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THE POTENTIAL VALUE OF MASS TREATMENT IN MALARIA ERADICATION

by

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1. Introduction

The present study of principles governing the potential effect of mass drug administration in malaria eradication is based on the quantitative assessment of the appropriate methodology through a computer model.

Eradication is normally considered on a national or other substantial scale involving very large numbers of people, though this is only the summation of numerous happenings in individual foci, from each of which the infection has first to be eradicated. The size of such foci depends principally upon the numbers of people put at risk by the existence of a single infection. Clearly only some limited number, henceforth called the transmission group, dependent on the distribution and living pattern of the population and of the mosquito carrier are put at risk in this way. It has already been pointed out that in limited communities the dynamics of infection tend to follow the general pattern seen in large populations so long as the actual number of cases is relatively high, but that there is marked divergence from this pattern when cases become few, and increasingly so when they number less than 10. Not only does the pattern then become irregular but "fade-out" tends to occur before one might have expected it on a deterministic

basis (Macdonald et al., 1967). The time at which this low finite number is reached naturally depends on the actual numbers originally infected as well as on the proportion per thousand population. The point may be seen in Table 1 which gives for an infinite population at risk the probable proportion who would remain infected under known conditions of holoendemic area in Tropical Africa if an 80% effective mass treatment were applied once every month. It can be seen that if the population involved were 100, low finite figures would be reached in about two months, for a population of 1000 they would be reached in about four months and for 10 000 in five or six months. It is difficult to imagine the circumstances in which 10 000 people would all be equally at risk from a single case, and indeed it is improbable that so many as 1000 are often at risk, and the more probable numbers involved lie between 1000 and 100. This rough statement can only be refined by experience in the checking of eradication programmes with the help of standards of expectation such as those now produced. In the meantime it might be legitimate to assume a size of the transmission group of between 100 and 1000, with normal values commonly below the centre of this range.

The stochastic process represents nature in that it includes provision for the working of chance. Cases do not decrease from week to week in accordance with an immutable law but in accordance with the operation of probability. The fact that one stochastic example ends in eradication within a certain time does not mean that others will. The mean rate of decline to low figures is shown by the deterministic curve, and the range of variation round it resulting from chance can be studied by running a stochastic programme a large number of times, say 100, on identical parameters. The machine time involved is considerable, and this is in consequence only possible as a step in the final checking process just before completion of the series. The general pattern is, however, discernible from experience of only a few such trials: the more abrupt the descent towards zero level, the less the scatter round the mean time of achievement; with a slow descent the scatter due to chance alone is great and may extend over years rather than months.

The normal process involves successive eradication from large numbers of small foci or groups. If the general progress is rapid, many contiguous groups may become almost abruptly free leaving only a few recalcitrant areas where prevention has been less effective. Less successful programmes in which the rate of decline of the parasite rate is slow would be expected to show wide divergence in the time at which individual groups or foci become free, some remaining infected for long periods through

the operation of chance with consequent long postponement of the time when surveillance alone could handle the situation. There can be little doubt that this is a common pattern during the late stages of eradication, though it does not exclude the possibility of measures having been wholly inadequate in some places or entire programmes.

Consideration of the laws of probability, as illustrated by computer techniques, puts it beyond question that this general principle must apply, and it must apply whether transmission groups are 100, 1000 or 5000 strong. It follows that intensity of prevention and speed in attaining results are highly significant contributors to an eradication process, and that every delay or lessening of effort may have an exaggerated final effect.

Several pilot projects, experimental schemes and actual eradication programmes in Africa have failed to eliminate malaria, though they have succeeded in reducing parasite rates to low levels. Many causes have operated, administrative and operational failure being not uncommon, but behind these has always been the fact that malaria carried perennially by Anopheles gambiae is resistant to eradication by insecticides alone however effective the administration and organization. Attempts to improve insecticidal technique have not been very promising. Adjuvant mass medication has long been advocated and has had a few trials (de Zulueta et al., 1964, and others) but has never been generally accepted, and this probably because successful examples have been regarded as exceptions, while the difficulties, cost, lack of information on regimes and expected results, have deterred others from the method. It seems logical therefore to make, first, a theoretical study of the probable efficacy of mass treatment regimes as adjuvants to or replacements for insecticidal programmes, and on this background to seek later experimental application.

2. The potential value of mass treatment

2.1 The therapeutic activity of brief treatments

An essential characteristic of mass treatment is that it is to be given to a very high proportion of the total population of an area, at approximately the same time. It almost always follows that treatment of any particular individual should be brief and not spread over a number of days. The theoretical efficacy of mass treatment does not differ from that of treatment given to individuals except as is determined by this feature of essential brevity of administration, and an examination of potential value

demands first an examination of the therapeutic activity of brief courses of treatment. The present examination is limited, except where specifically stated otherwise, to the treatment of falciparum malaria in communities with previous experience of the infection.

There have been many studies of the efficacy of single-dose or single-day treatment of falciparum malaria since 1947, but few have included an analysis of the long-term effect of treatment and the proportion of "radical cures" in contrast to the proportion of "clinical cures" which has in most cases been the prime interest. A large number of trials of proguanil were reviewed by Afridi (1947). The series included both falciparum and vivax infections and the results are not in all cases distinguishable. He concluded that a single-dose treatment with 0.3 g (300 mg) of proguanil produced a very high proportion of clinical cures but it could not be considered to provide a complete cure, or in later terminology, a radical cure. Macdonald & Rao (1950) arrived at very similar conclusions. Utilizing 0.3 g doses of proguanil in Ceylon they produced clinical cure in all, but found relapses in 3 of 26 falciparum cases, 9 of 26 vivax, 3 of 8 malariae, and 5 of 6 mixed infections, and summarized their findings by saying that single-dose chemotherapy could not be recommended as a radical cure. About this time trials were made with the 4-aminoquinolines, chloroquine and amodiaquine. Butts (1950) recorded happenings in 227 falciparum cases treated with sixteen dosage schedules of chloroquine, the most effective being a single-day treatment with two doses totalling 0.75 g (750 mg) base in one day, but he did not follow this to the demonstration of possible long-term relapses. Villarejos (1951) went into this aspect following administration of amodiaquine in a dose of 10 mg/kg as a single dose in one day, and found that this dose produced a radical cure of falciparum infections. This work was taken up by Hoekenga (1952) who treated 380 falciparum malaria cases with amodiaquine in doses ranging from 1.0 g to 0.4 g (1000-400 mg) in one day, and 220 falciparum cases with chloroquine of either 0.6 g or 0.45 g (600 mg - 450 mg) base on one day. He was not able to check with absolute certainty on the absence of relapses but recorded that careful observation revealed no relapses amongst these falciparum cases. Covell et al., (1955) commended single-dose treatment with 4-aminoquinolines but went no further than saying that a clinical cure, and sometimes a radical cure, may be expected.

Clyde (1958, 1961, 1967) has made a number of studies bearing on this point. In his earlier paper he records the treatment of 92 children, of whom 63 had active falciparum parasitaemia, with 225 mg chloroquine and 50 mg pyrimethamine. He found

one of 74 positive seven weeks later and 5 of 81 positive six months later, whence it may be inferred that the cure rate which he achieved was not less than 89%. He later studied the value of relatively small doses of chloroquine (120 mg for children of over five years of age) in treatment and recorded that in seven children all that could be observed for a long period in freedom from transmission was complete clearance of parasites lasting for at least three months. In his later review of the general subject he concludes that asexual parasitaemia is cleared and with P. falciparum radical cure is possibly attained by ingestion of the following single doses, applicable to children aged more than five years:

Mepacrine (Quinacrine)	300 mg
Proguanil (Chlorguanide)	300 mg
Chlorproguanil	20 mg
Pyrimethamine	25 mg
Chloroquine phosphate, or sulfate	120 mg
Amodiaquine	120 mg

In a recent study Pringle & Avery Jones (1966) record a careful analysis of the effects of a single dose of 300 mg chloroquine base on falciparum infections in a large number of Tanzanian children on whom observations were continued for a long period. It is concluded that the evidence favours the postulate that all blood infections which were present in children at the time of treatment were eliminated.

These studies reasonably support the widely held belief among malariologists that a single adequate dose of a 4-aminoquinoline produces the radical cure of a very high proportion of cases of falciparum malaria in people with previous experience of the infection, and it is therefore accepted as a basis for further study.

2.2 Mass treatment and vivax malaria

An examination has been made of the literature for comparable information on the efficacy of brief treatments of vivax infections, but no coherent picture has emerged, and for this reason the present study is confined to falciparum malaria. It is a most significant hiatus in knowledge of chemotherapy that it should appear impossible to quantify the many vague statements about the "suppression" of vivax malaria and the proportion of treated cases which are likely to relapse, together with the periods at which relapse is likely to occur. A typical textbook statement would be that most

vivax infections treated with a single dose of a 4-aminoquinoline drug would be expected to relapse after a period of suppression, and also that vivax infections can be made non-infective to mosquitos for a considerable period of time by the administration of appropriate doses of pyrimethamine. Either or both of these characteristics could be built into a model such as the one here described for falciparum malaria, but there are some conflicting records in the literature which suggest that this gives far too pessimistic an idea of the statistical probabilities following brief treatments of vivax malaria. As an example, Roy (1950) treating 297 patients with vivax malaria in Egypt, divided them into six groups receiving single doses of quinine dihydrochloride 2.0 g, and chloroquine diphosphate, amodiaquine, proguanil, chloroquine sulfate, and mepacrine, each in a dose of 0.6 g. He followed the cases for six months during which time there were two relapses of vivax malaria in the quinine group, five in the mepacrine group, six in the chloroquine sulfate group, four in the proguanil group, one in the amodiaquine group, and none in the chloroquine phosphate group. This picture could also be built into a model and could be matched by other sets of observations giving similar indications, but there is little point in building either type of assumption into a model until more certainty as to which is relevant is achieved.

2.3 Computer models of the effects of mass treatment

The efficacy of mass treatment depends on the chemotherapeutic efficiency of the drug and on the proportion of the population to whom it is administered, the combination of these two producing what is later referred to as the efficiency of mass treatment. A general knowledge of happenings in many places with particular knowledge of happenings in an area of Northern Nigeria (Kankiya) indicate that however effective the drug itself and however effective the system of administration, there must be some material omission from total coverage owing to the common absence of some members of a community at any time. In order to allow for failures due to therapeutic, administrative, or demographic causes, further work has been carried out on the assumption that the maximum attainable total efficiency is not likely to exceed 80%, and computer programmes have been run with this and lower efficiencies.

The efficiency of and the intervals between treatments have first been decided. Provision has then been made, at some early stage and then periodically at appropriate intervals, for the recovery of the chosen proportion of overt cases, without modification in the numbers of infections which are at the time incubating, either

in the mosquito or in man. This leaves an opportunity for infections to remain "in the pipeline" even should overt infections be totally eliminated. Programmes in this form have been operated in both deterministic and stochastic forms.

An initial study was made of the principles governing the potential effect of mass treatment, particular interest lying in its range of potential value and the extent to which this value might be modified by operational and epidemiological factors. It would have been possible to run programmes with treatment postulated at any interval down to consecutive days, but in view of the practical difficulties of an adequately supervised mass treatment programme the minimal practical interval was regarded as one month, with two months as a more likely working minimum. Initial trials indicated that mass treatment at such intervals could only lead to eradication if the reproduction rate was really low, below four or five. Though there are conditions where it might naturally be sufficiently low to make this method alone applicable, in most conditions the ruling rates would be too high, and mass treatment is here considered as an adjuvant to associated insecticidal attack.

The general pattern of these preliminary trials was that transmission was regarded as perennial except in certain stated examples: malaria was moderately unstable such as might well occur with a moderately anthropophilic vector under the partial influence of insecticides, and in stochastic examples transmission groups or communities were considered to contain 100 people.

It might be expected that the original picture would include a moderately high parasite rate, later declining under the influence of attack.

Another study (Macdonald et al., 1967) showed expected happenings under the influence of insecticidal attack alone producing reproduction rates ranging in their new values from zero to 1.0.

Figure 1 shows the expected effect of 80% effective mass treatment on such four sets of conditions, plus others in which the reproduction rate was 1.5, 2.0 and 4.0. Figure 2 repeats the same exercise for treatment every two months, other parameters being the same. Each set is shown deterministically because the object was to study the typical progress of happenings rather than the actual mechanism of final local eradication.

After each treatment there is marked reduction in the parasite rate, though never to the extent of the 80% reduction that the stated efficiency of treatment suggests. The reason is that treatments are here stated at the start of months, rates at the end: in the interval new cases have occurred, and have been derived from the infective reservoir of the previous month, before treatment was given. In all cases there has been some, and in a few a very substantial, restocking of the parasite reservoir during the month.

Examination of the two sets of results gives some indication of the potentialities and limitations of mass treatment of this general order of efficiency and periodicity: significant effect in reduction of the parasite rate to levels where "fade-out" might start to operate is only achieved when the intensity of transmission, as indicated by the reproduction rate, is low. Sustained low rates of 1, 2, 3 and such-like values are very rare in nature and it follows that the real value of mass treatment lies in its possible use as an adjuvant to insecticidal or other attack on transmission, and is to be judged by the extent to which such a combined mechanism is superior to a single one based on insecticide alone.

There is clearly a possibility of advantage where insecticidal attack alone is incapable of completely interrupting transmission. A different study showed that failure would have to be admitted in any insecticidal attack which did not reduce the reproduction rate well below 0.5, whereas even a four-monthly regime of 80% effective treatment might have converted this failure at 0.5 into almost brilliant success, and even at 1.5 into a satisfactory solution. A two-monthly regime could have produced rapid solution with a residual reproduction rate of 2.0, which without it would have constituted total failure.

This is, however, an understatement of the value of mass treatment. Even when insecticidal attack is totally successful in interrupting transmission, its effect in reducing the parasite rate is purely passive: it allows opportunity for natural elimination of infections without parallel restocking of the reservoir, and a minimum of three years is normally allowed for reduction to fade-out levels. Incomplete interruption has a slower effect and periods of four or more years are commonly needed. Even a four-monthly regime can totally transform this picture, bringing parasite rates down towards fade-out levels in a few months in place of years: the speed of decrease of the parasite rate is such that there should be little scatter round it, neighbouring localities reaching a fade-out point roughly simultaneously, thus making the early

ending of attack and start of consolidation possible. Mass treatment undoubtedly adds to the annual cost of attack, as has often been said, but the cost can only properly be judged as a total cost from start to finish, which should be substantially reduced.

These are great advantages but they are limited to conditions where the reproduction rate is low and they cannot therefore compensate for inefficient or inadequately mounted attack. They are so much related to low reproduction rates that every opportunity of associating mass therapy with low, or zero, transmission should be taken. Where malaria is seasonal the greatest advantage is to be gained by mass treatment during the period of low, or zero transmission, and indeed if a true zero level is not reached naturally it may be even more important to achieve it by insecticidal attack during this time than during the period of acknowledged transmission. Mass therapy has then an opportunity to reduce parasite rates to fade-out levels before the onset of transmission. Even if this is not achieved it should greatly reduce them, and continued therapy and attack during the transmission season may at least hold them, thus giving better opportunities for the next year. These points are illustrated in Figure 3 which gives (for slightly different epidemiological parameters) the effect of two-monthly regimes of 80%, 70% and 60% efficiency on transmission with a 7-month "off-season", (reproduction rate 1.0) and a 5-month acknowledged transmission season (reproduction rate 6.0). In each case transmission is started at the beginning of the dry season: in the first fade-out occurs before the onset of the transmission season, in the second only at the start of the next off-season, and in the third after yet another complete seasonal cycle. Localities similar to this last one would show considerable scatter about the mean time of disappearance, and the area as a whole would be judged a total failure of the process.

2.4 Preliminary data needed

The efficacy of treatment depends to a large extent on the intensity of transmission, and it is important to know for design purposes whether this can be assessed merely from the amount of malaria (the parasite rate) or whether it is necessary to evaluate individual factors, reproduction rate, biting habit and longevity as have been presented up to this point. This has been tested by taking three sets of epidemiological conditions all leading up to a 75% parasite rate: one a very stable set with a stability index of 10, a moderate set with an index of 1.0, and a very unstable set with an index of 0.1, and applying an identical mass treatment, 80%

effective every four months, to each. A 12-month cycle of operation, starting with an initial parasite rate of 75%, led to its reduction to 27% in the stable conditions, to 5.5% in the moderate, and 2.4% in the unstable. Repetition with epidemiological conditions leading to a parasite rate of 50% gave similar results.

Stability index $\frac{a}{-\log_e p}$, representing the mean number of bites on man taken by an average mosquito during its entire lifetime, and determining the stability of epidemiological conditions (Macdonald, 1952). Evaluation cannot therefore be limited to a simple estimate of intensity, but must include measurement of the stability index based primarily on the man-biting habit and secondarily on the longevity of the mosquito. However, for any major scheme, it is most desirable that a full analysis should be made beforehand of the entire epidemiological situation, and a complete programme fitted to it in the manner which has been described.

Another set of trials concerned the possibility of having misrepresented the recovery rate, and its effect. There are good grounds, already quoted, for taking 0.005 as a widely applicable value, and the maximum credible range would seem to lie between 0.01 and 0.0025. These three values have therefore been contrasted in sets of conditions otherwise identical, a stability index of 1.0, reproduction rate of 1.75 and an original parasite rate of 75%, to which has been applied a four-monthly treatment of 80% efficiency. Three treatments reduce the parasite rates to 10%, 4% and 2% in the cases with recovery rates of 0.01, 0.005 and 0.0025. These differences are material though not so great as to invalidate the entire process, and particularly not so because the principal criticism raised against the value of 0.005 is that it is suspected to be too high: there is a strong feeling that falciparum infections are longer lived in Africa. The authors do not concur in this, but know no suggestion that the postulated rate is too low. Therefore if it deviates from actuality it seems to produce results which are somewhat too conservative.

The procedure which we have carried out, and would advise, is that after completion of analysis of a situation, and of the effects of treatment, leading to choice of method a fresh analysis should be made based on these extreme values, with testing of the proposed regime on the resultant reconstituted picture. A fully acceptable regime should meet these extreme demands as well as those of the model prepared.

3. Conclusions

From these considerations it has been concluded that:

(1) Mass treatment could play a very effective part in the eradication of falciparum malaria, but in most conditions only as an adjuvant to insecticidal attack.

(2) The value is not limited to conditions where insecticides have failed or might fail, the speed which it introduces constituting a valuable factor in any programme.

(3) The probable value of mass treatment in the eradication of vivax malaria cannot be forecast in a comparable manner because knowledge of the quantitative effects of drugs in curing vivax malaria is too elementary.

(4) The most effective time for institution of mass treatment is during the period of minimal transmission. Effective strategy would always aim to gain the greatest possible control over both the reservoir of parasites and transmission during this period, regarding activity during the period of normal high transmission as largely a holding operation, in readiness for abrupt elimination in the succeeding off-season.

(5) Preliminary analysis of the malaria situation, along lines which have been described, is essential. The data required are measures of the stability index and the reproduction rate, in two seasons if appropriate. The raw material to be gained from the field are the man-biting habit of the vector, successive values of the parasite rate under control conditions to which mass treatment would be adjuvant, and of the longevity of the vector, in that order of importance. Where the man-biting habit has been shown to be low, measurement of mosquito longevity assumes diminishing importance.

SUMMARY

The process of eradication consists of successive elimination from numerous small foci, in which terminal happenings can only be studied by stochastic processes. These indicate the high significance of terminal "fade-out" when numbers become low, and of chance in determining the time when it occurs. The scatter round the mean time is determined largely by the slope of decline, and the significance of speedy reduction of parasite rates is emphasized. The therapeutic activity of brief courses of drugs on falciparum malaria in communities previously exposed to it is examined, and it is concluded that a single dose of 0.6 g of a 4-aminoquinoline produces radical cure in a

high proportion of such cases. No adequate data exists on which to make any comparable quantitative statement on the curative ability of brief courses of drugs on vivax malaria.

An examination of the possible effect of brief mass treatments has been made using computer techniques, limiting consideration to treatments which are 80% effective or less so, and applied at intervals of two or more months, these being thought of as practical limits in African working conditions. Potential value is judged as very high, but only as an adjuvant to insecticidal attack. A number of conclusions are reached on appropriate methodology and regime.

RESUME

Le processus normal d'éradication du paludisme implique l'élimination successive de l'infection dans un grand nombre de petits foyers ou groupes. Seule la méthode stochastique permet d'étudier les résultats ultimes. Cette méthode montre l'importance de la phase finale de la disparition de la maladie (c'est-à-dire du moment où le nombre de cas devient extrêmement faible) ainsi que le rôle joué par le hasard dans l'arrivée de ce moment. La dispersion autour du temps moyen dépend en grande partie de la pente de réduction de l'indice plasmodique; et les auteurs insistent sur l'importance de cette vitesse de diminution.

Si, d'une manière générale, l'éradication progresse vite, nombreux sont les groupes contigus qui peuvent rapidement être libérés de la maladie, à l'exception de quelques zones coriaces. Dans les programmes où la diminution de l'indice plasmodique est lente, on peut s'attendre à ce qu'il existe une divergence considérable entre les moments où les différents groupes ou foyers sont libérés, certain d'entre eux demeurant infectés pendant longtemps sous l'effet de facteurs aléatoires, de sorte que l'instant où la surveillance permettrait à elle seule de faire face à la situation s'en trouve considérablement retardé.

Plusieurs projets pilotes ou expérimentaux ou même des programmes d'éradication n'ont pas réussi à éliminer le paludisme en Afrique, bien que l'on soit parvenu à ramener à une valeur faible les indices plasmodiques.

On a procédé à une étude théorique de l'efficacité probable de schémas de traitement de masse destinés à remplacer ou à compléter les programmes d'application d'insecticides, en vue d'une application expérimentale ultérieure.

L'efficacité du traitement de masse dépend des qualités chimiothérapeutiques du médicament utilisé et de la proportion de la population à laquelle il est administré, l'association de ces deux facteurs constituant ce qu'on appelle l'efficacité du traitement de masse.

On a commencé par étudier les principes dont dépend l'effet possible du traitement de masse, en mettant plus particulièrement l'accent sur l'étendue des possibilités offertes par ce traitement et la manière dont on peut les développer en faisant intervenir divers facteurs opérationnels et épidémiologiques.

On a examiné l'activité thérapeutique de divers médicaments administrés pendant une courte période pour le traitement du paludisme à falciparum dans des collectivités déjà exposées, ce qui a permis de conclure qu'une dose unique de 0,6 g d'amino-4 quinoléine devrait donner une guérison radicale dans une proportion élevée de cas. On ne possède pas d'indications permettant d'établir une comparaison quantitative avec le même genre de traitement appliqué à des cas de paludisme à vivax.

Pour étudier l'effet possible de traitements de masse de courte durée, on a utilisé les techniques du calcul électronique, en ne prenant en considération que les traitements efficaces à 80 % ou moins et appliqués à deux mois d'intervalle ou davantage; on avait estimé en effet que ces conditions correspondaient aux limites pratiques dans les conditions de travail existant en Afrique.

L'examen de deux séries de résultats a fourni quelques renseignements sur les possibilités et les limites d'un traitement de masse répondant à ces caractéristiques approximatives d'efficacité et de périodicité : il n'est possible de ramener l'indice plasmodique à un niveau permettant "l'effacement" de la maladie que si l'intensité de la transmission, mesurée par l'indice de propagation, est faible. Il s'ensuit que la valeur réelle du traitement de masse réside dans sa possibilité d'emploi comme complément des opérations insecticides ou des autres formes de lutte contre la transmission; pour déterminer cette valeur, il faut donc voir dans quelle mesure cette méthode combinée est supérieure à l'utilisation des seuls insecticides.

De ces diverses considérations, on a conclu ce qui suit :

1) Le traitement de masse pourrait jouer un rôle très efficace dans l'éradication du paludisme à falciparum mais, dans la plupart des cas, uniquement comme complément des opérations insecticides.

2) Son intérêt ne se limite pas aux situations où les insecticides ont échoué ou risquent d'échouer, car il introduit un élément de rapidité qui peut jouer un rôle utile dans tout programme.

3) On ne peut évaluer de façon comparable la valeur du traitement de masse dans l'éradication du paludisme à vivax, car notre connaissance des effets quantitatifs des médicaments sur cette forme de paludisme est trop élémentaire.

4) Le moment le plus propice au lancement du traitement de masse se situe pendant la période de transmission minimale. Pour être efficace, un plan de lutte devrait toujours avoir pour objectif de diminuer le plus possible le réservoir de parasites et la transmission à titre de solution d'attente visant à préparer le terrain pour une élimination de la maladie au cours de la saison suivante de transmission minimale.

5) Il est indispensable de procéder, de la façon indiquée, à une analyse préliminaire de la situation du paludisme. Les données nécessaires sont l'indice de stabilité et l'indice de propagation, pour deux saisons s'il y a lieu. Les données brutes à recueillir sur le terrain sont, par ordre d'importance décroissante, l'anthropophilie des vecteurs, les valeurs successives de l'indice plasmodique dans les conditions de lutte où le traitement de masse serait un adjuvant et enfin la longévité du vecteur. Lorsque l'anthropophilie se révèle peu importante, la mesure de la longévité du moustique joue également un rôle moindre.

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TABLE 1. EXPECTED CHANGES IN THE PARASITE RATE FOLLOWING APPLICATION OF AN 80% EFFECTIVE MASS TREATMENT ONCE A MONTH IN STANDARD EPIDEMIOLOGICAL CONDITIONS DESCRIBED IN THE TEXT

Month	Parasite rate %
0	90.00
1	19.63
2	5.22
3	1.48
4	0.43
5	0.12
6	0.04
7	0.01
8	< 0.01

Figure 1. The expected effect of 80% effective mass treatment over 4 months subject to reproduction rates as shown on the figures and standard conditions stated in the text: deterministic version.

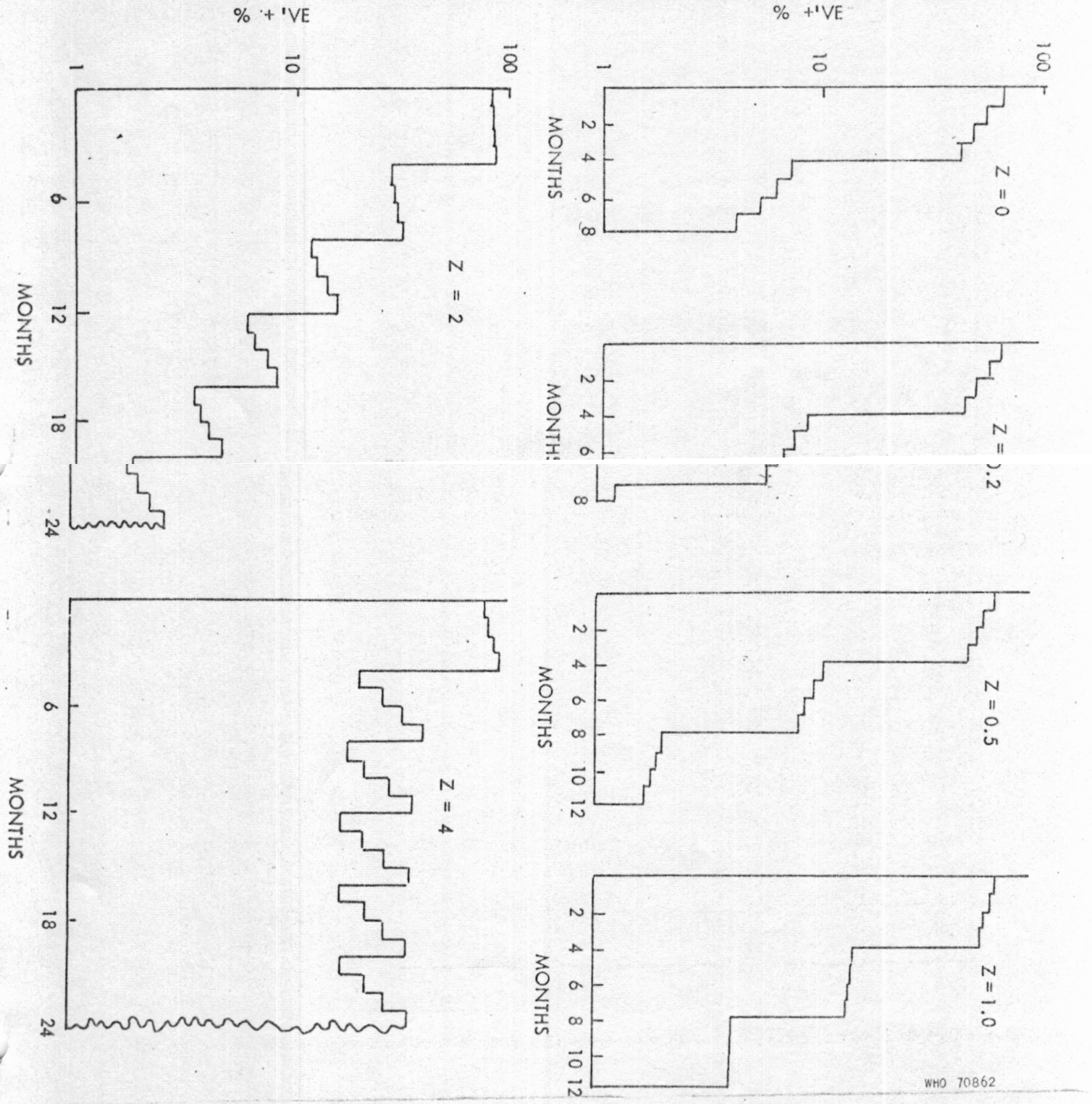
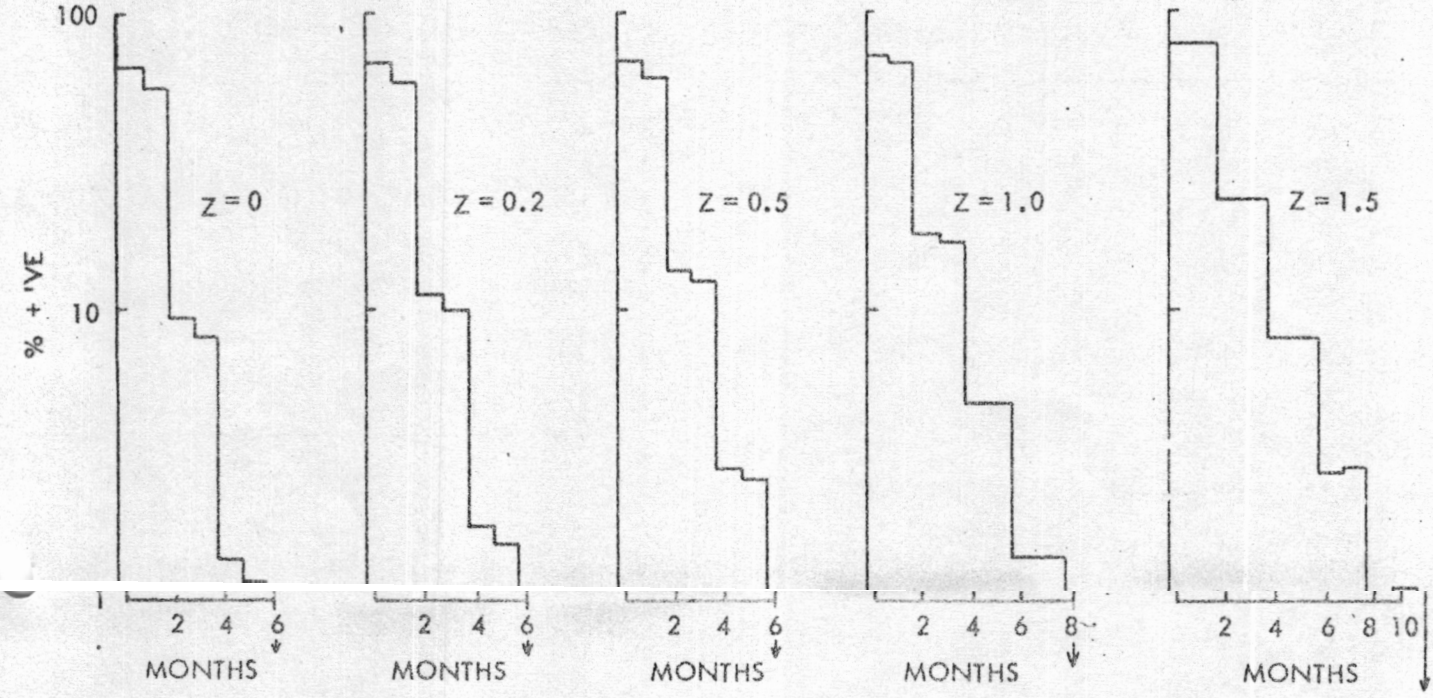


Figure 2. The expected effect of 80% effective mass treatment over 2 months on malaria subject to reproduction rates shown on the figures and standard conditions stated in the text: deterministic version.



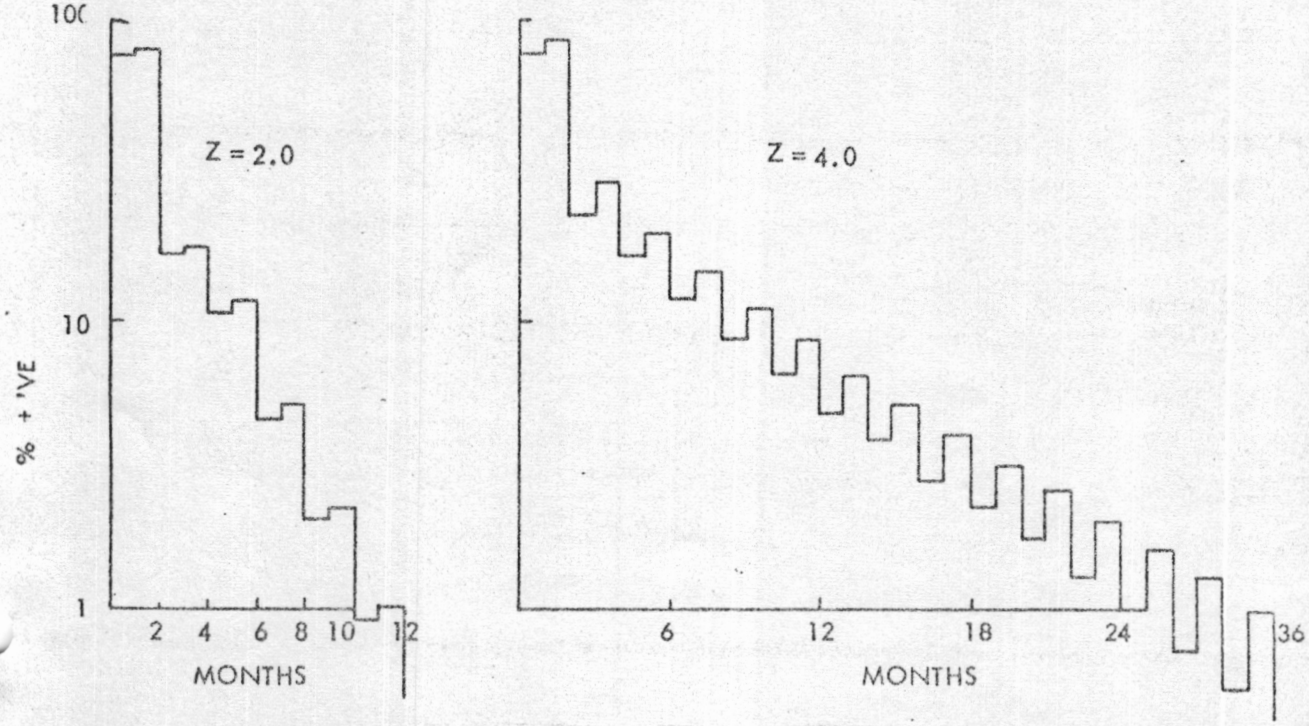


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FIGURE 3

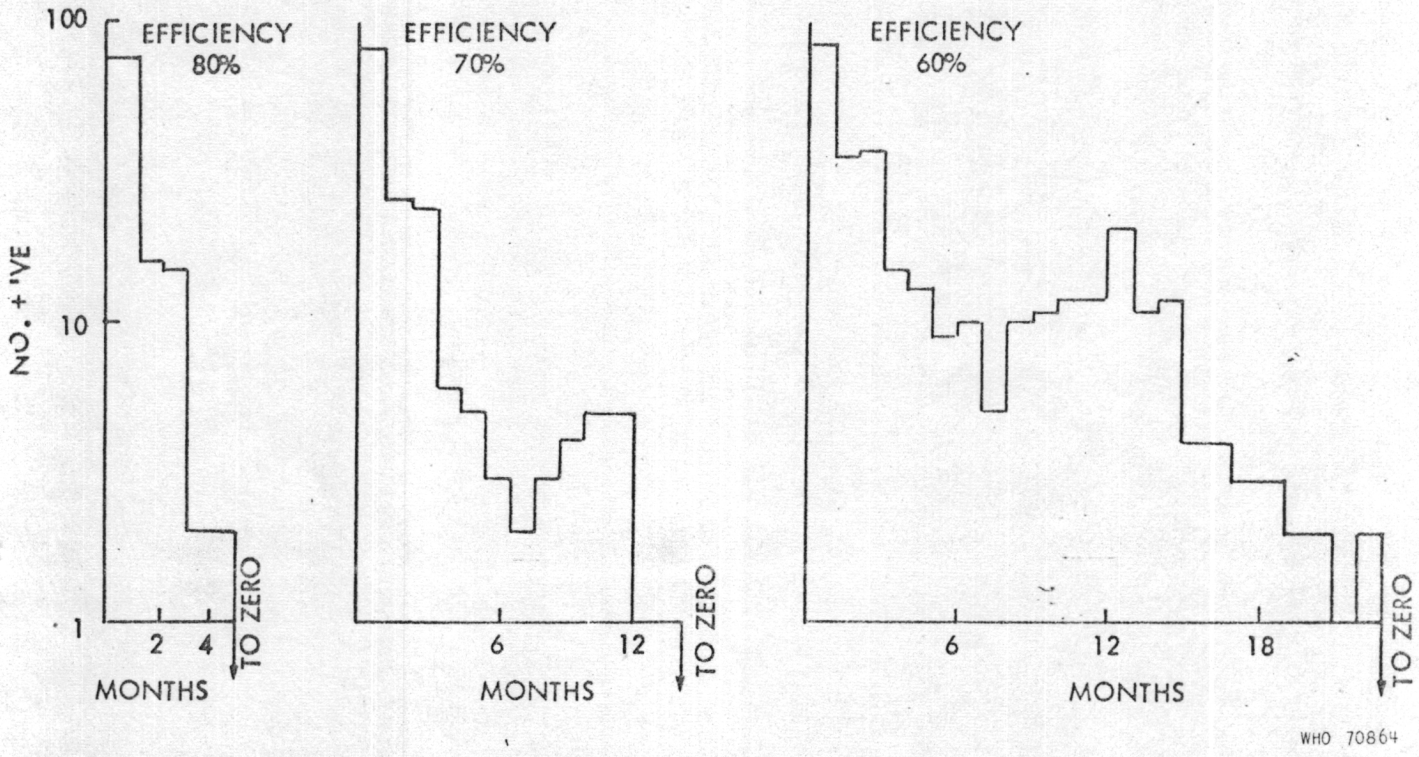

Figure 3. The expected effect of 80%, 70% and 60% efficient mass treatment every two months beginning at the start of the dry season on a simulated set of African conditions. These include a relatively low malarial season of 7 months and a high malarial season of 5 months in which, by insecticidal action, the reproduction rate has been maintained at 1 and 6 respectively: the probability of mosquito survival is maintained at 0.8 and the mean number of feeds on man per day by the vector mosquito is 0.5.

The purpose of the WHO/Mal series of documents is three-fold:

(a) to acquaint WHO staff, national institutes and individual research or public health workers with the changing trends of malaria research and the progress of malaria eradication by means of summaries of some relevant problems;

(b) to distribute to the groups mentioned above those field reports and other communications which are of particular interest but which would not normally be printed in any WHO publications;

(c) to make available to interested readers some papers which will eventually appear in print but which, on account of their immediate interest or importance, deserve to be known without undue delay.

It should be noted that the summaries of unpublished work often represent preliminary reports of investigations and therefore such findings are subject to possible revision at a later date.

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