

MALARIA CONTROL AT THE CROSS-ROADS! WHERE DO WE GO FROM HERE?

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Information on the world malaria situation released by the World Health Organization in 1985, indicates that not less than 5.5 million cases were recorded in 1983. These provisional figures represent only a part of the true picture; the data from tropical Africa were not included because of the incomplete and uncertain reporting from the large endemic areas of that continent. It has been estimated that of the total world population (1983) of some 4.7 billion about 2.2 billion live in parts of the world where malaria incidence has been reduced in varying degrees, but almost 400 million people in rural tropical areas are exposed to the full brunt of malaria infection. Not less than 373 million inhabitants of sub-saharan Africa live in endemic areas, where *Plasmodium falciparum* is the prevalent species. The *annual* number of clinical cases of malaria has been variously estimated at between 76 and 150 million cases.

A massive resurgence of the disease in south-east Asia seen during the years 1976-1978 has now decreased to 1973 levels, but there has been a slow rise of incidence in South and Central America, while the situation in Africa showed little change over the past decades.

We all know the main chapters of the sad saga of global malaria eradication and felt, often personally, the rise and fall of our hopes during the past 30 years.

True enough, the population living in previously endemic areas and virtually freed from malaria rose from 1.160 million in 1965 to 1.672 million in 1975. Malaria eradication has been attained in some 40 countries out of about 140 where the endemic disease was present. Nevertheless, it became obvious ten years ago that the advance of malaria eradication was grinding to a halt.

The causes of the resurgence of malaria that affected a number of countries during the period 1973-77 are complex. The importance of the general health services of the countries concerned was under-estimated. Too much reliance was placed on the residual house-spraying, in the belief that a single method would lead to the interruption of malaria transmission. As many programmes continued beyond the original target, faced with the complex technical and operational problems, several countries reduced their effort to control the disease. In some instances, the premature withdrawal of international and/or bilateral assistance accelerated the degradation of the programme. Difficulties of general nature (economic recession, increase of the cost of oil, insecticides, motor transport, equipment, etc.) had an adverse effect. Exophilic habits of some anopheline species, inaccessibility of outlying groups of houses, primitive structure of dwellings presented a number of obstacles. Other, and perhaps more serious difficulties were due to various administrative, socio-economic, financial and political problems, which often affect the improvement of health conditions in countries with inadequate basic health services and short of trained manpower.

The cloud of resistance of some *Anopheles* vectors to DDT grew steadily larger and soon extended to other insecticides.

By 1983 resistance to one or several insecticides had appeared in 57 species of *Anopheles* and this has affected the malaria control activities in 62 countries inhabited by 260 million people. Over one third of all malaria programmes face serious problems of resistance to current insecticides widely employed in agriculture. The last straw was the development of resistance of *P. falciparum* to chloroquine, our most reliable antimalarial drug. Large areas of resistance of *P. falciparum* to chloroquine, are present in some 20 countries of southern and south-eastern Asia and the northern areas of South America. Chloroquine resistant foci have been found now in at least 15 countries of tropical Africa and, as a result, the use of this compound has been restricted, to decrease the spread of the selection pressure on the parasite.

Re-examination of the global strategy of malaria eradication carried out in 1969 and 1978 by the World Health Organization recommended that in countries, where eradication did not appear to be feasible at the present time, malaria control programme may form a transitional stage.

Within the general agreement on the urgency of malaria control in order to maintain the gains of the previous decade two needs emerged: improvement of the basic health services in developing countries and better technical means of controlling the transmission of the infection. In 1980 the World Health Organization recommended adapting malaria control activities to the planning and implementation of the aims of primary health care. Over the past few years this concept of integration has been increasingly followed as a national health aim of malarious countries of the Third World.

The impact of such radical change was predictable. It confronted most of the countries concerned with the need to replace the rigid but simple philosophy of eradication by the flexible not time-limited and untried new approach to malaria control. Three important differences were notable.

In contradistinction to the principle of eradication, malaria control would have to concentrate on those areas, where endemicity is at the highest level with the greatest adverse effect on the population concerned. The difficulty in selecting such priority areas lies in the fact that in stable conditions of holoendemicity the adverse impact of the disease falls not on the whole indigenous population but primarily on its youngest non-immune groups.

The second major difficulty stemmed from the recognition, that in difference to the idea of an intensive effort towards a "permanent" goal of eradication, control of malaria is a long term commitment, commanding much patience and a steady devotion to an unspectacular and not well defined goal.

The third aspect of malaria control is that its operations cannot be carried out "by the book", according to some codified well defined specific rules, but must be flexible, adapted to changing epidemiological conditions and demanding not only a good knowledge of the area involved and available methods, but also close co-operation with the existing health services and the fullest support of the local community.

Some principles of this new approach to malaria control have often been repeated. Perhaps the most important of them is, that there should be a national commitment to support antimalaria activities as long as necessary, taking into consideration the country's capability to absorb and utilize fully any technical and financial assistance provided.

The second principle is that of feasibility. Whatever the target level of malaria control, there must be a reasonable conviction that the programme can be successfully implemented with the selected methods, the available manpower and financial resources. In view of the relevance of the programme to its predominantly rural ecology, the impact of (and on) agricultural practices and returns must be carefully considered.

Adaptability and flexibility are important principles which must take into account:

- a) The selection of the programme objectives, based on the appraisal of the situation, on the resources available, and on the potentialities for action;
- b) The definition of priority areas and/or population groups to be protected. In many instances, priority must be given to the protection of non-immune, most vulnerable groups;
- c) The availability of appropriate antimalaria measures that can be applied in priority areas and the definition of measures for application.

Much has been written about the integration of antimalaria activities with those of the general health services. Hurried and badly planned integration has often led to the disruption of well organized malaria control structure.

There is no doubt that a countrywide malaria campaign cannot be carried out without the full support of whatever type of health service exists in the country and the participation of the community. On the other hand, an antimalaria programme without a nucleus of specialists at the central level and trained manpower at the periphery is inconceivable.

Consequently where "vertical" antimalaria services exist and levels of malaria endemicity are high, those services should remain within the general health organization, to be available as a mobile and preventive branch of the central health authority. On the other hand, where no specialized services exist, some antimalaria activities could be carried out, by the primary health system, provided that the necessary experience exist or can be made available.

It seems that the present understanding of malaria control as a variant of "appropriate technology", may be successful only in a few countries. The very flexibility of malaria control and its adjustment to the local epidemiological and socio-economic condition requires alert, experienced and determined public health professionals at all levels. The shortage of such people is acute and the new training in this field must have a high priority.

Integration has been interpreted in different ways in various parts of the world. In the Americas, for example, integration was implemented by giving the existing malaria service other duties, principally field activities (e.g. surveys, surveillance) and control of other parasitic and communicable disease, including vaccination.

It seems that the Brazilian experience acquired during many years of *dedicated work in* the five main regions of this huge country offers a compromise between the former monolithic, vertical structure of malaria eradication and a horizontal system of health service, covering the primary health needs of its vast and varied population. This approach may be compared with a different national system (in one South American country) in which a malaria programme concentrated on one disease, with little if any support of general health services. The latter approach is spectacular and may achieve its aim, but the former is more permanent in the long run, better balanced and greatly preferable. The present malaria situation in Brazil indicates that in spite of some recent increase of number of cases in the Amazon region, the prospects of improvement are bright. Some active foci detected in 1982 in areas such as Goiás, Mato Grosso do Sul, Paraná and Santa Catarina were promptly and efficiently dealt with. Case detection exceeded the planned programme and the co-operation of the local health services was such, that nearly 90% of all cases were detected and treated. The main problems are limited to the Amazon area and closely related to the intense migratory movement in a region notoriously difficult for geographical, ecological and administrative reasons. It is a tribute to the organization and effort of the Brazilian central and peripheral health services that in these conditions the malaria situation had not deteriorated, while in the whole of this immense country with a population of 130 million only 19 million remain in the attack phase of the control programme.

Future development of malaria control depends on the new methods available for the attack on the parasite and on its vector. There have been many improvements of environmental approach for prevention of mosquito breeding by judicious source reduction methods. The extent to which control operations are capable of a substantial degree of malaria control is governed by technical, operational and economic considerations.

In long-term programmes priority should be given to environmental methods of control. In urban and peri-urban areas, this may be achieved by applying measures against the larval stage of the vector (chemical applications, environmental manipulations) or the adult stage (space spraying), together with elimination of breeding places of *Anopheles* mosquitoes. Residual insecticides should be reserved in rural areas for programmes where there are good prospects of control and for combating malaria outbreaks.

The collaborative research programme initiated by the WHO in the 1960s screened over 1,600 new chemical compounds for their insecticidal action and toxicological acceptability. A few organophosphates and carbamates showed great promise, but their costs of application are high. Some compounds such as synthetic pyrethroids and insect hormone analogues, have been developed and are being evaluated. However, in many parts of the world DDT and malathion are still most useful. Biological methods of mosquito control such as the toxin of *B. thuringiensis* are successful; larvivorous fish have been used with generally good results. Other predators, and parasitic agents have been assessed in the laboratory and in the field.

The search for new drugs was resumed 20 years ago; a tremendous drug-screening programme of the U.S. Army tested over 250,000 candidate compounds, came up with about six possible leads among 9-phenanthrene methanols and 4-quinoline methanols, of which two, namely mefloquine and halofantrine are most promising. Other drug or drug combinations including pyridine methanols, naphthoquinones and the Chinese "Qinghaosu" derived from *Artemisia annua*, and now synthesized as artemisinin, are being evaluated. "Targeting" of primaquine by various carrier systems is being explored.

The continuous culture of *P. falciparum* established by Trager and Jensen in 1976 brought the probability of a malaria vaccine closer to reality. Which of the three types of antigenic stimuli, viz. irradiated sporozoites, purified and lyophilized erythrocytic merozoites or perhaps some equivalent immunogenic antigens, produced by insertion of a plasmodial gene into a bacterium or yeast, combined with a carrier molecule and with an adjuvant, is going to be used as a prospective vaccine, time only will show. Before this materialises a number of difficult clinical trials will have to be completed; it may be premature to talk about the malaria vaccine as the ultimate technological solution of the problem of malaria control. The requirements for this vaccine are as high as the hopes connected with it.

It should be polyvalent for all species and strains of human plasmodia, it should produce an effective immune response at least for a year, it should be free from adverse effects of any

possible adjuvants, it should be fairly easily manufactured and stored and be adequate for mass administration in tropical developing countries. A tall order, indeed!

Over the past decade, the attempt to produce a malaria vaccine gathered an increasing momentum. It has been stimulated since the early 1970s by the U.S. Agency for International Development which built up a large group of contractual research projects; the same has been done by the UNDP/World Banc/WHO Special Programme which, since 1976, organized a multi-national scientific effort. The number of major research projects on malaria vaccines is probably well over 50 and the total funds appropriated are over \$ 20 million for the year 1985/86.

The recent resurgence of malaria and its slow present fall indicate how far we are from its conquest. It also emphasizes the role of malaria as one of the many factors at the core of the great dilemma of more rapid development of tropical countries. There is no denying that, in spite of the great achievements of the global programme a large reservoir of endemic malaria still remains over most of the globe.

The gradual erosion of our methods of attack on the mosquito vector and on the parasites causes much concern. There is much hope that the recent developments in molecular biology, biochemistry and especially immunology, will eventually produce new weapons against malaria. However, those of us who spent much of our lives in the tropics and especially in Africa believe, that the conquest of this disease, rooted in the physical environment and closely linked with the socio-economic conditions of their populations, cannot be achieved only by the new technical tools. Each of these tools will be needed, but their proper use will depend on less obvious factors and especially on the national will to relieve the poverty of the large rural areas and on the generous and sustained international aid.

Like Hydra, the monster of the Lernean marshes in Greek Argolis which had nine heads, malaria has not yet encountered its final Heraclean conqueror. Like Hydra, which grew two new heads as soon as one was cut off, malaria remains one of the main health problems of the developing tropical world.

The disappointment with the present results of malaria eradication and control must not lead to the doubt in the urgency of curbing this disease by any means at our disposal.

Fifty years ago a group of American and Brazilian doctors and sanitarians repulsed the invasion of *Anopheles gambiae* on Natal and the States of Ceará and Rio Grande do Norte in the North-East of Brazil. This has become a memorable page in the history of tropical medicine.

Despite all the new problems of malaria control at the present time, the message of my hasty and imperfect answer to the rhetorical question: *Where do we go from here?* is one of the justified hope. This is because the scientific progress, as well as the initiatives of the major international agencies and of many enlightened countries have created a better informed framework for health planning and for the continuation of our campaign against the mosquito borne diseases, that Oswaldo Cruz fought so courageously at the start of the present century.