

MALARIA CONTROL IN THE TWENTIETH CENTURY*

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I have been highly honored by the Society with the privilege of serving as your president and of presenting an address to the annual meeting. In similar circumstances, one of our former presidents, Dr. Clay Huff, with his characteristic modesty, once described the genesis of such an honor as "some quirk in the democratic process followed by this Society,"¹ but quirk, accident, or otherwise, I am most grateful.

Perhaps the most significant challenge to the president of this Society is that of selecting an appropriate topic for the presidential address. I suppose the usual course of events is to review, as far back as possible, the addresses given by presidents in the past. This can be a devastating experience, for one soon discovers that almost everything worth saying has already been said. A number of presidents have pointed with justifiable pride to the accomplishments of the past; others have pointed with equally justifiable alarm at the problems of the future. Still others have provided technical reviews of specific topics or philosophical discussions of the importance and trends of our endeavors in the field of tropical medicine. In selecting the topic, "Malaria Control in the Twentieth Century," it seemed possible to include a little of each of these elements, certainly not as eloquently as has been done in the past, but perhaps with the added perspective of a few more years of collective experience in the effort to defeat our age-old adversary.

The turn of the century found us with a new body of knowledge relative to the life cycle of the malaria parasite, which engendered great optimism in the hopes for controlling the disease. After the discoveries of Ross and others, it was inevitable that malaria control would be centered on the new knowledge of the vectorial role of the anopheline mosquito. At this time the reduction and control of malaria appeared to be a fairly simple matter.

Methods for eliminating mosquitoes with engineering techniques and with larvicides were known, and there was a specific therapeutic drug—which was something of a rarity in those early years. At any rate, there were suggestions for at least localized eradication of the disease, including pleas by Hoffman in 1915² for a National Committee on the Eradication of Malaria for the United States, and in 1916³ for eradication of malaria throughout the Western Hemisphere. The latter plea followed the adoption of a resolution by the Second Pan-American Scientific Congress in January 1916, "that all American countries inaugurate a well-considered plan of malaria eradication and control." Certainly early successes did little to discourage great hopes of defeating the "scourge of the tropics." The achievements of Gorgas and LePrince in Panama, Malcolm Watson in the Federated Malay States, and Cruz and Chagas in Brazil sparked many ambitious control projects in various parts of the world. Many of these efforts met with either lesser degrees of success or outright failure, and there began to be some disenchantment with the idea that the control of malaria was a simple matter.

By the end of the first quarter of the 20th century there was a growing realization that the control of malaria in the vastly differing areas where it existed might require vastly differing methods. As a result of early studies on the epidemiology of the disease and early control efforts, it became clear that an area might be amply endowed with anopheline mosquitoes and still be free of malaria; on the other hand, in some areas where the anopheline population had been "adequately" reduced, malaria continued to have a high incidence. Some recognition was being given to the idea that where malaria rates were decreasing significantly, such as in North America and in some areas of Northern Europe, there was little evidence that the specific efforts at malaria control were primarily responsible. All of this resulted in an opinion held by many that, except in extraordinary circumstances, efforts toward control of malaria by antimosquito measures were

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of little real value. Clearly, the discovery of the insect vector had not solved the malaria control problem.

At about the beginning of the second quarter of the century, under the leadership of the Malaria Commission of the League of Nations Health Organization, a new emphasis was placed on the use of chemotherapeutic methods. Attention was sharply recalled to the purpose of all antimalaria effort, that of lessening human suffering. The Commission, and many individual workers also, felt that the widespread use of antimalaria drugs, coupled with minimal larvicidal efforts and some extra effort toward killing adult anophelines in houses, would ultimately result in effective malaria control. This concept was not accepted by all workers; many steadfastly adhered to the mosquito control school. As Hackett stated in his classic, *Malaria in Europe*, "Certainly the appeal to quinization could not be expected to arouse much enthusiasm. It was a time-honored resource with a history of 300 years of constant defeat, always eagerly abandoned in favor of anything new and promising, wearily taken up again as the irreducible minimum of all relief work in malaria."⁴ It is safe to say that chemotherapeutic and adulticiding methods were given a fair trial around the malarious world, but even with the advent of pyrethrum extracts and the two new synthetic drugs, plasmochin and atebirin, the results were quite familiar: where malaria was on the wane, it continued to decline; in other areas the efforts met with failure.

From the ashes of many disappointments with both the chemotherapeutic and the antimosquito approaches, a third school of thought emerged, possibly in the long run more productive than either of the other two. A number of malariologists came to the conclusion that we did not know enough about the variability of malaria epidemiology or vector behavior to intelligently apply any method on a wide scale, and pressed for an intensive and continuing study of all aspects of the disease and its transmission. Thus the 30's and early 40's saw a return to primary emphasis on the development of better engineering methods for source reduction, further development and exploitation of larvicidal methods, and an expansion of biological studies of the vectors and their habits. All of this seemed to result in a further

reduction of malaria in areas with an established decline.

The advent of the Second World War brought the well-known problems of military malaria, but, as seems to be the case in all modern wars, it also brought an expansion of research and some promising solutions. With the end of the war malaria control entered a new age, with such new weapons as the chlorinated hydrocarbon insecticides and the 4-aminoquinoline antimalaria drugs. Control programs were quick to take advantage of the residual contact toxicity of DDT, dieldrin and other members of this new class of insecticides. Early successes with the use of the residual insecticides renewed hopes for eventual widespread control, and the goal of eradication again emerged.

The first serious proposals toward eradication in the United States were put forth by Louis Williams in 1943,⁵ and in 1945 the U. S. Public Health Service adopted what was in fact a national malaria eradication program, although it was initially called "The Extended Malaria Control Program." This was not greeted with optimism by all malariologists at this early date. In his presidential address to the National Malaria Society in 1945, Johnson stated, "We are frequently reminded of the possibility of eradicating malaria in the United States, now that it is at a low ebb. I feel that this is an untenable concept as we do not yet know in sufficient detail just where and under what conditions the disease occurs, or will occur, in its last natural habitat."⁶ Nevertheless, 2 years later the semantic facade was dropped and funds were appropriated by the U. S. Congress unequivocally for malaria eradication. By 1951 it appeared that malaria in the United States for all practical purposes indeed had been eradicated, or perhaps had disappeared, according to the standards set forth by the National Malaria Society.⁷ This Society then proceeded to merge with the American Society of Tropical Medicine to form our present organization—a very respectable, but perhaps premature, suicidal act.

The international consideration of malaria eradication was initiated by Dr. Fred Soper in 1950 in a proposal to the XIII Pan-American Sanitary Conference. As a result, the Pan-American Sanitary Bureau adopted hemispheric malaria eradication as an objective, somewhat hesitantly at first, but with growing enthusiasm and support. In

1954 the XIV Pan-American Sanitary Conference reiterated the resolve and the Office of Malaria Eradication of the Pan-American Sanitary Bureau was organized the same year. A year later, in 1955, the eradication concept became worldwide, when the VIII World Health Assembly came forth with a declaration for a worldwide program. The World Health Organization took the lead in establishing principles to provide a firm base for the great effort required to achieve the desired end, and thus was born what has often been described as the most ambitious and significant public health program of all time.

The response of the malaria situation to this new program during the next 20 years can now be viewed with some objectivity. During that time we have been flooded with figures from the international agencies showing, in the main, the continuing successes and promise of the eradication scheme. And, indeed there have been impressive local successes, though perhaps not always of the magnitude suggested by the statistics. There is no doubt that millions of people have been protected from malaria by programs utilizing residual insecticides. Eradication has been proclaimed and certified by WHO in 21 political or otherwise definable entities. In the Americas these have included a number of insular situations, the continental United States, and a part of Venezuela. At the end of 1974, of the total New World areas originally considered to be malarious, eradication was claimed for areas containing a population of over 90 million. Included in this figure are approximately 60 million from the continental United States—about two-thirds of the total. The United States also comprises about two-thirds of the land mass where eradication is claimed. Considering that malaria was extinct for all practical purposes in the United States prior to the initiation of the hemispheric campaign, suggests a possible bias in these optimistic figures. A similar situation exists in other areas of the world, with eradication being claimed principally in islands or in areas where malaria was at a low ebb or disappearing in temperate zone countries on the European continent.

Perhaps the most remarkable aspects of the malaria eradication concept have been the enthusiasm with which it was adopted and the perseverance in the face of adversity. The enthusiasm may not be difficult to understand. The new

residual insecticides were proposed as an effective single method which could be widely applied in rural situations at minimal cost, and in most cases optimistic predictions were made that 3 years of spraying and several more years of surveillance and mopping up of residual foci would see the job completed. For example, most of the Central and South American countries initiated their programs in 1956 and 1957 and set the target for completion of eradication at 6 years later. The eradication philosophy demanded such targets, because the recognized higher cost of an eradication program, as compared to a control program, could only be justified on a time-limited basis. During the ensuing 16 to 18 years there have been successes in some countries; in others the malaria incidence has either stabilized at moderate levels or has worsened after variable periods of improvement. Yet, even now, a dozen or more years after the original target date for eradication, some of these programs are still in operation, with continued hopes that another year or so of spraying will turn the tide.

After the past 20 years of experience, one might be able to make a reasonably good cost-benefit analysis of the global malaria eradication campaign. Such analyses seem to be in mode at the present, although they are usually of a prospective nature in the assessment of disease control priorities or the like. I am sure that my analysis would not be entirely the traditional consideration of economic growth, gross national product, dollar costs of programs, or other usual economic or sociologic measurements. Though highly important to the afflicted individual, even favorable changes in the morbidity or mortality rates may be of lesser importance than some of the costs. On the credit side, I have already cited the tangible gains in the reduction of malaria and its elimination in some areas. To infer the extent to which these gains may exceed those that would have resulted from efficient but less costly control programs would be purely conjectural.

Many side benefits from the malaria eradication campaign have been listed. Johnson⁸ has pointed out a number of these, and I am sure they are valid benefits. The organized malaria eradication programs have undoubtedly formed the first visible public health efforts in many developing countries; they have engendered cooperation in matters of public health among neighboring coun-

tries, and have strengthened the influence of the international organizations in the developing nations. The technology developed for the programs has most certainly benefited the control of other disease vectors.

What have been the costs of this effort? Estimates of financial cost are most readily available from the countries that have received substantial aid from the United States. If one considers only the 18 countries who were receiving U. S. assistance for malaria eradication programs in 1969, total expenditures for the 14 years between 1956 and 1969 amounted to approximately 790 million dollars. Of the total, about 450 millions were from U. S. sources—either grants, loans, or U. S.-owned local currencies. Thus in these countries alone, the total cost by now may have exceeded a billion dollars. Considering the large number of additional countries that have undertaken eradication programs, the worldwide cost could be double or triple that billion-dollar estimate. The only terms of reference for comparison of such costs are in the smallpox eradication program, which has cost something on the order of 250 million dollars during the past decade, 200 millions of which were provided by the affected countries. Can such costs be considered extravagant? Probably not, especially in these days when we are accustomed to multimillion dollar aircraft, billion dollar space explorations, and the like. Costs for malaria eradication programs probably represent only a few pennies per year per capita of the actual population of the malarious areas affected. If this had been the only cost of a noble experiment which was, at best, only partially successful, I am sure we would consider it money well spent. Unfortunately, this does not appear to me to be the case. While the fringe benefits may be considered significant by some, there are those who feel that the hidden costs have been disastrous.

At the inception of the worldwide eradication concept there were several major premises that were accepted. One was that with a single weapon, the application of a residual insecticide to the interior walls of houses, one could interrupt the transmission of malaria in almost any area willing and able to adopt this method. Another premise was that we had all the information that we needed to put this method to effective use and to eliminate malaria from most areas of the world—with the possible exception of Africa south of

the Sahara. Not only was it felt that no new information was needed, but it appeared that all we had learned in the past could now be ignored and forgotten. The *science* of malaria control, developed slowly and painfully from the beginning of the century to a relatively high state of sophistication, was almost overnight converted to the rather simplistic *technology* of malaria eradication, which basically required that one know how to deliver 2 grams of something to every square meter of a sometimes elusive interior wall, and to manage a hopefully ever-diminishing Kardex file of cases. The wide-ranging effects of this have been obvious. A legislative body could not be expected to provide financial support for basic malaria research when it was at the same time providing millions for malaria eradication with the virtual promise that in 5, 6, 7, or even 10 years the disease would be extinct. Neither could one expect much success in efforts to recruit some of the better minds to careers in malariology when articles were appearing in the major journals on the epidemiology of a disappearing disease. One would be a little suspicious of an individual who today decided that specialization on the epidemiology of smallpox would make a good career. There is little doubt that we have lost a generation of malariologists and a generation of malaria research, losses which will be difficult to recoup. Were there no voices to be heard in warning during this period? There were, but they received little credence and sometimes bitter condemnation as being persons of little faith and lesser knowledge. One of our very distinguished former presidents, Dr. Clay Huff, frequently called attention to our potential loss of malaria research and expertise, once most eloquently in his presidential address to this Society some 12 years ago.¹ I recommend rereading this address for a much more scholarly appraisal of the subject than I can provide. I would like to quote one short paragraph: “. . . the seeds of failure were sown when the nature of the eradication took the form it did. It assumed that we knew enough to abandon basic research and the training of personnel along lines which had proved to be efficacious even though more slowly than the promised quick eradication. In the midst of a mighty war it is a foolish nation which abandons research. I believe we cannot deny that the eradication program greatly depleted the sources of support for a continuation of

research and training in a highly complicated group of disciplines involved in the reduction of malaria.”

Such skepticism has not been well received until very recently by those dedicated to the maintenance of time-limited eradication programs. To suggest that malaria eradication might not be feasible in a country even after years of failure, or that a country was not ready to embark on an all-out time-limited eradication program, or that research was needed on vector bionomics, was considered sacrilege in some circles, and even brought forth innuendoes that a malariologist with such ideas was only bent on protecting his own career.

With all of this confidence and dedication, why did eradication fail? The usual answers to this question have emphasized the technical and administrative problems which have been encountered. The resistance of vectors to insecticides and failure to achieve adequate and timely financial support usually have been the major reasons cited for failures. To these have been added, somewhat more recently, the resistance of parasites to drugs, lack of trained personnel, failure to develop basic health services within countries, worldwide inflation and the energy crisis. Undoubtedly, the effects of these problems have been substantial, but there is also some reasonable doubt that eradication could have succeeded even if none of them had existed. The basic problems undoubtedly were those which characterize any lost cause—underestimation of the enemy and overconfidence in the available weaponry. In looking backward it seems inconceivable that we could have, even in the enthusiasm of the times, forgotten the lessons of the past. In 1931 Paul Russell expressed his respect for the vector of malaria and his dismay at the problems associated with its control.⁹ In his words, “Man ploughs the sea like a leviathan, he soars through the air like an eagle; his voice circles the world in a moment, his eyes pierce the heavens; he moves mountains, he makes the desert to bloom; he has planted his flag at the north pole and the south; yet millions of men each year are destroyed because they fail to outwit a mosquito.” Today, some 44 years later, we have added many accomplishments to Dr. Russell’s list, but we have still not outwitted the mosquito.

Early in the century the first disciples of the

Ross theory for the control of malaria through vector control began to note and to report problems associated with the variability of habits and habitats of the vectors in various parts of the world. Even before the turn of the century, in 1899, Daniels stated in reference to the larval habitats of the malaria mosquitoes in Central Africa, “To a large extent, not only each country but even locality differs in detail.”¹⁰ In his studies in India in 1900 and 1901, J. W. W. Stephens found that “Distribution of endemic malaria depends . . . on the district concerned, and must at present be attributed to undefined causes which we have termed the ‘regional factor’.”¹¹ Later, in 1913, in his textbook, *Tropical Medicine and Hygiene*,¹² Daniels stated in regard to anopheline control, that “For economic and efficient prophylaxis, a knowledge of the habits of each species is required, and it is found that the different species vary greatly in their habits, life history, and breeding places.” A few more examples: Knab, in 1913, “Treatises and manuals abound with general statements that all *Anopheles* are practically alike in habits and that observations on the habits of one species are applicable to any other. In fact there is great individuality in the habits of the different species, both as adults and during their developmental stages.”¹³ In 1925 Samuel Taylor Darling pointed out the fallacy of accepting for the control of *Anopheles* in the Southern United States those methods being used successfully in India, Italy or Panama.¹⁴ In 1929, Hackett, drawing on his already wide experience in dealing with anopheline behavior, reported on the “Differences in the habits of anophelines which transmit malaria in America, in Europe and in the Far East.”¹⁵ This is a classic, and like all of Hackett’s works deserves rereading from time to time. He states, “Our soundest knowledge may lead us astray . . . if we reason by analogy and take the lessons we have learned through hard work or bitter experience in one region and attempt without preliminary study to apply them in another. For if failure or disaster occurred in these cases, it was almost always due to the unexpected behavior of some anopheline mosquito.”

Differences in behavior in geographically separate and even seasonal populations of the same species continued to be reported from numerous sources. These behavioral differences could usually be related to the problems of mosquito

control or the ability of the strain or species to transmit malaria. There is a most interesting recent report by Elliott and de Zulueta on ethological or behavioral resistance in malaria vectors and behavioral response to intradomiciliary residual insecticides.¹⁶ They reviewed some 40 years of literature on the resting habits of anopheline vectors before the introduction of the residual insecticides. After reviewing 100 reports on 33 species, they concluded "that daytime resting patterns of the great majority of malaria vectors included facultative daytime exophily, even before this habit came to confer significant advantage for survival."

With the constant warnings of behavioral differences in anopheline vectors, and with many specific reports of vector exophily, it seems difficult now to understand how the single-purpose methodology for malaria eradication could have been accepted as the basis for the initiation and perseverance of the multinational, multimillion dollar programs.

It should not be implied that vector behavior was the only problem which might have been considered a serious impediment to eradication. There were substantial human behavioral, cultural, and economic factors which were equally important and equally underestimated. I can recall my first glimpse of an ongoing malaria eradication program, which had been for years based entirely on intradomiciliary residual DDT spraying, and seeing with some dismay the high percentage of the "houses" which had no conventional walls to spray. Wherever one looks in areas where malaria eradication programs have been in progress, one sees human behavior patterns which have militated against the effectiveness of the methods used. We invariably were surprised when only 50 to 60 percent of a population would accept prophylactic drugs being distributed on a regular basis free of charge. Yet during several decades how many children in the United States would have remained unvaccinated against smallpox had it not been widely required for school attendance? And how many children in this country today are not receiving the advantage of immunizations against the childhood and dread diseases which are almost universally available at no cost? Eradication implied perfection and total coverage with methods which were too often subject to modification by perverse human behavior. Needless to say, this

was not our first encounter with perverse human behavior in disease control programs, nor will it be our last.

Even after the introduction of DDT as a residual insecticide there were warnings. In 1949, Smith and Dy set an example which might well have been adopted by others, stating that they "considered it unwise to embark on a wide-scale DDT residual spraying operation without first being satisfied as to the effectiveness and practicability of the procedure under Philippine conditions, notwithstanding that it is an accepted modern method of control in other countries."¹⁷ They did indeed conclude from their careful study that DDT residual spraying of houses was *not* an effective malaria control procedure in the Philippines. Nevertheless, DDT spraying was subsequently widely used in that country. In 1948 Foy and his colleagues suggested that DDT had a minimal effect on the vector in Greece, where malaria appeared to be reduced equally in sprayed and nonsprayed areas.¹⁸ There were other early reports on the variable effectiveness of DDT spraying, on the conversion of anopheline populations to exophily, and on the human and vector behavioral characteristics which would diminish the applicability of the method.

In 1927, almost 50 years ago, the Second General Report of the Malaria Commission of the League of Nations Health Organization contained the following advice: "The history of special 'antimalarial campaigns' is chiefly a record of exaggerated expectations followed sooner or later by disappointment and abandonment of the work. This record of failure and disappointed hopes makes it clear that the only prospect of real progress lies in renewed activity in the continuous study of the disease in all its aspects." The Commission also stated, "nothing struck us more forcibly than the observation that in several of the countries which we visited, costly measures were being undertaken with an antimalarial purpose in circumstances in which such action was of very doubtful utility." Perhaps the truth of these observations is even more apparent today than it was 50 years ago.

My objective in reviewing our shortcomings of the past and our apparent disregard of history is not so much to be critical, but more an effort to improve our future prospects. The situation which exists today is anything but good, in spite of some

continuing optimistic reports. India, which during the late 1960's was reporting only a few hundred thousand cases of malaria annually, will by the most conservative estimates have 4 to 5 million cases this year, and some estimates have been double that figure. Pakistan has shown a similar resurgence. Sri Lanka, where case numbers had been reduced to very low levels, experienced an epidemic resurgence a few years ago and reported over 1.5 million cases between 1968 and 1970. The number of cases in Nepal multiplied about 6 times between 1972 and 1974. In the Americas, there has been little change in the overall case rates between 1962 and 1974. While some countries have shown improvement during that period, others have shown an upward trend of cases. In Central America, the combined number of reported cases in the two countries of Nicaragua and El Salvador almost exactly doubled between 1973 and 1974; and a further increase is predicted for the current year. Surinam showed a similar doubling of cases during the same period. But the statistics of past and present pluses and minuses have already been overdone; our main purpose should be to look to the future. Whatever gains have been made we should strive to maintain; we should be seeking ways to reverse deterioration of control where it is now apparent; and we should be seeking new ways to develop control programs in the highly endemic areas where eradication programs were never considered feasible.

Perhaps the first step necessary in the consideration of future malaria programs, regardless of whether we call them eradication programs or control programs, is to admit in a forthright way that we have thus far failed to either achieve eradication or even to achieve a technology which is adequate for this purpose. Eradication is an absolute term that demands a certain amount of perfection. Changing the rules or redefining perfection at this point will not alter the result. The highly efficient smallpox eradication program has eliminated the disease from more than 99 percent of the world—yet it will be a failure if the few remaining foci are not eliminated. We must accept the fact that we have, through what might be retrospectively termed a very expensive control program, eliminated malaria from a few areas and reduced morbidity and mortality in considerably larger areas, but we have not achieved widespread progress toward eradication of the disease.

It is quite understandable that the many countries which have expended for this purpose relatively large proportions of their health budgets for many years with great hopes and expectations of achieving this goal would be reluctant to accept failure and retreat to lesser goals. In this regard, the influence of the international organizations—the World Health Organization worldwide and the Pan American Health Organization in this hemisphere—will be a key factor and should be exerted as vigorously toward reorientation to a policy of sane, economical control programs as it was 20 years ago toward establishment of time-limited eradication as a policy. While such a reorientation of policy was first officially proposed in 1969 by the World Health Assembly's resolution on the needed revision of strategy of the eradication campaign, progress toward this goal has been slow. Resistance to change has been deeply entrenched in some countries—and indeed in some segments of the international organizations. During the past year or two, progress seems to have accelerated, perhaps stimulated by an ever-worsening situation. A very excellent summary of the past, present and future of malaria programs was provided by Lepes in 1974.¹⁹ While not being pessimistic, this review was highly realistic about our current needs in malaria programs and our prospects for the future. This paper, along with those of Janssens,²⁰ Weller,²¹ and Bruce-Chwatt,²² forms a tetralogy of presentations at the International Congresses in Athens 2 years ago, which together provide a superb view of the past, present and future of our sometimes faltering battle against malaria.

The 28th World Health Assembly in May 1975 adopted a resolution on the development of the antimalaria program which took note of the deteriorating situation and its grave consequences and recommended renewed efforts by individual countries to maintain malaria *control* programs within their ability to do so. It is of interest that the word "eradication" did not appear in this resolution. More recently, in September of this year, the Directing Council of the Pan American Health Organization adopted a significant resolution which also took note of the current problems and proposed a broad range of remedies. Perhaps the most significant recommendation was toward the "development of malaria control methodologies better adapted to the epidemiological and eco-

conomic conditions in each country." Along with official recognition of our need to retreat, at least temporarily, from our earlier goals, has come, albeit slowly, official recognition of our other immediate needs, including the reestablishment of research and training programs, the exploration of alternative methods, and the development of basic epidemiologic information for each of the vastly differing ecological situations which characterize the malarious areas of the world.

Research and training, the two casualties of the eradication concept, are now a generation behind—and we are almost to the point of not having the remaining resources to reinstate significant programs for either. Both need to be considered in the broadest sense. Research and development must include a full range of interests, from the most basic laboratory studies to the most practical of field investigations. Training must not be limited to the production of technicians, skilled only in the use of one or more practical methods, but must produce well-rounded classical malariologists.

The limited research which has been done during the past 20 years has provided no significant new means for controlling malaria. In the recent past it has been repeatedly pointed out that we now have all of the tools and methods that will be available in the foreseeable future for malaria control. The massive program in the United States toward the development of new chemotherapeutic agents turned up some promising compounds, but none appear so promising as to revolutionize the prophylaxis or therapy of malaria—and none seem to be nearing availability. Highly interesting results have been obtained on malaria immunology and immunogenesis, but it must be realized that we are still far far away from a useful product. Novel methods of vector control have been the subject of limited study, and to date show equally limited promise. The sterile male release method has shown some promise in one study and is now being subjected to a greater challenge in a field study in El Salvador, and studies on other genetically based methods are also still in the early developmental stages. The use of mosquito pathogens is being explored, but is also in an early stage of development. One can be hopeful that continued and expanded research in these fields will yield some

remarkable breakthrough, but such a breakthrough is something on which we cannot depend and for which we cannot sit back and wait. Jenner's discovery of efficient vaccination for smallpox came 100 years before the elucidation of the mosquito transmission of malaria. Yet it appears to have taken 175 years to translate this discovery into a technology that now seems to assure smallpox eradication. One wonders if it will take equally as long for the conquest of malaria after the development of the first crude immunogenic method.

In spite of this somewhat gloomy outlook for the immediate future, there is cause for encouragement. Many national governments, as well as the international health agencies, are beginning again to look at research as a necessity for progress and to support actively research efforts. This has been strongly evident in the recommendations and resolutions of a number of international groups. Although it is somewhat perplexing that the Resolution of the 28th World Health Assembly on the development of the antimalaria program did *not* specifically mention research as a need, the World Health Organization is indeed exploring new initiatives in tropical disease research. In a proposed new "Special Program for Research and Training in Tropical Diseases" malaria is one of six diseases under consideration. At present the disease problems to be considered include only two facets: Chemotherapy and Immunology—specifically immunization, in the case of malaria. The program would include basic and applied research and would concentrate initially on the development of research and training resources in emerging countries, principally in Africa. There will be a need for a significant response on the part of the developed nations in financial support, staffing and collaboration. This "Special Program" is now in its formative stages and hopefully will evolve into a viable and continuing research effort directed toward the short-term problems with immediate application to disease control, as well as the longer-term basic investigations which may eventually lead to the development of new and effective weapons. There is some danger at this point in overemphasizing the faint possibility of developing, through a concentrated effort, another panacea which will immediately solve all our problems—the one perfect drug, the one new insecticide, the one-shot lifetime immunization.

There is a dire current need for both types of research, and both should be fully supported. Our *immediate* needs are more in the resumption and extension of careful studies on the ecology of malaria wherever it exists, to enable us to apply intelligently and effectively whatever weapons we now have at hand. This should include a careful re-exploration of the long-neglected source reduction measures so important during the first 50 years of this century.

The U. S. government is currently investing some 10 to 15 million dollars annually in malaria-related research, with much of this being provided by the Department of Defense, principally for development of chemotherapeutic agents. The Agency for International Development, for many years a prime source of support for operational eradication programs in developing countries, is providing, at present, significant support for basic research in an effort to accelerate the development of an effective and practical immunizing agent. While this level of expenditure in the United States would seem generous for a disease that is not strictly one of our domestic problems, if we consider the world's disease problems to be our own, it does not seem very high. Even an expenditure of 100 million dollars annually would be equivalent to only about one dollar for each case and about 100 dollars for each infant or child death attributable to malaria on the African continent alone.

The other necessary component of progress, malariologic expertise, may present an even less encouraging outlook, although some measures are being taken to improve the situation. The pressing need of the developing countries is for skilled malariologists who can consider realistically the existing problems and can manage control programs which are not only tailored to fit the peculiar epidemiologic, ecologic and cultural characteristics of a given area, but also are within the constraints of health priorities and economic potential of a country. As pointed out previously, there is a growing recognition of this need, but thus far it has elicited more lip service than action. The broad training to produce such experts does not now seem to be available. The World Health Organization is collaborating with the Government of Iran in establishing a professional course of study which should provide such a background, and a similar program is under

consideration in the New World as a cooperative venture of the Government of Mexico and the Pan American Health Organization. Hopefully, both of these ventures will succeed and will spawn similar courses elsewhere. The developed countries of the world, including the United States, might well sponsor, with the cooperation and assistance of the international health organizations, the development of programs which would provide the needed graduate training for their own scientists as well as for those from the economically less favored countries. Certainly this would constitute a significant contribution to the promotion of health worldwide.

An accurate prediction of the progress that will be made toward eliminating malaria during the remaining 25 years of this century is impossible—even the maintenance of current levels of control will be difficult. One might approach the future with something between very cautious optimism and qualified pessimism. I have concentrated principally on the technical aspects of control, ignoring almost completely the major economic, social and political factors which may indeed be more important than anything technical in determining the success or failure of any disease control effort. Two of the major problems of our time, the energy crisis and the food crisis, will affect our progress, directly and indirectly. The need for energy will necessitate a rapid growth of hydroelectric impoundments and the need for food will require irrigation projects, both conducive to the expansion of endemic malaria foci and other water-related diseases. The old adage that "malaria flees before the plow" may well be invalid today, if it ever was valid, since man's expansion into newly developing agricultural areas may increase his risk of infection. The continuation and growth of worldwide inflation will serve to diminish proportionally the level of disease control effort. Malaria is not the only disease of consequence within its range and, thus, will have to compete with others in the health budgets of affected countries.

On the brighter side, while malaria may not always "flee before the plow," it often does flee from industrialization, urbanization and general economic and social improvement. Hopefully, trends in these directions will serve to ameliorate some of the negative factors mentioned above. Unfortunately, these are at best slow processes.

In the meantime, our immediate task should be to regroup and to utilize to the best of our scientific and economic ability the tools which we now have at hand. We are not bankrupt in weaponry—perhaps only a little less than solvent in expertise and resourcefulness. We have excellent insecticides that are still effective against adult and larval anophelines over a wide range of circumstances. We have excellent chemotherapeutic agents that are still widely effective. We have the know-how of a generation of malariologists who showed us how to achieve malaria control even before the modern weapons became available.

Great progress can still be made, even in nations where malaria is still man's number one disease problem or where it is rapidly returning to that status. The epidemiology of the disease and the behavior patterns of human and anopheline hosts must be reexamined carefully in every ecological niche as a basis for effective and economic application of a wide variety of control measures. Continuing research and training in practical malariology will be the keys to solution of problems which will face the control programs for the next several decades. Hopefully, new and expanded initiatives in more sophisticated laboratory research will at some time in the not-too-distant future yield the newer weapons which will make possible realization of the great dream of eradication.

It is incumbent on the international organizations and the more affluent countries to assist the developing world to the extent possible in continuing efforts to reduce the malaria problem. In doing so, they should not demand the perfection of an eradication program nor impose sophisticated methodologies which would be economic or technologic impossibilities if the countries were left to their own resources by the vagaries of international support.

There are many lessons that we should have learned well through our experience in the malaria eradication era. A particularly important lesson for the future is the danger of entering such a disease-eradication campaign without sufficient knowledge of the worldwide epidemiologic factors involved and without the availability of an adequate technology for control. The successes of the smallpox campaign will undoubtedly bring about renewed faith in the eradication concept,

and certainly there are diseases which would even now fit into this mold. But many others do not, and untimely proposals for eradication of such diseases as schistosomiasis or onchocerciasis, or even malaria, within a predictable time frame can lead only to disappointments and the ill-conceived expenditure of resources badly needed for other essential public health programs and for the development of the technology of disease control.

Others in the recent past have eloquently expressed these same concerns. Some of the past presidents of this Society, including particularly Drs. Huff,¹ Weller,²³ and Reeves,²⁴ have in their presidential addresses and other presentations provided much food for thought in our approaches to disease control and eradication, and I would highly recommend another look at the principles which they have discussed.

It will be interesting, at least for some of you, to look back from the perspective of the year 2000 to see what progress has been made in the last quarter of this century in the elimination of malaria as mankind's primary infectious disease problem. Hopefully, at that time it will be possible to say that we were able to rid ourselves of this disease only 100 years after the basic knowledge of its epidemiology became available. This is perhaps too optimistic an outlook, but we can make great strides toward that goal if, from this point, we recognize the problems that exist and begin our slow progress toward their solution.

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