Fever in the returning traveler

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Rob Stenstrom MD, PhD
St Paul’s Hospital Department of Emergency Medicine
University of British Columbia
Disclosure: I love to travel!
Take home points

1. Fever in the returning traveler is malaria until proven otherwise
2. Spectrum of disease presentation is variable depending on prior exposure and/or immunization
3. A high index of suspicion and thorough travel history are essential
4. You can’t know about all of the possible diseases; A history of travel should alert you to the possibility of a travel-related illness
Background and Epidemiology

In 2007, 812 million people crossed international borders
53 million travel from developed to developing world
Doubling in last 20 years

20-70% report travel related illness
Up to 5% will seek medical care
Tons of diseases to consider....

- AIDS
- African Trypanosomiasis
- Amebiasis
- American Trypanosomiasis (Chagas’ Disease)
- Bovine Spongiform Encephalopathy and Variant Creutzfeld-Jakob Disease
- Cholera
- Coccidioidomycosis
- Cryptosporidiosis
- Cyclosporiasis
- Dengue Fever
- Diptheria, Tetanus and Pertussis
- Encephalitis, Japanese
- Encephalitis, Tickborne
- Filariasis, Lymphatic
- Giardiasis
- Haemophilus influenzae Type b Meningitis and Invasive Disease
- Hepatitis A
- Hepatitis B
- Hepatitis C
- Hepatitis E
- Histoplasmosis
- Influenza
- Legionellosis
- Leishmaniasis
- Leptospirosis
- Lyme Disease
- Malaria
- Measles
- Meningococcal Disease
- Mumps
- Norovirus Infection
- Onchocerciasis (River Blindness)
- Plague
- Poliomyelitis
- Rabies
- Rickettsial Infection
- Rubella
- Schistosomiasis
- SARS
- Sexually Transmitted Disease
- Smallpox
- Steptococcus pneumoniae
- Traveler’s Diarrhea
- Tuberculosis
- Typhoid Fever
- Varicella (Chickenpox)
- Viral Hemorrhagic Fever
- Yellow Fever
TropNetEurope and multinational Geosentinel Surveillance Database (> 250,000 visits).

Most common infectious diagnoses related to travel:
1. Diarrhea (bacterial > parasitic)
2. Hepatitis A
3. Malaria
4. Dengue fever
5. Typhoid

Spectrum of Disease and Relation to Place of Exposure among Ill Returned Travelers. David O. Freedman, et al. NEJM, January 2006
Rare diseases are Rare!!

Ebola virus disease, Japanese encephalitis, rabies, tetanus, diphtheria, plague, tularemia, murine typhus, Rift Valley fever, poliomyelitis, primary amebic meningoencephalitis, anthrax, Hantavirus not reported once in over 40,000 cases of febrile returning travelers
The term VFR (Visiting Friends and Relatives) describes an immigrant, ethnically and racially distinct from the majority population of the country of residence, who returns to their country of origin to visit friends or relatives (CDC)
Common Causes of fever in the returned traveler

URTI
STI
UTI
Mono
Gastroenteritis
VTE
The travel history

• Get a (good) translator!
• Where visited/rural/urban
• For how long
• Pattern of fever/antipyretics
• Immunizations prior
• Prophylaxis
• Activities undertaken
• Sexual contacts
• Contact with animals
• Medications (immune-modulators)
• PMH (chemo, etc)
What is en/epidemic where they were?

- Pacific North West: *Cryptococcus gatti*: over 60 cases, 12% fatality rate; mostly completely healthy previously
- Ongoing E-coli outbreak in Europe
- New outbreak of measles in travelers returning from Europe mostly in non-immunized children; Major outbreak in France – 6 deaths.
Case: 42 year old male in Africa for 2 weeks

- On safari in Kenya; returned 3 weeks ago
- No PMhx; No specific immunizations
- Took Malaria prophylaxis
- **Symptoms**: Fever, malaise, anorexia, nausea, abdo pain
- **On exam**: N vitals, T 37.1° oral. Benign abdomen
- CBC, lytes BUN Creatinine urine dip all N
Case: 42 year old male in Africa for 2 weeks

- Fluids, gravol → home
- Returns the next day jaundiced

Diagnosis??
Hepatitis A Pathogenesis

- Ingestion
- Replication in oropharynx/GI tract
- Transported to liver - major site of replication
- Shed in bile, transported to intestines
- Shed in feces
- Brief viremia
- Cellular immune response: clinical disease and control

Incubation Period (15-50 days)
Hepatitis A

- After infectious diarrhea most common disease in travelers seeking medical help; most common vaccine preventable

- 1000 times more common than Yellow Fever Fatality rate of 0.5-1.3%; tends to be milder in children (70% asymptomatic)

- Cases of acute liver failure with Hepatitis A and (therapeutic) doses of Acetaminophen

- New inactivated HAV vaccines induce protective antibodies in more than 95% of recipients and offer protection estimated to last for 10 years

- Treatment: supportive
Hepatitis A distribution
Case:
51 year old male visiting Thailand

- Fever, extreme myalgias, arthralgias, rash
Dengue Fever:

- Aedes aegypti mosquito – day biting, common in cities
- Short incubation: 3-15 days
- Flavivirus with 4 antigenically distinct serotypes
- Immunity specific for each serotype
- *Most common cause of fever in the returning traveler from Asia/Indian sub-continent*
- Symptoms: Fever, myalgias (breakbone fever) arthralgias, headache, rash. Can be biphasic
- 60-70 cases per year in Canada (serologic test)
- CFR 5%
Distribution of Dengue fever and Aedes aegypti Mosquito
Dengue Haemorrhagic fever

- Uncommon in travelers
- Frequently fatal
- Associated with prior Dengue infection with another DF serotype
Case: 32 year old Female

Moved here from India 8 years ago
Returned from a visit home to India 12 days ago
Hx: Fever, myalgias, dark urine
Ex: Unwell
VS: Temp: 40°C
       BP: 90/55
       Pulse: 142
       Resp: 22, O₂ sat. 97%
Case:

- Labs: CBC: Hb 125, Platelets 110, WBC 3.1 with lymphopenia; Lytes BUN creatinine N Transaminases, LDH doubled; Lactate 1.8 (N) Bili 67; Blood smear: slight hemolysis

- Physical exam: Scleral icterus, splenomegaly
## Lab findings in disease states

<table>
<thead>
<tr>
<th>Finding</th>
<th>Disease</th>
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<tbody>
<tr>
<td>Hemoconcentration</td>
<td>Dengue</td>
</tr>
<tr>
<td>Thrombocytopenia, leukopenia</td>
<td>Malaria, Dengue</td>
</tr>
<tr>
<td>↑ transaminases</td>
<td>Malaria, Dengue, Typhoid</td>
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<tr>
<td>Hemolysis (↑ LDH, Bili)</td>
<td>Malaria, Hepatitis, yellow fever</td>
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<tr>
<td>Hypoglycemia</td>
<td></td>
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<tr>
<td>Eosinophilia</td>
<td>Parasitic infection; drug reaction</td>
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</table>
Malaria

• Female anopheles mosquito
• Incubation corresponds with liver stage of malaria parasite

**Incubation**

— *P. falciparum*  
  7 Days-8 weeks

— *P. vivax*  
  14 Days - 1 year

— *P. ovale*  
  14 Days - 1 year

— *P. malariae*  
  30 Days - 1 year

Semi-immune people such as immigrants and visitors from endemic areas and those taking chemoprophylaxis may have delayed onset of illness and mild symptoms.
MALARIA

- Risk of traveler acquiring malaria 200-500/100,000
- 60-70% of reported cases = falciparum (most from sub-Saharan Africa)
- 15% by P. vivax (the majority from the Indian subcontinent)
- 9% by P. ovale Case fatality rate = 3-5%
- 500 cases year in Canada
- 3-5 deaths per year (Canada)
- Now > 100 cases worldwide of “airport malaria”
MALARIA

• In any given year, nearly 10% of the global population will suffer from malaria.
• Risks for mortality include:
  – traveler's delay in seeking medical attention for fevers
  – inadequate access to parenteral therapy for severe malaria in Canada
  – delayed or inadequate care by Canadian physicians and hospitals.
Investigations

- CBC-diff
- Lytes, BUN, creatinine, gl-
- LFTs, transaminases
- **Thick and thin smear for malaria repeated (if neg q 8-12h x 3**
- Blood/urine/stool/culture
- ELISA for antibody detection, as indicated
- Radiography
DEET: N,N-Diethyl-meta-toluamide

One application of 25% lasts up to 5 hours
Not to face
Not in kids < 1 year old
**Not** on pets or St Paul’s staff who are prone to attempt licking themselves
Other bad actors:
Traveler's Diarrhea

• Common!
• Majority bacterial
• Loperamide and antibiotics good
• See Campana’s (better) talk
HIV, and other STIs
Rickettsial diseases

Rocky Mountain spotted fever, Q fever, etc

Short incubation period; 2-8 days
Headache, fever myalgias
Tick bite hx *absent* in 30%
Yellow fever

- Aedes mosquito; flavivirus
- Vaccine near 100% efficacy (10 years)
- Treatment supportive; 5% mortality
Typhoid fever

- Salmonella Typhi
- Fecal-oral transmission
- Fever, H/A, abdo pain, constipation; less frequently, diarrhea
- 3-4 weeks; Mortality 12-30% if untreated
- Blood cultures + in 60-70% of cases
- Treatment is fluoroquinolone or 3rd generation cephalosporin
Cholera

• Sudden Onset
  – Incubation 1 – 5 days
  – Therefore RARE in the returned traveler

• Vaccine
  – Reduces rate of infection by no more than 50%
  – effective for no more than 3-6 months

• Raw Shellfish: No es Bueno!
  – USA: sporadic cases from the Gulf of Mexico
  – Sporadic cases of travelers bringing contaminated seafood home
West Nile Virus: Confirmed cases in Canada – 2008

- Travel related
- Positive
Useful websites:

- http://www.CDC.gov/
- http://www.who
- http://www.malariajournal.com/content/8/1/202/comments
- http://medical-dictionary.thefreedictionary.com/Cerebral+malaria
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