The torments and blessings of the leprosy epidemiometric model

MF LECHAT

School of Public Health, Catholic University of Louvain, Department of Epidemiology, 30 Clos Chapelle-aux-Champs, 1200 Bruxelles, Belgium

1. Introduction

Mathematical models of diseases in populations, i.e. epidemiometric models, are not new. Such an approach was first used by Ross for malaria in 1911, and later applied to tuberculosis by Reed and Frost. The aim of these models is to quantify the dynamics of a disease in a population, that is to define, through a set of appropriate equations, how the variations of selected epidemiologic parameters are mutually related.

The use of computers, making possible to include a large number of variables, has greatly facilitated the development of such models. In 1962, Waaler et al. proposed a model for tuberculosis, from which originated the idea to try a similar method in the study of the epidemiology of leprosy (Lechat 1971).

The reason for applying this approach to leprosy was that for several decades large scale leprosy control campaigns had been organized in many areas of the world, still there was increasing doubt as to whether these efforts were fully effective in reducing the problem. In spite of intensive case-finding and mass treatment, the number of new patients was still significant. No convincing epidemiological evaluation had been carried out.

The specific objective of the ESLEP epidemiometric model for leprosy was therefore to study how the incidence of leprosy does relate to prevalence. If such a quantitative relationship can be established, it could become possible (1) to predict future incidences under present conditions of control; (2) to simulate how changes in the control measures affect incidence.

2. Method

The development of the model involved three main steps, summarized

as follows :

(1) Basic assumption

As mentioned, the purpose of the whole exercise is to calculate incidences of new cases as a result of prevalences of overt cases
 $(\text{incidence}) = f(\text{prevalence})$

This relation supposes one preliminary assumption, i.e. that the leprosy patient constitutes the sole reservoir of infection. There is no animal reservoir, and no inapparent carrier apt to transmit the disease.

This relation must be further expanded in two ways :

- (a) due to the accepted delay between infection and onset of disease, which may cover many years, this relationship must be rewritten

$$(\text{incidence})_t = f(\text{prevalence})_{t-j}$$

Where annual incidence is considered as dependent on past prevalences (j corresponding to the duration of the incubation period).

- (b) Patients not having the same capacity to transmit the disease, prevalence should be divided into various classes having different infective powers. Consequently, 8 classes of patients were distinguished, according first to the type of leprosy (bacteriologically positive or not) and further to treatment (duration, and attendance). This division is consistent with present knowledge on differential attack-rates in patients exposed to index-cases with various clinical types (Doull and Guinto), effect of treatment on incidence in contacts (Castellazi, Worth) and bio-assays in mice foot-pad (Rees, Shepard).

The basic equation becomes therefore :

$$(\text{incidence})_t = f \quad (\text{prevalences})_{t-j}$$

(2) Structure

~~Since there is~~ Since there is a continual interchange between the various classes of the population, including the patients, the dynamic of the disease can be represented in a schematic way, according to what is known of the natural history of the population (Fig. 1). It goes without saying that each of these categories should be precisely defined.

This structure postulates a certain number of simplifications, the main of which are (a) latent cases are non infective ; (b) there is no congenital leprosy ; (c) the population is uniformly susceptible ; (c) all latent cases develop overt disease except if dying in the meantime ; (d) there is no spontaneous cure without treatment ; (e) there is no transformation from the tuberculoid to

Fig. 1. - FLOW - CHART. LEPROSY MODEL

the lepromatous type (reversal reaction).

(3) Estimation of the parameters

Five categories of data are required in the model, i.e. (a) transition rates from one state to another ; (b) probabilities of transition, that is rates which are dependent on the duration of stay in one given class ; (c) ratio of lepromatous/tuberculoïd among the new cases ; (d) interval between infection and onset of disease, according to the type of leprosy (incubation/latency period) ; (e) infective capacity of the 8 different classes of patients, that is the number of persons infected per patient per year.

Averages for the three first categories were obtained from actual data collected on 35.000 patients in the Polambakkam Control Scheme, South India, for the period 1955-1970, representing some 320.000 person-year of observation.

Estimates for the distribution of the incubation-latency period and infective capacities were estimated by a least-square method from the data collected in the period 1955-1970.

3. Results

The model was run on a twenty years time period in order (a) to predict annual incidence under present control measures ; (b) to simulate incidence trends with different control methods. Simulations were achieved by manipulating the relevant parameters.

The main results were the following (Fig 2 and table 1).

- (1) Present control conditions, based on early case-finding (75 % of the new patients detected within 1 year of onset) and mass-treatment (15 % of patients abandoning treatment per year) are effective to reduce incidence in the long run. Incidence is reduced by 50 % after approximately 12 years.

It ensues that leprosy control cannot bring results overnight. Long-term planning and sustained efforts are required. The message is of special importance for international agencies and non-governemental organizations which at times display a tendency to expect short term results and go discouraged when so-called eradication was not soon materializing.

- (2) Further reduction in the interval between onset and detection (that is making detection earlier), as well as improvement in case-holding, as compared to present conditions, does not result in a significant reduction of incidence.

Fig. 2. Prediction of incidence with different control methods at various coverages over 20 - years period

This is important, in view of major efforts being often directed to improve those operational components of the leprosy control activities. The superiority of one of these two methods over the other will depend on their respective cost under local conditions. From an operational point of view, and with limited resources in personnel, one will have to choose strengthening early detection or pursuing patients having abandoned the treatment, depending on the cost of the required changes of activities.

- (3) Segregation of the bacteriologically positive patients for one year after detection, in addition to present control measures, is relatively effective. The reduction in incidence reaches 75 % after 20 years.

This constitutes an epidemiological argument against segregation, in addition to the economic, operational and psychological reasons which militate against it.

- (4) Elimination of all lepromatous (bacteriologically positive) patients does not bring about interruption of transmission, as shown by a persisting 0.4 per thousand incidence after 20 years.

This is in contradiction with the view that only the so-called open cases are responsible for spreading the disease, which found its way in oft repeated recommendation that when resources are limited, control should focus on these cases to the detriment of the others. It rather suggest the hypothesis that though much less infective, the tuberculoid cases could by their sheer number play a non insignificant role in the transmission. Hence, the necessity to implement adequate control and design appropriate treatment schedule for those patient (who at present are sometime somewhat improperly called paucibacillary cases).

- (5) Vaccination of the population with a BCG-type vaccine, whose effect was for long assumed to protect against the lepromatous type of leprosy, has little if no public health effect in the long run.

This observation indicates further that vaccine protection at the population level is another matter that effectiveness as demonstrated in clinical trials.

- (6) Specific vaccination for leprosy comes out by far as the most effective measure to drastically reduce incidence in the not too distant future. 87 % reduction in the predicted incidence is obtained after 20 years by vaccinating only 50 % of the population. With a 100 % vaccine coverage, incidence is

reduced to zero in 11 years.

It should be noted that the effect of vaccination is delayed. This is due to the prolonged incubation-latency period of leprosy, which in the model ranged from 1 to 8 years, and to the fact that simulations postulated no effect of vaccination in the individuals already infected.

The outright result is that research in the development of a vaccine constitute a major priority for the allocation of resources.

Incidentally, these simulations have been repeated using cost-indicators, to study the cost-effectiveness ratios of various control measures. It will only be mentioned that under the South-India conditions specific vaccination again comes out first, as the most cost-effective measure.

4. Difficulties

Turning from blessings to torments, the development of the model has raised a number of difficulties and even set backs, both from the technical and conceptual viewpoints.

- (1) Soon after the publication of the first results, our attention was raised on some errors in the formulation of the model, the major being the use of an unlimited population in which new cases were recruited. These errors have been corrected. A comparison of the simulation before and after modification of the programme showed that the initial results are valid as long as the prediction does not exceed 30 or 40 years.
- (2) The initial model did not take into account the age distribution of the population. It resulted in an underestimation of the death rates, and consequently an increasingly overestimated prevalence, as well as resulting incidences, over the years. A new model has been presently established, using the DYNAMO PACKAGE, which takes age into account.
This has necessitated the calculation of age-specific incidence rates in the population, which in itself constituted a side-study.
- (3) In order to be generalized, the model should be validated in other populations presenting the same epidemiological context. This is actually carried out by Jan De Vries at the University of Michigan School of Public Health in Ann Arbor, using the data accumulated in the Pogiri Leprosy Control Scheme, Andhra Pradesh, over the period 1962-1969.

- (4) Extension of the model to populations with other epidemiological characteristics (mainly different pattern of transmission) remains an open question.

5. Future

The availability of the DYNAMO package, much more convenient for simulation than the initial programme, opens the way for testing a number of hypothesis and simulations along several lines.

- (1) In its initial stage, the ESLEP model did not consider the following possibilities (a) resistance to leprosy, be it genetic or immunological ; (b) infection not followed by development of disease ; (c) spontaneous cure ; (d) infectivity of latent patients.
- (2) Dapsone-resistance can be simulated by introducing an additional class of lepromatous patients. Resistance in different proportions and with different rates of emergence, is present being simulated, in order to see how it affects incidence trends in the long run.
- (3) Other direct or indirect control measures can be studied, such as fast-acting treatment or birth control, this latter one by reducing the size of the cohorts of new susceptibles.
- (4) Testing of different mechanisms for the vaccination is now under consideration. As mentioned, the initial simulations postulated that the vaccine afford no protection to those individually already infected. Other hypothesis can be envisaged and their protective effect measured.

In the meantime, 10 years have elapsed since the initial prediction were established using the Polambakkam data as a baseline. Plans are being made to compare the expected incidence as predicted by the model with the actual data observed in the study population for the period 1971-1980.

Moreover, the development of the model has strongly pointed out the scarcity of valid epidemiological data in leprosy. More important, it revealed the want for an appropriate information system for collecting and retrieving epidemiological data in leprosy.

A major fall-out of the model has been the elaboration of a simple recording and reporting system of essential epidemiological data, developed jointly with WHO (OMSLEP). This system will hopefully help both in the epidemiological and the operational evaluations of leprosy control schemes in the future.

6. Conclusions

The major difference in the model approach to tuberculosis and leprosy is that in leprosy we cannot identify infection from disease. This black box, which can be called latency or incubation period or by whatever term, cannot be recognized. This from a methodological point of view has revealed a major difficulty.

The development of an appropriate test to recognize leprosy infection would drastically the prospects of epidemiological research in leprosy. It would then become possible to study how the disease is transmitted in the population, who get it, when, and under what circumstances.

This if necessary confirms once more that epidemiology cannot be dissociated from basic research, and that its achievements are closely dependent on progress in other fields, in this case immunology.

	Incidence at 20 years ‰	Reduction as % Initial inci- dence	% reduction vs present measures
1. Present control measures	1.08	60.2	
2. Improvement of case-holding	0.80	70.5	25.9
3. Earlier detec- tion	0.99	63.2	8.3
4. Segregation 80% lepomatous	0.76	72	29.6
5. B.C.G. - like vaccination 50%	0.98	60.6	9.3
6. Specific vacci- nation	0.34	87.4	68.5

Table 1. Prediction of incidence with different control methods at various coverages over a 20-years period

Acknowledgements

These studies were supported by grants received from the following associations members of ILEP (The International Federation of Anti-Leprosy Associations) : Damian Foundation Belgium, Amici dei Lebbrosi, Fondations Follereau France, Fondation Follereau Luxembourg, CIOMAL, Secours aux Lépreux Canada.

References

- Ross, R. The Prevention of Malaria, 2nd edit. Murray ed., London, 1911.
- 2 De Oliveira Costa Maia. Some mathematical developments on the epidemic theory formulated by Reed and Frost. Human Biol, 1952, 24, 167-200.
- 3 Waaler H, Geser A, Andersen S. The use of mathematical models in the study of the epidemiology of tuberculosis. Amer. J. Pub. Hlth, 1962, 52, 1002-1013.
- 4 Lechat M.F. An Epidemiometric approach for planning and evaluating leprosy control activities. Int. J. Leprosy, 1971, 39,2, 603-607.
- 5 Lechat M.F., Misson J.Y, Vellut C.M, Misson C.B, Bouckaert A. Un modèle épidémiométrique de la lèpre. Bull. Organ. mond. Santé, 1974, 51, 361-373.
- 6 Lechat M.F, Misson C.B, Bouckaert A, Vellut C. An Epidemiometric model of leprosy : a computer simulation of various control methods with increasing coverage. Int. J. Lepr. 1977, 45, 1, 1-8.
- 7 Lechat M.F, Vellut C, Misson C.B, Misson J.Y. Application of an economic model to the study of leprosy control costs. Int. J. Lepr. 1977, 46, 1, 14-24.
- 8 Lechat M.F, Vellut C, Misson C.B. The use and limitations of epidemiometric models in leprosy. A window on Leprosy. Gandhi Memorial Leprosy Foundation Silver Jubilee Commemorative volume, New Delhi 1978, 64-70.