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Modelling Hiv Infection of Macrophages and T Cells

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ABSTRACT : *We analyze a mathematical model of HIV (human immunodeficiency virus) in macrophages and T cells for stability. We report that there are two critical points: the disease-free equilibrium and endemic equilibrium. The method of analysis is based on Rene Descartes' theory of positive solutions. The results showed that the disease-free equilibrium (DFE) is asymptotically stable if the basic reproduction number* $R_o<1$ *and the endemic equilibrium is unstable if* $R_o>1$*. New theorems were formulated using the basic reproduction number* R_o*.*

KEYWORDS: *Macrophages, T cells, HIV/AIDS, critical points, basic reproduction number, disease-free equilibrium, endemic equilibrium.*

I. INTRODUCTION

Undoubtedly, HIV/AIDS pandemic is the greatest public disaster of modern times [21]. Since early 1980's when this pandemic became visible, it has continued to ravage the world population and the vast number of HIV infected individuals are in sub-Saharan Africa and are mainly due to heterosexual transmission [12]. More than 40 million people worldwide are infected with the HIV virus; women account for 50% of those infected [24]. During the past two decades, researchers have made significant progress in understanding the epidemiology of HIV/AIDS worldwide. Presently, these efforts have led to the reduction of the global spread of the disease. Mathematical models have been extensively used to study the transmission dynamics of HIV. (see [2, 5, 6, 12, 13, 14, 16, 20, 22, 24, 26] and the references therein). During the course of the disease, HIV may infect a variety of cell types. The dynamics of infection by HIV on macrophages and T cells has been studied by a number of authors (see [7,9,10,11,17,18,19,21,23] and the references therein). Since macrophages T cells are immune system of the body, HIV destroys these cells on invasion. In this paper, we consider the model which is proposed by Nowak et al [17], make a couple of changes of variable and then study the transformed equations for stability. We determine the dynamics of the extended model by a threshold quantity called the basic reproduction number (denoted by R_o), which measures the number of new cell infections that an infected cell can generate in a completely susceptible population. In particular, it is shown that the disease-free equilibrium is asymptotically stable if $R_o<1$ and the endemic equilibrium is unstable if $R_o > 1$.

II. MATHEMATICAL FORMULATION

We shall consider the differential system that describes the model of macrophages and T cell infection by HIV proposed by Nowak et al. [17]

$$
\begin{aligned}
x_1^1 &= \alpha - d_1 x_1 - a_1 y_1 \\
y_1^1 &= \beta_1 x_1 y_1 - a_1 y_1 \\
\omega^1 &= \varepsilon - f\omega - r\omega(y_1 + y_2) \qquad (1) \\
x_2^1 &= r\omega(y_1 + y_2) - d_2 x_2 - \beta_2 x_2 y_2 \\
y_2^1 &= \beta_2 x_2 y_2 - a_2 y_2
\end{aligned}
$$

where x_1 = uninfected macrophages
y_1 = infected macrophages
x_2 = uninfected T cells
y_2 = infected activated T cells
ω = resting T helpher cells
ε = production rate of resting T helpher cells
r = activation rate of resting T helpher cells
f = death rate of resting T helpher cells
α = production rate of uninfected macrophages
d_1 = death rate of uninfected macrophages
d_2 = death rate of uninfected T cells
β_1 = transmission rate of HIV in infected macrophages
β_2 = transmission rate of HIV in infected T cells
a_1 = death rate of infected macrophages
a_2 = death rate of infected T cells

Let $\eta = 1 - \frac{d_1 x_1}{\alpha}, \varepsilon = 1 - \frac{f\omega}{E}$. Substituting into equation (1), we obtain

$$\begin{aligned}
\eta^1 &= d_1\eta + \beta_1 y_1(1-\eta) \\
y_1^{\ 1} &= \frac{\beta_1\alpha(1-\eta)y_1}{d_1} - a_1 y_1 \\
\varepsilon^1 &= \frac{-f\varepsilon}{E} + f(\varepsilon - \varepsilon E) + \frac{r}{E}(E-\varepsilon E)(y_1+y_2) \\
x_2^{\ 1} &= \frac{r}{f}(E-\varepsilon E)(y_1+y_2) - d_2 x_2 - \beta_2 x_2 y_2 \\
y_2^{\ 1} &= \beta_2 x_2 y_2 - a_2 y_2
\end{aligned} \tag{2}$$

Lemma 1: The basic reproduction number of the model (2) for macrophages cell is

$$R_o = \frac{\alpha\beta_1}{d_1 a_1} \tag{3}$$

Lemma 2: The basic reproduction number of the model (2) for T cell is

$$R_o = \frac{\beta_2 r E\alpha}{d_2(r\alpha + fa_2)} \tag{4}$$

III. STABILITY RESULT

3.1 The Critical Points

The critical points of equation (2) are

$A_o = (0,0,0,0,0)$ and

$$A^* = \left(\begin{array}{l} \frac{\beta_1\alpha - a_1 d_1}{\beta_1\alpha}, \frac{\beta_1\alpha - a_1 d_1}{\beta_1 a_1}, \frac{-r(\beta_1\alpha - a_1 d_1)\beta_1 a_1 E}{\beta_1 a_1 - f\beta_1 a_1 + \beta_1 a_1 f(1-E)r(\beta_1\alpha - a_1 d_1)}, \\ \frac{-r[(E-\varepsilon E)\beta_1\alpha - a_1 d_1]}{fd_2\beta_1 a_1}, \frac{a_2 f d_2 \beta_1 a_1}{r\beta_2[(E-\varepsilon E)\beta_1\alpha - a_1 d_1]} \end{array} \right)$$

Where A_o is the disease – free equilibrium and A^* is the endemic equilibrium.

We shall need the following theorems in the analysis of the nature of the critical points.

Theorem 3. 1 [9].

Let $\frac{dx}{dt}$ = P(x,y), $\frac{dy}{dt}$ = Q (x,y) and X = $\begin{pmatrix} x \\ y \end{pmatrix}$

Let X_1 = $\begin{pmatrix} x_1 \\ y_1 \end{pmatrix}$ be a critical point of the plane autonomous system

X_1 = g(x) = $\begin{pmatrix} P(x,y)_1 \\ Q(x,y) \end{pmatrix}$, where P(x,y) and Q(x,y) have continuous first partial derivatives in a neighbourhood of X_1

(a) If the eigenvalues of A = $g^1(X_1)$ have negative real part then X_1 is an asymptotically stable critical point

(b) If A = $g^1(X_1)$ has an eigenvalue with positive real part, then X_1 is an unstable critical point.

Theorem 3.2 (DESCARTES' RULE OF SIGNS) [2]

The number of positive zeros (negative zeros) of polynomials with real coefficient is either equal to the number of change in sign of the polynomial or less than this by an even number (by counting down by two's)

3.2 Stability of the Disease-free equilibrium

Theorem 3.3

The critical point of the DFE is asymptotically stable if $a_1 > 0$, $a_2 > 0$, $d_1 > 0$, $d_2 > 0$, $r > 0$, $E > 0$, $f > 0$, and $R_o < 1$.

Proof

The Jacobian matrix of disease – free equilibrium at A_o is

$$J(A_o) = \begin{pmatrix} -d_1 & 0 & 0 & 0 & 0 \\ 0 & -a_1 & 0 & 0 & 0 \\ 0 & r & \frac{-f}{E} & 0 & 0 \\ 0 & \frac{rE}{f} & 0 & -d_2 & \frac{rE}{f} \\ 0 & \frac{rE}{f} & 0 & 0 & -a_2 \end{pmatrix}$$

The eigenvalues are given by

$$\left(-\lambda - d_1\right)\left(-\lambda - a_1\right)\left(-\lambda - \frac{f}{E}\right)\left(-\lambda - d_2\right)\left(-\lambda - a_2\right) = 0 \qquad (5)$$

Hence, $\lambda_1 = -d_1$, $\lambda_2 = -a_1$, $\lambda_3 = -\frac{f}{E}$, $\lambda_4 = -d_2$, $\lambda_5 = -a_2$.

Expanding equation (5), we have

$$-\lambda^5-\left(a_2+d_2+\frac{f}{E}+a_1+d_1\right)\lambda^4$$
$$-\left(a_2d_2+\frac{fa_2}{E}+\frac{fd_2}{E}+a_1a_2+a_1d_2+a_2d_1+d_1d_2+\frac{d_1f}{E}+a_1d_1+\frac{a_1f}{E}\right)\lambda^3$$
$$-\left(\frac{fd_2a_2}{E}+a_1a_2d_2+d_1d_2a_2+\frac{d_1fa_2}{E}+\frac{d_1d_2f}{E}+a_1a_2d_1+a_1d_1d_2+\frac{a_1d_1f}{E}+\frac{a_1a_2f}{E}+\frac{a_1d_2f}{E}\right)\lambda^2$$
$$-\left(\frac{d_1d_2f}{E}+a_1a_2d_1d_2+\frac{a_1d_1d_2f}{E}+\frac{a_1a_2f}{E}+\frac{a_1a_2d_2f}{E}\right)\lambda-\frac{a_1a_2d_1d_2f}{E}=0$$

(6)

By Rene Descartes's rule of signs if $a_1 > 0$, $a_2 > 0$, $d_1 > 0$, $d_2 > 0$, $r > 0$, $E > 0$, $f > 0$ in equation (5), then it follows that there are no change in signs which implies that there no positive solutions of equation (5).

Hence, all the eigenvalues $\lambda_1,\lambda_2,\lambda_3,\lambda_4,\lambda_5$ are negative. Thus, we conclude that the critical point A_o is asymptotically stable.

Using model parameter values in [17]: $\alpha=1$, $\beta_2=0.5$, $d_1 = 0.6$, $a_1 = 2$, then we calculate $R_o = 0.417$. This shows that R_o is less than unity. Hence, the DFE is asymptotically stable.

3.2 Stability of the Endemic Equilibrium

Theorem 3.4

The critical point A^* of the endemic equilibrium is unstable if $r > 0$, $E > 0$, $\alpha > 0$, $\beta > 0$, $a_1 > 0$, $d_2 > 0$, $f > 0$ and $R_o > 1$.

Proof

The Jacobian matrix of equation (2) at A^* is

$$J(A^*)=\begin{pmatrix} 0 & \frac{\beta_1\alpha-a_1d_2}{\beta_1a_1} & 0 & 0 & 0 \\ -d_1 & \frac{\beta_1\alpha-a_1d_1}{\beta_1\alpha} & \frac{rE}{f} & 0 & 0 \\ 0 & 0 & \frac{-r(\beta_1\alpha-a_1d_1)\beta_1a_1E}{\beta_1a_1-f\beta_1a_1+\beta_1a_1f(1-E)-r(\beta_1\alpha-a_1d_1)} & 0 & 0 \\ 0 & 0 & -d_2 & \frac{-r[(E-\varepsilon E)\beta_1\alpha-a_1d_1]}{fd_2\beta_1a_1} & \\ 0 & \frac{rE}{f} & 0 & 0 & \frac{a_2fd_2\beta_1a_1}{r\beta_2[(E-\varepsilon E)\beta_1\alpha-a_1d_1]} \end{pmatrix}$$

It is sufficient to show that at least one eigenvalues of the endemic equilibrium is positive. By solving

$$|A-\lambda I|=0 \qquad (7)$$

We claim that if $E > 0$, $f > 0$, $r > 0$, $a_1 > 0$, $a_2 > 0$, $d_1>0$, $d_2>0$ $\beta_1>0$, $\beta_2>0$ and $R_o > 1$, then by Rene Descartes' rule of sign, equation (7) has 2 negative roots and 3 positive roots given by

$$\lambda_1=\frac{\beta_1\alpha-a_1d_1}{\beta_1a_1},\quad \beta_1\alpha \gg a_1d_1$$

$$\lambda_2=\frac{\beta_1\alpha-a_1d_1}{\beta_1\alpha},\quad \beta_1\alpha \gg a_1d_1$$

$$\lambda_3 = \frac{-r(\beta_1\alpha - a_1 d_1)\beta_1 a_1 E}{\beta_1 a_1 - f\beta_1 a_1 + \beta_1 a_1 f(1-E) - r(\beta_1\alpha - a_1 d_1)}$$

$$\lambda_4 = \frac{-r[(E-\varepsilon E)\beta_1\alpha - a_1 d_1]}{fd_2\beta_1 a_1}$$

$$\lambda_5 = \frac{a_2 fd_2\beta_1 a_1}{r\beta_2[(E-\varepsilon E)\beta_1\alpha - a_1 d_1]}$$

Hence, the critical point A^* of the endemic equilibrium (2) is unstable.This completes the proof.

Using parameter values taken from [18]: $\beta_2 = 2$, E = 1, α =1, $d_2 = 0.6$, r =2, f =0.01, $a_2 = 0.5$, R_o =6.536. It shows that $R_o > 1$ and hence the critical point A* is unstable.

IV. DISCUSSION AND CONCLUSION

The mathematical analysis of our dynamical system revealed that the stability of the two critical points depends on the basic reproduction number R_o. Our results show that the DFE is asymptotically stable if $R_o<1$ while the endemic equilibrium is unstable when Ro>1. If $R_o<1$, an average infectious macrophages and T cell is unable to replace itself and the infection is temporal and dies out in time. If $R_o>1$, the infection persists and an epidemic results. This could lead to a wiping out of the macrophage and T cell populations and drive disease progression to AIDS. Consequently, the instability of the endemic equilibrium is of great concern to scientists and other stakeholders in the spread and control of HIV disease. Hence, the study of endemic instability is essential in predicting the future course so that prevention and intervention strategies can be effectively designed. Since macrophages and T cells are human system against attack by foreign particles, HIV prevention and therapeutic strategies should be vigorously pursued to combat the spread of the virus. Media alert of the disease, condom use, HIV vaccines and anti-retroviral drugs could lead to a reduction in the transmission of HIV if effectively utilized.

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