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Epidemiological Model of Typhoid Fever and its Use in the Planning and Evaluation of Antityphoid Immunization and Sanitation Programmes*

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An epidemiological model has been constructed for typhoid fever in a stable population in order to study the transmission of infection at different levels of endemicity. It involves a number of parameters representing the proportions of epidemiological subgroups in the population—such as the susceptible, the infected, and the immune—and rates of transition between the groups. Numerical values based on available evidence were assigned to the parameters, to provide a realistic simulation of stable endemicity.

Changes were then introduced in the values of some of the parameters in order to study the consequences of mass vaccination and improvements in general health conditions and sanitation, in particular on the incidence of disease.

The model shows that a single mass vaccination reduces the incidence of disease considerably, but the gain is largely lost after a few years. Repeated vaccinations at 5-year intervals will produce further decreases in incidence, though the additional gain becomes smaller at each consecutive vaccination.

The model was also used to estimate the possible effect of improvements in sanitation. The incidence decreases to a new level of stability when the transmission of the infection is reduced because of improved sanitation. The effect of sanitation is long-lasting and in this respect gives better results than vaccination.

The simultaneous application of mass vaccination and sanitation gives a cumulative effect, which in some cases tends to be close to the effect of sanitation alone.

The model was used to forecast the probable effect of preventive measures against typhoid fever, such as mass immunization and sanitation programmes, on a selected population in terms of prevention of disease, as well as in terms of relative costs and benefits. It provides a useful guide for the rational use of funds and the facilities to be set aside for typhoid fever control purposes.

Other possible uses of the model are briefly discussed.

The need to adjust the model in relation to specific conditions in the community is stressed, as is the need to readjust it to take into account changes in the pattern of life and the natural history of typhoid fever.

Typhoid fever is a public health problem primarily in endemic areas; accordingly, we have studied mathematical models for this disease in relation to endemic conditions.

The model has been constructed with a view to its possible use for forecasting trends of the natural course of infection and the effect of preventive measures—vaccination and sanitation—on such trends. For the sake of simplicity, stable endemic situations were taken as a basis for the model.

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The effectiveness of antityphoid vaccines has been evaluated (Cvjetanović & Uemura, 1965) in controlled field trials in endemic areas. The degree of protection conferred by various vaccines, and methods of production and testing, have been established (WHO Expert Committee on Biological Standardization, 1967), as well as immunization schemes and dosages (Yugoslav Typhoid Commission, 1964; Typhoid Panel, United Kingdom Department of Technical Co-operation, 1964; Hejfec et al., 1966; Cvjetanović & Tapa, unpublished data).

The effect of sanitation has been demonstrated (WHO Expert Committee on Enteric Infections, 1964), although the available information does not give a clear idea of the exact quantitative effectiveness of each particular component of environmental sanitation.

We therefore believe that the essential information is available for the construction of the model, in spite of certain inadequacies that make it difficult to determine exactly each specific factor and parameter in the model. For example, the effect of mass immunization cannot be expressed in simple equations that take into account only the protective effect of the vaccine and the numbers of people immunized and not immunized. There are other factors that influence the outcome of vaccination programmes—e.g., the sources of infection and routes of transmission, the size of the challenge dose, and the degree of exposure of the population. Furthermore, transmission from the known sources of infection, sick persons or carriers, to other people depends on various characteristics of the population such as state of immunity, food habits, occupation, customs, and personal hygiene.

Environmental sanitation, like immunization, has a considerable effect on the control of typhoid fever. However, many factors, such as level of education and economic status, play a role, and make the effect of specific sanitation measures much more difficult to determine than that of immunization programmes. All these factors should be taken into consideration in constructing and, in particular, in applying mathematical models to specific population groups.

It is hoped that the mathematical model will be used for determining the probable results and relative benefits and costs of mass immunization and sanitation programmes. An attempt has therefore been made to construct a simple model that will enable health workers to plan and apply an effective typhoid fever control programme within the limits of their financial means and available facilities and resources.

BASIC EPIDEMIOLOGICAL FACTORS

For the construction of any mathematical model, it is necessary to establish some basic epidemiological factors and parameters as a point of departure.

Natural history of typhoid fever

The natural history of typhoid fever is known and will not be described here except in so far as it concerns the construction of the model. Data on the natural history of the disease used in the construction of the model—i.e., incubation period, duration of illness, and relapse, morbidity, fatality, carrier, and other rates—were compiled from numerous studies in different countries. It was realized that the data obtained in one study frequently differ from the results of other studies. This is sometimes the result of differences in methods of investigation, laboratory techniques, and procedures of data collection and analysis, as well as of different environmental and other conditions. For the construction of the model, it was necessary to take some definite parameters as a starting-point.

Some of the prevailing opinions concerning these parameters (American Public Health Association, 1965) were critically appraised. Many of the parameters varied considerably, and it was necessary to come to some arbitrary compromises in order to arrive at definite numerical values to be used for the construction of the model.

Some of the basic values that were used are presented below:

Incubation period: range, 7–21 days; mean, 14 days
Duration of sickness: range, 14–35 days; mean, 28 days
Duration of relapse: range, 7–28 days; mean, 18 days
Frequency of relapses: 5% of cases
Proportion of cases: symptomatic (typical, febrile), 20%; asymptomatic (and mild), 80%
Case fatality rate: 1–10%; average, 3%
Carrier rate: chronic—range, 2–5%; average, 3%: temporary (mean duration, 90 days)—range, 7–20%; average, 10%
Incidence in endemic areas: 10–150 per 10 000 population

Infection was considered in the light of the complex host–parasite–environment relationships, and, as far as possible, from the quantitative point of view.

The host factor—number and immune status—was taken into account in constructing the model as this factor largely determines actual morbidity rates and levels of endemicity.

In some studies, a relationship has been demonstrated between age, sex, and socio-economic status and the typhoid morbidity rate; young age groups, females, and poor people being the most affected, while women, in particular, tended to be carriers for a longer period and were more difficult to cure. These and possibly other factors might be important in specific population groups but we have, for the sake of simplicity, omitted them in the construction of this model.

The parasite factor was also considered from the quantitative point of view and therefore the simple presence or absence of *Salmonella typhi* was not the only criterion for determining the risk of infection. The techniques used in some studies showed that carriers excrete regularly, rather than intermittently, a large and fairly constant number of organisms (Merselis et al., 1964). It seems that persons living under poor hygienic conditions in the vicinity of carriers are at high risk and frequently contract the disease.

Studies carried out on healthy volunteers (Hornick & Woodward, 1967) have shown that the ID_{50} is about 10^6–10^7 organisms, and that the ID_{25} is about 10^4 organisms. However, people in natural conditions are usually infected with a lower dose (Cvjetanović, 1957; Hornick & Woodward, 1967). In most of the communities with endemic typhoid, the microorganisms are spread widely by carriers and by convalescent and sick persons. Accordingly, infection may under favourable conditions be easily transmitted through contaminated food and water or on the hands. Infected persons and carriers are often found accidentally and *Salmonella* may be detected in the blood stream of apparently healthy persons (Watson, 1967). We have therefore considered that the parasite is more widely present than might be assumed from the incidence of clinical illness.

The morbidity rates in communities with different levels of endemicity of typhoid fever were determined from the available national statistical returns, but these data were critically appraised in the light of the many studies that have revealed much more infection than was indicated in health statistics reports.

For example, among 40 students in an army school stricken by a typhoid epidemic, 15 had *Salmonella typhi* in their faeces and/or blood, but only 2 had a febrile illness: 2 more had been subfebrile and in routine clinical and public health practice would never have been diagnosed as typhoid cases (*Vojna Epidemiologija*, 1966). The typical clinical illness, we believe, occurs in only a small proportion (perhaps 20%) of those infected.

While many studies have revealed that the rate of temporary and chronic carriers after an illness varies, it is usually about 10% for the former and about 3% for the latter (Ames & Robbins, 1943; Vogelsang & Bøe, 1948). However, in the older age groups the chronic carrier rate has been as high as 10% (Ames & Robbins, 1943), or even higher among those having typhoid concurrently with other conditions such as schistosomiasis (Saad El-Din Hathout et al., 1966) and cholelithiasis (Tynes & Utz, 1962).

There are other factors that must be taken into account when constructing mathematical models. For instance, superimposed infections may change greatly the susceptibility and resistance of the host, and thus alter the natural history of the disease. Studies in Egypt (Saad El-Din Hathout et al., 1966) have shown that the carrier rate or the rate of urinary excretors of *S. typhi* among people infected with schistosomiasis is much higher, and the carrier state lasts longer, than among otherwise healthy people. Moreover, the presence of urinary carriers in rural areas with much stagnant water and poor sanitation leads to extensive environmental contamination and to a high risk of infection. This fact has to be taken into account when our model is adapted for use in areas where schistosomiasis is a common disease.

The environment undoubtedly plays a role in the natural history of typhoid fever and it should not be neglected, since the risk of transmission of infection depends greatly on environmental conditions.

There may be a greater risk of infection in certain specific population groups—e.g., nurses and schoolchildren—owing to the environmental conditions to which they are exposed.

The transmission of typhoid fever varies under different climatic, socio-economic, and cultural conditions and determines, to a great extent, the level of endemicity and morbidity rates. The rapid decline of typhoid fever in the USA during the last few decades is primarily the result of rapid changes in environmental conditions and standards of personal hygiene (National Communicable Disease Center, 1967). We have taken these environmental factors into account in the construction of our model, and have considered them to be the most important and decisive factors determining the actual level of endemicity in a community.

Effectiveness of vaccines and mass immunization

The effectiveness of vaccines was calculated from the data obtained in various controlled field trials (Cvjetanović & Uemura, 1965). The degree of effective protection conferred by the vaccine was taken as being equal to that conferred by the most effective vaccines in the controlled trials. These were the acetone-dried and heat–phenol vaccines given in two doses; however, in endemic areas, similar results could be expected with only one dose (Typhoid Panel, United Kingdom Department of Technical Co-operation, 1964; Cvjetanović & Tapa, unpublished data).

In view of the field experience, it was considered that booster doses of an effective vaccine should be given about every 5 years, and this was applied in the model. For reasons of simplicity, these factors were applied to a homogeneous population.

In constructing the model, we did not make adjustments for differences in the risk of infection and consequently in the expected morbidity rates between various population groups, including differences between those who did and those who did not volunteer to be immunized. It has been observed that, for various reasons, volunteers contract disease less readily and less often than those who do not volunteer for vaccination. In one controlled field trial, the typhoid morbidity rate among volunteers belonging to the control group and receiving placebo was 13 per 1 000, while in non-volunteers in the same community it was 26 per 1 000 (Yugoslav Typhoid Commission, 1964). The ratio was thus 1: 2. In the same study, the difference in morbidity rates between volunteers and non-volunteers was especially great among populations exposed to a heavy challenge dose in a water-borne outbreak, the morbidity rates being in the ratio of 1: 11. This important fact should not be neglected as the immunization of a volunteering population tends to give results far below those that would be expected from the application of simple arithmetic.

For the above reasons, the " theoretical " effectiveness of typhoid vaccine, as determined in controlled field trials, differs from the " use " effectiveness in mass immunization campaigns. We have taken this into account and have made adjustments on the grounds of field experience (Yugoslav Typhoid Commission, 1964; Cvjetanović, 1957) to compensate for the differences in vaccine effectiveness in the volunteers and the non-volunteers.

There are other possible reasons why the impact of immunization on the natural course of infection in the community may not in fact follow the straightforward calculations based on effectiveness determined in controlled field trials and expressed as a percentage reduction of the incidence rates. The possibility that vaccine is less effective for the prevention of inapparent infection and its spread than for the prevention of clinical illness has not been fully evaluated in any field trial and we still lack reliable information. We did not try to speculate or to make adjustments in our model to take this into account but this may become necessary if further research brings forth more clear-cut information.

Effectiveness of sanitation

Environmental sanitation—primarily the disposal of excreta, but also water chlorination, food control, etc.—when introduced and practised regularly considerably lowers the level of transmission of infection. The transmission rate or force of infection could easily be reduced to half its former level by the construction of privies and the provision of sufficient safe water (Schliessman et al., 1958; Wolff & van Zijl, 1969). Environmental sanitation appears to be the determining factor in the transmission of infection.

For the purpose of the model, the introduction of a specific sanitation programme could be considered simply as changing the force of infection. The construction of latrines would result in a diminished rate of transmission of infection from carriers—e.g., to 50% of its original value—which is supported by field observations.

Sanitation campaigns that are not followed by sustained efforts to maintain adequate sanitary practices may produce only temporary results. However, when sanitation is introduced together with health education and improvement of living standards, the effects tend to be cumulative, resulting in a steady reduction of typhoid morbidity rates owing to the decline in the force of transmission of infection.

CONSTRUCTION OF THE MODEL FOR TYPHOID FEVER ENDEMICITY

Structure of the model

The general population was divided into subgroups identifiable in the natural course of typhoid fever. The natural history and epidemiological evolution of the infection in the population depends essentially

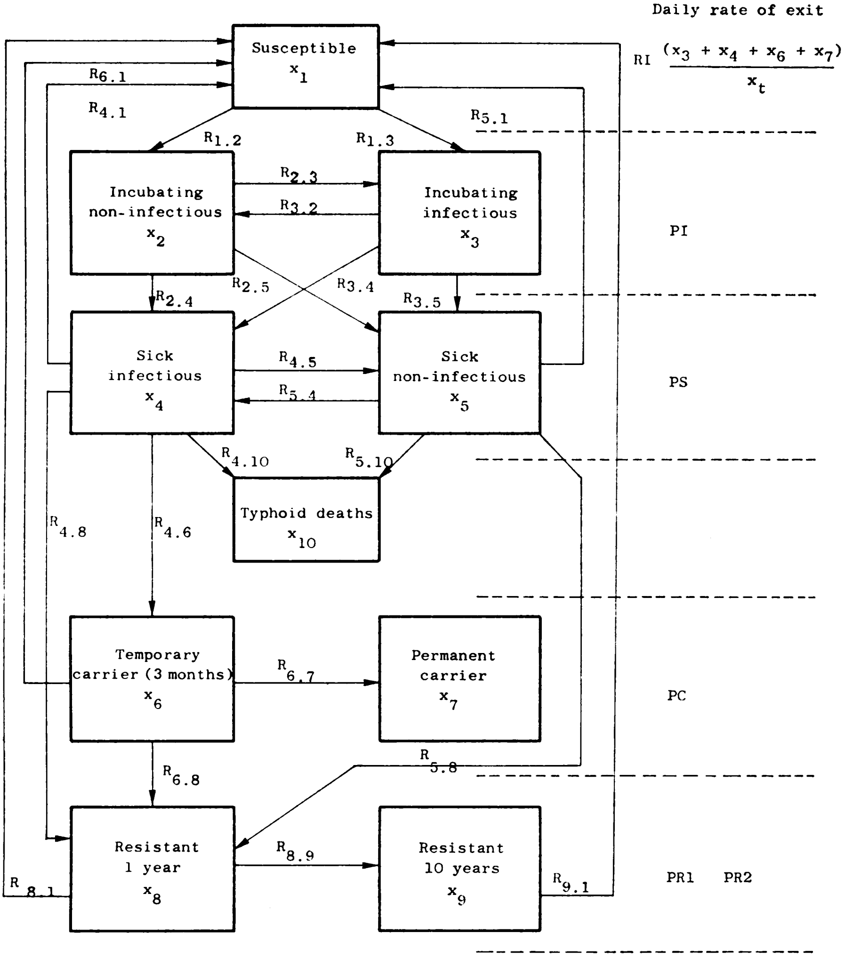

Fig. 1. Flow chart for epidemiological model of the natural course of typhoid fever.

on changes in the various classes of individuals over a period of time. The structure and the class symbols adopted to simulate the dynamics of typhoid fever in the population[1] are illustrated in the flow chart (Fig. 1).

It is not easy to estimate the numerous rates of transition directly from available quantitative evidence. It was found more convenient to consider the rate of transition as the product of the rate of change from one stage of the disease to the other stages (or rate of exit) by a coefficient of transfer, which would represent the relative size of the class moving to any other subgroup.

Epidemiological parameters and daily rates of change

The epidemiological parameters involved in the present model are specified below. The numerical values of the corresponding daily rates of change are also indicated. They should, however, be considered as possible values only. Other simulations of typhoid fever dynamics could easily be worked out with different levels for these quantities.

An infected person may or may not become sick. In the present model it was assumed that the same

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[1] The movement of births and deaths due to causes other than typhoid fever is not shown in the flow chart but was taken into consideration in the mathematical expression of the model.

Table 1. Matrix of coefficients of transfer $R_{i.j}$

Class of origin i	Class of destination j										Total
	1	2	3	4	5	6	7	8	9	10	
1	—	0.990	0.010	—	—	—	—	—	—	—	1.000
2	—	—	0.040	0.950	0.010	—	—	—	—	—	1.000
3	—	0.010	—	0.900	0.090	—	—	—	—	—	1.000
4	0.100	—	—	—	0.100	0.100	—	0.694	—	0.006 [a]	1.000
5	0.100	—	—	0.200	—	—	—	0.694	—	0.006 [a]	1.000
6	0.100	—	—	—	—	—	0.300	0.600	—	—	1.000
7	—	—	—	—	—	—	—	—	—	—	0.000
8	0.100	—	—	—	—	—	—	—	0.900	—	1.000
9	1.000	—	—	—	—	—	—	—	—	—	1.000
10	—	—	—	—	—	—	—	—	—	—	0.000

[a] Fatality rate is 0.03 of clinical cases. Assuming that 0.20 of classes x_4 and x_5 develop clinical symptoms, 0.006 of these classes are transferred to class x_{10}.

dynamics of disease apply equally well to both types of infection with respect to the ability to transmit the infection to other persons and to maintain or lose resistance status. In the mathematical development, therefore, these two types of infection were treated, as far as possible, as one group, and for convenience the term " sickness " is used below also for asymptomatic infections.

Period of incubation. The mean duration was fixed at 14 days. The daily rate of exit is therefore $PI = 0.07143$ per person under incubation.

Period of sickness. The mean duration was fixed at 28 days for both symptomatic and asymptomatic cases. In addition, it was assumed that 5% of affected persons would relapse for a mean period of 18 days. Hence the mean duration of the sickness period is $0.95 \times 28 + 0.05\ (28 + 18) = 28.9$ days per case. The daily rate of exit is therefore $PS = 0.03460$ per case.

Temporary carriers. The mean duration was fixed at 90 days. The daily rate of exit is therefore $PC = 0.01111$ per temporary carrier. The permanent carrier can exit only by death.

Resistants. The mean duration of short resistance was fixed at one year (365 days). The daily rate of exit is therefore $PR_1 = 0.002740$ per short resistant. The mean duration of long resistance was fixed at 10 years. The daily rate of exit is therefore $PR_2 = 0.0002740$ per long resistant.

Clinical or symptomatic cases. It was assumed that 20% of the persons passing through the sickness period are detected as typical acute clinical cases (symptomatic) (*Vojna Epidemiologija*, 1966). In this study, incidence rate refers to clinical cases only.

Mortality from typhoid. It was assumed that 3% of the clinical cases would die from typhoid fever. Therefore 0.6% of the daily exit of persons in the sickness period was allocated to typhoid deaths.

Natality and general mortality. For simplicity, a stable population was used in the model.[1] The annual birth rate and crude death rate (all causes) were both fixed at the same level of 20 per thousand. The daily rates are therefore $PB = PD = 0.0000548$ per person in the community.

Force of infection. The risk of transfer of infection to a susceptible individual is proportional to the proportion of infectious persons in the population and to a factor (RI) that is an expression of the force of infection. This factor is the resultant of the mean values of several parameters: frequency of contact,

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[1] An actual example of a growing population is treated in the section entitled " Use of the model for the planning of preventive measures ".

effective challenge dose, degree of susceptibility, etc.

In the present study, the factor *RI* will be considered as the main variable determining the pattern of the epidemiological characteristics of the population. Four different values of *RI* were successively entered in the model: 0.0018, 0.0020, 0.0025, and 0.0040 per susceptible and per infectious person per day.

Infectiousness. The infectious persons are: a small fraction of the persons incubating the disease, the majority of the sick, and all the carriers. The relative importance of each class was fixed as indicated in the matrix of coefficients of transfer (Table 1). The intensity of infectiousness was supposed to be constant for all persons in these classes.

Coefficients of transfer

All transfers from one epidemiological subgroup to another are represented in the flow chart (Fig. 1) by a set of coefficients $R_{i.j}$, which express at each stage of the disease the fraction of individuals transferred from class *i* to class *j*, out of all the individuals leaving class *i*.

The numerical values of the coefficients of transfer $R_{i.j}$ were derived from available epidemiological evidence (see Table 1).

It is recognized that many of these coefficients can vary over a wide range and that for some of them the range of variation is not even known. It would not, however, be difficult to simulate typhoid fever dynamics with other values for the coefficients of transfer.

Mathematical model

The mathematical relationship between the 10 classes of individuals defined in Fig. 1 is expressed in the following system of 10 equations, where the differentials dx_i are in fact finite daily increments, as all the rates were calculated on a daily basis:

$$
\begin{aligned}
dx_1 &= -(x_3 + x_4 + x_6 + x_7)(x_1/x_t)RI + (x_4R_{4.1} + x_5R_{5.1})PS + x_6R_{6.1}PC + x_8R_{8.1}PR_1 + x_9R_{9.1}PR_2 + \\
&\quad x_tPB - x_1(PD - dx_{10}/x_t) \\
dx_2 &= R_{1.2}(x_3 + x_4 + x_6 + x_7)(x_1/x_t)RI + x_3R_{3.2}PI - x_2(PI + PD - dx_{10}/x_t) \\
dx_3 &= R_{1.3}(x_3 + x_4 + x_6 + x_7)(x_1/x_t)RI + x_2R_{2.3}PI - x_3(PI + PD - dx_{10}/x_t) \\
dx_4 &= (x_2R_{2.4} + x_3R_{3.4})PI + x_5R_{5.4}PS - x_4(PS + PD - dx_{10}/x_t) \\
dx_5 &= (x_2R_{2.5} + x_3R_{3.5})PI + x_4R_{4.5}PS - x_5(PS + PD - dx_{10}/x_t) \\
dx_6 &= x_4R_{4.6}PS - x_6(PC + PD - dx_{10}/x_t) \\
dx_7 &= x_6R_{6.7}PC - x_7(PD - dx_{10}/x_t) \\
dx_8 &= (x_4R_{4.8} + x_5R_{5.8})\,PS + x_6R_{6.8}PC - x_8(PR_1 + PD - dx_{10}/x_t) \\
dx_9 &= x_8R_{8.9}PR_1 - x_9(PR_2 + PD - dx_{10}/x_t) \\
dx_{10} &= (x_4R_{4.10} + x_5R_{5.10})PS
\end{aligned}
$$

where $x_t = \sum_{1}^{9} x_i$

The annual number of cases is given by the formula:

$$\Sigma(x_2(R_{2.4} + R_{2.5}) + x_3(R_{3.4} + R_{3.5}))0.2\ PI$$

where the summation Σ is done over 365 days.

The annual number of typhoid fever deaths is simply given by the sum of dx_{10} over 365 days.

The above set of equations would constitute a system of differential equations if the daily rates were replaced by instantaneous rates of change. However, it was suspected that such a system could not be solved analytically with all mathematical rigour. On the other hand, the daily changes of the classes x_i are extremely small and can be calculated at high speed on the electronic computer. It was therefore decided to apply this technique in the simulation of typhoid fever dynamics.

In order to facilitate their interpretation, the numerical results of computer simulations actually produced will be presented here mainly in graphical form.

Table 2. Stable percentage distribution in population classes for different levels of force of infection (*RI*). Birth rate and crude death rate are both equal to 20 per thousand population

Population class	Daily force of infection (*RI*)			
	0.0018	0.0020	0.0025	0.0040
susceptible	94.5	84.9	67.3	41.7
incubating non-infectious	0.0244	0.0661	0.143	0.254
incubating infectious	0.00122	0.00331	0.00716	0.0127
sick infectious	0.0511	0.139	0.300	0.534
sick non-infectious	0.00583	0.0158	0.0342	0.0609
temporary carriers	0.0158	0.0430	0.0930	0.166
permanent carriers	0.966	2.62	5.73	10.3
short resistant	0.527	1.43	3.09	5.51
long resistant	3.96	10.7	23.3	41.5
total	100	100	100	100
annual typhoid incidence rate [a]	12.8	34.8	75.2	133.9
annual typhoid death rate [b]	4.3	11.7	25.3	45.1

[a] Per 10 000 population.
[b] Per 100 000 population.

APPLICATION OF THE MODEL TO EVALUATION OF THE EFFECT OF PREVENTIVE MEASURES

Stable endemicity

The first objective was to find the set of x_i values that would correspond to a stable endemic situation for a given value of the force of infection *RI*; it was then possible to study clearly the effect of specific preventive measures imposed upon the stable endemicity.

Several preliminary trials showed that situations corresponding to existing levels of endemicity were obtained with the following four values of the parameter *RI*: 0.0018, 0.0020, 0.0025, and 0.0040. The percentage distribution of the population in the various epidemiological classes, when the stable situation is reached,[1] are shown in Table 2 for the selected values of the force of infection.

It was found that the size of the epidemiological classes was almost linearly related to the reciprocal of the force of infection *RI*. This fact facilitated the derivation of a stable situation from another already known stable situation. It is thought that a stable level of endemicity can establish itself only if the rate *RI* remains above a certain critical value and that this value is a function of the birth and death rates. Further study in this direction might be fruitful.

Immunization

The mathematical model was then used to simulate the dynamic changes that would occur in the various epidemiological categories of the population under conditions of stable endemicity if mass immunization were carried out.

It was assumed that, by vaccination, a certain proportion of the susceptible persons was directly transferred to the short-resistant class. This proportion is measured by the efficacy of the immunization, which is itself the product of the immunization coverage and the effectiveness of the vaccine used. Ranges covering the more common values for these factors, as used for the computation of the resulting efficacy of the mass vaccination, are shown in Table 3.

The effects of different typical levels of efficacy of mass vaccination are analysed in the present study.

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[1] The mathematical problem consists of finding the set of values of x_i that simultaneously render null all the dx_i. Asymptotic solutions were obtained with the computer by successive trials covering long periods.

Table 3. Efficacy of vaccination against typhoid fever for various combinations of population coverage vaccine effectiveness

Population coverage	Effectiveness of vaccine		
	0.60	0.75	0.90
0.60	0.36	0.45	0.54
0.80	0.48	0.60	0.72
1.00	0.60	0.75	0.90

Single mass immunization. The effects of a single mass immunization on the annual incidence rate of typhoid fever as well as on the various epidemiological categories are shown in Fig. 2 for the two extreme levels of vaccination efficacy (36% and 90%). Separate graphs were drawn for each of the four levels of endemicity stability (see Table 2).

It is clearly seen that the sudden transfer of a certain proportion of susceptible persons to the resistant class has an immediate effect on the incidence rate (per 10 000 population), the importance of the decrease being, of course, directly related to the efficacy of the mass immunization. It is, however, observed that after this spectacular drop the incidence rapidly rises and that, depending on the initial level of endemicity, between 50% and 90% of the gain is lost 10 years later. The speed of the loss is then considerably reduced and the curve tends slowly to the initial stability level. This fact is believed to be a consequence of the delayed repercussion of the mass vaccination on the carriers (see Fig. 2).

Periodic mass immunization. The results of seven successive mass immunizations carried out at intervals of 5 years are illustrated in Fig. 3 for the situation characterized by a low endemicity level ($RI = 0.0018$) and a medium level of vaccination efficacy (60%).[1]

Repeated vaccinations largely compensate for the rapid loss in the benefit observed on the incidence curve after each immunization, but it is noted that the additional gain decreases at each subsequent inoculation. Nevertheless, the long-term level, which is established when the vaccination programme is interrupted, is considerably affected by the number of successive vaccinations carried out. In the example illustrated in Fig. 3, the long-term gain on the incidence curve is, after seven inoculations, at least four times as large as after only one immunization.

It is also interesting to observe the effect of periodic vaccinations on the carriers. Slight decreases occur after successive vaccinations, but the movement is less and less accentuated, and after the last immunization the curve sometimes shows a definite tendency to the re-establishment of the original level.

Improvements in sanitation

Any improvement in sanitation—mainly the disposal of excreta, but possibly also the provision of safe water, the adoption of hygienic habits, etc.—would result in a decrease in the risk of infection, as measured in this model by the force of infection RI (Fig. 4).

The shift in time of the size of each epidemiological subgroup x_i from one stability level to another was simulated with the model.

The thick lines of Fig. 4 show the pattern of change of the annual incidence rate (per 10 000 population), and of the percentages of carriers and of susceptible and resistant persons, on the assumption that a high force of infection ($RI = 0.0040$) is suddenly reduced, at the fifth year, to a lower level ($RI = 0.0020$) as a consequence of the reduction in the risk of transmission.

As seen in Fig. 4, the size of the various epidemiological classes will ultimately pass from the initial stability level to the new, more favourable, level of endemicity.

The 50% reduction in the force of infection causes an immediate decrease in the annual incidence rate to about 50% of its original level, followed by a temporary increase, most probably as a result of the slower decrease in the reservoir of infection (see the trend of the percentage of carriers in Fig. 4). A long-term decrease is then observed, bringing the incidence rate asymptotically to its new stability level.

Combined effect of immunization and sanitation

Fig. 4 also shows the additional gain on the incidence of the disease that can be expected from combined mass immunization and sanitation programmes with either single immunization or periodic vaccinations at 5-year intervals. For the present illustration, the degree of immunization efficacy was fixed at the medium value of 60% and the degree of efficacy of sanitation at a value of force of infection

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[1] Computer runs were also produced for other levels of these parameters but are not reported here.

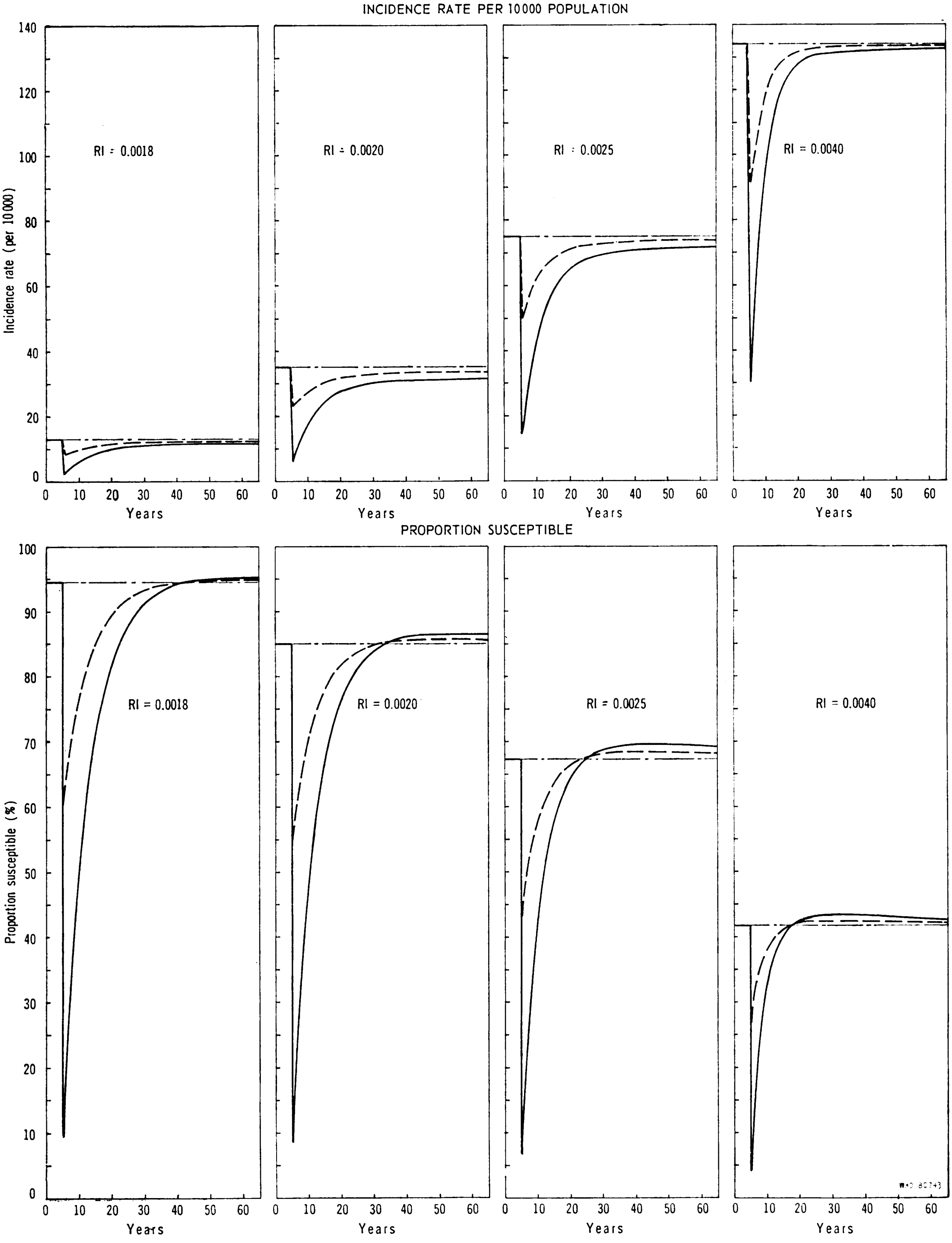

Fig. 2. Effect of a single mass vaccination on the dynamics of typhoid fever at different levels of endemicity and efficacy of vaccination: horizontal broken line—stability level; solid curve—efficacy of vaccination 36%; dashed curve—efficacy of vaccination 90%.

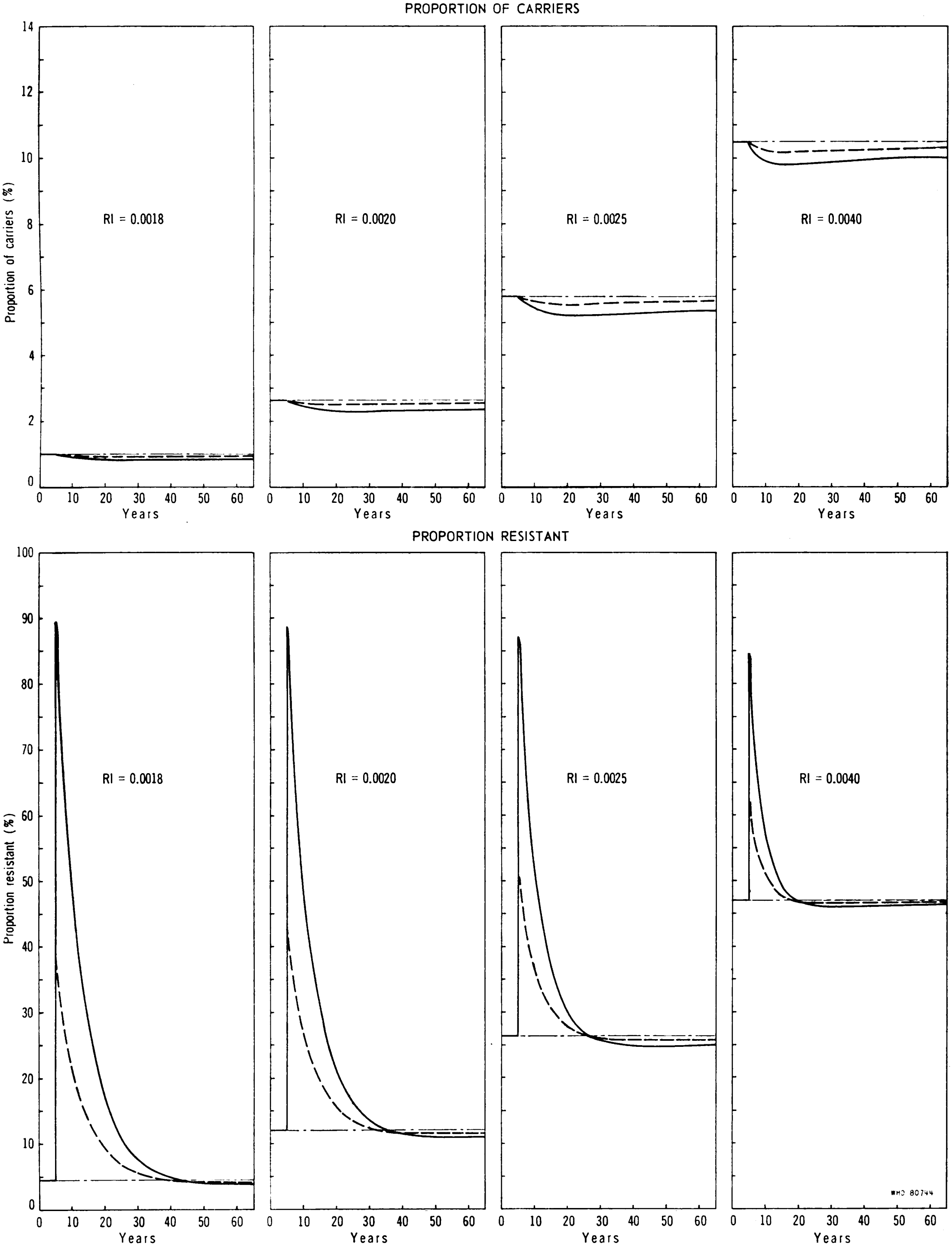

Fig. 2 (*concluded*)

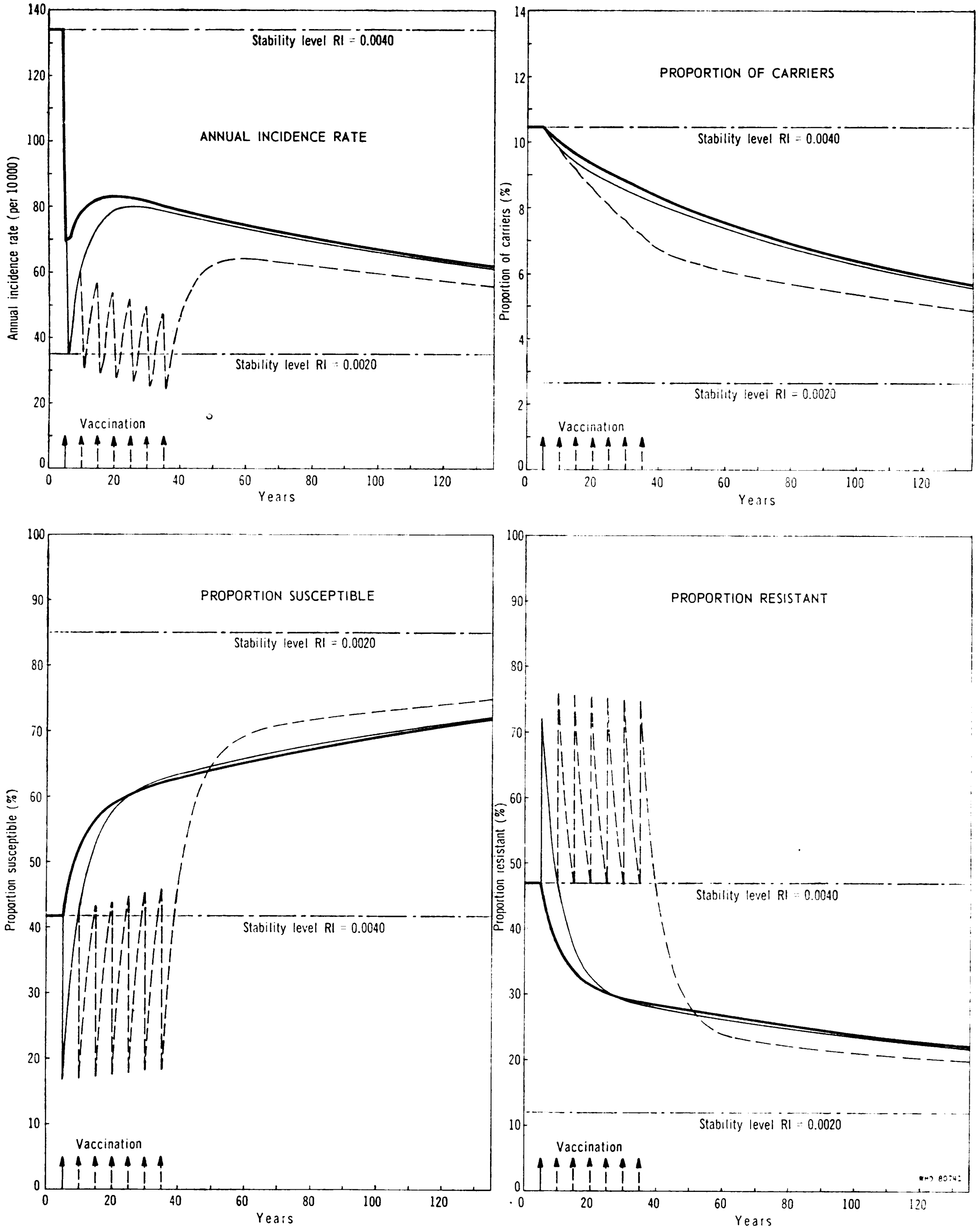

Fig. 3. Comparison of the effects of single and periodical mass vaccination on the dynamics of typhoid fever; efficacy of vaccination, 60 %: thick solid line—stability level for RI = 0.0018; thin solid line—1 vaccination; broken line—7 periodical vaccinations.

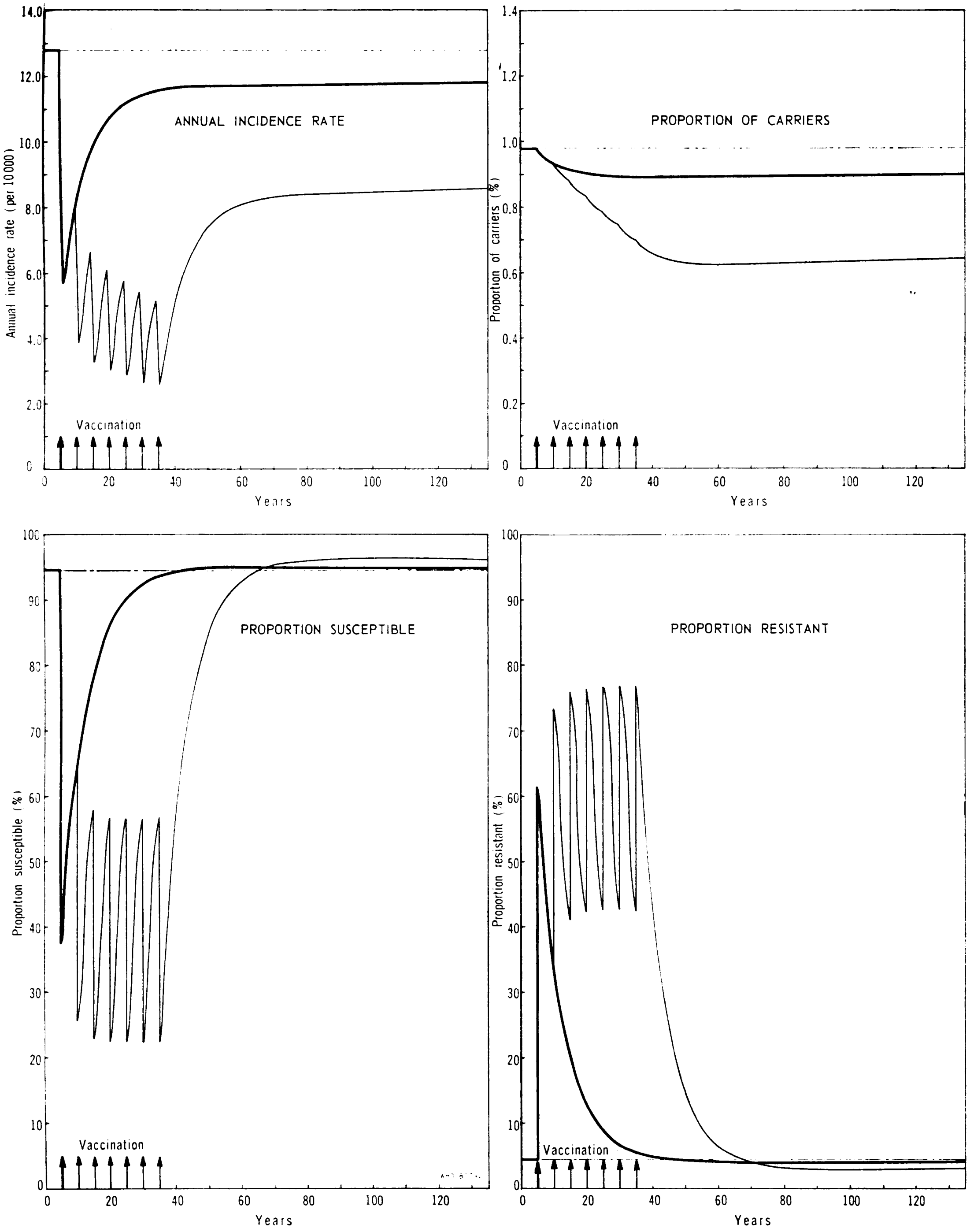

Fig. 4. Effect of a change in the force of infection on the dynamics of typhoid fever with or without mass vaccination: horizontal broken line—no vaccination; thick solid line—1 vaccination; thin solid line—7 periodical vaccinations.

50% lower than before the application of sanitary measures. Broadly speaking, the results of combined measures are quite comparable in the long run with those of improvements in sanitation alone. The main feature of interest is perhaps that the long-term benefit of immunization is largely governed by the permanent gain resulting from the favourable change in the force of infection resulting from the improvement of sanitation. This finding is of great importance for the long-term planning of control and, possibly, eradication of typhoid fever.

APPLICATION OF THE MODEL IN COST–BENEFIT EVALUATION

While the relative effectiveness of various preventive measures is of great practical interest to public health workers for both the planning and application of such measures, the costs and benefits must be taken into consideration in order to make the best use of available resources. We have therefore tried to apply our model to the evaluation of the relative merits of immunization and sanitation in the control of typhoid fever from the point of view of costs and benefits.

Determination of costs and benefits

Determination of the costs of vaccination and sanitation is not difficult. To the cost of the materials (vaccines, syringes, and needles; or latrines, water mains, etc.) was added the cost of transportation and manpower (professional and auxiliary). The benefits were calculated as the funds that would otherwise be spent on the treatment of typhoid cases, hospital and other expenses, as well as lost wages. We did not attempt to cost human lives in terms of money as some authors have done (Rice & Cooper, 1967). In view of this the actual benefits are always higher than can be presented by simple financial gains.

There were two main difficulties in the evaluation of costs and benefits, namely:

(1) The costs of immunization and treatment of cases, like other costs, differed greatly from country to country in view of the different stages of development of the medical services and the economy and the different socio-economic systems. In some countries, most of the cost of treatment was borne by individuals; in others, it was borne largely by the state (social or health insurance, for example). As the costs and benefits were differently distributed between individuals and state services, it was impossible to find a common international denominator and to express, in terms of one currency (e.g., US dollars) the costs and benefits that would be applicable generally.

(2) So far as sanitation is concerned, the benefits cannot be limited to its effect on typhoid alone. Sanitation affects other illnesses—enteric, parasitic, or skin infections—and leads to a rise in the standards of hygiene in general, and also brings (as in the case of water supplies) economic benefits.

We were therefore obliged to study each country or area separately, applying the same principles but taking into account specific conditions. The differences between the countries were so great that generalization was impossible.

We collected data on costs from several countries at various levels of development and with various socio-economic systems, and found that they can be roughly divided into several categories; for example:

(*a*) countries with a subsistence economy, the state being responsible for the provision of modest health services;

(*b*) countries with intermediate economic development, where the state has a limited financial responsibility for health matters and services;

(*c*) countries such as (*b*) in which the state has a greater financial responsibility for social and health matters and services;

(*d*) countries with a high degree of economic development, where the state has a limited responsibility for financing immunization and treatment of typhoid; and finally

(*e*) countries with a high degree of economic development where the state is largely (if not totally) responsible for providing free immunization, treatment, and wage compensation in case of illness.

Since typhoid fever is endemic and represents a problem in those countries with a lower level of development (*a*, *b*, *c*), we have limited our study to those categories.

Use of the model for long-term cost–benefit evaluation

Immunization and sanitation, even if envisaged as short-term programmes, have a long-lasting effect. The costs of initial investment are compensated over a long period of time. For practical reasons, a cost–benefit analysis should be considered on a long-term basis if one wishes to obtain meaningful information.

In view of the fact that conditions change with time, the cost–benefit analysis must be re-examined

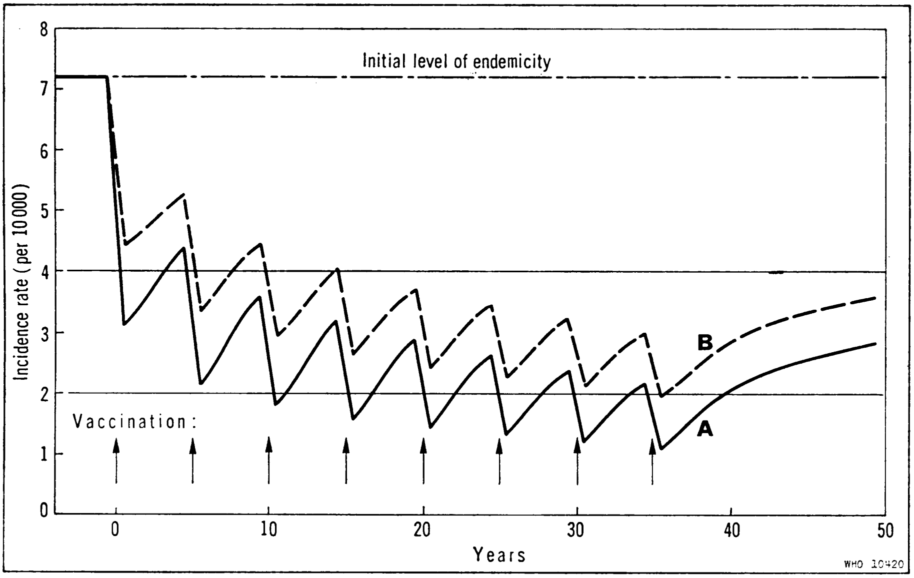

Fig. 5. Effect of eight successive mass vaccinations at five-year intervals on the annual incidence of typhoid fever. (A) = vaccination coverage, 75 %; vaccine effectiveness, 80 %; (B) = vaccination coverage, 50 %; vaccine effectiveness, 80 %.

from time to time in the light of these changes and should become a continuous process in the planning and evaluation of public health programmes.

Use of the model for the planning of preventive measures

The model can be used for the planning of preventive measures in various countries and areas only if the necessary parameters, as described above, are known and if the relevant information is collected. Some of the parameters and information may be available from existing statistical returns and others may have to be collected in special surveys or studies designed for this purpose.

Once the data are available, they can be fed into the model and into the computer to predict the trend of typhoid for years to come, assuming that no special preventive measures are taken in the meantime. The model can also be used to simulate the possible effect of the application of various immunization and/or sanitation programmes. On the grounds of costs and benefits, the merits of relevant preventive measures can be compared and those most suited to the goals envisaged and the resources available can be selected.

In order to illustrate these uses of the model with an example, we shall take actual data on the epidemiological situation in a small, typical Pacific island with an initial population of about 150 000. The annual birth rate was taken as 35 per 1 000 inhabitants, and the annual death rate as 8 per 1 000 population. The annual natural incidence of typhoid fever cases was taken at the level of 7.2 per 10 000 inhabitants. These data correspond closely to the actual situation in Western Samoa and resemble that in some other islands.

The effect of one type of vaccine in two different immunization campaigns with vaccination repeated at 5-year intervals (A = 75% coverage, B = 50% coverage) on the population of this island is presented in Fig. 5. This shows how the incidence of typhoid would decline after immunization and indicates that higher coverage of the population with the same type of vaccine would give better results. The data thus obtained could be used for cost-benefit analysis. The cost of immunization could be compared with the benefit derived from savings in the cost of treating the typhoid cases that would be prevented by immunization.

The effect of constructing privies is anticipated to produce a 50% drop in transmission owing to prevention of the spread of disease. Even if the effect of privy construction were smaller (e.g., 30%) it would still be considerable, as shown in Fig. 6, which

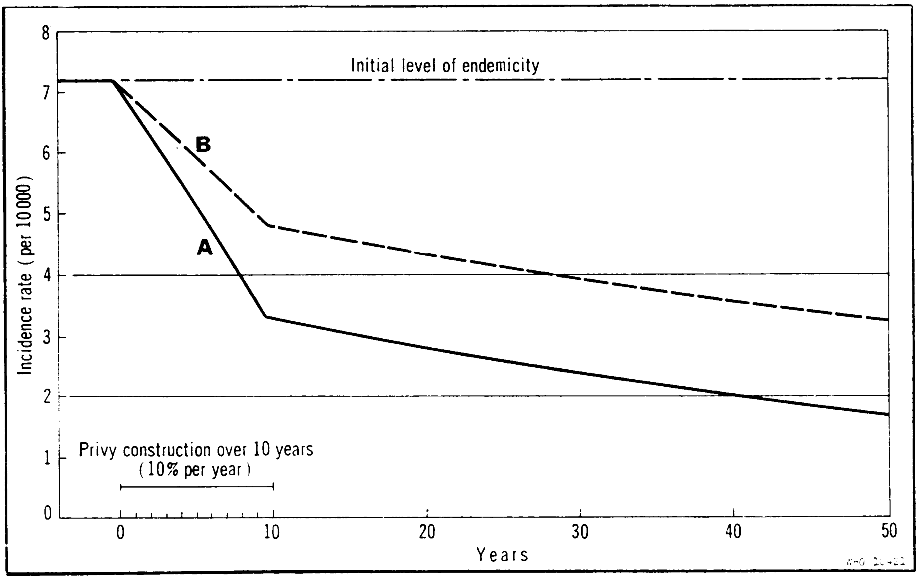

Fig. 6. Effect of privy construction on the annual incidence of typhoid fever. Effectiveness of privy construction: (A) = 50 % on transmission by carriers; (B) = 30 % on transmission by carriers.

presents the effect of a sanitation programme comprising construction of privies for the whole population over a 10-year period. The effect is long-lasting and produces a continuous decline in the incidence of typhoid owing to the gradual elimination of carrier-transmitted infection.

Fig. 7 shows the effect of sanitation—namely, privy construction—on the incidence of typhoid when construction is accomplished over a period of 5 years and covers the whole population (case A). This is compared with privy construction over a 10-year period (case B). It is obvious that only a small additional long-term gain is achieved by early construction of all privies. This simulation (Fig. 7) shows, as does Fig. 6, that the endemicity level of typhoid in this community would, as a result of sanitation, begin to decline steadily and continuously. The same data can also be used for cost–benefit analysis.

Fig. 8 compares the effect of privy construction alone with the cumulative effect of vaccination and privy construction combined, taking into account possible different levels of effectiveness of vaccination and sanitation. The effect of sanitation and vaccination is obviously greater, but a tendency to return to an earlier level of endemicity is obvious after immunization, whereas sanitation produces a definite and continuous downward trend in the endemicity level. It is therefore clear that sanitation would give a more permanent effect than immunization, although vaccination alone, or combined with sanitation, might, in the short run, be more effective for the control of typhoid fever.

In the present study, the numerical application of the cost–benefit calculation will be limited to three examples of single or combined activities drawn from the situations described above.

The cost factors have been determined from actual records available for the community and fixed as follows:

The estimated average cost of immunizing one person was taken as US$ 0.20, while the treatment of a typhoid fever case, including the cost of medical and paramedical personnel (but not lost wages), was estimated at US$ 100.00.

The average cost to the government of constructing a new, satisfactory privy or making sanitary an existing privy serving an average of six persons was estimated to be US$ 3.15. This represents the cost of the services of skilled manpower to aid and supervise construction or reconstruction of the privy. Other expenses of construction (unskilled labour and material) are readily borne by the population. The total cost of construction of a new, sanitary privy

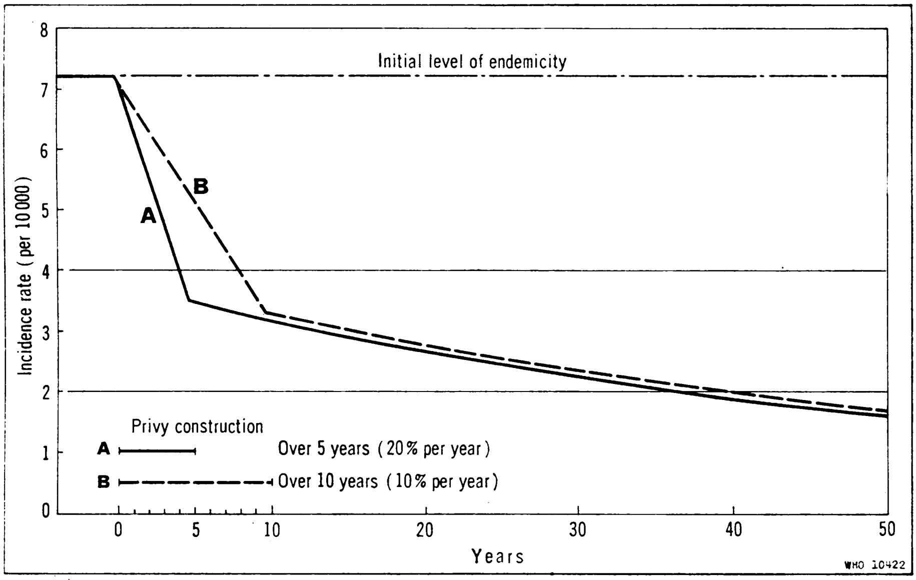

Fig. 7. Effect of rate of privy construction on the annual incidence of typhoid fever. Effectiveness of privy construction: 50 % on transmission by carriers.

excluding unskilled manpower and superstructure was estimated to be US$ 5.00. Thus the government's contribution represents over one half of the total cost of a new privy. The *per caput* cost of privy construction for the government is about $0.50 as compared with $0.20 for a single vaccination.

The costs and benefits are presented from the government's point of view, the government being fully responsible for the cost of immunization and treatment of cases, while contributing only partly to the cost of privies; the population would provide, free of charge, the necessary material and manpower for construction of the privies.

The actual computer runs are presented graphically (Fig. 9), and only final values for a 30-year period are given in Table 4.

Example of costs and benefits of vaccination campaigns. In the first graph of Fig. 9 (left), the cost of vaccination and the saving on case treatment are cumulated over time for an immunization programme corresponding to the situation illustrated in Fig. 5 (line A).[1] The cost of the first mass immunizations of 75% of the population would already be offset by savings on treatment in a 5-year period. After the third vaccination, owing to the decrease in case incidence, the difference between the cost of vaccination and the benefit on treatment is definitely positive and the balance is progressively augmented by the subsequent mass immunizations. One should not forget, however, that the incidence will slowly return to its initial level if vaccination activities are stopped.

Example of costs and benefits of privy construction. This example shows the cost of a programme for sanitation through the construction or improvement of privies. The parametric values and epidemiological effects of this programme were taken as described in Fig. 6 (line A). Furthermore, it was assumed that there was a necessity to rebuild or to make sanitary all the privies required by the population, the cost of material and manpower being borne by the population and the services of a sanitary inspector being provided by the government. The programme would cover a 10-year period and would then continue at a reduced rate to satisfy the needs of the annual population increase.

Fig. 9 (centre) shows that the savings resulting from the reduction in the number of typhoid fever

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[1] That is, vaccination at five-year intervals with an 80% effective vaccine of 75% of a community affected by a typhoid endemicity level of 7.2 per 10 000, the initial size of the population being about 150 000 and the natural annual growth 2.7%.

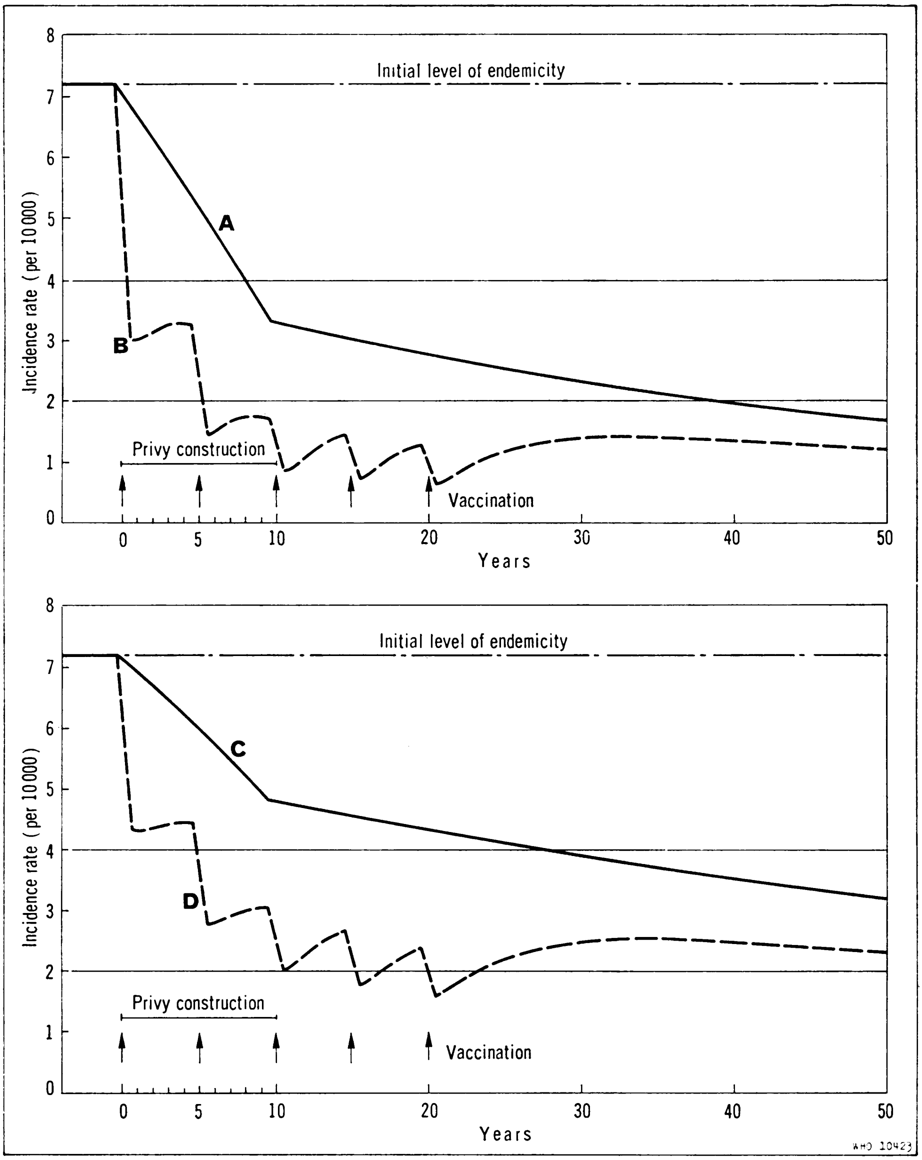

Fig. 8. Effect of privy construction and mass vaccination at different levels of effectiveness on the annual incidence of typhoid fever. (A) = privy construction only—effectiveness, 50 % on transmission by carriers; (B) = privy construction and vaccination—vaccination coverage, 75 %; effectiveness, 80 %; (C) = privy construction only—effectiveness, 30 % on transmission by carriers; and (D) = privy construction and vaccination—vaccination coverage, 50 %; effectiveness, 80 %.

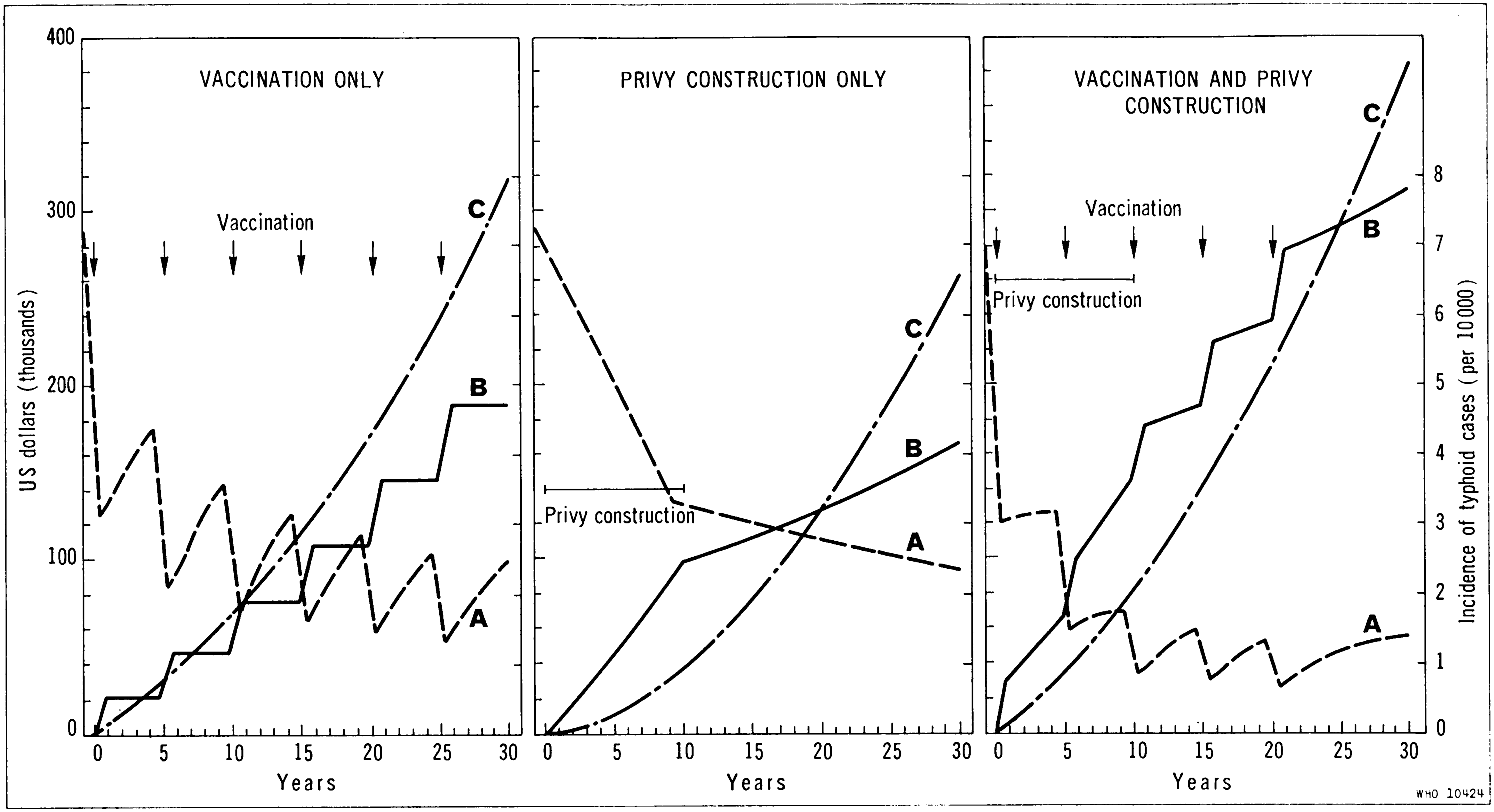

Fig. 9. Impact of different typhoid control programmes on the incidence of the disease and on the cumulative costs and benefits. (A) = incidence of typhoid cases (per 10 000 population); (B) = cumulative costs; (C) = cumulative benefits.

Table 4. Summary of the costs and benefits expressed in US $ of various different typhoid control programmes over a 30-year period in a population and under conditions characteristic of a Pacific island

Activity	Cumulative cost			Cumulative cost of treatment of typhoid cases [a]			Balance between cost and benefit
	Vaccination	Construction of privies	Total cost	Without activity	With activity	Benefit on treatment cost	
vaccination, single	21 924	—	21 924	477 900	367 300	110 600	+ 88 676
vaccination, repeated [b]	188 305	—	188 305	477 900	161 100	316 800	+ 128 495
privy construction	—	166 149	166 149	477 900	219 000	258 900	+ 92 751
vaccination [c] and privy construction	145 632	166 149	311 781	477 900	93 500	384 400	+ 72 619

[a] The values shown when divided by 100 give the respective numbers of cases.
[b] Six successive mass campaigns at five-yearly intervals.
[c] Five successive mass campaigns at five-yearly intervals.

cases grow slowly during the early years of the programme, and that the balance between the cost of privy construction and the benefit on case treatment starts to be positive only after 20 years. It should be observed that such a programme would ultimately lead to the eradication of the disease and thus provide an important and definite benefit (see Fig. 6). One should also take into account the beneficial effect of privies on other intestinal infections and the saving in lives and wages.

Example of costs and benefits of immunization and sanitation combined. The last example illustrates the impact of the combined strategy indicated for line B in Fig. 8. The cumulative cost of the five successive mass immunizations and the construction and improvement of privies (government contributions only) is presented in Fig. 9 (right), which also shows the corresponding benefits on case treatment expected from this programme. With the numerical values given to the parameters in this example, it is only after 25 years that the balance between cost and benefit begins to be positive, but in the meantime the disease would have been reduced to a considerably lower level than by any of the other control programmes.

The costs of vaccination and/or sanitation and the benefits obtained from savings on the treatment of prevented cases corresponding to the above three examples have been consolidated for a 30-year period in Table 4. In addition, the first line of the table shows the cost and benefit estimates corresponding to a single mass vaccination campaign with the same parametric values as in the first example of Fig. 9. The last two columns of this table show that the most favourable balance does not necessarily correspond to the greatest benefit as expressed in terms of saving on case treatment. In fact, as expected, the most substantial benefit results from combined immunization and sanitation, although the balance appears less satisfactory because the cost of this policy includes an expensive initial investment in privy construction.

It must be emphasized that these examples—limited by necessity to a single community in a developing country—considerably over-simplify the economic and financial treatment of the actual health problem and the strategy of control envisaged; for example, no allowance was made for interest on investments, for changes in absolute and relative costs of immunization, privy construction, and treatment that would occur in the lapse of time, or for numerous other factors.

In the preparation of control programmes numerous other possibilities arise in different communities and conditions. These could be analysed in a similar way. If, for example, the construction of privies proves unprofitable from a cost point of view for the government, when the government is responsible for the total or even half of the cost of construction, it may prove profitable if the population contributes 2/3 or 3/4 of the cost. When the proposed programmes, because of relatively high costs and low benefits, prove unacceptable to the health authorities, simulation would make it possible to explore alternative more beneficial approaches.

There are a number of economic and other factors not applied in the above examples that could be taken into account; for example, the secondary effects of control measures against typhoid fever, such as the effect of sanitation on the control of other enteric infections and intestinal parasites, or the effect of this control on the development of tourism.

The above examples of cost–effect and cost–benefit analysis showed that in a community resembling the population of Western Samoa, immunization and sanitation would give essentially the same results for about the same cost and that in selecting the most suitable control programme both would have to be considered in the light of local conditions.

A close inspection of local conditions in Western Samoa revealed, however, that the various districts of that country differ greatly in respect of incidence of typhoid fever and availability of water (necessary for the functioning of water-sealed latrines—the only satisfactory type of privy for these islands). Moreover, it was found that the cost of vaccination against typhoid fever could be significantly reduced if this antigen were combined with other vaccines (DPT) given to children. Such combined vaccination would cover only the younger age groups, as these are the only ones to receive DPT; however, it is precisely the very young age groups that are at highest risk of typhoid fever. Furthermore, in view of the serious financial limitations, the priorities in the control programme were determined, but the final analysis and plan of action demonstrated that the programme could be carried out all over the country without any appreciable increase of the Government's budget (but with continuing international assistance at the existing level).

In some districts with a water system, sanitation alone was shown to be the best long-term proposition for controlling typhoid fever, while in other areas, where incidence was very high and running water not available, vaccination was obviously of considerable benefit for a certain period of time until a water supply system and sanitary privies could be built.

It could be argued that such planning was possible earlier even without the help of a model. While there is probably some truth in this, there is no doubt that the model made it easier to prepare a sound programme. The above plan for typhoid control at present forms a part of the national health programme.

OTHER USES OF THE MODEL

So far, the examples have shown how the model can be used to simulate the effects of preventive measures and to analyse their costs and benefits, and how it can assist in the planning and evaluation of typhoid fever control programmes.

The model has other uses, such as the prediction of future trends of typhoid fever and the requirements in material and manpower for specific control projects.

We used the model in this way by applying recent typhoid fever morbidity data from certain countries and simulating present trends. Comparing data obtained through the model with actual incidence in the countries studied, we observed a regularity and parallelism in the declining trend. However, in Great Britain, the natural decline was recently much slower than the model had predicted. On checking this discrepancy it was found that the majority of the recent cases of typhoid fever in Great Britain were imported or occurred among immigrants. The trend towards eradication of the disease shown by the model was therefore not borne out by fact. However, eradication would still be possible if cases and carriers were no longer imported into the country.

This theoretical exercise demonstrates how the model could be used to explore the possibilities of eradicating typhoid fever in a country and to determine the factors to be taken into account should eradication be the aim of the health authorities.

DISCUSSION

The typhoid fever model that has been developed represents a simplified natural epidemiological process. Nevertheless, it could be used in its present form for drawing up long-term public health programmes concerning, in particular, the use of both vaccines and sanitation for control. Whenever this model is applied to an actual population, it is necessary to keep in mind the factors (mentioned in the introductory paragraphs of this article and in the section on epidemiological factors) that have not been included in the model. These factors differ from population to population. They should first be evaluated and then, if necessary, introduced according to their relative merits and importance.

Knowledge of the number of carriers in a population is helpful in determining the dynamics of typhoid fever and will differ by age groups according to the past incidence in these population groups. When most carriers are aged it should be expected, if other factors do not change, that they will be eliminated by death, and that a somewhat more favourable level of endemicity will be established. However, it should be mentioned that many elderly carriers represent a particular risk for the population since their standard of personal hygiene tends to deteriorate and they thus become a dangerous source of infection.

An increase of population under favourable environmental conditions should also lead to an improvement, particularly if the new generation is immunized. Where unfavourable conditions exist, an increase of population may lead to a deterioration, owing to overcrowding and general lowering of standards of living, sanitation, and personal hygiene. The growth of population should therefore be considered in the light of other pertinent epidemiological factors.

There are numerous other factors that may also have an important impact on the incidence of typhoid fever—e.g., natural calamities, superimposed infections such as schistosomiasis, and changes in food habits and standards of hygiene. It is the task of epidemiologists and public health workers to evaluate these factors critically and to use the mathematical model creatively in practice.

A few other factors should also be kept in mind, such as timing of the immunization campaign and selective protection of groups at high risk. The effect of mass immunization, as shown by the model, is of only a temporary nature. However, if it is repeated at the proper intervals and on sufficiently large portions of the population, immunization will lead to a definite decline in the endemic level of the disease. It must be realized, however, that while a more potent vaccine and a greater number of immunized persons signify a lower incidence of disease, they also mean an increased number of susceptible and a decreased number of resistant persons in the population. In practice, this means that once an immunization campaign has started it is important that it should continue if the gains made are not to be lost, since the carriers not eliminated by immunization represent a constant danger of further spread of infection. The effect of mass immunization campaigns should not be over-estimated as is often the case. Immunization campaigns have only temporary effects and, in addition, have other limitations as mentioned above.

The effect of sanitation is more spectacular and permanent. However, it is difficult to determine with certainty the degree of effectiveness in practice of any one of numerous sanitary measures or of their combinations: the effectiveness may be affected by additional health education and by changes in the standard of living.

A combined immunization and sanitation programme, while not much more effective than sanitation alone, is indicated, in particular, in cases of disaster when disruption of the normal sanitary installations and measures occurs and maximum protection is required.

We have limited ourselves, in this instance, primarily to evaluation of the effect of immunization and/or sanitation programmes on the natural course of typhoid in an endemic community, but other preventive measures could also be evaluated by use of the same model.

The model could also be used to evaluate the relative costs and benefits of immunization and/or other measures such as sanitation, treatment and isolation of cases, and treatment of carriers in various economic and epidemiological circumstances and at different levels of endemicity.

The effect of employing vaccines with increased potency or the effect of immunization of increased numbers of people in the campaigns can also be investigated. Finally, the model could be used for operational research in the evaluation of various public health programmes in terms of their costs and benefits, thus ensuring that the programmes set up give the best results possible with the financial means available.

No attempt has been made at this stage to determine the optimum use of funds for typhoid control in a wider public health programme, since it is difficult to evaluate all the economic and other consequences of an effective typhoid control or eradication programme. This would involve a complex study of balanced economic and health development and detailed cost–benefit analysis of numerous interrelated activities in the field of health and other spheres.

RÉSUMÉ

MODÈLE ÉPIDÉMIOLOGIQUE DE LA FIÈVRE TYPHOÏDE: SON EMPLOI DANS LA CONCEPTION ET L'ÉVALUATION DES PROGRAMMES DE VACCINATION ANTITYPHOÏDIQUE ET D'ASSAINISSEMENT

On a construit un modèle épidémiologique de la fièvre typhoïde en vue d'étudier les modalités de la transmission de l'infection à différents niveaux d'endémicité. Le modèle met en jeu un certain nombre de paramètres représentant les proportions des divers sous-groupes épidémiologiques de la population (par exemple: sujets réceptifs, sujets infectés et sujets immuns) et les taux de transfert d'un sous-groupe à un autre. Afin de simuler avec le maximum de réalité une situation endémique stable, on a attribué aux paramètres une valeur numérique basée sur les données actuellement connues. On a ensuite modifié les valeurs de certains paramètres de façon à étudier les conséquences de la vaccination de masse et de l'amélioration des conditions d'hygiène générale et de l'assainissement, en particulier sur l'incidence de la maladie.

Le modèle montre qu'une vaccination de masse unique entraîne une baisse très notable de l'incidence, mais que le bénéfice de l'opération est en grande partie dissipé après quelques années. La répétition des vaccinations à 5 ans d'intervalle a pour effet de réduire encore l'incidence, mais le gain additionnel obtenu par chacune d'elles s'amenuise de plus en plus.

Le modèle a été utilisé pour évaluer les conséquences éventuelles des mesures d'assainissement. L'amélioration des conditions d'hygiène, en contrecarrant la transmission de l'infection, amène l'incidence à un niveau stable plus bas. Cette action est durable et, à cet égard, l'assainissement donne de meilleurs résultats que la vaccination.

Le recours simultané à la vaccination de masse et aux mesures d'hygiène a un effet cumulatif qui, dans certains cas, se rapproche de celui qu'on obtient par l'assainissement seul.

On a aussi tiré parti du modèle pour prévoir les résultats probables des programmes de lutte antityphoïdique dans une population donnée, non seulement en termes de prévention de la maladie, mais aussi en termes de coût et de bénéfice relatifs. La méthode s'avère utile lorsqu'on désire utiliser de manière rationnelle les crédits et les moyens de lutte.

D'autres possibilités d'emploi du modèle épidémiologique sont brièvement évoquées.

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