The Ill Returning Traveler:
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Learning Objectives:
1. Introduce Travel Medicine as a bona fide medical specialty
2. Discuss the common symptoms of illness in returning travelers and subsequent implications
3. Highlight the geographic links for many tropical and travel-related infections
4. Outline the work-up and initial management of travel-related conditions
5. Review cases in Travel Medicine

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The Febrile Patient Back From the Tropics:

You are seeing a sick recently returned traveler from Africa.

He has a high fever (104°F), mild confusion, headaches and nausea.

What is this illness?

The Febrile Patient Back From the Tropics:

The problem: The body in illness has a limited vocabulary of symptoms

Many “tropical” diseases produce similar initial symptom complexes.

The Febrile Patient Back From the Tropics:

Is it Malaria?

A common and reasonable response would be to order a malaria smear and treat for Plasmodium malaria presumptively while awaiting results.

But what if the fever doesn’t go away and the malaria smear is inconclusive or delayed???
Ill-Returning Traveler
Clinical Presentations:
- Fever
- Diarrheal illness
- Rash
- Cough

All of these categories overlap and a returning patient may have just one of these symptoms or they may have all of them.

Major challenge is having to consider unfamiliar diseases—what could they have been exposed to on the trip?

Ill-Returning Traveler
Clinical Presentations:

Two Major Errors:

1. Not considering exotic diseases like Malaria!
2. Considering only exotic diseases!

Clinical & Diagnostic Error:

22 year old male patient who presents to the clinic with a 1 week history of bloody diarrhea and painful bowel movements several weeks after returning from a mission trip to Guatemala.

- What comes to mind?
Clinical & Diagnostic Error:

22 year old male patient who presents to the clinic with a 1 week history of bloody diarrhea and painful bowel movements several weeks after returning from a mission trip to Guatemala.

- What comes to mind?

Diagnostic Error:

Common Presenting Symptoms:
Fever:

- Fever in a returned traveler should prompt immediate evaluation for potentially life-threatening infections.
- Primary Concerns: Malaria, Typhoid, Dengue, Chikungunya, Katayama fever (acute schistosomiasis), Rickettsial infections, Leptospirosis, Meningococcal disease, Influenza, and Hepatitis.
- To name only a few of the possibilities!!
- Decision to workup as outpatient vs. inpatient
- Timing of presentation to healthcare
- If at real risk for malaria, should perform blood smears up to three times if necessary and consider starting empiric therapy with Atovaquone-Proguanil or Artemether-Lumefantrine.
- Many of these diseases respond to doxycycline (rickettsial diseases, leptospirosis, malaria) (albeit slowly)
- Tick Typhus

Initial Work-Up for the Febrile Traveler:

- CBC w/differential
- ESR
- Blood smear x 1-3 (thin & thick)
- Blood culture
- HIV antibody test
- Viral load (RNA)
- LFTs
- U/A
- Stool culture
- Stool O & P x 1-3
- Chest x-ray
- CMP
- Selected Serologies: (e.g., dengue, HIV, schisto; hepatitis panel)

Dengue Fever:

- Symptoms
  - Febrile Phase: sudden onset fever, headache, myalgia, rash
  - Critical Phase: hemorrhagic manifestation, abnormal d.d. of hemorrhages
  - Recovery Phase: abrupt relief of symptoms, few with complications

Diarrhea:
- Most acute travelers' diarrhea will have resolved by return or very soon thereafter (Rx ciprofloxacin, azithromycin, or rifaximin).
- Post-infectious IBS (negative workup) is the most common finding.
- Consider parasitic etiologies such as Giardia, Ameba, Cryptosporidium (Stool O&P, giardia and cryptosporidium stool antigen testing).
- Stool culture for bacterial pathogens such as Salmonella etc. (Misses Enterotoxigenic E. coli or ETEC).
- Consider Clostridium difficile stool toxin if antibiotics used abroad.
- Empiric treatment with Tinidazole or Metronidazole may be reasonable—covers parasites and C. diff.
- Remember to also consider non-travel diagnoses: e.g. IBD.

Rashes in Travelers:
- What was the exposure (location and environment), when did the rash begin, where did it spread, and how has it changed?
- Identify the primary lesion: And what it originally looked like!
- The predominant skin symptom is an important clue: itching suggests an allergic etiology and tenderness infection.
- Another clue is how the rash progresses. Centrifugal rashes start on the trunk and spread to the extremities (varicella) whereas centripetal rashes (dengue fever, rickettsial infections) do the opposite.
- Rash may be due to infestation (scabies), infection (Dengue Fever) or allergies to food items (Mangoes).

Cough:
- Usually indicates a respiratory illness but may be present with malaria or typhoid as well.
- URI: In a prospective study that followed nearly 800 Americans who traveled to developing countries, 26% experienced cough, sore throat or congestion.
- Influenza virus was detected in 38% of those with respiratory symptoms, followed by rhinovirus, adenovirus, and RSV.
- Influenza is the most common vaccine preventable illness in travelers.
- TB should always be considered.
- SE Asia: consider Melioidosis, an infection mimicking TB caused by the bacterium Burkholderia pseudomallei.
**Modes of Transmission for Travel-Related Illness:**

- Food and waterborne diseases
- Vector-borne diseases
- Zoonoses (diseases from animals)
- Sexually transmitted diseases
- Bloodborne diseases
- Airborne diseases
- Diseases transmitted from soil

**Diagnostic Work-Up & Considerations:**

1. Trip Itinerary
2. Geographic distribution of diseases
3. Create differential diagnosis based on signs and symptoms
4. Preventive strategies employed (vaccines, malaria chemoprophylaxis)
5. Epidemiologic exposures
6. Incubation periods
7. Laboratory results

**Step 1: The History**

- “Listen to your patient, (s)he is telling you the diagnosis”

Sir William Osler (July 12, 1849 - December 29, 1919)
Specific Oral Exposures for Tropical Infectious Diseases:

Undercooked food/untreated water; fecal-oral:
Cholera, HAV, Enteric fever, Non-typhoidal Salmonellosis, etc.

Unpasteurized dairy products:
Brucellosis, Tuberculosis, Salmonellosis, Listeriosis

Specific Exposures: Vector-Borne

Insects: Examples:
Mosquitoes: Dengue fever, Malaria, Yellow fever
Ticks: Rickettsial diseases, Tularemia
Sand flies: Leishmaniasis, Oroya fever
Reduvids: American Trypanosomiasis
Tsetse flies: African Trypanosomiasis
Fleas: Typhus, Plague
Specific Exposures (cont.)

Fresh water contact:
Leptospirosis, Schistosomiasis

Sexual contact:
Chancroid, Gonorrhea, Chlamydia, Syphilis, HSV, HBV, HIV, HPV

Animal contact:
Brucellosis, Plague, Q fever, Rabies, Tularemia, Anthrax, Viral Hemorrhagic Fevers

Specific Exposures (cont.)

Blood contact:
HBV, HCV, HIV, Malaria

Sick contacts (airborne):
Influenza, TB, Meningococcal disease

Soil contact:
Anthrax, Tetanus, Ascariasis, Trichuriasis

Incubation Periods for Tropical Infectious Diseases:

- Short:
- Medium:
- Long:
Incubation Period: Short (<10d)
- Dengue and Yellow Fever (Arboviruses)
- Leptospirosis
- Meningococcal disease
- Typhus and some Rickettsial fevers
- Plague

Incubation Period: Intermediate (10-21d)
- Amebiasis
- Plasmodium falciparum malaria
- Babesiosis
- Hemorrhagic fevers, including Lassa fever
- scrub typhus and some rickettsial diseases
- African trypanosomiasis
- Typhoid (Enteric) fever
- Brucellosis

Incubation Period: Prolonged (>21d)
- Viral Hepatitis
- HIV
- Rabies
- Tuberculosis
- P. vivax, P. ovale, & P. malariae infections
  First 3 months but can be up to 1 year later
- Visceral leishmaniasis
- Amebic liver abscess
- Filariasis
Characteristics of Ill-Returning Travelers – France 2014

230 patients hospitalized for travel-related illnesses.

- M/F ratio = 1.6; median age = 33 years
- 71% returning from sub-Saharan Africa
- Median duration of travel = 28 days (15-60d)
- Median time from return of travel to hospitalization = 13 days (7-21d)

Characteristics of ill-returning travelers – France 2014

Geographic disease associations (most common cause of fever):

- Africa: Malaria
- Asia: Dengue
- Latin America: Cutaneous Leishmaniasis
- Indian Ocean Islands: Chikungunya fever

Travel-Acquired Diseases (France 2014)

Hospitalized Subset:

- Malaria (49%) especially in patients returning from sub-Saharan Africa and without adequate chemoprophylaxis
- Pulmonary tuberculosis (n = 8)
- Viral hepatitis (n = 8)
- Typhoid fever (n = 6)
- HIV/AIDS (6 new diagnoses)
- Non-typhoid Salmonellosis (n = 5)
- Crimean-Congo hemorrhagic fever
Febrile illness was most likely from Africa and SE Asia.
Malaria was among the top 3 diagnoses from every region.
Over the past decade, dengue became the most common febrile illness from every region outside sub-Saharan Africa.
In sub-Saharan Africa, rickettsial disease was second only to malaria as a cause of fever.
Respiratory disease was most likely in Southeast Asia.
Acute diarrhea was disproportionately seen in travelers from south-central Asia.

Risk Profile for Travel Related Diseases

Travel Medicine Cases:
Case 1: The Medical Resident

A 28 y/o married female medical resident returned to her home country of Pakistan for 4 weeks. Never bothered with travel immunizations (VFR traveler) or visiting a travel clinic prior to departure.

CC: High sustained fever to 39.4°C; it began on the plane flight home

PE: Unremarkable

Case 1: Differential Diagnosis

- Malaria
- Enteric (Typhoid) fever
- Typhus
- Dengue fever
- Other febrile viral illness

Case 1: Diagnosis

Typhoid fever:

High persistent fever, abdominal discomfort and later “pea-soup” diarrhea, may be associated with faint “rose spots,” actually bacterial emboli, visible only in light-skinned individuals. These 2-3 mm macules are usually on the abdomen or lower chest and last 3-4 days. Dx: Culture of blood or bone marrow
Case 1: Typhoid Fever “Pea Soup Diarrhea”

Case 2: The Island Vacation

- 32 year old female traveled to Puerto Rico for a relaxing vacation, duration of 10 days.

CC: Fever to 39°C beginning 3 days after returning to the states.

She developed a diffuse rash on her 2nd day home.

Case 2: Differential Diagnosis

- Dengue
- Zika
- Acute HIV syndrome
- Chikungunya
- EBV
- Enteroviral illness
- Typhoid Fever
Case 2: Diagnosis
Dengue Fever

- Short incubation < 2 weeks
- Centripetal rash characterized by white islands of uninvolved skin in a red sea; biphasic fever
- Dx: DENV Detect IgM capture ELISA (after first 5 days of illness) or dengue reverse-transcriptase polymerase chain reaction (RT-PCR) testing (for viremia < 5 days)
  - A new NS-1 (nonstructural) protein assay may supplant PCR testing in the future.

Dengue Fever is characterized by:
- Fever
- Rash
- Muscle and joint pains

Aedes aegypti mosquito

Case 3: The Missionary

- A 28 year old missionary returning from Papua New Guinea with high fever (103°F), rigors, headache, anemia, jaundice and LQ tenderness. He took mefloquine during his trip but didn’t finish his pills after leaving the country. Exposed to lots of rats where he lived. He also skipped taking the Hepatitis A vaccine.
- Elevated unconjugated bilirubin level
- Hematocrit 35
- Palpable spleen
- Blood smears and LFTs pending

Case 3: Differential Diagnosis

- Hepatitis
- Malaria
- Leptospirosis
- Mononucleosis or a “mon0-like illness”
- Dengue
- Chikungunya
Case 3: Diagnosis:
Plasmodium Vivax Malaria

Case 4: The Roaming Musician

A 26 year old Department of Music graduate student who returned home having spent the summer in Senegal learning about African dance and music. She used local animal hides to make her own drums.

CC: During the past week, she has noted the onset of several mildly tender, black, scab-like lesions on her legs (some began before leaving Senegal). No fever noted.

Case 4: Differential Diagnosis

- Cutaneous tuberculosis
- Rickettsiosis
- Cutaneous diphtheria
- Cutaneous anthrax
Case 4: Diagnosis
Cutaneous Anthrax

SYMPTOMS:

1 CUTANEOUS ANTHRAX

The sore is painless, but it is surrounded by swelling. A scab often forms, and then dries and falls off within 2 weeks.

Case 5: Itchy Beach Rash

A 40-year-old woman who traveled to Barbados, spent time mostly on the beach. She later developed this itchy rash on her foot.

Diagnosis?
What organism is responsible?

Case 5: Diagnosis
Cutaneous Larva Migrans

There were many cats and their feces in the vicinity of the hotel but no dogs. Many individuals got cutaneous larva migrans in the same week at this hotel.

A common cause is *Ancylostoma braziliense*, a hookworm of cats and dogs.
**Take Home Messages:**

1. The body has a limited symptom “vocabulary” by which it can relay what is amiss.
2. There is no substitute for a thorough clinical history.
3. Strongly consider the recent geographic location of ill returning travelers when attempting to make a diagnosis.
4. When in doubt, empirically treat for the most life-threatening illness first.
5. Malaria should always be on the differential.

**References:**

6. Ray Smego, The Ill-Returning Traveler