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THE DYNAMICS OF MALARIA ERADICATION[1]

by

Professor Sh. D. Moshkovsky
Martsinovsky Institute of Medical Parasitology and Tropical Medicine
Ministry of Health, Moscow, USSR

1. INTRODUCTION

The best way for eradication of an infectious disease is the application of measures which interrupt the transmission of the disease directly and completely. This way is, however, neither always applicable nor most economical. Thus, in trying to eradicate malaria in vast areas it is in most cases impossible to interrupt transmission through a frontal attack by means of such radical methods, as, for instance, detection and immediate care of every single overt or asymptomatic case or complete destruction of the total vector population, or extermination of every infected mosquito before the maturation of sporozoites. Where such radical measures are inapplicable eradication may be achieved by means of measures with limited action. This possibility is based on the fact that the spread of anthroponoses occurs as a chain-process maintained only if the loss of prevalent cases is compensated for by the appearance of new ones. By a proper choice of measures even exerting only a partial effect, this compensation may become impaired, resulting in a decrease and eventual interruption of transmission of the disease.

After the necessary system of measures has been completely introduced into practice the spread of the disease may continue, though gradually declining, and cessation of transmission must occur within a certain time. The duration of this period and the pattern of the reduction of the endemic level are determined by the prevailing epidemiological conditions and by the system and scope of measures used. The study

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of the regularities governing this process constitutes the dynamics of eradication which is one of the most important parts of quantitative epidemiology. The aim of it is to calculate the size of measures (or, more exactly, the scale of changes in the situation) necessary for the eradication of the disease; to determine the time necessary to achieve this goal, and to predict the curve of the decline of prevalence under different circumstances.

2. QUANTITATIVE APPROACH

Schematically this calculation for malaria may be based on the theory of the endemic level developed by Ross. The main part of this theory consists in the proof that the endemic level (or the prevalence of malaria in the population) "M" is determined by two magnitudes, designated as epidemiological parameters (Moshkovski, 1943, 1950) representing the numerical values of the joint activities of the factors which determine the gain and loss of cases. The first parameter, communicability, (α) is the measure of the "facility of transmission" of the disease. In malaria, communicability corresponds to the average number of infective bites inflicted on the population in a unit of time by mosquitos which have fed on one infected person belonging to this population. The second epidemiological parameter: exhaustibility, (γ) indicates the average probability of the elimination of a case from the population (as a result of recovery or of loss through any other cause) within the same unit of time. The latter parameter represents a value which is the inverse of the average duration of the presence in the population of a person (who had been infected only once) in an infected state. This duration is therefore equal to $\frac{1}{\gamma}$. Hence the average number of infective mosquito bites derived from one infected person during the *whole* time of his presence (in an infected state) in the population is equal to $\alpha\frac{1}{\gamma}$. This value corresponds to the basic reproduction rate (z_o) of Macdonald (1952, 1957). Under stable conditions the numerical value of the theoretical endemic level (M) according to premises of Ross is represented by the equation:

$$M = 1 - \frac{\gamma}{\alpha} \quad . \; . \; . \; . \; . \; . \; . \; . \; . \; . \quad (I),$$

where M indicates the proportion of persons in whose body the parasite is present at the given moment.[1]

In spite of the extreme schematization of the premises on which equation (I) is constructed, this equation helps to understand a number of important features of the epidemiological process, particularly of the dynamics of malaria eradication.

Inherent in this equation is the "feed-back" principle warranting the restitution of the endemic level in case of fortuitous deviations not caused by changes in the ratio of the parameters α and γ.

Lasting shifts of the endemic level may be caused only by steady deviations of this ratio. With the decrease in the ratio $\frac{\gamma}{\alpha}$, M increases and vice versa. When $\frac{\gamma}{\alpha}$ becomes equal to 1, the limit value of M is zero, indicating the start of the drop of the prevalence which will continue until the disappearance of the disease.[2]

3. SCALE OF CHANGES PREREQUISITE FOR MALARIA ERADICATION

It is obvious that for the achievement of conditions resulting ultimately in malaria eradication, the ratio $\frac{\gamma}{\alpha}$ must be increased as many times (v) as $\frac{\gamma}{\alpha}$ is less than 1, or $\frac{1}{1-M}$-fold (because $\frac{\gamma}{\alpha} = 1-M$). Hence the equation for v (indicating the minimal scale of changes in the epidemiological conditions - prerequisite for malaria eradication) will be

$$v = \frac{1}{1-M} \quad . \; . \; . \; . \; . \; . \; . \; . \; . \; . \quad (II)$$

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[1] M may be much higher than the parasite index (P), estimated by a cross-section examination. The ratio between M and P may vary markedly in different foci and in various population groups in the same area.

[2] With $\frac{\gamma}{\alpha} = 1$, $\frac{\alpha}{\gamma}$ also becomes equal to 1 representing in Macdonald's system the critical value below which malaria cannot perpetuate itself in the population.

This equation indicates how many times must τ be increased or α decreased in order to build up conditions leading to malaria eradication.[1]

Figure 1 and Table 1 illustrate the equation (I). It will be seen that the scale of the necessary changes (v) increases the more steeply the higher the endemic level. The rise of v becomes extremely steep with the transition to areas where practically every person is affected (holoendemic areas). For instance, for a zone with 90% prevalence v should be 5 times as large as for a zone with 50% prevalence; with $M = 95\%$ v is twice as large as with $M = 90\%$; with $M = 99\%$ v is 10 times greater than with $M = 95\%$ and 50 times greater than with $M = 50\%$.

These calculations show that the eradication of malaria in holoendemic areas requires much more effort in comparison with areas of moderate or low endemicity. But they also show that after the first successes have been achieved, further increase in efforts will result in a more pronounced drop of the endemic level: conversion of a holoendemic region into a hyperendemic one requires tremendous changes in the epidemiological conditions; transition from a hyperendemic state into a mesoendemic one is easier, and still easier is the transition to the hypoendemic situation and eventually to complete eradication of the disease.

4. DEGREE OF REQUIRED CHANGES

In the application of equation (II) the following points must be taken into consideration. V indicates the <u>relative</u> degree of the required alteration, but a given relative alteration may under different conditions correspond to different absolute changes in the given factors. The bigger the volume of the factor under consideration, the greater is the degree of absolute alteration necessary to produce the indicated relative change. Thus, in order to produce a twofold reduction of an anopheline-breeding water surface of 100 hectares, it is necessary to drain 50 hectares. But if the surface is only 10 hectares, it will be enough to drain 5 hectares. For a fourfold diminution of the parasite reservoir, it is necessary to treat three-fourths of the population in the whole endemic region, and only one-fourth of the population if the prevalence is 33%.

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[1] If a rise of τ and a drop of α are brought about simultaneously, the increase of the ratio $\frac{\tau}{\alpha}$ is equal to the product of the respective changes.

On the other hand, all other conditions being equal, higher endemic levels correspond to higher values of any one epidemiological factor, the achievement of an equal *relative* diminution of α (or increase of $\frac{\gamma}{\alpha}$) at a high endemic level will require therefore a bigger *absolute* scale of the corresponding measures, as compared with a lower level.

Hence the difference between high and low endemic regions with regard to the volume of efforts required for eradication will generally be higher than that calculated from equation (II).

At the same time it is noteworthy that the amount of necessary efforts and expenditures by no means parallels the volume of the absolute changes required.

The ratio between the changes and the efforts may fluctuate tremendously in various areas and during different periods of malaria control and eradication. Thus, for instance, if highly productive anopheline breeding places are limited and accessible, a great reduction of the vector density may be achieved with small expense. On the contrary, with remote, widely scattered, hidden small breeding places control of the aquatic stages is very costly. The same technique applied to the same extent may produce a different effect under different conditions. For instance the higher the temperature, the relatively lower is the epidemiological effect of residual spraying because the resting period of the mosquitos on the treated walls during every gonotrophic cycle is shorter and the number of those cycles for each sporogonic cycle is less; hence there is less chance for the mosquito to be killed before the maturation of the sporozoites. Even for the same place the epidemiological effect of the use of residual insecticides is slower for quartan malaria than for falciparum and especially for vivax malaria (Moshkovski, 1951, 1957).

In different areas different measures must be chosen to make the programme of eradication most efficient and cheap. It is evident that the size of the necessary effort depends on the correct choice of the most vulnerable targets, on the suitability of the techniques and the perfection of their application. In some cases the desired result may be arrived at by means of a single technique. But with the more complicated situation and the higher endemic level more techniques must be combined. In using a system of joint measures the rule of multiplication of the effects must be applied (Moshkovski, 1950, pp. 183 and 192) according to which the effect of a system of measures is equal to the product of the effects of single measures. So if the first technique has reduced the vector density 10 times, the second has diminished the mean duration of the infectious period of a person 8 times, the third has lowered the accessibility of man to the mosquito 5 times,[1] the total diminution of communicability ( ) will reach 10 x 8 x 5^2 = 2000 times.

5. DYNAMICS OF MALARIA ERADICATION

5.1 If changes in the situation brought about are not less than those indicated by equation (II), i.e. if measures are introduced for a sufficient time warranting at least an equalization of the parameters and (e.g., systematic residual spraying and/or regular detection, and treatment of infected persons), a drop in the prevalence of malaria begins and eradication will be eventually arrived at. The pattern of this progressive reduction of the prevalence represents the proper dynamics of eradication.

The general equation of the dynamics of eradication is the same as that for the approach of the actual prevalence (m) of the disease in the population to the liminal endemic level (M) corresponding to the established values of the parameters α and γ:

$$m = \frac{M}{1 + n_o e^{-\alpha M t}} \quad \ldots\ldots\ldots\ldots \text{(III)}$$

This general equation (III) is derived from the same premises as equation (I).

m = actual prevalence of malaria at time t;

o = the base of natural logarithms;

t = time;

α = first epidemiological parameter;

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[1] This number is squared, as the reduction brings about not only a drop in the proportion of mosquitos becoming infected but also of those which, after having got sporozoites, obtained access to man.

$n_o = \frac{M}{m_o} - 1$; m_o the initial value of m.

When m increases ($M > m_o$) n_o is positive, when m decreases ($M < m_o$) is negative.

In accord with equation (III) the time for the drop of the prevalence from m_o to m is given by

$$t = \frac{\ln\frac{n_o}{n}}{\alpha M} \quad \dots\dots\dots\dots \text{(IV)}$$

where $n = \frac{M}{m} - 1$ (Moshkovski, 1950, pp. 264-277).

In cases when the numerical values of α and γ have been equalized and the limit value M is zero, equation (III) becomes

$$m = \frac{1}{1 + \alpha t} \quad \dots\dots\dots\dots \text{(V)}$$

This equation allows to calculate the course of the decrease of m from 1 (corresponding to holoendemicity) to $m = 0$ (eradication) (see Figure 2). If the initial prevalence is below 1 (or 100%) the drop of m follows the same curve, but the time scale begins at the point corresponding to the initial value of m as indicated in Figure 2. The time necessary to reach a given value of m is determined by equation

$$t = \frac{1 - m}{\alpha m} \quad \dots\dots\dots\dots \text{(VI)}$$

For a holoendemic area the time (t_{50}) necessary for transmission from $m_o = 1$ to $m = 0.5$ is equal to

$$t_{50} = \frac{1}{\alpha} = \frac{1}{\gamma} \quad \dots\dots\dots\dots \text{(VII)}$$

This period which may be designated as the "period of half decay" is thus equal to the mean duration of the presence of an infectious case in the population (see paragraph 2).

5.2 If the measures applied bring about a greater change in the parameter ratio than the minimal one indicated by (1), i.e. if γ becomes greater than α, the limit value of M becomes negative. This follows from equation (I) when $\frac{\gamma}{\alpha} > 1$.

Negative values of M indicate that under the new conditions the rate of withdrawal of prevalent cases is higher than the rate of the appearance of new ones. Negative values of the endemic level represent a measure of the epidemiological "safety margin" that would be established after completion of the eradication (see Moshkovski, 1950, pp. 235-236).

With negative values of M the dynamics of eradication follow equation (III) and the decline of the prevalence is more steep than when the size of the changes corresponds only to the minimum ($M = 0$)[1] (Figure 3).

If the change in the ratio $\frac{\gamma}{\alpha}$ does not reach the minimum indicated by equation (I) i.e. if the value of γ remains less than α, eradication will not be achieved, the endemic level will drop only to a certain value above zero. This new level will depend on the new value of the ratio $\frac{\gamma}{\alpha}$ according to equation (I).

Example: $\frac{\gamma}{\alpha} = 0.2$ corresponds to $M = 1 - \frac{\gamma}{\alpha} = 0.8$ (prevalence 80%)

For eradication a fivefold increase of the ratio $\frac{\gamma}{\alpha}$ is necessary (Table 1). If the increase is only threefold M will drop till $M = 1 - (0.2 \times 3) = 0.4$ or 40%. With a twofold increase of $\frac{\gamma}{\alpha}$ M will become $1 - (0.2 \times 2) = 0.6$, or 60%.

The curve for M will approach the limit 0.4 in the first instance and 0.6 in the second. The curve will follow equation (III). The absence of further decrease in such cases in spite of the continuation of the adopted control system

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[1] The equations (III) and (V) correspond to schemes of the so-called deterministic processes (for the definition of this concept see Bailey, 1957; Bartlett, 1960) and are based on the assumption of uniform distribution of the population and the disease. In reality epidemiology is concerned not with "smooth" functions but with discrete phenomena and finite assemblies with generally no uniform distribution both of population and of disease. Consequently the interruption of the chain-process (i.e. eradication occurs not at an infinity but at certain moments the distribution of which may be calculated from stochastic schemes (Figure 4)). For other correctives see Moshkovski, 1950, pp. 299-309; Macdonald, 1957.

(Figure 5) is often explained as the result of the depletion or loss of efficiency of the techniques applied. But actually the slowing off and eventual cessation of the reduction of M is the result of the approach to the limit value of M corresponding to the newly established ratio $\frac{\gamma}{\alpha}$. If the efficacy of the measures employed was diminished or it totally vanished, the prevalence would rise and in the last case it would reach the initial level. The mere fact that the prevalence remains at a lower level than before the introduction of the system of measures indicates that the system is efficient.

For further reduction of the endemic level and for ultimate eradication, the situation must be re-analysed and new techniques must be accepted or the intensity of the applied practices increased in order to attain the scope of changes indicated by equation (II). As mentioned above, intensification of the activities beyond this minimum will increase the speed of the eradication.

6. FINAL REMARKS

The Figures 2 to 5 show a decrease in the speed of the reduction of the prevalence with time. At the first glance this trend seems to be in contradiction with the conclusions of §3 where it was indicated that with a high endemic level it is very difficult to achieve a reduction, whereas later the result is attained with lower cost. The same paradox arises when comparing the speed of the reduction in the case of high and low levels.

This discrepancy is only apparent. The curves in Figures 2 to 4 refer to the trend beginning after the indicated degree of increase of the ratio $\frac{\gamma}{\alpha}$ has been reached. The difference between holoendemic, hyper- meso-and hypoendemic areas indicated in §3 refer to the volume of changes, efforts, expenses, etc. necessary to attain the equalization of the values of γ and α.

This volume of changes etc. is much higher in holoendemic than in hyperendemic etc. areas. But once the necessary system of measures is attained, a decline of the prevalence begins, the intensity of reduction being the greater, the greater the range between the existing level and the liminal (theoretical) one, like elastic tape contracts the quicker the more it is extended.

REFERENCES

Bailey, M. T. J. (1957) Mathematical theory of epidemics, London

Bartlett, M. S. (1960) Stochastic population models in ecology and epidemiology, London

Macdonald, G. (1952) Trop. Dis. Bull., 49, 813

Macdonald, G. (1957) The epidemiology and control of malaria, O.U.P., London

Moshkovski, Sh. D. (1943) Medical parasitology (Moscow), 5, 3; 6, 3

Moshkovski, Sh. D. (1950) Basic laws of epidemiology of malaria (in Russian), Moscow

Moshkovski, Sh. D. (1951) In: (Moshkovski, Sh. D. & Rashina, M. D., eds.) Epidemiology and medical parasitology for entomologists, pp. 207-209, Moscow

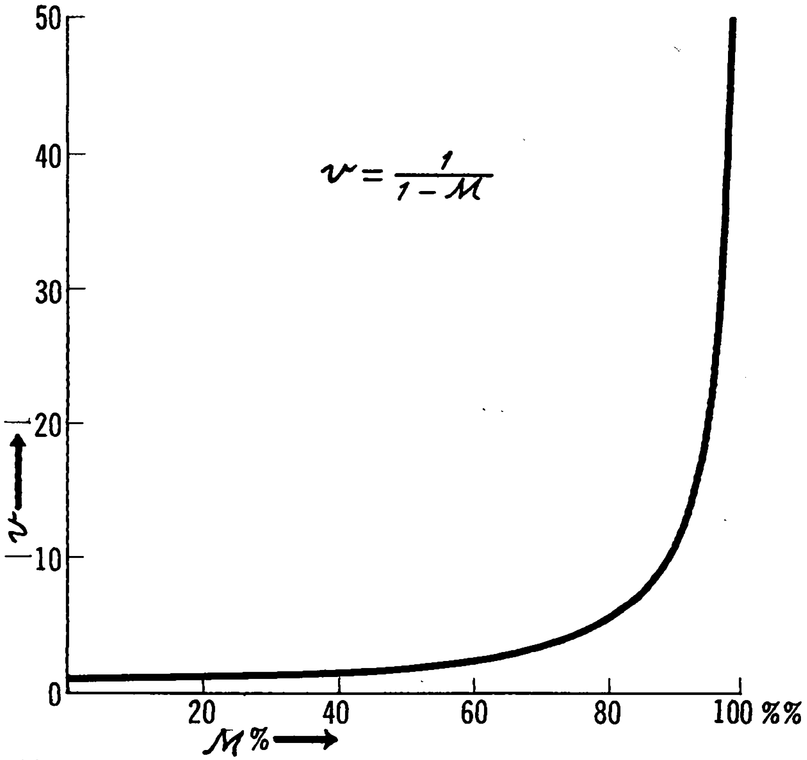
Moshkovski, Sh. D. (1957) In: Problems of regional pathology, pp. 114-116, Moscow

TABLE. VALUES OF V (SHOWING HOW MANY TIMES MUST THE RATIO $\frac{\tau}{\alpha}$ BE INCREASED TO ATTAIN CONDITIONS NECESSARY FOR ERADICATION) FOR DIFFERENT THEORETICAL VALUES OF THE ENDEMIC LEVEL M

M	V	M	V
1	1.01	60	2.5
2	1.02	65	2.86
3	1.03	70	3.33
5	1.05	75	4.00
10	1.11	80	5.00
15	1.18	85	6.67
20	1.25	90	10.0
25	1.33	95	20.0
30	1.43	97	33.3
35	1.54	98	50.0
40	1.67	99	100
45	1.82	99.9	1 000
50	2.00	99.9	10 000

FIG. 1

SIZE OF ALTERATIONS (in the joint action of the epidemiological factors) REQUIRED FOR MALARIA ERADICATION



M - ENDEMIC LEVEL (true prevalence of malaria in the population)
V - SIZE OF ALTERATIONS (how many times the basic reproduction rate must be decreased)

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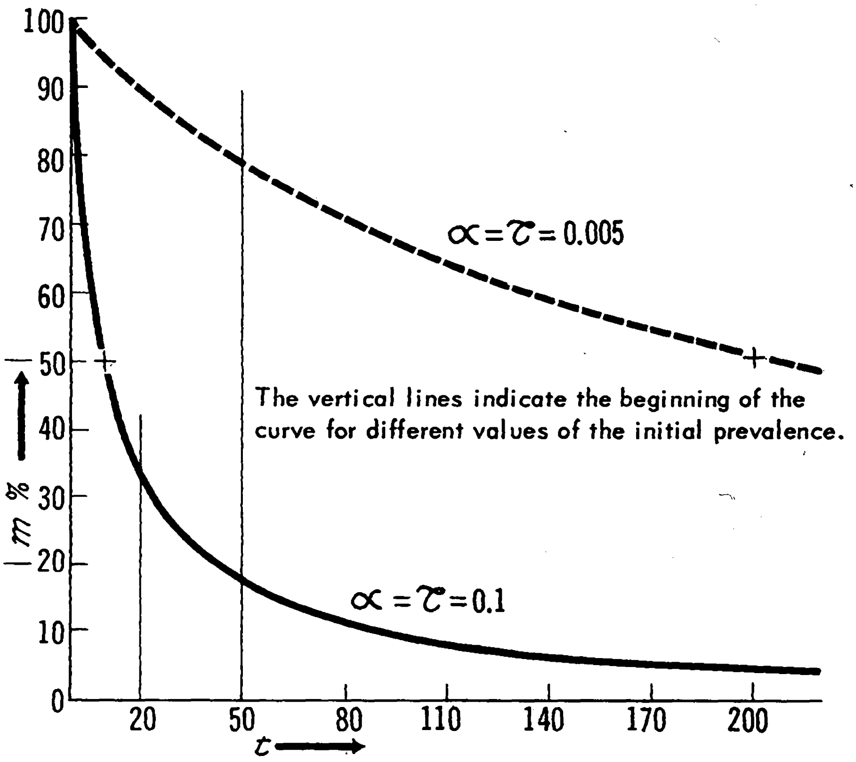
FIG. 2

THE DYNAMICS OF MALARIA ERADICATION IN A HOLOENDEMIC REGION

(beginning with the moment when the required alteration in the ratio $\frac{\tau}{\alpha}$ has been attained)



The vertical lines indicate the beginning of the curve for different values of the initial prevalence.

m- prevalence of malaria; t-time
+ - point of time when m-reaches 50%

α- first epidemiological parameter-COMMUNICABILITY
τ- second epidemiological parameter-EXHAUSTIBILITY

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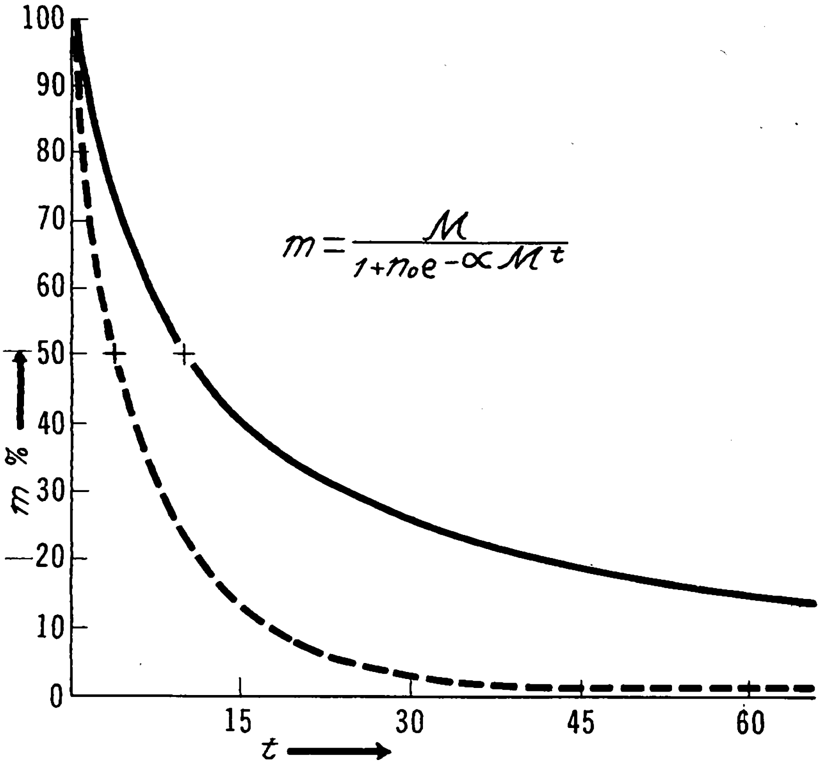
FIG. 3

DECLINE OF MALARIA PREVALENCE FROM INITIAL LEVEL 100%



Solid line
$\alpha = \tau = 0.1$ $M = 0$

Dashed line
$\alpha = 0.1$ $\tau = 0.2$ $M = -1$

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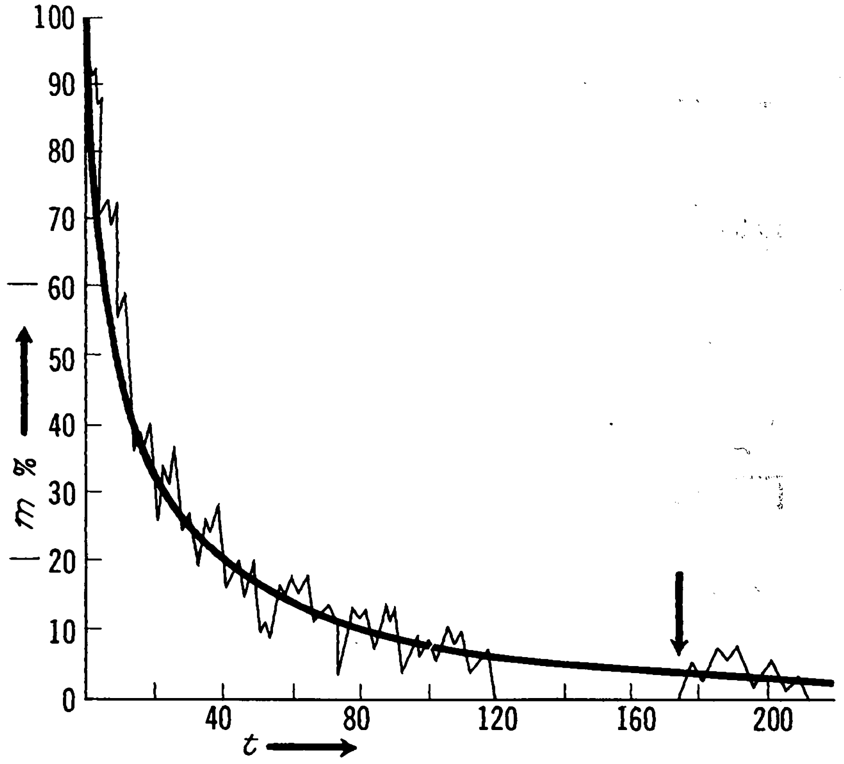
FIG. 4

STOCHASTIC FLUCTUATIONS (ZIGZAG LINE) OF THE PREVALENCE (m) IN THE COURSE OF MALARIA ERADICATION

Interruption of transmission occurs at the first drop to zero

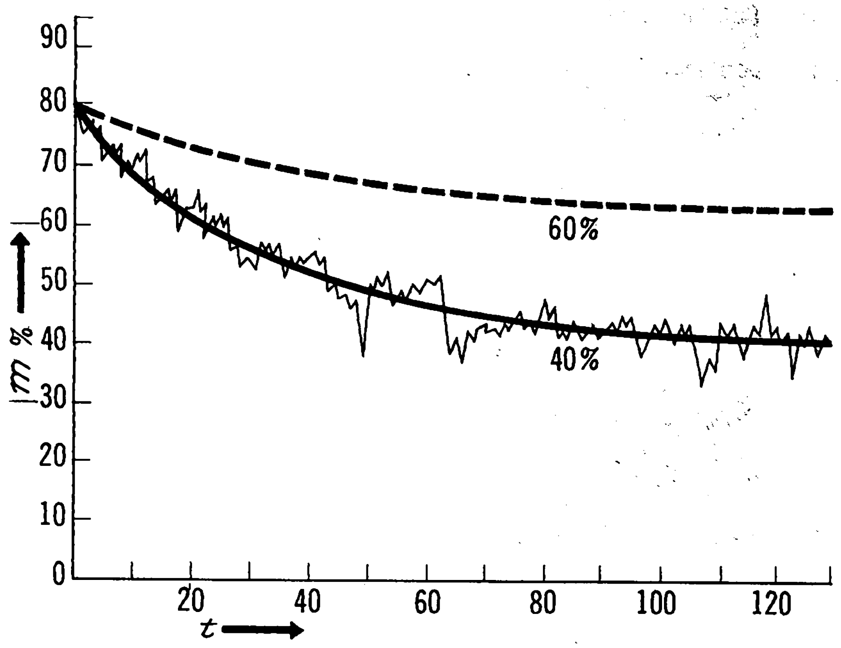


↓ REINTRODUCTION OF MALARIA FOLLOWED BY AN OUTBREAK WHICH TERMINATES VERY SOON IF THE ATTAINED CHANGES ARE MAINTAINED

WHO 4373

FIG. 5

DECLINE OF THE PREVALENCE FOLLOWING ON THE ADOPTION OF MEASURES
CAPABLE OF LOWERING THE ENDEMIC LEVEL ONLY TO
40%-SOLID LINE 60%-DASHED LINE



ZIGZAG LINE - FLUCTUATIONS OF THE PREVALENCE WITH THE APPROACH TO 40%
ALTHOUGH FORTUITIOUS DEVIATIONS CAUSE DECREASE BELOW THE LIMIT VALUE
(40%) THE PROCESS CONTINUES AND THE PREVALENCE OSCILLATES AROUND THE LIMIT

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