CHAPTER 3

A REFINED MODEL FOR GONORRHEA DYNAMICS

The population which needs to be described by a model for the transmission of gonorrhea consists of those sexually active people who could be infected by their contacts. The model in Chapter 2 assumes that this population is homogeneous and uniform; however, that model is too simple since the population is really quite heterogeneous. A suitable model should allow for heterogeneity by incorporating many groups. The division into groups could be done according to differences in sex, sexual contact rates, sexual behavior, age, geographic location, socioeconomic status, etc. For example, some individuals are more active sexually than others in the sense that they have more frequent changes of sex partners. Some infected people, especially women, are essentially asymptomatic and do not seek treatment while others have symptoms which cause them to seek treatment.

In section 3.1 we develop a model for a population divided into n groups or subpopulations. We show that **either the disease dies out naturally for all possible initial levels or the disease remains endemic for all future time.** Moreover, the numbers of infectives and susceptibles in each group approach nonzero constant levels, which are independent of initial levels. The effects of changes in the parameter values (corresponding to epidemiological changes) on a disease can be determined by examining the resulting changes in the endemic equilibrium levels.

A method of determining the contact rates among groups by using a proportionate mixing assumption is described in section 3.2. With this assumption the threshold quantity which determines whether the disease dies out or remains endemic is an average contact number. Models with different groups are considered in subsequent chapters.

3.1 A Gonorrhea Model with n Groups

Assume that the population is divided into n groups and let N_i be the size of the subpopulation in group i. We assume that each group is homogeneous in the sense that all individuals in the group are similar. They should have the same rates of contact with new sexual partners, the same mean durations of infection and the same likelihood of acquiring infection during a sexual encounter with an infectious partner. We assume that individuals are either susceptible or infectious and that infectious individuals in a group have the same

sexual behaviour and activity levels as susceptibles. Let $I_i(t)$ denote the prevalence in group i at time t so that the susceptible fraction in group i is $1-I_i(t)$. We measure time t in days.

Let λ_{ij} be the average number of adequate contacts (i.e., contacts sufficient for transmission) per unit time (one day) of an infective in group j with persons in group i. Since the susceptible fraction in group i is $1-I_i(t)$, the average number of susceptibles in group i infected per unit time by an infective in group j is $\lambda_{ij}(1-I_i(t))$ and the average number infected per unit time by N_jI_j infectives is $\lambda_{ij}N_jI_j(1-I_i(t))$.

Let d_i be the mean duration of infection in days for a person in group i. As in Chapter 2, we assume that each infective in group i has a fixed chance of recovering each day and that the probability is $1/d_i$. Thus the removal rate per day from the infectious class is N_iI_i/d_i. As noted in section 2.1, that this is equivalent to assuming that the durations of infection in group i have a negative exponential distribution (Hethcote and Tudor, 1980).

The differential equations for the model are

$$\frac{d}{dt}(N_iI_i) = \left(\sum_{j=1}^{n} \lambda_{ij}(N_jI_j)(1-I_i)\right) - N_iI_i/d_i \qquad [3.1]$$

with initial conditions $I_i(0) = I_{io}$ for $i=1,2,\ldots,n$. The first term in each differential equation is the rate of new infections or incidence in group i and the second term is the removal rate due to recovery. Figure 3.1 shows the susceptible and infective compartments and the transfer rates between compartments.

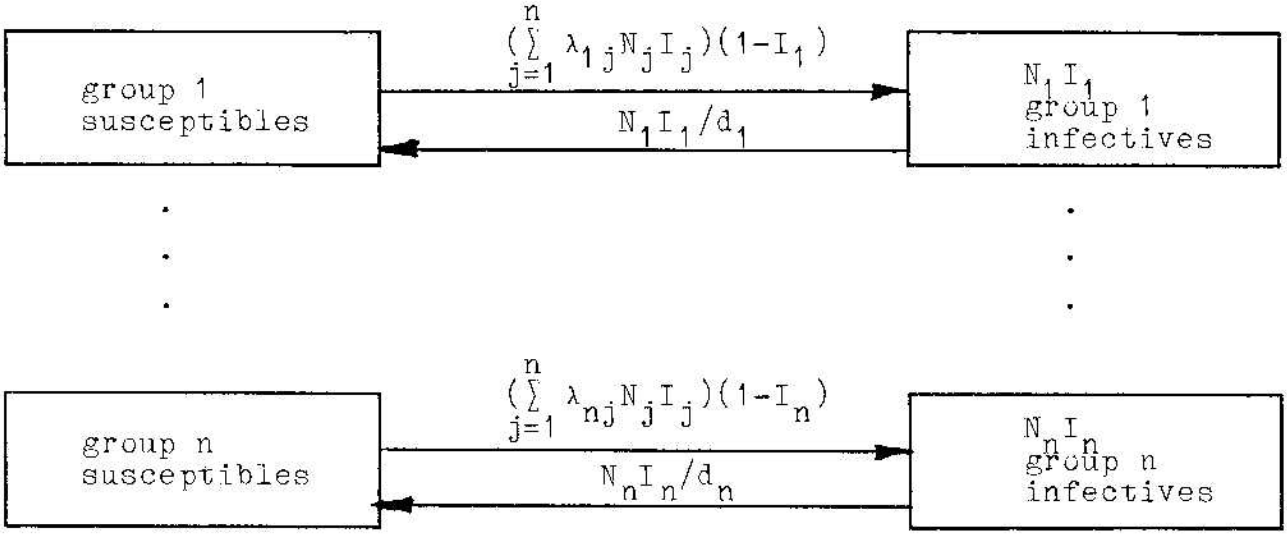

Figure 3.1 Flow diagram for the model [3.1]

Lajmanovich and Yorke (1976) proved that the model [3.1] is well posed. That is, unique solutions of [3.1] exist for all time, depend continuously on the initial data, and are always between 0 and 1. The nxn coefficient matrix A in the linearization of [3.1] is given by $A = L-D$ where $L = [\lambda_{ij}N_j]$ and D is a diagonal matrix with N_i/d_i as the entry in the ith row and column. Let $s(A)$ be the stability modulus of A, i.e., the maximum real part of the eigenvalues of A. They proved the following theorem.

THEOREM 3.1. Assume that the model is irreducible, that is, the population cannot be split into two subpopulations that do not contact each other. The solutions of [3.1] approach the equilibrium point at the origin if $s(A)\leq 0$ and they approach a unique positive equilibrium point if $s(A)>0$, provided there is some infection in some group initially.

Thus **gonorrhea will die out if the parameter values are such that $s(A)\leq 0$ and will approach an endemic steady state if $s(A)>0$.** One practical implication of the theorem above is that it allows us to focus on the positive equilibrium point and to see how it changes when parameter values change or when control procedures are added. Let $E_i>0$ be the equilibrium prevalence (the fraction of group i that is infectious at equilibrium). Thus the E_i are the solutions of the n simultaneous quadratic equations obtained when the right sides of [3.1] are set equal to zero. From the quadratic equations, 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. Figure 3.2 shows the typical behavior of solution paths as they approach an endemic equilibrium point.

One of the striking features of Theorem 3.1 is the qualitative dynamical conclusion that equations [3.1] have a unique equilibrium point, either strictly positive or zero, which is the limit of every solution starting out from a state where infection is present. Hirsch (1984) has shown that this conclusion also holds for a generalization of equations [3.1]. In his differential equations, the incidence and removal terms are given by functions which satisfy certain conditions. His model is so general that it is not possible to give a procedure for deciding whether the equilibrium point corresponds to an endemic steady state or to die out of the disease. However, the generality of his model strongly suggests that any observed fluctuations in the incidence are not due to the intrinsic dynamics of the disease so that they must be due to fluctuations in

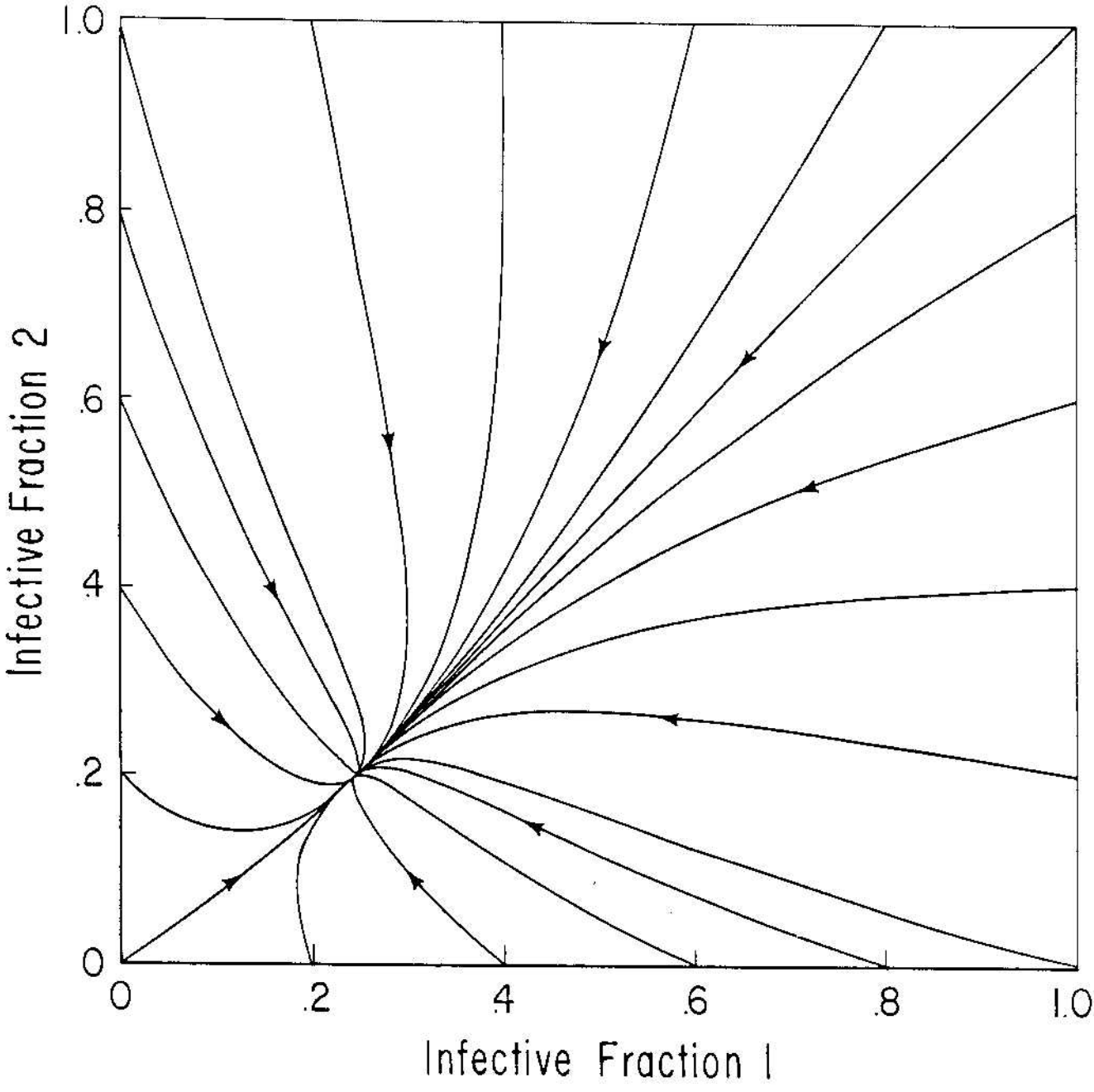

Figure 3.2. Solution paths approaching the endemic equilibrium point when $s(A) > 0$.

epidemiological or environmental factors or in reporting.

3.2 Proportionate Mixing Among Groups

The contact rates λ_{ij} in the contact matrix can be determined methodically by using some assumptions regarding the interactions of the groups. The "proportionate mixing" approach explained in Nold (1980) assumes that the number of adequate contacts between two groups is proportional to the relative sexual activities of the two groups. An encounter will refer to one or more episodes of sexual intercourse with a new partner. For example, if group 1 has 10% of all encounters and group 2 has 40% of all encounters, then in a proportionate mixing model, the fraction of all encounters which are between groups 1 and 2 is .10 × .40. The frequency of encounters is a better measure of sexual activity that is likely to transmit infection than the frequency of sexual intercourse, since encounters are new opportunities to become infected or to transmit the infection.

Let a_j be the activity level of group j, which is the average number of encounters of a person in group j per unit time. Thus $1/a_j$ is the average time between encounters for a person in group j. Let q_j be the probability that an infective in group j transmits the infection 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. Notice that the sum of each column in the mixing matrix M is 1. From these definitions it follows that the average number of adequate contacts per unit time of an infective in group j with different partners in group i is $\lambda_{ij} = a_j m_{ij} q_j$.

The average number of encounters per unit time is $A = \sum_{i=1}^{n} a_i N_i$. The fractional activity level of group i defined by $b_i = a_i N_i / A$ is a measure of the relative sexual activity of group i. Notice that $\sum_{i=1}^{n} b_i = 1$. The proportionate mixing assumption is that the **encounters of a person are distributed in proportion to the fractional activity levels**, i.e., $m_{ij} = b_i$.

The contact number k_j for group j, which is the number of adequate contacts made by a typical infective in group j during the duration of infection, satisfies $k_j = q_j a_j d_j$. If t_{ij} is the number of adequate contacts with group i of a group j infective during an average case, then $t_{ij} = \lambda_{ij} d_j = a_j m_{ij} q_j d_j = m_{ij} k_j$. The $n \times n$ matrix $T = [t_{ij}]$ is called the transmission matrix. In the proportionate mixing model, $t_{ij} = b_i k_j$.

The average contact number for this model with proportionate mixing is $\bar{K} = \sum_{i=1}^{n} b_i k_i$, which is the weighted average of the contact numbers of the groups with the fractional activity levels used as weights. It is the average number of persons contacted by an average infective during the infectious period. We now prove that this average contact number is a threshold parameter which determines whether gonorrhea dies out ($\bar{K}<1$) or remains endemic ($\bar{K}>1$).

The characteristic equation for the transmission matrix T is $\det(T-\alpha I) = (-1)^n \alpha^{n-1}(\alpha-\bar{K}) = 0$. We assume below that T is irreducible, which again means that the whole population cannot be split into two subpopulations which do not interact with each other. The lemmas below are from Nold (1980).

LEMMA 3.2. If T is a square matrix with nonnegative elements, then T has a real, simple eigenvalue p(T), called the Perron eigenvalue, which is equal to its spectral radius.

LEMMA 3.3. The outbreak eigenvalue $m_o = s(A)$ for [3.1] has the same sign as $r(T)-1$ where $r(T)$ is the spectral radius of T.

THEOREM 3.4. In the proportionate mixing model the solutions of [3.1] approach the origin if $\bar{K}<1$ and they approach a unique positive equilibrium if $\bar{K}>1$, provided there is some infection in some group initially.

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

We now develop some relationships that will be useful in later chapters. Using several definitions above, an algebraic manipulation leads to $\lambda_{ij}N_j/N_i = (k_i/q_i d_i)b_j q_j$ so that [3.1] becomes

$$\frac{dI_i}{dt} = \left(\sum_{j=1}^{n} b_j q_j I_j\right) \frac{k_i(1-I_i)}{q_i d_i} - \frac{I_i}{d_i} \qquad [3.2]$$

for $i = 1,2,\ldots,n$. This is a convenient form since the parameter values appearing are often available.

The endemic equilibrium prevalences E_i are found by setting the right sides of [3.2] equal to zero so they are the nontrivial solutions of

$$\left(\sum_{j=1}^{n} b_j q_j E_j\right) k_i (1-E_i)/q_i = E_i \qquad [3.3]$$

for i = 1,2,...,n. Define the <u>average equilibrium infectivity</u> h by

$$h = \sum_{j=1}^{n} b_j q_j E_j \ . \qquad [3.4]$$

The <u>fractional infectivity</u> of group j defined by

$$C_j = b_j q_j E_j / h \qquad [3.5]$$

measures the relative ability of group j to transmit the infection. From [3.3] and [3.4] we find that the endemic equilibrium prevalences E_i must satisfy

$$E_i = hk_i/(q_i+hk_i) \ . \qquad [3.6]$$

The equations [3.4] and [3.6] yield

$$\sum_{i=1}^{n} q_i b_i k_i/(q_i+hk_i) = 1 \qquad [3.7]$$

which is equivalent to an nth degree polynomial for h. For example if n=2, then the quadratic equation is

$$k_1 k_2 h^2 + [q_2 k_1 + q_1 k_2 - (q_1 b_1 + q_2 b_2) k_1 k_2]h - q_1 q_2 (\bar{K}-1) = 0 \ . \qquad [3.8]$$

The endemic prevalences are found from [3.6] using the positive root h of [3.8].

Since the incidence in group i is N_i times the summation terms in [3.2], the total incidence of the population per year divided by the population size (i.e., the number of cases per person per year) is

$$Y = \frac{365\left[\sum_{i=1}^{n} N_i \left(\sum_{j=1}^{n} b_j q_j E_j\right) k_i (1-E_i)/q_i d_i\right]}{\sum_{i=1}^{n} N_i} \ . \qquad [3.9]$$

Using [3.3] the number of cases per person per year satisfies

$$Y = \frac{365\left[\sum_{i=1}^{n} N_i E_i / d_i\right]}{\sum_{i=1}^{n} N_i} \ . \qquad [3.10]$$