

Dengue in the Americas: challenges for prevention and control

Dengue en las Américas: desafíos para su prevención y control

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Abstract

Dengue is the most important vector-borne disease in the Americas and threatens the lives of millions of people in developing countries. Imprecise morbidity and mortality statistics underestimate the magnitude of dengue as a regional health problem. As a result, it is considered a low priority by the health sector with no timely steps for effective control. Dengue is perceived as a problem of "others" (individually, collectively and institutionally), therefore responsibility for its control is passed on to others (neighbors, the community, municipality, health institutions, or other governmental agencies). With no precise risk indicators available there is little opportunity for timely diagnoses, treatment, health interventions or vector control (poor surveillance). Solutions only targeting the vector reduce the impact of interventions and there is no sustainable control. Without political commitment there are insufficient resources to face the problem. This paper discusses the challenges for prevention and control in the Americas.

Dengue; Communicable Disease Control; Disease Prevention

Introduction

Dengue is now the most important vector-borne disease in the Americas and threatens the health of millions of people that live in urban, suburban and rural environments. Clinical and public health services have been unable to diminish this disease since there is no vaccine available to prevent infection, no effective medical treatments that avert the development of severe symptoms and no sustainable control measures against the vector that guarantee protection of affected communities.

Dengue was initially identified as breakbone fever in 1790 in Philadelphia, U.S.A¹, and later spread throughout the Americas, until the Pan American Health Organization (PAHO) launched an *Aedes aegypti* eradication campaign to combat yellow fever in the 1950s and 1960s that came close to eliminating the vector from the continent². Although the geographical distribution of the vector is similar to its distribution before the eradication campaigns³, populations during the "eradication era" were principally rural. In the last 40 years, there has been intensive urbanization due to massive migration from agricultural areas to cities. Although urbanization in Latin America and the Caribbean had already reached 41% of the population by 1950, the population living in urban areas is expected to reach between 82 and 84% by 2030; by then the Latin America and Caribbean region will be the second most urbanized

in the world⁴. The current distribution of dengue vectors in the Americas is a fraction of their potential niche, especially with deteriorating social, environmental and economic conditions that have made vector control a more challenging goal nowadays than it was in the past.

Traditional approaches to dengue prevention and control have been inherited from the vertical programs that targeted vector elimination in domestic habitats, with the use of larvicides and insecticides in addition to breeding site elimination as the core of *Aedes* control strategies. The initial impact of the eradication campaign created the false impression that any vector control strategy could achieve similar reductions. During the 1990s *Ae. aegypti* control programmes shifted from large-scale spraying to community-based programmes, mainly due to the decentralization of health services, the breakdown of vertical control programs in the region and the lack of technical personnel. Failure to reduce efficiently vector densities have given way to the development and application of innovative approaches for community involvement, although with limited impact in the control of the overall spectrum of breeding sites in the household and peridomestic surroundings^{5,6}. The purpose of this review is to describe the challenges faced by prevention and control programs in addressing a major sanitary health problem in the region.

Dengue in numbers

Dengue is the most widely distributed viral hemorrhagic fever in the world^{7,8}. In the 1950s, only nine countries reported dengue, while today more than 100 countries worldwide with a combined population of more than 2.5 billion are at risk of dengue infection. The average number of cases reported yearly to the World Health Organization (WHO) rose from 908 during the 1950s to 514,139 in the 1990s⁹. Around 50 million cases are estimated to occur each year causing an average 24,000 deaths worldwide, and a 100% increase is predicted in the coming two to three decades¹⁰. During the 1980s an average 91,000 cases were reported annually by 25 countries. During the period from 2000 to 2006, an average of 545,000 cases was reported every year by 44 countries. Dengue statistics should be considered a proxy for real incidence. The upward trend and cyclical nature of dengue epidemics every three to five years, occurs at different moments in every country (Table 1). Although epidemic outbreaks are not temporally homogenous, reintroductions from one country to another also provoke increases in the risk of severe dengue infection¹¹. The first major dengue hemorrhagic epidemic in the Americas occurred in Cuba in 1981 and was caused by dengue 2 virus. From 1981 to 1996, 42,246 dengue

Table 1

Dengue incidence (rates per 100,000 inhabitants) in selected countries, 2000-2006.

Country	2000	2001	2002	2003	2004	2005	2006
Argentina	4.6	0.03	0.6	0.4	8.7	0.1	0.5
Bolivia	0.88	14.7	74.3	327.4	369.5	222.1	102.0
Brazil	136.1	239.4	452.4	198.1	65.4	118.1	200.8
Colombia	53.8	272.7	210.3	258.7	135.4	149.9	180.7
Costa Rica	434.6	818.2	314.5	606.3	290.0	1,165.2	345.1
Cuba	1.2	101.6	26.7	0	0	0.7	?
Dominican Republic	40.7	42.3	37.6	72.5	27.6	33.7	72.3
Ecuador	181.4	84.8	45.3	80.1	47.8	94.2	45.1
El Salvador	51.7	17.1	286.0	116.2	201.0	226.3	307.8
Guatemala	79.1	38.6	65.0	57.8	54.3	54.3	24.5
Honduras	210.4	138.0	490.8	251.8	303.7	286.6	128.3
Mexico	21.9	6.2	9.8	5.0	8.2	16.8	27.2
Nicaragua	144.2	40.4	41.4	53.7	19.9	31.6	25.9
Panama	11.1	53.3	24.5	10.1	12.9	137.9	145.6
Paraguay	441.8	0.7	33.2	2.4	2.9	7.2	75.8
Peru	21.4	89.4	34.0	13.9	37.5	24.4	14.2
Puerto Rico	62.9	132.4	73.5	94.5	83.2	144.3	77.0
Venezuela	87.3	337.7	152.9	109.6	124.6	171.3	149.9

Source: Pan American Health Organization. <http://www.paho.org/spanish/ad/dpc/cd/Dengue.htm> (accessed on Feb/2007).

hemorrhagic fever cases were reported in several countries, although 90% of these cases were from Venezuela (52%), Cuba (24%), Colombia (9%), Nicaragua (6%) and Mexico (3%). During the 2000-2006 period, 85,331 dengue hemorrhagic fever cases were reported from Colombia and Venezuela (61%), while 16% of cases were from Mexico (Table 2).

Although there is an overall ratio of 45 dengue fever cases reported for every dengue hemorrhagic fever case detected, the ratio of dengue /dengue hemorrhagic fever cases reported in Brazil (468) and Costa Rica (396) is very different from those reported in Honduras (17), Venezuela (13), Colombia (10) or Mexico (7). This variation is principally due to under-reporting of dengue cases in the countries with the lowest dengue/dengue hemorrhagic fever ratio and/or lack of severe dengue diagnosis in the countries with high ratios. In both scenarios, passive surveillance of dengue fever cases and failure of clinical diagnostic capacity hamper precise measurements of the magnitude and trend of this health problem and illustrate the problems faced by all surveillance systems: incomplete, inopportune and imprecise information (Table 2).

A practical framework for prevention and control

Dengue epidemiology has changed with time and the evolving clinical picture, social and cultural environments, vector control strategies and surveillance capabilities in the region must be addressed in an integrated manner, due to the complexity of factors involved in transmission dynamics, risk assessment and control potential. The purpose of the present framework (Table 3) is to describe what we know about dengue, the challenges associated with major transmission determinants, the problems faced by clinicians for dengue diagnosis and treatments of complications; the laboratory infrastructure required to support clinicians and public health workers, the inconveniences faced by surveillance systems, and the unmet needs of prevention and control strategies.

Table 2

Dengue hemorrhagic fever cases in selected countries, 2000-2006.

Country	2000	2001	2002	2003	2004	2005	2006	Total	Dengue fever/ dengue hemorrhagic fever ratio
Argentina	0	0	0	0	0	0	0	0	0
Bolivia	73	0	1	47	25	10	1	157	137,3
Brazil	59	679	2,607	713	77	433	628	5,196	467,7
Colombia	1,819	6,563	5,269	4,878	2,815	4,306	5,379	31,029	9,8
Costa Rica	4	37	27	69	11	52	64	264	395,7
Cuba	0	69	12	0	0	0	?	81	180,9
Dominican Republic	58	4	76	252	136	84	230	840	33,2
Ecuador	3	55	158	416	64	334	173	1,203	61,8
El Salvador	411	54	405	138	154	207	245	1,614	50,1
Guatemala	42	4	47	22	39	32	4	190	228,6
Honduras	314	431	863	458	2,345	1,795	636	6,842	17,4
Mexico	50	191	1,429	1,419	1,959	4,255	4,477	13,780	6,9
Nicaragua	636	458	157	235	93	177	52	1,808	10,2
Panama	3	7	5	0	4	2	5	26	287,1
Paraguay	0	0	0	0	0	0	0	0	0
Peru	0	251	13	15	35	16	4	334	188,6
Puerto Rico	24	36	23	5	11	19	7	125	210,7
Venezuela	2,186	6,541	2,979	2,246	1,986	2,681	2,476	21,095	13,4
Americas	5,667	15,500	14,374	10,994	9,810	14,557	14,429	85,331	44,8

Source: Pan American Health Organization. <http://www.paho.org/spanish/ad/dpc/cd/Dengue.htm> (accessed on Feb/2007).

Table 3

Practical framework for dengue prevention and control.

Primary determinants		Health services determinants					
Environmental	Biological risk factors	Clinical picture	Risk perception	Diagnosis	Treatment	Surveillance	Prevention and control
Physical: temperature, rainfall, altitude, vegetation, soil use/ Global: urbanization, population growth, migration; travel, industry responsibility (non-recyclable products)/Local: house conditions, Public services infrastructure, water management, education, social networks/ Knowledge, attitudes and perceptions	Vector: competence and capacity/ Virus: serotypes, virulence, sequence of infections/ Host: age, sex, immune response, herd immunity	Asymptomatic	Other health needs	Null	Null	Not perceived silent transmission	Infestation indices (opportunity & productivity)
		Febrile	Common disease self limiting	Very low	Self medication analgesics	Poorly recognized. Passive detection	Breeding site classification, Source reduction; chemical, biological, behavioural interventions
		Benign dengue		Low		Partially reported	
	nutrition, race, genetic traits	Severe fever	Requires health services	High with laboratory support	Specialized clinical care (fluid replacement)	(Passive and active) Incomplete morbidity and mortality statistics	Emergency control: source reduction, insecticide spraying, social mobilization
		Fever with hemorrhage					
		Dengue hemorrhagic fever/dengue shock fever (grades I, II, III, IV)					
Challenges	Pathogenesis	Assessment of WHO definition	Risk awareness. Behavior change	Identification of at risk populations, case management, laboratory and clinical infrastructure			Vaccine, effective vector control, sustainable community prevention and interventions

Major determinants of dengue transmission

Environmental

Dengue is considered a disease of the tropics due to its most recent geographic distribution, despite the fact that *Ae. aegypti* and breakbone fever were originally reported in temperate areas such as Philadelphia in the late 18th century. The perception of dengue as a tropical disease derives from its relationship with climate variables such as heavy rainfall, high temperatures, humidity and vegetation, which define the vector's ecological niche and are typically found in Southeast Asian countries where dengue and dengue hemorrhagic fever were initially recognized. The vector is extremely sensitive to meteorological conditions and seasonal variations which affect

its distribution and abundance in predictable annual cycling. Temperature influences dengue transmission by affecting vector density patterns, blood feeding habits and virus propagation in the mosquito^{12,13}.

Seasonal occurrence of dengue transmission can be attributed to the increase in breeding sites available during the rainy season or the need to accumulate water during droughts or dry seasons¹⁴. While these factors influence the density, productivity and stability of larval sites, its association with transmission patterns usually lags several weeks^{15,16}. Global climate changes have created great concern about the emergence of dengue in more temperate areas (with controversial conclusions), although predictions of dengue outbreaks in regions now free of the transmission, remain to be validated^{17,18}.

- **Global determinants**

Multiple factors favour viral transmission to humans by a mosquito vector: human population growth, rural-urban migration, and unplanned urbanization, characterized by the inadequacy of basic urban infrastructure with substandard housing conditions and insufficient water supply, sewage and waste management systems¹⁹. In addition, the uncontrollable massive proliferation of non-recyclable products (discarded plastic, metal and glass containers, tires) has resulted in a deteriorated environment, favouring an increase in mosquito breeding sites.

Today, cities are better communicated by more and faster means of transport, thereby creating urban networks where risks are easily disseminated from local to international settings. Population movements (migration and tourism) are important vehicles for spreading the serotypes and strains, and the co-circulation of multiple serotypes increases the potential for the emergence of dengue hemorrhagic fever/dengue shock syndrome²⁰. Routes of global trade provide natural sources for vector dispersion²¹, while a global economy means that no country is completely immune to the risks.

Dengue transmission is highly concentrated in urban settings, especially in those below a certain altitude range, above an average annual temperature, with a high population density and deficient public services infrastructure^{22,23}. However widespread distribution of dengue infection in rural areas is evident as surveillance systems and access to health services improve in those areas. The logistics of vector control strategies in disperse and low-populated areas is therefore complicated. The higher rates found in rural areas in Thailand are linked to a higher dependence on water storage during the dry season²⁴. Increase in dengue/dengue hemorrhagic fever among rural populations has also been observed in Central and South America, with similar prevalence rates in some urban and rural populations²⁵. A study from the Gulf coast of Mexico showed that 85% of the communities reporting dengue infection during the 1995-1998 period were rural and 65% of those were classified as extremely poor according to socioeconomic indicators²⁶. Despite its wide dispersion in rural areas, transmission primarily occurs in urban environments.

Ae. aegypti is an urban mosquito that is domesticated where population density, proximity to dwellings, and large and continuous production of breeding sites, all provide ideal conditions for transmission. It is highly dependent on the existence of man-made artificial contain-

ers widely used to deal with deficiencies and inconsistencies in domestic water supply. This situation must be analyzed not only from the individual perspective but also as a social problem where every member of the community has a role and a responsibility. Special emphasis should be placed on industry's role in producing new types of containers which may be massively introduced into the community, with no provision for adequate disposal. The burden of control strategies has shifted to the community, even though risk is influenced by factors that are external to the community's environment. Control strategies have focused responsibility only on the community, without regulating the role of industry, and its social responsibility regarding environmental health.

- **Local determinants**

Dengue should not be considered a poverty-related disease because it affects wealthy neighbourhoods as well, although the magnitude of risk can be moderated by the use of housing materials such as screens in doors and windows^{27,28}. In Taiwan, it was estimated that 63% of dengue infections could be eliminated if everyone lived in adequately screened homes²⁹. Even in comparable areas both with high vector abundance in an ideal climate such as the Mexican-Texas border, the primary determinant for dengue prevalence was socioeconomic. Improved housing conditions (the use of air conditioners) limited transmission even when *Ae. aegypti* infestation rates were remarkably high on both sides³⁰. Dengue infection rates in Southeast Asia have been declining, in part due to strong economic growth in many countries, and to improved housing standards and control programs, which have reduced vector populations³¹. Dengue transmission by *Ae. aegypti* has been associated with poor hygiene, and poor socioeconomic and literacy levels, especially for female heads of households^{32,33,34}.

Biological risk factors

The complex relationship between climate variables, mosquito abundance, human host density, and viral serotype define the potential heterogeneity of disease transmission patterns. Vectors need to contact infected and susceptible hosts, and therefore abundance, dispersion, mortality, genetic and tissue susceptibility to infection, feeding behaviour, and the extrinsic incubation period are the most important variables for dengue transmission dynamics^{35,36,37,38}.

Genetic analyses of dengue viruses have been useful to monitor the transmission of viral genotypes associated with the increase of severe cases³⁹. Dengue 2 (DEN-2) viruses belonging to the Southeast Asian genotype appear to be better adapted to mosquito transmission and are associated with more severe clinical outcomes. They are apparently displacing the American genotype of DEN-2 viruses in some regions of Latin America⁴⁰.

Universal susceptibility to infection implies natural risk for all exposed populations even though most people suffer only mild fevers when infected. Severe dengue develops where endemic transmission and co-circulation of different serotypes occurs. The role of age, sex, race and genetic background in the host population interact in different ways depending on the history of dengue in each country or region. The age distribution of dengue hemorrhagic fever cases in the Americas is different from that observed in Asia. Cases in Cuba and Venezuela include all age groups, although two thirds of the fatalities have been in children under the age of 15. Studies in Brazil describe a mean age range of 31-45 years. In Puerto Rico the mean age changed from under 15 years to 38 years between 1986 and 1991. Nevertheless, elderly groups in Puerto Rico had less haemorrhagic symptoms, similar case fatality rates, and were hospitalized as often as infants⁴¹.

Infection serotype and previous exposure history to other dengue serotypes are known to influence disease severity⁴². Primary infection with any of the four dengue serotypes is usually associated with mild disease, while increased susceptibility to dengue hemorrhagic fever/dengue shock syndrome occurs if the individual is infected with a second heterologous serotype. The immune basis for this hypothesis suggests that antibodies developed during the primary infection decline to sub-neutralizing levels and instead of mediating viral clearance, assist the new virus in infecting host macrophages, a phenomena known as antibody-dependent enhancement⁴³. Nevertheless, dengue hemorrhagic fever resulting from primary infections has increased over time from 1% in 1978 to 14% in 1997, but is associated with milder clinical symptoms⁴⁴. The risk of developing dengue hemorrhagic fever has been estimated at only 1-125 severe cases out of every 1,000 dengue infections in children⁴⁵ and it occurs 15 to 80 times more frequently in individuals experiencing a secondary infection although the reasons are still not clearly understood^{46,47}.

Health services determinants

Clinical profile

Infection with any virus serotype can produce a wide spectrum of clinical illness, ranging from asymptomatic nonspecific febrile syndrome, to severe and fatal hemorrhagic disease. While most patients go through an asymptomatic phase, those who have signs and symptoms develop a self-limiting illness considered benign that runs unapparent or mild in children. Dengue hemorrhagic fever and dengue shock syndrome are life-threatening illnesses associated with hemorrhage, thrombocytopenia and increased vascular permeability. The severe limit of the dengue spectrum is characterized by the sudden onset of hemoconcentration and hypoproteinemia and fever defervescence, but it has been difficult to adhere to the WHO case definition of hemoconcentration in certain settings, since there is no precise test that can accurately predict impending dengue vascular leakage, hipovolemia and shock⁴⁸. An important aim of the WHO classification system is to allow prompt identification of patients who are at greatest risk for developing severe dengue complications, thereby facilitating triage and appropriate use of clinical resources. Strict application of clinical criteria, however, underestimates the number of severe cases. Unfortunately, the WHO definition requires multiple and repeated clinical tests that are not available in countries with limited resources. Omission of the tourniquet test would impede detection of Grade I dengue hemorrhagic fever cases that represent 15-20% of all dengue hemorrhagic fever cases. Even early treatment is incompatible with diagnostic criteria, since appropriately hydrated cases will not present hemoconcentration⁴⁵. In Nicaragua, only 30% of infants in a study fulfilled strict dengue hemorrhagic fever/dengue shock syndrome criteria and the tourniquet test had a low sensitivity⁴⁹. Approximately 82% of Vietnamese children in shock were correctly identified using the narrow WHO classification system⁵⁰, although the tourniquet test had a sensitivity of only 41.6%⁵¹. Differences between disease patterns from Southeast Asia and the Americas can be traced to clinical practice, particularly to the failure of clinicians in the Americas to collect appropriate data to fulfil the requirements of the WHO case definition⁵². In Asia, better case management and intensive national programs to educate parents and medical staff improved early care and avoidance of over hydration of dengue hemorrhagic fever/dengue shock syndrome patients⁴³.

Risk perception and diagnosis

Dengue is not a medical priority for affected communities, since their social, economic and environmental priorities are more compelling than an inadvertent, mild fever solved by self medication which rarely requires clinical attention. At the family level, dengue is considered mild, and a common disease which does not require investment in time or money in health care, except when symptoms are severe. Even when studies have demonstrated that people in endemic countries recognized the disease and its link to the vector, control practices are not equivalent to knowledge about the disease or risk perception. In most regions, there is no appreciation or sense of urgency or risk associated with the worldwide deteriorating dengue situation. Cultural and practical issues related to water management at the domestic, community and urban levels are crucial to understanding risk assessment, and hence the development of effective control strategies. It is a common belief that control is only the responsibility of government agencies (vector control programs), which undermines individual actions, and a sense of community responsibility⁵³.

When faced with a dengue fever case, physicians require support from laboratories to confirm infection using paired blood samples, and/or to classify the stage and severity of clinical findings. In addition to the problem of inappropriate clinical diagnoses by unskilled physicians, there is an absence of quality serological diagnoses and viral isolation in endemic areas. Due to intensive dengue transmission in the region, countries are compelled to strengthen their laboratory capabilities in support of surveillance activities. By 1996, only 53 laboratories in 14 countries had serologic diagnostic capabilities using IgM antibodies; only 20 had resources to perform virus isolation, and only 11 used molecular techniques. Quality control performed from 1996 to 2001 demonstrated that only 87% of laboratories had excellent performance in their diagnostic capabilities with problems ranging from the irregular provision of antigens, dependency on the regional centers for kit distribution, different sensitivity among serologic tests, and the limited use of more specific diagnostic techniques⁵⁴.

Treatment

Dengue fever cases are usually treated with antipyretic drugs and analgesics (salicylates are counter indicated). Due to the progressive nature of the illness, repeated assessment during the febrile period may be necessary, with closely

monitored intravenous fluid replacement as the cornerstone of severe case management. Severe dengue requires expert care and hospitalization, even though the lack of clinical predictors of severe disease complicates diagnosis and timely treatment. The case fatality rate may be kept below 1% where skilled staff and facilities are available. In poor countries, it can be as high as 10%⁵⁵.

Surveillance

Dengue is a mandatory reportable disease that must be reported to the nearest epidemiology unit. The clinical spectrum of the infection, however, undermines surveillance activities, for several reasons. First, the most cases are asymptomatic and go undetected. The prevalence of asymptomatic children in Costa Rica varied from 2.9% in San Jose to 36.9% in the coastal region⁵⁶. During the 1970's, dengue swept through Colombia causing an extensive epidemic where more than half a million cases were estimated but most occurred silently for most of the period. The silent epidemic in the city of Salvador, Brazil, between 1998 and 1999 was estimated to have infected around 560,000 individuals, while the official notification system only recorded 360 cases⁵⁷. Asymptomatic cases and under-reporting contributed to a false panorama of dengue in these areas. Similar results were reported in central Brazil, where seroprevalence surveys estimated 340,000 cases and official reports only contained 9,544³².

Secondly, a large proportion of infected individuals have the mild form of the disease, which is perceived as not serious enough to warrant health care assistance. Dengue cases are misdiagnosed by medical personnel as a febrile syndrome, and therefore go unreported. When dengue fever is identified, regulatory guidelines require paired blood samples to confirm diagnosis, therefore only a small proportion of cases are diagnosed, confirmed and reported. Dengue statistics in the region under-report mild and classic cases, and are not designed to recognize all but the most severe cases. Confirmed cases face the same technical caveats as all laboratory tests required to comply with the strict WHO classification criteria. This situation explains why during 2006, only 4% of the total number of dengue cases were confirmed by laboratory tests (PAHO).

Finally, official notification systems register cases reported by the primary health care system, which is used mainly by uninsured populations. The diversity of public health institutions in each country complicates opportune case notification to surveillance and control programs. The

private health sector rarely complies with case notification, and consequently, important data is lost from a variety of health providers. Combined, these undermine coverage and access to the surveillance system. A dengue prevention program faces multiple operational problems due to the lack of sensitive identification of at-risk populations, and identification of infected versus diseased patients.

Prevention and control

Ae. aegypti is adapted to domestic and peridomestic environments, and breeds in different types of artificial containers, which are specifically used for water storage due to insufficient municipal supply. Even in areas with a continuous potable water supply, *Ae. aegypti* densities can be found in clean containers such as flower vases and fountains. Traditional entomological indices such as House or Premise Index (HI), Container Index (CI) and Breteau Index (BI), are used to monitor *Ae. aegypti*, although attempts to associate them with dengue transmission have failed due to the fact that these indices measure prevalence, not abundance, and because they do not discriminate between capacity or productivity. Other indices have been proposed to address the issue of productivity (Larval Density Index, the *Stegomyia* Index and the *Stegomyia* Larval Density Index), but are labor intensive and impractical⁵⁸. Pupal surveillance of *Aedes* vectors has been proposed as a more accurate measure of female mosquitoes as complementary to traditional larval surveillance. The Premise Condition Index offers a rapid assessment method of selected households for surveys, does not require larval identification or infested container and larval counts, and can be done from the outside and is quick. Its primary limitation is that it does not consider indoor breeding risks⁵⁹.

While source reduction is considered the most effective measure of vector control, it is important to distinguish sources that are controllable from those that are disposable, and those that are indoors versus outdoors. In Singapore, 79% of total breeding sites were indoors²⁹. In Fiji, surveillance and control strategies failed to define key container types, e.g. tyres and drums, which were responsible for most of the *Aedes* being produced⁶⁰. Studies in El Salvador have demonstrated that infested discarded cans, plastic containers and tire casings were risk factors for dengue infection with abundance-attributable fractions of 4%, 13% and 31%, respectively⁶¹.

Reduction of mosquito breeding in household water containers using larvicides, predatory

crustaceans, or elimination of discarded containers, and control of adult mosquitoes by spraying insecticides, requires continuous efforts by the communities, which are difficult to sustain, and for which effectiveness requires validation. Options for control, such as insecticide-treated window curtains, water container covers and controlled-release insect growth regulators may contribute to reduce densities of dengue vectors and dengue transmission⁶². Decreasing the carrying capacity of the mosquito's environment using frequent reduction of the vector breeding sites seems to be the most effective way to control disease but good entomological indices are required to monitor transmission risk, and evaluate the impact of different control strategies, whether physical, biological, chemical or behavioural.

Our ability to control *Ae. aegypti* is also limited since larvicides have *low coverage* in terms of the large pool of breeding sites present in any urban environment. Growing reluctance on the part of residents to accept their use in potable water, their expense, the increase in non essential water holding containers in the environment, and the increasing frequency of locked residences during the day has resulted in infrequent applications and inadequate coverage which affect long-term suppression⁶³. Insecticides are *short in reach* when it comes to effective penetration into the vector's resting places, and they are *short lived* in relation to female adult mortality. Studies conducted in Asia and the Americas, indicate that after the application of Ultra Low Volume (ULV), the adult population of mosquitoes returned to pretreatment levels within two weeks, and even with multiple applications, the impact on incidence was minimal⁶⁴.

Aside from these technical problems, there is no public health program with sufficient human resources to deal with all households in urban centers (*short response capacity*). National programs are under-funded, poorly managed and operate in isolation from other health care delivery elements. Field workers are poorly motivated and supervised, are underpaid and lack communication skills. Unfortunately, during low transmission periods, most individuals as well as government agencies lose interest in mosquito control, and hence subsequent vector population increases. Dengue control has been approached as a community responsibility by the public health community, and exclusive reliance on the community to assume full responsibility for vector control activities has been stressed even though it is a problem which requires resources and financing from different governmental agencies and municipal actors outside the health sector.

The domestic urban environment creates new risks associated with accelerated urbanization processes and this risk challenges the countries to respond with basic sanitary infrastructure. Intersectoral and multidisciplinary vector control programs are needed and several community based dengue control interventions have been reported from a wide variety of ecological and social environments, including: communication campaigns, educational initiatives, behavioral change, biological control efforts, integrated control projects and a mixture of the above strategies. Interventions that rely on educational strategies only, have less impact on behavior and entomologic indices⁶⁵. The evidence to show that community-based dengue control programmes alone, or those implemented in combination with institutional control activities, can enhance the effectiveness of dengue control programmes is weak⁶⁶.

Behavioral changes can help reduce the infestation of domestic containers, if individual community and institutional practices are correctly targeted. Changing behavior requires mobilizing social networks and organizations, as well as implementing firm public policies. A new relationship between governmental institutions and individuals is required and programs should be designed based on local sanitation structure, as well as community organization and roles for different family members. Programs should incorporate epidemiological surveillance, community participation, management of the environment and basic public services, case management, education, and effective vector control and training. Sustained dengue control requires partnerships among donors, the public sector, civil society, non-governmental organizations, the private sector, and the interactions between politicians, public health personnel, administrators, engineers, urban planners, and environmental groups, in order to strengthen existing intersectoral management structures in support of community actions^{67,68}.

Challenges

Countries in the Americas now face the irrefutable fact that social, economic and environmental conditions have converged to establish dengue as a major health threat to their populations. The enormous investment required for urban infrastructure in developing countries, will hardly be available in the near future, although adaptation of health services to avoid or prevent dengue transmission is feasible. Basic research must provide a better understanding of the immune

response, the antibody dependent enhancement mechanisms, virulence factors for the different genotypes and pathogenic pathways of severe dengue infection. Understanding the changing and severe clinical profile of dengue infection must be clarified for the development of safe vaccines and effective drugs for treatment. Clinical diagnoses of dengue cases will benefit and improve the identification of at-risk populations for severe dengue, although a strong laboratory-based surveillance system, intensive training of medical staff and strong medical infrastructure support for clinical diagnosis in endemic and high risk areas are also essential components.

Without vaccines, effective drugs, or sensitive diagnostic tests, the only available response to reduce disease severity and case fatality is clinical management through enhanced care supported by accessible, sensitive and specific useful diagnostic tests. These tools will help identify warning signs for severe disease and evidenced-based criteria for treatment procedures standardization⁶⁹. The current WHO/dengue hemorrhagic fever definition is an epidemiological tool to collect public health data on the incidence of symptomatic infection, as well as disease severity. This definition should be simple and reproducible, use readily available information, and should be applicable to the majority of cases without modification or reinterpretation. The current definition is not equally useful in all clinical care or epidemiological situations, nor does it reflect current practices in case treatment, hospital laboratory, and diagnostic methods⁴³.

An ideal dengue vaccine must be tetravalent, in order to protect against infection from all four serotypes. Recent initiatives focus predominantly on recombinant strategies based on infectious clone technology, DEN antigen-encoding viral and plasmid vectors and recombinant DEN antigens. Several multivalent dengue vaccines are in various stages of development, but none is close to regulatory approval. Live attenuated tetravalent dengue vaccines are being developed either through multiple passages of the virus in animal tissues and for cell culture, or through viral mutation combined with chimerization. The risk of developing severe dengue during a secondary infection has major implications for vaccination policy, since vaccines developed against one or two strains could theoretically prime populations for future epidemics of dengue hemorrhagic fever/dengue shock syndrome⁷⁰. The potential for immunization-mediated enhanced disease has given rise to the current goal, which is to produce solid immunity against all four serotypes with one or two vaccine doses. Once a safe vaccine becomes available for wide-scale evaluation, it

needs to be tested to measure protective efficacy and safety, since a major problem will be to differentiate potential vaccine-induced immune enhancement diseases. The 50 million dollars of support granted by the Bill and Melinda Gates Foundation to develop a paediatric dengue vaccine does not necessarily guarantee that a vaccine may be available for poor children in dengue endemic countries in the near future ⁷¹.

The development of improved entomological surveillance methods is crucial for timely vector control. Entomological indices must measure transmission risk thresholds and provide precise information to evaluate physical, biological, chemical or behavioural interventions. Breeding containers must be identified according to their abundance, potential productivity and control activities required for elimination of breeding risks (controllable vs. disposable). Productivity of key premises or breeding containers is an important issue since a low proportion of positive premises and containers are responsible for high productivity. As a result, limited resources are available to control high risk areas ⁷². Effective vector control should be based on timely detection of entomological risks which can then be tackled through community participation schemes supported by governmental actors and social stakeholders.

Community based health projects need to find the ingredients necessary to generate a continuous action to promote changes in behavior since they are expected to modify the environment where the problem arises. Sustainability

provides an additional difficulty for all strategies, because it requires not only continuity of actions, but also effectiveness. Although most community-based interventions emphasize this impact on behavioral changes of individuals, families and groups, they must also provoke changes in the behavior and responsibilities of institutions (health, education, municipal authorities, etc.) and other stakeholders. It is necessary to stress that preventive practices for dengue control, can only be modified or present when they are supported by efficient urban infrastructure.

Dengue is a complex disease that threatens the lives of millions of people in developing countries. Imprecise morbidity and mortality statistics undermine the study of factors associated with dengue transmission and its recognition as a major regional health problem. Dengue is perceived as a problem of "others" (individually, collectively and institutionally), and therefore responsibility for its control is passed on to others (neighbors, the community, municipality, health institution or other governmental agencies) and not fully appropriated by any. With no consistent or precise risk indicators (clinical, entomological, and epidemiological), there is little opportunity for timely diagnoses, treatment, health interventions or vector controls (poor surveillance). Solutions targeting only the vector reduce the impact of interventions. With ineffective interventions, there is no sustainable control and without population-based and political commitment, there are insufficient resources to address the problem.

Resumen

El dengue es la enfermedad transmitida por vector más importante en las Américas, que amenaza la vida de millones de personas. Las cifras subestiman la magnitud del problema y el dengue no figura como prioridad para las autoridades en salud y no se identifica como problema (baja percepción de riesgo), por lo que las medidas para el control se realizan tardíamente. El dengue se considera un problema de "otros" (individuo, colectividad, institucional) y la responsabilidad del control se desvía hacia otros (vecindario, comunidad, municipio, el Ministerio de Salud, etc.). Se carece de indicadores de riesgo precisos, por lo que no hay oportunidad para acciones de diagnóstico, tratamiento, prevención y control vectorial. Con intervenciones poco efectivas no hay control sostenible y sin compromiso político no hay recursos suficientes para enfrentar este problema sanitario. Este artículo aborda los desafíos para la prevención y el control del dengue en las Américas.

Dengue; Control de Enfermedades Transmisibles; Prevención de Enfermedades

Contributors

H. Gómez-Dantés designed the study, carried out a literature review and was responsible for writing in English the epidemiological and clinical elements as well as the design of the matrix. He also provided support to different sections with ideas and technical scientific contributions. J. R. Willoquet was responsible for writing the article and revising the English, contributing to the section about vectors and control, as well as providing support to the other sections with ideas and technical scientific contributions.

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