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Dengue, a re-emergent social problem in the Americas. Strategies for its eradication

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ABSTRACT

Dengue virus is considered one of the most important re-emergent viruses. It threatens roughly one third of the world's population, with more than 50 million cases reported each year in tropical and sub-tropical regions. Dengue re-emergency is caused by multiple environmental, social and economic factors, as well as by governmental health policies. Generally, poverty and inequality, existing in many countries, are behind all these factors. This is a review on dengue as a social problem in the American continent, its epidemiological situation and current eradication strategies. This paper also includes the particular situation of Cuba, a country that, as a consequence of the results obtained in public healthcare, the advances in scientific, technical and specifically biotechnological development, and the health policies implemented by the Cuban government, is the only Latin-American nation that has been able to control a disease such as dengue

Key words: Dengue, dengue virus, social problems, social factors, Cuba, poverty, epidemiology, eradication

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RESUMEN

Dengue, un problema social re-emergente en las Américas. Estrategia en su erradicación. El virus de dengue está considerado uno de los virus re-emergentes más importantes en la actualidad, constituyendo una amenaza a un tercio de la población mundial, con más de 50 millones de casos reportados cada año en regiones tropicales y sub-tropicales. La re-emergencia del dengue tiene su causa en múltiples factores tanto ambientales, como sociales, económicos y de políticas de salud de los gobiernos. En general, detrás de todos estos factores se encuentra la pobreza y la desigualdad existente en muchos países. Esta es una revisión de la situación del dengue como problema social en las Américas, la situación epidemiológica y las estrategias más actuales en su erradicación. Esta revisión incluye la situación particular de Cuba, donde los resultados obtenidos en el sector de la salud, el desarrollo científico-técnico y de la biotecnología y las políticas de salud seguidas por nuestro gobierno le han permitido ser el único país latinoamericano en lograr controlar enfermedades como el dengue.

Palabras claves: Dengue, virus de dengue, problema social, factores sociales, Cuba, pobreza, epidemiología, erradicación

Introduction

Thirty years ago, it was optimistically believed that scientific advances in hygiene and diagnosis methods, together with the development of new drugs and vaccines -which had already achieved a drastic reduction in the prevalence of diseases such as poliomyelitis and tuberculosis- would, in due time, lead to the control of the remaining infectious diseases. Today, infectious diseases are still within the main causes of morbidity and mortality worldwide, and in some cases their incidence is even increasing. An initial optimism has been replaced by a more thoughtful and realistic outlook as the close relationship between disease and the socioeconomic situation, in a changing and ever more globalized world, is being recognized.

Emergent infectious diseases are, in general, a group of recently appearing diseases, such as HIV/AIDS, Hantavirus pulmonary syndrome, Lyme disease, hemolytic uremic syndrome, Ebola virus hemorrhagic fever, and even more recently, avian influenza. In contrast, re-emergent infectious diseases have been known for a long time, but have recently had a significant increase in their incidence or a more widespread geographic localization, like dengue.

During the new millennium, issues such as quality of life, infectious diseases, chronic disorders, diseases associated to urbanization and climate changes are still important in the general health condition of the population. Paradoxically, in spite of the high cost, specialization, technological advances and pharmaceutical breakthroughs that characterize modern medicine, most of these problems remain unsolved. The wide array of available drugs to fight diseases and their causes and the ever growing funds to support the cost of health care have not been able, however, to achieve what 30 years ago was considered to be scientifically possible and economically feasible.

Climate change is one of the main worldwide ecological problems, and it is considered to be produced basically by the atmospheric accumulation of greenhouse effect gases, as a result of human activity [1]. Many of the organisms and biological processes associated to the transmission of infectious diseases are especially influenced by climatic variables such as temperature, precipitation and humidity. The foreseen growth of vector insect populations, as a direct result of climate change, increases the transmission potential of many infectious diseases [2, 3].

The incidence of dengue and dengue hemorrhagic fever have increased significantly in the last decades. Dengue virus is regarded as one of the most important re-emergent viruses, directly threatening one third of the world population and resulting in more than 50 million cases reported in tropical and sub-tropical areas. The emergence and re-emergence of dengue are

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due to multiple factors of environmental, social, economic and political nature, including national health care policies. These factors include failures in vector control programs, population growth, fast and unplanned urbanization, an increase in transportation by plane, an increase in the amount of non-biodegradable waste, the inefficiency of public healthcare infrastructure and a lack of funds for its improvement. In general, poverty and inequality stand behind most of these factors in many countries [4, 5].

Currently, the excessively high prices of medical care do not solve over 90% of the public healthcare problems, and the private medicine model of many countries has led to a strong privatization of this activity and an ever more commercial conception of health services [6].

Strong research into the social, environmental and economic risk factors mentioned above is vital for a better understanding of the challenges ahead and the available alternatives for the prevention and control of disease [7]. Although it is true that it is unacceptable to talk about social progress without mentioning scientific and technical progress, today we can say that social progress is not conceivable without the results of the biological sciences in general [8].

Cuba, through the progress in public health care together with the recent achievements in the field of biotechnology, has become a medical and scientific powerhouse. The health policies implemented by the government have allowed our country to become the only Latin American state that has controlled diseases such as dengue, setting an example for other nations of the world.

The purpose of this paper is to analyze the state of dengue as a social problem in the Americas, including its epidemiological situation and the strategies currently in place for its control. This review also specifically includes an assessment of the Cuban situation.

What is dengue?

Dengue is an acute viral disease transmitted by mosquitoes, that has produced an increase in morbidity and mortality in recent decades. Human beings are the main host for dengue virus, which uses mosquitoes of the genus *Stegomyia* (formerly *Aedes*) as its main vector for disease transmission, particularly the species *Stegomyia aegypti* (*Aedes aegypti*), also known as the vector for yellow fever.

Dengue virus is an arbovirus. This is an ecological term used to describe the viruses requiring blood-sucking arthropods to complete their life cycle. Arboviruses typically need at least two hosts, a vertebrate and an arthropod.

Taxonomically, dengue virus belongs to the *Flavivirus* genus (*Flaviviridae* family), together with other members such as Japanese Encephalitis Virus (JEV), West Nile Virus (WNV) and Yellow Fever Virus (YFV). It is usually divided into four different serotypes (DEN 1-4). Most dengue virus infections are asymptomatic, and those following a different clinical course present a variety of clinical symptoms, of which the most common one is an acute fever known as Dengue Fever (DF), that is very similar to other acute febrile states of viral origin such as those produced by influenza. However, in a small number of cases, dengue infections progress to spontaneous febrile hemorrhages (Dengue Hemorrhagic Fever, DHF) or, in more severe cases, to Dengue Shock Syndrome (DSS), characterized by circulatory failure [9].

Currently, between 2 500 to 3 000 million persons live in high-risk areas for dengue transmission. The annual estimates of hemorrhagic dengue cases are of about 500,000, and at least 21,000 deaths are reported every year, most of them in children. There have been dengue or DHF outbreaks in more than 100 countries [10].

History of Dengue in the region

Chinese texts from the years 265-420 A.D. mention a disease known as "water poison", attributed to flying insects that reproduced in the water. Dengue fever is an ancient disease, which spread throughout the world with the increase in international trade during the XVIII and XIX centuries [11]. The first clinical description of the disease later known as dengue was of 1780, in Philadelphia [5]. A report from Ehrenkranz *et al.* [12] in 1971 states that the pandemics of dengue in southern US and the Caribbean region can be divided into four periods: 1827-1884, 1885-1920, 1921-1950 and 1951-1970.

One of the most important factors in the spreading of dengue in previous centuries was the slave trade. *Aedes* reproduced on the slave trade ships, with the prisoners and their captors acting as viral reservoirs. At least 8 pandemics during the years 1779 to 1916 might have their origins in maritime ports of entry [13, 14].

The pandemics from the first period were characterized by the involvement of ports in the Caribbean, the Gulf of Mexico and the Atlantic. The most important clinical signs were arthralgias, obstetric complications and hemorrhages.

The second period is strongly linked to the Caribbean as the main commercial route for international trade in the region, and to railroads as the connection between North American cities. There were outbreaks reported in Texas, Bermuda, Cuba, Panama, Puerto Rico and Venezuela in the period from 1880 to 1920. The third period (1920-1950) is related to the increased urbanization in southern U.S., the rapid movement of the population due to mass migrations towards urban areas and the propagation of the mosquito, mainly during World War II, leading to an increase in dengue hemorrhagic fever [15].

The last period is linked to the accelerated growth of the population in the Caribbean region. The first laboratory isolate from the area was obtained during this period, in 1953, as documented by the report of Anderson and Downs [5].

There was a very effective control of the disease in most countries of the region during the 1950's and 1960's, as a side effect of the Pan-American Health Organization (PAHO)-sponsored programs for the control of *Aedes aegypti* to eliminate yellow fever and malaria. These programs eliminated the vector from more than 70% of the originally infected areas of the subcontinent [5, 15]. Unfortunately, they lost political support after this, with a subsequent proliferation

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and spread of the mosquito throughout the region in the 1970's and 1980's, for which governmental reaction for its control arrived too late [16]. Starting in the seventies, frequent episodes of re-colonization of the mosquito were observed. There were epidemics at the beginning of the decade in Jamaica, Puerto Rico, the Lesser Antilles, Haiti and Venezuela.

In 1985, a second *Aedes* species originating from Asia, *A. albopictus* (also known as the "Asian tiger") was detected in North America [17, 18]. *Established populations of this arthropod were found in Houston, Texas, arriving through used car tires imported from Asia* [19].

Besides the 4 periods described by Ehrenkranz *et al.* in 1971, there were also epidemic outbreaks which have appeared in the last 30 years of the XX century. These last decades have been characterized by an increase in the density of *Aedes aegypti* populations and their spread to most countries of the region, the co-circulation of several serotypes, the introduction of genotypes with the potential to cause hemorrhagic fever, the presence of hyperendemicity in several countries of the area, and the increase in the number of cases of dengue or hemorrhagic dengue. There have also been FHD outbreaks or epidemics in several countries.

In 1977, serotype 1 is introduced for the first time in the region, triggering a pandemic that started in Jamaica and spread to Cuba, Puerto Rico, Venezuela and the remaining countries of the Caribbean, Mexico, Central America and the northern parts of South America. There were more than 700 000 cases reported in the region from 1977 to 1980, with more than 400 000 cases of classic dengue fever in Cuba, a small island with a population of 10 million persons at the time [20]. The 80's witnessed the appearance of Dengue Hemorrhagic Fever (DHF) epidemic and the co-circulation of several dengue serotypes.

The first and so far biggest epidemic of DHF in the region was reported in Cuba in 1981, caused by dengue serotype 2 [21]. Out of the 344 203 reported cases, 10 312 had DHF. There were 158 deaths, 101 of which were children (figure 1).

Another important outbreak was reported in Cuba in 1997, caused by dengue serotype 2, with 3 012 confirmed cases, of which 205 evolved to DHF with 12 deaths in adults [23]. This outbreak coincided with an increase in the infestation index by *A. aegypti* in the area, caused by imports of automobile tires [24].

More recently, in 2001-2002, there was a new Cuban outbreak caused by serotype 3. There were 14 443 confirmed cases, 81 of them with DHF and 3 deaths, all of them in adults [5].

There were more than 1 million dengue cases reported in the region in the year 2002, 17 363 of which were DHF, with 225 deaths. According to the figures reported for 2004 by the Pan-American Health Organization (PAHO), the number of fatalities decreased to a total of 57 in that year, coinciding with an increase in the circulation of serotype 3. The 3 countries with the highest number of reported cases were Brazil (107 168), Venezuela (30 693) and Colombia (27 523). According to the latest PAHO data (of November 1st, 2005) there were 260 321 cases of DF in 2005, of which 2 861 correspond to DHF, with 68 deaths [25].

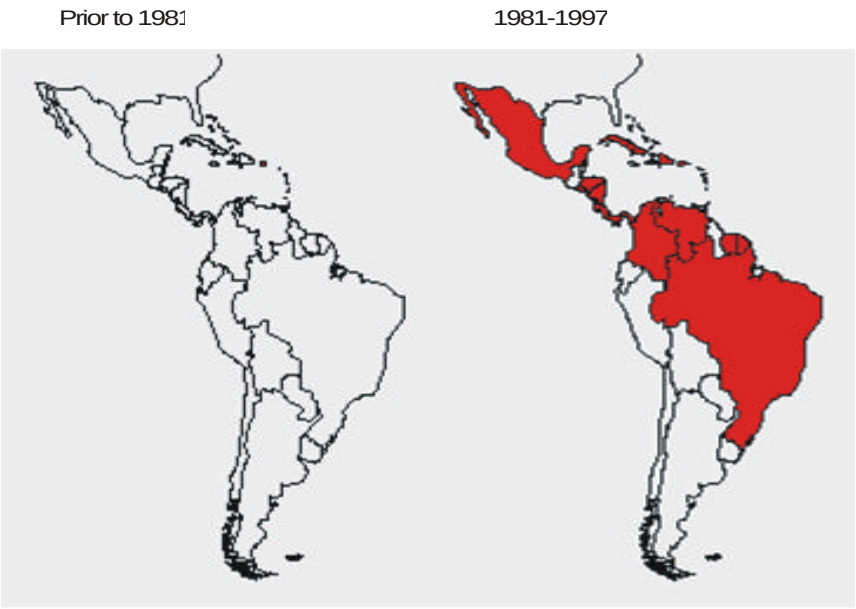

Figure 1. Geographical distribution of cases of dengue hemorrhagic fever confirmed by laboratories in the Americas (Red areas), prior to 1981 and from 1981 to 1997. Source: CDC 2001 [22].

The epidemiological and social conditions that increased the severity of the dengue hemorrhagic fever epidemic in Asia are also present in the Latin American continent. Currently, only Cuba, Uruguay and Chile are non-endemic countries for dengue [26].

Social issues related to the re-emergence of dengue in the area

The answer of Dr. John Snow -considered to be the father of modern epidemiology due to his persistence in determining the causes of cholera transmission and to the development of statistical mapping techniques in London in the 1850's upon being questioned about how to solve the epidemiological problems of the shores of the Thames river, was categorical: The sources of all those issues were poor healthiness, a lack of hygiene and inadequate living conditions. Health is a social problem, and its improvement depends on social actions. Science and society interact in many different ways [27].

Poverty, together with social differences, is increasing in most countries of the American continent. Pathologist Rudolf Virchow argued, back in 1848, that "Medical statistics will be our measuring rule: We will count lives one by one, and let us see where death takes its greater toll: on the workers, or in the privileged classes …"

Any analysis of the degree of scientific and technological development in the Latin America region will yield relatively low values for any conceivable indicator. The expenses in science and technology by Latin American countries are a little less than 8 000 million dollars a year, representing 2.3% of the worldwide expenditure in this sector [28]. For example, the amount invested by Latin America in science and technology is equivalent to the money poured into Research and Development (R & D) by General Motors alone, illustrating the existing gap

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between the region and developed countries on this issue.

The unprecedented growth of the population, uncontrolled and unplanned urbanization, the increase in poverty and an inadequate control of the environment are among the social and economic factors that stand behind the re-emergence of dengue [4, 29]. More than 80% of the population in Latin America is concentrated in urban areas. However, in most cities of the region urbanization is characterized by informal settlements and shanty towns without an appropriate supply of drinking water, drainage systems, waste management, public health care system or even electricity; where large amounts of utensils such as car tires and empty cans accumulate in open areas and become breeding grounds for dengue vector insects. These are mostly densely populated areas, with poverty as a common theme. According to PAHO estimates from 1996, about 196 million persons (roughly one-half of the population in the area) live in poverty in Latin America, implying a 42% increase in this indicator during the eighties, compared to a 22% population growth [30].

The increase in traveling, due both to migration and tourism, also constitutes an important element in the re-emergence of dengue in the region [29]. Another problem is the unstable economic situation, that together with the privatization of public health care systems in most of these countries has contributed to the deterioration of the infrastructure of health systems and, subsequently, of the vector control programs.

"Carrying out an emergency sanitization campaign is the easy part. The difficult thing is to implement a system guaranteeing routine sanitization, dictating orders and dispositions that are not just followed because of discipline, but as a result of persuasion and conviction. My first task now is to begin sanitary education, starting with myself…" These were the words of Finlay after being appointed as Superior Head of Sanitation in Cuba, 1901 [31].

In general, the most important factors that have determined an increase in dengue in the region are listed as follows:

1. Poverty.
2. Fast, unplanned urbanization
a) Dwellings without proper conditioning.
b) Crowding.
c) Lack of water, or lack of drinking water.
3. Failure in vector control programs
a) Lack of, or decrease in political will.
b) Appearance of resistance to insecticides.
c) Ineffective control measures.
4. Increase in flights.
5. More non-biodegradable waste.
6. Deterioration of public health care infrastructure and its funding.

Current strategies for eradication of the disease. Importance of social communication.

In spite of the considerable amount of effort invested in the development of a vaccine against dengue, and notwithstanding the significant progress which has already been made, the chances for an effective vaccine to be widely available during the next years are slim. This implies that currently and during the foreseeable future, controlling dengue will mean controlling the mosquito [4].

From 1995 to the present day, several strategies have been proposed by PAHO and the World Health Organization (WHO) for implementing the surveillance and control of dengue and DHF/DSS in different affected countries [32]. Although some states of the region have spent significant amounts of money on this, in general the situation has not improved. In 1996, 23 countries spent 331 million dollars and in 1997, 671 million dollars in control programs for the disease. However, the economic analyses made by PAHO indicate that an integrated control program based on coordinated actions to prevent, treat and eliminate mosquito breeding sites may reduce current expenditure by 30%.

The formerly implemented control programs had a very costly vertical structure, based on intermittent and largely ineffective fumigations with insecticides (chemical control) and where community involvement and health education were used only during outbreaks.

From 1999 on, dengue was formally included within the agenda of the Tropical Disease Research program (TDR) [33]. The high-priority goals of this agenda are social, economic and behavioral research; research on the vector, including its control; research on diagnostics, the pathophysiology of the disease, the characterization of the viral agent and work focused on the development of a vaccine.

In September 2001, during the 43rd Directive Council of PAHO, the Resolution on Prevention and Control of Dengue and Dengue Hemorrhagic Fever was unanimously approved by the health ministers from Latin American countries. The resolution (CD 43.R4) focuses its strategy on the management of programs through intersectoral partnerships and actions involving public health, environmental and educational sectors, granting special attention to the area of social communication for public health care through partnerships, management and social participation for achieving behavioral changes on individual and collective levels.

The official document OPS/HCP/HCT/208/02 lists ten key points for achieving these goals [34].

1. Integrated epidemiological and entomological surveillance.
2. Promotion and implementation of coordinated actions between public health, environmental and educational sectors, with the additional involvement, if possible, of trade, industry, tourism, and the legislative and legal branches.
3. An effective participation of the community.
4. An appropriate management of environmental issues and attention to basic services such as water supply, the management of liquid and solid waste, and of used tires.
5. Attention to inpatients and out patients.
6. Notification of the cases (clinical and confirmed cases, cases and deaths by DHF, circulating serotypes).
7. Inclusion of the topic of dengue/health in the formal educational curricula.
8. A critical analysis of the function and use of insecticides.

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9. Formal training of health workers and professionals (either in the medical or social sectors).

10. Preparation for emergencies, implementing mechanisms to deal with the presence of outbreaks and epidemics.

More recently, in 2003, a new resolution was passed by PAHO, promoting a methodology based on technical cooperation among countries[29] and creating the Integrated Management Strategy (IMS-Dengue), with the Technical Group on Dengue (TG-Dengue) as its executive branch.

The health organizations have to finally face the fact that the dimensions of the problem have long gone beyond the frontiers of the health care sector, which is no longer the sole entity responsible for its prevention and control. Currently, limiting the damage inflicted by dengue epidemics requires the involvement of every sector.

There are five strategic areas defined in the comprehensive management system for the prevention and control of dengue in the Americas, namely: social communication, entomology, epidemiology, laboratory and patient care.

A new PAHO-supported WHO/CDC initiative launched COMBI (Communication for Behavioral Impact) in 2003, which is a methodology for the planning and implementation of social communication programs with the goal of impacting and producing behavioral changes. This methodology, offers an innovative approach to social communication; it has been previously applied in diseases such as malaria, lymphatic filariasis, tuberculosis, leprosy and HIV/AIDS. It represents an organic combination of marketing, education, communication, promotion and mobilization approaches that synergize in achieving a common goal: having a behavioral impact and promoting program-community associations [35].

The epidemiological situation of dengue in the area places a high demand on comprehensive approaches for mosquito control that mix community participation with a reduction of the dependence on insecticides (chemical larvicides and adulticides). The prevention of epidemics needs a coordinated community effort to raise the awareness of DF and DHF, teaching how to recognize and control the transmitting mosquito.

This new challenge places the health sector in a completely new field of knowledge that constitutes an interface between epidemiological disciplines and social and communication sciences, required for implementing these new strategies. This is done by knowing what communities to work with, who are the leaders and what kind of leadership is necessary to organize prevention and control strategies, and the local socio-economic conditions that must be faced. As it is known that social factors can be used to explain and pinpoint modifiable habits and behavior, sectors with which to coordinate the preventive action must be identified, and any expectations on communal organizations must be placed in consideration.

Another strategy followed by WHO is a surveillance network named Dengue Net [36], which tries to standardize epidemiological and laboratory surveillance to increase the timely availability of basic dengue data for the regional control of the disease. This regional strategy promotes the participation of every country, and is currently integrated by 12 countries in the area, including Cuba.

Understanding the main factors behind health at the population level has highlighted the need to consider the ecosystem during the analysis of health at an individual level, and WHO has acknowledged the need to take the ecosystem into account for the detection of critical points for dengue transmission within a framework of comprehensive vector management [37].

The creation of Eco-clubs [38] in the area has also led to initiatives for the elimination of mosquito breeding areas. This requires the knowledge of the species and its habits, preferences and behavioral response to control measures, in order to maximize the efficiency of its elimination on scientific bases while simultaneously reducing its environmental impact as much as possible [39].

Cuba has followed a holistic approach known as EcoSalud [40], based on the ecosystem as a paradigm, which explains dengue epidemics as the result of complex interactions between its genetic history and economic, ecological and cultural forces [41].

Brazil has followed its own ecological initiative through a campaign with the motto "Recycling is life" for the collection and elimination of used car tires (figure 2). This has led to the destruction of one of the most important habitats for the larval stages of the mosquito. Car tires are being collected in several cities,

Figure 2. Poster of the ecological Project " to Recycle is life", of Brazil.

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and later processed for manufacturing shoes and other goods.

It is argued that health promotion must be the basis of new programs for fighting dengue, starting from the premise that health is a collective social asset. One of the challenges of promotion is centered on the fact that health is essential for social, economic and personal development, and is therefore crucial for the quality of life. On the other hand, the influence of political, economic, social, cultural and behavioral factors on health can either be positive, or negative.

A holistic perspective on promotion is very important in dengue, where changes must be promoted on individual, communitarian and institutional behavior due to the strong relationship between this health problem and the home environment, which in turns depends directly on human behavior. Promotion is targeted not only toward the community, but also toward the structure and organization of prevention and control programs.

A study on the contribution of social research to dengue control and preventative activities carried out in Fiji, in the South Pacific [42], showed that "…social research must be maintained throughout the course of community-based programs, to be able to make last-minute adjustments and mobilize the population. The traditional scheme -starting with a baseline-type research which is repeated at the end of the project or program- does not make it possible to optimize, in real time, the community mobilization methods in the course of the project. The frequent use of participative research also helps to shape the project, with the creation of new networks during research planning…" This highlights the importance of creating links between epidemiological knowledge and social and communication sciences. Epidemiology yields data on the vector, different viral serotypes, transmission routes, risk factors, and preventative measures and actions against potential outbreaks. While the program's effectiveness depends on the social and cultural knowledge of the community afflicted by dengue, including the main avenues for informal or formal communication on health and, more specifically, on disease prevention and control; other issues include the knowledge on the social determinants of certain habits, practices and behaviors - together with the means for their potential modification- without forgetting its established partnerships, leaderships and organizations.

The Cuban health system. Strategies for dengue control

The Cuban health system is universal, free, accessible, regionalized and comprehensive. Thanks to its health programs, diseases such as tetanus, malaria, whooping cough, meningococcal meningitis, post-parotiditis, rubella, measles and diphtheria have been eradicated.

The prevention of dengue in Cuba is based on the following basic principles: political will, effective inter-sector coordination, active community involvement, and the proper use of the current sanitary legislation. There is a comprehensive surveillance system in the country for the prevention of dengue, where community participation is present at every structural level, starting from political and governmental organizations and including the whole civil society.

In 1981, after controlling the dengue epidemic that took place in Cuba during that year, the National Campaign for the Eradication of *Aedes aegypti* was created. An extensive set of chemical and environmental measures were successfully taken, reducing infestation indices for the mosquito from 10.9% at the beginning of August, 1981, to 0.007% in April, 1984 [43]. No viral activity was detected between 1982 and 1996 [44]. Currently, 2.4 million convertible Cuban pesos are spent yearly on dengue prevention, of which 70% is exclusively devoted to vector control [45]. The latter involves the participation of 24 000 health workers, 30 000 family doctors and 120 000 children [46].

Another important principle applied in our country is that dengue prevention must be environmentally sound [47]. Currently, there is worldwide consensus on the political priority of environmental conservation issues [48]. Dengue is the main re-emergent vector-transmitted disease in Cuba. Due to its geographic location, viral transmission occurs through epidemic outbreaks, which means that a high proportion of our population is sensitive to at least one viral serotype. Given that a dengue vaccine is not available, dengue prevention is mainly through an ecosystem sanitation point of view that is based on the following principles [47]:

1. The concept of health must be placed within the perspective of the concepts of physical and socio-economic environments
2. Socio-economic and health-related aspects must be linked to traditional environmental values
3. Environmental concepts must be incorporated into the decision-making process for health interventions
4. The values and risk perception of the community must be taken into account and used at all stages of analysis and evaluation of the interventions

Biotechnology in Cuba and its involvement in the fight against dengue

The results obtained in the public health sector, together with the rapid development of science and technology driven by the recent breakthroughs in the field of biotechnology, have allowed the country to become a medical and scientific powerhouse. The standards attained by biotechnology in Cuba are comparable even to those of developed countries, and are the result of a comprehensive health system, governmental efforts, and highly qualified human resources.

Cuba has invested heavily on the development of science and technology, prompted by a well defined political position that conceives them as means for social development and to cover important human needs, such as health and nutrition [49]. The Cuban pharmaceutical industry has played a major role in our biotechnological development, by focusing the research in this field on human health issues. The creation of the Scientific Pole in 1981 showed to way toward the structure of science under a socialist model, making this new technology not only a valuable contribution to health and nutrition, but a new economic sector [50].

The Scientific Pole, located at the western part of Havana, is a complex formed by the more than 50

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research centers which is one of the biggest systems of its kind worldwide. Currently, the country had the widest reaching immunization program in the world, vaccinating against 13 diseases, 8 of which are directly manufactured in the country. Additionally, there is ongoing research in at least 20 vaccine-related projects, highlighting the social engagement of science in Cuba [51]. The large number of institutions created for research, production and marketing, which currently employ thousands of researchers, ensure that neither the US commercial blockade nor the shortage of funds derived from it have been able to hamper the reach of this program.

Some of the most relevant achievements of Cuban biotechnology in the fight against infectious are the vaccine against group B meningococci, unique in the world, the production of recombinant alfa-Interferon, the Transfer Factor, a recombinant vaccine against Hepatitis B (HB), diagnostic kits, a *Haemophilus influenzae* vaccine [52], and the tetravalent vaccine Trivac HB (immunizing against diphtheria, tetanus, pertussis and hepatitis B), which was included in the national immunization program in March, 2005.

Cuba has been able to stop all dengue outbreaks, by the active participation of institutions of the Scientific Pole and other sectors of the public health system on epidemiological surveillance, prevention and eradication of this virus. A number of current research projects in several scientific institutionsare now looking for an effective immunogen and increasing their knowledge on of the pathogenesis and epidemiology of this disease.

The contributions of the IPK to the scientific knowledge on different infectious diseases have made it a reference institution in the world for pathologies such as dengue. One of the main scientific results of IPK is a study on the hemorrhagic form of the disease in different population groups. This center is currently a PAHO/WHO collaborating center for the study of dengue and its vector.

IPK now works jointly with the CIGB in obtaining a recombinant vaccine against the virus, with promising results during preclinical tests in animals and it is an innovative contribution to the quest for a preventive immunogen against this disease [53]. Other projects are focused on obtaining antiviral drugs for dengue at CIGB, and this center also works on the development of diagnostic kits for the detection of dengue, with the help of the IPK.

The CIE is currently manufacturing 24 diagnostic kits against 15 diseases that are being used thoughout the country, including a diagnostic system against dengue.

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