Hot from the Tropics! Fever in the returned traveler workshop

UHN Conference 2015

Case 1: General approach to fever in the returning traveller

Exercise 1: Location of travel and pathogens

Pearls:

1. Focus on what’s common...i.e. the first column.
2. In all areas of the world, with the exception of Europe, malaria is a common infection, and is the **most common** infection encountered in those returning from Sub-Saharan Africa.
3. In the Caribbean, Central America and South America - dengue and malaria are most common infections encountered in returning travellers
4. In Southeast Asia and South central Asia, dengue and malaria are common, but enteric fever is also common - **70% of enteric fever is seen here**
5. In Sub Saharan Africa - tickborne ricketssia and acute schistosomiasis become a concern

Exercise 2: Effectiveness of vaccination and prophylaxis

Pearls:

1. Travelers visiting friends and family are a higher risk group because they are less likely to seek pre-travel counsel, obtain vaccination or prophylaxis
2. Malaria prophylaxis and Typhoid vaccine are **not** 100% effective
3. There is no prophylaxis for dengue

Exercise 3: Relevance of incubation period

Pearls:

1. When asking about travel history ask as far back as 6 months (some say 1 year)
2. Malaria can present in all time frames. Falciparum typically presents earlier than later compared to vivax
   a. Approximately 80% of patients with P. falciparum malaria develop symptoms within one month of returning from travel
   b. Only 36% of patients with P. vivax infection presented for medical care during the first month after return, about 20% were first seen more than six months after return, and 3 percent >1 year
3. Dengue typically presents within one week from exposure
Exercise 4: What investigations do you want to order?

Pearls:

1. Typhoid blood cultures are most sensitive in the first two weeks. Stool cultures are positive 3rd-5th weeks.
2. Dengue serology (Ig M) sensitivity and specificity of more than 93% if performed on or after the fifth day. Acute- and convalescent-phase serologies may be needed to confirm diagnosis as there is cross reactivity with other diseases (four time increase in Ig G or Ig M)

Exercise 5: Case wrap-up

Pearls:

1. Dengue is a viral illness transmitted by a mosquito bite, and not through human contact.
2. Most cases of Dengue are self-limiting: characterized by:
   a. Abrupt onset of fever, headache (often retro-orbital), severe myalgia/joint pain (so called Breakbone Fever)
   b. Rash (Confluent erythematous rash across chest, back, arms, legs with multiple discrete areas of sparing) in 50%
   c. Nausea, vomiting, abdominal discomfort
   d. Leucopenia, thrombocytopenia, increased hematocrit
3. Look for the following warning signs that can signal progression to more severe disease:
   a. Abdominal tenderness
   b. Persistent vomiting
   c. Clinical fluid accumulation
   d. Mucosal bleed
   e. Lethargy/restlessness
   f. Liver enlargement > 2 cm
   g. Increase hematocrit (by 20%) with rapid decline in platelets
4. Dengue hemorrhagic fever and shock occur in 1% of cases
5. Treatment is supportive
6. Admit if any warning signs

Case 2: A case of enteric fever
**Exercise 1: What is the differential diagnosis?**

**Pearls:**

1. If the clinical presentation is 2 weeks after exposure the likelihood that we are dealing with dengue or chikungunya decreases significantly

**Exercise 2: Match the following laboratory results to the following diseases: dengue, malaria, typhoid fever, acute schistosomiasis?**

**Pearls:**

1. Basic bloodwork findings are non-specific; they may help with your diagnosis, but should not be relied on

**Exercise 4: The next day you are working another shift. The charge nurse hands you a stack of cultures to follow up on. In it you find the culture results of your patient. The culture reads: gram-negative bacilli; final report pending. What is your differential diagnosis now? What do you do next?**

1. Enteric fever is caused by gram negative bacteria - Salmonella typhi and salmonella paratyphi A, B, C after ingestion of food or water contaminated with feces
2. Your initial blood tests can give you a clue to the underlying pathogen, but are very non-specific. Always do cultures. The diagnosis of typhoid fever is made using blood culture in the first 2 weeks. Stool cultures do not become positive until the 3rd week. Forget about the Widal test.
3. Do not forget to repeat malaria screens. The two diseases can co-exist.
4. Recall that typhoid vaccination only protects against Typhoid and NOT paratyphoid strains. Maximal protection against Typhoid is 75%, and this declines to 50-60% by 3 years.
5. Many cases of enteric fever do NOT present with pathognomic features (Rose spots, relative bradycardia, constipation) especially early on in the disease.
6. Most cases of typhoid fever we see in the Western world will be in the first week or two of the disease, presenting with non-specific constitutional symptoms (gradual onset fever, chills, diaphoresis, anorexia, dry cough, dull frontal h/a, myalgias)
7. “Rose spots” on central torso is seen in only 5-30% = 2-4 mm pink papules which fade on pressure seen in the second week.
8. Resistance to antibiotics is on the rise specially cases on Indian sub-continent. Follow up on the sensitivities.
9. Typhoid fever is a reportable disease to public health: it’s easily transmitted; carriers (3% of untreated patients) can spread the disease and need to be treated; patients can relapse.

Case 3: Malaria

Exercise 1: Based on the travel pattern, what are you most concerned about? What tests do you order?

Pearls:

1. The febrile traveller to a malaria endemic area should be considered to have malaria until proven otherwise.
2. The minimum basic tests for returned travelers presenting with fever include:
   a. Complete blood count with differential; liver enzymes; electrolytes; creatinine
   b. Malaria smears ± antigen detection dipstick at least 3 times over 24-48 hours
   c. Blood cultures x 2
   d. Urinalysis (± urine culture)
3. Other tests can be considered based on history, symptoms and epidemiology:
   a. Chest x-ray
   b. Consider NP swabs, sputum C&S, AFB if consistent with history and symptoms
   c. Stool culture (Salmonella, Shigella, Campylobacter, Yersinia, E. coli O157:H7)
   d. Stool for ova and parasites (Cyclospora, Cryptosporidium, Entamoeba histolytica, Giardia), consider C. Diff toxin
   e. Dengue serology (if incubation likely 2 weeks)
   f. Consider saving acute and convalescent serology for further testing if no diagnosis within 2 weeks
   g. STI testing
   h. HIV testing

Exercise 2: Are there any clinical features or lab findings (other than microscopy) that can aid in your diagnosis?

1. The clinical presentation and supplemental lab tests are not reliable!
2. However, some clinical and lab findings may be helpful in determining severity of illness, thereby guiding management.
Exercise 3:

Which malaria species are you concerned about? What treatment options are available for different malaria species? What are some considerations in choosing treatment medication for malaria infection?

1. Focus on prompt diagnosis and initiation of rapid treatment for malaria especially if severe malaria is suspected based on clinical picture. The patient may deteriorate rapidly!
2. Parenteral artesunate is recommended as first-line treatment for severe P. falciparum malaria in Canada, with parenteral quinine as an alternative. The PHAC website lists hospital pharmacies which stock both artesunate and quinine in Canada (grouped by region) along with contact info.
3. Exchange transfusion may have benefits for treating hyperparasitemic cases of P. falciparum.
4. The use of steroids to treat severe or cerebral malaria has been associated with worse outcomes and should be avoided.
5. The treatments of choice for uncomplicated P. falciparum malaria depends on chloroquine resistance and use of chemoprophylaxis.
6. Treatment for uncomplicated malaria should consist of a drug different to that used for prophylaxis.
7. To prevent relapses of P. vivax and P. ovale malaria, primaquine phosphate should follow chloroquine treatment. (Avoid primaquine in pregnancy and G6PD deficiency!)

Exercise 4:

Case evolution: The thick and thin smear for our patient shows falciparum malaria with a parasitemia level of 8%. How would you treat this patient and what is your disposition?

Pearls:

1. The overall case-fatality rate of falciparum malaria varies from about 1% to 5% and increases to 20% for those with severe malaria
2. High index of suspicion and prompt diagnosis = rapid initiation of treatment for severe malaria
Exercise 5:

Consider these clinical scenarios and questions:

- A pregnant woman from Indonesia presents with *P. vivax* malaria. What do you need to consider prior to initiating treatment?
- A development assistant arrives in Central Africa. It is his first journey abroad. Three days later he develops fever to 40°C. He was taking Chloroquine and Proguanil and thinks that he cannot have malaria. What do you think?
- A woman is brought in with high fever upon returning from a 3 week trip to Nicaragua. She looks unwell. Your colleague thinks that it might be severe malaria and quickly injects an ampoule of Chloroquine IV. What is he risking?
- Are patients with sickle cell anemia “immune” to malaria?
- Is there a malaria vaccine available?

Pearls:

1. Think Malaria! Malaria is very common; a very important cause of mortality and morbidity in (sub)tropical areas. Malaria must be ruled out in all patients presenting with fever post travel to endemic areas.
2. Four main parasites: *Plasmodium falciparum, P. vivax, P. ovale, P. Malariae* but occasionally infection with zoonotic malaria, such as *P. knowlesi*, may be regionally important (Southeast Asia)
3. Severe malaria is most commonly caused by infection with *P. Falciparum*. The diagnosis should be made early and treatment initiated rapidly.
4. Symptoms may vary: atypical, fever/rigors, anaemia, kidney failure, splenomegaly, altered level of consciousness.
5. Clinical diagnosis is not reliable. Diagnosis should be confirmed via thick & thin smear (gold standard), rapid antigen-detection or DNA-based methods (currently only used for quality assurance, not readily available). You need 3 negative smears over 24-48 hours to rule out malaria.
6. Chemoprophylaxis does not guarantee immunity. There is also increasing resistance of mosquitoes to various insecticides and increasing resistance of parasites to chloroquine in many regions (so even though precautions were taken, infection may still be present).
7. Beware of counterfeit medication purchased abroad for prophylaxis or treatment (i.e. ineffective chemoprophylaxis and/or treatment received abroad). This is very common and patients may have been ineffectively chemoprophylaxed and/or treated for malaria (or other illness) while abroad.
8. Vaccination is still in the experimental stage.
Case 4: Undifferentiated rash

Exercise 1:

Which diseases may present with a rash and fever following travel to the tropics?

Pearls:

1. Dengue and chikungunya as well as rickettsial infection are common causes of rash and fever in travelers returning from endemic areas.
2. Consider travel history, vaccination and potential exposures (especially in areas where outbreaks may be common ie. measles in unvaccinated populations, meningitis belt)
3. Don’t forget about STIs and non-infectious causes of rash and fever. (Acute HIV, secondary syphilis, disseminated gonococcal infection, vasculitis)
4. In addition, an adverse drug reaction, which calls for immediate interruption of therapy, must be considered.

Exercise 2: Match the rash to the disease.

Pearls:

1. Dengue, chikungunya and rickettsiosis are frequent causes of cutaneous rash and fever after a trip in the (sub)tropics.
2. Septicaemia due to meningococci is life-threatening and must be ruled out after travel to endemic areas in non-vaccinated individuals.
3. A disease that occurs after a trip does not necessarily need to have an exotic aetiology.
4. Consider uncommon diseases during outbreaks (Ebola) or preventable diseases in the unvaccinated (Measles)
5. Do not forget that STIs, cosmopolitan infections, non-infectious conditions as well as drug eruptions may manifest at any time.
6. Travel pattern and timing as well as labs may be helpful in determining cause of rash/fever.