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A Mathematical Model for HBV

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ABSTRACT

In this paper we present an epidemic model for hepatitis of type B. In this model essential factors for this epidemic are appeared. The factors are susceptibility, expositive factor, vaccination, infection, and recovery. Asymptotical stability in disease free equilibrium points is investigated. Also asymptotical stability in endemic equilibrium point is considered. We show that another equilibrium point is not asymptotically stable.
KEY WORDS. Asymptotic stability; Hepatitis; Epidemiology; Hyperbolic point; Endemic equilibrium point.

INTRODUCTION

Population studies as a biological topic is the reason for many interesting results in mathematical sciences ([3], [5], [6], [8], [9],[10], [11]). In this paper we are going to present a model to describe the method of infection for the virus of hepatitis of type B.
To describe this model we consider five boxes, which called susceptible, latent or exposed, infectious, vaccination and recovery box.
We know that in many infectious diseases there is an exposed period after transmission of infection from susceptible to potentially infective members. Moreover potential infective people can transmit infection. If the exposed period is short, then we ignore potential infection in the model. In the infections with long exposed period this parameter can't be ignored.
In the case of vaccination before the beginning of an epidemic, we must consider both exposed period and the period of treatment. In HBV we accept with such situation. HBV produce by Hepadena virus, with DNA genome. That's exposed period is approximately three months, and then jaundice significant will be appearance.
More than 2 billion people have been infected with the hepatitis B virus. An estimated 600000 people die each year due to the acute of hepatitis B.
The virus incubation period is 90 days on average, but can vary from about 30 to 180 days. HBV maybe detected 30 to 60 days after infection and persist for widely variable periods of time.
We often used HBV vaccination for children and adults in the susceptible people and the exposed period.
In this paper we consider an epidemiological model. We divided the population into five classes: susceptible, latent or exposed,infectious, vaccination and recovered. We denote their sizes by S, E, I, V and R respectively [4]. We used of the abbreviation SEIVR for this model. A susceptible individual first goes through exposed period after infection before becoming infectious. We also assume that a fraction m of the susceptible individuals and a fraction α of the exposed period will be used forvaccination.
In section 2, the SEIVR model, R_o and R_1 are formulated.
We present a condition for asymptotical stability of the disease-free equilibrium points in section 3.
The asymptotical stability of the endemic equilibrium point $Q_*$is considered in section 4.
In section 5,we investigate asymptotical stability for another equilibrium point of HBV model.

2 MODEL FORMULATION

With the notations of previous section the size N(t) of total population in time t for HBV consideration is: S(t) +E(t)+I(t)+v(t)+R(t).We denote the transmission rate (per capita) byβ.$\mu$and$\lambda$are the natural mortality rate and the birth rate respectively. We denote the recovery rate in class I byγ.Also we denote the leaving rate of the exposed class by k.
In SEIVR the fractions m and α denote per unit time of susceptible people and the people in the exposed period who are selected for vaccination. Also σ denotes the fraction of vaccinated members who became infected.
We denote the rate of removal from the vaccinated class by η.
f denotes the fraction of γI members who leaving the infected class at time t to the recovery class and the remaining fraction (1-f)dies because of disease. Moreover we suppose that the fraction $f_v$of ηV members leaving the vaccination class at time t.
So we can deduce the following mathematical model.

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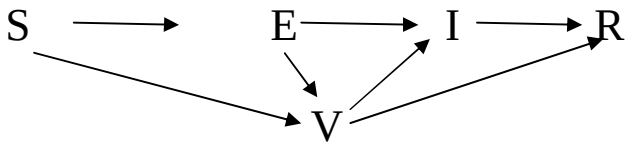
$$\begin{cases} \dot{S} = -\beta SI + \lambda N - \mu S - \mathfrak{m}S \\ \dot{E} = \beta SI - \mu E - \alpha E - (1-\alpha)kE \\ \dot{I} = (1-\alpha)kE - (\mu-\gamma)I + \beta\sigma IV \\ \dot{V} = \alpha E + \mathfrak{m}S - \sigma\beta IV - \eta V \\ \dot{N} = -(1-f)\gamma I - (1-fv)\eta V\mu + \lambda N - \mu N \\ \dot{R} = \gamma IF + \eta V f v - \mu R \end{cases} \quad (1.1)$$

Flowchart of this model is



We would like to calculate the basic reproduction number R_0,if there is no any vaccination in population before anepidemic. In this case we suppose the infection is divided into two disease stages or compartments ([9],[4]). Let the (i,j) entry of the transition matrix T is the rate individuals in stage j progress to stage i, and the (i,j)entry of the infection matrix F is the number of new infections at stage j caused by contact with diseased individuals in stage i.

In the initial stages of the epidemic, we can assume S_0 is near the disease free value so $V_0 = 0$ and we approximate the middle two equations for E and I with the linear system

where A= $\alpha + (1-\alpha)k + \mu$.

In this linearization ,we have separated the dynamics into two parts. The first matrix which we denote it by F is the matrix of transition rates, and the second matrix which we denote is by T is a matrix of infection rates.

So

and

$$T=\begin{pmatrix} \alpha + (1-\alpha)k + \mu & 0 \\ -(1-\alpha)k\mu + \gamma & \end{pmatrix} .$$

Thus

$$FT^{-1} = \begin{pmatrix} \frac{\beta S_0(1-\alpha)k}{(\mu+\gamma)(\alpha+(1-\alpha)k+\mu)} & \frac{\beta S_0}{\mu+\gamma} \\ 0 & 0 \end{pmatrix}$$

We know that R_0 is the eigenvalue of FT^{-1}[1].So

$$R_0 = \frac{\beta S_0(1-\alpha)k}{(\mu+\gamma)(\alpha+(1-\alpha)k+\mu)}$$

If there exist vaccination at the beginning of an epidemic then S_0+V_0=K=N_0.

In this case we suppose the infection is divided into3 disease stages or compartments, which areI, E, and V.

Since

$$\begin{pmatrix} \dot{E} \\ \dot{I} \\ \dot{V} \end{pmatrix} = \begin{pmatrix} \alpha + (1-\alpha)k + \mu & 0 & 0 \\ -(1-\alpha)k\mu + \gamma & 0 & \\ -\alpha & 0 & \eta \end{pmatrix} \begin{pmatrix} E \\ I \\ V \end{pmatrix} - \begin{pmatrix} 0 & \beta S_0 & 0 \\ 0 & 0 & \beta\sigma V_0 \\ 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} E \\ I \\ V \end{pmatrix}.$$

If

$$F = \begin{pmatrix} 0 & \beta S_0 & 0 \\ 0 & 0 & \beta\sigma V_0 \\ 0 & 0 & 0 \end{pmatrix}$$

and

$$T = \begin{pmatrix} \alpha + (1-\alpha)k + \mu & 0 & 0 \\ & -(1-\alpha)k\mu + \gamma & 0 \\ -\alpha & & 0 \qquad \eta \end{pmatrix}$$

then

$$FT^{-1} = \begin{pmatrix} \frac{\beta S_0(1-\alpha)k}{(\mu+\gamma)(\alpha+(1-\alpha)k+\mu)} & \frac{\beta S_0}{\mu+\gamma} & 0 \\ \frac{\beta\sigma\alpha V_0}{\eta(\alpha+(1-\alpha)k+\mu)} & 0 & \frac{\beta\sigma V_0}{\eta} \\ 0 & 0 & 0 \end{pmatrix}.$$

So themethod for calculationR_1 presented in[1]implies

$$R_1 = \frac{1}{2}\left(\frac{\beta S_0(1-\alpha)k}{(\mu+\gamma)\ (\alpha+(1-\alpha)k+\mu)}\right.$$
$$\left. + \sqrt{\frac{\beta^2 S_0^2(1-\alpha)^2k^2}{(\mu+\gamma)^2(\alpha+(1-\alpha)k+\mu)^2} + \frac{\beta^2\sigma S_0\alpha V_0}{\eta(\alpha+(1-\alpha)k+\mu)}}\right).$$

3. ASYMPTOTICAL STABILITY ANALYSIS

From the biological consideration, the phase space of the model is:

$$T_0 = \{(S,E,I,V,N): 0 \le S + E + I + V \le N\}$$

If there is no vaccination in population then $V_0 = 0, I_0 = 0\ and E_0 = 0$. Before an epidemic outbreak if $\lambda = \mu$ then the point $Q_0 = (K,0,0,0,K)$ is the disease free equilibrium point of the model, it exists for all non negative values of the parameters.

Theorem 1.In themode (1.1)ifR_0<1 then $Q_0$is asymptotically stable.

Proof.The linearization of the system(1.1)at the equilibrium point Q_0 is

$$\begin{pmatrix} -(\mu+m) & 0 & -\beta K & 0 & \lambda \\ 0 & A\beta K & 0 & 0 & \\ 0 & (1-\alpha)k-(\mu+\gamma) & 0 & 0 & \\ m\alpha & 0 & -\eta & 0 & \\ 0 & 0 & -(1-f)\gamma-(1-f_v)\eta & 0 & \end{pmatrix}$$

where A= - $(\alpha + (1-\alpha)k + \mu)$.

Its characteristic equation withthe eigenvalue $\acute{\lambda}$ is

$$[(\alpha + (1-\alpha)k + \mu + \acute{\lambda})(\mu + \gamma + \acute{\lambda}) - \beta K(1-\alpha)]$$
$$((\mu + m + \acute{\lambda})\,\acute{\lambda}(\eta + \lambda) + m\acute{(}1 - f_v)\lambda\eta) = 0.$$

So

$$\left(\acute{\lambda}^2 + a_1\acute{\lambda}\ + a_2\right)(\acute{\lambda}^3 + b_1\acute{\lambda}^2 + b_2\acute{\lambda}\ + b_3) = 0,$$

where

$a_1 = 2\mu + \gamma + \alpha + (1-\alpha)k > 0,$
$a_2 = (\alpha + (1-\alpha)k + \mu)(\mu + \gamma) - \beta K(1-\alpha)k$
$= (\alpha + (1-\alpha)k + \mu)(\mu + \gamma)(1 - R_0),$
$b_1 = \mu + m + \eta,$
$b_2 = \mu(\mu + m),$
$b_3 = m(1 - f_v)\lambda\eta.$

Since R_0<1thena_2>0. So both eigenvalues in theequation of degree 2 have negative real parts. And it is obvious that b_1>0,b_2>0 and b_3>0.Also

$$b_1b_2 = (\mu + m + \eta)\mu(\mu + m) > m\mu\eta > m\mu\eta(1 - f_v).$$

So b_1b_2>b_3.By Hurwitz criterion ([2], [7], [6] and [8])the disease free equilibrium Q_0 is locally asymptotically stable.

If there is vaccination in the population then before an epidemic outbreak I_1=0,N_1= $\frac{(\mu+m)S_1}{\lambda}$ and $V_1 = \frac{mS_1}{\eta}$,

where $\lambda = \frac{\mu(\mu+m)}{mf_v+\mu}andf_v = \frac{\mu}{\eta}$.

Theorem 2.In the SEIVR model (1.1)ifR_1<1,η+mf_v>m and $\lambda f_v > \mu$ then the equilibrium point $Q_1 = \left(S_1, 0, 0, \frac{ms_1}{\eta}, \frac{(\mu+m)S_1}{\lambda}\right)$ is asymptotically stable.

Proof. The linearization of the system (1.1)at the equilibrium point Q_1 is

$$\begin{pmatrix} -(\mu+m) & 0 & -\beta S_1 & 0 & \lambda \\ 0 & A-\beta S_1 & 0 & 0 & \\ 0 & (1-\alpha)k & B & 0 & 0 \\ & m\alpha-\beta\sigma V_1-\eta & 0 & & \\ 0 & 0 & -(1-f)\gamma-(1-f_v)\lambda-\mu & & \end{pmatrix}$$

where$A = -(\alpha + (1-\alpha)k + \mu)$and $B = -(\mu + \gamma + \beta\sigma V_1)$.
The characteristic equation is

$$(\acute{\lambda}^2 + (\alpha + (1-\alpha)k + 2\mu + \gamma + \beta\sigma V_1)\acute{\lambda} + (\alpha + (1-\alpha)k + \mu)$$
$$(\mu + \gamma + \beta\sigma V_1) - \beta(1-\alpha)kS_1)(\acute{\lambda}^3 + (2\mu + \eta + m - \lambda)$$
$$\acute{\lambda}^2 + \big((\mu-\lambda)(\mu+\eta+m) + \eta(\mu+m)\big)\acute{\lambda} + (\mu-\lambda)(\mu+m)\eta +$$
$$(1-f_v)\lambda m\eta = 0$$

We know$\lambda = \frac{\mu(\mu+m)}{mf_v+\mu}$. So we can see easily that$b_1>0$.

$$b_2 = ((\mu-\lambda)(\mu+m+\eta) + \eta(\mu+m) = -\mu m(1-f_v)(\mu+m+\eta) +$$
$$\eta(\mu+m)(mf_v+\mu)\frac{1}{mf_v+\mu} = (-\mu m(\mu+m+\eta) + \mu m f_v(\mu+m+\eta) + \eta(\mu+m)mf_v + \eta\mu(\mu+m))\frac{1}{mf_v+\mu} = (\mu^2(\eta+mf_v-m) + m\big((\mu+\eta)f_v-\mu\big) + 2m\mu\eta f_v\frac{1}{mf_v+\mu} > 0,$$

and

$$b_3 = \eta(\mu-\lambda)(\mu+m) + (1-f_v)\lambda\eta m = \frac{\mu m(f_v-1)}{mf_v+\mu}\eta(\mu+m) +$$
$$(1-f_v)\lambda\eta m = (1-f_v)(\lambda\eta m - \mu\eta m(\mu+m)\frac{1}{mf_v+\mu})$$
$$= \frac{1-f_v}{mf_v+\mu}\big(\lambda\eta m(mf_v+\mu) - \mu\eta m(\mu+m)\big)$$
$$> \frac{1-f_v}{mf_v+\mu}\Big(m^2\mu\eta + m\lambda\mu\eta - \mu\eta m(\mu+m)\Big) > 0.$$

In the theorem we assume that $\eta + mf_v > m$.
We can see easily that

$$2\mu + m + \eta - \lambda > (1-f_v)\lambda, \qquad (1)$$

also

$$(1-f_v)\mu(\mu+m+\eta) < (mf_v+\mu)\eta.$$

So

$$(1-f_v)\frac{\mu(\mu+m)}{mf_v+\mu}(\mu+m+\eta) < \eta(\mu+m),$$

and

$$(1-f_v)\lambda(\mu+m+\eta) < \eta(\mu+m).$$

Thus

$$(1-f_v)\lambda(\mu-\lambda)(\mu+m+\eta) > \eta(\mu+m)(\mu-\lambda) \qquad (2)$$

and

$$b_1b_2 = (2\mu+m+\eta-\lambda)\big((\mu-\lambda)(\mu+m+\eta) + \eta(\mu+m)\big)by(1)$$
$$> (1-f_v)\lambda\big((\mu-\lambda)(\mu+m+\eta) + \eta(\mu+m)\big) = (1-f_v)\lambda m\eta + (1-f_v)\lambda\big((\mu-\lambda)(\mu+m+\eta) + \mu\eta\big) > (1-f_v)\lambda m\eta + (1-f_v)\lambda(\mu-\lambda)(\mu+m+\eta)by(2)$$
$$> (1-f_v)\lambda m\eta + \eta(\mu-\lambda)(\mu+m) = b_3.$$

By Hurwitz criterion([2], [7]. [6] and [8]) the disease free equilibrium point Q_1 is asymptotically stable.

4 ENDEMIC EQUILIBRIUM POINTS

To calculate the endemic equilibrium Q_*=(S_*, E_*,I_*,V_*,N_*).We solve

$$-\beta S_*I_* + \lambda N_* - (\mu+m)S_* = 0;$$
$$\beta S_*I_* - \alpha E_* - (1-\alpha)kE_* - \mu E_* = 0;$$
$$(1-\alpha)kE_* - (\gamma+\mu)I_* + \beta\sigma I_*V_* = 0;$$
$$\alpha E_* + mS_* - \beta\sigma I_*V_* - \eta V_* = 0;$$

and

$$-(1-f)\gamma I_* - (1-f_v)\eta V_* + \lambda N_* - \mu N_* = 0.$$

We have

$$S_* = \frac{\lambda N_*}{\mu+m+\beta I_*} \qquad (3),$$

$$E_* = \frac{\beta I_*}{\alpha+(1-\alpha)k+\mu}\frac{\lambda N_*}{\mu+m+\beta I_*} \qquad (4),$$

$$V_* = \frac{\mu+\gamma}{\sigma\beta} - \frac{(1-\alpha)k\lambda N_*}{\sigma(\alpha+(1-\alpha)k+\mu(\mu+m+\beta I_*)} \quad (5),$$

and

$$N_* = \frac{((\mu+\gamma)(\sigma\beta I_*+\eta)\sigma(\alpha+(1-\alpha)k+\mu)}{m\sigma(\alpha+(1-\alpha)k+\mu)+\eta(1-\alpha)k+(\alpha+(1-\alpha)k)\beta\sigma I_*}\frac{\mu+m+\beta I_*}{\lambda\sigma\beta} = \frac{1}{\lambda-\mu}((1-f)\gamma I_* + (1-f_v)\eta V_{*)}. \quad (6)$$

If $\lambda - \mu < 0$ then $N_* < 0$.So there is no equilibrium point. So we suppose that $\lambda - \mu > 0$ and I_* satisfies

$$AI_*^2 + BI_* + C = 0 \quad (7),$$

where

and

$$-\frac{\eta(\mu+m)(\mu+\gamma)(\alpha+(1-\alpha)k+\mu)}{\lambda\beta} + \frac{1}{(\lambda-\mu)\sigma\beta}(1-f_v)$$
$$\eta^2(1-\alpha)k(\mu+\gamma).$$

Moreover I_* is the positive solution of Eq.(4.5).
A little bit calculation on (4.5) implies that:
If we consider $2\mu + m - \lambda > 0, then C > 0$,
If $\lambda f > \mu$, then $A < 0$.So (4.5) has a unique positive solution.
If $\lambda f < \mu$, then $A > 0$, and we have the following three cases:
i. If $B < -2\sqrt{AC}$ then (4.5) has two different positive solutions.
ii. If $B = -2\sqrt{AC}$ then (4.5) has a unique positive solution $I_* = \frac{-B}{2A}$.

iii. If $B > -2\sqrt{AC}$ then(4.50 has no positive solution.
Remark 4.1. System (1.1) has a bifurcation at $B^2 = 4AC$ if and only if $\lambda < \mu$.
Theorem 3. If $\beta S_* > 1$ and $N_* < \frac{1}{\lambda+\gamma-m}$ then Q_* is asymptotically stable.

Proof. We define a Lyapunov function L= $\frac{S}{I}$[2]. It is easy to verify that L $(Q_*) > 0$. We suppose that U is a neighborhood of Q_* such that

$$U = \left\{(S,E,I,V,N): \beta S > 1, N < \frac{1}{\lambda+\gamma-m}\right\}.$$

So

$$\dot{L} = \frac{\dot{S}I - I\dot{S}}{I^2} = \frac{1}{I^2}\left[(-\beta SI + \lambda N - (\mu+m)S)I - \left((1-\alpha)kE - (\mu+\gamma)I + \beta\sigma IV\right)S\right] \leq$$
$$\frac{1}{I^2}(-\beta SI^2 - \beta\sigma SIV + \lambda NI + (\gamma-m)SI)$$
$$= \frac{1}{I}(-\beta S(I+\sigma V) + \lambda N + (\gamma-m)S)$$
$$\leq \frac{1}{I}(-\beta S + \lambda N + (\gamma-m)S)$$
$$\leq \frac{1}{I}(-\beta S + (\lambda+\gamma-m)N) \leq \frac{1}{I}(-\beta S + 1) < 0.$$

Thus $\dot{L}$(Q)<0 for all Q∈ U. So Q_* is asymptotically stable.□

5 ANOTHER EQUILIBRIUM POINT FOR HBV

In this section we show that there is another equilibrium point for (1.1). For this purpose we assumethat there are no disease deaths i.e. f=f_v =1. Thus $\lambda = \mu$, so the birth rate and natural mortality rate are equal. Thus we find the equilibrium point $Q_* = (S_*, E_*, I_*, V_*, N_*)$ where S_*, E_*, V_* and N_* are the same as the pervious section. And I_* is the positive solution of the equation

$$AI_*^2 + BI_* + C = 0,$$

where

$$A = \frac{-\sigma\beta(\lambda+\gamma)(\alpha+(1-\alpha)k+\lambda)}{\lambda}, B = \frac{-\eta(\alpha+(1-\alpha)k+\lambda)(\lambda+\gamma)}{\lambda}, and C = \frac{-\eta(\lambda+m)(\lambda+\gamma)(\alpha+(1-\alpha)k+\lambda)}{\lambda\beta}.$$

If $\eta > 4\sigma(\lambda+m)$ then there is only one positive solution I_*.
To mention the final result of this paper we need the following theorem of[9].

Theorem 4. Let A be an n×n matrix with real entries. For A to be stable, it is necessary and sufficient that
i. the second compound matrix $A^{[2]}$ of A is stable;
ii.$(-1)^n det\ (A) > 0$.
Theorem 5. The equilibrium point Q_* is not asymptotically stable.
Proof . Linearization of the system (1.1) at the equilibrium point Q* is

$$\begin{pmatrix} -(\beta S_*\mu + m) & 0 & -\beta S_* & 0 & \lambda \\ \beta I_* & A & \beta S_* & 0 & 0 \\ 0 & (1-\alpha)k & B & \beta\sigma I_* & 0 \\ m & \alpha & -\sigma\beta V_* - \eta & 0 & \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

where $A = -(\alpha + (1-\alpha)k + \mu)$ and $B = -(\mu + \gamma) + \beta\sigma V_*$.
So det J= 0.Thus theorem 4 implies $Q_* is$ not asymptotically stable
In another case if $V_* = 0$ then

$$\frac{\lambda N}{\mu+m+\beta I} = \frac{(\mu+\gamma)(\alpha+(1-\alpha)k+\mu)}{\beta(1-\alpha)k} =$$
$$\frac{1}{\beta}\frac{(\mu+\gamma)(\eta+\beta\sigma I)(\alpha+(1-\alpha)k+\mu)}{m\sigma(\alpha+(1-\alpha)k+\mu)+\eta(1-\alpha)k+(\alpha+(1-\alpha)k)\beta\sigma I}.$$

So

$$I_* = \frac{-m\sigma(\alpha + (1-\alpha)k + \mu)}{\alpha\beta\sigma} < 0$$

Since I_* can not be negative then in this case there is no equilibrium point .

CONCLUSION

In this paper we present a model for HBV, which contains vaccination and exposed period. The consideration of this model from dynamical point of view can be atopic future research.

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