

Mathematical epidemiology of HIV and sexually transmitted infections

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On November 23rd, 2004, WHO and UNAIDS launched a new report on the global HIV/AIDS epidemic. According to the report, the number of newly infected adults and children during 2004 was estimated to be 4.9 million. Totally 39.4 million people were estimated to live with HIV all over the world. The report also pointed out the increase is especially remarkable in East Asia, Eastern Europe and Central Asia. We must recognize that HIV/AIDS is still an enormous threat to mankind.

As to the situation in Japan, there is still a constant increase of HIV infected persons. The rate of HIV positive blood donors during 1987-2004 shows very stable exponential growth except for the very early years. Based on the regression coefficient, there has been 12.5% increase per year. This implies that the number of newly infected individuals becomes doubled in 5.9 years. We cannot overlook the serious impact of HIV/AIDS in Japan.

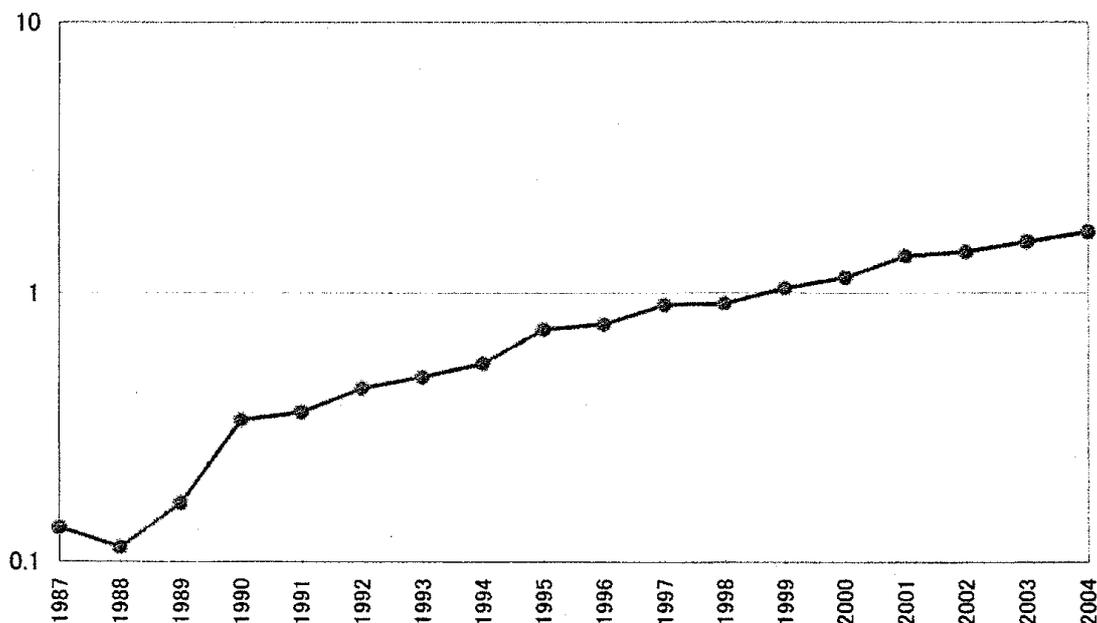


Fig. 1 The rate of HIV positive blood donors in Japan during 1987-2004 (per 100,000)

To understand the implication of the present observation and consider preventive policies, mathematical models can play an important role (Anderson and May, 1988, 1991; Anderson *et al.*, 1991). We can predict the future spread of HIV and evaluate the effect of proposed preventive strategy by using a mathematical model. Even a very simple mathematical model can be expected to predict essential time course of the spread. In addition to such simple models, there is a back calculation method to predict AIDS cases using the relationship that HIV infected individuals develop AIDS following some specific statistical distribution of incubation time. Mathematical models have advantage in long term prediction whereas back calculation in a short term prediction. I would like to review some of these mathematical approaches to HIV/AIDS and other sexually transmitted infections.

Simple mathematical models

A simple mathematical model of infectious diseases without considering immunity is called SIS model. It is a compartment model represented by a set of differential equations. Here the variable S represents the susceptibles and the variable I represents the infecteds. When immunity is considered, an additional variable R is added representing the recovered or removed and called SIR model. The SIS model is described as follows:

$$\frac{dS}{dt} = \lambda - \mu S - \beta c \frac{I}{S+I} S + fI$$

and

$$\frac{dI}{dt} = -\mu I + \beta c \frac{I}{S+I} S - fI.$$

In this model λ represents constant birth rate. The parameter μ represents mortality, f is a recovery rate, β is transition probability and c is the rate of contact per person per unit time. The parameters β and c are mathematically redundant but separated because of practical purpose. The above model does not distinguish male and female, which are considered to be essential in sexually transmitted infections. In this model, additional mortality due to the infection is disregarded because sexually transmitted infections are usually less lethal than other infectious diseases. The SIS model incorporating male and female is expressed as follows:

$$\frac{dS_m}{dt} = \lambda_m - \mu_m S_m - \beta_m c_m \frac{I_f}{S_f + I_f} S_m + f_m I_m,$$

$$\frac{dS_f}{dt} = \lambda_f - \mu_f S_f - \beta_f c_f \frac{I_m}{S_m + I_m} S_f + f_f I_f,$$

$$\frac{dI_m}{dt} = -\mu_m I_m + \beta_m c_m \frac{I_f}{S_f + I_f} S_m - f_m I_m$$

and

$$\frac{dI_f}{dt} = -\mu_f I_f + \beta_f c_f \frac{I_m}{S_m + I_m} S_f - f_f I_f.$$

The subscript m represents for male and f for female. Then we have prevalence rates of male and female at equilibrium as follows:

$$\frac{I_m^*}{N_m} = \frac{\beta_m c_m \beta_f c_f - (\mu_m + f_m)(\mu_f + f_f)}{\beta_f c_f (\mu_m + f_m + \beta_m c_m)}$$

and

$$\frac{I_f^*}{N_f} = \frac{\beta_m c_m \beta_f c_f - (\mu_m + f_m)(\mu_f + f_f)}{\beta_m c_m (\mu_f + f_f + \beta_f c_f)}.$$

Here N is the sum of S and I . If all the parameters are the same between male and female, this model is reduced to the first one not involving the difference of male and female. These models serve as the basic framework of more complicated models of infectious diseases. Dividing one variable into two or more subclasses according to some important characteristics, such as age and/or sexual activity, is a typical approach to constructing more realistic model. The importance of heterogeneity in sexual activity is most emphasized and the concept of 'core', the subpopulation of higher sexual activity, has been proposed (Hethcote and York, 1984).

Pair formation models

One important characteristics of human population is the formation of a pair consisting of one male and one female in which sexual contact is usually restricted. There are models incorporating such a pair formation (Dietz, 1988; Waldstätter, 1989). The models are consisted of variables of single male, single female and a pair of male and female. Another important characteristic is that the restriction is not absolutely complete. Thus such a model also has a variable representing CSW (commercial sex worker). There are two states, susceptible and infected, for each individual, the number of equations of the pair formation

model is considerably large.

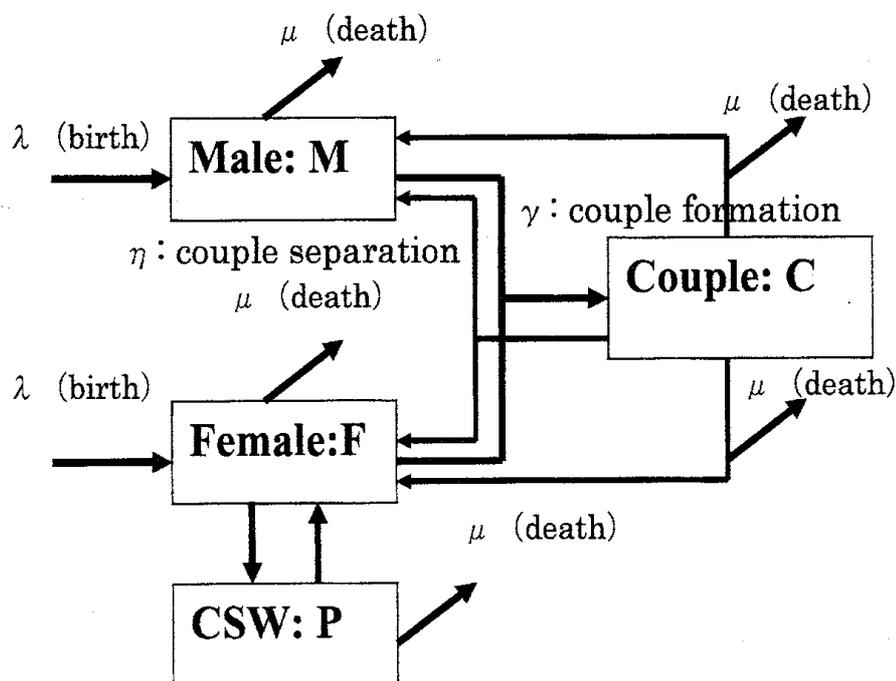


Fig. 2 The scheme of pair formation model with commercial sex workers

Kakehashi(1998) analyzed the invasion of HIV in Japan using a pair formation model. Setting the involved demographic parameters as close as possible to the actual Japanese situation, the condition for HIV to spread was investigated. The result of the analysis suggested that HIV cannot spread if CSW did not exist. Sensitivity analyses for the stability of disease free equilibrium were carried out for unknown parameters and the results were illustrated as the domain in parameter space. The Latin hypercube sample of parameter set indicated that critical transmission probability is 0.66%(SD=0.17%), a level smaller than the higher range of reported transmission probability.

The increase of infected persons is expected to grow exponentially in the early stage of the spread. Kakehashi(2000) also analyzed on the initial growth rate using the pair formation model. According to the model, the initial exponential growth rate of infected persons can be calculated as the maximum eigenvalue of the Jacobian matrix evaluated at the disease free equilibrium. Setting the maximum eigenvalue to be the same as the observed growth rate, we can obtain the reliable range of unknown parameters.

Age structured models

Age is one of the most influential attribute in sexually transmitted infections. There are more realistic models in which age and sexual activity is considered (Garnett and Anderson,

1993). The age specific incidence rates of sexually transmitted infections show typical pattern which has a peak at the most sexually active age. Using the incidence data of sexually transmitted infections in Japan, the age specific pattern is analyzed in Kakehashi(2003).

Back calculation

Back calculation is a statistical method to estimate HIV infected persons from the data on AIDS cases (Brookmeyer and Gail, 1988, 1994). If $a(t)$ and $h(t)$ represent the numbers of AIDS case and HIV infected persons at time t , and besides the probability density function of incubation time is described by $w(t|\theta)$ with parameter θ , there is a relationship:

$$a(t) = \int w(t-s|\theta)h(s)ds.$$

If we assume $h(t)$ is exponential, we can calculate the growth rate by maximum likelihood method using AIDS case data. This method is also useful to investigate the consistency of HIV and AIDS data and the distribution of time interval between the report of HIV and that of AIDS. The analysis is applied, for example, to the data in Southeast Asia (Suhama and Kakehashi, 2000).

The combination with differential equations is discussed in Rao and Kakehashi(2004)

Discussion

We so far reviewed some mathematical approaches to the spread of HIV and sexually transmitted infections. Some sophisticated methods have been already developed but there still exists the need for more reliable models. Mathematical approach to the spread of infectious diseases is not only of academic value but also of practical importance. We would like to continue our challenge in this field.

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