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On Modeling Hepatitis B Transmission Using Cellular Automata

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Hepatitis B transmission is shown to be difficult to model using differential equations, but easily modeled using cellular automata.

KEY WORDS: Hepatitis B; cellular automata; globally stable.

1. INTRODUCTION

Hepatitis B is an important disease in many countries.[1] It has the property that persons who contract it divide into a small ($\cong 5\%$ of infectives) core (carrier) group which are asymptomatic and are infective for the rest of their lives but with low infectivity. The rest of the infected have much shorter period during which they are infective (typically 20 days) yet they have a much higher (typically an order of magnitude) infectivity. Then they get long term (not necessarily life long) immunity.

Modelling HB transmission requires combining both groups with their varied time scales of infectivity. This makes it difficult to use differential equations[2, 3] to model the real problem. A possible approximation is to neglect the difference in time scales and average transmission rates for both groups (approximately 5:1 for the core group[1] since the duration of the infectivity is included). This will be done in Section 2. A more realistic approach is to include this time difference explicitly. In Section 3 this will be made using the powerful tool of cellular automata.[4–6]

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2. A DIFFERENTIAL EQUATION MODEL

Denote the susceptibles of the core group by S_1, the infectives by I_1 and the corresponding cases for the non-core group by S_2, I_2 respectively. Since HB is fatal to significant number of the core group also it is important to include newly born children, the total number of population is not conserved. Motivated by the work of Brauer *et al.*[3] the following model is proposed:

$$\begin{aligned}
\dot{S}_1 &= rS_2 - a_1 S_1[I_1 P_1 + (1-P_1) I_2] \\
\dot{I}_1 &= a_1 S_1[I_1 P_1 + (1-P_1) I_2] - \sigma I_1 \\
\dot{S}_2 &= -rS_2 - a_2 S_2[(1-P_2) I_1 + P_2 I_2] + \alpha \\
\dot{I}_2 &= a_2 S_2[(1-P_2) I_1 + P_2 I_2] - \gamma I_2
\end{aligned} \tag{1}$$

Where a dot means differentiation with respect to time. The assumptions of the model are:

(1) Susceptibles are recruited from non-core into core groups at a rate r.

(2) There is probability P_1 (P_2) that a core (non-core) infected will transmit the disease to a core (non-core) susceptible.

(3) The core infected persons are removed (by death or recovery) at rate σ. Non-core ones recover at rate fly and become immune.

(4) There is a rate α of new non-core susceptibles.

(5) The mixing between all susceptibles and infected is homogenous.

Since the average transmission rate, (including the infectivity duration) in developing countries, for core group is much higher than that of non-core group it is assumed that

$$a_1 > a_2, \qquad P_1 = 1, \qquad P_2 = 0 \tag{2}$$

Hence the model becomes

$$\begin{aligned}
\dot{S}_1 &= rS_2 - a_1 S_1 I_1 \\
\dot{I}_1 &= a_1 S_1 I_1 - \sigma I_1 \\
\dot{S}_2 &= -rS_2 - a_2 S_2 I_2 + \alpha \\
\dot{I}_2 &= a_2 S_2 I_2 - \gamma I_2
\end{aligned} \tag{3}$$

The unique steady state is given by

$$S_1 = \sigma a_1, \qquad S_2 = \sigma I_1 / r, \qquad I_2 = a_2 \sigma I_1^2 / (r\gamma)$$
$$I_1 = \tfrac{1}{2}\{ -r/a_2 + \sqrt{(r/a_2)^2 + 4\alpha r/\sigma a_2}\} \tag{4}$$

the characteristic polynomial of the steady state (4) is given by

$$\lambda^3 + \lambda^2[r + (a_1 + a_2) I_1] + \lambda a_1 I_1[\sigma + r + a_2 I_1] + \sigma a_1 I_1[r + 2a_2 I_1] = 0 \tag{5}$$

Using Routh-Horowitz criteria,[2] all the roots of this polynomial have negative real parts hence we conclude

Proposition. The system (3) has a unique steady state (4) which is asymptotically (hence globally) stable.

Although this model is an approximation to the real situation it has some interesting consequences: The disease is expected to be endemic (i.e., remain for long time) since both I_1, I_2 are nonzero. Vaccination is expected to reduce the number of possible susceptibles. But as (4) shows that eradication of the disease requires $\alpha \to 0$, i.e., most individuals who are susceptible to become core have to be protected. This agrees with that of ref. 1. It also indicates that it may be difficult to eradicate HB.

3. CELLULAR AUTOMATA MODEL FOR HB

A way to include the short range character of HB disease transmission is to model it on a lattice.[4] Each site i has a state we denote it by (1) to represent susceptible, (2) to represent infective, (3) to represent carrier (core) and (4) to represent immune. Rules are put to represent the spread of the HB disease. Two phases appear, in the first the disease does not spread and in the second it does.

Our Models will be formulated in terms of cellular automata[4–6] defined as follows: Let $G = (V, E)$ be a graph, $V(E)$ is the set of vertices (edges) of G. An automata network is a triplet $\{G, Q, F\}$ where Q is the set of states of the sites (vertices) of G. F is the set of transition rules e.g., $\forall$ vertex i, F_i: $QU_i \to Q$ define the state of i according to the states of the sites in the neighborhood of U_i of i. The mathematical properties of cellular automata have been studied in ref. 7.

Using the language of DP[5] the model is $1+1$ (1-space + 1-time) dimensions. The lattice (spatial) dimension is $N = 300$ and $t = 5000$. There are two parameters P_1, P_2 where P_1 is the probability of infection and P_2 is the probability that a carrier becomes noninfective (e.g., cured or vaccinated etc.).

In the previous section the following approximations have been made: First the difference of infectivity time is neglected. Second, the loss of immunity after infection in non-core groups has been neglected. Third, homogeneous mixing between susceptibles and infected is assumed. Cellular automata (CA) helps us to improve on these approximations. It is a discrete dynamical system in both time and scale. We take each time step to be equal to the typical infectivity period of a non-core infected (($\cong 20$ days).

Thus non-core infected survive only for one time step then they change their state into immune. Only new non-core infected will exist in the following time step. On the other hand core infected continue to accumulate and only change their state to immune with probability P_2. Thus the first approximation has been avoided. We also assume that immune can be susceptible with fixed probability (say 2%). This rectifies the second approximation. Finally it is assumed that a susceptible becomes infected with probability P_1. This avoids the homogeneity assumption.

Therefore the following rules are proposed as HBCA rules: The state $S(i)$ is assigned to each vertex i at time t. $S(i)=1$ for susceptible, $S(i)=2$ for infective, $S(i)=3$ for carrier and $S(i)=4$ for Immune (recovered). The automata rules are:

(i) If $S(i)=1$ and $(S(i\pm 1)=2$ or $S(i\pm 1)=3)$ then $S1(i)$ will be infected (i.e., $S1(i)$ will be 2 or 3) with probability p_1 else $S1(i)=1$. If $S1(i)$ is infected then $S1(i)=2$ with probability.95 else $S1(i)=3$.

(ii) If $S(i)=2$ then $S1(i)=4$.

(iii) If $S(i)=3$ then $S1(i)=3$ with probability p_1 else $S1(i)=4$.

(iv) If $S(i)=4$ then$S1(i)=1$ with probability 0.02, where $S(i\pm 1)=k$ means that at least one of the two neighbours must be $k(k=2, 3)$ and $S1(i)$ is the state at the ith site at time $t+l$.

The phase space is shown in Fig. 1. In our simulations we take $N=300$ and $t=5000$.

In Fig. 1 region I (II) is the one in which the disease does not (does) spread. It is clear that, according to this model, HB will not spread if the probability p_2 that the carrier is cured is $p_2<0.986$. This shows that carriers play a crucial role in HB spread. Hence its eradication requires that carriers should be treated. Also vaccination policies should be designed to reduce the number of potential carriers. Since it is known[1] that early infection increases the possibility of being a carrier, universal child vaccination should be administered. Furthermore targetted adult vaccination should be made to specific groups with high transmission rates e.g., drug addicts (sharing needles) and homosexuals. Also due to the long time for the carrier state one should not expect to observe drastic reduction

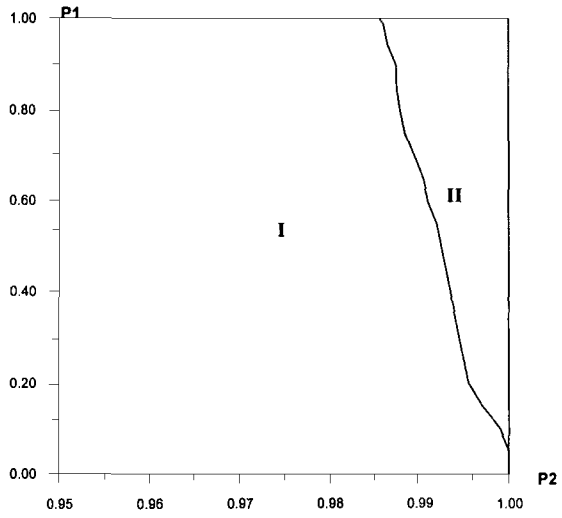

Fig. 1. Region I the disease will not spread. In region II it will spread.

of HB infective shortly after vaccination programs start. It may take 2–4 decades till their effect becomes tangible.

It is interesting that using mathematical models as a guide to vaccination strategies is gaining increasing support from the specialists.[8]

Finally we like to comment on the relation between epidemic models and contact processes.[9, 10] In the standard one dimensional contact process each site has two possible states e. g. $\{0, 1\}$. The evolution rules are:

(i) If $S(t, i) = 0$ (i.e., empty) and at least one of its neighbours is occupied, then $S(t + l, i) = 1$ with probability p_1.

(ii) If $S(t, i) = 1$, then $S(t + l, i) = 0$ with probability p_2.

This model is equivalent to susceptible-infected (SI) model. It is not clear to us how to contact processes can accommodate some epidemic features e.g., carriers, incubation etc.

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