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Global dynamics of a staged-progression model for HIV/AIDS with amelioration

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ABSTRACT

We consider a mathematical model for HIV/AIDS that incorporates staged progression and amelioration. Amelioration as a result of HAART treatment is allowed to occur across any number of stages. The global dynamics are completely determined by the basic reproduction number R_0. If $R_0 \leq 1$, then the disease-free equilibrium (DFE) is globally asymptotically stable and the disease always dies out. If $R_0 > 1$, DFE is unstable and a unique endemic equilibrium (EE) is globally asymptotically stable, and the disease persists at the endemic equilibrium. The proof of global stability utilizes a global Lyapunov function.

1. Introduction

For infectious diseases progressing through a long infectious period, infectivity or infectiousness can vary greatly over time. The progression of a typical HIV infection can take eight to ten years before the clinical syndrome (AIDS) occurs, and the progression goes through several distinct stages, marked by drastically different $CD4^+$ T-cell counts and viral RNA levels. HIV-infected individuals are highly infectious in the first few weeks after infection, then remain in an asymptotic stage of low infectiousness for many years, and become gradually more infectious as their immune system becomes compromised, until they develop AIDS.

Since the advent of highly active antiretroviral therapy (HARRT) in 1996, there has been remarkable improvement on the survival rate of HIV-infected patients. On an individual level, the viral load of averted treatment can help patients ameliorate to higher CD4+ counts and prolong patients' lives. On the population level, treatment can prolong the infectious period of HIV-infected individuals during which they may continue transmission and may even resume risky sexual or drug activities. This can have negative effects to the control and interventions of the epidemics. To fully evaluate the overall effectiveness of the antiretroviral therapies on the disease spread of HIV/AIDS, it is important to investigate the long term impact of amelioration on the population dynamics of the HIV transmission.

Mathematical modeling is a useful tool in better understanding disease dynamics, making prediction of disease outbreak and evaluations of prevention or intervention strategies. In [1,2], models of HIV infection in vivo were studied. Global properties of disease models in cellular levels were analyzed in [3,4] and recently, small world networks was derived for HIV modeling by discrete event simulation models [5].

Variability of infectiousness over time has been modeled in the literature by Markov chain models, or staged-progression (SP) models (see e.g. [6–17]). Longini et al. [14] used six stages of HIV infection for individuals who have not developed full-blown AIDS to model the progression of HIV infection. Current HAART treatments are able to significantly lengthen patients'

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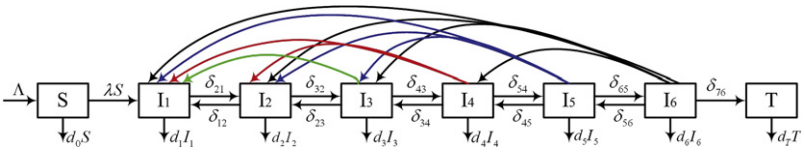

Fig. 1. The transfer diagram for model (1).

life spans. It is possible for ameliorated HIV patients to move from advanced stages back to any earlier infectious stages [8,15]. In this paper, we present a 6-stage SP model with arbitrary amelioration so that ameliorated patients can move to any of the less advanced stages. Our model is a natural generalization of those in [18,15,19], in which amelioration can only occur one stage at a time. Our goal is to establish the global dynamics of the 6-stage model with arbitrary amelioration and to investigate the effects of amelioration on the disease dynamics.

We prove that the global dynamics is completely determined by the basic reproduction number R_0. If $R_0 \leq 1$, then the DFE is globally asymptotically stable and the disease always dies out. If $R_0 > 1$, then DFE becomes unstable, and a unique EE exists in the interior of feasible region. For the case of bilinear incidence, we prove that EE is globally asymptotically stable. Our results contain earlier global-stability results in [18,15,19] when the number of stages is less than or equal to 6.

The paper is organized as follows. The 6-stage SP model is presented in Section 2 and its basic properties are given in Section 3. In Section 4, the basic reproduction number is derived using the method of next generation matrix. The global stability of EE for the bilinear incidence is proved in Section 5.

2. A 6-stage SP model with arbitrary amelioration

To formulate an SP model with disease progression and arbitrary amelioration, the total host population is partitioned into the following compartments: the susceptible (S), the infectious (I_i) whose members are in the i-th stage of the disease progression, $i = 1, \ldots, 6$, and the terminal compartment (T), where individuals are non-infectious due to inactivity. In the case of HIV infection, the terminal compartment consists of people with active AIDS and they typically either become sexually inactive or isolated from the infection process, thus their infectivity is negligible. One also assumes that there is no recovery from the disease, and thus the only exit from the compartment T is death. Let δ_{ij} $(i > j,\ i = j + 1)$ be the mean progression rate from the j-th stage to the i-th stage and δ_{ij} $(i < j)$ the rate of amelioration from the j-th stage to the i-th stage, respectively, for $i, j = 1, 2, \ldots, 6$. Here, we allow individuals in the j-th stage to be able to move to any other i-th stage as the result of HARRT treatment. Let λ_i be the transmission coefficient for the infection of a susceptible from an infectious in the class I_i, which takes into account of average number of contact and probability of infection for each contact, then the total incidence is given by $\lambda = \sum_{i=1}^{6} \lambda_i I_i S f(N)$, where $N = S + \sum_{i=1}^{6} I_i$ is the total active population. Here we assume that the density dependence of the incidence is given by a function $f(N)$ which will be specified below (see also [18]). Average death rate for susceptible compartment is d_0, d_i for the compartment I_i, which may include death due to infection, and d_T for the active disease compartment. It is assumed that the inflow to susceptible is a constant Λ. The population transfer among compartments are schematically depicted in the transfer diagram in Fig. 1. All parameters in the model are assumed to be positive. We remark that if $\lambda_i = 0$ for some i, then the compartment I_i will be regarded as a latent compartment. Thus, our model includes, as a special case, models of $SE_1 \cdots E_m I_1 \cdots I_k R$ type, for $m + k = 6$. Obviously this 6-stage model can be extended to any finite n-stage model, and $SE_1 \cdots E_m I_1 \cdots I_k R$ type models as a special case, for $m + k = n$.

Based on the preceding assumptions and the transfer diagram, the following system of ordinary differential equations is derived for the SP model with variable amelioration

$$\begin{cases} S' = \Lambda - d_0 S - \lambda S, \\ I_1' = \lambda S - (d_1 + \delta_{21}) I_1 + \delta_{12} I_2 + \delta_{13} I_3 + \delta_{14} I_4 + \delta_{15} I_5 + \delta_{16} I_6, \\ I_2' = \delta_{21} I_1 - (d_2 + \delta_{12} + \delta_{32}) I_2 + \delta_{23} I_3 + \delta_{24} I_4 + \delta_{25} I_5 + \delta_{26} I_6, \\ I_3' = \delta_{32} I_2 - (d_3 + \delta_{13} + \delta_{23} + \delta_{43}) I_3 + \delta_{34} I_4 + \delta_{35} I_5 + \delta_{36} I_6, \\ I_4' = \delta_{43} I_3 - (d_4 + \delta_{14} + \delta_{24} + \delta_{34} + \delta_{54}) I_4 + \delta_{45} I_5 + \delta_{46} I_6, \\ I_5' = \delta_{54} I_4 - (d_5 + \delta_{15} + \delta_{25} + \delta_{35} + \delta_{45} + \delta_{65}) I_5 + \delta_{56} I_6, \\ I_6' = \delta_{65} I_5 - (d_6 + \delta_{16} + \delta_{26} + \delta_{36} + \delta_{46} + \delta_{56} + \delta_{76}) I_6, \end{cases} \tag{1}$$

and $T' = \delta_{76} I_6 - d_T T$. The incidence form is λS, where the force of infection

$$\lambda = f(N) \sum_{i=1}^{6} \lambda_i I_i \tag{2}$$

is density dependent. We assume that the function $f(N)$ satisfies the following assumptions.

(H) $f(N) > 0, \quad f'(N) \leq 0, \quad$ and $\quad |N f'(N)| \leq f(N), \quad$ for $N > 0$.