MODELING THE DYNAMICS OF T4-CELLS COUNTS IN AN HIV-INFECTED INDIVIDUAL

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Abstract

In this work, we examined the stages of HIV progression to AIDS and proposed a stochastic model of the number of T4 – cells counts in an HIV infected person. The mean number of T4 – cells in each disease phase is obtained and the conditions for a stable level of CD^+4 – lymphocyte cells in an infected host are suggested. The need for antiretroviral therapies to sustain this level is emphasized.

Keywords: *Lymphocytes, antiretroviral therapy, helper cells, transfer rate constant.*

INTRODUCTION

The *CD^+cells* lymphocytes cells, sometimes called T4 - cells are often the primary targets of the HIV-virus in an infected host, and gradual decline from their normal level of 900 *m/l* is associated with sequence of progression stages towards AIDS in the host and provides us with information on when to start zidovudine and other antiviral treatments (Hethcote *et al*, 2002). However decline in the level of T4 Lymphocytes cells in an infected host follow a sequence of phases, the pre-antibody phase, where an individual is infected but not antibody seropositive. Some individuals at this stage may experience acute illness. The asymptomatic phase includes persons who are infected and antibody seropositive. The symptomatic phase occurs when individual develop an abnormal hematologic indicator or prodromal illness, such as persistent and generalized lymphadenopathy or oral candidiasis (Hethcote *et al*,2002) and the last stage is the clinical AIDS phase. However progression from HIV to AIDS in children is significantly different from that of adult. Some children are known to progress more rapidly than others. Children born with HIV infection are known to survive only within the first five years of infection. However, in this work we are only concerned with adult progression stages to AIDS in line with the five phases of transmission of the disease, and so we provided estimates of the mean number of *T4–cells* present in an infected person at various stages of the disease. Other approaches to HIV and AIDS modeling can be seen in the works of Hethcote *et al*, (2002), Waema and Olowofeso (2005), Iwurnor C.C.C (1999), Bailey N.T.J. (1964, 1975) Chiang, C. (1968) and Rao B. V. (2006).

Model Assumptions

We assume the following five clinical stages from HIV-infection to AIDS and death due AIDS as,
Stage one: pre-antibody stage
Stage Two: Asymptomatic stage
Stage three: Symptomatic stage
Stage Four: AIDS Stage
Stage Five: Death state from the disease

An individual with *CD^+cells* in the HIV infected host stages is assumed to be due to non disease and disease death, from HIV-virus.

Let the probability that a cell dies due to HIV –infection, during the time interval, $(t, t + \Delta t)$ be $\beta n\Delta t + 0(\Delta t)$ the probability that a cell in phase j replicate itself during the time interval $(t, t + \Delta t)$ be $n\lambda j\Delta t + 0(\Delta t)$ the probability that a cell in phase j dies due to nature during the time interval $(t, t + \Delta t)$ be $\mu_j n\Delta t + 0(\Delta t)$ and the probability that a cell survived to the next stage during the time interval $(t, t+\Delta t)$ be $n v_{ij}\Delta t + 0(\Delta t), I, j=1,...,5$

Where β is the disease induced death rate due to AIDS in stage four, λj is the cell replication rate in state j, μ_j is the $Cd4^+$ death rate in state j and v_{ij} are the transfer rate constant from state i to state j n is the cell counts at time t and $0(\Delta)$ is an infinitesimal quantity that goes to zero as Δ goes to zero

Model Formulation

Pre-antibody state

Let the conditional probabilities associated with change in the number of $T4-cells$ in an infected host be,

$$\Pr ob(X(t+\Delta t)=n+1/X(t)=n)=n\lambda_1\Delta t+0(\Delta t)$$

$$\Pr ob(X(t+\Delta t)=n+2/X(t)=n)=0(\Delta t)$$

$$\Pr ob(X(t+\Delta t)=n-1/X(t)=n)=\mu_1 n\Delta t+n\nu_{12}\Delta t+0(\Delta t)$$

$$\Pr ob(X(t+\Delta t)=n-2/X(t)=n)=0(\Delta t)$$

$$\Pr ob(X(t+\Delta t)=n/X(t)=n)=1-n\lambda_1\Delta t-n\mu_1\Delta t-n\nu_{12}\Delta t+0(\Delta t)$$

Where $Xt()$ is number of T4 - cells in an infected host at time t

Let $ob\ X_1\ t\ =n\ \ X\ \ =c_1$ be the conditional probability of the size of the T4-cells in the first phase.

Then,

$$P_n(t+\Delta t)=P_n(t)(1-(\lambda_1+\mu_1+\nu_{12})n\Delta t)+P_{n-1}(t)(n-1)\lambda_1\Delta t)+P_{n+1}(t)(\mu+\nu_{12})(n+1)\Delta t)$$

$$P_n(t+\Delta t)-P_n(t)=-(\lambda_1+\mu_1+\nu_{12})n\Delta tP_n(t)+(n-1)\lambda_1\Delta tP_{n-1}(t)+(n+1)(\mu_1+\nu_{12})P_{n+1}(t)$$

$$\frac{P_n(t+\Delta t)-P_n(t)}{\Delta t}=-n(\lambda_1+\mu_1+\nu_{12})P_n(t)+(n-1)\lambda P_{n-1}(t)+(n+1)(\mu_1+\nu_{12})P_{n+1}(t)$$

Where $P_n()$ is the probability of the size of the T4- cells counts in an infected host at time t

Allowing Δt go to zero, leads to the Chapman differential equation,

(1) $$\frac{dP_n(t)}{dt}=-n(\lambda_1+\mu_1+\nu_{12})P_n(t)+(n-1)\lambda_1P_{n-1}(t)+(n+1)(\mu_1+\nu_{12})P_{n+1}(t)$$

(2) $$\frac{dP_0(t)}{dt}=(\mu_1+\nu_{12})P_1(t)$$

Let the associated probability generating function of the size of the $T4-cells$ be,

(3) $$G(X;t)=E(X^n)=\sum_{n=0}^{\infty}P_n(t)X^n$$

From the Chapman -Kolmogorov differential equation we have,

$$\sum_{n=1}^{\infty}\frac{d}{dt}P_n(t)X^n =$$

$$-(\lambda_1+\mu_1+\nu_{12})\sum_{n=1}^{\infty}nP_n(t)X^n+\lambda_1\sum_{n=1}^{\infty}(n-1)P_{n-1}(t)X^n+(\mu_1+\nu_{12})\sum_{n=1}^{\infty}(n+1)P_{n+1}(t)X^n$$

$$\frac{\partial G(X;t)}{\partial t}-P_0'(t)=-(\lambda_1+\mu_1+\nu_{12})X\frac{\partial G(X;t)}{\partial X}+\lambda X^2\frac{\partial G(X;t)}{\partial X}+(\mu_1+\nu_{12})(\frac{\partial G(X;t)}{\partial X}-P_1(t))$$

Substituting the value of $P_0'(t)$ into the above equation leads to the following.

$$\frac{\partial G(X;t)}{\partial t}=-(\lambda_1+\mu_1+\nu_{12})X\frac{\partial G(X;t)}{\partial X}+\lambda X^2\frac{\partial G(X,t)}{\partial X}+(\mu_1+\nu_{12})\frac{\partial G(X;t)}{\partial X}$$

$$\frac{\partial G(X;t)}{\partial t}=[((\lambda_1+\mu_1+\nu_{12})-X\lambda)X-(\mu_1+\nu_{12})]\frac{\partial G(X;t)}{\partial X}$$

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The auxiliary equations are,

(4) $$\frac{dt}{1}=\frac{dX}{((\lambda_1+\mu_1+\nu_{12})-X\lambda_1)X-(\mu_1+\nu_{12})}=\frac{dG(X;t)}{0}$$

$$\frac{dt}{1}=\frac{dX}{(X-1)(\mu_1+\nu_{12}-\lambda_1X)}=\frac{\partial G(X;t)}{0}$$

(5) Let $G(X;t)=C_1$ and

$$\frac{X-1}{\mu_1+\nu_{12}-\lambda_1X}\exp(-(\mu_1+\nu_{12}-\lambda_1)t)=C_2$$

We let $C_1=f(C_2)$ and from the initial condition; we find the auxiliary function to be,

(6) $$G(X;t)=f(\frac{X-1}{\mu_1+\nu_{12}-\lambda_1X}e^{-(\mu_1+\nu_{12}-\lambda_1)t})$$

When t = 0, $G(X;0)=X^c=f(\frac{X-1}{\mu+\beta+\nu_{12}-\lambda X})$ for $|X|<1$

$$\text{Let}\theta=\frac{X-1}{\mu_1+\nu_{12}-\lambda_1X},\quad X=\frac{1+\theta(\mu_1+\nu_{12})}{1+\theta\lambda_1}.$$

(7) $$f(\theta) = \frac{1+\theta\alpha)}{1+\theta\lambda_1}, \quad \alpha = \mu_1 + \nu_{12}$$

$$\text{Putting } \theta = \frac{X-1}{\mu_1 + \nu_{12} - \lambda_1 X} e^{-(\mu_1+\nu_{12}-\lambda_1)t}$$

From equation (6) we have,

(8) $$G(X;t) = \left(\frac{(1-e^{-(\alpha-\lambda)t})\alpha - X(\lambda - \alpha e^{-(\alpha-\lambda)t})}{\alpha - \lambda e^{-(\alpha-\lambda)t} - \lambda X(1-e^{-(\alpha-\lambda)t})}\right)^c$$

(9) $$E(X(t)) = \frac{\partial G(X,t)}{\partial X}/_{X=1} = ce^{-(\alpha-\lambda_1)t}$$

(10)
$$Var(X(t) = E(X(t)(X(t)-1) - E(X(t)) + [E(X(t))]^2 =$$

$$c\left(e^{-(\alpha-\lambda_1)t} + ce^{-2(\alpha-\lambda_1)t} + \frac{e^{-(2\alpha-\lambda_1)t}(2e^{\alpha t}\lambda_1 - e^{\lambda_1 t}(\alpha - c\alpha + \lambda_1 + c\lambda_1))}{\alpha - \lambda}\right)$$

(11) $$E(X(t)(X(t)-1) = \frac{\partial^2 G(X;t)}{\partial X^2}/_{X=1}$$

Asymptomatic State,

Assume that change in the number of $T4-cells$ in this stage is due to cells replication, death due to infection and natural and transition to the next stage. We then obtain the following associated conditional probabilities with this change in the size of the $T4-cells$ in this stage,

$$Prob(X_2((t+\Delta t) = n+1/X(t) = n) = (\lambda_2 + \nu_{12})n\Delta t + 0(\Delta t)$$

$$Prob(X_2(t+\Delta t) = n+2/X(t) = n) = 0(\Delta t)$$

$$Prob(X_2(t+\Delta t) = n-1/X(t) = n) = (\mu_2 + \nu_{23})n\Delta t + 0(\Delta t)$$

$$Prob(X_2(t+\Delta t) = n-2/X(t) = n) = 0(\Delta t)$$

$$Prob(X_2(t+\Delta t) = n/X(t) = n) = 1 - (\lambda_2 + \mu_2 + \nu_{12} + \nu_{23})n\Delta t + 0(\Delta t)$$

Let $Prob(X_2(t) = n/X(0) = c_2)$ be the conditional probability of the size of the T4 cells in stage two.

The probability that the number of $T4-cells$ in an infected host in the stage two is n, at time $(t+\Delta t)$ is obtained by considering all the three possibilities leading to the n events as follows,

$$P_n(X_2(t+\Delta t) = P_n(t)(1-(\lambda_2+\mu_2+\nu_{12}+\nu_{23})n\Delta t + 0(\Delta t) + P_{n-1}(t)((\lambda_2+\nu_{12})n\Delta t + 0(\Delta t))$$

$$P_{n+1}(t)((\mu_2+\nu_{23})n\Delta t + 0(\Delta t)$$

$$P_n(t+\Delta t) - p_n(t) = -(\lambda_2+\mu_2+\nu_{12}+\nu_{23})n\Delta t P_n(t) + (\lambda_2+\nu_{12})(n-1)\Delta t P_{n-1}(t)$$

$$(\mu_2+\nu_{23})(n+1)\Delta t P_{n+1}(t)$$

The Chapman-Kolmogorov differential equations are given by,

$$(11) \qquad \frac{d}{dt}P_n(t) = -(\lambda_2+\mu_2+\nu_{12}+\nu_{23})nP_n(t)$$

$$+(\lambda_2+\nu_{12})(n-1)P_{n-1}(t) + (\mu_2+\nu_{23})(n+1)P_{n+1}(t)$$

$$(12) \qquad \frac{d}{dt}P_0(t) = (\mu_2+\nu_{23})P_1(t)$$

We adopt the probability generating function in (3), then the associated Chapman-Kolmogorov differential equation are obtained as,

$$\sum_{n=1}^{\infty}\frac{d}{dt}P_n(t)X_2^n =$$

$$-(\lambda_2+\mu_2+\nu_{12}+\nu_{23})\sum_{n=1}^{\infty}nP_n(t) + (\lambda_2+\nu_{12})\sum_{n-1}^{\infty}(n-1)P_{n-1}(t) + (\mu_2+\nu_{23})\sum_{n=1}^{\infty}(n+1)P_{n+1}(t)$$

$$\frac{\partial G(X_2;t)}{\partial t} - P_0'(t) =$$

$$-(\lambda_2+\mu_2+\nu_{12}+\nu_{23})X_2\frac{\partial G(X_2;t)}{\partial X_2} + (\lambda_2+\nu_{12})X_2^2\frac{\partial G(X_2;t)}{\partial X_2} + (\mu_2+\nu_{23})(\frac{\partial G(X_2;t)}{\partial X_2} - P_1(t))$$

Using equation (12), we get the associated partial differential equation,

$$\frac{\partial G(X_2;t)}{\partial t} =$$

$$-(\lambda_2+\mu_2+\nu_{12}+\nu_{23})X_2\frac{\partial G(X_2;t)}{\partial X_2}+(\lambda_2+\nu_{12})X_2{}^2\frac{\partial G(X_2;t)}{\partial X_2}+(\mu_2+\nu_{23})(\frac{\partial G(X_2;t)}{\partial X_2}$$

$$\frac{\partial G(X_2;t)}{\partial t}=(X-1)(\lambda_2 X+\nu_{12}X-\mu_2-\nu_{23})\frac{\partial G(X_2;t)}{\partial X_2}=0$$

The auxiliary equations are,

(13) $$\frac{dt}{1}=\frac{dX_2}{(X-1)(\lambda_2 X+\nu_{12}X-\mu_2-\nu_{23})}=\frac{dG(X_2;t)}{0}$$

(14) $$G(X;t)=C_3$$

(15) $$\frac{X-1}{M_2X-M_1}=\exp((M_2-M_1)t), \qquad M_1=\mu_2+\nu_{23}, \quad M_2=\lambda_2+\nu_{12}$$

(16) $$\frac{X-1}{M_2X-M_1}e^{-(M_2-M_1)t}=C_4, \quad G(X;0)=X^{C_2}=f(\frac{X-1}{M_2X-M_1}), \ t=0.$$

$$\text{Let}\theta=\frac{X-1}{M_2X-M_1}, \text{ for all } |X|<1, \qquad X=\frac{M_1\theta-1}{M_2\theta-1}$$

(17) $$f(\theta)=\frac{M_1\theta-1}{M_2\theta-1}. \quad \text{Put } \theta=\frac{X-1}{M_2X-M_1}e^{-(M_2-M_1)t}$$

The required expression for the probability generating function is also obtained as,

(18) $$G(X;t)=(\frac{(M_1e^{-(M_2-M_1)t}-M_2)X-M_1(e^{-(M_2-M_1)t}+1)}{M_2(e^{-(M_2-M_1)t}-1)X-M_2e^{-(M_2-M_1)t}-M_1})^{c_2}$$

(19) $$E(X(t))=\frac{(M_2-M_1)}{M_1+M_2}c_2\exp(-(M_2-M_1)t)$$

$$E(X(t)(X(t)-1)) = \frac{\partial^2 G(X;t)}{\partial X^2}/_{X=1} = \frac{1}{M_1+M_2)^2}(c_2 \exp(-(M_2-M_1))\ x$$

$$((c_2-1)M_1 \exp(M_1 t) - ((\exp(M_1 t) - 2\exp(M_2 t) + c_2 \exp(M_1 t)M_2))$$

(20) $$\mathrm{Var}(X(t)) = E(X(t)(X(t)-1)) + E(X(t)) - [E(X(t))]^2 =$$

$$\frac{(M_2-M_1)c_2 \exp(-(M_2-M_1)t)(1+\exp(-(M_2-M_1)t)M_1 + (1-\exp(-(M_2-M_1)t)M_2)}{(M_1+M_2)^2}$$

Symptomatic State

Change in the size of third stage $T4-cells$ counts is assumed to be due to transition to and from the stage, coursed by natural, disease induced death and cell replication respectively.
The conditional probabilities associated with these dynamics are given as,

$$\Pr ob(X(t+\Delta t) = n+1/X(t) = n) = (\lambda_3 + \nu_{23})n\Delta t + 0(\Delta t)$$

$$\Pr ob(X(t+\Delta t) = n+2/X(t) = n) = 0(\Delta t)$$

$$\Pr ob(X(t+\Delta t) = n-1/X(t) = n) = (\mu_3 + \nu_{34})\Delta t + 0(\Delta t)$$

$$\Pr ob(X(t+\Delta t) = n/X(t) = n) = 1-(\lambda_3 + \mu_3 + \nu_{23} + \nu_{34})n\Delta t + 0(\Delta t)$$

$$\Pr ob(X(t+\Delta t) = n-2/X(t) = n) = 0(\Delta t)$$

Let $\Pr(ob)/(0.X_3) = n \quad X \quad = c_3$ be the conditional probability of the size of the

T4 -cells in stage three.

The probability that the number of $T4-cells$ in this stage at time $(t, t+\Delta t)$ is n is,

$$P_n(X_3(t+\Delta t) = P_n(t)(1-(\lambda_3 + \mu_3 + \nu_{23} + \nu_{34})n\Delta t + 0(\Delta t) + P_{n-1}(t)((\lambda_3 + \nu_{23})n\Delta t + 0(\Delta t))$$

$$P_{n+1}(t)((\mu_3 + \nu_{34})n\Delta t + 0(\Delta t)$$

$$P_n(t+\Delta t) - p_n(t) = -(\lambda_3 + \mu_3 + \nu_{23} + \nu_{34})n\Delta t P_n(t) + (\lambda_3 + \nu_{23})(n-1)\Delta t P_{n-1}(t)$$

$$(\mu_3 + \nu_{34})(n+1)\Delta t P_{n+1}(t)$$

The Chapman-Kolmogorov differential equations are,

$$\frac{d}{dt}P_n(t) = -(\lambda_3 + \mu_3 + \nu_{23} + \nu_{34})nP_n(t) \tag{21}$$

$$+(\lambda_3 + \nu_{23})(n-1)P_{n-1}(t) + (\mu_3 + \nu_{34})(n+1)P_{n+1}(t)$$

$$\frac{d}{dt}P_0(t) = (\mu_3 + \nu_{34})P_1(t) \tag{22}$$

The associated partial differential equation is,

$$\frac{\partial G(X_2;t)}{\partial t} = -(\lambda_3 + \mu_3 + \nu_{23} + \nu_{34})X_2\frac{\partial G(X_2;t)}{\partial X_2} \tag{23}$$

$$+(\lambda_3 + \nu_{23})X_2^{\,2}\frac{\partial G(X_2;t)}{\partial X_2} + (\mu_3 + \nu_{34})(\frac{\partial G(X_2;t)}{\partial X_2}$$

$$\frac{\partial G(X_2;t)}{\partial t} = (X-1)(\lambda_3 X + \nu_{23}X - \mu_3 - \nu_{34})\frac{\partial G(X_2;t)}{\partial X_2} = 0$$

The auxiliary equations are,

$$\frac{dt}{1} = \frac{dX_2}{(X-1)(\lambda_3 X + \nu_{23}X - \mu_3 - \nu_{34})} = \frac{dG(X_2;t)}{0} \tag{24}$$

$$G(X;t) = C_4 \tag{25}$$

$$\frac{X-1}{\alpha_2 X - \alpha_1}e^{-(\alpha_2-\alpha_1)t} = C_4, \quad \alpha_1 = \mu_3 + \nu_{34}, \quad \alpha_2 = \lambda_3 + \nu_{23} \tag{26}$$

$$G(X;t) = f(\frac{X-1}{\alpha_2 X - \alpha_1}e^{-(\alpha_2-\alpha_1)t}),\ G(X;0) = X^{C_3} = f(\frac{X-1}{\alpha_2 X - \alpha_1}),\ t = 0. \tag{27}$$

$$\text{Let}\theta = \frac{X-1}{\alpha_2 X - \alpha_1}, \text{ for all } |X| < 1, \qquad X = \frac{\alpha_1\theta - 1}{\alpha_2\theta - 1} \tag{28}$$

$$f(\theta) = \frac{\alpha_1\theta - 1}{\alpha_2\theta - 1}.\ \text{Put}\ \theta = \frac{X-1}{\alpha_2 X - \alpha_1}e^{-(\alpha_2-\alpha_1)t} \tag{29}$$

The probability generating function is,

$$G(X;t) = \left(\frac{(\alpha_1 e^{-(\alpha_2-\alpha_1)t} - \alpha_2)X - \alpha_1(e^{-(\alpha_2-\alpha_1)t} + 1)}{\alpha_2(e^{-(\alpha_2-\alpha_1)t} - 1)X - \alpha_2 e^{-(\alpha_2-\alpha_1)t} - \alpha_1}\right)^{c_3} \tag{30}$$

$$E(X(t)) = \frac{(\alpha_2 - \alpha_1)}{\alpha_1 + \alpha_2} c_3 \exp(-(\alpha_2 - \alpha_1)t) \tag{31}$$

$$\mathrm{Var}(X(t)) = E(X(t)(X(t)-1)) + E(X(t)) - [E(X(t))]^2 = \tag{32}$$

$$\frac{(\alpha_2 - \alpha_1)c_3 \exp(-(\alpha_2 - \alpha_1)t)(1 + \exp(-(\alpha_2 - \alpha_1)t)\alpha_1 + (1 - \exp(-(\alpha_2 - \alpha_1)t)\alpha_2)}{(\alpha_1 + \alpha_2)^2}$$

AIDS State:

The conditional probabilities associated with change in the size of stage four

$T4 - cells$ counts are given by,

$$\Pr ob(X(t+\Delta t) = n+1 / X(t) = n) = (\lambda_4 + \nu_{34})n\Delta t + 0(\Delta t)$$

$$\Pr ob(X(t+\Delta t) = n+2 / X(t) = n) = 0(\Delta t)$$

$$\Pr ob(X(t+\Delta t) = n-1 / X(t) = n) = (\beta + \mu_4 + \nu_{45})\Delta t + 0(\Delta t)$$

$$\Pr ob(X(t+\Delta t) = n / X(t) = n) = 1 - (\lambda_4 + \mu_4 + \beta + \nu_{34} + \nu_{45})n\Delta t + 0(\Delta t)$$

$$\Pr ob(X(t+\Delta t) = n-2 / X(t) = n) = 0(\Delta t)$$

Let $\Pr(X(t) = n \mid X_4 = c_4)$ be the conditional probability of the size of the T4-cells in stage four

Then,

$$P_n(X(t+\Delta t) = P_n(t)(1 - (\lambda_4 + \mu_4 + \beta + \nu_{34} + \nu_{45})n\Delta t + 0(\Delta t) + P_{n-1}(t)((\lambda_4 + \nu_{34})n\Delta t + 0(\Delta t))$$

$$P_{n+1}(t)((\mu_4 + \beta + \nu_{45})n\Delta t + 0(\Delta t)$$

The Chapman-Kolmogorov differential Equations are,

$$\frac{d}{dt}P_n(t) = -(\lambda_4 + \mu_4 + \beta + \nu_{34} + \nu_{45})nP_n(t) \tag{33}$$

$$+ (\lambda_4 + \nu_{34})(n-1)P_{n-1}(t) + (\mu_4 + \beta + \nu_{45})(n+1)P_{n+1}(t)$$

$$\frac{d}{dt}P_0(t) = (\mu_4 + \beta + \nu_{45})P_1(t) \tag{34}$$

The associated partial differential and auxiliary equations are,

$$\frac{\partial G(X_2;t)}{\partial t} = (X-1)(\lambda_4 X + \nu_{34}X - \mu_4 - \beta - \nu_{45})\frac{\partial G(X_2;t)}{\partial X_2} = 0 \tag{35}$$

$$\frac{dt}{1} = \frac{dX_2}{(X-1)(\lambda_4 X + \nu_{34}X - \mu_4 - \beta - \nu_{45})} = \frac{dG(X_2;t)}{0} \tag{36}$$

$$G(X;t) = c_5 \tag{37}$$

$$\frac{X-1}{\eta_2 X - \eta_1}e^{-(\eta_2-\eta_1)t} = c_6, \qquad \eta_1 = \beta + \mu_4 + \nu_{45}, \qquad \eta_2 = \lambda_4 + \nu_{34} \tag{38}$$

Using similar augments an in equations (27) - (29) ,with the initial number of $T4-cells$ counts at time 0, assumed to be c_4. The probability generating function of the average number of cells and their variance are,

$$G(X;t) = \left(\frac{(\eta_1 e^{-(\eta_2-\eta_1)t} - \eta_2)X - \eta_1(e^{-(\eta_2-\eta_1)t} + 1)}{\eta_2(e^{-(\eta_2-\eta_1)t} - 1)X - \eta_2 e^{-(\eta_2-\eta_1)t} - \eta_1}\right) \tag{39}$$

c_4

$$E(X(t)) = \frac{(\eta_2 - \eta_1)}{\eta_1 + \eta_2}c_4 \exp(-(\eta_2 - \eta_1)t) \tag{40}$$

$$\mathrm{Var}(X(t)) = E(X(t)(X(t)-1)) + E(X(t)) - [E(X(t))]^2 = \tag{41}$$

$$\frac{(\eta_2 - \eta_1)c_4 \exp(-(\eta_2 - \eta_1)t)(1 + \exp(-(\eta_2 - \eta_1)t)\eta_1 + (1 - \exp(-(\eta_2 - \eta_1)t)\eta_2)}{(\eta_1 + \eta_2)^2}$$

The limiting mean numbers of cells in each of the four phases arerespectively,

$$c, \quad \text{if} \quad \alpha > \lambda_1 \tag{42}$$

$$\frac{(M_2 - M_1)}{M_1 + M_2}c_2, \qquad \text{if } M_2 > M_1 \tag{43}$$

$$\frac{(\alpha_2 - \alpha_1)}{\alpha_1 + \alpha_2}c_3, \qquad \text{if } \alpha_2 > \alpha_1 \tag{44}$$

$$\frac{(\eta_2 - \eta_1)}{\eta_1 + \eta_2}c_4, \qquad \text{if } \eta_2 > \eta_1 \tag{45}$$

(46) If $\alpha > \lambda, \quad M_2 > M_1, \quad \alpha_2 > \alpha_1, \quad \eta_2 > \eta_1$.

The intensity of transition from stage i to state j also satisfy,

$$\nu_{1'2} > \lambda_1 - \mu_1, \quad \nu_{23} - \nu_{12} > \lambda_2 - \mu_2, \quad \nu_{34} - \nu_{23} > \lambda_3 - \mu_3, \nu_{45} - \nu_{34} > \lambda_4 - t$$

$$t = \mu + \beta$$

(47) However, if $\alpha < \lambda, \quad M_2 < M_1, \quad \alpha_2 < \alpha_1,$ and $\eta_2 < \eta_1,$
The transition intensities from state i to state j satisfy the following

$$\nu_{12} < \lambda_1 - \mu_1, \quad \nu_{23} - \nu_{12} < \lambda_2 - \mu_2, \nu_{34} - \nu_{23} < \lambda_3 - \mu_3, \ \nu_{45} - \nu_{34} = \lambda_4 - t$$

Equation (46) represents a gradual decay of the $CD+$ *lymphocyte*cells which is often the target of health providers, while (47), represents a faster one not often desired and reflects the scenario infected host often tries to avoid.

CONCLUSION

Slowing down the transfer rate constants from each disease phase to another will help to slow the rate of progression to AIDS from HIV infection and prolong the productive life of an infected individual. In this case conditions (46) will have to be realized to achieve this. However this involves the use of antiretroviral and other treatment therapies to help slow down the decay process of the infected helper cells.

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