BU-1193-M

Models for Sexually Transmitted Diseases with Recruitment

S. P. Blythe
Department of Statistics and Modelling Science
Strathclyde University
Glasgow G11XH, Scotland

F. Brauer
Department of Mathematics
University of Wisconsin
Madison, Wis. 53706, USA

C. Castillo-Chavez
Biometrics Unit
Cornell University
Ithaca, NY 14853

J. X. Velasco-Hernandez
Departmento El Hombre y su Ambiente
Universidad Autonoma Metropolitana Xochimilco
Mexico City, D.F., Mexico

Abstract

Models are formulated for the spread of a sexually transmitted disease in a core population of sexually very active members who are recruited from a larger meta-population of less sexually active individuals. The recruitment rate is assumed to depend on the perceived prevalence of disease in the core population. Two different situations are considered. One is for a fatal disease (such as AIDS) with homosexual transmission, a one-sex model for which some results are outlined. The second is for a disease with recovery (such as gonorrhea) with heterosexual transmission, a two-sex model for which some preliminary partial results are obtained.

Key words: Sexually transmitted diseases, recruitment models
1991 Mathematics Subject Classification 92D30

1. Introduction

In sexually transmitted diseases there is good indication that the core group consisting of the most sexually-active members of the population is responsible for most cases of the disease [Hethcote & Yorke (1984)]. Members may enter this core group from the population at large, and the rate of entrance into (or departure from) the core group should be included in an attempt to model the incidence of disease in the core group.

We shall study the spread of sexually transmitted disease in a core population, viewing recruitment into the core population as a demographic process. We consider both a one-sex model, as would be natural in studying homosexual transmission of HIV/AIDS, and a two-sex model, as would be natural in studying heterosexual transmission of gonorrhea. The main difference between one-sex and two-sex models is in the mixing of members to produce transmission of disease. Analytically, the main difference is that twice as many variables are needed for a two-sex model.

The new ingredient which we are introducing is the incorporation into the model of recruitment rates which depend on the perceived state of the disease. In particular, we consider the possibility that the recruitment rate could be a decreasing function either of the size of the infective population or of the fraction of the core population which is infective. We shall see that this may produce an unstable endemic equilibrium with sustained oscillations, a situation which can not arise if the recruitment is not dependent on the disease state.

As our results for the one-sex model will appear elsewhere [Blythe, Brauer, & Castillo-Chavez, to appear], we give only a description of the model and a statement of the results. Our analysis of the two-sex model is preliminary, and includes a formulation of the model with a partial analysis of a special case. We propose to carry on the analysis elsewhere.

We consider only models with constant natural death rates and constant recovery or disease-related death rates, producing systems of ordinary differential equations. More general transition rates would lead to differential-difference equation or Volterra equation models.

2. Single-sex models

We consider a core population of sexually very active individuals having total population size N. At time t there are $S(t)$ members susceptible to a sexually transmitted disease and $I(t)$ members who have been infected by the disease in the core group, $N = S + I$. The population dynamics are described by the model

$$\frac{dS}{dt} = g(S,I) - \mu S - \hat{C}(N)SI \tag{1}$$

$$\frac{dI}{dt} = \hat{C}(N)SI - (\mu + \sigma)I.$$

In this model, $g(S, I)$ represents the net rate at which members are recruited into the susceptible class of the core population from a larger meta-population. It is assumed that the effects of the infection within the population do not influence the demographic processes in the meta-population but that they may influence the recruitment rate $g(S, I)$. It is reasonable to assume that

$$g_I(S, I) \leq 0.$$

Two cases of particular interest are

(i) The recruitment rate depends only on the size of the infective class,

$$g(S, I) = G_1(I), \quad G_1'(I) \leq 0. \tag{2}$$

(ii) The recruitment rate is a function of the fraction of the core population which is infective,

$$g(S, I) = G_2\left(\frac{I}{S+I}\right), \quad G_2'\left(\frac{I}{S+I}\right) \leq 0. \tag{3}$$

We also require

$$g(0, I) \geq 0$$

as departure from the population is impossible if there are no susceptibles. We assume that the population has a carrying capacity K in the absence of disease, so that

$$g(K, 0) = \mu K, g_s(K, 0) < \mu.$$

The constants μ and σ are respectively the per capita death rate in each class from causes other than the disease and the per capita rate of departure from the infective class either through death from the disease or through recovery from the disease and transition out of the core population. For a disease such as HIV/AIDS, the term σI represents not recovery but transition from the infective (HIV positive) class to the class of those with AIDS symptoms, who are assumed to be sexually inactive. As our model includes neither a removed class in the core population nor a return from the infective class to the susceptible class, we are essentially restricted to a universally fatal disease such as HIV/AIDS. We could modify the model to apply to a disease such as gonorrhea by including an internal recruitment term in the equation for S. In the next section we shall describe a two-sex model of this type.

We assume in (1) that $C(N)$ is the number of contacts per infective in unit time and

$$\hat{C}(N) = \frac{C(N)}{N};$$

thus the number of contacts per infective in unit time is a function of total population size N and the number of new infections in unit time is $\hat{C}(N)SI$. It is reasonable to assume

$$C(N) \geq 0, C'(N) \geq 0, \hat{C}'(N) \leq 0 \tag{4}$$

for $N > 0$ [Brauer (1990), Castillo-Chavez et al 1989 a,b,c]. We define the constant

$$\beta = \hat{C}(K).$$

The model (1) has been analyzed elsewhere [Blythe, et al, to appear], and here we shall only state the basic results: There is always a disease-free equilibrium $(K, 0)$ which is asymptotically stable if the basic reproductive number

$$R_0 = \frac{\beta K}{\sigma + \mu}$$

is less than 1 and unstable if $R_0 > 1$. If $R_0 > 1$ there is at least one endemic equilibrium. If

$$[\hat{C}(N) + S\hat{C}'(N)][\sigma + \mu - g_I(S, I)] + S\hat{C}'(N)[g_s(S, I) - \mu] \geq 0$$

at all points (S, I) with $g(S, I) = \mu N + \sigma I$, which is satisfied at least in the special cases (2) and (3), the endemic equilibrium (S, I) is unique, and it is asymptotically stable if and only if

$$g_s(S, I) < \mu + \hat{C}(N)I. \tag{5}$$

In the special case (2), the condition (5) is always satisfied and thus there is a unique endemic equilibrium which is asymptotically stable. In the special case (3), instability and sustained oscillations around the endemic equilibrium are possible.

The model (1) is not appropriate for a disease such as gonorrhea, where infectives recover and presumably return to the susceptible class in the core population. While we could modify the model (1) to allow for this, we prefer to formulate a two-sex demographic recruitment model of this type.

3. A general two-sex model

We now consider a core population of sexually very active individuals having total population size $N = N_f + N_m$, where N_f is the total female population size and N_m is the total male population size. At time t there are $S_f(t)$ female and $S_m(t)$ male members susceptible to a disease transmitted by heterosexual contact and $I_f(t)$ female and $I_m(t)$ male members who have been infected by the disease. We assume that there are recruitment functions $g_f(S_f, I_f)$ for females and $g_m(S_m, I_m)$ for males with

$$\frac{\partial g_f}{\partial I_f}(S_f, I_f) \leq 0, \frac{\partial g_m}{\partial I_m}(S_m, I_m) \leq 0.$$

Let μ and σ be constants representing respectively the per capita death rate in each class from causes other than the disease and the per capita rate of recovery from infection and return to the susceptible class.

Let C_m denote the number of contacts per male in unit time and C_f the number of contacts per female in unit time. We assume that the ratio C_m/N_f is a function $\hat{C}_m$ of the total female population size and that the ratio C_f/N_m is a function $\hat{C}_f$ of the total male population size. Then the balance relation between male and female contacts [Castillo-Chavez & Busenberg (1991)] requires that

$$N_m C_m = N_f C_f$$

or

$$\hat{C}_m(N_f) = C_m/N_f = C_f/N_m = \hat{C}_f(N_m). \tag{6}$$

In analogy with (4), we assume

$$\hat{C}'_m(N_f) \leq 0, \hat{C}'_f(N_m) \leq 0$$

We now have, as a basic two-sex model for a disease (like gonorrhea) with recovery without immunity and return to the susceptible class, the four-dimensional system.

$$\begin{aligned}
S'_f &= g_f(S_f, I_f) - \mu S_f + \sigma I_f - \hat{C}_m(N_f) S_f I_m \\
I'_f &= \hat{C}_m(N_f) S_f I_m - (\mu + \sigma) I_f \\
N'_f &= g_f(S_f, I_f) - \mu N_f \\
S'_m &= g_m(S_m, I_m) - \mu S_m + \sigma I_m - \hat{C}_f(N_m) S_m I_f \\
I'_m &= \hat{C}_f(N_m) S_m I_f - (\mu + \sigma) I_m \\
N'_m &= g_m(S_m, I_m) - \mu N_m.
\end{aligned} \tag{7}$$

It is convenient to use I_f, N_f, I_m, N_m as variables and to replace S_f and S_m by $N_f - I_f, N_m - I_m$ respectively.

The conditions for an equilibrium of (7) are

$$\hat{C}_m(N_f) S_f I_m = (\mu + \sigma) I_f, g_f(S_f, I_f) = \mu N_f) \tag{8}$$

$$\hat{C}_f(N_m) S_m I_f = (\mu + \sigma) I_m, g_m(S_m, I_m) = \mu N_m.$$

Because of (6), these imply

$$S_f I_m^2 = S_m I_f^2 \tag{9}$$

The coefficient matrix of the linearization of (7) at an equilibrium (I_f, N_f, I_m, N_m) is

$$\begin{bmatrix} -I_m\hat{C}_m(N_f) - (\mu+\gamma) & I_m\{\hat{C}_m(N_f) + S_f\hat{C}'_m(N_f)\} & S_f\hat{C}_m(N_f) & 0 \\ -\frac{\partial g_f}{\partial S_f} + \frac{\partial g_f}{\partial I_f} & \frac{\partial g_f}{\partial S_f} - \mu & 0 & 0 \\ S_m\hat{C}_f(N_m) & 0 & -I_f\hat{C}_f(N_m) - (\mu+\gamma) & I_f\{\hat{C}_f(N_m) + S_m\hat{C}'_f(N_m)\} \\ 0 & 0 & -\frac{\partial g_m}{\partial S_m} + \frac{\partial g_m}{\partial I_n} & \frac{\partial g_m}{S_m} - \mu \end{bmatrix} \tag{10}$$

If $I_f = 0$ at an equilibrium, then $N_f = S_f$, $g_f(N_f, 0) = \mu N_f$ and this implies $S_f = N_f = K_f$, the female carrying capacity. It follows from (9) that $I_m = 0$ and then $S_m = N_m = K_m$, the male carrying capacity. At the disease-free equilibrium, the coefficient matrix is

$$\begin{bmatrix} -(\mu+\sigma) & 0 & \beta K_f & 0 \\ -\frac{\partial g_f}{\partial S_f} & \frac{\partial g_f}{\partial S_f} - \mu & 0 & 0 \\ \beta K_m & 0 & -(\mu+\sigma) & 0 \\ 0 & 0 - \frac{\partial g_m}{\partial S_m} + \frac{\partial g_m}{\partial I_m} & \frac{\partial g_m}{\partial S_m} - \mu & \end{bmatrix}$$

where

$$\beta = \hat{C}_m(K_f) = \hat{C}_f(K_m).$$

In view of the carrying capacity conditions

$$\frac{\partial g_f}{\partial S_f}(K_f, 0) < \mu, \frac{\partial g_m}{\partial S_m}(K_m, 0) < \mu.$$

The condition that the characteristic equation's roots have negative real parts reduces to the condition that the roots of

$$\begin{bmatrix} \lambda+\mu+\sigma & -\beta K_f \\ -\beta K_m & \lambda+\mu+\sigma \end{bmatrix}$$

have negative real part. This equation is

$$(\lambda+\mu+\sigma)^2 - \beta^2 K_f K_m = 0,$$

$$\lambda^2 + 2(\mu+\sigma)\lambda + [(\mu+\sigma)^2 - \beta^2 K_f K_m] = 0$$

and the stability conditions are $\mu + \sigma > 0$, which is satisfied automatically, and

$$(\mu + \sigma)^2 - \beta^2 K_f K_m > 0,$$

or

$$R_0 = \frac{\beta\sqrt{K_f K_m}}{\mu + \sigma} < 1.$$

At an endemic equilibrium, with $I_f > 0$, $I_m > 0$, it follows from (8) that

$$\hat{C}_f(N_m)\hat{C}_m(N_f)S_f S_m = (\mu + \sigma)^2,$$

$$C_f(N_m)C_m(N_f)S_f S_m = (\mu + \sigma)^2 N_m N_f.$$

Under the assumption that $C_f(N_m)$ and $C_m(N_f)$ are increasing functions, in analogy with (4),

$$C_f(N_m) \leq C_f(K_m) = \beta K_m, C_m(N_f) \leq \beta K_f$$

and thus

$$(\mu + \sigma)^2 \leq \beta^2 K_m K_f \cdot \frac{S_f}{N_f} \cdot \frac{S_m}{N_m} \leq \beta^2 K_m K_f.$$

Therefore an endemic equilibrium can exist only if $R_0 > 1$, and the disease-free equilibrium is unstable.

From (10) we see that the characteristic equation at an endemic equilibrium is a fourth degree polynomial equation. The coefficients in this equation are sufficiently complicated to make this equation intractable in general. In the next section we shall consider a special case of the model for which some stabililty analysis is possible.

The model (7) is not restricted to sexually transmitted diseases. Instead of viewing it as a two-sex model, we could consider it as a two-special model for a disease with vector transmission. For this purpose, the functions g_f and g_m represent birth rates rather than recruitment rates, and the transition rates μ and σ should not be the same for both species. In addition, the relation between C_m and C_f is not symmetric. If males correspond to hosts and females correspond to vectors, the females determine the rate of contact and we would view (6) as expressing C_m in terms of C_f, so that C_m can be eliminated.

We shall explore models for vector-transmitted diseases elsewhere. In such models the parasite time scale may be much faster than the host time scale, and it might be reasonable to approximate by a reduced model with only one time scale.

Symmetric two-sex models

Because of the difficulties in analyzing the model (7), we shall specialize in two ways. As the specializations assume a symmetry between the two sexes, they are quite inappropriate for vector-transmitted disease models

(i) We assume proportional mixing

$$C_m = \beta N_f, C_f = \beta N_m \tag{11}$$

These forms satisfy the balance law (6) and they imply

$$\hat{C}_m(N_f) = \hat{C}_f(N_m) = \beta, \hat{C}'_m(N_f) = \hat{C}'_f(N_n) = 0.$$

(ii) We assume that the recruitment function is the same for both sexes, that is, that there is a function g of two variables such that

$$g_f(S_f, I_f) = g(S_f, I_f), g_m(S_m, I_m) = g(S_m, I_m). \tag{12}$$

Then the male and female carrying capacities K_m and K_f are equal,

$$K_m = K_f = K.$$

We define a symmetric equilibrium of (7) to be an equilibrium with $S_f = S_m$, $I_f = I_m$. We see from (7) that a symmetric equilibrium (S, I) is an intersection of the vertical line $\beta S = \mu + \sigma$ with the curve $g(S, I) = \mu(S + I)$ running from a point on the I-axis in the $S - I$ plane to the point $(K, 0)$. Thus under the assumptions (11), (12), the system (7) has a unique endemic equilibrium if the contact number, which is now given by

$$R_0 = \frac{\beta K}{\mu + \sigma}$$

exceeds 1.

If (7) has a non-symmetric equilibrium, say with $S_f < S_m$, since (8) implies that

$$S_f S_m = \left(\frac{\mu + \sigma}{\beta}\right)^2,$$

we have

$$S_f < \frac{\mu + \sigma}{\beta} < S_m.$$

Then, again from (8),

$$(\mu + \sigma) I_f = \beta S_f I_m < (\mu + \sigma) I_m,$$

so that $I_f < I_m$; it follows that $N_f < N_m$. In the special case $g(S,I) = G_1(I)$, we obtain a contradiction since

$$\mu N_f = G_1(I_f) \geq G_1(I_m) = \mu N_m.$$

Thus in the special case (2) there can not be a non-symmetric equilibrium. However, in general, non-symmetric equilibria can occur. In particular, it is possible to construct examples with

$$g(S,I) = G_2\left(\frac{I}{S+I}\right)$$

which have non-symmetric equilibria.

Under the hypotheses (11) and (12), the coefficient matrix of the linearization at an endemic equilibrium (I_f, T_f, I_m, T_m) is

$$\begin{bmatrix} -\beta I_m - (\mu+\gamma) & \beta I_m & \beta S_f & O \\ -\frac{\partial g}{\partial S} + \frac{\partial g}{\partial I} & \frac{\partial g}{\partial S} - \mu & O & O \\ \beta S_m & 0 & -\beta I_f - (\mu+\gamma) & \beta I_f \\ 0 & 0 & -\frac{\partial g}{\partial S} + \frac{\partial g}{\partial I} & \frac{\partial g}{\partial S} - \mu \end{bmatrix}.$$

The characteristic equation of a symmetric equilibrium $I_f = I_m = I$, $N_f = N_m = N$ is

$$\left(\lambda + \mu - \frac{\partial g}{\partial S}(\lambda + \mu + \sigma + \beta I) + \beta I\left(\frac{\partial g}{\partial S} - \frac{\partial g}{\partial I}\right)\right]^2 - \left[\beta S\left(\lambda + \mu - \frac{\partial g}{\partial S}\right)\right]^2 = O$$

or

$$\left[(\lambda + \mu - \frac{\partial g}{\partial S}(\lambda + \mu + \sigma + \beta I) + \beta I\left(\frac{\partial g}{\partial S} - \frac{\partial g}{\partial I}\right) - \beta S\left(\lambda + \mu - \frac{\partial g}{\partial S}\right)\right].$$

$$\left[\left(\lambda + \mu - \frac{\partial g}{\partial S}\right)(\lambda + \mu + \sigma + \beta I) + \beta I\left(\frac{\partial g}{\partial S} - \frac{\partial g}{\partial I}\right) + \beta S\left(\lambda + \mu - \frac{\partial g}{partial S}\right)\right] = 0.$$

Since this is a product of quadratic factors, we have the necessary and sufficient conditions for asymptotic stability of the endemic equilibrium

$$\mu - \frac{\partial g}{\partial S} + \mu + \sigma + \beta I - \beta S > 0 \tag{13}$$

$$\mu - \frac{\partial g}{\partial S} + \mu + \sigma + \beta I + \beta S > 0 \tag{14}$$

$$\left(\mu - \frac{\partial g}{\partial S}\right)(\mu + \sigma + \beta I) + \beta I\left(\frac{\partial g}{\partial S} - \frac{\partial g}{\partial I}\right) + \beta S\left(\mu - \frac{\partial g}{\partial S}\right) > 0 \tag{15}$$

$$\left(\mu - \frac{\partial g}{\partial S}\right)(\mu + \sigma + \beta I) + \beta I\left(\frac{\partial g}{\partial S} - \frac{\partial g}{\partial I}\right) - \beta S\left(\mu - \frac{\partial g}{\partial S}\right) > 0. \tag{16}$$

The condition (14) is weaker than (13) and may be discarded. Only one of the conditions (15) and (16) is needed. If

$$\frac{\partial g}{\partial S} < \mu \tag{17}$$

the condition (16), along with (13), is necessary and sufficient for asymptotic stability. If

$$\frac{\partial g}{\partial S} > \mu. \tag{18}$$

the conditions (15) and (13) are necessary and sufficient for asymptotic stability.

Because $\beta S = \mu + \sigma$, the condition (13) is equivalent to

$$\frac{\partial g}{\partial S}(S, I) < \mu + \beta I. \tag{19}$$

If (17) holds, then (19) follows and (16) reduces to $\frac{\partial g}{\partial I} < \mu$, a consequence of $g_I(S, I) \leq 0$. Thus the condition (17) by itself implies asymptotic stability. If (18) holds, then (15) reduces to

$$\frac{\partial g}{\partial S} < \mu + \frac{\mu - \frac{\partial g}{\partial I}}{2(\mu + \sigma)}\beta I. \tag{20}$$

The condition (20) is more restrictive than (19) if

$$\frac{\mu - \frac{\partial g}{\partial I}}{2(\mu + \sigma)} < 1,$$

or

$$\frac{\partial g}{\partial I} > -\mu - 2\sigma. \tag{21}$$

Thus stability is implied by the set of conditions (18), (20), (21), and also by the set of conditions (18), (19), and

$$\frac{\partial g}{\partial I} < -\mu - 2\sigma.$$

In the one-sex model, stability of the endemic equilibrium is implied by the single condition (5), analogous to (19). Thus it would appear that the endemic equilibrium is less likely to be stable for a two-sex model than for a one-sex model. This is misleading, because our two-sex model involves recovery and our one-sex model was for a fatal disease, and also because the difference in mixing is a qualitative difference between the two types of models. Some numerical simulations with parameter values similar to those

which produce oscillation in a one-sex model indicate stability; apparently the two-sex model is less likely to generate oscillations than the one-sex model.

5. Conclusions

We have exhibited a new possible cause for oscillations in models for the spread of communicable diseases, namely a recruitment rate into the population under study which depends on the state of the disease. This is of particular importance for sexually transmitted diesases, where much evidence points to the importance of a core population of sexually very active members. There is also ample observed evidence that the perceived state of a sexually transmitted disease is a powerful influence on patterns of sexual behavior, in particular on recruitment into the core population.

Our investigations indicate that much more study of such models is needed to learn about the effectiveness of disease management measures. We have considered only linear death rates and transition rates out of the infective classes, and it is quite possible that more general distributions of infective periods could exhibit more complicated behavior. Another factor which could be important is the possibility that there could be a time-lag between observation disease prevalence and recruitment into the core population.

While our two-sex model results are quite fragmentary, they indicate that one-sex and two-sex models can not be used interchangeably in describing sexually transmitted disease. It is clear that the nature of the mixing process is extremely important in studying sexually transmitted diseases, probably much more important than in the study of other types of disease.

Acknowledgements

This research has been partially supported by NSF grant DEB-9253570 to C C-C. In addition, this research has been partially supported by the Army Research Office through the Mathematical Sciences Institute at Cornell University.

References

S. Blythe, F. Brauer, & C. Castillo-Chavez, (to appear), Demographic recruitment in sexually transmitted disease models, to appear.

F. Brauer (1990), Models for the spread of universally fatal diseases, J. Math. Biology 28, pp. 451-462.

C. Castillo-Chavez & S. Busenberg (1991), On the solution of the two-sex mixing problem, Lecture Notes in Biomathematics 92, Springer-Verlag, (S. Busenberg & M. Martelli, eds.), pp. 50-98.

C. Castilllo, K. L. Cooke, W. Huang & S. A. Levin (1989a), The role of infectious periods in the dynamics of acquired immunodeficiency syndrome (AIDS), Lecture Notes in Biomathematics, 81, Springer-Verlag, (C. Castillo-Chavez, S. A. Levin & C. Shoemaker, eds.), pp. 177-189.

_____ (1989b), The role of long incubation periods in the dynamics of HIV/AIDS, Part 1: Single population models, J. Math. Biology, 27, pp. 373-398.

_____ (1989c), On the role of long incubation periods in the dynamics of HIV/AIDS. Part 2: Multiple group models, Lecture Notes in Biomathematics 83, Springer-Verlag (C. Castillo-Chavez, ed.), pp. 200-217.

H. W. Hethcote & J. A. Yorke (1984), Gonorrhea: Transmission Dynamics and Control, Lecture Notes in Biomathematics 56, Springer-Verlag.