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An Epidemiometric Model of Leprosy: A Computer Simulation of Various Control Methods with Increasing Coverage[1]

M. F. Lechat, C. B. Misson, A. Bouckaert and C. Vellut[2]

Epidemiometric models are useful tools to predict and simulate trends of diseases under various epidemiologic conditions, evaluate control methods, and compare cost and effectiveness of possible strategies ([3]). An epidemiometric model of leprosy has been developed, using the data collected in the Polambakkam leprosy control scheme, South India, from 1954 to 1970. Structure of this model was described previously ([4]). Preliminary results included a number of test-simulations under various control conditions over a 20 year period, using incidence as the epidemiologic criterion of effectiveness. This study presents the full range of simulations for these various control methods, which were considered at different coverages of application.

MATERIALS AND METHODS

Using the model previously described, the incidence of leprosy has been computer simulated at 5, 10, 15 and 20 years, under a number of different control conditions.

[2] M. F. Lechat, M.D., D.T.M., Dr.P.H., Professor of Epidemiology; C. B. Misson, Research Associate, Department of Epidemiology; A. Bouckaert, M.D., D.T.M., Assistant Professor, Department of Epidemiology, School of Public Health, Catholic University of Louvain, 1200 Brussels; C. Vellut, M.D., Medical Officer, Leprosy Center, Polambakkam 603309, India.

The following control measures, available or still in the developmental stage, were considered:

0. Unmodified leprosy control as carried out at present in the study population, based on early detection and regular treatment.

I. Vaccination with a BCG like type-specific vaccine 100% effective for preventing development of leprosy as the lepromatous type and converting potential lepromatous cases into tuberculoids.

II. Vaccination with a disease-specific vaccine 100% effective for preventing leprosy.

III. Improvement over present conditions in case-holding to treatment.

IV. Isolation of lepromatous patients for one year after detection.

The reference control strategy used as a base line for comparisons presents the following features which are relevant to simulations:

a) The probability of abandoning treatment (defined as absence from treatment for one calendar year) is dependent on the number of years since treatment was initiated. It follows a negative exponential distribution with means = 0.377 for lepromatous patients and 0.469 for tuberculoid patients.

b) The transition rate for resuming treatment is independent from the duration of interruption of treatment. The annual transition rates are 0.317 for lepromatous patients and = 0.143 for tuberculoid patients.

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c) The ratio of lepromatous to total new cases is taken as 0.145 (i.e., 14.5% of the individuals develop leprosy as the lepromatous type).

These parameters were obtained from the study population, numbering 35,200 patients observed yearly for 16 years (1955-1970), using uniformly trained personnel and standard operational criteria.

Simulations were carried out by modifying the relevant parameters in the equations of the model governing the number of infective cases over the preceding years. All simulations took into account a 1% annual increase of the target population.

For methods I to IV, ten simulations were carried out, corresponding to different coverages, i.e., 10, 20, . . ., 100%, of the control method being tested. Indifferently, these percentages of application could be looked at as different effectiveness of the methods. For example, coverage of 70% of the population with a vaccine that is 100% effective is equivalent to coverage of 100% with a vaccine 70% effective. Similarly, if isolation is poorly efficient, strict isolation of 70% of the patients could be equated with a 70% efficient isolation of 100%. For improvement of case-holding (simulation III), this corresponds to reducing by 10, 20, . . ., 100% the probability of abandoning treatment over the whole range of successive years.

RESULTS

Predictions of incidence over 5, 10, 15 and 20 years are given in Figures 1-3, with present control strategy taken as reference. In Figures 4 and 5, the 10th and 20th year effectiveness of each control method as compared to present strategy has been plotted as a function of the percentage of coverage. This is a first step for further cost-effectiveness analysis.

DISCUSSION

The relative effectiveness of the four simulated control methods is sharply contrasted.
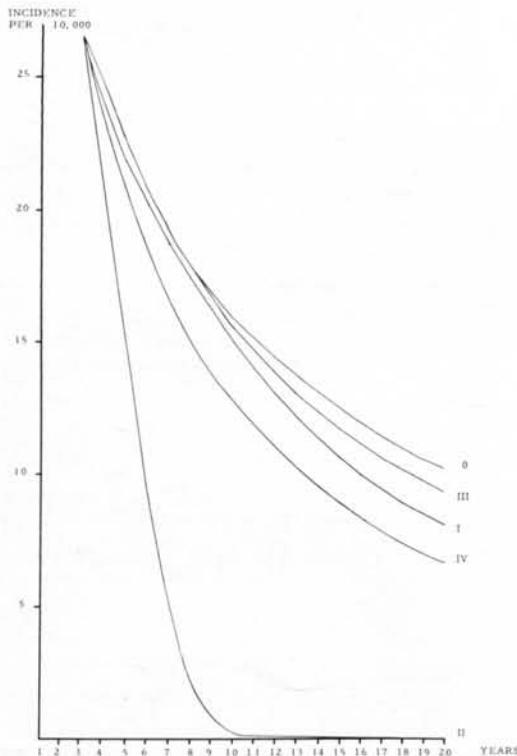

FIG. 1. Prediction of incidence with five control methods at 100% coverage: 0. Present leprosy control measures; I. Vaccination with a BCG-like vaccine; II. Vaccination specific for leprosy; III. Improvement in case holding as compared to present drop-out rates; IV. Isolation of lepromatous patients for one year after detection.
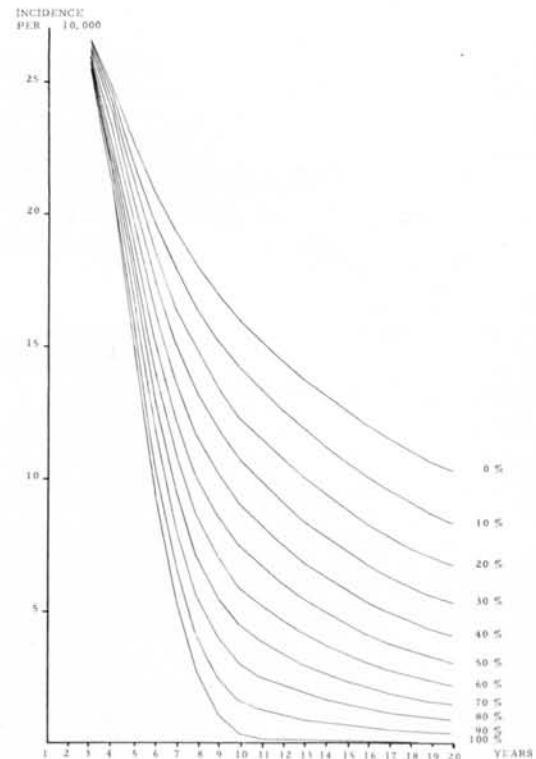

FIG. 2. Prediction of incidence with vaccination of the population by a leprosy-specific vaccine at different coverage; 0 refers to present leprosy control measures.
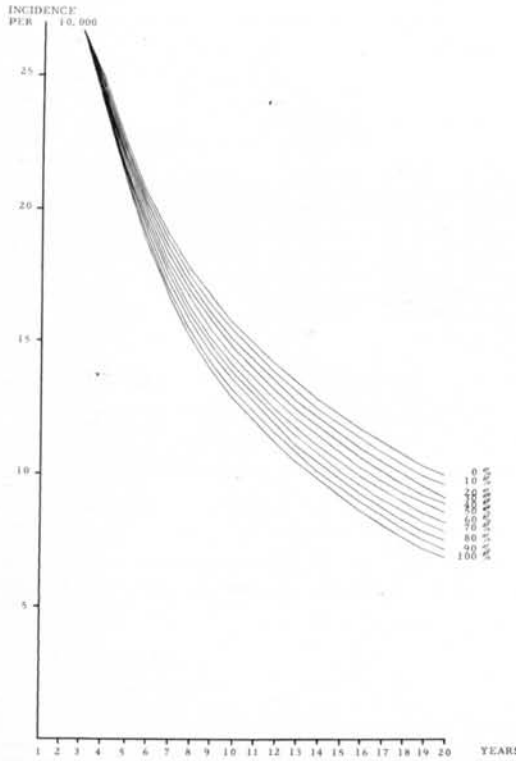
FIG. 3. Prediction of incidence with isolation for one-year of newly detected lepromatous cases, different proportion of patients isolated; 0 refers to present leprosy control measures.

As observed in preliminary simulations with a 50% coverage, a BCG-like vaccination (I) is not likely to bring a major reduction in total incidence of new cases over a 20 year period. The full range of simulations, with vaccinations from 10% to 100% of the population, yields incidences of 10.03 to 8.13 new cases per 10,000 population after 20 years, i.e., a 2% to 21% incidence reduction as compared to continuation of the present methods (10.28 per 10,000 population).

As can be expected from a vaccine, the assumed effect of which is to convert potential lepromatous into tuberculoid cases, following this method is especially noticeable after 15 years. Due to the relatively prolonged incubation period (ranging from 1 to 8 years with a mean of 2.2 years for lepromatous leprosy in the model), cases already infected and in the latent stages escape the effect of vaccination.

With a BCG-like vaccination, the number of new tuberculoid cases at five and ten years increases as compared to the present method. Cases which, in the absence of vaccination, would have been lepromatous are now turn-
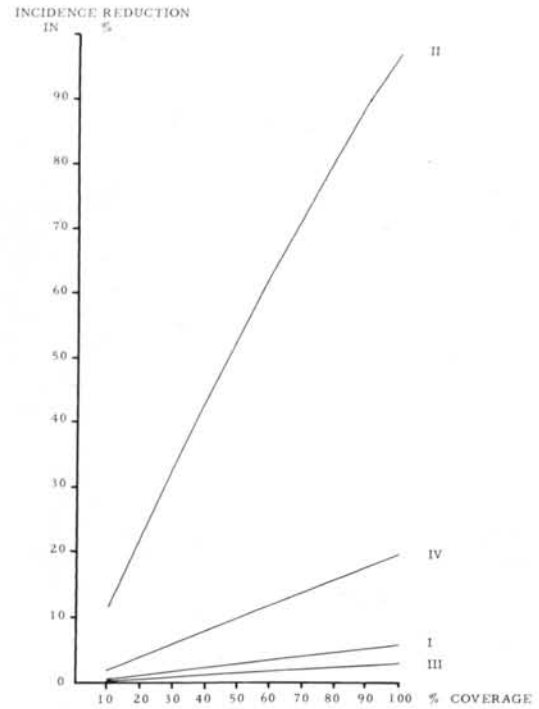

FIG. 4. Tenth year effectiveness of various control methods for reducing incidence as related to coverage of application (numbers refer to method, see text).
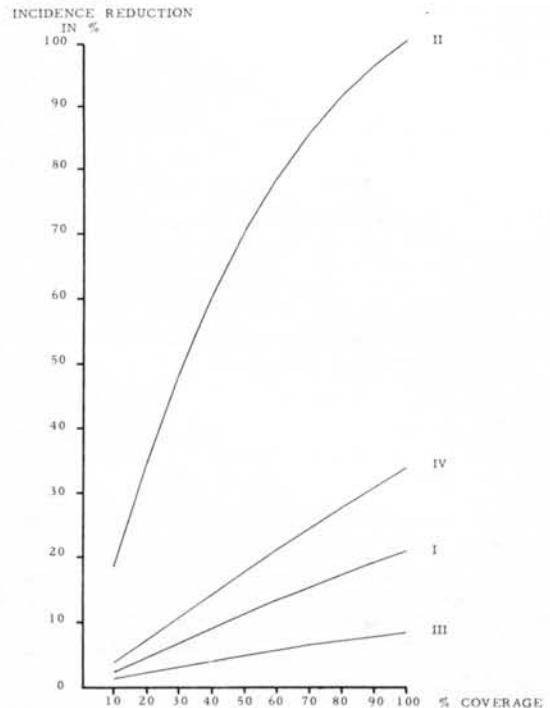

FIG. 5. Twentieth year effectiveness of various control methods for reducing incidence as related to coverage of application (numbers refer to method, see text).

TABLE 1. *Compared incidence with low-coverage leprosy specific-vaccine and high-coverage type-specific vaccine.*

Method	Incidence per 10,000			
	5 years	10 years	15 years	20 years
BCG-like vaccine 100%	21.64	15.05	10.66	8.13
BCG-like vaccine 90%	21.84	15.14	10.82	8.31
BCG-like vaccine 80%	21.94	15.23	11.00	8.51
Specific leprosy vaccine 10%	21.95	14.19	10.60	8.37
Present methods unchanged	22.72	16.01	12.52	10.28

ing to develop the tuberculoid type. Longer incubation period for tuberculoid leprosy as deduced from the model (4.0 years) can also contribute to prolong this effect. It is only at the 15th year that the number of new tuberculoid cases starts also to decrease as compared to the no-vaccination situation. This indicates that a BCG-like vaccination will have little effect on the long-term incidence of leprosy.

Although, on an individual basis, exposure to lepromatous leprosy is associated with the highest risk of transmission ([1]), tuberculoid cases in most countries constitute the largest reservoir. Though less infective, the tuberculoid type of the disease may therefore constitute the major factor for continuation of transmission, at least in those areas where a large proportion of patients are affected with it.

The effectiveness of a BCG-like type of vaccine will therefore depend on the proportion of lepromatous leprosy in the population (14.5% in the model situation). Where lepromatous leprosy constitutes a large share of the patients, it will likely be more effective than in other areas of the world which are characterized by a small lepromatous to total patient ratio. This is the case in Latin America. In Africa, where the majority of the patients are affected with the tuberculoid type, 93 to 97% in some countries ([2]), the effect of such a vaccination will be close to nil ([4]). There is at present no specific vaccine for leprosy. Simulations show that a specific vaccination will, in the long run, be by far the most effective control method for leprosy. Efforts invested in the development of such a vaccine are worth continuing and increasing.

A 100% coverage of the population with an effective vaccine will interrupt transmission after ten years, with 0.25 new cases per 10,000 population. This corresponds to the residual cases with a maximum of eight years' incuba-

tion period and two years or more delay between onset and registration for treatment, which according to the values of the model constitutes 0.19% of potentially latent cases infected prior to vaccination time. No new cases will appear from the 13th year. A 10% coverage of the population with a specific vaccine is approximately as effective as a 100% coverage with a lepromatous-protecting BCG-like vaccine (Table 1) in controlling incidence at the 5th to 15th year time horizons.
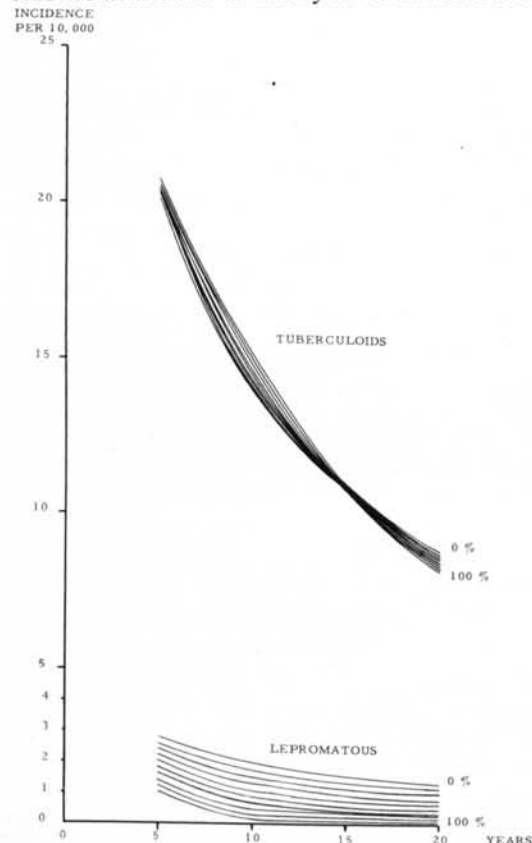

FIG. 6. Prediction of incidence for lepromatous and tuberculoid cases over 5 to 20 years with a BCG-like vaccine—(Method I) at 10% to 100% coverage.

Compared to other methods, specific vaccination with 20% coverage is as effective for controlling the disease as is isolation of all the lepromatous patients for one year after detection. This again is clearly in favor of investing in research for the development of a vaccine as the highest priority for leprosy control.

Specific vaccination has the further advantage of bringing a greater reduction in incidence as related to increased coverage (Figs. 7-10) than any other method. A 90% incidence reduction is achieved at approximately 8.0 years with 100% vaccination-coverage, and respectively 10.0 years and 16.0 years with 90% and 80% coverages. Since it would be unreasonable to expect a 100% coverage, it follows that high though incomplete coverages can also result in drastically reducing incidence if more time is afforded. This is important, since it provides the decision maker with quantified alternatives at different time horizons. Cost will differ according to the schedule adopted to achieve given targets in incidence reduction.

Incidence is a major indicator of effectiveness for the epidemiologist. It provides a measurement of the transmission of the disease. Health managers, however, can be more interested in the total number of patients at different time horizons. Long-term results can be less attractive in terms of fi-

nances or political engineering than short-term returns.

The number of patients prevented, i.e., reduction in incidence, after 20 years is less factual than the crude load of patients, that is prevalence, in the 20 years to come. This is definitely important for governments and funding agencies. Although effective in the long-run, some methods .are likely to temporarily increase the number of patients in the first few years of the program. Such is, for example, the reduction of the delay between onset of the disease and registration for treatment (not considered in this study), and also to a slighter extent type-specific vaccination (due to a longer incubation period of tuberculoid leprosy in the model). The model answers these questions by predicting total prevalence at 5, 10, 15 and 20 years (Fig. 11).

For long-term planning, prediction of prevalence at a given year in the future is less important that the cumulative prevalence of cases over time. This is the time-integral of prevalences expressed in person-years. A computer program has been prepared which yields cumulative prevalence for each of the simulated control methods, according to population coverages. It also calculates the reduction in cumulative prevalence for different control methods at various coverages (Table 2).
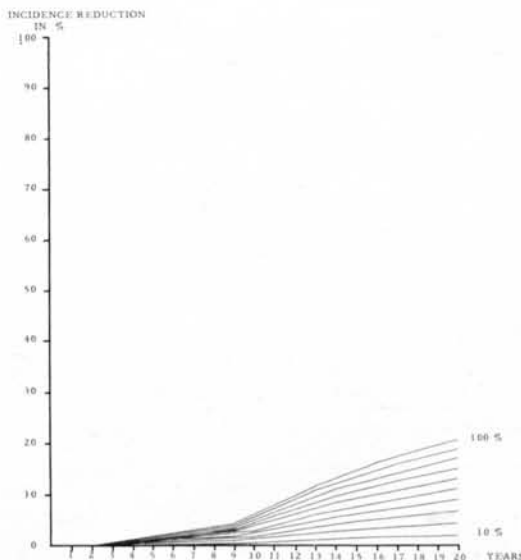

FIG. 7. Vaccination with a BCG-like vaccine, 1-20 years reduction of incidence, in percent, present control methods taken as base lines.
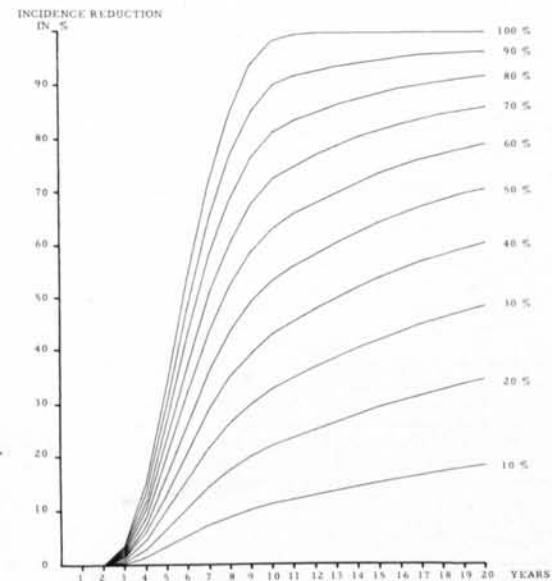

FIG. 8. Vaccination specific for leprosy, 1-20 years reduction of incidence, in percent, present control methods taken as base lines.
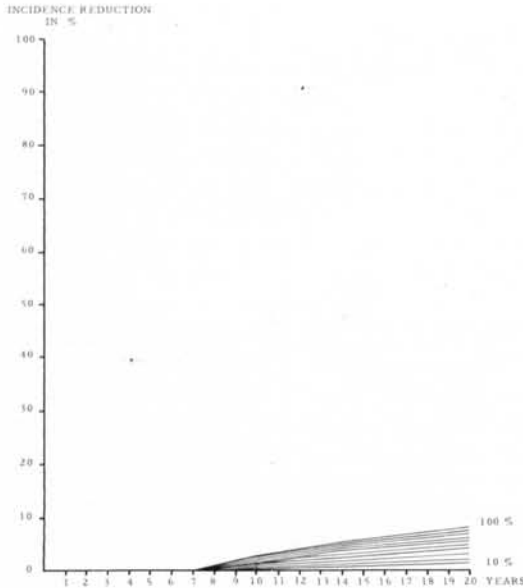
FIG. 9. Improvement in case holding compared to present drop-out rates, 1-20 years reduction of incidence, in percent, present control methods taken as base lines.
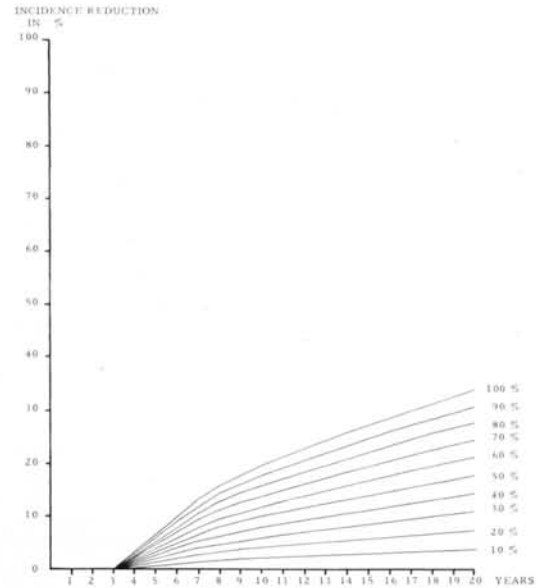

FIG. 10. Segregation of lepromatous patients for one year after detection, 1-20 years reduction of incidence, in percent, present control methods taken as base lines.

CONCLUSIONS

Different control methods for leprosy were computer simulated using a previously described model. Four methods were compared: I) a BCG-like type-specific vaccination which converts potentially lepromatous patients into tuberculoids; II) a specific vaccination for leprosy; III) improvement of case-holding, i.e., reduction in the rate of abandon of treatment; IV) isolation of lepromatous patients for one year after detection. These methods were simulated at different rates of coverages, ranging from 10% to 100%.

Reduction of incidence was taken as the indicator of effectiveness. Incidences were predicted at 5, 10, 15 and 20 year time horizons. Under all circumstances, specific vaccination was the most effective method. Segregation of 100% of the lepromatous patients for one year after detection is similar in effects to vaccination of 20% of the population. Determination of iso-effectiveness according to methods and coverages provides the base lines for cost-effectiveness analysis. In addition to incidence, health managers and funding agencies can be concerned with the num-

TABLE 2. *Case-load (cumulative prevalence) in person-years for 10 and 20 years, vaccination with leprosy specific vaccine at different coverages.*

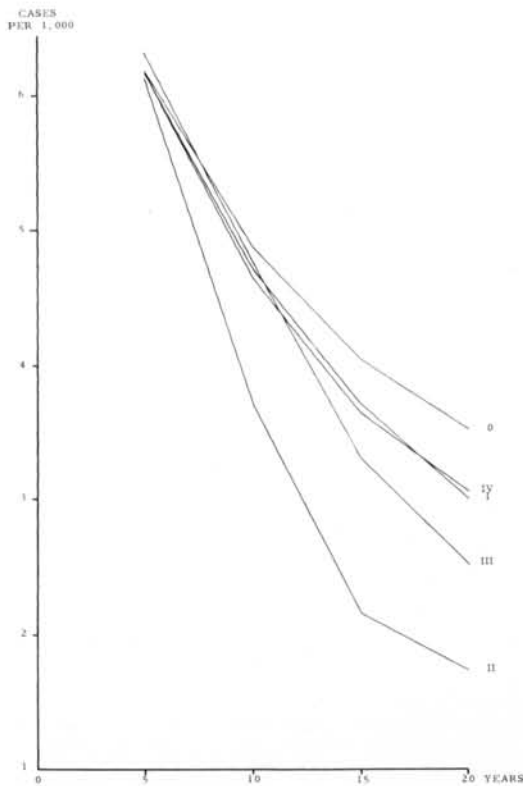| Percent coverage	10 years		20 years	
	cumulative prevalence	% reduction	cumulative prevalence	% reduction
0	59.097	—	104.116	—
10	58.402	1.2	100.678	3.4
20	57.716	2.4	97.200	6.7
30	57.033	3.5	93.907	9.2
40	56.355	4.7	90.800	12.8
50	55.681	5.8	87.866	15.7
60	55.014	7.0	85.105	18.3
70	54.351	8.1	82.501	20.8
80	53.691	9.2	80.050	23.2
90	53.037	10.3	77.746	25.4
100	52.389	11.4	75.586	27.5

FIG. 11. Prediction of prevalence, 5, 10, 15, 20 years with five control methods at 100% coverage: 0. Present leprosy control measures; I. Vaccination with a BCG-like vaccine; II. Vaccination specific for leprosy; III. Improvement in case holding as compared to present drop-out rates; IV. Isolation of lepromatous patients for one year after detection.

ber of patients remaining in treatment in the course of the years, that is annual prevalence, and total case-load, that is cumulative prevalences over time. A computer program has been designed which predicts these two parameters under various assumptions of the model.

SUMMARY

An epidemiometric model of leprosy has been developed to predict and simulate trends of leprosy under various control conditions. This model, whose structure was previously described, is based on data collected in the Polambakkam leprosy control scheme in South India over a 16 year period, from 1954 to 1970. Incidence of leprosy has been computer simulated at 5, 10, 15 and 20 years. The following control measures, some of them still in the developmental stage, were considered: a) unmodified leprosy control as carried out in the study population, based on early detection and regular treatment; b) vaccination with a BCG-like type vaccine effective for preventing development of leprosy as the lepromatous type and converting potentially lepromatous cases into tuberculoid ones; c) vaccination with a disease specific vaccine supposed to be 100% effective in preventing leprosy; d) improvement over present conditions in case-holding; e) isolation of lepromatous patients for one year after detection. The methods tested were simulated at different ranges of coverage, ranging from 10% to 100%, and compared to the results predicted with the present control strategy taken as base lines.

Under all circumstances, specific vaccination was the most effective method. A 100% coverage of the population with an effective vaccine will interrupt transmission after ten years. A 90% incidence reduction is achieved at approximately eight years with 100% coverage, 10.5 years with 90% coverage, and 18 years with 80% coverage. Compared to other methods, specific vaccination with 20% coverage is as effective for controlling the disease as isolation of all the lepromatous patients for one year after detection. This clearly stresses research in the development of a vaccine as the highest priority for leprosy control.

A computer program has also been designed which predicts annual prevalences and cumulative prevalences over time, since these parameters can be of particular interest to governments and funding agencies. These data provide the base lines for cost-effectiveness analysis of leprosy control.

RESUMEN

Se desarrolló un modelo epidemiométrico de la lepra para predecir y simular el curso de la enfermedad bajo diferentes condiciones controladas. Este modelo, cuya estructura se ha descrito previamente, está basado en los datos colectados en el programa de control de Polambakkan, al Sur de la India, durante el período comprendido entre 1954 y 1970. Por computadora se simuló la incidencia de lepra para 5, 10, 15 y 20 años. Se consideraron las siguientes medidas de control, algunas de las cuales aún están en la etapa de desarrollo: a) el control de la lepra como se hace actualmente en el estudio de una población, basado en la detección temprana y en el tratamiento regular de los casos; b) la vacunación con una

vacuna del tipo del BCG, efectiva para prevenir el desarrollo de la lepra en su forma lepromatosa y para convertir los casos potencialmente lepromatosos en tuberculoides; c) la vacunación con una vacuna específica, considerada como 100% efectiva en la prevención de la lepra; d) el mejoramiento de las condiciones actuales en el manejo de los casos, y e) el aislamiento de los pacientes lepromatosos durante un año a partir de su detección. Los métodos analizados se simularon a diferentes grados de cobertura, variando del 10% al 100%, y se compararon con los resultados predecidos por el programa de control actual.

Bajo todas estas circunstancias, el método de vacunación específica resultó el más efectivo. Abarcando al 100% de la población con una vacuna efectiva, la transmisión de la enfermedad se interrumpiría en 10 años. Una reducción del 90% en la incidencia de la enfermedad se lograría en 8 años abarcando al 100% de la población, en 10.5 años abarcando al 90% de la población, y en 18 años abarcando al 80% de la misma. Comparada con los otros métodos, la vacunación específica, abarcando al 20% de la población, resulta tan efectiva como el aislamiento de todos los pacientes durante un año después de su detección. Estos resultados señalan claramente que la investigación tendiente al desarrollo de una vacuna tiene la más alta prioridad para el control de la lepra.

También se ha diseñado un modelo de computación que permite predecir las prevalencias anuales y las prevalencias cumulativas en el tiempo. Estos parámetros pueden ser de un particular interés para los gobiernos y las instituciones o dependencias relacionadas con la Salud Pública.

Estos datos proporcionan la base para el análisis del costo y la efectividad de los programas para el control de la lepra.

RÉSUMÉ

On a mis au point un modèle épidémiométrique de la lèpre qui permet de prédire et de simuler les tendances épidémiologiques de la lèpre dans une série de conditions définies par des méthodes de contrôle différentes. La structure de ce modèle a été décrite précédemment. Le modèle est basé sur des données récoltées dans la zone de Polambakkam, dans le Sud de l'Inde, au cours d'une période de 16 ans, de 1954 à 1970. L'incidence de la lèpre a été simulée sur ordinateur à des délais de 5, 10, 15 et 20 ans. Les méthodes suivantes de contrôle, dont certaines sont encore au stade des recherches, ont été considérées: a) la méthode actuellement utilisée pour le contrôle de la lèpre dans la région, basé sur le dépistage précoce et le traitement régulier; b) la vaccination par un vaccin ayant des effets semblables à ceux parfois attribués au BCG, et se traduisant par le développement d'une lèpre tuberculoïde chez des malades qui autrement auraient évolué vers le type lépromateux; c) la vaccination par un vaccin spécifique contre la lèpre, dont on suppose qu'il est efficace à 100% pour prévenir la maladie; d) l'amélioration des conditions actuelles d'assiduité au traitement; e) l'isolement temporaire des malades lépromateux pendant une année suivant leur dépistage. Les méthodes étudiées ont été simulées à différents taux de couverture, variant de 10 à 100%. Les résultats ont été comparés à ceux auxquels on pourrait s'attendre avec les méthodes actuelles de contrôle, tels qu'ils ont été prédits par le modèle.

Dans tous les cas, la vaccination spécifique s'est révélée la méthode la plus efficace. D'après les données du modèle, une réduction d'incidence de 90% est obtenue après environ 8 ans si 100% de la population est vacciné, après 10,0 années si 90% est vacciné, et après 16 ans pour une couverture de vaccination de 80%. Lorsqu'on compare la vaccination spécifique aux autres méthodes de contrôle de méthode qui ont été étudiées, on constate qu'une vaccination spécifique de 20% de la population seulement est aussi efficace pour contrôler la maladie à long terme que l'isolement temporaire de tous les malades lépromateux pendant une année après leur détection. Ceci montre de manière indubitable que la mise au point d'un vaccin constitue aujourd'hui une très haute priorité de la recherche appliquée dans le domaine du contrôle de la lèpre.

On a également mis au point un programme d'ordinateur qui permet de prédire les prévalences annuelles, ainsi que les prévalences cumulées au cours des années. Ces paramètres peuvent en effet présenter un intérêt particulier pour les gouvernements et les organismes qui financent les campagnes de contrôle contre la lèpre.

Ces données fournissent le point de départ d'une analyse coût-bénéfice des méthodes utilisées pour le contrôle de la lèpre.

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