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ADVISORY GROUP ON MALARIA ERADICATION STRATEGY

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THE GENESIS AND THE DEVELOPMENT OF MALARIA ERADICATION

1. A global problem

Malaria, though now principally a disease of the tropical and sub-tropical areas of the world, has existed in the vast majority of countries from north-west Russia to southern Argentina. Within the last half-century, it has been endemic in areas inhabited by over two-thirds of the world's population (i.e. estimated at 2400 million out of 3400 million in 1966). Twenty years ago it was estimated that some 300 million people suffered from clinical attacks of the disease each year and that the disease caused directly about 3 million deaths annually.

Despite the high figure of annual deaths, and though it is often a major cause of infant mortality, particularly in highly endemic areas, the importance of malaria consists mainly in the chronic invalidism it produces in the rural populations. It leads to an increased number of deaths from other causes and impairs physical and mental development. Wherever it has existed, human progress has been inhibited and the country's development retarded. The utilization of many potentially fertile areas of the world had been barred by its presence; other areas, in which human activities had encouraged the breeding of the vector anopheline mosquitos, had to be abandoned.

2. Malaria control

From the beginning of the century various attempts had been made in many countries to control malaria. The methods available during the first four decades however, depended mainly on expensive permanent measures to prevent mosquito

breeding or repetitive measures such as larviciding. These could only be employed in relatively confined urban areas or for special population groups in rural areas where economic or considerations could support their use; they rarely offered hope of a final solution and needed to be continued indefinitely. Control of malaria in rural areas was, therefore, beyond the economic capacity of countries and territories in the tropics.

The advent of residual insecticides, especially DDT, and the experience gained in its large-scale use, during the Second World War, have provided new possibilities for the control of vector-borne diseases. These new advances meant that widespread rural populations could now benefit. The value of residual insecticides in this connexion was rapidly appreciated by a number of governments and they were introduced by enthusiastic public health workers for wide-scale malaria control operations in such countries as Ceylon, Greece, Guyana, India, Italy, Mauritius, USSR, United States of America and Venezuela.

Although certain synthetic antimalarials had been produced in the second and third decades of this century, their value was not fully recognized until quinine became in short supply during the Second World War. At this time extensive research was undertaken and a number of additional useful antimalaria compounds were developed. These various suppressive and curative compounds provided complementary control methods with the residual insecticides.

3. The World Health Organization and malaria control

The World Health Organization had inherited a long tradition of international co-operation in the fight against malaria going back to the establishment of the Pan American Sanitary Bureau in 1902 and to the Malaria Commission of the League of Nations. As was to be expected, therefore, the importance of the public health problem of malaria and the need to give antimalaria activities priority were recognized from the inception in 1946 of the Interim Commission of WHO. The first World Health Assembly in July 1948 based on the recommendations of the Expert Committee on Malaria of the Interim Commission, decided to provide malaria control demonstration teams to

countries requesting such assistance. DDT residual spraying was the main method of control recommended. By the end of 1949, seven malaria control demonstration teams were in operation in different parts of Asia.

4. Evolution of the concept of malaria eradication

At this time the employment of these insecticides was considered generally as an advanced method of control and as with any other method their continued use year by year was envisaged. However, experience in Venezuela, one of the earliest large-scale antimalaria operations using residual insecticides in rural areas, and in Ceylon, Guyana, India and Italy soon indicated that eradication of malaria could be achieved even without the complete extermination of the vector, by ensuring, through residual insecticides, that the infected mosquitos were killed off before their developing infection reached the stage when it could be passed on to man.[1]

With transmission halted for a period of about three years most of the parasite reservoir in man would die out even without treatment and the remaining parasitaemia could be eliminated by treatment, including those cases of the longer-living *Plasmodium malaria* which, however, has only a limited infective potentiality. Hence malaria could be eliminated even without attempting actual eradication of the vector mosquito.

Confirmation of this concept was fortuitously provided in Greece where residual insecticide spraying had been applied each year since 1946. In 1951, due to shortage of DDT, it was decided to withhold spraying in the islands of Crete and the Peloponnese where, according to the evidence, transmission had been interrupted by the end of 1949. In Crete, a system of public health vigilance introduced to find malaria cases, showed no indigenous cases - thus proving that if transmission was fully interrupted for a few years, spraying could be withheld without indigenous malaria reoccurring.

On the basis of these experiences from different parts of the world, was born the concept of a time-limited programme of completely eliminating malaria. Such a programme could now be undertaken over the rural areas, where the disease was of the highest public

[1] During this period, normally of about 12 days, between the female mosquito becoming infected and the malaria parasites reaching the stage when they can be passed on to man, the insect takes blood meals at two or three day intervals and on each occasion is likely to rest on the walls of the house.

health importance, as a capital investment and not a permanently recurring cost. It would not only have the benefit of reducing human suffering by eliminating the heavy burden of malaria deaths and sickness, but also make available the man-power needed for developing agricultural land in many of the tropical and subtropical areas of the world.

5. Vector resistance to insecticides

In 1951, the development of resistance of the vector Anopheles sacharovi to DDT was reported in Greece which reinforced the desirability of adopting a time-limited approach to eradication of malaria and demonstrated that the residual insecticides could not be depended on to continue their effectiveness indefinitely. Confirmation that this phenomenon was not an isolated instance became evident when the same condition was reported in Anopheles quadrimaculatus in the United States of America and soon other reports from various parts of the world showed that it was likely to become widespread. With the danger of resistance developing it was obvious that the larger the area in which eradication techniques could be effectively adopted as rapidly as possible the greater and more rapid would be the success of eliminating the disease on a wide basis and preventing its re-establishment. It is against the background of these factors that in October 1954, the Fourteenth Pan American Sanitary Conference in Santiago, Chile, stressed the danger of prolonged control programmes with the consequent hazard of the development of resistant strains of Anopheles and emphasized the urgency in achieving the eradication of malaria by converting all control programmes into eradication programmes. In November 1954, it was recommended in a formal resolution at the Second Asian Malaria Conference at Baguio, Philippines, that the ultimate goal of a nation-wide malaria control programme be eradication of the disease. The following year in Mexico, the Eighth World Health Assembly resolved that the Organization should take the initiative to provide technical advice and co-ordinate resources in the implementation of a programme having as its objective the world-wide eradication of malaria.[1]

For this large-scale expansion of activities, the Eighth World Health Assembly established a Malaria Eradication Special Account to receive voluntary contributions in cash and kind. Later the major part of the Organization's assistance to the

[1] WHA 8.30.

malaria eradication programme was incorporated within the regular budget. Up to the end of December 1967 it is estimated that the Organization will have expended over US$ 85 million on the malaria eradication programme including funds made available through the United Nations Expanded Programme for Technical Assistance. During the same period UNICEF has provided supplies and equipment to a large number of programmes to a value of over US$ 60 million.

6. Malaria eradication

Thus the Organization became instrumental in stimulating and guiding the most extensive public health operation ever undertaken. In developing the methodology for malaria eradication all the methods then available, including chemotherapy and larviciding, were considered and it was recommended that residual insecticides would be the main instrument in the attack against malaria not only on the grounds of efficiency, but also for economic reasons. Malaria, poverty and lack of development are inseparables in the rural tropics. The regular administration of antimalarial drugs over a period of time to rural communities not only demands an elaborate organization beyond the capacity of most of the countries concerned, but even the acceptance of the drug regimens for the duration of eradication is difficult to ensure. Prevention of mosquito breeding by attacking the larval forms in water is generally impracticable in rural areas and it becomes more expensive per person the lower the population density. In contrast, the use of DDT as a house spray, once or twice a year, demands a comparatively small mobile organization, while its cost, which depends on the number of houses to be sprayed does not vary substantially in most instances with the population density.

7. Review of methods and criteria of malaria eradication

7.1 Formative principles

On the basis of experience developed in the several countrywide malaria eradication programmes then in operation the WHO Expert Committee on Malaria in 1956 laid down the principles and practice of malaria eradication which it defined as the ending of transmission of malaria and the elimination of infected cases in a campaign limited in time and carried out to such a degree of perfection that, when it comes to

an end, there is no resumption of transmission.[1] This Committee emphasized the need to plan the whole programme on a total coverage basis throughout its eight to ten year duration in four phases, preparation, attack, consolidation and maintenance.[2]

Total coverage, in the preparatory phase involved a reconnaissance of all malarious territory, the mapping and numbering of all housing units to be sprayed; in the attack phase it meant the periodic spraying of every house, in such a way that the inner walls remained lethal to mosquitos during the whole transmission season, requiring spraying operations to be carried out at the appropriate time in a highly efficient manner. Only by such a total coverage in space, time and quality could the necessary degree of perfection be attained indispensible for interruption of transmission, the essential basis for eradication of the disease.

Year by year, as experience of the eradication programme accumulated, the methodology recommended was reviewed and continuously adapted to the needs. Initially, in the general enthusiasm for this vast public health task, and in many instances encouraged by the dramatic results of their large-scale control operations, a number of countries adopted the concept of eradication without the necessary detailed planning or assurance of resources to cover the whole duration of the programme.

Recommendations were, therefore, made for the minimum conditions which should be fulfilled before a malaria eradication programme received the technical approval of the Organization.

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[1] Wld Hlth Org. techn. Rep. Ser. (1957) 123

[2] Preparatory - the time devoted to preparation for attack operations and includes the completion of the epidemiological and geographical reconnaissance, establishment of services and training of staff; attack - during which antimalarial measures aimed at interrupting transmission are applied on a total coverage basis throughout the operational area; consolidation - follows the attack phase, is characterized by active, intense and complete surveillance with the object of eliminating any remaining infections and proving eradication of malaria; maintenance - the period which begins when the criteria of malaria eradication are met in an operational area and which will continue until world-wide eradication has been achieved. (Vide Terminology of Malaria and of Malaria Eradication, 1963, World Health Organization, Geneva).

7.2 Training

In the field of training two aspects were covered - the training of national staff and that of the international advisers. The traditional procedure for recruiting the latter category had been to seek them among leading professionals of the national services. However, the rapid expansion of the malaria eradication programme demanded such a considerable number of specialized personnel to reinforce the national staff that specific provision had to be made to train these advisers in the techniques of malaria eradication.

Training of national staff has been carried out at two levels, within the country and abroad. The more senior categories of staff, responsible for the planning, top supervision and assessment of the programme, were in general trained at international centres, while the lower supervisory and junior grades of staff were trained within their own country. International malaria eradication training centres were established by the Organization to meet the special programme needs for training of the higher categories of staff, both international and national and well over 2000 have received training at these centres. At the national training centres many times this number were instructed in the principles and practice of malaria eradication.

Initially with the very large numbers requiring training courses could not be highly specialized but as the programme developed special courses were given particularly to medical officers to enable them to acquire a deeper knowledge of the epidemiology of malaria in order to enable them to deal with technical problems which arose.

7.3 Surveillance and evaluation

Although the need for a system of surveillance was recognized when the global eradication programme was launched, it was not until 1960 that its detailed methodology was developed and the full extent of the operations required realized.

As for spraying operations, a surveillance mechanism must also be based on total coverage, both in time and space, to discover, investigate and eliminate continuing transmission and the parasite reservoir and to provide the data for the substantiation of interruption of transmission and of eradication.

As most of the endemic areas of the world, where eradication was undertaken, did not have rural health services covering the entire population it was necessary to organize an extensive surveillance machinery consisting of a case detection system with a dynamic element whereby every household was visited at periodic intervals and a static element through health institutions and voluntary collaborators in each community to provide facilities for treatment and blood examination of every fever case.

While the necessary personnel, equipment and facilities for undertaking the spraying operations were provided for by most governments embarking on malaria eradication, in many instances, the organization needed for surveillance was not fully foreseen. This has led to serious difficulties in deciding on the appropriate time for the withdrawal of spraying, which has to be based on data obtained through an adequate surveillance machinery. Consequently some spraying operations were terminated prematurely and transmission of malaria became re-established in the absence of adequate case detection and ensuing remedial action through an efficient surveillance organization. Thus the defects in planning and organization led to inevitable technical reverses in some programmes. In others, as the best expedient, spraying operations had to be prolonged as a precautionary measure until the surveillance mechanism could be fully established.

The epidemiological standards for withdrawal of spraying and for confirmation of eradication of malaria were first laid down in 1960, but these standards were revised in the light of experience accumulated in the field. The progress of individual eradication projects can now be assessed in a more critical way, not only in order to determine the appropriate time when individual areas can safely be assigned to a more advanced phase of the programme, but also, even in the early years of the attack operations, it is possible to foresee when a programme is not going according to plan with the methods of attack being used and remedial action can be promptly taken.

Frequent use is made of an external audit system whereby experienced assessors unconnected with the execution of the programme in the particular country carry out this type of evaluation.

7.4 Participation of the general health services

Initially much emphasis was placed on the development of national malaria eradication services with a semi-autonomous status within the health framework of the country. Such a status was considered necessary in many programmes during their

early stages to ensure the rapid evolution and operational efficiency of the mass campaign. Unfortunately in some instances due to the autonomous nature of the eradication programme there was lack of co-ordination and co-operation between the general public health services and the malaria eradication services. The need for the close involvement of the public health services in providing the static element in surveillance operations has already been mentioned. There must also be a co-ordinated and concurrent development of these services so that they may be capable of taking over the responsibility for vigilance operations, after eradication of malaria has been achieved, to prevent its re-establishment. Frequently this concurrent development did not take place. It therefore became apparent that before a programme started, firm plans must be made and resources be available to ensure that the health services would have the required coverage during the later stages of the attack phase to assist adequately in case detection operations and that, by the end of the consolidation phase, would have developed sufficiently to undertake the whole vigilance needed to prevent re-establishment of malaria. Hence greater emphasis is now laid on the role of general public health services of a country in the malaria eradication programme from its inception and particular attention is paid to ensure that the plan of operations for the malaria eradication programme fits into the health sector of the over-all national socio-economic plan.

7.5 Laboratory services

In the eradication programme, proof of the disappearance of malaria is basically dependent on the examination of blood slides in the laboratory. Thousands of slides are examined, none of which may contain parasites, yet each occasional positive blood slide must be spotted. In order to secure a higher degree of accuracy, the cross checking of all positive slides and 10 per cent. of negative slides in a separate laboratory is now standard practice. Standard techniques are laid down for the preparation and processing of blood slides. Similarly, field practices and techniques in entomology have also been improved and modified in the light of experience. Working manuals in blood examination, entomology and in other technical operations have been prepared and made available to national programmes. In order to ensure understanding of particular terms employed in malariology by the thousands of workers on the subject in different parts of the world, a standardized terminology in English, French, Spanish and Russian was issued.

7.6 Inter-country co-ordination

One of the causes of prolongations of programmes has been their unequal development in neighbouring countries with common epidemiological features, whereby the more advanced programmes must continue attack activities in border areas until the contiguous country reaches the same stage. In Europe in 1959 this was successfully overcome by a co-ordinated plan with a target date set for all to reach the consolidation phase in the same year - by 1963. A similar plan covering the Common Market Countries of Central America and Panama has not been fully implemented due, until recently, to lack of resources. Elsewhere inter-country co-ordination has been encouraged by the arranging at regular intervals of what are termed border meetings between neighbouring countries.

7.7 Pre-eradication programmes

For areas where it was not feasible, under the conditions obtaining, to undertake malaria eradication, pre-eradication programmes have been developed with the over-all objective of gradually building up the technical, administrative and operational facilities for the eventual launching of a full scale malaria eradication programme. This was originally intended to provide the stimulation and concurrent development of the necessary basic foundations for such a programme, namely the health infrastructure and the malaria service. A subsidiary but immediate objective was the institution of appropriate anti-malarial measures to reduce malaria mortality and morbidity, particularly in children. These programmes were brought into operation particularly in Africa where little progress had been made in the eradication of malaria.

There is no doubt that malaria is a most important communicable disease in Africa and that its ultimate eradication from the continent is desirable for the benefit and well-being of its peoples, and also to lessen the hazard of the disease to other countries by the elimination of the vast reservoirs of malaria infection. However, in the savannah areas of this continent, in addition to the administrative and operational difficulties, a practical method of interrupting transmission of malaria has not yet been found.

Since the inception of this type of programme in 1960, only three countries have in fact advanced from pre-eradication to an eradication programme, none of these being in tropical Africa. Field experience, has in general proved that the concurrent development of the malaria service and the basic health service is impractical due to shortage of suitable man-power and limitations in financial resources in the countries concerned. In many countries the peripheral and intermediate echelons of the basic health service will need to be built up almost ab initio on a countrywide scale involving large capital and recurrent costs and a long-term training programme.

Thus, it has become necessary to devote more time and effort to the development of basic health services and for the most part limit antimalarial measures to the provision of treatment to sufferers from the disease. However, ultimately external and national resources must be made available to introduce the public health measures needed to overcome malaria in Africa.

8. Technical problems and approaches to their solution

8.1 Problem areas

In a biological programme of such complexity as malaria eradication, it could not be expected that the use of the single attack measure of spraying of residual insecticides, even where resistance of the vector mosquito was not a problem, would be applicable or continue to be applicable in all situations. The need was early recognized for adapting the methods of attack to suit local epidemiological factors relating to man, the mosquito and the parasite. A constant search was made for alternative methods to be used where necessary either in conjunction with spraying operations or alone.

It has, for example, been found in certain areas that despite total, complete, regular and sufficient coverage with residual insecticides transmission of malaria persists. Such areas have been called problem areas and although sensu stricto their extent is limited to about one per cent. of the total population under the eradication programme, they are of considerable significance as sources of imported malaria into areas already freed from the disease and have an operational and psychological importance out of proportion to their extent. The factors responsible for the existence of these areas are mainly related to the resistance of the anopheline

vector and to extra-domiciliary transmission related to the habits of man or the mosquito. These problem areas persist when the means available for tackling them are inadequate and the problem may frequently be overcome by using a combination of known and well-tried attack measures, properly carried out under adequate supervision.

In order to overcome the problem of resistance of the mosquito to the commonly employed insecticides, a programme for testing and screening of new residual insecticides in a series of collaborative laboratories and by field trials was instituted in 1960 and later, other types of imagicides and larvicides were tested in this programme. Through this activity over 1300 compounds have been screened and as a result alternative insecticides are now available for use against the adult and larval forms of the mosquito in certain special situations. However, none of the newer residual insecticides have the wide range of applicability of DDT with its relatively low cost, long residual action and relative non-toxicity to man.

8.2 Complementary use of chemotherapy

A number of years ago, in 1958, it was recommended that, while essential in the consolidation phase as a curative measure, drugs could also be employed during the attack phase as a complementary measure to reduce the parasite load of the community and hasten the interruption of transmission. Alone, mass drug administration using tablets has not, in general, proved feasible due to the frequency of dosage, the extent of coverage of the populations required and the elaborate organization needed. However, antimalarial drugs incorporated in a fundamental food element such as salt have proved their value in certain communities where spraying operations may be impracticable due to the topography of the country of habits of the people, as in the hinterland of Guyana and among nomadic populations in Iran.

Although the employment of drugs at an effective dosage within an eradication programme as a complementary attack measure has proved its worth, the development of resistance of some strains of Plasmodium falciparum to the commonly used aminoquinoline drugs in parts of South America and South East Asia limits to some extent the scope of their use in these areas.

The differing responses of strains of parasites and of people to antimalarial drugs has been recognized for many years since it was originally reported with quinine in the last century, but it was not until 1960 that resistance of the falciparum parasite to chloroquine was first observed. A methodology has been developed for assessing the degree of resistance found and alternative treatment schedules are available. It should be emphasized that the best available means to prevent the spread of drug resistance is to ensure that measures to interrupt transmission should receive the highest priority.

8.3 Research

As technical problems have arisen, research has been stimulated to overcome them. With the development of the malaria eradication programme, a changing emphasis on various aspects of research is obvious. In the early years of the programme, the Organization focused its main attention on the technical aspects of application of residual insecticides, the assessment of the duration of activity of various formulations, the absorptive action of surfaces on which the insecticides were sprayed and the development of efficient spraying equipment.

Later, attention was given to studies on the resistance of malaria vectors to residual insecticides and the development of a standardized technique for assessment of vector susceptibility. More recently there has been increasing interest in the quantitative epidemiology of malaria, in the epidemiology of disappearing malaria, in new immunological techniques that might be valuable for case detection, in genetic aspects of malaria infection in man, in the vectorial capacity of Anopheles, in genetic studies on systematics of Anopheles and on their pattern of response to insecticides. Development of resistance of malaria parasites to 4-aminoquinolines had led to a considerable programme of research in searching for new drugs and in standardizing the laboratory screening of potential antimalarials. Field research for developing a method of interruption of transmission in savannah areas of Africa by combined use of insecticides and drugs is now in progress.

Since 1957 well over 200 research agreements have been made by the Organization with institutes and over the last three years an average of 40 agreements per year have been made.

9. Administrative and operational difficulties

Under the very diverse administrative and operational factors affecting most of the malarious countries, only a few could adhere to the original time targets set in their eradication plans and delays and setbacks occurred causing disappointment and concern to the government and to the assisting agencies. These delays have added to the problem of sustaining the national interest in the programme.

Many of the setbacks were aggravated by the lack of flexibility in the government's financial regulations which delayed the tackling of problems immediately they occurred. Few administrative departments of governments realize the importance of timing in funding, provision of supplies and spraying - delays of a few weeks can adversely affect the long-term programme targets.

Frequently when the incidence of the disease has been brought down to a low level, funds for the programme are reduced and inevitably further outbreaks occur. It is thus essential to keep alive the spirit of the combat against the disease until it has been eradicated.

10. Present status of the programme (see map in A20/P&B/1, page 6)

In 1958, in areas with about 280 million, it was considered that the disease had been eradicated and a further 60 million people were said to be free from the risk of endemic malaria. By the end of September 1967, out of the 1670 million people living in the originally malarious areas regarding which information is available, (excluding mainland China, North Korea and North Viet-Nam) over 1000 million live in areas now freed from the risk of endemic malaria and a further 240 million are benefiting from programmes under attack operations (Figure 1). The population of areas in which the Organization has assisted programmes amounts to just under 1000 million and pre-eradication programmes in areas with another 190 million people have also been supported by the Organization. Out of the 34 countries where eradication of malaria is reported to have been obtained, 10 have been entered in the WHO Official Register of areas where malaria eradication has been achieved. In addition there are 18 other countries still undertaking eradication programmes which already have areas with a population of over 470 million in the maintenance phase.

11. Prospects

However, the rate of progress in respect of malaria eradication is slowing down due to difficulties experienced in developing new programmes, amongst the 400 million people needing them. Other difficulties, mainly administrative and financial, are hampering further progress in some of the countries which have embarked on malaria eradication programmes.

The day when global eradication of malaria will become a reality is dependent not only on technical considerations, but to an even greater extent on the availability of resources and facilities and the ability of countries to build up effective rural health services to sustain the eradication of the disease. In many instances, particularly in Africa, the competing demands for the limited national resources of men and materials by operations vital to the national interest make it at present unrealistic to expect adequate priority to be given to malaria eradication even where the disease is the most important problem. Massive external assistance is therefore needed to build up the health services required for the systematic control and eventual eradication of malaria. Nevertheless such external assistance can never be completely a substitute for a country's resources. Ultimate success will depend on the national conviction that the eradication of malaria is an urgent need for the benefit of its peoples and its economy.

FIGURE 1

CHANGES IN THE DISTRIBUTION OF POPULATION IN THE ORIGINALLY MALARIOUS AREAS OF THE WORLD BY PHASE OF MALARIA ERADICATION BETWEEN 1958 AND 1967