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Zika threatens to become a huge worldwide pandemic

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ABSTRACT

The *Aedes aegypti* mosquito which transmits Zika virus (as well as dengue, chikungunya and yellow fever) represents a high risk for global transmission. This virus comes from Africa, the Zika forest in Uganda, where it was discovered in 1947 in a rhesus monkey. In May 2015, the first local cases were recorded in Brazil, surpassing 1.5 million cases in December of the same year. By March 2016, local transmission of Zika was recognized in 34 countries. Its clinical condition is similar to dengue febrile illness, although milder. The final geographical distribution area is constantly expanding. Recently, it has been associated with cases of Guillain-Barré syndrome in Brazil, Colombia, El Salvador, Venezuela and Suriname. Microcephaly was documented in Brazil. This article discusses some factors that contributed to the spread of Zika virus in South America. Climate change associated with the events of the phenomenon of “El Niño” is also analyzed. The biggest concern is how quickly Zika is spreading around the world and that it could be far more dangerous than previously thought. Zika virus infection, by its explosive potential, has every chance of becoming a global pandemic.

1. Introduction

Charles Franklin Craig was a distinguished researcher in the field of tropical medicine who contributed to the study of dengue in 1907. Therefore, it is appropriate to remember him in the context of the resurgence of dengue and other infections transmitted by *Aedes aegypti* (*Ae. aegypti*). In 1954, Albert Sabin made a review of the existing knowledge about dengue. A considerable amount of information has been accumulated since then and much has been learned about the dengue virus, its epidemiology and pathogenesis. Unfortunately, no progress has been made in controlling the *Ae. aegypti* mosquito, as well as in preventing the diseases it transmits [1].

Unfortunately, in the first decade of the 20th century, the *Ae. aegypti* has invaded again almost every country in the American region, which had achieved its eradication during 1950 and 1960. Furthermore, it is in most tropical countries where the vector reaches the highest density. The biggest problem is given by the uncontrolled urbanization in many tropical cities in the world, and the general ignorance of the diseases transmitted by the vector mosquito [2].

The world has changed in the last 50 years and it is not surprising that the *Ae. aegypti* has also changed. There was an explosion in the number of artificial containers that are the ideal larval habitat for this mosquito. These include many non-biodegradable containers, plastics which are used as household consumer goods, car tires, and many other artificial containers that hold water, which are found at homes [3].

2. Importance of the spread of the Zika virus

Until 2007, only 14 sporadic human cases have been reported worldwide in some countries in Africa and Asia. However, in the last decade, cases have expanded to new territories leading to outbreaks in several Pacific Islands [4]. The outbreak in 2007 on the island of Yap (Micronesia) was the first Zika virus outbreak outside Africa and Asia [4–6].

Later, between 2013 and 2014 there was another outbreak in the French Polynesia that spread to New Caledonia [7]. Since then, there have been cases of Zika virus disease in the Cook Islands, the Solomon Islands, Samoa, Vanuatu and Easter Island (Chile) [4]. In May 2015, an outbreak of Zika virus started in Brazil, which initially affected the states of Bahia

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and Rio Grande do Norte [8]. Upon detection in Brazil, local transmission has been identified in most countries of the region of the Americas. The strain which was identified in these outbreaks is of Asian origin [9].

3. Importance of *Ae. aegypti* vector

Ae. aegypti is the main vector of 4 important diseases: dengue, yellow fever, Chikungunya and Zika. The mosquito bites during daylight and it is characterized by living in the domestic habitat. It mates, feeds, rests and lays its eggs in areas where humans live and in the surroundings [10].

Several records have shown the elimination or significant reduction of yellow fever and dengue by controlling the *Ae. aegypti*. Mosquito control leads to the reduction and elimination of the disease. In this regard, it should be recalled that the construction of the Panama Canal was possible when the surgeon of the United States Navy, William Gorgas, could stop the transmission of yellow fever among workers, eliminating mosquito growth sites. Later, Ferd Soper, from the Rockefeller Foundation, continued a successful eradication program during the fifties and sixties, which allowed to extinguish the transmission of yellow fever and dengue in most of South and Central America [11].

Through aggressive vector control efforts in South America, outbreaks of yellow fever and dengue fever began to decline and by the end of 1960 these infections had been almost eradicated in tropical regions of the continent. However, as many programs were suspended during the 70s, the *Aedes* mosquito breeding resumed. Towards the middle of the 90s, maps that indicated the vector geography resemble maps made 30 years ago [12].

Zika and dengue are distributed in the poorest urban areas of the tropics. These infections are part of the forgotten tropical diseases which mainly affect poor populations. Unfortunately, the absence of public health policies in several countries has allowed the resurgence of these mosquito-borne infections [13].

Ae. aegypti does not tolerate cold winters and it is currently limited to tropical and subtropical regions. Its expansion to regions free of dengue (*e.g.* the southern provinces of Argentina: Chubut, Santa Cruz) could occur if human behavior and culture allow adequate exposure to the mosquito (*e.g.* water storage and presence of artificial containers where larvae may develop) [11].

4. Why did the spread of dengue contribute to the Zika emergence?

Dengue epidemics worldwide have become larger and more frequent. The incidence of the severe and fatal form of the disease has increased dramatically in recent years in developing countries. There are several reasons for the defeat. A phenomenon that facilitated the spread of dengue began in the 1960s, when the airplane was extensively used for traveling for commercial purposes. This has provided the ideal mechanism for transporting dengue virus located in the body of an infected person [14].

Nobody ignores that the ease that exists nowadays to travel by plane makes it almost inevitable for a vector such as *Ae. aegypti* to be carried around the world through flights [15].

Dengue is also one of the most serious consequences of the growth of unplanned urbanization in developing countries. The tropical urbanization which has been accelerated in recent decades has greatly increased population density and geographical distribution of the vector. In addition, global migration movements enhance the spread of vectors and viruses. When the human population migrates from rural areas to cities, the ideal environmental conditions (proliferation of breeding sites) for increasing *Aedes* mosquitoes are created [16]. On the other hand, poverty complicates the efforts of communities or individuals to carry out effective protection measures. Even when control resources exist, they are inefficiently applied [17].

The lack of general knowledge about the diseases which are transmitted by the vector mosquito is also important. In addition, citizens of most tropical countries expect and require state bodies to control the mosquitoes that breed in the domestic environment, which are mainly present due to inappropriate accumulation of water that is stored in household containers. Unfortunately, and due to its paternalistic nature, most governments still promise results that they cannot achieve to control the mosquito [18].

5. Zika and climate change

Transmission of infectious diseases is sensitive to climatic conditions, especially diseases like dengue or Zika, in which the virus has a life cycle outside the human body. Viruses that are transferred by insects are exposed to climatic environment. Climate changes may affect the transmission of infectious diseases including temperature, humidity, rainfall, and soil humidity [19].

Zika epidemic clearly shows that climate change is already affecting human health. Climate change can affect health through several ways, for example, the increase in frequency and intensity of heat waves, heavy rains, increased floods and droughts. In Latin America, the impact of extreme heat wave in human health can be exacerbated by increased humidity. The overall balance of the effects of this phenomenon on health is negative and the population of developing countries is particularly vulnerable to adverse effects [20].

Many of the most serious public health consequences related to climate change are being experienced by the world's poorest nations because of their geographical location. In addition, poor education, low income, lack of water, lack of health policies, difficult access to health care and other contextual factors reduce the ability to react to the threat of Zika in developing countries [21].

Therefore, climate change acts as an amplifier of the health risks of the poorest people, who are suffering a great increase in diseases by *Ae. aegypti* in comparison to rich people and less vulnerable populations [22].

The current financial crisis of the poor and indebted countries of South America spreads doubts about the global model to reduce health inequalities. Undoubtedly, climate change is an important component in the spread of Zika virus, but it is difficult to separate it from human factors. Changes in human behavior such as massive deforestation, dam construction, the extinction of natural predators, and changes in biodiversity, have increased the risk of exposure to mosquitoes [23].

Moreover, unlike dengue, geographic expansion of Zika virus vector finds a new population without proper immunity, which increases the number of potential infected people. It is clear that climate change is a potentially very important factor to produce short-term effects, such as new epidemics of Zika and even pandemic risk [24].

The summer of 2016 (December to March in the Southern Hemisphere) shows a lack of capacity in public health in Latin American countries to deal with the epidemic of Zika and dengue [25]. One of the goals of the fight against Zika is the development and production of countermeasures. Unfortunately, the indifference of decision makers in public health and their inability to establish strategies in medium and long term have been favorable factors for the *Ae. aegypti* spread [26].

This has caused that geographical areas where the Zika virus is expanding are unprepared to deal with the growing epidemic. Residents in the cities of Latin America, including the major capitals, are likely to suffer the most severe consequences of the disease, including severe illness and death [27].

There are a lot of people who lack infrastructure and have little land to plan its use. It is essential to work in urban settlements to mitigate the vulnerability of those most disadvantaged. For example, the agenda of governments should include reforestation to lower the risk of flooding. Poverty reduction, especially in improving housing conditions and access to potable water, should reduce the vulnerability caused by climate change [28]. Many inhabitants of the outlying areas of large cities in Latin America are marginalized.

There are neighborhoods that lack electricity, running water, garbage collection, paved streets, sewers and drains for rain. With this vulnerability, low-income people living in urban areas are more susceptible to suffer a more intense exposure to *Ae. aegypti* [29,30].

6. Large scale fumigation

Since the early twentieth century, it was thought that the most effective method for preventing diseases caused by mosquitoes is one that points to the adult vector, which transmits the pathogen [31].

However, the dominant paradigm to suppress the *Ae. aegypti* should be directed to the immature mosquito (eggs and aquatic larvae), which does not usually survive long enough to transmit the virus [32].

This does not exclude the need to target adult vectors in places near human beings through the use of pesticides directly into homes, in order to reduce the survival of infected mosquitoes. Control into homes can be achieved by fumigating indoors, but these actions are often hampered by limited access to houses and limited resources [33].

For decades, it has been said that the most effective way to control the adult mosquito in urban areas is using insecticides, particularly malathion. It has been used on units installed on trucks and airplanes. Another method is to fumigate from house to house with adulticide insecticides and on the periphery up to 150 m. These methods were responsible for reducing malaria, yellow fever and other vectors, thus allowing the construction of the Panama Canal at the beginning of the twentieth century [34].

Unlike malaria controls, in which insecticides interrupt the transmission of *Anopheles* mosquitoes, this method has not been effective for *Ae. aegypti*. Unfortunately, it has taken decades to realize that it has little or no impact on the wild population of *Ae. aegypti*. The application of insecticides on mounted units has the same impact on the mosquito and human populations.

The insecticides applied with spray have more impact on human population than on mosquitoes, and in most cases the method has been used for *Ae. aegypti* [35].

Fumigation in airplanes or trucks has often limited effectiveness against *Ae. aegypti* because the steam does not penetrate inside buildings where adult mosquitoes are at rest, although it is often used in emergencies as “a visible symbol of government action” in many Latin American countries [36].

Again, as the Zika is a problem related to domestic sanitation, the existence of breeding ground is due to specific human behavior (individual, community and institutional) that favors them because any container capable of retaining water is a potential breeding for *Aedes* eggs [33].

7. *Ae. aegypti* mosquito breeding ground

Ae. aegypti has predominantly domestic habits; most of the time, it stays inside homes and just leaves them in search of sites for oviposition in containers with hard edge, mainly in household containers where water is stored uncovered [34].

There is a variety of man-made containers in patios, which collect rainwater or are filled with water by people, where dengue vectors are developed. Get rid of unused containers, protect containers in use with adjusted covers, and daily change water trough for animals and vases can reduce the risk of Zika infection [35].

Water storage containers must be kept clean and closed so that mosquitoes cannot use them as aquatic habitat. Common containers in which eggs become adult dengue mosquitoes are: natural plant containers, artificial containers, and containers that people use to collect rainwater [36]. *Aedes* inside homes just sit on wet and dark surfaces to avoid dying from desiccation, making several jumps (flights) during the day before resting again [37].

As the dengue is a problem linked to home sanitation, its emergency is specifically associated with human behavior (individual or in the neighborhood) that favors the existence of breeding, since any container capable of retaining water is a potential breeding for *Aedes* eggs. Several containers have been identified, such as [38,39]: 1. Bottles; 2. Soda water bottle caps, empty tin cans, barrels with water; 3. Containers on the roof to collect rainwater (also called “clunkers”); 4. Tanker, cisterns, wells; 5. Used tires; 6. Other artificial containers that hold water, which are found in the domestic environment: buckets, tubs, basins; 7. Puddles; 8. Vases and flower vases; 9. Troughs for animals; 10. Plate under pots; 11. Swimming pools, decorative garden fountains; 12. Mechanical scrap (abandoned or discarded cars); 13. Boats and rafts; 14. Holes in trees, leaf axils, holes in stones; 15. Ceilings, awnings and gutters of the roofs; 16. Tires, pots; 17. Coconut shells; 18. Common city areas where there are concentrations of people such as: bus stations, prisons, churches, parks, squares, schools; 19. Septic tank; 20. Cemeteries.

Cemeteries are considered great sources of mosquitoes and in the last decade the results of over 30 studies related to mosquitoes in cemeteries have been published. Among the 31 species found which breed in cemeteries in 16 countries, the *Ae. aegypti* and *Aedes albopictus* were the most frequent [40]. In general, cemeteries are very suitable habitats for mosquitoes that feed on artificial containers given the large availability of sources they need (for example, sugar substances, blood, shelter or containers full of water) [41].

Mosquito breeding sites are found in and around the house: the female lays eggs in clean or almost clean water stored containers, which creates the opportunity for mosquito breeding.

Any stagnant water is a breeding ground for mosquitoes (sites of proliferation) and most of them are caused by man [42,43].

8. What can educators teach the community to prevent the production of *Ae. aegypti*?

Ae. aegypti, especially due to the lack of municipal water, results in the storage of domestic water [32]. The removal of breeding ground is a measure of great impact if it corrects "a historical social disadvantage": the lack of potable water. Moreover, insufficient urban care as the accumulation of garbage, create reservoirs suitable to contain rainwater, which are conditions ideal for the development of larvae. The best approach to control Zika depends on intensive work on the environment to reduce the amount of available vectors and the provision of potable water. The mosquito lives with people in the same house or in a perimeter of up to 100 m. Survival and spread of mosquito intimately depends on the way of life of the family.

The only option to make that the problem Zika does not become increasingly worse is to reduce the incidence of disease, and the only way to achieve it is to control *Ae. aegypti* by removing places of larval development [38]. There is unanimity in considering the elimination or reduction of populations of *Ae. aegypti* as an effective and tested method for disease prevention [42].

9. Community participation in the elimination of *Ae. aegypti*

A common denominator of success in prevention was the ability and commitment to maintain a mosquito control program. The successful implementation of programs requires careful planning, but in order to have a lasting effect, they must be sustainable indefinitely. Community involvement is essential for success, but this is a complementary alternative to traditional surveillance and control campaigns [44].

A remarkable fact is that community participation is generally high in epidemic times. This emphasizes the need for continuous surveillance by health personnel to ensure the effectiveness and sustainability of community participation initiatives. Sustainability over time will be enhanced by the availability of tools which are easy to use, based on evidence. Besides allowing officials of public health to discuss policies that have an impact on public health, it is required to ensure the supply of resources, make efficient use of limited resources, advocate the necessary funds and obtain programmatic freedom in decision-making [45].

At its most basic (city) level, the development of *Ae. aegypti* infection can be eliminated simply by preventing the vector to access to containers with water, which are necessary for the development of immature mosquitoes. *Ae. aegypti* lays its eggs and completes its development in household water and its surroundings and vector elimination will succeed only if all members of the community participate [46]. The activities that neighbors should do include control of household containers: turn, destroy, cover, protect with lid or avoid water storage in all containers that are capable of breeding mosquito larvae. Also, all those containers that are not useful for the inhabitants of the house should be discarded [47].

People who eliminate mosquito habitat remain vulnerable if their neighbors do not do it. If a neighborhood is free from breeding, it is certain that there will not be cases of Zika. It is now clear that a worthwhile long-term goal for mosquito control is to convince people that transmission mostly occurs in the home environment. People, without being aware of the disease and its risks, help to create conditions for the survival and spread of the vector. It is necessary to place the responsibility for urban mosquito control accordingly with the citizens of the community. Instead of learning to accept responsibility for their own health destiny, people sometimes become dependent on the leaders. The result is a generation that blames the government for a disease that exists, at least in part, because people refuse to participate in practices to reduce larvae in the neighborhood [48].

There is no government and health system capable of solving the problem without the active and aware participation of every person and an organized community action. Community action to eliminate mosquito breeding sites seems to be the only effective and permanent method to prevent or control the spread of Zika. It is necessary to promote behavioral changes not only in the community, but also in how the prevention and control programs are structured [49].

Interventions that are being carried out in Latin American countries are not working. They are not successful actions or sustainable over the years because they have had a very expensive and vertical structure, based on chemical control (use of insecticides) and because they use community participation and health education only in case of epidemics or emergencies. While public participation is essential, the crucial need for political commitment has been repeatedly highlighted as one of the most important components of control programs regardless of the method used [50].

10. Guillain-Barré syndrome (GBS) and other neurological complications

During the outbreak in the French Polynesia and New Caledonia, an increase of neurological complications that could be related to Zika virus infection was first observed. Between November 2013 and February 2014, 74 cases of neurological or autoimmune disease were reported in the epidemic area, including 42 cases of GBS [51]. The possibility of producing other neurological syndromes (meningitis, meningoencephalitis and myelitis) was also described in this outbreak.

In the recent epidemic in Brazil, the appearance of neurological syndromes related to a recent history of Zika virus infection has also been recorded. In 2015, Brazil reported more than 1 700 cases of GBS. Venezuela, Colombia, El Salvador and Suriname have also reported an unusual increase in cases of Guillain-Barré between December 2015 and February 2016 [9].

11. Microcephaly and other neurological disorders in newborns

Zika virus infection has also been related to the onset of neurological disorders in newborns. Brazil has reported more than 5 000 suspected cases of microcephaly from the beginning of 2015 until the epidemiological week 5 of 2016. Most of these cases are located in the northeast of the country [52].

Moreover, health authorities in the French Polynesia have recently reported an unusual increase in malformations of the central nervous system during the period 2014–2015, which coincides with Zika virus outbreaks on the island. During this period, there were 17 reported neurological malformations in newborns and antibodies against Zika virus were found in samples of 4 mothers, suggesting a possible infection during pregnancy [53].

In the USA, the Department of Health of Hawaii has confirmed on January 15, 2016 the identification of Zika virus in a newborn with microcephaly, whose mother lived in Brazil in May 2015. Between December 2015 and January 2016, the detection of ocular lesions in infants with microcephaly was also reported. In these cases, most mothers had manifested symptoms consistent with Zika virus infection during the first trimester of pregnancy [54].

It has been recently confirmed the presence of Zika virus in a fetus of 32 weeks in Slovenia, whose mother had traveled to Brazil and had become infected in the 13th week of pregnancy. The fetus had microcephaly with calcifications in brain tissue and placenta. The Zika virus was detected by PCR and electron microscopy in the brain tissue of the fetus. This finding reinforces the hypothesis of association between virus infection and development of neurological malformations [55].

Pregnant women are the highest risk group. Recommendations and actions of promotion and prevention should be directed to them, based on the available evidence linking Zika virus infection with the appearance of congenital anomalies. Pregnant women or who are trying to become pregnant and planning to travel to areas affected by Zika virus transmission could consider postponing the trip if not essential. If it is not possible to delay the trip, they should take extra precautionary measures to avoid mosquito bites [56].

Men returning from areas affected with local transmission of Zika virus should consider using condoms during sex with pregnant women or women who may become pregnant during 28 days, if they have not had symptoms consistent with Zika infection and for a period of 6 months, in the case of having had laboratory-confirmed disease. Blood donations must be delayed for 28 days in case of travel to risk areas [57,58].

12. Why are dengue and Zika tropical diseases rapidly expanding?

Unfortunately, in the first decade of the twentieth century, *Ae. aegypti* has invaded again almost all Latin American countries that had achieved eradication during 1950 and 1960 [15]. Currently, Zika is a disease that spreads rapidly in the tropics of the world and causes serious illness including Guillain-Barré and congenital malformations [51].

Some factors that have contributed to the emergence of Zika are [24]: emergence of the world as a global village, unplanned urbanization, inadequate health service, improper disposal of feces and development of vector resistance to insecticides.

Some things that are expressed in the foregoing may be “uncomfortable”. However, the time that has passed honestly talks about the problem of emerging diseases that have been ignored for many years to the point of not even having reliable statistics [59]. One of the failures is in epidemiological surveillance. It is a set of actions that provide knowledge, detection or prevention of any changes in the determinant and decisive factors of individual or collective health, in order to recommend and take prevention and control measures. The problem we encounter when monitoring is that the reported cases are not always representative of the reality of the population.

This states that we should worry about making a wise interpretation of surveillance data through understanding and detecting at which points data get lost and what information bias results from these losses [60]. There is no correlation between reported cases and what happens in reality. It is like seeing a part of the whole thing. It is like seeing only the tip of a large iceberg. This is likely to lead to underestimate its importance [61].

One of the main limitations of surveillance is that their numbers depend on patients who consult a doctor, without this step, and the disease will not be officially registered. In population studies based on attenuated symptoms of fever and myoarthralgia, only 5%–20% of those who develop an acute disease consulted the doctor [62].

Many of the people who attended the consultation were the ones who perceived their symptoms as more severe or who had prolonged demonstrations. Often the case record gets lost, because sometimes people, due to fear of the diagnosis that they could be given, do not go to medical facilities, when they should do so [63].

In addition, if the patient visits the doctor, often the professional does not ask for blood samples for diagnosis, except in cases of greater severity. On the other hand, the answer of patients upon the request to undergo a blood test is another point at which data are lost because several of the patients who are asked a diagnostic test do not do it [64]. Furthermore, not all laboratories routinely screen serum samples for the presence of antibodies. Moreover, when a negative serology result is found in the laboratory, an infection is not dismissed. Even worse, in some reference laboratories, samples are not processed due to lack of supplies, resulting in a loss of a substantial proportion of cases involved in the epidemic. Self-medication is common among the population for certain symptoms such as headache or fever and so these cases are not part of the statistics. From the point of view of public health, the diagnosis is very important since management differs depending on the clinical symptoms [65].

Data use at different points along the chain of surveillance (from the patient to official statistics) is often described as a pyramid. When the disease in the community is studied, there is discordance between the amount of people who take primary care and the reported disease in a national survey.

The disease in the community is the base of the pyramid, while cases reaching official statistics are the apex. This shows that, in comparison to cases in official statistics, real cases in the community are much higher [66].

The general consensus is that in Latin America underreporting is common. Another feature that varies by region is the proportion of population covered by national surveillance systems. The national data sets have different amounts of information, and a few use standard case definitions. All these factors make it very difficult to obtain sensible conclusions on the burden of Zika and other infections by *Ae. aegypti* or to make valid comparisons between different health regions in a country [67].

There are huge data gaps in developing countries about epidemics of mosquito-borne diseases. Moreover, little progress was made on how the population perceives the infections transmitted by *Ae. aegypti* as a problem involving human behavior [68]. It was not possible to motivate people enough to clean up the community and eliminate mosquito breeding sites to the point in which mosquito density is low enough to prevent the spread of epidemics of dengue and Zika. And that is why this goal in Latin America has been so frustrating [69].

In underdeveloped countries, changing behavior may not be easy or quick, as it is a generation that has been led to believe that the government can do better. In fact, the dengue and Zika epidemic in 2015–2016 can be used to encourage this behavior change. If that happens, an unfortunate event would have been used. It is known that it will take many years to achieve the goal, but also that if the result is correct, it will be successful to prevent the coexistence of two simultaneous epidemics, Zika and dengue [70–72].

It is important to start now. We should not wait. Otherwise, we will probably have to prepare for a scene of major epidemics of dengue and Zika widespread uncontrollably throughout the American continent. Blind trust in the last 50 years as regards reducing mosquito breeding may seem logical, given the domestic habitat of the vector, but obviously it does not work in most communities at risk due to lack of cooperation in the neighborhood and the lack of public health policies [73–75].

Surely, this has strengthened the rapid development of epidemics of dengue and Zika which is affecting us. *Ae. aegypti* is more prevalent now than at any other time in history [76]. Again, political turmoil in developing countries will set out difficult questions to answer in a world where mosquitoes can move, but where efficient actions are frequently stopped [77,78].

13. Conclusions

The 2015–2016 dengue epidemics are the worst in the history of Latin America. This is the result of decades of governments that have been true predators of public health. It is not wise to underestimate the dengue virus. In the best of cases, it makes people sick. In the worst cases, it kills. They did not focus on the 2008–2009 epidemic and prevention programs were abandoned [79–81].

Proof of this is that in 2016, in the city of Buenos Aires, local transmission of dengue and Zika was recorded. It is the first time since 1870, when there was a yellow fever epidemic, that there are millions of *Ae. aegypti* mosquitoes in Buenos Aires [1]. This is also happening in the great capitals of Latin America. The health system is in crisis: hospitals are not stocked, there is little medical staff and nurses, people have to wait more than 5 h in hospitals and there are no supplies for laboratory testing. But what is more serious is the concealment of the number of people infected and killed by dengue. The actual figures would exceed official statistics 7 times. Moreover, large cities are full of potential habitats of the *Ae. aegypti* mosquito. This explains why we are losing the battle against dengue. This explains, due to mismanagement in health in Latin America, why the Zika epidemic has become the “Perfect Storm”. Half of the global population is at risk of getting a disease transmitted by *Ae. aegypti*. Again, the health catastrophe in Latin America shows that we are the greatest threat to public health, and the *Ae. aegypti* mosquitoes are not.

Conflict of interest statement

I declare that I have no conflict of interest.

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References

[1] Troncoso AR. Vector-borne diseases. In: Troncoso AR, editor. *Dengue and dengue hemorrhagic fever: its history and resurgence as a public health problem, progress and challenges*. Buenos Aires: Cuentahilos Press; 2010, p. 167-77.
[2] Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL, et al. Global trends in emerging infectious diseases. *Nature* 2008; **451**: 990-3.
[3] Gubler DJ. Dengue, urbanization and globalization: the unholy trinity of the 21st century. *Trop Med Health* 2011; **39**: 3-11.
[4] Duffy MR, Chen TH, Hancock WT, Powers AM, Kool JL, Lanciotti RS, et al. Zika virus outbreak on Yap Island, Federated States of Micronesia. *N Engl J Med* 2009; **360**(24): 2536-43.
[5] Lanciotti RS, Kosoy OL, Laven JJ, Velez JO, Lambert AJ, Johnson AJ, et al. Genetic and serologic properties of Zika virus associated with an epidemic, Yap State, Micronesia, 2007. *Emerg Infect Dis* 2008; **14**: 1232-9.
[6] Cao-Lormeau VM, Roche C, Teissier A, Robin E, Berry AL, Mallet HP, et al. Zika virus, French Polynesia, South Pacific, 2013. *Emerg Infect Dis* 2014; **20**(6): 1085-6.
[7] Dupont-Rouzeyrol M, O'Connor O, Calvez E, Daurès M, John M, Grangeon JP, et al. Co-infection with Zika and dengue viruses in 2 patients, New Caledonia, 2014. *Emerg Infect Dis* 2015; **21**(2): 381-2.
[8] Cardoso CW, Paploski IA, Kikuti M, Rodrigues MS, Silva MM, Campos GS, et al. Outbreak of exanthematous illness associated with Zika, chikungunya, and dengue viruses, Salvador, Brazil. *Emerg Infect Dis* 2015; **21**(12): 2274-6.
[9] Lee J. Zika virus infection: new threat in global health. *J Korean Med Sci* 2016; **31**(3): 331-2.
[10] Yamey G, Torreele E. The world's most neglected diseases. *BMJ* 2002; **325**: 176-7.
[11] Medlock JM, Hansford KM, Schaffner F, Versteirt V, Hendrickx G, Zeller H, et al. A review of the invasive mosquitoes in Europe: ecology, public health risk, and control options. *Vector Borne Zoonotic Dis* 2012; **12**(6): 435-47.
[12] Monath TP. Yellow fever. In: Service MW, editor. *The encyclopedia of arthropod-transmitted infections*. Wallingford: CAB International; 2001, p. 571-7.
[13] Weaver SC, Reisen WK. Present and future arboviral threats. *Antivir Res* 2010; **85**: 328-45.
[14] Hayes EB. Zika virus outside Africa. *Emerg Infect Dis* 2009; **15**(9): 1347-50.
[15] Woolhouse MEJ, Gowtage-Sequeria S. Host range and emerging and reemerging pathogens. *Emerg Infect Dis* 2005; **11**(12): 1842-7.
[16] Monath TP. Yellow fever. In: Monath TP, editor. *The arboviruses: epidemiology and ecology*. Boca Raton: CRC Press; 1988, p. 139-241.
[17] Hennessey M, Fischer M, Staples JE. Zika virus spreads to new areas – region of the Americas, May 2015–January 2016. *MMWR Morb Mortal Wkly Rep* 2016; **65**: 55-8.
[18] Weaver SC. Vector biology in viral pathogenesis. In: Nathanson N, editor. *Viral pathogenesis*. New York: Lippincott-Raven; 1997, p. 329-52.
[19] Brady OJ, Golding N, Pigott DM, Kraemer MU, Messina JP, Reiner RC Jr, et al. Global temperature constraints on *Aedes aegypti* and *Ae. albopictus* persistence and competence for dengue virus transmission. *Parasit Vectors* 2014; **7**: 338.
[20] Campbell KM, Lin CD, Iamsirithaworn S, Scott TW. The complex relationship between weather and dengue virus transmission in Thailand. *Am J Trop Med Hyg* 2013; **89**(6): 1066-80.
[21] Carrington LB, Seifert SN, Armijos MV, Lambrechts L, Scott TW. Reduction of *Aedes aegypti* vector competence for dengue virus under large temperature fluctuations. *Am J Trop Med Hyg* 2013; **88**: 689-97.
[22] Lambrechts L, Paaijmans KP, Fansiri T, Carrington LB, Kramer LD, Thomas MB, et al. Impact of daily temperature fluctuations on dengue virus transmission by *Aedes aegypti*. *Proc Natl Acad Sci U S A* 2011; **108**: 7460-5.

[23] Carrington LB, Armijos MV, Lambrechts L, Scott TW. Fluctuations at a low mean temperature accelerate dengue virus transmission by *Aedes aegypti*. *PLoS Negl Trop Dis* 2013; **7**: e2190.

[24] Nagao Y, Thavara U, Chitnumsup P, Tawatsin A, Chansang C, Campbell-Lendrum D. Climatic and social risk factors for *Aedes* infestation in rural Thailand. *Trop Med Int Health* 2003; **8**: 650-9.

[25] Richardson K, Hoffmann AA, Johnson P, Ritchie S, Kearney MR. Thermal sensitivity of *Aedes aegypti* from Australia: empirical data and prediction of effects on distribution. *J Med Entomol* 2011; **48**: 914-23.

[26] Estallo EL, Lamfri MA, Scavuzzo CM, Almeida FF, Introini MV, Zaidenberg M, et al. Models for predicting *Aedes aegypti* larval indices based on satellite images and climatic variables. *J Am Mosq Control Assoc* 2008; **24**: 368-76.

[27] Johansson MA, Dominici F, Glass GE. Local and global effects of climate on dengue transmission in Puerto Rico. *PLoS Negl Trop Dis* 2009; **3**: e382.

[28] Barbazan P, Guiserix M, Boonyuan W, Tuntaprasart W, Pontier D, Gonzalez JP. Modelling the effect of temperature on transmission of dengue. *Med Vet Entomol* 2009; **24**: 66-73.

[29] Carrington LB, Seifert SN, Willits NH, Lambrechts L, Scott TW. Large diurnal temperature fluctuations negatively influence *Aedes aegypti* (Diptera: Culicidae) life-history traits. *J Med Entomol* 2013; **50**: 43-51.

[30] Rohani A, Wong YC, Zamre I, Lee HL, Zurainee MN. The effect of extrinsic incubation temperature on development of dengue serotype 2 and 4 viruses in *Aedes aegypti* (L.). *Southeast Asian J Trop Med Public Health* 2009; **40**: 942-50.

[31] Liang G, Gao X, Gould EA. Factors responsible for the emergence of arbovirus; strategies, challenges and limitations for their control. *Emerg Microbes Infect* 2015; **4**(3): e18.

[32] Eisen L, Beaty BJ, Morrison AC, Scott TW. Proactive vector control strategies and improved monitoring and evaluation practices for dengue prevention. *J Med Entomol* 2009; **46**(6): 1245-55.

[33] Llinás GA, Gardenal CN. Phylogeography of *Aedes aegypti* in Argentina: long-distance colonization and rapid restoration of fragmented relicts after a continental control campaign. *Vector Borne Zoonotic Dis* 2012; **12**: 254-61.

[34] Morrison AC, Gray K, Getis A, Astete H, Sihuincha M, Focks D, et al. Temporal and geographic patterns of *Aedes aegypti* (Diptera: Culicidae) production in Iquitos, Peru. *J Med Entomol* 2004; **41**: 1123-42.

[35] Ayorinde A, Oboh B, Otubanjo O, Alimba A, Odeigah P. Some toxicological effects of a commonly used mosquito repellent in Lagos State, Nigeria. *Res J Environ Toxicol* 2014; **8**: 46-52.

[36] Koou SY, Chong CS, Vythilingam J, Lee CY, Ng LC. Insecticide resistance and its underlying mechanisms in field populations of *Aedes aegypti* adults (Diptera: Culicidae) in Singapore. *Parasit Vectors* 2014; **7**: 471.

[37] Basso C, Caffera RM, García da Rosa E, Lairihoy R, González C, Norbis W, et al. Mosquito-producing containers, spatial distribution, and relationship between *Aedes aegypti* population indices on the southern boundary of its distribution in South America (Salto, Uruguay). *Am J Trop Med Hyg* 2012; **87**: 1083-8.

[38] Rubio A, Cardo MV, Vezzani D. Tire-breeding mosquitoes of public health importance along an urbanization gradient in Buenos Aires, Argentina. *Mem Inst Oswaldo Cruz* 2011; **106**: 678-84.

[39] Díaz-Nieto LM, Maciá A, Perotti MA, Berón CM. Geographical limits of the southeastern distribution of *Aedes aegypti* (Diptera, Culicidae) in Argentina. *PLoS Negl Trop Dis* 2013; **7**: e1963.

[40] Soliani C, Rondan-Dueñas J, Chiappero MB, Martínez M, Da Rosa EG, Gardenal CN. Genetic relationships among populations of *Aedes aegypti* from Uruguay and northeastern Argentina inferred from ISSR-PCR data. *Med Vet Entomol* 2010; **24**: 316-23.

[41] Vezzani D, Albicócco AP. The effect of shade on the container index and pupal productivity of the mosquitoes *Aedes aegypti* and *Culex pipiens* breeding in artificial-containers. *Med Vet Entomol* 2009; **23**: 78-84.

[42] Kilpatrick AM, Randolph SE. Drivers, dynamics, and control of emerging vector-borne zoonotic diseases. *Lancet* 2012; **380**(9857): 1946-55.

[43] Vasilakis N, Cardosa J, Hanley KA, Holmes EC, Weaver SC. Fever from the forest prospects for the continued emergence of sylvatic dengue virus and its impact on public health. *Nat Rev Microbiol* 2011; **9**(7): 532-41.

[44] Vezzani D, Carbajo AE. *Aedes aegypti, Aedes albopictus*, and dengue in Argentina: current knowledge and future directions. *Mem Inst Oswaldo Cruz* 2008; **103**: 66-74.

[45] Chadee DD. Resting behaviour of *Aedes aegypti* in Trinidad: with evidence for the re-introduction of indoor residual spraying (IRS) for dengue control. *Parasit Vectors* 2013; **6**: 255.

[46] Reiter P. Oviposition, dispersal, and survival in *Aedes aegypti*: implications for the efficacy of control strategies. *Vector Borne Zoonotic Dis* 2007; **7**: 261-73.

[47] Harrington LC, Edman JD, Scott TW. Why do female *Aedes aegypti* (Diptera: Culicidae) feed preferentially and frequently on human blood? *J Med Entomol* 2001; **38**: 411-22.

[48] Adler PB, Hillerislambers J, Levine JM. A niche for neutrality. *Ecol Lett* 2007; **10**: 95-104.

[49] Heintze C, Velasco Garrido M, Kroeger A. What do community-based dengue control programmes achieve? A systematic review of published evaluations. *Trans R Soc Trop Med Hyg* 2007; **101**: 317-25.

[50] Lloyd LS, Winch P, Ortega-Canto J, Kendall C. Results of a community-based *Aedes aegypti* control program in Merida, Yucatan, Mexico. *Am J Trop Med Hyg* 1992; **46**: 635-42.

[51] Oehler E, Watrin L, Larre P, Leparc-Goffart I, Lastere S, Valour F, et al. Zika virus infection complicated by Guillain-Barre syndrome—case report, French Polynesia, December 2013. *Euro Surveill* 2014; **19**: 20720.

[52] Zanluca C, Melo VC, Mosimann AL, Santos GI, Santos CN, Luz K. First report of autochonous transmission of Zika virus in Brazil. *Mem Inst Oswaldo Cruz* 2015; **110**(4): 569-72.

[53] Choumet V, Desprès P. Dengue and other flavivirus infections. *Rev Sci Tech* 2015; **34**: 473-8. 462–72.

[54] Oliveira Melo AS, Malinger G, Ximenes R, Szejnfeld PO, Alves Sampaio S, Bispo de Filippis AM. Zika virus intrauterine infection causes fetal brain abnormality and microcephaly: tip of the iceberg? *Ultrasound Obstet Gynecol* 2016; **47**: 6-7.

[55] Akolekar R, Beta J, Picciarelli G, Ogilvie C, D'Antonio F. Procedure-related risk of miscarriage following amniocentesis and chorionic villus sampling: a systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 2015; **45**: 16-26.

[56] Petersen EE, Staples JE, Meaney-Delman D, Fischer M, Ellington SR, Callaghan WM, et al. Interim guidelines for pregnant women during a Zika virus outbreak – United States, 2016. *MMWR Morb Mortal Wkly Rep* 2016; **65**: 30-3.

[57] Musso D, Roche C, Robin E, Nhan T, Teissier A, Cao-Lormeau VM. Potential sexual transmission of Zika virus. *Emerg Infect Dis* 2015; **21**(2): 359-61.

[58] Patiño-Barbosa AM, Medina I, Gil-Restrepo AF, Rodriguez-Morales AJ. Zika: another sexually transmitted infection? *Sex Transm Infect* 2015; **91**: 359.

[59] Rey JR, Lounibos P. [Ecology of *Aedes aegypti* and *Aedes albopictus* in the Americas and disease transmission]. *Biomedica* 2015; **35**(2): 177-85.

[60] Coffey LL, Forrester N, Tsetsarkin K, Vasilakis N, Weaver SC. Factors shaping the adaptive landscape for arboviruses implications for the emergence of disease. *Future Microbiol* 2013; **8**(2): 155-76.

[61] Wong PS, Li MZ, Chong CS, Ng LC, Tan CH. *Aedes (Stegomyia) albopictus* (Skuse): a potential vector of Zika virus in Singapore. *PLoS Negl Trop Dis* 2013; **7**(8): e2348.

[62] Ioos S, Mallet HP, Leparc Goffart I, Gauthier V, Cardoso T, Herida M. Current Zika virus epidemiology and recent epidemics. *Med Mal Infect* 2014; **44**(7): 302-7.

[63] Faye O, Freire CCM, Iamarino A, Faye O, de Oliveira JVC, Diallo M, et al. Molecular evolution of Zika virus during its emergence in the 20(th) century. *PLoS Negl Trop Dis* 2014; **8**(1): e2636.

[64] Seccacini E, Lucia A, Zerba E, Licastro S, Masuh H. *Aedes aegypti* resistance to temephos in Argentina. *J Am Mosq Control Assoc* 2008; **24**: 608-9.

[65] Kroeger A, Nathan MB. Dengue: setting the global research agenda. *Lancet* 2006; **368**: 2193-5.
[66] Visintin AM, Laurito M, Diaz LA, Benítez Musicant G, Cano C, Ramírez R, et al. New records of mosquito species (Diptera: Culicidae) for Central and Cuyo regions in Argentina. *J Am Mosq Control Assoc* 2009; **25**: 208-9.
[67] Bernardini Zambrini DA. Neglected lessons from the 2009 dengue epidemic in Argentina. *Rev Saude Publica* 2011; **45**: 428-31.
[68] Gwatkin DR, Guillot M, Heuveline P. The burden of disease among the global poor. *Lancet* 1999; **354**: 586-9.
[69] Nafziger EW, Auvinen J. The economic causes of humanitarian emergencies. In: Nafziger EW, Stewart F, Vayrynen R, editors. *War, hunger and displacement: the origin of humanitarian emergencies*. Oxford: Oxford University Press; 2000, p. 91-145.
[70] Kelly-Hope L, Ranson H, Hemingway J. Lessons from the past: managing insecticide resistance in malaria control and eradication programmes. *Lancet Infect Dis* 2008; **8**: 387-9.
[71] Hemingway J, Beaty BJ, Rowland M, Scott TW, Sharp BL. The innovative vector control consortium: improved control of mosquito-borne diseases. *Trends Parasitol* 2006; **22**: 308-12.
[72] Gubler DJ. The changing epidemiology of yellow fever and dengue, 1900 to 2003: full circle? *Comp Immunol Microbiol Infect Dis* 2004; **27**: 319-30.
[73] Messina JP, Brady OJ, Pigott DM, Brownstein JS, Hoen AG, Hay SI. A global compendium of human dengue virus occurrence. *Sci Data* 2014; **1**: 140004.
[74] Messina JP, Brady OJ, Scott TW, Zou C, Pigott DM, Duda KA, et al. Global spread of dengue virus types: mapping the 70 year history. *Trends Microbiol* 2014; **22**(3): 138-46.
[75] Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, et al. The global distribution and burden of dengue. *Nature* 2013; **496**(7446): 504-7.
[76] Reiner RC Jr, Perkins TA, Barker CM, Niu T, Chaves LF, Ellis AM, et al. A systematic review of mathematical models of mosquito-borne pathogen transmission: 1970–2010. *J R Soc Interface* 2013; **10**(81): 20120921.
[77] Smith DL, Perkins TA, Reiner RC Jr, Barker CM, Niu T, Chaves LF, et al. Recasting the theory of mosquito-borne pathogen transmission dynamics and control. *Trans R Soc Trop Med Hyg* 2014; **108**(4): 185-97.
[78] Nguyet NM, Duong TH, Trung VT, Nguyen TH, Tran CN, Long VT, et al. Host and viral features of human dengue cases shape the population of infected and infectious *Aedes aegypti* mosquitoes. *Proc Natl Acad Sci U S A* 2013; **110**(22): 9072-7.
[79] Seley C, Avrutin P, Rossi L, Hahnm M, Troncoso A. Dengue research needs related to surveillance and emergency response. *Prensa Med Argent* 2009; **96**: 215-29.
[80] Martinez FN, Gonzalez LJ, Gabriela F, Laura R, Troncoso A. The chikungunya threat: the globalization of vectorborne diseases. *Prensa Med Argent* 2009; **96**: 671-80.
[81] Erica RW, Paula A, Celeste S, Laura R, Troncoso A. Community participation in dengue prevention and control: an urban neglected tropical disease. *Prensa Med Argent* 2009; **96**: 185-95.