Travel Medicine

David Fessler, MD, MPH
Division of General Medicine and Primary Care
Division of Infectious Diseases
Beth Israel Deaconess Medical Center

themindfulword.org
Phone message:
Patient leaving for Nigeria next month for 3 weeks to see family. 10 weeks pregnant. Requesting valium for flight. Please advise.
Pre-travel counseling on disease prevention is highly individualized, can be complex and time-consuming

• Routine and travel-specific immunizations
• Malaria chemoprophylaxis
• Travelers Diarrhea
• Food/Water safety
• Insect protection
• High-altitude medicine
• Diving/marine medicine
• Jet lag, motion sickness
• Sun protection, temperature extremes
• Special needs travelers
  • Pregnancy
  • Immunosuppressed
  • Complex medical needs
Pre-travel counseling on disease prevention is highly individualized, can be complex and time-consuming

• Routine and travel-specific immunizations
• Malaria chemoprophylaxis
• Travelers Diarrhea
• Food/Water safety
• Insect protection
• High-altitude medicine
• Diving/marine medicine
• Jet lag, motion sickness
• Sun protection, temperature extremes
• Special needs travelers
  • Pregnancy
  • Immunosuppressed
  • Complex medical needs
Cause of Death in US Overseas Travelers

- Cardiovascular Disease: 49.0%
- Injury (Unintentional): 22.0%
- Infectious Disease: 1.0%
- Others/Unknown: 5.5%
- Cancer: 5.9%
- Suicide/Homicide: 2.9%
- Medical: 13.7%
Online Resources for Travel Health

CDC Traveler’s Health
http://www.cdc.gov/travel/

WHO International Traveler and Health
http://www.who.int/ith/en/

State Department Travel Advisories
http://travel.state.com

Paid subscription online services
• Up-to-Date
• Shoreland Travax
2012 U.S. Resident International Travelers

Total U.S. travelers to international destinations: 28,502,000

Destinations:
- Europe: 36%
- Caribbean: 24%
- Asia: 19%
- South America: 7%
- Central America: 7%
- Middle East: 6%
- Africa: 3%
- Oceana: 2%

Only 12 % had pre-travel visit with physician

45% of travelers listed “Visiting Family and Friends” as purpose of trip
Travelers visiting family and friends

Significantly increased risk of illness while abroad
• Eating local food
• Drinking local water
• Accomodations with less stringent hygiene
• Perception of immunity to various endemic infections
  • Less likely to take malaria prophylaxis
  • Less likely to be vaccinated prior to trip
The Pre-Travel Visit

- Risk Assessment
- Risk Communication
- Risk Management
The Pre-Travel Visit

- Risk Assessment
  - Detailed itinerary
    - Countries/regions with duration in each area
    - Departure/return dates
    - City/rural
    - Anticipated activities
- Risk Communication
- Risk Management
The Pre-Travel Visit

• Risk Assessment
  • Detailed itinerary
  • Patient-centered risk assessment
    • Vaccination history
    • Medical history
      • Allergies
      • Relevant medical conditions
      • Medications
      • Pregnancy
  • Risk Communication
  • Risk Management
The Pre-Travel Visit

• Risk Assessment
• Risk Communication
• Risk Management
The Pre-Travel Visit

• Risk Assessment
• Risk Communication
• **Risk Management**
  • Travelers Diarrhea prevention/treatment
  • Malaria prevention/insect precautions
  • Vaccine recommendations
  • Other advice relevant to itinerary and patient

Handouts on vaccines, insect precaution, food/water safety, destination-specific health issues available on CDC travel site.
Estimated Monthly Incidence Among Travelers in Developing Countries

- Travelers' diarrhea: 20%-40%
- Malaria (no chemoprophylaxis West Africa)
- Influenza A or B
- Dengue infection (symptomatic)
- Animal bite with rabies risk
- PPD conversion

- Hepatitis A
- Typhoid (South Asia, N/W/Central-Africa)
- Tick borne encephalitis (rural Austria): 0.01%
- Hepatitis B
- Typhoid (other areas)
- HIV-Infection
- Fatal accident: 0.0001%
- Cholera
- Legionella infection
- Japanese Encephalitis: 0.0001%
- Meningococcal disease
- Poliomyelitis

CDC 2014 Yellowbook
http://www.cdc.gov/travel/
Travelers’ Diarrhea

• Occurs in 30-60% of travelers
  • 80-90% due to bacterial pathogens
• Most common pathogens:
  • E. coli (especially ETEC)
  • Campylobacter
  • Shigella
  • Salmonella
  • Viruses (norovirus, etc)

• Parasites relatively uncommon, but become more likely with lengthy travel or protracted symptoms
  • Giardia, Entameoba, Cyclospora, Isospora, Cryptosporidium
Tips for Food/Water Safety

• Wash hands before eating, either with soap & water or alcohol-based gel
• Drink/brush teeth with bottled or boiled water
  • Avoid tap water, ice cubes, pre-opened water bottles
• Avoid food purchased from street vendors
• Make sure food is fully and recently cooked
• Avoid unpasteurized dairy products
• Avoid raw fruits/vegetables unless traveler peels them

parentsconnect.com  growcookeat.com  myfrenchkitchen.wordpress.com
“Boil It, Cook It, Peel It, or Forget It”

Intuitive, but is it effective?
• No change in incidence of travelers diarrhea over last 50 years

Poor adherence to food/water safety advice?
• Surveys show same poor adherence compared to 15 years ago
  • Travelers’ desire to sample local foods
  • Carefree attitude, alcohol

Does it work even if advice is followed?
• Some risk elements out of travelers’ control
  • Even “safe” foods easily contaminated by other foods, improper handling, or prolonged storage
• No clear evidence that incidence decreased in travelers closely adhering to food/water safety advice
Prevention of Travelers’ Diarrhea

Bismuth subsalicylate (Pepto-Bismol)
- Anti-microbial, anti-secretory, and toxin absorption properties
- 40-65% protective for prevention of travelers’ diarrhea
- Standard dosing: two tablets qid - inconvenient
- Side effects: Black tongue and stool
- Impairs absorption of doxycycline
- Contraindications: Pregnancy, advanced CKD, aspirin allergy
- Precautions:
  - Bleeding with use of anticoagulants
  - Risk of toxicity when used with other salicylates
Prevention of Travelers’ Diarrhea

Probiotics
Probably safe, but not routinely recommended due to questionable efficacy

• Single RCT showed efficacy of daily Lactobacillus GG over placebo
  • 47% protection (3.9% vs 7.4% with diarrhea on given day)
• Another RCT with 245 travelers showed no protective benefit with twice daily Lactobacillus LA compared to placebo

Hilton, J Travel Med 1997;4:41
Briand, Clin Infect Dis 2006;43:1170
Prevention of Travelers’ Diarrhea

Prophylactic Antibiotics
• Very efficacious (up to 90%)
• Main concerns are drug resistance and balancing benefits/toxicities
• Growing resistance has already made tetracyclines and TMP-SMX ineffective, and fluoroquinolone resistance is spreading quickly

Rifaximin
• Intraluminal, non-absorbed rifamycin derivative
• No efficacy against invasive infections like Campylobacter or Shigella
• FDA approved for treatment (not prevention) of travelers diarrhea
• RCT of 210 student travelers to Mexico showed good efficacy of Rifaximin (600mg daily) compared to placebo over 14 days
  • 73% protection (20% vs 48% developed diarrhea, p<0.001)

Martinez-Sandoval, J Travel Med 2010;17:111
Travelers’ Diarrhea

Early Self-Treatment

• In general, should focus on early self-treatment rather than prophylaxis, offering prophylaxis only for high risk patients
• Usually ciprofloxacin 500mg bid x 1-3 days
• In pregnancy, or in South/Southeast Asia with high incidence of fluoroquinolone-resistant Campylobacter:
  • Azithromycin 500mg daily x 1-3 days

• Anti-motility agents usually safe, controversial in severe disease due to concerns about prolonged bacterial carriage

• High fevers, bloody stools, lack of resolution should prompt medical evaluation
Estimated Incidence Per Month of Infections and Fatal Accidents Among Travelers in Developing Countries in 2010

- Travelers’ diarrhea: 20%-40%
- Malaria (no chemoprophylaxis West Africa)
- Influenza A or B: 1%
- Dengue infection (symptomatic)
- Animal bite with rabies risk
- PPD conversion
- Hepatitis A
- Typhoid (South Asia, N/W/Central-Africa)
- Tickborne encephalitis (rural Austria): 0.01%
- Hepatitis B
- Typhoid (other areas)
- HIV-infection
- Fatal accident: 0.001%
- Cholera
- Legionella infection
- Japanese encephalitis: 0.0001%
- Meningococcal disease
- Poliomyelitis

CDC 2012 Yellowbook
http://www.cdc.gov/travel/
# Pre-Travel Immunizations

<table>
<thead>
<tr>
<th>VACCINE</th>
<th>AGE GROUP</th>
<th>19-21 years</th>
<th>22-26 years</th>
<th>27-49 years</th>
<th>50-59 years</th>
<th>60-64 years</th>
<th>≥ 65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza **</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tetanus, diphtheria, pertussis (Td/Tdap) **</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicella **</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human papillomavirus (HPV) Female **</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human papillomavirus (HPV) Male **</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zoster **</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measles, mumps, rubella (MMR) **</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumococcal 13-valent conjugate (PCV13) **</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumococcal polysaccharide (PPSV23) **</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningococcal TL **</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis A **</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B **</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenza type b (Hib) **</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **1 dose annually**
- **Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs**
- **2 doses**
- **3 doses**
- **1 dose**
- **1 or 2 doses**
- **1 dose**
- **1 or 2 doses**
- **1 dose**
- **1 or more doses**
- **2 doses**
- **3 doses**
- **1 or 3 doses**

Caviar, Truffles, and Travel Vaccines

Out of Pocket Costs for BIDMC Travel Clinic

• Travel visit: $115
• Administration of first vaccine: $80
• Administration of each additional vaccine: $39

Vaccine costs:
• Yellow fever: $204
• Inactivated typhoid: $204
• Oral typhoid: $89
• Menactra: $319
• Rabies: $628 (x3!)
• Japanese Encephalitis: $421 (x2!)

Patients should call the insurer first!
Typhoid Vaccine

1) Injectable polysaccharide vaccine (Typhim Vi, Typherex)
   • One IM dose given at least 2 weeks before travel
   • 50-70% effective
   • Good for two years

2) Oral live attenuated vaccine (TY21a, Vivotif)
   • Oral capsules on days 0,2,4,6, given 1 week before travel
   • 50-80% effective
   • Good for five years
   • Contraindicated in immunosuppressed, pregnancy

   • 80% of US cases in returning travelers coming from Mexico, India, Phillipines, Pakistan, El Salvador, and Haiti.
   • Neither vaccine effective against other strains of salmonella
Pre-Travel Immunizations

Estimated Incidence Per Month of Infections and Fatal Accidents Among Travelers in Developing Countries in 2010

- Travelers' diarrhea: 20%-40%
- Malaria (no chemoprophylaxis West Africa)
- Influenza A or B
- Dengue infection (symptomatic)
- Animal bite with rabies risk
- PPD conversion
- Hepatitis A
- Typhoid (South Asia, N/W/Central-Africa)
- Tickborne encephalitis (rural Austria): 0.01%
- Hepatitis B
- Typhoid (other areas)
- HIV-infection
- Fatal accident: 0.001%
- Cholera
- Legionella infection
- Japanese encephalitis: 0.0001%
- Meningococcal disease
- Poliomyelitis

CDC 2012 Yellowbook
http://www.cdc.gov/travel/
# Malaria in the United States

## Table 1. Number of malaria cases* among U.S. military personnel and U.S. and foreign civilians — United States, 1970–2011

<table>
<thead>
<tr>
<th>Year</th>
<th>U.S. military personnel</th>
<th>U.S. civilians</th>
<th>Foreign residents</th>
<th>Status not recorded</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>36</td>
<td>767</td>
<td>306</td>
<td>169</td>
<td>1,278</td>
</tr>
<tr>
<td>2004</td>
<td>32</td>
<td>775</td>
<td>282</td>
<td>235</td>
<td>1,324</td>
</tr>
<tr>
<td>2005</td>
<td>36</td>
<td>870</td>
<td>297</td>
<td>325</td>
<td>1,528</td>
</tr>
<tr>
<td>2006</td>
<td>50</td>
<td>736</td>
<td>217</td>
<td>561</td>
<td>1,564</td>
</tr>
<tr>
<td>2007</td>
<td>33</td>
<td>701</td>
<td>263</td>
<td>508</td>
<td>1,505</td>
</tr>
<tr>
<td>2008</td>
<td>19</td>
<td>510</td>
<td>176</td>
<td>593</td>
<td>1,298</td>
</tr>
<tr>
<td>2009</td>
<td>18</td>
<td>661</td>
<td>201</td>
<td>604</td>
<td>1,484</td>
</tr>
<tr>
<td>2010</td>
<td>46</td>
<td>1,085</td>
<td>368</td>
<td>192</td>
<td>1,691</td>
</tr>
<tr>
<td>2011</td>
<td>91</td>
<td>1,098</td>
<td>386</td>
<td>350</td>
<td>1,925</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Area or region</th>
<th>No.</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>1057</td>
<td>(67.4)</td>
</tr>
<tr>
<td>Asia</td>
<td>338</td>
<td>(21.5)</td>
</tr>
<tr>
<td>Central America/Caribbean</td>
<td>99</td>
<td>(6.3)</td>
</tr>
<tr>
<td>South America</td>
<td>33</td>
<td>(2.1)</td>
</tr>
<tr>
<td>Oceania</td>
<td>6</td>
<td>(0.4)</td>
</tr>
<tr>
<td>Unknown</td>
<td>37</td>
<td>(2.4)</td>
</tr>
<tr>
<td>Total</td>
<td>1,571</td>
<td>(100)</td>
</tr>
</tbody>
</table>

## Plasmodium species

<table>
<thead>
<tr>
<th>Plasmodium species</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
</tr>
<tr>
<td>P. falciparum</td>
<td>948</td>
</tr>
<tr>
<td>P. vivax</td>
<td>420</td>
</tr>
<tr>
<td>P. malariae</td>
<td>50</td>
</tr>
<tr>
<td>P. ovale</td>
<td>51</td>
</tr>
<tr>
<td>P. knowlesi</td>
<td>0</td>
</tr>
<tr>
<td>Mixed</td>
<td>21</td>
</tr>
<tr>
<td>Undetermined</td>
<td>435</td>
</tr>
<tr>
<td>Total</td>
<td>1,925</td>
</tr>
</tbody>
</table>

## Category

<table>
<thead>
<tr>
<th>Category</th>
<th>No.</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visiting friends and relatives</td>
<td>607</td>
<td>(55.4)</td>
</tr>
<tr>
<td>Tourist</td>
<td>45</td>
<td>(4.1)</td>
</tr>
<tr>
<td>Missionary or dependent</td>
<td>96</td>
<td>(8.8)</td>
</tr>
<tr>
<td>Business representative</td>
<td>78</td>
<td>(7.1)</td>
</tr>
<tr>
<td>Student or teacher</td>
<td>32</td>
<td>(2.9)</td>
</tr>
<tr>
<td>Air crew or sailor</td>
<td>10</td>
<td>(0.9)</td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
<td>(0.3)</td>
</tr>
<tr>
<td>Unknown</td>
<td>224</td>
<td>(20.5)</td>
</tr>
</tbody>
</table>

---

Preventing Mosquito Bites

Physical protection
• Limit exposure to standing water
• Long sleeved shirt, long pants, socks, wide brim hat
• Light-colored clothing
• Screened and/or air conditioned rooms
• Permethrin-impregnated bed nets

Insect Repellents
• DEET (10-35% for casual exposures, 35-50% for intense exposures, or high heat/humidity)
• Icaridin, PMD (lemon eucalyptus oil)
• Permethrin-treated clothing
• Area repellents (mosquito coils, aerosolizers, etc)
Malaria Chemoprophylaxis Cases

19F traveling to Haiti for 2 weeks for service work.
• No medical issues or allergies, not pregnant.

42M traveling to Bangkok and towns along the Thai-Cambodian border.
• History of hypertension, no drug allergies

28F, 24 weeks pregnant, traveling to Nigeria to see family.
• No other medical issues, no drug allergies

Chemoprophylaxis options
a) Chloroquine
b) Mefloquine (Lariam)
c) Atovaquone/proguanil (Malarone)
d) Doxycycline
e) Other
Malaria Chemoprophylaxis

**Chloroquine**
Widespread resistance, but still agent of choice in sensitive areas
- Haiti, DR, Caribbean, parts of Central America, most of Middle East

**Dosing:**
Weekly, starting 1 week before departure, and continuing for 4 weeks after return

**Adverse effects:**
- Generally well tolerated
- Uncommon: GI intolerability, dizziness, pruritis in dark-skinned people (up to 25%) due to drug concentrating in skin
- May exacerbate psoriasis or other pruritis symptoms
- Keratopathy, retinopathy reported in long-term use
Malaria Chemoprophylaxis

Mefloquine (Lariam):
Drug resistance rare, except in isolated areas in southeast Asia

Dosing:
Weekly, start 2 weeks before, continue 4 weeks after return

Neuropsychiatric side effects:
Wide variability in reported incidence and severity
• Well-tolerated vivid dreams: up to 25%
• About 5% have to discontinue drug due to side effects such as anxiety, depression, nightmares, insomnia, dizziness
• Seizures, psychosis, encephalopathy rare: ~1/10,000

Precautions/Contraindications:
Significant psychiatric disease, seizure disorder, QT prolongation
Malaria Chemoprophylaxis

**Atovaquone/Proguanil (Malarone):**
- Only sporadic reports of drug resistance
- Cost considerations aside ($3-4/day) used by many as agent of choice in chloroquine-resistant areas

**Dosing:**
- Daily, start 1 day before departure and continue 7 days after return

**Adverse effects:**
- Very well tolerated. Rare GI side effects, headache, insomnia, rash

**Precautions/Contraindications:**
- Renal insufficiency (GFR<30)
- Pregnancy class C due to lack of safety data for atovaquone
Malaria Chemoprophylaxis

**Doxycycline**
- No reports of drug resistance
- Useful in those traveling to chloroquine-resistant areas who can’t tolerate mefloquine or afford atovaquone/proguanil

**Dosing:**
- Daily, start 1 day before departure, continue 4 weeks after return

**Adverse effects:**
- GI side effects, phototoxicity

**Precautions/Contraindications:**
- Pregnancy, breast feeding, children under 8
Malaria Chemoprophylaxis in Pregnancy

Pregnant travelers should generally avoid travel to malarious areas
• Increased risk of severe malaria, increased maternal and fetal death
• Sequestration of parasites in placenta, with IUGR, premature delivery, anemia, congenital malaria

• If travel unavoidable, personal protection measures are critical
• DEET thought to be safe, though limited data in 1st trimester

Chemoprophylaxis:
• Chloroquine safe in sensitive areas
• Mefloquine only option in chloroquine-resistant areas
  • Safety data exists during 2nd and 3rd trimester, but limited data in 1st trimester
Drug Interactions with Anti-Malarials

**Warfarin:** Atovaquone-proguanil may reduce metabolism and boost INR

**Anti-arrhythmics:** Caution with Mefloquine, which can increase QTc

**Immunosuppressives:**
- Chloroquine, doxycycline, and mefloquine can raise cyclosporine levels
- Doxycycline and mefloquine increase tacrolimus levels
- No significant interactions with atovaquone-proguanil

**Antiretrovirals:**
- Mefloquine may modestly reduce protease inhibitor levels
- NNRTIs may modestly reduce mefloquine efficacy
Malaria Chemoprophylaxis Cases

19F traveling to Haiti for 2 weeks for service work.
• No medical issues or allergies, not pregnant.

**Chloroquine**

42M traveling to Bangkok and towns along the Thai-Cambodian border.
• History of hypertension, no drug allergies

**Atovaquone/proguanil (Malarone), or Doxycycline**

28F, 24 weeks pregnant, traveling to Nigeria to see family.
• No other medical issues, no drug allergies

**Avoid travel if at all possible. If travel unavoidable:**

**Mefloquine (Lariam)**
Phone message:
Patient leaving for Ghana next month for 3 weeks to see family. 10 weeks pregnant. Requesting valium for flight. Please advise.

Malaria Prophylaxis?
Vaccines?
Access to Medical Care?
DVT Risk?
Food/Water Safety?

Pregnancy
Phone message:

*Patient leaving for Ghana next month for 3 weeks to see family. 10 weeks pregnant. Requesting valium for flight. Please advise.*

**High risk scenario:**
- Malaria-endemic area with limited chemoprophylaxis options
- Yellow-fever endemic area, vaccine pregnancy class “C”
- “Visiting friends and family”
  - Potential risks for food/water borne illness
- Access to obstetric care?

Consider deferring trip if possible
If travel unavoidable:
- Mefloquine, travel vaccines (incl. YFV), lots of counseling!
Summary

• Much pre-travel preparation can happen in a primary care office
  • Hep A, Typhoid, Cipro, travel counseling, +/- malaria prophylaxis can take care of the majority of travelers

• Online, updated resources for destination-specific information

• Travel clinic preferable for those requiring Yellow Fever vaccine, pregnancy, immunosuppression
  • Make sure travel visit is covered
  • Have patient bring full vaccination record
Thank you!
References

• Keystone JS, Kozarsky PE, Freedman DO, Northdurft HD, Commor BA, ed. Travel Medicine, 2nd ed., Mosby Elsevier.