Fever in the Returning Traveler

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Learning objectives

1. Evaluate the returned pediatric traveler with a non-localizing fever;
2. Identify the key history and exam components in evaluating a returned traveler with a fever.
First patient Monday morning...

- Toddler febrile to 39° x 2 days, nausea, loose stools
- Fully immunized, healthy
- No fever now
- Well-appearing with non-focal physical exam

Sick, not sick, possibly sick?
Disposition of the well febrile child

- Viral illness
- No further evaluation needed
- Anticipatory guidance
- “Oh, we returned from Lahore 2 weeks ago, after visiting our family for 10 days. He was fine until this past weekend, when these symptoms developed.”
Every traveler should be presumed to have malaria, right?

How do I treat malaria?

Does he need to be hospitalized?

Could this be typhoid? Do you treat with fluoroquinolones? At what age can you give this to a child?

And what about rickettsial infections? How are they diagnosed? Do I give doxycycline empirically?
Fever acquired in US

- UTI
- Pneumonia
- Viral

Fever acquired during travel*

- Dengue
- Enteric
- Malaria
- Viral

*1849 children/6978 travelers with ‘fever’ reported to GeoSentinel.
It’s a small world

• Who is traveling?
  – Over 900 million international trips each year†
  – 2012: 66.6 million international arrivals in US‡

• Why are we traveling? *

† WHO
‡US Travel Association
* GeoSentinel Surveillance Network 2007
Visiting friends & relatives

- 27% of international tourism in 2011
- VFR travelers have higher risk of malaria & typhoid fever
- Younger, longer trips, remote destinations
- Risk perception
- Fewer financial resources for prophylaxis
- Less likely to access pre-travel advice
## Approach to fever in a traveler

| Geography | • Where did the family travel?  
|          | • Exposures during travel |
| Timing   | • Time to fever onset  
|          | • Fever course |
| Signs and Symptoms | • Clinical and exam findings |
| Classic Features | • Know the classic associations |
Where did they travel?

Geography

No. cases per 1000 diagnoses
Case 1

- 9 year old healthy male
- returning from 6wk trip to Afghanistan 10 d ago
- 10 days of nausea, vomiting and diarrhea
- 7 days of fever
- VS: T 39.1 HR 108 RR 21 BP 119/88
- Exam:
  - Mild scleral icterus
  - mild TTP over RUQ >> LUQ with hepatosplenomegaly and hyperactive bowel sounds
  - nontender scabbed rash over b/l LE c/w bug bites
No typhoid vaccination
+ malaria prophylaxis
Ate at all you can eat buffet week prior to leaving Afghanistan
# Time to fever onset

## Table 2

| Incubation periods for common and severe infections acquired during travel |
| --- | --- | --- |
| **Short (<10 d)** | **Medium (11–21 d)** | **Long (>30 d)** |
| Typhoid | Malaria | Reactivation malaria |
| **Denque** | Typhoid | Tuberculosis |
| Rickettsial | Hepatitis A | Leishmaniasis |
| Meningitis/encephalitis | Schistosomiasis | Filariasis |
| Chikungunya | Amebic liver abscess | Schistosomiasis |
| Salmonellosis | Leptospirosis | Rabies |
| Shigellosis | Q-fever | African trypanosomiasis |
| VHF | African trypanosomiasis | Enteric protozoal |
| Influenza | Brucellosis | Enteric helminthic |
| Legionella | VHF | |
| Mononucleosis | Rickettsial | |
| | HIV Seroconversion | |

*Abbreviations: HIV, human immunodeficiency virus; VHF, viral hemorrhagic fever.*
Typhoid

- *Salmonella typhi and paratyphi*
- Gram negative rods
- “Enteric Fever”
Initial management

- Complete blood count
- Blood and stool cultures
- Empiric oral antibiotics: Cefixime, Cipro, Azithro
- Discuss resistance patterns of typhoid with CNMC outpatient Infectious Disease on call at (202)476-5000.
- Consult CDC Yellow Book: refer to ED for malaria screen if indicated
Resistance patterns for Typhoid

- Endemic disease
- Multidrug-resistant strains reported
- Nalidixic acid–resistant strains reported
# Typhoid Fever

## Geography
- South Central Asia

## Timing
- 5-21 days
- Gradual increase in fever

## Signs and Symptoms
- Abdominal pain, fever, chills, HSM, n/v
- Mimics dengue, malaria, viral illness
- Diarrhea > constipation (in children)

## Classic Features
- Rose spots (5-30%)
- Relative bradycardia
Rose Spots

- Specific to typhoid
- “Blanching erythematous maculopapular lesions”
- 2-4 mm diameter
- Reported in 5-30% cases
- Usually on anterior trunk
- Easily missed on dark skinned patients
- Early in course – Week 1-2
Case 2

- 3 yo female returned from travel to Nigeria
- visited relatives
- returned 5 days ago
- 5 days of fever, rigors, and vomiting.
- Mom reports she is “lethargic”
- VS: T 38.8 HR 124 BP 100/45 RR 36
- normal exam
- No malaria prophylaxis
- No travel vaccines
- Visiting family
- There for 2-3 weeks
### Time to fever onset

#### Table 2

**Incubation periods for common and severe infections acquired during travel**

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<thead>
<tr>
<th>Short (&lt;10 d)</th>
<th>Medium (11–21 d)</th>
<th>Long (&gt;30 d)</th>
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<td>Reactivation malaria</td>
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<td>HIV Seroconversion</td>
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*Abbreviations:* HIV, human immunodeficiency virus; VHF, viral hemorrhagic fever.
# Malaria

| Geography       | Sub-Saharan Africa  
|-----------------|---------------------
|                 | SE Asia, S Asia (Indian subcontinent), Central/South America, parts of Caribbean |
| Timing          | $P.\text{falciparum}$ is most dangerous and the most rapid onset of all types (7-30 days)  
|                 | $P.\text{ovale}, P.\text{vivax}, P.\text{malariae}$: subacute (> 30d) |
| Signs and Symptoms | Persistent fever, chills, headache, malaise, diarrhea, HSM, jaundice  
|                 | Mimics: typhoid, viral hepatitis, dengue |
| Classic Features | Acute isolated fever  
|                 | Patterned persistent fever (30%) |
Initial management

**Severe Illness**
- Refer to ED
- Notify CNMC Outpt ID Re: patient
- May need PICU for IV quinidine

**Positive Smear + Mild Illness**
- ED will initiate therapy
- Hgb, LFTs, UA (hemoglobinuria)
- ID may consider outpatient management

**Negative Smear**
- ED will discuss with ID on call
- Observation/admission per ID
Malaria

• Most common cause of serious febrile illness and death in returned traveler
• Thin smear - presence of parasites, count, speciation
• Thick smear - more sensitive (can take hours)
• Positive smear →
  – Parasitemia count as a percentage (confirmed by our lab or ID)
  – Lab will autoconfirm with Binax test

\[ P. falciparum \]
Malaria Rapid Diagnostic Test (RDT)

- *P. falciparum*
  Sensitivity: 99.7%
  Specificity: 94.2%*

- *P. vivax*
  Sensitivity: 93.5%
  Specificity: 99.8%

*for parasitemia levels >5,000 parasites/µl
Severe Disease

• If...
  – Parasitemia >=5%
  – Cerebral malaria (sz, AMS, confusion, coma, increased ICP)
  – Hemoglobinuria, renal failure (“blackwater fever”), acute tubular necrosis
  – Respiratory distress, coagulopathy, shock, acidosis, or hypoglycemia

• Tx: IV quinidine (consider exchange transfusion)
  – Serial ECGs to monitor QRS interval
  – Monitor for hypoglycemia
  – PICU admit
“Malaria Belt”

Place of residence of pediatric malaria cases treated at Children’s National Medical Center 1999-2006 (n = 93)

J of Travel Med. 2011. 18(3):153-160
# Labs

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Typhoid</th>
<th>Malaria</th>
<th>Dengue</th>
<th>Viral illness</th>
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<tbody>
<tr>
<td>Leukopenia</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
<td>(EBV leukocytosis) lymphocytic predominance</td>
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<tr>
<td>Anemia</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
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<tr>
<td>Low platelets</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
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<tr>
<td>Transaminitis</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
</tr>
<tr>
<td>Hyponatremia</td>
<td></td>
<td>+ (severe)</td>
<td>+ (severe)</td>
<td></td>
</tr>
<tr>
<td>Coagulopathy</td>
<td>+/-</td>
<td>+ (severe)</td>
<td>+ (severe)</td>
<td></td>
</tr>
<tr>
<td><strong>Diagnostic TEST</strong></td>
<td><strong>Blood cultures</strong></td>
<td><strong>Thick and Thin Smear</strong></td>
<td><strong>Acute and Convalescent Titers</strong></td>
<td><strong>Titers</strong></td>
</tr>
</tbody>
</table>
Returned Traveler with Fever

Sick
- Send to ED for evaluation. Call (202) 476-5433 for referral to ED

Not Sick
- Consult CDC Yellow Book
- Consider ED eval for malaria if from endemic region, call (202) 476-5433
- Discuss with Outpatient ID on call (202) 476-5000
Summary

• “History is 90% of diagnosis”
• Malaria & typhoid are important causes of fever
• Viruses are common everywhere
• Broader differential in sicker patients
• Know your resources – CDC Yellow Book, Infectious Disease, Dermatology
Important Resources

• CDC Yellow Book

• CDC Travelers’ Health


References


