# Dengue Virus: Another Type of Immigrant

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**ABSTRACT**

Dengue is a hemorrhagic virus contracted via the bite of a mosquito. Due to extreme changes in weather, increasing travel and immigration from tropical and subtropical climates, and increasing numbers of mosquito-borne illnesses, dengue virus infection presents a growing threat to the United States. The purpose of this article is to present etiology, pathology, management, and the latest treatment of dengue virus to prepare advanced practice nurses for early assessment and treatment of dengue virus.

**Keywords:** dengue, hemorrhagic fever, virus



A 6-year-old Latino male presented to urgent care with fever and body aches. A complete blood count indicated thrombocytopenia. The child's medical history included eczema and allergy to penicillin. A systemic examination was unremarkable. His parents were instructed provide hydration with a solution containing zinc, electrolytes, and glucose, along with a prescription for an antibiotic. In 2 days, the child presented to the emergency room with worsening fever, chills, fatigue, abdominal cramps, and bilateral petechiae on his lower extremities. Laboratory results indicated worsening thrombocytopenia and a positive antibody test for dengue virus with immunoglobulin M (IgM) 10.1 and immunoglobulin G (IgG) 0.32 (normal IgM and IgG $< 0.9$). The child was admitted to the hospital and given IV fluids, antipyretics, and nonsteroidal inflammatory drugs for 4 days. At discharge the boy's parents were advised to schedule a 2-week follow-up appointment with the general practitioner.

An estimated 2.5 billion people around the world are at risk to acquire dengue virus infection and 50 million will become infected within 1 year.[1] Due to extreme changes in weather, increasing travel, emigration from tropical and subtropical climates, and increasing numbers of mosquito-borne illnesses, dengue virus infection presents a growing threat to the United States. As a result, the Centers for Disease Control and Prevention (CDC) added dengue fever and viral hemorrhagic fever to the list of nationally notifiable diseases, which is a list of diseases that must be reported at local, state, territorial, federal, and international levels for purposes of monitoring, controlling, and preventing outbreaks.[2] The 2010 finalized data from the National Notifiable Diseases Surveillance System reported 690 cases of dengue virus infection and 10 cases of dengue hemorrhagic fever in the US.[3]

The prevalence of dengue virus raises concern due to its capacity to become epidemic and threaten the blood supply, which has caught the attention of the media, health-care professionals, and the general public. A retrospective study of cerebrospinal fluid and serum samples (n = 3,768), collected from 2003 to 2005 at the City of Houston Department of Health and Human Services Public Laboratory, identified 47 cases of dengue virus.[4] Postevaluation of 42 hospital records showed that 43% of cases met the World Health Organization (WHO) criteria for dengue fever, but at the time of hospital admission no dengue virus tests were performed due to lack of surveillance for the disease.[4] In March, 2011 the Miami-Dade County Health Department confirmed a second case of locally acquired dengue fever.[5]

Presentation of the etiology, pathology, management, and latest treatments for dengue virus are of critical importance. A search for "dengue virus" articles in PubMed (July 2014) yielded over 12,331 articles. Only 28 articles included clinical assessment, treatment, and diagnostic technologies from the last 5 years. Information from national and international agencies dealing with disease surveillance and prevention were also included. Exclusion factors include

case studies, genetic manipulation experiments, co-infection studies, medical devices, and alternative medicine.

As dengue virus enters the US and infection rates increase, advanced practice nurses will play critical roles in early assessment and treatment. Due to the pathogenicity of the virus, advanced practice nurses need to be aware of the symptoms, diagnostic technologies, potential for vaccines, and prevention methods.

## CHARACTERISTICS AND CLASSIFICATIONS OF DENGUE

Dengue is an RNA virus belonging to the family *Flaviviridae* with four serotypes (DENV1, DENV2, DENV3, and DENV4). Exposure to one serotype does not convey immunity to the remaining serotypes, but it does provide lifelong immunity to that specific serotype. DENV1 and DENV4 are often associated with a primary infection, whereas DENV2 and DENV3 are twice as likely to result in dengue hemorrhagic fever.[6] The extensive range of symptoms makes it hard to determine direct associations with serotype. Symptoms of subsequent infections become more severe as a result of cross-reacting antibodies. DENV2 occurs commonly as a secondary infection with higher monocyte counts and prolonged activated partial thromboplastin times.[7] A surveillance study from 2005 to 2010 showed that DENV3 was associated with musculoskeletal and gastrointestinal manifestations, and DENV4 was linked to respiratory and cutaneous manifestations.[8] Sequential or secondary infection may occur between serotypes or with other viruses.[9,10]

Dengue virus is transmitted by the *Aedes aegypti* and *Aedes albopictus* mosquitoes. Once the dengue virus enters the cells of the mosquito during a blood meal, the nucleocapsid is uncoated and viral RNA is translated as a single polyprotein.[11] The virion is made up of three structural proteins and seven nonstructural proteins.[11] An immune response pathway is initiated upon viral entrance into the mosquito.[12] The virus migrates to the salivary glands of the mosquito and is transferred during sequential blood meals to humans. Once infected, dengue virus can be transmitted through blood transfusions, organ transplants, or from mother to fetus.

The origins of dengue virus are traced to infectious cycling between nonhuman primates and mosquitoes.[13] DENV1 and DENV2 were identified in 1943 in Japan and in 1945 in Hawaii.[13] Over 70 years of epidemiologic and genetic data of dengue virus indicates progression occurred from Asia to the Americas between 1943 and 1981 with peaks reported between 2005 and 2009.[13] By 2013, Mexico, India, Indonesia, Africa, and Brazil reported the presence of all four dengue virus types.[13]

### Classifications of Dengue

Classification of dengue virus manifestations has been questionable due to variance of presenting symptoms and cross-reactivity among serotypes and other diseases. Mounting questions have suggested a need for new guidelines, classification, and case definitions.[14] The first dengue disease classification system was developed by the WHO in the 1960s during fever outbreaks in Thailand. This original classification system identified dengue at three levels of differentiation: dengue fever; dengue hemorrhagic fever; and dengue shock syndrome.[14] Dengue fever was defined as an acute febrile illness with two or more symptoms of headache, retro-orbital pain, myalgia, arthralgia, rash, hemorrhage, or leukopenia.[15,16] Classification of dengue hemorrhagic fever has four requirements: fever lasting 2 to 7 days; positive tourniquet test or spontaneous bleeding; platelet counts $\leq$ 100,000/mm$^3$; and evidence of plasma leakage.[15] Dengue shock syndrome was classified by internal hemorrhage, shock, platelet count $\leq$ 50,000/mm$^3$, and plasma leakage with hematocrit values $\geq$ 20% of the normal value for age and gender.[15]

Studies addressing changes in the classification system based on symptom presentation led to an updated diagnostic recommendation by the WHO in 2009. A study of febrile patients (n = 14,595) indicated that symptoms of myalgia, back pain, arthralgia, and bruising are more common in adults than children.[17] Myalgia and gastrointestinal symptoms showed significant differences between primary and secondary infections with myalgia reported more frequently in secondary infection ($P = .001$) and gastrointestinal symptoms more prevalent in primary infection ($P = .022$).[17] However, no significant differences in symptoms were observed among the serotypes.[17]