Dengue and Chikungunya Virus Infections

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Disclosure of Potential for Conflict of Interest

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FINANCIAL DISCLOSURE

• None

• Consultant: Shorelands Inc.
WHO estimate: 50 million cases/year

Occurs in all tropical countries, currently epidemics in Latin America / Caribbean / India
Dengue: the agent

• A flavivirus
  – Single stranded RNA virus, types 1 - 4

• Vector: Aedes mosquitoes (day-biting)
Dengue: types of transmission

Epidemic dengue

• Single strain sweeps through a susceptible population with incidence of infection reaching 25-50%
  – Risk to travelers is high during the epidemic but low between epidemics

Hyperendemic dengue

• Continuous circulation of multiple serotypes
• Overall risk to travelers is higher than epidemic dengue
Dengue: clinical

- Incubation: 4-7 days (range: 3-14)
  - Many asymptomatic

- **Classic dengue fever**
  - Fever
  - Headache
  - Retro-orbital pain
  - Marked muscle and joint pains
  - Hemorrhagic features not limited to DHF
Dengue: clinical

- **Dengue ± warning signs (dengue fever)**
  - Constitutional symptoms including fever: 90%
  - HA, eye pain, body pain, and joint pain: 63-78%
  - Rash: ~50%
  - GI: >50%
  - Diarrhea: 30%
  - Respiratory: ~33%
  - Conjunctival injection, pharyngeal, erythema, lymphadenopathy, hepatomegaly: 20-50%
Dengue: clinical

• **Severe dengue**
  (formerly dengue hemorrhagic fever, dengue shock)
  – Immune enhancement following infection with heterologous or different strain
  – Vascular permeability (plasma leakage syndrome)
    • Hemoconcentration, pleural effusion, ascites
  – Marked thrombocytopenia with bleeding tendency
  – Hepatomegaly and/or abnormal liver function
  – CNS dysfunction
Dengue - Diagnosis

- Generally a clinical diagnosis
- Serology, acute and convalescent titers
- PCR, plaque reduction neutralization test (PRNT)

- Nonspecific laboratory findings:
  - Leukopenia
  - Thrombocytopenia
  - Transaminase elevation
Dengue

• Treatment
  – Supportive

• Prevention
  – Vector avoidance
This patient has conjunctival hemorrhage, spontaneous epistaxis, and platlets of 32K. Does he have Severe Dengue?
The answer is NO
He does not meet the WHO definition:

1) fever
2) hemorrhagic manifestations (or a positive tourniquet test)
3) platelets less than 100K
   and
4) one piece of evidence of increased plasma leakage (pleural effusion, ascites, hematocrit increased 20% over normal or drop of 20% with hydration, or hypoproteinemia).
Dengue

• Thrombocytopenia often occurs with uncomplicated dengue so that hemorrhage without plasma leakage does not constitute DHF.
Prevention - Dengue

- Personal protection measures to prevent mosquito bites
- Day biting *Aedes* mosquito
- Clean up breeding sites
- Peridomestic mosquitoes that like to breed in clean water, such as rain water collected in discarded water bottles or other containers
Chikungunya: the agent
A la Jay Keystone – “Dengue with arthritis”

• An Alphavirus
• Vector: *Aedes* mosquitoes
• Chikungunya means “that which bends up”.

![Chikungunya virus](image1.png)
![Aedes mosquito](image2.png)
Approximate Global Distribution of Chikungunya Virus, by Country, 2010

2004: Kenya
Indian Ocean islands

2007: Italy
2006: India
2010: France

2012
Cambodia
Indonesia
Philippines
Bhutan
PNG

2011: New Caledonia

Reunion: 1/3 population infected

Chikungunya: clinical

- Incubation period: 3-7 days (range: 2-12)
- Symptoms
  - Fever - usually ends abruptly after 2 days
  - Arthralgia/arthrits, HA, insomnia and prostration
    - last up to a week
  - rash, conjunctivitis, photophobia, fatigue
  - In middle age, joint pains may last 4-10 weeks,
    longer in elderly
  - Rarely fatal
Chikungunya

• Diagnosis
  – Viral culture, not readily available
  – RT-PCR
  – Serology (cross react with O’nyong’nyong virus and Semliki Forest virus)

• Treatment
  – NSAIDs
  – Chloroquine (for anti-inflammatory properties)?

• Prevention
  – Vector avoidance
QUESTIONS????
And then Malaria cases...
Reliable supply / standby therapy

- Higher risk of malaria – may be prescribed a full malaria treatment course to carry with them
- If ill, seek immediate medical attention for diagnosis
- Can then treat with the full treatment course they are carrying with them

- Avoids the risk of inappropriate drug-drug interactions
- Avoids counterfeit medicines
- Does not deplete local supplies of medicines

- Malarone and Coartem are now options
Take Home Messages

• Malaria is an important risk for many travelers
• Prevention is key
  – Assessment of risk of exposure
  – Prevention of anophelene bites
  – Assessment of appropriate prophylaxis
  – *** Fast and appropriate medical care in event of malaria
  – EDUCATE health care providers
Now you can prevent some cases...
Mr D is a 28-year-old healthy male. Travelling for 12 weeks, backpacking with a friend to Kenya, Tanzania, Uganda and Zambia. He is in good health, has no allergies, and is not on any medications. He will be travelling during the months of February, March, and April.
• What would you recommend for malaria prevention?
Africa

• WHO:
• Canada/CDC:
• EU:

Actually in agreement – this is a high risk area for CRPF.
All advise ATV/PG; Doxycycline; Mefloquine (Primaquine)
• Would you give him stand-by treatment/reliable supply?
Would you give him stand-by treatment (SBT) - reliable therapy?

Will he be able to get to medical attention if ill?
Will he be able to get safe drugs for treatment?
Will drug other than his prophylaxis be available?
What would you recommend for him to do about malaria prevention after he is treated for an episode of malaria??
His “friend” is actually his wife and figures that this will be a good, relaxed time to try to get pregnant.

What would you advise her about malaria prevention?
Recommendations for Pregnancy

• Travel to malaria risk area during pregnancy not recommended
• Risk for Mom and Babe
• Limited to CQ (no use in Africa) and MQ (some recommend only after the first trimester, more recently expanded to full pregnancy)
The Jones family are off to the Dominican Republic to visit a resort for a two week well deserved vacation. (Marg 33, Joe 34, Sally 5, Mikey 3)

What are you going to recommend about malaria prevention?
Dominican Republic

- **Areas with malaria:** All areas (including resort areas), except none in the cities of Santiago and Santo Domingo.
- **Estimated relative risk of malaria for US travelers:** Low
- **Drug resistance:** None
- **Malaria species:** *P. falciparum* 100%
- **Recommended chemoprophylaxis:** Atovaquone-proguanil, chloroquine, doxycycline, or mefloquine

2012 CDC Yellow Book
John and Tim are about to embark on an adventure through South East Asia. They have already blown the bankroll and plan to take in Cambodia, Vietnam, Thailand, and Laos over 12 weeks.

What would you advise about malaria prevention?
South East Asia – Malaria Recommendations
Some areas with both chloroquine AND mefloquine resistance

Bed nets?

What do you do for individuals in and out of risk areas?
• 34 year old man on eco-adventure in Borneo

• What would you recommend for malaria prevention?
Area of CRPF

Potential risk of leptospirosis with flooding and also risk for rickettsiosis
Malaria Decision Aid
Incorporating the ‘Ottawa Malaria Decision Aid’ into the standard pre-travel consultation process and assess its impact on a traveller’s malaria chemoprophylactic decision.
Traveller calls travel clinic to book pre-travel appointment (TOH) or emails request for appointment (Health Canada). Recruitment script is presented either as an email attachment (Health Canada) or directly by the clerk (TOH).

Is the traveller interested in learning more about the study? 

YES, Traveller is provided with study website address to learn more about the study (Health Canada and TOH). Completes screening questions (inclusion/exclusion criteria) online.

Does the traveller qualify for the study?

YES, Question on study website asking if traveller would like to participate.

NO, Traveller follows standard pre-travel process.

NO, Participants register online in order to complete the questionnaire.

Travellers Randomized

STANDARD CARE ARM

Traveller completes pre-appointment questionnaire online.

Traveller attends Pre-Travel consultation.

Traveller completes post-consultation questionnaire online.

Traveller completes post-travel questionnaire online once they return from travels and one week after malaria pills are finished.

DECISION AID ARM

Traveller completes pre-appointment questionnaire online.

Traveller completes Decision Aid section online.

Traveller attends Pre-Travel consultation.

Traveller completes post-consultation questionnaire online.

Traveller completes post-travel questionnaire online once they return from travels and one week after malaria pills are finished.

Figure 2. Traveller’s progress through the Ottawa Malaria Decision Aid Study.
IMPORTANT RESOURCES:

- Health Canada (www.travelhealth.gc.ca) [CATMAT]
- US CDC (www.cdc.gov)
- World Health Organization (www.who.int)
- International Society of Travel Medicine (www.istm.org)