Reemergence of Dengue Fever in Argentina as a Result of Climate Change

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Abstract

Argentina has recently experienced a tremendous increase in reported incidents of dengue fever, including the appearance of a novel deadly form of the disease. Dengue fever is a vector-borne viral disease for which there is no vaccine or viable treatment. Climate variability, including the rise in temperature, humidity, and precipitation, has affected the spread of the disease by providing enhanced conditions for the dengue fever vector. It is important for countries to make a joint effort to decrease the combustion of fossil fuels, in order to limit the spread and intensity of dengue fever.

Introduction

The World Health Organization estimates that 50 million cases of dengue fever are reported annually and that 2.5 billion people in 100 countries (40 percent of the world's population) are potentially at risk.[1] Over the past decade, reported incidents of dengue fever have risen drastically. The mosquito that transmits dengue fever, *Aedes aegypti*, was eradicated from Argentina in 1963. However, the disease reemerged in 1997 as a more severe form of the disease, dengue hemorrhagic fever.[2] This was the first reported case of this lethal derivative of dengue fever. Studies have linked an increase in global temperature to a rise in this vector-borne disease. The mosquito that carries the dengue virus is particularly abundant in tropical regions. Continuously hot and humid weather with an abundance of rain create ideal breeding grounds for *A. aegypti*. Global warming, even by 1°C, has an impact on the reproduction and survival rate of the infectious agent and its associated vector organism.[2] In addition, climate change can increase the geographic distribution of the disease, spreading dengue fever to higher latitudes and elevations.[3] Dengue fever is now at epidemic proportions, and understanding its strong association with climate change can help the medical community face its biggest challenge: stopping the spread of the disease. Climatic variability, including changes in temperature, humidity, and precipitation, will affect dengue fever vectors and hosts, consequently increasing the risk of disease transmission in Argentina.

Dengue fever consists of a variety of symptoms, all of which occur after a sudden high fever. People experience searing joint and eye pain, body rashes, and severe headaches. During the more uncommon form of the disease, dengue hemorrhagic fever (DHF), patients experience uncontrollable gastrointestinal bleeding that can result in circulatory failure and death.[4] Dengue fever is caused by four viral serotypes, or closely related but distinct viruses: DEN-1, DEN-2, DEN-3, and DEN-4. Exposure to one of the viruses provides lifelong immunity to that particular virus, however, the probability of contracting DHF increases by 50% after exposure to one of the other three serotypes.[4] No effective vaccine or drug treatment is yet available; therefore, management of the disease has relied on insecticides and eradication of breeding sites.

The adult *Ae. aegypti* mosquitoes feed during the day, preferring to lay their eggs in moist areas such as water storage containers. To elucidate the relationship between climate change and dengue fever, it is important to understand that water is an essential part of a mosquito's life cycle. *Ae. egypti* lay their eggs on damp soil that gets covered by water. In the next stage, larvae need to live in the water, which is why mosquitoes often breed in specific habitats such as ponds and marshes.[5] Although eggs can survive desiccation for many months, water is required for the ovipositional (egg laying) stage for a mature egg to hatch, explaining why rainfall is an important factor for the mosquito's survival.[5] Finally, the newly-emerged mosquito must remain on the surface of the water for a few days to allow its body to dry and harden.[2,5] Increased precipitation can therefore directly affect the number of breeding sites available for mosquitoes that carry dengue fever.

The late 20th century earth has experienced a drastic warming of global temperatures. Scientists project that by 2100, global temperatures will increase 1-3.5 °C from where they stand currently.[6] These findings are significant, especially compared to the 0.5 °C increase in temperature of the past century.[6] Climate change will exacerbate the incidence of dengue fever in Argentina by creating a larger geographic distribution for *Ae. aegypti*. Since humans are a delicacy for the peridomestic *Ae. aegypti*, the potential feeding frenzy caused by global climate change puts them at a high risk for infection. Warming in cooler regions can increase the range at which mosquitoes can survive and thus transmit the disease. Optimal vector capacity is around 30-32 °C, owing to a reduction in the mosquito's incubation period.[6] Watts et al. analyzed the effect of temperature on the ability of *A. aegypti* to transmit the DEN-2 virus serotype.[7] In the first experiment, a strain of *A. aegypti* fed on DEN-2 infected rhesus monkeys. The mosquitoes were incubated at 20, 24, 26, and 30 °C for 25 days at 4-7 day intervals.[7] Subsequently, when the mosquitoes were allowed to bite a rhesus monkey, only the mosquitoes maintained at 30 °C transmitted the DEN-2 virus. To explore the influence of temperature further, a second experiment, in which the incubation periods changed to 30, 32, and 35 °C, showed that the rate of transmission increased with an increase in temperature.[7] Furthermore, the incubation period decreased from 12 days for mosquitoes at 30 °C to 7 days for mosquitoes at 32 and 35 °C.7 Other studies confirm these findings and note that shortening a dengue virus's incubation period by five days would have a three-fold increase in the rate of transmission.[8] These results provide confirmation that vector efficiency is temperature-dependent, and that the mosquitoes can infect organisms much faster at higher temperatures.[8]

The development of *A. aegypti* is also sensitive to warming waters, which allow larvae to mature in a shorter time period.[9] In addition, larvae will have a greater capacity to produce more offspring during the transmission period.9 In warmer climates, adult female *A. aegypti* feed more frequently and digest blood faster.[10] Dengue transmission is particularly confined to tropical and subtropical regions because freezing temperatures destroy overwintering eggs and larvae of the mosquito[10]. Even at colder temperatures, viral development is slow, and mosquitoes are unlikely to survive long enough to become infectious[10].

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As the climate warms, not only can vectors expand the disease to northern latitudes, but new vector species can also be introduced to tropical regions. When dengue fever reemerged in northern Argentina, the province of Misiones reported the presence of *Ae. albopictus* for the first time in the country.[11] Misiones has a subtropical climate with no dry season, which makes the region one of the most humid provinces in Argentina[11]. Similar to *A. aegypti*, *Ae. albopictus* is a container-dwelling mosquito whose larvae usually develops in water-filled tires, flower vases, and other artificial containers[12]. The females deposit desiccation-resistant eggs on walls of these containers[12]. Their eggs hatch when the container is flooded. Interestingly, *Ae. albopictus* is an ecological generalist, adapted to both temperate and tropical climates and can, therefore, occupy a wide range of suitable container habitats.[12] Alto et al. conducted a laboratory experiment to see how temperature changes can affect the population dynamics and hence the range expansion of *Ae. Albopictus*.[13] Constant temperatures of 22°, 24°, and 26 °C were used to measure mortality and emergence rates across the entire life cycle of the mosquitoes.[13] Populations at 26 °C had a significantly greater intrinsic rate of increase (r) and lower asymptotic densities (K), which signified high fecundity, short generation time, and early mature onset with higher temperatures.[13] Lower K at 26 °C could result if mosquito populations experienced a greater daily mortality rate, since with an increased rate of production, *Ae. albopictus'* resources also become depleted more quickly due to competition.[13] Even at 24 °C, *Ae. albopictus* populations yielded shorter development times.[13] Another study by Alto et al. also reveals the effect of both temperature and precipitation on the current distribution of *Ae. Albopictus*.[14] Populations of *Ae. albopictus* were again maintained at 22, 24, and 26 °C; however, each caged population for each temperature was assigned to one of three precipitation regimes: 25%, 90%, and 100% dry.[14] Variation in precipitation did not have a significant effect on the size of adult populations, unless their aquatic habitats dried completely.[14] In fact, drying caused considerable mortality of both larvae and pupae, confirming the mosquito's dependence on water. In this study, greater temperatures coupled with either 25 or 90% drying resulted in a population growth.[14] Based on this data, populations of *Ae. albopictus* in warmer regions with a probability of summer drought are likely to experience an increase in production as long as container habitats do not completely dry out. The experiment also revealed that adult size decreased at higher temperatures.[14] Interestingly, since a small body size is one of the characteristics of r-selection, these findings confirm the results of other studies that showed mosquitoes experiencing an increased r-value with elevated temperature.[14] The conditions of this study also closely resemble air temperatures and mean water concentrations in and around tires during the mosquito's active season.[14] These results suggest that warmer temperatures paired with adequate precipitation will contribute to the northward expansion of *Ae. albopictus*.

Since studies have shown that, with rising temperatures, Aedes mosquitoes experience increased competition and decreased body size, Alto et al. examined the effects of larval competition between *A. aegypti* and *Ae. Albopictus*.[10] Competitive interactions between larvae may carry over to the adult mosquito and alter its ability to become infected and subsequently transmit the virus.[10] Studies performed on *Ae. triseriatus*, a tree hole breeding mosquito, demonstrated that resource competition among larvae produce smaller adults that transmit La Crosse virus at higher rates.[15] The experiment revealed that interspecific competition between the two species of mosquitoes was more significant than intraspecific competition within the same species.[10] To determine how larval competition affects the transmission of disease, adult female mosquitoes were fed a blood mixture containing Sindbis virus (SINV).[10] Increased competition was associated with enhanced vector potential or increased susceptibility to infection. Significantly, the two Aedes species differed in susceptibility and dissemination. *A. albopictus* was more likely to develop an infection than *A. Aegypti*.[10] Conversely, although *A. aegypti* experienced lower infection rates, the mosquito transmitted the vector more frequently.[10] The effects of competition on viral infection using SINV applies to arboviruses like dengue. Although the role of global warming was not explicitly mentioned in the study, it can be deduced that since an increase in temperature results in decreased mosquito size and increased competition, Aedes mosquito will become infected and transmit the dengue fever more frequently. Therefore, changes in climate strongly influence dissemination of vector-borne diseases.

The appearance of *Ae. albopitus* in Argentina shows that, as a result of climate change, dengue fever will not only extend into regions previously devoid of disease, but new species of mosquitoes carrying the infectious agent will also increase the transmission of dengue fever to already endemic regions. This change in transmission dynamics of the virus increases the chance of developing secondary dengue infections, an important risk factor for DHF.[16] The new areas of mosquito invasion are temperate regions that border endemic zones.[16] In these regions, humans and *A. aegypti* can coexist, yet transmission of the disease is unlikely due to lower temperatures. Leading climatologist, Jonathan Patz, explains that with rising temperatures, people in previously uninfested areas will be especially vulnerable to disease onset since they do not have immunity to the disease.[17] Increasing temperature, even by less than one degree, will increase a virus's epidemic potential, allowing more mosquitoes to transmit the disease[17]. Furthermore, global warming also decreases the size of *A. aegypti* larvae, which results in smaller adult mosquitoes that need to feed multiple times to develop their eggs, thereby, increasing the rate of transmission.[10]

The potential for a dengue fever epidemic was projected by a general circulation model (GCM) of global climate change. Among the three GCM's, the average annual increase in temperature was about 1.16 ° by 2050.[18] For regions already at risk for the disease, the epidemic potential rose by an average of 31-47%.[18] Also, endemic locations are at a higher risk of DHF due to an increase in transmission. Hopp and Foley created a numerical model using the response of *A. aegypti* to climate variations from 1958 to 1995 in order to examine the global-scale relationships between climate, *A. aegypti* populations, and cases of dengue fever.[19] As evidenced by the northward and southward seasonal shifts in distribution, the modeled mosquito population is greatly influenced by temperature.[6] The most significant association arises between variations in mosquito larvae densities and temperature.[19] The climatologists additionally found that the strongest relationship between the modeled mosquito and temperature variation occurs in the moist tropical regions.[19] These findings provide further evidence of the role of climate in mosquito development and survival.

Humidity, another climate variable, has been examined as a contributing factor to an increase occurrence of dengue fever. Hales et al. created an empirical model displaying the geographical limits of dengue fever transmission on the basis of vapor pressure, which is a measure of humidity.[20] Since humidity is usually high where temperature and rainfall levels are elevated, vapor pressure is a good marker of dengue fever distribution.[20] In fact, the scientists showed that current limits of dengue fever

transmission can be modeled with 89% accuracy on the basis of long-term vapor pressure.[20] If humidity remained at baseline values with the projected increases in population, by 2055, 3.2 billion people will be at risk for dengue fever.[20] However, if humidity increased, as predicted by a global circulation model, and the same population increase would have occurred, 4.1 billion people would be at risk of the disease.[20] Different generated circulation models repeatedly predict that dengue's epidemic potential significantly increases with a small rise in temperature. These studies are not trying to make a claim that climate change is the only factor contributing to the increase in the spread and intensity of dengue fever; instead, the experiments illustrate that climate change is an important factor to consider when implementing reforms to combat the disease.

Climate anomalies, including changes in the El Niño Southern Oscillation (ENSO), can also be connected to the resurgence of dengue fever in Argentina. A correlation analysis of past ENSO events and dengue epidemics across northern South America and the Indonesian archipelago showed a strong relationship between these two variables.[21] Of the six El Niño episodes that occurred between 1965 and 1993, only the 1993 ENSO was not associated with a rise in the incidence of dengue fever.[21] All of the epidemics were associated with warmer temperatures, which is reasonable since the El Niño effect refers to a warming of sea surface temperatures.[21] The model also showed that DHG transmission increased following the onset of the rainy season.[21] The dengue epidemic that occurred in northern Argentina in 1998 also took place following the onset of rainfall. La Niña, which is associated with the cold phase of ENSO, appeared to have an insignificant effect on the occurrence of dengue epidemics, since there was no epidemic seen in or following a La Niña year.[21] These findings confirmed previous studies that show an increase in the incidence of dengue fever with warmer temperatures, resulting from a lengthened mosquito life span and increased rate of viral replication.[22] Warmer temperatures also contribute to drought conditions in many places during El Niño, which is why the overall relationship between average rainfall and incidence of disease remains unclear. Even though the study considered the increases in population, other factors such as rapid urbanization, and a decline in public health services increases the availability of mosquito breeding sites. To further elucidate the relationship between precipitation and dengue fever, Wiwanitkit (2006) investigated the correlation between the two variables. He transformed the geographical data into the rainfall and the infective rate into the prevalence of the disease.[23] A significant association between rainfall and the number of clinical cases of dengue fever was observed.[23] Although temperature likely has the most direct effect on the incidence of dengue fever, Wiwanitkit's results provide support for a direct relationship between rainfall and the disease.[23]

Argentina is currently experiencing the biggest epidemic of dengue fever since its reemergence in the late 1990s. Although many experts say that increased global travel and urbanization transport *A. aegypti* to new areas, it is global warming that enables the mosquitoes to settle permanently in new locations. In Chaco, in northern Argentina, there have already been 11,363 confirmed cases of the disease; however, many political officials, including Argentina's Health Minister, underreport the number of cases, partially due to fear of damaging the country's international reputation.[24] Even though internal political pressures interfere with Argentina's ability to combat dengue fever, a multitude of actions can be taken to stop the spread of disease.

Currently, public health administrators are educating people, especially in poor rural areas, about the importance of removing potential breeding sites around their homes[24]. Also, treating standing water with insecticides could radically decrease dengue's reach. Since no effective vaccine has yet been developed, the only method of preventing dengue fever is by fighting the mosquito vectors. It has been repeatedly shown that environmental conditions strongly influence the abundance and geographic distribution of the principle dengue mosquito, *A. aegypti*. Assuming that climate change is inevitable is not only incorrect, but detrimental to the human population. Human activities, mainly the burning of fossil fuels, have significantly increased the amount of greenhouse gases in the atmosphere, enhancing the greenhouse effect. Elevated carbon dioxide levels contribute significantly to an increase in global temperatures, which, in turn, worsens the outbreak of dengue fever. Climate change can even affect the disease indirectly through a decrease in agriculture, which may lead to increased urbanization and spread of disease in cities.[25] Therefore, waiting for the earth to stop warming is not a solution. Industrialized countries are emitting the most carbon dioxide, contributing to the spread of infectious diseases in tropical regions. For example, Argentina is not contributing significantly to the emission of greenhouse gases, yet it has experienced a resurgence of dengue fever due to global warming. Stopping the transmission of dengue fever, as well as other tropical diseases, requires a united effort of all countries, especially the top emitters of carbon dioxide.

Argentina's Health Ministry has recently launched a national campaign to educate people about the importance of wearing insect repellant and covering exposed body parts. Authorities have linked the spread of dengue fever in the northern provinces of Argentina to the epidemic in neighboring Bolivia.[26] Experts are saying that Bolivia is currently experiencing the worst outbreak in the country's history. The National Meteorology Service forecasting unit reports exceedingly elevated spring and summer temperatures averaging 37 °C.[26] Precipitation during the warm season (November through April) has supplied *A. aegypti* with ideal living conditions, resulting in over 60,000 reported cases of dengue fever from January to April of 2009.[26] Widespread fear among Bolivians has caused a tremendous increase in migration to neighboring countries, such as Argentina and Brazil. The healthcare systems in poverty-stricken countries, such as Bolivia, are severely underfunded. Hospitals are overflowing with diseased victims, many of whom have to wait outside to get treatment. A lack of resources and education is fueling the spread of dengue fever, partially because poor people often unintentionally provide homes for mosquitoes by keeping plastic containers and tires outside.

As dengue fever increasingly threatens populations worldwide, scientists are fervently trying to find a viable treatment. Since there are four serotypes of the dengue virus, it has been very difficult to create a vaccine that would target all four strains of the virus. Raviprakash et al. recently created a tetravalent dengue virus vaccine using a complex adenovirus vector as well as incorporating genes from all four dengue virus types.[27] When rhesus monkeys were injected with this vaccine, they displayed high antibody levels that neutralized all of the viral serotypes.[27] Furthermore, when the monkeys were injected with each of the four strains of dengue virus, the scientists saw either complete or significant protection against the four strains.[27] This vaccine has the potential of treating millions of people at risk of dengue fever. Maiztegui et al. (1997) conducted a clinical study to evaluate the efficacy of Candid 1, a live attenuated Junin virus vaccine, which is targeted for treating Argentine hemorrhagic fever. The fatality ratio for untreated patients for this disease is 15-30%.[28] Previously, no vaccines

have been available for the prevention of the illness that is a major health concern among Argentinean agricultural workers. This study had a large sample of patients: 3255 people received the vaccine and 3245 received a placebo.[28] The vaccine yielded a protective efficacy of 84%, representing the first successful vaccine for preventing a disease caused by an arenavirus.[28] However, the duration of the vaccine is still unknown and needs to be looked into further.

In addition to finding viable vaccines, scientists have also tried genetic manipulations as a means of terminating the spread of dengue fever. Xi et al. discovered that the Wolbachia bacterium is capable of stopping the transmission of the dengue virus[29]. Although about a third of the mosquito population carries this bacterium in the wild, *A. aegypti* does not possess it.[29] Although the scientists have not yet found the exact mechanism by which Wolbachia stops the virus from replicating, their findings have significant potential medical implications.[29] The bacterium can be used as a method of controlling dengue fever, since Wolbachia can only be passed between mosquitoes.[29] Fu et al. generated a new strain of flightless female *A. aegypti* that would die quickly in the wild, reducing transmission of dengue fever.[30] Interestingly, males of this strain can fly, but they are incapable of biting.[30] When the genetically altered males breed with wild-type female mosquitoes, their offspring are incapable of flying.[30] Releasing this new breed of mosquitoes into the wild could significantly decrease the dissemination of dengue fever.

Dengue fever is the most important vector-borne viral disease globally. Argentina is currently suffering a major outbreak of the disease, and has recently experienced a new fatal form, dengue hemorrhagic fever. Changes in climate, most notably and increase in temperature, humidity, and precipitation, have contributed to the increase in the mosquito population that carries the dengue virus, and subsequently an increase in the transmittance of the disease. Clearly, Argentina is vulnerable to variations in climate due to its geographical location. A major step towards curbing the spread of fatal disease is to decrease the combustion of fossil fuels which causes an increase in greenhouse gas emission. This will lead to a decrease in global warming and help terminate the spread and intensity of dengue fever. Since dengue fever affects over 50 million people worldwide, a joint effort on the part of all nations needs to take place in order to decrease global warming and fatal disease.

References

1. Watstein, S., and Jovanovic, J. (2003). Statistical handbook on infectious diseases (Westport, Conn.: Greenwood Press).

2. Aviles, G., Rangeon, G., Vorndam, V., Briones, A., Baroni, P., Enria, D., and Sabattini, M.S. (1999). Dengue reemergence in Argentina. Emerg. Infect. Dis. 5, 575-578.

3. Hellmann, J.J., Byers, J.E., Bierwagen, B.G., and Dukes, J.S. (2008). Five potential consequences of climate change for invasive species. Conserv. Biol. 22, 534-543.

4. Tapia-Conyer, R., Mendez-Galvan, J.F., and Gallardo-Rincon, H. (2009). The growing burden of dengue in Latin America. J. Clin. Virol. 46 Suppl 2, S3-6.

5. Wearing, H.J., and Rohani, P. (2006). Ecological and immunological determinants of dengue epidemics. Proc. Natl. Acad. Sci. U. S. A. 103, 11802-11807.

6. Githeko, A.K., Lindsay, S.W., Confalonieri, U.E., and Patz, J.A. (2000). Climate change and vector-borne diseases: a regional analysis. Bull. World Health Organ. 78, 1136-1147.

7. Watts, D.M., Burke, D.S., Harrison, B.A., Whitmire, R.E., and Nisalak, A. (1987). Effect of temperature on the vector efficiency of Aedes aegypti for dengue 2 virus. Am. J. Trop. Med. Hyg. 36, 143-152.

8. McLean, D.M., Clarke, A.M., Coleman, J.C., Montalbetti, C.A., Skidmore, A.G., Walters, T.E., and Wise, R. (1974). Vector capability of Aedes aegypti mosquitoes for California encephalitis and dengue viruses at various temperatures. Can. J. Microbiol. 20, 255-262.

9. Padmanabha, H., Soto, E., Mosquera, M., Lord, C.C., and Lounibos, L.P. (2010). Ecological Links Between Water Storage Behaviors and Aedes aegypti Production: Implications for Dengue Vector Control in Variable Climates. Ecohealth

10. Alto, B.W., Lounibos, L.P., Higgs, S., and Juliano, S.A. (2005). Larval Competition Differentially Affects Arbovirus Infection in Aedes Mosquitoes. Ecology 86, 3279-3288.

11. Tejerina, E.F., Almeida, F.F., and Almiron, W.R. (2009). Bionomics of Aedes aegypti subpopulations (Diptera: Culicidae) from Misiones Province, northeastern Argentina. Acta Trop. 109, 45-49.

12. Higa, Y., Yen, N.T., Kawada, H., Son, T.H., Hoa, N.T., and Takagi, M. (2010). Geographic distribution of Aedes aegypti and Aedes albopictus collected from used tires in Vietnam. J. Am. Mosq. Control Assoc. 26, 1-9.

13. Alto, B.W., and Juliano, S.A. (2001). Temperature effects on the dynamics of Aedes albopictus (Diptera: Culicidae) populations in the laboratory. J. Med. Entomol. 38, 548-556.

14. Alto, B.W., and Juliano, S.A. (2001). Precipitation and temperature effects on populations of Aedes albopictus (Diptera: Culicidae): implications for range expansion. J. Med. Entomol. 38, 646-656.

15. Reese, S.M., Mossel, E.C., Beaty, M.K., Beck, E.T., Geske, D., Blair, C.D., Beaty, B.J., and Black, W.C. (2010). Identification of super-infected Aedes triseriatus mosquitoes collected as eggs from the field and partial characterization of the infecting La Crosse viruses. Virol. J. 7, 76.

16. Gubler, D.J. (2002). Epidemic dengue/dengue hemorrhagic fever as a public health, social and economic problem in the 21st century. Trends Microbiol. 10, 100-103.

17. Patz, J.A. (2009). Factors affecting global environmental public health. WMJ 108, 279, 281.

18. Patz, J.A., Martens, W.J., Focks, D.A., and Jetten, T.H. (1998). Dengue fever epidemic potential as projected by general circulation models of global climate change. Environ. Health Perspect. 106, 147-153.

19. Hopp, M. J. & Foley, J. A. (2003), Worldwide fluctuations in dengue fever cases related to climate variability. Clim. Res. 25, 85–-94.

20. Hales, S., de Wet, N., Maindonald, J., and Woodward, A. (2002). Potential effect of population and climate changes on global distribution of dengue fever: an empirical model. Lancet 360, 830-834.

21. Rohani, P. (2009). The link between dengue incidence and El Nino southern oscillation. PLoS Med. 6, e1000185.

22. Fuller, D.O., Troyo, A., and Beier, J.C. (2009). El Nino Southern Oscillation and vegetation dynamics as predictors of dengue fever cases in Costa Rica. Environ. Res. Lett. 4, 140111-140118.

23. Wiwanitkit, V. (2006). An observation on correlation between rainfall and the prevalence of clinical cases of dengue in Thailand. J. Vector Borne Dis. 43, 73-76.

24. Seijo, A. (2009). Dengue 2009: chronology of an epidemic. Arch. Argent. Pediatr. 107, 387-389.

25. Galama, J.M. (2001). Emergent viral infections. Ned. Tijdschr. Geneeskd. 145, 616-619.

26. Duenas, J.C., Llinas, G.A., Panzetia-Dutari, G.M., and Gardenal, C.N. (2009). Two different routes of colonization of Aedes aegypti in Argentina from neighboring countries. J. Med. Entomol. 46, 1344-1354.

27. Raviprakash, K., Wang, D., Ewing, D., Holman, D.H., Block, K., Woraratanadharm, J., Chen, L., Hayes, C., Dong, J.Y., and Porter, K. (2008). A tetravalent dengue vaccine based on a complex adenovirus vector provides significant protection in rhesus monkeys against all four serotypes of dengue virus. J. Virol. 82, 6927-6934.

28. Maiztegui, J.I., McKee, K.T.,Jr, Barrera Oro, J.G., Harrison, L.H., Gibbs, P.H., Feuillade, M.R., Enria, D.A., Briggiler, A.M., Levis, S.C., Ambrosio, A.M., Halsey, N.A., and Peters, C.J. (1998). Protective efficacy of a live attenuated vaccine against Argentine hemorrhagic fever. AHF Study Group. J. Infect. Dis. 177, 277-283.

29. Xi, Z., Khoo, C.C., and Dobson, S.L. (2005). Wolbachia establishment and invasion in an Aedes aegypti laboratory population. Science 310, 326-328.

30. Fu, G., Lees, R.S., Nimmo, D., Aw, D., Jin, L., Gray, P., Berendonk, T.U., White-Cooper, H., Scaife, S., Kim Phuc, H., et al. (2010). Female-specific flightless phenotype for mosquito control. Proc. Natl. Acad. Sci. U. S. A. 107, 4550-4554.