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A Mathematical Model of Virus Neutralizing Antibody Response

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Abstract: Controlling the spreads of the disease is a primary goal of health administrators. In this study, we examine a mathematical model of virus neutralizing antibody response using a stability of the model based on Perron theorem. It is shown that the spread of the disease can be controlled if the critical parameter $R = \frac{\delta B^*}{\mu_6} < 1$, where δB^* is the scale initial value of B cells and μ_6 is the death rate of the free virus.

Key words: Spread, neutralizing, control, disease, mathematical model, antibody response

INTRODUCTION

Mathematical models of virus neutralizing antibody response have been examined by many Scientists. As a first approximation, Bocharov and Romanyukhu (1994) described the numbers of antibody forming cells required to produce the neutralizing IgG antibody titers observed during the early phase of Vascular Somatitis Virus (VSV) neutralizing immunoglobulin response. Since the pioneering work of Bell (1971) many mathematical models of B- cell activation and antibody production have been developed (Bruni *et al*., 1975, 1978; Marchuk and Petrov, 1987; Merrill, 1987; Mohler *et al*., 1980; Bocharov and Romanyukhu, 1994). Of particular interest in the study is the work of Funk *et al*. (1998) and Ayodele (2003).

MATHEMATICAL MODEL

In this study, we consider the following system of equations:

$$\frac{dB_0}{dt} = -\mu_1\left(B_0 - B^*\right) - \varepsilon VB_0 \quad (1)$$

$$\frac{dB_1}{dt} = \varepsilon VB_0 - qB_1 \quad (2)$$

$$\frac{dB_2}{dt} = qB_1 - qB_2 \quad (3)$$

$$\frac{dA_M}{dt} = qB_2 - \mu_2 A_M - S(t)A_M \quad (4)$$

$$\frac{dA_G}{dt} = S(t)A_M - \mu_3 A_G \quad (5)$$

$$\frac{dM}{dt} = f_1 A_M - \gamma_1 VM - \mu_4 M \quad (6)$$

$$\frac{dG}{dt} = f_2 A_G - \gamma_2 VG - \mu_5 G \quad (7)$$

$$\frac{dV}{dt} = \delta VB_0 - \gamma_1 m^{-1} VM - \gamma_2 g^{-1} VG - \mu_6 V \quad (8)$$

Where

- B_0 - B cells specific to vascular somatitis virus.
- B_1 - Activated B cells.
- B_2 - Proliferating B cells.
- B^* - Number of VSV- specific B cells in unprimed mice.
- A_M - Antibody forming cells producing Ig M.
- A_G - Antibody forming cells producing Ig G.
- M - Neutralizing Ig M antibody.
- G - Neutralizing Ig G antibody.
- μ_1 - Generation rate of virus specific precursor B cells from bone marrow.
- ε - Activated rate of vascular somatitis virus specific to B cells.
- S(t) - Rate at which IgM secreting antibody forming cells switch to IgG production in the presence of T cells help.
- q - Expansion rate.
- f_1 - Production rate of A_M.
- f_2 - Production rate of A_G.
- γ_1 - Rate at which IgG molecule bind to virus.
- γ_2 - Rate at which IgM molecule bind to virus.

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$\gamma_1 m^{-1}$ - Rate at which free virus (V) is neutralized by IgM (M) antibody.

$\gamma_2 g^{-1}$ - Rate at which free virus (V) is neutralized by IgG (G) antibody.

μ_2, μ_3, μ_4, μ_5 and μ_6 are the death rate of A_M,A_G,M,G and V respectively (μ_i>0)

δ - Rate at which dV/dt depends on VB_0

STABILITY OF ZERO SOLUTION

Theorem: Let R = $\delta B^*/\mu_6$. The zero solution is stable if R<1. Otherwise the zero solution is unstable.

Theorem (Perrons): Let x = Ax+f (x,t) where A has all eigenvalues negative real parts. Let f be real and continuous for small |x| and t≥0 and f(x,t) = 0|x| as |x|→0 uniformly in t, t≥0. Then the zero solution of x = Ax+f(x,t) is uniformly asymptotically stable.

Proof: We need Perrons' theorem to prove the theorem above.

Let

$$x = 1 - \frac{B_0}{B^*}$$

Then the system becomes

$$\frac{dx}{dt} = -\mu_1 x + \varepsilon V - \varepsilon V x \quad (9)$$

$$\frac{dB_1}{dt} = \varepsilon VB^* - \varepsilon VB^* x - qB_1 \quad (10)$$

$$\frac{dB_2}{dt} = 2^{\frac{10}{16}} qB_1 - qB_2 \quad (11)$$

$$\frac{dA_M}{dt} = qB_2 - \mu_2 A_M - S(t)A_M \quad (12)$$

$$\frac{dA_G}{dt} = S(t)A_M - \mu_3 A_G \quad (13)$$

$$\frac{dM}{dt} = f_1 A_M - \gamma_1 VM - \mu_4 M \quad (14)$$

$$\frac{dG}{dt} = f_2 A_G - \gamma_2 VG - \mu_5 G \quad (15)$$

$$\frac{dV}{dt} = \delta VB^* - \delta VB^* x - \gamma_1 m^{-1} VM - \gamma_2 g^{-1} VG - \mu_6 V \quad (16)$$

Let Z = (x, B_1, B_2, A_M, A_G, M, G, V)

Then the system (8)-(16) is essentially

$$Z' = AZ + f(Z) \quad (17)$$

$$\text{Since } S(t) = \begin{cases} 0, \ t \le 3.5 \ \text{days} \\ \frac{1}{10} e^{3(t-4.5)}, 3.5 < t \le 7 \ \text{days} \\ 180, \ t < 7 \ \text{days} \end{cases}$$

Where

$$A = \begin{pmatrix} -\mu_1 & 0 & 0 & 0 & 0 & 0 & 0 & \varepsilon \\ 0 & -q & 0 & 0 & 0 & 0 & 0 & \varepsilon B^* \\ 0 & 2^{\frac{10}{16}} q & -q & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & q & -\mu_2 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\mu_3 & 0 & 0 & 0 \\ 0 & 0 & 0 & f_1 & 0 & -\mu_4 & 0 & 0 \\ 0 & 0 & 0 & 0 & f_2 & 0 & -\mu_5 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \delta B^* - \mu_6 \end{pmatrix}$$

Hence |A-Iλ| = 0 gives

$\lambda_1 = -\mu_1$, $\lambda_2 = -q$, $\lambda_3 = -q$, $\lambda_4 = -\mu_2$, $\lambda_5 = -\mu_3$, $\lambda_6 = -\mu_4$, $\lambda_7 = -\mu_5$, $\lambda_8 = -\mu_6 + \delta B^*$

Since μ_i>0, and q>0 then the zero solution is uniformly asymptotically stable if $-\mu_6+\delta B^*$ <0 i.e. R<1. So by Perrons theorem, the zero solution is asymptotically stable if R<1.

Remark: In the model of Funk *et al.*(1998) δ = 0, μ_6= 0, hence the zero solution of Funk *et al.*(1998)model is unstable.

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