FEVER IN THE RETURNING TRAVELER

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Objectives

• To discuss the approach to fever in the returning traveler
• To understand the resources available when approaching a patient that will be traveling or who has traveled internationally
• To review a few interesting case presentations of fever in individuals returning from various parts of the world
• To gain an understanding of the importance of pre-travel counseling
FEVER IN THE RETURNING TRAVELER

NOT a comprehensive review of infections!
Who are we talking about?

- People who have traveled internationally
  - Adventure/leisure
  - Visiting friends/relatives (VFR)
  - Medical work
- People who are moving to or visiting the U.S. from another country
Why is this topic important? Health of travelers

- Millions of US travelers make international trips every year
- 20-70% of travelers from industrialized countries to developing countries report some illness associated with travel
  - 8% become ill enough to seek health care during or after travel
  - Higher incidence of illness in individuals that visit family/friends
- Should be considered a medical emergency
  - Most are not fatal, but some are emergencies: malaria, dengue (and other hemorrhagic fevers)
- Understanding the signs, symptoms, and epidemiology of these diseases (or how to find that information) can aid in timely diagnosis
Why is this topic important? Public health

- Travel affects the presence or introduction of vector-borne diseases
  - E.g., locally acquired dengue in Florida, measles at Disneyland
- Detection can alert public health and medical communities to disease outbreaks before they spread to the general population
Fever in the returning traveler

- GeoSentinel Network report from 1997-2011
  - Large, worldwide, multicenter database (6 continents)
  - Records information about international travelers with new, travel-related illness
    - Inpatient and outpatient
  - Most common diagnoses: malaria, diarrheal disease, and systemic disease (fever)

http://www.express.co.uk/life-style/health/469986/How-to-prevent-scarlet-fever
GeoSentinel Surveillance Sites

FIGURE 1. Locations of GeoSentinel surveillance sites* and network members†

* N = 54.
† N = 235.
Excludes people immigrating to the US

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No.</th>
<th>(%)</th>
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<tbody>
<tr>
<td>Born/Residence in US</td>
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<tr>
<td>Born in the United States</td>
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<tr>
<td>Residence in the United States</td>
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<td><strong>Reason for travel</strong></td>
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<td>Tourism</td>
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<td>Missionary/volunteer/researcher/aid worker</td>
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<td>Visiting friends and relatives</td>
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<td>Business</td>
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<td>Student</td>
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<td>Military</td>
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<td>Medical tourism</td>
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<tr>
<td>Missing</td>
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<td>(&lt;1)</td>
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<td>Expatriate</td>
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<td><strong>Pretravel encounter</strong></td>
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<td>Yes</td>
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<td>No</td>
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<tr>
<td>Unknown</td>
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<tr>
<td>Missing</td>
<td>560</td>
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</tr>
<tr>
<td>Syndrome/System grouping</td>
<td>No. (%)</td>
<td>Syndrome/System grouping</td>
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<td>----------------------------------------------</td>
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<td>Acute diarrhea</td>
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<td>Diarrhea, acute unspecified</td>
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<td>Diarrhea, acute bacterial</td>
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<td>Giardiasis</td>
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<td>Amebas, other (Escherichia hartmani, E. nana,</td>
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<td>E. coli, E. polecki)</td>
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<tr>
<td>Campylobacter</td>
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<td>Gastrointestinal other</td>
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<td>Strongyloides, simple intestinal</td>
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<td>Blastocystis Sp.</td>
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<td>Pain, abdominal</td>
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<td>Esophagitis</td>
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<td>Gastritis, Helicobacter pylori positive</td>
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<td>Plasmodium falciparum malaria</td>
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<td>Viral syndrome (no rash)</td>
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<td>Dengue, uncomplicated</td>
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<td>Febrile illness unspecified (&lt;3 weeks)</td>
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<tr>
<td>Epstein-Barr virus</td>
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<tr>
<td>Dermatologic</td>
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</tr>
<tr>
<td>Insect bite/sting</td>
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<td>(15)</td>
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<tr>
<td>Nonfebrile rash of unknown etiology</td>
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<td>(10)</td>
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<tr>
<td>Fungal infection (superficial/cutaneous mycosis)</td>
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<td>(7)</td>
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<tr>
<td>Cutaneous leishmaniasis</td>
<td>100</td>
<td>(6)</td>
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<tr>
<td>Skin and soft tissue infection</td>
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<td>(6)</td>
</tr>
<tr>
<td>Chronic diarrhea</td>
<td>1,100</td>
<td>(8)</td>
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<tr>
<td>Irritable bowel syndrome, post-infectious</td>
<td>605</td>
<td>(55)</td>
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<tr>
<td>Chronic unknown diarrhea</td>
<td>351</td>
<td>(32)</td>
</tr>
<tr>
<td>Irritable bowel syndrome</td>
<td>44</td>
<td>(4)</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>31</td>
<td>(3)</td>
</tr>
<tr>
<td>Postinfectious lactose intolerance</td>
<td>15</td>
<td>(1)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Abbreviations: STDs = sexually transmitted diseases; ob/gyn = obstetric/gynecologic.</th>
</tr>
</thead>
<tbody>
<tr>
<td>* N = 13,059.</td>
</tr>
<tr>
<td>† The five most common diagnoses are provided for the seven most common syndrome/system groupings.</td>
</tr>
</tbody>
</table>
Start your evaluation with the basics

- Careful history and physical is key!
- Remember: common things are common, but don’t want to miss a serious illness (e.g., *falciparum* malaria)
- Ask your questions multiple ways
  - “Pets” may not mean snakes, frogs, or birds to some people
  - Get detailed if an answer seems like it may lead somewhere or is insufficient
    - They may have been drinking *bottled water*, but were using *ice* made from tap water
What do you need to ask?

- Duration and chronology of ALL symptoms
- Countries/Areas visited and activities
  - Urban vs. rural
  - Camping, hiking, outdoors
  - Swimming or rafting
  - Hotel/resort or home
- Length of stay
- Pre-travel vaccines and medications on trip

- Exposures
  - Food – meats, fish, cooked vs raw
  - Dairy – pasteurized vs. raw
  - Water – drinking, food washing, sources of water
  - Animals – bites, petting zoos, other contact
  - Medical facilities – did they visit or work in one? What kind of facility?
  - Sick contacts (others on trip, people they visited)
  - Insect bites
  - Sexual contacts
# Fever chronicity

<table>
<thead>
<tr>
<th>Acute</th>
<th>Chronic</th>
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</thead>
<tbody>
<tr>
<td>Viral syndrome</td>
<td>TB</td>
</tr>
<tr>
<td>Sepsis</td>
<td>HIV</td>
</tr>
<tr>
<td>Typhoid</td>
<td>Malaria</td>
</tr>
<tr>
<td>Leptospirosis</td>
<td>Brucella</td>
</tr>
<tr>
<td>Malaria</td>
<td>Helminthic/parasitic infection</td>
</tr>
<tr>
<td>Rickettsial disease</td>
<td>Rheumatologic</td>
</tr>
<tr>
<td></td>
<td>Autoinflammatory</td>
</tr>
<tr>
<td></td>
<td>Oncologic</td>
</tr>
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</table>
Consider incubation periods

<table>
<thead>
<tr>
<th>Incubation period</th>
<th>Possible Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10 days</td>
<td>Arbo viruses (dengue and yellow fevers), viral hemorrhagic fevers, enteric bacterial and viral infections, <em>Rickettsiae</em>, plague, influenza, anthrax, food poisoning, pneumonia</td>
</tr>
<tr>
<td>11-21 days</td>
<td>Falciparum malaria, leptospirosis, typhoid, rickettsiosis, African trypanosomiasis, brucellosis, enteric protozoan infections, hepatitis, <em>Strongyloides</em>, cutaneous myiasis, scabies, tungiasis, Lyme disease</td>
</tr>
<tr>
<td>&gt; 30 days</td>
<td>Malaria, tuberculosis, hepatitis, enteric protozoal and helminthic infections, HIV, leishmaniasis, schistosomiasis</td>
</tr>
</tbody>
</table>

What do you look for?

- Physical exam should help guide your differential
  - No physical exam findings – more systemic illness; rely more on history and exposures
  - Hepatomegaly – hepatitis, mono, liver helminth, malaria, leptospirosis
  - Splenomegaly – malaria, Brucella, dengue, typhoid
  - Abdominal tenderness – traveler’s diarrhea, parasite/helminth
  - Rash – viral exanthem, parasite (e.g., cutaneous larva migrans), meningococcal disease, rickettsial disease
What do you order?

• **Consider your differential first**
  • Always think of malaria in a region where exposure is possible!
    • Thick and thin smears x3, separate by 12h
  • Consider Quantiferon-GOLD (blood) or placing a PPD for evaluation of tuberculosis
  • CBC
  • +/- liver function tests
  • +/- stool culture or other evaluation
What do you order?

• Blood cultures
  • Helpful to let the lab know what you’re looking for if you have an idea

• Specific PCR and/or Antibody titers
  • PCR: looks for the DNA or RNA of a target organism
  • Antibody tests: tests for proteins made by the immune system specific to the organism of interest
  • Have to know what you are testing
  • Can often be expensive, take time for results to come back, or difficult to find a lab to do the test
Complete blood count (CBC) generalizations

• White blood cells
  • Neutrophils
    • Usually high with bacterial illness
    • Can be low with malaria, HIV
  • Lymphocytes
    • May be high in viral illness (e.g., mononucleosis), rickettsial disease
  • Eosinophils
    • High in parasite/helminth infections
• Hemoglobin/hematocrit
  • Anemia may indicate hemolysis (can go with malaria) or chronic disease
• Platelets
  • May be low in viral or rickettsial illness
  • May be high in more chronic inflammatory processes

Antimicrobials

• Need to know the basics about drug resistance in various areas
  • E.g., Ciprofloxacin resistance among many GI pathogens in Asia
  • Malaria: Chloroquine resistance in most places other than the Carribbean, some parts of Central America, and a few places in the Middle East
• This information can be obtained from the CDC, other journal publications, or by talking to travel clinic
When in doubt...

- Consult local travel clinic or Infectious Diseases consultant
PUTTING THESE EVALUATION TACTICS TO USE
• **Primary goal: Illustrate the importance of history and physical exam**
  - A thorough history, including exposures, can help guide your differential
  - Physical exam findings can also help guide the differential
  - These, in conjunction with knowledge or literature about regions traveled, help narrow what to consider for your diagnosis and workup
    - Limits cost
    - Can limit time to treatment, if required

• **Secondary goal**
  - Understand the importance of pre-travel counseling and how this can help avoid illnesses seen in individuals returning from travel
SOUTH AFRICA

45yo woman with 3 days fever, chills, headache, myalgias. Just returned from 2 week safari in South Africa

Althaus F, et. al. *IJID*. 2010;14S:e274-6
Mackowiak PA. *CID*. 2004;39:700-1
History of present illness

• 9 days PTA (>1wk into trip), noticed large bug bites on legs and face while on safari in South Africa
• 4d PTA, returned home from South Africa
• 3d PTA, fever, chills, headache, myalgias started
• 1d PTA, noted rash – initially just a few non-itchy spots, then increased in number and became itchy
• All other review of systems negative
What else do we need to know?

- **PMH:** Otherwise healthy woman
- **Travel:** Trip was 2 weeks long and included safari in the park
- **Insects:** Multiple insect bites, thinks mosquitoes mostly, but not sure
- **Animals:** No contact with wild game
- **Sick contacts:** Others on the trip have similar lesions and fever
- **Food/water:** Drank bottled water and ate fully cooked meats
- **Medications:** Taking malaria prophylaxis during trip (Malarone)
- **Immunizations:** Has had standard immunizations, but has not had any additional vaccines prior to travel
Physical Exam

- **Vitals**: Febrile (39°C), but otherwise normal
- **General**: Mildly ill appearing, in no distress
- **HEENT**: Bilateral conjunctival injection. Mucus membranes moist. No discharge from eyes or nose.
- **Neck**: No meningismus. Some muscle tenderness bilaterally.
- **Respiratory/Cardiac/Abdominal**: Normal
- **Skin**:
  - ~30 erythematous papules 1-8mm in size, itchy, on abdomen and limbs. Spares palms and soles.
  - 1-2 lesions with central, darker, purple/black hue as in photos on right (one on leg, one on cheek)
- **Lymph nodes**: No abnormal lymph nodes
- **Neurologic**: Normal

Right: Althaus F, et. al. *IJID.* 2010;14S:e274-6
What is on your differential? What do you want to do?
Differential

- Rickettsial disease
- Plague
- Anthrax
- Chikungunya
- Trypanosomiasis
- Superinfected insect bite
- Other viral exanthem
Evaluation

- CBC:
  - WBC count 4.5 (70%N, 24%L)
  - Hgb/Hct normal, plt 180
- Thick and thin smears: No parasites detected
- Blood culture: Negative
- Extra serum obtained for antibody titers
Further evaluation

- Chikungunya and dengue IgM negative (acute), follow-up: negative IgG and IgM convalescent titers
- Acute and convalescent serologies sent for *Rickettsia africae*
  - Sent because of eschars, constellation of other symptoms, and exposures
  - Acute titers: IgM 1:32, IgG negative
  - Convalescent titers (sent 8 weeks afterwards): IgM 1:64, IgG 1:128
# Tick-borne Rickettsioses affecting international travelers

<table>
<thead>
<tr>
<th>Human disease</th>
<th>Organism</th>
<th>Principal vectors</th>
<th>Geographic distribution</th>
<th>Reported in international travelers</th>
</tr>
</thead>
<tbody>
<tr>
<td>African tick bite fever</td>
<td><em>Rickettsia africae</em></td>
<td><em>Amblyomma</em> ticks</td>
<td>Sub-Saharan Africa, French West Indies</td>
<td>Yes</td>
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<tr>
<td>Mediterranean spotted fever</td>
<td><em>Rickettsia conorii</em></td>
<td><em>Rhipicephalus</em> &amp; <em>Haemaphysalis</em> ticks</td>
<td>Mediterranean littoral to Indian subcontinent, sub-Saharan Africa</td>
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<td>Indian tick typhus</td>
<td>Indian tick typhus <em>rickettsia</em></td>
<td><em>Rhipicephalus</em> ticks</td>
<td>India</td>
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<td>Astrakhan fever</td>
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<td><em>Rhipicephalus</em> ticks</td>
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<td><em>Rhipicephalus</em> ticks</td>
<td>Eastern Mediterranean littoral, SW Europe</td>
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<td>Rocky Mountain spotted fever</td>
<td><em>Rickettsia rickettsi</em></td>
<td><em>Dermacentor</em> &amp; <em>Amblyomma</em> ticks</td>
<td>North and South America</td>
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<td>Queensland tick typhus</td>
<td><em>Rickettsia australis</em></td>
<td><em>Ixodes</em> ticks</td>
<td>Eastern Australia</td>
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<td><em>Rickettsia aeschlimannii</em></td>
<td><em>Hyalomma</em> &amp; <em>Rhipicephalus</em> ticks</td>
<td>Mediterranean area, Morocco, sub-Saharan Africa</td>
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<td>North Asian tick typhus</td>
<td><em>Rickettsia sibirica</em></td>
<td><em>Dermacentor</em> &amp; <em>Haemaphysalis</em> ticks</td>
<td>Former Soviet Asia, China, European Russia</td>
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<td>Flinder’s island spotted fever</td>
<td><em>Rickettsia honei</em></td>
<td>Ticks of several genera</td>
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<td><em>Dermacentor</em> ticks</td>
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<td>Central and northern Europe</td>
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<td><em>Hyalomma</em> ticks</td>
<td>Mongolia, France, sub-Saharan Africa</td>
<td>No</td>
</tr>
</tbody>
</table>

Jensenius M, et al. IJID. 2004. 8;139-146
African Tick Bite Fever (ATBF)

- **Organism:** *Rickettsia africae*
  - Obligate intracellular Gram-negative, rod-shaped bacterium
  - Present in ~30-70% of *Amblyomma* ticks
  - Lipopolysaccharides cross-react with other *Rickettsia* species in diagnostic testing

- **Vector:** *Amblyomma variegatum* and *Amblyomma hebraeum* ticks
  - Hard tick
  - Tall grasses and good amount of rainfall (sub-Saharan Africa)
  - All three developmental stages of the tick can transmit disease
  - Hosts: cattle, sheep, horses, donkeys, pigs, giraffes, buffaloes, antelopes, and warthogs
Distribution

Amblyomma variegatum

Amblyomma hebraeum

http://www.afrivip.org/sites/default/files/Ticks_identification/ixod_ambl.html
Transmission of *Rickettsia africae*

- Incubation period 5-10 days
- This type of tick “attacks” a host, multiple ticks attack single host
  - Responds to increased CO2, humidity, vibration, and change in ambient temperature (from body temperature)
  - Most likely why there are multiple lesions typically found and cases are clustered
  - Typically attack the legs, then crawl to warm, moist areas: axillae, neck, groin, behind knee
Risks and prevention for travelers

- Risk factors include: hunting, staying in a rural area, not using repellent
- Short- and long-term travelers all at risk
- Cause of up to 26% of fevers in travelers returning from Sub-Saharan Africa
- Prevention
  - Insect repellent with DEET (25-50%)
    - Safe for children over 2mo
    - Lasts for several hours, but needs to be reapplied if out longer
  - Permethrin treated clothing and gear

Clinical Presentation of ATBF

- Triad seen in up to 75% of patients:
  - Fever
  - Rash (up to 45% of patients)
    - Typically maculopapular (15-23% of patients) or vesicular (0-21% of patients)
    - Usually mild and often is missed
  - Inoculation eschar ("tache noir")
    - Characteristic, seen slightly more often than the rash (53-100% of patients)
    - Usually multiple
    - Ring of erythema surrounding black eschar
- Myalgias, headache, neck pain
- Lymphadenopathy in region of eschar
  - Not common but more sensitive
- Cases typically present in clusters of people who have been traveling together
Laboratory diagnosis

- **Acute and convalescent serologies**
  - Helps to draw blood to freeze at initial presentation
  - Convalescent serology can be done 2-12 weeks after symptom onset
    - Should run at the same time as acute serology
    - Not helpful with acute diagnosis, but confirms diagnosis later

- **PCR from eschar tissue**
  - Available for research purposes, not diagnostic

- **Culture**
  - Less often used, since the organism is intracellular
  - From eschar tissue
Treatment

- Doxycycline: 100mg BID for at least 3 days after fever subsides and evidence of clinical improvement
  - Treatment typically 5-14 days
- Treat presumptively, since serology may not be positive yet
- Clinical improvement typically starts within 48-72 hours of starting treatment
HAITI

30yo male medic on 2 week medical trip to Haiti returning with 48h fever and now with rash and joint pain
HPI

- May 2014 spent 2 weeks in Haiti working at a hospital in Port au Prince
- 9 days into the trip, developed fever and pain in multiple joints (elbows, wrists, knees, shoulders)
  - Fever lasted 48 hours
- Following resolution of fever, developed diffuse rash on trunk, extremities, and palms of hands
- Returned home with continued rash and severe joint pain
  - Taking acetaminophen with minimal relief
- Presented 1 day after returning home due to symptoms (6 days into illness)
Exposures/PMH

- **PMH:** Otherwise healthy
- **Ill contacts:**
  - No other medical personnel ill
  - Treating patients in a hospital with many types of illnesses, some with fever and joint pain
- **Immunizations:**
  - Typhoid vaccine within the past 2 years
  - Otherwise appropriately vaccinated
- **Food/water:** Drinking bottled water only and eating fully cooked food (mostly rice and beans) prepared at the hospital or at the UN
- **Insects:** Multiple mosquito bites, not using repellent
- **Animals:** No interactions with animals during trip
- **Other activities:** No swimming or fresh water exposures
- **Medications:** Taking malaria prophylaxis (chloroquine)
Physical Exam

- Afebrile, other vital signs normal
- **HEENT**: Mild bilateral conjunctival injection. No discharge from eyes or nose. Mucus membranes moist. No oral lesions.
- **Neck**: Normal range of motion
- **Respiratory/Cardiac**: Normal
- **Abdominal**: Normal
- **Skin**: Diffuse maculopapular rash with 1-3mm lesions on arms, legs, trunk, hands
- **Lymph nodes**: No enlarged lymph nodes
- **Musculoskeletal**: No swelling of joints, but severely limited range of motion due to pain in hands, wrists, elbows, ankles, and knees
- **Neurologic**: Normal
What is on your differential? How would you evaluate?
Differential diagnosis

- Dengue fever
- Chikungunya
- Malaria
- Leptospirosis
- Rickettsial disease
- Other viral exanthem
- Post-infectious arthritis
- Rheumatologic condition

http://www.cdc.gov/chikungunya/hc/clinicalevaluation.html
Evaluation

- CBC: WBC 4, Hgb/Hct normal, Plt 150
- Thick and thin smears negative x3
- Acute titer for dengue: Negative
- Acute titer for chikungunya: Positive IgM
Chikungunya virus

- First described in 1950s in Tanganyika
  - Swahili that translates: “to become contorted”
- Initially in Africa and Asia, now spread to the Americas and Caribbean
  - First **locally spread** case in the Americas in 2013 (St. Martin)
  - Central and South America 2014

http://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0002921
Countries where chikungunya has been reported as of 10/2015

http://www.cdc.gov/chikungunya/geo/
Chikungunya virus

- **Vector:** *Aedes albopictus* and *Aedes aegypti*
- **Transmission:**
  - *A. aegypti* typically bite during the day
  - Mosquitoes typically near dwellings with water basins or in areas with standing water
  - Highest presence during rainy seasons
  - Reports of *in utero* transmission if mom viremic around the time of delivery
- **Reservoir:** Primates (human and non-human)
- **Virus:**
  - RNA virus in *Togaviridae* family
  - Incubation period of 3-7 days (range 1-12)
Clinical Presentation

- Some asymptomatic (up to 20%)
- Severe polyarthralgia
  - Symmetric, usually elbows, wrists, hands, knees, ankles, feet
  - Lasts days to weeks to months
  - Sometimes arthritis
- Myalgias
- High fever
  - Lasts 2-4 days, up to 1 week
- Maculopapular rash ~50%
  - Usually after the fever resolves
  - Does not spare palms or soles
- Other symptoms include:
  - Conjunctivitis
  - Nausea/vomiting
  - Lymphadenopathy
  - Headache
Evaluation

- Acute and convalescent titers for chikungunya
  - Can test separately (acute then convalescent if acute titers were negative)
  - Some commercial labs, CDC, and some state health departments
- RT-PCR for chikungunya
  - Useful in 1st week of illness while viremic
  - Some commercial labs, CDC, and state departments
Differentiating chikungunya vs. dengue?

• Difficult to do
  • Both with arthralgias, fever, and can have rash
  • Both reported in the same regions and have the same vector
• Some people report more debilitating joint pain with chikungunya (subjective)
  • Joint pain can last much longer with chikungunya
• Shorter fever course with chikungunya?
• Ultimately, laboratory diagnosis
  • Serologies for both chikungunya and dengue available
• Treat pain/fever with acetaminophen until dengue can be ruled out
Management

- Rest, hydration
- NSAIDs for joint pain
  - Can use acetaminophen if dengue still on differential
  - If have been afebrile for >48h and no warning signs for dengue, may switch to NSAIDs
- Steroids may help with joint pain
- Protect from mosquito bites, particularly during first week while viremic
Prevention for travelers

• Mosquito netting
• Window and door screens
• Insect repellent
  • At least 20% DEET
• Long sleeves and pants/socks
  • Tuck them in!

http://www.cdc.gov/chikungunya/hc/clinicalevaluation.html
TIME FOR A BREAK!

KEEP CALM AND WEAR INSECT REPELLENT

Protect yourself from mosquito bites that spread West Nile and chikungunya.
CENTRAL AMERICA

16yo healthy male with 3 week history of fever and “knots” in muscles, began during mission trip to Costa Rica
Timeline of symptoms/History of Present Illness

- Mission trip to Costa Rica 6/25-7/12/15
  - 7/7 Emesis x2
  - 7/9 Muscle pain and swelling in legs
  - 7/12 Legs remained swollen, arms started with similar symptoms
- Travel back home on 7/12
  - 7/13 Fever started, night sweats, leg/arm swelling continue
  - 7/16 Fever continued, noticed “knots” in calves, triceps, and thighs
HPI, continued

• 7/20 to PCP:
  • Complete blood count (CBC): WBC 13.5 (N68%, L13%, M3%, E15% - abs 2000)
  • Hemoglobin 13.9, Hematocrit 43.2, Platelets 557
  • Malaria smear normal x1
  • Dengue fever serology negative
• 7/21-7/26: Nighttime fevers to ~101, able to participate in regular activities and afebrile during the day
• 7/29-7/30: New “knots” in abdominal wall and upper chest. Phone consult with Infectious Diseases.
• 7/31: ID evaluation
Review of Systems

- **Constitutional**: + Fevers, night sweats
- **HEENT**: No red eyes, + sore throat 2 days ago
- **CNS**: No headache or vision, gait, or speech changes
- **Respiratory**: No concerns
- **Cardiovascular**: No concerns
- **GI**: No diarrhea or abdominal pain; + vomited x2 at beginning of illness
- **GU**: No concerns
- **MSK**: “knots” in arms, legs, upper chest, and abdomen
- **Skin**: No rashes or lesions
- **Heme/Lymph**: No concerns
PMH/Social History

- Previously healthy, no prior surgery or hospitalizations
- No significant family history
- NKDA
- Immunizations up to date
  - Typhoid vaccine in May 2015
Travel/Exposures

• Estes Park hiking trip 4/2015
• Travel to Florida Keys 6/2015
• Climbed 14er on 6/23/15
• Travel to Costa Rica 6/25-7/12/15
  • Accommodations: Hotel and host family
  • Food: Drank local water and ate local food; host family served fresh cheeses and a pork specialty from the area
  • Activities: Mixing concrete with a local organization; some hiking, + mosquito bites
• Animals: None
• No risk factors for HIV or tuberculosis
• No known sick contacts. Parents unsure whether anyone else from the trip is sick.
Physical examination

- **Vitals**: No fever, normal heart rate, blood pressure, and respiratory rate
- **General**: Pale, well-nourished, in no distress
- **HEENT**: Normal
- **Neck**: Normal
- **Respiratory/Cardiovascular**: Normal
- **Abdomen**: Nondistended. Tenderness to palpation along midline.
- **GU**: Normal
- **Skin**: No rashes or lesions
- **Lymph Nodes**: No enlarged lymph nodes
- **Neuro**: Normal
Physical Examination - Musculoskeletal

- Multiple hard, well-defined masses with tenderness to touch and no redness
  - Neck: 0.5x3cm mass in the muscle of the right neck
  - Abdomen:
    - Right upper quadrant with 1.5cm round mass
    - Left lower quadrant with 1cm x 2cm mass
  - Arms:
    - Left and right triceps with 7cm x 5cm mass
    - Right and left forearms with 1cm x 2cm mass
  - Legs:
    - Left lateral quadriceps with 4cm x 3cm mass
    - Left medial calf with 6cm x 4cm mass
    - Right calf with 5cm x 4cm mass
What is on your differential?
What would you do to evaluate?
Evaluation (7/31/15)

- **CBC:**
  - WBC 12.4 (65%N, 14%L, 3.5%M, **16.4%E – absolute 2030**)
  - Hgb 12, Hct 36, Plt 472
- **CMP:** Normal except AST 77, ALT 53, Albumin 3.1
- **CK:** 435 U/L (high)
- **CRP:** 14.1 mg/dL (high)
- **ESR:** 32 mm/hr (high)
Does this change your differential?
Differential – fever, muscle masses, eosinophilia

- Parasitic infection
  - *Trichinella*
  - *Toxocara*
  - *Taenia solium* (cysticercosis)
Remainder of evaluation 7/31

- MRI Brain: Normal
- Echocardiogram: Normal
- Ultrasound of masses: No cysts noted
- Toxocara, trichinella, and cysticercus Ab sent (send-out)

- Highest likelihood: trichinella – pork exposure, masses in muscles, swelling of arms and legs, and fever
Trichinellosis

- A public health issue:
  - Control efforts for pork
  - Wild game
  - Newer outbreaks in domestic sheep, goats, cattle
Trichinella spp.

Table 2
*Trichinella* species and related genotypes, their natural cycles, main hosts, and distribution areas

<table>
<thead>
<tr>
<th>Trichinella species or genotype</th>
<th>Cycle</th>
<th>Main hosts</th>
<th>Distribution area</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>T. spiralis</em></td>
<td>Domestic and Sylvatic</td>
<td>Swine, carnivores, rats</td>
<td>Cosmopolitan</td>
</tr>
<tr>
<td><em>T. nativa</em></td>
<td>Sylvatic</td>
<td>Carnivores</td>
<td>Arctic and subarctic regions</td>
</tr>
<tr>
<td><em>Trichinella T6</em></td>
<td>Sylvatic</td>
<td>Carnivores</td>
<td>Southern Canada, northern USA</td>
</tr>
<tr>
<td><em>T. britovi</em></td>
<td>Sylvatic</td>
<td>Carnivores</td>
<td>Temperate areas of the Palearctic region</td>
</tr>
<tr>
<td><em>Trichinella T8</em></td>
<td>Sylvatic</td>
<td>Carnivores</td>
<td>South Africa and Namibia</td>
</tr>
<tr>
<td><em>Trichinella T9</em></td>
<td>Sylvatic</td>
<td>Carnivores</td>
<td>Japan</td>
</tr>
<tr>
<td><em>T. murrelli</em></td>
<td>Sylvatic</td>
<td>Carnivores</td>
<td>USA</td>
</tr>
<tr>
<td><em>T. nelsoni</em></td>
<td>Sylvatic</td>
<td>Carnivores</td>
<td>Africa south of the Sahara</td>
</tr>
<tr>
<td><em>T. pseudospiralis</em></td>
<td>Sylvatic</td>
<td>Mammals and birds (carnivores and omnivores)</td>
<td>Cosmopolitan</td>
</tr>
<tr>
<td><em>T. papuae</em></td>
<td>Sylvatic, domestic?</td>
<td>Swine</td>
<td>Papua New Guinea</td>
</tr>
</tbody>
</table>

Clinical presentation: Acute Phase

- Fever, excessive sweating
- Diarrhea, vomiting
- Eyelid and facial edema (17-100%)
  - Varies based on host allergic reaction to the organism
- Myalgias (74-97%)
  - Trunk, upper/lower extremities, neck
- Hemorrhagic lesions (25%)
- CNS (after 2-4 weeks of disease)
  - Headache
  - Transient tinnitus or dizziness
  - Decreased DTRs
- Severe disease or if not treated in early stage
  - Anisocoria, facial nerve paresis, Babinski reflex +
## Laboratory evaluation

### Parallels Clinical Course
- Leukocytosis (>15,000)
  - Appears within 2-5 weeks
- Hypokalemia
- Anti-trichinella antibodies
  - IgE appear first, but rarely detected
  - IgG and IgM appear (week 2)
- Hypoproteinemia, hypoalbuminemia (severe disease)

### Unrelated to Clinical Course
- Eosinophilia (1,000-19,000)
- Increased CPK and AST
  - 2-5 weeks into disease
Clinical presentation: Late stage

- 5-7 weeks after infection (larvae are encapsulated)
- Signs and symptoms disappear
- Laboratory parameters return to normal
Other organ involvement

- **Heart:**
  - Transient parasitemia
  - Do not encapsulate in myocardium
  - Eosinophilic infiltrate may be present

- **Eye:**
  - Conjunctivitis, uveitis, retinitis, or optic neuritis
  - Usually seen during acute stage

- **CNS:**
  - If severe infection, can penetrate CNS tissues
Treatment

- Eliminate intestinal form to prevent muscular invasion
- Available: Albendazole
  - Adults: 400mg/dose BID for 5-14 days, may repeat
  - Children: 10mg/kg/day for 5-14 days, may repeat
- Others (not available): Mebendazole, Thiabendazole
- Steroids: Suppress signs/symptoms of hypersensitivity in acute phase (not required in benign disease)
THE PHILIPPINES

12mo returning from visiting family in the Philippines for 4 weeks, now with fever, URI symptoms, and rash
HPI

- March/April 2014 travel to Philippines to visit family for 4 weeks
- Returned to the US on 4/12
- 4/13: Developed redness of both eyes, cough, and runny nose. Fever started later that night.
- 4/14: Evaluated by PCP due to above symptoms. Diagnosed with viral illness.
- 4/17: Fever continues. Rash noted on face.
  - Described as a lot of pink spots
- 4/18: Returns to PCP with rash all over body and on face, fever, and slight redness of eyes
Exposures/PMH

- **PMH:** No severe or chronic illnesses
- **Immunizations:** Immunized through 6 months, but left for trip before 12mo well-child check
- **Food/water:**
  - Drinks pasteurized milk
  - Fully cooked food
- **Medications:** None
- **Animals:** No animal exposures
- **Insects:** Several mosquito bites, healing
- **Sick contacts:** Several other young children in the family with fever/rash about 1 week before patient left
- **Activities:** No freshwater swimming or exposure, no camping or hiking
Physical Exam

- **Vitals:** Afebrile, all normal
- **General:** Mildly ill appearing, but in no acute distress
- **HEENT:** Conjunctivae mildly injected. No discharge from eyes or nose. Mucus membranes moist. Several 2mm white macules on buccal mucosa.
- **Neck:** Symmetric, 0.5cm submandibular lymph nodes, full range of motion
- **Cardiac:** Normal
- **Respiratory:** Normal
- **Abdomen:** Normal
- **Skin:** Diffuse maculopapular rash with 1-3mm lesions on face, trunk, arms, buttocks, and legs. Lesions on face coalescing into patches.
- **Neuro:** Normal
- **Musculoskeletal:** Normal
What is on your differential? What would you do?
Differential diagnosis

- Measles
- Chikungunya
- Leptospirosis
- Kawasaki disease
- Adenovirus
- Enterovirus
Evaluation

- CBC: Low WBC count
- CRP: 2.1mg/dL
- ESR: 15mm/hr
- Blood culture: Negative
- Thick and thin smears: Negative
- Measles IgM: Positive, 1:16
Measles

- Caused by Rubeola virus
- Family *Paramyxoviridae*
- Transmission: Respiratory/droplet from person to person
- Incubation period: 8-12 days
- Most contagious in prodromal stage through day 4-5 of rash

Measles

• 20 million people infected each year, worldwide
• Declared eliminated from the US in 2000
  • Outbreaks still occur (e.g., Disneyland in 2014)
• The majority of measles cases in the US are in unimmunized individuals that traveled internationally
  • Become infected while traveling and return to the US and infect others
Measles Worldwide

• Still a problem being addressed
  • Common in many developing countries
  • More than 20 million people are affected per year

• WHO campaign to reduce measles-related deaths
  • In 2013, 84% of children worldwide received 1 dose of the measles vaccine by 1yo
  • Estimated to have prevented 15.6 million deaths
  • Still have much work to do
Clinical Presentation

- Prodrome: High fever, runny nose, cough, non-purulent conjunctivitis
- Koplik spots ~3d after initial symptoms
- Rash
  - Typically starts 3-7 days after initial symptoms
  - Maculopapular rash
  - Appears on face, then becomes generalized
    - Can be more confluent on face/head
  - Lasts 4-7 days
- Exam can include tonsillar and lymph node hypertrophy
Complications

• More common if < 5yo or > 20yo
• Include:
  • Diarrhea
  • Pneumonia
  • Ear infection
  • Encephalitis
  • Subacute sclerosing panencephalitis
    • Rare, but fatal
    • Occurs 7-10 years after initial infection
    • More frequently occurs if infected at < 2yo
Evaluation

- Can be diagnosed clinically based on symptoms
- Confirm with measles IgM (serum) or RT-PCR (throat swab)
- CBC: Leukopenia and lymphopenia
Prevention for Travelers

- MMR (Measles-mumps-rubella) is part of childhood vaccine schedule
  - Typically given at 12-15mo, then again at 4yo
  - If 12mo – 3yo, can give second MMR as long as > or = 28d after first MMR
  - One dose is 93% effective if given at > or = 12mo
- Children 6mo-11mo can receive one dose of MMR prior to travel
  - 85% effective if administered at 9mo
  - Does not count towards the required 12mo and 4yo vaccines
WHAT HAPPENS WHEN THEY DON’T HAVE A RASH?
• A good history of the illness and detailed exposure history is key to narrow your differential
• Many of these illnesses discussed today can but don’t always have a rash
• Laboratory studies can be an adjunct to your clinical suspicion
• Malaria, TB, and HIV should remain in the back of your mind
• Common things are common
PRE-TRAVEL COUNSELING

...an ounce of prevention...
Talk to your patients!

- Advise even before they consider travel, so they know where to go
- Many patients will come at the last minute or not at all
  - Difficult to immunize or fill Rx
- Goal is to prevent or limit travel-related illness, regardless of reason for travel

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No.</th>
<th>(%)</th>
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<tbody>
<tr>
<td>Born/Residence in US</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Born in the United States</td>
<td>7,597</td>
<td>(76)</td>
</tr>
<tr>
<td>Residence in the United States</td>
<td>9,942</td>
<td>(99)</td>
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<tr>
<td>Reason for travel</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tourism</td>
<td>3,799</td>
<td>(38)</td>
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<tr>
<td>Missionary/volunteer/researcher/aid worker</td>
<td>2,438</td>
<td>(24)</td>
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<td>Visiting friends and relatives</td>
<td>1,661</td>
<td>(17)</td>
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<tr>
<td>Business</td>
<td>1,492</td>
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<tr>
<td>Student</td>
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<td>(6)</td>
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<tr>
<td>Military</td>
<td>18</td>
<td>(&lt;1)</td>
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<tr>
<td>Medical tourism</td>
<td>9</td>
<td>(&lt;1)</td>
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<tr>
<td>Expatriate</td>
<td>33</td>
<td>(&lt;1)</td>
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<tr>
<td>Missing</td>
<td>1,154</td>
<td>(12)</td>
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<td>Pretravel encounter</td>
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<tr>
<td>Yes</td>
<td>4,451</td>
<td>(44)</td>
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<tr>
<td>No</td>
<td>4,134</td>
<td>(41)</td>
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<tr>
<td>Unknown</td>
<td>887</td>
<td>(9)</td>
</tr>
<tr>
<td>Missing</td>
<td>560</td>
<td>(6)</td>
</tr>
</tbody>
</table>
General guidance

• Food
  • Restaurants should be reputable
  • Avoid street food
  • Make sure food is served hot and fully cooked
  • Fruits and veggies should be able to be peeled

• Water
  • Avoid ice cubes and fresh fruit juices
  • Check that caps on bottles are intact (and haven’t been filled with tap water)

• Animals
  • Avoid, if possible
  • If bitten, rinse thoroughly for 5 minutes, then seek medical care

• Remember to discuss good hand hygiene and general safety!

Vaccines

- Make sure everyone traveling is up to date on usual vaccines
  - Accelerated schedules available for children
- Travel vaccines – know your area or how to find info
  - CDC: www.cdc.gov/travel/destinations/traveler [/insert country]
  - Make sure they receive vaccines in time to become immune
Other medications

- Malaria prophylaxis
  - Understand areas of resistance to chloroquine
- Prophylactic medications (traveler’s diarrhea)
  - Increasing antibiotic resistance
- Ensure they refill Rx for any important, existing medications
Resources for pre-travel counseling

- Physician: PCP, Travel Medicine specialist, Infectious Diseases consultant
- CDC website: www.cdc.gov/travel/
- WHO International Travel and Health website: www.who.int/ith
- Fit For Travel (for travelers from the UK, but helpful): www.fitfortravel.scot.nhs.uk/
- TraVax: http://www.travax.nhs.uk/
QUESTIONS?
Thank you!
Resources

- WHO pandemic and endemic disease information http://www.who.int/csr/disease/en/
Resources

Resources

- [http://www.cdc.gov/measles/about/signs-symptoms.html](http://www.cdc.gov/measles/about/signs-symptoms.html)