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WORLD-WIDE MALARIA ERADICATION: PAST, PRESENT AND FUTURE

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In the United States today, "malaria" is a word that stimulates little more than mental pictures of tropical jungles and rain forests, yet only 25 years ago it was synonymous with recurrent illness and suffering for hundreds of thousands of citizens. As recently as 1936 incidence reached a high peak in the southeast, where at that time the disease was normally endemic, and as late as 1943 a small epidemic occurred at Battle Creek, Michigan, a relatively northern locale.

Throughout history, our country, together with most of the warm countries of the world, had suffered under the onslaught of this disease. But its cause was not determined until 1880 when Dr. Lavaran in Algeria discovered the agent, a parasite in the blood. The mode of spread was not established until 1898 when Ronald Ross, working in India, proved that the parasite is transmitted by mosquitoes. Almost simultaneously Brassi, Bignami, and Bastianelli, in Italy, came to the same conclusion but with the added point of research that the parasite must undergo at least a ten-day period of development in the mosquito's body before the insect can transmit infection.

Of equal importance was the finding that the parasite could develop only in mosquitoes of a single genus, the *Anopheles*. Over the ensuing years, it was learned that not all species of *Anopheles* feed on man often enough to be of any significance in the transmission of malaria, that the different species have considerably different habits. Some prefer to rest indoors in the daytime, others outdoors. Some prefer to lay their eggs in the quiet waters of a swamp, others along the edge of mountain streams, or in puddles, or ponds, or springs. These and other pertinent facts became known through patient research and observation extending over a period from 1900 to 1940 and later.

Once the medical world had accepted these facts concerning the epidemiology of malaria, its attacks against the disease were concentrated on two vulnerable points in the chain of transmission—the parasite in man, and the transmitting insect in nature. In the early part of this century, the only drug known to be effective against the parasite in man was quinine. But although it was used in massive and repeated doses, both prophylactically and therapeutically, little success was achieved in control of malaria by this means alone.

Better results were obtained through attacks upon the mosquito itself, largely by the use of chemical larvicides and by drainage. Initially, however, there was considerable resistance to this approach to control, for many authorities believed it economically impossible. Despite these doubts, in the Canal Zone from 1904-1914 Gorgas and LePrince demonstrated the effectiveness and economy of malaria control by larviciding methods. Others followed in their pioneering footsteps, and by the beginning of World War II a considerable technology had developed around the use of three larvicides—oil, paris green, and pyrethrum.

For many years oil was used as a larvicide. Spread as a thin surface film on the waters of mosquito-breeding areas, it killed the larvae by cutting off their vital supply of oxygen. After 1921, paris green was used extensively. Applied in a diluent of dust to the water's surface, it was ingested by feeding larvae and killed them. Pyrethrum came into use during the late years of the larviciding period. But supplies were limited and the price remained high, so it was used only on a small scale.

The basic weakness of all of the larvicides was the need for frequent application. None remained effective for more than a few days, so they had to be reapplied at least as often as the length of the larval cycle, or approximately weekly. In some cases larviciding was supplemented by drainage to obtain better control for longer periods. However, programs of larviciding and drainage were expensive, and their costs could be justified only in densely populated areas. Through the years, therefore, urban areas received adequate protection but rural areas seldom did.

War circumstances, of course, justified the expenditure of a considerable effort on malaria control. In the United States during World War I, more than 40 control projects in 15 states protected 1,750,000 civilians and 800,000 military personnel. In World War II, the United States Public Health Service and the Armed Forces conducted 2,200 malaria control projects in war areas in 24 states. These programs, coupled with an increased standard of living after the war, reduced malaria in this country to the lowest point in its history and suggested that eradication of the disease in the United States was possible.

During the later years of World War II, the possibility of attack against the adult mosquito rather than the larvae asserted itself. Attempts had been made in this direction as early as 1936 by Park-Ross and deMeillon in South Africa, who sprayed pyrethrum in kerosene on the daytime resting places of the vector. This preparation killed the adult mosquito before the parasites could develop in its body. However, it had little residual effect, and spraying had to be repeated weekly. Even so, this was no more frequent than was required for larviciding. The method proved to be effective and sufficiently low in cost to be used in the rural tropics.

Prior to this time most malaria control had been confined to the urban areas of the more highly developed countries, but the development of techniques for attack against the adult mosquito made possible malaria control, and eventually eradication, in many parts of the world.

The discovery of DDT, an insecticide with long-lasting residual effectiveness, permitted development of truly economical adulticiding procedures. While DDT, the compound, is too well known to merit description here, the details of its application to malaria control may not be such common knowledge and, hence, bear sketching here. It was in 1939 that Müller, while screening compounds for their effectiveness against moths, found that DDT was ideal and that it also killed many other insects. Most exciting was the fact that for several months it continued to kill insects coming in contact with it.

During World War II, the potential value of DDT to the Allied war effort was recognized in official intelligence circles, and samples reached the United States in the early years of the war. Here it was placed in the hands of the United States Public Health Service, the Department of Defense, and the United States Department of Agriculture. At the USDA's laboratory in Orlando, Florida, the long-lasting insecticidal qualities of the compound were first observed. For periods of several months, mosquitoes were destroyed when they rested on surfaces that had been sprayed with solutions of the compound.

With this new weapon the frequency of attack against malaria could be reduced from a daily schedule, in the case of drugs used against the parasite in humans, or a weekly schedule, in the case of larvicides used against the mosquito vectors, to a spraying schedule of only a few times a year. This development put malaria control within economic reach even of rural areas and made eradication a possibility.

The first large-scale use of DDT was directed to actual war operations in the Pacific Theatre where malaria was a strong factor in many campaigns. At the end of the war, when thousands of the returning troops carried malaria in their bodies,

there was definite danger that they would spark a dangerous resurgence of the disease in this country. To counteract this threat, the United States Public Health Service and the departments of health of some 14 states cooperated in an extensive program of malaria control with DDT, which was becoming available in significant quantities. The use of larvicides, screening, and drainage was slowly displaced by the simple and inexpensive spraying of DDT upon the walls of each habitation in the endemic areas. The results of this program exceeded even the more optimistic predictions, and malaria in the southern states dropped lower and lower. Possibly the rate of decline, if not the final result, was strongly influenced also by improvements in the general standard of living which occurred in the post-war years, and by the common use in almost every household of the convenient and newly available insecticides in aerosol containers; but the DDT spraying program was probably the decisive factor.

As the program progressed, spots completely free of the disease began to appear in traditionally malarious areas, thus allowing efforts to be concentrated in the more stubborn areas. The disease began to disappear, and malariologists, much to their delight, found as a distinct possibility the Utopia often dreamt of, but seldom accomplished—the complete eradication of a major disease from a country.

That the success in the United States was not a fortunate accident of nature was soon demonstrated by similar success in Italy (1). The Pontine Marshes south of Rome were infamous as malarious areas for centuries before Missiroli and his co-workers began the application of DDT and chlordane as residual insecticides. Today this area is free of the disease, is producing large quantities of agricultural products, and is as healthy as any area of Italy. This success was repeated in other sections of Italy, including Sardinia, until the disease is virtually unknown in the peninsula today

Similar results were achieved in other parts of the world, notably in South America, and the concept of world-wide malaria eradication began to evolve. This level of progress was not reached, however, without discouraging set-backs and a full complement of technical problems. Among these, the development of resistance by houseflies *(Musca domestica)* was noticed as a warning signal as early as 1948, and insecticide resistance in a vector of malaria was suspected in Greece in 1949. To counteract this threat, insecticides other than DDT were used Probably all of those available have now been tried, at one time or another, in the laboratory or field. At present the Agency for International Development Expert Panel on Malaria recommends that DDT be used until resistance develops. Dieldrin should then be the first substitute, and malathion the second (2). Baytex may also be considered, but it is more expensive than the others and more toxic to man and animals.

When dieldrin has been used, generally it has been applied every six months. It should be used only in the localized areas where DDT resistance has been demonstrated, and specific safety precautions must be observed in its application, for its use without adequate precautions has produced numerous cases of poisoning among spray crews

Because of the resistance problem, eradication of malaria cannot take the slow and easy course that has frequently characterized control programs in the past. Instead, the strategy must be well planned in advance, the operational organization established, and all preparations made so that a concerted attack may be conducted country-wide and results accomplished before resistance in the vectors of any area can become a major problem.

A variety of factors and [illegible] as have a bearing on eradication programs. Among t[illegible] [illegible]ems relating to the human population are nomadism, i[illegible] [illegible]ation, pilgrimages, and fringe habitation. Among those relating to the vector are the outdoor feeding and resting habits of these mosquitoes, and their habits or actions relative to the host and to insecticide-treated surfaces. Climatic factors include the effects of humidity and temperature on the duration and intensity of residual action. Housing problems relate first to the type of surface to be treated (whether plaster, wood, or other material; whether painted, papered, finished otherwise, or bare; and whether clean, or filmed with soot, dirt, or grease), and, finally, to needs for post-treatment modifications to prevent reinfestations. Despite the obstacles, world-wide malaria eradication is moving forward A survey of the extent of the world problem in 1957 showed a total world population of 2.7 billion. Of this number, more than a billion lived in malarious areas—466 million of them protected by control programs and 702 million not protected (Table I).

TABLE I

Extent of the Malaria Problem, 1957

World Population	2,737,000,000
Population Not at Risk	1,569,900,000 (57.3%)
Population at Risk but Protected or About to be Protected	466,000,000 (17.0%)
Population at Risk, Not Protected	702,100,000 (25.7%)

Source of Data: WHO International Protection Against Malaria, 1957.

In September 1958, eradication had been practically achieved in nine countries, was well advanced in seven, was being started in forty-six, and was being planned in fourteen (Table II).

TABLE II

Extent of the Malaria Problem, 1958

	Countries	Population at Risk, millions
Eradication Practically Achieved	9	51.8
Eradication Very Advanced	7	13 1
Eradication Being Implemented	46	576 0
Eradication Being Planned	14	125 3
Totals, Protected or About to be Protected	76	766.2
Eradication Not Yet Planned	64	401.9

Source of Data: WHO Report of Expert Committee on International Quarantine. International Protection Against Malaria, WHO/1Q/67-October, 1958.

This left 402 million still exposed but unprotected By January of 1960, eighteen countries had achieved eradication, protecting additional populations of 108 million previously subject to attack. In sixty-six countries, eradication programs were in progress and would protect another 893 million people. In thirty-two countries with a total population of 209 million persons exposed to malaria, programs were getting underway or were in the planning stages. In only thirty-seven countries, where 43 million persons were at risk, were there no plans for malaria eradication. Details may be found in Table III

There have been exceptions to the general success indicated by this record of achievement. Most notable, no doubt, is in Africa, where great areas of the continent have remained endemic for malaria throughout man's span of memory. Various factors have contributed to this incomplete success. For one thing, in the area south of the Sahara desert, a highly efficient vector, *Anopheles gambiae,* spreads falciparum malaria to hundreds of thousands of people each year, despite a partial tolerance among the populace developed over many generations. Here, under unusual conditions, the disease has moved out from this endemic area into contiguous areas, where people not normally subject to exposure have become infected.

Other factors in Africa's continuing malaria problem include: unstable political situations, long seasons of transmission, sometimes extending throughout the entire year; labor migrations; wide dispersal of habitations in jungle areas; lack of roads and other facilities to enable transportation and communication; nomadism, poverty, and illiteracy; and lack of trained professional and administrative personnel to give necessary directions to the programs.

TABLE III

Extent of the Malaria Problem, 1960

1. Eradication completed (18 countries or territories including a population of 108 million living in once-malarious areas)

Barbados	Lithuania (USSR)
Byelo-Russia (USSR)	Moldavia (USSR)
Chile	Martinique
Corsica (French)	Netherlands
Cyprus	Puerto Rico
Gaza Strip	Singapore
Hungary (understood to be eradicated)	Tobago
	Ukraine (USSR)
Italy	United States
Latvia (USSR)	

2. Eradication program in operation (66 countries, 893,501,000 exposed to malaria before initiation of program)

Afghanistan	Guatemala	Philippines
Albania	Honduras	Portugal
Algeria	India	Portuguese India
Argentina	Indonesia	Romania
Bolivia	Iran	Ryuku Islands
Brazil	Iraq	Sarawak
British Guiana	Israel	Spain
British Honduras	Jamaica	St. Lucia
Bulgaria	Jordan	Surinam
Burma	Laos	Swaziland
Cambodia	La Reunion	Thailand
Ceylon	Lebanon	Trinidad
China (Taiwan)	Libya	Turkey
Colombia	Malagasay (Rep. of)	UAR-Egypt
Costa Rica	Mauritius	UAR-Syria
Dominica	Mexico	Union of South Africa
Dominican Republic	Nepal	USSR
Ecuador	Nicaragua	Venezuela
El Salvador	Panama	Vietnam (Rep. of)
French Guiana	Panama Canal Zone	Yugoslavia
Greece	Paraguay	Zanzibar and Pemba
Grenada	Peru	
Guadeloupe		

3. Preparing for malaria eradication

A. Plan of operation—program suspended

Haiti (3 million exposed to malaria)

B. Pre-eradication survey (5 countries, 85 million exposed to malaria)

Bechuanaland	Pakistan	Somaliland (UK)
Korea (Rep. of)	Saudi Arabia	

C. Pilot project (14 countries, 58 million exposed to malaria)

Cameroons, State of	Nigeria	Sudan
Dahomey, Republic of	North Borneo	Togo
Ethiopia and Eritrea	Senegal	Uganda
Liberia	Somalia	Voltaic Republic
Netherlands New Guinea	South Rhodesia	

D. Negotiations underway for a malaria eradication program (12 countries, 62 million exposed to malaria)

Angola	Ghana	Mozambique
Belgian Congo	Guinea	Ruanda-Urundi
Central African Rep.	Malaya	Sierra Leone
Cuba	Morocco	Tunisia

4. No malaria eradication program yet contemplated (37 countries, 43 million exposed to malaria)

Aden Protectorate	Ivory Coast (Rep. of)	Nyasaland
Australia	Japan	Papua & New Guinea
Bahrein	Kenya	Portuguese Guinea
Bhutan	Macao	Qatar
Brunei	Maldive Islands	Sao Tome & Principe
Cameroons (Br.)	Mauretania (Rep of)	Solomon Islands
Cape Verde Islands	Muscat and Oman	South West Africa
Chad (Rep. of)	New Hebrides	Spanish Guinea
Comoro	Niger (Rep. of)	Spanish N. Africa
Congo (Rep. of)	North Rhodesia	Sudan (Rep. of)
Gabon (Rep. of)		Tanganyika
Gambia (Rep. of)		Timor
Hong Kong		Trucial Oman
		Yemen

Source of Data: ICA Expert Panel on Malaria. Report and recommendations on malaria: a summary. *Amer. J. Trop. Med. & Hyg.* 10(4): 459-460, July, 1961.

Certain parts of the continent have fared better: In the Cameroons and Liberia, particularly, intense efforts have blocked transmission. Such intensive operations probably could produce equal success in other parts of the continent, but, on a per capita basis, the widely dispersed rural population would make this an expensive and perhaps ineffective program.

However, a newly developed mosquito-control technique may add another weapon to the campaign against malaria, not in Africa alone but in any other area where the disease may persist. This technique, the slow release of an insecticidal vapor over a long period of time, was developed following the observation of Mathis and co-workers, in 1958, that mosquitoes held in test spaces died when minute quantities of vapor from a container of commercial fly bait reached them (3). The bait was formulated with malathion and DDVP, and the latter proved to be the main source of the lethal vapor.

The potential advantages of a malaria-control program using such a simple procedure instead of the conventional spraying of insecticides were obvious. The technique was envisaged as one in which a container of DDVP, mixed with a carrier that would allow very slow dispersal, could be hung in the room to be protected. Such a program would require much less complex administrative detail, would require fewer and less skilled laborers, and would obviate such problems as the variations in effectiveness of insecticides resulting from differences in the surfaces treated.

Laboratory and field trials of the technique were begun in 1959. Susceptible, adult female *Anopheles quadrimaculatus* held in test chambers were exposed to DDVP vapors for four hours at various concentrations Vapor concentrations of DDVP greater than 0.010 μg per liter produced average mortalities of 95 per cent or better (4). This concentration appears to be quite critical, for concentrations between 0.007 and 0.010 μg of DDVP per liter of air resulted in mortalities of 10 to 90 per cent. These findings are reflected in ventilation studies under field conditions, which showed that increasing numbers of dispensers were needed to achieve 100 per cent mortality as the open areas of the test chamber walls increased (5).

A dispenser has been develop[illegible] for field trials that provides required concentrations over a [illegible]cted period of time. Its active unit is a cartridge compo[illegible] of DDVP mixed with a wax carrier. (This formulation [illegible] not yet been published but a paper describing it is now in press (6).) The cartridge, which is six to seven inches long and approximately an inch in diameter, is hung in the room to be treated, generally near the ceiling, or just under the roof in unceiled houses.

With the DDVP-residual-fumigant technique, the residual spraying technique, and possibly others still to be developed, malaria is under increasing attack. Malaria has already been eradicated from large parts of the world. It is being eradicated

from others. Under the combined efforts of the field worker, the research scientists, and the industries that produce the needed products, malaria can and will be eradicated from this earth so that mankind may live in large areas of the world where its threat is now ever present.

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