CHAPTER 4

MODELING GONORRHEA IN A POPULATION WITH A CORE GROUP

In the early 1970s, the prevalent idea was that "gonorrhea is everybody's problem". It was recognized that everyone who was sexually active could get gonorrhea and, consequently, the screening program in the United States started in 1972 was designed to identify asymptomatic women by doing culture testing of as many women as possible. This screening program has been described in section 1.3.

In this chapter we study the core group: the group of individuals who are sexually very active and are efficient transmitters. The existence of a core group suggests that methods especially designed to identify and cure core members might be a more effective use of the resources available for gonorrhea control since the **real objective of control is to prevent cases.** A core-noncore model is developed in section 4.2 and parameter values such as sexual activity levels and average durations of infection are estimated. In the calculations **the core is less than 2% of the population** and consists of people who are 10 times as sexually active as noncore members. Remember that our measure of sexual activity is the frequency of new partners and that all individuals modeled are sexually active. Cases in the core are only 13% of the incidence; yet 16.7% of the encounters are with core members and **60% of all infections are directly caused by core members.** Thus a small core group can be very important in the transmission of gonorrhea.

Various control procedures such as screening and contact-tracing are discussed in section 1.3. When screening and rescreening are compared in section 4.3, the calculations show that **rescreening is approximately four times as effective per number of individuals tested as screening** in reducing total incidence. As described in section 4.3 and in (WHO, 1978, p. 107), the National Strategy to Control Gonorrhea was revised in 1975 to include retesting and rescreening. The two strategies for contact investigation compared in section 4.4 are contact-tracing individuals named as infectors and contact-tracing infectees.

Recall from section 1.3 that if scientists eventually are able to develop a vaccine for gonorrhea, then it will probably give only short term immunity. Because of this limitation it is particularly valuable to examine ways of using a vaccine. The two vaccination strategies for potential vaccines compared in section 4.5 are vaccination of

random individuals in the population at risk and vaccination of persons just after they have been treated for gonorrhea. Calculations in that section show that **post-treatment vaccination is about five times as effective per number of persons immunized as random vaccination** in the population.

The concept of a core is important in understanding gonorrhea dynamics from a clinical perspective. The quotation below is by R. K. St. John and J. W. Curran (1978) of the Venereal Disease Control Division of the Centers for Disease Control.

> "Increasing emphasis is being placed on intervention strategies for the core population described by Drs. Yorke, Hethcote and Nold. Patients who have repeated infections in relatively short periods (three to six months) are clearly part of the core. Brooks, Darrow, and Day studied 7,347 patients from venereal disease clinics and retrospectively identified 492 patients who had had repeated infections. **This small number of patients was responsible for 21.6% of all cases of gonorrhea in the local county and 29.4% of all the cases seen in the clinic.** Membership in these high-risk groups constantly changes as variations in patients' sexual behavior lead individuals into or out of the group. Identification of these individuals while their risk of infection is high may have major impact on transmission of the disease. Studies are under way to determine which risk factors can be used to identify this group a priori so that attempts can be made through periodic screening to keep these patients free of disease for longer periods. [Emphasis added.]"

The quotation below is from a 1978 report of a World Health Organization scientific group (WHO, 1978, p. 116).

> "The Group observed that, in the USA, the decision to carry out culture screening of non-symptomatic women was based on the assumption that the major cause of the gonorrhoea epidemic was the large reservoir of such women. This assumption is no longer in vogue in that country, and decisions for control are now based on the concept of core transmitters of disease, which postulates that a relatively small proportion of the population is contributing to the maintenance of the epidemic and that it is precisely this group of transmitters that is particularly important. Further disease models are needed for the development of innovative approaches to the problem of gonorrhoea control."

4.1 The Concept of a Core Group

If the contact number is greater than one and the initial susceptible fraction of the population is near one, then the initial

infectee number is greater than one so that the prevalence for the disease will initially increase. The prevalence cannot increase indefinitely since it is bounded above by one. A factor which limits the prevalence of a disease is called a saturation factor. For diseases whose infection confers immunity, the saturation factor is acquired immunity. The average prevalence of such a disease is limited by the fact that some adequate contacts of an infective do not result in transmission since the contacted person is immune. Immunity acquired by infection or vaccination is the saturation factor for diseases such as measles, chickenpox, mumps, rubella, poliomyelitis, diphtheria and whooping cough. For influenza a mutation to a new strain can lead to a new epidemic since individuals may not be immune to the new strain.

Gonorrhea is an exception; most other directly-transmitted diseases confer significant levels of immunity. Since gonococcal infection does not appear to confer protective immunity or substantial resistance, acquired immunity cannot be a saturation factor for gonorrhea. An adequate contact of an infective will not result in transmission of gonococcal infection only if the contacted individual is also an infective. This is called the preemption effect since an already infectious individual cannot be infected by another infective. Strictly speaking the infected individual could acquire an additional strain. **Preemption seems to be the only possible saturation factor for gonorrhea** since infection does not confer immunity.

The effects of the screening program were used in our simplistic one population model in section 2.3 to estimate that the contact number σ is 1.40 so that the prevalence $1-1/\sigma$ before screening would be 0.29. If the initial prevalence is below 0.29, then the prevalence approaches this value monotonically, but does not exceed 0.29 because of the preemption effect. Thus saturation occurred in that model when the prevalence reached 0.29.

We now use crude estimates to calculate the prevalence in another way. We estimate that the actual yearly incidence of gonorrhea in the United States is 2.0 million and that the population at risk is approximately 20 million. If the average duration of infection is one month, then the number of cases at any given time is 166,667 which is less 1% of the at-risk population. Since less than 1% of the contacts of an average infective are also infectious, preemption is not an important limiting factor when the population is considered to be one large, uniform, homogeneously-infected population. If preemption at

1% were enough to stop incidence from increasing, then the large current screening program (which is estimated to discover and cure 10% of infectious women) would have caused gonorrhea to die out.

Of course, the population is not homogeneously infected and uniform since some individuals have more sex partners than others. Thus the preemption that limits gonorrhea must be occurring in a subset of the at-risk population. The sexually active population could be divided into subgroups according to sex, age, race, sexual practices, number of sex partners, etc. The population in the groups with high prevalence (with prevalences of at least 20%) are lumped together and called the core. **There is a significant preemption effect in the core.**

There is no sharp division of the population at risk into the core and noncore since the heterogeneous population is made up of many groups. However, it is convenient conceptually and computationally to think of the core and the noncore as the only groups in the sexually active population being considered. If half of the infected individuals (half of 166,667 people) were in the core and the prevalence for the core were 20%, then the core would have 416,667 members or about 2% of the 20 million people assumed to be at risk. Thus the core can be a small percentage of the population at risk.

The significance of the core can be determined by a thought experiment. We observe that prevalence in the noncore is small (≈1%) so that no saturation is occurring there. In addition some cases there come from contacts with core members. We conclude that the contact number is less than one in the noncore. Suppose now that all individuals in the core were instantaneously cured and permanently immunized against gonococcal infection. Since cases infected by the core would no longer occur, the noncore prevalence would decrease and the infectee number for the entire population would decrease to a value less than one. Before the immunization the infectee number was greater than one for the core and less than one for the noncore; immediately after the immunization it is zero for the core and decreased for the noncore. Since there is no saturation in the noncore, the susceptible fraction of the population is approximately one so that the contact number is approximately equal to the infectee number. Thus the contact number for the noncore is less than one after the immunization so that gonorrhea would die out. In other words, since nonzero equilibrium prevalence required saturation in some group, if the core is immunized so that there is no saturation, then the equilibrium prevalence cannot be nonzero. Thus all cases are

caused directly or indirectly by the core: **the core causes gonorrhea to remain endemic.**

Some efforts have been made to identify core groups by their characteristics (Rothenberg, 1982;Potterat, Rothenberg, Woodhouse et al, 1983). Homosexual men (Darrow et al., 1981; Judson et al., 1980) and prostitutes (Darrow and Pauli, 1983) may be core group members because of their frequent and anonymous sexual contacts, the social and legal impediments to their medical care, and their lack of referral of sex partners. An overall infection rate of 27% among street prostitutes was found in one city studied recently (Potterat et al., 1979). Gonorrhea was detected in 20% of women arrested for prostitution in Atlanta, Georgia (Conrad et al., 1981). There is some evidence that women with gonococcal Pelvic Inflamatory Disease are core group members because their sexual contacts are often infected and frequently asymptomatic (Wiesner and Thompson, 1980; Potterat et al., 1980). It is possible to identify high risk individuals by characteristics such as age, sex, race and census tract (Rothenberg, 1982). One study of possible core group members in a small community showed that 3% of the population was responsible for 27% of the gonococcal infections (Phillips, Potterat, Rothenberg et al., 1980). Intervention with high risk groups is an efficient use of resources since their importance in overall disease transmission is disproportionate to their numbers.

Groups with high rates of infection definitely are geographically clustered, often in an inner city (Potterat, et al. 1980; Wiesner, 1979; Rothenberg, 1982). The abstract of a paper, The Geography of Gonorrhea: Empirical Demonstration of Core Group Transmission, by Rothenberg (1983) is given below.

> "The pattern of reported gonorrhea in Upstate New York (exclusive of New York City) in the years 1975-1980 is one of intense central urban concentration, with concentric circles of diminishing incidence. The relative risk for gonorrhea in these central core areas, compared to background state rates, is 19.8 for men and 15.9 for women, but as high as 40 in selected census tracts. Prevalence appears to approach 20% in some areas, the level postulated by current epidemiologic models for continuing endemic transmission. These core areas are characterized by high population density, low socioeconomic status and a male to female case ratio of one or lower. Contact investigation data suggest that sexual contact tends to exhibit geographic clustering as well. These observations provide support for narrow focusing of epidemiologic resources as a major disease control strategy."

4.2 The Core-Noncore Model

When part of the population differs from the rest in some epidemiologically significant way, it is desireable to consider the simplest model which concentrates on that difference. Here we use a model with a core group and a noncore group in order to determine the implications of having one group more active than the other. Two group models have the additional advantage that the equilibrium prevalences are easy to obtain with a hand calculator. However, the core-noncore model ignores distinctions between women and men and does not allow different groups with different durations of infection. A more refined model involving eight groups is considered in Chapter 6. There the equilibrium point is more difficult to calculate so a computer is used.

Here we divide the population into two groups based on the frequency of new sexual encounters. Let I_1 be the prevalence for the core (the very active group) and I_2 be the prevalence for the noncore (the active group). In order to do some calculations with the proportionate mixing model [3.2] with n=2, we must choose some parameter values. Let the average number of days between encounters be 5 days for core members and 50 days for noncore members so that the activity levels defined in section 3.2 are $a_1 = 1/5$ and $a_2 = 1/50$. Assume that the ratio N_1/N_2 of the sizes of the groups is 1/50 so that the core is about 2% of the sexually active population being considered. Let the average durations of infection, d_1 and d_2, both be 25 days. Here we assume that all new encounters are adequate contacts so that $q_1 = q_2 = 1$. Thus the core-noncore model is an initial value problem with the differential equations

$$\frac{dI_i}{d\tau} = \frac{k_i}{d_i}(b_1I_1+b_2I_2)(1-I_i) - \frac{I_i}{d_i} \qquad [4.1]$$

for i = 1,2. A flow diagram for this model is given in figure 4.1.

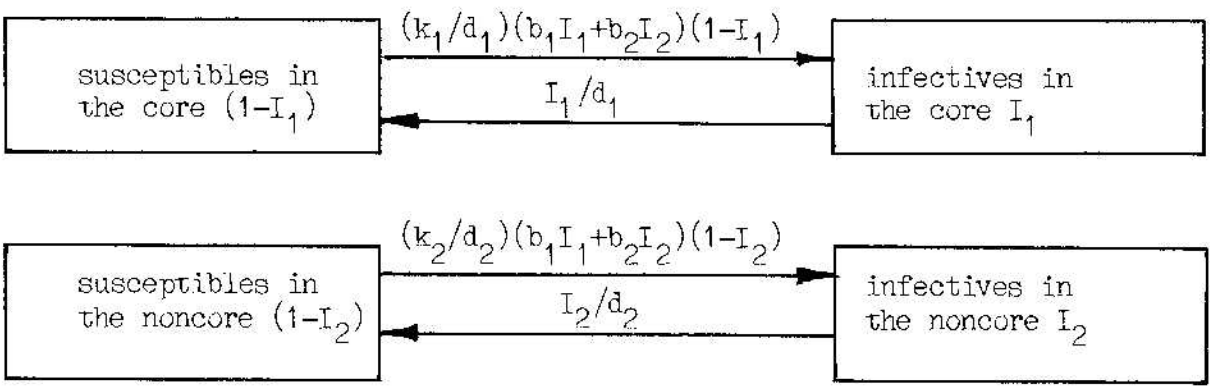

Figure 4.1 Flow diagram for the core-noncore model.

The difference between the groups is that core members are 10 times as active as noncore members. Without checking details, we might estimate roughly that a core member is 10 times as likely to become infected and has 10 times as many opportunities to transmit the infection while infected. Hence each core member might be expected to infect 100 times as many people as a noncore member. This calculation is not precise since it ignores the saturation in the core: an infective core member cannot be infected. We now see what the model predicts in detail.

Using definitions and equalities in section 3.2, we find that the contact numbers are $k_1 = 5$ and $k_2 = 0.5$ so that the average core member has adequate contacts with 5 people during the infectious period while each noncore person has adequate contacts with an average of 0.5 persons. The fractional activity levels are $b_1 = 1/6$ and $b_2 = 5/6$ so that 1 out of 6 encounters is with a core member and 5 out of 6 are with a noncore member. Thus 1/36 of the encounters are between two core members, 10/36 are between a core member and a noncore member and 25/36 are between two noncore members.

The average contact number $\bar{k}$ is 1.25 so that by Theorem 3.4, gonorrhea remains endemic and the prevalences approach the equilibrium values E_1 and E_2. From equation [3.8] the average equilibrium infectivity h is 0.078 so that the equilibrium prevalences are $E_1 = 0.28$ and $E_2 = 0.038$ from [3.6]. Thus 28% of the encounters of a susceptible with a core member result in infection while for encounters with a noncore member the figure is only 3.8%. From [3.5] the fractional infectivities are $C_1 = 0.60$ and $C_2 = 0.40$ so that for this model **60% of all infections are caused by core members.** Thus the core causes 1½ times as many infections as the noncore even though he core is 50 times smaller. Thus for this model **a core member causes 75 times as many infections as a noncore member** (compare this with our original estimate of 100). From [3.10] the cases per person per year is Y = 0.62. Cases in the core group are 13% of the total incidence at equilibrium.

The calculations above show that **a small core group can be very important in the spread of gonorrhea.** The core is less than 2% of the population above and cases in the core are only 13% of the incidence; yet because core members are 10 times as sexually active as noncore members, 16.7% of the new encounters are with core members and 60% of all infections are caused by core members.

4.3 Screening and Rescreening Strategies

The following quotation is from the report of a World Health Organization scientific group (WHO, 1978, p. 105).

> "The mistaken assumption that every case of gonorrhoea is equally important for the spread of disease must be dispelled. Failure to treat gonorrhoea cases among groups with a high rate of disease transmission significantly limits the chances of success."

The general technique which we use is to change the differential equation to incorporate a control procedure such as screening. Then we solve for the new equilibrium. The drops in the equilibrium prevalence and incidence are a result of the control procedure. We can also calculate how many cases are prevented for each person discovered and treated via the screening program. The number of cases prevented includes all the cases in the chain of transmissions: primary, secondary, tertiary cases, etc.

First consider a strategy of screening individuals at random in the sexually active population. Let g be the fraction of the population being screened for gonorrhea by culture testing per day so that the yearly fraction screened is 365 times g. The fraction of those identified and cured by screening is gI_i for each group. When modified to include screening, the model [4.1] for the prevalences becomes

$$\frac{dI_i}{dt} = \frac{k_i}{d_i}(b_1I_1 + b_2I_2)(1-I_i) - \frac{I_i}{d_i} - gI_i \ . \qquad [4.2]$$

for $i = 1,2$. The average contact number becomes

$$\bar{K} = \frac{b_1k_1}{1+gd_1} + \frac{b_2k_2}{1+gd_2} \qquad [4.3]$$

The equations for the equilibrium prevalences E_1 and E_2 are

$$\frac{k_i}{1+gd_i}(b_1E_1+b_2E_2)(1-E_i) = E_i \qquad [4.4]$$

for $i = 1,2$. These equations are similar to [3.3] except that each k_i is replaced by $k_i/(1+gd_i)$.

We now calculate the effect of screening 1/2 of the sexually active population per year using the parameter values for the core-noncore model in section 4.2. Using $g = 1/730$ the quadratic equation

yields h = 0.067 so that the equilibrium prevalences are E_1 = 0.24 and E_2 = 0.031. The cases per person per year calculated from [3.10] is Y = 0.53 which is a reduction of 13.9%. **For each 5.8 people screened there is a yearly reduction in incidence of 1 person.** The number of discoveries due to screening is $g(N_1E_1+N_2E_2)$ and the number screened is $g(N_1+N_2)$ so that the percent of those screened who are discoveries is 3.5%. The percent of people screened who are in the core is 13.2%.

Now consider a rescreening strategy where treated infectives return several weeks after their cure to be retested for gonococcal infection. These people who are rescreened could be infected by a new partner or reinfected by the old partner who is still infectious. Let f be the fraction of infectives who are rescreened and let the rescreening rates be proportional to the fractions removed from the infectious classes several weeks earlier. Since the several week delay is unimportant near the equilibrium, we assume that the fraction removed due to rescreening is the fraction f of recoveries screened times the recovery rate I_i/d_i times the prevalence I_i. The model [4.1] modified to include rescreening becomes

$$\frac{dI_i}{dt} = \frac{k_i}{d_i}(b_1I_1+b_2I_2)(1-I_i) - \frac{I_i}{d_i} - \frac{fI_i^2}{d_i} \qquad [4.5]$$

for i = 1,2. The equations for the equilibrium prevalences are

$$k_i(b_1E_1+b_2E_2)(1-E_i) = (1+fE_i)E_i \qquad [4.6]$$

for i = 1,2. These equations cannot be manipulated to give a quadratic equation like [3.8] for h, but they can be solved numerically for given parameter values.

Let us calculate the effect of rescreening 1/2 of the infected individuals using the parameter values given in section 4.2. Using f = 1/2, the equilibrium prevalences are E_1 = 0.206 and E_2 = 0.027 so that h = 0.057. The cases per person per year calculated from [3.10] is Y = 0.46 which is a reduction of 25.3%. Rescreening 1/2 of the infectives corresponds to rescreening a number equal to 23.1% of the total population per year. **For each 1.5 people rescreened, there is a yearly reduction in incidence of 1 person.** The number of discoveries due to rescreening is $f(E_1^2N_1/d_1+E_2^2N_2/d_2)$ and the number rescreened is $f(E_1N_1/d_1+E_2N_2/d_2)$ so that the percent of those rescreened who are discoveries is 5.1%. The percent of people rescreened who are in the core is 13.2%.

Thus **rescreening is approximately four times as effective per**

number of individuals tested as screening in reducing incidence. The intuitive reason why rescreening is more effective than screening is that since rescreened individuals were infected before, they are more likely to be core group members and, consequently, more likely to be infectious again when rescreened. Moreover, discovering and curing a core member who can spread the infection to many others is more effective in reducing prevalence than discovering and curing a noncore member. Thus **rescreening is one method of focusing the culture testing on members of the core group,** who are the efficient transmitters.

In 1975 there was a change in the gonorrhea control program in the United States. It was recognized that there is a core group of efficient transmitters and that they are more likely to become reinfected shortly after treatment (Henderson, 1974b). The new strategies are described below (Henderson, 1974a).

> "3. National Strategies to Control Gonorrhea
>
> The major thrust of these strategies is the rescreening of gonorrhea patients after treatment for this disease. The elements of this overall strategy can be summarized into three points:
>
> a. For infected persons both men and women:
>
> (1) Counsel to refer sex partners for examination and treatment; and
>
> (2) Counsel to return one week after treatment for a test-of-cure culture posttreatment culture) and 4-6 weeks after treatment for a rescreening culture.
>
> b. For all patients with positive posttreatment followup cultures or with positive rescreening cultures, special efforts will be made to have their sexual partners referred for examination and treatment.
>
> c. Improve clinical and laboratory services in both the public and private sectors to provide accurate diagnosis, effective therapy, and maximum utilization of services by persons at high risk of infection."

It is estimated that some of the 5% who are positive for gonorrhea on retesting after one week are treatment failures and some are reinfections (Henderson, 1975b). The first group is important because they may have PPNG and the second group is important because they and their sex partners may be more important transmitters, i.e., core

group members. Rescreening after 4-6 weeks yields about 5-20% positive cultures in clinics. Rescreening is designed to identify individuals who are rapidly reinfected and, consequently, are in the core group of more efficient transmitters. The Director of the VD Control Division of the Center for Disease Control stated that (Henderson, 1974b) "the intended impact of these 'new' program elements is to shift program resources from routine screening in general populations to highly targeted testing and counselling in populations with reinfections of recent origin."

The results of rescreening have varied from place to place. In those areas where it has been found to be effective, it has been continued. The following quotation is illustrative (Miles, 1978).

> "Post-treatment culturing and rescreening at 4-6 weeks were first looked at as an activity that might be expendable to reduce laboratory support costs since it was done basically to monitor the effectiveness of therapy. However, it was discovered that a positivity rate of better than 5-6% was being achieved and that almost none of these patients were treatment failures. This was a substantially higher rate than most providers obtained on initial culture, much less a reculture. Most notable was the fact that almost no resources were being expended to identify these additional infections. This group of patients was being reinfected between the time of treatment and reculture. Without a doubt, these patients and their sex partners are among the most important transmitters of gonorrhea and by identifying them through rescreening and applying intensive epidemiology, we may more directly affect the incidence of gonorrhea than by all other control activities combined. Therefore, our resources in Indiana were retargeted in 1976 to reach this important group of patients through rescreening in the venereal disease clinics."

4.4 Contact Investigation Strategies

Contact investigation or tracing procedures have been described in section 1.3. The quotation below is from Rothenberg (1982).

> "Resources available for contact interviewing and contact tracing are limited. A coherent plan for targeting these resources, selecting priority patients--is economically mandated. This approach is founded on a theoretical basis as well: high risk groups may be directly or indirectly responsible for most disease transmission (Yorke, Hethcote and Nold, 1978)."

Here we consider the effects of two different contact investigation strategies. These strategies are also analyzed using an eight group model in Chapter 6. One strategy is to contact-trace

individuals named as potential **infectees** or people to whom the disease may have been spread by the cases being considered. The other strategy is to contact-trace individuals named as **infectors**, i.e., the individuals from whom the cases being considered obtained their gonococcal infection. Anecdotal information suggests that infected individuals can usually correctly identify the person who infected them.

Assume that the daily number of people contact traced, found to be infectious and cured is a fraction f of the daily incidence. That is, for each current case, f other cases are cured as a result of contact tracing. If infectees are contact traced, then they are typical infectives so that the daily number contact traced are divided between the core and noncore in proportion to the incidences of the core and noncore. If infectors are traced, then those traced are divided between core and noncore in proportion to the numbers of infections caused by the core and noncore. The infectivity C_i defined in section 3.2 is the probability that the infection came from group i. The infectors are proven transmitters and so are more likely to be in the core than a random infected person.

In section 4.2 the calculations showed that the core accounts for 13% of the incidence so that 13% of randomly chosen cases would be core members. Thus 13% of the infectives found by contact tracing infectees would be core members. Since 60% of all infections were transmitted by core members, 60% of the infectives found by contact tracing infectors would be core members. It is clearly more important to identify and cure core members since they are the efficient transmitters. The typical noncore infective contacts 0.5 individuals when infectious while the typical core infective contacts 5, so there is a significant increase in cases prevented by curing a core infector, even if that individual is likely to be reinfected soon. The more detailed calculations below and in Chapter 6 verify this prediction.

If infectees are contact traced, then a fraction f of the incidences in each differential equation are removed by contact tracing. Thus the differential equations for the prevalences become

$$\frac{dI_i}{dt} = (1-f)\frac{k_i}{d_i}(b_1I_1+b_2I_2)(1-I_i) - \frac{I_i}{d_i} \qquad [4.7]$$

for i = 1,2. The equilibrium prevalence equations are similar to [3.3] except that each k_i is replaced by $(1-f)k_i$. Using the parameter values in section 4.2, we model a control procedure in which 1% of the infectees (f = 0.01) are traced and cured. One reason for choosing f = .01 is so that it would be implementable in practice. Calculations

show that h = 0.075 so that E_1 = 0.27 and E_2 = 0.036. The cases per person per year calculated from [3.10] is Y = 0.59 which is a reduction in incidence of 5.1%. **For each infectee contact traced and cured, there is a reduction in incidence of 5.34 people.**

If infectors are traced, then the number traced and cured is f times the total daily incidence. This number is divided between the core and noncore in proportion to the infectivities, $C_i = b_iI_i/(b_1I_1+b_2I_2)$, which measure the relative ability of group i to transmit the infection (cf. equation [3.6]). Thus the fractional removal rates for i = 1,2 due to contact tracing are

$$\frac{C_i f(\text{incidence})}{N_i} = \frac{b_iI_i}{b_1I_1+b_2I_2}\frac{f}{N_i}\left[\frac{N_1k_1}{d_1}(1-I_1) + \frac{N_2k_2}{d_2}(1-I_2)\right](b_1I_1 + b_2I_2)$$

$$= a_iI_if\ \frac{a_1N_1(1-I_1) + a_2N_2(1-I_2)}{A}$$

$$= \frac{k_i}{d_i}I_if\,[1-(b_1I_1 + b_2I_2)]$$

Thus the differential equations for the prevalences become

$$\frac{dI_i}{dt} = \frac{k_i}{d_i}[b_1I_1 + b_2I_2][1 - (1-f)I_i] - (1+fk_i)\frac{I_i}{d_i} \qquad [4.8]$$

for i = 1,2. The equilibrium fractional prevalences satisfy

$$[k_i/(1+fk_i)][b_1(1-f)E_1 + b_2(1-f)E_2][1 - (1-f)E_i] = (1-f)E_i \qquad [4.9]$$

for i = 1,2. These equations are similar to [3.3] except that E_i is replaced by $(1-f)E_i$ and k_i is replaced by $k_i/(1+fk_i)$. Thus the quadratic equation approach given in section 3.2 can also be applied here. Using the parameter values in section 4.2, we find that if 1% of the infectors (f=.01) are traced and cured, then h = .069, $.99E_1$ = .247 and $.99E_2$ = .033. The cases per person per year is Y = 0.55 which is a reduction of 11.0%. **For each infector contact traced and cured, there is a reduction in incidence of 12.3 people.**

For tracing either infectees or infectors, f = .01 corresponds to successfully tracing and curing a number of infectives equal to 1% of the incidence. Thus according to this two group model curing a certain number of infectors by contact tracing is approximately twice as effective in reducing incidence as curing the same number of

infectees by contact tracing. A model in Chapter 6 involving eight groups shows that tracing infectors is three times as effective as tracing infectees.

4.5 Vaccination Strategies

The efforts to develop a gonorrhea vaccine are described in section 1.3. The quotation below is from the report of the WHO scientific group (WHO, 1978).

> "One potential application of mathematical models for gonorrhoea is to predict the impact of preventive measures (e.g., vaccination) or of changes in case-finding or in efficacy of treatment (e.g., increased failure rates due to increased prevalence of β-lactamase-producing gonococci). Such projections could be useful in planning control programmes."

Here we investigate the effectiveness of two vaccination strategies. The general vaccination strategy is vaccination of individuals chosen at random from the population at-risk. The post-treatment strategy is vaccination of persons just after they have been treated for gonorrhea. Since it is likely that those who become immune due to vaccination will have only temporary immunity, let r be the average period of temporary immunity. Vaccine efficacy, which is the fraction of those vaccinated who become immune, can be much less than one.

For the general vaccination strategy let the daily rate of individuals in the ith group becoming immune due to vaccination be uN_iS_i. Let class R_i contain the people temporarily removed from the susceptible-infective interaction by immunity due to vaccination. The differential equation model [4.1] becomes

$$\begin{aligned} \frac{dI_i}{dt} &= \frac{k_i}{d_i}(b_1I_1 + b_2I_2)S_i - \frac{I_i}{d_i} \\ \frac{dS_i}{dt} &= -\frac{k_i}{d_i}(b_1I_1 + b_2I_2)S_i - uS_i + \frac{(1-S_i-I_i)}{r} + \frac{I_i}{d_i} \end{aligned} \qquad [4.10]$$

for $i = 1,2$. The fraction of the population which is temporarily immune is $R_i = 1 - S_i - I_i$. A flow diagram is given in Figure 4.2.

If we set the right sides of [4.10] equal to zero and add, then $S_i = (1-I_i)/(1+ru)$ so that the equilibrium points satisfy these equations. Thus the equilibrium prevalences satisfy

$$\left[\frac{k_i}{1+ru}\right] (b_1 E_1 + b_2 E_2)(1-E_i) = E_i \qquad [4.11]$$

or i = 1,2. These equations are similar to [3.3] except that each k_i is replaced by $k_i/(1+ru)$.

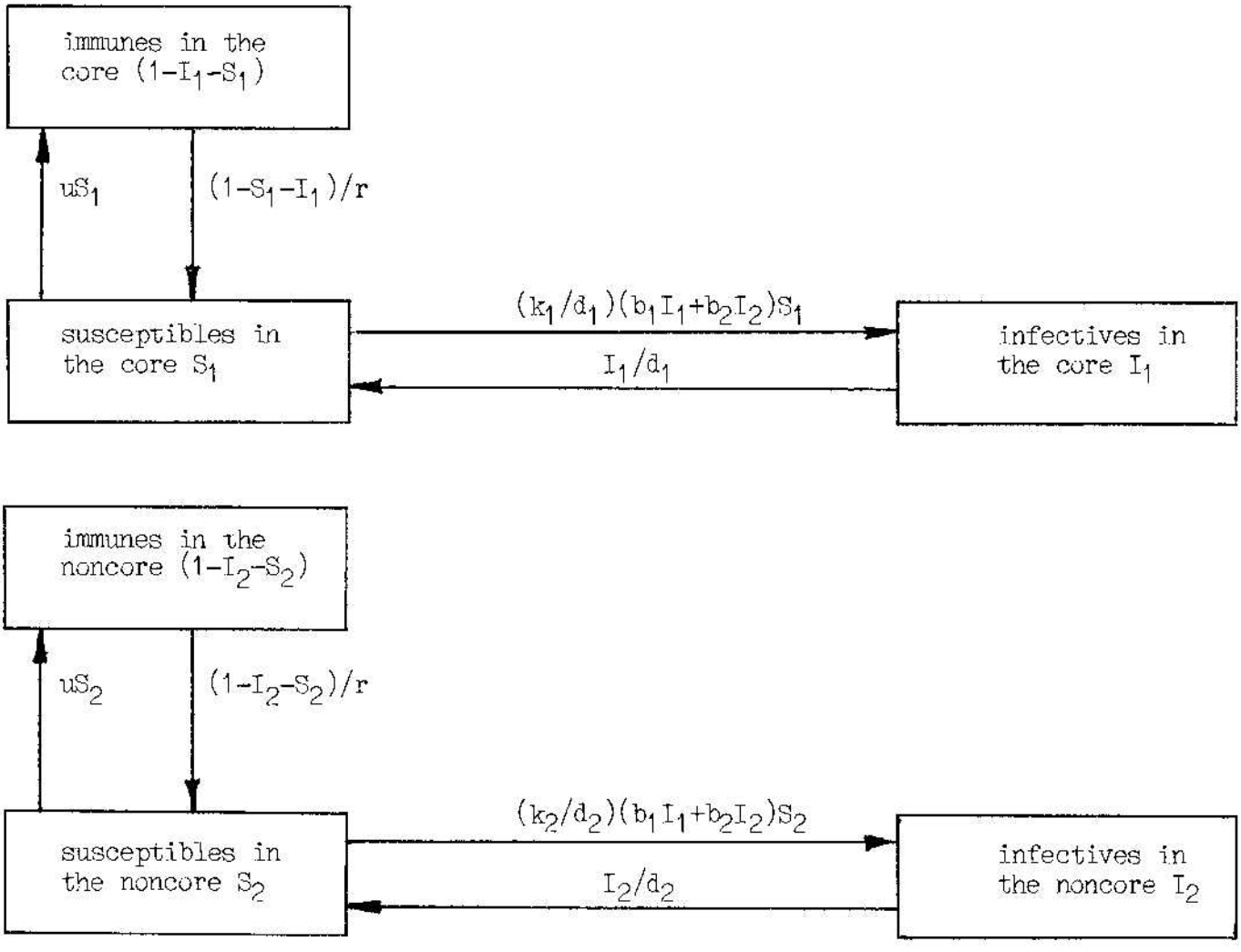

Figure 4.2 Flow diagram for the general vaccination strategy.

We now calculate the effect of randomly immunizing 1/20th of the population per year (u=1/7300) when the average period of temporary immunity is 6 months. Note that ur = 0.025 would also correspond to immunizing 1/40th of the population with average immunity of 1 year or to immunizing 1/10th with average immunity of 3 months. Using the parameter values for the core-noncore model in section 4.2, the equilibrium infectivity h is 0.070 so that the equilibrium prevalences are E_1 = 0.25 and E_2 = 0.033. The cases per person per year is Y = 0.54 which is a reduction of 12.4%. When 1/20th of the population is immunized by vaccination per year and the average immunity is 6 months, **there is a yearly reduction in incidence of 1.53 people for**

each person immunized by general vaccination.

A vaccine could be very effective in controlling gonorrhea. Note that for a vaccine which gives an average immunity of 6 months, the calculations suggest that random immunization of 1/2 of the general population each year ($ur \geq 0.25$) would cause gonorrhea to disappear. Of course, vaccination would need to be continued forever at the same or a higher level to prevent an outbreak from an imported case.

We now analyze the post-treatment vaccination strategy in which the fraction f of the people treated are immunized by vaccination (possibly just after their treatment). We assume that the people treated are typical of the infectives. Let r be the average period of temporary immunity. The differential equations [4.1] become

$$\frac{dI_i}{dt} = \frac{k_i}{d_i}(b_1 I_1 + b_2 I_2)S_i - \frac{fI_i}{d_i}$$

$$\frac{dS_i}{dt} = -\frac{k_i}{d_i}(b_1 I_1 + b_2 I_2)S_i + \frac{(1-f)I_i}{d_i} + \frac{(1-S_i-I_i)}{r} \qquad [4.12]$$

for $i = 1,2$. Again the fraction of the population which is temporarily immune is $R_i = 1 - S_i - I_i$. A flow diagram is given in Figure 4.3.

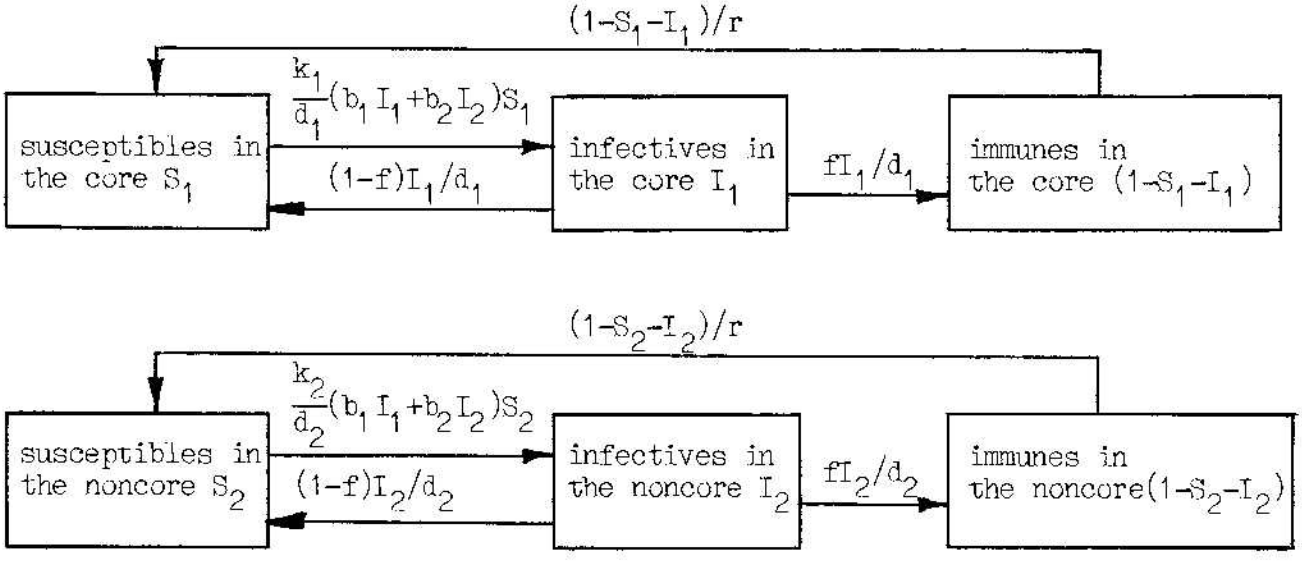

Figure 4.3 Flow diagram for the post-treatment vaccination strategy.

If we set the right sides of [4.12] equal to zero and add, then the equilibrium points must satisfy $S_i = 1 - I_i(1+fr/d_i)$. Thus the equilibrium prevalences satisfy

$$k_i(b_1E_1 + b_2E_2)[1-E_i(\frac{1+fr}{d_i})] = E_i \qquad [4.13]$$

for i = 1,2. These equations can be made similar to the equilibrium equations [3.3] except that E_i is replaced by $(1+fr/d_i)E_i$.

Assume that 1/5 of the infectives are immunized by vaccination and the average immunity r is 6 months. Note that fr = 36.5 days would also correspond to immunizing 1/10 of the infectives with an average immunity of 1 year or to immunizing 2/5 of the infectives with an average immunity of 3 months. Using the parameter values in section 4.2, the average equilibrium infectivity h is 0.032 so that the equilibrium prevalences are E_1 = 0.11 and E_2 = 0.015. From [3.10] the cases per person per year is Y = 0.25 which is a reduction of 59.4%. Immunizing 1/5 of the infectives corresponds to immunizing a number equal to 5.0% of the total population per year. **For each person immunized by vaccination just after being treated** for a gonococcal infection, **there is a yearly reduction in incidence of 7.3 people.**

Hence **post-treatment vaccination is approximately 5 times as effective per person immunized as random vaccination.** Of course the random vaccination is restricted to the population being modeled where everyone is sexually active. Intuitively, post-treatment vaccination is better since core members (who are more often infected and are more efficient transmitters) are more likely to be temporarily immunized by post-treatment vaccination.