Update in Travel Medicine
Brian S. Schwartz, MD
Associate Professor
UCSF, Division of Infectious Diseases

Lecture outline
1. Why should you know about travel medicine?
2. Who needs pre-travel care?
3. The pre-travel visit
4. Post-travel evaluation

International travelers
• ~1 billion travelers cross international boarders each year
• 60 million traveled from the US internationally
  – Almost half traveled to a developing country

Travelers crossing international borders

Reason for travel and 2 most frequent destinations

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1. Why should you know about travel medicine?
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What is the magnitude of travel related morbidity/mortality?

- 20-70% report some illness
- 1-5% seek medical attention
- 0.05% evacuation
Who should seek pre-travel care?

• Travelers to resource poor settings

• Travelers with significant medical issues

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Pre-travel consultation

1. Assessing the health of the traveler
2. Assessing the risk of travel
3. Education
4. Vaccination
5. Prescribing prophylactic/self-treatment

Pre-travel consultation

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Exacerbation of comorbidities is the predominant cause of death in US Travelers:

- Cardiovascular Disease: 49%
- Injury: 22%
- Infection: 1%
- Other/Unknown: 6%
- Cancer: 6%
- Suicide/Homicide: 3%
- Medical: 14%


Pre-travel consultation

1. Assessing the health of the traveler
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Assessing the risk of travel

- Destination(s)
- Season
- Duration of stay
- Planned activities
- Accommodations
- Purpose of travel

Pre-travel consultation

1. Assessing the health of the traveler
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3. Education
4. Vaccination
5. Prescribing prophylactic/self-treatment
Educational topics
- Insect avoidance
- Injury prevention
- Safe food and water
- Altitude
- Safe sex
- Animal avoidance
- Evacuation insurance/access to med care

Insect avoidance
- Vector-borne diseases are common travel-associated infection

Mosquitos
- Viruses
  - Dengue fever
  - Chikungunya fever
  - Zika virus
  - Jap. encephalitis
  - Yellow fever
  - WNV
- Protozoa
  - Malaria
- Helminths
  - Filariasis
- Insects
  - Botfly
Dengue fever

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

Dengue fever: worldwide distribution


Dengue fever: clinical disease

- Incubation: Short (4-7 days)
- Clinical Manifestations:
  - Fever, headache, joint and muscle aches
  - Nausea and vomiting
  - Rash
- Lab abnormalities:
  - Leukopenia, thrombocytopenia, transaminitis
- Dengue Hemorrhagic Fever/Shock
  - Occurs 3-7 days into illness, often with end of fever

Dengue rash

flushing erythema  3-5 days  Dengue rash

1-2 days post onset of symptoms

Morbilliform eruption w/ petechiae and islands of sparing

Dengue diagnostics

Guzman MG. Nature Reviews Micro. 2010

Dengue on the Big Island (Hawaii) 2015-16 Outbreak!


Chikungunya fever in the Americas!

- Came to Caribbean in 2013 \(\rightarrow\) C America \(\rightarrow\) S America
  - 1.7 million cases
- 679 cases reported in US in 2015

Chikungunya fever

- Transmitted by Aedes mosquitoes
- Incubation period 2-4 days (1-14)
- Clinical manifestations (resolved within 7d)
  - Fever + Polyarthralgias 2-4 days later
  - Rash: \(\sim\) 50%, maculopapular
- Labs:
  - Lymphopenia, thrombocytopenia, transaminitis
- Severe complications/deaths in elderly

http://www.cdc.gov/chikungunya/geo/united-states.html
Lab features of Chikungunya vs. Dengue

<table>
<thead>
<tr>
<th></th>
<th>Chikungunya</th>
<th>Dengue</th>
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<tbody>
<tr>
<td>Lymphopenia</td>
<td>+++</td>
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<tr>
<td>Neutropenia</td>
<td>+</td>
<td>+++</td>
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<tr>
<td>Thrombocytopenia</td>
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<td>+++</td>
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<tr>
<td>Hemoconcentration</td>
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**Diagnosis and Treatment Chikungunya**

- Lab diagnosis with IgM/PCR:
  - CDC and DPH of CA, NY, FL
  - Focus labs
- Treatment:
  - Supportive
  - Avoid NSAIDs or aspirin until Dengue excluded

**Zika virus**

- Transmitted by Aedes mosquitoes
- Incubation period 2-4 days (1-14)
- Clinical manifestations (resolved within 7d)
  - fever, rash, joint pain, conjunctivitis
- Severe complications rare
Zika virus risk areas

Zika virus associated microcephaly

- Recommendations to pregnant women
  - Avoid travel to Zika risk areas
  - If visited risk area
    - CDC has testing
  - No treatment available
  - No vaccine
- Sexual transmission
  - Men to avoid intercourse or use condoms with pregnant partners

http://www.cdc.gov/mmwr/volumes/65/wr/mm6502e1er.htm?s_cid=mm6502e1er_e

Zika vs. Dengue vs. Chikungunya

<table>
<thead>
<tr>
<th>Features</th>
<th>Zika</th>
<th>Dengue</th>
<th>Chikungunya</th>
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</thead>
<tbody>
<tr>
<td>Fever</td>
<td>++</td>
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<tr>
<td>Rash</td>
<td>+++</td>
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<tr>
<td>Conjunctivitis</td>
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<td>Arthralgia</td>
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<tr>
<td>Myalgia</td>
<td>+</td>
<td>++</td>
<td>+</td>
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<tr>
<td>Headache</td>
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<td>+</td>
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<tr>
<td>Hemorrhage</td>
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<td>++</td>
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<tr>
<td>Shock</td>
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<td>+</td>
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</table>

Botfly

*Dermatobia hominis*

Flies

- Protozoa
  - Leishmaniasis
- Helminths
  - Loa loa

Geographic distribution of cutaneous leishmaniasis

- Old world
  - Dry, arid conditions
- New world
  - Forested areas

Returning from Panama

Returning from Costa Rica
Returning from Portugal

Returning from Israel

Returning from Brazil

Ticks
- African tick-bite fever
- Lyme disease
- Tick-borne encephalitis
**African Tick Bite Fever**

- *Rickettsia africae*
- Aggressive Bont ticks live on undulates and in grassy areas

**Clinical Presentation**

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


**African tick-bite fever: Tache noire**

**African tick-bite fever: skin findings**
Treatment

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

How to prevent insect exposure?

- Avoid outbreaks
  - [www.cdc.gov/travel](http://www.cdc.gov/travel)
- Avoid high risk periods
  - Keep indoor from dusk to dawn (malaria)
- Physical barriers
  - Proper clothing and bed nets
- Insect clothing

Insect repellents

- Which ones are effective?
  - DEET*
  - Picardin*
  - Oil of Lemon Eucalyptus
  - IR3535
  - Permethrin (not on skin)
- Which ones are not effective?
  - Citronella
  - Wristbands, candles, fans, etc.
- Order: Sunscreen → repellent

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**Product** | **Active Ingredient** | **Complete Protection Time**
---|---|---
OFF Deep Woods | DEET (24%) | 302 minutes
Picardin 20% (Sawyer) | Picardin (20%) | >300 minutes
Sawyer Controlled Release | DEET (20%) | 234 minutes
OFF Skintastic | DEET (8%) | 112 minutes
OFF Skintastic for kids | DEET (4.75%) | 88 minutes
Avon Skin So Soft + IR3535 | IR3535 (7.5%) | 23 minutes
Herbal Armor | Citronella (12%) | 14 minutes

Educational topics

- Insect avoidance
- Injury prevention
- Safe food and water
- Altitude
- Safe sex
- Animal avoidance
- Evacuation insurance/access to medical care

Preventable causes of death in US travelers

- Vehicle accident, 735
- Homicide, 533
- Suicide, 357
- Accidental death, 282
- Drowning, 329
- Drug-related, 467
- Execution, 13
- Maritime accident, 31
- Disaster, 131
- Air accident, 82
- Accident other, 332
- Terrorist, 52
- Suicide, 357
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- Homicide, 533
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Food and water safety

- Many common travel-related infections are transmitted by contaminated food/water
  - Travelers' Diarrhea
  - Hepatitis A
  - Hepatitis E
  - Typhoid fever
  - Parasitic infections
Prevention of food-borne disease

- Most studies failed to correlate guideline adherence to risk of travelers’ diarrhea
- *Where* you eat < *what* you eat!
- Safe options?
  - Drinks: Bottled H2O, soft-drinks
  - Foods: Hot, processed, packaged, peeled

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Vaccine preventable diseases

- Routine vaccination should be up to date
- Required vaccines
- Travel-related vaccines
### Travel-related vaccines

- Hepatitis A*
- Typhoid fever*
- Yellow fever*
- Meningococcal infection
- Japanese encephalitis
- Polio vaccine
- Rabies vaccine
- Hepatitis B

### Hepatitis A

**Transmission:**
- Food/water

**Vaccine (inactivated):**
- Intramuscular: Hep A and Hep A/B (Twinrix)
- Life-long protection after 2nd dose (6 mo)
- Ok to give up until departure in most patients

**Immune globulin:**
- < 2 wks pre-travel and < 12 mo, > 40 yr, liver dz, IS

### Typhoid Fever

**Transmission:**
- Food/water

**> 400 cases annually US**
- Travel #1 risk factor

**2 vaccines (50-80% protective):**
- Intramuscular (inactivated) – booster Q2 years
- Oral (live attenuated) – booster Q5 years

### Yellow Fever

- Mosquito transmitted
- YF Risk: illness (death)
  - W. Africa: 50(10)/100,000
  - S. America: 5(1)/100,000
- Vaccine required/regulated
- Side effects rare but significant
  - > risk for 60 yr
Other travel-related vaccines

- Japanese encephalitis
- Meningococcus
- Polio vaccine
- Rabies vaccine
- Hepatitis B

Pre-travel consultation

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Prophylactic/self-treatment medications for travelers

- Malaria*
- Travelers’ diarrhea*
- Altitude illness
- Jet lag
- Motion sickness
- Common infections (UTI, SSTI, yeast infection)

Malaria in the US

Malaria in the US

• What: 70% Plasmodium falciparum
• Where: 72% cases from Africa
• Who:
  – 54% - “visiting friends and relatives”
  – 3% - “tourists”
  – 6 deaths in 2012


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</td>
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<tr>
<td></td>
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<td>Con: $</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>Chloroquine-susceptible</td>
<td>Weekly; 4 wks post</td>
<td>Pro: Weekly</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Con: GI upset</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>All</td>
<td>Daily; 4 wks post</td>
<td>Pro: $</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Con: Photos; GI</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>Mefloquine-susceptible</td>
<td>Weekly; 4 wks post</td>
<td>Pro: $, ok in preg, kids</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Con: Dreams, avoid psych/Seiz.</td>
</tr>
</tbody>
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Treatment


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

DuPont HL. Annals of Internal Medicine. 2005
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”

A new tool for you to get your patients ready for travel

http://gtten.travel/prep/prep

- Provide destination specific recs using CDC data
- Generates a medical note to cut and paste into EMR

Lecture outline

1. Why should you know about travel medicine?
2. Who needs pre-travel care?
3. The pre-travel visit
4. Post-travel evaluation
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.

Top 5 complaints in returning travelers leading to MD visit

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How to determine etiology of fever in returned traveler

Patients need immediate evaluation

- Destination(s)
- Incubation period
- Exposures
- Exam findings/labs
- Prophylaxis/immunizations

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

Exposures?
- Insect or animal exposures?
- Fresh water exposure?
- What did they consume?
- Other ill travelers?
- Sexual activity?

Specific symptoms or exam findings?
- Symptoms
  - Abdominal pain?
  - Headache?
- Exam findings
  - Rash?
  - Lymphadenopathy?
  - Arthritis?

Prophylaxis?
- Vaccinations?
  - Which ones?
  - Timing of vaccinations?
- Malaria prophylaxis?
  - Appropriate agents?
  - Taken appropriately?
Initial testing?
- CBC w/ differential
- LFTs
- Blood cultures x 2
- Thick and thin blood smear x 2
- Urinalysis
- CXR
- Additional testing based on history/exam

Top 5 complaints in returning travelers leading to MD visit
- Fever without localizing findings
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Acute diarrhea
- Most likely travelers’ diarrhea
- Consider empiric treatment
  - Ciprofloxacin, azithromycin, rifaximin

Top 5 complaints in returning travelers leading to MD visit
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Freedman DO. NEJM. 2006.
5 most common dermatological diagnoses in returning travelers

- Cutaneous larva migrans
- Insect bite
- Skin abscess
- Superinfected insect bite
- Allergic rash

Lederman ER. J Infect Dis. 2008

Top 5 complaints in returning travelers leading to MD visit

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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

Top 5 complaints in returning travelers leading to MD visit

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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

Summary

- Travel health risks are dependent on underlying medical conditions as well as itinerary, duration of travel, purpose of travel, and planned activities
- Travelers should be up to date on routine and travel-specific vaccinations
- Travelers should be given prophylactic and self-treatment medications as appropriate
- Recommend evacuation insurance to travelers, particularly those at high-risk
- A febrile returning traveler is a medical emergency

Connor BA. Clin Inf Dis. 2005