

# A Model of the Transmission of Dengue Fever with Larval Competition and the Insecticide Application on Control of the Vector

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**Abstract:** Dengue fever is a viral disease endemic in many areas of the world. About two-thirds of the world's population live in areas infested with dengue vectors, mainly *Aedes aegypti*. Dengue causes a spectrum of illnesses in humans ranging from clinically inapparent to severe and fatal hemorrhagic disease. A variety of methods have been used in order to control *Aedes* mosquitoes. Chemical control, with the use of insecticides, is a widely used technique. There is much controversy over the impact of insecticide applications on *Aedes aegypti* populations and their impact on dengue transmission is even more difficult to assess. In this paper, we present a dynamic model of dengue transmission and study the impact of mosquito control efforts on a simulated epidemic. The dengue model is a mathematical description of transmission of one serotype of dengue virus between host and vector population groups in a constant environment. The model is based on the SEIR models of infectious disease epidemiology. For the mosquito population, we include the model of larval competition proposed by Gurney and Nisbet in 1983. The control of the vector by the insecticide application, according to the model, obtained small impact on the incidence of the disease, even when the percentile of reduction was high. On the other hand, there is an effective decrease in the transmission of the disease when insecticide applications are accomplished during the peak of the prevalence, once the transmission is decreased in a moment in that the disease can not be reinstalled inside of the population.

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## 1 Introduction

Dengue is a disease that generates about a thousand deaths a year in the world and whose epidemics have serious socioeconomic consequences. It has been demanding the development of strategies that can reduce its morbidity and mortality [1]. Globally, the dengue viruses are considered the most important arboviral (virus transmitted by insects) transmitted for human beings, due the number of infected people as well as the number of deaths [2]. The mosquito *Aedes aegypti*, together with the mosquito *Aedes albopictus*, represents a great problem for the human population, because both have the capacity to act as vector of the urban yellow fever, of the dengue fever and of the dengue hemorrhagic fever (DHF) [3].

The dengue is an infectious disease, and there are four virus serotypes of dengue called DEN-1, DEN-2, DEN-3 and DEN-4, from the genus *Flavivirus*. The natural hosts for the dengue viruses are the

human beings (only capable of to develop clinical manifestations), the mosquitoes of the genus *Aedes* and small primates (which just develop viremia). Infection for anyone of the four serotypes can provoke a wide spectrum of reactions in the human being, from mild, nonspecific viral syndrome to severe hemorrhagic disease and death [4].

Although in the last years the understanding of the structure of *Flavivirus* has had an accentuated progress, many studies will still be necessary in order to produce an effective vaccine. Then, it is necessary to reinforce the control of the disease through the vector, which can be made through controlling programs integrating biological controlling, insecticides and preventive methods to avoid the formation of new foci of the mosquito.

## 2 Methodology

In relation to the problem exposed in the section 1, it was developed a system that accomplishes the simulation of a dengue epidemic with the employment or not of insecticides [5].

This system is based on the epidemic model SEIR of infectious diseases for the human population and, the model with age distribution proposed by Gurney and Nisbet [6] for the mosquito population. There are many hypotheses that can be established in the construction of the model, so that this model approach about some social and biological mechanisms that influence the propagation of the disease.

The population is divided in compartments or classes that move with the time and that represent the different states of the disease. People of all the ages and both sexes are included and, in relation to the mosquito population, only adult females are admitted.

The hypotheses that are established in the model are the following:

- The total human population  $N$  is constant;
- The vital dynamics, that is, the births (recruitments) and the deaths for the two species, it is also considered. The births only happen in the class of the susceptible;
- The acquisition of maternal protection in the humans and the transovarial transmission in the mosquitoes is not included in the model;
- All the births and all the deaths happen at same rates and all the new-borns are susceptible. Only natural deaths are included in the model, being supposed that the disease doesn't cause deaths (classic dengue);
- The model supposes homogenous mixing, that is, the populations are confined to a particular geographic area, small enough that each bite has an equal probability of being taken from any particular human.

With relationship to the hypotheses that must be adjusted in the model, in order to include the hypothesis of larval competition for food, we have:

- There are only two significant life history stages:
  - ◆ A larval stage with duration  $\tau_L$  and population  $L(t)$ ;
  - ◆ An adult stage with duration  $\tau_A$  and population  $A(t)$ .
- Uniform competition: The largest source of limitation of resources is in the larval stage, where it is natural to assume that a certain larva competes equally with another for food.

In the case of the mosquito *Aedes aegypti*, the larvae compete for the food that drops in the reservoirs where they are located. Thus, it is natural to choose the rate of per capita mortality of the larvae as dependent just of the total number of individuals of the population and it is given, therefore, for

$$D_L = aL(t).$$

- Assuming that there is not limitation of resources in the adult stage, we will have naturally that the rate of mortality of the adults  $D_A$  is constant.
- Since the larvae are infertile, the per capita fecundity of the larvae is zero ( $\beta_L = 0$ ). About the adults, the per capita fecundity is independent of the density and, therefore,  $\beta_A$  is constant, since in this stage the supplies of food are not limited.

The compartments that represent the state variables for the human population are represented for:

$S_h(t)$  = Number of susceptible individuals in the instant  $t$ ;

$E_h(t)$  = Number of exposed individuals in the instant  $t$ ;

$I_h(t)$  = Number of infected individuals in the instant  $t$ ;

$R_h(t)$  = Number of recovered individuals in the instant  $t$ .

The compartments that represent the state variables for the mosquito population, besides  $L(t)$ , are represented for:

$S_v(t)$  = Number of susceptible adult mosquitoes in the instant  $t$ ;

$E_v(t)$  = Number of exposed mosquitoes in the instant  $t$ ;

$I_v(t)$  = Number of infected mosquitoes in the instant  $t$ .

For the population of the vector the class of those recovered is not considered since, once these are infected, they stay in this class to the death, once the expectation of life of the vector is quite short (about three to eight days).

The system of first-order differential equations (1)-(2) provides the model of dengue fever transmission with larval competition.

The equations (1) represent the human population, the equations (2) represent the mosquito population,  $\delta_A = 1/T_{lv}$  and the variable  $P(t)$  represents the probability of survival of the larvae. The quantities

$IL$  and  $IA$  represent the inoculation of larvae and adult mosquitoes.

The set of values attributed to the parameters, in order to simulate a dengue epidemic, is available in the table 2 and it was extracted from [7], [8] and [9].

$$\begin{cases} \frac{dS_h}{dt} = \frac{N_h}{T_{lh}} - S_h \left( I_v \frac{c_{vh}}{N_h} + \frac{1}{T_{lh}} \right) \\ \frac{dE_h}{dt} = S_h I_v \frac{c_{vh}}{N_h} - E_h \left( \frac{1}{T_{iit}} + \frac{1}{T_{lh}} \right) \\ \frac{dI_h}{dt} = \frac{E_h}{T_{iit}} - I_h \left( \frac{1}{T_{id}} + \frac{1}{T_{lh}} \right) \\ \frac{dR_h}{dt} = \frac{I_h}{T_{id}} - \frac{R_h}{T_{lh}} \end{cases} \quad (1)$$

$$\begin{cases} \frac{dL}{dt} = \beta_A S_v + IL - P[\beta_A S_v(t - \tau_L) + IL(t - \tau_L)] - \alpha L^2 \\ \frac{dP}{dt} = \alpha P[L(t - \tau_L) - L] \\ \frac{dS_v}{dt} = P[\beta_A S_v(t - \tau_L) + IL(t - \tau_L)] + IA - \delta_A S_v - S_v I_h \frac{c_{hv}}{N_h} \\ \frac{dE_v}{dt} = S_v I_h \frac{c_{hv}}{N_h} - E_v \left( \frac{1}{T_{eit}} + \frac{1}{T_{lv}} \right) \\ \frac{dI_v}{dt} = \frac{E_v}{T_{eit}} - \frac{I_v}{T_{lv}} \end{cases} \quad (2)$$

### 3 Parameters and Initial values

The initials values attributed for state variables for the model of dengue fever transmission are related in the table 1.

**Table 1** - Initials values for State variables for the model of dengue fever transmission.

State variable	Initial value
Susceptible host	10.000
Exposed host	0
Infectious host	0
Resistant host	0
Susceptible vector	20000
Exposed vector	0
Infectious vector	1
Larvae	0
Probability of survival of the larvae	1

**Table 2** - Parameter values for the model of dengue fever transmission.

Name	Symbol	Base value
Transmission probability, host to vector	$a_{hv}$	0,75
Transmission probability, vector to host	$a_{vh}$	0,75
Bites per susceptible vector per day	$b_s$	0,5
Bites per infectious vector per day	$b_i$	1,0
Effective contact rate, host to vector	$c_{hv} = a_{hv} b_s$	0,375
Effective contact rate, vector to host	$c_{vh} = a_{vh} b_i$	0,75
Host life span	$T_{lh}$	25.000 days
Vector life span	$T_{lv}$	4 days
Intrinsic latent period	$T_{iit}$	5 days
Extrinsic latent period	$T_{eit}$	10 days
Host infection duration	$T_{id}$	3 days
Per capita fecundity	$\beta_A$	1,31 eggs per day
Adult death rate	$\delta_A$	0,25 adults per day
Larval stage duration	$\tau_L$	18,5 days

The expression (3) provides the basic reproductive number ( $R_0$ ) for the model of transmission of dengue fever with uniform larval competition.

$$R_0 = \frac{c_{hv} c_{vh}}{\delta_A} \frac{T_{lv}}{T_{lv} + T_{eit}} \frac{T_{id}}{T_{id} + T_{lh}} \frac{T_{lh}^2}{T_{lh} + T_{iit}} \frac{A^*}{N_h} \quad (3)$$

The term  $A^*$  represents the number of adult mosquitoes at equilibrium and can be obtained from the expression (4).

$$A^* = \frac{1}{\alpha \tau_L^2 (\beta_A - \delta_A)} \ln^2 \left( \frac{\beta_A}{\delta_A} \right) \quad (4)$$

Using the values of the tables 1 and 2 in (3), we obtain the result  $R_0 = 1,928$ . In this case, the average number of secondary infections produced when one infected individual is introduced into a population where everyone is susceptible is 1,928. At equilibrium, each infection will on average produce exactly one secondary infection [10].

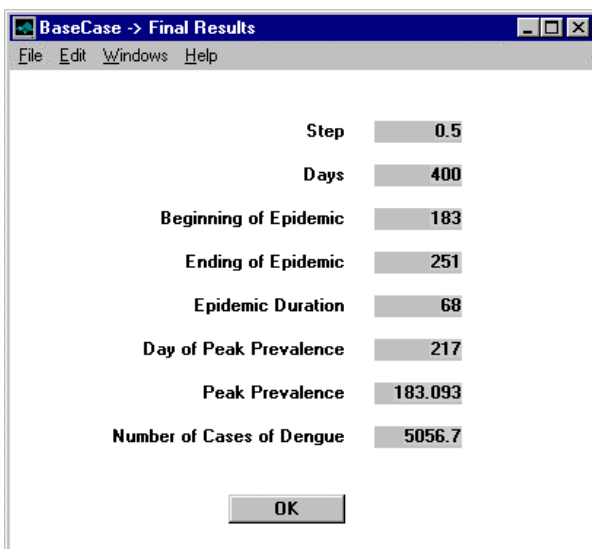
## 4 Implementation

The system that simulates the process of transmission of dengue fever was implemented using the tool MATLAB®. The numerical method used in the solution of the model represented by the system of first-order differential equations (1)-(2) was the Adams-Bashforth-Moulton predictor-corrector method [11].

The following information about a epidemic can be obtained from the system:

- Day of the beginning of the epidemic;
- Day of ending of the epidemic;
- Duration (in days) of the epidemic;
- Daily incidence: number of new cases per day;
- Prevalence: number of existent cases in certain day;
- Day of the peak of the prevalence;
- Number of prevented cases, in relation to the base case (where there is not insecticide application) in the situations in that insecticides are applied.

The fig. 1 shows the final results window that contains the results of an epidemic of dengue fever based in the model (1)-(2), in the base case (with no application of insecticide).

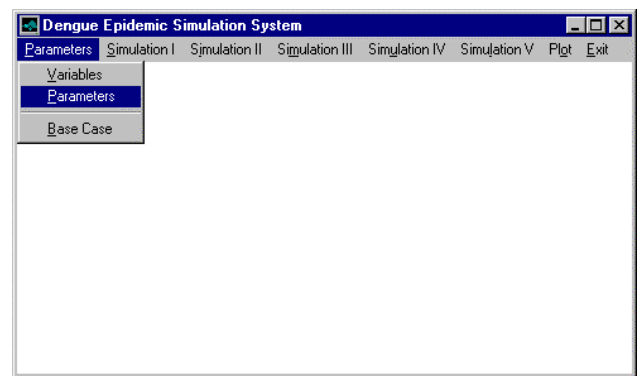


**Fig. 1** - Final results of the base case.

In this system there is the possibility of plotting graphics that contain information about an epidemic such as the prevalence and the incidence in a given day.

In addition to the model (1)-(2), other four models of transmission of dengue fever were implemented, in order to analyze the differences between the models in terms of number of cases of dengue fever and the dynamics of the vector population.

The fig. 2 shows the main screen of the dengue epidemic simulation system, with a menu of options that contains the necessary information for a simulation.



**Fig. 2** – Main menu of the dengue epidemic simulation system.

## 5 The Vector Control

According to the approach used for [8], the epidemic will begin when the prevalence exceeds 1% of the population. We adopt in this work the same approach.

The insecticide application is treated as an abrupt decrease in the population of the vector, in agreement with a percentage defined initially, which starts in any day after the beginning of the epidemic and with applications in consecutive or alternate days (seven days apart).

Some of the analyzed situations are the following:

- The total number of cases of dengue versus day after the beginning of the epidemic in that begins the application of the insecticide.
- The number of cases prevented versus day after the beginning of the epidemic in that begins the application of the insecticide.

The percentiles of decrease in the vector densities analyzed were 30%, 45%, 75% and 90% and four and seven applications of insecticide were analyzed, besides of one in the successive applications.

## 6 Conclusion

This work was designed and implemented in order to contribute for a theoretical evaluation of the effectiveness of the programs of chemical control of the vector, as well as to illustrate the theoretical hypothesis used in the modeling and simulation of a deterministic model of transmission of the dengue.

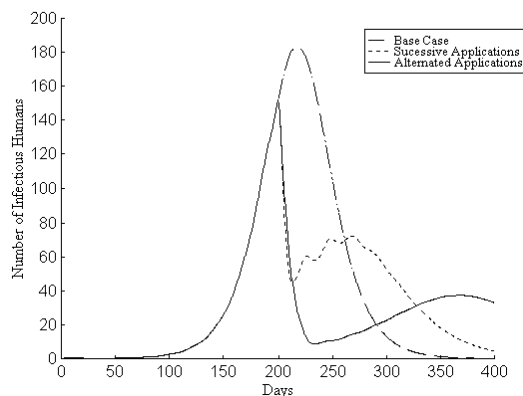
We can affirm that the impact of the programs of reduction of the vector in the community theoretically presented, in terms of the number of cases of dengue for the approached situations, was small. It is possible to affirm that the benefits in medical terms seem few, with a small impact on the incidence of the disease. Even when the percentile of reduction of the vector is high, the impact on the incidence is small. Such statement is illustrated by the table 3, which presents the best results of four applications of insecticide with a 90% reduction of the vector population.

**Table 3** - The maximum impact of four insecticide applications with a 90% reduction of the vector population on the course of the epidemic.

Results	Applications on consecutive days	Applications on alternate days (seven days apart)
Day of application of insecticide	218	208
Beginning of the epidemic	183	183
End of the epidemic	225	216
Day of peak of prevalence	217	209
Number of cases of dengue	4184,93	3257,66
Cases prevented	871,77	1799,04
Cases prevented (%)	17,24	35,58

Alternated applications have a larger impact than successive applications in the course of an epidemic. Such statement is also illustrated in the table 3, for the specific case of four applications with a 90% reduction of the vector population.

The fig. 3 illustrates the prevalence (number of existing cases) for four applications with a 90% reduction in the vector population with beginning on day 198, where we can compare the base case with successive and alternated applications.



**Fig. 3** – Impact of four applications of insecticide given at successive and intercalated days on a prevalence in the base case epidemic in an immunologically naive population. Each application reduces the adult mosquito population by 90%.

In the peak of the prevalence, each person generates, on the average, a new case of dengue. Thereafter, as the number of susceptible continues to decrease, the epidemic decreases and tends to disappear. Applications prior to the peak of the prevalence have a temporary depression in the transmission according to the fig. 3.

For these reasons, the best results for the analyzed cases, in terms of cases prevented, were obtained in applications close to the day of the peak of the prevalence.

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