

Dengue Fever/Dengue Hemorrhagic Fever

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Abstract

In September 2009 the first documented, locally acquired cases of Dengue Fever in eighty years were diagnosed in individuals living in or visiting Key West, Florida. Dengue Fever is a mosquito-borne viral illness found throughout the tropics. There are four serotypes of the disease, which is accepted as the most common arthropod-borne disease in the world. Dengue Hemorrhagic Fever and Dengue Shock Syndrome are clinical variants of this disease, which have significant morbidity and mortality. *Aedes aegypti* is the mosquito species which carries the disease. *A. aegypti* breeds exclusively in standing fresh water and bites humans exclusively. The disease has a large percentage of clinically asymptomatic cases. When symptomatic, common symptoms are frontal headache, fever, and severe musculoskeletal pain. There are no currently approved vaccines.

Introduction

The first documented cases of locally acquired Dengue Fever (DF) in the Florida Keys in eighty years (forty years for the state of Florida) were diagnosed in the summer and fall of 2009.¹ This disease is commonly found in the tropics and is considered endemic to such vacation spots as Puerto Rico and the Virgin Islands. Also known as “breakbone fever,” due to the intense pain experienced by some patients, this illness is caused by a member of a family of viruses known as hemorrhagic fevers. Dengue Fever is a mosquito-borne (*Aedes aegypti* and rarely the *Aedes albopictus* species) disease with no apparent animal reservoir. The disease can also be transmitted via both blood transfusion and transplacentally during pregnancy. The initial case in the Florida Keys was found in a tourist who visited Key West and returned home to New York where she was diagnosed. The Centers for Disease Control and Prevention (CDC) deployed a team from its Dengue Branch in Puerto Rico to Key West in September 2009 after two additional cases in “locals”

were diagnosed. An extensive study of the local population was completed with the results showing a large number of IGM and IGG-positive individuals.

History

Illnesses consistent with DF are well documented throughout history. Dr. Benjamin Rush first described “bilious remitting fever” in the modern medical literature during an outbreak in Philadelphia, PA. in 1780. His account noted the general population had named the illness “breakbone fever.” The word “dengue” may be derived from the Swahili “Ka-Dinga pepo,” which means a cramp-like seizure from an evil spirit.² The exact origin of the disease is in question. Both the U.S. and the Japanese militaries were impacted by DF during the Pacific Campaign of World War II. DF was rare in North America and the Caribbean basin after World War II due to aggressive spraying programs. DENV-1 (see description below) was first seen in Cuba in 1977. The first case of Dengue Hemorrhagic Fever seen in the Americas was in Cuba in 1981 when DENV-2 was introduced to the island. Dengue Hemorrhagic Fever (DHF) was first documented in 1953 in Manila, the Philippines.³

Epidemiology

The disease Dengue Fever/Dengue Hemorrhagic Fever is caused by four closely related viruses (Flaviviridae family) DENV-1, DENV-2, DENV-3 and DENV-4. The four variants are indistinguishable clinically. The viruses are composed of a single strand of RNA, which is in the same genus as the Yellow Fever and West Nile viruses. Between 500,000 and one million individuals worldwide contract Dengue Fever/Dengue Hemorrhagic Fever annually, making it the most common arthropod-borne disease in the world.⁴ The disease is very common to urban environments in the tropics, and it is estimated that tens of millions of U.S. travelers visit endemic

areas annually.⁵ In the United States twenty-six states require the reporting of dengue infections. It is felt that competent mosquito vectors are located in twenty-eight of the fifty states.⁶ There are two passive surveillance systems run by the CDC. One is compiled from state health departments, while the other, ArboNet, also accepts reports from private laboratories. As well, there is a disease specific surveillance system run by the World Health Organization (WHO), known as DenguNet, which tracks cases worldwide. Isolated outbreaks of DF have been seen along the Texas/Mexico border intermittently between 1986 and 2005, and a large outbreak, 122 cases, occurred in Hawaii in 2001-2002. The Hawaii outbreak included at least one autochthonous case.⁷

Pathophysiology/Clinical Disease

The incubation period of DF in the mosquito is 8-12 days followed by an additional 3-14 days in the human host. This is followed by clinical disease lasting 3-7 days. The virus is easily passed from mature female mosquitoes to their offspring, and an infected mosquito is infectious throughout its lifespan. The levels of clinical dengue infection range from asymptomatic infection to critically ill patients with hemorrhage and shock. Case definitions are:

A. Asymptomatic or mild infection

Very common and by definition few or no symptoms besides fever

B. Dengue Fever (DF)

Fever and two or more of the below:

- a) Retro-orbital/ocular pain
- b) Headache
- c) Rash
- d) Myalgias
- e) Arthralgias
- f) Leukopenia
- g) Hemorrhagic symptoms not meeting the definition of DHF

C. Dengue Hemorrhagic Fever (DHF)

Meets criteria for Dengue Fever plus:

- a) Thrombocytopenia (less than 100,000 cells per mm²)
- b) Evidence of plasma leakage manifested by hemo-concentration (increase in hematocrit >20% of normal for age or a decrease < 20% after rehydration) or pleural effusion, ascites, or hypo-proteinemia.

D. Dengue Shock Syndrome (DSS)

Meets all of the criteria for DHF plus:

signs of shock; i.e., rapid pulse, narrow pulse pressure, and, most importantly, poor end organ perfusion.⁸

It is well established that individuals will develop antibody and lifelong immunity to the specific variant that they contracted as well as a transient immunity to all four of the variants. Only

when a second, third, or fourth infection (i.e., with a different variant) is contracted does the possibility of developing a clinical case of hemorrhagic disease occur. Transplacental transfer of maternal antibody can put an infant at risk for DHF.⁹

Differential Diagnosis

As fever and headache are the primary symptoms seen in DF, similar illnesses will drive the differential diagnosis process. Meningitis, encephalitis, and sinusitis are some of the etiologies of fever and headache that must also be considered. The lack of respiratory symptoms, such as sore throat and cough, make illnesses such as influenza less likely. A history of travel to a tropical environ should be elicited. Currently, the lack of such travel should remove DF from the differential.

Diagnostic Studies

DF is confirmed in reference laboratories using polymerase chain reaction (PCR) technology, which makes confirmation of the diagnosis during a case of clinical disease very unlikely. There is also PCR cross reactivity between the Dengue virus and several other similar organisms, such as West Nile Fever.¹⁰ The cases found in Key West were all DENV-1. Again, this information, if and when available, will almost certainly be reported long after the resolution of clinical disease. Routine diagnostic studies, such as a complete blood count (CBC), coagulation studies, and serum chemistries, will be of little value in the diagnosis of the disease but important in the management of the more complex cases. As long as there is only one variant of the disease found locally and the patient has no prior history of DF (i.e., prior travel), the hemorrhagic forms should not be an issue. In locations, such as Asia, where all four variants are found, DHF or DSS are of real concern.

Therapeutics

As with many viral illnesses, supportive measures are the cornerstone of therapy. In the more routine cases, analgesia may be the only therapeutic requirement. The uncommon cases of hemorrhagic disease may require more aggressive interventions, such as volume support, aggressive hemodynamic monitoring, and potentially transfusion of blood products including platelets.

Public Health Interventions

The primary public health intervention regarding mosquito-borne disease is the reduction in mosquito breeding habitat. Monroe County, Florida, the home of Key West, has an extensive mosquito control apparatus run by a Mosquito Control Board. Aggressive spraying, both airborne and on land, with trucks has been accelerated. The geographic location of the cases in Key West is in an area known as Old Town. This area is covered by large trees and foliage typical of many tropical cities and is likely impervious to spraying. The reduction of standing

water, probably best through a public education program, will likely have the best outcome. As the *A aegypti* mosquito breeds solely in standing fresh water, an intervention that focuses on reduction of these breeding habitats has been shown to be the most successful. Programs, such as those seen in Cuba in the early 1980s and Singapore in the 1990s, which focused on paramilitary style neighborhood programs have been the most successful.¹¹ There are no currently approved vaccines for DF, although several are being investigated.

Re-emerging Disease

The return of DF to the Florida Keys is another example of re-emerging diseases. DF has been described as one of the most common re-emerging infections.¹² It is currently unknown specifically how the disease re-established itself, but in a time of worldwide air travel, legal and illegal immigration, and international commerce, it should be no surprise that this has occurred. Key West is a mere ninety miles from Cuba, and it is not uncommon for “rafters” to land unannounced on its shores. It is possible the disease has actually been in the mosquito population in Key West and the Lower Keys for an extended timeframe. As stated above, much of the disease is asymptomatic or very mild and would therefore elude detection. The diagnosis of the tourist who returned home to New York may have opened an investigation into a disease not as new (to Florida) as might be originally thought. Primary care providers throughout the United States, Canada, and Europe should routinely include a travel history in all evaluations of a febrile patient.

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