KMITL Sci. J. Vol. 5 No. 2 Jan-Jun 2005

RISK OF INFECTION TO TOURISTS VISITING AN DENGUE FEVER ENDEMIC REGION

Puntani Pongsumpun[1,*] and I-Ming Tang [2]
[1] Department of Mathematics and Computer Science, Faculty of Science,
King Mongkut's Institute of Technology Ladkrabang, Chalongkrung Road,
Ladkrabang, Bangkok 10520, Thailand
[2]Department of Physics, Faculty of Science, Mahidol University,
Rama 6 Rd., Bangkok 10400, Thailand

ABSTRACT

A mathematical model is used to study the risk of infection by the dengue virus for tourists visiting a dengue fever endemic region. The SIR (S = susceptible, I = infectious and R = recovered) model is used. The human population is separated into two populations, host and tourists. The infection rate of dengue virus depends on the immune status of the human. We assume that tourists have less immunity than the members of the host population. We use standard dynamic analysis method for analyzing mathematical model. The local stability conditions for the endemic state are determined from the value of the reproduction number for the disease. The infectious tourist fractions are calculated as a function of the length of time the tourist stay in the region. The risk of infection grows as the tourists stay longer.

KEYWORDS: dengue disease, transmission model, tourist, stability

1. INTRODUCTION

Dengue disease is a mosquito-borne disease caused by dengue virus. Four serotypes of the dengue virus exist and are called DEN1, DEN2, DEN3 and DEN4. Infection by one type of the virus confirms permanent immunity to further infections by the infecting strain and temporary immunity to the others. The disease is usually found in tropical region of the world. This disease can be transmitted to human by biting of infected *Aedes Aegypti* mosquitoes [1]. This species lives in close with humans in most tropical urban areas. Biting activity is greatest in the morning for several hours after daybreak and in the late afternoon for several hours before dark. It may feed all day indoors. This mosquito breeds in artificial water containers such as discarded tires, cans, barrels and flower vases, all of which are usually found in the domestic environment.

Dengue fever (DF) is characterized by the rapid development of the illness that may last from five to seven days with headache, joint and muscle pain and a rash [2]. The rash develops on the feet or legs three to four days after the beginning of the fever. The illness is characterized by a sudden onset of fever, intense headache, joint and muscle pain, loss of appetite, vomiting and diarrhea, and rash. Dengue hemorrhagic fever (DHF) is the severe form of dengue fever. It is usually the result of a second infection in a person having pre-existing antibodies to a different stain. DHF is associated with loss of appetite, vomiting, high fever, headache and abdominal pain. Shock and circulatory failure may occur. Dengue fever may occur in people of all ages who are exposed to infected mosquitoes. The disease occurs mainly in tropical Asia and the Caribbean, usually during the rainy seasons in areas with high numbers of infected mosquitoes. The symptom of dengue patients may occur from four to twelve days after exposure to an infected mosquito. Current data suggests that the immune

*Corresponding author. Tel: 662-3264344 ext. 320 Fax: 662-3264341 ext. 284
E-mail: kppuntan@kmitl.ac.th

status (i.e., having had a previous dengue infection), age, and genetic background of the human host are the most important risk factors for developing dengue disease [3].

We are interested in this paper on the risk of infection of tourists who visit dengue fever endemic regions. There are reports of increased number of tourists to Thailand who are being infected with dengue virus. In a study of Swedish tourist's [4], 71% of the imported dengue cases during 1998-99 were infected in Thailand. A similar preponderance was seen among Israel tourists during 1994-1995 [5]. A special report issued by the surveillance net TropNetEurop [6] point out that during 2002, 61.4% of the 68 reported cases (among German or Swiss tourists) had become infected while they were visiting Ko Phangan and Ko Samui, two islands in the Gulf of Thailand. During the previous three years, only 20.4% of the imported dengue cases among this group of tourists originated in Thailand. The average duration of the tourists in these three studies was three to four weeks. A prospective study of Israeli tourists to tropical countries who stay a long time (at least three months) indicates that the incident rate of dengue infection for these travelers may be as high as 600 per 100,000 travelers [7].

Another reason for being interested in the risk of infection to tourists is a recent comment made about another disease, malaria. Labbe *et al.* [8] pointed out that "*Analysis of imported malaria in travelers may represent a novel surveillance system* for detecting *drug-resistant malaria*". Looking at infections only in persons residing in endemic regions, it may not be possible to determine whether a new strain of the virus or parasite is more virulent than the old. Partial immunity to the old strain may have developed in the people who are constantly exposed to the old strain. The new strain may lead to a higher incidence of infection not because it is more virulent but because the populace has developed a level of immunity to the old. Expose the new and old strains to tourist would not encounter the problem since the tourist would not have any immunity to either strain.

2. MATHEMATICAL MODEL

We formulate the mathematical model by first separating the population into two groups, human and vector population. We then divide the human population into hosts and tourist. The host population is the people who stay permanently in the region. The tourist is the person who stays in the region for a length of time (θ) between 10 days and 3 months. Each of the human population is divided into three classes, susceptible, infectious, and recovered populations. A susceptible person is one who is both not immune and not infectious. An infectious person is one who is both infected and can transmit the dengue virus to the mosquitoes. This occurs only during the period of viremia. A recovered person is the infected person after the viremia stage until after they recover from dengue infection. We assume that none of tourists carry the virus when they enter into the region. Because the host population has been exposed to the virus for most of their life, they will have developed some immunity to the dengue virus. Therefore, the infection rate in the host population should be less than that in the tourist. We take the total numbers of hosts and tourists to be constant. The host population should be greater than the number of tourists. We assume that there is only one type of dengue virus present and that the disease-related death rate is negligible. We divide the vector population into two classes: susceptible and infectious vector population. The mosquitoes never recover from infection.

The time rate of change for each population class is equal to the number of population entering minus the number of population leaving. Letting

$\bar{S}_h(t)$ denotes the number of susceptible host population at time t,

$\bar{I}_h(t)$ denotes the number of infectious host population at time t,

$\bar{R}_h(t)$ denotes the number of recovered host population at time t,

$\bar{S}_t(t)$ denotes the number of susceptible tourist at time t,

$\bar{I}_t(t)$ denotes the number of infectious tourist at time t,

$\bar{R}_t(t)$ denotes the number of recovered tourist at time t,

$\bar{S}_v(t)$ denotes the number of susceptible vector population at time t,

$\bar{I}_v(t)$ denotes the number of infectious vector population at time t.

The rate of change for each class of human and vector population is given by [9];

$$\begin{aligned}
\frac{d}{dt}\bar{S}_h &= \eta N_T - \nu_h \bar{S}_h \bar{I}_v - \mu_h \bar{S}_h, \\
\frac{d}{dt}\bar{I}_h &= \nu_h \bar{S}_h \bar{I}_v - (\omega + \mu_h)\bar{I}_h, \\
\frac{d}{dt}\bar{R}_h &= \omega \bar{I}_h - \mu_h \bar{R}_h, \\
\frac{d}{dt}\bar{S}_t &= P - \nu_t \bar{S}_t \bar{I}_v - ((1/\theta) + \mu_h)\bar{S}_t, \\
\frac{d}{dt}\bar{I}_t &= \nu_t \bar{S}_t \bar{I}_v - ((1/\theta) + \omega + \mu_h)\bar{I}_t, \\
\frac{d}{dt}\bar{R}_t &= \omega \bar{I}_t - ((1/\theta) + \mu_h)\bar{R}_t, \\
\frac{d}{dt}\bar{S}_v &= C - \nu_v(\bar{I}_t + \bar{I}_h)\bar{S}_v - \mu_v \bar{S}_v \\
\frac{d}{dt}\bar{I}_v &= \nu_v(\bar{I}_t + \bar{I}_h)\bar{S}_v - \mu_v \bar{I}_v
\end{aligned} \qquad (1)$$

with the conditions

$$N_T = \bar{S}_h + \bar{I}_h + \bar{R}_h, \quad N_r = \bar{S}_t + \bar{I}_t + \bar{R}_t \text{ and } N_v = \bar{S}_v + \bar{I}_v \qquad (2)$$

where N_T is the total number of host population,

N_r is the total number of tourist,

η is the birth rate of the human population,

ν_h is the infection rate of dengue virus from vector to host human,

ν_t is the infection rate of dengue virus from vector to tourist,

ν_v is the infection rate of dengue virus from human to vector,

μ_h is the death rate of the human population,

ω is the recover rate of the human population,

P is the rate at which the tourists entering into the region,
$1/\theta$ is the rate at which the tourist leaving the region,
C is the constant recruitment rate of the mosquito,
μ_v is the death rate of the vector.

We assume that the total numbers of host population, tourist and vector populations are constant. Thus the rates of change for the total host population, tourist and vector population are equal to zero. This gives $\eta = \mu_h$ for the human population. The total number of tourist is given by $N_r = P/((1/\theta)+\mu_h)$ while the total number of vector is $N_v = C/\mu_v$. We now normalize (1) by letting

$$S_h = \frac{\bar{S}_h}{N_T}, I_h = \frac{\bar{I}_h}{N_T}, R_h = \frac{\bar{R}_h}{N_T}, S_t = \frac{\bar{S}_t}{N_r}, I_t = \frac{\bar{I}_t}{N_r}, R_t = \frac{\bar{R}_t}{N_r} \quad \text{and}$$

$$S_v = \frac{\bar{S}_v}{N_v}, I_v = \frac{\bar{I}_v}{N_v}.$$

This gives

$$\begin{aligned}
\frac{dS_h}{dt} &= \mu_h(1 - S_h) - \rho_h S_h I_v, \\
\frac{dI_h}{dt} &= \rho_h S_h I_v - (\omega + \mu_h) I_h, \\
\frac{dS_t}{dt} &= ((1/\theta) + \mu_h)(1 - S_t) - \rho_t S_t I_v, \\
\frac{dI_t}{dt} &= \rho_t S_t I_v - ((1/\theta) + \omega + \mu_h) I_t, \\
\frac{dI_v}{dt} &= (\rho_{v,t} I_t + \rho_{v,h} I_h)(1 - I_v) - \mu_v I_v,
\end{aligned} \tag{3}$$

where $\rho_h = \nu_h(C/\mu_v)$, $\rho_t = \nu_t(C/\mu_v)$, $\rho_{v,h} = \nu_v N_T$, $\rho_{v,t} = \nu_v N_r$

with the three conditions

$$S_h + I_h + R_h = 1, \; S_t + I_t + R_t = 1 \quad \text{and} \quad S_v + I_v = 1. \tag{4}$$

3. ANALYSIS OF THE MATHEMATICAL MODEL

3.1 ANALYTICAL RESULTS

The equilibrium points are found by setting the right hand side of (3) equal to zero. This gives

1) The disease free equilibrium point $M_1 = (1,0,1,0,0)$ and
2) The endemic disease equilibrium point, $M_2 = (S_h^*, I_h^*, S_t^*, I_t^*, I_v^*)$ where

$$S_h^* = \frac{1}{1+\varphi_1 I_v^*}, \tag{5}$$

$$I_h^* = \frac{\varphi_2 I_v^*}{1+\varphi_1 I_v^*}, \tag{6}$$

$$S_t^* = \frac{1}{1+\varphi_3 I_v^*}, \tag{7}$$

$$I_t^* = \frac{\varphi_4 I_v^*}{1+\varphi_3 I_v^*} \tag{8}$$

$$I_v^* = \frac{-D_1 + \sqrt{D_1^2 - 4D_2 D_0}}{2D_2} \tag{9}$$

where

$$D_2 = \mu_v \varphi_3 (Y_0 + \varphi_1) + \rho_{v,t} \varphi_1 \varphi_4, \tag{10}$$

$$D_1 = \mu_v \varphi_3 (1 - Y_0) + \mu_v (Y_0 + \varphi_1) + \rho_{v,t} \varphi_4 (1 - \varphi_1), \tag{11}$$

$$D_0 = \mu_v (1 - Y_0) - \rho_{v,t} \varphi_4, \tag{12}$$

such that $\varphi_1 = \frac{\rho_n}{\mu_h}$, $\varphi_2 = \frac{\rho_n}{\omega + \mu_h}$,

$$\varphi_3 = \frac{\rho_t}{(1/\theta) + \mu_h} \text{ and } \varphi_4 = \frac{\rho_t}{(1/\theta) + \omega + \mu_h} \tag{13}$$

and

$$Y_0 = \frac{\rho_{v,h} \varphi_2}{\mu_v} > 1 \tag{14}$$

In this study, we are interested in the infections that occur in regions endemic in the dengue disease. To determine the local stability of the DF endemic equilibrium point, we need to find the characteristic equation for the endemic equilibrium point. Following the usual procedure for finding it, we get

$$\lambda^5 + g_4 \lambda^4 + g_3 \lambda^3 + g_2 \lambda^2 + g_1 \lambda + g_0 = 0 \tag{15}$$

where

$$g_4 = \rho_h \left(\frac{1}{\varphi_1} + \frac{1}{\varphi_2} + \frac{1}{\varphi_3} + \frac{1}{\varphi_4} + 2I_v^* \right) + \rho_{v,h} \varphi_2 S_h^* + \rho_{v,t} \varphi_4 S_t^*, \tag{16}$$

$$\begin{aligned} g_3 = {} & \rho_h^2 \left(\frac{1}{\varphi_1 \varphi_2} + \frac{1}{\varphi_1 \varphi_3} + \frac{1}{\varphi_1 \varphi_4} + \frac{1}{\varphi_2 \varphi_3} + \frac{1}{\varphi_2 \varphi_4} + \frac{1}{\varphi_3 \varphi_4} \right) \\ & + \rho_h^2 I_v^* \left(\frac{1}{\varphi_1} + \frac{1}{\varphi_3} + 2\left(\frac{1}{\varphi_2} + \frac{1}{\varphi_4} \right) + I_v^* \right) \\ & + \rho_h \left(\rho_{v,h} \varphi_2 S_h^* \left(\frac{1}{\varphi_1} + \frac{1}{\varphi_3} + \frac{1}{\varphi_4} \right) + \rho_{v,t} \varphi_4 S_t^* \left(\frac{1}{\varphi_1} + \frac{1}{\varphi_2} + \frac{1}{\varphi_3} \right) \right) \\ & + \rho_h I_v^* \left(\rho_{v,h} S_h^* (1 + 2\varphi_2) + \rho_{v,t} S_t^* (1 + 2\varphi_4) \right), \end{aligned} \tag{17}$$

$$
\begin{aligned}
g_2 \;=\; & \rho_h^3\left(\frac{1}{\varphi_1\varphi_2\varphi_3}+\frac{1}{\varphi_1\varphi_2\varphi_4}+\frac{1}{\varphi_1\varphi_3\varphi_4}+\frac{1}{\varphi_1\varphi_3\varphi_4}\right)\\
& +\rho_h^3 I_v^*\left(\left(\frac{1}{\varphi_1\varphi_2}+\frac{1}{\varphi_2\varphi_3}+\frac{1}{\varphi_1\varphi_4}+\frac{1}{\varphi_2\varphi_4}+\frac{1}{\varphi_3\varphi_4}\right)+I_v^*\left(\frac{1}{\varphi_2}+\frac{1}{\varphi_4}\right)\right)\\
& +\rho_h^2\rho_{v,h}S_h^*\left(\begin{array}{l}\varphi_2\left(\dfrac{1}{\varphi_1\varphi_3}+\dfrac{1}{\varphi_1\varphi_4}+\dfrac{1}{\varphi_3\varphi_4}\right)+\\ I_v^*\left(1+\dfrac{1}{\varphi_1}+\dfrac{1}{\varphi_3}+\dfrac{1}{\varphi_4}+\dfrac{\varphi_2}{\varphi_1}+\dfrac{\varphi_2}{\varphi_3}+2\dfrac{\varphi_2}{\varphi_4}+I_v^*(1+\varphi_2)\right)\end{array}\right) \qquad (18)\\
& +\rho_h^2\rho_{v,t}S_t^*\left(\varphi_4\left(\frac{1}{\varphi_1\varphi_2}+\frac{1}{\varphi_1\varphi_3}+\frac{1}{\varphi_2\varphi_3}\right)+I_v^*\left(1+(1+\varphi_4)\left(\frac{1}{\varphi_1}+\frac{1}{\varphi_2}+\frac{1}{\varphi_3}\right)\right)\right)\\
& +\rho_h^2\rho_{v,t}I_v^{*2}S_t^*(1+\varphi_4)\;,
\end{aligned}
$$

$$
\begin{aligned}
g_1 \;=\; & \rho_t^4\left(\frac{1}{\varphi_1\varphi_2\varphi_3\varphi_4}+I_v\left(\frac{1}{\varphi_1\varphi_2\varphi_4}+\frac{1}{\varphi_2\varphi_3\varphi_4}\right)+I_v^2\frac{1}{\varphi_2\varphi_4}\right)\\
& +\rho_h^3\rho_{v,h}S_h^*\left(\frac{1}{\varphi_3}\left(\frac{\varphi_2}{\varphi_1\varphi_4}+I_v^*\left(1+\frac{1}{\varphi_1}\right)\right)+\frac{I_v^*}{\varphi_4}\left(1+(1+\varphi_2)\left(\frac{1}{\varphi_1}+\frac{1}{\varphi_3}\right)\right)\right)\\
& +\rho_h^3\rho_{v,h}S_h^*I_v^{*2}\left(\left(1+\frac{1}{\varphi_1}\right)+(1+\varphi_2)\left(\frac{1}{\varphi_4}\right)\right) \qquad (19)\\
& +\frac{\rho_h^3\rho_{v,t}S_t^*}{\varphi_1}\left(\frac{\varphi_4}{\varphi_2\varphi_3}+I_v^*\right)+\frac{\rho_t^3\rho_{v,t}S_t^*}{\varphi_2}\left(I_v^*\left(1+\frac{1}{\varphi_1}\right)\right)\\
& +\frac{\rho_h^3\rho_{v,t}S_t^*I_v^*}{\varphi_3}\left(\frac{1}{\varphi_1}+\frac{1}{\varphi_2}\right)+\frac{\rho_t^3\rho_{v,t}\varphi_4I_v^*S_t^*}{\varphi_2}\left(\frac{1}{\varphi_1}+\frac{1}{\varphi_3}\right)\\
& +\rho_h^3\rho_{v,t}S_t^*I_v^*\left(I_v^*\left(1+\frac{1}{\varphi_1}+\frac{1}{\varphi_3}\right)+I_v^*\frac{\varphi_4}{\varphi_2}\right)
\end{aligned}
$$

$$
g_0=\rho_h^4\rho_{v,h}I_v^*S_h^*\left(\frac{1}{\varphi_4}\right)\left(1+\frac{1}{\varphi_1}\right)\left(I_v^*+\frac{1}{\varphi_3}\right)+\frac{\rho_h^4\rho_{v,t}I_v^*S_t^*}{\varphi_2}\left(1+\frac{1}{\varphi_3}\right)\left(I_v^*+\frac{1}{\varphi_1}\right) \qquad (20)
$$

The stability of the endemic equilibrium point can be determined by using Routh-Hurwitz criteria as follows:

i) $g_i > 0$ for $i = 0, 1, 2, 3, 4,$

ii) $g_2 g_3 g_4 > g_2^2 + g_4^2 g_1,$

iii) $(g_1 g_4 - g_0)(g_2 g_3 g_4 - g_2^2 - g_4^2 g) > g_0 (g_3 g_4 - g_2)^2 (g_2 g_3 g_4 - g_2^2 - g_4^2 g)$

After we check the three conditions above, we found that the endemic equilibrium point is locally stability when

$$Y > 1$$

where

$$Y = \nu_v \nu_h \frac{(C/\mu_v)N_T}{\mu_v(\omega + \mu_h)}$$

The quantity Y" = $\sqrt{Y}$ is the basic reproductive number of the disease, it gives the average number of secondary patients that one patient can produce if introduced into a susceptible human. So we can reduce the outbreak of dengue disease in the endemic region when the basic reproductive number (Y") greater than one.

3.2 NUMERICAL RESULTS

The values of the parameter used in this study are $\mu_h = 0.0000391$ per day. This corresponds to a life expectancy of 70 years in human. The mean life of mosquito is 14 days that is $\mu_v = 0.071$ per day. We assume that tourists have less immunity than the host population. Thus the infection rate with dengue virus in the tourist should be greater than in the host human. Numerical solutions of (3) are shown in the following figures.

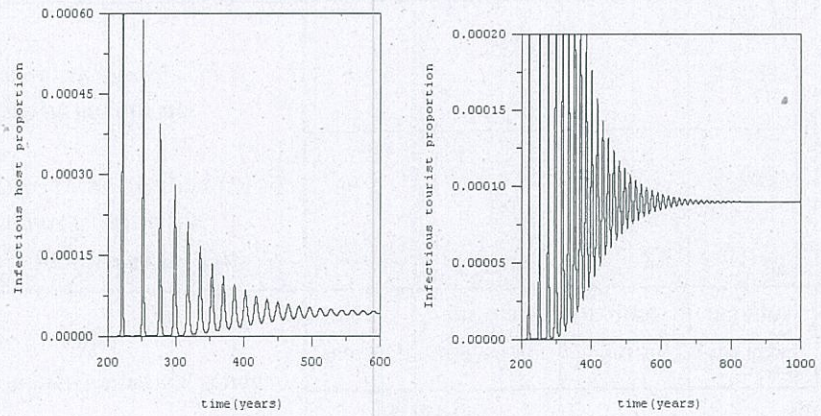

Figure 1. Numerical solution of (3) yield the time series solutions of the infected host population and tourist population. The values of the various parameters in the model are: $\theta = 90$ days, $\mu_h = 0.0000391$ day^{-1}, $\mu_v = 0.071$ day^{-1}, $\rho_h = 0.5$ day^{-1}, $\rho_t = 0.7$ day^{-1}, $\rho_{v,t} = 0.0225$ day^{-1}, $\rho_{v,h} = 0.075$ day^{-1}, $\omega = 1/3$ day^{-1}, $Y = 1.62206$ and $Y^{\cdot\cdot} = 1.2736$.

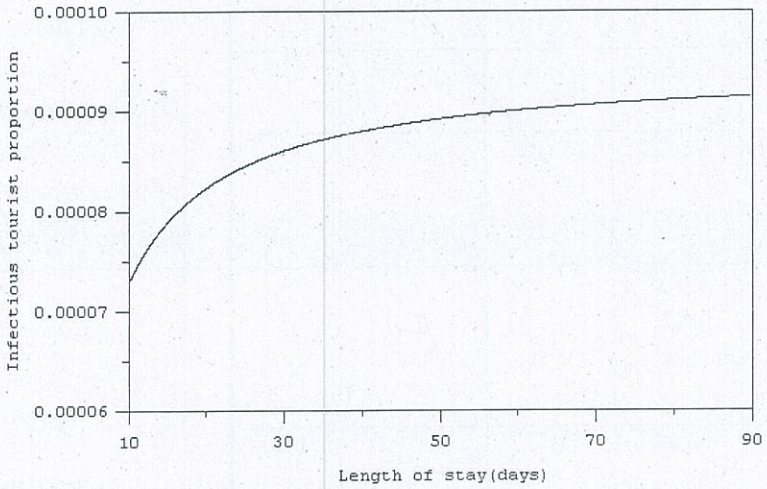

Figure 2. Equilibrium values of infectious tourist proportion as a function of the time they stay in an endemic area with $\mu_h = 1/(365\times70)$ day^{-1}, $\mu_v = 1/14$ day^{-1}, $\rho_h = 0.5$ day^{-1}, $\rho_t = 0.7$ day^{-1}, $\rho_{v,t} = 0.0225$ day^{-1}, $\rho_{v,h} = 0.075$ day^{-1}, $\omega = 1/3$ day^{-1}.

4. DISCUSSION AND CONCLUSION

From figure 1, we see that as time increase, the infected host population oscillates towards the equilibrium value $I_h^* = 0.0000462331$ and the infected tourist population oscillates towards its equilibrium value $I_t^* = 0.000088$. The equilibrium values of the other populations are $S_h^* = 0.606202$, $S_t^* = 0.992869$ and $I_v^* = 0.0000508505$. The imaginary part of complex root is approximately 0.001055, meaning that the period of oscillation is $2\pi/0.001055$ days or approximately 16.3 years. We then use the computer simulation to show how the number of infected tourist increases as they stay longer. We have varied the length of stay of the tourist from 10 days to three months as in figure 2. We see that the infected tourist population increases until it converges to a constant value. This indicates that the risk of infection with dengue virus to the tourist increases as they stay longer.

REFERENCES

[1] World Health Organization. **1997** Dengue *Haemorrhagic fever*: Diagnosis treatment and control, Geneva.

[2] Gubler, D.J. **1998** Dengue and Dengue Hemorrhagic Fever. *Clinical Microbiology Review*, *11*, 450-496.

[3] Kuno, G. **1995** Review of the Factors Modulating Dengue Transmission. *Epidemiological Review*, *17*, 321-334.

[4] Lindback, H., Lindback, J., Tegnell, A., Janzon, R., Vene, S. and Ekdahl. **2003** Dengue Fever in Travelers to the Tropics, 1998 and 1999. *Emerging Infectious Diseases* [serial online] available from http//www.cdc. gov/ncidod/EID/vol9no4/02-0267.htm.

[5] Schwartz, E., Mendelsen, E. and Sidi, Y. **1996** Dengue Fever among Travelers. *The American Journal of Medicine*, *101*, 516-520.

[6] TropNetEurop Sentinel Surveillance. **2002** *Dengue Fever in 2002. Special Report* 23.06.02.

[7] Schwartz, E., Moskovitz, A., Postasman, I., Peri, G., Grossman, Z. and Alkan, M.L **2000** Changing Epidemiology of Dengue Fever in Travelers to Thailand. *European Journal of Clinical Microbiology Infecious Diseases*, *19*, 784-786

[8] Labbe, A.C., Patel, S., Crandall, I. and Kain, K.C. **2003** Molecular Surveillance System for Global Patterns of Drug Resistance in Imported Malaria. *Emerging Infectious Diseases Journal*, *9*, 33-36.

[9] Esteva, L. and Vargas, C. **1998** Analysis of a Dengue Disease Transmission Model. *Mathematical Biosciences*, *150*, 131-151.