On the estimation of infected erythrocytes in *Plasmodium falciparum* malaria patients

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Intra-host models describe the dynamics of the interaction of parasites (viruses, bacteria, protozoans, ...) within the host. These models have been used to understand the population dynamics and evolution of *Plasmodium falciparum* in the host. Most of these models are, related to the seminal Anderson, May and Gupta's model [1]:

$$\begin{cases} \dot{x} = \Lambda - \mu_x x - \beta x m, \\ \dot{y} = \beta x m - \mu_y y, \\ \dot{m} = r\mu_y y - \mu_m m - \beta x m, \end{cases} \tag{1}$$

where x is the concentration of uninfected erythrocytes in the blood, y is the concentration of infected erythrocytes, and m the concentration of free merozoites. Experimental analysis has shown that the dynamics of *Plasmodium falciparum* might change according to its "age", i.e., the stage of its life cycle. Hence, a model, where the dynamics of the healthy cells are coupled with an age-structured model for the infected cells and the dynamics of free merozoites, is needed and has been considered [2, 3]:

$$\begin{cases} \dot{x} = \Lambda - \mu_x\, x - \beta\, x m, \\ \dot{y_1} = \beta\, x m - (\gamma_1 + \mu_1)\, y_1, \\ \dot{y_2} = \gamma_1\, y_1 - (\gamma_2 + \mu_2)\, y_2, \\ \vdots \\ \dot{y_n} = \gamma_{n-1}\, y_{n-1} - (\gamma_n + \mu_n)\, y_n, \\ \dot{m} = r\, \gamma_n\, y_n - \mu_m\, m - \beta\, x m. \end{cases} \tag{2}$$

One of the characteristics of *Plasmodium falciparum* is *sequestration*: mature parasitized erythrocytes sequester in the microvasculature of various organs including the brain and only immature forms of the parasite can circulate freely and are seen on peripheral blood smears. It is known that antimalarial drugs act preferentially on different stage of parasite development [2]. In practice, to know a patient's stage of infection, the total parasite concentration $\sum_{i=1}^{n} y_i$ in the patient is needed. However, only the peripheral infected erythrocytes (young parasites $y_1 + y_2 + \dots y_k$, for some $k < n$), also called *circulating*, can be observed (seen on peripheral blood smears) and the other ones (sequestered: $y_{k+1}, \dots y_n$) are hidden and cannot be observed. There is no clinical method of measuring the sequestered infected cells directly.
All parameters in (2) can be estimated by biological considerations, *except* the parameter β which is the Red Blood Cells (RBC)'s rate of infection. This rate of infection is generally unknown (and difficult to estimate) in epidemic models.
We give a method for the estimation of the sequestered infected erythrocytes and by the way the total parasite burden of the patient using the the measures of the peripheral infected erythrocytes and without using the unknown parameter β. We apply this estimation method using real data that have been collected when malaria was used as therapy for neurosyphilis by the US Public Health Service.

Références

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