Travel health risks vary according to:

**WHERE:** industrialized vs developing countries

**WHEN:** season e.g. rainy vs dry

**HOW LONG:** duration

**WHAT FOR:** tourism, business, VFR

**HOW:** hygiene expected: high (5*) vs low (back packer)

special activities: diving, high altitude, hunting, camping

**HOST STATUS:** Healthy vs pre-existing condition

---

Travel Medicine on the Web

Center for Disease Control  

The International Society of Travel Medicine  

International Association for Medical Assistance to Travelers  

American Society of Tropical Medicine and Hygiene  

The State Department (Travel warnings)  
[http://travel.state.gov/travel/](http://travel.state.gov/travel/)

The Yellow Book (Health Information for International Travel)  
http://EINSTEIN.YU.EDU/GLOBAL
Classification of Travel Immunizations

- Routine
- Required to cross international borders
- Recommended according to risk of exposure
Adult Immunizations

- Td every 10 years
- Measles (MMR) born >1957
- *Meningococcus univ. students res.
- **Influenza annually
- Varicella susceptible
- Pneumococcus > 65yrs +/- illness
- Hepatitis A/B susceptible
- iPolio booster (>18y)

*New conjugate vaccine
**Travel vaccine
Yellow Fever Immunization

sub-Saharan Africa (urban) and tropical S. America (sylvatic)

Usually safe effective vaccine (AE=1:131,000*)

International regulations require proof of vaccination (international immunization card i.e. “Yellow Card”)

*egg allergy: rash, urticaria, asthma

Risk of YF Vaccine

All: Viscerotropic 3-5 per million (YF-AVD)
Neurotropic 2-3 per million (YF-AND)

By age: <50 yrs: 2-5 per million = 1:200,000
>50 yrs: 20 per million = 1:50,000

23 cases YF - AVD since 1996 (61% fatal)
Elderly travelers (> 60) or those with hx of thymus dysfunction (17%)

M. Cetron, ASTMH, Denver, Nov.12, 2002
Hepatitis A is the most frequent vaccine preventable disease of travelers

Morbidity & Mortality of Hepatitis A

10% (1-14 yr) hospitalized
20% (15-39 yr) hospitalized
adult time off work ~ 4 wks
mortality > 40 yr ~ 2%
< 40 yr ~ 0.15%
Risk of Hepatitis A with Travel

3 case/1000/month (tourist routes) to 20 case/1000/month (off tourist routes: back packers, campers)

1 case/10,000-20,000/month (DR, Mexico)

- Steffen R, JAMA, 1994;272:885-9
- De Serres, JTM, 2002;9:10-16

Hepatitis A Vaccines

HAVRIX® (GlaxoSmithKline)
VAQTA® (Merck)
- Inactivated viral vaccines
- 2 doses, 6 to 18 months apart
- Effective almost immediately
- 10 years (maybe lifetime protection)
Risk of Hepatitis B with travel

Expatriates:
all cases: ~ 1 case/1000/month
symptomatic only: 1/2000/month

Short-term: 1/2000 - 1/10,000/month

Steffen R. Vaccine 1993;11:518-20
Combined Hepatitis A/B Vaccine*  
3-Dose Schedule:

- **Traveler (usual)** → 0, 1 and 6 mo

- **Last-minute traveler** → 0, 7 and 21 days
  +/- booster at 1 year

*Twinrix®, GlaxoSmithKline.

Combined Hepatitis A/B Vaccine

- short-term travelers
- sexually active
- accident prone
- chronic disease
- close contact with locals
- long-term travelers (≥ 3 months)
- expatriate workers
- occupational risk groups
Typhoid Fever in Travelers, 1994–1999

Source: 50% of cases from 3 countries
- India              30%
- Pakistan        13%
- Bangladesh    6%

Reason for travel: 77% of cases: VFRs
Duration of travel: 48% for <4 weeks
Age: 25% were <10 years of age

Typhoid Vaccines

Vi capsular polysaccharide vaccine (im)
Ty21a live attenuated (PO)

96% sero (+) at 2 wks
Efficacy @ 50 - 80% (adults)
Vi q2-3yrs; Ty21a q5yrs

New Conjugate Typhoid Vaccine (not in USA)
>90% efficacy in children 2-5yo, 5-15 yo, and adults
Cholera

Cholera Vaccines

- No vaccine currently available in US
- Low risk for routine travelers (0.01-0.001/month stay)
- Treated with rehydration + antibiotics**
- Best prevention: avoid uncooked shellfish*, bottled water, cooked food
Pre-exposure rabies immunization

<table>
<thead>
<tr>
<th>Risk</th>
<th>Population</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuous</td>
<td>lab workers</td>
<td>test q 6 mo</td>
</tr>
<tr>
<td>Frequent</td>
<td>vets, spelunkers</td>
<td>test q 2 yrs</td>
</tr>
<tr>
<td>Infrequent</td>
<td>episodic/exposure risk</td>
<td>no testing or booster</td>
</tr>
</tbody>
</table>

Travel over 1 month in duration
Remote location with difficult access to care

Rabies Vaccines (Pre+Post)

Pre-exposure:
- HDCV 0,7,21 or 28d ID*/IM
- PCEC 0,7,21 or 28d IM
- RVA 0,7,21, or 28 IM (RabAvert)

Post-exposure:
- non-immunized:
  - RIG** 20mg/kg x1 +
  - HDCV 0,3,7,14,28 IM
- immunized:
  - HDCV 0,3 IM
  - PCEC 0,3 IM
  - RVA 0,3 IM
2,000,000 pilgrims each year

Meningococcal Immunization

- Immunization required only to Mecca for Hajj
- In S-S Africa regular epidemics serogp A or C in “Meningitis Belt” (Mali to Ethiopia)
- Serogroup A most common outside US
- C and B can also cause epidemic disease
- Vaccine A, C, Y and W135 (no B) (OMP GpB)
- Asplenia, C₃ C₅ -C₉ deficiencies, lab personnel
- Pre-adolescent (11-12), Adolescents (HS/15), college freshmen
Meningococcal Vaccines
Menactra® + Menomune®

Menactra: meningococcal polysaccharide diphtheria toxoid conjugate vaccine A,C, Y, W-135 (11 - 55yrs)

Both vaccines contain 3 out of the 4 serogroup providing coverage for 67% of meningococcal disease overall and up to 83% in the adolescent population.

Four serogroups (C, Y, W-135 and B) endemic in the U.S.

No B serogroup vaccine available in the U.S. (or the U.K.), but MenZB

Japanese B Encephalitis

Rural India + China, SEA, Indonesia, Korea, E. Russia
For travel over 30 days especially to rural farming areas
Associated with pigs

High incidence of mild (20%) to serious (0.6%) vaccine events
IXARO 2 doses separated by 28 days
The Advisory Committee on Immunization Practices recommends JE vaccine for travelers who plan to spend ≥1 month in endemic areas during the JEV transmission season. This includes long-term travelers, recurrent travelers, or expatriates who will be based in urban areas but are likely to visit endemic rural or agricultural areas during a high-risk period of JEV transmission. Vaccine should also be considered for the following:

Short-term (<1 month) travelers to endemic areas during the JEV transmission season, if they plan to travel outside an urban area and their activities will increase the risk of JEV exposure. Examples of higher-risk activities or itineraries include:

1. spending substantial time outdoors in rural or agricultural areas, especially during the evening or night;
2. participating in extensive outdoor activities (such as camping, hiking, trekking, biking, fishing, hunting, or farming); and
3. staying in accommodations without air conditioning, screens, or bed nets.

Travelers to an area with an ongoing JE outbreak.

Travelers to endemic areas who are uncertain of specific destinations, activities, or duration of travel.

Vaccine Spacing

Live viral antigens if not given on same day should be separated by at least 28 days or immune response may be blunted (except OPV, MMR, oral typhoid)

Chloroquine/mefloquine can interfere with IM Rabies Vaccine

Oral Typhoid should not be taken concurrently with proguanil and delayed >24hrs after mefloquine and any antibiotic

TB testing and live virus antigen either together or at least 4-6 wks apart to avoid interference
Immunocompromised Traveler and HIV

Killed vaccines can be used, but immune response may be blunted

Avoid live vaccines in patients with AIDS, leukemia, lymphoma other malignancies and during treatment with immune suppressive drugs.

With CD4+ over 500 (in HIV) MMR and other live vaccines have been used. Yellow fever can be used in asymptomatic HIV-infected travelers, but incidence of side effects may be higher.

Varicella vaccine

~95% of U.S. adults have antibodies

Immunization Summary

Immunize according to risk and not to country visited, except yellow fever and menigococcus which are required for travel.

Hepatitis A and B are the most frequent vaccine preventable infections

Typhoid and Hepatitis A are indicated for most travelers.

Malaria is the major infectious risk for travelers

300 million infections and 3 million deaths annually
30,000 European and N. American travelers infected annually
4% mortality (P.f.); 20% with severe cases involving Cerebral malaria, ARDS, PE, oliguria, <5gm Hg, seizures, BF, lactic acidosis, and/or hypoglycemia (<40mg%)
Malaria Endemic Areas

- P. falciparum - gametocyte
- P. falciparum – ring stages
P. malariae - band stage (trophozoite)

P. malariae rosette (segmented merozoite stage)

P. vivax

Schüffner’s dots
Traveler’s malaria

<table>
<thead>
<tr>
<th>Purpose</th>
<th>UK (n=1710)</th>
<th>USA (n=695)</th>
</tr>
</thead>
<tbody>
<tr>
<td>family visit</td>
<td>56%</td>
<td>23%</td>
</tr>
<tr>
<td>tourists</td>
<td>12%</td>
<td>12%</td>
</tr>
<tr>
<td>business</td>
<td>6%</td>
<td>9%</td>
</tr>
<tr>
<td>students</td>
<td>-</td>
<td>9%</td>
</tr>
<tr>
<td>missionaries</td>
<td>-</td>
<td>11%</td>
</tr>
<tr>
<td>Peace C.W.</td>
<td>-</td>
<td>2%</td>
</tr>
</tbody>
</table>

MMWR 2001;50:SS1-44; Eurosurveillance 1998;3:40
No prophylaxis = malaria

<table>
<thead>
<tr>
<th>Chemo.</th>
<th>USA</th>
<th>UK</th>
<th>Canada</th>
</tr>
</thead>
<tbody>
<tr>
<td>none</td>
<td>84.2%</td>
<td>81%</td>
<td>97%</td>
</tr>
<tr>
<td>MFQ</td>
<td>5.8%</td>
<td>4%</td>
<td>3%</td>
</tr>
</tbody>
</table>


Acquired Immunity-Adults

Following many exposures clinical immunity develops

Limits symptomatic disease

Neither sterile or permanent i.e. “semi-immune”

Species and stage specific

Passively transferred from immune mother to fetus
Who dies from Traveler’s Malaria?

USA & Canada (n=21) | Total
---|---
no chemo. | 21 | 100%
Delay seeking care | 1 | 5%
Missed by MD | 13 | 62%
Lab misDx | 9 | 43%
misRx | 11 | 52%

*Kain et al. CMAJ 2001;164:654*

Prophylaxis for Chloroquine-Resistant Malaria

<table>
<thead>
<tr>
<th>Drug</th>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mefloquine</td>
<td>Weekly</td>
<td>Neuropsychiatric ADRs</td>
</tr>
<tr>
<td>(Lariam®)</td>
<td>Most ADRs first 3 doses</td>
<td>1-2 weeks pre; 4 weeks post</td>
</tr>
<tr>
<td></td>
<td>Moderate cost $$</td>
<td></td>
</tr>
</tbody>
</table>

ADR = adverse drug reaction.
Mefloquine: Contraindications

- Active depression
- History of convulsions
- History of psychosis or major psychiatric disorder
- A recent history of:
  - Depression
  - Anxiety disorder

http://www.lariam.com (Lariam®, mefloquine hydrochloride).
Website provided by Roche Laboratories Inc.

Prophylaxis for Chloroquine-Resistant Malaria

<table>
<thead>
<tr>
<th>Drug</th>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atovaquone-Proguanil (Malarone®)</td>
<td>Causal Px (kills liver stages)</td>
<td>Daily Gastrointestinal ADRs</td>
</tr>
<tr>
<td></td>
<td>Moderate cost $$</td>
<td>1-2 days pre; 1 weeks post</td>
</tr>
</tbody>
</table>
Atovaquone/proguanil (Malarone)

- tissue schizonticide $\Rightarrow$ causal for Pf (not Pv/Po)
- dose: adults: 250mg Atov/100mg Pro daily $\Rightarrow$ food
  - ped: 62.5/25 $\Rightarrow$ food
- 1 day before $\Rightarrow$ 1 wk after exposure
- efficacy: 95 - 100% Pf; ~85% Pv
- adverse events: GI upset, headache, rash, cough

Prophylaxis for Chloroquine-Resistant Malaria

<table>
<thead>
<tr>
<th>Drug</th>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxycycline</td>
<td>Highly effective (84-100% protection); suppressive</td>
<td>Daily Gastrointestinal problems Photosensitivity</td>
</tr>
<tr>
<td></td>
<td>low cost $</td>
<td>children &lt; 8 yrs. and pregnancy</td>
</tr>
</tbody>
</table>
Doxycycline

Adverse effects:
- Photosensitivity (UVA & UVB blockers = TiO$_2$/ZnO)
- Nausea, vomiting (take with food)
- Esophageal ulcer (take with fluids)
- Candida vaginitis (carry antifungal)

Primaquine Prophylaxis

8-aminoquinolone
tissue schizonticide so causal prophylaxis

Dose: 30 mg (base) = 2 tabs/day, 1 day before and 1 week after exposure

Efficacy: 85-95% (Pf + Pv) in 3 studies:
- Irian Jaya, Kenya & Colombia
Primaquine Prophylaxis

Adverse events: GI upset, met Hb
Contraindicated in G6PD deficiency, pregnancy

Take with food and screen for G6PD

Prophylaxis for Chloroquine-Resistant Malaria - summary

<table>
<thead>
<tr>
<th>Drug</th>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mefloquine (Lariam®)</td>
<td>Moderate cost $$ $11.40/dose</td>
<td>Neuropsychiatric problems 1-2 weeks pre; 4 weeks post</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>Lowest cost $ $0.70/day</td>
<td>Daily; sunburn; gastrointestinal; vaginal yeast infection; 1 day pre, 4 weeks post</td>
</tr>
<tr>
<td>Primaquine</td>
<td>Safety, convenience; $2/d</td>
<td>G6PD level</td>
</tr>
<tr>
<td>Atov/proguanil (Malarone®)</td>
<td>Safety 2 day pre; 7 days post</td>
<td>Daily, Highest cost $$ $5.60/day</td>
</tr>
</tbody>
</table>
Prophylaxis & Pregnancy

Chloroquine safe
Mefloquine safe 2nd, 3rd trimesters
No evidence of abortion or defects 1st trimester
Chloroquine + proguanil
postpone pregnancy ~ 3 months post mefloquine
DEET

Mean Protection (min)

<table>
<thead>
<tr>
<th>Repellent</th>
<th>Protection (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEET (24%)</td>
<td>300</td>
</tr>
<tr>
<td>DEET (6.7%)</td>
<td>234</td>
</tr>
<tr>
<td>Skin-so-soft\textsuperscript{TM}</td>
<td>10</td>
</tr>
<tr>
<td>Citronella (10%)</td>
<td>20</td>
</tr>
<tr>
<td>Eucalyptus (Repel, Fite\textsuperscript{TM})</td>
<td>~240</td>
</tr>
</tbody>
</table>

picaridin (Bayrepel 19.2% was equivalent to DEET)

*Fradin et al. NEJM 2002;347:13 compared 7 repellents in 15 participants*

DEET safety

Mosquitoes disease to 700 million/yr
DEET > 8 billion appl. (2 mill/yr)

REMARKABLE safety profile

- <50 case of serious toxic effects since 1960
- >75% resolved without sequelae

most problems in those with long-term high dose
no clear association of adverse events with concentration

DEET use in Children

30% DEET safe in children > age 2 mo.
Avoid hands, eyes, under clothing
Wash off with soap and water after risk
Apply once daily
Avoid excessive use

Picaridin

OIL of LEMON EUCALYPTUS*

*P-menthane - 3,8 - diol
Travelers Diarrhea

Sudden onset >3 loose stools/24h over 4-5 days (85%), n/v, cramps or pain, tenesmus, stool urgency, dysentery, fever

Sequelae:
40% modify activities
20% confined to bed
1% hospitalized
2% chronic diarrhea > 1 mo.
TRAVELERS DIARRHEA

Boil it, cook it, peel it, or forget it!
Easy to remember…
...Impossible to do !*

TD: Clinical

Sudden onset: 1/3-70% in 1st 2 wks.
≥3 loose stools/24h over 4-5 days (85%)*
*+n/v, cramps or pain, tenesmus, stool urgency, dysentery, fever

sequelae:
- 40% modify activities
- 20% confined to bed
- 1% hospitalized
- 2% chronic diarrhea > 1 mo.
Traveler Diarrhea Pathogens

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>ETEC</td>
<td>30%</td>
</tr>
<tr>
<td>EAEC</td>
<td>26%</td>
</tr>
<tr>
<td>Othersa</td>
<td>7%</td>
</tr>
<tr>
<td>Mixedb</td>
<td>20%</td>
</tr>
<tr>
<td>None identifiedc</td>
<td>37%d</td>
</tr>
</tbody>
</table>

a. Includes Salmonella sp, Shigella sp, Campylobacter sp (10-18%), Vibrio sp, Aeromonas hydrophilia, Pleisomonas shigelloides, (E.histolytica, Cyclospora, C. parvum, G. lamblia <15%), and rotovirus (2.5%)
b. Patients with >1 enteric pathogen
c. Patients with TD and no agent identified
d. From 51% previously

Travelers Diarrhea Treatment

<table>
<thead>
<tr>
<th>Severity</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>mild:</strong></td>
<td>none; loperamide; BSS</td>
</tr>
<tr>
<td>1-2 stools/24 hr</td>
<td></td>
</tr>
<tr>
<td><strong>moderate:</strong></td>
<td>add single dose antibiotic</td>
</tr>
<tr>
<td>&gt; 3 stools/24 hr</td>
<td></td>
</tr>
<tr>
<td><strong>severe:</strong></td>
<td>Continue antibiotic x 3 d plus loperamide or BSS</td>
</tr>
<tr>
<td>&gt; 6 stools/24 hr and fever or blood</td>
<td></td>
</tr>
</tbody>
</table>

Antibiotics used: Quinolone, Azithromycin, Doxycycline
TD Pediatric Treatment
(>2yrs)

- Azithromycin 10mg/kg qd x2d*+ORS
- Doxycycline C-I in children <8y +ORS*
- Ciprofloxacin 10mg/kg qd x 2d +ORS

(Widespread resistance to TMP/S and doxycycline by enteric organisms)