3rd COURSE: IMPLEMENTATION OF BIOLOGICAL CONTROL OF MOSQUITOES USING BACTERIAL BIOINSECTICIDES

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SATELLITE SYMPOSIUM: MOSQUITO VECTOR BORNE TROPICAL DISEASES AND BIOLOGICAL CONTROL

CONFERENCE ABSTRACT:

USING *B. thuringiensis* subsp. *israelensis* (Bti) IN DENGUE VECTOR CONTROL PROGRAMS IN SOUTH AND SOUTHWESTERN BRAZIL

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Recent Historical Background

Back in 1996 A. David Brandling-Bennett and Francisco Pinheiro from the Pan American Health Organization (Washington, D.C., USA) published an interesting point of view, under the title "Infectious Diseases in Latin America and the Caribbean: Are They Really Emerging and Increasing?" (*EMERGING INFECTIOUS DISEASES* V.2 [1], January-March). Accordingly to dengue and dengue hemorrhagic fever (DHF) they recalled important aspects, such as:

During the 1950s and 1960s, under the leadership of the Pan American Health Organization (PAHO), most countries in the Americas successfully reduced or eliminated infestation with the vector *Aedes aegypti.* Many local eradication programs, however, were not sustained and the mosquito reinfested all the Latin America except for Chile and Uruguay. As a consequence, dengue spread throughout the region, causing severe epidemics or even pandemics during the 1970s and 1980s.

Between 1968 and 1980, only 60 suspected or confirmed cases of DHF were reported, all by five countries in and around the Caribbean. After the 1981 DHF outbreak in Cuba, reports of DHF in the Americas markedly increased. The Cuban epidemic was the most notable event in the history of dengue in the Americas: almost 400,000 cases of dengue, over 10,000 cases of DHF, and 158 deaths were reported. The Cuban authorities implemented a successful vector control program and the country is still virtually free of *Ae. aegypti*. After this outbreak, cases of DHF continued to occur in the Americas, although at relatively low levels, until 1989 when another large epidemic with 2,500 cases of DHF occurred in Venezuela. Since then, Venezuela has reported large numbers of DHF cases every year, and in 1995 the country reported the largest outbreak of dengue/DHF in its history: almost 30,000 dengue cases and 5,000 DHF cases. Since 1968, 25 countries of the Americas have reported more than 35,000 confirmed or suspected DHF cases and approximately 500 deaths.

In 1995, dengue and DHF activity in the region was higher than in any year except 1981. As of November, countries in the Americas had reported more than 200,000 dengue cases and 6,000 DHF cases, and approximately 90 deaths. **Brazil** has had the largest number of dengue cases, but more than 80% of the DHF cases occurred in Venezuela. The reinvasion of the Americas by dengue virus type 3, which had been absent for 16 years, has increased the threat of large epidemics

and consequent risk for DHF. This serotype was isolated in Panama and Nicaragua at the end of 1994, and in 1995 it spread to other Central American countries (except Belize) and Mexico, causing severe outbreaks. High levels of infestation with *Ae. aegypti* are common from the United States to Argentina, making it likely that dengue epidemics will increase in frequency and severity.

Currently, dengue is endemic in virtually all countries with *Ae. aegypti*, and epidemics occur periodically.

Until December 2000 Brazil suffered virus type 1 and 2 dengue epidemics, and the type 3 spread from Nova Iguaçu, Rio de Janeiro, from that time to the present.

Finally, Brandling-Bennett and Pinheiro asked: Are dengue increasing in the region or are we simply seeing the results of better reporting of a persistent problem? OK, we agree that probably both factors are at work.

The CDC (CDC Dengue Fever Home Page- Atlanta, USA) indicate that dengue is the most important mosquito-borne viral disease affecting humans; its global distribution is comparable to that of malaria, and an estimated 2.5 billion people live in areas at risk for epidemic transmission. Each year, tens of millions of cases of dengue fever occur and, depending on the year, up to hundreds of thousands of cases of DHF. The case-fatality rate of DHF in most countries is about 5%; most fatal cases are among children and young adults. It must me controlled!

Dengue Control and Mosquito Vector Control

According to the CDC Home Page, “the reasons for the dramatic global emergence of dengue/DHF as a major public health problem are complex and not well understood. However, several important factors can be identified. First, effective mosquito control is virtually nonexistent in most dengue-endemic countries. Considerable emphasis for the past 20 years has been placed on ultra-low-volume (UBV) insecticide space sprays for adult mosquito control, a relatively ineffective approach for controlling *Ae. aegypti*.”

It must be noted here that the most important aspect, the first one, should be what the CDC pointed as the last one. The medical or clinical surveillance. The CDC text is: “Lastly, in most countries the public health infrastructure has deteriorated. Limited financial and human resources and competing priorities have resulted in a "crisis mentality" with emphasis on implementing so-called emergency control methods in response to epidemics rather than on developing programs to prevent epidemic transmission. This approach has been particularly detrimental to dengue control because, in most countries, surveillance is (just as in the U.S.) very inadequate; the system to detect increased transmission normally relies on reports by local physicians who often do not consider dengue in their differential diagnoses. As a result, an epidemic has often reached or passed transmission before it is detected”. In few words, is to say that if you can readily detect fever cases and isolate possible dengue symptomatic patients, makes no difference if you have the vector on the neighborhood. Is to say: dengue control irrespective of dengue vector control.

The common sense for pest or vector CONTROL is the reduction of an existing population to a level below an economic or transmission risk, respectively. But considering a little wide period of time, and for a given area, controlling a pest or vector population may be understood as avoiding its introduction and subsequent growth. Our point of view has been that regarding to dengue vector control, the first approach should be avoiding its ‘production’. And then, at second, its elimination or

reduction. As we know many attempts on education and community participation for breeding site reduction has been done. The results indicate however that very few attempts have been entomologically evaluated, let's say, taking in account and comparing vector larval or adult densities before and after the intervention. And from that publications reporting entomological evaluation, very few indicate a reduction of dengue risk. The conclusion is that we are failing to avoid dengue vector spread and population growth, and then, we have to control *Ae. aegypti* in the simple sense of killing their eggs, larvae, pupae and adults.

Evolution of larval control strategies – Southwestern Brazil.

In the last decades, the main attempts to control *Ae aegypti* in the States of Rio de Janeiro and São Paulo started in 1985, carried out in this late State by SUCEN (State Department for Disease Control). Rio de Janeiro experienced a major epidemic during 1986 with probably two times the official number of 700,000 dengue cases.

At that time, a vector surveillance program for São Paulo State detected the presence of the mosquito in 30 out of 654 towns. And since then organophosphate insecticides are being used to routine control. Larval foci are treated with the larvicide temephos, and for adult control residual perifocal spraying with fenitrothion was recommended. We have today 478 tows (74.1%) infested and dengue transmission was confirmed to at least 154 of these.

Unfortunately in Brazil the use of Bti for dengue vector control has been almost always associated to the concern with a possible failure of the chemical control. It seems that the policy is: Temephos as choice. If not possible, due to resistance, so we have to use Bti based products.

The susceptibility of *Ae. aegypti* to temephos and Bti was firstly investigated by me and Modolo (SUCEN) from larvae field collected during April 1987 in Campinas, SP. We evaluate both larvicides alone and as a mixture, in order to investigate a possible integrated control. Due to the survival of the assayed larvae to a temephos concentration more than two times that established by WHO as the resistance diagnostic dose, we conclude for a urgent need for full multiple-concentration tests to confirm resistance among Brazilian populations of *Ae aegypti*. But it was only in 1996 that SUCEN implemented an annual program for monitoring the susceptibility of *Ae. aegypti* to insecticides in São Paulo by means of larval and adult bioassays. And since 2000 SUCEN staff has been also investigating the levels of esterase and acethylcholinesterase activity by biochemical tests.

A national dengue control approach in Brazil (actually an Eradication Plan) was launched by the Ministry of Health in June 1996. Although strongly based upon the chemical control, it was at least mentioned the 'production' of *Bacillus thuringiensis israelensis* (Bti). Few months before (April 1996) it was held at Rio de Janeiro a PAHO meeting discussing a report about *Aedes* and dengue control in Americas and the feasibility of eradication programs. From that report, based on a questionnaire answered by 28 countries, it was clear that the common choice was the chemical control by the use of the larvicide temephos and UBV treatments with malathion for adult control. Also, the report pointed out an increasing use of pyretroids. The mention for the use of Bti (400 liters) was related to Argentina during the period from 1991 to 1995, comparing to 16,000 Kg of chemicals used in the same period. Although personally I never checked for that information, I doubt such

Bti was used for *A aegypti* control. I went to Argentina three times (1994, 1997 and 1998) for scientific meetings and the concern for dengue vector control there was only starting by those late years (1997 and 1998).

After been intensively used for eleven years, resistance to temephos was firstly suspected only in 1997 in the state of Rio de Janeiro by FNS (National Foundation for Health) and confirmed in the next year by the IBEX, the Brazilian Army Biological Institute. Galardo *et al.* (2001) found mortality from 23.5 to 74% to the Diagnostic Concentration (DC) of 0.012 ppm a.i. in 7 municipalities in the State. And besides resistance, human intoxication to the chemical insecticides becomes also a problem. In 1998 many FNS officials were removed from field work due to insecticide contamination, by handling granular temephos and products such as malathion and fenithrothion for spatial ULV. Laboratory tests carried out by FNS confirmed the intoxication. The consequence was that in 1999 FNS carried out an auction for Bti and methoprene (an insect growth regulator) products and bought a corn cob formulation (about 19 tons) and ALTOSID.

In September, 2000 the problem was discussed and we presented both products for the Dengue Operational Managers (DOM), in the state of Rio de Janeiro (91municipalities), in a two days forum. The results where presented at the 3rd International Congress of Vector Ecology – Barcelona, Spain. Interviewing the DOM one year later, we concluded for some important technical and social problems related with the broad use o Bti in Rio de Janeiro. The DOM said that: decentralization seems to help for regional (and local) solutions. They where not optimist about dengue epidemics next summer (January 2002) in Rio de Janeiro. They used that lot of granular Bti all over the State during 2001. They felt the product as a good choice (efficient and safe). BUT they whished something better - a soluble formulation that do not clog and with a longer lasting residual effect. They faced some additional problems during the routine work with the community, such as alleged allergies, alleged dog, cat and chicken intoxication or even casualty, and people refusing to accept granular Bti treatment, in any breeding places, induced by someone else that experienced clog problems. Also, they where dreaming about Administrative - Political stability and good training courses. They wanted good work conditions, stability, good salary for them and for the field work agents they coordinate (receiving that time ~20 US$/week). And finally, they where unanimously in considering EDUCATION and elimination of breeding sites the key factor for dengue prevention.

Although a little bit difficult to assert the exact amount of Bti used for dengue control during the last 4 years in Brazil, some companies inform that the amount of the corn cob granular formulation used was around 160, 250, 150 and 45 tons respectively. Additionally, around 60 tons a novel water dispersible granules (WDG) formulation has been used during the two late years (2002 and 2003).

In the last years Brazilian government through the national health foundation (FNS) has been implementing a nation-wide decentralisation of health programs and endemic diseases control. Public funds have been as much as 400 millions Euros (one billion Reais R$) a year, allocated to about 3,000 municipalities all over the country. By April last year, during a meeting for State dengue coordinators, FNS inform that Bti based products where available for those localities where larval resistance to organophosphates where detected. And if confirmed an auction for temephos this year of around 6,000 ton, we can expect the same policy for the next years. (See also the abstract: P. Vilarinhos, “Control of Dengue in Brazil – Actual Situation and Perspectives” in the present Symposium)

ANDRADE, C.F.S. & M. MODOLO, 1991. Susceptibility of *Aedes aegypti* larvae to temephos and *Bacillus thuringiensis* var. *israelensis* in integrated control. Rev. Saúde públ. São Paulo, 25(3): 184-187.

SANTOS. L.U., SOUZA, A.B., ANDRADE, F.C. & SOUZA, C.E.P. 1994. Uso de *Bcillus thuringiensis israelensis* como agente controlador de mosquitos em um cemitéio. Ver. Patol. Tropical 23(2):151-158.

A.K.R. Galardo, L.A. Braga & S.S. Soares. EVALUATION OF TEMEPHOS SUSCEPTIBILITY IN *AEDES AEGYPTI* IN RIO DE JANEIRO, BRAZIL. XXI International Congress of Entomology, Foz do Iguaçu, Brazil, 2001. ABSTRAC 4976.

C.F. Andrade, J. R. Duarte, Z. Martins & J. Campos. Training dengue operational managers for swapping temephos by *Bacillus thuringiensis israelensis* in the *Aedes* control program in the State of Rio de Janeiro, Brazil. 3rd International Congress of Vector Ecology – Barcelona, Spain. 16/21 September 200.1

CAMPOS G. J. & ANDRADE C.F.S. 2001 Susceptibilidade Larval de duas Populações de *Aedes aegypti* (Diptera, Culicinae) a inseticidas químicos. Revista Saúde pública 35 (3): 232-236.

CAMPOS J. & C.F ANDRADE**.** Larval susceptibility to chemical insecticides of *Aedes aegypti* and *Culex quinquefasciatus* populations Rev. Saúde Pública, SP,USP37(4), 2003.

Vilarinhos P. 2001 Current status of the National Program to Fight against *Aedes aegypti* in Brazil In: Symposium: Vector Control Programs with Economic and Technologic Considerations Organizers: Norbert Becker (Germany), Jean Marc Hougard (France) and Jack E. Hazelrigg (USA).