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On multi-strain flu model

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ABSTRACT

In this paper we present a multi-strain model for flu including an immune response term. The model is presented and discussed. Also we argue that there are two worrying aspects that may indicate the possibility of appearance of new strains in Egypt. © 2013 Trade Science Inc. - INDIA

KEYWORDS

Multi-strain;
Flu.

INTRODUCTION

Multi-strain diseases are gaining importance. This is exemplified by the recent review in Lancet[1] about multi-strain diseases. It can be summarized by the following points:

There is no formal definition for multi-strain diseases.

Multi-strain diseases are the norm not the exception.

Multi-strain diseases can significantly affect the dynamics, treatment and control strategies of the disease.

In some cases multi-strain phenomena can be helpful for the patient through the competition between different strains.

Mathematical models for multi-strain viruses can be quite useful. In fact trying to anticipate the new strains experimentally is quite difficult[2].

Spatial effects of epidemics can be important. Typically they are difficult to quantify. Mathematical models can help in this problem.

In sec.2 the single strain model is presented and discussed. Also we argue that the added immune response term represents some basic properties of the immune system and that it should be included to study longer term behavior of the disease. The mathematics is similar to multi-strain hepatitis C virus[3] but the conclusions are quite different. In sec. 3 the multi-strain model is investigated. Conclusions are presented.

THE SINGLE STRAIN MODEL

The fractional order multi-strain model is given by

$$\begin{aligned} D^{\alpha}T &= s - dT - (1-\eta)\beta VT, \\ D^{\alpha}I &= (1-\eta)\beta VT - \delta I(1 - I/c_2), \\ D^{\alpha}V &= (1-\varepsilon_p)pI - cV, \end{aligned} \qquad (1)$$

Where $0 < \alpha \leq 1$, T represents uninfected cells, 1 represents infected cells and V represents virus. The model assumes that uninfected cells are produced at a constant rate s, die at rate, d, per cell and are infected at constant rate β. Infected cells are lost at a rate δ per cell. Viral particles (virions) are produced at rate p per infected cells and cleared at rate c per virion. Typically, infection is treated using Tami flu. The efficacy of treatment in blocking virion production and reducing new infections are described by two parameters, ε_p and η,

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respectively. For example, a treatment efficacy in blocking virion production of 95% corresponds to ε_p=0.95. Setting V to be proportional to I one gets the reduced system:

$$DT = s - d\,T - a\,I\,T,$$
$$DI = a\,I\,T - b\,I(1-\frac{I}{c}). \quad (2)$$

Where *a,b,c,d,s* are positive constants. There are three equilibrium points of the system (2). The first is the disease free $(T=\frac{s}{d},\ I=0)$ and two endemic states (T_1, I_1^*) and (T_2, I_2^*) where

$$T_j = \frac{b}{a}(1-\frac{I_j^*}{c}), \quad j=1,2,$$
$$I_1^* = \frac{c}{2}\{(1-\frac{d}{ac})+[(1-\frac{d}{ac})^2-(\frac{4}{c})(\frac{s}{b}-\frac{d}{a})]^{(1/2)}\},$$
$$I_2^* = \frac{c}{2}\{(1-\frac{d}{ac})-[(1-\frac{d}{ac})^2-(\frac{4}{c})(\frac{s}{b}-\frac{d}{a})]^{(1/2)}\} \quad (3)$$

The locally asymptotic stability condition for the disease free state is

$$\frac{s}{d} < \frac{b}{a} \quad (4)$$

The locally asymptotic stability conditions for the two endemic states are:

$$0 < I_j^* < \frac{d}{(b/c-a)} \quad (5)$$

$$2(\frac{as}{b}-d) > (a-\frac{d}{c})I_j^*, \quad j=1,2 \quad (6)$$

THE MULTI-STRAIN MODEL

The model is given by:

$$DT = s - dT - a_1I_1T - a_2I_2T$$
$$DI_1 = a_1I_1T - b_1I_1(1-I_1/c_1) + g_1I_2$$
$$DI_2 = a_2I_2T - b_2I_2(1-I_2/c_2) + g_2I_1, \quad (7)$$

where *a1,a2,b1,b2,c1,c2,s,g1,g2* are positive constants and I1, I2 are the two strain infectives.

There are several equilibrium solutions: The disease free state $(T = s/d,\ I_1 = I_2 = 0)$. Four one strain endemic states given by $(T_{ij},I_{ij},0)$ and $(T_{2j},0,I_{2j})$, j=1,2 where

$$T_{1j} = (b_1/a_1)(1-I_{1j}/c_1),$$
$$I_{11} = \{(1-d/a_1c_1)+[(1-d/a_1c_1)^2-(4/c_1)(s/b_1-d/a_1)]^{(1/2)}\}c_1/2,$$
$$I_{12} = \{(1-d/a_1c_1)-[(1-d/a_1c_1)^2-(4/c_1)(s/b_1-d/a_1)]^{(1/2)}\}c_1/2, \quad (8)$$

$$T_{2j} = (b_2/a_2)(1-I_{2j}/c_2),$$
$$I_{21} = \{(1-d/a_2c_2)+[(1-d/a_2c_2)^2-(4/c_2)(s/b_2-d/a_2)]^{(1/2)}\}c_2/2,$$
$$I_{22} = \{(1-d/a_2c_2)-[(1-d/a_2c_2)^2-(4/c_2)(s/b_2-d/a_2)]^{(1/2)}\}c_2/2. \quad (9)$$

The multi-strain equilibrium solutions are given by the system:

$$s - dT - a_1I_1T - a_2I_2T = 0,$$
$$a_1I_1T - b_1I_1(1-I_1/c_1) + g_1I_2 = 0,$$
$$a_2I_2T - b_2I_2(1-I_2/c_2) + g_2I_1 = 0. \quad (10)$$

The local asymptotic stability of the single healthy state is given by

$$\frac{s}{d} < \frac{b_1}{a_1}, \quad \frac{s}{d} < \frac{b_2}{a_2} \quad (11)$$

$$(b_1 - \frac{a_1s}{d})(b_2 - \frac{a_2s}{d}) > g_1g_2 > 0 \quad (12)$$

The local asymptotic stability of the one strain endemic states are:

$$h_1 > 0, \quad h_3 > 0, \quad h_1h_2 > h_3 \quad (13)$$

For the state $(T_{ij},I_{ij},0)$ we have:

$$h_1 = d + b_1 + b_2 + (a_1 - 2b_1/c_1)I_{1j} - (a_1 + a_2)T_{1j} \quad (14)$$

$$h_2 = -a_1dT_{1j} - g_1g_2 + b_1(1-2I_{1j}/c_1)(d+a_1I_{1j}) + (-a_2T_{1j}+b_2)[d-a_1T_{1j}+b_1+(a_1-2b_1/c_1)I_{1j}], \quad (15)$$

and

$$h_3 = (-a_2T_{1j}+b_2)\{-a_1dT_{1j} + b_1(1-2I_{1j}/c_1)(d+a_1I_{1j})] + g_2[-g_1(d+a_1I_{1j}) + a_1a_2I_{1j}T_{1j}]. \quad (16)$$

For the state $(T_{2j},0,I_{2j})$ we have:

$$h_1 = d + b_1 + b_2 + (a_2 - 2b_2/c_2)I_{2j} - (a_1 + a_2)T_{2j} \quad (17)$$

$$h_2 = -a_2dT_{2j} - g_1g_2 + b_2(1-2I_{2j}/c_2)(d+a_2I_{2j}) + (-a_1T_{2j}+b_1)[d-a_2T_{2j}+b_2+(a_2-2b_2/c_2)I_{2j}], \quad (18)$$

and

$$h_3 = (-a_1T_{2j}+b_1)\{-a_2dT_{2j} + b_2(1-2I_{2j}/c_2)(d+a_2I_{2j})] + g_1[-g_2(d+a_2I_{2j}) + a_1a_2I_{2j}T_{2j}]. \quad (19)$$

We have the following conclusions:

The term added in equation (1) represents the well known high and low zone tolerance of the immune response (There is no immune response if the antigen number is either too high or too low[4]) since it vanishes for

both limits $1 \to 0$ and $1 \to c_2$. Immune response is significant for long time virus dynamics.

Since multi-drugs are strongly recommended to avoid drug resistance it is proposed that a further drug should be used.

Multi-strain phenomena is quite important. It exists in many diseases e.g. Flu, HCV Tb etc… It may cause the failure of treatment and /or vaccination protocols.

There are two worrying aspects about the possibility of the appearance of new strains of flu in Egypt. The first is the typical use of Tami flu for the past three years or more. Multi drugs are strongly recommended for multi-strain diseases.

The second is that the European vaccine for H1N1 required two shots. Some people did not take the second shot. Weak vaccination is a standard stimulus for virus mutation.

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