Fever in returning traveler: Survey of select tropical diseases

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Discussion outline

1. Background: illness in travelers
2. Approach to traveler illness
3. 5 Cases of common tropical diseases

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Illness in returning travellers

• Post-travel illness is common
  • 22-64% of returning travelers
• Majority fall into 4 general categories:
  • systemic febrile illness
  • acute diarrhea
  • dermatologic disorder
  • non-diarrheal GI disorder
Relative frequency of diagnostic categories

Among 17,353 patients in GeoSentinal network (CDC, ISTM)
### Systemic febrile illness (n = 3907)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malaria</td>
<td>35%</td>
</tr>
<tr>
<td>Dengue</td>
<td>10</td>
</tr>
<tr>
<td>Mononucleosis</td>
<td>3</td>
</tr>
<tr>
<td>Rickettsial infection</td>
<td>3</td>
</tr>
<tr>
<td>Salmonella typhi or S. paratyphi infection</td>
<td>3</td>
</tr>
<tr>
<td>No specific cause reported</td>
<td>41</td>
</tr>
</tbody>
</table>

### Acute diarrhea (n = 3859)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parasitic diarrhea (e.g. giardiasis, amebiasis)</td>
<td>35%</td>
</tr>
<tr>
<td>Bacterial diarrhea (e.g. SSYCE)</td>
<td>27</td>
</tr>
<tr>
<td>Unspecified and viral diarrhea</td>
<td>40</td>
</tr>
</tbody>
</table>

### Dermatologic disorder (n = 2947)

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insect bite</td>
<td>19%</td>
</tr>
<tr>
<td>Cutaneous larva migrans</td>
<td>13</td>
</tr>
<tr>
<td>Allergic rash or reaction</td>
<td>11</td>
</tr>
<tr>
<td>Skin abscess</td>
<td>10</td>
</tr>
<tr>
<td>Mycosis</td>
<td>6</td>
</tr>
<tr>
<td>Animal bite</td>
<td>5</td>
</tr>
<tr>
<td>Leishmaniasis</td>
<td>4</td>
</tr>
<tr>
<td>Myiasis</td>
<td>4</td>
</tr>
<tr>
<td>Mite infestation (e.g. scabies)</td>
<td>2</td>
</tr>
</tbody>
</table>

### Non-diarrheal GI disorder (n = 1421)

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intestinal nematodes (e.g. strongyloides, ascaris)</td>
<td>24%</td>
</tr>
<tr>
<td>Gastritis or peptic ulcer disease</td>
<td>13</td>
</tr>
<tr>
<td>Acute hepatitis</td>
<td>12</td>
</tr>
</tbody>
</table>

Travel history

- Countries visited -- urban or rural
- Duration of stay in each place
- Accommodations
- Vaccines and chemoprophylaxis
- Sex or other intimate contact
- Animal and arthropod exposures
- Needle and blood exposures
- Food, water, and soil exposures
## Incubation periods

<table>
<thead>
<tr>
<th>Short (&lt;10 days)</th>
<th>Intermediate (10-12 days)</th>
<th>Long (&gt;21 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malaria</td>
<td>Malaria</td>
<td>Malaria</td>
</tr>
<tr>
<td>Influenza</td>
<td>Viral hemorrhagic fevers</td>
<td>Hepatitis A, B, C, E</td>
</tr>
<tr>
<td>Arboviral infections including</td>
<td>Typhoid fever</td>
<td>Schistosomiasis (Katayama fever)</td>
</tr>
<tr>
<td>dengue, yellow fever</td>
<td>Scrub typhus</td>
<td>Leishmaniasis</td>
</tr>
<tr>
<td>Plague</td>
<td>Q fever</td>
<td>Amoebic liver abscess</td>
</tr>
<tr>
<td>Enteric bacterial infections including</td>
<td>Relapsing fever (Borrelia spp)</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>including paratyphoid fever</td>
<td>African trypanosomiasian</td>
<td>Filarialast</td>
</tr>
<tr>
<td>African tick bite fever</td>
<td>Brucellosis</td>
<td>HIV</td>
</tr>
<tr>
<td>Spotted fever group (including</td>
<td>Leptospirosis</td>
<td></td>
</tr>
<tr>
<td>Rocky Mountain spotted fever)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: Leggat P. Assessment of febrile illness in the returning traveller. Australian Family Physician. 2007:36(5).
Laboratory tests

- Common initial labs:
  - CBC with differential
  - Thick/thin blood malaria films
  - LFTs
  - Cultures of blood and stool
  - UA and urine culture

- Other tests based on history and initial findings:
  - E.g. serological tests, string test, splenic bx, etc.
Cases:
common tropical diseases in returning travellers
Clinical case

• 18yo M student returns from 1-month trip to SE Asia 4 days ago

• P/w:
  • high-grade fever
  • headache / pain behind eyes
  • bone and muscle aches
  • blanching rash

Dengue

• Most prevalent mosquito-borne viral disease
• Ranges from mild febrile illness to life-threatening shock
• >50 million infections each year
• >2.5 billion at risk in ~100 countries

Dengue transmission

- Transmitted by female *Aedes* mosquito
- Dengue viruses 1-4
- Infection with one serotype doesn’t protect against others
- Sequential infections risk dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS)

Classic dengue presentation

- Incubation period 3-14 days
- Acute febrile illness
- Retro-orbital pain
- Marked muscle and bone pain ("break-bone fever")
- Rash...
DHF and DSS

• Dengue hemorrhagic fever:
  1. fever 2-7 days
  2. increased vascular permeability
  3. thrombocytopenia (<100k)
  4. hemorrhagic tendency

• Dengue shock syndrome:
  • above, plus shock

[ Image of dengue-related hemorrhage on arm. Available at: http://www.niaid.nih.gov/SiteCollectionImages/topics/denguefever/michaelRossmannStory.JPG ]
Dengue diagnosis

- Mostly a clinical diagnosis
- Lab: elevated HCT, low platelet, elevated LFTs
- In resource-rich settings....
  - serology testing
  - virus detection (culture, RT-PCR)
Dengue treatment

• Classic dengue fever:
  • supportive care (fluids, antipyretics, etc.)

• DHF/DSS:
  • plus, prn PRBCs, platelets, IVFs
Dengue prevention

- Reduce mosquito exposure
- Day-biter, so long clothing and DEET vs bednets
- Tetravelent vaccines in development
- Public health control of mosquitoes and mosquito-breeding sites
Clinical case

• 22yo M U.S. soldier returns from Afghanistan

• P/w:
  • several-month h/o intermittent low-grade fever
  • growing, non-painful ulceration on left hand
  • not responding to any topical treatment
Leishmaniasis

• Parasitic disease spread by bite of female sandfly

• Two forms:
  • Cutaneous leishmaniasis
  • Visceral leishmaniasis (aka, Kalazar)

• Leish & HIV worsen one another
Leishmaniasis life cycle

Cutaneous leish. presentation

- Several cutaneous forms
- Ranging from lesion at site of bite to destruction of mucosal areas
- Lesions develop over weeks-years
- Recurrences possible
**Visceral leish. presentation**

- Fever (for weeks)
- Vomiting and diarrhea
- Cough
- Fatigue
- HSM
- Anemia, thrombocytopenia

Leishmaniasis diagnosis

- Identify amastigotes within affected tissue
- Biopsy of skin or spleen (or marrow, lymph node)
- Montenegro test
- Serology

Leishmaniasis treatment

- First line:
  - Sodium stibogluconate (SbV) OR meglumine antimonate x3-4 weeks IV/IM
- Others:
  - Amphotericin B, pentamidine, miltefosine

Rx of cutaneous leish reduces risk of mucosal leish
Leishmaniasis prevention

• No vaccine available :(

• Limit exposure
  • avoid dusk/dawn biting, long sleeves, window screens, fine-mesh/insecticide-treated bednets

• Insecticide spraying of sandflies (particularly in epidemics)

• Control animal reservoirs
Clinical case

- 17yo F returns after a 1-month trip to Malawi with schoolmates. 6 weeks later...

- P/w:
  - mild fever with flu-like symptoms
  - generalized urticarial rash
  - Recalls h/o resolved rash after swimming
  - Labs show eosinophilia

Schistosomiasis

• Infection by 3 related parasitic blood flukes, often chronic
  • S. hematobium (bladder)
  • S. mansoni (GI, liver)
  • S. japonicum (GI, liver)

• Second most socioeconomically devastating parasitic disease after malaria
Schistosomiasis distribution

• >200 million currently infected (1 in 30)
• >200,000 deaths annually

Schistosomiasis life cycle

Schistosomiasis presentation

• Acute:
  • Swimmer’s itch / rash
  • Katayama fever (fever, urticaria, eosinophilia, cough, HSM)

• Chronic:
  • terminal hematuria
  • bloody diarrhea
Schistosomiasis complications

- Ectopic eggs and worms:
  - Papillomas in GU system
  - Calcification of bladder
  - Cor pulmonale
  - Liver fibrosis
- Neuroschistosomiasis

Schistosomiasis
diagnosis

• Adult worms inaccessible; look for eggs
  • mid-day urine
  • concentrated fecal smear
• Occasionally useful:
  • serology, rectal bx, radiological changes, 
    eosinophilia
Schistosomiasis treatment

• Praziquantel
• 40-60mg/kg x 1-3 doses, depending on spp.
• Repeat treatment in 3 months to kill previously maturing worms
• +/- steroids to reduce immune response
Schistosomiasis prevention

- Limit exposure to endemic fresh water
- Chlorinate or filter water of cercariae
- Eliminate snail habitat
- Mass treatments of school children where prevalence >40%
  - may treat only those w/dipstick hematuria
Clinical case

• 19yo M presents after living with family in East Africa for several years

• P/w:
  • Several-year h/o episodes (lasting several hours) of migrating, pruritic, raised, linear rashes
  • Lesions have been peri-anal, trunk, etc.

Strongyloidiasis

- Small bowel infection with the barely-visible roundworm, *Strongyloides stercoralis*
- Individuals become infected through contact with contaminated soil

Strongyloidiasis

life cycle

Strongyloidiasis presentation

- Acute s/sx (although usually asymptomatic):
  - itchy eruption where larvae entered
  - cough, wheeze, abdominal pain, diarrhea
- Chronic s/sx:
  - larva currens, GI sx
- Hyperinfection syndrome in immunosuppressed
Strongyloidiasis diagnosis

- Clinical diagnosis
  - eosinophilia, diarrhea, larva currens
- Stool microscopy
- Duodenal string test
- Serology
Strongyloidiasis treatment

- Options:
  - Ivermectin (most effective)
  - Albendazole
  - Thiabendazole (least effective)
- Second course after 2 weeks for chronic/severe infections
Strongyloidiasis prevention

• Footwear

• Screen at-risk individuals before giving steroids or immunosuppressive therapy

• Also consider screening for amebiasis and TB
Clinical case

• 12yo F returns from recent 1-month trip to west Africa after accompanying parents on a medical service trip
• P/w:
  • 1-week persistent high-grade fevers
  • abdominal pain, diarrhea
  • PE: febrile, unwell, abdominal distention and tenderness
  • New-onset rash...
Typhoid

- Life-threatening infection caused by bacteria *Salmonella typhi* and *S. paratyphi*
- Fecal-oral transmission
- 21.5 million/yr
- 400 cases in U.S., 75% acquired internationally

Typhoid life cycle

- Asymptomatic carriers most important reservoirs
- Ingestion of contaminated water/food
- Bacteria attach and penetrate GI
- Spread through body via macrophages

[ Image of “Typhoid Mary,” Available at: http://history1900s.about.com/od/1900s/a/typhoidmary.htm ]
Typhoid presentation

• Fever
• Quite unwell, malaise, abdominal pain, diarrhea
• Rose spots
• Complications:
  • intestinal perforation/hemorrhage
  • shock, organ failures

Typhoid diagnosis

• Blood culture (best)
• Other:
  • string capsule
  • aspirate of rose spots, CSF, abscess, marrow
• Widal test (low sensitivity/specificity)
Typhoid treatment

- Chloramphenicol (or amox, cotrimoxazole) was first line
- Fluoroquinolones (cipro), CTX, azithro now used due to increasing resistance
- Steroids if severe sx (delirium, coma, shock)
- Surgical resection (not just suturing) of perforations
Typhoid prevention

• Treatment of chronic carriers
  • “Typhoid Mary”

• Carriers have nidus in gallbadder (fecal carriers) or urinary tract (urinary carriers)

• Two vaccines:
  • Killed IM vaccine (booster after 2yrs)
  • Live oral Ty21a (3-4 doses over 5 days, booster after 5yrs)
Conclusion (1)

- Illness is relatively common amongst travellers
- Diagnosis assisted by history, incubation period, exam, simple labs
- Today, we discussed....
Conclusion (2)

Dengue

virus via Aedes, fever/pain/rash, DHF/DSS, clinical dx, supportive care

Leishmaniasis

sandfly, cutaneous/visceral forms, dx find amastigotes, rx sodium stibogluconate

Schistosomiasis

blood fluke, chronic tissue disruption, look for eggs in urine/stool, rx praziquantel

Strongyloidiasis

soil worm infects GI, usually no sx, larva currens, hyperinfection, rx ivermectin

Typhoid

fecal-oral, fever/unwell/GI/rosepots, dx culture/string/Widal, rx cipro +/- steroids