Re-emergence of dengue in Argentina: Historical development and future challenges

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Abstract

After 82 years of the absence of dengue in Argentina, a dengue outbreak occurred in the northern provinces of the country in 1998. *Aedes aegypti,* the vector mosquito, was eradicated in the 1960s, mainly due to the use of residual insecticides at an enormous cost of resources and through a vertical health programme. Since then, the country has gradually become reinfested due to the deterioration of the surveillance system and vector control programmes. At present, DENV-1 to 3 have been found in circulation and 3162 cases of dengue fever (DF) have been reported in the country. However, as autochthonous cases have been recorded during this epidemic only, the disease is still not considered endemic in the country, although there is a regular occurrence of outbreaks in neighbouring countries.

The control strategies currently being used are the same ones as used in the past century although socioeconomic and demographic conditions have greatly changed. Consequently, alternative methods are proposed as potential tools to establish new ways of controlling the vector, which is the only way of preventing new outbreaks in the region.

Keywords: Dengue; Argentina; Control strategies; *Aedes aegypti*.

Introduction

Argentina is the southern-most country in Latin America. With a surface area of 3 761 274 km^2, it has a wide diversity of geographical areas such as the cold and dry steppes of Patagonia, the Pampa grasslands, the humid and dry Chaco region and the jungle highlands or "yungas" in the north[1]. The great climatic and topographic diversity of this vast extension of land determines different forms of fauna and flora, as well as different types of human settlements that develop different lifestyles and socioeconomic activities that are directly related to their environment.

The growth of urban centres, viz. the city of Buenos Aires, where nearly 40% of the country's population is concentrated[2], in conjugation with movement of people from and to the neighbouring countries, supported by congenial environmental conditions in the north and centre, render this country prone to explosive epidemic outbreaks. The prevailing

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socioeconomic aspects of Latin America in general and Argentina in particular, especially the extreme polarization of resources, are extremely relevant in the re-emergence of dengue.

During the mid-20th century, the health authorities of American countries, together with the Pan American Health Organization (PAHO), carried out important *Ae. aegypti* eradication campaigns, which were developed in Argentina in 1965[3]. However, by the end of the 1980s, the country was re-infested by the mosquito, a situation that currently prevails[4].

The present article describes some of the variables that contributed to the re-emergence of dengue in Argentina, placing particular emphasis on mosquito vector control, and discusses possible contributions to the current vector control strategies.

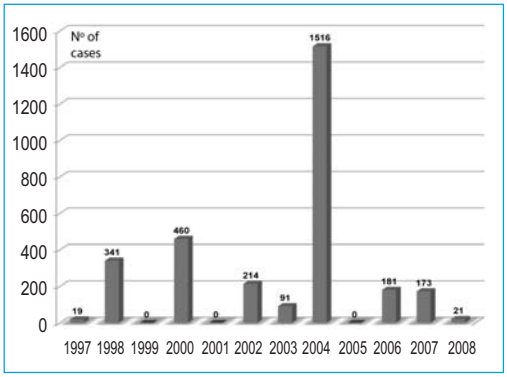
History of dengue fever in Argentina

The first outbreak of dengue in Argentina was recorded by Nicolás Gaudino[5] in 1916. The virus entered the country via Paraguay and affected the provinces of Corrientes and Entre Ríos. Although no cases were reported in the city of Buenos Aires, it affected 50% of the mesopotamic population.

Since then, in Argentina, the disease was not recorded for 82 years, in spite of the occurrence of severe outbreaks in the Caribbean and Central America in the 1960s, and the later appearance of dengue haemorrhagic fever (DHF) in the Cuban epidemic of 1981 which spread to all the other American countries except Canada and Uruguay[6]. During those eight decades, dengue was considered a problem affecting south-east Asia and other far-off regions. However, it has slowly re-entered our continent via Central America. Today, almost all the American countries from Mexico to the southern tip of the continent are affected by this disease[7].

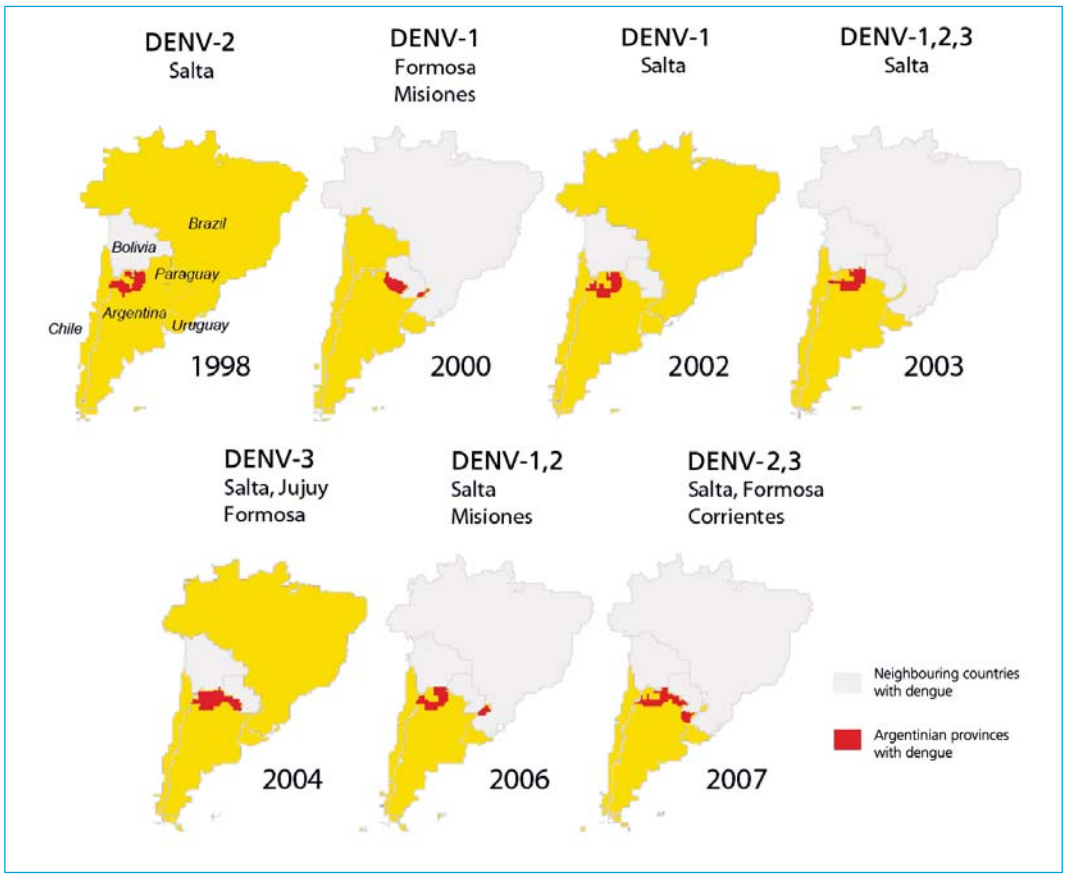
In 1998, there was an epidemic caused by DENV-2 restricted to the Chaco-Salta region of Argentina, with its epicentre in the city of Tartagal. The epidemic reached its peak in May[8], which caused several hundreds of cases of dengue fever (DF) (incidence rate: 45/10 000 inhabitants). All indications suggest that the virus was introduced from Bolivia[9]. However, this was just the beginning. Since then, a series of outbreaks have occurred in Argentina – in 1998, 2000, 2002, 2003, 2004, 2006, 2007 and 2008 (Figure 1). Five provinces, namely Salta, Jujuy, Corrientes, Formosa and Misiones reported autochthonous cases. More than 70% of the cases were reported in the province of Salta[10]. Only imported cases were reported in 2005, among people having travelled to Bolivia, Paraguay, Brazil, Puerto Rico and Nicaragua. Figure 2 shows the provinces affected by the outbreaks, active serotypes and relationship with outbreaks in neighbouring countries. At present, the outbreaks of dengue in Argentina have always

Figure 1: Dengue fever cases in Argentina since the re-emergence of the disease



Source: Sistema Nacional de Vigilancia de la Salud (National System of Surveillance of Health), National Ministry of Health of Argentina

Figure 2: Outbreak localization and its relationships with outbreaks in border countries by year, province and circulating serotype in Argentina, 1998–2007



Source: Sistema Nacional de Vigilancia de la Salud (National System of Surveillance of Health), National Ministry of Health of Argentina

had a direct relationship with neighbouring countries, with the entry of viraemic subjects to initiate transmission. As such, Argentina is still considered a non-endemic country[11]. Three serotypes have been detected in Argentina since the first emergency situation, and have only appeared simultaneously in 2003 in the province of Salta.

In addition to DENV-2, serotypes DENV-3 and DENV-4 started circulating in the north-eastern frontier with limited epidemic potential until 2004, when there was an extended outbreak with thousands of DENV-3 cases in several cities of the Chaco-Salta region. Despite the circulation of several serotypes in successive years and sequential infections, no clinical cases of DHF had been detected[12].

In 2006, the situation in the north-eastern frontier was aggravated by floods. Dengue outbreaks were recorded in the area of Embarcación in Salta and Puerto Iguazú in Misiones due to DENV-1. Sixty-nine cases were

detected in Salta and 112 in Misiones, all of which were confirmed by a laboratory or epidemiological nexus[13]. This was followed by yet another outbreak in north-eastern Argentina and Iguazú (province of Misiones): where 55 and 90 cases were reported in the Chaco-Salteño area and in Iguazú respectively. The latter cases were mostly imported through the significant flow of people in the "triple frontier" area around the falls[14].

Towards the end of 2006, the authorities of Paraguay reported cases of dengue in the city of Asunción, which rapidly developed into a great epidemic. Like in the beginning of 2006, DENV-3 probably entered from Brazil via the state of Mato Grosso. With the entry of new DENV-3 serotype, the population of Asunción, which was previously exposed to DENV-1 in 1999-2000, presented DHF cases as expected due to sequential infections. This event marked a turning point in the history of dengue in the region as it was the first time that this severe clinical form was recognized in Paraguay[15]. Although by mid-February 2007 there were under 20 cases of DHF, serious cases of classical dengue were detected without plasma extravasation, and the physiopathological and clinical event defining DHF. Such DENV-3 cases had been previously observed in Brazil. The affected individuals presented acute attacks in one or several parenchyma: myocarditis, brain haemorrhage, or hepatocellular deficiency. Acute symptoms appeared 48–72 hours after the onset of dengue, sometimes in the absence of any apparent bleeding and without the haematocrit modifications as normally observed in DHF. The term *"visceral dengue"* has recently been coined to name this clinical variant, which must be carefully considered in the event of circulation of DENV-3. Due to the dengue epidemic situation in Paraguay, Argentine provinces are now considered high-risk areas[16].

Historical evolution of *Ae. aegypti* in Argentina

At the beginning of the 20th century, *Ae. aegypti* was present in every American country except Canada, from the southern states of United States to Buenos Aires, Argentina. In Argentina, it was widely distributed, covering 14 provinces in the northern and central regions of the country[17]. In 1947, a continental programme coordinated by PAHO was launched to eradicate yellow fever and its vector, *Ae. aegypti*[18]. It started out as a highly successful campaign and by 1954 and 1962 achieved its goal in 18 continental countries, including Argentina. Since 1962, only three additional countries have managed to eradicate this vector. During the 1970s, the support for mosquito surveillance and control programme got slackened, with the result that *Ae. aegypti* re-infested. By 1995, *Ae. aegypti* had a distribution similar to that in the 1940s before the eradication effort was initiated. Only Bermuda and Chile remained free of this infestation[19].

Presence of *Ae. albopictus*

In August 1998, the presence of *Ae. albopictus* was reported in the locality of San Antonio, province of Misiones; in February 2004 it was also found in Eldorado, another locality in Misiones. These are the first reports of this species in our country[20,21,22]. In the surveillance studies performed during February and March of 2007 in the open spaces and suburbs of the city of Puerto Iguazú, 24 foci of *Ae. albopictus* were detected, 18 of which were shared with *Ae. aegypti*[23]. The presence of *Ae. albopictus* conveys a potential risk in the epidemiological context of the region regarding the circulation and transmission of dengue, yellow fever and other related arboviruses[24].

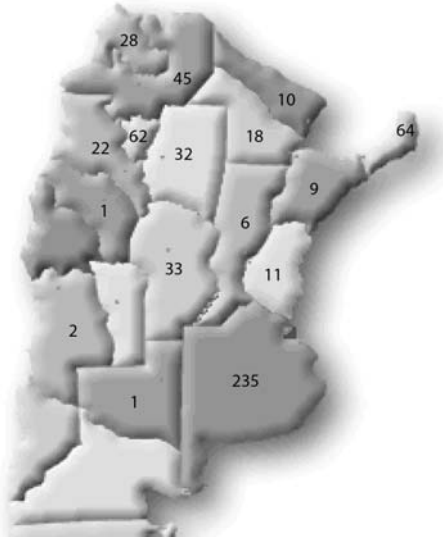
Current situation

The reinfestation of this region with *Ae. aegypti* forced the authorities to re-launch monitoring and control activities based on the new criteria of health service decentralization established by PAHO. According to these norms, the National Government transferred the responsibility of monitoring and control activities to the local municipalities, contributing to them with supplies and staff training. This new modality made it necessary to modify old criteria used by the centralized system, generating local difficulties in the provincial facilities regarding their resources and staff training. Furthermore, it is still difficult to combine criteria regarding the monitoring method, rational purchase of supplies (equipment, insecticides, security equipment, etc.) and development of control activities[25].

The high-risk situation of viral transmission still prevails in several localities in north Argentina despite the intervention of national, provincial and local governments, as well as of NGOs, that have been working on vector control for several years. The *Ae. aegypti* indices are still high enough to produce autochthonous outbreaks. In most municipalities (Figure 3), the House Index (HI) (*Ae. aegypti* breeding sites/houses inspected) remains over 10%[26]. Therefore, the entire northern region of the country must be considered a high-risk area. The current floods in Santa Cruz de la Sierra, Bolivia, put the provinces of Salta and Jujuy in an outbreak-prone area with the additional risk of yellow fever transmission as the flooded rural areas being evacuated lie in the jungle yellow fever-endemic zone.

In 2008, 2 996 183 tourists arrived in Argentina from dengue-endemic neighbouring countries, 285 073 of which entered from Paraguay. Approximately 46% of these tourists arrived by plane. In 2008 >2 400 000 Argentines left the country via Buenos Aires

Figure 3: *Ae. aegypti* infestation in Argentina by province. Cumulative values of 2008. Numbers indicate municipalities with the presence of the vector



Source: Sistema Nacional de Vigilancia de la Salud (National System of Surveillance of Health), National Ministry of Health of Argentina

to travel to dengue-endemic countries. The level of migration in border areas, especially in the tropical regions of northern Argentina, is under-reported[27]. The number of imported dengue cases in Buenos Aires and other cities of Argentina detected during the current period is substantially higher than the number detected in previous years.

During 2008, the National Ministry of Health reported only 28 cases of dengue in the country, 9 of which were imported. National government workers together with the local provincial staff of Salta are currently carrying out intense house-by-house control activities against mosquito breeding sites, with the collaboration of the community and using insecticide space spraying. These activities have

extended to the border town of Yacuiba in coordination with the health workers of this Bolivian district. No dengue deaths have been reported as yet in Argentina[28].

Current control strategies

Ever since the outbreak in Tartagal in 1998, all the routine and emergency activities recommended for the control of dengue were implemented in the country by the National Ministry of Health. The monitoring, control and evaluation methods implemented were the classical methods used for many years in similar situations[29,30]. The necessary supplies and equipment were purchased and field workers were trained on their correct usage. An emergency control strategy included the application of ultra low volume (ULV) thermal fog spray treatments, portable mist blowers, and house-by-house focal treatment. Simultaneously, diffusion activities were carried out to alert the population of the current situation. Adulticide treatments were only performed during epidemics and not as a means of prevention.

The active substances used were Temephos® sand granules as a larvicide, and the organophosphate Sumithion® and the pyrethroid Deltamethrin® as adulticides in spatial sprays in an oily base using gas oil as solvent. These are obviously not the best tools for implementing control activities in urban areas where the inhabitants suffer a high degree of exposure to the insecticides used.

Innovation in control strategies

Although certain epidemic outbreaks were controlled in some areas of northern Argentina, the inadequacy of implementing actions extrapolated from similar situations in other countries or regions with different socioeconomic conditions was soon obvious. We needed to modernize, improve, change and/or adapt future vector control strategies to meet our national and local requirements.

Some social events have triggered these changes. For example, focal treatments in Argentina were possible due to the implementation of social plans during the 2001 recession for the unemployed, who were obliged to contribute four working hours for vector control activities. However, since the economic recovery of the country, these plans were de-activated and now it is impossible to carry out these activities. Major constraints included security risk, refusals, locked houses, etc. These obstacles and inconveniences required the development of alternative strategies.

The CIPEIN, Pest and Insecticide Research Centre, in Buenos Aires, Argentina, is a World Health Organization Collaborating Centre for the evaluation of Chagas disease and dengue vector resistance. Among other tasks, it carries out basic and operational research studies with the object of optimizing control activities for insect vectors of human disease. Among the Centre's many contributions to mosquito control, we can mention the development of new active substances (permethrin *cis*-isomer, permethrin *trans*-isomer)[31,32,33], isolation of natural products with insecticide properties[34,35] and new insecticide formulations as fumigants in cans or tablets[36,37], Insect Growth Regulators (IGR) formulations in sand[38], and ULV formulations for spatial treatments[39].

Another proposal is the use of adulticides in complete cycles throughout the city, in addition to the control of immature forms, as a control strategy in case of an imminent outbreak of dengue. In countries like Argentina, this type of methodology would be particularly important due to the short periodicity of risk of transmission, which is generally from January

to April, coinciding with the period of higher temperatures and greater rainfall. Furthermore, the outbreaks of dengue in Argentina are closely associated with the epidemiological situation in neighbouring countries, evidenced by the coincidence in time and circulating serotypes in each affected area. Therefore, it has been suggested that the control of adult mosquitoes in border areas with epidemiological risk is a strategy that might avoid autochthonous outbreaks and, at the same time, is cost-beneficial at an incidence of more than 29 cases for every 1000 inhabitants[40].

However, developing such a tool is only part of the vector control challenge. To supplement focal house-to-house treatment, and in the frame of an integral mosquito vector control, a combination of treatments has been proposed that involves spraying a larvicidal-adulticidal mixed formulation[41] using units set up on vehicles in addition to intra-domiciliary actions performed by the dwellers themselves. This proposal is currently under evaluation and could constitute an efficient alternative for controlling this disease.

In spite of the lack of an extended success of campaigns based only on the use of insecticide tools, other strategies of vector control without chemical treatment involving the community have not been organized either. A good review of the achievements of the community-based dengue control programmes was done by Heintze et al.[42].

The PLICOV (Latin American Programme for Innovation in Vector Control) initiative was conceived due to the need of regional countries to develop novel strategies, which can be adapted to the particular situation of each country[43]. A group of six countries, comprising of Argentina, Bolivia, Peru, Panama, Cuba and Colombia, are jointly developing evaluation and control activities of new tools to verify their potential use for vector control in our continent. This objective has been supported not only by field studies, but also by laboratory research carried out in Latin American countries.

Resistance to insecticides

As recommended by the World Health Organization[44], the main preventive activities include monitoring of *Ae. aegypti* oviposition and larviciding sites. Since 1998, extensive chemical control operations were performed in the northern part of Argentina. A massive control programme began in 2002 in Clorinda (Formosa)[45] and in 2003 in Iguazú (Misiones), carried out by the Mundo Sano Foundation in collaboration with the National Ministry of Health, the local municipal government, and CIPEIN. The insecticides generally used in the event of an outbreak were temephos for larvicidal treatment in water containers (focal treatment) and *cis*-permethrin as an adulticidal ULV formulation (spatial treatment). For the control strategies to succeed it is important to know the level of susceptibility to the insecticides used, because the development of resistance could lead to control failures[46]. Therefore, our Centre implemented the first monitoring programme in Argentina in the cities of Clorinda and Iguazú, based on a protocol established during a meeting of the Latin American Network for Vector Control held in Iguazú (Misiones) in December 2004[47], and compared the susceptibility data obtained to the mosquito reference strain at CIPEIN. The results indicated an incipient resistance to temephos in these mosquito populations, posing an alert for this region. The Brazilian Ministry of Health considers that Resistance Ratio (RR) values of 3 are a reason to alternate temephos with another insecticide such as *Bacillus thuringiensis* var. *israelensis* or methoprene[48]. No control failures have been observed yet, but if these values rise to 10, the current control strategies would need to be completely revised[49].

Conclusions

The vertical plans of the mid-20th century based on the mobilization of huge resources and DDT, and centred on the eradication of *Ae. aegypti*, the vector, provided extraordinary results. However, their application in the current situation is highly impracticable and, as demonstrated by Brazil, not only a budgetary issue.

Judging by the progression of the disease in our continent, and in the world in general, the problem is far from being solved. The complex situation that Argentina and the rest of the South American countries face not only depends on the development of new active substances or more efficient formulations, but also on adopting an integral approach to the problem that includes active participation of all parties, reasonable allocation of resources, cost-benefit analyses, insecticide-resistance monitoring, establishing adequate entomological and epidemiological surveillance and, most importantly, the political will.

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