April 7th is World Health Day. The theme this year is "Malaria Eradication—a World Challenge". Four statements from the World Health Day message given by Dr M. G. Candau, Director-General of the World Health Organization, provide the plan for this special issue:

- In 1960, malaria remains a constant threat to more than 1000 million human beings.
- Malaria strikes first at a country's most precious resource—its young children.
- There must be no slackening of effort until the last remaining case has been tracked down and cured.
- The eradication of malaria is a challenge to all the world. In this age, when man thinks he is about to set foot on the moon, he should be capable of stamping out one of his worst enemies of his own planet.
Thousands of teams, tens of thousands of vehicles, millions of tons of materials, hundreds of millions of houses to spray, hundreds of millions of blood samples to be examined, drugs to be transported by the ton, maps to be drawn up by the thousand, the movements of millions of migrants to be observed...

MEXICO: The army takes part
Malaria in the world today

This map shows in broad lines the world’s effort against malaria. Strict cartographic accuracy of the 148 malarial countries or territories has not been attempted.
Areas without malaria

Areas with malaria

Areas where only occasional cases occur

Areas where malaria is being eradicated

Areas where the eradication programme is in the preparatory stages

Areas without an eradication programme

Areas where some species of malaria-transmitting mosquitoes are resistant to insecticides
The secret of malaria:

The link between mosquito and parasite
The life of the parasite

1. A female anopheles mosquito sucks a sick person's blood that contains sexual forms of malaria parasites.
2. Cysts, produced by the sexual malaria parasites, develop in the stomach of the mosquito.
3. Malaria parasites, fully developed and multiplied, are present in the salivary glands of the mosquito. The healthy person bitten by the mosquito becomes infected.
4. The parasites first develop in the liver of the infected person.
5. Then the parasites develop and multiply in the red blood cells of the infected person. This phase coincides with attacks of malaria, with fever, anaemia and other symptoms often leading to death.
6. Sexual forms of the parasite develop in the blood of the infected person.
For the first time in the history of mankind

The nations form a coalition to fight a single disease

A venture without precedent in human history is the present world-wide campaign to stamp out malaria. Never before have concerted international forces on such a scale been deployed against a single disease. Never before have doctors, engineers, laboratory workers and helpers of all kinds been mobilized in such large numbers in so many different countries to combat the same evil. Never before has a scheme been launched that so intimately affects the living conditions of such vast numbers of the earth's inhabitants.

In this year 1960, twelve hundred million human beings are living under the constant threat of malaria. It is not a spectacular disease; its victims show no wounds or mutilations to excite our pity; it comes upon them as they sleep, in the stillness of the night, carried by the mosquito. It is the "fever" long believed to be inescapable in tropical countries, more of a nuisance than an illness, people said.

The truth is that malaria is a disaster, and its terrible consequences (among that third of the world's population which already has more than its fair share of disease and poverty) cannot be easily visualized in countries that are free of it. Malaria epidemics can be just as destructive as plague epidemics. Those

*Dr C. A. Alvarado, Director of the WHO Division of Malaria Eradication, Professor G. Macdonald, Director of the Ross Institute in London, Professor P. G. Sergeiev, Vice-President of the USSR Academy of Medical Sciences.
who live in malaria-ridden areas, however, have become resigned to it, and accept it as a natural part of their everyday life. Its victims are quite unaware of the physical and moral deterioration it has brought about as through countless centuries it has sapped their strength, robbed them of initiative, and made them vulnerable to other, more deadly infections. Moreover, it is estimated that malaria accounts for 10-15 per cent of infant mortality in these countries.

The ultimate aim of the campaign is to eliminate the disease, to wipe it off the face of the globe, never giving up until the very last case in the remotest corner of the earth has been tracked down.

The time has come for malaria to take its place in history alongside the Flood and the ancient plagues.

World strategy

The necessity for this giant undertaking was unanimously recognized by the representatives of all the governments attending the Eighth World Health Assembly in Mexico City in 1955. The World Health Organization was given charge of this world-wide operation which was to be something quite new in medical history.

This was to be a health programme presenting many features of a military campaign, and one whose aim was not merely the surrender, but the extermination of the enemy. An antimalaria army came into being, with its intelligence service, its supply lines, its transport facilities, its arms and munitions depots, its logistics offices, its general staff and high command: the last an office of modest dimensions in Geneva. It is occupied by Dr C. A. Alvarado, Director of WHO's Division of Malaria Eradication and chief of 329 malaria experts now at work in 73 different countries.

"We are engaged on a monster programme", Dr Alvarado admits. "It calls for tens of thousands of teams, and millions of tons of supplies and equipment. Hundreds of millions of homes must be visited, hundreds of millions of blood tests carried out, and tons of drugs supplied. Thousands of lorries, cars, bicycles, donkeys, camels, elephants and boats are needed. We must co-ordinate the work of hundreds of laboratories, help establish contacts and exchange of information between hundreds of research and laboratory workers, arrange meetings of experts, translate reports from many different countries so that they can be understood in the others.

"This drive to wipe out malaria also means making thousands of maps, taking a census of population in the affected areas, keeping a check on the movements of millions of nomads, giving lectures, and holding open-air discussions with villagers to convince them of the need for the action being taken.

"Malaria eradication", declares Dr Alvarado, "is above all an organizational and administrative problem, for we now know almost all we need to know about its scientific and technical aspects and researchers are working hard on the few

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A considerable financial effort

The figures below show how malaria eradication campaigns were financed in 1958. The World Health Organization and the Pan American Health Organization worked closely together with the United Nations Children's Fund and the International Co-operation Administration of the United States. In 1958, the joint efforts of these organizations covered 29% of world expenditure on malaria. The remaining 71% was met separately by the governments of the countries where campaigns are being fought.

1958 expenditures in millions of dollars

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<tr>
<th>Source</th>
<th>Expenditure (Millions of Dollars)</th>
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<tr>
<td>Governments</td>
<td>77.5</td>
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<td>International Co-operation Administration of the United States</td>
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<td>United Nations Children's Fund</td>
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<td>World Health Organization</td>
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<td>Pan American Health Organization</td>
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<td><strong>Total</strong></td>
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removing unknowns. But malaria eradication is also a question of money. According to estimates, the campaign costs rather less than one dollar for each human being freed from the menace of malaria. "It is also a question of perseverance, for any slackening in the drive to eradicate malaria might create doubts concerning the whole conception of eradication and the obvious benefits that will accompany it. Any hesitation at this time could shake people's confidence in the authority and good judgement of those United Nations bodies whose function it is to improve the health of the masses throughout the world.

"Malaria eradication is indeed a challenge to every country of the world."

For thousands of years malaria remained a mysterious affliction, which seemed connected with the presence of marshes or other unhealthy surroundings. The foul smells arising from stagnant water were also held responsible. The first step towards solving the mystery was the discovery by a Frenchman, Laveran, in 1880, that malaria was caused by a parasitic organism, a haemosporidium (plasmodium). In 1898, a British doctor, Ronald Ross, showed that the parasite of bird malaria is transmitted by female mosquitoes, and the same year Italian scientists proved that the human para-
site is carried by Anopheles mosquitoes.

Up to that time malaria patients had been treated with cinchona bark, which later became quinine. Blood-letting was also practised. Whenever they could, people would move away from areas that were believed unhealthy, thus, without realizing it, escaping the risk of contact with mosquitos. Water management and drainage schemes were also carried out.

During the building of the Panama Canal, special squads were kept busy killing the mosquitos in the huts which housed the workmen. Attempts were also made to destroy the mosquito larvae with substances known to be poisonous to them (gas-oil, Paris Green).

These were the methods employed up to the Second World War; they were both expensive and troublesome, since the merest puddles likely to provide a breeding ground for mosquitos had all to be treated. Furthermore, as a WHO report tells us, such operations could be carried out only "in communities of a marked demographic, economic or strategic value". In plain language that meant that only a few privileged groups received favoured treatment because they lived on highly-productive agricultural land or in prosperous mining areas, or else in places where troops were stationed. "As a consequence", the report states,
"the areas of control were mere dots on the malaria map of a country."

It was the discovery of DDT by a Swiss, Paul Müller, who was awarded the Nobel Prize for it, that completely changed the outlook in the fight against malaria after the Second World War.

It transformed malaria control into a simple operation of spraying this "residual" insecticide on the inside walls of dwellings, where the mosquitoes rest after feeding on human blood. The poison killed off the mosquitoes. Malaria sufferers were then given medical treatment, and the spread of the disease was thus halted.

It seemed that the battle had been won. At last the antimalaria campaigns would extend beyond the privileged areas to all the villages and hamlets where they were most badly needed. It would be possible for the first time to estimate the time and money required on the basis of the size of the population to be protected and the average wall surface to be sprayed per head. The amount of insecticide needed, the number of spraying pumps, the manpower involved and so on could then be accurately worked out.

The war against malaria had entered a new phase in which science and logistics were paramount. The way was now open for the huge eradication programme that was soon to be launched.
A DISASTROUS DISEASE

The eradication of malaria will free humanity from a ruinous disease that is a disgrace to our time. Other diseases may decimate a population; malaria can depopulate a whole region. Throughout history it has driven men off vast tracts of fertile land. Those it does not kill it enslave. And those that stay on, drag out a miserable existence.

These are facts that no one questions. Yet conclusive proofs of the economic benefits resulting from malaria eradication are difficult to obtain. Nevertheless, the reports that WHO receives from all over the world provide some valuable indications about the economic, social and human significance of the present anti-malaria drive.

- In Afghanistan, about one million peasants lived under the constant shadow of malaria, and some of the most fertile land could not be cultivated because of the ravages of the disease. The total cost of antimalaria operations from 1949 to 1959 did not exceed $750,000, whereas malaria was the cause of a yearly loss of earnings amounting to about $20,000,000.

- In Ceylon, the disappearance of malaria has resulted in a saving of about $30,000,000 per year, that is, six times the total expenditure on the ten-year antimalaria campaign.

- In India, the figures supplied by Dr K. Viswanathan, malaria adviser at the WHO Regional Office in New Delhi, are really astronomical. He estimates that the annual economic losses caused by malaria in that country are in the neighbourhood of $500,000,000, corresponding to loss of wages, loss of output, etc., affecting the fifty million Indians who fall victims to the disease every year. On the other hand, he has calculated that the total cost of a malaria eradication programme of several years' duration in India would not exceed $190,000,000, i.e. much less than half the amount of the present yearly losses.

- In Mexico, where 175,000,000 dollars' worth of economic damage is caused every year by malaria, the total cost of the five-year eradication programme is expected to be about $20,000,000.

- In the Philippines, the uprooting of malaria has made possible many projects which previously were out of the question: construction of roads, opening of mines, and building of houses and industrial premises.

- In Thailand, it has been estimated that fifty million agricultural worker-days were lost each year on account of malaria. This equals a rice harvest of $15,000,000, whereas the cost of the malaria eradication programme from 1954 to 1958 was $500,000 per year.

- In French Guiana, infant mortality decreased by more than 50 per cent since the large-scale anti-malaria operations carried out in 1949-1951.

- In Nigeria, according to a survey, babies born of malaria-infected mothers weighed on an average about 150 g (5 oz.) less than ordinary babies.

- In Greece, says Dr Belios, Director of the Malaria Department, the average height of army recruits has increased by 4.5 cm since malaria has practically disappeared from that country.

- In Sardinia, this was what Dr Paul F. Russell of the Rockefeller Foundation saw when he revisited the island after an interval of 20 years. "When I first visited Sardinia in 1929, I was distressed by the pitiable condition of many of the children in malarious villages. In a typical street there would almost always be sad little creatures with large bellies and pale faces sitting listlessly in the doorways of their homes. When I last visited Sardinia in 1950, after malaria had been eradicated, the village children everywhere seemed to be playing vigorously, kicking balls and romping about in a normal healthy manner, with rosy cheeks and without swollen bellies, a vivid and striking contrast that left no doubt in my mind about the beneficial effects of malaria eradication.

"In the same year I visited Oristano, in Western Sardinia. This marshy area had been so malarious that it gave rise to a local proverb: 'Chi va al Oristano resta al Oristano (Who goes to Oristano stays in Oristano)'. Here Mussolini carried out a huge 'bonification' that failed because the drainage did not stop malaria transmission; the land could not be profitably farmed because local and imported labourers rapidly became incapacitated by malaria. But in 1950, malaria had been eradicated and prosperous farmers were the rule in this area. In fact, later in the year I was told that the successful harvest had created several 'lire millionaires'. There was no room for doubt about the economic benefits."
Reconnaissance patrol in the Himalayan foothills

For ten days, a 'World Health' photographer, Eric Schwab, went with a WHO sanitary whose job it was to organize the supply lines for the malaria campaign in the mountains of Nepal.
In Pokhara, at the foot of Anapurna mountain, sanitarian MacInnes starts his survey.

In the high mountain villages, the only way of transporting the tons of supplies that will be needed during the forthcoming malaria campaign is to use porters.
The long trek of sanitarian MacInnes from Pokhara to Kathmandu
Evening duty: filling in the map

In the mountain villages, storage space for the supplies needs to be found

Good relations with the population
At 6000 feet above sea level, the reign of the mosquito ceases.

Up to here the malaria campaign will be pursued but no higher: in Nepal, the malaria mosquito is not found above 6000 feet.

The task is completed: MacInnes travels back to Kathmandu and makes his report to the Nepalese authorities.
ONCE UPON A TIME there was a happy young couple. They loved one another dearly. But Fate was envious of their bliss: one day, Death came and took the young wife away.

Overwhelmed with grief, the husband would not think of burying her. But the work of Death is the same for everyone and her body began to return to dust. The sight was too much for the villagers and, rather than part from his wife, the young man chose to go away. He became a pariah rejected by everybody and went to live on the river, leaving his sampan only to fetch food from the nearest village.

Finally, because of his stubborn will to keep the object of his love, the Genii took pity on him. One of them appeared to him as he was drifting on the river in deep grief and despair. "It is in my power to help you," the Genie said "but you should know that it is not always wise to change one's destiny. You should learn to accept your fate. However, if you really want it, I shall make your wife live again... I hope you will not live to regret it."

The husband said that this was his fondest hope. He would never regret.
LET IT BE DONE AS YOU WISH... the Genie said. He pricked the man's finger letting out a drop of blood which fell on the dead body of the girl. And lo, she was alive again, as beautiful and as fresh as ever.

The young couple decided to continue living on the river. But one night, coming back from the village where he had gone for food, the husband could not find his lovely wife. The sampan was empty. She was gone. He called for her but she did not answer. Yet he had not far to go to find her. She had left home to live with a man on a boat nearby. Her husband begged her to return, but it was of no avail. She did not want to come back. She would simply follow her will.

He tried to tell her how ungrateful she was. Was it not to him that she owed her second life?

Standing on the prow of the next sampan, the young woman answered him back, and they argued a long time. In the end she said she would have no more to do with him. He could have his drop of blood back.

She snatched a long pin from her hair and pricked her finger. A pearl of blood sprang out and rolled into the river. With it went the life that her husband had given back to her. Her body fell again into dust and drifted gently on the water. Slowly, the dust changed into tiny grubs, from which mosquitoes were born.

The husband then remembered the words of the Genie. He did not bewail his unfaithful wife. He married again and had many children, from whom we all descend.

As for the faithless one, she cannot overcome her anger and grief. She has been changed into a mosquito. She harasses mankind with her buzzing, thus expressing her sorrow, and she stings us trying to steal back the drop of blood which would give her life again.
The malaria campaign in Iran has reached the neighbourhood of Shiraz. Here is how a "World Health" photographer, Philip Boucas, saw modern science and technology penetrating the landscapes that were sung by the greatest Persian poets.
To check the effectiveness of the insecticide, mosquitos are placed in these cones.
villagers in Kazerun wonder whether insecticide is still effective

All malaria cases are carefully recorded and detailed statistics drawn up.

All houses are clearly marked to show when they have been sprayed.
Here Dr Emilio Pampana, who was the first Director of Malaria Eradication in WHO, tells some of his reminiscences and estimates the chances of total victory over the disease to which he devoted the best part of his life
I was in great hurry; I was going to be married and my fiancée had just arrived from Italy to join me. She has assisted me since as my best friend and helper. But my suddenly getting up in the middle of a class to go and get married caused quite an uproar.

A few days after our wedding, I accepted an appointment as medical officer to a mining company in the Chocó, a narrow strip between the Andes and the Pacific in Colombia. I spent seven years there.

**Into the wilds**

It was a very interesting experience: the Chocó had not yet been fully explored from the medical point of view. When we arrived there was no electricity, no running water, and fifty yards from our adobe house the jungle began, where one had to cut one’s way with a machete. Often I had to do microscope work at night, and the kerosene lamp attracted swarms of insects. If I left any blood slides unprotected overnight, there was nothing left on them in the morning. The insects had eaten everything. But in spite of our hard life, I felt continually excited and happy to be a physician and to have equipped myself to deal with tropical diseases. We both felt, my wife and I, that we were going to be very useful in this particular place.

However, my first patient made me feel very unhappy. In London, I had attended a couple of lectures in dentistry during the tropical medicine course and this had enabled me to include a few instruments for dental extraction in my kit. Now my first patient turned out to be a dental case. I succeeded in getting a good analgesia, but the tooth broke and I was unable to pull out the roots. I felt quite frustrated, but fortunately the patient never came back.

The Chocó was said to be the second wettest area in the world with a yearly rainfall averaging 300 inches. Its climate was typical of the equatorial rain forest. Relapsing fever, which was extremely widespread, could of course be treated with neoarsphenamine, which was also a miracle drug for relapsing fever. It became so popular that people came from remote villages, sometimes travelling five or six days by canoe, to ask for a shot of “914”. Amoebiasis was still treated with emetine and bismuth and anti-yoeliosis with oil of chenopoïdium. A local product, *leche de higueron*, was used against *Trichuris* infections and to obtain some I instructed one of my boys to “milk” a suitable fig tree (*Ficus glabrata*) in the jungle. As prophylactic and curative drug against malaria at the beginning of my tropical career, there was nothing but quinine. True, it could often save lives, but quite a number of patients, particularly children, came too late. Blackwater fever was not rare and caused high mortality. In some cases patients recovered, but I am not sure whether it was the treatment I gave them which saved their lives.

The appalling morbidity of malaria and the tragedy of death from blackwater fever were my real teachers in preventive medicine. We knew that if malaria could be prevented, blackwater fever would also be prevented. We also knew that larval control could prevent most of the morbidity from malaria and that a daily
dose of quinine could prevent, if not infection, at least the clinical manifestations of malaria. I was more convinced every day that the efforts and money spent to cure a few cases would help save more lives and prevent much sickness, if only such resources were devoted to prevention. Antilarval measures and sanitation were applied in the small areas of the camps so that malaria could no longer be contracted there. Unfortunately, a number of employees had to spend many nights in outlying localities which could not be protected.

We went back to England for a vacation and I took my Diploma of Tropical Medicine and Hygiene there. During our stay in Surrey (I commuted every day between the school in London and our house in the country) my wife, who had always been taking her daily quinine, decided to discontinue it. I came home one night and found her with high fever. The local doctor had been called, but guessing that she was suffering from a tropical ailment he thought it best to wait for my return. It was malaria. The following day the students at the London School could see a couple of slides with a rich culture of Plasmodium vivax. They also heard a lesson on the primary latency of vivax infections, possibly facilitated by daily quinine, but terminated as soon as the quinine was stopped.

After seven years work in the equatorial forest, completely isolated from medical research, I felt the need of going back to university life. I also wanted to devote myself to preventive medicine. I became one of the assistants of Professor G. Sanarelli at the Institute of Hygiene of Rome University. Professor Sanarelli was one of the few senators who had not accepted fascism and was an easy target for those who wanted to discredit him. He was an old "Fasceur" and had tried to introduce the use of BCG in Italy, but had failed because of his antifascism.

That was the time of the bontica integrale and the reclamation of all malarial areas in Italy, especially the Pontine Marshes. For me the work done in the Pontine marshes near Rome was of the greatest interest. Thus began my close association with the great malariologists of the Roman school: G. Bastianelli, A. Masirolli, G. Raffaele and many others.

**International work**

After a few years in Rome, I took the *libera docenza*, which entitled me to lecture at the University. The same year, on the suggestion of Professor Sanarelli, I accepted an appointment in the Health Section of the League of Nations with the task of helping to reorganize public health services in a South American republic.

Before going there, however, Dr L. Rajchman, Medical Director of the section, asked me to study different types of public health developments in some European countries, where great progress had been made despite limited economic resources. When I returned to Geneva, the South American country for which I had been recruited was involved in a war and the reorganization of public health was postponed *sine die*. I agreed to remain in Geneva as assistant to Professor M. Circa, then Secretary of the Malaria Commission, whom I succeeded when he returned to Roumania.

My first official journey took me to Yugoslavia, Italy and Spain. Part of this journey was made in the company of Wenyon, Sir Malcolm Watson and L. Hackett; throughout I was with another great malariologist, J. M. Sinton.

In those days, Spain was a good example of the efficiency and the limitations of the treatment of malaria. Clinical severity was controlled, but transmission and endemicity did not decrease.

The Malaria Commission of the League had secured the collaboration of five different institutes to carry out a plan of comparable experiments with the then new antimalarials: the mepercin and pamaquin of today. These trials were carried out in France (Algeria), Italy (Sardinia), Malaya, Roumania and the USSR. It was during our visit to Russia that we became acquainted for the first time with the "anti-relapse treatment" which is still today one of the features of malaria eradication in the Soviet Union and other Peoples' Republics.

In Algeria, the experiments were undertaken under the direction of Edmund Sergent in an area of the Atlas mountains. The laboratory was in a newly built hotel which had only a front, all the rooms having been carved in the rock. From our hotel, we would ride on Arab horses down the valleys and along the wadis. Wherever we stopped, we were offered milk, dates and sweets which attracted masses of flies. But even the hygienist cannot refuse refreshments offered to him in a spirit of friendly hospitality. Those flies were a good lesson for a young international civil servant.

More than on the new drugs, the interest of malariologists was focussed on experimental human malaria. A few years before, in Vienna, Wagner von Jauregg had found that general paralysis patients would often be cured, and still more often improved, if they developed malaria. Hence, the inoculation of malarial blood or the feeding of infected mosquitoes on patients had become standard treatment and enabled malariologists to study in man a disease which could not be transmitted to experimental animals. Man had become the guinea-pig, and the malaria therapy centres in the U.K., the U.S.A., Italy, Roumania, and other countries, brought in very important contributions to our knowledge of the disease. One of these was the limited duration of most malarial infections, which was later to become the basis of our concept of malaria eradication.

In 1936, I served as a member of a commission which had been asked to prepare an Intergovernmental Conference on Rural Hygiene in the Far East. This involved extensive travel.

The Conference took place in Bandenong the following year. Reading its reports today one is appalled at the poor prospects there were for antimalarial work in this part of the world. Some twenty years later, malaria eradication work was going ahead in most of this vast area.

In 1938, the world political situation was deteriorating rapidly. Italy withdrew from the League and I decided to resign. I returned to Rome where I spent most of
my time at the Malaria Institute. In 1943, the League of Red Cross Societies invited me to Geneva to organize and direct the Health and Relief Bureau. As I had not participated in the Second World War, I considered it a great privilege to serve the Red Cross. In 1947, however, the newly constituted World Health Organization's Interim Commission asked me to organize the struggle against malaria, and I resigned from the League.

**Progress**

By 1947, malaria control had become feasible even in rural areas, which gave point to Paul F. Russell's forcible slogan that no country was so poor as to afford not to control malaria. Though I was convinced that the residual insecticides would eventually eradicate the disease, I never believed that they were a panacea which would make it unnecessary to base the work on sound epidemiological footing.

For seven years, WHO helped governments in every field leading to malaria control, the objective being to delete malaria from the list of public health problems. My generation has been fortunate enough to keep its sense of the wonderful. As a child in Florence, I saw one of the first motorcars and one of the first aeroplanes. I well remember the first time I listened to a radio broadcast in the Chocó camp, when members of General Byrd's expedition sent Christmas messages to their families in America. Having experienced such beginnings one is still able to react emotionally to progress, though it has become to us almost a habit. It was so for my generation of malaria workers when the residual insecticides appeared. I still experience amazement today when I think of what can be done with them and the prospects they opened to us.

In 1949, the first WHO malaria teams were sent into the field. At the end of the year I went to see them at work in India, in Pakistan, in Thailand. They included doctors, engineers, entomologists, public health nurses, all new to their career as international public health officials. They had to create a new tradition of service, in spite of unfamiliar surroundings, isolation in rural areas and a strange cultural, linguistic and religious environment. They had to have faith. They succeeded. They made the way easier for their successors who were later scattered in most malaria-stricken countries.

To these field malariologists, the world-wide use of modern tactics against the disease is very largely due. But then came the time when a great change in strategy was suggested. For economic reasons, Greece had to interrupt its spraying campaign in Crete and the Peloponnesus. It was then discovered that after many years of total coverage, the source of infection was so depleted that no dire consequences resulted from the cessation of spraying.

It was also in Greece that a case of anopheline resistance to DDT was found for the first time. These two findings prompted the adoption of a new strategy, the objective of which was the eradication of malaria. This implied the termination of antimalarial activities after a limited period and the end of the former system of "control", which, to be effective, had to be continued year after year.

The present malaria eradication programme is described elsewhere in this issue, but I have often been asked to say how I see its future. I believe that in a few years malaria can be eradicated from the face of the earth—except, for the time being, in tropical Africa.

One of the reasons which prompted WHO to adopt the new strategy was the alarm caused by the development of DDT resistance in Anopheles sacharovi in Greece. It was only one species, but by the end of 1955, resistance had been found in five anopheline species. It now has been discovered in 17 and it seems likely that resistance will be found in more. Nevertheless, I do not think this will prove an invincible obstacle. After all, the areas where the insecticide-resistant vectors are to be found are inhabited by less than five per cent of the total human population in areas under insecticide spraying programmes—and these species are generally susceptible to other insecticides. I am much more concerned about the attitude of some governments towards eradication. I am convinced that unless governments are deeply aware of the enormous responsibilities they undertake when they decide to eradicate malaria and, unless they take all the necessary budgetary and administrative measures, the objective will not be attained. Too much lip-service is being paid to the glorious idea of malaria eradication, but it is often forgotten that unless the government as a whole considers the programme as one of its own high priority projects and not merely as a pet project of the ministry of health, failure will be more likely than success. Already it is for lack of recognition of this, that most programmes were forced to increase the number of years of total coverage spraying. It may happen that during the course of the programme the ministry of finance decides to cut down the next year's budget of the eradication project by, let us say, 10%; the consequence will be that the spraying campaign may have to be prolonged for another year, which will cost more 100%. Or it may happen that in spite of the malaria eradication service being adequately staffed and well supplied with equipment and transport, the absence of suitable legislation allows a number of houses to remain unsprayed; this also will have as a consequence the need for prolonging the campaign or worse, the impossibility of interrupting transmission.

The reservation I have made about tropical Africa is, I hope, only temporary; I am confident that in a few years we shall have found a method of interrupting transmission even there. It will, of course, cost more effort and more money to eradicate malaria in this area. But I like to think that when malaria no longer exists in the Americas, in Asia, in the Western Pacific and even in North and South Africa, the privileged populations of these areas will unite to assist tropical Africa—not only on account of human solidarity, but in order to prevent the return of a disease which then could come only from Africa.
Counterthrust of the laboratories to mosquito resistance

The research work of entomologists, geneticists and biochemists pave the way for malaria eradication and yield considerable savings in time and money.

At first sight, it seems like a straightforward fight between man and mosquito. The female of the Anopheles mosquito bites a malaria sufferer and sucks up the malaria parasite together with his blood. Two weeks later she is able to pass on the infection by biting a healthy person. To break the chain of infection, therefore, all that is needed is to kill the mosquito before the malaria parasite has had time to develop within its body and become a danger for the next person bitten.

The whole theory of malaria eradication is based on the mosquito's habit of resting on interior walls after it has fed on someone's blood, and on the possibility of spraying those walls with "residual" insecticides that will kill all the mosquitoes settling on them over a period of several months. Yet in actual practice, intricate problems arise. The world-wide campaign to stamp out malaria is aimed at protecting twelve hundred million human beings, widely different in their way of life and habits. The majority live in villages difficult to reach and far from any main roads. Such people regard as intruders those who come to spray the walls of their homes. In some places the houses have no walls, only a primitive roof. In others, the mosquito does not settle on the walls, but prefers to go and digest the blood of its victims in some outdoor retreat away from the houses. Elsewhere the mosquito bites only outside. It may happen that the mosquito is irritated by the presence of the insecticide and learns to avoid it, or else does not settle long enough for the poison to take effect.

A still more serious problem is that of resistance to the insecticide. It was this that prompted the decision of the WHO Member Governments at the Eighth World Health Assembly in Mexico City in 1955 to declare all-out war on malaria. It had become imperative to stamp out the disease from the world before all the species of malaria-carrying mosquitoes would develop resistance to the insecticides used.

Alarm Sounded in 1951

Almost everywhere until then, the fight against malaria had been carried on in a spirit of optimism. The spraying of the inside walls of houses with insecticides went on without
undue haste; when one village had been done, the workers moved on to the next. More and more districts were gradually being protected against the disease. The work went on, slowly but steadily, the idea being that with perseverance and plenty of time it would sooner or later be possible to treat all the malarial regions of the earth.

It was in 1951 that the cry of alarm first went up: "The insecticide we are using is no longer active!" This was the first counter-attack; the mosquito was putting up resistance. At first, resistance was assumed to be the result of the mosquito becoming accustomed to the insecticide as is the case with alcoholics or drug-addicts whose intake of alcohol or drugs is constantly increasing and yet producing less and less effect. The mosquitoes too, seemed to become inured to bigger doses of insecticide, which at last failed to kill them. They appeared to have "acquired" immunity.

Out of this situation was born the idea of world-wide malaria eradication. It was decided to replace piecemeal campaigns by total war. The operation, it was realized, must be completed while the insecticide continued to kill and before the hitherto sporadic resistance became general. This resistance was believed to be due to spraying at insufficient strength, thus giving the mosquitoes a chance to grow accustomed to the insecticide. The essence of the eradication policy was therefore to make an all-out effort to engage in mass slaughter of the malaria-carrying mosquitoes for the length of time required to cure the existing malaria victims and eliminate the infection. After that, even if the mosquitoes...
This machine reveals the hidden paths of resistance

Radioactive tracers are used at Slough, England, to find out what happens to the insecticide in the mosquito.

came back, there would no longer be any infection for them to spread.

If the idea had ever been entertained that it might be possible to eliminate once and for all the malaria-carrying species of mosquitoes, it was now abandoned. The mosquito had given its answer.

The mechanism of resistance

Then it was the turn of the entomologists, the geneticists and the biochemists to launch their counter-attack, and this time the battle was engaged in the laboratories.

Mosquitoes take very kindly to life in confinement. From all over the world, mosquito eggs, tiny grey specks, are sent by post in boxes or in ordinary envelopes, to the famous Ross Institute of Tropical Medicine in London. Twenty-four hours later the eggs hatch out, and the larvae that are fed, one item of their diet being baby-food wriggle in powder form, the same that builds bonny British babies.

In a week's time, in cages of very fine netting, the adults begin to fly. The males are fed on sugar, the females on blood which is sometimes taken from an entomologist's forearm but more frequently from the shaved belly of a guinea-pig. The mosquitoes are then exposed to insecticides, and those that resist are separated from those that do not. The next step is mating: "resisters" are mated with "resisters", "non-resisters" with "non-resisters", and then "resisters" with "non-resisters". Some species of mosquitoes refuse to mate in captivity, and for them a few entomologists have succeeded in carrying out artificial insemination.

From these couples come new families, which may be resisters, non-resisters or hybrids, each reacting in their own way to the various insecticides to which they are exposed. Scores of generations are studied in this way, and their behaviour is carefully noted.

The rôle of an enzyme

This patient, meticulous research work has made it possible for entomologists and geneticists to determine with some accuracy the nature of this phenomenon of resistance.

Mosquitoes do not acquire resistance, they are born with it; in fact it can now be affirmed that even before the residual insecticides were invented, some individual mosquitoes were already "resisters". They had in them the genes of resistance, and were protected even against insecticides that were still in the future.

It has now been established beyond doubt that at first the insecticide killed off the susceptible mosquitoes. The remainder, the resisters, all survived and multiplied, producing a whole new population of mosquitoes gradually less and less affected by the lethal properties of the insecticide.

The scientists then set about finding out something more about the mechanism of resistance. In the case of a particular insecticide they discovered that, fortunately for the mosquito and unfortunately for us, its organism contains an enzyme which sets about altering the chemical composition of the insecticide by dissociating the atoms which make the substance toxic. The insecticide manufacturers were informed of this discovery, and their chemists are now trying to develop an insecticide which will become more effective when acted upon by the enzyme in the mosquito's organism.

There are unfortunately other insecticide troubles besides mosquito resistance. For instance the walls to be sprayed may interfere with the action of the insecticide. There are walls which soak up the insecticide and prevent it from doing its lethal work, and there are walls which decompose it and render it harmless.

Then there is the good housewife, anxious to keep her house clean, who whitewashes or papers her walls, thus covering up the insecticide.

All these factors have to be taken carefully into account in organizing a world antimalaria campaign.
On a swampy island a few miles from Savannah, the Communicable Disease Center of the United States Public Health Service has set up a laboratory where the resistance of mosquitoes to insecticides is investigated. The scientists are testing new insecticides and working on an insect-killing fumigant that will have long-acting effect.
The latest techniques

A DEAD-AND-ALIVE count of mosquitoes is made

RADIOACTIVE TRACERS for the study of insecticides

COBALT 60 CHAMBER to irradiate insects
From cinchona bark
to medicated salt

There is a whole battery of drugs against malaria. Some are preventive drugs, taken as a protective measure by visitors to malarious regions, and some are effective in treating malaria sufferers. One might then ask whether the present campaign for the eradication of malaria is on the right lines with its complicated insecticide spraying operations, its delicate laboratory work, the enormous transport problem involved, and the costly army of workers needed. Would it not be simpler to distribute drugs to everyone living in malarious areas? In this way malaria sufferers would be cured and others protected. The reply of the experts is: “No.”

In the first place, the experts say that the antimalarial drugs only keep the blood parasite at bay for a short time; scarcely one week, in fact. This means that an immense and very efficient organization would be needed for the regular distribution of drugs over vast territories with widely-scattered, and often nomadic, inhabitants. Then the population would soon tire of
THE PINOTTI METHOD: an anti-malarial drug is mixed with salt (above). Anti-malarial salt being distributed in New Guinea (below). The method was first tried experimentally in Brazil.

coming so often for treatment. It would be difficult to persuade people who were not feeling ill to take drugs regularly over a long period, and almost impossible to ensure that everybody, including children, was getting the proper dose.

Nevertheless, the antimalarial drugs play an extremely important and indeed essential role in the eradication campaign, particularly in the final phases.

Here again, however, a problem arises that only the laboratories can solve. They must try to produce a drug which maintains its efficacy for a long enough period and which can be given in a single dose at long intervals.

The scientists are therefore directing their efforts to finding a drug that can be injected. One advantage is that some people may feel more confidence in a treatment that hurts than in tablets which are merely swallowed without discomfort. Another is that an injection is more difficult to evade during mass campaigns in which the whole population is treated.

The discovery of modern antimalarial drugs was an indirect consequence of the two world wars. The first synthetic products were obtained in the laboratory between 1924 and 1927 by the Germans who had been working on the problem since their quinine supplies were cut off by the war. From 1939 to 1945 it was the Allies who manufactured products to replace the cinchona bark which no longer arrived from Japanese-occupied Java. They had also found a number of synthetic antimalarial drugs on German prisoners-of-war captured in North Africa.

Through a strange series of coincidences in the inter-war period, research work on synthetic antimalarials opened the way to further progress in two apparently unrelated fields: the behaviour of the malaria parasite in the human organism, and the treatment of syphilitic nervous disorders.

In order to test the effectiveness of the new drugs, European research workers needed malaria patients. These were rare in Europe and—understandably—the few attending a hospital preferred to be given treatment rather than be used as guinea-pigs. The solution was to find people willing to be inoculated with malaria. The neuro-syphilitic cases provided the answer.

This story goes back to the time of Hippocrates who, five centuries before Christ, recognized that violent fevers sometimes had a beneficial effect on sufferers from certain diseases. Galen, seven centuries later, described the cure of an epileptic after an attack of quartan fever. In the nineteenth century, some observers found that certain mental patients were returned to sanity after an access of fever (malaria, typhoid fever). In 1917, an Austrian psychiatrist for the first time inoculated malaria into nine patients suffering from general paralysis, and three of them were cured.

It was in England that an Indian sailor from Madagascar disembarked in 1925, shivering with malaria, and went for treatment to the Horton Hospital, Epsom. He was treated, but a little of his blood infected with the malaria parasite, Plasmodium vivax, was carefully preserved. This strain of the parasite was maintained in the laboratory, and over a period of thirty years it has been used to infect sixty-eight thousand mosquitoes, which in turn have infected ten thousand neurosytphilitic patients suffering from general paralysis. Many of these patients have left the Horton Hospital, cured. The others, by consenting to be first infected with and then cured of malaria, have made it possible to determine the limitations of quinine, to test certain modern drugs and, finally, to establish the fact that the liver plays an important role in the development of the malaria parasite.

With the discovery of penicillin, the queen of drugs against syphilis, antimalarial drugs can no longer be tested in this way.

Although control of malaria with drugs alone has not been found generally practicable, quite a new method is being employed in Brazil.

The Brazilian eradication campaign was making slow progress in the vast, impenetrable forests of the Amazon basin. Three million people live there under the menace of malaria. Most of their houses have no walls and consist only of a roof over four supports. The mosquitoes, after biting, go outside in the open to rest. Many nomads move about the country according to season and availability of agricultural work. The usual technique of spraying therefore offers little chance of interrupting transmission of the disease.

A Brazilian specialist, Dr Mario Pinotti, conceived the idea of adding an antimalarial drug to the cooking salt used at every meal by the people of the Amazon basin—in the same way as iodine is added to the salt in regions where goitre is present in endemic form.

After forty days' use of the antimalarial salt there were only two cases among the nine hundred inhabitants of the experimental zone. One was a newly-born, breast-fed baby, and the other a stranger who had only been in the zone for the last three days.

In view of these results, the World Health Organization has asked scientists to undertake further laboratory research.
Not a single case must remain...

The earth will not be truly and finally rid of malaria until the very last case has been tracked down and treated, until the possibility of infection has ceased to exist.

THE EXAMPLE OF GREECE: 1 million cases and 10,000 deaths in 1938. In 1958, there were only 1,200 cases. There are smiles again in the rice fields of Skala.
The aim of the world campaign to eradicate malaria is the complete and unconditional liberation of twelve hundred million human beings in 148 different countries or territories throughout the world.

At the present time, according to the information available to WHO, anti-malaria operations are proceeding, although at different stages, in 92 countries or territories with a total population of one thousand million. Taken together, this already constitutes the greatest co-ordinate public health programme that has ever been known—yet in 56 more countries and territories, with two hundred million inhabitants, a beginning has not been made.

There are already thirteen countries and territories which register only a few malaria cases yearly, either occurring sporadically or brought in from outside, and given us, as it were, a preview of what may very soon happen in the greater part of the world if there is no slackening in the overall effort.

Listen to what Dr Emilio Pampana, the first WHO Director of Malaria Eradication, has to say:

"There is no doubt about it, malaria eradication will be an established fact within 10 or 20 years from now, at least as far as Europe, Asia, Africa and North America are concerned—but only if we go about it in earnest, and waste no time. The world malaria eradication campaign has often been compared to a war, and rightly so, but you cannot wage war by halves! It demands an all-out effort.

A sound budget

"The first essential is a regular and sufficient supply of funds for as long as necessary. If part of the budget is cut at any stage, the whole campaign may collapse. No one would ask a surgeon to economize on the anaesthetic in the middle of an operation and thereby risk the life of his patient. The same applies to eradication campaigns—there can be no question of cutting down expenditure once operations are under way.

"It is therefore essential that the different countries joining in the battle should be assured of enough munitions and resources to see them through to the final victory. The World Health Organization and other international bodies can assist in this. It is essential also that heads of states, leaders of governments, and politicians should understand that the campaign in which their countries are engaged is of real practical value not only for themselves but for the world at large.

"It is when the final stage of eradication is reached that the worst difficulties will arise. Then malaria will almost have disappeared and the great mass of the people will be free of it. People quickly lose interest in a disease which no longer alarms them. When that time comes, a political leader may be more ready to provide funds for the erection of a public building bearing his name than for the maintenance of an unspectacular malaria watchdog service which will cost a great deal less.

"I am quite sure that in about ten years from now most of the world will have been freed from this scourge. Then Africa's turn will come, for malaria in that continent presents complexities and difficulties that have not yet been entirely overcome—for instance the particular behaviour of the mosquitos that carry the disease, the people's way of life, the widely-scattered population, inadequate communications, transport difficulties, and so on.

"We may be confident, however, that when the time comes the countries of the world will make it a point of honour to join forces to overthrow the last strongholds of malaria in Africa. Indeed it will be to everybody's interest to do so, for the continued presence in the heart of our planet of such a reservoir of infection would be intolerable at that time."

Professor G. Macdonald, Director of the Ross Institute of Tropical Hygiene in London, and chairman of the last WHO Expert Committee on Malaria, takes the view that the world cannot claim to be finally rid of malaria until the very last case has been detected and treated, and the infection has completely disappeared.

"Before we can really talk of malaria eradication," says Professor Macdonal, "before we can use the word in its true sense, we must revise our way of thinking.

Proof negative

"Imagine the predicament of a public prosecutor if asked to prove, not as is usual, that a crime has been committed in his town, but the contrary, that a crime has not been committed. At first he would be nonplussed, but then he would probably try to produce the negative proof by using all the machinery set up for producing positive proof. He would have the town combed by his policemen and inquiry agents until it had been established beyond all question that there was no weapon, no victim, and no murderer.

"The same thing will happen with regard to malaria. The surveillance services in the countries claiming to have achieved eradication will sooner or later have to stop looking for the remaining cases and set out to prove the complete absence of any infection. Only when that has been done will it be possible to speak of eradication of malaria.

"Before very long, I suppose, the world will be faced with the most tricky phase of the present campaign—that of dealing with residual cases. If they are neglected, it will be impossible to claim that eradication is complete, because the danger of reinfection, however slight it may seem, will still threaten the world. If both infection and mosquitos exist anywhere, the two are bound to meet sooner or later, and we would be back where we started.

"This is how I see the future of malaria eradication: first of all, very careful preliminary work in the laboratories; then a very swift and intensive campaign in the field; finally, the establishment of a control service whose objective is to obtain conclusive proof that the last trace of infection has disappeared.

"Naturally these three stages cannot be carried through without good administrative services, good communications, a well-informed general public, the most conscientious work and, last but not least, money. And I am convinced that the funds will be forthcoming when those who hold the purse-strings are given proof—positive proof—that the undertaking is sound.

"I do not underestimate the countless difficulties in the way of such an achievement: shortage of research workers, technicians, administrative staff, and so on. Then there is the problem of the nomads which is one of the most complex now facing us."

The wanderers

The vast seasonal migrations involving millions and millions of human beings constitute a problem which requires more and more careful attention as malaria eradication campaigns enter their final phases.

These migrants may be shepherds moving to fresh pastures, peasants leaving their valleys during the summer, seasonal workers, people going to industrial towns to find employment, or pilgrims crossing entire continents to visit their holy places. Any of these may have eluded the anti-malaria campaign and all are potential smugglers of the malaria parasite into areas which have been cleared of it.

As the world campaign to eradicate malaria approaches its goal, and the moment draws near to prove that malaria has ceased to exist, antimalarial operations will gradually become incorporated in routine public health and international quarantine measures, as has already happened in the case of other ancient plagues such as yellow fever.
world health

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