

# THE CHALLENGE OF CONTROLLING ARBOVIRUSES IN BRAZIL

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**Abstract** This paper discusses the challenges of the control of dengue and yellow fever in Brazil. Yellow fever, a vaccine preventable disease, has re-emerged in its sylvatic cycle, in regions of Brazil that were free of transmission for more than 60 years. Severe adverse events following vaccination limit the use of the vaccine. Dengue emerged in Brazil in 1986. It has since become hyperendemic. Control measures based on vector control seem to be ineffective. New tools are urgently needed to fight both arboviruses.

**Key Words** Arboviruses, dengue, yellow fever, epidemiology, control

## INTRODUCTION

Yellow fever and dengue are the main arboviruses of public health importance in Brazil. The aim of this presentation is to discuss the challenges to their control in Brazil

## YELLOW FEVER

The first two epidemics of yellow fever (YF) in Brazil occurred in Recife, in 1685, and in Salvador, in 1686. During the following two centuries, major Brazilian cities were periodically afflicted by deadly YF epidemics. During the 19th century, Rio de Janeiro, then the Brazilian capital, suffered summer epidemics every year. YF was considered an obstacle to the development of the country.

In late 19th century, Finlay and co-workers demonstrated vector transmission of YF, and opened a new alternative to its control. In early 20th century, as a result of vector control activities, urban YF transmission cycle was interrupted first in São Paulo and Rio de Janeiro, the two major cities of the country, and later in all in Brazilian cities.

The 1930s decade was marked by two important facts: the development of the live attenuated vaccine, and the discovery of the sylvatic transmission cycle of YF. Brazil was one of the field sites for the efficacy trials of the YF live attenuated viral vaccine, developed by South African researcher Max Theiller. Brazil was also one of the first countries to introduce the vaccine in its YF control program, in late 1930s.

The threat of the re-emergence of urban yellow fever lead to the resolution of the Pan American Health Organization (PAHO) to recommend that member-states should conduct an eradication campaign of YF vector insect, *Aedes aegyptii*. From 1950s to early 1970s extensive vector control activities were conducted by most Latin American countries, and *A. aegyptii* was virtually eliminated from all countries, but Venezuela and some Caribbean islands.

Since the 1940s decade, sylvatic YF occurrence was almost entirely restricted to the “traditional” endemic regions: the Amazon Region and the Central-Western Brazilian plains. These two regions cover two-thirds of the country’s surface, but less than 15% of its population. YF vaccine was extensively used in the population of these regions, during mass vaccination campaigns, as well as for travelers to these regions.

The 1970s decade was also marked by the military dictatorship that ruled the country since 1964. The military plan to transform Brazil into a regional power included the occupation of the Amazon and Central-Western Regions. Two new states were created, Rondonia and Mato Grosso do Sul, and incentives were offered to people interested in colonizing the new agricultural border. The occupation of rainforest and “cerrado” (the South American savannah) by farmers and ranchers has continued till present days, and probably has had consequences on YF occurrence.

The intense dissemination of *A. aegyptii* in Latin America and the widespread dissemination of dengue brought back the fear of re-emergence of the urban cycle of YF. That led PAHO to recommend in 1996 that the whole population of the endemic countries should be vaccinated against YF. Brazilian Government decided to take the

challenge seriously, and developed massive vaccination campaigns, planned to reach the whole country, starting from the traditional endemic regions, followed by the states bordering them, and later the Eastern part of the country. From 1998 to 2000 some 50 million people were vaccinated, in what was probably the largest YF vaccine campaign ever. But in 2000 the occurrence of two deaths due to what later was characterized as YF vaccine-induced viscerotropic disease led to the interruption of the mass vaccination campaigns.

The same year was marked by the occurrence of an outbreak of YF among tourists visiting a national park around Brasília, the Brazilian capital. The park's outbreak was the first of a series of YF sylvatic cycle outbreaks, in states that were thought to be YF free. In the following decade, YF outbreaks were reported in the states of Minas Gerais, São Paulo, Paraná and Rio Grande do Sul. Outbreaks also occurred in neighboring countries to the South, Paraguay and Argentina. Vaccination was intensified as a response to the outbreaks, and the number of vaccine induced viscerotropic disease also increased.

The summer outbreaks of 2009 and 2010, in the States of São Paulo and Rio Grande do Sul, although small (26 cases in SP and 19 in RS), reached to the headlines of major newspapers, TVs and internet sites. That created panic, including in areas of these states where no transmission had been detected. There was a rush for vaccines, and millions of people were vaccinated, most of them in low or no risk areas. That has also contributed to increase the number of vaccine induced YF.

The ecologic and demographic changes of the past 40 years in North and Central-Western Brazil, have probably led to intense pressure on primates populations of these regions, as well as in increased probabilities of transportation of sylvatic YF vectors and even its reservoir animals from endemic regions to new areas. That is probably related to the re-emergence of YF transmission in regions that remained YF free for more than 60 years.

Urban YF cycle did not re-emerge in Brazil. The large vaccine coverage among the population of "traditional" endemic regions restricts the number of potential carriers to new areas. On the other hand, *A. aegyptii* infestation rates in Brazilian cities might not be high enough to re-install YF transmission. The proposal of once again to vaccinate the whole Brazilian population is hindered because of the occurrence of vaccine induced viscerotropic disease. In areas where the risk of YF transmission is low, would it be justified to submit the people to the risk of a fatal adverse event? FIOCRUZ, the Brazilian public vaccine manufacturer is currently working in the development of less reactogenic vaccines. That might be the way out to the Brazilian yellow fever control program.

## DENGUE

Unlike yellow fever dengue's occurrence was not reported during Brazilian colonial times, nor after the country's independence. That all would change for good during the 1980ies. Dengue virus emerged twice: in 1981, in the Northernmost tip of Brazil, and in 1986, in Rio de Janeiro. The first reported outbreak occurred in Boa Vista, the capital of then Federal Territory of Roraima. Some 11,000 cases were reported in a population of 40,000, and DENV-1 and DENV-4 were identified. That outbreak did not spread to the rest of the country. Roraima was then a federal territory. Its administration was directly controlled by the military and access to non-residents was restricted.

In 1986 DENV-1 emerged in Rio de Janeiro, as did DENV-2 in 1990 and DENV-3 in 2000. These three serotypes became endemic in most regions of the country. IN 1986 Brazil became aware that the vector was no longer eradicated, but also it became clear that traditional control strategies no longer worked. In the 25 years since its emergence, dengue has become hyperendemic, with periodic epidemic peaks (1998, 2002, 2008, 2010). The largest epidemic occurred in summer 2009-2010, when almost 1 million cases were reported. Despite huge efforts and a considerable budget allocated to the dengue control program, the disease seems to follow its "natural" course.

In late 2010 the emergence of DENV-4 was detected in the Northern states of Amazonas and Roraima. Later, in the first months of 2011, its transmission has been confirmed in several states. A new countrywide epidemic is predicted for next summer. Since the 1970ies a huge demographic change is going on: the migration of millions of people from rural areas to the Brazilian cities. Nowadays more than 60% of Brazilians live in cities. Cities infrastructure did not grow enough to handle all that growth. Sub-standard housing, the proliferation of the "favelas", insufficient water supply, limited sewage systems, inadequate garbage collection and final destination, all contribute to the spread of *A. aegyptii*. At the same time, the widespread use of plastic cases and packs also contributed to the increase in mosquitoes infestation.

In 1988 a new constitution was approved and the country begun its re-democratization process. A new public health law was approved in 1990, and it installed the National Public Health System (SUS). With SUS, vector

control activities, which were under federal responsibility were decentralized to the municipalities. There were just not enough manpower and equipment to be decentralized to all 5,565 municipalities in which the country is divided. Even so, decentralization meant an increase in budget, manpower and equipment allocated to dengue control activities. In 2010 approximately R\$ 1 billion was transferred from the federal budget (Ministry of Health) to states and municipalities for dengue control activities. It is estimated that direct investment from these two levels amounts the same value. It might be not enough, but definitely is not a small amount of resources. And still, it apparently has had no impact in reducing dengue epidemics. Critics say it is a waste of money. Defenders say epidemics would have been worse without it.

Meanwhile, for the ones involved in dengue epidemiology and control there seems no reason to be optimistic. A huge epidemic is predicted with the emergence of DENV-4 in 2011. The trend to an increase in the occurrence of more severe cases in younger ages will probably continue. New tools to fight dengue epidemics are desperately needed. One of the large multinational pharmaceutical corporations has promised its dengue vaccine to be available in 2015. That might be some hope!

### REFERENCES CITED

- Brasil. Ministério da Saúde.** Manual de Vigilância Epidemiológica da Febre Amarela. 1999, Brasília, Ministério da Saúde, 60 pp
- Brasil/Ministério da Saúde.** Isolamento do sorotipo DENV4 em Manaus. Atualização em 03/02/2011, assessed in May 12, 2011.
- Brasil/Ministério da Saúde.** Isolamento do sorotipo DENV4 em Roraima. Atualização em 24/09/2010, assessed in May 12, 2011.
- Monath TP.** Yellow fever vaccine, in: Plotkin SA & Orenstein WA, Vaccines, 4th ed. Saunders, Philadelphia, 2004. Chapter 40: 1095-1176
- Osanai CH, Rosa APAT, Tang A, Amaral RS, Passos ADC & Tauil PL.** Surto de dengue em Boa Vista, Roraima. Rev Inst Med Trop São Paulo. 1983; 25(1):53-4
- PAHO.** Actualización sobre la fiebre amarilla en las Américas. Boletín Epidemiológico OPS 2000, 21(2):13.
- Siqueira Jr JB, Martelli CMT, Coelho GE, Simplicio ACR & Hatch DL.** Dengue and dengue hemorrhagic fever, Brazil, 1981 – 2002. Emerging Infectious Diseases 2005, 11(1):48-53
- Teixeira MG, Costa MCN, Barreto F & Barreto ML.** Dengue: twenty-five years since reemergence in Brazil. Cad Saude Publica 2009, 25(S1):S7-S18
- Teixeira MG, Costa MCN, Barreto ML & Motta E.** Dengue and dengue hemorrhagic fever epidemics in Brazil: what research is needed based on trends, surveillance and control experiences. Cad Saude Publica 2005, 21(5):1307-15
- Vasconcelos PFC, Luna E et al.** Serious adverse events associated with yellow fever 17DD vaccine in Brazil. The Lancet 2001, 358:91-97
- Vasconcelos PFC, Costa ZG, Rosa EST, Luna E et al.** Epidemic of jungle yellow fever in Brazil, 2000: implications of climatic alterations in disease spread. Journal of Medical Virology 2001, 65:598-604.
- Vasconcelos PFC.** Yellow fever in Brazil: thoughts and hypothesis on the emergence in previously free areas. Rev Saude Publica 2010, 44(6):1144-9.

