Ill returning traveler
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I have no disclosures

International travel in 2010
- 940 million travelers crossed international boarders
- 60 million traveled from the US internationally – Almost half traveled to a developing country

What is the magnitude of travel related morbidity/mortality
- 20-70% report some illness
- 1-5% seek medical attention
- 3% report fevers
- 0.1-0.01% require medical evacuation
- 1/100,000 – death

Travelers crossing international borders

Exacerbation of comorbidities is the predominant cause of death in US Travelers:
- Suicide/Homicide 3%
- Cancer 6%
- Other/Unknown 6%
- Infection 1%
- Injury 22%

Hill DR. CID. 2006

Preventable causes of death in US travelers 2008-2010

- Air accident, 82
- Disaster, 131
- Drowning, 329
- Drug-related, 67
- Execution, 13
- Homicide, 533
- Maritime accident, 31
- Terrorist, 52

Illness in returned travelers: 2007-2011

- Gu/sti, 3%
- Derm, 21%
- Febrile, 25%
- Resp, 12%
- Neuro, 2%

Top 5 complaints in returning travelers leading to MD visit

- Fever without localizing findings
- Acute diarrhea
- Dermatological disorders
- Chronic diarrhea
- Nondiarrheal gastrointestinal disorders

Freedman DO. NEJM. 2006.

Fever

- 2-3% of American/European travelers to developing countries
  - 39% fever when abroad
  - 37% fevers abroad and home
  - 24% fevers at home only
- Medical emergency

Hill DR. J Trav Med. 2000

How to determine etiology of fever in returned traveler?

- Destination
- Incubation period
- Exposures
- Exam findings/labs
- Prophylaxis/immunizations

Freedman DO. NEJM. 2006.
**Incubation period**: Etiology of fever according to interval after travel

<table>
<thead>
<tr>
<th>Days post-travel</th>
<th>Proportion of Diagnoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>7</td>
<td>7.7%</td>
</tr>
<tr>
<td>14</td>
<td>14.1%</td>
</tr>
<tr>
<td>21</td>
<td>21.4%</td>
</tr>
<tr>
<td>28</td>
<td>28.7%</td>
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<tr>
<td>35</td>
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<tr>
<td>42</td>
<td>42.3%</td>
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<td>49</td>
<td>49.6%</td>
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<tr>
<td>56</td>
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<tr>
<td>63</td>
<td>64.2%</td>
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<tr>
<td>70</td>
<td>71.5%</td>
</tr>
<tr>
<td>77</td>
<td>77.8%</td>
</tr>
<tr>
<td>84</td>
<td>85.1%</td>
</tr>
<tr>
<td>91</td>
<td>92.4%</td>
</tr>
<tr>
<td>98</td>
<td>98.7%</td>
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</tbody>
</table>

**Proportion of Diagnoses**
- **Malaria**: 71%
- **Other**: 4%
- **CMV/EBV**: 2%
- **Dengue**: 1%
- **Typhoid**: 2%
- **P. falciparum**: 8%
- **P. vivax**: 35%
- **Other**: 42%

**Exposures?**
- Insect or animal exposures?
- Fresh water exposure?
- What did they eat/drink?
- Other ill travelers?
- Sexual activity?

**Specific symptoms or exam findings?**
- Symptoms
  - Abdominal pain
  - Arthralgias
- Exam findings
  - Rash
  - Jaundice
  - Ocular changes

**What kind of prevention measures were used?**
- Vaccinations?
  - Which ones?
  - Timing of vaccinations?
- Malaria prophylaxis?
  - Appropriate agents?
  - Taken appropriately?

**Case 1**
29 year-old paleontologist returned 3 days ago from a 3 week research trip to southern Bangladesh complaining of fever.

He complains of high fevers and now diffuse myalgias.

**Initial testing?**
Initial testing?
- Complete blood count
- Liver function tests
- Blood cultures
- Thick and thin blood smears (malaria)
- Urinalysis
- Chest x-ray
- Additional testing based on history/exam

Skin and Labs
- 2.1 > 37 < 67
- Cr: 0.8
- AST: 78
- ALT: 93
- AP: 88
- Bili: 0.7

Your DDx?

Dengue fever
- 50-100 million infections/year
- Mosquito vector (daytime)
- Urban and rural

Dengue fever: worldwide distribution

Dengue fever: clinical disease
- Incubation: 4-7 days
- Clinical Manifestations:
  - Severe headache, joint and muscle aches
  - Nausea and vomiting
  - Rash
- Dengue Hemorrhagic Fever/Shock Syndrome
  - Occurs 3-7 days into illness, often w/ end of fever
- Labs: leukopenia, thrombocytopenia, ↑ LFTs

Dengue rash

Flushed erythema
1-2 days post onset of symptoms

Morbilliform eruption
w/ petechiae and islands of sparing


Dengue fever: treatment and prevention

- Treatment: supportive
- Prevention of mosquito exposure
  - Avoid endemic areas
  - DEET
  - Permethrin

Dengue in Hawaii!!

- In 2001-2002 > 1,000 infected on 3 islands
- No *Aedes aegypti* were found
- *Aedes albopictus* was able to transmit dengue
- Returning traveler to Hawaii infected with dengue after visiting French Polynesia


Chikungunya fever

http://www.cdc.gov/chikungunya/

Chikungunya in the Caribbean!

http://www.cdc.gov/chikungunya/
Chikungunya fever

- Incubation period 2-4 days (1-14)
- Clinical manifestations
  - Fever
  - Polyarthralgias 2-4 days later: Hands/ankles
  - Rash ~ 50%, maculopapular, hyperpigmentation
- Labs: Lymphopenia, thrombocytopenia, ↑ LFTs
- Severe complications/deaths in elderly

Chikungunya: diagnostic testing

- Serological testing (IgM/IgG) available via CDC and Quest Diagnostics (via Focus Labs)

Case 2

- 63 year-old male with no PMH returned from a 10 day vacation to South Africa with complaints of fever, myalgias, and rash.

History cont.

Physical Exam

- VS: 38.5, 76, 128/70, 16, 99% RA
- Lymph:
  - 1 cm R inguinal LAD, mild tenderness
- Skin:
  - right waistband region, 1.5 x 1 cm ulcer w/ mild surrounding erythema non-painful
  - ~20, 0.2-0.3 cm papulo-vesicular lesions on trunk, flank, back, forehead, extremities
Labs and Microbiology

**Hematology**
- \ / 2.8 \ ---214 / 47 \ Diff
  - Poly - 31%
  - Lymph - 51%
  - Mono - 15%
  - Eos - 2%
  - Baso - 1%

**Chemistry**
- Chem 7 - wnl
- LFTS - wnl; UA - wnl

**Micro**
- 7/18 - Bld Cx X 2 – NGTD
- 7/18 – thin/thick - neg

Your DDx?

African Tick Bite Fever

**Clinical Presentation**
- Fever
- Headache
- Muscle aches
- Inoculation eschar, often multiple
- Regional lymph node swelling
- Rash


Jensenius, Lancet ID 2003
African tick-bite fever

“Tache noire”

Treatment

• Doxycycline 100 mg BID x 7 days or until 48h after defervescence
• Symptoms often improve 24-48h after initiation of treatment


Case 3

• 28 year-old male returned 3 weeks ago from a trip to Kenya
• Last week developed fever (up to 103), occasional hives, and occasional cough/wheezing

Physical Exam

• T-101, V55
• HEENT: oropharynx clear
• CHEST: clear
• CV: RRR no M
• ABD: soft, no HSM
• EXT: WWP
• DERM: faint diffuse maculopapular rash

Labs

• 8>40<320
• Eos: 6.0
• AST-55, ALT-63, AP & Bili-wnl
• Cr-0.9
• CXR - clear

Exposures

• Swam in a fresh water lake
  — After swimming in lake he developed an “itchy rash” which resolved in a few days
• No uncooked food/unfiltered water
• Denies exposure to sick contacts
• Sexually active with girlfriend
Fever and Eosinophilia?

- Strongyloides
- Acute schistosomiasis (Katayama fever)
- Visceral larva migrans (toxocariasis)
- Hookworm
- Ascariasis
- Cutaneous larva migrans
- Filariasis
- Trichinosis

Eosinophilia in returning travelers

<table>
<thead>
<tr>
<th></th>
<th>SE Asia</th>
<th>Ind. subcont.</th>
<th>Mid East</th>
<th>Asia other</th>
<th>S. &amp; C. America</th>
<th>Sub-Saharan Africa</th>
<th>Oceania</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of cases</td>
<td>0%</td>
<td>10%</td>
<td>20%</td>
<td>30%</td>
<td>40%</td>
<td>50%</td>
<td>60%</td>
</tr>
</tbody>
</table>

Diagnostics

- Bld cx x 2 – NGTD
- Thick/thin smear – negative
- Schisto IgG - positive

Schistosomiasis

Gryseels B. Lancet '06
Swimmer's itch (12-24 hrs)

Katayama Fever (2-6 wks)

Chronic Infx
- Gut
- Urine
- Liver
- Other (months-yrs)

Diagnosis
- Micro
  - Stool O&P
  - Urine O&P
- Serology
- Histology

Gryseels B. Lancet '06

Treatment
- Praziquantil is the treatment of choice
  - Not active against immature forms
  - Katayama fever, repeat 6-8 weeks later (+/-steroids)

Case 4
- 45 year-old Russian business man presents to urgent care with fever and rash for several days. He also complains of cough, nasal congestion, and itchy eyes
  - He has been in San Francisco for 1 week for a conference. He otherwise has no past medical history

Morbilloform eruption and fever in returning traveler

http://children.webmd.com/
Measles cases in US 2001-2013

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6236a2.htm

Case 5

- 34 y/o M presents with fever
- Returned 2 wks ago from a 3 wk trip to Ghana
- Received hep A, typhoid, yellow fever vaccines
- Drank bottled water, cooked his food paying close attention to preparation
- Used treated bed net, no malaria prophylaxis

Exam

- T-102.3, 110, 123/67, 20, 99% RA
- HEENT: oropharynx clear
- CHEST: clear
- CV: RRR no M
- ABD: soft, no HSM
- EXT: WWP
- DERM: clear

Labs

- WBC: 8
- HCT: 35
- PLT: 90
- AST: 33, ALT: 36, Alk Phos 67, TBili: 1.9
- Cr: 0.9
- CXR - clear

DDx of fever without any localizing symptoms in returned traveler?

Malaria

Freeman DO. NEJM 2008
**Lifecyle of P. falciparum**

- Sporozoites
- Trophozoite
- Merozoites
- Schizont
- Hepatocyte
- RBC

**Malaria prevention**

- Low risk: *Insect avoidance, consider chemoprophylaxis in certain travelers*
  - vulnerable travelers
  - immigrants visiting friends/relatives
  - prolonged travel (> 1 mo)
  - unreliable access to medical care
- Moderate-high risk: *Chemoprophylaxis*

**Malaria chemoprophylaxis**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Areas of use</th>
<th>Directions</th>
<th>Pro/cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atovaquone/proguanil</td>
<td>All</td>
<td>Daily; 1 wk post</td>
<td>Pro: Minimal SEs, Con: $\uparrow$</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>Chloroquine -susceptible</td>
<td>Weekly; 4 wks post</td>
<td>Pro: Weekly, Con: GI upset</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>All</td>
<td>Daily; 4 wks post</td>
<td>Pro: $\downarrow$, Con: Photos; GI</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>Mefloquine -susceptible</td>
<td>Weekly; 4 wks post</td>
<td>Pro: $\downarrow$, ok in preg, kids, Con: Dreams, avoid psych/Seiz.</td>
</tr>
</tbody>
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**Travelers’ diarrhea (TD)**

- #1 travel-related illness: 30-70% of travelers
- Pathogens:
  - Bacteria 80-90%: ETEC, campy, shigella, salmonella
  - Viruses 10%: Norovirus, rotavirus
- Course:
  - Bacterial and viral diarrhea lasts 3-5 days
  - Longer durations suggests other diseases

**Prevention of TD**

- Prevention
  - Avoidance of contaminated food/water
- Prophylaxis
  - Bismuth subsalicylate 2 tabs QID
  - Rifaximin 200 mg PO QD-BID (vs. placebo)
  - TD: 15% vs. 54% in Mexican travelers

Freedman DO. NEJM. 2006.
Self-treatment of TD
- Ciprofloxacin:
  - 500 mg PO BID for 1-3 days
- Azithromycin: SE Asia, children, pregnancy
  - 500 mg PO QD x 3 days or 1000 mg PO x 1
- Rifaximin: not for invasive infections
  - 200 mg PO TID x 3 days
- Loperamide: not for invasive infections
  - Added benefit, use in “emergency”

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Cutaneous larva migrans
- Treatment:
  - Albendazole 400 BID x 3-7d OR
  - Ivermectin 200 mcg/kg QD x 1-2d
- Prevention: wear shoes in risk areas

Freedman DO. NEJM. 2006.
Cutaneous leishmaniasis

Protozoa
*(single-celled eukaryotes)*

- **GI/GU**
  - Entamoeba
  - Giardia
  - Cryptosporidium
  - Trichomonas

- **Blood**
  - Plasmodium
  - Babesia

- **Tissue**
  - Trypanosoma
  - Leishmania
  - Toxoplasma

Returning traveler from Costa Rica

Returning traveler from Portugal

Returning traveler from Israel

Returning traveler from Brazil
Leishmaniasis: Clinical disease

Visceral  Cutaneous  Mucosal

Distribution of species by clinical disease

L major  L aethiopica  L tropica

L infantum

Visceral

Cutaneous

L donovani  L braziliensis  L panamensis

L mexicana  Mucosal

Distribution of species by geography

L panamensis  L braziliensis

New World

L infantum  L aethiopica

Old World

L donovani  L tropica  L major

Where do you get it? Cutaneous

Clinical manifestations

- Incubation period: 1-4 weeks
- Morphology:
  - Small raised bump → ulcer (months)
  - May grow as large as 5 cm
- Not painful in most cases
- Often self-resolves within 6 months

How do you get it?

Sand fly
Mucocutaneous disease

- Caused by only a few species
  - *L. braziliensis*
  - *L. panamensis*
- Weeks to years
- Ulcerations that eventuate in mutilating destruction of the oropharynx


Diagnosis

- Skin biopsy: sterile, full-thickness punch-biopsy specimens at the active border of the lesion
- Aspiration for culture and PCR testing
- Coordinate testing with CDC
  - Frank Steurer (tele: 404-718-4175; email: fsteurer@cdc.gov; fax: 404-718-4195)


Treatment

- Key factors
  1. species
  2. extent of disease
  3. comorbidities
- Options:
  - No treatment
  - Topical: Paromomycin
  - Intralesional injections: Antimony
  - Systemic: Antimony; Ampho B; Miltefosine; Azoles

L. guyanensis- Ambisome

L. panamensis- miltefosine (FDA IND)
L infantum – posaconazole then topical amphotericin (study)

L major – topical paromomycin

Other skin lesions that might “bug” your patients
**Returning traveler after an Amazonian trek**


**Botfly**

**Returning researcher from Ethiopia**

**Tungiasis**

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Freedman DO. NEJM. 2006.

**Chronic diarrhea**

- Protozoal infections
  - Giardia
  - Cryptosporidium
  - Entamoeba histolytica
  - Other: Cyclospora, isospora, etc...
- Other infections
  - C. difficile colitis
- Non-infectious etiologies
Evaluation of chronic diarrhea

- Bacterial culture
- Stool O&P x 3
- Other tests
  - Giardia antigen
  - Stool AFB stain (cryptosporidium, isospora, etc.)
  - Stool Cryptosporidium antigen
  - Stool Entamoeba histolytica antigen

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Freedman DO. NEJM. 2006.

Nondiarrheal gastrointestinal disorders

- Intestinal nematode infection
  - Strongyloides, schistosomiasis, ascaris
- Gastritis/PUD
- Acute hepatitis
  - Hepatitis A, E, B
- Constipation

Evaluation of nondiarrheal gastrointestinal disorders

- Check LFTs
- CBC w/ differential (eos?)
- Stool O&P x 3
- Serology: Strongyloides and schistosoma IgG
- GI referral for other diagnoses

Post-infectious irritable bowel syndrome

- 3-10% of travelers after episode of TD
- Diagnosis of exclusion
- Last months - years

Connor BA. Clin Inf Dis. 2005

Summary

- Fever (with rash) and cutaneous diseases are very common in returning travelers
- A systematic approach to diagnosis includes a detailed travel history and for febrile patients laboratory testing is often indicated