CHAPTER 7

THE HIV TRANSMISSION DYNAMICS MODEL FOR FIVE MAJOR RISK GROUPS

Chapters 2 and 3 have focused on modeling the transmission dynamics of HIV and the progression to AIDS for homosexual men. That model is now expanded in Section 7.1 to include five major risk groups: homosexual (and bisexual) men, homosexual (and bisexual) men who are intravenous drug users, intravenous drug users (IVDUs), heterosexual partners of IVDUs and neonates of female IVDUs and heterosexual partners. In this model the homosexual men have homosexual partnerships within their own group and also with homosexual–IVDUs. The IVDUs have needle–sharing partnerships with other IVDUs and also with homosexual–IVDUs. Obviously, the heterosexual partners of IVDUs have sexual partnerships with people who are IVDUs. Perinatal transmission occurs from the female IVDUs and the female heterosexual partners. Figure 7.1 summarizes the risk groups and possible routes of transmission of HIV infection. The fitting procedure for the five–group model is outlined in Section 7.2. This model with the first three risk groups is used for New York City in Chapter 8. The full model is used for regional comparisons in Chapter 10.

The five risk groups above are chosen since they account for 94% of the adult/adolescent cases and 78% of the perinatal pediatric cases with known source of infection reported through December, 1991 in the United States (CDC: 1992). See Tables 1.1 to 1.3. The model does not include other heterosexual contacts, hemophiliacs, blood transfusion recipients, and children with other perinatal transmission. It is not reasonable to include more risk groups in an initial model for a local population. Blood transfusion recipients (2% of AIDS cases) could be included, but blood banks are regional instead of local. Similarly, the incidence in hemophiliacs (1% of all AIDS cases) is quite uniform throughout the United States, so this is a nationwide phenomenon instead of a local phenomenon, particularly since the blood factor concentrate is prepared in a few places and distributed nationwide. It is probably not necessary to include a separate population of bisexual men since heterosexual contacts with bisexual men accounts for only 651 out of 206,392 AIDS cases in the United States through December 1992. It is not possible to include people or sexual partners born in pattern II countries since the immigration times and HIV status of these people is not known.

7.1 The General Model

Recall that the homosexual men are subdivided into active and very active subpopulations. In the modeling of homosexual men in San Francisco (SF), the 10% of the homosexual men in the very active class were ten times as sexually active as those in the active class (the parameter values are $F = 0.10$ and $R = 10$). Here the IVDU population is also subdivided into these two activity level classes based on their number of needle–sharing partners per month.

The needle–sharing contacts are modeled in a way analogous to the homosexual contacts in that there is an average number of new needle–sharing partners per month and there are probabilities of transmission per new needle–sharing partner that are dependent on the stage of

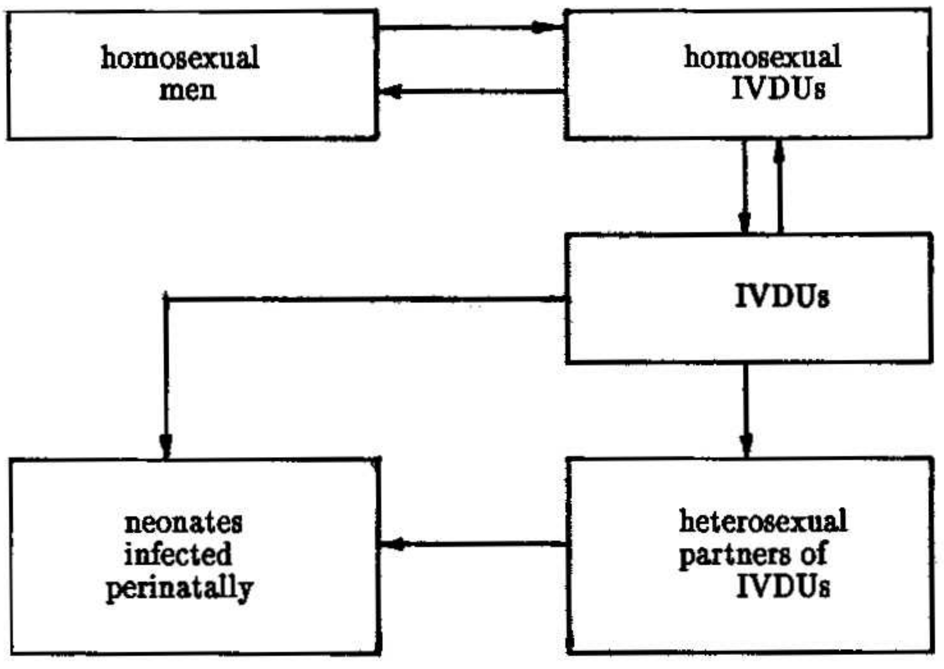

Figure 7.1 Risk groups and infection transmission connections.

infection of the partner just as for homosexual partners. As indicated previously the homosexual–IVDUs have both homosexual partners and needle–sharing partners.

The progression of HIV infecteds to AIDS has been developed carefully as a sequence of stages in Chapter 2 and the same progression is used for all adult risk groups in this general model. The progression for children has also been described in Chapter 2. The progression variables and parameters in Figure 3.1 and Table 3.1 now exist for all five risk groups: the homosexual men with suffix H, the homosexual–IVDUs with suffix B for both, the IVDU population with suffix D for drug user, the population of heterosexual partners of IVDU with suffix P for partners, and the neonates with suffix C for children. Thus the model consists of five sets of finite difference equations for the numbers in each compartment, which are similar to those in Figure 3.2. All populations except the heterosexual partners and children are subdivided into very active and active subgroups where the activity is either sexual or needle–sharing partnership formation. For example, the quantities for homosexual men are QVH, SVH, XH(1), ···, XH(8), QAH, SAH, YH(1), ···, YH(8), ZH(1), ···, ZH(6) and ZAIDSH.

The suffixes H, D, B, P and C are also used for other parameter values. For example, QHH, QHD, QHP and QHC are the probabilities of transmission of HIV infection by an infective in an asymptomatic stage during a homosexual partnership, needle–sharing partnership, heterosexual partnership, and childbirth, respectively. The quantities PAH, PAD and PAP are the average number of new homosexual, needle–sharing and heterosexual partnerships per month.

As in the model for homosexual men, the fraction η of new partnerships are distributed by proportionate mixing and the fraction $1-\eta$ of new partnerships occur internally to each group. The total incidences in the active and very active subpopulations are the sums of the internal incidences and the external proportionate mixing incidences. The incidences with suffixes H and

D on the variables and parameters are used for homosexual partners and needle–sharing partners, respectively. Thus the incidence for homosexual men is the sum of the internal and external (proportionate–mixing) homosexual incidences given in Section 3.2, where each parameter and variable now has the suffix H. For the IVDUs, the incidence is the sum of similar internal and external needle–sharing incidences, with suffix D. Thus the incidence in the active subpopulation of IVDUs is

$$\left[\sum_{i=1}^{m} (1-\mathrm{ETAD}) * \rho_i * \mathrm{PHD} * \omega_i * \mathrm{QHD} * \mathrm{YD}(i)\right] * \frac{\mathrm{SAD}}{\mathrm{QAD}-\mathrm{YD}(m+1)}$$

$$+ \sum_{i=1}^{m} \mathrm{ETAD} * \rho_i * \mathrm{PHD} * \omega_i * \mathrm{QHD} * [\mathrm{R} * \mathrm{XD}(i)+\mathrm{YD}(i)] * \frac{\mathrm{PHD} * \mathrm{SAD}}{\mathrm{CD}},$$

where

$$\mathrm{CD} = \mathrm{PHD} * (\mathrm{QAD} - \mathrm{YD}(m+1)) + \mathrm{R} * \mathrm{PHD} * (\mathrm{QVD}-\mathrm{XD}(m+1)),$$

and the incidence in the very active subpopulation of IVDUs is

$$\left[\sum_{i=1}^{m} (1-\mathrm{ETAD}) * \rho_i * \mathrm{R} * \mathrm{PHD} * \omega_i * \mathrm{QHD} * \mathrm{XD}(i)\right] * \frac{\mathrm{SVD}}{\mathrm{QVD}-\mathrm{XD}(m+1)}$$

$$+ \sum_{i=1}^{m} \mathrm{ETAD} * \rho_i * \mathrm{PHD} * \omega_i * \mathrm{QHD} * [\mathrm{R} * \mathrm{XD}(i)+\mathrm{YD}(i)] * \frac{\mathrm{R} * \mathrm{PHD} * \mathrm{SVD}}{\mathrm{CD}}.$$

The homosexual–IVDUs are considered to have both homosexual partnerships and needle–sharing partnerships. The incidence in the homosexual–IVDUs with suffix B is the sum of both the homosexual and needle–sharing incidences.

The incidence for the heterosexual partners of IVDUs is not given by the incidences above, but is given by

$$\sum_{i=1}^{m} \rho_i \times \mathrm{PAP} \times \omega_i \times \mathrm{QHP} \times [\mathrm{XD}(I)+\mathrm{YD}(I)] \times \frac{\mathrm{SAP}}{\mathrm{QAP}-\mathrm{YP}(M+1)}.$$

Note that the IVDUs do not have two activity levels in mixing with heterosexual partners and the heterosexual partners have only one activity level. This incidence term for the heterosexual partners of IVDUs is a very simple version of a complicated process. Although heterosexual partnerships with IVDUs are constantly being formed and dissolved, it is difficult to model this pairing process. The incidence term above assumes that people in the population of heterosexual partners of IVDUs are mixing with the IVDUs and forming partnerships. It is helpful to think that this population is a changing amalgamation consisting of those who have been or currently are or will become heterosexual partners of IVDUs. The incidence expression above seems to be the simplest way to model heterosexual partners of IVDUs.

The incidence of perinatal HIV infections is the product of the fecundity rate FC (children born per female per month), the probability QHC of transmission by an asymptomatic mother to a neonate and the weighted sum of infected females. The weighted sum of female IVDUs is the sum of the products of the relative weights of transmission, the fraction PIW of IVDUs who are women and the number of infected IVDUs. The weighted sum of female heterosexual partners is the sum of the relative weights of transmission, the fraction PHW of heterosexual partners who are females and the number of infected heterosexual partners. The sum of these two is the weighted sum of infected females. Thus the incidence of perinatal HIV infections is

$$FC \times QHC \times \left[\sum_{i=1}^{m} \rho_i \times \omega_i \times PIW \times [XD(I)+YD(I)] + \sum_{i=1}^{m} \rho_i \times \omega_i \times PHW \times YP(I) \right]$$

7.2 The Fitting Procedure

The fit criteria given in Section 6.1 for the model for homosexual men in San Francisco must be expanded for this more general model. As before, the first criterion for the simulations is that the parameter values must be consistent with the *a priori* parameter estimates obtained from data. Since estimates of HIV incidence are generally not available, the second criterion is now that the yearly AIDS incidences in the risk groups in the simulations must be close to the yearly AIDS incidence data supplied by the Centers for Disease Control (CDC).

Many of the parameter values in the model are fixed at their estimated values, but some are allowed to vary to give the best fit. For example, the population sizes of the homosexual men, IVDUs and heterosexual partners of IVDUs are all fixed, but the population size of the homosexual–IVDUs is varied in order to obtain the best fit to the AIDS incidence data in this population. The migration rates and natural mortality rates are fixed at the estimated values.

The parameters related to the progression through the stages (m and γ_i for $i = 1, \cdots, 7$) are all fixed and equal to the values found in Chapter 2. Other fixed parameter values are the probabilities (or proportions) of transmission QHH, QHD and QHP per asymptomatic partner, the parameters ω_k which multiply these QH values to determine the probability of transmission by a stage k infective and the parameters ρ_k which are the fractions still active in stage k.

The predicted AIDS cases in the five risk groups in the NYC model must be close to the delay–adjusted AIDS incidence. The number of AIDS cases per year are not linearly independent so that a hypothesis of the chi–square goodness of fit test is not satisfied. Nevertheless the chi–square value of the sum of the squares of the observed minus the expected divided by the expected values is computed as a measure of the fit. Separate chi–square sums are also computed for each of the five risk groups.

The fit to the AIDS incidence data in the population of homosexual men is obtained by varying the initial average number PASH of partners per month, the year STRH in which reduction in partners starts and the yearly reduction factor RDNH. Similarly, the fit to the AIDS incidence data in the IVDU population is obtained by varying the analogous parameters

PASD, STRD and RDND. The fit to the AIDS incidence data in the homosexual–IVDU population is obtained by adjusting the population size NSIZEB.

The fitting procedure involves choosing parameter values sequentially with those subject to the most uncertainty chosen last or adjusted to fit the AIDS incidence data. Fixed values are used for many parameters such as population sizes, migration rates, natural mortality rates, number of stages, stage transition rates, probabilities of transmission by asymptomatic infectives, multiplying factors for probability of transmission and fractions still active in the stages, activity level fractions and ratios, and the transfer rate constants between the activity levels.

After the parameters above are fixed, the reduction starting years STRH and STRD are chosen and the size NSIZEB of the homosexual–IVDU population is chosen. Initial guesses are made for four parameters: the average numbers of partners per month (PASH and PASD), and the yearly reduction factors (RDNH and RDND). A Fortran computer program uses the IMSL subroutine BCONF to find the values of these four parameters which minimize the sum of the chi–square values for the homosexual men, homosexual–IVDUs and IVDUs. This program is similar to FIT10.FOR listed in the Appendix.

After the simulation model has been fit to the IVDUs, then the model is fit to the heterosexual partners of IVDUs by varying only one parameter, the average number PAP of new heterosexual partners per month. After both the IVDUs and their heterosexual partners have been fit, then the model is fit to the perinatal cases by varying only one parameter, the fecundity rate FC. This program is similar to IVDU10.FOR listed in the Appendix.

7.3 Discussion of the Model

Epidemiological modelers attempt to capture the essential features of an epidemiological process in a precisely stated model. Of course, the models are extreme simplifications of the complex human and biological processes that contribute to the spread of an infectious disease, but they can be very useful in attempting to understand the basic epidemiological mechanisms. The art of epidemiological modeling is to formulate a model so that it has enough complexity to be consistent with all observations, but is not more complicated than necessary to fit the data. Thus there is a balance between the goals of simplicity and realism.

The model formulated here for the spread of HIV in the five risk groups shown in Figure 7.1 attempts to capture the essential aspects in a relatively simple model. This model consists of five sets of nonlinear difference equations similar to those in Figure 3.2 for compartments similar to those in Figure 3.1. The model incorporates the major transmission mechanisms of homosexual and heterosexual intercourse, needle–sharing by IVDUs and perinatal infection.

Heterogeneity in sexual and needle–sharing behavior is reflected by the division of each population of homosexual men, homosexual IVDUs and IVDUs into two subgroups consisting of those who are active and those who are very active. The model includes migration into and out of the risk populations, normal, non–HIV related deaths, and changes in sexual (or needle–sharing) behavior by some individuals. Because there is no solid data on changes in the sizes of the risk groups over time, the modeling here assumes that the population sizes remain constant. The subdivision into only two sexual (or needle–sharing) activity levels is reasonably simple, but it is consistent with the survey data and it is adequate to fit the HIV and AIDS incidence data. Based on four surveys of homosexual behavior, it is estimated in Section 5.2 that for two sexual activity levels, ten percent of the population has ten times as many new sexual partnerships per month. The corresponding needle–sharing parameters are estimated in Section 8.2.4.

Heterogeneity in behavior is an important factor in the transmission of sexually transmitted diseases. Hethcote and Yorke (1984) explored the effects of heterogeneity in the transmission of gonorrhea and found that a "core" group of sexually very active, highly–efficient transmitters were central to the transmission and persistence of gonorrhea. One of the major barriers to a better understanding of the HIV transmission process is the lack of information on the social, sexual and needle–sharing mixing which occurs between subgroups of the risk groups. Many authors have used a modeling approach to explore the effects on HIV transmission and AIDS of behavioral heterogeneity and different mixing structures. Attempts have been made to estimate the entries in contact or mixing matrices from survey data. Papers exploring sexual mixing and heterogeneity include: Ahlgren et al. (1990), Anderson (1988a, 1988b), Anderson and May (1991), Blythe and Anderson (1988), Blythe and Castillo–Chavez (1989), Busenberg and Castillo–Chavez (1991), Cardell and Kanouse (1989), Castillo–Chavez et al. (1989), Hyman and Stanley (1988, 1989), Jacquez et al. (1988, 1989), Knox (1986), Koopman et al. (1989), Pickering (1986), Sattenspiel and Simon (1988) and Simon and Jacquez (1992). Papers modeling HIV transmission in IVDUs include Blower et al. (1991) and Kaplan et al. (1989, 1990).

Staged progression has become the standard way to model the long infectious period leading to AIDS. Here the progression from HIV infection to AIDS is modeled by a sequence of seven infectious stages with AIDS as the seventh stage and death due to AIDS as the eighth stage. The mean times in each stage are given in Chapter 2 for both clinical staging and T4–cell count staging. The infectivity and amount of sexual activity vary with the stage of infection. The relative infectivity and relative sexual activity compared to those in the asymptomatic stage are estimated in Sections 5.1.1 and 5.1.2.

The HIV incidence terms are all based on the principle of mass action; i.e., the incidence is directly proportional to the product of the number of susceptibles and the number of infectives in the stages. The simplest formulation for the interactions between subgroups of a risk group is based on the assumption of proportionate mixing. In this case the activity levels are specified for each subgroup and then the new partnerships of a person are distributed in proportion to the activity levels and population sizes of the subgroups (Hethcote and Yorke, 1984). Thus a person is more likely to have a new partner from a more active subgroup than from a less active subgroup. This assumption of proportionate mixing has the immense advantage that the n^2 entries in the $n \times n$ contact matrix can be estimated from n pieces of information (Hethcote and Van Ark, 1987). Unfortunately, this proportionate mixing assumption does not seem to be realistic since very active people seem to be much more likely to form new partnerships with other very active people. The next simplest formulation for subgroup interactions seems to be a convex combination of proportionate mixing and internal mixing (in which people mix only with their own subgroup). This formulation, which was used in modeling gonorrhea (Hethcote and Yorke, 1984, p. 83), is now often called preferred mixing (e.g., Jacquez et al., 1988, 1989). In the modeling here, the incidences are formulated with preferred mixing and the convex combination parameter η is adjusted to fit the data.

As indicated in Section 7.1, the incidence terms for HIV transmission between needle–sharing IVDUs are also formulated with preferred mixing. It may seem strange to use the same form for the incidence terms for homosexual men and for IVDUs; however, this same form is based on the following similarities. People in both groups do form partnerships that consist of one or more contacts (homosexual or needle–sharing). Bath houses or gay bars might be analogous to shooting galleries as places where multiple partnerships occur. The number of contacts and duration of partnerships vary greatly in both populations so that the very active and active categories are a simplification for both populations. People in both populations can have multiple simultaneous partnerships and the incidence terms account for this somewhat since this behavior could correspond to frequent partner change. Thus the incidence term above is a simplification for both populations, but is reasonable for both populations.

There are data from sexual behavior surveys which show that the average partnership rate of homosexual men in some cities has changed over time (see Section 5.3.2). There are also some indications that the needle–sharing behavior of IVDUs may have decreased over time (see Section 8.2.4). Here changes in behavior are modeled by specifying the initial average number of new partners per month, the starting and stopping dates for changes in the partnership rate and the yearly reduction factor.

Modeling HIV transmission and AIDS in heterosexual partners of IVDUs is handled with the simplest possible formulation. The HIV incidence for these heterosexual partners is proportional to the number of new partnerships per month of heterosexuals with IVDUs; consequently, the only parameter to be adjusted in the fitting process is the average number of IVDU partners per month of heterosexuals. Although there is some evidence that the probability of heterosexual transmission is different depending on whether the infected person is male or female (Padian et al., 1991), this possible asymmetry is not included in our model. If this asymmetry were included, then the model would need separate classes for male and female IVDUs and for male and female heterosexual partners of IVDUs. This more complicated model would have more parameter values to be estimated, and this might be difficult since the yearly AIDS incidence is often small and erratic in the risk groups of female IVDUs and their male heterosexual partners. The simple model used here works well in fitting the AIDS incidence data for heterosexual partners.

The modeling of perinatal transmission from HIV–infected mothers to their newborn children before, during or just after birth is also modeled in the simplest way possible. The perinatal HIV incidence involves only the fecundity rate (birth rate), the probability of transmission during birth and the number of HIV–infectious females. The progression of perinatally–infected children to AIDS is modeled using the two–track staging system given in Section 2.3. For further clarification of the incidence terms or other aspects of the model, see the sample computer programs in the Appendix.