



Fever in the Returned Traveller

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Disclosures

Relationship with Commercial interests:

- *Speakers Bureau/ Honoraria :*
AstraZeneca, Sunovium

Objectives

1. Background
2. General Approach
3. Various presentations
 1. Fever and rash
 2. Fever and Gastrointestinal symptoms
4. Emerging Infections and Outbreaks



Case 1

- ▶ 29 year old male presents to emergency department with high spiking fevers, headache and confusion
- ▶ Previously healthy
- ▶ He travelled 2 ½ months. Returned 1 ½ weeks ago after visiting relatives in Zambia. Well during travel.
- ▶ Developed intermittent fever, fatigue one week ago. SOB over past few days



Background: Practical Approach to Fever in Returned Traveller

▶ 25% Rule

- ▶ 25% of febrile returned travellers have a self limited process which resolves within 24 hrs
- ▶ 25% have a potentially serious illness
- ▶ Differentiate between minor self-limited processes and progressive life-threatening illness



YOU'VE GOT THE WORST
CASE OF WHATEVER THIS
IS, I'VE EVER SEEN.



5 Questions to Ask in Approach to Patient and History Taking

1. What is most likely? (Geography)
2. What is most probable? (Timing)
3. Is this infection treatable?
4. Is this infection transmissible?
5. Did this predate travel?

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graph TD; A[Practical Approach to Fever in Returned Traveller] --> B[Geographic Risk Factors]; A --> C[Non Geographic Risk Factors];
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Practical Approach to Fever in Returned Traveller

Geographic Risk Factors

Non Geographic Risk Factors

Most Common Causes of Fever - Geographic (GeoSentinel)

1. Malaria (21-48%)
2. Unspecified febrile illness (9-24%)
3. Respiratory (4-24%)
4. Gastroenteritis (2-14%)
5. Dengue (3-8%)
6. Typhoid (0.8-6%)
7. Viral hepatitis (0.6-13%)



Location of Travel in Returned Ill Travellers)

	Sub-Saharan Africa	SE Asia	South Asia	Caribbean & Central/S.America
Systemic febrile illness	49%	34%		25%
				Exception of
				Caribbean
Malaria	42-62%	7-13%	14%	8% <1%
Dengue	<1%	16-32%	14%	9% 23%
Salmonella	<1%	3%	14%	2-3%
Resp Sx's	10%	17%		13%
Diarrhea	10%	17%		15%
No Dx	19%	22%		26%

Practical Approach to Fever in Returned Traveller

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graph TD; A[Practical Approach to Fever in Returned Traveller] --> B[Geographic Risk Factors]; A --> C[Non Geographic Risk Factors]; C --> D[1. UTI<br/>2. URTI<br/>3. STI<br/>4. PE/DVT<br/>5. Non-travel causes];
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Geographic Risk Factors

Non Geographic Risk Factors

1. UTI
2. URTI
3. STI
4. PE/DVT
5. Non-travel causes

Practical Approach to Patient and History Taking

1. Geography - what is most likely
2. What is most probable?
 - ▶ Timing of presentation
 - ▶ Case: 1 ½ weeks post travel to Zambia
 - ▶ However, was travelling 2 ½ months



Timing of Presentation

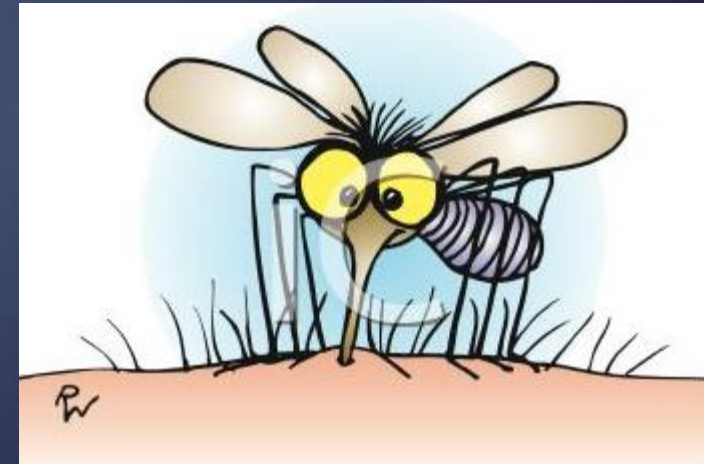
- ▶ Early (< 14 days)
 - ▶ Arboviruses
- ▶ Intermediate (< 1 month)
- ▶ Late (>3 months)



Malaria & HIV can be early & late

Most Common in Etiologies for Early Presentation (<14 days)

- ▶ **Arboviruses** (Dengue, Yellow Fever, West Nile, Japanese encephalitis, Tick Borne Encephalitis, Chikungunya, Zika . . .)
- ▶ Anthrax
- ▶ Brucella
- ▶ Diphtheria
- ▶ Ehrlichiosis
- ▶ Hantavirus
- ▶ **HIV**
- ▶ **Influenza**
- ▶ Acute Histoplasmosis
- ▶ Leptospirosis
- ▶ **Lyme**
- ▶ **Malaria**
- ▶ **Measles**
- ▶ Meilioidosis
- ▶ **Meningococcal**
- ▶ Plague
- ▶ Psittacosis
- ▶ Q fever
- ▶ Rabies
- ▶ Relapsing fever
- ▶ **Rickettsia**
- ▶ **Toxoplasmosis**
- ▶ Trichinosis
- ▶ Tularemia
- ▶ **Typhoid/paratyphoid**



Most Common Etiology Intermediate Incubation (< 1 month)

- ▶ Amebic liver abscess
- ▶ Brucellosis
- ▶ Flukes – Clonorchis, fasciola, schistosomiasis
- ▶ Coccidiomycosis
- ▶ CMV
- ▶ Hepatitis A,C,E
- ▶ HIV
- ▶ Leishmaniosis (visceral)
- ▶ Rubella
- ▶ Toxoplasmosis
- ▶ Trypanosomiasis (African, American)



Most Common Etiology Late Presentation (>3 months)

- ▶ Amebic liver abscess
- ▶ Bartonellosis
- ▶ Brucellosis
- ▶ Flukes – clonorchis, fasciola
- ▶ CMV
- ▶ Filariasis
- ▶ Gnathostomiasis
- ▶ Hepatitis B, C
- ▶ HIV
- ▶ Leishmaniasis, visceral
- ▶ Lyme disease
- ▶ Malaria
- ▶ Melioidosis
- ▶ Fungal – penicilliosis, histoplasmosis
- ▶ Rabies
- ▶ Syphilis
- ▶ Trypanosomiasis
- ▶ Tuberculosis
- ▶ Visceral larva migrans (toxocariasis)



Return to Case

Given timing and location, what is the most likely etiology?

- a. Malaria
- b. Malaria
- c. Malaria

Practical Approach to Patient and History Taking

2. What is most probable?

- ▶ Timing of presentation
- ▶ Based on history and clinical findings
 - ▶ Pretravel preventative measures
 - ▶ Exposures

Patient History - 1

i. Pre-travel preparation:

- ▶ Immunizations (travel vaccines AND childhood vaccines)
- ▶ Malaria prophylaxis

ii. Location

- ▶ Include stopovers

iii. Timing

- ▶ Arrival/departure dates, onset symptoms in relation to travel

Patient History - 2

- iv. Treatment sought while travelling
- v. Did symptoms pre-date travel?
- vi. General history
 - ▶ ? Preceding illness, other health condition

Patient History - 3

vii. Exposures

- ▶ Blood and body fluid exposure
- ▶ Bites (insects and animals)
 - ▶ Mosquitoes, sandflies, fleas, ticks
- ▶ Other animal contact
- ▶ Activities
 - ▶ Caving, fresh water exposures
- ▶ Ingestions
 - ▶ Unpasteurized dairy, shellfish, uncooked meat, uncooked fish
- ▶ Sick contacts



Case 1 continued

▶ Patient History:

- ▶ Originally from Zambia – immigrated to Canada 15 years ago
- ▶ Travelled to rural areas in Zambia
- ▶ No pre-travel medical visit
- ▶ Married. Travelled with wife

Review of Systems

▶ Fever pattern

- ▶ Continuous (typhoid, typhus)
- ▶ Intermittent/relapsing (malaria, TB, borrelia)

▶ Neuro

▶ Resp – Loeffler's syndrome

▶ GI

▶ GU – hematuria, genital lesions

▶ MSK – swellings, arthritis, arthralgias

▶ Skin - Viral exanthems

▶ Coagulopathy

Physical Exam

- ▶ General
- ▶ Neuro
 - ▶ LOC, meningismus, focal deficits
- ▶ HEENT
 - ▶ Conjunctival changes
- ▶ Respiratory
- ▶ CVS
- ▶ Abdomen
 - ▶ HSM
- ▶ Reticuloendothelial system
 - ▶ LN's, hemorrhagic manifestations
- ▶ MSK
- ▶ Skin
 - ▶ GU lesions, skin rashes

Back to Case: Physical Exam

- ▶ General

- ▶ Patient looks ill.

- ▶ T 40C, HR 126, BP 105/70, RR 26

- ▶ HEENT

- ▶ Respiratory

- ▶ CVS

- ▶ Abdomen

- ▶ Splenomegaly

- ▶ Reticuloendothelial system

- ▶ Neuro

- ▶ Confused, no meningismus

- ▶ MSK

- ▶ Skin

Back to Case – Differential Diagnosis:

- ▶ Most probable:
 - ▶ Malaria
- ▶ DDX includes:
 - ▶ Viral hemorrhagic fever
 - ▶ Rickettsial
 - ▶ Meningococcal
 - ▶ Sepsis

Potentially Life Threatening Conditions - What Not to Miss

- ▶ Malaria
- ▶ Hemorrhagic manifestations
 - ▶ Viral hemorrhagic fever
 - ▶ Meningococcemia
 - ▶ Leptospirosis
 - ▶ Plague
 - ▶ Rickettsial infections
 - ▶ Vibrio infection
 - ▶ DIC
- ▶ Respiratory distress
- ▶ Hypotension or hemodynamic instability
- ▶ Confusion, lethargy, stiff neck, focal neurologic findings

3 - Is this Infection Transmissible?

Isolation Precautions Required in:

	Airborne Precautions	Droplet Precautions	Contact Precautions
Respiratory Symptoms	X (TB)	X (viral infection)	
Fever and Rash		X	
Meningitis Syndrome		X	
Hemorrhagic Fever		X	
Diarrhea			X

Investigations: Fever in Returned Traveller

Labs

- CBC and diff, Liver enzymes, Cr, GFR, PTT, INR
- BC x 2
- Blood smear x 3 for malaria and rapid diagnostic test
- Urinalysis

CXR

Pearls

- ▶ Leukopenia – dengue, typhoid, Brucella, rickettsia, acute HIV
- ▶ Thrombocytopenia – malaria, dengue, Brucella
- ▶ Eosinophilia – migratory stage of helminths (acute HIV, fungal infections, occasionally viral infections)
- ▶ LFT abnormalities – viral hepatitis, leptospirosis, rickettsia, Q fever, relapsing fever, yellow fever, amebic abscess, brucellosis, typhoid, hemorrhagic fever, dengue

Investigations:

Further testing dependent on exposures and other factors

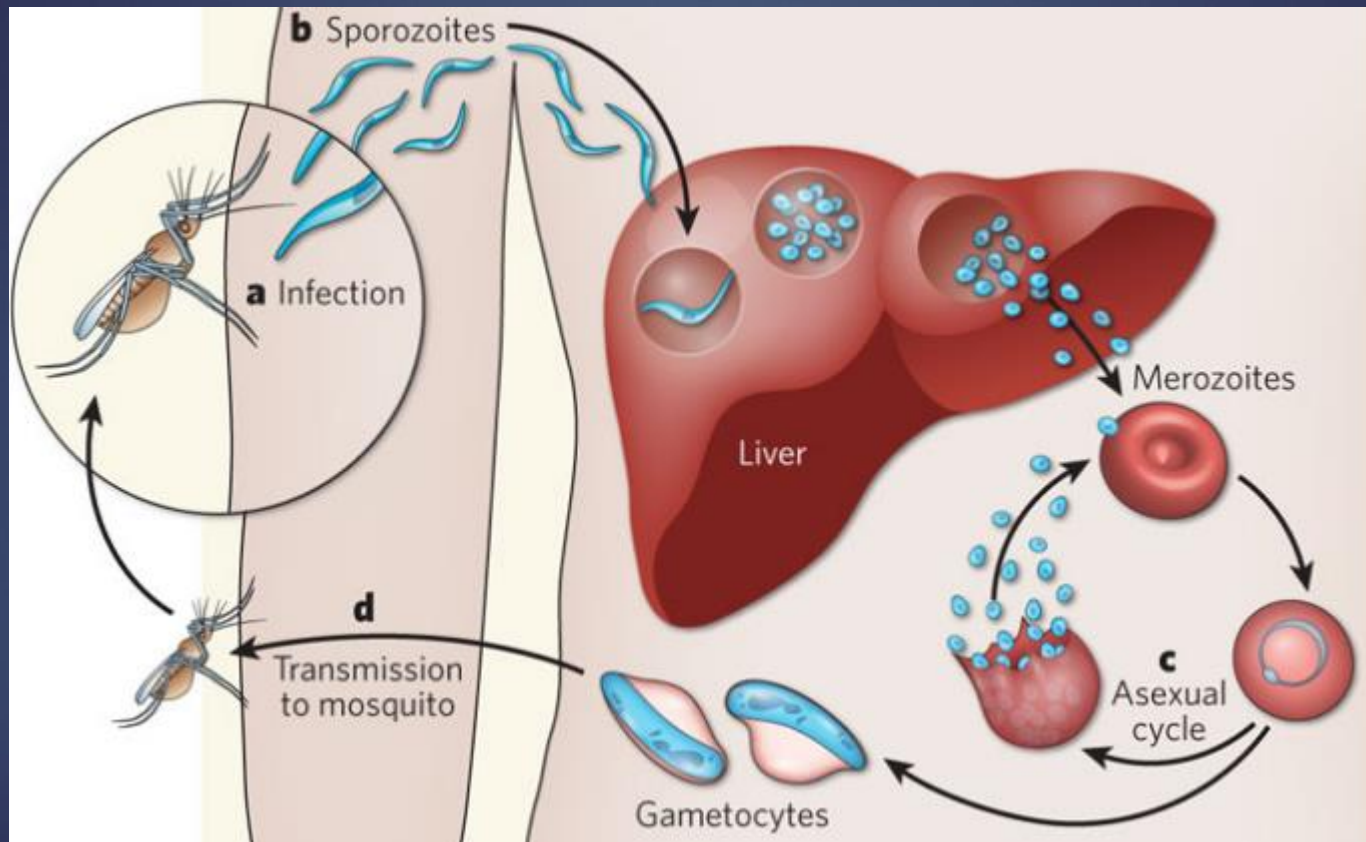
- Stool for C&S, blood, leukocytes, O&P (C diff)
- Serologies (HIV, syphilis, viral hepatitis, EBV, CMV) consideration serologies rickettsia, arboviruses, leptospirosis etc
- Urinary antigen (legionella)
- STI screen
- CSF
- Blood smears – malaria, babesia, borrelia, filarial
- Sputum – AFB and mycobacterial culture, fungal stains and culture
- Other imaging
- Biopsy (BM, skin, lymph nodes, masses)

Test for non-infectious etiologies (TSH, autoimmune etc.)

Return to Case - Investigations

- ▶ Hb 102, PLT 83, WBC 12.1
- ▶ Cr 115, random glucose 4.3
- ▶ P falciparum rapid test positive, smear 0.1% parasites
- ▶ CXR – clear
- ▶ CSF – Clear, WBC 2, RBC 3, glucose 4.0, protein 48, gram stain negative

Malaria



Malaria

- ▶ **Emergency - Most frequent infectious cause of death in returned traveller**
- ▶ Incubation period:
 - ▶ 10-14 days, 90% of cases present within 1 month of last exposure
 - ▶ *P vivax* or *P ovale* may present months to years post infection
- ▶ Symptoms:
 - ▶ Fever, flu-like viral illness, chills, headache, myalgia
 - ▶ Dry cough, abdominal pain

MCHUMOR by T. McCracken



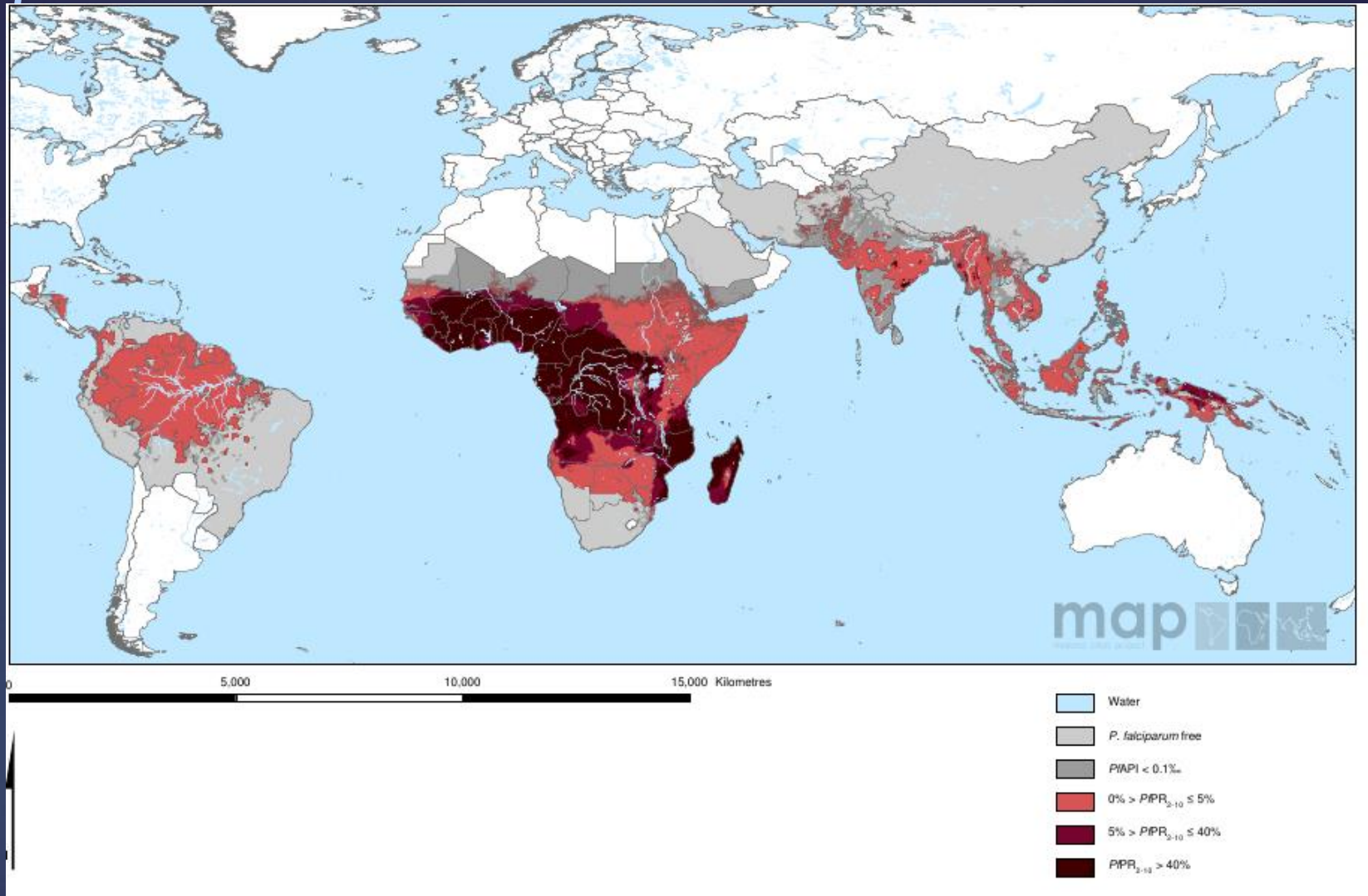
"Off hand, I'd say you're suffering from an arrow through your head, but just to play it safe, I'm ordering a bunch of tests."

**MALARIA MAY OFTEN
BE PRESENT
WITH A COINFECTION**

Malaria Approach

1. Is this *p. falciparum*?

P. falciparum



[Malar J](#). 2011 Dec 20;10:378. doi: 10.1186/1475-2875-10-378.

A new world malaria map: *Plasmodium falciparum* endemicity in 2010.

[Gething PW](#)¹, [Patil AP](#), [Smith DL](#), [Guerra CA](#), [Elyazar IR](#), [Johnston GL](#), [Tatem AJ](#), [Hay SI](#).

Malaria Approach

1. Is this *p. falciparum*?
2. Is this severe or complicated infection?

Severe Malaria

► Definition:

- One or more of the following in the absence of an alternative cause and in the presence of *P. falciparum* parasitemia

- Impaired consciousness (GCS <11)
- Prostration – generalized weakness (unable to sit, stand, walk w/o assistance)
- Multiple convulsions - >2 in 24 hrs
- Acidosis – pH < 7.25, bicarb <15 mmol/L, venous lactate 5 or greater
- Hypoglycemia - <2.2 mmol/L
- Severe anemia – Hb <50, HCT 15% or less
- Renal impairment – Cr >265 mcmmol/L, BUN >20 mmol/L 3mg/dL
- Respiratory distress
- Pulmonary edema
- Significant bleeding
- Shock
- Hemoglobinuria
- Jaundice
- *P falciparum* parasitemia >5%

- May occur with other severe forms of malaria (*P. vivax* and *P. knowlesi*)

Severe Malaria

► Definition:

- One or more of the following in the absence of an alternative cause and in the presence of *P. falciparum* parasitemia

Presence of End Organ Failure

- Impaired consciousness (GCS <11)
- Prostration – generalized weakness
- Respiratory distress
- Pulmonary edema
- Significant bleeding
- Shock
- Hemoglobinuria
- Jaundice
- *P falciparum* parasitemia >5%
- Impaired renal function – serum creatinine >2.5 mg/dL
- Metabolic acidosis – bicarb <15 mmol/L, venous lactate 5 or greater
- Hypoglycemia - <2.2 mmol/L
- Severe anemia – Hb <50, HCT 15% or less

- May occur with other severe forms of malaria (*P. vivax* and *P. knowlesi*)

Malaria Approach

1. Is this *p. falciparum*?
2. Is this severe or complicated infection?
3. Has the infection been acquired in an area of known drug resistant malaria?
 - ▶ Chloroquine resistance
 - ▶ Mefloquine resistance
4. Is there a co-infection?
5. Was prophylaxis used? Avoid the same drug

Empiric Management - 1:

► If any concern of falciparum malaria:

► **ADMIT**

► Start empiric treatment

1 - Artesunate IV

(followed by doxycycline OR
atovaquone/proguanil)

OR

2 - Quinine IV

PLUS doxycycline OR clindamycin

Empiric Management - 1:

- ▶ If any concern of falciparum malaria:
 - ▶ ADMIT
 - ▶ Start empiric treatment
- ▶ Supportive: anticonvulsants, IV glucose and fluids, antipyretics, antibiotics, blood transfusion
- ▶ Every 2-4 hour assessments
- ▶ Repeat labs q 6 hrs: parasitemia, Hb/HCT, glucose, lactate

Empiric Management - 2:

- ▶ If ill, treat with ceftriaxone empirically
 - ▶ 2 gm q 12 hrs if concern of meningitis
- ▶ Consider doxycycline (rickettsia or leptospirosis)
- ▶ For sepsis syndrome, be concerned regarding ESBL organisms – consider carbapenem (meropenem)

Objectives

1. Background
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 - ▶ Malaria
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Case 2 – Fever and Rash

- ▶ 48 year old woman presenting to emergency department with fever, severe muscle aches, headache and back pain which started abruptly 2 days ago
- ▶ Chills a couple of days previously and mild macular rash
- ▶ She returned from Bangkok 4 days ago on a business trip



► What is the first thing we ask ourselves?

Is this transmissible?

Is this Infection Transmissible?

Isolation Precautions Required in:

	Airborne Precautions	Droplet Precautions	Contact Precautions
Respiratory Symptoms	X (TB)	X (viral infection)	
Fever and Rash		X	
Meningitis Syndrome		X	
Hemorrhagic Fever		X	
Diarrhea			X

2. Approach to Fever and Rash (Flu-like symptoms)

- ▶ Same ddx as non-travellers (HIV, syphilis, EBV, CMV, measles, meningococcal, vasculitis etc.)
- ▶ Arbovirus - early viral hemorrhagic fevers
- ▶ Typhoid
- ▶ Rickettsia
- ▶ Leptospirosis
- ▶ Measles
- ▶ Relapsing fever
- ▶ Acute African trypanosomiasis
- ▶ Malaria

Case 2 continued

▶ History:

- ▶ Exposures – nil
- ▶ Attended travel clinic prior to travel. Told that as she was solely in Bangkok, malaria prophylaxis not necessary
- ▶ PMHx – borderline DM, hypothyroid
- ▶ No meds

Case 2 continued

- ▶ Physical Exam:

- ▶ Looks stable

- ▶ T 38.6, BP 118/72, P 102, RR 18

- ▶ Conjunctival injection, pharyngeal erythema, subcentimetre anterior cervical lymphadenopathy, generalized maculopapular rash



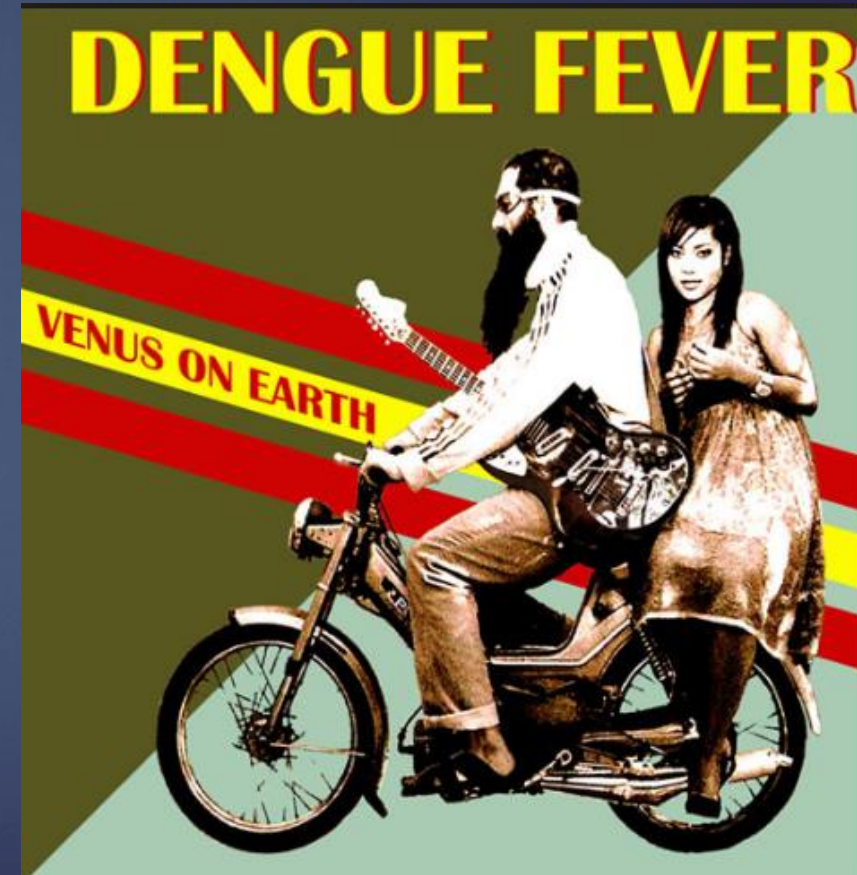
Case 2 continued

▶ Investigations:

- ▶ WBC 3.2, PLT 58, INR 1.2, GFR 55, AST 87
- ▶ Urinalysis - bland
- ▶ BC, UC pending
- ▶ CXR normal

Given the timing and location,
what is the most likely diagnosis?

- ▶ Dengue
- ▶ Typhoid
- ▶ CMV, EBV
- ▶ Malaria



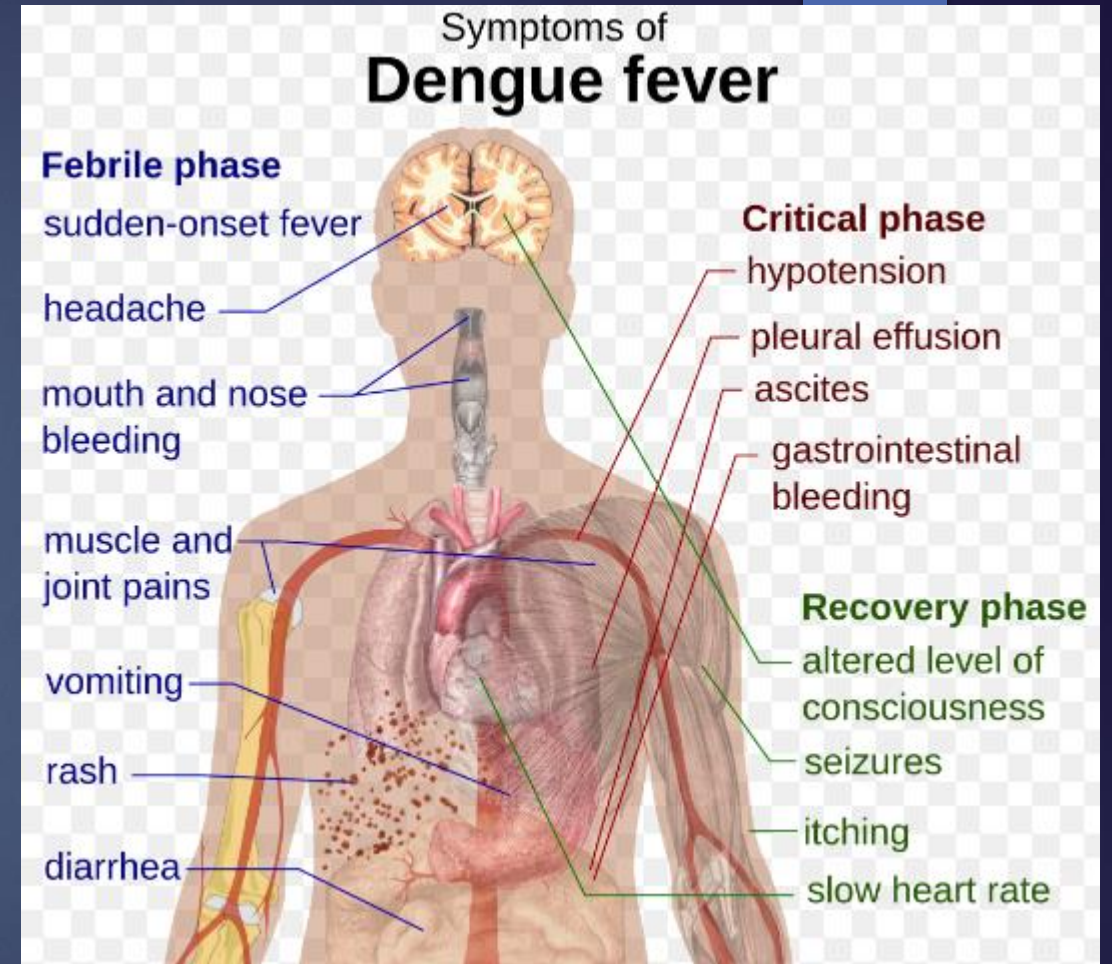
WHO Dengue Map



- Most common in SE Asia (Thailand), Caribbean, South Pacific and Central America
- Predominantly urban (business travellers at risk)

2 - Dengue

- ▶ Incubation: 2-7 days post mosquito bite
- ▶ Symptoms:
 - ▶ “breakbone fever”
 - ▶ Severity ranges between
 - ▶ Asymptomatic
 - ▶ Dengue fever
 - ▶ Dengue Hemorrhagic Fever with shock syndrome
- ▶ Diagnosis: serology



Dengue



- ▶ After acute illness:
 - ▶ Frequently a post-viral fatigue lasting up to 6 months
 - ▶ Patient Education:
 - ▶ If travelling to dengue endemic region in future, there is a risk of developing dengue **hemorrhagic** fever

Hemorrhagic Fevers

▶ DDx:

- ▶ DIC from “typical bacteria”
- ▶ Meningococcus
- ▶ Rickettsiae
- ▶ Dengue
- ▶ Viral hemorrhagic fever
- ▶ Malaria
- ▶ Typhoid

▶ Treatment:

- ▶ Supportive
 - ▶ Hydration, acetaminophen, transfusion if required

Unlikely if > 3 weeks since travel
If suspected **MUST:**
1 – isolate
2 – notify Public Health

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Approach to Fever & GI Symptoms

- ▶ Diarrhea - work up typically not warranted
 - ▶ If fever present - further work-up warranted
- ▶ Investigations:
 - ▶ Stool for C&S, O&P, (C diff)
 - ▶ BC if looks unwell
 - ▶ Liver enzymes, CBC, Cr, GFR, lytes, coags
 - ▶ Viral hepatitis serology

Typhoid and Paratyphoid fever

- ▶ Incubation: typically 1 week, may be as long as 3 weeks
- ▶ Transmission: fecal-oral route
- ▶ Endemic risk: Anywhere. Mainly in tropics and locations with poor sanitation. Indian subcontinent has 10x risk
- ▶ Prevention:
 - ▶ Vaccine 60-70% effective

Typhoid and Paratyphoid Fever

► Clinical course:

- Insidious onset (unlike malaria, dengue, viral infection)

► Signs and symptoms:

- Fever – gradual, crescendoing over days
- Relative bradycardia (pulse-temperature dissociation)
- Abdominal pain, bowel perforation, GIB, peritonitis
- “Rose spots”
- Hepatosplenomegaly
- Bacteremia



Typhoid and Paratyphoid Fever

▶ Dx:

- ▶ BC (within 1st week illness)
- ▶ Stool (urine culture); occasionally bone marrow culture
- ▶ Labs: anemia, leukopenia/cytosis, abn liver enzymes

▶ Treatment:

- ▶ **Ceftriaxone 2 gm IV q 24 hrs x 7-14 days**
- ▶ Azithromycin
- ▶ Ciprofloxacin

Objectives

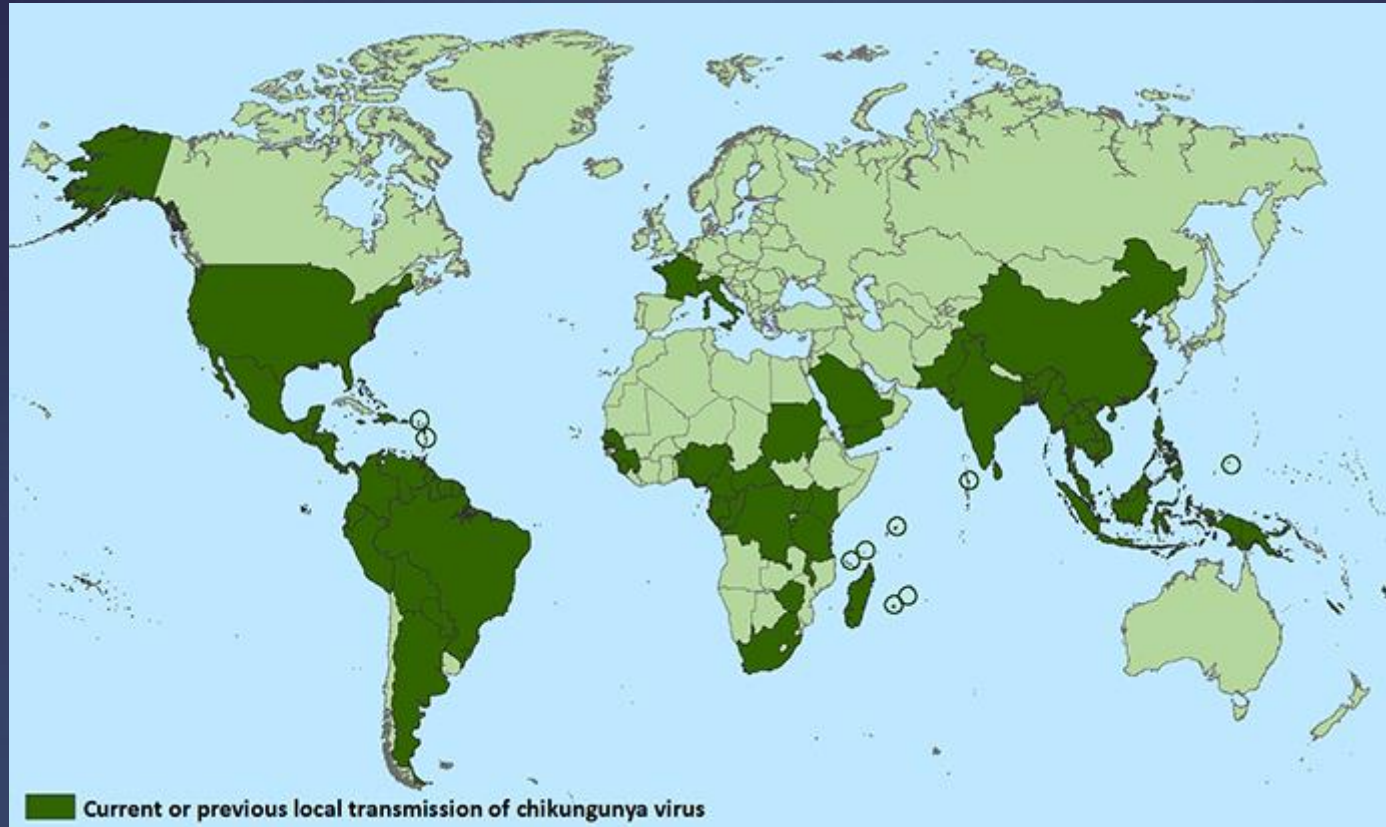
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Chikungunya

- ▶ Transmission:
 - ▶ Arthropod borne: *Aedes aegypti*,
Aedes albopictus
 - ▶ Transfusion, organ transplantation,
nosocomial, vertical
- ▶ Incubation: 2-4 days (range 1-14)

Chikungunya Map as of April 22 2016 (CDC)



- First isolated from mosquitoes and humans during an outbreak in Tanzania in 1952-53
- Late 2013 - first local transmission identified in the Americas, initially in the Caribbean countries and territories

Chikungunya

“That which bends up”, “Stooped walk”

Clinical Manifestations:

- ▶ Abrupt onset symptoms
- ▶ Fever , malaise, polyarthralgia
- ▶ Maculopapular rash in 40-75%

Diagnosis: Serology

Treatment:

- ▶ Supportive
- ▶ Anti-inflammatory
- ▶ No effective antivirals

Chikungunya Disease



TIMELINE OF ZIKA VIRUS



APRIL 1947

Zika virus first discovered in Uganda's Zika forest on a rhesus monkey.



1952

First human case recorded during outbreak of jaundice in eastern Nigeria

Micronesia's Yap Island experiences outbreak with a total of 49 confirmed and 59 probable cases.

APRIL 2007

Zika virus spreads through the French Polynesian islands. No deaths were reported but many people were hospitalized.

OCTOBER 1ST, 2013

1960s - 1980s

Human cases are confirmed through blood tests. No deaths or hospitalizations are reported, but studies consistently show widespread human exposure to the virus.

[Read more](#)

The disease is mapped as it moves from Uganda to western Africa and Asia in the first half of the 20th century.



**Partners In
Research**

FEBRUARY 1, 2014

Local transmission of the virus was confirmed on Easter Island off the coast of Chile.

30 October 2015

Brazil reports an unusual increase in the number of cases of microcephaly among newborns.

MAY 15TH, 2015

Brazil reports its first case of the virus.



Brazil declares a state of emergency with 2 700 babies in Brazil being born with microcephaly.

DECEMBER 24TH, 2015

Canada and the US advise pregnant women to postpone travel to a number of South American countries.

JANUARY 15TH, 2016

JANUARY 20TH, 2016

Almost 4 000 cases of microcephaly were reported in Brazil with 90% of cases in the country's northeast and 6% in the southeast.



Zika Virus

- ▶ 3 lineages: 2 African and 1 Asian
 - ▶ Asian lineage most recent in Pacific and Americas
- ▶ Transmission:
 - ▶ Mosquito borne
 - ▶ Vertical
 - ▶ Sexual
 - ▶ Transfusion
- ▶ Incubation: typical incubation flaviviruses is 3-14 days

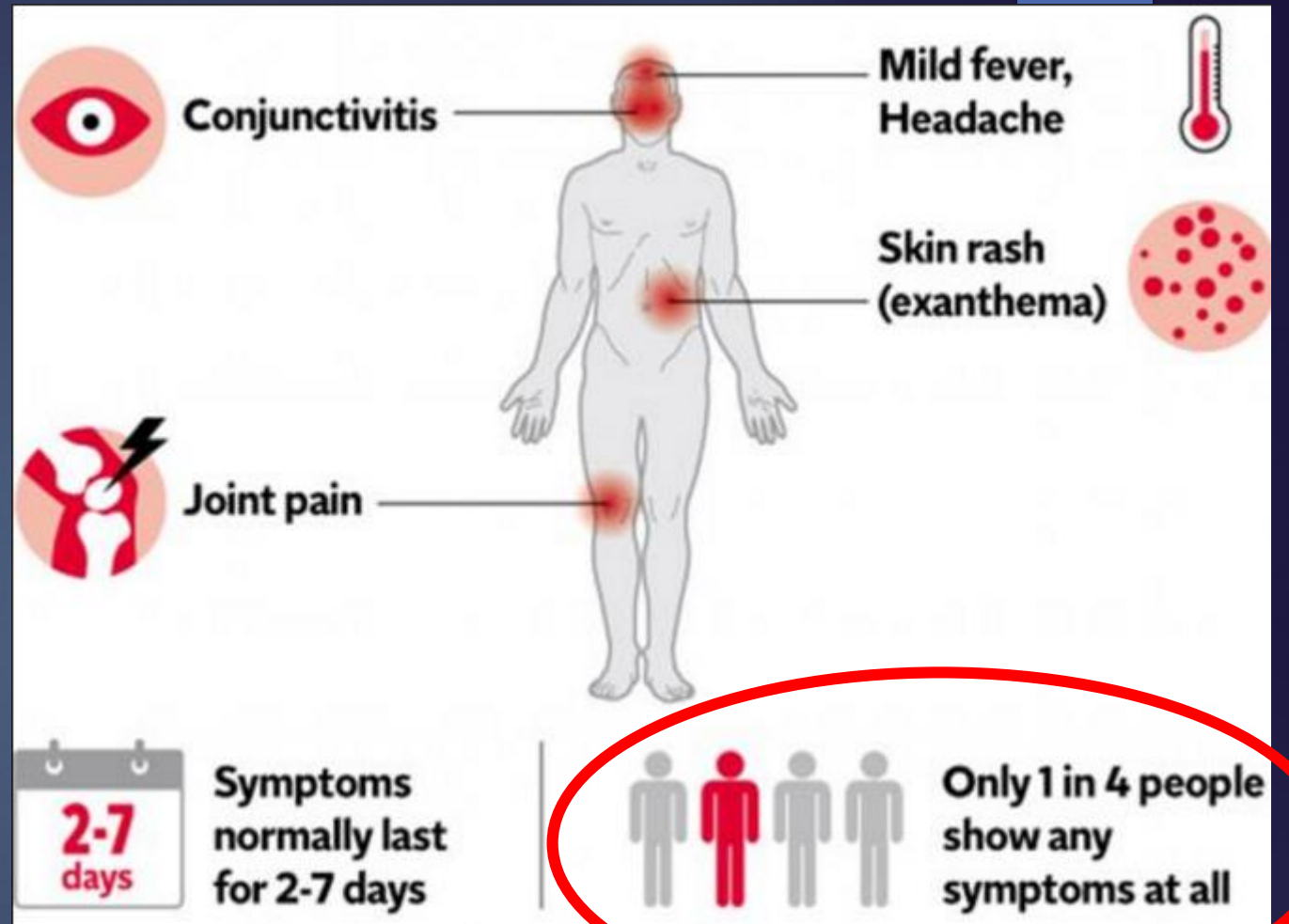
Zika Virus

► Neurologic:

- Meningoencephalitis
- Guillian Barre syndrome

► Fetal:

- Microcephaly, fetal death, growth restriction, CNS lesions, ventricular calcifications, abnormal amniotic fluid, abnormal cerebral or umbilical artery flow, ocular malformations



Zika

- ▶ 14 vaccine developers working on 23 projects of vaccine development (USA, France, Brazil, India, Austria)

Zika Testing

BCCDC updated Sept 15 2016

Clinical Presentation	Recommended Tests
Pregnant women (regardless if symptomatic)	Submit specimen as per acutely ill
Acutely ill: <ul style="list-style-type: none">• 2 or more symptoms AND• Symptom onset within 2 weeks of travel AND• Currently symptomatic or onset symptoms in last 5-10 days	<ol style="list-style-type: none">1. Blood for PCR RNA Zika virus detection2. Zika serology (urine and NP swab)

Zika Testing

BCCDC updated Sept 15 2016

Clinical Presentation	Recommended Tests
Recovered: 1. Zika symptoms AND onset within 2 weeks of travel 2. No longer symptomatic and symptom onset > 10 days ago	1. Zika serology Send one month after symptoms resolve
Asymptomatic • No symptoms consistent with Zika virus	1. Zika serology Send one month post travel

Zika – CDC Preconception Counselling Guidance

MMWR Oct 7, 2016

- ▶ Men - asymptomatic but exposed to Zika virus:
 - ▶ Wait 6 months after last possible exposure before attempting to conceive with partner
- ▶ Asymptomatic partners with possible exposure and are NOT trying to conceive but want to limit partner's risk – no unprotected sex for:
 - ▶ Men: at least 6 months
 - ▶ Women: at least 8 weeks
- ▶ Pregnant women – consider postponing nonessential travel to affected countries

Zika



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Management of Fever in Returned Traveller

1. What is most likely?
 - ▶ Geographic vs. nongeographic etiologies
2. What is most probable?
3. What infection control precautions are required?
4. Did this predate travel?
5. What is the severity (or risk of severity) of illness?



Barriers to Change

- ▶ Exposure
- ▶ Differentiating severe infection from self-limited processes
- ▶ Lack of history



Thank you



Websites for Outbreaks

- ▶ Center for Disease Control and Prevention – Health Information for International Travel under Travelers' Health and updates on travel-related infections
 - ▶ <http://wwwnc.cdc.gov/travel/notices/>
- ▶ World Health Organization
 - ▶ <http://www.who.int/en/>
- ▶ ProMed
 - ▶ <http://www.promedmail.org/>
- ▶ Update: Interim Guidance for Preconception Counseling and Prevention of Sexual Transmission of Zika Virus for Persons with Possible Zika Virus Exposure — United States, September 2016
 - ▶ http://www.cdc.gov/mmwr/volumes/65/wr/mm6539e1.htm?s_cid=mm6539e1_w

Appendix – Brief explanation of various infections

- ▶ **Amoebiasis** – caused by protozoa *Entamoeba histolytica*. Infection via fecally contaminated food, water, or hands. Presents with i) intraluminal GI symptoms ii) colitis (invasive GI disease) iii) amoebic abscess iv) extraintestinal manifestations – pulmonary, cardiac, brain. Treatment: If invasive disease, treat with metronidazole followed by paramomycin. Intraluminal disease treated with paramomycin
- ▶ **Anthrax** – bacterial infection (*Bacillus anthracis*) which can be in spore form. Associated with animal or animal hide exposure, bioterrorism, heroin outbreak. 3 main syndromes – cutaneous, inhalation, gastrointestinal tract (may cause meningitis). IC – standard precautions. Post exposure prophylaxis for aerosolized exposure. 3 doses anthrax vaccine, ciprofloxacin or doxycycline. Treatment: fluoroquinolone + meropenem + linezolid

- ▶ **Brucella** – zoonotic bacterial infection caused by contact with fluids from infected animals or unpasteurized milk/cheese, undercooked meat, lab workers. Presents with fever, constitutional symptoms, arthralgia, myalgia, hepatosplenomegaly, localized symptoms of any body system. PEP required for lab workers. Treatment: doxycycline + streptomycin OR rifampin
- ▶ **Chagas disease – *Trypanosoma cruzi***. Transmitted by triatomine (rejuvid or kissing beetle) defecating during blood meal and inoculating wound. In central and south America. Swelling at site of bite; generalized nonspecific symptoms such as malaise, fever, anorexia, occasionally myopericarditis. Chronic infection can cause myocarditis or esophageal or colonic motility disorders
- ▶ **Diphtheria** – caused by a gram positive bacillus (*Corynebacterium diphtheria*). Respiratory or cutaneous presentation. Treatment: erythromycin or Penicillin G (antitoxin). Close contact screening, may require treatment/vaccination.
- ▶ **Erlichiosis/anaplasmosis** – intracellular bacteria. Vector for erlichiosis (Lone Star tick); anaplasmosis (*Ixodes scapularis*). Systemic symptoms, rash, neurologic symptoms, myocarditis. Treatment: doxycycline

- ▶ **Filariasis** – nematodes that inhabit the lymphatics and subcutaneous tissue. Transmitted by various mosquito vectors, dependent on location/subtype. Acute infection – adenolymphangitis, fever, tropical pulmonary eosinophilia. Chronic infection – lymphedema, chyluria, hematuria, proteinuria
- ▶ **Gnathostomiasis** – tissue nematodes. Predominantly SE Asia, Asia, S and Central America, some regions of Africa. Infection through ingestion of undercooked or raw freshwater fish, eels, frogs, birds, reptiles. Symptoms include migratory localized swellings associated with pain, edema, pruritus, erythema
- ▶ **Hantavirus** – virus transmitted by contact with rodents - typically transmitted by aerosol of rodent feces, urine, saliva. Presents as hemorrhagic fever with renal syndrome or cardiopulmonary syndrome. Treatment: supportive
- ▶ **Leishmaniasis** – protozoa transmitted by sandflies. Frequently asymptomatic. May present with fever, malaise, weight loss, splenomegaly (hepatomegaly). Cutaneous or systemic presentation.

- ▶ **Leptospirosis** – a spirochete. Infection usually due to exposure to environmental sources, animal urine contaminated water (freshwater exposure in sports) or soil, infected animal tissue (rodent infested regions). May be mild or subclinical to fatal. Fever, rigors, myalgias, headache, conjunctival suffusion, cough, GI symptoms, rash. Treatment: doxycycline
- ▶ **Liver flukes** – trematodes (*Clonorchis*, *Opisthorchis* – East Asia from eating undercooked fish; *Fasciola* - from eating infected vegetation)
- ▶ **Melioidosis** – caused by intracellular gram negative bacteria *Burkholderia pseudomallei*. Bacteria is an environmental saprophyte in soil and fresh water. Predominantly in SE Asia, South Asia, China, and Australia. Transmitted via percutaneous inoculation inhalation, aspiration, occasionally ingestion. May cause acute or chronic infection. Symptoms include pneumonia, skin ulcers or abscesses, bacteremia, any systemic presentation. Treatment: ceftazidime vs. carbapenem.

- ▶ **Plague** – caused by the gram negative coccobacillus *Yersinia pestis*. Transmitted by fleas from rodents and wild and domestic animals. Predominant syndromes are febrile gastrointestinal, or pseudoappendicitis. Also extraintestinal.
- ▶ **Psittacosis** – intracellular bacteria *Chlamydia psittaci*, transmitted by bird predominantly. Typically presents with respiratory syndrome, but may have systemic symptoms. Treatment: doxycycline
- ▶ **Q fever** – caused by intracellular bacteria *Coxiella burnetii*. Human infection typically related to exposure with infected livestock, but may be associated with other pets or wild animals. Presents with acute or chronic infection. May cause culture negative infective endocarditis, any systemic syndrome. Treatment: doxycycline
- ▶ **Relapsing fever** – caused by spirochete *Borrelia*. Fever is sudden in onset, followed by afebrile hypotensive periods. Generalized symptoms. May be louse borne or tick borne. Treatment: tetracyclines, penicillin

- ▶ **Schistosomiasis** – fluke which infections humans through penetration of skin from freshwater contact. Acute infection – may be asymptomatic vs acute systemic hypersensitivity febrile syndrome. Chronic infection may affect urinary vs GI system. May cause portal hypertension, neurologic disease, pulmonary disease. Treatment for chronic infection: paramomycin
- ▶ **Toxocariasis (visceral larva migrans)** – *Toxocaris canis* or *catis*. Infection via ingestions of eggs from contaminated hands, soil, fomites. Typically asymptomatic. Eosinophilia is common. May cause ocular or visceral involvement (especially hepatic or pulmonary involvement).
- ▶ **Trichinosis** – nematode *Trichinella*. Transmitted by ingesting raw or undercooked meat (bears, foxes, pigs, birds etc). Typically presents with muscle pain, swelling, weakness. May have other systemic symptoms including GI. Treatment with antiparasitics if significant symptoms.

- ▶ **Trypanosomiasis** – caused by protozoa via bite from tsetse fly
- ▶ **African Trypanosomiasis** – two separate types
 - ▶ **East African (*trypanosoma brucei rhodesiense*)** - more acute form.
 - ▶ **West and Central Africa (*Trypanosoma brucei gambiense*)** – more chronic form.
 - ▶ Early infection - headache, fever, malaise, arthralgias. May have chancre from bite and lymphadenitis, especially of posterior cervical nodes.
 - ▶ Late infection – meningoencephalitis
- ▶ **Tularemia** – caused by GNB *Francisella tularensis*. Transmission via contact with animal or biting insect (predominantly flies), also lab workers, . Various presentations – ulceroglandular, glandular, oculoglandular, pharyngeal, typhoidal, pneumonic. Treatment: antibiotics dependent on presentation. Antibiotic prophylaxis for lab workers

Symptomatic Differential Diagnosis

- ▶ Fever pattern
 - ▶ Continuous (typhoid, typhus)
 - ▶ Remittent (TB, African trypanosomiasis)
 - ▶ Intermittent/relapsing (malaria, TB, borrelia)
- ▶ Neuro - malaria, meningitis (meningococcal), typhoid, rickettsia, encephalitis (arbovirus or other viral), East African trypanosomiasis, rabies
- ▶ Resp – loeffler's syndrome, fungal (coccidio/histoplasmosis), typical and atypical bacterial pathogens, TB legionella, influenza, Q fever
- ▶ GI – viral hepatitis, enteric fever, gastroenteritis, amoebiasis, flukes
- ▶ GU – schistosomiasis, STI's, UTI
- ▶ MSK – arboviruses (chikungunya), toxocariasis, gnathostomiasis
- ▶ Skin - Viral exanthems (rubella, varicella, mumps, HHV6), dengue, spotted or typhus group rickettsiosis, typhoid fever, parvovirus B19
- ▶ Coagulopathy - Meningococcemia, leptospirosis, other bacterial pathogens a/w coagulopathy, malaria, viral hemorrhagic fever

Regions of Malaria Resistance

Chloroquine resistance – if in doubt, do NOT use chloroquine

- ▶ *P. falciparum* resistance in most areas (exceptions Central America west of the Panama Canal, Haiti, the Dominican Republic, and most of the Middle East)
- ▶ *P. vivax* resistance in Papua New Guinea or Indonesia.
- ▶ Mefloquine resistance
 - ▶ SE Asia