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EPIDEMIOLOGICAL ASPECTS OF MALARIA ERADICATION IN THE EASTERN MEDITERRANEAN REGION

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### I INTRODUCTION

Species of plasmodia causing malaria of <u>homo sapiens</u> have adopted such a chain of feeding in their parasitic life, probably since the early development of man, that this scourge has accompanied mankind throughout known history. With their specific relationship to the host, plasmodia have proved that on the scale of phylogenetic development they have advanced a step further, which at the same time affords proof of their very long-standing development into the species we know today.

It is well-known that malaria as a disease is widely distributed on our planet and that half of the world population of today was originally exposed to the risk of infection. The only reason that plasmodia have not become a cosmopolitan species lies in the fact that the sexual cycle of development in the definite host-anopheline mosquitoes requires, first, the presence and maintenance of anophelines, and second, favourable temperature of the environment for the completion of the sporogonic cycle.

There are many written documents to be found throughout the recorded history of mankind mentioning malaria allegorically, as it was understood by contemporaries of the period when the observations were made. On the basis of such documents, Celli a well-known Italian malariologist, made an epidemiological assessment of malaria at the beginning of this century in Campagna Romana, at a time when secular waves of epidemics of malaria were, on the one hand, causing misery to the population and, on the other hand, giving rise to prosperity in agriculture during the periods without epidemics of malaria.

It is generally accepted that malaria reached its climax in Europe in the middle of the Eighteenth Century, and since then malaria has followed a trend of epidemiological declination towards disappearance. In other words, little by little malaria has been losing grounds formerly conquered. A similar observation was made in relation to the North American continent since the Civil War. This natural disappearance of malaria was caused primarily by the change in the behaviour of mankind, and in Europe it somehow coincided with the era when man adopted two new things in his life: first, to invent a bed to sleep on instead of lying on the floor, and second, to separate himself from his domestic animals, constructing separate shelters for them. The natural disappearance of malaria, however, as would be the case with any other disease, is a slow process, and it is therefore necessary for man to undertake artificial measures to accelerate its final disappearance.

During the period from 1881 - when plasmodium was discovered by C.A. Laveran - until 1939, when the insecticidal effect of Dichlorodiphenyl trichloroethane (DDT) was learnt, many facts - biological and epidemiological - were made known. But in spite of the fact that our knowledge has increased tremendously regarding plasmodia, their life-cycle in man and mosquito, the pathologic alteration of human tissue and the possibilities for controlling the disease, today we still need more knowledge regarding the epidemiology of malaria in different parts of the world.

### II MALARIA ERADICATION CAMPAIGNS

### 1. The Concept of Eradication and the Global Malaria Eradication Campaign

The concept of the eradication of a communicable or transmissible (arthropodborne) disease is based on the feasibility of interrupting contact or transmission between an infected (germ-carrier) and non-infected human being (recipient), and then in the absence of continuing transmission to clear up the parasite (germ) reservoir persisting in man. Many elements are to be known concerning the parasite (germ) and the man (the host), and also concerning the vector if a transmissible disease is involved, before the eradication of a disease can be declared feasible. This is why, in spite of the tremendous advancement in medical science today, we are still not in a position to embark on the eradication of all communicable diseases because we do not have the means by which we can make it feasible. In addition to this, there are germs parasitizing man and animals (domestic and wild), which can complete their life cycle either through man, within human society, or separately in open nature (natural focus of disease). In the latter case the danger of failure to eradicate such a disease will persist either because man may enter the focus of the infection and become infected or the infected animals may bring the germ into human dwellings, thus presenting possibilities for the renewed and subsequently continued infection of man. A classical example is sylvatic yellow fever: while in South America man enters the natural focus of yellow fever, in West Africa the infected monkeys visit human dwellings where they are bitten by <u>Aedes simpsoni</u> who in turn become infected and transmit the virus to man.

As far as malaria is concerned, experience gained in some ten years of the application of synthetized insecticides with residual effect has shown that transmission of malaria can be interrupted. Indeed, insecticides with

residual effect are meant to affect the sporogonic cycle of the development of plasmodia. As is well known, if the sporogonic cycle cannot be completed, then transmission of malaria is impossible; thus the first basic requirement in the concept of eradication is achieved. To satisfy the second part of the concept, i.e. to clear up the parasite reservoir, there are two possibilities: first, to keep the human population free from transmission for a period of three to five years, which period corresponds in general to the natural longevity of infection of plasmodia in a human body; and second, to accelerate the disappearance of the parasite reservoir by administering antimalarial drugs of radical effect to all known parasite carriers. As soon as the feasibility of such a procedure was demonstrated, the concept for and criteria of malaria eradication were laid down. Subsequently, the Eighth World Health Assembly, held in Mexico in 1955, declared the intention to embark on a global campaign for the eradication of malaria. Today, just one decade after the historic resolution was passed in respect of malaria eradication, it is to be noted that over 800 million people originally exposed to the risk of malaria infection are now free from that risk, which proves the feasibility of the whole enterprise of eradication of malaria.

# 2. Epidemiological Considerations in a Malaria Eradication Campaign

Celli was the first who, in 1925, described his observations on a typical variation of the seasonal trend of a malaria epidemic under natural conditions, in respect of geographical position and climatic conditions of a Thus, according to Celli there were three types of malaria epigiven area. demics in Europe; namely, North European, North Italian and South Italian Later, Simitch, T. described the Balkan type of malaria, which is types. similar to the South Italian but is still specific in its trend. During the period between Celli and the era of DDT, some other types of the seasonal trend of malaria were recognized (India, tropical areas). It is very natural that insecticides with residual effect, when applied in malaria control or eradication, have entirely changed the picture of the incidence of malaria, and the natural pattern of malaria incidence is no longer taken into consideration in the evaluation work of a modern malariologist.

However, beside the wonderful progress achieved in the global malaria eradication campaign, we have also witnessed failures in interrupting transmission in certain areas of the world where standard techniques were applied in the attack. In other areas, the response of malaria to attack measures

was rather weak and consequently the progress of the eradication campaign was slow.

There is no doubt that the resistance developed by mosquitoes to the insecticides applied is playing an important role in the difficulties - or even failures - encountered in malaria eradication campaigns. One should not ignore the importance of the resistance of plasmodia to antimalarial drugs, although this has not as yet been considered as the most important problem so far met.

Biologically speaking, the development of mosquito resistance to insecticides is a natural consequence of artificial selection forced by the repeated pressure of insecticides against the natural population of mosquitoes. Of course, different species have a quicker or slower reaction, but ultimately this should happen to all species.

Today, after ten years of experience in malaria eradication campaigns, we are well aware that we should follow the old axiom: "To fight an enemy one should first learn it".

The knowledge accumulated during the first four decades of the century in respect of the epidemiology of malaria has greatly assisted in the implementation of malaria eradication campaigns, but for its continuation more knowledge is required in the light of changed natural conditions for the survival of plasmodia. It is to be appreciated that ecological conditions (including geographical, climatic and behaviouristic conditions of both man and mosquite) are declisive for the survival and reproduction of plasmodia. This principle should be observed in the planning and implementation of antimalarial measures.

# 3. <u>Malaria Eradication Campaigns in Countries of the Eastern Mediterranean</u> Region

The enthusiastic drive towards the global eradication of malaria was followed by several countries of the Region. Iran, Iraq, Israel, Jordan, Lebanon, Libya, Pakistan and the Syrian Arab Republic adopted the policy by which they have converted their malaria control activities into eradication campaigns. Cyprus should also be included in this group, being a country where a mosquito eradication campaign carried out between 1949 and 1952 resulted in the disappearance of malaria. While figuring among the above-mentioned countries, Israel is an exceptional case because of the extensive health facilities existing in the country with a high number of medical and paramedical personnel. Due to such facilities and to the well-planned and executed eradication activities, in the absence of technical obstacles the malaria eradication campaign has already reached the maintenance phase.

Significant progress was made in other countries having implemented malaria eradication programmes in 1957-1958, but set-backs have also been experienced in the past two-three years in the form of focal outbreaks or even re-establishment of transmission. The first problem to hamper the smooth progress of malaria eradication campaigns was the resistance of <u>A.</u> <u>stephensi</u> to chlorinated hydrocarbons, which was detected in south Iran and south Iraq in the period 1960-1961. The initial progress made in these two countries resulted in the withdrawal of spraying, and consequently since 1961 in south Iran and 1962 in south Iraq transmission has been re-established.

Apart from obstacles of a technical nature such as those experienced with the resistance of <u>A. stephensi</u>, in some countries the reappearance of malaria was due rather to the weaknesses of epidemiological activities which failed to detect the persisting parasite reservoir and thus, in the presence of vector species, transmission was made possible.

Chronologically, it was in Lebanon that malaria first demonstrated its disobedience and where in 1962, just a few kilometres from Beirut, with the presence of a few parasite carriers actually belonging to another country, <u>P. vivax</u> took advantage of favourable circumstances for its reproduction, and as a result more than 180 cases were detected in a couple of months. Intensive surveillance, with additional spraying, was needed to eliminate this focus and the last indigenous case was detected in that area in 1963. Syria and Jordan were victims of a similar experience in 1963 and 1964, respectively. While in the Syrian Arab Republic, in the second half of 1963, a number of active foci of transmission were detected with a total of 700 cases for the whole country, in Jordan, in the first year after the withdrawal of attack measures - namely in 1964 - transmission took a rather natural trend and, as a result, nearly 800 cases were detected, most of them in the Jordan Valley.

There is no doubt that such an experience may adversely affect the enthusiastic drive towards the eradication of malaria. However, we should analyse the situation critically and direct our attack and consolidation activities in such a way that persisting foci of transmission can be eliminated. In this respect, reasons for the development of the epidemiological situation as experienced in the above-mentioned countries are discussed hereunder.

The basic requirement for a successful malaria eradication campaign is a thorough geographical reconnaissance in respect to human dwellings and the population as well as to the geographical distribution - potential and factual - of malaria as a disease, thus enabling total coverage with antimalarial measures. Unfortunately, this requirement was not fulfilled in most of the eradication campaigns in our Region. As a consequence, "total coverage" with insecticides was never achieved, nor was the complete interruption of transmission. To illustrate this point with a specific example let us take Syria, where in 1963 and part of 1964 malaria reappeared in localities and areas which were considered non-malarious. During the period 1958-1963, coverage provided by the spraying campaign was as follows:

Total number of		5 P	R	A Y	E I	)
to be exposed to the risk of Malaria	1958	1959	1960	1961	1962	1963
5 785	3 043	2 548	3 037	1 818	1 425	271

While the partial coverage by insecticides produced a pressure on the transmission of malaria, keeping the number of detected cases between 200 and 350, as soon as this pressure was reduced in 1963 the number of detected cases grew to over 600 in that year. There are similar examples in other countries.

Besides total coverage with insecticides being of utmost importance in order to assure the complete interruption of transmission, a mechanism of detection of melaria on a total coverage basis is to be established so that the epidemiological development can be closely followed-up, thus enabling the thorough assessment of the programme in respect of the appropriate time for the withdrawal of attack measures. Here again, there are several examples to be drawn from countries of our Region where the premature withdrawal of attack measures resulted in reestablishment of transmission. For example, in Jordan, a country where the progress of the malaria eradication programme was rather impressive, a total of 289 and 151 cases were detected during 1962 and 1963, respectively. However, these cases were detected in 90 and 123 localities in 1962 and 1963, respectively, which shows that there was a large number of localities with parasite carriers, presenting excellent potentialities for the renewal of transmission. In fact, after withdrawal of attack measures in 1964, transmission of malaria was re-established in the Jordan Valley and as a result nearly 800 cases were detected during that year.

# 4. <u>Epidemiological Activities in Malaria Eradication Campaigns in the</u> Eastern Mediterranean Region

Surveillance operations aiming at the detection of parasite reservoirs were implemented during the late attack phase in all countries of the Region having launched a malaria eradication programme. Surveillance operations were introduced in 1959 and 1960 in Iran, Iraq, Jordan, Lebanon, Libya and the Syrian Arab Republic, while in Pakistan they were introduced in 1962, in the second year of the attack phase in zones where the malaria eradication programme started in 1960.

The development of the case detection mechanism in countries of the Region which adopted surveillance operations on a regular basis has passed through difficult stages as in other areas of the world.

A surveillance operation can only be successful, as is well known, if the total population is covered by it and if the same criterion in the screening of a disease is strictly utilized. The screening device in the detection of malaria cases - the fever - is not strictly observed in most instances. There is an objective reason for this, and that is the fact that the fever is not checked by a thermometer and thus it is left to the population to declare it on the basis of its subjective feeling. As long as such an otherwise objective screening device is not objectively judged, its objectiveness becomes subjective. Consequently, if the main criterion for the detection of malaria cases is not strictly applied, a certain number of parasite carriers may remain hidden, or be detected only after transmission is re-established. The concept of "total coverage in space and time" with surveillance operations, though accepted as <u>conditio</u> sine <u>qua</u> non in active case detection, has not always been followed, with the same consequenbes as the failure to observe the main criteria for the detection of malaria bases.

This applies to active case detection carried out by surveillance agents regularly at a fortnightly or monthly interval from door to door.

As far as the "institutional" detection of malaria cases is concerned, it is to be stated that the inadequate development of the rural health infrastructure, together with a negative ratio of doctors to the population, not only made the so-called "passive case detection" insufficient, but also had is a consequence that large areas remained uncovered by this method of ietection.

However, in spite of these facts, surveillance operations have been constantly improving during the last four years, and the results achieved are rather encouraging.

From data recorded and made available, it has been noted that in countries at an advanced stage of the malaria eradication programme, the regular case detection mechanism - institutional (passive case detection) and at nome (active case detection) - is gaining quantitatively and qualitatively in comparison with other methods of detection that are applied ad hoc, as for example "epidemiological investigation" and "mass blood examination". In other words, in the assessment of epidemiological activities we are evaluating several elements related to the total number of slides taken throughout a year from the population of a given area, the inter-relationship of the sources of slides taken (through different methods of detection) as well as the positivity rate of slides taken separately through a specific method of detection. It is assumed that if a minimum of ten per cent of the population is examined throughout a year, this number should be sufficient to secure the detection of malaria cases. It is further expected that most of the slides would be collected through the regular case detection mechanism, i.e. through active and passive case detection. Presumably, the positivity rate of slides collected through active and passive case detection should be similar since fever is to be used as a screening device in both systems.

Referring to the statement made in a previous paragraph about the quantitative and qualitative improvement of surveillance in the past four years, it is to be mentioned that this statement was made on the basis of the following facts:

- i. While in 1961 only 4% of the total number of slides were collected through passive case detection, in 1962 and 1963 the number increased to 9.3% and 19.05%, respectively. The same percentage of passive case detection was maintained in 1964, but the absolute figure was even higher than in 1963.
- ii. The positivity rate of slides taken through mass blood examination in 1961 was rather high, reaching 27.2% of all positive cases reported from eight countries in the Region. If the <u>ad hoc</u> investigation of the population gave such a high positivity rate, it means that the regular case detection mechanism failed in its task. However, since then, the positivity rate of slides detected through mass blood examination has decreased and for 1962, 1963 and 1964, it was found to be 14.1%, 6.5% and 3.5%, respectively.
- iii. The epidemiological investigation and follow-up of confirmed malaria cases has shown a solid trend of quantitative and qualitative improvement during the last four years. This statement is supported by the fact that while in 1961 only 2.4% of the total slides collected in countries in the Region were collected through epidemiological investigation, in 1962, 1963 and 1964 the percentage increased to 4.1, 6.3 and 7.8, respectively. In addition, as a result of improved regular surveillance, the positivity rate of slides taken through epidemiological investigation has been constantly decreasing during the last four years from 2.4% in 1961 to 0.67% in 1964.

Another characteristic of the surveillance operations in countries of the Region is that active case detection was and continues to be the most powerful method of detection. This is of course due to the inadequate number of rural health dispensaries to cover all the population under malaria risk. On the other hand, as in other countries of the world, the personnel of health institutions have not become "malaria minded" and therefore passive case detection has to be imposed by the malaria service.

There is another aspect of epidemiological activities in a malaria eradication campaign. This is the method of dealing with a confirmed malaria case. Besides the radical treatment which should follow immediately after the detection, a case should be epidemiologically investigated and classified. The same should be done with the locality - focus - where the case was found. This procedure has become an everyday practice in all countries having areas in the consolidation phase. There is still room for improvement where the classification of malaria cases as "relapses" and "imported" are concerned, but there is no doubt that the present trend will lead to such a level of accuracy that the epidemiological requirements can be entirely satisfied.

It is also encouraging to note that with the epidemiological investigation of cases and foci, as well as with their classification, the idea of the prevention of reintroduction of transmission is gaining more and more attention. Thus, for example, Jordan and Lebanon have recently supplemented effective measures in this respect, while in Israel the control of immigrants was established four years a jo.

The necessity of prompt evaluation of epidemiological data is more and more appreciated by malaria eradication services in the countries of our Region, and quite a number of trained epidemiologists are assigned to the programmes, mostly at country or district level. In Pakistan, for example, an evaluator is assigned at zonal level and made responsible for the epidemiological evaluation and assessment. As malaria eradication programmes are progressing further, the need for well-trained and experienced malaria epidemiologists becomes more and more apparent. WHO, and particularly the Regional Office for its part, has assisted and will certainly continue to assist the Governments by providing fellowships for malariologists to be trained in malaria epidemiology either through courses or through study tours.

The technical difficulties encountered in the malaria eradication programmes of the Region have stimulated epidemiological studies and research. Thus, quite a number of such research programmes were carried out in Iran with encouraging results.

Summarizing the epidemiological activities in the countries of our Region having launched malaria eradication programmes, it can be stated that significant progress has been achieved in this field. Thus, the prospects are good. With further consolidation of these activities and measures undertaken accordingly, the elimination of foci can be expected fairly soon in Jordan, Libya and the Syrian Arab Republic. The resistance and/or tolerance of <u>A. stephensi</u> in Iran and Iraq to chlorinated hydrocarbons, which has created an obstacle to the smooth progress of eradication, is being studied, and it is hoped that with strengthened operations and eventual application of combined attack measures, this difficulty can be overcome.

#### III DISCUSSION

In previous paragraphs, some general features of malaria epidemiology have been discussed, as well as the experience gained in countries of the WHO Eastern Mediterranean Region having launched malaria eradication programmes and the epidemiological activities being carried out.

As already mentioned, the epidemiology of malaria varies from one area to another; therefore the transmission season, the natural pattern of malaria endemo-epidemics, should be thoroughly studied.

The epidemiology of malaria in countries of the Middle East, i.e. in Iran, Iraq, Israel, Jordan, Lebanon and the Syrian Arab Republic, is characterized by its seasonal nature. Thus the transmission starts sometime in May (south Iraq, south Iran and Jordan) or in June (other countries), reaching its peak sometime in October, with the highest incidence of malaria cases in November. Another characteristic of the epidemiology of malaria in the above-mentioned countries is that, under favourable climatic conditions, vectors such as A. stephensi, A. superpictus and A. sergenti can develop high density of their population within a relatively short time. which in turn may produce a high rate of transmission even if the existing parasite reservoir in human beings is very low. If we add to this fact that the population inside the human dwellings is mostly dense and that localities are usually surrounded by suitable breeding places, the potential dimension of transmission becomes easily understood. This is why a malaria epidemic acquires an explosive character in many areas of countries in the The best example of this is the epidemic which occurred in Middle East. Basrah City in 1963 where in two cycles of transmission, for an approximate period of ten weeks, over 2 000 cases were detected.

Besides these characteristics of malaria related to the parasite and the vectors, in countries of the Middle East the behaviour of man also

influences the epidemiological pattern of malaria. Nomadism and seasonal movement of labour contributes to the renewal of transmission in areas already freed from malaria. This problem needs careful attention and study. At the same time, nomadism and/or seasonal movement of population may require additional supplementary antimalarial measures by including this part of the population under the regular surveillance operations and protecting it, at least during the transmission season, by administering antimalarial drugs. In this respect the experimental administration of medicated salt in a field trial in Iran gave very encouraging results.

The question now is how to cope with this somewhat controversial aspect of malaria in the Middle East, namely with its instability which at the same time has the potentiality to develop into an explosive epidemic.

The answer is not very simple, but in any case the intensity of antimalarial measures must be planned in conformity with the epidemiological characteristics of malaria, as experienced in given areas. This means that thorough epidemiological, including entomological, observations are to be made and assessed throughout a malaria eradication campaign.

It has already been mentioned in this paper that epidemiological activities have been improving during the past four years and that the prospects are good. It can be expected that the experience already gained in malaria eradication programmes will further contribute to the strengthening of the epidemiological part of malaria eradication operations, which will no doubt ultimately facilitate the elimination of persisting foci of malaria in countries being in an advanced stage of eradication. It is also assumed that experience gained in some countries of our Region with the epidemiology of malaria will be beneficially utilized in others having recently embarked on malaria eradication or in countries where a malaria eradication programme is to be launched in the near future.

### IV CONCLUSIONS AND RECOMMENDATIONS

Summarizing the above statements and discussions on the general and specific epidemiology of malaria as related to the countries of the WHO Eastern Mediterranean Region, as well as the experience already gained in epidemiological activities and studies in malaria eradication programmes, the following conclusions can be drawn: 1. Geographical reconnaissance in respect of the population, their dwellings and the thorough delimitation of malarious areas has not been completed prior to embarking on malaria eradication in most countries of the Eastern Mediterranean Region (with the exception of Pakistan). This has caused difficulties necessitating the application of attack measures for a longer period than originally expected. In some instances, attack measures have to be applied in areas which were previously considered as non-malarious.

2. In countries of the Middle East the specific epidemiology of malaria, manifesting its unstable but explosive character with vectors capable of creating obstacles of a technical nature (resistance, exophily), and with an ever-moving population (nomads, seasonal labour), has certainly contributed to the difficulties experienced, besides the incomplete geographical reconnaissance and incomplete coverage of the population by attack measures.

Epidemiological studies, stimulated by technical problems and operational difficulties, have been carried out with encouraging results.

3. Epidemiological activities, particularly surveillance operations, have been implemented in the late attack phase of eradication programmes. Surveillance operations have passed through difficult stages as in other parts of the world, but substantial improvement has been noticed during the last four years. Active and passive case detection, being organized on the basis of total coverage "in space and time", has shown quantitative and qualitative improvement, although there is still room for further progress. However, the fact remains that there is a noticeable yearly increase in the number of slides taken through the regular case detection mechanism. Consequently ad hoc investigations, such as the "mass blood examination" of a certain group of the population, is taking the place it should, while previously this constituted one of the main sources for collecting slides.

4. Due to the fact that the development of rural health services has not reached the total coverage of the rural population in most countries of the Region, the role to be played by the general health services in the detection of malaria cases did not reach its expected strength. Thus, the active case detection carried out by a surveillance agent belonging to the malaria eradication service was and remains the main method of detection. It is to be pointed out however that the role of the general health services in a malaria eradication campaign is realized and recognized more and more by all countries having reached an advanced stage of malaria eradication, and appreciable efforts can be observed in this respect.

On the grounds of the experience gained with malaria epidemiology and epidemiological activities in the course of eradication programmes in countries of our Region, it is to be recommended:

A. To strengthen further the epidemiological service of eradication programmes by increasing the manpower and raising the qualifications of the staff, thereby enabling better and more intensive epidemiological activities, particularly in countries in an advanced stage of malaria eradication. In this respect the following details regarding these activities are suggested:

- the lapse of time between the collection of slides and their micro-
- scopic examination should be reduced and should never be more than seven days;
- the radical treatment should promptly follow the confirmation of a positive case;
- the epidemiological investigation of a malaria case and its locality, as well as appropriate classification and follow-up, should be carried out within a reasonable time. Only this, together with immediate remedial measures applied on the basis of the epidemiological findings, will prevent the re-establishment of transmission in an area already freed from malaria;
- the importance of collection and processing of epidemiological data can never be overemphasized. It must be noted that a critical analysis of the epidemiological situation, promptly and permanently carried out, will facilitate adequate planning of activities and will spare us unpleasant surprises;
- applied epidemiological including entomological research in central laboratories and in the field should be stimulated further, as results thereby achieved have already proved encouraging.

B. Although strictly speaking it has less epidemiological bearing, the necessity for further development and strengthening of the general health services - particularly in respect of its coverage of the rural population and its role in the detection of malaria cases - is to be emphasized.

Indeed, if the general health services do not take an active part in malaria eradication programmes, the final goal of eradication can scarcely be achieved.