Faculdade de Saúde Pública

VOLUME 34
NÚMERO 3
JUNHO 2000
p. 214-22

Revista de Saúde Pública

Journal of Public Health

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YANG Hyun M [a] and Marcelo U Ferreira[b] *Assessing the effects of global warming and local social and economic conditions on the malaria transmission* Rev. Saúde Pública, 34 (3): 214-22, 2000 www.fsp.usp.br/rsp

Rev Saúde Pública 2000;34(3):214-22
www.fsp.usp.br/rsp

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Keywords
Malaria, transmission#. *Anopheles,* parasitology#. Plasmodium, physiology#. Temperature#. Socio-economic factors#. Epidemiology models. Insect vectors. Host parasite relations.

Abstract

Objective
To show how a mathematical model can be used to describe and to understand the malaria transmission.
Methods
The effects on malaria transmission due to the impact of the global temperature changes and prevailing social and economic conditions in a community were assessed based on a previously presented compartmental model, which describes the overall transmission of malaria.
Results/Conclusions
The assessments were made from the scenarios produced by the model both in steady state and dynamic analyses. Depending on the risk level of malaria, the effects on malaria transmission can be predicted by the temperature ambient or local social and-economic conditions.

Descritores
Malária, transmissão#. Anopheles, *parasitologia#. Plasmodium, fisiologia#. Temperatura ambiente#. Fatores socioeconômicos#. Modelos epidemiológicos. Insetos vetores. Relações hospedeiro-parasita.*

Resumo

Objetivo
Apresenta-se um modelo matemático mostrando como esse instrumento pode ser importante para descrever a transmissão de malária.
Métodos
Baseado no modelo proposto previamente, foram quantificados os efeitos de dois fatores que podem afetar a transmissão da malaria: a temperatura ambiente e as condições socioeconômicas locais.
Resultados/Conclusões
A quantificação foi feita estudando o modelo proposto no estado estacionário e na sua dinâmica. Dependendo do nível de risco de malária, os principais efeitos na transmissão de malária são devidos à temperatura ambiente ou às condições socioeconômicas.

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The publication of this article was subsidied by Fapesp (Process nº 00/01601-8).
Submitted on 8/2/1999. Reviewed on 3/1/2000. Approved on 2/2/2000.

INTRODUCTION

Based on the mathematical model developed by Yang[16] to describe quantitatively the overall picture of malaria transmission, the possible effects of global warming and local social and economic conditions on the epidemiology of malaria were assessed.

There has recently been a growing interest on the effects of global warming on the epidemiology of malaria and other vector-borne diseases.[11,13] Due to the "greenhouse effect", the global annual average temperature at the surface of the Earth is expected to increase between 1.0 to 3.5°C by the year 2100. The impact of global warming is currently considered by the World Health Organization as one of the greatest public health challenges for the next century.[11] Higher ambient temperatures within the range of 20-31°C affect malaria transmission in several ways: (a) development of *Anopheles* is shortened; (b) biting capacity of female mosquitoes is increased since their gonadotrophic cycle (interval between bloodmeals) is shortened; and (c) the extrinsic incubation period of *Plasmodium* decreases logarithmically. As a result, small increases in temperature can result in large increases in the vectorial capacity of mosquitoes, defined as the daily potential number of inoculations originated in an infectious person.[8]

Therefore the effect of global warming on malaria transmission, for instance, has been examined in terms of increased vectorial capacity.[7,8] However, the impact of temperature changes may be disproportionately higher in populations with low levels of antimalarial immunity, such as children and adults coming from malaria-free regions.[9]

Another aspect of malaria risk is related to local conditions. The change in malaria transmission can be associated with social and economic conditions (e.g., prevailing health care services and sanitation improvements). In most endemic areas of malaria the effect of a temperature increase on the disease transmission seems limited, however changes in social and economic conditions are far more important than a temperature shift.[7]

The epidemiological impact of temperature changes and social and economic conditions on malaria incidence in communities with different levels of acquired immunity was analyzed. To do this, in the section 2 some results are transported from the model presented by Yang.[16] The mathematical formulas are numerically treated to furnish some epidemiological scenarios in the section 3 and in the section 4 these results are commented.

METHODS

The system of dynamic equations and the steady state equilibrium points are transported from Yang,[16] and the range over which the model's parameters can vary are discussed.

For humans, the seven compartments are: susceptible (x_1), incubating (x_2), infectious (x_3), immune (x_4), partially immune (x_5), non-immune but with immunological memory (x_6), and incubating after reinfection (x_7). The fractions of the host population are described by the following system of differential equations

$$\begin{cases} \dot{x}_1(t) = \mu + (\theta+\alpha)x_2(t) + \pi_3 x_6(t) - [hy_3(t)+\mu]x_1(t) \\ \dot{x}_2(t) = hy_3(t)x_1(t) - (\theta+\gamma_1+\mu+\alpha)x_2(t) \\ \dot{x}_3(t) = \gamma_1 x_2(t) - (\gamma+\mu)x_3(t) \\ \dot{x}_4(t) = \gamma x_3(t) + hy_3(t)x_5(t) + \gamma_1 x_7(t) - (\pi_1+\mu)x_4(t) \\ \dot{x}_5(t) = \pi_1 x_4(t) - [hy_3(t)+\pi_2+\mu]x_5(t) \\ \dot{x}_6(t) = \pi_2 x_5(t) + \theta x_7(t) - [hy_3(t)+\pi_3+\mu]x_6(t) \\ \dot{x}_7(t) = hy_3(t)x_6(t) - (\theta+\gamma_1+\mu)x_7(t) \end{cases} \quad (1)$$

where μ and α are, respectively, the natural and differential mortality rates of human host, θ is the natural resistance rate against malaria, γ_1^{-1} and γ^{-1} are the average periods, respectively, to initiate the production of gametocytes and to build up an effective immune response, π_1, π_2 and π_3 are, respectively, rates at which protective immunity, partial immunity and immunological memory are lost, and h is the inoculation rate. The quantity $y_3(t)$ is the proportion of infectious mosquitoes.

The mosquitoes population is divided into three compartments Y_1, Y_2 and Y_3, which are, respectively, the number of susceptible, incubating (infected but non-infectious), and infectious mosquitoes. The mosquito population is described by the following system of equations

$$\begin{cases} \dot{Y}_1(t) = \phi\dfrac{\sigma_1(T)}{\sigma_1(T)+\mu_e(T)}[Y_1(t)+Y_2(t)+Y_3(t)] - [fx_3(t)+\mu'+\alpha']Y_1(t) \\ \dot{Y}_2(t) = fx_3(t)Y_1(t) - [\sigma_2(T)+\mu'+\alpha']Y_2(t) \\ \dot{Y}_3(t) = \sigma_2(T)Y_2(t) - (\mu'+\alpha')Y_3(t) \end{cases} \quad (2)$$

where μ' and α' are, respectively, the natural and induced mortality rates of mosquitoes, ϕ and $\mu_e(T)$ are, respectively, the rates of oviposition and of eggs becoming non-viable, $\sigma_1^{-1}(T)$ and $\sigma_2^{-1}(T)$ are, respectively, the duration of the cycle from egg to mature adult and the duration of sporogony in the mosquito, and f is the transmission rate. Even though the rate of oviposition may depend on temperature,[8] that is designated by symbol T, is restricted and dependent only on the parameters σ_1, σ_2 and μ_e.

The equation systems (1) and (2) have two equilibrium points. The first one is the disease-free community,which is given by

$$\begin{cases} y_1 = 1 \\ y_i = 0\,; \quad \text{for } i = 2 \text{ and } 3 \end{cases} \tag{3}$$

for vector population, and for host population.

$$\begin{cases} x_1 = 1 \\ x_i = 0\,; \quad \text{for } i = 2, 3, \ldots, \text{ and } 7, \end{cases} \tag{4}$$

The second one is malaria at endemic levels, given by

$$\begin{cases} y_1(x_3) = \dfrac{\mu'+\alpha'}{fx_3+\mu'+\alpha'} \\ y_2(x_3) = \dfrac{fx_3(\mu'+\alpha')}{[\sigma_2(T)+\mu'+\alpha'](fx_3+\mu'+\alpha')} \\ y_3(x_3) = \dfrac{x_3}{c_1x_3+c_2}, \end{cases} \tag{5}$$

for the vector population and for the host population,

$$\begin{aligned} x_1(x_3) &= b_2x_3+b_3 \\ x_2(x_3) &= b_1x_3 \\ x_4(x_3) &= \frac{[hx_3+(\pi_2+\mu)(c_1x_3+c_2)] \times}{\pi_1\pi_2(\theta+\gamma_1+\mu)(c_1x_3+c_2)^2} \\ &\quad \frac{\times [h(\gamma_1+\mu)x_3+(\theta+\gamma_1+\mu)(\pi_3+\mu)(c_1x_3+c_2)]}{\pi_1\pi_2(\theta+\gamma_1+\mu)(c_1x_3+c_2)^2}(b_4x_3+b_5) \\ x_5(x_3) &= \frac{h(\gamma_1+\mu)x_3+(\theta+\gamma_1+\mu)(\pi_3+\mu)(c_1x_3+c_2)}{\pi_2(\theta+\gamma_1+\mu)(c_1x_3+c_2)}(b_4x_3+b_5) \\ x_6(x_3) &= b_4x_3+b_5 \\ x_7(x_3) &= \frac{h(b_4x_3+b_5)x_3}{(\theta+\gamma_1+m)(c_1x_3+c_2)}, \end{aligned} \tag{6}$$

plus a third degree polynomial to determine x_3, given by

$$A(x_3)^3 + B(x_3)^2 + Cx_3 + D = 0 \tag{7}$$

The auxiliary variables b_1, b_2, b_3, b_4, b_5, c_1 and c_2, and the coefficients of the polynomial A, B, C and D can be found in Yang.[16]

Finally, the *basic reproduction ratio* R_0 is given by

$$R_0 = \frac{\gamma_1}{\theta+\gamma_1+\mu+\alpha} \times \frac{f}{\gamma+\mu} \times \frac{\sigma_2(T)}{\sigma_2(T)+\mu'+\alpha'} \times \frac{h}{\mu'+\alpha'}, \tag{8}$$

which is a product of four terms.[16]

The model can be analyzed with steady state equilibrium values[3] and dynamic state.[15] The steady state analysis is performed by calculating the equations (5), (6) and (7), which are the equilibrium points, considering a chosen set of values for the parameters. The time-dependent solution of the equation systems (1) and (2), from the initial values until the system reaches a new equilibrium point, enables the dynamics analysis. Both dynamic and steady state analyses depend heavily on the R_0 value given by the equation (8).

To obtain useful epidemiological information, the actual values for the model's parameters must be known. Since their values can vary a lot, Table 1 shows the range and the mean value that the model's parameters can assume.

Table 1 - The values found in the literature for the parameters of the model. The symbols d and y stand, for days and years, respectively.

Parameter	Range	Mean
θ^{-1} (d)	1 – 4 [6]	2.5
γ_1^{-1} (d)	15 – 19 [5]	17
γ^{-1} (d)	50 – 150 [14]	100
π_1^{-1} (d)	40 – 60 [14]	50
π_2^{-1} (y)	0.2 – 5 [4]	2.6
π_3^{-1} (y)	1 – 20 [4]	10.5
μ^{-1} (y)	50 – 55 [4]	52.5
α^{-1} (y)	2,450 – 2,964	2,707
ϕ (eggs/d)	25 – 65 [5]	45
μ'^{-1} (d)	10 – 14 [5]	12
α'^{-1} (d)	98 – 191.8	144.9
$\sigma_1^{-1}(T)$ (d)	10 (31 °C) – 26 (20 °C) [8,10]	18
$\sigma_2^{-1}(T)$ (d)	8 (31 °C) – 22 (20 °C) [8,10]	15
$\mu_e^{-1}(T)$ (d)	0.020 (31 °C) – 0.052 (20 °C)	0.036

Note: The index numbers in the second column (range) refer to the bibliographic references listed in the end of the article.

As can be noted, the table above was obtained from the literature for the parameters θ, γ_1, γ, π_1, π_2, π_3, μ, ϕ, μ', $\sigma_1(T)$ and $\sigma_2(T)$. Regarding the differential (α) and induced (α') mortality rates, it was assumed a decrease of about 2% and 6% respectively in the expected life span. Finally, $\mu_e(T)$ was calculated applying the equation

$$\mu_e(T) = \sigma_1(T)\left(\frac{\phi}{\mu'+\alpha'} - 1\right),$$

which is the equation (4) given in Yang.[16]

The focus will be on the effects on malaria transmission due to temperature changes and social and economic conditions prevailing in a community. For this reason, the temperature is considered as independent parameters θ, γ_1, γ, π_1, π_2, π_3 and ϕ as being related, roughly and indirectly, to the general social and economic conditions; and the temperature is of course considered as dependent parameters $\mu_e(T)$, $\sigma_1(T)$ and $\sigma_2(T)$ as being related to temperature changes. Also, three representative risk areas of malaria are considered by assigning particular values for the inoculation h and transmission f rates.

With regard to the temperature independent parameters, it is being assumed that they are related to social and economic conditions prevailing in the community. For instance, they can be used as an indicator of the health care system effectiveness in identifying promptly new malaria cases, their sanitation condition and economic activity, which can be responsible for deforestation. It is possible to characterize, with due caution, the lower bounded values of Table 1 as representative of good social and economic conditions. Here is the rationale. Note that the values in Table 1 are given in terms of the periods of time (the inverse of the respective rates) which decrease as the rates increase. Observe that the lower bounded values of the parameters reveal a quick acquisition of immunity (represented by a large value of γ) and also a rapid natural recovery period (represented by a large value of θ). Both features can be associated to the effectiveness of the health care system in identifying and treating malaria infected individuals (represented by an additional increase in θ), and providing the individuals some kind of protection (vaccine when available). As explained in Yang,[16] the quick immunity response and drug treatment can lead to the early differentiation of the merozoites to sexual gametocytes (represented by a large value of γ_1). Nevertheless, the quick immunity response can induce protection for a limited amount of antigens, which results in quick loss rates of acquired (fully and partially protective) immunity (represented by a large value of π_1 and π_2) and immunological memory (represented by a large value of π_3). Finally, the surrounding environment can be adverse to the vector proliferation (represented by a low value of ϕ). Hence, the lower bound values of Table 1 can be associated with a community with good social and economic conditions. Conversely, the upper bound values can be related to a community with deteriorating social and economic conditions. Based on what was discussed, the indices 1, 2 and 3 are introduced to describe a community with good, intermediate, and deteriorating social and economic conditions.

In regard to the temperature dependent parameters, the values presented in Table 1 are related to lower temperature (20°*C*), intermediate temperature (between 20-31°*C* but close to 21.5°*C* because the shape of the curve of parameters as a function of the temperature follows a hyperbolic curve), and higher temperature (31°*C*). To these parameters, the indices 1, 2 and 3 to are introduced to describe areas of low, intermediate, and high temperature. Note that when temperature increases from 20°*C* to about 21.5°*C*, the values of temperature dependent parameters increase from the lower bound to the mean ones.[10] When the remaining 9.5°*C* in the temperature increases, the parameters are allowed to grow from the mean values to the upper bounded values.

Both social and economic conditions and temperature were subdivided in 3 classes. For that, there are 9 possible combinations of the model's parameters values given in Table 1. They are denoted them as P_{ij}, which appears hereafter and throughout the text, for each possible case, with i=1, 2 and 3 and j=1, 2 and 3. The first subscript i stands for the social and economic conditions, and the second subscript j for the temperature. Because of that, for temperature independent parameters it was assigned 1 for lower bound values, 2 for the mean values and 3 for upper bound values on the range of parameters. For temperature dependent parameters it was assigned 1 for the values corresponding to upper bound (20°*C*), 2 to the mean values (21.5°*C*), and 3 to those corresponding to the lower bound (31°*C*) on the range of parameters.

Finally, the inoculation rate h and the transmission rate f, both being dependent on the average number of mosquito bites in humans, measure the level of interaction between these populations. Three levels of human exposure to the mosquito are analyzed, to reproduce low, intermediate and high contact of human hosts with mosquito populations. Note that both h and f can be dependent on temperature (vectorial capacity), social and economic conditions (bed-net and deforestation), and other climate changes (*El Niño* phenomenon).

In the next section, based on the above results and the values of the model's parameters, the effects of global warming and social and economic conditions on malaria epidemiology are assessed.

RESULTS

The effects of different levels of acquired immunity among human hosts and the influence of temperature on the parameters related to vectors on malaria transmission are assessed. For that, the 9 possible combinations of the values shown in Table 1 were taken into account.

First is the steady state analysis. Tables 2 to 4 show the values of the equilibrium point and the *basic reproduction ratio* for 3 sets of values for h and f.

Table 2 analyzes the situation where a community is in a low risk area of malaria, where h=0.07 and f=0.13 (both in $days^{1}$).

A broad range of *basic reproduction ratios* (0.075-1.91) is seen, but they remain at lower values. Lower

Table 2 - The equilibrium values (in percentage) of human and mosquito populations and the *basic reproduction ratio* R_0 for h=0.07 and f=0.13 (both in *days*$^{-1}$). The notation P_{ij} (see the text), where (i,j) = 1, 2 and 3, are related to the chosen values for the parameters.

	P_{11}	P_{12}	P_{13}	P_{21}	P_{22}	P_{23}	P_{31}	P_{32}	P_{33}
x_1	100	100	100	100	100	100	87.8	70.6	53.3
x_2	0	0	0	0	0	0	0.03	0.08	0.12
x_3	0	0	0	0	0	0	0.27	0.61	0.93
x_4	0	0	0	0	0	0	0.14	0.49	1.21
x_5	0	0	0	0	0	0	3.24	8.70	15.8
x_6	0	0	0	0	0	0	8.56	19.4	28.6
x_7	0	0	0	0	0	0	0.01	0.02	0.06
y_1	100	100	100	100	100	100	99.6	99.0	98.5
y_2	0	0	0	0	0	0	0.28	0.55	0.59
y_3	0	0	0	0	0	0	0.17	0.48	0.96
R_0	0.075	0.097	0.14	0.43	0.55	0.75	1.14	1.43	1.91

values of R_0 mean that small efforts can lead to the eradication of the disease. The 6 cases P_{11} to P_{23} show that the disease cannot develop itself in this community ($R_0 \leq 1$). However, if cases P_{31}, P_{32} and P_{33} (referred as $P_{3.}$, the deteriorating social and economic conditions regardless the temperatures) are considered, it is possible to note that the disease can develop itself at a low endemic level in the community.

Consider the deterioration of the social and economic conditions in a community. There is a transition from disease-free ($P_{2.}$) to malaria at endemic levels ($P_{3.}$), due to deteriorating social and economic conditions. Note that a community who lives in higher temperatures suffers more the effects of deterioration of social and economic conditions, a case where the disease can develop itself at a prevalence rate of 53.3%. The deteriorating conditions favor about 46.7% of the susceptible individuals to have their first exposure to the parasite (the region was previously malaria-free), which can result in an increased number of severe malaria disease.

Consider the effect of the increasing temperatures in a low malaria transmission area. This effect can only be seen in the case that reproduces deteriorating ($P_{3.}$) social and economic conditions. The increasing temperatures are responsible for a low variation on the *basic reproduction ratio*, from 1.14 to 1.91. However, the proportion of susceptible individuals (x_1) is reduced from 87.8 % to 53.3 %. The increasing temperatures favor about 34.5 % of the susceptible individuals to have their first exposure with the parasite. Observe that half of this variation occurs when the temperature increases 1.5°*C*. The decreasing in the number of susceptible individuals is transferred to individuals who are partially immune (x_5) and non-immune but with immunological memory (x_6). But the number of incubating individuals after reinfection (x_7) is almost negligible. The proportion of infectious mosquitoes is situated below 1%.

When there is a transition from malaria-free to endemic levels, there is a more pronounced effect on malaria transmission due to the changes in the social and economic parameters at higher temperatures. Therefore, in a low malaria transmission area, the presence deteriorating social and economic conditions is much more hazardous than the temperature changes.

Table 3 analyzes a community at an intermediate risk of malaria, where h=0.25 and f=0.17 (both in *days*$^{-1}$).

A broad range of the *basic reproduction ratio* is seen, with its intermediate values varying from 0.35 to 8.90. Cases P_{11}, P_{12} and P_{13} (good social and economic conditions) represent a malaria disease-free community, but in other 6 cases P_{21} to P_{33} malaria is at endemic levels.

Table 3 - The equilibrium values (in percentage) of human and mosquito populations, and the *basic reproduction ratio* R_0, for h=0.25 and f=0.17 (both in *days*$^{-1}$). The notation P_{ij} is accordingly to Table 2.

	P_{11}	P_{12}	P_{13}	P_{21}	P_{22}	P_{23}	P_{31}	P_{32}	P_{33}
x_1	100	100	100	50.7	40.1	29.4	19.2	15.4	11.5
x_2	0	0	0	0.18	0.21	0.22	0.16	0.16	0.16
x_3	0	0	0	1.05	1.21	1.31	1.28	1.26	1.22
x_4	0	0	0	2.08	3.51	6.04	7.29	9.52	12.9
x_5	0	0	0	15.2	20.2	26.3	38.5	42.1	45.9
x_6	0	0	0	30.7	34.6	36.4	33.3	31.2	27.9
x_7	0	0	0	0.11	0.18	0.28	0.28	0.33	0.38
y_1	100	100	100	98.1	97.8	97.6	97.2	97.3	97.4
y_2	0	0	0	1.29	1.28	1.01	1.73	1.46	1.00
y_3	0	0	0	0.65	0.95	1.40	1.03	1.27	1.64
R_0	0.35	0.45	0.64	2.01	2.56	3.49	5.35	6.68	8.90

Consider the deterioration of the social and economic conditions. There is a transition from disease-free ($P_{1.}$) to malaria at endemic levels ($P_{2.}$), and the transition from these levels to higher ones ($P_{3.}$). Note that a community living in higher temperatures suffers more with the worsening of social and economic conditions, where the disease can develop itself at a prevalence rate of 53.3%. The deteriorating social and economic conditions favor about 70.6% of the susceptible individuals to have their first exposure to the parasite (the region was previously malaria-free). In another situation, when the disease was previously established, the community living at lower temperature suffers more the effects of the worsening of social and economic conditions, resulting in 31.5% of the susceptible individuals to have their first exposure to the parasite.

Consider the effect of the increasing temperatures in an intermediate malaria transmission area. This effect can be seen in cases that reproduce intermediate ($P_{2.}$) and deteriorating ($P_{3.}$) social and economic conditions. The increase in temperatures leads to a low variation on the *basic reproduction ratio*, from 2.01 to 8.90. There is a greater change from case P_{21} to case P_{23}, which decreases the susceptible individuals in 21.3%, which is a greater proportion than from case P_{31} to case P_{33}. Also, half of this variation occurs when the temperature increases 1.5°*C*. At this temperature change, the increasing rate for individuals who are partially immune (x_5) is greater than for individuals who are non-immune but have immunological memory (x_6). The proportion of immune individuals (x_4) also increases, but the proportion of infectious individuals (x_3) remains at a low value. The number of incubating individuals after reinfection (x_7) is still small, but about 10-*time*s greater in relation with the previous situation. The proportion of infectious mosquitoes is situated around 1%. The *basic reproduction ratio* showed a broader variation than that of the previous situation.

Again, when there is a transition from malaria-free to endemic levels, malaria transmission is more dangerous if a community lives in deteriorating social and economic conditions at higher temperatures. However, when the disease is already established in the area, the worsening of social and economic conditions in a community who lives at lower temperatures has a great effect on malaria transmission.

Table 4 analyzes the situation where a community is under high-risk of malaria, where *h*=0.90 and *f*=0.25 (both in $days^{-1}$).

The *basic reproduction ratio* varies a lot, from 1.86 to 47.1. The higher values of R_0 mean that only greater efforts can lead to the disease eradication (in general, only disease control). All 9 cases show the disease at endemic levels. In this situation, excluding cases P_{11}, P_{12} and P_{13}, the proportion of infectious individuals remains at low values. Changing from case P_{11} to case P_{33}, the proportion of immune and partially immune individuals increases dramatically. The proportion of infectious mosquitoes is situated around 2%, but in for case P_{13} it is 4.41%. Also, in this case, there is the highest proportion of incubating individuals after reinfection.

Consider the deteriorating social and economic conditions in a community. There is a transition from disease at low endemic levels ($P_{1.}$) to intermediate prevalence ($P_{2.}$), and a transition from these to higher endemic levels ($P_{3.}$). If social and economic conditions are deteriorating from good to intermediate, then there is an increase in new cases of malaria (48.11%) at lower temperatures (P_{11} to P_{21}). This finding is in opposition to what was found in previous cases, especially when the disease was not established. In this situation (high risk), the effects of worsening social and economic conditions at lower temperatures contribute more to malaria transmission.

Consider the effect on malaria transmission due to increasing temperatures in a high-risk malaria area. This effect can be seen in all situations that reproduce good ($P_{1.}$), intermediate ($P_{2.}$) and deteriorating ($P_{3.}$) social and economic conditions. When the temperature increases, about 25.6% of the susceptible individuals will have their first exposure to the parasite. Half of this variation occurs when the temperature increases 1.5°*C*. In this situation, the variation in malaria prevalence is much

Table 4 - The equilibrium values (in percentage) of human and mosquito populations, and the *basic reproduction ratio* R_0, for h=0.90 and f=0.25 (both in $days^{-1}$). The notation P_{ij} is accordingly to Table 2.

	P_{11}	P_{12}	P_{13}	P_{21}	P_{22}	P_{23}	P_{31}	P_{32}	P_{33}
x_1	57.8	45.3	32.2	9.69	7.63	5.57	3.65	2.91	2.18
x_2	0.97	1.13	1.20	0.20	0.19	0.17	0.13	0.12	0.11
x_3	3.23	3.77	3.99	1.18	1.11	1.01	0.99	0.94	0.89
x_4	8.28	14.0	22.9	21.2	25.5	31.5	32.4	37.2	43.7
x_5	6.53	8.65	10.7	39.8	40.8	41.0	49.0	47.4	44.4
x_6	22.8	26.5	27.9	27.3	24.2	20.2	13.4	11.0	8.28
x_7	0.38	0.66	1.04	0.57	0.60	0.63	0.46	0.45	0.43
y_1	93.2	92.1	91.7	96.8	97.0	97.3	96.9	97.0	97.2
y_2	4.84	4.91	3.89	2.10	1.71	1.14	1.96	1.60	1.08
y_3	2.00	2.97	4.41	1.06	1.26	1.58	1.16	1.39	1.76
R_0	1.86	2.40	3.38	10.7	13.5	18.5	28.3	35.4	47.1

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more pronounced at lower temperatures when a community lives in good social and economic conditions.

Regarding to the range of allowed values to *h* and *f*, only the variation of the parameter *f* was constrained to obtain the proportion of infectious mosquitoes (which is equivalent to sporozoite rate measured in field surveys), varying from 0.17% to 4.41%. On the range of variation of both parameters, the above three tables show a strong effect of the temperature and the level of immunity on malaria transmission.

The effect of variation of the parameters *h* and *f* on malaria transmission is now analyzed. Both parameters can be influenced by many factors. The transition from low to intermediate risk community reveals that the transition from case P_{23}^{L} (Table 2) to case P_{23}^{I} (Table 3) shows the highest variation in malaria prevalence (70.6%), while for the intermediate to high risk communities, the transition from case P_{13}^{I} (Table 3) to case P_{13}^{H} (Table 4) shows the highest variation in malaria prevalence (67.8%). The superscripts *L*, *I* and *H* stand, respectively, for low, intermediate, and high risk of malaria. It was observed, however, that at higher temperatures the effects of malaria transmission is seen mostly among individuals living in more favorable social and economic conditions. A trend of the same magnitude is seen in the variation of malaria prevalence in all ranges of temperature variation, except for the change from intermediate to high risk transmission in a community with extremely deteriorating social and economic conditions (a minor effect is seen in the transmission P_{33}^{I} [Table 3] to case P_{33}^{H} [Table 4] with a 9.32% variation).

Second, the numerical simulations of the systems of equations (1) and (2) are considered. The purpose of the dynamic simulation is to show how the disease reaches the steady state. The ordinary differential equations are solved by the 4th order Runge-Kutta method.[12]

Only three situations were analyzed regarding the temperature and the focus was on three regions: disease-free community, but potentially under risk (Southeast Brazil); disease at low endemic levels (Amazon region and Southeast Asia); and disease at high endemic levels (Africa). To the first region can be assigned lower bound values for parameters which do not depend on the temperature, and for those which depend on the temperature, the upper bound values (20°*C*). To the second region, mean values were assigned to parameters that are dependent and not dependent on the temperature. Finally, the last area is characterized by upper bound values for parameters which do not dependent on the temperature, and lower bound values (31°*C*) for those which depend on the temperature.

Figure 1 shows a disease-free region (Southeast Brazil), and the case corresponding to P_{11} of Table 2 was chosen, with R_0=0.075. This case takes into account the temperature of 20°*C*, and values corresponding to lower bound for temperature independent and upper bound for temperature dependent parameters. This is a community with relatively good social and economic conditions, situated in an area relatively protected against malaria transmission and at lower temperatures. The assumed initial values are (in percentage): x_1=10, x_2=20, x_3=20, x_4=15, x_5=15, x_6=10, x_7=10, y_1=60, y_2=20 and y_3=20.

Observe that the disease is eradicated in the first years after the outbreak of an epidemic, despite the initial high prevalence of malaria.

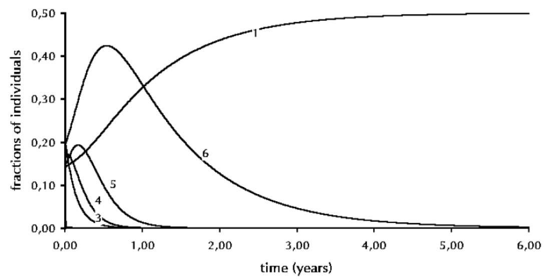

Figure 1 - The time-dependent classes of individuals corresponding to P_{11} of Table 2 are showed (the curves corresponding to their classes are labeled by their respective numbers). The relatively low valued fractions x_2 and x_7 do not appear, and the actual fraction x_1 is obtained by multiplying the vertical axis by a factor 2.

In the next two simulations, the following initial conditions (in percentage) were considered: x_1=99.8, x_2=0.1, x_3=0.1, x_4= x_5= x_6= x_7=0, y_1=100 and y_2= y_3=0. The purpose is to analyze the development of the disease at endemic levels when a small number of malaria cases is introduced into a disease-free community.

Figure 2 presents the disease at a low endemic level region (Amazon region and Southeast Asia) and case P_{22} of Table 3 was considered, with R_0=2.56. This case takes into account temperatures between 20-31°*C* (near 21.5°*C*), and mean values for the parameters. It is a community with intermediate social and economic conditions, situated in an area of low malaria transmission and at intermediate temperatures.

There is a strong fluctuation in all dynamic variables. The first epidemic outbreak has a duration of 3 *years* (see x_3), and the second outbreak has its peak delayed in about 6 *years*.

Figure 3 shows the disease at high endemic level region (Africa), which corresponds to P_{33} of Table 4, with R_0=47.1. This case takes into account a tempera-

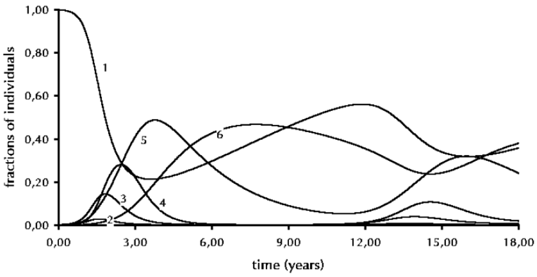

Figure 2 - The time-dependent classes of individuals corresponding to P_{22} of Table 3 are showed. The relatively low valued fraction x_7 does not appear.

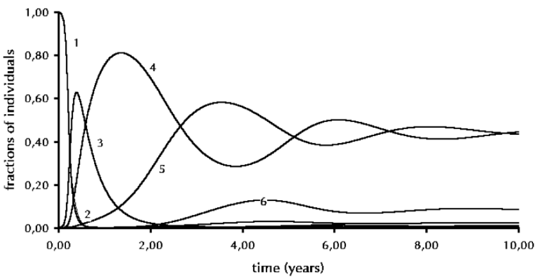

Figure 3 - The time-dependent classes of individuals corresponding to P_{33} of Table 4 are showed. The relatively low valued fraction x_7 does not appear.

ture of 31°*C*, and values corresponding to upper bound for temperature independent and lower bound for temperature dependent parameters. It is a community with relatively deteriorating social and economic conditions, situated in an area of relatively great risk of malaria transmission and at higher temperatures.

The first epidemic peak is much more accentuated, and subsequent peaks decrease more rapidly than in the previous case.

When the malaria region is at endemic levels, if the parameters are changed to drive the *basic reproduction ratio* to below unity, then the disease can be eradicated from the community during the first two years of a controlling effort, seen in Figure 1. However, Figures 2 and 3 show that, if the controlling effort is not carried out consistently, then there will be new cases of malaria, and there will be damped oscillations until a new endemic level is reached.

Finally, Table 5 shows the eigen-values corresponding to the equilibrium points considered in the dynamic simulation.

As cited in Yang,[16] the equilibrium point is stable if all eigen-values have negative real part. The first case (P_{11}) shows an exponential decay until it reaches the disease free situation, because all eigen-values are real and negative, except for one which is zero, accordingly to Yang.[16] The other two cases (P_{22} and P_{33}) show damped oscillations until they reach the malaria at endemic levels. Both cases present complex eigen-values.

DISCUSSION

The temperature in malaria transmission plays an important role. For instance, the increase in the temperature around 1.5°*C* leads the malaria-free environment to low endemicity, or the occurrence of malaria disease from low to high endemicity. Therefore, as reported before in the literature, the effects of global warming on malaria transmission is a major challenge in the next years.[8] The situation where social and economic conditions associated parameters varied was also analyzed. The effects of variation in these parameters are much stronger than the effects of increasing ambient temperatures, as expected.[7] However, the effects of social and economic conditions on malaria transmission must be considered, because these effects were assessed indirectly by interpreting the values assigned to the temperature independent parameters.

Also, inoculation and transmission rates can have a broad range of variation in the same region. For example, when there is deforestation or irregular rainfall (*El Niño* phenomenon), the interaction between the human host and the mosquito vector can be changed. Therefore, if case P_{11} of the intermediate transmission

Table 5 - The eigen-values corresponding to the equilibrium points P_{11} (Table 2), P_{22} (Table 3) and P_{33} (Table 4). Re and Im stand for the real and imaginary parts of a complex number, respectively.

	Case P_{11}		Case P_{22}		Case P_{33}	
	Re	Im	Re	Im	Re	Im
λ_1	-0.00005	0	-0.462	0	-0.32	0
λ_2	-1.06	0	-0.460	0	-0.31	0
λ_3	-0.15	0	-0.13	-0.02	-0.19	0
λ_4	-0.12	0	-0.13	0.02	-0.09	0
λ_5	-0.018	0	-0.02	0	-0.03	0
λ_6	0	0	-0.0002	-0.002	-0.001	-0.004
λ_7	-0.025	0	-0.0002	0.002	-0.001	0.004
λ_8	-0.014	0	-0.002	-0.0001	-0.004	0
λ_9	-0.003	0	-0.002	0.0001	-0.002	0
λ_{10}	-1.07	0	-0.00005	0	-0.00005	0

(Table 3) is compared with one of the higher transmission (Table 4), there is a dangerous change, from disease-free to relatively high malaria endemic levels. Based on that, the data observed in the Amazon region can fit in this model. There was observed about 1% of infectious mosquitoes[2] and around 45% of individuals without antibodies against malaria parasite.[1] Among them, besides the susceptible individuals, there are incubating, infectious, non-immune but with immunological memory, and incubating after reinfection individuals. Therefore, this community can be explained by case P_{32} of Table 3, a community with extremely deteriorating social and economic conditions living in intermediate temperatures at an intermediate risk of malaria.

The *basic reproduction ratio* increased from case P_{11}^{L} (Table 2) to case P_{33}^{H} (Table 4). Since this parameter is associated with secondary infections among mosquito populations originated by one single infectious mosquito, hence in case P_{11}^{L} (and all others with $R_0 \leq 1$) there will be a natural eradication of malaria when malaria infection at any rate is introduced in the community. On the other hand, in case P_{33}^{H} (and all others with $R_0 > 1$), malaria disease is at endemic levels because each infectious mosquito can infect more than one susceptible mosquito. For that, controlling or eradication efforts increase with increasing R_0.

The climate, social and economics changes, and environmental changes due to rainfall or deforestation showed to influence dramatically malaria prevalence. The variation in the temperatures interferes much more with the pattern of the prevalence among individuals in a community with good social and economic conditions than that those living in extremely deteriorating social and economic conditions. Also, almost half of the decrease in susceptible individuals occurs during a temperature variation of about 1.5°C. However, the variation in the transmission parameters has a more pronounced effect in a community with good social and economic conditions living at higher temperatures.

Finally, it is more realistic that a region's social and economic conditions (deterioration or improvement) should be managed by humans rather than temperature variation. Therefore, in regions where there is a malaria risk, a good management of the surrounding environment and the existence of a good health care system can avoid the outbreak of malaria transmission in the area.

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