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A Model of Infectious Disease with Latent, Acute and Chronic Phases

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Abstract: A general model is presented for infectious diseases which have a latent stage of infection before the infected persons enter into acute phase. Patients may recover from acute stage or they enter into chronic phase. After recovery from acute or chronic phase they become susceptible again. For such a model a basic reproductive number R_0 is obtained. It is found that the disease-free equilibrium point is locally stable if $R_0 < 1$, whereas if $R_0 > 1$ the disease-present equilibrium point is locally stable and it is globally asymptotically stable when the rate of recovery is sufficiently large. Results of numerical simulation are also reported here.

Keywords: Dynamical system, endemic equilibrium, epidemic, global stability, non linear incidence.

I. INTRODUCTION

In recent years there have been great advances in mathematical modeling of infectious disease dynamics. Mathematical modeling has made a substantial impact on our thinking and understanding of the transmission dynamics of malaria, dengue fever, hepatitis C, HIV – infection etc. Epidemiological factors crucial to the dynamics of such diseases include long and variable periods of infectiousness.

An epidemiological model is said to be of SIS type if the susceptible become infectious and then are susceptible again upon recovery from the infection. Epidemiological models for gonorrhea, hepatitis C and some other bacterial diseases are of SIS type. Models of SIS type have been considered by Zhou (1994), Busenberg and Cooke (1993) and many others[1,2].

Reade et. al.(1998) studied the dynamics of a disease in which an individual upon infection will first exhibit acute signs of disease, then before total recovery progress to a chronic stage[3]. After recovery the individual will be susceptible only to subsequent bouts of chronic infection. Their model is appropriate for diseases like feline calicivirus and feline herpes virus infection in cats, foot and mouth disease in cattle.

Keeping in view the characteristics of hepatitis C, Luo and Xiang (2012) considered an endemic model with acute and chronic stages[4]. Diagnosis of hepatitis C is very difficult and so far no vaccine is available. The disease is transmitted through peoples' direct contacts. After the primary infection a host stays in a latent period before becoming infectious. In the acute stage of hepatitis C, the common symptoms are fatigue and jaundice. Luo and Xiang (2012) assumed that the hepatitis C patients go through the chronic stage and a person, after recovery from the chronic stage, becomes susceptible again[4]. The last assumption is reasonable since there is no evidence that immunity develops by the successful treatment of hepatitis C.

In the present paper, the epidemiological model of Luo and Xiang (2012) is modified by considering the possibility of recovery from chronic stage as well as from acute stage[4]. The reason is that the recovery from acute stage is more probable than that from the chronic stage. For the model presented here we have found a basic reproductive number R_0 .We have determined equilibrium points both for the cases $R_0 < 1$ and $R_0 > 1$ and we have discussed stability criterion for the two equilibrium points. The paper is organized as follows: Section II formulates the model; Section III studies the existence of the equilibrium points; Section IV shows global asymptotic stability analysis and spread of disease by numerical simulation.

II.THE SIS MODEL WITH AN EXPOSED PERIOD

Here we consider the spread of an infectious disease in a host population of size N which follows the following IVP in absence of disease :

$$\dot{N}(t) = (b - d)N, \qquad N(0) = N_0 \qquad (2.1)$$

Here b is the birth rate constant and d is the death rate constant. Solution of the IVP (2.1) is given by $N(t) = N_0 e^{rt}$, where $r = b - d$. Clearly, population size N grows or decays exponentially according as $r > 0$ or $r < 0$. N remains constant when $r = 0$; i.e., when $b = d$.

We part the host population into four classes : susceptible – $S(t)$, exposed – $E(t)$, patients in acute phase – $A(t)$, patients in chronic phase – $C(t)$. At any time t,

$$S(t) + E(t) + A(t) + C(t) = N(t) \qquad (2.2)$$

Equations governing the SIS model with an exposed period are the following:-

$$\dot{S}(t) = bN - \frac{\lambda AS}{N} - \frac{\mu CS}{N} - dS + \alpha A + \beta C \qquad (2.3)$$

$$\dot{E}(t) = \frac{\lambda AS}{N} + \frac{\mu CS}{N} - (d + \epsilon)E \qquad (2.4)$$

$$\dot{A}(t) = \epsilon E - (d + k + \alpha)A \qquad (2.5)$$

$$\dot{C}(t) = kA - (d + \beta)C \qquad (2.6)$$

Here ϵ is the rate at which an exposed person goes into acute phase and k is the rate at which an acute status – patient turns into chronic phase. α and β are the recovery rates from acute state and chronic state respectively. The

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terms $\lambda AS/N$ and $\mu CS/N$ appearing in equations (2.3) and (2.4) are non-linear incidence terms. The incidence of a disease implies the number of new cases per unit time. The contact rates λ and μ are, in general, functions of N. For standard incidence λ and μ are assumed to be constants. Clearly, $b, d, \lambda, \mu, \epsilon, k, \alpha, \beta$ are positive constants. Equations (2.3) – (2.6) are subject to the following initial condition :

$$S(0) = S_0, E(0) = E_0, A(0) = A_0, C(0) = C_0 \quad (2.7)$$

where $S_0 + E_0 + A_0 + C_0 = N_0$.
We now introduce the following dimensionless variables

$$S' = \frac{S}{N}, E' = \frac{E}{N}, A' = \frac{A}{N}, C' = \frac{C}{N} \quad (2.8)$$

In dimensionless form equations (2.2) – (2.6) become the following :-

$$S + E + A + C = 1 \quad (2.9)$$

$$\dot{S} = b - \lambda AS - \mu CS - dS + \alpha A + \beta C \quad (2.10)$$

$$\dot{E} = \lambda AS + \mu CS - (d + \epsilon)E \quad (2.11)$$

$$\dot{A} = \epsilon E - (d + k + \alpha)A \quad (2.12)$$

$$\dot{C} = kA - (d + \beta)C \quad (2.13)$$

In which primes have been dropped out.

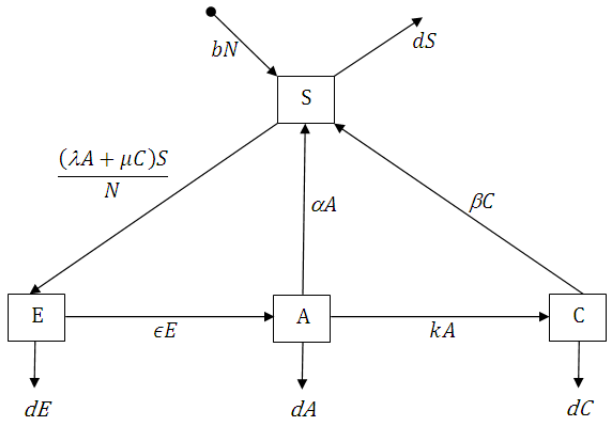

Fig. 1: Transfer diagram for the SIS model with an exposed period.

III. EXISTENCE OF THE EQUILIBRIUM POINTS

When the size of the host population is constant in absence of disease, b = d. Because of the constraint (2.9), one of the four equations (2.10) – (2.13) become redundant. Substituting $S = 1 - E - A - C$ in equations (2.11) – (2.13) we get the following equations :

$$\dot{E} = (\lambda A + \mu C)(1 - E - A - C) - (b + \epsilon)E \quad (3.1)$$

$$\dot{A} = \epsilon E - (b + k + \alpha)A \quad (3.2)$$

$$\dot{C} = kA - (b + \beta)C \quad (3.3)$$

Properties of the system of equations (2.10) – (2.13) can be deduced from the properties of the system of equations (3.1) – (3.3) in the invariant region :

$$\Gamma_0 = \{(E, A, C) \epsilon R^3 : E \geq 0, A \geq 0, C \geq 0, E + A + C < 1\}$$

Equilibrium points of the system of equations (3.1) – (3.3) can be obtained by solving the following equations

$$(\lambda A + \mu C)(1 - A - C) = (\lambda A + \mu C)E + (b + \epsilon)E \quad (3.4)$$

$$\epsilon E = (b + k + \alpha)A \quad (3.5)$$

$$kA = (b + \beta)C \quad (3.6)$$

Clearly, system of equations (3.1) – (3.3) admits the disease–free equilibrium point $(E, A, C) = (0,0,0)$, which is the trivial solution of the equations (3.4) – (3.6). The non-trivial solution of the equations (3.4) – (3.6) is given by (E^*, A^*, C^*) where is the basic reproductive ratio. (E^*, A^*, C^*) is an interior point of Γ_0 when $R_0 > 1$.

$$E^* = \left(\frac{b + k + \alpha}{\epsilon}\right) A^*$$

$$A^* = \left(\frac{b + \beta}{k}\right) C^*$$

$$C^* = \epsilon k \left(1 - \frac{1}{R_0}\right) / [(b + \beta)(b + k + \alpha + \epsilon) + \epsilon k]$$

where

$$R_0 = \frac{\epsilon \{\lambda (b + \beta) + \mu k\}}{(b + \epsilon)(b + \beta)(b + k + \alpha)} \quad (3.7)$$

IV. STABILITY ANALYSIS AND DISCUSSION

Theorem 4.1: System of equations (3.1) – (3.3) admits the disease – free equilibrium $E^f = (0,0,0)$ which is locally stable if $R_0 < 1$.
Proof: The existence of the disease – free equilibrium point E^f is shown in Section III. We now prove that E^f is locally stable.
The Jacobian matrix of the system of equations (3.1) – (3.3) is given by

$$J = \begin{bmatrix} -\lambda A - \mu C - b - \epsilon & \lambda (1 - E - 2A - c) - \mu C & -\lambda A + \mu (1 - E - A - 2C) \\ \epsilon & -b - k - \alpha & 0 \\ 0 & k & -b - \beta \end{bmatrix} \quad (4.1)$$

The characteristic equation of J is given by

$$x^3 + P_1 x^2 + P_2 x + P_3 = 0 \quad (4.2)$$

where

$$P_1 = \lambda A + \mu C + 3b + k + \alpha + \beta + \epsilon$$

$$P_2 = \epsilon\lambda E + \lambda A (2b + k + \alpha + \beta - 2\epsilon) + \epsilon\lambda C + \mu C (2b + k + \alpha + \beta + \epsilon) + (b + \beta)(b + k + \alpha) + (b + \epsilon)(2b + k + \alpha + \beta) - \epsilon\lambda$$

$$P_3 = \{\epsilon\lambda (b + \beta) + \epsilon\mu k\}E + \lambda A \{(b + \beta)(b + k + \alpha) + 2\epsilon (b + \beta) + \epsilon k\} + \epsilon k\mu A + \mu C \{(b + \beta)(b + k + \alpha) + \epsilon(b + \beta) + 2\epsilon k\} + \epsilon\lambda (b + \beta)C + (b + \epsilon)(b + \beta)(b + k + \alpha) - \epsilon\lambda (b + \beta) - \epsilon\mu k$$

At the point E^f, $P_1 > 0$. $P_3 > 0$ whenever $R_0 < 1$.
If $R_0 < 1$,

$$\epsilon\lambda (b + \beta) < \epsilon\{\lambda (b + \beta) + \mu k\} < (b + \epsilon)(b + \beta)(b + k + \alpha)$$

$$\Rightarrow \epsilon\lambda < (b + \epsilon)(b + k + \alpha)$$

$$\therefore P_1 P_2 - P_3 > (b + \beta)(b + k + \alpha)(2b + k + \alpha + \beta) + (3b + k + \alpha + \beta + \epsilon)(b + \epsilon)(b + \beta) + b(b + \epsilon)(b + k + \alpha) + \epsilon\mu k > 0.$$

Hence the theorem is proved.

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Theorem 4.2 : The system of equations (3.1) – (3.3) admits disease – present equilibrium point $E^p = (E^*, A^*, C^*)$ if $R_0 > 1$. E^p is a stable node or focus when $P_1P_2 - P_3 > 0; E^p$ is an unstable node or focus when $P_1P_2 - P_3 < 0; E^p$ is a center when $P_1P_2 - P_3 = 0$.

Proof : Existence of E^p is shown in Section III.

At the point $E^p, P_1 > 0$.

$$P_3 = [(b+\beta)(b+k+\alpha)\{\lambda(b+\beta)+\mu k\}/k + (b + \beta)\{\lambda(b+\beta)(b+k+\alpha) + 2\epsilon\lambda(b+\beta) + \epsilon\lambda k + \epsilon\mu k\}/k + \{\mu(b+\beta)(b+k+\alpha) + \epsilon\mu(b+\beta) + 2\epsilon\mu + \varepsilon\lambda(b+\beta)\}]C^* + (b+\epsilon)(b+\beta)(b+k+\alpha) - \{\varepsilon\lambda(b+\beta) + \epsilon\mu k\}$$

$$> (b+\epsilon)(b+\beta)(b+k+\alpha)\left(1-\frac{1}{R_0}\right) > 0, if\ R_0 > 1.$$

Thus, the nature of the equilibrium point E^p depends on the sign of $P_1P_2 - P_3$.

Theorem 4.3: The endemic equilibrium point E^p is globally asymptotically stable in the interior of Γ_0 if $R_0 > 1$.

Proof: We prove the theorem using the geometric approach of Li and Muldowney (1996)[5].

Let $D = \{(E, A, C)\epsilon R^3 : E > 0, A > 0, C > 0, E + A + C < 1$. Clearly, D is open set and simply connected and $f \epsilon C^{'}(D)$ where the system of equations (3.1) – (3.3) is identified as

$$\dot{x} = f(x) \qquad (4.3)$$

E^p is unique equilibrium point of the system (4.3) within D.

When $P_1P_2 - P_3 > 0, E^p$ is a stable point and there exists a compact absorbing set $K \subset D$ which follows from the boundedness of the solution of (4.3).

The second additive compound matrix is given by

$$J^{(2)} = \begin{bmatrix} -(\lambda A+\mu C) - 2b - k - \alpha - \epsilon & 0 & \lambda A - \mu(1-E-A-2C) \\ k & -(\lambda A+\mu C) - 2b - \beta - \epsilon & \lambda(1-E-2A-C) - \mu C \\ 0 & \epsilon & -2b-k-\alpha-\beta \end{bmatrix}$$

We consider the matrix valued function P as follows :-

$$P = P(E, A, C) = diag\left\{1, \frac{A}{C}, \frac{A}{C}\right\}$$

Then $P_f = \nabla p_{ij} \cdot f(x)$

$$P^{-1} = diag\left\{1, \frac{C}{A}, \frac{C}{A}\right\}$$

$$P_f P^{-1} = diag\left\{0, \frac{\dot{A}}{A} - \frac{\dot{C}}{C}, \frac{\dot{A}}{A} - \frac{\dot{C}}{C}\right\}$$

$$B = P_f P^{-1} + PJ^{(2)}P^{-1}$$

We write B in block form as follows:-

$$B = \begin{bmatrix} B_{11} & B_{12} \\ B_{21} & B_{22} \end{bmatrix}$$

where

$$B_{11} = -(\lambda A + \mu C) - (2b + k + \alpha + \epsilon),$$

$$B_{12} = \left[0, \frac{C}{A}\{\lambda A - \mu(1 - E - A - 2C)\}\right],$$

$$B_{21} = \begin{bmatrix} kA/C \\ 0 \end{bmatrix},$$

$$B_{22} = \begin{bmatrix} \frac{\dot{A}}{A} - \frac{\dot{C}}{C} - (\lambda A + \mu C + 2b + \beta + \epsilon) & \lambda(1 - E - 2A - C) - \mu C \\ \epsilon & \frac{\dot{A}}{A} - \frac{\dot{C}}{C} - (2b + k + \alpha + \beta) \end{bmatrix}$$

We choose the vector norm $|.|$ in R^3 as follows :- $|(x, y, z)| = max\{|x|, |y + z|\}$. Let $\sigma(\cdot)$ denote the Lozinskii measure wrt this norm. Using the method of estimating $\sigma(\cdot)$ in Li and Muldowney (1996) we have $\sigma(B) \leq sup\{g_1, g_2\}$ where $g_1 = \sigma_1(B_{11}) + |B_{12}|, g_2 = \sigma_1(B_{22}) + |B_{21}|$. Here $|B_{21}|, |B_{12}|$ are matrix norms wrt the L^1 vector norm and σ_1 denotes the Lozinskii measure wrt the L^1 norm. Therefore,

$$\sigma_1(B_{11}) = -(\lambda A + \mu C) - (2b + k + \alpha + \epsilon)$$

$$\sigma_1(B_{22}) = \frac{\dot{A}}{A} - \frac{\dot{C}}{C} - (\lambda A + \mu C + 2b + \beta)$$

$$|B_{12}| = \frac{C}{A}\{\lambda A - \mu(1 - E - A - 2C)\}$$

$$|B_{21}| = kA/C$$

Thus,

$$g_1 = -(2b + k + \alpha + \epsilon) - \frac{\mu C}{A}(1 - E - 2C)$$

$$g_2 = \frac{kA}{C} + \frac{\dot{A}}{A} - \frac{\dot{C}}{C} - (\lambda A + \mu C + 2b + \beta)$$

g_1, g_2 can be rewritten as follows

$$g_1 = \frac{\dot{A}}{A} - b - \frac{\epsilon(E + A)}{A} - \frac{\mu C}{A}(1 - E - 2C) \leq \frac{\dot{A}}{A} - b$$

,provided (1 –E -2C) > 0, i.e., if α is sufficiently large.

$$g_2 = \frac{\dot{A}}{A} - b - (\lambda A + \mu C) \leq \frac{\dot{A}}{A} - b$$

$$\therefore \sigma(B) \leq \frac{\dot{A}}{A} - b \qquad (4.4)$$

Along each solution $\big(E(t), A(t), C(t)\big)$ to the system of equations (3.1) – (3.3) with $(E_0, A_0, C_0)\epsilon K$, we have

$$\frac{1}{t}\int_0^t \sigma(B)\, ds \leq \frac{1}{t} ln\frac{A(t)}{A_0} - b \qquad (4.5)$$

$$when\ t \to \infty, \bar{g}_2 \leq -b/2 < 0 \qquad (4.6)$$

Thus, by the theorem of Li and Muldowney, it follows that the endemic equilibrium point E^p is globally asymptotically stable in D if $R_0 > 1$. In order to observe how the disease spreads in the system we have performed numerical simulation. We have assumed that initial population is 1,00,000 when there is neither acute nor chronic patient, only certain percentage of people are in latent stage of infection. In Fig. 2 we have plotted total infected people (A + C) against time. In Fig. 3 we have displayed how number exposed person decays with time.

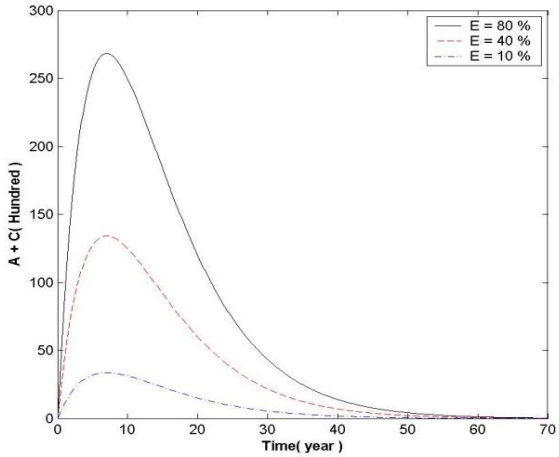

Fig. 2: (A + C) against t, b = 15 per thousand, $\lambda = .3,\ \mu = .7,\ \epsilon = .02, k = .06, \alpha = .3,\ \beta = .05$.

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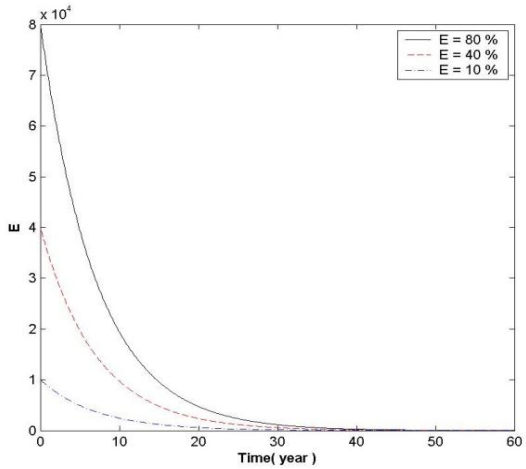

Fig. 3: E against t, b = 15 per thousand, $\lambda = .3,\ \mu = .7,$ $\epsilon = .02, k = .06, \alpha = .3,\ \beta = .05.$

V. CONCLUSION

This study provides a transmission dynamic model of infectious diseases which have three different phases of infection, namely, latent stage, acute stage and chronic stage. This model is appropriate for diseases like hepatitis C, tuberculosis etc. Till date there is no vaccine for hepatitis C and BCG vaccine used for tuberculosis has some limitations. In the epidemiological model presented here three phases of infection have been taken into account. It is assumed that recovery is possible from both acute and chronic stage. It is true, in general, that early diagnosis and early treatment results in early recovery. So, recovery from acute stage is more probable than that from the chronic stage of infection. After carrying out stability analysis of equilibrium points it is found that if the basic reproductive number R_0 is less than 1 then the disease-free equilibrium point is locally asymptotically stable and if R_0 is greater than 1 then the endemic equilibrium of the system is locally stable and it is globally asymptotically stable when the rate of recovery from the acute stage of infection is sufficiently large. We have also shown how the disease breaks out by numerical simulation.

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