A Safe Retreat?

Illness in the Returning Traveller

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Presented at the University of Ottawa's 31st Annual Pediatric Refresher Course, Children's Hospital of Eastern Ontario, Ottawa, Ontario, October 2006.

Increased recreational travel, globalization of economies, immigration and more Canadian families returning overseas to visit friends and relatives (VFR) has increased the frequency of international travel. VFR patients may be at higher risk because of longer length of travel and perceived immunity to local pathogens, such as malaria. The Center for Disease Control and Prevention (CDC) and the Public Health Agency of Canada (PHAC) maintain websites that can help the clinician distinguish geographically-focused infections.

The approach to travel-related illness is distinct in that the clinician needs to first rule out treatable infections that are likely to cause death and consider diseases of public health risk. Routine, cosmopolitan diseases can also be acquired while travelling but should never be assumed since mortality with some travel-related illnesses can be very high. Other infections, which present with more specific symptoms without fever, such as skin rashes or diarrhea, are less life-threatening and can be managed less acutely.

Pertinent points on history in persons with fever and recent (within six months) travel include:

- dates,
- duration,
- mode of travel,
- urban or rural residence,
- pre-travel prophylaxis and immunizations and
- whether they were tourists vs. VFR.

The three most common important causes of non-specific fever in the returning traveller are:

- malaria,
- typhoid and
- dengue fever.

Malaria

Malaria is the most frequent cause of systemic febrile illness in the returning traveller and carries a mortality rate as high as 20% in severe cases. Those particulary at risk for death include:

- children,
- pregnant women and
- non-immune travellers.

The risk of acquiring malaria is highest in Africa. Physicians should consult the CDC or PHAC websites for a complete list of countries where malaria is endemic. *Plasmodium (P) falciparum* is the most life-threatening of the four species of malaria. *P. vivax* and *P. ovale* cause a more indolent picture, but can have a long latency and may relapse due to the ability of the parasites to remain dormant in the liver.

Table 1

General guidelines for the treatment of uncomplicated or severe malaria

Uncomplicated *Plasmodium (P) falciparum*
- Atovaquone/proguanil taken for 3 days p.o.

OR
- Quinine or quinidine with doxycycline or clindamycin

Severe *P. falciparum*
(metabolic acidosis, severe anemia, central nervous system changes)
- Intravenous quinine
- Monitored bed
- Transfusion or exchange transfusion
- Committee to advise on Tropical Medicine and Travel statement for nearest center for supply

Incubation period

The incubation period ranges from eight to 25 days, but may be longer. The symptoms are often non-specific, but usually include:
- fever (that may be constant or intermittent),
- headache,
- nausea,
- chills,
- vomiting and/or diarrhea,
- myalgias,
- arthralgias and
- cough.

Routine, cosmopolitan diseases can also be acquired while travelling but should never be assumed since mortality with some travel-related illnesses can be very high.

Fever may be absent at the time of medical assessment in up to 40% of patients. Splenomegaly and hepatomegaly often occur, especially in chronic infections.

At least three malaria smears (thick and thin) are indicated in persons who have visited a malaria endemic area and who present with a febrile illness. Additional work up should include:
- a complete blood count,
- a platelet count,
- blood cultures,
- creatinine,
- liver enzymes,
- chest radiograph, or
- lumbar puncture, if appropriate.

Thrombocytopenia and anemia are also common.

Treatment

Malaria is a medical emergency. Initially, all cases or persons highly suspected of having malaria should be admitted and treated as chloroquine-resistant *P. falciparum* until speciation is available. Consultation with an Infectious Diseases expert should be sought. Every hospital pharmacy should have oral medication available for dispensing depending on the severity of the disease (Table 1). Parenteral quinine dihydrochloride may be obtained through the Canadian Malaria Network (http://www.phac-aspc.gc.ca/tmp-pmv/quinine/index.html). Patients infected with *P. vivax* or *P. ovale* should also receive treatment with primaquine phosphate after the initial treatment to eradicate the liver hypnozoites that remain in order to prevent malaria relapses. However, primaquine phosphate should only be administered if there is a normal amount of glucose 6-phosphate dehydrogenase enzyme.

Typhoid fever

Typhoid (enteric) fever is caused by *Salmonella typhi* and *Salmonella paratyphi*. They are acquired by fecally-contaminated water or food. Travellers to the following endemic areas are at greatest risk:

- the Indian subcontinent,
- Southeast Asia,
- South America,
- Central America,
- Africa and
- Eastern Europe.

Antimicrobial resistance has been reported to:

- ciprofloxacin,
- sulfonamides and
- tetracyclines.

A history of vaccination does not rule out the diagnosis as the vaccine is only 50% to 80% protective.

Incubation period

The incubation period is usually seven to 14 days. The symptoms may be biphasic, presenting with an initial enterocolitis with diarrhea lasing several days, with resolution and then recurrence of more non-specific symptoms. Symptoms may include:

- fever,
- chills,
- rash,
- diaphoresis,
- hepatosplenomegaly,
- headache,
- myalgias,
- confusion,
- psychosis and
- apathy.

At least three malaria smears (thick and thin) are indicated in persons who have visited a malaria endemic area and who present with a febrile illness.

Constipation can occur in 10% to 20% of those affected and as few as 20% may have abdominal pain. Patients may look unwell and may have hepatosplenomegaly on exam. Leukopenia and thrombocytopenia may also be present. Blood, stool and sometimes bone marrow cultures should be obtained.

Treatment

Initial treatment should include cefotaxime or ceftriaxone with modification once susceptibilities are known.

Dengue fever

Dengue is caused by a flavivirus, transmitted by day-biting *Aedes (A) aegypti* mosquitoes who breed in stagnant water, frequently in urban areas. Areas at risk include:

- Southeast Asia (especially Thailand),

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Take-home message

- Travel-related illness is becoming more common. Always proceed to consider the worst case scenario
- Malaria must be considered in a person with a fever or a history of a fever who has travelled to a malaria-endemic area in the prior six months
- Malaria is a medical emergency; three malaria smears 12 hours apart is standard of care
- Typhoid fever is generally diagnosed using blood cultures and empiric therapy should include third generation cephalosporins as quinolone resistance is high
- Dengue fever is common and also caused by a day-biting mosquito

- the South Pacific,
- Central America and
- the Caribbean.

Incubation period

The incubation period can vary from two to 14 days. Symptoms may consist of:
- high fever,
- chills,
- headache,
- myalgias and
- a classic erythematous reticulate rash over the:
  - thorax,
  - face and
  - flexion areas.

Also characteristic are:
- lymphocytosis,
- neutropenia and
- elevated aminotransferases.

Repeated infections can present as hemorrhagic dengue or shock syndrome with:
- hyponatremia,
- hypoproteinemia and
- circulatory collapse.

Serology (IgM and IgG) or dengue are helpful but may not be available acutely. Bacterial sepsis and malaria should always be ruled out with blood cultures and smears.

Management

Management is supportive, including:
- rest,
- fluids,
- antipyretics and analgesia and
- transfusion where indicated.

Use of the following should be avoided:
- steroids,
- non-steroidal anti-inflammatory drugs and
- acetylsalicylic acid. Dx

Resources
1. Arguin P, Kozarsky PE, Navin AW, et al: *Health information for international travel (CDC Yellow Book).* Mosby-Year Book, Atlanta, 2005-2006.
2. Freedman DO, Weld LH, Kozarsky PE, et al: Spectrum of disease and relation to place of exposure among ill returned travellers. N Engl J Med 2006; 354(2):119-30.