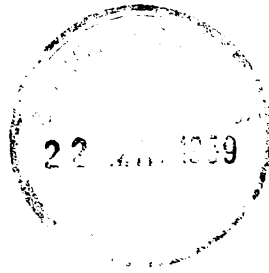


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MECHANISM AND PROCEDURES OF SURVEILLANCE IN MALARIA
ERADICATION¹

by

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1. INTRODUCTION

In malaria control there is no danger of resurgence of the disease as long as control measures are recurrently continued. When the strategy is changed to eradication the campaign is limited in time and within that period a complete interruption of transmission should be secured. What is more important, there should be no resumption of transmission after the campaign comes to an end. Two things are necessary to secure this objective. One is that the campaign is carried out to a high degree of perfection, through total, speedy and efficient coverage of the entire malarious area with any degree of autochthonous transmission. The second is that there should be an active search for malaria cases in every locality and a determination through careful epidemiological investigation whether they are imported, sporadic, induced, introduced or indigenous.² It is this latter procedure that constitutes the basic part of surveillance. But it does not end with a mere case finding or malaria detection programme, and an epidemiological determination of the origin of malaria cases. It includes the steps that have to be taken in order that "primary" cases thus detected do not lead to further infection.

¹ Prepared as a working paper at the request of the Secretary of the Expert Committee on Malaria (seventh session) which met in Lisbon from 15-23 September 1958.

² The terms "imported", "sporadic", "induced", "introduced" or "indigenous" are used as defined in the sixth report of the Expert Committee on Malaria. (Athens, 1956)

The concept of eradication and of surveillance as an integral part of its terminal phases - whenever it may be originated - is thus epidemiological and does not necessarily include within it the biological challenge of a total elimination of human plasmodia.

In resorting to surveillance to substantiate the claim of malaria eradication one need not necessarily find a total absence of any indigenous autochthonous malaria but only evidence that cases of this category are so few that in practice, after adequate treatment, they do not lead to an equal or increasing number of subsequent cases arising therefrom.

2. PERIOD OF ESTABLISHMENT OF SURVEILLANCE

The period during which surveillance should be established would depend on (a) the amount of malaria originally prevalent, (b) its responsiveness to residual insecticide spraying, (c) the status of rural health services (d) relative costs of continued spraying with limited surveillance and consolidating spraying with full surveillance with a view to effect earlier withdrawal of spraying especially to forestall resistance.

2.1 When to begin surveillance? Surveillance in a composite sense will be needed only when transmission has been almost completely interrupted. At an earlier stage the workload will be too heavy. The reduction of (a) spleen rates in children 2-9 years to below 10% - (many workers including the writer feel it should be to below 5% to allow for possible omissions in palpating spleens of Hackett size 1), (b) parasite rates in children 2-9 years to below 1%, and (c) infant parasite rates to zero, are suggested as indications that the stage of interruption of transmission has been reached. Surveillance may be established in the year following the reduction of these rates below the prescribed limits.

During this year spraying will continue. Surveillance will thus commence in the attack phase, generally towards its end. In countries or areas in which even a single spraying is likely to bring about such reduction, surveillance may need to be established at the very beginning of eradication procedures. Surveillance

may also be adopted at the very commencement of the attack phase for training purposes and in order to overcome a possible reluctance of governments to provide additional personnel and funds at a later stage of the programme when malaria has been greatly reduced and the demand for more men and money appears superfluous. Such an organization will help in rendering better supervision of the spraying programme. In areas where malaria is shown to be in some measure "refractory" to residual insecticides, the implementation of a full-scale active surveillance procedure from the very commencement of the attack phase may be attended by a complete interruption of transmission which might not result from spraying even when the latter method was continued for a number of years.

2.2 How long to continue surveillance? The maintenance of surveillance after withdrawal of spraying serves three purposes: (1) the prompt detection of malaria cases and their treatment, so that these primary cases do not generate secondary cases; (2) the adoption of measures including resumption of spraying in circumscribed areas, in order to prevent the further spread of transmission, should residual foci of infection be discovered; and (3) the establishment of the claim of malaria eradication through an intensive investigation of malaria morbidity. In order to establish a claim for malaria eradication as laid down in the sixth report of the Expert Committee on Malaria, active surveillance has to be continued for at least two years after the withdrawal of spraying.

2.3 Maintenance of surveillance. Surveillance will have to be a continuing process, but after the stage of consolidation, during which special staff are appointed for the purpose, further surveillance in a less intense and more limited activities may be incorporated into general health service.

2.4 Relative costs of continued spraying without surveillance and of surveillance towards the end of the attack phase along with spraying. In some countries, organized surveillance may prove considerably more costly than one or two additional cycles of spraying. The latter might, therefore, be a more economical way of bringing about complete interruption of transmission. Additional cycles of spraying dictated on grounds of economy or greater feasibility should, however, be

undertaken only if there is no apparent danger of the development of resistance in the vector species. In any case, after the completion of such additional sprayings surveillance must be established in an adequate and random sample of the population in order to substantiate an eventual claim for eradication.

The randomization of the sample must be in terms of units of villages and must include areas which before the commencement of spraying operations could be grouped under distinct epidemiological zones. The necessity for an entire village to be included arises out of the range of flight and infiltration of the vector species. The adequacy of the size of the sample population would have to be judged in terms of the statistical requirements to substantiate a nil incidence in the total universe.

3. SURVEILLANCE PROCEDURES

These include:

- 3.1 Active search for cases through a special surveillance organization establishing contact at stated frequencies with every householder.
- 3.2 Passive search for cases through notification by patients, medical practitioners or other agencies.
- 3.3 Treatment of detected cases with suitable drugs and in appropriate dosage. The general practice consists of treatment of all fever cases without awaiting microscopic diagnosis with a single dose of 4-aminoquinolines (chloroquine or amodiaquine). In some countries pyrimethamine is also administered along with 4-aminoquinolines. In others 8-aminoquinolines are given in microscopically diagnosed cases (5-day treatment in falciparum malaria and 14-day treatment in vivax and quartan malaria). In India it is proposed to provide a five-day course with 8-aminoquinolines in all infections.
- 3.4 Epidemiological investigation of proved malaria cases with a view to determining if they are imported, sporadic, induced, introduced or indigenous.

3.5 Adoption of protective measures, including resumption of spraying when necessary, when indigenous malaria cases are discovered.

3.6 Entomological studies. In determining the frequency of visits to be made to houses in active surveillance, one has to take into account the effect of the spraying operations on the density of the vector species.

When the vector species is eradicated or nearly completely eradicated, the need for active surveillance is practically nil, except for substantiating the claim for eradication. The question of spotting autochthonous malaria cases and radically treating them does not arise. The cases of malaria will consist only of sporadic, imported or induced types. They will not be of introduced or indigenous types. The former types of infections would die out naturally even in the absence of any specific measures of treatment. Instances of such a happening should be comparatively rare although in India the only place where malaria has been eradicated also happens to be the area where the vector species has been nearly completely eradicated.

In areas where the vector species was very greatly reduced as a result of spraying operations it may have nevertheless a tendency to reappear with variable speeds after the discontinuation of spraying. The frequency of surveillance visits may be at longer intervals in the earlier stages and may need to be made at shorter intervals later on. This may be possible with the staff provided in the first instance by reason of their getting better acquainted with the local conditions; in other cases it may be necessary to appoint additional staff in the later phases of the programme. In areas where complete interruption of transmission has been effective almost solely through the mechanism of interception of the vector and without any material reduction of the vector density, the frequency of visits may have to be at shorter intervals. On the other hand, a vector species of this type usually has a very low anthropophilic index and the number of secondary cases arising in one incubation interval may be much less than in the case of vector species with a much higher anthropophilic index.

In the light of the above possibilities, the frequency of visits has to be determined by the scrutiny of the various factors involved in the basic reproduction of malaria. For present purposes, Macdonald's formula might be modified to give the average number of secondary cases which might be produced by a typical primary case in the interval between two visits. $Z = \frac{ma^2bc p^n}{\log_e p} \times \frac{1}{d}$ where d is the interval in days between two visits. The factor c has been added to Macdonald's formula to provide for the nightly turnover and some of the bites of the infective vector species which may be insufficient for the purpose of feeding proving sufficient for purposes of infection. With respect to vector species of sufficiently high vectorial capacity, the product bc may be taken to be roughly unity, and hence both the factors may be ignored.

The mosquito which alights on the skin of man may inject saliva with sporozoites, on the skin, but before it follows it up with the process of feeding it may be disturbed and it may be obliged to feed upon another man. Thus during the same night one mosquito may attempt to feed on more than one person and thus tend to infect more than one person in one night. The factor c will thus be always greater than unity, while the factor b will always be less than unity.

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- ¹ z - the reproduction rate, or number of secondary infections distributed by a single primary case
- m - the anopheline density in relation to man
- a - the average number of men bitten by one mosquito in one day
- b - the proportion of those anophelines with sporozoites in their glands which are actually infective
- p - the probability of a mosquito surviving through one whole day
- n - the time taken for completion of the extrinsic cycle
- e - the base of natural logarithms, 2.71828

(Macdonald, G. (1957) The Epidemiology and Control of Malaria, Appendix 1, p. 111)

Three illustrations are furnished below of the expansion of this formula with respect to some of the vector species in India and Ceylon for a frequency of visits of 30 days' interval and an assessment of the maximum number of secondary cases from one gametocyte carrier.

A. fluviatilis (Kanara District, Mysore State, India)

Maximum value of \underline{m} (for two-and-a-half years after discontinuance of spray - the maximum period so far observed) is 0.01. Maximum value of $\underline{a} = 0.5$ and of $\underline{p} = 0.95$ (from Dr Viswanathan's records of oocyst and sporozoite rates), $\underline{n} = 10$.

$$\underline{Z} = 0.01 \times 0.5 \times 0.5 \times 12 \times 30 = 0.9.$$

A. minimus (Assam, India and Nepal)

Maximum value of $\underline{m} = 0.05$, $\underline{p} = 0.9$ (from Viswanathan's records of oocyst and sporozoite rates in Assam), $\underline{n} = 12$. Maximum value of $\underline{a} = 0.5$.

$$\underline{Z} = 0.05 \times 0.5 \times 0.5 \times 2.7 \times 30 = 1.0.$$

A. culicifacies

Value of \underline{m} varies widely from 0.05 (Mysore State, India) to 2 or 3 or even 5 to 10; $\underline{n} = 10$. \underline{p} varies from 0.775 (Russell and Rao in Pattukottai) to 0.85 (assumed in Ceylon). \underline{a} varies from 0.025 (several parts of India to perhaps 0.15 (Ceylon).

When $\underline{m} = 0.05$)
 $\underline{a} = 0.025$) $\underline{Z} = 0.05 \times 0.025 \times 0.025 \times 0.3 \times 30$, which is very small.
 $\underline{p} = 0.775$)

There will be no autochthonous transmission and no need for surveillance.

When $\underline{m} = 0.05$)
 $\underline{a} = 0.15$) $\underline{Z} = 0.05 \times 0.15 \times 0.15 \times 1.2 \times 30$, which is also small.
 $\underline{p} = 0.85$)

When $\underline{m} = 3$)
 $\underline{a} = 0.15$) $\underline{Z} = 3 \times 0.15 \times 0.15 \times 1.2 \times 30 = 2.43$.
and $\underline{p} = 0.85$)

If the maximum limit of $\underline{Z} = 2.43$ and the average taken as 1, one month's frequency of visit will be adequate when the mosquito density in relation to man at night is 3, its anthropophilic index is 0.3, and the daily survival rate is 0.85. Naturally

if the value of \underline{m} goes up higher than 3 there will be need for more frequent visits than once a month. In India, except in epidemic regions and years, anthropophilic index is seldom as high as 0.1. Hence in culicifacies areas in India for all practical purposes once a month frequency of visits will be adequate when the value of \underline{m} is even as high as 10. (When $\underline{m} = 10$, $\underline{a} = 0.05$, $\underline{p} = 0.85$ and $\underline{n} = 10$, $\underline{Z} = 10 \times 0.5 \times 0.5 \times 1.2 \times 30 = 0.9$.) In India culicifacies appears to be greatly reduced in density after 5 or 6 years of spraying and only very low densities have so far been met with in the limited areas where spraying has been withdrawn. Hence, while one month's interval will be needed, say, about two years after discontinuance of spray, even longer intervals would prove adequate earlier.

In Ceylon, on the other hand, where there is a jungle reservoir for Anopheles culicifacies the speed of reappearance in the dry belt and the density of A. culicifacies are greater in magnitude, but even under such conditions once a month interval of visits would perhaps be adequate.

4. SURVEILLANCE ORGANIZATION

4.1 Active surveillance in the consolidation phase. The surveillance procedures should cover the entire population in the eradication area. This is essential for the detection of residual reservoirs of infection and their adequate treatment. When transmission is greatly reduced infant-parasite rates may be nil but low grade autochthonous transmission may still occur. Only house-to-house visits would help in the detection of fever cases and the determination of malaria cases among them. It is only then that residual reservoirs may be effectively treated and rendered non-infective to the local mosquitos. Only if in a total coverage indigenous malaria cases are proved to be absent would the claim for eradication be substantiated. Random sample surveys and defining confidence intervals would help in inferring eradication within the limits of probability, but they are inadequate for the purposes of radical treatment of reservoirs of infection and for a certain substantiation of eradication.

In areas with well developed rural health service the rural health service personnel may be utilized for surveillance, but they would need to be supplemented

by special surveillance staff unless the eradication service contains adequate personnel for this purpose even during the attack phase of spraying. The frequency of visits has to be determined, depending on the local epidemiology of the disease. The surveillance organization is also utilized in some countries for determining parasite rates among infants or children born after the commencement of spraying or even in older age-groups of population. In some countries it is only used for detection of fever cases by house-to-house visits, for treating them and, after microscopic confirmation, for making epidemiological investigations. The number of personnel needed would depend on the workload which may be assigned in surveillance procedures.

With poorly developed health services surveillance may need the full complement of staff to be appointed as part of the malaria eradication service either in the very beginning or when the load of transmission is greatly reduced. A staffing pattern common in some countries is one inspector for every 2000 houses with 10 000 population. It varies from 5000 to 25 000 population.

With partially developed health services the staffing pattern would vary depending on the extent of development of rural health service. The regular health staff and the special malaria surveillance staff should together be sufficient to provide one surveillance agent for every 10 000 population.

4.2 Passive surveillance in the consolidation phase. A passive search for cases will be facilitated by the co-operation of hospitals, dispensaries, private practitioners, voluntary agents and by patients themselves notifying malaria cases. This has the advantage that the responsibility is thrown on the householder to notify fever and take treatment which he will observe every day if his health consciousness is stimulated. In active surveillance the householder will await the personnel's visit and the treatment will follow the visit.

Passive surveillance may be logical and sensible as a permanent measure for getting information on fever cases and through them on malaria cases. During the phase of maintenance passive surveillance would perhaps be the only feasible measure, but whether epidemiologically speaking passive surveillance would be satisfactory in the consolidation phase depends upon the degree of public

consciousness, the number of passive surveillance agents and the efficiency with which they operate.

Essential differences between eradication and control depend on the totality of coverage, the efficiency of coverage and the speed of coverage of spraying operations; the same applies to the phase of surveillance in which it is important to have total coverage, efficient coverage and speedy coverage. Passive surveillance cannot lend itself to a full accomplishment of these factors in the race against time that malaria eradication procedures have to provide for.

Central and regional organizations are of utmost importance. There should be a regional laboratory and an epidemiological service. In some countries for every ten surveillance personnel there is a doctor for supervision and epidemiological investigation. He is assisted by a technician. After successful residual spraying programmes there are in some countries 20 to 40 fever cases per 1000 population in a year. A technician should be capable of handling about 40 to 50 slides per day or about 20 000 to 15 000 slides per year.

There should thus be one technician for every 30 to 40 surveillance personnel each detecting about 400 fever cases per year if the technician has no other blood examinations to do. Where technicians are provided on a more liberal scale they also carry out mass blood examinations (not limited to fever cases) in representative areas. The work of the regional laboratory should be test-checked at the central laboratory. Likewise regional epidemiological investigations should be scrutinized by the central organization. Further, the central organization may have a mobile investigation team to study problem areas or to test-check the surveillance procedures in the field. Checks by central and regional organizations by mass parasitological surveys are particularly necessary in passive surveillance. Even in active surveillance, which is confined to the examination of fever cases, they serve as a useful check on the efficiency of detection of malaria parasite carriers. In epidemic areas the central organization should continue to have entomological units to make entomological assessment after the discontinuance of the special surveillance staff two or three years after withdrawal of spraying.

4.3 Maintenance phase. On the conclusion of the consolidation phase two or three years after the withdrawal of spraying, surveillance which would need to be continued for all time as in other communicable diseases may be entrusted to the regular health staff. The malaria surveillance personnel, by reason of their proved service and popularity with the people, may well form the nucleus of rural health services, in areas where such services are under-developed. There will thus be continuity of efficiency in malaria surveillance and development of multi-purpose health services.

4.4 Surveillance during the attack phase. The organization described above during the consolidation phase will be established during the last year of the attack phase when surveillance will be concurrent with spraying. Indeed, in countries where it is considered necessary to provide surveillance operations right at the beginning of the attack phase in order to provide for better supervision of spraying and to get well-trained in surveillance, the organization described under consolidation may be introduced right at the beginning of the attack phase itself. During the course of training in certain areas the staff may be engaged in two directions. The first will be the post-operational evaluation in indicator districts in order to study the rate of descent of malaria transmission. In these indicator districts such work may also be combined with the organization of surveillance procedures. Until well-trained, the latter cannot be expected to be well-organized.

The routine malarimetric data however could be more easily compiled to give in a rough way evidence of the rate of descent of malaria transmission. With such evidence the results of surveillance procedures during the training period may be compared. Later however when surveillance procedures are well established they will be far more sensitive and the compilation of routine malarimetric data in the indicator districts would no longer be necessary.

5. SPECIAL STUDIES IN SURVEILLANCE

As surveillance is a relatively new concept, its procedures are often empirical. However completely medical institutions may diagnose and report malaria cases they will only form a small or large proportion of the totality of malaria prevalent in

the country. Some special studies seem essential in order to determine the nature and pattern of surveillance procedures. These may include the following investigations:

(1) The most feasible procedure for detecting all reservoirs of infection. Would house-to-house visiting inquiring about the history of fevers reveal all reservoirs? Some reservoirs may be symptom free on account of a persistence of 'antitoxic' immunity and hence fail to be detected as a 'fever' case. Would repeated visits find them with febrile symptoms at some stage? Would they, in the meantime engender any secondary cases in the absence of spraying operations? Or, on account of the persistence of immunity, would their gametocyte load and their role of infectivity be small? If not, would mass microscopic examinations be necessary or would an examination of children born in the post-operative period and fever cases be adequate? Whatever answers to these questions could be furnished in theory, the problems will not be settled otherwise than by practical pilot experiments in the field.

(2) The extent of fever morbidity after malaria has been almost completely eliminated and the proportion of malaria under different pre-eradication epidemiological conditions. The former would determine the load of microscopic examination and the quantities of antimalarial drugs needed.

(3) The most effective means of approach to householders. Would the supply of a few simple drugs for treating minor ailments improve the efficiency of surveillance in countries with practically no rural medical aid?

(4) The most effective organization at the centre and in the regions for laboratory service in order to furnish results of blood examination in the shortest period of time. What is the role of mobile microscopy using McArthur's portable microscope? How to ensure efficient blood examination when a very large proportion of the slides will be negative? (Dr Gabaldon has suggested the introduction of P. berghei into the slides so that the microscopists have to find a few known positives among the slides examined each day.) Some workers find girl microscopists more conscientious in their work than men.

(5) Simple but adequate methods of recording and reporting.

(6) Maximum period up to which parasitaemia may be allowed to continue before radical treatment is given and the frequency of visits absolutely essential in order to be able to spot reservoirs and treat them before they become effectively infective: this may vary under different pre-existing epidemiological conditions.

(7) Correlation of primary "cases" (reservoirs of infection) with secondary cases under different epidemiological conditions such as (a) unaffected vector densities and achievement of interruption of malaria by interception of the vector, (b) vector densities returning to prespraying levels in areas where spraying has brought about reduction of vector species and its withdrawal is followed by increasing density, (c) man-biting frequency, (d) daily survival rate, and (e) nocturnal turnover of the vector species. These factors have a great bearing on the adoption of suitable measures including resumption of spraying when indigenous malaria is found to occur. The basic reproduction rate depending on the above factors and the usual period of malaria transmission in a year would determine when spraying would need to be resumed. The minimal time between primary and secondary cases in falciparum and vivax malaria (about 4 to 5 weeks in the former and about 3 weeks in the latter) has to be correlated with the mosquito factors and the usual period of transmission. When the season of transmission is short the theory of reproduction of malaria after its near-complete elimination would perhaps render resumption of spraying needless and treatment of primary 'cases' would consolidate and maintain eradication. When the season is prolonged the speed of onset of secondary cases is important. In low-grade transmission it may be sufficient to intensify treatment procedures without resuming spraying except, perhaps, locally. In higher grades of transmission resumption of spraying may become necessary. Whatever the initial speed of onset, in all grades sooner or later a substantial proportion of the people may be affected and hence the need for adoption of suitable measures at the appropriate time. What this appropriate time is would need to be determined for each area with its known epidemiology.

(8) Significance of enlarged spleens found in surveillance. A casual enlarged spleen found during surveillance may be the result of repeated persplenitis on account of attacks of malaria acquired in the pre-spraying period or in the earlier part of the attack phase and the inability of the spleen to revert to its original size. Such a condition may or may not be attended with parasitaemia. Even if it is attended with parasitaemia, there would be a fair amount of immunity with the result that the gametocyte output will be relatively small and the infective role of the reservoir will also be small. In such cases, while treatment of the individual may be desirable and necessary, drug treatment of the contacts in the same house or in neighbouring houses would not serve any useful purpose. Enlarged spleens with parasitaemia may also occur among imported cases. For them too, of course, only individual treatment would be called for. The third type of enlarged spleen detected during surveillance may reflect some transmission in the recent past, but this will be even better indicated in the morbidity survey that will form part of surveillance procedures.

6. SURVEILLANCE AND LEGISLATION

Legislation may be needed in some countries to cover (a) entry of surveillance personnel into houses to make inquiries, (b) taking of blood slides from fever cases and (c) notification of malaria cases. Legal provision for (a) and (b) exists in some countries and executive instructions regulate notification from medical institutions. No law will be of any avail if it cannot be effectively implemented and governments may be chary of legislating if there is a danger of the legal process being held to ridicule on account of impossibility of implementing it. On the other hand, a law need not necessarily be implemented through a court process. The threat implied in an issue of legal notices may itself secure compliance. In urban areas and in most countries in rural areas with well-developed health services, such legislation may be desirable and fruitful.

7. SURVEILLANCE AND MOVEMENT OF POPULATION

Surveillance of unstable populations is a different problem. In some areas provision is made for treatment outposts on the boundaries of eradication areas to treat all nomads with 4-aminoquinolines and pyrimethamine. Their blood is taken for examination but treatment is provided without awaiting the result, and entry into the eradication area is allowed. In large-scale engineering works or congregations as in fairs and festivals in eradication areas, in addition to surveillance, residual spraying is continued even after complete interruption to prevent the hazard of introduced malaria.

8. INTERNATIONAL ASPECTS OF SURVEILLANCE

There can be no restriction on movement of individuals but where large groups immigrate into a country for pleasure, business, work, or to attend religious or other large gatherings, blanket treatment and adequate local spraying of insecticides to prevent introduced malaria would be advisable. When malaria is eradicated in a country its borders are not safe unless on the other side malaria is either absent, eradicated or under eradication. Regulation of movement of population is not feasible though desirable. The only effective safeguard is establishment of eradication procedures on both sides either by direct negotiation between the countries or with international assistance. The introduction of a non-indigenous vector species refractory to insecticides may endanger the successful completion of an eradication programme. Likewise, the introduction of infective anophelines from across the border may result in a small epidemic though such a chance is generally small. Facilities should be made available for the free, full and frequent exchange of epidemiological information and of reports on the progress of the eradication programmes. In all these matters WHO can play a most useful part.