# CHAPTER 6

## MODELING GONORRHEA IN A POPULATION DIVIDED INTO EIGHT GROUPS

In Chapters 4 and 5, the population was divided into two groups. Here the population is divided according to sex, the level of sexual activity and whether the infections are symptomatic or asymptomatic. There are eight groups representing the eight combinations, such as the male-highly active-asymptomatic group. This population dynamics model is used to compare the effectiveness of six control methods for gonorrhea involving population screening and contact tracing of selected groups. A condensed version of the results in this chapter appeared in a paper (Hethcote, Yorke and Nold, 1982).

In section 6.1 the eight groups are described and the system of eight nonlinear ordinary differential equations is given. The number of independent contact rates among people in the eight groups is reduced by using proportionate mixing assumptions in section 6.2. It is shown that a contact number determines whether the disease dies out or remains endemic. The six gonorrhea control methods considered involve screening of women and men, contact tracing women and men who are infectees and contact tracing women and men who are infectors. The six control methods are incorporated into the eight group model in section 6.3.

Estimates of parameters used in the equations are described in section 6.4. Some values of parameters are found from current data and estimates of epidemiologists while other values such as the levels of sexual activity are found indirectly so that incidences and prevalences are consistent with observations and so that the effects of the screening program correspond to observed incidence changes. A computer program finds the endemic equilibrium levels for a given parameter set for each of the six control methods. This program is described in section 6.5; a listing of the program and a sample output are given in appendices. A table summarizing the calculations for six different parameter sets is given in section 6.6.

Since gonococcal infection in a woman can lead to pelvic inflammatory disease and sterility, our criterion for the effectiveness of a control procedure is the extent to which the equilibrium prevalence (and hence the number of months of infection) in women is reduced when the control is added to the equations. The calculations in section 6.6 show that discovering (and curing) **an infectious woman**

**by tracing infectors** of diagnosed men **is more effective** in this sense **than** discovering (and curing) an infectious woman by **screening**, and **the latter is more effective than** discovering (and curing) an infectious woman by **tracing contacts** of diagnosed men. The calculations also show that the relative effectiveness of using the corresponding procedures to discover infectious men instead of women is approximately the same. Of course, it is more difficult to discover infectious men because male prevalence is much lower.

The control procedures are small supplements added onto the current screening program. The calculations assume that the suplementary control procedures all discover the same number of individuals per unit time, namely, a number equal to 1% of the incidence in women. All calculations are made when the prevalences are at equilibrium. In section 6.7 we will consider conclusions from the model, the relative difficulties of discovering one individual by each of the procedures and implications for gonorrhea control strategies. The results of our theoretical modeling are meant to advise gonorrhea control strategists and clinicians.

## 6.1 The Model for a Heterogeneous Population

Gonorrhea transmission occurs in a population in which some infectives are more active sexually than others, in which probabilities of transmission per sexual contact are quite different for men and women, and in which some infectives are asymptomatic with long durations of infection while others are symptomatic with shorter durations. A model with eight groups is needed to incorporate all of these essential aspects. Although sexually transmitted diseases are a major health problem among homosexuals, there does not seem to be much transmission between the homosexual population and the heterosexual population. Consequently, we consider a heterosexual population, i.e., we assume that all contacts are heterosexual. The population considered here is the sexually active women who are the target of the screening program in the United States and their male partners.

The four groups of women have odd indices (1,3,5,7) and the four groups of men have even indices (2,4,6,8). Let $N_i$ denote the size of the group i. Since the sizes of the odd (even) index groups can be divided by the total number of women (men) in the population, we assume that $N_i$ is the fraction of women or men in group i. Hence

$$N_1 + N_3 + N_5 + N_7 = 1 \text{ and } N_2 + N_4 + N_6 + N_8 = 1.$$

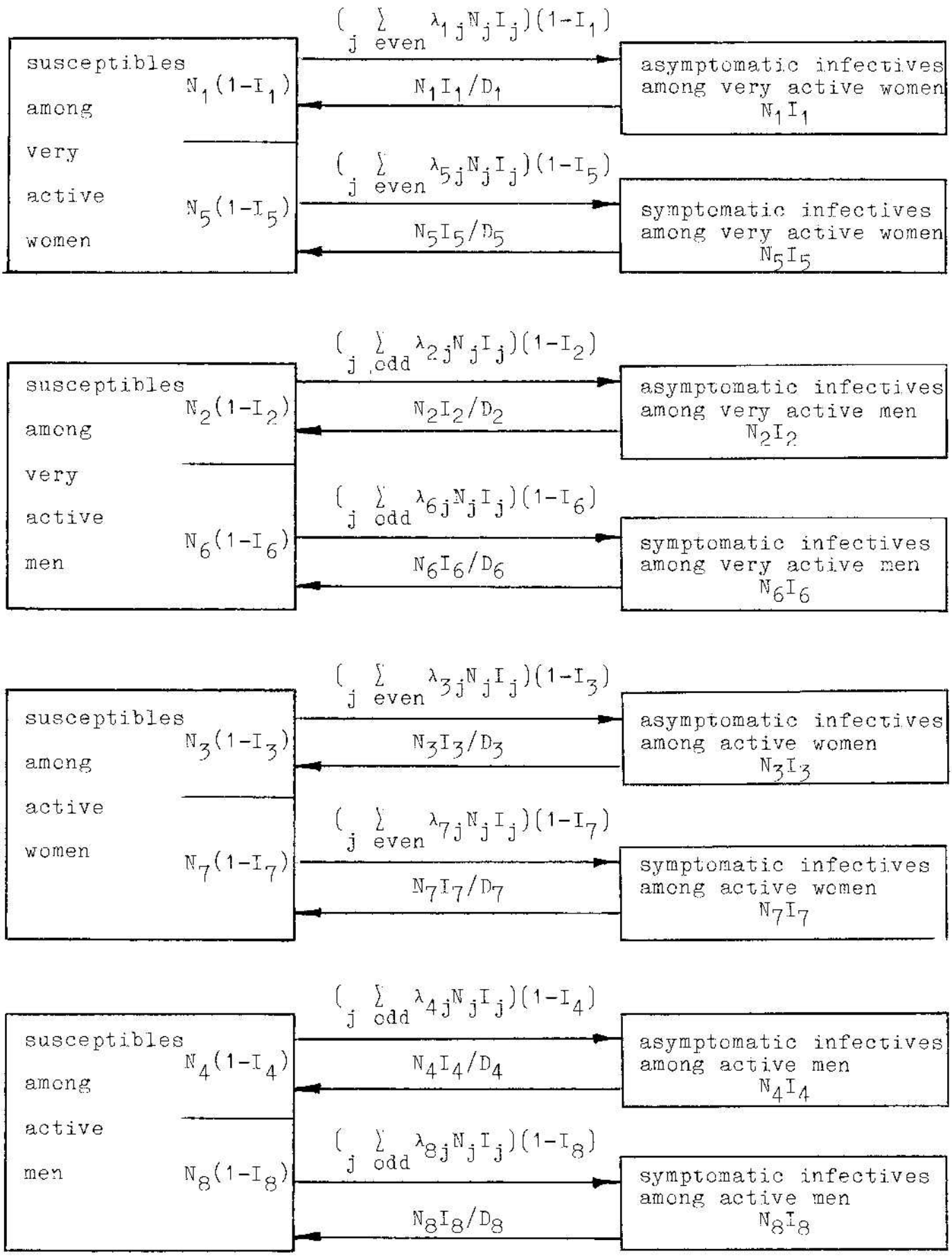


Figure 6.1. Flow diagram for the eight group model.

As indicated in Chapter 1, gonococcal infection does not confer resistance or immunity against reinfection so that individuals in each group are either susceptible or infectious. As in section 3.1, the prevalence in group i at time t (in months) is $I_i(t)$ and the susceptible fraction of the population is $1-I_i(t)$.

If the **symptoms** of an infection **are sufficient to cause the person to seek medical treatment,** then the person is **symptomatic;** otherwise, the person is asymptomatic. As before, the sexual activity is measured by the frequency of encounters (cf. section 3.2). Group 1(2) consists of very active women (men) who are asymptomatic when they are infectious. Group 3 (4) consists of active women (men) who are asymptomatic when infectious. Group 5 (6) consists of very active women (men) who are symptomatic when infectious. Group 7 (8) consists of active women (men) who are symptomatic when infectious. Of course, the actual population is very diverse so that it does not divide clearly into groups; however, it is convenient conceptually and computationally to assume the existence of these groups so that the effectiveness of various control procedures can be evaluated and compared.

The model consists of the differential equations and initial conditions presented in section 3.1 with n=8.

$$\frac{d}{dt}(N_i I_i) = \sum_{j=1}^{8} \lambda_{ij}(1-I_i)N_j I_j - N_i I_i / D_i \qquad [6.1]$$

$$I_i(0) = I_{io} \qquad i = 1,2,\ldots,8. \qquad [6.2]$$

Note that here $\lambda_{ij} = 0$ if i+j is even since there are only heterosexual contacts in the model. We assume that the $\lambda_{ij}$ are fixed and do not vary seasonally. Here we use one month as the unit time so $D_i$ is the mean duration of infection in months. A flow diagram for this model is given in figure 6.1. Modifications of the equations [6.1] to include control procedures will be described in section 6.3.

The first challenge in dealing with a model of this complexity is choosing the parameters in a simple and rational way, in a way sufficiently clear that the reader can feel confident that a reasonable collection of parameter choices has been tested. There are, after all, thirty two nonzero $\lambda_{ij}$s, eight $N_i$s and eight $D_i$s. Reducing the number of parameters will be a major concern in this chapter.

In the model, we have separated women into groups according to whether or not their infections are asymptomatic. Wiesner and

Thompson (1980) state that the infected individual's ability to recognize symptoms of gonococcal infection and then get medical treatment may vary significantly from person to person. However, it is also reasonable to assume that very active women are distributed between being asymptomatic and symptomatic when infectious in a random manner. Our model is consistent with this assumption if we assume that the susceptibles among very active women are sometimes asymptomatic and sometimes symptomatic. Similar remarks also apply to the other groups. Other models involving asymptomatics have also been considered (Kemper, 1978; Bailey, 1979; Cooke, 1982).

As in the earlier models we will consider the positive equilibrium point and how it changes when parameter values change or when control procedures are added. Let $E_i$ be the endemic equilibrium prevalence in group i. Then the $E_i$ are the solutions of the 8 simultaneous quadratic equations obtained by setting the right sides of [6.1] equal to zero. Since the first term in each differential equation corresponds to the incidence (number of new cases per unit time), the equilibrium incidence in group i is equal to the equilibrium prevalence $E_i$ times the group size $N_i$ divided by the mean duration $D_i$ (cf. section 2.1).

## 6.2 The Contact Matrix

The contact matrix has 32 zero entries and 32 positive entries which must be determined. As in section 3.2, we will initially use a proportionate mixing approach to determine these contact rates, i.e., we assume that the number of encounters between groups of women and men is proportional to the relative sexual activities of the groups.

Let $A_j$ be the activity level of group j which is the average number of encounters (with different partners) of a person in group j per unit time. Let $Q_j$ be the probability that an infective in group j transmits the disease during an encounter with a susceptible, i.e., that there is an adequate contact. Let $M_{ij}$ be the fraction of encounters made by an average infective of group j with persons in group i. Hence $\Sigma_i M_{ij} = 1$ for each j. The matrix M is called the mixing matrix. Using these definitions it follows that the average number of encounters per unit time of an infective in group j with different partners in group i is $A_j M_{ij} = \lambda_{ij}/Q_j$ .

The fact that each sexual encounter involves one man and one woman requires that the average number of encounters per unit time for women (sum of $A_i N_i$ over odd indices) must equal the average for men (sum of $A_i N_i$ over even indices); we denote this value by A. We define

the activity fraction $B_i$ of groups i by $B_i = A_i N_i / A$. Hence

$$B_1 + B_3 + B_5 + B_7 = 1 \quad \text{and} \quad B_2 + B_4 + B_6 + B_8 = 1.$$

We assume all $A_i > 0$ so that all $B_i > 0$. The proportionate mixing assumption is that the encounters of a person are distributed in proportion to the activity fractions of the groups of the opposite sex, i.e., $M_{ij} = B_i$ for all i and j such that i + j is odd. Note that the proportionate mixing formulation here is different from that in section 3.2 since there are groups of women and men here with heterosexual contacts.

We let $K_j > 0$ denote the contact number for group j, which is the number of adequate contacts made by a typical infective of group j during the duration of infection so that $K_j = Q_j A_j D_j$. The number of adequate contacts $T_{ij}$ of a group j infective with group i during an average case satisfies $T_{ij} = \lambda_{ij} D_j = A_j M_{ij} Q_j D_j = M_{ij} K_j$ We call the matrix $[T_{ij}]$ the transmission matrix. **Proportionate mixing means that**

$$\mathbf{T_{ij} = B_i K_j}$$

**for i+j odd** and $T_{ij} = 0$ for i+j even. Notice that the matrix $[T_{ij}]$ is determined by 16 values, the $B_i$s and $K_j$s.

The second generation contact number for this model with proportionate mixing is

$$K = \Big( \sum_{i \text{ odd}} B_i K_i \Big) \Big( \sum_{j \text{ even}} B_j K_j \Big),$$

where the first factor is the average number of men adequately contacted by an average infectious woman during her infectious period, and the second factor is the average number of women adequately contacted by an average infectious man. Thus K is the number of women contacted in two generations, that is, by an infectious woman through her contacts with men (first generation) and their contacts with other women (second generation). The theorem below means that **this second generation contact number is a threshold parameter which determines whether the disease dies out** ($K < 1$) **or remains endemic** ($K > 1$). The second generation contact number has the same intuitive interpretation as in section 5.1.

The characteristic equation for the transmission matrix $[T_{ij}]$ is $\det([T_{ij}] - \alpha I) = \alpha^6(\alpha^2 - K) = 0$ . This equation follows from a detailed calculation using properties of determinants. Notice that $[T_{ij}]$ is

irreducible since all $B_i$s and $K_j$s are positive. Recall that irreducibility implies that the whole population cannot be split into two subpopulations which do not interact with each other.

THEOREM 6.1 In the proportionate mixing model, the solutions of equations [6.1] approach the origin if $K \leq 1$ and they approach a unique positive equilibrium if $K > 1$.

PROOF. From the characteristic equation and Lemma 3.2, the Perron eigenvalue $p(T) = K^{1/2}$ is equal to the spectral radius $r(T)$. By Lemma 3.3, $r(T) = K^{1/2} \leq 1$ is equivalent to the outbreak eigenvalue satisfying $m_0 = s(V) \leq 0$. The theorem now follows from Theorem 3.1.

The proportionate mixing assumption is not always completely reasonable, since a very active person may be more likely to have an encounter with a very active person. Very active people may know how to seek very active people. In the extreme case where very active (active) people only have encounters with very active (active) people, then the encounters of a person are distributed in proportion to the fractional activity levels of the opposite sex group with the same activity level. Thus there is proportionate mixing within the very active subpopulation and within the active subpopulation, but there is no interaction between these subpopulations. The mixing matrix for this model has 48 zero entries and 16 positive entries.

Since the actual mixing is probably somewhere between the extremes of proportionate mixing in the entire population and proportionate mixing in the activity levels, we use a mixing matrix M which is 1-G times the mixing matrix for proportionate mixing plus G times the mixing matrix for proportionate mixing in the activity levels. The fraction G between 0 and 1 is called the selectivity constant.

## 6.3 Six Control Methods

The reduction of pelvic inflammatory disease (PID) is a primary goal of gonorrhea control activities. Some infected women develop PID; consequently, it is reasonable to assume that a reduction in the months of infection of women in the population would cause a corresponding reduction in PID. Therefore **our criterion for the effectiveness of a control procedure is the percentage reduction in prevalence for women.** This is equivalent to measuring the percentage reduction in total months of infection for women each year. Reduction in incidence is a less useful criterion, because control procedures can

cure people and make them available for new infections, so that two cases might occur where there would otherwise have been one case of long duration.

The six control methods are screening and targeted contact tracing procedures which are designed to discover infectious women and men so that they can be cured. Let C be proportional to the number of women being screened per unit time. The $R_i$ are the relative rates at which women are discovered and cured by screening in the various groups. C is an adjustable parameter measuring the effort put into the screening program so that $CR_i$ is the rate at which women are discovered and cured in group i. For each of the six supplementary control procedures, there are analogous terms that we denote by E and $P_i$. Equations [6.1] are modified to include C and E as follows:

$$\frac{d}{dt}(N_i I_i) = \sum_{j=1}^{8} \lambda_{ij}(1-I_i)N_j I_j - N_i I_i/D_i - CR_i - EP_i \qquad [6.3]$$

Our objective is to compare the effects of the six control methods when they are implemented at low levels as supplements to the existing screening program. To be comparable we choose the value of E for each method so that the discoveries are 1% of the incidence in women, i.e.,

$$\sum_{i=1}^{8} EP_i = (.01) \sum_{i \text{ odd}} \sum_{j=1}^{8} \lambda_{ij}(1-I_i)N_j I_j .$$

The six control methods are described below.

Type 1W: Screening of Women

Screening of women consists of culture testing of women at certain health facilities. Screening of women is currently the primary control method in the United States. The number of infectious women discovered by screening is proportional to the prevalence. If the prevalence is doubled in a group, then twice as many will be discovered by screening. Thus

$$R_i = I_i N_i \quad \text{for } i \text{ odd}$$

and $R_i = 0$ for i even. Since the type 1W supplementary program also corresponds to screening, $P_i = I_i N_i$ for i odd and $P_i = 0$ for i even.

Type 1M: Screening of Men

This procedure is analogous to type 1W with roles reversed so that $P_i = I_i N_i$ for i even and $P_i = 0$ for i odd. (We remark that screening of men produces so few discoveries that it is generally

impractical.)

Type 2W: Contact Tracing Women Who Are Infectees

An infectee is a person to whom the gonococcal infection has been spread by the reference case (the patient who has come in for treatment) and the infector is the source of the gonococcal infection in the reference case. The supplementary control procedure 2W consists of discovering women infectees by tracing and culture testing women who are named as contacts (but not as the infector) by diagnosed men. Infected men of group j are diagnosed (and cured) at rate $I_j N_j / D_j$ and the average man in group j during the duration of his infection infects $\lambda_{ij}(1-I_i)D_j$ women in group i. Therefore, the number of female infectees per unit time in group i is

$$P_i = \sum_{j \text{ even}} \lambda_{ij}(1-I_i)I_j N_j \quad \text{for i odd}$$

and $P_i = 0$ for i even. Hence type 2W discoveries are distributed in proportion to the rate at which new cases occur in the female groups, i.e., in proportion to the incidence.

Type 2M: Contact Tracing Men Who Are Infectees

This procedure is analogous to type 2W with roles reversed so that $P_i = \sum_{j \text{ odd}} \lambda_{ij}(1-I_i)I_j N_j$ for i even and $P_i = 0$ for i odd. Note that 2W and 2M involve tracing contacts and do not include tracing the named infector or source of the infection.

Type 3W: Contact Tracing Women Who Are Infectors

In this procedure, infectious women are identified through the men they infect. The probability that a diagnosed man has been infected by a woman in group i is proportional to the rate at which infections are caused by women in group i. Hence the discoveries are distributed using

$$P_i = \sum_{j \text{ even}} N_i I_i \lambda_{ji}(1-I_j) \quad \text{for i odd}$$

and $P_i = 0$ for i even.

Type 3M: Contact Tracing Men Who Are Infectors

In this procedure, the discoveries are distributed using

$$P_i = \sum_{j \text{ odd}} N_i I_i \lambda_{ji}(1-I_j)$$

for i even and $P_i = 0$ for i odd.

Screening and control types 1W and 1M change the usual removal terms in [6.3] so that [6.3] is like [3.1], but with modified durations. Control types 2W and 2M change the incidence terms in [6.3] so that [6.3] is like [3.1] when the terms in [6.3] are combined, but with a different contact matrix. The signs of the entries are unchanged for small supplementary control efforts. Control types 3W and 3M modify the linear and quadratic terms in [6.3], but for small E [6.3] is like [3.1] with a different contact matrix and different durations. Since the models with controls are forms of [3.1], they are covered by Theorem 3.1. Thus we can examine the coordinates $Y_i$ of the endemic equilibrium point corresponding to specific epidemiologic and control parameters. As indicated in the introduction to this chapter, control procedures are compared by comparing their effect on the equilibrium prevalence in women.

## 6.4 Parameter Estimation

The following three criteria are used as reasonable restrictions on the parameter sets for the model:

1. **the incidence for men must be slightly larger than the incidence for women;**

2. **the prevalence for women must be approximately 3% of the population of women at risk;**

3. **discovering 10% of the infective women by population screening must result in a 20% decrease in incidence in men.**

The first criterion is based on observed gonorrhea incidence (Wiesner and Thompson, 1980; CDC, 1981a) The second criterion is used because prevalences exceeding 3% seem unrealistic as discussed in section 4.1. Yorke, Hethcote and Nold (1978) estimated using a trend analysis that approximately 10% of all actual cases of gonorrhea in women in the United States were discoveries of the culture-screening program. They also estimated that the result of this discovery of 10% of infectious women was an approximately 20% decrease in actual incidence in men. The third criterion corresponds to these estimates.

The system [6.3] contains 48 parameters: 32 positive $\lambda_{ij}$, 8 $D_i$ and 8 $N_i$. Under some simplifying assumptions described below, **the 48 parameters can be reduced to the following 8:** the duration of infection for all asymptomatics ($D_a$), the duration of infection for all symptomatics ($D_s$), the fraction of men who are asymptomatic when infectious ($A_m$), the fraction of women who are asymptomatic when infectious ($A_w$), the ratio (J) of the transmission probabilities during an encounter by an infectious man and by an infectious woman,

the fraction (F) of the women or men who are in the very active groups, the ratio (H) of the sexual activity of the very active to the active persons, and the selectivity constant (G). These constants and estimates for them are discussed below.

We assume that there is one typical mean duration for the four groups of asymptomatics and another for the four groups of symptomatics. The duration ranges for asymptomatic women and men are estimated to be 3-12 months and 3-6 months, respectively (Wiesner and Thompson, 1980). The duration ranges for symptomatics are estimated to be 3-45 days for women and 2-30 days for men (Wiesner and Thompson, 1980). Hence we use $D_a$ = 6 months and $D_s$ = .25 or .5 month. The results depend primarily on the ratio $D_a/D_s$ so that halving or doubling both $D_a$ and $D_s$ has only a slight effect on the relative merits of the control procedures. We assume that the fractions which are asymptotic when infectious are $A_w$ = .6 for women and $A_m$ = .1 for men. These parameter values lead to results which are consistent with estimates in Wiesner and Thompson (1980) that: 30-60% of the incidence in women are asymptomatics; asymptomatics are 80-98% of the prevalence in women and, consequently, are responsible for 80-98% of the transmissions; 2-5% of the incidence in men are asymptomatics and asymptomatic men account for 60-80% of the prevalence in men and hence 60-80% of the transmissions.

During sexual intercourse the probability of transmission from an infectious woman to a susceptible man is estimated to be .2 to .3 while the probability of transmission from an infectious man is approximately .5 to .7 (Wiesner and Thompson, 1980). Because an encounter involves one or more sexual intercourses, the transmission probability for women might be .5 while the transmission probability for men could be .9. The model requires an estimate of the ratio J of the transmission probability for men to that for women. This ratio J is taken to be 2 or 1.

Assume that the fraction F who are in the very active groups and the ratio H of sexual activity of the very active to the active persons is the same for women and men. In our model, we assume that 1 to 3% of the population is very active and that very active people are 5 to 10 times as sexually active as active people. The population size fractions $N_i$ can be calculated by using $N_1 = (F)(A_w)$, $N_3 = (1-F)(A_w)$, $N_5 = F(1-A_w)$, $N_7 = (1-F)(1-A_w)$ and analogous formulas for $N_2$, $N_4$, $N_6$ and $N_8$.

The contact numbers $K_i$ (relative to $K_1$) are found from the durations $D_i$, the population sizes $N_i$, the transmission probability

ratio J and the activity level ratio H by using

$$K_2 = \frac{K_1 D_2 J}{D_1} (N_1 + N_5 + \frac{N_3+N_7}{H})/(N_2 + N_6 + \frac{N_4+N_8}{H})$$

$K_3 = K_1 D_3/(D_1 H)$, $K_4 = K_2 D_4/(D_2 H)$, $K_5 = K_1 D_5/(D_1)$, $K_6 = K_2 D_6/(D_2)$, $K_7 = K_1 D_7/(D_1 H)$, and $K_8 = K_2 D_8/(D_2 H)$. These relationships are derived by using $K_i = Q_i A_i D_i$, $A_1 = HA_3 = A_5 = HA_7$, $A_2 = HA_4 = A_6 = HA_8$, and the conservation of encounters. The contact number $K_1$ determines the absolute level of sexual contacts and is chosen so that the third criterion is satisfied as explained in the next paragraph. The contact numbers and the durations are used to determine the activity levels. These activity levels and the population size fractions are used to determine the mixing matrices for the proportionate mixing model and for the model with proportionate mixing within activity levels. The selectivity constant G which combines these two mixing matrices is chosen so that the second criterion is satisfied. If G is zero, prevalences in the model are usually unrealistically high. The selectivity constant G measures the correlation between the activity level of the infectious person and the activity level of the sexual partner. The correlation coefficient can be shown to be

$$r = G[(\frac{1-G}{1+FH-F} + G)(\frac{H(1-G)}{1+FH-F} + G)]^{-1/2}$$

In the proportionate mixing model (when G is zero), the correlation coefficient r is zero.

The constant C in [6.3] is adjusted so that 10% of the equilibrium incidence in women is discovered by population screening. The third criterion requires that the absolute level of sexual contacts is adjusted so that the result is a 20% decrease in incidence in men. If the absolute level were too low, then the prevalences would be zero or the addition of C could be sufficient to drive the prevalences to zero. If the absolute level were too high, then the addition of population screening would cause only a small change in incidence in men. The correct absolute level of sexual contacts is determined by an iterative process using a separate computer program.

The extra cure rate is supplementary since it is a small control effort added onto the existing population screening program. For the supplementary control procedures, E is chosen so that the number of extra discoveries are equal to 1% of the equilibrium incidence in women. Hence the supplementary control procedures are directly comparable since they all involve the same number of discoveries.

## 6.5 The Computer Programs

Computer programs have been written to find the endemic equilibrium point from the simultaneous quadratic equations obtained by setting the right sides of [6.3] equal to zero. The input requested by the programs are values related to the eight essential parameters described in the previous section. The programs first construct the contact matrix $[\lambda_{ij}]$, and then solve the differential equations [6.3] numerically using Euler's method until the prevalences are near the equilibrium levels. Finally these good approximations are used as starting values in Newton's method to find the coordinates of the equilibrium point. Although a model with 8 groups is considered here, similar computer programs have been used to compare control procedures for models with 4 and 12 groups.

The computer program FINDK uses an iterative procedure to find the value of the contact number $K_1$ of the first group so that if the number of women discovered by general population screening is 10% of the incidence in women, then there is a 20% decrease in the incidence in men. The computer program GCCONT requests input parameter values and then produces output tables consisting of prevalences, incidences, percent changes and preventions for five cases: the model with no control procedure, the model with general population screening and then the model with general population screening plus one of the three supplementary control procedures 1W, 2W or 3W for women. The computer program SCRMEN is similar except that it produces output for the 3 supplementary control procedures 1M, 2M or 3M for men. Appendix 1 contains the listing of the computer program GCCONT. This program contains many remark statements which explain the steps in the program. The programs FINDK and SCRMEN are modifications of the GCCONT. These computer programs were written in the BASIC language by Annett Nold and Herb Hethcote.

Appendix 2 contains a sample run of GCCONT showing input parameter values and output tables. This sample run produces the data for 1W, 2W and 3W in Table 6.1 corresponding to parameter set 1. Note that $N_1 + N_3 = .60$ and $N_2 + N_4 = .10$ so that .6 of the women and .1 of the men are asymptomatic when infectious. Since $N_1 + N_5 = .02$ and $N_2 + N_6 = .02$, 2% of the women and men are very active. The average durations are $D_a = 6$ months for asymptomatics and $D_s = .5$ months for symptomatics. The sexually active groups are 10 times as active as the less active groups, the transmission probability ratio is 2 and the selectivity constant is .2. Notice that the three criteria given in the previous section are satisfied. In particular note that the

value $K_1$ = 9.238 determined by FINDK causes a 20.0018% decrease in the monthly incidence in men due to general population screening of women. Although the output tables contain detailed information, the sentences at the bottom of each output table contain the most useful information. The percentage decreases and cases prevented corresponding to 1W, 2W and 3W for parameter set 1 were obtained from these sentences.

## 6.6 Comparison of the Supplementary Control Procedures

In Table 6.1 we present the results of calculations with six different parameter sets. Six of the parameters are somewhat arbitrary, namely, the fraction F of the population in the very active groups, the selectivity constant G, the ratio H of sexual activity of very active persons to active persons, the duration $D_a$ of asymptomatics, the duration $D_s$ of symptomatics and the transmission probability ratio J. Therefore we compute the equilibria with several sets of values of these parameters. Thus the parameters F, G, H, J, $D_a$, $D_s$ take on a variety of values, while the other essential parameters are fixed at the values given in section 6.4. The three criteria given in section 6.4 for a parameter set to be reasonable are satisfied for these parameter sets.

As described earlier, we use the percentage decrease in the population prevalence in women as the measure of the effectiveness of a supplementary control procedure. In Table 1 the percentages can be compared directly since each of the six supplementary procedures results in the same number of discoveries. For parameter set number 1, type 3W control (supplementary tracing of infectors of diagnosed men) is 1.9 times as effective per discovery in reducing prevalence as type 1W control (supplementary population screening) and is 2.8 times as effective per discovery as type 2W control (supplementary tracing of contactees of diagnosed men). Control procedure type 3M is 2.2 times as effective per discovery as type 1M and is 5.4 times as effective per discovery as type 2M. Types 1M and 3M are slightly more effective than 1W and 3W, respectively, while 2M is less effective than 2W.

Another measure of the effectiveness of a supplementary control procedure is the number of cases in women and men prevented by the discovery and cure of one infectious person through this procedure. To evaluate the number prevented, the new equilibrium is found when a certain number of cases per day are cured. Then we can determine how much incidence has dropped, that is, how many fewer women and men are

TABLE 6.1

Summary of Output From the Computer Program
for Various Input Parameter Sets

| Parameter Set Number | | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|---|
| F = fraction in very active groups | | .02 | .01 | .03 | .02 | .02 | .02 |
| H = sexual activity ratio | | 10. | 10. | 5. | 10. | 10. | 10. |
| G = selectivity constant | | .2 | .2 | .5 | .2 | .2 | .2 |
| r = correlation coefficient | | .08 | .08 | .31 | .08 | .08 | .08 |
| $D_a$ = duration of asymptomatics | | 6. | 6. | 6. | 6. | 6. | 12. |
| $D_s$ = duration of symptomatics | | .5 | .5 | .5 | .25 | .5 | .5 |
| J = transmission probability ratio | | 2. | 2. | 2. | 2. | 1. | 2. |
| population prevalence with general population screening | women | .028 | .031 | .027 | .028 | .026 | .028 |
| | men | .011 | .012 | .011 | .010 | .015 | .010 |
| population incidence with general population screening | women | .009 | .010 | .009 | .010 | .008 | .005 |
| | men | .011 | .012 | .012 | .014 | .015 | .07 |
| percentage decrease in prevalence in women due to supplementary control procedure | 1W | 4.4 | 4.2 | 4.1 | 4.3 | 4.3 | 4.3 |
| | 2W | 3.0 | 2.9 | 2.7 | 2.7 | 2.9 | 2.7 |
| | 3W | 8.4 | 8.1 | 5.5 | 7.9 | 8.3 | 7.9 |
| | 1M | 4.8 | 4.7 | 4.5 | 5.9 | 2.9 | 5.9 |
| | 2M | 2.0 | 2.0 | 1.8 | 1.6 | 1.3 | 1.6 |
| | 3M | 10.7 | 9.8 | 6.3 | 12.9 | 6.1 | 12.9 |
| cases in women and men prevented per person and cured by the supplementary control procedures | 1W | 6.5 | 6.0 | 6.1 | 6.8 | 8.3 | 6.8 |
| | 2W | 4.5 | 4.2 | 4.2 | 4.4 | 5.7 | 4.4 |
| | 3W | 16.3 | 15.3 | 9.9 | 16.7 | 20.6 | 16.7 |
| | 1M | 8.7 | 8.2 | 8.1 | 11.4 | 6.4 | 11.4 |
| | 2M | 3.8 | 3.6 | 3.5 | 3.3 | 3.0 | 3.3 |
| | 3M | 19.9 | 17.9 | 11.9 | 25.7 | 13.9 | 25.7 |

being infected each day. Using parameter set number 1, the cases in women and men prevented by the discovery of one infectious woman by type 3W are 2.5 times the preventions by type 1W and 3.6 times the preventions by type 2W control. The cases prevented by the discovery of one infectious man by type 3M control are 2.3 times the preventions by type 1M and 5.2 times the preventions by type 2M. Thus the control procedures have the same relative merits using this measure of effectiveness.

The heterogeneity of the population is a result of the sexual activity ratio H, the ratio $D_a/D_s$ of durations of asymptomatics and symptomatics, and the relative likelihood $A_w/A_m$ of a case being asymptomatic. Since parameter sets 2 and 5 describe populations which are approximately as heterogeneous as that of parameter set 1, the percentages are approximately the same. Since parameter set 3 describes a less heterogeneous population than parameter set 1, the percentage decreases in prevalence in women are lower and the ratios are lower than for parameter set 1. Parameter sets 4 and 6 describe more heterogeneous populations than parameter set 1 and the ratios of the percentage decreases in prevalence in women are greater for 3M, 1M and 2M. In a homogeneous population where all people have the same sexual activity levels ($H = 1$) and the same durations ($D_a = D_s$), the procedures 1W, 2W and 3W are equally effective per discovery and the methods 1M, 2M and 3M are equally effective. From the data in Table 1 and other calculations, we conclude that the more heterogeneous the populations, the larger the ratio of the effectiveness of the control procedures.

Types 3W and 3M are more effective because they have a high likelihood of identifying very active people and a high likelihood of identifying asymptomatics. Although types 1W and 1M tend to identify aymptomatics, they are not very effective in finding very active people. Control types 2W and 2M are not very effective in finding either very active or asymptomatic persons. For example, for parameter set 1, the probability that a discovery is a very active person is .20, .23 and .71 for types 1W, 2W and 3W, respectively; and the probability that a discovery is asymptomatic is .93, .57 and .91 for types 1W, 2W and 3W, respectively.

In section 6.4 we assumed that .6 of the women and .1 of the men are in groups where individuals are asymptomatic when infectious. For parameter set 1, asymptomatic women are 57% of the incidence and are 93% of the prevalence; asymptomatic men are 8% of the incidence and are 63% of the prevalence. Hence asymptomatic women (men) account for

93% (53%) of the transmissions. Although the percentages for asymptomatic men are not quite in the estimated ranges specified in section 6.4 they are closer to the ranges for this parameter set than for the many other parameter sets attempted. Hence these values justify a posteriori the above choices of these two parameter values.

## 6.7 Discussion

The eight group model is more realistic than the two group models considered in earlier chapters. The comparison of the strategies studied in this chapter seemed to require a model in which all eight groups interact. Use of the eight group model reveals that tracing infectors is approximately three times as effective as tracing infectees. This result is more realistic than that obtained in section 4.4 using the two group model.

Earlier we defined the core as the union of those groups whose prevalence exceeds 20%. From the calculations for parameter set 1 with screening in Appendix 2, we see that the prevalences of the very active asymptomatic groups are 41% for women and 50% for men. These prevalences are much higher than for the other six groups. Thus the model suggests that the core should consist of very active women and men who are asymptomatic when infectious. However, since it is not understood why some cases are asymptomatic and others are symptomatic, it is also useful to calculate prevalences when asymptomatics and symptomatics are merged. The epidemiologist who is trying to identify the core would not be able to tell whether a particular person is potentially symptomatic or asymptomatic and, consequently, would look at these merged populations. By using the data in Appendix 2, we find that the prevalence for all very active women is 27% and the prevalence for all very active men is 12%. **From this vantage point, the core would consist of all very active women.**

Results which are consistent over a range of acceptable parameter values can be considered to be robust predictions of the model. An example of a robust result is that the relationship between the effectivenesses of the supplementary control procedures is always the same for this model; specifically, infector tracing (type 3W or 3M) is more effective per discovery than population screening (type 1W or 1M) and population screening is more effective per discovery than infectee tracing (type 2W or 2M). Although the magnitude of the ratios of the effectivenesses are not robust since they depend on the particular parameter set, we observe that the greater the heterogeneity of the population in terms of the differences in sexual activity and the

differences in durations between asymptomatics and symptomatics, the larger the ratios of the effectivenesses of the control types.

The relationship between the effectiveness of the supplementary control types is explained as follows. Asymptomatics are more important transmitters than symptomatics because they are infectious longer. Very active persons are more important transmitters because they contact more people while they are infectious. Infector tracing (types 3W and 3M) is the most effective control procedure because it is more likely to identify both asymptomatics and very active people; population screening (types 1W and 1M) is next in effectiveness because it is more likely to identify asymptomatics; and infectee tracing (types 2W and 2M) is the least effective control procedure per discovery because it is not more likely to identify either asymptomatics or very active people.

The discoveries by the supplementary control procedures are all set equal to 1% of the incidence in women so that all of them are comparable. Since there are approximately 1.0 million women infected each year, each supplementary control procedure would have to identify and cure an extra 10,000 people. We estimate that type 1W would require screening at least an additional 500,000 women per year (Yorke, Hethcote and Nold, 1978). Control types 2W and 3W would require testing contacts of the approximately 600,000 infectious men reported annually. It would therefore be necessary to identify and cure one extra infectious contact for each 60 reported men for type 2W control or one more infector for each 60 reported men for type 3W control. Since about 400,000 women are reported annually, it would be necessary to identify and cure one extra male infectee for each 40 reported women for type 2M control or one more male infector for each 40 reported women for type 3W control.

In constructing the model it is assumed that infectors can be clearly distinguished from contacts so that type 3W is distinct from type 2W and type 3M is distinct from type 2M. Even though identifications of infectors versus contactees will not always be accurate, we still feel that concentrating on tracing people named as infectors is a reasonable practical goal. If only the most recent contacts of the reference cases are traced, then the infectors might be consistently missed. A control program which takes advantage of the findings here is one based on interviewing, in which the interviewer raises the question about the infector and whether this person might be brought in for treatment. Field studies could give valuable ideas on conducting interviews to identify infectors.

Tracing persons named as infectors would sometimes lead to infectees; however, the program would still be more effective than a program which puts no emphasis on finding infectors. The program proposed is modest in scale since it only requires that one extra infector be identified for every 40-60 cases of the opposite sex.

The relative merits of the various control procedures depend not only on the effectiveness per discovery in reducing prevalence, but also on the costs of discovering an infective by the procedures. Some investigators believe that infectives can often identify their infectors. Hence the person named as the infector is often the actual infector and this person (especially an asymptomatic) is often still infectious when contacted and checked. It might be necessary to contact and check more than one person identified as a contact (not the infector) of the reference case in order to find another infective. Since only a few people would have to be contacted, the cost of a discovery and cure by tracing infectors and infectees might be low. Yorke, Hethcote and Nold (1978) estimated that about fifty women must be checked by general population screening (type 1W) in order to discover one infectious woman (excluding people who would be identified without culture screening). However, an add-on culture test for someone who is already being examined is substantially cheaper than the cost of tracing and examining a suspected infector or infectee. Since the prevalence in men is very low, the cost of discovering an infectious man by population screening could be so high that type 1M control is impractical. The results of our analysis of this model are meant to advise gonorrhea control strategists and clinicians.

If the cost in dollars or the relative costs could be estimated for the discovery and cure of one person by each of the procedures, then the cost per prevention of a new case could be computed for each of the control procedures. Comparison of the costs per prevention would show which of the six procedures is the most efficient use of the resources available for gonorrhea control. Different cities or states may find that different control procedures are more effective because of the special characteristics of their population.