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Malaria dynamics with long incubation period in hosts

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ABSTRACT

Motivated by the empirical observation of the bimodal distribution of the incubation time of *P. vivax* in Korea, we analyze a mathematical model for malaria transmission dynamics that features two distinct exposed classes in the human population. The short-term incubation period is modeled by exponential distribution, while it is assumed that the long-term incubation period has fixed length. Then we formulate the model as a system of delay differential equations. We identify the basic reproduction number $\mathcal{R}_0$ and show that it is a threshold parameter for the global dynamics of the model. If $\mathcal{R}_0 \leq 1$, the disease-free equilibrium is globally attractive, while the disease uniformly persists in the human and mosquito populations when $\mathcal{R}_0 > 1$. Furthermore, for the special case of lifelong immunity, we prove that the endemic equilibrium is globally asymptotically stable.

1. Introduction

According to recent research, 104 countries or territories are at risk of malaria [1]. In addition to its health toll, malaria imposes a heavy economic burden on endemic countries [2]. One of the most common types of malaria is caused by *Plasmodium vivax*. The parasite *P. vivax* can remain dormant in liver cells in a form called *hypnozoite*, leading to an increased incubation period. *P. vivax* strains from different regions of the world have different length of incubation time [3]. Recent analyzes of the incubation period of *P. vivax* malaria in Korea have confirmed that the incubation times have a bimodal distribution, with a clear distinction of short-term and long-term incubations [4].

The basic models of Ross and Macdonald used ordinary differential equations to understand the dynamics of malaria transmission [5,6]. The incubation period was incorporated first by Sharpe and Lotka [7] as a discrete time delay. The delayed Ross–Macdonald model was later analyzed in [8,5,9]. It was concluded that prolonging the incubation periods reduces the prevalence of the disease. Other researchers expressed the incubation period by exponential distribution, letting the latent compartment decay exponentially in the absence of inflow from the infectious compartment [10,11], thus formulating the models by systems of ordinary differential equations.

Xiao and Zou [12] considered a general probability function $P(t)$ describing the latency distribution, in order to reflect the fact that the latency period varies from individual to individual. They show that when the basic reproduction number is less than one, the disease will eventually die out. When the basic reproduction number is greater than one, they consider two specific forms for $P(t)$: (i) $P(t)$ is an exponential function; (ii) $P(t)$ is a step function. In both cases, when the basic reproduction number is greater than one, they show that the disease will persist. Moreover, under additional conditions, all admissible positive solutions converge to the unique endemic equilibrium. They have generalized the conclusion of Ruan et al. [9] that longer incubation periods lead to lower prevalence of the infection, regardless of the specific form of the distributions.

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Based on empirical observation of the bimodality of the incubation times of *P. vivax* in Korea, Nah et al. [13] separated the exposed class in their model into short-term and long-term exposed classes. They describe $P(t)$ as a weighted sum of two exponential functions. However, according to the empirical investigations, no cases had incubation time between 15 and 32 weeks [4]. In this sense, it is more realistic to describe $P(t)$ as a weighted sum of an exponential function and a step function, as it provides a better approximation of the observed phenomenon.

In this paper, we analyze a *P. vivax* malaria transmission model describing $P(t)$ as a weighted sum of an exponential function and a step function, which means we model the short-term incubation periods by exponential distribution, while we assume that the long-term incubation period has fixed length. In Section 2, we construct the model and discuss its fundamental properties.

In Section 3, we define the basic reproduction number, and show that it is a threshold parameter determining the extinction or the persistence of the disease. Further, in the special case of lifelong immunity, we prove the global stability of endemic equilibrium when the basic reproduction number is greater than one.

2. Model description and basic properties

2.1. Model formulation

Let us denote by $e_H(t)$, $s_H(t)$ and $i_M(t)$ the fraction of exposed human population, the fraction of susceptible human population and the fraction of infective mosquito population at time t, respectively. We define the transmission coefficient as

$$\alpha := abm,$$

referring to Table 1 for the description of the parameters. Denote by ξ the mortality rate of human population. Then the fraction of the exposed human population at time t is given by

$$e_H(t) = \int_0^\infty \alpha s_H(t-u) i_M(t-u) P(u) e^{-\xi u} du,$$

where $P : \mathbb{R}_+ \to [0, 1]$ and $P(u)$ denotes the probability that an individual is still being in the exposed class u units of time after entering the exposed class, provided that this individual survived this period, which has probability $e^{-\xi u}$.

We separate the exposed individuals into two distinct classes. Following [14], we use the exponential distribution for the short-term incubation period (with average $1/\eta$), while we assume a fixed time τ for every individual with long-term incubation period. Let $p \in (0, 1)$ be the probability that an exposed individual experiences a short-term incubation period upon a successful contact with an infected mosquito. Then we can specify $P(u)$ as

$$P(u) = pP_s(u) + (1-p)P_l(u),$$

where

$$P_s(u) := e^{-\eta u}, \qquad P_l(u) := \begin{cases} 1, & u \in [0, \tau], \\ 0, & u \in (\tau, \infty). \end{cases}$$

Let us denote by $e_H^s(t)$ and $e_H^l(t)$ the fraction of exposed human population with short-term incubation period and with long-term incubation period at time t, respectively. It holds that

$$e_H(t) = e_H^s(t) + e_H^l(t).$$

Then we obtain

$$\begin{aligned} e_H^s(t) &= \int_0^\infty p\alpha s_H(t-u) i_M(t-u) P_s(u) e^{-\xi u} du \\ &= \int_0^\infty p\alpha s_H(t-u) i_M(t-u) e^{-(\eta+\xi)u} du, \end{aligned} \tag{1}$$

$$\begin{aligned} e_H^l(t) &= \int_0^\infty (1-p)\alpha s_H(t-u) i_M(t-u) P_l(u) e^{-\xi u} du \\ &= \int_0^\tau (1-p)\,\alpha s_H(t-u) i_M(t-u) e^{-\xi u} du. \end{aligned} \tag{2}$$

One can differentiate $e_H^s(t)$ with respect to t to get the ordinary differential equation

$$\frac{de_H^s(t)}{dt} = p\alpha s_H(t) i_M(t) - (\eta + \xi)\, e_H^s(t).$$

The fraction of human population progressing to the infectious class per unit of time at time t, after experiencing either the short- or long-term incubation period, is given by $\eta e_H^s(t) + (1-p)\alpha s_H(t-\tau) i_M(t-\tau) e^{-\xi\tau}$. We denote by $i_H(t)$ the fraction