

## DECISIONS

# Fever and rash in a woman returning from the Caribbean

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**F**our days after a Caribbean vacation, a 31-year-old woman presents to her family physician with fever, rash and myalgia. On examination, she appears well. Her blood pressure is 116/90 mm Hg, her heart rate is 95 beats/min, and her temperature is 38.6°C. She has a diffuse, faint macular rash. Laboratory investigations show a leukocyte count of  $2.5$  (normal  $4.0$ – $11.0$ )  $\times 10^9/L$  and normal hemoglobin and platelets levels. Three thick and thin blood films performed 12 hours apart show no evidence of malarial parasites, and blood cultures yielded negative results.

## What is the most likely diagnosis?

The patient's presentation is highly suggestive of dengue, the most common cause of fever in travellers who have recently returned from Latin America, including the Caribbean.<sup>1</sup> Dengue is an acute viral illness transmitted by *Aedes* mosquitoes throughout the tropics and subtropics, mainly in urban and periurban areas.<sup>2</sup>

Dengue infection rates have increased dramatically in the past 50 years,<sup>3</sup> with current worldwide incidence approaching 390 million cases per year.<sup>2</sup> In North Americans returning from the Caribbean, South America, South-East Asia and South-Central Asia, dengue is a major cause of febrile illness and occurs more often than malaria.<sup>1,3</sup> Popular tourist destinations for Canadians, including Cuba, the Dominican Republic, Martinique, Mexico and Hawaii, have experienced recent dengue outbreaks.<sup>4,5</sup>

Physicians should consider dengue in febrile patients presenting within two weeks of return from an endemic area, although a shorter incubation period of five to seven days is most typical.<sup>3</sup> Common concurrent symptoms during the initial febrile phase include retro-orbital headache, myalgia, vomiting and an early, nonspecific macular rash.<sup>3</sup> In the immediate period around defervescence, known as the critical phase, patients are at risk of hemorrhage and complications related to increased vascular permeability. A distinct rash characterized by diffuse erythema with islands of sparing (areas of uninvolved skin)

typically appears just before recovery. Leukopenia, thrombocytopenia and transaminitis frequently occur. Combined symptoms and laboratory findings are more highly predictive of dengue infection, which is 71 times more likely in travellers with both fever and rash and 230 times more likely in those with fever, rash and leukopenia.<sup>3</sup>

## What diagnostic tests should be performed?

In any returning traveller who is ill, it is essential to initially rule out severe and potentially life-threatening infections requiring specific treatment, including malaria, typhoid fever, bacterial sepsis, influenza and rickettsial disease.<sup>3</sup> Chikungunya virus has been isolated recently in the Caribbean and should also be considered in returning travellers with fever.<sup>4</sup> Serologic testing for dengue lacks sensitivity in the acute setting, with only 50% of patients having detectable IgM antibodies on day 4 of illness.<sup>5</sup> A fourfold rise in convalescent IgG titres measured more than 14 days after symptom onset retroactively confirms dengue infection but rarely influences management because patients have already recovered. If available, enzyme-linked immunoassays or polymerase chain reaction assays targeting the viral NS1 antigen or its nucleic acids are helpful for the diagnosis of dengue in the early febrile period.<sup>5</sup>

## Should this patient be admitted to hospital?

Dengue in travellers is usually a mild, self-limited illness managed in an outpatient setting.<sup>5</sup> Less than 1% of travellers acquire the life-threatening constellation of severe plasma leakage, hemorrhage, end-organ damage and shock.<sup>3,6</sup> However, severe symptoms are possible. In one European cohort, 11% had internal hemorrhage, shock, plasma leakage or severe thrombocytopenia, and 23% required hospital admission.<sup>6</sup> Warning signs suggesting the need for hospital admission include abdominal pain or tenderness, persistent vomiting, third spacing (i.e. shifting of fluids into interstitial spaces), spontaneous

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mucosal bleeding, lethargy or restlessness, liver enlargement by more than 2 cm and increased hematocrit concurrent with rapidly decreasing platelet counts.<sup>5</sup> Physicians should consider inpatient monitoring for older patients, those with substantial medical comorbidities, infants and pregnant women.<sup>5</sup>

### How should this patient be monitored?

Patients receiving outpatient treatment for dengue need close follow-up. During the three- to seven-day febrile period and the ensuing 24- to 48-hour critical phase around defervescence, patients require almost daily complete blood counts and monitoring for severe dengue symptoms.<sup>5</sup>

### What treatment should be started?

Management includes supportive care and treatment of complications such as bleeding, fever, hypovolemia and electrolyte disturbances.<sup>5</sup> Acetaminophen is the appropriate choice for musculoskeletal pain and fever, and patients should be warned to avoid nonsteroidal anti-inflammatory drugs (NSAIDs) owing to an increased risk of bleeding.<sup>5</sup> A recent Cochrane review showed that corticosteroids are not beneficial, and may even be harmful compared with placebo, for the treatment of severe dengue.<sup>7</sup> Patients can expect a complete recovery, although some may experience prolonged postinfectious fatigue that will gradually resolve with time.

### What should I tell this patient about dengue prevention in the future?

The best prevention for dengue is to avoid mosquito bites. Wearing long-sleeved clothing and using a repellent that contains at least 30% DEET (diethyltoluamide) is the most effective way to elude day-biting *Aedes* mosquitoes. Prior dengue infection confers lifelong immunity to the infecting serotype, but only transient immunity to other

viral serotypes. More than one of the four dengue serotypes may cocirculate within an endemic area, and reinfection with a different serotype increases the risk for clinically severe dengue.<sup>5</sup> No effective dengue vaccine is currently available; however, this is an active area of research.<sup>8</sup>

### Case revisited

The patient received counselling related to appropriate hydration, avoidance of NSAIDs and monitoring for severe dengue symptoms. She was managed as an outpatient with daily follow-up and complete blood counts. Her fever and myalgia persisted for four days, and she took acetaminophen for symptom relief. Twenty-four hours after fever resolution, her platelet count decreased to 100 (normal 150–400) × 10<sup>9</sup>/L but returned to normal over the following 72 hours. Signs or symptoms suggestive of severe dengue did not develop. The patient remained fatigued in the two-week period following her acute illness but ultimately recovered fully.

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#### Patient and physician resources for the prevention, diagnosis and management of dengue fever

- Interactive map of worldwide dengue activity, [www.healthmap.org/dengue](http://www.healthmap.org/dengue)
- Physician information: clinical management of dengue, [www.cdc.gov/dengue/clinicalLab/clinical.html#links](http://www.cdc.gov/dengue/clinicalLab/clinical.html#links)
- Patient information: protecting yourself from mosquito bites, <http://travel.gc.ca/travelling/health-safety/insect-bite>