Modeling and R_0 estimation of the 2010 Dengue Hemorrhagic Fever Outbreak in Hermosillo Sonora.

S. Díaz-Infante[a,*], J. A. Montoya Laos[b], D. Olmos Liceaga[b], P. A. Reyes Castro[c]

[a] *CONACYT-Universidad de Sonora, Departamento de Matemáticas, Universidad de Sonora Blvd. Rosales y Luis Encinas S/N, Col. Centro, Hermosillo, Sonora, C.P. 83000, México*
[b] *Departamento de Matemáticas, Universidad de Sonora Blvd. Rosales y Luis Encinas S/N, Col. Centro, Hermosillo, Sonora, C.P. 83000, México*
[c] *Centro de Estudios en Salud y Sociedad, El Colegio de Sonora, Avenida Obregón No. 54, Colonia Centro, C.P. 83000, Hermosillo, Sonora. México*

Abstract

We model and estimate the basic reproductive number of Dengue and Dengue Hemorrhagic Fever outbreak of the 2010 from Hermosillo Sonora. Our results suggest that serotype DENV-2 of the Dengue virus and the cross infection risk enhancement hypothesis, could explain the incidence of Dengue Hemorrhagic Fever cases reported by Secretaria de Salud del Estado de Sonora.

Keywords: Differential Equations; Dengue Hemorrhagic Fever; Boot strap;

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1. Introduction

State the objectives of the work and provide an adequate background, avoiding a detailed literature survey or a summary of the results.

Objectives. Our objective is to explain the dengue hemorrhagic outbreak that occurred in the city of Hermosillo, Sonora in2010.

Severity. Dengue Classic Fever (DCF) Dengue Hemorrhagic Fever (DHF) description.

ADE hypothesis. Dengue Virus Serotype 1 (DENV-1), Dengue Virus Serotype 2 (DENV-2) reinfection as cause of hemorrhagic.

Background. It was reported that in 2010 there was present only DENV-1 circulating in Hermosillo (Tesis de Pablo. La referencia que menciona ya no se encuentra disponible por internet.)

*Corresponding author
Email addresses: saul.diazinfante@unison.mx (S. Díaz-Infante), montoya@unison.mx (J. A. Montoya Laos), daniel.olmos@unison.mx (D. Olmos Liceaga), preyes@colson.edu.mx (P. A. Reyes Castro)

2. Material and methods

Provide sufficient detail to allow the work to be reproduced, with details of supplier and catalogue number when appropriate. Methods already published should be indicated by a reference: only relevant modifications should be described.

2.1. Data

Data description (Pablo).

Socioeconomic description: homogeneity according to population density index.

Model

Our work aims to explain the DHF cases reported in the Hermosillo's 2010 outbreak. Particularly, our aim is to provide evidence based on a mathematical model and statistical parameter estimation that a second strain (DENV-2) was also present in the city in 2010, and thus being responsible for the presence of DHF.

Thus, our formulation only considers the time of the epidemic and supposes that at this period, the DENV-2 serotype invades for the first time the city. We understand theDHF cases as a consequence of reinfection with the DENV-2 serotype. That is, a fraction of individuals with immunity to serotype DENV-1—acquired by past outbreaks—increments their susceptibility to the DENV-2, and consequently develops hemorrhagic with a certain probability.

T

Important Hypothesis (Daniel-Saúl)

Permanent immunity. Accordingly to WHO (1997 (accessed May, 2018), infection of Dengue caused by a serotype DEN-i induces long-life immunity to reinfection with this strain. Then, we assume in our formulation that a susceptible individual previously infected with Dengue of serotype DEN-i only could acquire Dengue of a different serotype. We also suppose that a susceptible individual who never get infected before, could obtain Dengue by any of serotypes DENV-1, or DENV-2, but only for a single time and during the outbreak period.

ADE hypothesis. The processes and factors that produce DHF are still unclear. There is evidence that reinfection with a different serotype enhances the probability of developing plasma vascular permeability—the Antibody Dependent infection Enhancement (ADE) hypothesis (see, e.g. Halstead, 1992, p. 295). But there also exist studies that report first infection DHF cases Streatfield et al. (1993). We consider in our formulation the ADE hypothesis, that is, only a fraction of the second reinfection with serotype DENV-2 develops vascular leaking.

DENV-2 report circulation in Hermosillo.

Asymptomatic and reported cases. We assume that the 95% (pendiente) of the DCF are asymptomatic, whereas for DHF all the cases are reported. Therefore, the class $Y_{-1}^{[h]}$ accounts for all the DHF cases, whereas a fraction $p = 0.05$ of the sum $I_1+I_2+Y_{-1}^{[c]}$ represent the confirmed cases of DCF.

Incluir citas de los porcentages de asintomáticos, http://www.who.int/en/news-room/fact-sheets/detail/dengue-and-severe-dengue says that about75% is asymptomatic

chastel2012.pdf

Homogeneity about the early outbreak stage. Define the infection forces as

$$\begin{aligned} A_{I_1} &= \frac{\beta_M b}{N_H} I_1, \qquad A_{I_2} = \frac{\beta_M b}{N_H} I_2, \\ A_{Y_{-1}^{[h]}} &= \frac{\beta_M b}{N_H} Y_{-1}^{[h]}, \qquad A_{Y_{-1}^{[c]}} = \frac{\beta_M b}{N_H} Y_{-1}^{[c]}, \\ B_{M_1} &= \frac{\beta_H b}{N_H} M_1, \qquad B_{M_2} = \frac{\beta_H b}{N_H} M_2 \, . \end{aligned} \tag{1}$$

Vector transmission dynamics. Define

$$A_\bullet := A_{I_1} + A_{I_2} + A_{Y_{-1}^{[h]}} + A_{Y_{-1}^{[c]}}$$

as the total human infection force, that is, the sum of all human contributions to the vector infection. Then we describe the mosquito disease dynamics by

$$\begin{aligned} \frac{dM_S}{dt} &= \Lambda_M - A_\bullet M_S - \mu_M M_S \\ \frac{dM_1}{dt} &= A_{I_1} M_S - \mu_M M_1 \\ \frac{dM_2}{dt} &= \left(A_{I_2} + A_{Y_{-1}^{[h]}} + A_{Y_{-1}^{[c]}} \right) M_S - \mu_M M_2 \end{aligned} \tag{2}$$

Here M_S, is the vector susceptible class and M_1, M_2 respectively denotes the vector Infected classes with DENV-1 and DENV-2.

Host disease dynamics. Susceptible individuals (S) become infected for the first time with DENV-1 or DENV-2 after a successful mosquito bite and move to classes I_1 and I_2, respectively. From here, they move to a recovered class R_S, and for the rest of the epidemic they are immune to any serotype. S_{-1} are the individuals who obtained DENV-1 in previous years are susceptible only to DENV-2 for the current year. They can become infected with DENV-2 and the outcomes are DF ($Y_{-1}^{[c]}$) or DHF ($Y_{-1}^{[h]}$). Finally, all the infected individuals eventually move to the recovered class $R_{S_{-1}}$.

For our model, μ_H is the human death rate; α_c and α_h are the recovery rates from DCF and DHF, respectively; b is the number of bites per week per mosquito and β_H is the effectiveness of the bite. From the current hypothesis our model is given by

$$\begin{aligned} \frac{dS}{dt} &= \mu_H N_S - (B_{M_1} + B_{M_2})S - \mu_H S \\ \frac{dI_1}{dt} &= B_{M_1} S - (\alpha_c + \mu_H) I_1 \\ \frac{dI_2}{dt} &= B_{M_2} S - (\alpha_c + \mu_H) I_2 \\ \frac{dS_{-1}}{dt} &= \mu_H N_{S_{-1}} - \sigma B_{M_2} S_{-1} - \mu_H S_{-1} \\ \frac{dY_{-1}^{[c]}}{dt} &= (1-\theta)\sigma B_{M_2} S_{-1} - (\alpha_c + \mu_H) Y_{-1}^{[c]} \\ \frac{dY_{-1}^{[h]}}{dt} &= \theta \sigma B_{M_2} S_{-1} - (\alpha_h + \mu_H) Y_{-1}^{[h]} \\ \frac{dR}{dt} &= \alpha_c \left(I_1 + I_2 + Y_{-1}^{[c]} \right) + \alpha_h Y_{-1}^{[h]} - \mu_H R \end{aligned} \tag{3}$$

Here, we take $N_H = N_S + N_{S_{-1}}$ as the total number of individuals. For our formulation N_H, N_S and $N_{S_{-1}}$ remain constant. N_S is the total number of individuals that are involved in the first infection dynamics ($N_S = S + I_1 + I_2 + R_S$). On the other hand $N_{S_{-1}}$ is the total number of individuals involved in the reinfection dynamics ($N_{S_{-1}} = S_{-1} + Y_1^{[c]} + Y_1^{[h]} + R_{S_1}$). All the recovered individuals in both classes belong to the recovered class

$R = R_S + R_{S_{-1}}$ as our dynamics are considered only for one year.

Fix $\Lambda_\cdot = N_\cdot$.

Include information about the 2 strains

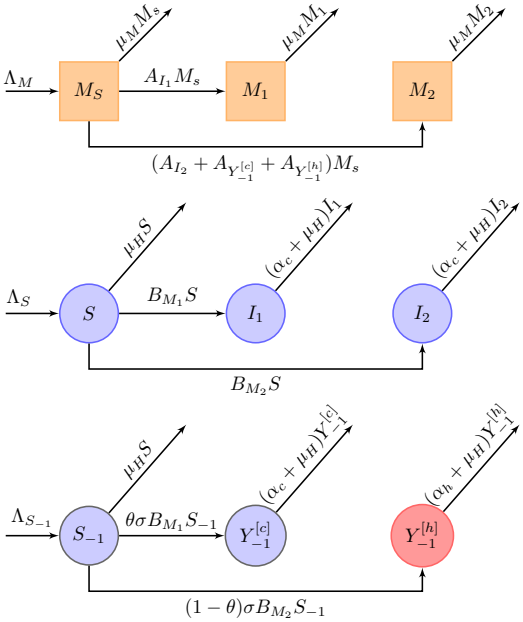

Figure 1: Flow diagram of model (3)

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Basic reproductive number. The disease free equilibrium results

$$FDE = \left(\frac{\Lambda_M}{\mu_M}, 0, 0, N_H - N_{S_{-1}}, 0, N_{S_{-1}}, 0, 0, 0\right).$$

get a relation for the initial grow phase parameter

Using the next generation operator method reported as in Feng and Velasco-Hernández (1997), we obtain the basic reproductive number

$$\begin{aligned} \pi_R &:= \frac{\beta_H \beta_M b^2 \Lambda_M}{\mu_M^2 N_H^2} \\ R_{01} &:= \pi_R \left(\frac{N_H - N_{S_{-1}}}{\alpha_c + \mu_H} + \frac{(1-\theta)\sigma N_{S_{-1}}}{\alpha_c + \mu_H} \right) \\ R_{02} &:= \pi_R \frac{\sigma\theta N_{S_{-1}}}{\alpha_h + \mu_H}, \\ \mathcal{R}_0 &:= \sqrt{R_{01} + R_{02}}. \end{aligned} \tag{4}$$

$$\begin{aligned} \psi &:= \frac{\beta_M b N_M}{\mu_M N_H} \\ R_{0c} &:= \sqrt{\psi \left(\frac{\beta_H b N_S}{(\alpha_c + \mu_H) N_H} + \frac{\beta_H b (1-\theta)\sigma N_{S_{-1}}}{(\alpha_c + \mu_H) N_H} \right)} \\ R_{0h} &:= \sqrt{\left(\frac{\beta_M b N_M}{\mu_M N_H} \right) \left(\frac{\sigma\theta N_{S_{-1}}}{(\alpha_h + \mu_H) N_H} \right)} \\ \mathcal{R}_0 &:= \sqrt{R_{0c}^2 + R_{0h}^2}. \end{aligned} \tag{5}$$

In this equation, R_{0c} and R_{0h}, are the basic reproductive numbers for classical and hemorrhagic dengue cases, respectively. From here, R_0 provides a measure of how DF and DHF infected people influence the presence of new dengue cases (Either DF or DHF). R_{0h} measures the new hemorrhagic cases that arise from one hemorrhagic infected individual in a population of $N_{S_{-1}}$ susceptible to strain 2 individuals, meanwhile R_{oc} provides a measure of how many new individuals will obtain DC fever (DF?) from an individual that has or has not have acquired dengue previously (from an individual that has either DF or DHF).

Observe that this R_0 differs in some way to the traditional R_0 where two different serotypes are involved (Feng and Velasco-Hernández (1997) include citations of R_0 for two serotypes). This follows from the idea that we are interested in classic and hemorrhagic cases rather than the predominance of a serotype.

Discuss above parameters units. Weeks or days

2.2. R_0 estimation (Montoya)

We suppose that the number of cases of classic and hemorrhagic dengue are observed at time points $t_1, \ldots t_n$. Here we assume that these processes follow a Poisson distribution with mean $\lambda_h(t) = Y^{[h]}_{-1}$ and $\lambda_c(t) = Z$, where

$$\frac{dZ}{dt} = p\left(I_1 + I_2 + Y^{[c]}_{-1}\right). \tag{6}$$

In our case the vector of parameters of the ordinary differential equations model is $\psi = (\psi_1, \psi_2)$, where $\psi_1 = (\beta_H, \beta_M)$ is regarded as unknown and $\psi_2 = (\alpha_c, \alpha_h, b, \mu_H, \mu_M, \sigma, \theta, p)$ is known in advance. We write $\lambda_h(t)$ and $\lambda_c(t)$ as $\lambda_h(t; \psi_1)$ and $\lambda_c(t; \psi_1)$ to emphasize this fact.

We use the likelihood approach to estimate the vector parameter ψ_1 based on an observed sample ....

3. Results

Results should be clear and concise.

Modeling Results (Saúl-Daniel).

Data analysis (Saúl-Montoya).

R_0 and parameter inference (Montoya).

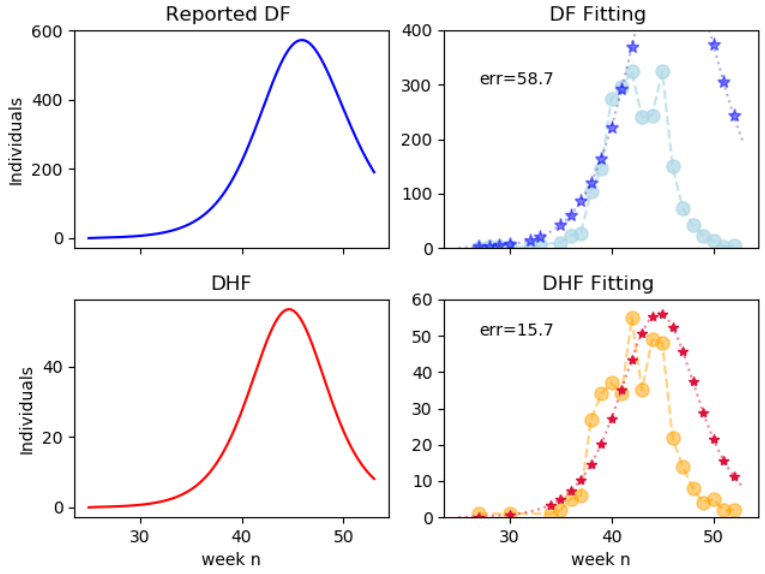

Figure 2: DF and DHF numerical solutions versus Dengue data from 2010 Hermosillo outbreak. Python code and data in https://github.com/SaulDiazInfante/Two-strains-dengue-model-data-fitting/tree/master/StochasticSearchPySimplifiedModel

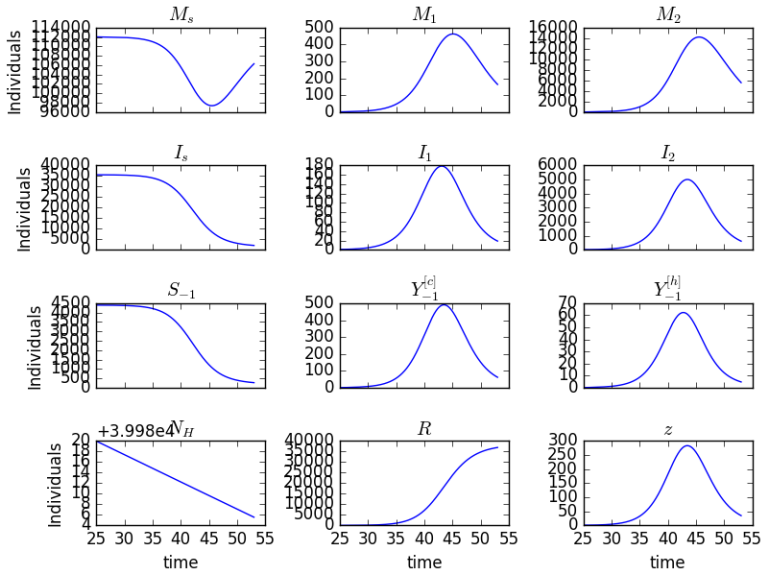

Figure 3: Evolutions of each stage.

Symbol	Meaning
M_S	Number of susceptible mosquitoes.
M_1, M_2	Number of infected mosquitoes with virus serotype DENV-1 or DENV-2.
S	Susceptible host population which, never has acquired dengue.
S_{-1}	Susceptible host population which is immune to serotype 1.
I_1, I_2	First time infected host population by serotype 1 and 2, respectively.
$Y_{-1}^{[h]}$, $Y_{-1}^{[c]}$	Second time infected host population with serotype 2, with DHF and DCF, respectively.

Table 1: Meaning of variables. Here we omit the explicit dependence of time.

4. Discussion

This should explore the significance of the results of the work, not repeat them. A combined results and Discussion section is often appropriate. Avoid extensive citations and discussion of published literature.

In our results we obtained $R_{0c} > 1$ and $R_{0h} < 1$. This means that for this outbreak, the presence of DHF cases, cannot trigger on its own new DHF cases and in general, $R_{0h} < 1$ would imply an exponential decay on the number of infected individuals. However, the small DHF outbreak arises despite the value of R_{0h} as there is an increase in infected mosquitoes of the serotype 2 due to the presence of the S individuals, which initially is close to N_S. Therefore, DHF dynamics is a consequence of the intensity of the outbreak of DF, given by serotype 2.

5. Conclusions

The main conclusions of the study may be presented in a short Conclusions section, which may stand alone or form a subsection of a Discussion or Results and Discussion section.

In this work we have presented a mathematical model to understand the 2010 dengue outbreak that occurred in Hermosillo, Mexico. The model includes infected classes of classic and hemorrhagic versions of dengue in order to adjust the observed data. To our knowledge, there is no published work

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Symbol	Meaning	Reference	Range	units
$M_S(0)$	Initial number of			
$M_1(0)$,	susceptible and infected			
$M_2(0)$	mosquitoes.			
N_H	Total Susceptible population	INEGI (see section 2.1)	283 493	
b	Biting rate	Yasuno M (1990)	[10.36 , 33.39]	meals/week
Λ_S	Human birth rate		$\mu_H \cdot (N_H - N_{S_{-1}})$	week^{-1}
$\Lambda_{S_{-1}}$	Human birth rate		$\mu_H \cdot N_{S_{-1}}$	week^{-1}
Λ_M	Vector birth rate		$\mu_M \cdot N_M$	week^{-1}
μ_M	vector mortality rate	YANG et al. (2009)	[0.252, 0.763]	week^{-1}
μ_H	Human mortality	—	0.000 273 973	week^{-1}
β_H	Human infection			
	probability by vectors	Feng and Velasco-Hernández (1997)	(0, 0.05]	—
β_M	Vector infection			
	probability by humans	Feng and Velasco-Hernández (1997)	(0, 0.05]	—
α_c	Mean recover rate			
	from Classic Dengue	Pinho et al. (2010)	[0.581, 1.75]	week^{-1}
α_h	Mean recover rate	Pinho et al. (2010)	[0.581, 1.75]	week^{-1}
	from Hemorrhagic Dengue			
σ	Susceptibility to serotype			
	DENV-2.	Feng and Velasco-Hernández (1997)	(0, 5)	
p	Ratio of asymptomatic cases	Balmaseda et al. (2006), Chastel (2011, 2012)	$[\frac{1}{60}, \frac{1}{30}]$	—
θ	Probability of			
	acquire DHF			
	as second infection			

Table 2: Parameter description

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Parameters (time in weeks) for figs. 2 and 3		
$\Lambda_M = 30\,702.613\,900\,6,$	$\Lambda_S = 10.238\,593\,423\,3,$	$\Lambda_{S_{-1}} = 1.137\,621\,491\,48,$
$\alpha_c = 0.686\,615\,937\,276,$	$\alpha_h = 1.413\,100\,922\,56,$	$b = 12.712\,233\,341\,8,$
$\beta_H = 0.047\,848\,897\,773\,3,$	$\beta_H = 0.047\,848\,897\,773\,3,$	$\beta_M = 0.036\,106\,599\,564\,8,$
$\mu_H = 0.000\,273,$	$\mu_M = 0.307\,170\,720\,093,$	
$\sigma = 1.806\,480\,946,$		
$\theta = 0.188\,750\,185\,7,$		
$p = 0.126\,295\,209\,216,$	$h = 0.000\,189\,285\,714\,286,$	
$S(0) = 35\,598.0,$	$I_1(0) = 1.0,$	$I_2(0) = 1.0,$
$M_S(0) = 120\,000,$	$M_1(0) = 10,$	$M_2(0) = 10,$
$S_{-1}(0) = 4400.0,$	$Y_{-1}^{[c]}(0) = 0.0,$	
$Y_{-1}^{[h]}(0) = 0.0,$	$z(0) = 0.252\,590\,418\,433,$	$Rec(0) = 0.0,$

Table 3: Parameters of numerical example