Travel Medicine

Megan Shaughnessy, MD, MS, CTropMed®, CTH®
Infectious Disease Staff Physician
Assistant Professor of Medicine, University of Minnesota
Medical Director of International Travel Medicine Clinic
Director of International Education
Hennepin County Public Health Clinic
Hennepin Healthcare system
Overview

- Travel Medicine background
- Travel Medicine at Hennepin Healthcare
- Pre travel consultation
- Post travel infection concerns

No conflicts of interest to report
International travel background

- International travel is increasing
  - 435 million in 1990 → 1.2 billion travelers in 2015
  - Trips to developing regions increased 31% → 47% of all travel
- Reason for travel is changing
  - Tourism ↓, visiting friends and relatives ↑
    - ~ 150 million people live outside their birth country
  - 14% of US college students study abroad, 46% in non-European country
  - Medical tourism
- Only 44% of international travelers from the US see a medical provider prior to travel
  - Only 10-20% of these in a dedicated travel clinic
    - More errors occur with travel advice from non travel clinics
    - Travel services may be limited

Harvey MMWR 2013;63:1-23.
The next infectious disease outbreak is just a plane ride away...
Recent travel related concerns

- Travelers contribute to the global spread of infectious diseases, including novel/emerging diseases
  - Zika
  - Chikungunya
  - MERS-CoV
  - SARS
  - Measles
  - Viral hemorrhagic fevers (Ebola)
  - Multidrug resistant organisms (MDROs)
COVID-19

- Drastic and precipitous decrease in travel
  - During 2020, US TSA screened 39% of the number passengers that were screened during 2019
  - November 2020: London Heathrow Airport, Frankfurt Airport, and Singapore Changi Airport were approximately 12%, 13%, and 1.9% (respectively) of the number of passengers compared to November 2019.

- Travel returning, but new and changing challenges
  - COVID testing for entry
  - Vaccination?
HCMC International Travel Medicine Clinic

- Sees patients of all ages, including families traveling together
  - In person and now telephone visits
- Providers who are ID trained who are available for post travel related infection concerns
- Dedicated clinic staff (RN, MA, providers)
- Specialty pharmacy partner
- Provides travel related vaccines and medications, including YF vaccine (formerly a Stamaril EAP site)
- Now provides COVID-19 PCR testing with < 24 hour turnaround time
- Clinic back line for providers/clinic staff: redacted for posting
Travelers in primary care clinics

• When possible- refer to travel clinic!
  ▫ Make sure routine immunizations are up to date
  ▫ Delay live virus vaccines in case others (YF) needed at travel visit, unless long duration prior to travel
  ▫ Check titers if unknown status for hepatitis A, B, MMR, varicella

• What to do if travel clinic referral not possible?!?
  ▫ Call!
  ▫ Consult your resources
Travel resources

- [www.cdc.gov/travel](http://www.cdc.gov/travel)
- Global TravEpiNet ([http://gten.travel/prep/prep](http://gten.travel/prep/prep))
- [www.headinghomehealthy.org](http://www.headinghomehealthy.org)
- Shoreland Travax
- CDC Yellow book
- Travel Medicine, Jay Keystone
- Oxford Handbook of Tropical Medicine
Pre travel consultation

- Components of a pre travel visit:
  - Assessing risk
  - Counseling on medical conditions
  - Counseling on travel related issues
  - Medications
  - Vaccines
Assessing risk

• Patient specific
  ▫ Age, medical history, medications, allergies, pregnancy, etc.

• Trip specific
  ▫ Departure date, length of stay
  ▫ Destination(s), urban vs rural
  ▫ Reason for travel
  ▫ Lodging
  ▫ Food
  ▫ Transportation
  ▫ Activities
Special travel populations

• Visiting friends and relatives (VFR)
  ▫ Refers to immigrants ethnically/racially distinct from the majority population of their country of residence who return home to visit friends and/or relatives
  ▫ Typically traveling from high-income to low-income country
  ▫ Most commonly travel to Sub-Saharan Africa
  ▫ Duration between immigration and travel back to home country varies widely, but most often > 4 years
    • Waning malaria immunity
  ▫ Includes second generation immigrants who were born in the country of residence
    • Younger age
    • Risks are slightly different than first generation
VFR travelers

Increased exposure to pathogens
  ▫ Staying in remote rural areas
  ▫ Close contact with local population
  ▫ High-risk food/beverages
Less likely to seek pre-travel advice (only 16%)
  ▫ Less likely to receive travel vaccinations
  ▫ Less likely to take malaria chemoprophylaxis
Last minute travel
More prolonged stay in visiting country
Special travel populations

Immunocompromised travelers: HIV/AIDS, transplant, steroids/anti-TNF, etc.

- 2015 study: 60% had traveled internationally in past 10 years, 45% to high risk destinations

- **Areas of concern**
  - Travel may cause problems with underlying disease
  - Host country may not be able to provide needed medical care
  - May be unable to receive live vaccinations, decreased response to other vaccines
  - Travel related medications may interact with chronic medications
  - May be more susceptible to infection and/or more severe manifestations of infection

- Need early referral to travel clinic

Bialy Intern Med J 2015
Special travel populations

• Pediatric travelers
  ▫ Incomplete routine vaccine series
  ▫ Too young for recommended vaccines
  ▫ Dosing/administrations of medications
  ▫ Increased risk of travelers' diarrhea, including severe dehydration
  ▫ More severe manifestations of other diseases
Special travel populations

Pregnant travelers

- 2\textsuperscript{nd} trimester generally regarded as safest for travel
- Potential contraindications for travel
  - Medical risk factors
  - OB risk factors
  - Destination specific factors
- Complicating factors
  - Live virus vaccines
  - Malaria prophylaxis
  - Travelers diarrhea
  - Unique, higher risk pathogens
- Similar complications/considerations for breast feeding travelers
Counseling on chronic conditions

- Notification of PCP and/or specialists
- Full supply of chronic medications
- Medication letter, especially if controlled substances
- Epi pen
- Anticipation/planning for potential problems
- Medical care at destination
- Overseas medical and evacuation insurance
Counseling on travel related issues

- Food/Water safety
- Insect avoidance
- Animal bites
- Road safety, other safety concerns
- DVT prevention
- Water
- Altitude
- Sea sickness
- Motion sickness
- Jet lag
- STDs/high risk behaviors
- Medical care while abroad
- Cruise ships
- Mass gatherings
Medications

• Medical kit of OTC medications
  ▫ Pain/fever meds, antidiarrheal, constipation, antacids, antihistamine, decongestants, creams (hydrocortisone, antifungal), etc.

• Preventative medications
  ▫ Malaria chemoprophylaxis: atovaquone-proguanil (malarone), mefloquine, doxycycline, [tafenoquine]
  ▫ Altitude: acetazolamide (Diamox)
  ▫ Sea sickness/Motion sickness: scopolamine, meclizine
  ▫ HIV: PEP (truvada + dolutegravir) OR PrEP (truvada)

• Self treatment
  ▫ Travelers diarrhea
  ▫ Yeast infections
  ▫ Symptom based treatment for malaria (if chemoprophylaxis not an option)
## Malaria chemoprophylaxis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Usage</th>
<th>Adult Dose</th>
<th>Pediatric Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atovaquone-proguanil</td>
<td>Prophylaxis in all areas</td>
<td>Adult tablets contain 250 mg atovaquone and 100 mg proguanil hydrochloride.</td>
<td>Pediatric tablets contain 62.5 mg atovaquone and 25 mg proguanil hydrochloride.</td>
<td>Begin 1–2 days before travel to malarious areas. Take daily at the same time each day while in the malarious area and for 7 days after leaving such areas. Contraindicated in people with severe renal impairment (&lt;30 mL/min). Atovaquone-proguanil should be taken with food or a milky drink. Not recommended for prophylaxis for children weighing &lt;5 kg, pregnant women, and women breastfeeding infants weighing &lt;5 kg.</td>
</tr>
<tr>
<td>Dapone</td>
<td>Prophylaxis in all areas</td>
<td>100 mg orally, daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mefloquine</td>
<td>Prophylaxis in areas with mefloquine-sensitive malaria</td>
<td>250 mg base (250 mg salt) orally, once/week.</td>
<td>≤9 kg: 4.4 mg/kg base (5 mg/kg salt) orally, once/week.</td>
<td>Begin ≥2 weeks before travel to malarious areas. Take weekly on the same day of the week while in the malarious area and for 4 weeks after leaving such areas. Contraindicated in people allergic to mefloquine or related compounds (quinine, quinidine) and in people with active depression, a recent history of depression, generalized anxiety disorder, psychosis, schizoaffective, other major psychiatric disorders, or seizures. Use with caution in people with psychiatric disturbances or a previous history of depression. Not recommended for people with cardiac conduction abnormalities.</td>
</tr>
</tbody>
</table>
# Malaria chemoprophylaxis

<table>
<thead>
<tr>
<th>Malaria chemoprophylaxis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chloroquine</strong></td>
<td><strong>Tafenoquine</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Prophylaxis only in areas with chloroquine-sensitive malaria</td>
<td>Prophylaxis in all areas</td>
</tr>
<tr>
<td>300 mg base (500 mg salt) orally, once/week</td>
<td>200 mg orally</td>
</tr>
<tr>
<td>5 mg/kg base (8.3 mg/kg salt) orally, once/week, up to maximum adult dose of 300 mg base</td>
<td>Not indicated in children &lt;16 years old</td>
</tr>
<tr>
<td>Begin 1–2 weeks before travel to malarious areas. Take weekly on the same day of the week while in the malarious area and for 4 weeks after leaving such areas. May eradicate parasitemia.</td>
<td><strong>PART</strong> indicated for people who had prolonged exposure to <em>P. vivax</em> or <em>P. ovale</em> or both. Administered as a single dose. Contraindicated in people with G6PD deficiency. Also contraindicated during pregnancy and lactation unless the infant being breastfed has a documented normal G6PD level.</td>
</tr>
</tbody>
</table>

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1. All people who take chloroquine or chloroquine-resistant *Plasmodium* should have a documented normal G6PD level before starting the medication.
Travelers’ diarrhea

- Most common condition reported by travelers
- 30-70% of travelers, depending on the destination
  - Low risk countries: US, Canada, Australia, New Zealand, Japan, northern and western Europe
  - Intermediate risk countries: Eastern Europe, South Africa, Caribbean islands
  - High risk areas: Asia, Africa, the Middle East, Mexico, Central and South America
- Risk factors: from high-income countries, children/young adults, reduced gastric acid, adventure tourists, low cost accommodation, cruise ships
- Consuming fecally contaminated food/water
- Hand hygiene practices of traveler, people at destination (restaurants, etc.)
Etiology of travelers’ diarrhea

- **80-90% Bacterial pathogens**
  - *E. coli* (enterotoxogenic)
  - *Campylobacter jejuni*
  - *Shigella* spp.
  - *Salmonella* spp.

- **5-8% Viral pathogens**
  - Norovirus, rotavirus, astrovirus

- **Protozoan pathogens**
  - *Giardia intestinalis*
  - *Cyclospora cayetanensis* in certain regions: Nepal, Peru, Haiti, Guatemala
  - *Entamoeba histolytica, Cryptosporidium parvum*: uncommon in travelers
  - Others: *Isospora, Microsporidia, Dientamoeba fragillis*
Symptoms

- Incubation period
  - 6-48 hours for bacterial, viral
  - 1-2 weeks for protozoa
- Duration (without treatment)
  - Bacterial: 3-5 days
  - Viral: 2-3 days
  - Protozoa: weeks to months
- Malaise, anorexia, abdominal cramps, watery diarrhea, nausea/vomiting (10-25%, especially viral)
Travelers’ diarrhea and fever

• 1/3 of patients with travelers diarrhea have low grade fever
• Dysentery: fever, bloody stool
  ▫ *Shigella*
  ▫ *Campylobacter*
  ▫ Enterohaemorrhagic *E. coli*
  ▫ *Salmonella*
  ▫ *Yersina*
  ▫ *E. histolytica*
  ▫ *Clostridium difficile*
## Travelers diarrhea self treatment

### Table 2-10. Travelers’ diarrhea treatment recommendations

#### Therapy of mild travelers’ diarrhea
- Antibiotic treatment is not recommended in patients with mild travelers’ diarrhea.
- Loperamide or BSS may be considered in the treatment of mild travelers’ diarrhea.

#### Therapy of moderate travelers’ diarrhea
- Antibiotics may be used to treat cases of moderate travelers’ diarrhea.
- Fluoroquinolones may be used to treat moderate travelers’ diarrhea.
- Azithromycin may be used to treat moderate travelers’ diarrhea.
- Rifaximin may be used to treat moderate, noninvasive travelers’ diarrhea.
- Loperamide may be used as adjunctive therapy for moderate to severe travelers’ diarrhea. Antimotility agents alone are not recommended for patients with bloody diarrhea or those who have diarrhea and fever.
- Loperamide may be considered for use as monotherapy in moderate travelers’ diarrhea.

#### Therapy of severe travelers’ diarrhea
- Antibiotics should be used to treat severe travelers’ diarrhea.
- Azithromycin is preferred to treat severe travelers’ diarrhea.
- Fluoroquinolones may be used to treat severe, nondysenteric travelers’ diarrhea.
- Rifaximin may be used to treat severe, nondysenteric travelers’ diarrhea.
- Single-dose antibiotic regimens may be used to treat travelers’ diarrhea.

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1 These treatment recommendations were developed prior to the approval of rifaximin 557 in the United States. Because it is in the same category of antimicrobial drug as rifaximin and because they have the same mechanism of action, rifaximin 557 can be considered as an alternative to rifaximin.

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Increasing risk of MDRO colonization!
Vaccines

• Catch up to date on routine vaccines!
  ▫ Influenza
  ▫ Hepatitis A/B
  ▫ MMR
  ▫ Tdap
  ▫ Polio
  ▫ Pneumococcus
  ▫ Varicella/Zoster

• May need titers: Hepatitis A/B, MMR, Varicella

• Pediatric travelers: early vaccination for Hepatitis A, MMR, Varicella
Travel vaccines

- Hepatitis A: 2 dose series (0, 6 months)
  - Licensed age 12 months and up; Now recommended for age 6-11 months but doesn’t count towards routine series
  - Routinely given in US childhood vaccination series since 2008
- Typhoid
  - IM: inactive vaccine, 2-3 years protection, ≥ 2 yrs
  - Oral: live, 5 years protection, more effort by patient, ≥ 6 yrs
- Polio booster
  - Some countries require 1 adult booster, document on ICVP (“yellow card”)
- Rabies
  - Pre exposure series: 0, 7, 21-28 days. Eliminates need for RIG and fewer post exposure vaccines
- Cholera vaccine
  - Available for adults but limited use
Meningococcal vaccines

- Conjugate vaccines
  - Menactra (9 mo – 55 yrs)
  - Menveo (2 mo – 55 yrs)
- Common off label use in adults > 55 years of age
- Meningitis belt of Africa
- Required for Hajj travelers
  - Document on ICVP ("yellow card")
- Booster every 5 years (more frequently for younger children)
Japanese encephalitis (JE)

- Mosquito vector (daytime)
- True incidence of infection in endemic countries unknown
  - Potential for long term neurological sequela
- Rarely reported in travelers
- JE vaccine (Ixiaro)
  - 0, 28 days. Booster at 1 yr
    - Can accelerate to 0, 7 days for adults
  - Select travelers? Prolonged stays, rural areas
  - Expensive!
Yellow fever vaccine

- Live virus vaccine with rare, serious side effects
  - Viscerotropic or neurotropic disease (1-2 in 125,000 administered doses)
- Age 9 mo and above, precaution > 60 yrs
- Can only be given at licensed clinics, ICVP documentation
- Lifetime protection (previously 10 yr booster) unless immunocompromised

Table 4–23. Countries with risk of yellow fever (YF) virus transmission⁴

<table>
<thead>
<tr>
<th>AFRICA</th>
<th>CENTRAL AND SOUTH AMERICA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angola</td>
<td>Ethiopia², Gabon, Ghana, Guinea, Guinea-Bissau, Kenya², Liberia, Mali², Mauritania², Niger⁴</td>
</tr>
</tbody>
</table>

Table 4–27. Countries that require proof of yellow fever (YF) vaccination from all arriving travelers⁴

- Angola
- Burundi
- Cameroon
- Central African Republic
- Chad
- Congo, Republic of the
- Côte d’Ivoire
- Democratic Republic of Congo
- Gabon
- Ghana
- Guinea-Bissau
- Mali
- Niger
- Nigeria
- Sierra Leone
- South Sudan
- Togo
- Uganda

Definitions by the World Health Organization as countries or areas where YF has been reported currently or in the past and vectors and animal reservoirs currently exist. See current Annex.
Illnesses in returned travelers

- Up to 64% of international travelers returning to US self-report an illness related to their travel
  - Only 8% see a physician
- Most frequently reported illness categories in GeoSentinel surveillance network study from US clinic sites 1997-2011:
  - Acute diarrhea: 22%
  - Other GI: 15%
  - Febrile/systemic illness: 14%
    - Malaria, viral syndrome, dengue, EBV
  - Dermatologic: 12%
  - Chronic diarrhea: 8%
  - Respiratory: 8%
  - Nonspecific: 5%

Harvey MMWR 2013;63:1-23.
Fever in returned travelers

- Most serious illness in returned travelers
- May not be febrile at time of presentation
- Febrile patients more likely to need hospitalization, particularly if elderly
- Multidrug resistant organisms present and increasing globally, other infection control concerns
- Malaria is most common specific diagnosis and most common cause of death in febrile travelers
  - Fever in a traveler to a malaria endemic area is a medical emergency!

Formulating a differential in a febrile traveler

- Location(s) of travel
  - Epidemiology of infectious diseases
- Dates of travel
  - Incubation period
- Associated symptoms
Specific diagnoses for systemic febrile illness

Table 3. Etiologic Diagnoses within Selected Syndrome Groups, According to Travel Region.\textsuperscript{a}

<table>
<thead>
<tr>
<th>Syndrome and Cause</th>
<th>All Regions</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>
<th>Other or Multiple Regions\textsuperscript{f}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic febrile illness (n = 1907)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specific pathogen or cause reported\textsuperscript{g}</td>
<td>594</td>
<td>459</td>
<td>527</td>
<td>446</td>
<td>738</td>
<td>512</td>
<td>547</td>
<td>454</td>
</tr>
<tr>
<td>Malaria\textsuperscript{h}</td>
<td>352</td>
<td>63</td>
<td>133</td>
<td>113</td>
<td>522</td>
<td>139</td>
<td>130</td>
<td>234</td>
</tr>
<tr>
<td>Dengue\textsuperscript{i}</td>
<td>104</td>
<td>216</td>
<td>123</td>
<td>118</td>
<td>7</td>
<td>142</td>
<td>311</td>
<td>33</td>
</tr>
<tr>
<td>Mononucleosis (due to Epstein-Barr virus or cytomegalovirus)\textsuperscript{j}</td>
<td>31</td>
<td>70</td>
<td>69</td>
<td>79</td>
<td>10</td>
<td>17</td>
<td>32</td>
<td>63</td>
</tr>
<tr>
<td>Rickettsial infection\textsuperscript{k}</td>
<td>31</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>36</td>
<td>10</td>
<td>16</td>
<td>24</td>
</tr>
<tr>
<td><em>Salmonella</em> typhi or <em>S. paratyphi</em> infection\textsuperscript{l}</td>
<td>29</td>
<td>22</td>
<td>25</td>
<td>17</td>
<td>7</td>
<td>10</td>
<td>26</td>
<td>24</td>
</tr>
<tr>
<td>No specific cause reported\textsuperscript{m}</td>
<td>406</td>
<td>541</td>
<td>473</td>
<td>514</td>
<td>282</td>
<td>478</td>
<td>453</td>
<td>546</td>
</tr>
</tbody>
</table>

Febrile illnesses with global distribution

- Urinary tract infections
- Respiratory infections
  - Bacterial pneumonia
  - Tuberculosis
  - Influenza (season is year round in the tropics)
  - Other respiratory viruses
- Hepatitis A, B, C, E
- Sexually transmitted diseases (HIV, HSV)
- CMV, EBV
- Measles
- Meningococcus (higher rates in meningitis belt of Africa)
- Histoplasmosis and other fungal infections
- Toxoplasmosis (although higher rates in parts of world- Brazil)
- Legionellosis
# Common infections by incubation period

<table>
<thead>
<tr>
<th>Disease</th>
<th>Usual incubation period (range)</th>
<th>Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incubation &lt; 14 days</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chikungunya</td>
<td>2–4 days (1–14 days)</td>
<td>Tropics, subtropics</td>
</tr>
<tr>
<td>Dengue</td>
<td>4–8 days (3–14 days)</td>
<td>Tropics, subtropics</td>
</tr>
<tr>
<td>Encephalitis, arboviral (Japanese encephalitis, tickborne encephalitis, West Nile virus, other)</td>
<td>3–14 days (1–20 days)</td>
<td>Specific agents vary by region</td>
</tr>
<tr>
<td>Enteric fever</td>
<td>7–18 days (3–60 days)</td>
<td>Especially in Indian subcontinent</td>
</tr>
<tr>
<td><strong>Acute HIV</strong></td>
<td>10–126 days (10 days to 6 weeks)</td>
<td>Worldwide</td>
</tr>
<tr>
<td>Influenza</td>
<td>1–3 days</td>
<td>Worldwide, can also be acquired while traveling</td>
</tr>
<tr>
<td>Legionellosis</td>
<td>5–6 days (2–10 days)</td>
<td>Widespread</td>
</tr>
<tr>
<td>Leptospirosis</td>
<td>7–12 days (2–26 days)</td>
<td>Widespread, most common in tropical areas</td>
</tr>
<tr>
<td>Malaria, <em>Plasmodium falciparum</em></td>
<td>6–30 days (98% onset within 3 months of travel)</td>
<td>Tropics, subtropics</td>
</tr>
<tr>
<td>Malaria, <em>P. vivax</em></td>
<td>8 days to 12 months (almost half have onset &gt;30 days after completion of travel)</td>
<td>Widespread in tropics and subtropics</td>
</tr>
<tr>
<td>Spotted-fever rickettsiae</td>
<td>Few days to 2–3 weeks</td>
<td>Causative species vary by region</td>
</tr>
<tr>
<td>Zika virus infection</td>
<td>3–14 days</td>
<td>Widespread in Latin America, endemic through much of Africa, Southeast Asia, and Pacific Islands</td>
</tr>
</tbody>
</table>
# Common illnesses by incubation period, cont.

<table>
<thead>
<tr>
<th>Incubation 14 Days to 6 Weeks</th>
<th>Encephalitis, arboviral, enteric fever, acute ( HIV; ) leptospirosis; malaria</th>
<th>See above incubation periods for relevant diseases</th>
<th>See above distribution for relevant diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amebic liver abscess</td>
<td>Weeks to months</td>
<td>Most common in resource-poor countries</td>
<td></td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>28–30 days (15–50 days)</td>
<td>Most common in resource-poor countries</td>
<td></td>
</tr>
<tr>
<td>Hepatitis E</td>
<td>26–42 days (2–9 weeks)</td>
<td>Widespread</td>
<td></td>
</tr>
<tr>
<td>Acute schistosomiasis (Katayama syndrome)</td>
<td>4–8 weeks</td>
<td>Most common in sub-Saharan Africa</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Incubation &gt;6 weeks</th>
<th>Amebic liver abscess, hepatitis E, malaria, acute schistosomiasis</th>
<th>See above incubation periods for relevant diseases</th>
<th>See above distribution for relevant diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B</td>
<td>90 days (60–150 days)</td>
<td>Widespread</td>
<td></td>
</tr>
<tr>
<td>Leishmaniasis, visceral</td>
<td>2–10 months (10 days to years)</td>
<td>Asia, Africa, Latin America, southern Europe, and the Middle East</td>
<td></td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>Primary, weeks; reactivation, years</td>
<td>Global distribution, rates and levels of resistance vary widely</td>
<td></td>
</tr>
</tbody>
</table>

CDC Yellow book
# Febrile illnesses according to common clinical findings

## Table 5-04. Common clinical findings and associated infections

<table>
<thead>
<tr>
<th>COMMON CLINICAL FINDINGS</th>
<th>INFECTIONS TO CONSIDER AFTER TROPICAL TRAVEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever and rash</td>
<td>Dengue, chikungunya, Zika, rickettsial infections, enteric fever (skin lesions may be sparse or absent), acute HIV infection, measles</td>
</tr>
<tr>
<td>Fever and abdominal pain</td>
<td>Enteric fever, amebic liver abscess</td>
</tr>
<tr>
<td>Undifferentiated fever and normal or low white blood cell count</td>
<td>Dengue, malaria, rickettsial infection, enteric fever, chikungunya, Zika</td>
</tr>
<tr>
<td>Fever and hemorrhage</td>
<td>Viral hemorrhagic fevers (dengue and others), meningococcemia, leptospirosis, rickettsial infections</td>
</tr>
<tr>
<td>Fever and arthralgia or myalgia, sometimes persistent</td>
<td>Chikungunya, dengue, Zika</td>
</tr>
<tr>
<td>Fever and eosinophilia</td>
<td>Acute schistosomiasis, drug hypersensitivity reaction, fascioliasis and other parasitic infections (rare)</td>
</tr>
<tr>
<td>Fever and pulmonary infiltrates</td>
<td>Common bacterial and viral pathogens, legionellosis, acute schistosomiasis, Q fever, leptospirosis</td>
</tr>
<tr>
<td>Fever and altered mental status</td>
<td>Cerebral malaria, viral or bacterial meningoencephalitis, African trypanosomiasis, scrub typhus</td>
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<tr>
<td>Mononucleosis syndrome</td>
<td>Epstein-Barr virus infection, cytomegalovirus infection, toxoplasmosis, acute HIV infection</td>
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<tr>
<td>Fever persisting &gt;2 weeks</td>
<td>Malaria, enteric fever, Epstein-Barr virus infection, cytomegalovirus infection, toxoplasmosis, acute schistosomiasis, brucellosis, tuberculosis, Q fever, visceral leishmaniasis (rare)</td>
</tr>
<tr>
<td>Fever with onset &gt;6 weeks after travel</td>
<td>Plasmodium vivax or ovale malaria, acute hepatitis (B, C, or E), tuberculosis, amebic liver abscess</td>
</tr>
</tbody>
</table>
Initial evaluation of the febrile traveler

- Important to identify infections that are:
  - Rapidly progressive and/or potentially fatal
  - Public health concern
  - Treatable
- Approximately 25% of patients remain undiagnosed, but generally recover
Important questions to ask

- PMHx, surgeries, medications (chronic and new)
- Immunization history, especially travel vaccinations
- Travel itinerary (specific locations and dates)
- Type of accommodation
- Malaria chemoprophylaxis
  - Compliance is key- before, during, and after
- Use of bed nets and insect repellent
Important questions to ask, cont.

- **Travel activities/exposures:**
  - Water source
  - Food: raw meat, seafood, unpasteurized dairy, street food, uncooked fruits/vegetables
  - Insect bites
  - Freshwater activities (swimming, rafting, etc.)
  - Soil contact
  - Adventure travel (spelunking, ecotourism)
  - Animal exposures, especially bites
  - Sexual contact (19-26% of travelers report a new sexual contact during travel, <25% condom use)
  - Needle exposures: Tattoos, piercings, IVDU
  - Hospitalizations and other medical care (injections, transfusions, medical tourism, etc.)
  - Sick contacts
  - Mass gatherings (Hajj)
General laboratory evaluation

• Malaria evaluation
  ▫ Multiple peripheral blood smears and rapid diagnostic tests (Binax)
• Complete blood count with differential (eosinophils)
• Basic metabolic panel
• Liver enzymes
• Urinalysis
• Cultures of **blood** +/- urine
• Chest Xray
• Stool evaluation if symptoms present
• Specific diagnostic assays as applicable
  ▫ Not always reliable or readily available
Potentially fatal febrile illnesses in travelers

• Influenza
• Malaria
• Dengue fever
• Typhoid (enteric) fever
• Rickettsial infections
• Leptospirosis
• Many rarer causes
  ▫ Viral hemorrhagic fevers
  ▫ Yellow fever
  ▫ Anthrax
  ▫ Plague
  ▫ Melioidosis
  ▫ Bartonella (Oroya fever)
Empiric treatment

- Malaria
  - Artemisinin-based combination therapies
- Typhoid
  - Ceftriaxone
- Rickettsial disease
  - Doxycycline
- Leptospirosis
  - Doxycycline
- Travelers diarrhea?
  - Fever with diarrhea is an indication to treat (also bloody diarrhea)
    - Azithromycin preferred due to resistance concerns, least likely to increase risk of Hemolytic Uremic Syndrome
- Routine infections (pneumonia, UTI, cellulitis, etc.)
Febrile illnesses of public health concern

- Viral hemorrhagic fevers
  - Ebola and others (Marburg, Lassa, Crimean-Congo hemorrhagic fever)
- Severe acute respiratory infections
  - Influenza
  - MERS-CoV
  - SARS
  - COVID-19
- Measles
- Varicella
- Monkeypox
- Pulmonary tuberculosis
- Meningococcal meningitis
Summary

• Travel contributes to the global spread of infectious diseases
• Travelers should be seen in an International Travel Medicine clinic
  ▫ Pre travel counseling
  ▫ Post travel illness management
Questions?

• Megan.Shaughnessy@hcmed.org
• www.hcmed.org/clinics
  ▫ Travel Medicine
References

- Shoreland Travax, accessed 5/6/2019
Zika

- Flavivirus transmitted by Aedes mosquitoes
- 1/5 people infected symptomatic
  - Fever, conjunctivitis, rash, headache, arthralgias/myalgias
  - Incubation period 3-14 days
- Fetal malformations
- Epidemiology
  - First identified in 1947 in Uganda
  - Prior to 2007: sporadic infections in Africa and Asia
  - 2007: outbreak in Yap islands; spread throughout Pacific islands
  - 2014: spread to Central and South America
  - Miami-Dade County Florida 6-10/2016, Brownsville Texas 10-11/2016
MERS-CoV

- Middle East Respiratory Syndrome, caused by a Coronavirus
  - Fever, cough, shortness of breath → pneumonia and ARDS
- More than 2,200 cases since 2012, case fatality rate 36%
- Saudi Arabia
  - UAE, Jordan, Qatar, Oman, Kuwait, Yemen, Lebanon, Iran
- Camels: primary reservoir, spread to humans via aerosols or body fluids
- 30 imported cases, including to the US (2 cases in 2014, unrelated)
- Health care workers account for approximately 20% of cases
Measles virus

- Incubation period 7-21 days
- One of most contagious diseases
  - 90% of people susceptible and exposed → infected
- First measles vaccine introduced in US 1963
  - MMR introduced in 1971, second dose recommended 1989
- Regular outbreaks in US related to international travel and low vaccination rates
  - MN outbreaks 2011 (Somali child visiting Kenya, 21 cases) and 2017 (75 cases)
  - 2015 multistate outbreak (147 cases) originating in Disneyland
  - 2019 to date: > 700 cases, greatest number since 1994
Ebola virus

- Viral hemorrhagic fevers
  - Lassa (MN case), Marburg, Crimean-Congo hemorrhagic fever
- Direct contact with infected blood and body fluids
  - Airborne transmission “not thought to occur”
- Incubation period: 2-21 days (average 10)
- Symptoms: fever, malaise, GI, hemorrhage
  - Mortality rate 20-80%
- 2014 outbreak: largest ever at 22,000 cases
  - Originated in Guinea, spread to Liberia and Sierra Leone
  - Locally acquired cases in Spain and US
- Current outbreak in Democratic Republic of Congo, 2nd largest ever
  - Started July 2018, >1500 cases to date
  - No spread outside of DRC
**MDROs**

- **Enterobacteriaceae:**
  - Extended-spectrum Beta-lactamase (ESBL)
  - Carbapenem-resistant (CRE)
    - NDM (New Delhi Metallo-beta-lactamase)
- **Salmonella typhi**
- **Salmonella, Shigella, Campylobacter**
- **Gonorrhea**
- **Acinetobacter**
- **MDR and XDR Tuberculosis**

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**Hospital Wastewater Releases of Carbapenem-Resistance Pathogens and Genes in Urban India.**
Lamba M, Graham DW, Ahammad SZ.

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**India: ‘Superbug’ Gene Found in Environment**
By DONALD G. McNEIL, Jr. APRIL 7, 2011

Bacteria containing an antibiotic-resistant “superbug” gene have been found in 2 of 51 tap water samples in New Delhi and in dozens of puddles and pools that children could play in, according to a report published Thursday in the journal *Lancet Infectious Diseases*. A team from Cardiff University in Britain found the gene, NDM-1, in 11 different types of bacteria, including...
Medical tourism

- Traveling to another country for medical care
  - Cheaper
  - Immigrant returning to home country
  - Procedure not available in US
- Hundreds of thousands of US residents yearly
- Common locations: Thailand, Mexico, Singapore, India, Malaysia, Cuba, Brazil, Argentina, and Costa Rica
- Common procedures
  - Cosmetic surgery
  - Dentistry
  - Cardiac surgery
  - Others: transplant, joint replacements, oncology care, IVF
- Challenges/risks
  - Infection control: MDROs, nontuberculous mycobacteria, etc.
  - Communication issues
  - Counterfeit, poor quality, and/or expired medications
  - Flying after a procedure (blood clots)
Diagnoses according to travel region (developing world)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>All Regions (N=17,353)</th>
<th>Caribbean (N=1115)</th>
<th>Central America (N=1338)</th>
<th>South America (N=1671)</th>
<th>Sub-Saharan Africa (N=4524)</th>
<th>South Central Asia (N=2403)</th>
<th>Southeast Asia (N=2793)</th>
<th>Other or Multiple Regions (N=3517)</th>
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† This category includes travel to West Asia, Northeast Asia, eastern Europe, Oceania, North Africa, or Antarctica (1668 travelers) or to multiple developing regions, for which ascertainment of exposure was impossible (1486 travelers).
‡ P<0.01 for the comparison among regions.

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‡ P<0.01 for the comparison among regions.
# Common illnesses by travel site

## Table 5-02. Common causes of fever, by geographic area

<table>
<thead>
<tr>
<th>GEOGRAPHIC AREA</th>
<th>COMMON TROPICAL DISEASE CAUSING FEVER</th>
<th>OTHER INFECTIONS CAUSING OUTBREAKS OR CLUSTERS IN TRAVELERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caribbean</td>
<td>Chikungunya, dengue, malaria (Haiti), Zika</td>
<td>Acute histoplasmosis, leptospirosis</td>
</tr>
<tr>
<td>Central America</td>
<td>Chikungunya, dengue, malaria (primarily <em>Plasmodium vivax</em>), Zika</td>
<td>Leptospirosis, histoplasmosis, coccidioidomycosis</td>
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<tr>
<td>South America</td>
<td>Chikungunya, dengue, malaria (primarily <em>P. vivax</em>), Zika</td>
<td>Bartonellosis, leptospirosis, enteric fever, histoplasmosis</td>
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<tr>
<td>South-central Asia</td>
<td>Dengue, enteric fever, malaria (primarily non-falciparum)</td>
<td>Rickettsia</td>
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<tr>
<td>Southeast Asia</td>
<td>Dengue, malaria (primarily non-falciparum)</td>
<td>Chikungunya&lt;sup&gt;1&lt;/sup&gt; infections</td>
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<tr>
<td>Sub-Saharan Africa</td>
<td>Malaria (primarily <em>P. falciparum</em>), tickborne rickettsiae (main cause of fever in southern Africa), acute schistosomiasis, dengue</td>
<td>African trypanosomiasis, chikungunya, enteric fever, filariasis</td>
</tr>
</tbody>
</table>

<sup>1</sup> Not included in table.
GeoSentinel Surveillance Network

Established in 1995, maintained by CDC

54 clinics sites, 235 network members

HealthPartners Center for International Health, Regions Hospital, St Paul

26 countries, 6 continents

Collects demographic, travel, and clinical diagnosis surveillance data from ill international travelers

Rapid messaging system between all sites and network members

Harvey MMWR 2013;63:1-23.
Persistent diarrhea

- Diarrhea > 2 weeks:
- Most common etiology from GeoSentinel study:
  - Postinfectious irritable bowel syndrome 55%
  - Unknown 32%
  - Irritable bowel syndrome 4%
  - Ulcerative colitis 3%
  - Postinfectious lactose intolerance 1%
- Often not infectious!
  - Exception- protozoan pathogens
    - *Giardia* most common, upper GI symptoms predominate
  - Rare exception- bacterial pathogens
    - Children with enteroaggregative or enteropathogenic *E. coli*
    - *C. difficile*

Harvey MMWR 2013;63:1-23.