

A Model for HIV in Asia

STAVROS BUSENBERG Mathematics Department, Harvey Mudd College, Claremont, California

KENNETH COOKE Mathematics Department, Pomona College, Claremont, California

AND

YING-HEN HSIEH Department of Applied Mathematics, National Chung-Hsing University, Taichung, Taiwan

Received 20 January 1994; revised 31 August 1994

ABSTRACT

A model is proposed in which the spread of HIV/AIDS in the community is mainly due to the sexual interaction between a core group of female prostitutes and young unmarried males. Several threshold parameters are obtained that determine persistence of endemic proportions, persistence of total population, and the persistence of infective population given the extinction of endemic proportions in a population tending to infinity. Conditions are given for the existence of multiple endemic equilibria as well as the existence of multiple stable equilibria with separatrix and their asymptotic behavior and biological significance are discussed. In all cases, global analysis is accompanied by bifurcation diagrams, and numerical examples are provided for some particular cases of interest. This model was proposed with the recent rapid growth of the HIV/AIDS epidemic in Asia in mind.

1. INTRODUCTION

Transmission of the human immunodeficiency virus (HIV) is continuing in all affected regions, but in south and southeast Asia there appears to be an explosive growth in the prevalence of infection. In 1987, HIV infections among prostitutes in Thailand were rare, but by late 1991 almost 15% nationwide were infected according to Mann [15]. By 1 July, 1991, only 106 AIDS cases had been reported officially in Thailand [6], but the 1992 overall estimate is between 300,000 and 500,000 HIV-infected [18]. As of 1 July, 1991, only 65 AIDS cases had been reported in India [15], but by early 1992 an estimated 1 million people were infected with the virus as reported by Wallace [23]. In all,

MATHEMATICAL BIOSCIENCES 128:185-210 (1995) © Elsevier Science Inc., 1995 655 Avenue of the Americas, New York, NY 10010

0025-5564/95/\$9.50 SSDI 0025-5564(94)00072-8 at least 1-1.5 million Asian adults had been infected by 1992 according to [18]. With the increasing international travel to and from Asia (the second most common destination for travelers from the United Kingdom after sub-Saharan Africa according to Hawkes et al. [9]), it is a situation to be concerned with.

This very rapid spread in Asia is due, at least in part, to the widespread use of prostitutes, or "sex workers" as they are called. In many countries, promiscuous sexual behavior is condoned for men as long as the women are prostitutes. It is said that Bombay, India has more than 200,000 prostitutes, and according to a recent survey as many as 30% are infected [23], and the percentage is growing rapidly (see Figure 2 in [18]). In addition, the blood supply in India is not universally screened for HIV. In Thailand also, prostitution is a central problem, and the government has begun programs to distribute condoms and an education program for boys to dissuade them from visiting prostitutes. Nevertheless, an explosion of HIV infection seems to have been taking shape in the last few years. According to [18], infection levels of 44% were found in female sex workers in the northern part of Thailand. By December 1991, women at antenatal clinics in Thailand were tested HIV positive at a mean rate of 1.0%, blood donors at 1.25%, and military conscripts (men of age 21) at 2.98% nationwide. Although the early spread was mainly in the intravenous drug-using community, today the vast majority of new cases are members of the general population contracting HIV infections through heterosexual intercourse.

It is reported that in these Asian countries, married individuals have relatively few extramarital sexual encounters or divorces. In a 1990 survey of partner relations in Thailand [19], 84.7% of the male respondents currently married reported having no outside sexual encounters in the previous 12 months. As can be expected, the number is much higher for males in the rural regions (88.4%) than in urban areas (73%). The corresponding numbers for female respondents are 99.6%, 99.8%, and 99%, respectively. One should note, however, that cultural norms in Thai society opposing women having premarital or extramarital sex would favor some underreporting. Moreover, the same survey reports that only 12.2% of the married men had paid for sex in that time period while the figures were 35.9% for never-married males and 50% for formerly married men. In a survey of new army recruits involving 21-year-old young men from rural Thailand, 73% said that their first sex experience had been with a sex worker, and virtually all had visited prostitutes by the time they were 21 [23]. Hence the major source of customers of the sex industry in Thailand is the single male population. A 1990 survey [19] also reported that only 5.3% of all respondents were divorced, widowed, or separated.

In this paper we formulate a mathematical model that explicitly takes account of prostitution and demography. To obtain a model that emphasizes these aspects and yet is amenable to mathematical analysis, we make various simplifying assumptions, which are explained below. We explore in a qualitative and quantitative way how prostitution and other factors affect the rate of spread and prevalence levels of infection.

Another model that also includes heterosexual transmission and prostitution is given by Waldstätter [22]. The model in [22] is similar to ours in that it contains a group of prostitutes, a group of single males, a group of single females, and groups of pairs. It contains four kinds of pairs, whereas we have put all those with at least one infected partner into one group. It is more general than ours in that prostitutes can interact with men who are either single or in a couple, and also in allowing break-up of pairs. On the other hand, in [22], when a prostitute retires she is removed completely from the population, whereas in our model she moves to the single female group and may eventually enter a pair. Study [3] has shown that many sex workers in Thailand retire to reintegrate into village society without much difficulty. Also, in [22] recruitment into the core is assumed to be constant rather than proportional to the number of single males as in our model. Waldstätter gives a partial stability analysis of the disease-free equilibrium but no other analysis. He leaves open questions about endemic equilibria or limiting proportions of infectives. Our simplifying assumptions have allowed us to perform a complete analysis of our model.

Our analytical results are formulated in terms of several key quantities, which are combinations of the biological and sociological parameters in the model. Among the more important of the latter are the contact rate of prostitutes (number of sexual contacts per unit time), the immigration and emigration rates among prostitutes, and the transmission probabilities of infection. The combination quantities include the basic reproductive number R_0 , which is often used as a predictor for whether an epidemic can occur or be sustained, but as we shall see there are other important quantities that must be considered.

In Section 2, we formulate the model. In Sections 3 and 4, we describe some mathematical results that have been proved. The proofs themselves are in part put in an Appendix. In Section 5 we include some numerical examples and bifurcation diagrams for some particular cases of interest, and in Section 6 we discuss the biological interpretation of the threshold parameters.

2. THE MODEL

The model considers heterosexual transmission of HIV in a community in which married persons have negligible extramarital affairs and in which almost all premarital sexual activities are between young men and a core group of female prostitutes or "sex workers." The 1990 Partner Relations Survey in Thailand [19] reported that 43.5% of the never married/partnered male respondents had had at least one sexual association in the previous 12 months while 99% of the never married/partnered female respondents had had no sexual association in the previous 12 months, and we note the similarly high percentage for females with no sexual partners other than their spouse. One should note, however, that in a study of sexual networking in Thailand by Napaporn et al. [16], only 37% of the males with multiple partners surveyed had no noncommercial sex partners (other than their spouses), exposing the need for further study on sexual networking in Thai society.

We therefore consider four population groups: the core group, young unmarried males, young unmarried females, and married couples. Within each group, there is a further division into infected and susceptible (noninfected) individuals. Thus we introduce the following symbols.

 F_0 = number of susceptible core females,

 f_0 = number of infective core females,

 M_1 = number of susceptible unmarried young males,

 m_1 = number of infective unmarried young males,

 F_1 = number of susceptible noncore young females,

 f_1 = number of infective noncore young females,

 S_2 = number of couples in which both partners are susceptible,

 I_2 = number of couples in which one or both partners are infective.

The numbers of young males and females refer to those who are sexually active. We make note of the following assumptions, which we make because we wish to focus on the role of prostitution as the primary mode of spread.

Assumptions. Homosexual and drug activity are not included in this model. Sexual contact of single males other than with prostitutes is negligible, since unmarried females who are not in the core have a negligible amount of sexual contact. Individuals in pairs do not have extramarital contacts. There is no break-up of pairs. All *couples* are either susceptible or infective.

 $\alpha^*(M_1 + m_1)$, the rate at which core females are recruited, is assumed to be proportional to the number of young men. α^* , a positive

constant less than 1, is the constant of proportionality at which the core prostitutes are recruited. The "supply and demand" hypothesis is intuitively plausible. It also allows us to obtain a complete analysis of the model that would not have been possible with a constant recruitment rate.

- μ_i and $\overline{\mu}_i$ (*i* = 0, 1, 2), removal rates due to death or removal from the geographic area or withdrawal from sexual activity in various populations. For the sake of brevity, we hereafter refer to this as the rate of removal.
- c_f , the contact rate or number of sexual contacts per unit time for core females.
- c_m , the contact rate or number of sexual contacts per unit time for young males.
- β , the male-to-female transmission probability per sexual contact.
- $\overline{\beta}$, the female-to-male transmission probability per sexual contact.
- $\rho_0, \overline{\rho}_0$, the respective rates at which susceptible and infective core females "retire" and move to the young female population category. A 1992 survey of 1012 commercial sex workers in Thailand [2] reported that the mean age of the commercial sex workers surveyed is 22.4 years, and 54% said they started this profession at age 19 or younger; hence a typical currently working sex worker would have worked approximately 3.5 years. Many of those surveyed responded that after their debt to their employer was paid off, they would like to return home to work on a farm or start their own business in the rural village.
- $\sigma_1, \overline{\sigma}_1$, the pairing rate of susceptible and infective young males who form couples.
- 2b, the per capita rate at which new mature individuals enter the young male and young female groups (births per susceptible couple times the survival fraction). A 1:1 sex ratio is assumed.
- ω , a factor multiplying b for births to infective couples, represents the reduced probability at which children of infective couples will survive to enter the sexually active population compared to children of noninfective couples.

We assume the following hypotheses on these parameters:

H1. $c_m(m_1 + M_1) = c_f(f_0 + F_0).$

H2'. $\overline{\mu}_0 + \overline{\rho}_0 > \mu_0 + \rho_0$.

The first hypothesis states that the total number of contacts made by males with females per unit time is equal to the total number of contacts made by females with males per unit time. An underlying assumption implicit in H1 is that $c_f > c_m$, since the total number of young males, $m_1 + M_1$, must be larger than that of core females $f_0 + F_0$.

We note then that we have

$$\alpha^*(m_1 + M_1) = \alpha(f_0 + F_0), \tag{1}$$

where $c_m \alpha = c_f \alpha^*$. Since our model does not postulate constant population sizes, the parameters c_m , c_f , α , and α^* will in general vary with time or according to the state of the system and the preference of the individuals. Several authors have commented on this modeling problem, including Huang et al. [12], Lin et al. [14], and Lepont and Blower [13]. Lepont and Blower [13] suggested several possible approaches: (1) Assume c_m is constant and solve for $c_f(t) = c_m(m_1 + M_1)/(f_0 + F_0)$, which they termed "female flexibility"; (2) "male flexibility," which is similar but holding c_f constant; (3) "alternate flexibility," where c_m and c_f are assumed to be constant sequentially; (4) "opposite sex availability," where the contact rates are modified in proportion to the change in the availability of the opposite sex. However, evidence so far from Thailand, while indicating that condom use has increased in sex worker populations, does not show a major decrease in number of sex workers or in contact rates (T. Brown, personal communication). The study by Bhassorn et al. [2] reported that although awareness of AIDS among the commercial sex workers is high, most of the sex workers surveyed said that they would continue working in this profession for economic reasons. The data from Thailand in general do not suggest what might be a realistic choice or set of choices. Consequently, in this paper we take these parameters to be constant as a first approximation. Our equations and results therefore may be regarded as approximating the real situation, and we hope they will provide useful benchmarks for further studies. Hopefully, with more future studies on sexual patterns of these Asian societies, we can further explore this issue.

A second implication of H1 is that the ratio between the number of core females and the number of single males remains constant even while the size of the population varies. However, this is consistent with our "supply and demand" hypothesis, where the core prostitutes are recruited in constant proportion to the number of single males.

The second hypothesis is based on the plausible assumption that the rate of "removal" plus "retirement" from the group of infected core females is greater than the same rate for susceptible core females. The following hypothesis will also be required in some of what follows.

H3'. $\overline{\mu}_1 + \overline{\sigma}_1 + \alpha > \overline{\mu}_0 + \overline{\rho}_0$.

Hypothesis 3', which is somewhat less intuitive, says that the rate of "removal" plus pairing of infected males, plus the recruitment rate α , is greater than the rate of "removal" plus "retirement" for infected core females. This assumption, along with H2', will make our model equations well posed.

An important additional assumption concerns the nature of the mixing of subgroup members. General discussions of mixing may be found in [4, 5], where general axioms are formulated. Here, we assume so-called proportional mixing. The incidence rate of new infections within the core group may then be written as

H4.
$$c_f \beta F_0 \frac{m_1}{m_1 + M_1} = c_m \beta F_0 \frac{m_1}{f_0 + F_0}$$
.

The quantity on the left may be justified as the product of c_f , the number of contacts of a core female, times the number of susceptible core females, times the fraction $m_1/(m_1 + M_1)$ of contacts that are with infected males, times the probability β of transfer of infection per contact. The quantity on the right is equal, because of H1. It is also reported by Padian et al. [17] that the male-to-female transmission probability β .

We now write the equations of our model. The prime denotes differentiation with respect to time t. Explanations of the various terms will follow the equations.

$$F'_0 = \alpha^* (m_1 + M_1) - \mu_0 F_0 - \rho_0 F_0 - c_m \beta \frac{F_0}{f_0 + F_0} m_1, \qquad (2a)$$

$$f_0' = c_m \beta \frac{F_0}{f_0 + F_0} m_1 - \overline{\mu}_0 f_0 - \overline{\rho}_0 f_0, \qquad (2b)$$

$$M'_{1} = b(S_{2} + \omega I_{2}) - c_{m} \overline{\beta} \frac{f_{0}}{f_{0} + F_{0}} M_{1} - \mu_{1} M_{1} - \sigma_{1} M_{1}, \qquad (2c)$$

$$m_{1}' = c_{m} \,\overline{\beta} \frac{f_{0}}{f_{0} + F_{0}} M_{1} - \overline{\mu}_{1} m_{1} - \overline{\sigma}_{1} m_{1}, \qquad (2d)$$

$$S_2' = \sigma_1 \frac{M_1 F_1}{f_1 + F_1} - \mu_2 S_2, \qquad (2e)$$

$$I_{2}' = \sigma_{1} \frac{M_{1}f_{1}}{f_{1} + F_{1}} - \overline{\mu}_{2}I_{2} + \overline{\sigma}_{1}m_{1}, \qquad (2f)$$

$$F_{1}' = b(S_{2} + \omega I_{2}) + \rho_{0}F_{0} - \mu F_{1}$$

$$- \frac{F_{1}}{f_{1} + F_{1}} (\sigma_{1}M_{1} + \overline{\sigma}_{1}m_{1}), \qquad (2g)$$

$$f_1' = \overline{\rho}_0 f_0 - \overline{\mu}_1 f_1 - \frac{f_1}{f_1 + F_1} (\sigma_1 M_1 + \overline{\sigma}_1 m_1).$$
(2h)

The last term in Equation (2a) represents the incidence of new infections, as previously explained. The first term represents the recruit-

ment of new core females, which (as already stated) is assumed to be proportional to the number of young males. We have in mind a situation in which the population under study is in an urban area and the recruits are drawn from rural areas, as is usually the case in Thailand [2]. Since we are not modeling the rural population, we are implicitly assuming an unlimited resource for recruitment. (Alternatively, it could be assumed that recruitment is from within the studied population, but a recruitment term of the form $\alpha^* (m_1 + M_1)$ might then be more appropriate.) The next two terms represent "removal" and transfer out of the core group either back to the rural population or into the noncore female group as shown here in Equations (2g), (2h). The first term in Equation (2b) is the incidence of newly infected, and the other two terms are similar to those in Equation (2a).

In Equation (2c), bS_2 gives the rate of birth and survival to maturity of young males from susceptible pairs, and $b\omega I_2$ the same rate for young males from infected pairs. There is no similar term in the equation for m'_1 , Equation (2d), because vertical transmission is not included in the model. The second term in Equation (2c) and the first term in Equation (2d) represent incidence of infection of males due to contact with core females. [The ratio $f_0 / (f_0 + F_0)$ is the proportion of infected females in the core.] The terms $\mu_1 M_1$ and $\overline{\mu}_1 m_1$ are for "removals," and the terms $\sigma_1 M_1$ and $\overline{\sigma}_1 m_1$ give the rate at which males form new pairs.

We now explain the terms representing formation of pairs. More general discussion of such pairing functions may be found, for example, in Hadeler et al. [8] or Waldstätter [22]. If $\sigma_1 M_1$ is the rate at which susceptible males form pairs, we may assume that these are formed with susceptible and infected females according to their respective proportions. Let ϕ_{00} , ϕ_{10} , ϕ_{01} , and ϕ_{11} denote the rate of formation of pairs from young males and females in which both are susceptible, the male is infected but not the female, the female is infected but not the male, and both are infected, respectively. Then

$$\phi_{00} = \sigma_1 M_1 F_1 / (f_1 + F_1), \tag{3}$$

$$\phi_{01} = \sigma_1 M_1 f_1 / (f_1 + F_1). \tag{4}$$

Similarly, if $\overline{\sigma}_1 m_1$ is the rate at which infected young males form pairs, then

$$\phi_{10} = \overline{\sigma}_1 m_1 F_1 / (f_1 + F_1), \tag{5}$$

$$\phi_{11} = \overline{\sigma}_1 m_1 f_1 / (f_1 + F_1). \tag{6}$$

Now Equation (3) represents the rate of addition of susceptible pairs (the S_2 equation); the sum of (3) and (5) gives the rates of removal of

susceptible females into pairs; the sum of (4) and (6) gives the rates of removal of infected females into pairs; and the sum of (4)–(6) gives the rate of formation of new pairs with one or both parties infected (the I_2 equation). The positive term in the S'_2 and I'_2 equations should be clear, and the negative terms represent "removal." Finally, the F'_1 equation contains a birth term and the term $\rho_0 F_0$ representing emigration from the core. The meaning of the terms in the f'_1 equation should now be clear. We have assumed that the term $\bar{\rho}_0 f_0$, representing migration out of the core, is the only source of infected young females and that there is no rerecruitment from the f_1 group back into the core.

3. EQUILIBRIA OF THE MODEL

By using hypothesis H1, we may replace $\alpha^*(m_1 + M_1)$ by $\alpha(f_0 + F_0)$ and then decouple the equations for F_0 , f_0 , and m_1 from the others. Moreover, by redefining μ_0 to be the former $\mu_0 + \rho_0$, $\overline{\mu}_0$ to be the former $\overline{\mu}_0 + \overline{\rho}_0$, and $\overline{\mu}_1$ to be the former $\overline{\mu}_1 + \overline{\sigma}_1$, we may write these equations in the following simpler forms:

$$F'_{0} = \alpha (f_{0} + F_{0}) - \mu_{0} F_{0} - c_{m} \beta \frac{F_{0}}{f_{0} + F_{0}} m_{1}, \qquad (7)$$

$$f_0' = c_m \beta \frac{F_0}{f_0 + F_0} m_1 - \overline{\mu}_0 f_0, \qquad (8)$$

$$m_{1}' = c_{f} \overline{\beta} f_{0} - c_{m} \overline{\beta} \frac{f_{0}}{f_{0} + F_{0}} m_{1} - \overline{\mu}_{1} m_{1}.$$
(9)

Hypotheses H2' and H3' now take the forms

H2. $\overline{\mu}_0 > \mu_0$

and

H3. $\overline{\mu}_1 + \alpha > \overline{\mu}_0$.

Note that H2 and H3 together imply $\overline{\mu}_1 + \alpha > \mu_0$.

We now introduce the notation

$$T_0 = f_0 + F_0$$
, $y_1 = \frac{F_0}{T_0}$, $y_2 = \frac{f_0}{T_0}$, $y_3 = \frac{m_1}{T_0}$.

Simple calculation then gives the following equations.

$$T'_{0} = T_{0} (\alpha - \mu_{0} y_{1} - \overline{\mu}_{0} y_{2}), \qquad (10)$$

$$y'_{1} = (\alpha - \mu_{0}y_{1})(1 - y_{1}) - c_{m}\beta y_{1}y_{3} + \overline{\mu}_{0}y_{1}y_{2}, \qquad (11)$$

$$y'_{2} = (1 - y_{2})(c_{m} \beta y_{3} - \overline{\mu}_{0} y_{2} + \mu_{0} y_{2}) - \alpha y_{2}, \qquad (12)$$

$$y'_{3} = y_{2} \left[c_{f} \overline{\beta} - c_{m} \overline{\beta} y_{3} + (\overline{\mu}_{0} - \mu_{0}) y_{3} \right] - y_{3} (\overline{\mu}_{1} + \alpha - \mu_{0}), \quad (13)$$

with $y_1 + y_2 = 1$ and $0 \le y_3 \le c_f / c_m$. It is easy to see from these equations that the positive orthant in $y_1 y_2 y_3$ space is invariant. Now we shall consider the two-dimensional system, which we obtained from (11) and (13),

$$y_{1}' = \left[\alpha + (\overline{\mu}_{0} - \mu_{0}) y_{1} \right] (1 - y_{1}) - c_{m} \beta y_{1} y_{3},$$
(14)

$$y_{3}' = (1 - y_{1}) \left[c_{f} \overline{\beta} - (c_{m} \overline{\beta} - \overline{\mu}_{0} + \mu_{0}) y_{3} \right] - y_{3} (\overline{\mu}_{1} + \alpha - \mu_{0})$$
$$= c_{f} \overline{\beta} - (c_{m} \overline{\beta} + \overline{\mu}_{1} - \overline{\mu}_{0} + \alpha) y_{3} - y_{1} \left[c_{f} \overline{\beta} - (c_{m} \overline{\beta} - \overline{\mu}_{0} + \mu_{0}) y_{3} \right].$$
(15)

System (14), (15) is well posed by H2 and H3, that is, $0 \le y_1 \le 1$, $0 \le y_3 \le c_f/c_m$. Our first result concerns equilibria and phase plane analysis for this system. One equilibrium is $(y_1, y_3) = (1, 0)$, and a straightforward calculation shows that at any other equilibrium (y_1, y_3) , y_1 must satisfy the quadratic equation

$$h(y) \coloneqq Ay^2 + By + C = 0,$$

where

$$\begin{split} &A = (\ \overline{\mu}_0 - \mu_0) \Big(c_m \ \overline{\beta} - \overline{\mu}_0 + \mu_0 \Big), \\ &B = c_m \ \overline{\beta} \big(c_f \beta + \alpha \big) - (\ \overline{\mu}_0 - \mu_0) \big(c_m \ \overline{\beta} - \overline{\mu}_0 + \overline{\mu}_1 + 2 \alpha \Big), \\ &C = - \alpha \Big(c_m \ \overline{\beta} - \overline{\mu}_0 + \overline{\mu}_1 + \alpha \Big). \end{split}$$

The following result is proved in the Appendix in the usual way, by examining the eigenvalues of the linearization.

PROPOSITION 1

Assume that H1–H4 hold. Then the disease-free equilibrium at (1,0), abbreviated DFE, of system (14), (15) is locally asymptotically stable if $R_f < 1$ and unstable if $R_f > 1$, where

$$R_f^2 = \frac{c_m c_f \beta \overline{\beta}}{\left(\alpha + \overline{\mu}_0 - \mu_0\right) \left(\alpha + \overline{\mu}_1 - \mu_0\right)}, \qquad R_f > 0.$$

If H_1 , H_2 , and H_4 hold but H_3 does not, then the above holds if $\overline{\mu}_1 + \alpha > \mu_0$, but (1,0) becomes unstable if $\overline{\mu}_1 + \alpha \le \mu_0$.

 R_f determines the local stability of DFE. In some cases it determines whether the infectious fractions will die out, while in other cases it

merely determines whether bifurcation can occur. All this will be made clear shortly in the next theorem. We should add, at this point, that R_f is *not* the basic reproduction number for the infectious populations in our model because the issue here is the persistence of endemic fractions. The basic reproduction number for the infectious populations will be given in Section 4.

We now examine the question of existence, uniqueness, and stability of equilibria with $0 < y_1 < 1$. Several cases must be considered, depending on the sign of the quantity A. Observe first that

$$c_m \,\overline{eta} + \overline{\mu}_1 - \overline{\mu}_0 + lpha = \left(c_m \,\overline{eta} - \overline{\mu}_0 + \mu_0
ight) + \left(\,\overline{\mu}_1 + lpha - \mu_0
ight)$$

Since H3 implies C < 0, there are only three possible cases: (I) A > 0; (II) A = 0; (III) A < 0. We describe all three cases in Theorem 2.

THEOREM 2

The existence, uniqueness, and stability result for positive equilibrium of system (14), (15) is summarized in Table 1.

Before turning to a discussion of the full model, we shall complete the analysis of the two-dimensional system (14), (15). Theorem 2 is proved in the Appendix, as is also the following.

PROPOSITION 3

Assume that H1-H4 hold. Then system (14), (15) has no periodic solution (periodic orbits, homoclinic loops, or oriented phase polygons)

| | | R_{f} | Number of positive equilibria | Stability ^a |
|-----------|-------|------------|-------------------------------|------------------------|
| Case I. | A > 0 | >1 | 1 | AS |
| | | ≦1 | 0 | — |
| Case II. | A = 0 | >1 | 1 | AS |
| | | <u>≤</u> 1 | 0 | — |
| Case III. | A < 0 | >1 | 1 | AS |
| | | =1 | $0(A \geq C)$ | |
| | | | $1(\overrightarrow{A < C})$ | AS |
| | | <1 | $0\left(B^2 < 4AC\right)$ | _ |
| | | | $1 \left(B^2 = 4AC \right)$ | Stable |
| | | | $2(B^2 > 4AC)$ | One AS, the other |
| | | | | unstable |

 TABLE 1

 Evistance Uniqueness and Stability of Positive Equilibrium

^aAS = locally asymptotically stable.

with orbit in the invariant set

$$S = \{(y_1, y_3) : 0 < y_1 < 1, 0 < y_3 < c_f / c_m\}.$$

Now we are in position to give the following theorem, based on Theorem 2 and Proposition 3.

THEOREM 4

(1) If $A \ge 0$, then the DFE at (1,0) is globally asymptotically stable (abbreviated G.A.S.) within the set S if $R_f \le 1$. If $R_f > 1$, then the unique endemic equilibrium is G.A.S. within S.

(2) If A < 0, then the above result still applies unless (i) $R_f = 1$ and A < C or (ii) $R_f < 1$ but $B^2 \ge 4AC$. For case (i), DFE is linearly stable but not attracting in S. So the unique endemic equilibrium is G.A.S. in S. For case (ii), when $B^2 > 4AC$ there are two endemic equilibria in S, the one with smaller y_1 value is asymptotically stable and the other unstable. The stable manifold of the unstable endemic equilibrium divides S into two regions that are the domains of attraction for the asymptotically stable endemic equilibrium and the asymptotically stable DFE. Hence we have a saddle-node connection. When $B^2 = 4AC$, we have a saddle-point bifurcation of the previous case, so there is a unique endemic equilibrium. The stable manifold of the endemic equilibrium once again divides S into two regions that are the domains of attraction for itself and DFE.

See the proof in the Appendix.

4. ANALYSIS OF THE COMPLETE MODEL EQUATIONS

We now turn to a discussion of the full model given in system (2). Let $T_0 = f_0 + F_0$, and let $N_0 = f_0 + F_0 + m_1 + M_1 = (1 + c_f / c_m)T_0$ be the total population of sexually active persons. Then

$$T_{0}' = f_{0}' + F_{0}' = \alpha (f_{0} + F_{0}) - \mu_{0}F_{0} - \overline{\mu}_{0}f_{0}$$

= $[\alpha - \mu_{0} - (\overline{\mu}_{0} - \mu_{0})y_{2}]T_{0},$

and

$$N'_{0} = N_{0} \big[\alpha - \mu_{0} - (\overline{\mu}_{0} - \mu_{0}) y_{2} \big].$$

Define R_1 by the equations

$$R_1 = \begin{cases} \alpha / \mu_0 & \text{if } R_f \leq 1, \\ \alpha / \left[\mu_0 + \left(\overline{\mu}_0 - \mu_0 \right) y_2^* \right] & \text{if } R_f > 1, \end{cases}$$

where y_2^* denotes an endemic equilibrium value of y_2 .

LEMMA 5

Assume case I or II ($A \ge 0$). If $R_1 < 1$, then $N_0(t)$ tends to 0 as t tends to ∞ . If $R_1 > 1$, then $N_0(t)$ tends to ∞ . The asymptotic rate of decrease or increase is $\alpha - \mu_0 = \mu_0(R_1 - 1)$ if $R_f < 1$ and $[\mu_0 + (\overline{\mu}_0 - \mu_0)y_2^*](R_1 - 1)$ if $R_f > 1$.

Proof. If $R_f \le 1$, then y_2 tends to zero, so the limiting equation is $N'_0 = N_0 [\alpha - \mu_0] = N_0 \mu_0 (R_1 - 1)$. If $R_f > 1$, the limit equation is $N'_0 = N_0 [\mu_0 + (\overline{\mu}_0 - \mu_0) y_2^*](R_1 - 1)$, and the result follows at once from these scalar equations.

THEOREM 6

Assume case I or II. The limiting values of variables F_0 , f_0 , m_1 , M_1 are as indicated in Table 2, where R_0 is defined to be

$$R_0^2 = c_m c_f \beta \overline{\beta} / \overline{\mu}_0 \overline{\mu}_1.$$

Proof. First suppose that $R_f \leq 1$. Since the disease-free equilibrium of system (14), (15) is asymptotically stable by Proposition 1, there are no periodic orbits by Proposition 3, and all solutions in the first quadrant are bounded, it follows from the Poincaré-Bendixson theorem that the disease-free equilibrium (1,0) is globally asymptotically stable. Thus y_1 tends to 1, $y_2 = 1 - y_1$ to 0, and y_3 to 0. We know from Lemma 5 that N_0 tends to 0 if $R_1 < 1$, and to ∞ if $R_1 > 1$. If $N_0 = f_0 + F_0 + m_1 + M_1$ tends to 0, then each of these four variables tends to 0 since they are nonnegative, and this establishes the first row in Table 2. If $R_f > 1$, the proportions tend to the endemic equilibrium. It follows from Lemma 5 that if $R_1 < 1$, N_0 tends to 0 and hence f_0 , F_0 , m_1 , M_1 all tend to 0 automatically, independent of the value of R_0 . Likewise for $R_1 > 1$, where N_0 tending to ∞ implies that all variables tend to ∞ . Note that in this case $R_0 > 1$ follows naturally. The first three rows in Table 2 have now been proved.

| Т | A | B | L | Æ | 2 |
|---|---|---|---|---|---|
| | | | | | |

| R_{f} | R_1 | R_0 | $N_0(t)$ | (y_1, y_2, y_3) | (F_0, f_0, m_1, M_1) |
|---------|-------|------------------|----------|-------------------------|------------------------------------|
| ≤1 | < 1 | < 1 ^a | 0 | (1,0,0) | (0, 0, 0, 0) |
| >1 | < 1 | | 0 | (y_1^*, y_2^*, y_3^*) | (0, 0, 0, 0) |
| >1 | >1 | $> 1^{a}$ | ∞ | (y_1^*, y_2^*, y_3^*) | $(\infty, \infty, \infty, \infty)$ |
| ≤1 | >1 | <1 | 00 | (1, 0, 0) | $(\infty, 0, 0, \infty)$ |
| ≤1 | >1 | >1 | ∞ | (1, 0, 0) | $(\infty, \infty, \infty, \infty)$ |

Limiting Values of Variables for Cases I and II

^aAutomatically satisfied.

Continuing with the case $R_f \leq 1$, now suppose that $R_1 > 1$ so N_0 tends to ∞ . The differential equations for f_0 and m_1 are

$$f_0' = c_m \beta \frac{y_1}{y_1 + y_2} m_1 - \overline{\mu}_0 f_0, \qquad (16)$$

$$m_{1}' = c_{f} \overline{\beta} f_{0} - c_{m} \overline{\beta} \frac{y_{2}}{y_{1} + y_{2}} m_{1} - \overline{\mu}_{1} m_{1}.$$
(17)

Since (y_1, y_2) tends to (1, 0), the limiting equations are

$$f_0' = c_m \beta m_1 - \overline{\mu}_0 f_0, \qquad m_1' = c_f \overline{\beta} f_0 - \overline{\mu}_1 m_1.$$

This is a linear system with eigenvalues given by

$$\lambda_{1},\lambda_{2}=\frac{-\left(\overline{\mu}_{0}+\overline{\mu}_{1}\right)\pm\left[\left(\overline{\mu}_{0}-\overline{\mu}_{1}\right)^{2}+4c_{m}c_{f}\beta\overline{\beta}\right]^{1/2}}{2};$$

hence one is always negative, and the other is positive if and only if $R_0 > 1$.

It is clear that when $R_0 > 1$, there is one eigenvector in the first quadrant on which motion is away from the origin and another eigenvector in the second quadrant on which motion is toward (0,0) in the f_0m_1 plane. That is, the origin is a saddle point, and all trajectories in the first quadrant tend away from (0,0). By Thieme's extension of a theorem of Markus (Theorem 1.6 in Thieme [20]) with ω extended to include ∞ , the solutions of system (16), (17) tend to ∞ .

When $R_0 < 1$, the eigenvalues are negative. By the same theorem (unextended), f_0 , m_1 tend to 0.

Now consider M_1 . Since $y_3 = m_1 / (f_0 + F_0) = c_f m_1 / [c_m (m_1 + M_1)]$ and $N_0 = (c_m / c_f + 1)(m_1 + M_1)$, it follows that

$$M_{1} = \frac{N_{0} \left[1 - \left(c_{m} / c_{f} \right) y_{3} \right]}{1 + c_{m} / c_{f}}$$

 $0 \le y_3 < c_f / c_m$ and y_3 tends to zero since $R_f \le 1$. Consequently M_1 tends to 0 if N_0 tends to 0, and M_1 tends to ∞ if N_0 tends to ∞ .

Clearly, R_0 is the basic reproduction number that determines whether the infectious populations f_0 and m_1 will die out or not. A biological interpretation of this expression will be given later in Section 6.

As for case III, Table 2 is still valid if any one of three conditions is met: (i) $R_f > 1$ or (ii) $R_f = 1$ and $A \ge C$ or (iii) $R_f < 1$ and $B^2 < 4AC$.

However, if (a) $R_f = 1$ but A < C or (b) $R_f < 1$ but $B^2 \ge 4AC$, the asymptotic behavior of the population depends on the initial value of the population, as stated in Theorem 4. In other words, (y_1, y_3) could go to either the DFE (1,0) or an endemic equilibrium (y_1^*, y_3^*) depending on which domain of attraction the initial value is in. Hence the subgroups (F_0, f_0, m_1, M_1) also could go to $(0, 0, 0, 0), (\infty, 0, 0, \infty)$, or $(\infty, \infty, \infty, \infty)$ depending on where the population starts from initially. We summarize the result for cases (a) and (b) in Table 3.

Table 3 follows directly from Table 2, except that the limiting value of (y_1, y_2, y_3) is placed in the first column because the value of R_1 depends on the asymptotic value of (y_1, y_2, y_3) ,

$$R_1^* = \begin{cases} \alpha / \mu_0 & \text{if } (y_1, y_2, y_3) \to (1, 0, 0), \\ \alpha / [\mu_0 + (\overline{\mu}_0 - \mu_0) \overline{y}_2] & \text{if } (y_1, y_2, y_3) \to (\overline{y}_1, \overline{y}_2, \overline{y}_3). \end{cases}$$

Here $(\bar{y}_1, \bar{y}_2, \bar{y}_3)$ could be any endemic equilibrium. R_0 remains the same as in Table 2.

5. BIFURCATION DIAGRAMS AND NUMERICAL EXAMPLES

Figure 1 is a bifurcation diagram that illustrates case III (A < 0) when $R_f = 1$. The vertical axis is y_3 , and the horizontal axis is C/A. The horizontal line $y_3 = 0$ is the DFE, which is always locally stable in this case. When $C/A \le 1$, the DFE is globally asymptotically stable. When C/A > 1, there exists a unique endemic equilibrium with $y_3 > 0$, which is globally asymptotically stable.

Figure 2 is the bifurcation diagram for case III when $R_f < 1$. The vertical axis is again y_3 , but the horizontal axis is now $B^2/4AC$. The line $y_3 = 0$ is the DFE, which is always locally asymptotically stable. For $B^2/4AC < 1$, the DFE is also globally asymptotically stable. At $B^2/4AC = 1$, the DFE becomes only locally asymptotically stable and there is a unique endemic equilibrium. When $B^2/4AC > 1$, it splits into two branches. The upper branch is locally asymptotically stable, and the lower branch is unstable.

| (y_1, y_2, y_3) | R_1^* | R_0 | N_0 | (F_0, f_0, m_1, M_1) |
|---|---------|-----------------|-------|------------------------------------|
| $(1,0,0)/(\bar{y}_1,\bar{y}_2,\bar{y}_3)$ | <1 | <1 ^a | 0 | (0,0,0,0)/(0,0,0,0) |
| $(\bar{y}_1, \bar{y}_2, \bar{y}_3)$ | >1 | $> 1^{a}$ | 00 | $(\infty, \infty, \infty, \infty)$ |
| (1,0,0) | >1 | <1 | 8 | $(\infty, 0, 0, \infty)$ |
| (1,0,0) | >1 | >1 | 8 | $(\infty, \infty, \infty, \infty)$ |

 TABLE 3

 Limit Values of Variables for Cases III(a) and III(b)



200

FIG. 2. Bifurcation diagram for case III (A < 0) when $R_f < 1$.

We now provide two numerical examples to illustrate that the above cases can really occur.

Example 1. Let $c_m \overline{\beta} = 1$, $c_f \beta = (3.165)^2$, $\alpha = 1$, $\overline{\mu}_1 - \mu_0 = 2.165$, and $\overline{\mu}_0 - \mu_0 = 2.165$. It follows that

$$A = -2.522225$$
, $B = 4.522225$, $C = -2$, and $R_f = 1$.

Since A < C, from Table 1 we expect DFE (1,0) to be stable with an asymptotically stable positive equilibrium (y_1^*, y_3^*) .

Indeed the roots of $h(y) = Ay^2 + By + C = 0$ are

$$y_{11} = C/A = 2/2.522225, \qquad y_{12} = 1.$$

We already know tr J < 0 for both y_{11}, y_{12} . Now

$$\det J(y_{11}) = \frac{1 - y_{11}}{y_{11}} \left(Ay_{11}^2 - C \right) = \frac{1 - y_{11}}{y_{11}} 0.4140986 > 0,$$

so that both eigenvalues are negative and y_{11} is asymptotically stable.

det J(1) = 0 so that y_{12} has one negative eigenvalue and an eigenvalue equal to 0. Hence it is stable. Note that as A approaches C from below, we have a bifurcation point at A = C where the endemic equilibrium no longer exists and DFE becomes G.A.S. in S. (See Theorem 4.)

Example 2. Let $c_m \overline{\beta} = 1$, $c_f \beta = 10$, $\alpha = 1$, $\overline{\mu}_1 - \mu_0 = 2.165$, and $\overline{\mu}_0 - \mu_0 = 2.165$. Now we have

$$A = -2.522225, \quad B = 4.505, \quad C = -2, \quad R_f^2 = \frac{10}{3.165^2} < 1,$$

and

$$B^2 - 4AC = 0.117225 > 0.$$

Therefore, from Table 1 we expect two positive equilibria, one asymptotically stable and the other unstable, in addition to the asymptotically stable DFE.

Once again solving h(y) = 0, we get

$$y_{11} = 0.82518781, \qquad y_{12} = 0.96093357.$$

From Theorem 4, we expect y_{11} to be asymptotically stable.

We again know tr J < 0.

$$\det J(y_{11}) = 0.2825289 \frac{1 - y_{11}}{y_{11}} > 0,$$
$$\det J(y_{12}) = -0.3290053 \frac{1 - y_{12}}{y_{12}} < 0.$$

Hence (y_{11}, y_{31}) is asymptotically stable and (y_{12}, y_{32}) is a saddle point, where y_{3i} is the value of y_3 corresponding to y_{1i} (j = 1, 2).

It is interesting to note that in this case an influx of some number of infectives could possibly result in an initial condition that would lead to the asymptotically stable endemic equilibrium; that is, the disease would become endemic even with a small R_f (<1). Unfortunately, without any detailed real data on a core group of prostitutes, we are still unable to determine whether these theoretical cases are feasible in the real world.

6. BIOLOGICAL SIGNIFICANCE OF THE THRESHOLD PARAMETERS

We now return to the original notation of $\mu_0 + \rho_0$ instead of μ_0 , $\overline{\mu}_0 + \overline{\rho}_0$ instead of $\overline{\mu}_0$, and $\overline{\mu}_1 + \overline{\sigma}_1$ instead of $\overline{\mu}_1$. We first note that the asymptotic behavior of the system is rather straightforward for $c_m \overline{\beta} + \mu_0 + \rho_0 \ge \overline{\mu}_0 + \overline{\rho}_0$, that is, cases I and II. From Table 2 we see that the threshold parameter R_f determines whether the endemic fractions will die out in cases I and II. In case III, bifurcation occurs if $R_f \le 1$. We can rewrite A as

$$\mathcal{A} = \left(\overline{\mu}_0 + \overline{\rho}_0 - \mu_0 - \rho_0\right)^2 \left(\frac{c_m \overline{\beta}}{\overline{\mu}_0 + \overline{\rho}_0 - \mu_0 - \rho_0} - 1\right).$$

The sign of A clearly depends on whether the fraction in the second term is greater than or less than unity. Here $c_m \overline{\beta}$ is the rate at which a susceptible young man is infected if he makes contact with a population of all infected core females, and $\overline{\mu}_0 + \overline{\rho}_0 - \mu_0 - \rho_0$ is the removal plus retirement rates of these core females *due to infection*. Therefore if the former term dominates over the latter, R_f simply determines whether the endemic fractions will die out. On the other hand, if the removal/retirement of the infected core females caused by infections is greater than the rate at which they infect susceptible males, it results in an increase in the pool of susceptible core females as well as susceptible young men. This tends to destabilize the system, and $R_f \leq 1$ no longer

guarantees that the endemic fractions will go to zero. More interestingly, in this case the relative sizes of the initial populations could determine whether the endemic fractions will persist. R_f , restricted to be nonnegative, can be viewed as the geometric mean of the relative strengths of the disease transmission of the two infective groups, that is, m_1 and f_0 , versus their proportional dilution via AIDS-related excess removal rates and the increase of susceptible core female proportion α .

The asymptotic population size is determined by R_1 , which measures simply recruitment of susceptible core females versus removal with the presence of disease taken into account. It is interesting to note that the birth rate b is absent from the expression for R_1 . This can be interpreted as saying that the persistence of population depends not on the births of individuals but on the recruitment of disease-free core females, regardless of whether the disease will persist. When the total population N_0 tends to ∞ and the infective proportion $y_2 + y_3$ goes to 0, the basic reproduction number R_0 determines whether the infective population goes to 0 or ∞ . Clearly, R_0 is simply the geometric mean of the ratios of disease transmission to removal for infective young males and infective core females. Hence it is the mean number of secondary infections caused by one infective entering a susceptible population.

When $\overline{\mu}_0 + \overline{\rho}_0 > c_m \beta + \mu_0 + \rho_0$ (i.e., A < 0), the asymptotic proportions depend on the initial values as well as the threshold parameter R_f ; consequently R_1 also depends on the initial proportions. This illustrates the importance of $\overline{\mu}_0 + \overline{\rho}_0$. That is, if $\overline{\mu}_0 + \overline{\rho}_0$ is sufficiently large (i.e., greater than $c_m \overline{\beta} + \mu_0 + \rho_0$), then even if the DFE is stable ($R_f \le 1$), it will not be globally stable. Biologically, this could be interpreted as follows: If the effect of the disease on increasing removal rate is so large that $\overline{\mu}_0 + \overline{\rho}_0 > \mu_0 + \rho_0 + c_m \overline{\beta}$, it will have a destabilizing impact on the system by making the dynamics more complicated. Qualitatively, the asymptotic behavior of the system becomes dependent not only on the threshold parameters but also on the initial conditions. We also note that the well-posedness of system (14), (15) requires H3, that is, $\overline{\mu}_1 + \overline{\sigma}_1 + \alpha > \overline{\mu}_0 + \overline{\rho}_0$. Hence an increase in $\overline{\mu}_0 + \overline{\rho}_0$ tends to destabilize the system by allowing unbounded solutions.

Our model also enables us to study the dependence of endemic levels on the various parameters (α , c_f , c_m , β , $\overline{\beta}$, R_0 , etc.) by computing the endemic proportions y_2 and y_3 as functions of the parameters via the expressions for A, B, and C. However, in many cases the resulting analytic expressions for the endemic proportions involve the square root of $B^2 - 4AC$ and it is difficult to obtain meaningful interpretations. One simple case is case II, A = 0, $R_f > 1$, where $y_1 = -C/B$ and the endemic proportion of the female sex workers is

$$y_2 = \frac{R_f^2 - 1}{R_f^2 - G},$$

where $G = (\overline{\mu}_0 - \mu_0)/(\alpha + \overline{\mu}_0 - \mu_0)$.

It is obvious that y_2 increases toward 1 as R_f increases. It also can be shown easily that y_2 is a decreasing function of α (note that R_f also depends on α). This makes sense because increasing the supply of sex workers α would dilute the endemic proportion. On the other hand, the endemic proportion for single males is

$$y_3 = \frac{\left(\alpha + \overline{\mu}_0 - \mu_0\right) R_f^2 y_2}{c_m \beta}$$

Given that y_2 decreases with α , y_3 is also a decreasing function of α ; that is, an increase in the supply of sex workers would decrease the infection level among the single males because the dilution of infection level in female sex workers decreases the probability that a customer will encounter an infected sex worker. Similar but more complicated expressions for other cases can also be obtained.

An open question of interest is, What is the effect of screening and/or treatment in the core group as a control measure for the spread of disease? Some models on screening and/or treatment in the whole community (e.g., [1, 10, 11, 21]) have shown that such a control measure is beneficial only under certain conditions on the parameters. Would things be different if it were done on the core group? We will not pursue this question in this work.

APPENDIX

PROOF OF PROPOSITION 1

The Jacobian matrix of system (14), (15) is

$$J = \begin{bmatrix} (1-y_1)(\overline{\mu}_0 - \mu_0) - [\alpha + (\overline{\mu}_0 - \mu_0)y_1] - c_m \beta y_3 & -c_m \beta y_1 \\ - [c_f \overline{\beta} - (c_m \overline{\beta} - \overline{\mu}_0 + \mu_0)y_3] & - (1-y_1)[c_m \overline{\beta} - \overline{\mu}_0 + \mu_0] - (\overline{\mu}_1 + \alpha - \mu_0) \end{bmatrix}$$

At $y_1 = 1$, $y_3 = 0$, the matrix has

tr
$$J = -\left[\alpha + \overline{\mu}_0 - \mu_0\right] - \left[\alpha + \overline{\mu}_1 - \mu_0\right],$$

det $J = \left[\alpha + \overline{\mu}_0 - \mu_0\right] \left[\alpha + \overline{\mu}_1 - \mu_0\right] - c_f c_m \beta \overline{\beta}.$

Under H2 and H3, the trace is negative and the determinant is positive if and only if $R_f < 1$. If H2 holds but H3 fails, so that $\overline{\mu}_1 + \alpha < \overline{\mu}_0$, then the same result holds if $\overline{\mu}_1 + \alpha > \mu_0$. On the other hand, det J < 0 if $\overline{\mu}_1 + \alpha \leq \mu_0$, and the equilibrium is unstable.

PROOF OF THEOREM 2

Case I. A > 0. By H3, h(0) = C < 0. If $R_f > 1$, then

$$h(1) = \left(\alpha + \overline{\mu}_1 - \mu_0\right)\left(\alpha + \overline{\mu}_0 - \mu_0\right)\left(R_f^2 - 1\right) > 0.$$

There is exactly one root in (0,1) and hence one endemic equilibrium (y_1, y_3) .

Using the fact that at positive equilibrium we have

$$c_m \beta y_1 y_3 = (1 - y_1) \left[\alpha + (\overline{\mu}_0 - \mu_0) y_1 \right],$$

the Jacobian of system (14), (15) can be put in the form

$$J = \begin{bmatrix} -\frac{\alpha}{y_1} - (\overline{\mu}_0 - \mu_0)y_1 & -c_m \beta y_1 \\ -\frac{(\alpha + \overline{\mu}_1 - \mu_0)}{c_m \beta y_1} [\alpha + (\overline{\mu}_0 - \mu_0)y_1] & -(1 - y_1)(c_m \overline{\beta} - \overline{\mu}_0 + \mu_0) - (\overline{\mu}_1 + \alpha - \mu_0) \end{bmatrix}.$$

Then

$$\operatorname{tr} J = -\frac{\alpha}{y_1} - (\overline{\mu}_0 - \mu_0) y_1 - \frac{(1 - y_1)A}{\overline{\mu}_0 - \mu_0} - (\overline{\mu}_1 + \alpha - \mu_0),$$
$$\operatorname{det} J = \frac{1 - y_1}{y_1} [Ay_1^2 - C].$$

Clearly, if $R_f > 1$, then tr J < 0 and det J > 0 so y_1 is asymptotically stable.

If $R_f \leq 1$, then $h(1) \leq 0$ and $h''(y_1) = 2A > 0$ imply that there is no root in (0, 1).

Case II. A = 0. A = 0 implies that $c_m \overline{\beta} = \overline{\mu}_0 - \mu_0$, and consequently

$$\begin{split} R_f^2 &= \frac{c_f \beta(\,\overline{\mu}_0 - \mu_0)}{\left(\,\alpha + \overline{\mu}_0 - \mu_0\right)\left(\,\alpha + \overline{\mu}_1 - \mu_0\right)},\\ B &= \left(\,\overline{\mu}_0 - \mu_0\right)\left(c_f \beta - \overline{\mu}_1 - \alpha + \mu_0\right),\\ C &= -\alpha\left(\,\overline{\mu}_1 + \alpha - \mu_0\right). \end{split}$$

If $R_f > 1$, then $B > \alpha(\overline{\mu}_1 + \alpha - \mu_0) = -C$, and there exists a unique root $y_1 > 0$ where $y_1 = -C/B < 1$. In this case, tr J < 0, det J > 0, and y_1 is again asymptotically stable.

If $R_f \leq 1$, then $B \leq -C$ and there is no root for h(y) = 0 in (0, 1).

Case III. A < 0. First denote the smallest positive root of h(y) = 0 by y_{11} . If $R_f > 1$, then h(1) > 0 and there is exactly one root in (0, 1). Therefore $B^2 > 4AC$ and -B/2A > 0. First, we have

$$\operatorname{tr} J = -\frac{\alpha}{y_1} - (\overline{\mu}_0 - \mu_0) y_1 + y_1 \frac{A}{\overline{\mu}_0 - \mu_0} + \frac{C}{\alpha} < 0.$$

Also A < 0, C < 0 implies B > 0 and

$$y_{11} = \frac{-B + \sqrt{B^2 - 4AC}}{2A} < 1,$$

so that

$$Ay_{11}^2 - C = \frac{\sqrt{B^2 - 4AC}}{2A} \left[\sqrt{B^2 - 4AC} - B \right] > 0.$$

Thus det J > 0, and y_{11} is once again asymptotically stable.

If $R_f = 1$, then h(1) = A + B + C = 0 and there are two possibilities. If $A - C \ge 0$, then $y_{11} = 1$ and there is no root in (0,1). However, if A - C < 0, then y_{11} is the unique positive root in (0,1). In this case $2A + B = -\sqrt{B^2 - 4AC}$ and $y_{11} = -(A + B)/A = C/A$.

It follows that

$$Ay_{11}^2 - C = \frac{C}{A}(C - A) = -\frac{C}{A}(2A + B) = \frac{C}{A}\sqrt{B^2 - 4AC} > 0.$$

Hence det J > 0 and y_{11} is asymptotically stable.

If $R_f < 1$, there are three possibilities, we will discuss each in turn.

(a) $B^2 < 4AC$, and there is no root in (0,1).

(b) $B^2 = 4AC$, and $y_1 = -B/(2A)$ is the unique root in (0,1). Consequently,

$$Ay_1^2 - C = \frac{B^2}{4A} - C = \frac{1}{4A} [B^2 - 4AC] = 0$$

and y_1 is stable.

(c) $B^2 > 4AC$, there are two positive roots in (0,1):

$$y_{11} = \frac{-B + \sqrt{B^2 - 4AC}}{2A}, \qquad y_{12} = \frac{-B - \sqrt{B^2 - 4AC}}{2A},$$

with $y_{12} > y_{11}$. Moreover,

$$Ay_{11}^2 - C = \frac{\sqrt{B^2 - 4AC}}{2A} \left[\sqrt{B^2 - 4AC} - B \right] > 0$$

and

$$Ay_{12}^2 - C = \frac{\sqrt{B^2 - 4AC}}{2A} \left[\sqrt{B^2 - 4AC} + B \right] < 0.$$

Hence y_{11} is asymptotically stable and y_{12} is unstable.

PROOF OF PROPOSITION 3

Clearly, S is invariant from system (14), (15). We apply the Dulac criterion in region S. Let $f_1(y_1, y_3)$ and $f_3(y_1, y_3)$ denote the expressions in the right-hand sides of Equations (14) and (15), respectively. Let $g(y_1, y_3) = 1/y_1y_3$. Then we find

$$\begin{split} \frac{\partial}{\partial y_1}(gf_1) &= \frac{\partial}{\partial y_1} \left\{ \frac{1}{y_3} \left[\frac{\alpha}{y_1} + (\overline{\mu}_0 - \mu_0 - \alpha) - (\overline{\mu}_0 - \mu_0) y_1 \right] - c_m \beta \right\} \\ &= \frac{1}{y_3} \left[-\frac{\alpha}{y_1^2} - (\overline{\mu}_0 - \mu_0) \right] < 0, \\ \frac{\partial}{\partial y_3}(gf_3) &= \frac{\partial}{\partial y} \left\{ \left(\frac{1}{y_1} - 1 \right) \left[\frac{c_f \overline{\beta}}{y_3} - \left(c_m \overline{\beta} - \overline{\mu}_0 + \mu_0 \right) \right] \right. \\ &\qquad \left. - \frac{1}{y_1} \left(\alpha + \overline{\mu}_1 - \mu_0 \right) \right\} \\ &= \left(\frac{1}{y_1} - 1 \right) \left(- \frac{c_f \overline{\beta}}{y_3^2} \right) < 0 \end{split}$$

in S. By the Dulac criterion, there is no periodic solution in S.

PROOF OF THEOREM 4

Part (1) follows directly from Theorem 2 and Proposition 3. The same is true for part (2) when $R_f > 1$, or $R_f = 1$ and $A \ge C$, or $R_f < 1$ and $B^2 < 4AC$.

For cases (i) and (ii) in (2), we first consider $R_f < 1$ and $B^2 > 4AC$. We let (y_{11}, y_{31}) be the endemic equilibrium with the smaller y_1 value and (y_{12}, y_{32}) be the one with the larger y_1 so that (y_{11}, y_{31}) is asymptotically stable while (y_{12}, y_{32}) is the saddle point. Since there is no periodic solution of any type in S, the stable manifold of (y_{12}, y_{32}) must intersect the boundary of S and divides S into two regions. It follows then (also from Proposition 3) that the two regions must be the domains of attraction for (y_{11}, y_{31}) and DFE (1,0), both of which are asymptotically stable. At (1,0), the Jacobian of (14), (15) is

$$J = \begin{bmatrix} -(\overline{\mu}_0 + \alpha - \mu_0) & -c_m \beta \\ -c_f \overline{\beta} & -(\overline{\mu}_1 + \alpha - \mu_0) \end{bmatrix}.$$
 (A1)

Since $R_f < 1$, both eigenvalues are negative. It is easy to show that one eigenvector has positive slope and the other has negative slope. Hence DFE is a node because S is an invariant rectangle and (1,0) is the lower right vertex of S. To show that (y_{11}, y_{31}) is also a node, we use the transformation $x = y_1 - y_{11}$, $y = y_3 - y_{31}$, so that system (14), (15) becomes

$$\begin{aligned} x' &= \left[\alpha + (\overline{\mu}_0 - \mu_0)(x + y_{11}) \right] (1 - x - y_{11}) - c_m \beta(x + y_{11})(y + y_{31}), \\ y' &= (1 - x - y_{11}) \left[c_f \overline{\beta} - (c_m \overline{\beta} - \overline{\mu}_0 + \mu_0)(y + y_{31}) \right] \\ &- (y + y_{31}) (\overline{\mu}_1 + \alpha - \mu_0). \end{aligned}$$
(A2)

(A2) can be rewritten as

$$\begin{pmatrix} x \\ y \end{pmatrix}' = A \begin{pmatrix} x \\ y \end{pmatrix} + \begin{pmatrix} f_1 \\ f_2 \end{pmatrix},$$
 (A3)

where A is the Jacobian of (A2) at (0,0) and

$$f_1(r,\theta) = -(\overline{\mu}_0 - \mu_0)\cos^2\theta r^2,$$

$$f_2(r,\theta) = (c_m \overline{\beta} - \overline{\mu}_0 + \mu_0)\cos\theta\sin\theta r^2$$

are the nonlinear terms of (A2) in polar coordinates. It is obvious that $f_i(r, \theta) = o(r)$ as $r \to 0^+$ for i = 1, 2. By Theorem (5.1) in Coddington and Levinson [7, p. 384], an improper node of the linearized system of (A3) is also an improper node for (A3). Therefore it suffices to show that (0,0) is an improper node for the linearized system of (A3). To this aim we consider the eigenvalues of the matrix A in (A3). Since A < 0, $R_f < 1$, and $B^2 > 4AC$, the two eigenvalues of A are real, distinct, and negative. Thus we have shown that (y_{11}, y_{31}) is an improper node and we have a saddle-node connection.

As $B^2 \rightarrow 4AC$, (y_{11}, y_{31}) approaches (y_{12}, y_{32}) so that at $B^2 = 4AC$, we have a saddle-point bifurcation where (y_{12}, y_{32}) becomes stable with its stable manifold dividing S into two regions. Again by Proposition 3,

every orbit in the region with (1,0) on its boundary will go to the asymptotically stable node at (1,0), while orbits in the other region will be attracted to (y_{12}, y_{32}) .

For the remaining case (i), $R_f = 1$, A < C; DFE is stable and the unique endemic equilibrium is asymptotically stable. The eigenvalues of the Jacobian matrix in (A1) are

$$\lambda_1 = 0, \qquad \lambda_2 = -\left(\overline{\mu}_1 + \overline{\mu}_0 + 2\alpha - 2\mu_0\right) < 0.$$

Let $(u_i, v_i)^T$ be the eigenvector of J corresponding to λ_i . Then we have

$$\frac{u_1}{v_1} = -\frac{c_m \beta}{\overline{\mu}_0 + \alpha - \mu_0} < 0,$$
$$\frac{u_2}{v_2} = -\frac{\overline{\mu}_1 + \alpha - \mu_0}{c_\ell \overline{\beta}} > 0.$$

Once again, since (1,0) is at the lower right vertex of the invariant rectangular set S, only the eigenvector manifold corresponding to the zero eigenvalue is contained in S. It follows that DFE is not attracting for S. Hence, by Proposition 3, we deduce that the unique endemic equilibrium must be G.A.S.

This work was supported in part by U.S. National Science Foundation research grants and in part by grant NSC 82-0208-M005-027 from the National Science Council of the Republic of China. We thank an anonymous referee for several suggestions that resulted in improvements in this article. Stavros Busenberg died on April 3, 1993.

REFERENCES

- 1 R. M. Anderson, S. Gupta, and R. M. May, Potential of community wide chemotherapy or immunotherapy to control the spread of HIV-1, *Nature* 350:356-359 (1991).
- 2 L. Bhassorn, C. Noppavan, T. Penporn, and A. Wattana, *The Demographic and Behavioral Study of Female Commercial Sex Workers in Thailand*, Institute of Population Studies, Chulalongkorn University, Bangkok, 1993.
- 3 T. Brown and W. Sittitrai, Estimates of recent HIV infection levels in Thailand, Research Report No. 9, Program on AIDS, Thai Red Cross Society, Bangkok, 1993.
- 4 S. Busenberg and C. Castillo-Chavez, A general solution of the problem of mixing of subpopulations and its application to risk- and age-structured epidemic models for the spread of AIDS, *IMA J. Math. Appl. Med. Biol.* 8:1-29 (1991).
- 5 C. Castillo-Chavez and S. Busenberg, On the solution of the two-sex problem, in Differential Equations Models in Biology, Epidemiology and Ecology (Lect. Notes Biomath. 92), S. Busenberg and M. Martelli, Eds., Springer-Verlag, Berlin, 1991, pp. 80-98.

1 2

. .

- 6 J. Chin, Present and future dimensions of the HIV/AIDS pandemic, VII Int. Conf. AIDS, Florence, 1991, Program and Abstracts.
- 7 E. A. Coddington and N. Levinson, Theory of Ordinary Differential Equations, McGraw-Hill, New York, 1955.
- 8 K. P. Hadeler, R. Waldstätter, and A. Wörz-Busekros, Models for pair formation in bisexual populations, J. Math. Biol. 26:633-649 (1988).
- 9 S. Hawkes, G. J. Hart, A. M. Johnson, C. Shergold, E. Ross, K. M. Herbert, P. Mortimer, J. V. Parry, and D. Mabey, Risk behaviour and HIV prevalence in international travelers, *AIDS* 8:247-252 (1994).
- 10 Y. H. Hsieh, Modelling the effect of screening in HIV transmission dynamics, in Differential Equations Models in Biology, Epidemiology and Ecology (Lect. Notes Biomath. 92), S. Busenberg and M. Martelli, Eds., Springer-Verlag, Berlin, 1991, pp. 99-120.
- 11 Y.-H. Hsieh and J. X. Velasco-Hernandez, Community treatment of HIV-1: initial stage and asymptotic dynamics, *Biosystems* (in press).
- 12 W. Huang, K. L. Cooke, and C. Castillo-Chavez, Stability and bifurcation for a multiple-group model for the dynamics of HIV/AIDS transmission, SIAM J. Appl. Math. 52:835-854 (1992).
- 13 F. LePont and S. M. Blower, The supply and demand dynamics of sexual behavior: implications for heterosexual HIV epidemics, J. AIDS 4:987-999 (1991).
- 14 X. Lin, H. W. Hethcote, and P. van den Driessche, An epidemiological model for HIV/AIDS with proportional recruitment, *Math. Biosci.* 118:181-195 (1993).
- 15 J. M. Mann, AIDS—the second decade; a global perspective, J. Infect. Dis. 165:245-250 (1992).
- 16 H. Napaporn, A. Bennet, and J. Knodel, *Sexual Networking in a Provincial Thai* Setting, AIDS Prevention Monograph Series Paper No. 1, Bangkok, 1992.
- 17 N. S. Padian, S. C. Shiboski, and N. P. Jewell, Female-to-male transmission of human immunodeficiency virus, J. Am. Med. Assoc. 266:1664–1667 (1991).
- 18 W. Sittitrai and T. Brown, The Asian AIDS epidemic, Congressional Forum on the HIV/AIDS Pandemic, Washington, DC, June 23-25, 1992.
- 19 W. Sittitrai, P. Phanuphak, J. Barry, and T. Brown, Thai Sexual Behavior and Risk of HIV Infection: A Report of the 1990 Survey of Partner Relations and Risk of HIV Infection in Thailand, Program on AIDS, Thai Red Cross Society, and Institute of Population Studies, Chulalongkorn University, Bangkok, 1992.
- 20 H. Thieme, Convergence results and Poincaré-Bendixson trichotomy for asymptotically autonomous differential equations, J. Math. Biol. 30:755-763 (1992).
- 21 J. X. Velasco-Hernandez and Y. H. Hsieh, Modelling the effect of treatment and behavioral change in HIV transmission dynamics, *J. Math. Biol.* 32:233-249 (1994).
- 22 R. Waldstätter, Pair formation in sexually-transmitted diseases, in *Mathematical and Statistical Approaches to AIDS Epidemiology* (Lect. Notes Biomath. 83), C. Castillo-Chavez, Ed., Springer-Verlag, Berlin, 1989, pp. 260–274.
- 23 C. P. Wallace, AIDS fuse is lit in Asia, Los Angeles Times, Jan. 7, 1992, pp. A1-A11.