Travel Medicine 2015

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Phone message:
Patient leaving for Nigeria next month for 3 weeks to see family. 10 weeks pregnant. Requesting valium for flight. Please advise.
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
• Travax.com
A 24 year old woman books an urgent care visit with you. She has been experiencing 3 days of high fever to 103.5°F. Yesterday, she started a faint, lacy rash over her torso and this morning developed pain and swelling in her wrists and ankles. She returned from a weeklong trip to St. Thomas a week ago.

• What could this patient have done to reduce the risk of acquiring this infection?
• What would you advise her about prognosis and treatment?
Lindsay Lohan Reveals She Has Chikungunya: Rare, Untreatable Virus

Lindsay Lohan, Dec. 30

Click For More Pics Of Lindsay

Suspected and confirmed chikungunya cases by month
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)
Chikungunya

Natural History:
Fevers last 3-5 days
• Joint symptoms persist in ~80% of patients
• Arthralgias or inflammatory arthritis, tenosynovitis
• Mean duration: 6 months in some studies

Treatment:
Supportive care: NSAIDs, Tylenol
No antiviral treatments found to be effective
No established treatments for prolonged joint symptoms
Small cases series have described efficacy with DMARDs for those with persistent inflammatory arthritis
• Hydroxychloroquine
• Methotrexate
• Corticosteroids
Causes of Fever in the Returning Traveler: Location, Location, Location

- Retrospective study of 17,353 travelers presenting to GeoSentinel clinics at 30 sites on 6 continents 1996-2004
- Looked at travelers returning from 6 regions of developing world
- Most frequent causes of fever (per 1000):

<table>
<thead>
<tr>
<th></th>
<th>Global</th>
<th>Caribbean</th>
<th>Central America</th>
<th>South America</th>
<th>Sub-Saharan Africa</th>
<th>South-Central Asia</th>
<th>Southeast Asia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malaria</td>
<td>352</td>
<td>65</td>
<td>133</td>
<td>133</td>
<td>622</td>
<td>139</td>
<td>130</td>
</tr>
<tr>
<td>Dengue</td>
<td>104</td>
<td>238</td>
<td>123</td>
<td>138</td>
<td>7</td>
<td>142</td>
<td>315</td>
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<tr>
<td>Rickettsial infections</td>
<td>31</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>56</td>
<td>10</td>
<td>16</td>
</tr>
<tr>
<td>Typhoid/Paratyphoid</td>
<td>29</td>
<td>22</td>
<td>25</td>
<td>17</td>
<td>7</td>
<td>141</td>
<td>26</td>
</tr>
<tr>
<td>No cause reported</td>
<td>406</td>
<td>541</td>
<td>473</td>
<td>554</td>
<td>282</td>
<td>478</td>
<td>453</td>
</tr>
</tbody>
</table>

Freedman et al. *NEJM* 2006; 354:119
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/
A 35 year old woman tells you at her annual visit that she is leaving tomorrow for a week-long vacation to Mexico City. She is otherwise healthy, and is confident she is not pregnant.

1) How would you advise this patient about behavioral steps she can take to minimize the risk of travelers’ diarrhea?

2) What pharmacologic options would you consider for prevention or treatment of travelers’ diarrhea
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
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
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**
Safe, but not routinely recommended due to unclear 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 antibiotic-related 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
- Meta-analysis of four RCTs showed efficacy at preventing travelers’ diarrhea (RR 0.41, p<0.00001)
- Often not covered by insurers, high out-of-pocket cost

Hu, J Travel Med 2012;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 or levofloxacin 500mg qd 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)
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- Poliomyelitis

CDC 2014 Yellowbook
http://www.cdc.gov/travel/
A 45-year-old man with history of rheumatoid arthritis on infliximab sees you in clinic for a blood pressure check. Hand on the doorknob, he mentions that he is excited for his trip to India next month.” Further investigation reveals that he will be spending a week at the Hilton in Mumbai for business. Afterwards, he is flying to New Delhi and Agra to see the Taj Mahal. He leaves in 4 weeks.

1) What travel-related infections is this immunocompromised patient at increased risk for?
2) What routine vaccines do you want to verify this patient has received?
3) What travel-specific vaccines would you consider for this patient? How does his immunocompromised status affect this decision?

TNFα-blocker associated infections:
• TB
• Listeria
• Legionella
• Endemic fungi
  • Histoplasma
  • Coccidioides

livingwithra-nan.blogspot.com
### Figure 2. Vaccines that might be indicated for adults based on medical and other indications

<table>
<thead>
<tr>
<th>VACCINE ▼</th>
<th>INDICATION ▶</th>
<th>Pregnancy</th>
<th>Immuno-compromising conditions (excluding human immunodeficiency virus [HIV])</th>
<th>HIV infection CD4+ T lymphocyte count</th>
<th>Men who have sex with men (MSM)</th>
<th>Kidney failure, end-stage renal disease, receipt of hemodialysis</th>
<th>Heart disease, chronic lung disease, chronic alcoholism</th>
<th>Asplenia (including elective splenectomy and persistent complement component deficiencies)</th>
<th>Chronic liver disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza*</td>
<td></td>
<td></td>
<td>1 dose ILV annually</td>
<td>1 dose ILV or LAIV annually</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>1 dose Tdap each pregnancy</td>
<td></td>
<td></td>
<td>Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicella*</td>
<td></td>
<td></td>
<td>Contraindicated</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>3 doses through age 26 yrs</td>
<td>3 doses through age 26 yrs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human papillomavirus (HPV) Male*</td>
<td></td>
<td></td>
<td>3 doses through age 26 yrs</td>
<td>3 doses through age 21 yrs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Zoster*</td>
<td></td>
<td></td>
<td>Contraindicated</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>Contraindicated</td>
<td>1 or 2 doses</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>1 dose</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Pneumococcal polysaccharide (PPSV23)*</td>
<td></td>
<td></td>
<td></td>
<td>1 or 2 doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningococcal*</td>
<td></td>
<td></td>
<td></td>
<td>1 or more doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis A*</td>
<td></td>
<td></td>
<td></td>
<td>2 doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B*</td>
<td></td>
<td></td>
<td></td>
<td>3 doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Pre-Travel Immunizations

Indicated adult immunization up to date (see Fig 10.1)?

- no
  - Tetanus/diphtheria, Polio
  - MMR, Varicella, Pneumococcal, Influenza

- yes
  - Crossing an international border or country requiring yellow fever for entry?
    - no
      - Yellow fever
    - yes
      - Hepatitis A ± Typhoid

- yes
  - Food and water risk?
    - no
      - Hepatitis B, Rabies, Tuberculin skin test
    - yes
      - Special risks?
        - Travel to a yellow fever endemic/infected zone
        - Travel to sub-Saharan Africa or the Hajj
        - Travel to rural areas of South and SE Asia
        - Adventure travel
        - Anticipate any new sexual partner, body fluid exposure in healthcare or institutional setting
        - Aid or refugee worker
        - Cruise ship travel, chronic disease
        - yes
          - Yellow fever
          - Meningococcal
          - Japanese encephalitis
          - Hepatitis B, Rabies
          - Hepatitis B
          - Cholera
          - Influenza

Malaria Prevention

Malaria Chemoprophylaxis

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

42M moving to Namibia for a year for missionary work
• 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 in the United States

## Table 1. Number of malaria cases* among U.S. military personnel and U.S. and foreign civilians — United States, 1970-2012

<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>
<th>Area or region</th>
<th>No.</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>33</td>
<td>701</td>
<td>263</td>
<td>508</td>
<td>1,505</td>
<td>Africa</td>
<td>1151</td>
<td>(77.3)</td>
</tr>
<tr>
<td>2008</td>
<td>19</td>
<td>510</td>
<td>176</td>
<td>593</td>
<td>1,298</td>
<td>Asia</td>
<td>183</td>
<td>(12.2)</td>
</tr>
<tr>
<td>2009</td>
<td>18</td>
<td>661</td>
<td>201</td>
<td>604</td>
<td>1,484</td>
<td>Central America/Caribbean</td>
<td>64</td>
<td>(4.3)</td>
</tr>
<tr>
<td>2010</td>
<td>46</td>
<td>1,085</td>
<td>368</td>
<td>192</td>
<td>1,691</td>
<td>South America</td>
<td>37</td>
<td>(2.5)</td>
</tr>
<tr>
<td>2011</td>
<td>91</td>
<td>1,098</td>
<td>386</td>
<td>350</td>
<td>1,925</td>
<td>Oceania</td>
<td>7</td>
<td>(0.5)</td>
</tr>
<tr>
<td>2012</td>
<td>43</td>
<td>1,121</td>
<td>328</td>
<td>195</td>
<td>1,687</td>
<td>Unknown</td>
<td>47</td>
<td>(3.2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total</td>
<td>1,489</td>
<td>(100)</td>
</tr>
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</table>

## Table 2. Plasmodium species and category among U.S. military personnel and U.S. and foreign civilians — United States, 2012

<table>
<thead>
<tr>
<th>Plasmodium species</th>
<th>2012</th>
<th>Category</th>
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<tbody>
<tr>
<td></td>
<td>No.</td>
<td>(%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>P. falciparum</em></td>
<td>985</td>
<td>(58.4)</td>
</tr>
<tr>
<td><em>P. vivax</em></td>
<td>280</td>
<td>(16.6)</td>
</tr>
<tr>
<td><em>P. malariae</em></td>
<td>54</td>
<td>(3.2)</td>
</tr>
<tr>
<td><em>P. ovale</em></td>
<td>59</td>
<td>(3.5)</td>
</tr>
<tr>
<td><em>P. knowlesi</em></td>
<td>0</td>
<td>(0)</td>
</tr>
<tr>
<td>Mixed</td>
<td>21</td>
<td>(1.2)</td>
</tr>
<tr>
<td>Undetermined</td>
<td>288</td>
<td>(17.1)</td>
</tr>
<tr>
<td>Total</td>
<td>1,687</td>
<td>(100)</td>
</tr>
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<td></td>
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</tbody>
</table>

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 1-2 weeks before departure, and continuing for 4 weeks after return

Adverse effects:
• Uncommon: GI intolerability, neuropsychiatric symptoms, pruritis in dark-skinned people
• Keratopathy, retinopathy reported in long-term use

Contraindications/precautions:
• G6PD deficiency, pre-existing retinopathy or CNS diseases
• May exacerbated porphyria or psoriasis
Malaria Chemoprophylaxis

Mefloquine (Lariam):
Drug resistance rare, except along Thai-Cambodian and Thai-Burmese borders

Dosing:
Weekly, start 1-2 weeks before, continue 4 weeks after return

Neuropsychiatric side effects:
Wide variability in reported incidence and severity
• Well-tolerated vivid dreams: up to 25%
• Nightmares, insomnia, depression: 1/200 to 1/600
• Seizures, psychosis, encephalopathy: 1/6,000 to 1/10,000

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

Atovaquone/Proguanil (Malarone):
• Only sporadic reports of drug resistance
• Cost considerations aside, 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

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
Malaria Chemoprophylaxis Cases

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

**Anything, including Chloroquine**

42M moving to Namibia for a year for missionary work
• History of hypertension, no drug allergies

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

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 Nigeria next month for 3 weeks to see family. 10 weeks pregnant. Requesting valium for flight. Please advise.

Pregnancy

Malaria Prophylaxis?

Vaccines?

Access to Medical Care?

DVT Risk?

Food/Water Safety?
Phone message:
*Patient leaving for Nigeria 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

• Fever in the returning traveler: location, location, location!
• 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
• Keystone JS, Kozarsky PE, Freedman DO, Northdurft HD, Commor BA, ed. Travel Medicine, 2nd ed., Mosby Elsevier.
Thank you!