

## CHAPTER 2

### A SIMPLE MODEL FOR GONORRHEA DYNAMICS

The SIS model in section 2.1 where susceptibles become infectious and then susceptible again is based on the careful description in Chapter 1 of the characteristics of gonorrhea: **there is negligible protective immunity, negligible latent period and negligible seasonal oscillations.** It is the simplest possible model since it assumes that gonorrhea transmission occurs in one uniform, homogeneous population. The population represented by the model would necessarily consist only of those individuals at high risk who are also efficient transmitters. Thus people who are less active sexually would not be represented in this model. While the model restricts attention to this group, the model does not indicate the size of this group. Notice that this model ignores the epidemiological differences between women and men.

This model introduces notation and, like the more refined models later in this monograph, it has a threshold which determines whether the disease dies out or approaches an endemic equilibrium point. The incidence at the endemic equilibrium in the model depends on specific parameter values and this equilibrium will move as these parameter values change. The concept in section 2.2 of a **moving equilibrium provides a basis for understanding observed changes and for predicting changes in incidence** resulting from changes in epidemiological factors. In section 2.3 the **rapid response of gonorrhea incidence to epidemiologic changes is justified by both observations and calculations.**

The SIS model considered here gives us a theoretical framework to use in drawing simple conclusions. We can now see the fallacies in a variety of ideas that were widely held. In the seventies some observers thought that the increase in reported gonorrhea incidence was similar to exponential growth and that it would continue to increase exponentially. For example, a Scientific American (1976) news article stated, "Today gonorrhea is an epidemic disease out of control. . . . Reversing the exponential increase in gonorrhea calls for a two-pronged attack: . . ." A few people thought that the gonorrhea epidemic would follow a classic epidemic curve as observed for an SIR model without vital dynamics; thus they expected incidence to rise to a peak and then decrease. The gonorrhea model presented in this chapter and the concepts of a moving equilibrium and rapid response

which follow from the model provide a careful analysis and correct the misconceptions above.

## 2.1 One Population Model for Gonorrhoea

Assume that the population considered has a constant size  $N$  which is sufficiently large that the sizes of each class can be considered as continuous variables instead of discrete variables. The fractions of the population that are susceptible and infectious at time  $t$  are  $S(t)$  and  $I(t)$ , respectively. The fraction  $I(t)$  is called the prevalence. As noted in section 1.4 the exposed class of latent individuals is ignored since the latent period is very short. There is no acquired protective immunity.

The contact rate  $\lambda$  is the average number of adequate contacts of an infective per day. An adequate contact is a direct contact during sexual intercourse which is sufficient for transmission of infection if the individual contacted is susceptible. Thus the average number of susceptibles infected per day by the infective class of size  $NI$  is  $\lambda NI$ . Here the contact rate  $\lambda$  is assumed to be fixed and does not vary seasonally. We remark that the population is uniform and homogeneously infected in the sense that each person having an adequate contact has the same probability of contacting an infective (namely, the probability  $I(t)$ ).

Here we let  $d$  be the average infectious period and assume that the average infective has a  $1/d$  chance of recovering on any day, independent of how long the person has been infected. This assumption is equivalent to the assumption that individuals recover and become susceptible again at a rate proportional to the number of infectives  $NI$  with proportionality constant  $1/d$ . It is also equivalent to the assumption that the duration of infection has a negative exponential distribution (Hethcote, Stech and van den Driessche, 1981c).

Since  $S(t) = 1 - I(t)$ , the initial value problem for the number of infectives is

$$\frac{d}{dt}(NI(t)) = \lambda NI(t)(1-I(t)) - NI(t)/d, \quad NI(0) = NI_0 \quad [2.1]$$

After division by  $N$ , the differential equation and initial condition for the prevalence  $I(t)$  become

$$\frac{dI}{dt} = \lambda I(1-I) - I/d, \quad I(0) = I_0 \quad [2.2]$$

For this model the contact number  $\sigma$  defined in section 1.5 is equal to

the product of the daily contact rate  $\lambda$  and the average infectious period  $d$  in days. Figure 2.1 shows the susceptible and infective compartments and the transfer rates between compartments.

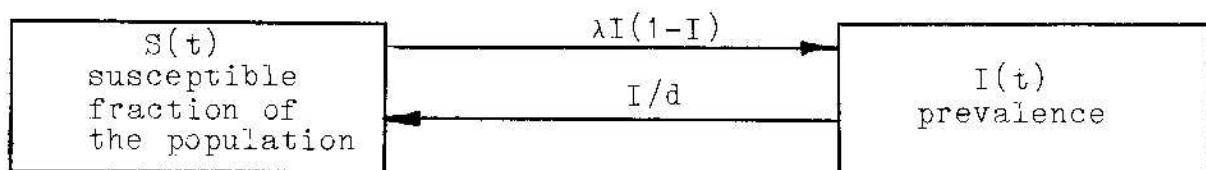


Figure 2.1 Flow diagram for the model [2.1].

The solution of [2.2] has the explicit form

$$I(\tau) = \begin{cases} \frac{e^{(\sigma-1)\tau/d}}{\sigma(e^{(\sigma-1)\tau/d} - 1)/(\sigma-1) + 1/I_0} & \sigma \neq 1 \\ \frac{1}{\lambda\tau + 1/I_0} & \sigma = 1 \end{cases} \quad [2.3]$$

The asymptotic results below follow from this solution.

If the contact number satisfies  $\sigma < 1$  and initially there is at least one infective, then the infectee number  $\sigma S(\tau)$  always satisfies  $\sigma S(\tau) < 1$  so that the average infective is replaced by less than one infective. Thus the disease will eventually die out (i.e.,  $I(t) \rightarrow 0$  as  $\tau \rightarrow \infty$ ) since the average infective is not being replaced by at least one new infective.

If the contact number satisfies  $\sigma > 1$ , then the average infective can be replaced if the susceptible fraction of the population is high. In this case, the disease remains endemic and the prevalence  $I(\tau)$  approaches the positive equilibrium or steady state value  $1-1/\sigma$  as  $t$  approaches  $\infty$ . At the endemic equilibrium point, the susceptible fraction of the population  $S$  is  $1/\sigma$  so that the infectee number satisfies  $\sigma S = 1$  as predicted in section 1.5. In summary we point out that the **contact number 1 is the threshold which determines whether the disease dies out ( $\sigma < 1$ ) or remains endemic ( $\sigma > 1$ )**.

The contact number depends on both the disease and the population being considered. A contact number may be greater than 1 in one population and less than 1 in another. For example, the male gay community has a large number of diseases that do not usually propagate heterosexually: rectal warts, hepatitis B and AIDS (Acquired Immuno-deficiency Syndrome).

In Chapter 1 we defined incidence as the number of new infectives per unit time. The daily incidence in our model [2.1] is  $\lambda NI(1-I)$ . Since we deal with fractions of the population in our mathematical models such as [2.2], we have defined prevalence as the fraction  $I(t)$  of the population that is infectious at a given time as opposed to the number  $NI(t)$  of people in the population who are infectious. For this and subsequent models, **when the disease is at an equilibrium, the prevalence times the population size is equal to the incidence times the duration.** Here we see this from [2.1] since the derivative of  $NI(t)$  is zero at an equilibrium point. We remark that epidemiologists usually define prevalence as the number of infectious individuals at a given time so that their relationship is that prevalence equals incidence times duration.

## 2.2 Changes in Incidence: A Moving Equilibrium

The epidemiologic factors of a disease are the characteristics of the disease and its environment that affect transmission. **Epidemiologic factors include sociological aspects** such as contact rates among individuals and among subpopulations, sizes of the affected population and subpopulations, social and economic conditions, psychological attitudes and control programs. **They also include clinical aspects** such as average durations of the incubation, latent and infectious periods, virulence of the agents and their resistance to certain treatments, and availability and quality of medical care. The epidemiologic factors at a given time determine a theoretical equilibrium or steady state level and if the epidemiologic factors do not change, the actual incidence will approach this equilibrium level. In the model in section 2.1, the prevalence  $I(t)$  approaches  $(1-1/\sigma)$  and the incidence approaches  $N(1-1/\sigma)d$ .

Before the theoretical equilibrium level is reached, the magnitude or relative importance of the epidemiologic factors may change and thus define a new theoretical equilibrium level. Although the theoretical equilibrium levels may never be reached, the actual incidence will be close to the theoretical equilibrium since the approach to equilibrium is rapid in comparison to changes in the theoretical equilibrium (see the next section). Thus we can think of gonorrhea incidence as having a moving equilibrium where the movement is due to changes in epidemiologic factors.

Figure 1.2 in Chapter 1 shows that the reported incidence of gonorrhea increased each year from 1957 to 1975. Reported incidence in the United States increased by a factor of about 4 between 1960 and

1975. Because of the increased awareness of the seriousness of gonococcal infection in women and the screening program started in the United States in 1972, the reporting of gonococcal infections in women may be better in the seventies than in the sixties. Changes in reported cases in men may correspond better to changes in actual incidence so that the actual incidence of gonorrhoea from 1960 to 1975 may be increased by a factor of approximately 3 instead of 4 (Yorke, Hethcote and Nold, 1978). The approach presented above would explain this increase as the result of continuous changes in the epidemiologic factors. Factors often mentioned as possible causes of the increased incidence include changes in sexual behavior and population mobility, changes in gonococcal resistance to antibiotics and changes in methods of contraception (WHO, 1978).

There is considerable evidence of changed sexual behavior in the United States (and elsewhere). Between 1967 and 1974, premarital intercourse rates rose 300 percent for white women and 50 percent for white men (NIAID, 1980). A national survey of college students in 1976 showed rates of premarital coitus were 74 percent for both sexes. Sexual activity among adolescents is clearly increasing. The percentage of sexually experienced never-married women who have had more than one sex partner increased from 38.5% in 1971 to 49.9% in 1976 (NIAID, 1980).

The demographic factors that correlate best with gonorrhoea incidence are age, race, marital status, socioeconomic status and urban residence (WHO, 1978). Changes in demographic factors are often ignored, yet they could cause significant changes in incidence. For example, if all other epidemiologic factors remained fixed, then a change in the size of the high case rate age group should cause a proportional change in gonorrhoea incidence. Since the 18-24 age group has the highest age specific case rates in the United States (American Social Health Association, 1975; Zaidi et al, 1983) the increase in size of this age group by a factor of 1.7 between 1960 and 1975 (Bureau of the Census, 1977) could have been one important cause of the increase in reported gonorrhoea incidence. Reported incidence is approximately ten times as high in the black population (WHO, 1978) on a per capita basis and the black population in the 18-24 age group increased by a factor of 1.9 between 1960 and 1975. Since the size of the 18-24 age group is projected to decrease by a factor of 0.86 in the United States from 1975 to 1990 (Bureau of the Census, 1977) a corresponding decrease in gonorrhoea incidence might be expected if other epidemiologic factors remained constant.

Since 1975 the reported incidence of gonorrhoea has been approximately constant. Although this suggests that an equilibrium level may have been reached, some epidemiologic factors have probably changed since 1975. Sexual activity among young people has probably continued to increase. The number of people in the high-risk age groups was expected to reach a maximum in 1983 (NIAID, 1980). The screening program initiated in 1972 has become larger and probably more effective. There has also been some indication that the fear of genital herpes has reduced the number of casual sexual contacts. Thus the almost constant observed incidence of gonorrhoea is almost certainly a balance among factors which tend to increase and to decrease incidence. Of course, there is no way to measure the changes in these factors accurately enough to give quantitative predictions of the movement of the equilibrium.

### 2.3 Changes in Incidence: Rapid Response

Not only does the incidence of gonorrhoea change as epidemiologic conditions change, but, in fact, the **incidence changes rapidly in response to epidemiologic changes**. As an example of rapid response, if all venereal disease clinics in a region were suddenly closed, then the actual incidence of gonorrhoea in that region would increase sharply to a new level within a few months. However, if the epidemiologic change occurred in steps over a period of time, then the incidence changes would also occur over the period of time. As examples of rapid response, we cite the regularly observed increases in national reported cases approximately four weeks after Christmas and New Year's Day when most treatment facilities are closed and people have different patterns of interaction. These increases are of short duration so that the incidences quickly drop back to the usual levels. Another example is the seasonal changes in gonorrhoea incidence due to seasonal changes in epidemiologic conditions (Yorke, Hethcote and Nold, 1978).

A crude estimate of the contact number can be obtained by using screening data from 1973-1975. As mentioned in section 1.3 it has been estimated that in 1975 the screening program for women discovered 10% of all gonococcal infections in women. If the 10% detected occur randomly among those with gonococcal infections, then the average infectious period is reduced by 10%. Using a trend line analysis on the reported incidence in men, it has been estimated that the effect of the screening program in 1975 was a 20% decrease in incidence in men (Yorke, Hethcote and Nold, 1978). If the incidence in women is

also reduced by 20% and their duration is reduced by 10%, the prevalence is reduced by a factor of  $(0.8)(0.9) = 0.72$  by the screening program. Using the simple model in section 2.1, we can equate two expressions for the prevalence with screening

$$1 - 1/(\sigma) = 0.72(1 - 1/\sigma)$$

**This equality yields a contact number  $\sigma$  of 1.40.**

This value of  $\sigma$  yields estimates of the rates of response of  $I(t)$ . The linearization of [2.2] near  $I=0$  is  $dI/dt = (\sigma-1)I/d$ ,  $I(0) = I_0$ . Thus if the initial infective fraction  $I_0$  is very small, then  $I(t) = I_0 e^{(\sigma-1)t/d}$  so that the doubling time for  $I(t)$  is  $t_d = d(\ln 2)/(\sigma-1)$ . For example, if the contact number is  $\sigma = 1.4$  and the average duration  $d$  is 1 month, then the doubling time is 1.7 months. This estimates the doubling time if gonorrhoea were introduced into a new population or if a new virulent strain such as PPNG were introduced. The concept of rapid response to epidemiologic changes is consistent with this rapid initial increase of the prevalence.

We can also obtain an estimate from  $\sigma$  of the speed of approach to equilibrium. If  $I(t) = 1 - 1/\sigma + V(t)$ , then the linearization of [2.2] around the equilibrium point  $1 - 1/\sigma$  is  $dV/dt = -(\sigma-1)V/d$ . This differential equation has solution  $V(t) = V_0 e^{-(\sigma-1)t/d}$  so that the half life is  $t_h = d(\ln 2)/(\sigma-1)$ . Thus the halving time near the endemic equilibrium point (the time a nonequilibrium prevalence takes to get half way to the equilibrium from its current position) equals the doubling time near the trivial equilibrium point. If  $\sigma = 1.4$  and  $d = 1$  month, then **the distance from the endemic equilibrium point is halved every 1.7 months.** Thus the rate of approach to the endemic equilibrium point is also rapid, which is consistent with the idea of rapid response.