Abstract.

In this note, we report on the formulation and mathematical analysis of single and multiple group models for the spread of the human immuno-deficiency virus (HIV), which is the etiological agent for the acquired immuno deficiency syndrome (AIDS).

Results on the robustness of a single group model are stated for specific and arbitrary survivorship functions. In addition, we provide with the first results that show that multiple group models can have multiple endemic equilibria.

Results on the dynamics for models for the sexual transmission of the human immuno-deficiency virus

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by

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In this note, we report on the formulation and mathematical analysis of single and multiple group models for the sexual spread of the human immuno-deficiency virus (HIV), which is the etiological agent for the acquired immunodeficiency syndrome (AIDS).

First we consider a single sexually active homosexual population, and concentrate on describing the dynamics of AIDS within this sub-population. We further subdivide this sub-population into three groups of active individuals: S(uninfected), I(HIV-infectious), and A(AIDS-infectious). In addition , we make the simplifying (but probably realistic assumption) that A-individuals (i.e. individuals with "full-blown" AIDS) are sexually inactive; consequently, they do not contribute to the dynamics of AIDS.

Λ denotes the"recruitment" rate into S; μ, the natural mortality rate; d, the AIDS-induced mortality; and λ, the transmission rate per infectious partner. More specifically, λ is given by the product of two (assumed) constant parameters: i, the probability of transmission per contact with an infectious individual, and ϕ, the average number of contacts per sexual partner. C(T) denotes the mean number of sexual partners an average individual has per unit time, given that the sexually active population is T (i.e. S + I). In general, C(T) will increase linearly for small T and saturate for large T; we assume only that C(T) is a nondecreasing function of T. The factor I/T denotes the probability that a randomly-selected individual will be infectious. Using these definitions we conclude that for a homogeneously-mixed sexually active population, the incidence rate (i.e. the number of new cases per unit time) is given by $\lambda C(T)SI/T$. We now let P(s) represent the conditional probability that an individual, if still alive, will be infectious s time units after infection. Clearly, P(s) is non-negative and non-increasing; furthermore, P(0) =1, and we

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assume that $\int_0^\infty P(s)\,ds < \infty$. Note that $-P'(x)$ denotes the rate of removal of individuals from group I into group A, x time units after infection.

With these preliminaries, we arrive at the following distributed delay model for the sexual spread of HIV/AIDS:

$$(1) \qquad \frac{dS(t)}{dt} = \Lambda - \lambda C(T(t))S(t)\frac{I(t)}{T(t)} - \mu S(t),$$

$$(2) \qquad I(t) = I_0(t) + \int_0^t \lambda C(T(x))S(x)\frac{I(x)}{T(x)} e^{-\mu(t-x)} P(t-x)\,dx,$$

$$(3) \qquad A(t) = A_0(t) + A_1 e^{-(\mu+d)t} + \int_0^t \{\int_0^\tau \lambda C(T(x))S(x)\frac{I(x)}{T(x)} e^{-\mu(\tau-x)}[-P'(\tau-x)e^{-(\mu+d)(t-\tau)}]dx\}d\tau,$$

where the functions (with compact support) $I_0(t)$, $A_0(t)$, and the constant A_1, are introduced to take care of the initial conditions.

This model is a generalization of those of Anderson et al. (1988), Anderson and May (1987), and Blythe and Anderson (1988). Our single group model results generalize and confirm the local results and numerical simulations done by Blythe and Anderson (1988) for specific forms of P(s) when C(T(t)) is assumed to be constant.

Results for the single group model

For $P(s) = e^{-\alpha s}$ we (Castillo-Chavez et al. 1989a, 1989b) have shown that:

1. The disease-free state $(\frac{\Lambda}{\mu},0)$ is a globally asymptotically stable equilibrium, if and only if, the reproductive number $R \equiv \lambda C(\frac{\Lambda}{\mu})\frac{1}{\mu+\alpha} \leq 1$.

2. If $R > 1$, then there is a unique endemic state, which is a global attractor for all positive solutions.

Thus R plays a fundamental role in the dynamics of the disease, controlling whether or not the disease can be maintained.

We can generalize for an arbitrary P(s) as follows:

3. The infection-free state is a global attractor whenever the reproductive number

$$R = \lambda C(\frac{\Lambda}{\mu}) \int_0^\infty e^{-\mu s} P(s) ds \leq 1.$$

4. If $R > 1$, then the limiting system

$$\frac{dS}{dt} = \Lambda - \lambda C(T(t)) S(t) \frac{W(t)}{T(t)} - \mu S(t) ,$$

$$I(t) = \int_{-\infty}^{t} \lambda C(T(x)) S(x) \frac{W(x)}{T(x)} e^{-\mu (t-x)} P_I(t-x) dx ,$$

has a unique endemic state, which is locally asymptotically stable.

Formulation of the n-group model

The single group models are the most easily obtained. However, as has been observed for other sexually-transmitted diseases, it is key to take into account the heterogeneity of populations with regard to sexual behavior and other characteristics. To this end, we now consider n sexually active sub-populations each divided into three classes S_i, I_i, and A_i. We assume that mixing between groups is proportionate to their sexual activity (i.e. proportionate mixing). Hence, the i^{th}-incidence rate is given by the following expression:

$$B_i(t) = C_i(T(t)) \sum_{j=1}^{n} p_{ij}(t) \lambda_{ij} I_j(t) , \text{ where } p_{ij}(t) = \frac{C_j(T(t)) T_j(t)}{\sum_{k=1}^{n} C_k(T(t)) T_k(t)} ,$$

where $T_k(t) = S_k(t) + I_k(t)$, and where the functions C_i are nondecreasing.

In addition, we rescale the dynamics of transmission by setting $\sigma_i = \frac{1/\mu}{1/\alpha_i}$. With this notation, with definitions analogous to those of our single population model, and with exponential removal (i. e. $P_i(s) = e^{-\alpha_i s}$) , we arrive at the following model $(4,\mu)$:

$$(4.1,\mu) \qquad \frac{dS_i(t)}{dt} = \Lambda_i - (B_i(t) + \mu)S_i(t),$$

$$(4.2,\mu) \qquad \frac{dI_i(t)}{dt} = B_i(t)S_i(t) - \mu(\sigma_i + 1) I_i(t),$$

$$(4.3,\mu) \qquad \frac{dA_i(t)}{dt} = \alpha_i I_i(t) - (d + \mu) A_i(t), \quad i = 1,2,..,n.$$

To describe our results for this model, we now define the probability $\kappa(i,T^*)$ by:

$$\kappa(i, T^*) = \frac{C_i(T^*)\frac{\Lambda_i}{\mu}}{\sum_{k=1}^{n} C_k(T^*)\frac{\Lambda_k}{\mu}}, \text{ where } T^* = \sum_{k=1}^{n}\frac{\Lambda_k}{\mu}, \; i = 1, 2, ...n,$$

and also introduce the matrix, L given by $L = \left[\frac{C_j(T^*)\lambda_{ij}\kappa(i)}{\sigma_i + 1}\right]_{nxn}$, and the function $H(\mu) = L - \mu E$, where E is the nxn identity matrix.

Local stability result for the general n-group model

5. Let $M(H(\mu)) = \sup\{\text{Re } \rho : \det(\rho E - H(\mu)) = 0\}$. Then there is a unique μ_0 such that

$$M(H(\mu)) \begin{cases} < 0 \text{ if } \mu > \mu_0 \\ = 0 \text{ if } \mu = \mu_0 \\ > 0 \text{ if } \mu < \mu_0 \end{cases}.$$

Furthermore the infection-free state $\bar{S} = (\frac{\Lambda_1}{\mu},\ldots,\frac{\Lambda_n}{\mu},0,\ldots,0)$ is locally asymptotically stable provided that $M(H(\mu)) < 0$.

Bifurcation results for the n-group model

Assume that $C_i(T) = c_i$ (a constant), for i = 1,2,..,n; L is irreducible; and μ_0 is such that $M(H(\mu_0)) = 0$. Introduce the expression

$$h(\mu_0) = \sum_{i=1}^{n} \bar{I}_i I_i \sum_{j=1}^{n} (c_i b_{ij} - \mu_0 \sigma_j) I_j,$$

where

$I = (I_1,\ldots,I_n)$ and $\bar{I} = (\bar{I}_1,\ldots,\bar{I}_n)$ are positive eigenvectors of $H(\mu_0)$ and $H^T(\mu_0)$ corresponding to the zero eigenvalue, respectively (T denotes the transpose in this case). The existence of these positive eigenvectors (i.e. all entries are positive) is guaranteed by M-matrix theory. We (Huang et al. 1989a, 1989b) have established the following bifurcation results:

6. If $h(\mu_0) \neq 0$, then μ_0 is a bifurcation point. More specifically, if $h(\mu_0) > 0$ ($h(\mu_0)<0$) then there is an $\epsilon > 0$ and unique continuously differentiable functions S and I mapping $(\mu_0 - \epsilon, \mu_0] \rightarrow R_+^n$ ($[\mu_0, \mu_0 + \epsilon) \rightarrow R_+^n$) such that $(S(\mu_0),I(\mu_0)) = (\frac{\Lambda_1}{\mu},\ldots,\frac{\Lambda_n}{\mu},0,\ldots 0)$ and $(S(\mu),I(\mu))$ is a positive endemic equilibrium of $(4,\mu)$. Furthermore this endemic equilibrium is locally asymptotically stable for each μ in $(\mu_0 - \epsilon, \mu_0)$ (unstable for each μ in $(\mu_0,\mu_0 + \epsilon)$).

7. For each μ in $(0, \mu_0)$, the system $(4,\mu)$ has a positive endemic equilibrium.

8. If $h(\mu_0) < 0$, then there is an $\epsilon > 0$, such that the system $(4,\mu)$ has at least two positive equilibria for each μ in $(\mu_0,\mu_0 + \epsilon)$.

Conclusion

In this note we have stated our analytical results for models of the sexual spread of HIV/AIDS. Our first conclusion is that our single group models are robust, in the sense that only "simple" dynamics are possible. In addition (see Castillo-Chavez et al. 1989a, 1989b) we have shown that the reproductive number is not significantly affected by the shape of the survivorship function, assuming that the function is biologically reasonable. Our second conclusion is that the idea of a reproductive number for a multiple group model is a very elusive one. Furthermore, we see that the "generalized" thinking that S-I-R epidemic models do not have multiple equilibria is not accurate, and hence the possibility for complex dynamics is certainly real. We must add that we have stated our results under the assumption of proportionate mixing. There is now a strong belief that this is not the appropriate form of mixing in which to study the dynamics of HIV/AIDS. Blythe and Castillo-Chavez (1989) recently have formulated a general framework for mixing and have used it to generate more general forms of mixing. We are extending the results of this note to include some these forms. Finally, we note that the above models have assumed that all infectious individuals are equally infectious. We have modified our single group model to include variable infectivity, and it appears that variable infectiousness does not play a significant role in the qualitative dynamics of our single group model (see Castillo-Chavez et al. 1989c), but can significantly affect quantitative values such as the initial rate of spread and the saturation level of cases. The numerical simulations of Hyman and Stanley (1988) show that the transient dynamics for a similar model can be very sensitive to changes in the infectivity.

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