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THE ANALYSIS OF AN HIV/AIDS MODEL WITH VACCINATION

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ABSTRACT. In this paper an ordinary differential equation mathematical model for the HIV/AIDS epidemic model with vaccination is presented. The dynamic of this epidemic model is analyzed, and an optional vaccine efficacy is put forward. The reproductive number, R_v, is defined, which is the number of secondary cases that one infected individual will cause through the duration of the infectious period. The disease-free equilibrium is globally asymptotically stable when $R_v < 1$ and unstable when $R_v > 1$. The existence of at least one endemic equilibrium point is proved for all $R_v > 1$. Based on the center manifold theory, the stability of the endemic equilibrium point is given. Theoretical results show that under a planned control the number of HIV infected and AIDS individuals will be eliminated.

1. Introduction. The Human Immunodeficiency Virus (HIV) is the causative agent of Acquired Inexpediency Syndrome in humans (AIDS). The transmission of HIV/AIDS is a serious problem to human health. It is largely transmitted by the homosexual, IV drug user, or through blood transfusion and mother-to-child transmission [**4**]. The main objective is to control them and prevent their transmission [**3**]. It is significant to study these infectious diseases theoretically through dynamic methods.

It is important to conduct widespread programs in which this disease is controlled in people who are infected with it. Candidate vaccines are on trial in several places to obtain definitive information about their efficacy in inducing protection against infection. It is hoped that these vaccines will reduce susceptibility to infection as well as reduce the level of infections of the vaccinated individuals who subsequently become infected. The application of vaccination programs has the likely

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effect of inducing behavioral change in those individuals subjected to it. Blower and McLean [**1**] have pointed that a mass vaccination campaign can increase the severity of the disease if the vaccine being supplied resulted in only 50 percent coverage and 60 percent efficacy. If the campaign is not accompanied by a change in behavior, Kribs-Zaleta and Velasco-Hernandez [**7**] have found that a vaccination campaign could fail to control the disease.

Mathematical models have been used to determine the ability of an imperfect vaccine to control other infectious diseases, and some of the findings have been corroborated by clinical studies (see [**2, 5, 6, 8, 9**] for general references). In this paper, HIV/AIDS infectious disease dynamic models with vaccination have been established firstly according to the properties of these infectious diseases. And, secondly, the dynamic of this epidemic model is analyzed, including the stability of an infection-free equilibrium and an endemic equilibrium. At last, an optional vaccine efficacy is put forward.

2. The HIV/AIDS model with vaccination. In this paper, we analyze the dynamics of the SIA model that is based on subdividing the whole population of an area or a country into five compartments, namely: unvaccinated susceptible individuals ($S_1(t)$), vaccinated susceptible individuals ($S_2(t)$) and the HIV-infected individuals in primary ($I_1(t)$), secondary ($I_2(t)$) and AIDS ($A(t)$) populations, so that the total population size is

$$N(t) = S_1(t) + S_2(t) + I_1(t) + I_2(t) + A(t). \tag{2.1}$$

2.1. The unvaccinated susceptible. The susceptible population is increased by recruitment of individuals (either by birth or immigration), and reduced by infected, which may be acquired via contact with infected individuals in either of the three infected classes (with effective contact rate β), by vaccination (at a rate ξ) and by natural death (at a rate μ). The parameters η_1 and η_2 account for the assumed reduced infectivity of infected individuals in the infected stage. This gives:

$$S_1' = bN - \frac{\beta(\eta_1 I_1 + \eta_2 I_2)}{N} S_1 - \xi S_1 - \mu S_1. \tag{2.2}$$

2.2. Vaccinated susceptible individuals. The population of vaccinated individuals is increased by vaccination of the susceptible.

Since the vaccine does not confer immunity to all vaccine recipients, vaccinated individuals may become infected but at a lower rate than unvaccinated. The vaccinated class is thus diminished by this infection and by natural death (at a rate μ). Here, ε accounts for the efficacy of the vaccine-induced protection against infection. It is assumed that the vaccine does not offer 100 percent protection against infection. This gives:

$$S_2' = \xi S_1 - \frac{\beta(\eta_1 I_1 + \eta_2 I_2)(1-\varepsilon)}{N} S_2 - \mu S_2. \tag{2.3}$$

2.3. HIV-infected individuals in primary. HIV-infected individuals in primary is increased by infection of unvaccinated susceptible individuals and diminished by natural death (at a rate μ) and by progression to the AIDS stage (at a rate σ_1). This gives

$$I_1' = \frac{\beta(\eta_1 I_1 + \eta_2 I_2)}{N} S_1 - \sigma_1 I_1 - \mu I_1. \tag{2.4}$$

2.4. HIV-infected individuals in secondary. HIV-infected individuals in secondary is increased by progression to the secondary infection stage, and diminished by natural death (at a rate μ) and by progression to the AIDS stage (at a rate σ_2). This gives

$$I_2' = \frac{\beta(\eta_1 I_1 + \eta_2 I_2)(1-\varepsilon)}{N} S_2 - \sigma_2 I_2 - \mu I_2. \tag{2.5}$$

2.5. Individuals in the AIDS stage. The population is generated by progression to the AIDS stage (at rates σ_1 and σ_2), and diminished by natural death (at a rate μ) and disease-induced death (at a rate δ). This gives

$$A' = \sigma_1 I_1 + \sigma_2 I_2 - \delta A - \mu A. \tag{2.6}$$

The model is governed by the following system of ordinary differential equations:

$$
\begin{cases}
S_1' = bN - \dfrac{\beta(\eta_1 I_1 + \eta_2 I_2)}{N} S_1 - \xi S_1 - \mu S_1, \\
S_2' = \xi S_1 - \dfrac{\beta(\eta_1 I_1 + \eta_2 I_2)(1-\varepsilon)}{N} S_2 - \mu S_2, \\
I_1' = \dfrac{\beta(\eta_1 I_1 + \eta_2 I_2)}{N} S_1 - \sigma_1 I_1 - \mu I_1, \\
I_2' = \dfrac{\beta(\eta_1 I_1 + \eta_2 I_2)(1-\varepsilon)}{N} S_2 - \sigma_2 I_2 - \mu I_2, \\
A' = \sigma_1 I_1 + \sigma_2 I_2 - \delta A - \mu A.
\end{cases} \tag{2.7}
$$

It is assumed that all state variables and parameters of the model are nonnegative. The rate of change of the total population, obtained by adding equations, is given by

$$
N' = bN - \mu N - \delta A. \tag{2.8}
$$

Introducing nondimensional variables $x_1 = S_1/N$, $x_2 = S_2/N$, $x_3 = I_1/N$ and $x_4 = I_2/N$, the variable A does not appear in the first four equations of (2.7). To make the problem solvable while retaining the broad features of the model, we make the assumption $\sigma_1 = \sigma_2 = 0$. This assumption eliminates the AIDS class and leads to a reduced system

$$
\begin{cases}
x_1' = b - \beta(\eta_1 x_3 + \eta_2 x_4) x_1 - \xi x_1 - b x_1, \\
x_2' = \xi x_1 - \beta(1-\varepsilon)(\eta_1 x_3 + \eta_2 x_4) x_2 - b x_2, \\
x_3' = \beta(\eta_1 x_3 + \eta_2 x_4) x_1 - b x_3, \\
x_4' = \beta(1-\varepsilon)(\eta_1 x_3 + \eta_2 x_4) x_2 - b x_4.
\end{cases} \tag{2.9}
$$

Our model is still a variable population model, and our original objective of investigating the effects of vaccinating susceptible individuals can be undertaken and is not affected by the simplifying assumption that leads to (2.9).

To simplify the calculation of steady states, we let $\gamma = 1 - \varepsilon$. A detailed analysis concerning the existence and stability of the equilibrium points will be done in the following section.

3. Existence and stability of equilibria.

3.1. Disease-free equilibrium (DFE). This model has a disease-free equilibrium, obtained by setting the righthand sides of (2.1) to zero, given by

$$E^0 : (x_1^0, x_2^0, x_3^0, x_4^0) = \left(\frac{b}{b+\xi}, \frac{\xi}{b+\xi}, 0, 0 \right).$$

Following [**11**], the linear stability of E^0 is obtained using the next generation matrix for the system (2.9) as follows. Using the notation in [**11**], the nonnegative matrix F and the singular matrix V, the new infection terms and the remaining transfer terms respectively, are given by

$$F = \begin{pmatrix} b\beta\eta_1/(b+\xi) & b\beta\eta_2/(b+\xi) \\ \xi\beta\gamma\eta_1/(b+\xi) & \xi\beta\gamma\eta_2/(b+\xi) \end{pmatrix}, \tag{3.1}$$

$$V = \begin{pmatrix} b & 0 \\ 0 & b \end{pmatrix}. \tag{3.2}$$

The vaccination reproduction number of infection, denoted by R_v, is then given by $R_v = \rho(FV^{-1})$, where ρ is the spectral radius. It follows that

$$R_v = \frac{b\beta\eta_1 + \xi\beta\gamma\eta_2}{b(b+\xi)}. \tag{3.3}$$

From the above we draw a conclusion as follows:

Theorem 3.1. *If $R_v < 1$, the disease-free equilibrium E^0 is globally asymptotically stable.*

The threshold R_v is known as the vaccinated reproduction number of infection. It measures the average number of new HIV cases generated by a single HIV infected individual during the course of his or her infection in the presence of a vaccination program. A similar threshold, known as the basic reproduction number, is obtained by setting $\xi = 0$ and $\gamma = 1$ in R_v giving

$$R_0 = \frac{\beta\eta_1}{b}. \tag{3.4}$$

The R_0 is the average number of secondary cases generated by a single infected individual in a completely susceptible population. And the reproduction number,

$$R_1 = \frac{\beta\eta_2}{b}, \tag{3.5}$$

defines the number of secondary infections due to the infective, who as susceptibles were vaccinated against the disease.

3.2. Existence of the endemic equilibrium. Using the reproduction numbers defined above, we can now examine the existence of the equilibrium. In terms of model parameters, equation (2.9) for x_3^* can be written as

$$x_3^*\{(R_v - \gamma R_0)(x_3^*)^2 - 2(R_v - R^c)x_3^* + (R_v - 1)\} = 0, \tag{3.6}$$

where R^c is given by

$$R^c = \frac{b(\gamma R_0 + 1) - \gamma(b+\xi)}{2b} = \frac{1}{2}\gamma\left(R_0 - \frac{b+\xi}{b}\right) + 1. \tag{3.7}$$

From (3.6) we see that either $x_3^* = 0$, a solution which gives the disease-free equilibrium, $x^0 = ((b/b+\xi), (\xi/b+\xi), 0, 0)$, or

$$(R_v - \gamma R_0)(x_3^*)^2 - 2(R_v - R^c)x_3^* + (R_v - 1) = 0, \tag{3.8}$$

which gives the endemic equilibrium $x^* = (x_1^*, x_2^*, x_3^*, x_4^*)$. From (3.8), we obtain

$$x_3^* = F_\pm(R_v - \gamma R_0, R_v - 1) = F_\pm(\cdot),$$

where

$$F_+(\cdot) = \frac{(R_v - R^c) + \sqrt{D}}{R_v - \gamma R_0},$$

$$F_-(\cdot) = \frac{(R_v - R^c) - \sqrt{D}}{R_v - \gamma R_0},$$

and

$$D = (R_v - R^c)^2 - (R_v - \gamma R_0)(R_v - 1).$$

It is evident that, as R_v tends to γR_0 for $R_v > 1$, the solution $x_3^* = F_+(\cdot)$ is unbounded, while the solution $x_3^* = F_-(\cdot)$ is bounded since $\lim_{R\to\gamma R_0} F_-(\cdot) = (\gamma R_0 - 1)/(\gamma R_0 - 1 + \tau)$, where $\gamma R_0 + \tau \neq 1$ and $\tau = (\gamma(b+\xi))/b$. We can see that only $x_3^* = F_-(\cdot)$ is a solution for $R_v > 1$. For $R_v < 1$, only $x_3^* = 0$ is a solution. These results can be summarized as follows:

Theorem 3.2. *Consider system* (2.9). *If* $R_v > 1$, *then for all* $\gamma R_0 > 0$, *there exists a unique endemic equilibrium point corresponding to* $x_3^* = F_-(\cdot)$ *while if* $R_v < 1$, *then the disease free equilibrium point is the only feasible solution, and the two solutions coalesce at* $R_v = 1$.

3.3. Stability of the endemic equilibrium. We use the theory of center manifolds to establish the stability of the endemic equilibrium point $x_3^* = F_-(\cdot)$. Consider system (2.9) which can be decomposed into linear and nonlinear parts as follows:

$$\dot{y} = f = Ay + G(y) \tag{3.9}$$

where $y = (y_1, y_2, y_3, y_4)^T = (x_3, x_4, x_1, x_2)^T$,

$$A = \begin{pmatrix} -b + \dfrac{b\beta\eta_1}{b+\xi} & \dfrac{b\beta\eta_2}{b+\xi} & 0 & 0 \\ \dfrac{\beta\gamma\eta_1\xi}{b+\xi} & -b + \dfrac{\beta\gamma\eta_2\xi}{b+\xi} & 0 & 0 \\ -\dfrac{b\beta\eta_1}{b+\xi} & -\dfrac{b\beta\eta_2}{b+\xi} & -(b+\xi) & 0 \\ -\dfrac{\beta\gamma\eta_1\xi}{b+\xi} & -\dfrac{\beta\gamma\eta_2\xi}{b+\xi} & \xi & -b \end{pmatrix}$$

$$G(y) = \begin{pmatrix} \beta y_3(\eta_1 y_1 + \eta_2 y_2) \\ \beta\gamma y_4(\eta_1 y_1 + \eta_2 y_2) \\ -\beta y_3(\eta_1 y_1 + \eta_2 y_2) \\ -\beta\gamma y_4(\eta_1 y_1 + \eta_2 y_2) \end{pmatrix}.$$

The disease-free equilibrium is the line $(x^0, 0)$, and the local stability of the disease-free equilibrium changes at the point $(x^0, 0)$. We use

the results of center manifold theory in [**11**] to show that there are nontrivial equilibria near the bifurcation point $(x^0, 0)$. The procedure requires the evaluation of the following constants:

(3.10)
$$a = \sum_{i,j,k=1}^{m} v_i w_j w_k \left(\frac{1}{2} \frac{\partial^2 f_i}{\partial x_j \partial x_k}(x^0, 0) + \sum_{l=m+1}^{n} \alpha_{lk} \frac{1}{2} \frac{\partial^2 f_i}{\partial x_j \partial x_l}(x^0, 0) \right),$$

and

$$b = \sum_{i,j=1}^{n} v_i w_j \frac{\partial^2 f_i}{\partial x_j \partial x_k}(x^0, 0), \tag{3.11}$$

of the normal form equation

$$\dot{u} = au^2 + b\rho u + o(3), \tag{3.12}$$

where f_i are given by (3.9), and $o(3)$ denotes terms of third order and higher in u and ρ. It is easy to show that the righthand side of (2.12) satisfies the conditions stated in [**11**]. At the disease free equilibrium, $\rho = R_v - 1 = 0$, the matrix $[\alpha_{lk}] = -Q^{-1}P$ is given by

$$-Q^{-1}P = \begin{pmatrix} -\dfrac{b\beta\eta_1}{(b+\xi)^2} & -\dfrac{b\beta\eta_2}{(b+\xi)^2} \\ \dfrac{\beta\eta_1\xi(b-\gamma(b+\xi))}{b(b+\xi)^2} & \dfrac{\beta\eta_2\xi(b-\gamma(b+\xi))}{b(b+\xi)^2} \end{pmatrix}, \tag{3.13}$$

resulting in $a < 0$ and $b > 0$. We can get the following theorem by applying the theorem which is given in [**11**].

Theorem 3.3. *If a and b are defined by* (3.10) *and* (3.11)*, then there exists a $\delta > 0$ such that*

(i) *If $a < 0$, then there are locally asymptotically stable endemic equilibria near x^0 for $0 < \rho < \xi$.*

(ii) *If $a > 0$, then there are unstable endemic equilibria near x^0 for $-\delta < \rho < 0$.*

Clearly, the solution $F_-(\cdot)$ which exists for $R_v > 1$ is locally asymptotically stable. A branch of super-threshold endemic equilibrium

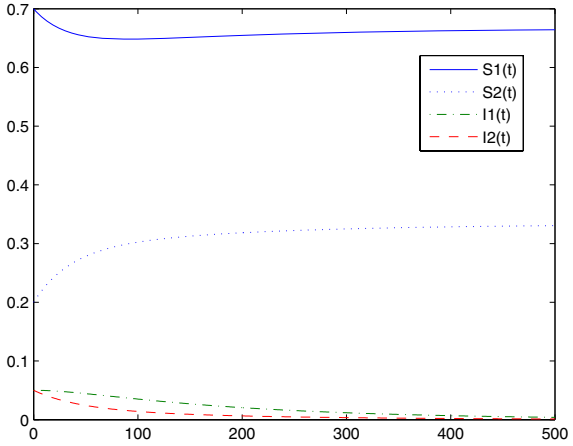

FIGURE 1. When $b = 0.02$, $\beta = 0.1$, $\eta_1 = 0.19$, $\eta_2 = 0.1$, $\xi = 0.01$; $\gamma = 0.6$, $R_v = 0.733 < 1$, $S_1(t)$ and $S_2(t)$ approach their steady state values while if $I_1(t)$ and $I_2(t)$ approach zero as time goes to infinity, the disease dies out.

points exists near the disease-free equilibrium point at $R_v = 1$; this bifurcation is said to be supercritical. It is clear from Theorem 3.3 that, provided $R_v > 1$, the disease cannot clear from the population. The simulations are as in Figures 1 and 2.

4. Optional vaccine efficacy. The long-term expectation is that vaccination will be the major control strategy for HIV/AIDS. In this section, we address the problem in which vaccination is available to a proportion of the population: We seek to derive conditions under which vaccination alone can slow down or eradicate the disease. The reproduction number in the presence of a vaccination strategy ξ is obtained by setting

$$R_v = \frac{b}{b+\xi} R_0 + \frac{\gamma\xi}{b+\xi} R_1, \tag{4.1}$$

which is a decreasing function of ξ with $R_v(0) = R_0$, $R_v(\infty) = \gamma R_1$ and hence $R_0 > \gamma R_1$. When $R_0 < 1$, the disease cannot develop into an epidemic; hence, in this case, vaccination is not necessary. If $R_0 > 1$, we want to consider the following problem: What vaccination strategy reduces the reproduction number R_v below the threshold of one? We

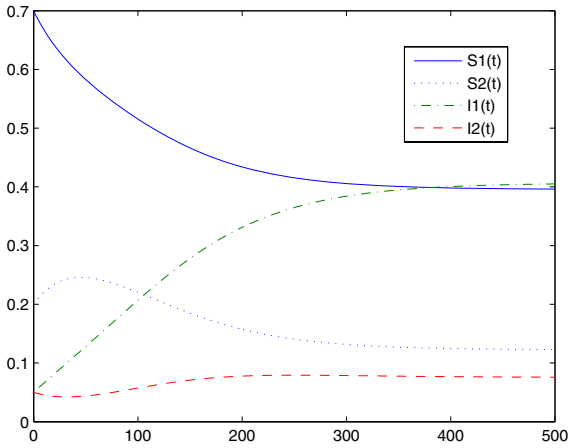

FIGURE 2. When $b = 0.02$, $\beta = 0.15$, $\eta_1 = 0.3$, $\eta_2 = 0.2$, $\xi = 0.01$; $\gamma = 0.6$, $R_v = 1.8 > 1$, all the components $S_1(t)$, $S_2(t)$, $I_1(t)$ and $I_2(t)$ approach their steady state values as time goes to infinity; the disease becomes endemic.

formulate this as a problem for finding the critical value ξ^* for which a vaccination program succeeds in slowing down or in eradicating the disease. This involves the following steps. First, the difference between the reproduction numbers R_0 and R_v satisfies the Hsu Schmitz [**10**] condition

$$R_0 - R_v = \frac{\xi}{b+\xi}(R_0 - \gamma R_1) > 0, \tag{4.2}$$

and secondly, differentiating R_v with respect to ξ gives

$$\frac{dR_v}{d\xi} = -\frac{b(R_0 - \gamma R_1)}{(b+\xi)^2} < 0. \tag{4.3}$$

Lastly, we determine the critical fraction ξ^* for which the vaccination program succeeds in reducing R_v below the threshold of one. It is easy to show that ξ^* is given by

$$\xi^* = \frac{b(1 - R_0)}{\gamma R_1 - 1} > 0, \tag{4.4}$$

and that it exists for $R_0 > 1 > \gamma R_1$. Note that, for $R_0 > \gamma R_1 > 1$, there is no ξ for which $R_v < 1$. Hence, for $R_0 > \gamma R_1 > 1$ the disease

will remain endemic in the population. Thus, we have the theorem as follows:

Theorem 4.1. *The disease can be eliminated if* $\xi > \xi^*$ *when* $R_0 > \gamma R_1 > 1$, *and the disease will remain endemic in the population if* $R_0 > \gamma R_1 > 1$.

5. Discussion. In this paper, we analyze the SIA model of HIV/AIDS with vaccination. We first examine the SIA model of disease under the vaccination. And then the dynamics of this epidemic model is analyzed. We find that the disease-free equilibrium is globally asymptotically stable when $R_v < 1$ and unstable when $R_v > 1$. We prove the existence of at least one endemic equilibrium point for all $R_v > 1$. In this paper, based on the center manifold theory, we give the stability of the endemic equilibrium point. Last, an optional vaccine efficacy is put forward. We have obtained a condition under which vaccination would succeed in slowing down the disease, which is $R_0 > \gamma R_1 > 1$; thus, under a planned control, the number of the HIV/AIDS individuals will be eliminated.

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