applied first.

PICARIDIN — Picaridin, which appears to be better tolerated on the skin than DEET, is used against flies, mosquitoes, chiggers and ticks. It is available in concentrations of 5-20%. The 20% formulation (Nattapelt 8 Hour; GoReady, and others) has been shown to repel mosquitoes for up to 8 hours.

PYRETHROIDS — Permethrin (Duranon, Permanone, and others), a synthetic pyrethroid insecticide available in liquid and spray form, can be used on clothing, mosquito nets, tents and sleeping bags for protection against mosquitoes and ticks. After application to clothing, it remains active for several weeks through multiple launderings. The combination of DEET on exposed skin and permethrin on clothing provides increased protection. Using pyrethroid-impregnated mosquito nets while sleeping is helpful when rooms are not screened or air-conditioned. Long-lasting insecticide-treated nets that maintain effective levels of insecticide for at least 3 years are available.

SOME OTHER INFECTIONS

DENGUE — Dengue fever is a viral disease transmitted by mosquito bites that occurs worldwide in tropical and subtropical areas, including cities. Outbreaks have occurred in recent years in Southeast Asia, South Asia, sub-Saharan Africa, the South Pacific and Australia, Central and South America, and the Caribbean and there have been sporadic reports in the Middle East. Dengue fever has also been reported in US travelers vacationing at popular tourist destinations in Puerto Rico, the US Virgin Islands and Mexico. Prevention of mosquito bites during the day, particularly in early morning and late afternoon, is the primary way to protect against dengue fever; no vaccine is currently available.

LEPTOSPIROSIS — Leptospirosis, a bacterial disease that occurs in many domestic and wild animals, is endemic worldwide, but the highest incidence is in tropical and subtropical areas. Transmission to humans usually occurs through contact with fresh water or damp soil contaminated by the urine of infected ani-
Advice for Travelers

mals.68 Travelers at increased risk, such as adventure travelers and those who engage in recreational water activities, should consider prophylaxis with doxycycline 200 mg orally once a week, beginning 1-2 days before and continuing throughout the period of exposure. No human vaccine is available in the US.

NON-INFECTIONOUS RISKS OF TRAVEL

Many non-infectious risks are associated with travel. Injuries, such as traffic accidents and drowning, account for the majority of preventable travel-related deaths. Sunburn also occurs in many travelers.

ACUTE ALTITUDE ILLNESS — Rapid exposure to altitudes >8,000 feet (2500 meters) may cause acute mountain sickness (AMS). Symptoms include headache, fatigue, nausea, anorexia, insomnia, and dizziness; pulmonary and cerebral edema can occur.69 There is evidence for a genetic predisposition.70 Sleeping altitude appears to be especially important in determining whether symptoms develop. The most effective preventive measure is pre-acclimatization by a 2- to 4-day stay at intermediate altitude (6000-8000 feet) and gradual ascent to higher elevations.

If rapid ascent to >9100 feet (2800 meters) sleeping altitude cannot be avoided, acetazolamide, a carbonic anhydrase inhibitor taken in a dosage of 125 mg twice daily (or 500 mg daily with the slow-release formulation Diamox Sequels) beginning the day before ascent and continuing at high altitude for 2 days or longer, decreases the incidence and severity of AMS.71 The recommended dose for children is 2.5 mg/kg (max 125 mg) every 12 hours. Although acetazolamide, a sulfone, has little cross-reactivity with sulfa drugs, hypersensitivity reactions to acetazolamide are more likely to occur in those who have had severe (life-threatening) allergic reactions to sulfa drugs.72 Dexamethasone (Decadron, and others) 2 mg every 6 hours or 4 mg every 12 hours has also been shown to prevent AMS in adults. It is not recommended for children.

Severe symptoms can be treated by descent to a lower altitude or by giving supplemental oxygen. When descent is impossible, dexamethasone 4 mg every 6 hours (preferably) or acetazolamide 250 mg every 12 hours, may be used to treat AMS. Dexamethasone, possibly combined with acetazolamide, should be used for cerebral edema. Sustained-release nifedipine (Procardia XL, and others), 20 mg every 8 hours or 30 mg every 12 hours may be helpful for prevention and treatment of pulmonary edema.

VENOUS THROMBOEMBOLISM — Prolonged immobilization, particularly during air travel, increases the risk of lower extremity deep vein thrombosis (DVT). Travelers with risk factors for thrombosis (past history of thrombosis, recent surgery, obesity, malignancy, pregnancy, advanced age, limited mobility, thrombophilic disorders, increased platelets) are at even higher risk. Nevertheless, flight-related symptomatic pulmonary embolism is rare.73 To minimize the risk, long-distance travelers should be advised to walk around frequently, exercise calf muscles while sitting, and drink extra fluids.74 Properly fitted compression stockings can decrease the risk of asymptomatic DVT.75 Giving a single dose of a low-molecular-weight heparin as prophylaxis to travelers at high risk reduced the incidence of asymptomatic DVT in a clinical trial.76

JET LAG — Disturbance of body and environmental rhythms resulting from a rapid change in time zones gives rise to jet lag, which is characterized by insomnia, daytime sleepiness, decreased quality of sleep, diminished physical performance, loss of concentration, irritability and GI disturbances. It is usually more severe after eastward travel.77 A variety of interventions have been tried, but none are proven to be effective. Shifting daily activities to correspond to the time zone of the destination country before arrival along with taking short naps, remaining well hydrated, avoiding alcohol and pursuing activities in sunlight on arrival may help. The dietary supplement melatonin (0.5-5 mg started on the first night of travel and continued for 1-5 days after arrival) has been reported to facilitate the shift of the sleep-wake cycle and decrease symptoms in some patients. A program of appropriately timed light exposure and avoidance in the new time zone may adjust the “body clock” and reduce jet lag.78 In one study, zolpidem (Ambien, and others) started the first night after travel and taken for 3 nights was helpful.79 A randomized, double-blind study found that the stimulant armodafinil (Nuvigil) 150 mg/d in the morning for 3 days increased wakefulness after eastward travel through 6 time zones.80

MOTION SICKNESS — Therapeutic options for motion sickness remain limited.81 A transdermal patch of the prescription cholinergic blocker scopolamine can decrease symptoms. Transderm Scop is applied to the skin behind the ear at least 4 hours before exposure (some experts recommend applying it 6-8 hours before) and changed, alternating ears, every 3 days. Oral promethazine (Phenergan, and others) is a highly sedating alternative. Over-the-counter drugs such as dimenhydrinate (Dramamine, and others) or meclizine (Bonine, and others) are less effective, but may be helpful for milder symptoms.
20. CDC. Recommendation of the Advisory Committee on Immunization Practices (ACIP) for use of quadrivalent meningococcal conjugate vaccine (MenACWY-D) among children aged 9 through 23 months at increased risk for invasive meningococcal disease. MMWR Morb Mortal Wkly Rep 2011; 60:1391.
46. CDC. Recommendation of the Advisory Committee on Immunization Practices (ACIP) for use of quadrivalent meningococcal conjugate vaccine (MenACWY-D) among children aged 9 through 23 months at increased risk for invasive meningococcal disease. MMWR Morb Mortal Wkly Rep 2011; 60:1391.
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64. SP Frances et al. Laboratory and field evaluation of commercial repellent formulations against mosquitoes (diptera: culicidae) in Queensland, Australia. Aust J Entomol 2005; 44:431.
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The expected outcome of the CME Program is to increase the participant’s ability to know, or apply knowledge into practice after assimilating, information presented in materials contained in Treatment Guidelines.

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The objective of this activity is to meet the need of healthcare professionals for unbiased, reliable and timely information on treatment of major diseases. The Medical Letter expects to provide the healthcare community with educational content that they will use to make independent and informed therapeutic choices in their practice.

Participants will be able to select and prescribe, or confirm the appropriateness of the prescribed usage of the drugs and other therapeutic modalities discussed in Treatment Guidelines with specific attention to clinical evidence of effectiveness, adverse effects and patient management.

Upon completion of this program, the participant will be able to:
1. Discuss the recommendations for use of vaccines available for US travelers
2. Review the recommendations for malaria prophylaxis and treatment of travelers’ diarrhea for US travelers
3. Determine the appropriate vaccinations and malaria prophylaxis for an individual patient based on their travel destination.

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Questions start on next page
1. A 65-year old man with diabetes is leaving next week on a 1-month African safari. He asks if he should be vaccinated against hepatitis A. You tell him:
   a. he doesn’t need hepatitis A vaccine for travel to Africa
   b. he should receive 2 doses of hepatitis A vaccine before he leaves
   c. it is too late to be vaccinated so he should receive immune globulin 0.06 mL/kg IM
   d. he should receive an initial dose of hepatitis A vaccine and immune globulin 0.02 mL/kg IM

2. A 25-year old woman is planning to travel to Mexico for a week for spring break. She has not been previously immunized against hepatitis B. You should tell her:
   a. hepatitis B vaccination is required for all travelers to Mexico
   b. Mexico is considered low-risk for hepatitis B so she doesn’t need to be vaccinated
   c. she should consider being vaccinated if she may engage in a risky behavior such as getting a tattoo or having unprotected sexual contact with a new partner while on vacation
   d. she doesn’t need to be vaccinated because she is staying for <2 weeks

3. Which Japanese encephalitis vaccine is both FDA-approved for use in children and currently available in the US?
   a. Ixiaro
   b. JE-Vax
   c. both Ixiaro and JE-Vax
   d. none of the above

4. Which meningococcal vaccine is FDA-approved for use in children ≥9 months old?
   a. Menomune
   b. Menveo
   c. Menactra
   d. all of the above

5. A healthy 19-year old man from the US is traveling in India and is bitten by a potentially rabid dog. He received 3 doses of rabies vaccine before leaving the US. What should he receive now?
   a. 2 doses of rabies vaccine
   b. 4 doses of rabies vaccine
   c. human rabies immune globulin
   d. 5 doses of rabies vaccine and human rabies immune globulin

6. Yellow fever vaccine should not be used in patients who:
   a. have symptomatic HIV infection
   b. are immunosuppressed
   c. have cancer
   d. all of the above

7. Cholera vaccine is:
   a. recommended for routine use in travelers
   b. is available in the US
   c. is recommended for those who plan to work in refugee camps
   d. is part of the primary childhood immunization schedule in the US

8. Which of the following is recommended to treat travelers’ diarrhea due to fluoroquinolone-resistant Campylobacter?
   a. azithromycin
   b. ciprofloxacin
   c. clindamycin
   d. loperamide

9. Rifaxmin:
   a. is recommended for patients with travelers’ diarrhea who have fever and bloody stool
   b. is not effective for prophylaxis of travelers’ diarrhea
   c. is highly bioavailable with significant systemic toxicity
   d. is about as effective as ciprofloxacin for treatment of diarrhea due to Escherichia coli

10. Mefloquine would be an option for malaria prophylaxis in which of the following patients:
    a. a 42-year old woman with depression traveling to Nigeria
    b. a 30-year old pregnant woman traveling to Brazil
    c. a 50-year old man with atrial fibrillation traveling to southern Vietnam
    d. a 12-year old boy with epilepsy traveling to India

11. Among the most effective drugs used for prevention of chloroquine-resistant malaria, the one generally best tolerated is:
    a. atovaquone/proguanil
    b. mefloquine
    c. doxycycline
    d. primaquine phosphate

12. Which of the following is true?
    a. DEET applied after sunscreen can decrease the effectiveness of sunscreen.
    b. Sunscreen applied after DEET can increase absorption of DEET.
    c. Sunscreen should be applied before DEET.
    d. all of the above