Journal of the Nigerian Association of Mathematical Physics
Volume **15 (November, 2009), pp 443 - 446**

A note on the effect of affinity hemodialysis on *T*-cell depletion

[1]R. O. Ayeni, T. O. Oluyo and A. M. Okedoye
Department of Pure and Applied Mathematics
Ladoke Akintola University of Technology, Ogbomoso, Nigeria

Abstract

We modify existing mathematical models for HIV that account for observation from hemodialysis. Of particular interest are the criteria under which the disease infected equilibrium could be stable we indicate treatment that is adequate to significantly lower gp 120 levels and help T cells to recover to normal level.

Keywords
Affinity dialysis, HIV/AIDS, Envelope proteins gp 120, criteria for stability.

1.0 Introduction

1.1 What is Known

The hallmark of HIV disease is the gradual loss of CD4+ *T* cells, which ultimately leaves the immune system unable to defend against opportunistic infections. While the mechanism through which HIV causes AIDS is imperfectly understood, the clinical data suggest that in addition to the loss of infected *T* cells, a large number of uninfected T cells are dying and that HIV – derived envelope proteins appear to be intimately involved. The major HIV envelope hlycoprotein *gp* 120 has been shown to have profound biological effects in vitro. *gp* 120 causes CD4 +*T* cells to undergo apoptosis. Binding of gp 120 to CD4+ cells in the presence of anti-envelope antibodies and complement opsonizes the cells, targeting them for clearance. The combined effect is the destruction of uninfected immune cells [1,2,3,4,5,6,7, and 8].

1.2 Model for AIDS incorporating stem cell depletion and gp 120 biological effects

Table 1.1

Production

$$S \xrightarrow{k_1} T$$: *T*- Cell production from stem cells

$$T + V \xrightarrow{k_2} T_i$$: Infection of *T* cell

[1]Corresponding author
[1]Telephone: +234-0803-722-9790

$$T_i \xrightarrow{k_3} V + P$$: Production of Virus and *gp* 120

$$P + T \overset{k_4}{\leftrightarrow} PT$$: Reversible gp 120 binding to normal *T* cells

Clearance

$$T \xrightarrow{d_1}$$: death normal *T* cell death rate

$$T_i \xrightarrow{d_2}$$: death clearance of infected *T* cells

$$V \xrightarrow{d_3}$$: Clearance viral clearance rate

$$P \xrightarrow{d_4}$$: Clearance *p* 24 clearance rate

$$PT \xrightarrow{d_5}$$: Clearance *gp* 120-induced apostosis and clearance,

where *T* denotes healthy cell, T_i is the infected *T* cell, *v* is virus, ρ is the concentration of *p* 24. We further assume that λ is the rate of recovery of T_i.

2.0 Mathematical model

Arising from table 1.1, the appropriate mathematical equations are

$$\frac{dS}{dt} = - k_1 S\left(1 - \frac{T}{T_0}\right) \tag{2.1}$$

$$\frac{dT}{dt} = k_1 S\left(1 - \frac{T}{T_0}\right) - k_2 TV - d_1 T - d_5 \frac{10PT}{k_4} + \lambda T_i \tag{2.2}$$

$$\frac{dT_1}{dt} = k_2 TV - d_2 T_i \tag{2.3}$$

$$\frac{dV}{dt} = k_3 T_i - d_3 V \tag{2.4}$$

$$\frac{dP}{dt} = 0.777V - d_4 P \tag{2.5}$$

The present model essentially modifies [7] model by assuming that some T_i essentially recover and become healthy because even weakly treatment of dialysis would be adequate to significantly lower *gp* 120 levels and help *T* cells recover to normal levels as long as stem cells remain available [4]

3.0 Stability analysis

The critical points are (0, 0, 0, 0, 0) and $\left(S_0\,,\,T_0,\,\frac{d_1 d_4 k_3 T_0{}^2}{0.777\alpha},\,\frac{d_1 d_4 T_0}{0.777\alpha},\,\frac{d_1 T_0}{\alpha}\right)$,

where $\alpha = (\lambda - d_2)\,\frac{d_3 d_4}{k_3(0.777)} - \frac{d_3 10 T_0}{k_4}$. The point (0, 0, 0, 0, 0) is the disease free

equilibrium. The point

$$\left(S_0\,,\,T_0,\,\frac{d_1 d_4 k_3 T_0{}^2}{0.777\,\alpha},\,\frac{d_1 d_4 T_0}{0.777\,\alpha},\,\frac{d_1 T_0}{\alpha}\right), = (S_0\ T_0,\,a,\,b,\,c)$$

is the infected equilibrium.

Let $\phi = S - S_0\,,\ \Psi = T - T_0,\ x = T_i - a,\ y = v - b,\ z = p - c$. Then

$$\frac{d\phi}{dt} = -\frac{S_0 \psi}{T_0} + nonlinear\,terms \tag{3.1}$$

$$\frac{d\psi}{dt} = \frac{S_0\psi}{T_0} - k_2 T_0 y - k_2 b\psi - d_1\psi - \frac{10 d_5 c\psi}{k_4}\ \frac{-10 d_5 T_0}{k_4} + \lambda x + nonlinear\ terms \tag{3.2}$$

$$\frac{dx}{dt} = k_2\ T_0 y + k_2\ b\psi - d_2\,x \tag{3.3}$$

$$\frac{dy}{dt} = k_3\,x - d_3\,y) \tag{3.4}$$

$$\frac{dz}{dt} = 0.777\ y - d_4 z \tag{3.5}$$

So the relevant matrix is

$$\begin{bmatrix} 0 & -\frac{S_0}{T_0} & 0 & 0 & 0 \\ 0 & 0 & \lambda & -k_2 T_0 & -\frac{10 d_5 T_0}{k_4} \\ 0 & 0 & -d_2 & k_2 T_0 & 0 \\ 0 & 0 & k_3 & -d_3 & 0 \\ 0 & 0 & 0 & 0.777 & -d_4 \end{bmatrix}$$

The eigenvalue μ satisfies

$$\mu^2\,(d_4 + \mu)\left((d_2 + \mu)(d_3 + \mu) - k_3 k_2 T_0\right) = 0$$

Hence μ = 0 twice. Or

$$\mu_1 = \mu_2 = 0,\ \mu_3 = -d_4$$
$$\mu_4 = \left\{-\left(d_2 + d_3\right) - \sqrt{\left(d_2 + d_3\right)^2 + 4k_2 k_3 T_0}\right\}/2$$
$$\mu_5 = \left\{-\left(d_2 + d_3\right) + \sqrt{\left(d_2 + d_3\right)^2 + 4k_2 k_3 T_0}\right\}/2$$

4.0 Discussion of results

The infected equilibrium is unstable since some eigenvalues have non- negative real values and may lead to full blown AIDS. To ensure stability of the infected point, it necessary to ensure that the stem cell is not depleted. This is the subject of another paper.

Reference

[1] M.D. Hazenberg, D. Hamann, H. Schuitemaker and F.T. Miedema (2000) Cell depletion in HIV – 1 infection. How CD4+T cells go out of stock Nat Immunol vol. 1 pp 285 – 289.

[2] T.O. Oluyo (2007): A mathematical model of HIV epidemic/verification using data obtained under contact tracing on Nigeria, Ph.D Thesis, LAUTECH, Ogbomoso, Nigeria.

[3] T.O. Oluyo and R.O. Ayeni (2007): A mathematical model of virus neutralizing antibody response Research J. Appl Sciences vol 2 pp 889 – 891.

[4] R.H. Tullis, D. Scammura and J. Ambrus (2002): Affinity hemodialysis for antiviral therapy with specific application to HIV J. Theor Med. Vol. 3 pp 157 – 166.

[5] R.H. Tullis R.P. Duffin, M. Zech and J.L. Ambrus (2002) Affinity hemodialysis for aantiviral Therapy 1. Removal of HIV – 1 from cell culture supernatants plasma and blood. Ther Apher vol. 6 pp 213 – 220.

[6] M.A. Stafford, L. Covey, Y. Cao, E.S. Daar, D.D. Ho and A.S. Perelson (2000): Modelling Plasma virus concentration during primary HIV infection, J. Theoretical Biology vol. 203 pp 285 – 301.

[7] R.H. Tullis (2004): Mathematical model of the effect of affinity hemodialysis on the T-Cell depletion leading to AIDS. Blood purification vol 22 84 – 91.

[8] R.H. Tullis, R.P. Duffi, M. Zech and J.L. Ambrus (2003): Affinity hemodialysis for antural therapy II. Removal of HIV -1 viral proteins from cell culture supernatants and whole blood; Blood purification vol 21, pp 58 -63.