Triage for Travel-related diseases
Not always a walk on the beach!
Philippe Lagacé-Wiens, MD, FRCPC, DTM&H
plagacewiens@dsmanitoba.ca

Transparency declarations
I lead a life mostly taken up by work. When I don't work, I like gardening, tending to chickens, cats and kids. When I get spare time, I love playing with my kids and spending quality time with my wife.

I have little time to entertain the idea of fancy drug/vaccine dinners or relationships with industry. I have no friends in the pharma/vaccine industry. My wife works for the Public Health Agency of Canada. PHAC has a lot of money recommends a lot of vaccines, some of which are for travellers but I had nothing to do with these recommendations.

The following specific drugs are mentioned in my talk: azithromycin, amoxicillin, TMP-SMX, chloramphenicol and artesunate. I have no financial relationship with the manufacturers or distributors of these drugs.

In short, I have nothing to declare relevant to the content of this presentation.

Outline
- Tropical and travel medicine background: Geography, risk factors, exposures, prevention.
- Key syndromes in geographical medicine
- Key diseases – presentation, incubation, diagnosis, morbidity and mortality: Malaria, Dengue, Typhoid
- Case studies and interactive fun
- Key points an conclusions

Travel-associated illness: Cosmopolitan vs. Geographical
- Cosmopolitan illnesses are those that may occur anywhere but onset was temporally related to travel.
- Many are very serious (e.g. PE, MI, CVA, pneumonia etc.)
- Should be managed in the ER like they are in non-travellers.
- Not the focus of this session
- Geographical illnesses are those which are destination specific.
- Many are serious
- Most are unfamiliar to Canadian HCPs
- Many present as non-specific illnesses.
- Some can progress rapidly and unpredictably.

Geographical medicine backgrounder
- Recent (even remote) travel may dramatically affect a differential diagnosis.
- Identifying key points of travel history during triage can help identify patients at risk for severe diseases.
- Geography (location of travel), symptoms and timing of onset are the most critical pieces of information for triage.
- Serious travel-related illness is uncommon but not rare.
- 22-64% of travellers experience illness when travelling to the developing world.
- 8% of travellers to the developing world seek medical advice while travelling or upon return.
- 11% of those that seek medical attention require hospitalization.
- ~5.1% of those that seek medical attention die. (~4000/yr deaths worldwide)

Geography – Key points
- North America, Europe and Australia are considered destinations without significant risk of the most serious geographical infectious diseases.
- Severe presentations of cosmopolitan travel-related illness may still occur:
  - Severe influenza, PE, Pneumonia, arboviral infections etc...
  - Travellers often have mixed itineraries and require probing.
  - All destinations within 6 months a good start.
- Central America, Mexico, Caribbean destinations have low incidence of serious travel related illness.
- But... High tourist traffic → 14.1% of travel-related healthcare contacts from these destinations.
Geography – Key points

- South America has moderate to high risk of serious travel-related illness.
  - Actual risk depends on specific destination and travel style.
- Sub-Saharan Africa has high risk of serious travel related illness.
  - Exact risk depends on a number of factors.
- North Africa generally less risk.
- South and South-East Asia has high risk of serious travel-associated illness.
  - Destination-specific.

Geosentinel survey (N = 17,353)

<table>
<thead>
<tr>
<th>Destination</th>
<th>N (%) of ill travellers from this destination</th>
<th>% of ill travellers that require hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caribbean</td>
<td>1115 (6.4)</td>
<td>5</td>
</tr>
<tr>
<td>Central America</td>
<td>1326 (7.6)</td>
<td>4</td>
</tr>
<tr>
<td>South America</td>
<td>1675 (9.7)</td>
<td>6</td>
</tr>
<tr>
<td>Sub-Saharan</td>
<td>4524 (26.1)</td>
<td>18</td>
</tr>
<tr>
<td>South Asia</td>
<td>2403 (13.8)</td>
<td>10</td>
</tr>
<tr>
<td>South East Asia</td>
<td>2793 (16.1)</td>
<td>11</td>
</tr>
</tbody>
</table>

Beyond geography – defining risk

- Incubation period plays an important role in triage
  - Most serious travel-related viral infections have incubation periods <21 days.
  - Most falciparum malaria cases present with in 1 month of return – but beware the exceptions and effect of prophylaxis.
- Travel Style:
  - Cruise ship, resort and urban travel <-- lower risk of serious travel-related disease.
  - VFR, adventure travel, “backpacking”, rural exposures, isolated destinations <-- higher risk.

VFRs – worth special consideration

- Travellers that are Visiting Friends and Relatives in developing countries are at highest risk of serious travel-associated infections.
  - Riskier activities
    - Low rate of pre-travel advice (~16%)
  - High risk destinations and travel styles
    - Up to 8x more likely to get malaria and 5x more likely to get a febrile illness than non-VFRs to same destination.

Key syndromes in geographic medicine

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Likelihood of being a “Serious” illness</th>
<th>% of ill travellers hospitalized</th>
<th>Important examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic febrile illness</td>
<td>High</td>
<td>46%</td>
<td>Malaria, Dengue, Typhoid, Hepatitis, EBV, HIV</td>
</tr>
<tr>
<td>Diarrhoeal illness</td>
<td>Moderate</td>
<td>15%</td>
<td>Shigellosis, Campylobacter ETEC, viral enteritis</td>
</tr>
<tr>
<td>Respiratory illness</td>
<td>Moderate</td>
<td>24%</td>
<td>Acute respiratory distress, pneumonia, tuberculosis</td>
</tr>
<tr>
<td>Genitourinary tract infection</td>
<td>Moderate</td>
<td>20%</td>
<td>Pyelonephritis, PID, UTI, STD</td>
</tr>
<tr>
<td>Dermatological illness</td>
<td>Moderate</td>
<td>20%</td>
<td>Acute cutaneous reaction, cellulitis, furuncle, acne</td>
</tr>
<tr>
<td>Non-diarrhoeal GI disorder</td>
<td>Low</td>
<td>No data</td>
<td>Intestinal obstruction, gastritis, hepatitis</td>
</tr>
</tbody>
</table>

† Likelihood of a serious may vary dramatically according to destination!!
Key geographical diseases

- Malaria, Dengue and Typhoid are the serious travel-related illnesses most likely to be encountered.
- Generally present as systemic febrile illness with or without localizing features.
- Severity of malaria (in particular) not always clinically apparent.
- Lab tests, blood smears, +/- imaging are required to assess severity.
- Timely intervention is lifesaving.

Malaria

- Human malaria is caused by one of 5 species of Plasmodium:
  - P. falciparum
  - P. vivax
  - P. ovale
  - P. malariae
  - P. knowlesi
- All are transmitted by stains of Anopheles mosquitoes
- Usually short lasting
- Can only be diagnosed with an appropriate lab test.
- Thick and thin blood smears (Gold standard) and RDTs (not available in Manitoba)

Malaria geography

- Risk of malaria in a one month stay (without prophylaxis)
  - Oceania (PNG, Papua [Irian Jaya], Solomon Islands and Vanuatu) 1:20
  - Sub-Saharan Africa 1:50
  - Indian subcontinent 1:500
  - Southeast Asia 1:500
  - South America 1:2,500
  - Central America and the Caribbean 1:10,000.
### Severe malaria criteria (WHO)

#### Clinical
- Impaired consciousness
- Prostration
- Failure to feed (usually applies to children)
- >2 seizures in 24h
- Respiratory distress
- Shock or systolic BP <70 in adults and <50 in children
- Jaundice plus evidence of other vital organ dysfunction
- Haemoglobinuria
- Spontaneous bleeding
- Pulmonary oedema (radiological)

#### Laboratory
- Hypoglycaemia (blood glucose <2.2)
- Bicarbonate <15 mmol/l
- Anaemia (Hb < 50 g/l)
- Haemoglobinuria
- Hyperparasitaemia (>2% in “non-immune”)
- Lactate >5 mmol/l
- Creatinine >265 μmol/l

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### Malaria management

#### Diagnosis of malaria

#### Uncomplicated
- From endemic area (premunition)
  - Consider outpatient oral therapy

#### Severe
- Not from endemic area (traveller, VFR) or pregnant
  - Admit for monitoring oral tx
  - Follow response

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### Dengue

- Four serotypes exist.
- Incubation 3-14 days (usually 4-7)
- No vaccine exists.
- Dengue virus is transmitted by day-biting Aedes sp. mosquitoes.
- Disease spectrum ranges from asymptomatic to haemorrhagic fever and death.
- Can only be definitively diagnosed with an appropriate lab test.
  - Serology or PCR - only available in reference labs.

#### Dengue – the disease

- Dengue fever, Dengue Shock Syndrome and Dengue Hemorrhagic fever are recognized syndromes.
- Dengue fever typically presents as undifferentiated febrile illness.
- Fever, rash, joint pain, headache, myalgias are common symptoms.
- Petechiae, purpura, mucosal bleeding, adenopathy, conjunctivitis may be seen.
- Positive tourniquet test.
- Dengue haemorrhagic syndrome (DHS)
  - Dengue fever with evidence of haemorrhage or capillary fragility.
  - MFD (Grade I DHS: definite, positive tourniquet test) to severe (Grade III and IV - overt significant haemorrhage).
- More likely to occur if previously infected with Dengue.

#### Dengue Shock Syndrome (DSS)
- DHS with evidence of shock (lactic acid, low BP, end organ damage).

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### Tourniquet test

- Inflating a BP cuff to between systolic and diastolic pressure for 5 minutes will trigger petechiae in patients with fragile capillaries.
- Commonly positive in Dengue fever.
  - >10 new petechiae per square inch suggests Dengue fever.
  - >20 per square inch suggests DHS.
- Non specific and should only be used in the right clinical context.

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### Dengue Geography

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[Guerrant et al. Tropical Infectious Diseases 3rd edition](http://www.tropicalinfectiousdiseases.com/)

[Guerrant et al. Tropical Infectious Diseases 3rd edition](http://www.tropicalinfectiousdiseases.com/)
Dengue warning signs

- Danger signs in patients with possible dengue are helpful for identifying patient with more urgent need for evaluation.
- Abdominal pain/tenderness
- Persistent vomiting
- Oedema (in any location)
- Lethargy or restlessness
- Hepatomegaly
- Thrombocytopenia and hemococoncentration (capillary leak)
- Positive tourniquet sign.
- Evidence of haemorrhage or bleeding
- Shock, haemorrhage, impaired consciousness are signs of severe dengue.

Dengue management

- There is no specific treatment for dengue.
- Supportive care (fluids, blood products, supportive care for shock).
- Steroids are not helpful.

Typhoid

- Typhoid fever is caused by the bacteria Salmonella enterica serotype Typhi (often called Salmonella Typhi).
- More rarely Salmonella serotype Paratyphi can cause the disease.
- Incubation is 3 to 60 days (usually 8 – 14)
- Acquired by eating contaminated food or drinking contaminated water.
- Does not typically cause diarrhoea.
- A vaccine exists (~50 - 60% effective) and prevention strategies work.
- Once ingested, bacteria crosses the gut, enters the bloodstream and can lead to shock, coma, CNS dysfunction, psychosis, GI haemorrhage and perforation.
- Overall mortality ~1%, mortality with severe disease is ~20%.
- Can only be diagnosed with an appropriate lab test
- Usually a blood culture

Typhoid – The disease

- Illness begins with malaise, myalgias and fevers that reach 40ºC.
- Rose spots appear in ~20% of Caucasians.
- Abdominal discomfort, headaches, fatigue and depression frequently occur. Constipation is common, diarrhoea is rare.
- Intestinal haemorrhage is a relatively common (~1%) complication and may lead to septic shock and death.
- Psychosis, hepatitis, osteomyelitis, endocarditis, meningitis and septic arthritis are rare complications.
- Relapses occur in ~8% without treatment, 10-35% with antibiotic treatment (amoxicillin, TMP-SMX, chloramphenicol) and are very rare with fluoroquinolone, azithromycin or ceftriaxone treatment.

Rose spots

- Subtle salmon-coloured patches, usually on chest, back and abdomen.
- Blanch with pressure.
- Only seen in fair skin.
- Only seen in 20% of fair-skinned.

Typhoid - Geography

- Typhoid – The disease
- Rose spots appear in ~20% of Caucasians.
- Abdominal discomfort, headaches, fatigue and depression frequently occur. Constipation is common, diarrhoea is rare.
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- Can only be diagnosed with an appropriate lab test
- Usually a blood culture
Risk of typhoid

- Varies greatly based on destination:
  - 1/3,000 travellers for travel to the South Asia (high risk)
  - 1/50,000–100,000 for travel to Sub-Saharan Africa, North Africa and the Middle East, or South America (intermediate risk)
  - < 1/300,000 for travel to the Caribbean and Central America (low risk).

Typhoid – warning signs

- Typhoid fever should be suspected in any traveller from an endemic area with a fever.
- Signs of severe illness include shock, CNS dysfunction, severe abdominal pain, obtundation, prolonged illness or prolonged fever (lasting > 1 week), melena.
- Presence of these requires urgent evaluation.

Management

- Management depends on severity, but all cases should be treated with antibiotics.
- Supportive care, ensuring a response to treatment (careful follow-up).
- Uncomplicated cases can be treated as outpatients with careful monitoring.
  - Oral fluoroquinolone or oral azithromycin where resistance is common (e.g. South and South East Asia).
  - Complicated cases require inpatient care.
    - IV fluoroquinolone or 3rd generation cephalosporin

You give me fever!

Case #1

- 29 year old male returns from Ghana after a 4 week holiday visiting friends and relatives.
- Presents to the ER 10 days after his return with sudden onset chills, fever, body aches.
- Has a severe headache.
- Did not seek pre-travel advise, took no prophylaxis and received no travel vaccines.
- Resided with his family near the town of Tamale, ate with his family, drank well water and slept without a bed net.
- Initial assessment shows a blood pressure of 100/65, temperature of 38.8º, tachycardia and respiratory rate of 28. No jaundice is noted, patient appear well hydrated and extremities seem well perfused. Rapid glucose is 4.2.

Question #1

- Could this be a serious travel-related illness?
  1) Yes
  2) No
  3) Possibly, but it’s rather unlikely
Question #2

- What serious tropical diseases are present in his destination?
  1. African tick typhus
  2. Malaria
  3. West-nile virus
  4. Chagas disease
  5. All of the above

Question #3

- What risk factors are present?
  1. The patient is of African origin
  2. The patient is partially immune to malaria
  3. The patient did not get malaria vaccination
  4. The patient was visiting friends and relatives

Question #4

- If it is malaria, is it severe malaria or uncomplicated malaria?
  1. Severe
  2. Uncomplicated
  3. Can’t tell

Follow-up

- He is sent to the waiting room after his assessment.
- 2 hours later, a health care aide asks the triage nurse to reassess as he is not responsive.
- On examination, the patient is convulsing, has a BP of 65/40 and is in respiratory distress.

What’s going on?

- Fever in a returned traveller is a medical emergency that requires close monitoring.
- Blood cultures, malaria smears are essential.
- 3 malaria smears > 8 hours apart should always be taken in patients suspected of having malaria.
- Other lab work is critical to rule out severe malaria.
- May confirm a diagnosis of severe malaria before clinical signs.
- Being from an endemic area does not confer immunity.
- Premunition is lost within ~ 1 year once exposure to malaria stops.

Guerrant et al. Tropical Infectious Diseases 3rd edition

Bloodwork

- Hgb 60
- Plt 30
- WBC 14.1 (N diff)
- Na 130, K 4.1, Cl 102, HCO₃ 14 mmol/L
- Glucose 3.9
- Cr 180
- Lactate 8 mmol/L
- AST 144, ALT 180
- Hemoglobinuria noted on urinalysis

African Journal of Biotechnology Vol. 9(10), pp. 1397-1401
Blood smear – 22% parasitaemia

DIAGNOSIS: SEVERE MALARIA

Malaria management

Uncomplicated

Severe

From endemic area (premunition)

Not from endemic area, premunition, or traveller

Hospitalized, treated with IV antimalarials

Artesunate based regimens are preferred for severe malaria.

Rash and fever

36 year old Canadian man returned from a holiday trip in Bangkok 8 days ago and presents with fever for the past four days.

Severe frontal headache, photophobia, muscle aches, severe back pain, nausea.

Noted conjunctival bleeding and a rash yesterday.

Stayed in tourist areas only, mainly Bangkok and Phuket.

Was exceedingly careful about avoiding risky foods and water.

Stayed in high class hotels but did daily excursions at numerous tourist sites. Used a mosquito net at night and stayed in air-conditioned hotels.

Took no malaria prophylaxis and received HAV, HBV, influenza and routine vaccines.

Initial investigations show T 39ºC, BP 112/77, HR 95, RR 16, glucose normal.

A rash and petechiae are noted.

Rash and fever

Case #2

Rash

Eyes
Petichiae

Question #1

Could this be a serious travel-related illness?
1) Yes
2) No
3) Possibly, but it’s rather unlikely

Question #2

What serious tropical diseases are present in his destination?
1. Tsutsugumushi fever
2. Malaria
3. Dengue
4. Typhoid
5. All of the above

Question #3

What risk factors are present?
1. The patient did not take malaria prophylaxis, which he should have!
2. The patient was exposed to day-biting mosquitoes
3. The patient did not get Dengue vaccination
4. The patient was visiting friends and relatives
5. All of the above

Question #4

What is the most likely diagnosis in this patient?
1. Malaria
2. Tsutsugumushi fever
3. Dengue
4. Hendra virus infection
5. Rabies

Worse case scenario...

He is sent to the waiting room.
4 hours later, another patient informs you he has vomited a large amount of blood and is lethargic.
On examination, he has epistaxis and hematemesis. BP is 90/70, HR is 120 and he has cool extremities.
Lab investigations

- Hgb 148, Pt 20, WBC 14 (40% lymphs, atypical forms noted), Hematocrit is 70%
- Na 138, K 5.1, HCO3 22
- Glucose 4.8
- AST 69 ALT 88

Dengue

- Combination of clinical presentation (fever, aches, rash, petechiae) and travel history make this diagnosis all but certain.
- Lab test (serology or PCR) can confirm the diagnosis.
- Management is supportive → fluids, expanders, blood products as required.
- Mild Dengue haemorrhagic fever can progress to DSS relatively quickly.
- Fall in platelets and rise in hematocrit often precedes shock.

Boil it, Peel it, Cook it or forget it!

Case #3

A 24 year old male originally from Bangladesh now living in Winnipeg returns from Bangladesh after visiting friends and relatives.

One week after returning, he felt unwell with rigors, fever (measured at 39.5ºC) and significant malaise. He presents 10 days after the onset of persistent fever.

He reports myalgias, weakness, fatigue and severe headache. He reports significant insomnia.

While in Bangladesh, he lived with his relatives and ate, drank and lived as they did. He had not sought any pre-travel advice or vaccines.

Initial assessment reveals a somnolent but rousable patient. T 38.7ºC, BP 112/77, HR 71, RR 16, glucose normal.

Question #1

- Could this be a serious travel-related illness?
  1) Yes
  2) No
  3) Possibly, but it’s rather unlikely

Question #2

- What serious tropical diseases are present in his destination?
  1. Hepatitis A
  2. Malaria
  3. Dengue
  4. Typhoid
  5. All of the above
Question #3

What risk factors are present?
1. The patient did not take malaria prophylaxis, which he should have!
2. He did not get hepatitis or any other vaccines.
3. He drank nasty water.
4. The patient was visiting friends and relatives.
5. All of the above

Question #4

What is the most likely diagnosis in this patient?
1. Malaria
2. Hepatitis A
3. Dengue
4. Typhoid
5. Rabies

Fever in a traveller is an emergency!

- Malaria smears, blood cultures and evaluation is essential!
- Blood counts, platelet counts, renal and liver function can help make a diagnosis and guide therapy.

Update

- He is triaged quickly and assessed by the EMO.
- Splenomegaly is noted, otherwise normal exam.
- Malaria smears are negative x 2.
- WBC 3.8, Pt 70, Hgb 155
- AST 62, ALT 72
- Creatinine 69
- Blood cultures are ordered.
- 4 hours into his admission, he complains of severe abdominal pain and is tender and guarding...

Typhoid fever

- South Asia has the highest incidences of Typhoid fever in the world.
- Malaria and Dengue, as well as other diseases are present.
- Complications include sepsis, intestinal perforation and haemorrhage and seeding of any organ.
- Risk of complications increases with duration of illness, presence of CNS dysfunction, shock at presentation.
- Treatment is supportive PLUS appropriate antibiotic therapy.

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The honeymooners

Case #4
The honeymooners

- A 24 year old female returns from her July honeymoon in Italy where she stayed only in four and five star hotels and traveled by train.
- Their honeymoon started in Rome with travel south to Naples and north along the Adriatic Sea to Venice.
- They returned to Winnipeg 10 days ago with no previous symptoms. Upon return, she had a mild headache and felt tired.
- On examination, she is afebrile, normotensive, and vitals within normal limits.
- Physical exam is unremarkable.

Question #1

- Could this be a serious travel-related illness?
  1) Yes
  2) No
  3) Possibly, but it’s rather unlikely

Question #2

- What serious tropical diseases are present in his destination?
  1. Malaria
  2. Dengue
  3. Typhoid
  4. All of the above
  5. None

Question #3

- What risk factors are present?
  1. Italians
  2. Mosquitoes
  3. Her husband
  4. Other tourists
  5. Her friends back home (when she got back)
  6. All of the above

Question #4

- What is the most likely diagnosis in this patient?
  1. Malaria
  2. West Nile virus infection
  3. Dengue
  4. Typhoid
  5. Rabies

Teaching point

- Destination is important!
- Italy has no significant "tropical" diseases that warrant emergent investigation or management.
- Italy has WNV, Chickungunya and Toscana virus – relatively common insect-borne illnesses. Enteroviruses circulate in the summer too...
- Bottom line: The destination suggests that this patient can be triaged like any other presenting from Canada.
The hyperactive colon

Case #5

22 year old previously healthy female presents to emergency for evaluation of profuse diarrhoea for 2 days.
Returned from a 14 day trip to Jamaica 3 days ago.
Did not take malaria prophylaxis, received HAV vaccine, recombinant cholera toxin B vaccine and routine vaccines.
Having 8-10 watery BMs per day x 2 days, no bloody stools, only vomited twice.
On examination, looks unwell, but is alert and responsive. Is afebrile, blood pressure is 110/65, heart rate is 89.

Question #1

Could this be a serious travel-related illness?
1) Yes
2) No
3) Possibly, but unlikely.

Question #2

What potentially serious tropical diseases are present in her destination?
1. Cholera
2. Dengue
3. Yellow fever
4. All of the above
5. None

Question #3

What is the most likely diagnosis?
1. Cholera
2. Malaria
3. Too much beer
4. Traveller's diarrhoea
5. Dengue

Question #4

What does the Dukoral™ vaccine prevent?
1. Traveller's diarrhoea
2. Cholera
3. Norovirus infection
4. Enteric Salmonella
5. Campylobacter
Question #5

- How should she be managed?
  1. Azithromycin and loperamide
  2. Supportive care (hydration, anti-nauseants, anti-diarrhoeals)
  3. Supportive care and ciprofloxacin.
  4. Malaria smears, stool cultures, examination for parasites and treat according to cause.

The weird and wacky

- Tropical medicine specialists evaluating returned travelers frequently entertain rare or exotic diagnoses.
- Travel-related cases of Ebola virus disease, Japanese encephalitis, leptospirosis, diphtheria, plague, malaria, murine typhus, Rift Valley fever, poliomyelitis, primary amoebic meningoencephalitis, and filariasis or yellow fever are exceedingly rare.
- Geosentinel survey (now >25,000 travelers seeking care) has yet to identify a single case of these.
- Hantavirus, VHFs other than Dengue, cholera, melioidosis, African sleeping sickness, Chagas disease may occur in travelers too, but are very rare.
- "Fever in a returned traveler is an emergency" will usually catch even these rare diagnoses.
- High degree of suspicion, appropriate tests and consultations will help identify them, should they occur!

Summary and Conclusions

- Recent travel can change the differential diagnosis significantly - always ask.
- Risk of severe travel-associated infection depends on destination, exposures and risks - always ask about them in travelers.
- The common serious travel-related infections are malaria, typhoid and dengue.
- Returned travelers from at-risk destinations with undifferentiated fever are at high risk of having a serious illness.
- Close monitoring and reassessment is key.
- Can progress rapidly and are potentially deadly.