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Climate Change and Dengue Fever: Are They Connected?

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Climate Change and Dengue Fever: Are They Connected?

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Introduction

Dengue virus is the most common mosquito born disease worldwide and is an endemic infection in many tropical and subtropical habitats, especially areas where poor public health infrastructure makes it difficult to control. According to the Centers for Disease Control and Prevention (CDC), the dengue virus is a leading cause of febrile illness among travelers returning from Latin America.[1] The dengue virus is a member of the family Flaviviridae and is transmitted to humans by the vector *Aedes* mosquitos, most frequently the *Aedes aegypti* mosquito, and secondarily by *Aedes albopictus*. Dengue infection results in a spectrum of clinical disease, ranging from asymptomatic to death. Infection with dengue virus is a significant global health challenge as an estimated 390 million infections occur annually.[2] The number of annual infections continues to rise, with the reason for this growth being multifactorial. Suspected factors playing a role include climate change, urbanization, population growth, poor sanitation, poor public health infrastructure, international travel, international trade, precipitation, and geographic mosquito expansion. [2-8] In recent years, autochthonous dengue cases have even been reported in the United States; a region which had not seen reports of dengue for 75 years.[3]

There are four antigenically distinct dengue virus serotypes (DENV-1 to DENV-4), and infection with one serotype provides lifelong immunity to the infecting serotype; however, cross protection against the other three is temporary, typically lasting about two years.[8,9] The dengue virus is transmitted most commonly by *Aedes aegypti*, and these mosquitos typically acquire the virus through the ingestion of infected human blood. Upon initial infection, people may remain asymptomatic or can develop a self-limited disease that manifests with a combination of fever, headache, retroorbital pain, weakness, maculopapular rash, myalgias, arthralgias, and minor bleeding.[1,8,10] The combination of these symptoms is known as dengue, or breakbone, fever.

Infection may lead to more severe conditions known as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). The most recent WHO classification system classifies DHF and DSS as severe dengue, and this may present with persistent vomiting, hematemesis, abdominal pain, hematochezia, increased mucosal bleeding, dyspnea, shock, and death.[1] Severe dengue is most commonly seen in young children and those re-infected by a separate dengue serotype.[8,11,12]

Dengue not only causes great suffering to those infected, but it also has significant economic and societal impact. Societal cost for prevention, medical care, surveillance, and lost-productivity vary, but estimates are as high as $39 billion per year worldwide and $1 to $4 billion each year in the Americas.[10,13] The development of therapeutics and vaccinations could play an important role in decreasing the societal cost of this disease.

Currently, healthcare workers have ineffective ways of predicting which patients will progress to the severe spectrum of disease. Despite its global presence, treatment options remain sparse, with prevention and supportive care being the most highly recommended options. Supportive care includes hydration, fever control with acetaminophen or sponge baths, and the avoidance of aspirin and NSAIDs to decrease bleeding risk.[1] The hope for the development of an effective vaccination remains, but vaccine trials thus far have shown poor effectiveness in people without pre-existing immunity.[14,15] Because it is highly prevalent and poor treatment options currently exist, global research efforts should be undertaken to improve educational strategies that address vector control and prevention in endemic areas. The populations with the highest risk of contracting dengue are shown to be within Central and South America as well as South Asia.[2]

It is frequently hypothesized that climate change will play a dramatic role on future geographical distribution of mosquito borne diseases such as dengue. The earth's climate is constantly changing, and over the past three centuries the earth has experienced a period of warming.[16] According to the National Aeronautics and Space Administration (NASA), mean global temperature has increased by 1.9°F since 1880, and 18 of the 19 warmest years on record have occurred since 2001.[17] This trend is attributable to the greenhouse effect, which is a consequence of when gases such as carbon dioxide, methane, water vapor, and nitrous oxide accumulate in the atmosphere and trap heat radiating away from Earth.[18] The burning of fossil fuels, such as coal and oil, is the single largest source of greenhouse gas emissions, accounting for 72% of all gases.[19] Regardless of the cause, increasing temperature will likely impact dengue infection and societal cost in future years.

This paper will explore whether climate change plays a role in the prevalence, incidence, and transmission of dengue infections within the Americas. In addition, other variables contributing to the spread and prevention of dengue will be addressed as well as the impact dengue has on the Costa Rican population.

Background

Epidemiologic trends of dengue infection

Dengue virus is a common arthropod born virus that is a major global health issue impacting millions. The first reported epidemics of dengue like illness in the Americas were reported in the 1600s.[6] Since this time, dengue infection has increased significantly both in the Americas and worldwide. The WHO reports that dengue burden has increased by 2,450 fold between 1955 and 2010.[20] From 1955-1959, there were 908 annual global cases reported to the WHO. Between 2000-2007, this increased to over 900,000 cases reported annually; and in 2010, there were

2,204,516 reported cases.[20] In the Americas, dengue is also increasing; in 2000 there were 400,519 cases of reported dengue, whereas in 2013 this increased to 2,386,386 cases.[9] Incidence rates in the Americas have also risen on a per capita basis from 16.4/100,000 people in the 1980s, 35.9/100,000 in the 1990s, to 71.5/100,000 in 2000-2007.[7] Additionally, the number of dengue hemorrhagic fever cases has also grown from 0.2/100,000 in the 1980s to 1.7/100,000 in 2000-2007.[7]

The first global estimates of dengue infections were calculated in the late 1980s to early 1990s, and these were based on approximations of the population at risk and assumed annual infection rates. The World Health Organization (WHO) currently estimates that 50-100 million infections occur annually, with 20,000 resulting in death.[20] Recent estimates by Bhatt et al. estimate that 390 million people (range 284-528 million) are infected each year, with 96 million (range 67-136 million) manifesting clinically.[2]

Bhatt et al. argues that WHO estimates were calculated informally, so new calculation methods were developed to predict true infection incidence based on the global population in 2010. The goal of the study by Bhatt et al. was to compile estimates of both apparent and inapparent dengue infection. To do this, they created a statistical model using 8,309 geo-records of dengue occurrence that incorporated environmental and socioeconomical transmission factors within each 5 km x 5 km area globally. This model was run several hundred times and then compared to previous studies looking at dengue incidence, and from this they were able to develop estimates of both apparent and inapparent infection. From this model, it was estimated that there were 96 million apparent dengue infections in 2010, with an additional 294 million inapparent infections.[2]

Impact of climate change and temperature on dengue

Increases in global dengue infection is complex and multifactorial. Several causes have been implicated in the surge of dengue, such as climate change, temperature, precipitation, urbanization, population growth, poor sanitation, poor public health infrastructure, poor vector control measures, international travel, international trade, and increased global mosquito distribution.[2-8]

Several statistical models have demonstrated that local temperature and levels of rainfall have a strong influence on dengue transmission, and Bhatt et al. suggest that these are the greatest two risk factors.[2,5,12,21,22] Temperature plays a critical role because it has been implicated in mosquito biting rate, mosquito development, virus incubation time, mosquito survival, and egg laying by mosquitos.[2,3,22-26] Dengue is a climate sensitive disease, and most countries demonstrate seasonal variation in dengue infections; incidence tends to be higher during rainy and warm seasons. A recent systematic review of 33 articles suggested that temperatures of 22℃ to 29℃ are the optimal temperature for dengue transmission.[27] In a study by Tun-Lin et al., they found egg, larvae, pupae, and adult mosquitos in all stages of life survive best and become infectious in temperatures of 20℃ to 30℃.[25] Rohani et al. demonstrated that as temperatures increase from 26℃ to 30℃, dengue virus detection in the salivary glands of *Aedes* mosquitos decreases from 9 days to 5 days.[28] Similarly, Watts et al., reported detection times of 7 days at 32℃ and 12 days at 30℃.[26] The differences in reported incubation times of these studies is likely due to the fact that the detection time was measured differently.

In addition to absolute temperature playing a role, diurnal temperature range (DTR) is also important as narrower DTR's lead to increased infectivity at the same mean temperature.[29] With increasing temperatures worldwide, mosquitos harboring dengue are now spreading to less

commonly habituated areas such as the United States. In 2001, after 56 years without autochthonous dengue reports, 122 laboratory confirmed cases of dengue were reported in Hawaii.[30] Between 2015-2016, 264 cases of dengue were confirmed by the Hawaii Department of Health, and only 26 of these were from travelers visiting Hawaii. Similarly, from 2009-2012, 75 years after the last report of dengue activity in Florida, a dengue outbreak resulted in 103 reported autochthonous cases.[30]

Several statistical models have predicted that climate change will play a profound role on increasing dengue incidence and prevalence. In a study by Hales et al., the authors concluded that based on climate trends, the total population at risk of contracting dengue will increase from 1.5 billion people in 1990 to 5-6 billion people in 2085. This compares to an estimated 3.5 billion people in 2085 if climate were to remain constant. [31] Another modeling study by Colon-Gonzalez et al. showed that limiting global warming to less than or equal to 1.5 ℃ above preindustrial temperature levels in Latin America could reduce annual dengue cases by 3.3 million per year.[32] Ryan et al. evaluated different climate warming scenarios and the impact these would have on *Aedes* virus transmission. They revealed that by 2050, temperature increase would intensify transmission risk of *Aedes* mosquitos, impacting nearly half a billion people. [33] In this study, their analysis was broken down further to evaluate the impact climate will have on *Aedes* mosquitos in individual regions. Here, central America and the United States are considered areas of high transmission risk, with projections for increases in populations at risk ranging from 21.9-31.1 million and 20.6-32.1 million in Central America and North America respectively by 2050. [33]

Urbanization and globalization have also shown to play an important role in dengue spread. Urbanization is important because in these highly populated areas, inadequate water

drainage and waste management systems can lead to conditions that increase the risk of infection transmission.[4] The role of clean water management is also crucial because in an environment with stagnant water, the *Aedes* mosquitos can complete their development. Eggs are laid in water containers such as pot plants, drains, and water tanks. These eggs then hatch into larvae, which will eventually develop into mosquitos.[3,5] Data from Costa Rica supports this hypothesis, as there is an inverse relationship between dengue incidence and households without access to water; this is possibly due to the fact that those without water need to store it in containers therefore supplying a reproduction site for mosquitos.[9] Globalization is thought to play a role in reemergence of dengue in Costa Rica as increased travel and trade can re-introduce the disease into areas where it was once eliminated.[8]

Impact of dengue infection and prevention strategies in Costa Rica

Dengue is the most important mosquito born disease affecting Costa Rica over the past decades.[8] In the 1950's – 1970's, dengue epidemics were rare as control campaigns, marked by the introduction of the Pan American Health Organization (PAHO) in the Americas, lead to the eradication of *Aedes aegypti* mosquitos as part of the yellow fever control campaign.[4] However, control campaigns were discontinued in the 1970's causing the *Aedes aegypti* mosquitos to make its reemergence and by the 1990's these mosquitos regained a geographic distribution similar to their pre-eradication population.[6] This is significant because dengue has been a major societal cost to the Costa Rican population. In a report by the Costa Rica Social Security Fund (CRSSF), approximately $1.23 million were spent on dengue care in 2002 and $1.45 million in 2003.[8] The continued prevention of dengue transmission is problematic due to the difficulty in controlling the *Aedes* vector. *Aedes* mosquitos have a propensity to adapt to human environments which allows them to recover from elimination efforts. Eggs can withstand months of draught

and upon reintroduction of water, they are able to hatch.[3] In Costa Rica, the Ministry of Health is responsible for the direction of health surveillance and guidelines. Guidelines produced by the ministry of health for dengue control include the use of insecticides, environmental care, inspection of homes, and community education on preventing mosquito bites. Other prevention strategies include sleeping in well screened accommodations, wearing clothing that cover the arms and legs, and avoiding mosquito breeding sites such as standing water or flower pots.[1]

Tetravalent vaccine trials are currently underway as this type of vaccine is needed to protect against the four different dengue serotypes. A recent phase III trial showed that although the live tetravalent vaccine, Dengvaxia, raised dengue antibodies, individuals were still poorly protected.[11] Furthermore, seronegative individuals receiving the vaccine were at a higher risk of hospitalization due to dengue infection complications. Interestingly, partially immune individuals that received Dengvaxia had decreased dengue related complications. This has resulted in Dengvaxia being licensed in several countries where there is at least 50% seroprevalence, and preferable 70% seroprevalence.[11]

Methods

This report was an Augsburg University Physician Assistant Master's Project approved literature review. All articles investigated were written in English. The PubMed search engine was used to identify relevant scientific studies to help answer the research questions. The PubMed search criteria included articles published from January 1, 2000 to the present. These dates were chosen to identify articles that addressed more recent public health concerns. Search terms included: 1) ("dengue") AND ("fever") AND ("Costa Rica" OR "Latin America" OR "Central America"), 2) ("dengue") AND ("fever") AND ("climate" OR "temperature"), 3) ("dengue") AND ("fever") AND ("epidemiology"), 4) ("dengue") AND ("fever") AND ("cost" OR "economics"), 5)

("dengue") AND ("fever") AND ("population growth" OR "urbanization"), 6) ("Aedes") AND ("climate change"), 7) ("mosquito" AND "climate change"), 8) ("climate change") and ("evolution") and ("cause"). These search terms were also used on Google to identify relevant online articles from sources such as the CDC, WHO, and NASA. Additionally, articles were identified and included through cross-referencing of the publications identified from the original PubMed and Google search. Articles prior to January 1, 2000 were included from cross references. All articles were analyzed and those with adequate and supportive information were used in this study.

To investigate the impact of *Aedes* mosquitos and dengue on the people of Costa Rica, a two-question survey was developed, and interviews were conducted with native Costa Rican's. Interview questions included: 1) What preventative measures have been implemented at home and in the community to protect against contracting the dengue virus? 2) Do you have places with stagnant water within or surrounding your home?

Discussion

After reviewing the literature, the current data suggests that dengue prevalence is continually increasing in the Americas and is an issue that should not be overlooked. From 2000 to 2013, dengue has increased by nearly 6-fold within the Americas.[7] This is significant because those infected by dengue can develop debilitating clinical symptoms which may ultimately result in death. Several studies have been performed to estimate annual global infection rates, but many have failed to account for apparent and inapparent infection totals. Bhatt et al. estimated that nearly 300 million people worldwide are infected annually without manifesting clinical symptoms.[2] This is important on a global standpoint because asymptomatic patients still function as a host for the mosquito to contract and then spread the virus.

As infection rates continue to rise, many studies have considered the correlation between dengue and climate change. In a study evaluation dengue in Mexico, a modeling system that incorporated factors such as temperature and rainfall suggested that annual dengue infections could increase 18% by 2030, 31% by 2050, and 42% by 2080.[32] Other climate change prediction modeling systems by Ryan et al, Hales et al, and Gonzalez-Colon et al. found similar results in that increasing temperatures will lead to increases in dengue transmission.[31,33,34] In the studies by Tun-lin et al. and Rohani et al., it was demonstrated that as temperatures become warmer, mosquitos are more likely to become infectious faster.[25,28] With a mosquitos limited lifespan, earlier infectivity would maximize the amount of time for virus transmission to another host. If the development time of the virus is greater than the life span of the mosquito, transmission will not occur. Furthermore, as a result of climate change, increasing global temperatures may allow countries once uninhabited by dengue virus to facilitate an environment in which these mosquitos are able to thrive.

Urbanization and globalization have also been indicated as playing a role in the incidence and transmission of dengue. In places with dense populations, the virus is able to spread more readily from host to mosquito to a new host. In areas of smaller populations, the virus is able to be contained easier as there are fewer people to become infected. In cases of globalization, as dengue spreads geographically, the chances of worldwide infection will increase as well.

Currently, there are no effective licensed vaccines to prevent the acquisition of dengue. Though recent vaccination trials have shown a high safety profile with partial efficacy for dengue prevention, the reduction in efficacy against dengue transmission was still lower than anticipated.[14,15] Since vaccines have been to this date ineffective, insecticide sprays are commonly used with mixed results. Currently, the best evidence of prevention strategies is

cleaning water filled containers that harbor the larvae. Unfortunately, this also has had mixed results due to the poor sustainability of these measures, with them only being followed during times of epidemics.[9]

Augsburg University's Physician Assistant program recently traveled to Costa Rica for a Master of Arts leadership course. While visiting the rural community of Boruca, Randall Fernández, a leader within the community, discussed an outbreak of dengue ten years ago that infected three people. When asked what local preventative measures were implemented throughout the community to protect against contracting dengue, he explained the village took several precautions. This included wearing protective clothing and staying inside during dusk when the mosquitos are most active. Additionally, people who had been infected were isolated in order to prevent the virus from spreading. Mr. Fernández stated that local pamphlets, such as the one provided by the CDC (Figure 1, Appendix), emphasize preventative measures such as mosquito nets and bug spray, but many in the community do not implement these precautions consistently because they have not experienced the virus enough to be concerned (R. Fernández, personal communication, July 5th, 2019).

The Physician Assistant program also visited Longo Mai, a small agricultural village in Costa Rica. Here, the homes had unenclosed roofs and kitchens without walls that were open to the outside environment. Four families were interviewed in Longo Mai and asked if they had stagnant water within or surrounding their homes. Each family admitted to having water buckets underneath their kitchen sinks to catch water that spilled from the faucet. Although they did not drink out of them, the buckets were commonly infested with gnats, flies and other insects. In addition, their showers were not equipped with drainpipes that redistributed excess water far away from their homes. Instead, they placed a hole in the lower wall for the water to drain out

into the yard, causing water to flood that area (Longo Mai families, personal communication, July 6th-7th, 2019). The homes in these communities also rely on natural ventilation, so doors and windows are often left open. With many not having appropriate barrier methods such as screens, mosquito entry increases and therefore risk of transmission. The lack of air conditioning is also a concern in warm climate areas, as people seek coolness in the shade, a place where *Aedes aegypti* mosquitos like to feed.

From these encounters, it was demonstrated that although Costa Rica's Ministry of Health aims to educate and implement prevention strategies, further outreach and follow-up is needed in smaller villages. Education should include discussions on the use of physical barriers such long sleeve shirts and pants, as well as screened sleeping accommodations. Implementation of household strategies to remove standing water is of utmost importance as several of the research papers studied demonstrated that stagnant water is a critical component of dengue breeding. Government funding could also be provided to help people from lower socioeconomic areas. These funds could go towards building roofs to separate the inside of the homes from the outside environment as well as helping with the purchase of mosquito nets and insecticides.

Conclusion

In conclusion, the current available research demonstrates that dengue continues to be a significant health problem in the Americas, with both temperature and climate change playing a significant role on the increasing incidence and prevalence of this disease. In isolation, studies show that as temperatures increase, so does the infectivity and transmissibility of dengue mosquitos. With recent trends in global climate warming, this allows us to hypothesize that as our planet continues to warm, the control of this disease will become more difficult.

On a global scale, public awareness must be made to reduce activities that result in the production of greenhouse gases. On a smaller scale, further research is needed to help develop and support targeted educational efforts and policies that address the spread of the *Aedes vector.* Research efforts should focus on ways to improve local surveillance systems, especially in areas of high incidence, and initiatives should be undertaken to help increase public awareness of this disease. As vector control programs can be costly and difficult to maintain long term, research should focus on the development of effective vaccines. Through implementation of prevention initiatives and effective vaccines, global incidence will decrease resulting in less economic and societal cost.

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Appendices

Definitions of terminology used in this study:

Autochthonous: “Originating in the place where found; said of a disease originating in the part of the body where found, or of a disease acquired in the place where the patient is located.”[35]

Vector: “An invertebrate animal capable of transmitting an infectious agent among vertebrates.”[36]

Dengue symptoms:

- Fever
- Headache
- Muscle and joint pains
- Nausea / vomiting
- Rash
- Hemorrhagic manifestations

If you have these symptoms, ask your physician to order a test for dengue.

Alarm signs:

- Intense abdominal pain
- Persistent vomiting
- Abrupt change from fever to hypothermia, with sweating and prostration.
- Restlessness or somnolence.

Immediately consult your doctor if any of these appear.

Treatment:

- Rest, drink plenty of fluids and consult a physician.
- **Avoid pain relievers that contain aspirin** and non steroidal anti-inflammatory medications such as ibuprofen. Acetaminophen or paracetamol may be used.

To eliminate mosquito breeding sites and reduce the risk of dengue, check around your house and empty water from buckets, cans, flower pots and other items.

If you have dengue:

- **Avoid mosquito bites while you have a fever.**
- Don't let mosquitoes bite you. They can infect other members of your family with dengue after biting you.
- Use mosquito barriers until the fever subsides, to prevent day-biting mosquitoes from biting a sick person, becoming infected, and then biting someone else.
- Rest in a screened room or under a bed net.
- Use insect repellents and spray insecticide indoors if there are mosquitoes.

For more information:

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Estado Libre Asociado de Puerto Rico
Departamento de Salud

CENTERS FOR DISEASE CONTROL AND PREVENTION

1324 Cañada Street
Puerto Nuevo
San Juan, Puerto Rico 00920

Phone: 787-706-2399
Fax: 787-706-2496

www.cdc.gov/ncidod/dvbid/dengue/index.htm
www.salud.gov.pr

Revised: October, 2008

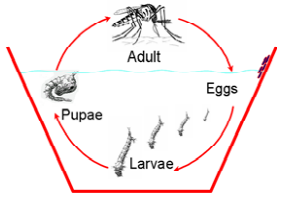
CENTERS FOR DISEASE CONTROL AND PREVENTION

Protect yourself from mosquito bites and dengue

Actual size of an *Aedes aegypti* mosquito →

Figure 1. Educational pamphlet for communities at high risk for dengue infection [37]

Dengue is carried by the *Aedes aegypti* mosquito, which can be found in the home.



This mosquito lays its eggs on the walls of water holding containers that are found around the home. Eggs hatch when submerged in water. Within 8 days the mosquito can complete its life cycle from egg, to larvae, to pupae and to an adult flying mosquito.

To help reduce the mosquito population in your community and the risk of exposure to dengue, eliminate larvae that grow in stored water.

If you have mosquitoes in your house:

- Eliminate any containers where the mosquito can lay her eggs, either by emptying the water, covering them or turning them upside down.

- Keep mosquitoes outside by fixing or installing window and door screens. Don't give mosquitoes a place to breed. A small amount of water can be enough for a mosquito to lay her eggs.

- Look around every week for possible mosquito breeding places. Empty water from buckets, cans, pool covers, flower pots and other items that aren't being used. Clean pet water bowls daily. Check if rain gutters are clogged. If you store water outside or have a cistern, make sure it's covered up. Encourage your neighbors to do the same.

If you have problems with the water supply in your area and you have to store water:

- Wash the interior of containers with a brush or sponge, to remove mosquito eggs that might be present, before filling them with water.

- Keep containers with water tightly sealed so that mosquitoes can not get inside and lay eggs. If you observe mosquito larvae, empty the container to eliminate any mosquito eggs.

Incorrect

Correct

In order to prevent the *Aedes aegypti* mosquito from laying its eggs in containers where you store water, keep it covered.

Remember that after the rain… there are more mosquitoes

Some mosquitoes lay eggs in the walls of artificial (plastic, metal, glass) containers with fresh water. Other mosquitoes prefer dirty water in trenches or brackish water in swamps to reproduce. In only one week these eggs can hatch and grow into adult mosquitoes.

Immediately after the rain, SEARCH for and ELIMINATE all WATER accumulated in containers and help your community to PREVENT DENGUE.

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Author(s) of Work(s): Chelsey Rilatos & Dr. Alicia Quella

Depositor's Name (Please Print): Chelsey Rilatos

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