Dengue outbreaks in Hawai‘i After WWII – A Review of Public Health Response and Scientific Literature

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Abstract

The four serotypes of dengue virus (DENV) cause the most important and common arthropod-borne viral diseases in humans. There have been three major dengue outbreaks in Hawai‘i since 1946. The most recent and largest outbreak occurred on Hawai‘i Island in 2015-2016. This article reviews the public health response to dengue outbreaks over the period 2001-2016, as well as scientific literature on dengue outbreaks in Hawai‘i. As summarized in the assessment by the Centers for Disease Control and Prevention in 2015, Hawaii's response to the dengue outbreak was timely, appropriate, and well-coordinated. All facets of a public health response to the outbreak were adequately addressed, but communications and medical entomologic capacities could be improved. The observations of Aedes aegypti on Hawai‘i Island and of its co-localization with confirmed human cases highlight the importance of continuous vector surveillance and entomologic research. In-depth studies on the molecular epidemiology, entomology, and epidemiological investigation would provide new insights into the latest outbreak and into strategies to combat DENV and other arboviruses in the future.

Keywords

Dengue virus, Outbreak, Hawaii, Hawai‘i

Abbreviations

CDC = Centers for Disease Control and Prevention
DENV = Dengue Virus
ZIKV = Zika Virus
DF = Dengue Fever
DHF = Dengue Hemorrhagic Fever
DSS = Dengue Shock Syndrome
WHO = World Health Organization
HDOH = Hawai‘i Department of Health
DLI = Dengue-Like Illness
DEET = N,N-Diethyl-meta-Toluamide

Introduction

Dengue is a tropical disease spread among the human population by mosquitoes carrying the dengue virus (DENV). There are four serotypes, DENV1 through DENV4. DENV belongs to the genus *Flavivirus* of the family *Flaviviridae*, which includes several arthropod-borne viruses causing significant human diseases, such as West Nile virus, Japanese encephalitis virus, yellow fever virus, tick-borne encephalitis and Zika virus (ZIKV).[1,2] DENV is transmitted by *Aedes* mosquitoes, including *A. aegypti* and *A. albopictus*. Following DENV infection, individuals can be asymptomatic, or manifest with flu-like symptoms including fever, headache, retro-orbital pain, myalgia, arthralgia and rash, known as classical dengue fever (DF).[1,3] In some individuals it can progress to the more severe forms of the disease, dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), characterized by severe thrombocytopenia, hemorrhage, plasma leakage and shock that can lead to death.[1,3] A study in 2013 estimates that approximately 390 million individuals are infected with DENV every year, and about a quarter of them present with apparent diseases.[4] Infection with one DENV serotype provides long-lived protection against the same serotype but not other serotypes; epidemiological studies have shown that secondary DENV infection with a different serotype has a higher risk of developing severe disease, DHF/DSS, compared with primary infection.[1] While several dengue vaccine candidates have been in different phases of clinical trials for several years, only one, Dengvaxia from Sanofi Pasteur, is currently licensed in a limited number of countries. The efficacy of Dengvaxia is ~60% overall and ~40% among the dengue naïve population, who have never been exposed to DENV in the past. Due to safety concerns, Dengvaxia is no longer recommended for dengue-naïve individuals and was suspended in some countries like the Philippines recently.[5-7]

DENV1 was first isolated in Japan in 1943, followed by DENV2 in Hawai‘i in 1945.[2] Dengue is spread to Hawai‘i when individuals are exposed and infected by DENV out-of-state during their travels to endemic regions, and upon their return introduce the virus to *Aedes* mosquito populations in Hawai‘i. The indoor-feeding *A. aegypti*, known as the principal vector, is more efficient in DENV transmission compared with *A. albopictus*, which is more common in Hawai‘i. During the past three decades, population growth, urbanization, lack of effective mosquito control, increasing travel and other factors have contributed to the global emergence of dengue especially in developing countries[2,8] According to the Centers for Disease Control and Prevention (CDC), dengue is endemic in the following United States (U.S.) territories: Puerto Rico, the U.S. Virgin Islands, American Samoa, and Guam. At least 100 countries are endemic for dengue in Asia, the Pacific, the Americas, Africa, and the Caribbean.[9]

There have been three dengue outbreaks in Hawai‘i since 1946: on Maui, O‘ahu and Kaua‘i in 2001-2002, on O‘ahu in 2011, and on Hawai‘i Island (Big Island) in 2015-2016. During the most recent (2015-16) outbreak, there were 264 confirmed cases, 238 of which were residents of Hawai‘i Island.[10] This article reviews the public health response to dengue outbreaks over the period 2001-2016, as well as scientific literature on research of the dengue outbreaks in Hawai‘i. Despite the revised World Health Organization (WHO) case definition (dengue, dengue with warning signs, and severe dengue) published in 2009, this review uses the traditional case definition (DF, DHF, DSS) to be consistent with several references cited.[2]

Methods

The authors searched and reviewed reports from government, state and organizations, as well as published literature through the PubMed database. Searching with the key words "Dengue outbreak" and "Hawaii", as of October 12, 2017 resulted in a total of 27 articles, of which 17 were excluded due to non-Hawai'i (such as Marshall Island, South Pacific, Puerto Rico, etc) or non-dengue topics (such as West Nile virus, etc.). The remaining 10 articles (references 11 to 14 and 16-21) together with the references cited in these articles were reviewed.

Results

Outbreak in 2001-2002

The 2001 outbreak started in May 2001 and lasted into 2002. In total, there were 122 confirmed cases (92 on Maui, 26 O'ahu and 4 Kaua'i) of the DENV1 serotype. The virus was most likely imported by travelers from the Society Islands in French Polynesia, which at the time was undergoing a much larger dengue epidemic with over 33,000 falling ill from February to November of 2001.[11] This was supported by a molecular epidemiological study of sequences encoding the envelope-protein of DENV1 isolates, which showed that two strains of DENV1 were introduced to Hawai'i: one from Tahiti, which was identified in most of the isolates, and one from Samoa, identified in a single isolate.[12,13]

A study noted that confirmation of the outbreak in Hawai'i was delayed by the lack of in-state capacity to test for dengue at the time.[14] After the CDC confirmed the Hawai'i outbreak on September 21, 2001, the Hawai'i Department of Health (HDOH) immediately sent out a statewide email alert to physicians asking them to test all patients for dengue if they exhibited dengue-like illness (DLI), defined as "fever or chills plus two or more of the following symptoms: myalgia, headache, arthralgia, eye or retroorbital pain, rash, or hemorrhagic manifestation." Eighty nine percent of the laboratory-positive cases presented with DLI.[11] There were cases with hemorrhagic symptoms, but none with DHF or DSS, in contrast to the Society Islands outbreak in which 45% of the hospitalized cases presented with DHF, and some with symptoms of DSS.[11] Several possibilities may account for the difference in disease severity between the two outbreaks; one being that the population of the Society Islands, compared with that of Hawai'i, are more likely to have had a previous DENV infection and thus experience a secondary DENV infection, which has been shown to have a higher risk of causing DHF/DSS than primary DENV infection.[1,15]

Among the many public health measures implemented in Hawai'i were: free laboratory testing for all suspected cases, active surveillance at over 50 medical facilities in Hawai'i, a patient-tracking system, the utilization of Epi-X (an online CDC resource for public health professionals), assistance with phlebotomy, lectures on dengue given at local medical centers, press releases (eg, daily case counts, information on how to eliminate breeding sites), and more.[11]

Vector control during the outbreak included actively reducing mosquito populations and educating people on specific prevention methods. This was accomplished by spraying insecticide in a 200-meter radius around case homes (adulticiding), and by breeding site control through elimination of standing water and collection of trash that could hold standing water.[11,14,16] Public health authorities performed private and public property inspections to identify buildings in close proximity to large mosquito/larvae populations and mosquito breeding sites, even rolling out door-to-door source reduction campaigns. During the DENV1 outbreak on Maui, a seroepidemiological survey of a community with a high incidence of dengue, in comparison with another community with low incidence, reported that about half of the inspected properties contained mosquito larvae, suggesting a "need for more effective community mosquito control." The same study also identified the presence of birds in one's house or yard as "significantly associated with infection," and posited that *A. albopictus* may be attracted to birds or to environmental conditions that birds reside in.[17]

During the outbreak, HDOH vector control staff conducted entomological surveys in 29 communities on O'ahu, Maui, Moloka'i, and Kaua'i to identify the species responsible for transmitting DENV.[11] The species was found to be *A. albopictus*, compared with *A aegypti* which is a less competent vector for transmitting DENV but more common in Hawai'i. The islands' vegetation provides an ideal habitat for *albopictus*, which prefers to live in non-urban areas. A study of the vector-to-host ratio map confirmed that most cases in O'ahu were found in areas with "sparse settlements," as opposed to the population-dense city of Honolulu.[18]

The state of Hawai'i launched aggressive campaigns and responded proactively to provide the public with information, support, and transparency on the nature of the disease and updates on the outbreak. The HDOH held media interviews, public service announcements, and town meetings, and developed a dengue education website. Educational brochures for travelers and tourists were distributed at car rental agencies and hotels. In Hana, individuals were posted at highway checkpoints to distribute mosquito repellent and educational materials about dengue.[11,14]

A previous study suggested that, given the variation between communities in attending public information sessions or accessing media sources, public relations responses should be customized by community.[14] Due to the dependence of Hawaii's economy on tourism, the epidemiologic and vector control response "had to balance the need for protective action...with the need to avoid discouraging tourism."[14] However, a study of a group of 4,000 people who visited Hawai'i at the peak of the dengue outbreak showed that only "94 (3%) experienced a DLI either during their trip or within 14 days of departure," and 27 of the 94 tested were found to be negative for anti-DENV IgM antibodies. Researchers concluded that individuals who visited Hawai'i during the 2001 outbreak had a low risk for DENV infection.[19]

DLI can be presented by other acute febrile illnesses including viral and bacterial diseases, such as leptospirosis which is prevalent in Hawai'i. A study investigated anti-leptospira IgM

antibody in 1206 patients, who had DLI but were negative for dengue, and reported 54 leptospirosis cases during the 2001 outbreak.[20] The study identified three clinical symptoms (rash, chills and petechiae) significantly less common among leptospirosis cases compared with dengue cases, and indicated that many leptospiral infections in Hawai'i go undiagnosed. Another study in 2005 examined serum samples from seven Hawaiian residents who recalled experiencing flu-like symptoms during the WWII, and found the presence of antibodies to DENV1 more than 60 years after the 1943 dengue outbreak in Hawai'i.[21]

Outbreak in 2011

The second of the three dengue outbreaks in the 21st century began in February 2011 in Pearl City, O'ahu. An HDOH news release on March 24, 2011 announced two confirmed and two suspected cases of dengue on O'ahu, and stated that a medical alert had already been sent out to physicians "advising them to consider potential DENV infection in persons with compatible symptoms, request appropriate laboratory testing, and report all suspected cases to the HDOH". In total, there were 4 dengue cases; all were infected near their homes by mosquitoes.[22]

During the time, the HDOH immediately initiated several precautionary measures including additional testing, surveying and a mosquito control plan for the areas where cases were probably infected. Updated information regarding vector source reduction (such as cleaning up breeding sites, emptying standing waters, checking gutters, etc) and protection against mosquito bites (such as repellant containing 20%-30% DEET or picaridin to skin and clothing, window screens, lighter-colored clothing, etc) were provided on the HDOH website.[22]

Outbreak in 2015-2016

The most recent dengue outbreak in Hawai'i started in September 2015 on Hawai'i Island, primarily in South Kona.[10] Two-hundred sixty-four confirmed dengue cases (218 adults and 46 children) were reported. It was the largest outbreak of dengue in a non-endemic area of the U.S. since 1946. The 2015 and 2001 outbreaks were similar in scale. One difference between the two outbreaks was that fears surrounding the 2015 outbreak were followed by fears of ZIKV spreading in Hawai'i, given that the *Aedes* mosquito transmits both DENV and ZIKV. The 2015 outbreak happened to occur around the same time that many countries were experiencing Zika outbreaks, and the WHO declared Zika a Public Health Emergency of International Concern on February 1, 2016.[23]

The mayor of Hawai'i County, William P. Kenoi, declared a state of emergency on Hawai'i Island on February 2, 2016.[24] The state of emergency included the suspension of a county law allowing tires to be deposited at Hawai'i County landfills; discarded tires collect small pools of water that serve as prime breeding spots for *Aedes* mosquitoes. Several activities also occurred well before the state of emergency. The HDOH updated its website to include an online map of disease risk areas that was routinely updated until April 20, 2016. [10] Electronic information and resources on DF and mosquitoes were provided, including brochures in Spanish, Samoan, Marshallese, Japanese, Ilokano, Hawaiian, English, Chuukese, Tongan, and Tagalog. Also, phone lines to call for additional information or to report suspected cases of infection were made available. The state also launched a disease education campaign called "Fight the Bite."[10]

In a report assessing the state's response to the outbreak, the CDC lauded the extensiveness of Hawai'i County's community outreach efforts to encourage individuals to protect against and report infection.[25] Overall, it considered Hawaii's outbreak response a "model for others." However, it recommended a greater social media presence and the organization of online information in a more user-friendly manner, and repeated its past recommendation to customize public relations responses at the community level. Moreover, a CDC team member failed to find information about dengue at the few selected hotels and airports that he visited; while not from a systematic evaluation, the observation appears to contrast with the 2001 outbreak response tactic of distributing information at tourist- and traveler-heavy areas.[25] Indeed, efforts to distribute information were ongoing as the outbreak progressed, so information likely reached more areas and individuals. The same CDC report stated that the epidemiologic surveillance was "timely and sufficiently sensitive to monitor temporal trends and geographic patterns of spread."[25] However, the report suggested future assistance from the CDC, describing the epidemiological resources as "taxed" and hypothesizing that another outbreak or significant health event would overwhelm state resources. For example, the report found that all of Hawai'i depends on two HDOH entomologists stationed in Honolulu.

Regarding entomologic control, the state aimed to reduce mosquito populations by adulticiding, primarily around case homes where individuals had been infected, as well as around schools. The CDC cited the amount of dense vegetation around households, long distances between households, unoccupied homes, homeowner and farm owner opposition to chemicals, and the scarcity of staff and equipment as factors preventing more widespread, standardized adulticiding (ie, at non-case properties).[25] The state also employed "mosquito surveys," larvicidal mechanisms by which standing water was dumped out or treated with soapy water. The soapy water treatment is not standardized or scientifically proven to be larvicidal in the field.[25,26] Laboratory testing of DENV, on the other hand, had improved since the 2011 outbreak, and in 2015 were done in-state within 1-2 days of sample receipt at the State Laboratories Division in Honolulu.[25]

The first scientific report of the 2015-2016 outbreak by the Hawai'i Dengue Response Team has been published.[27] Two studies on the mosquitoes in Hawai'i before this outbreak provide important insights into the outbreak.[28,29] They reported the presence of *A. aegypti*, the principal vector of DENV, on Hawai'i Island, and interestingly the distribution of *A. aegypti* co-localizes with the distribution of human cases, mainly in the east and west coasts of Hawai'i Island, including Hilo and Kona and Keelakekau.[10,28]

Conclusion

Compared with dengue-hyperendemic regions, the three dengue outbreaks in Hawai'i since 1946 were relatively small with less than 300 confirmed cases, no DHF or DSS cases, and comprised a single serotype during each outbreak. The public health response including disease surveillance and testing capacities has greatly improved.[25] As summarized in the CDC report in 2015 for the most recent outbreak, the response of the HDOH to the dengue outbreak has been timely, appropriate and well-coordinated between the state and county. All facets of a public health response to the outbreak have been addressed adequately, including community outreach, surveillance, diagnostic testing, medical care, and vector control, although communications and medical entomologic capacities could be improved.[25]

The 2001-2002 outbreak may have been limited in scale due to the transmission by the less competent vector *A. albopictus*.[11] However, the most recent outbreak took place on Hawai'i Island, where the more competent vector *A. aegypti* was present and co-localized with the confirmed human cases, raising concerns of the role of *A. aegypti* and/or *A. albopictus* in this outbreak and/or for future outbreaks of DENV or other arboviruses (including ZIKV and chikungunya virus, both transmitted by the two species). Continuous vector surveillance and entomologic research in Hawai'i are needed. Although the most recent outbreak has passed, dengue and other arboviral diseases continue to pose a very real threat to Hawai'i and similar regions. A limitation of this review is the lack of peer-reviewed scientific papers associated with the two most recent outbreaks. Future studies on the molecular epidemiology, entomology, epidemiological investigation and risk factors would provide new insights on the introduction and spread of DENV in the Hawai'i Islands. This multidisciplinary approach and collaboration is exemplified by a recent investigation of ZIKV in Florida.[30] This information is not only important for the scientific community to understand the largest dengue outbreak in non-endemic regions of the U.S. since 1946, but is also relevant to local community and public health sectors. New strategies based on research done in Hawai'i to fight against DENV and other arboviruses in the future are critically needed.

Conflict of Interest

None of the authors identify any conflicts of interest.

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