TROPICAL DISEASES

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Many millions of the people living in tropical regions of the world are cut off from the main stream of social and economic progress. Victims of a heavy burden of disease as well as of harsh economic circumstances, they are not free to choose and plan a better future.

There is a growing awareness of these special problems of the tropical countries, and one main channel of response is through the work of the World Health Organization (WHO) and the United Nations Development Programme (UNDP). It is clear that health is an integral part of development; healthy people are more effective and, in turn, development is essential to provide the resources necessary for improved health. Health and development are therefore inextricably interlinked and any strategy for improvement must be based upon this reality.

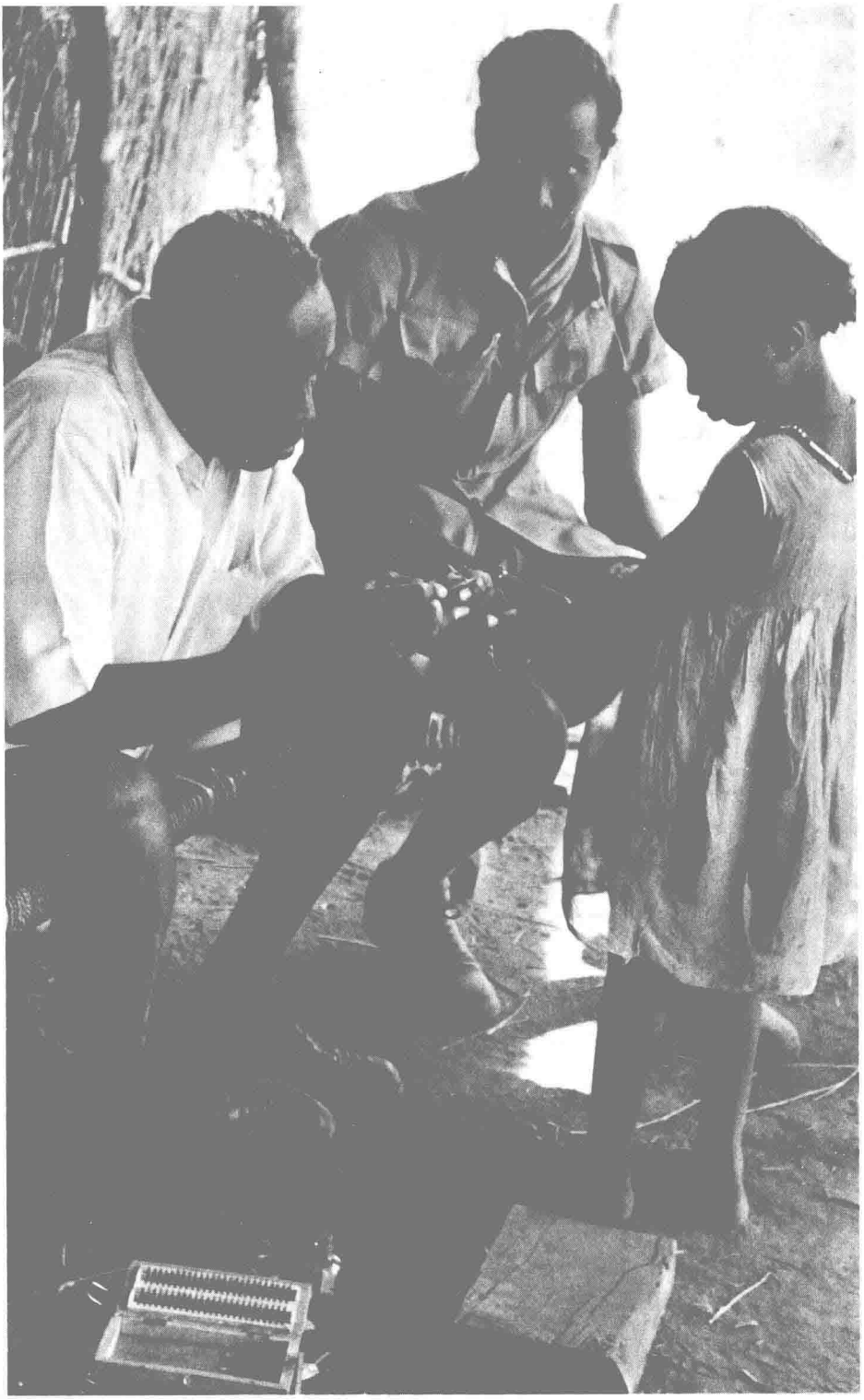
There is a wide range of existing knowledge and technology to be coordinated and exploited. A new dam to improve water supplies and provide irrigation and power, training in practical ways to avoid disease, better use of available drugs and vaccines, and a more favourable social and economic climate—these are some of the developments which will bring change and benefit. But in considering all the efforts now being made, it is clear that there is one aspect which, although of high priority, is not receiving adequate attention. The technical tools now available to control many of the tropical diseases are inadequate, or ineffective. It has, for example, repeatedly been shown that existing insecticides and

drugs for malaria control are unable to stop transmission of the disease throughout very large areas of Africa. Present remedies for other major tropical diseases—schistosomiasis, filariasis, trypanosomiasis, leprosy and leishmaniasis—are not practicable for large-scale use in many tropical countries. New tools are therefore needed.

WHO and UNDP recently launched a new Special Programme for Research and Training in Tropical Diseases to obtain these new tools. Fundamental to this Programme is the involvement of the world's leading scientists and research institutions. But of equal importance is the fullest possible involvement of the tropical countries themselves so that they may become competent, through training and research, to deal with their own disease problems. We commend this booklet to your reading as an account of the challenges and opportunities. We hope to enlist your support for a plan of action which holds a genuine promise for human betterment.

Dr H. Mahler
Director-General WHO

Mr B. Morse
Administrator UNDP



A medical worker takes a blood sample from a child in Sudan, where mosquito resistance to DDT resulted in a recrudescence of malaria and threatened to ruin one of the most promising development programmes in Africa.

left to dry out every few days, never remaining full for a whole week—the time required for the complete development of mosquitos from egg to adult. This, together with the use of larvicides and the speedy treatment of the relatively few malaria cases, kept the disease under control.

Gradually, secondary crops were added: millet, wheat, groundnuts and, later on, rice. This meant that the periodical drying out of the canals had to be abandoned, with the result that larvae of *Anopheles gambiae*, the principal malaria-transmitting mosquito in the region, could reach maturity.

Malaria strikes

In 1950, after a season of particularly heavy rains, malaria struck. It spread rapidly from village to village, affecting thousands of people within weeks. More than half of the total labour force of the Gezira was infected by *Plasmodium falciparum*, the predominant parasite species in the region and responsible for the severest form of malaria. Hundreds of people died, and so many were weakened that fully one-third of the crops went unharvested. To the incalculable human cost was added the economic loss of about 10 million dollars.

This marked the beginning of a long, costly fight against malaria and its vectors—mosquitos. These insects gradually developed resistance against major insecticides: first to dieldrin, then to DDT. A World Health Organization survey in 1970 revealed "an extraordinary high tolerance of mosquitos to DDT". The use of DDT was abandoned in the Gezira. Larviciding became irregular and by 1974 it was entirely discontinued owing to a shortage of larviciding oil. Meanwhile, malaria progressed.

In 1961, a survey of 16 villages had shown that malaria was endemic in 7 of them. By 1975, it was endemic in all of the 16. In some villages, more than half of the people were infected with malaria.

A major effort is now under way and an attempt is being made to use massively all available weapons against malaria. Armies of "mosquito men" have been trained to spray malathion, a new insecticide to which mosquitos are still susceptible. Households are regularly surveyed and drugs are used on a large scale in the hope of reducing transmission. Larviciding operations have been resumed, and experiments are under way to test the possibility of seeding canals with fish that feed on mosquito larvae.

Nevertheless, a parasite transmitted by a mosquito has endangered one of the most promising and dynamic developments in Africa. Who can tell what the Gezira would be like today had not a tiny micro-organism, invisible to the naked eye, interfered with man's will to better his lot?

Disease as a way of life

But this is only a small part of the picture. Dr David Rowe of the WHO Special Programme for Research and Training in Tropical Diseases writes:

"It is difficult for those living in temperate climates with good standards of public health and medical care to realize the impact of disease on rural communities in the tropics. For example, if you happen to be born and grow up in rural Africa you are liable to harbour four or more different disease-producing organisms simultaneously. And yet, as a parent, you must be fit enough to work, or your

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The waters of the Nile bring fertility to Egypt and Sudan, but they also harbour a water snail that transmits the small worms that cause schistosomiasis.

A medical assistant in the Gezira examines a malaria patient.

In Mexico : the face of malaria.

In Africa : examination of nasal mucus for the presence of the leprosy bacillus.

family will starve. In your village every child at times suffers the paroxysms of malaria fever and you and your wife will mourn the death of one or two children from this disease. The snails in the village pond carry schistosomiasis, and you do not consider it unusual when your children pass blood in their urine."

"You take for granted the disfigured faces and fingerless hands of the beggars in the village street suffering from leprosy. If you live near a river where blackflies breed, one in ten of your friends and neighbours will be blind in the prime of life. You know that waves of killing diseases such as measles and meningitis and perhaps sleeping sickness are liable to strike your village. But, lacking effective remedies, you tend to philosophize in the face of sickness. You make the effort to walk the ten miles to the nearest dispensary when you or your child is ill, but there may be no remedies, and it may be too late..."

The enemies within

Malaria is one of the most widespread diseases in the world, affecting some 200 million people. In some regions, malaria transmission is so intense that present efforts at mosquito control and disease treatment are totally inadequate.

In Africa, about one-fourth of all adults suffer from malarial fever at one time or another, and others are infected though they have developed a relative immunity and rarely have attacks. After the age of 12 months, almost every child in tropical Africa has malaria; at least one million children die of the disease every year. In other countries, such as India and Sri Lanka, where malaria had regressed before, it is now resurgent.

Schistosomiasis (Bilharziasis)

Schistosomiasis is an insidious and debilitating disease caused by small worms belonging to the group of parasites called trematodes or flukes. The adult schistosome worms live in the blood vessels of infected persons. The most widespread species is *Schistosoma mansoni*, which affects the bowel and is prevalent throughout Africa, the Middle East, and eastern parts of South America. Three other species also commonly infect man, two of which affect the intestine while one damages the bladder and, later, parts of the urinary system.

The eggs of the parasite are passed out in the faeces or urine of infected people and develop into larvae in fresh water. Here, they infect freshwater snails, in which they multiply, and then release large numbers of free-swimming larvae (known as cercariae) which can penetrate through the skin of a person entering the water.

Once in man, the larvae find their way into the small blood vessels of the large intestine or bladder, where they mature into adult worms of both sexes (the female lives in a fold along the body of the male).

The females are egg-laying machines. For possibly five years eggs are laid continuously and this process may last as long as 20 years in a small proportion of patients. Eggs that are not excreted lodge in either the bladder and adjacent organs of the genito-urinary system, when *S. haematobium* is the infecting parasite, or in the intestine and liver, when *S. mansoni* or *S. japonicum* is the invader.

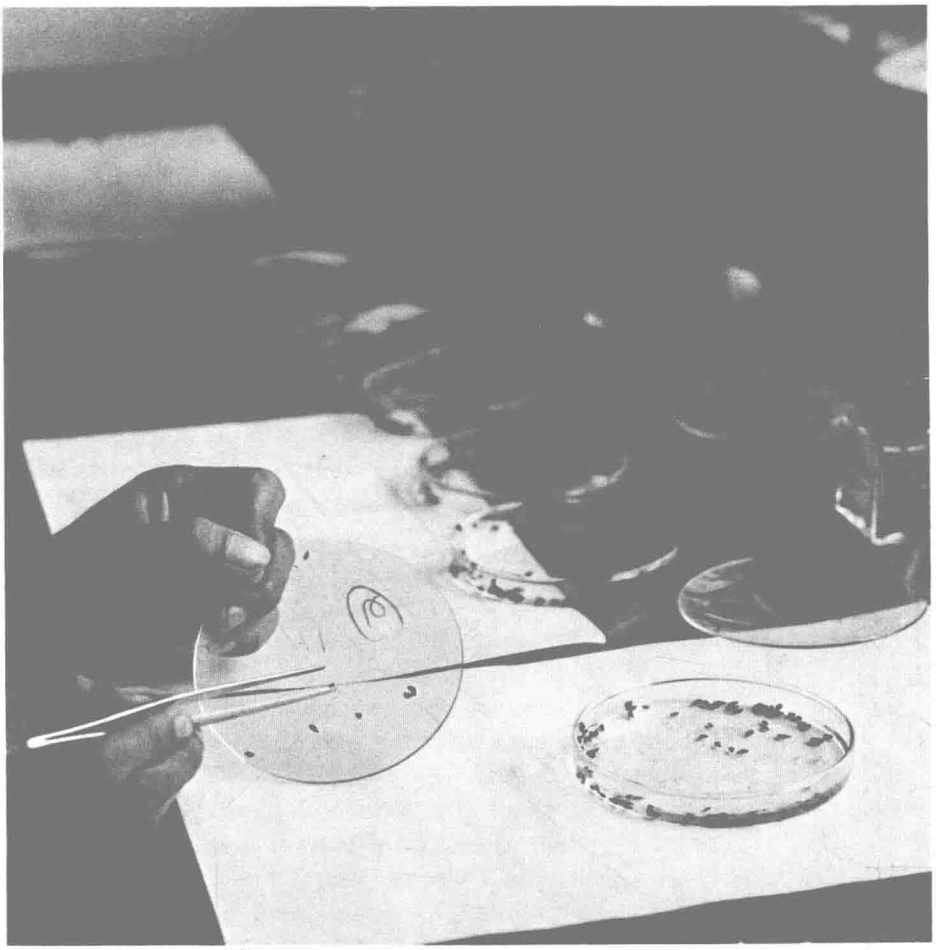
In the advanced stages of urinary schistosomiasis the constant passage of blood in the urine is characteristic and the small contracted bladder induces difficulty

and marked frequency in urination. In some tropical areas, schistosomiasis of the bladder is associated with cancer.

During the later stages of the intestinal types of schistosomiasis, lack of appetite, nausea and loss of weight are frequent together with intermittent bouts of diarrhoea and passage of blood in the stools. The liver and spleen enlarge, fluid collects within the abdomen producing a bloated belly while, in contrast, the remainder of the body shows emaciation.

Individual cases can be cured, but the injection of anti-schistosomal drugs, some of which contain antimony, can cause serious side-effects.

Schistosomiasis is often a disease of rural development, as artificial lakes and irrigation canals are sources of infection containing very large numbers of larvae. This problem has been encountered in Egypt and Sudan since the building of the High Dam at Aswan, and in Ghana as a result of the construction of the Akosombo Dam on Lake Volta. Similar problems have afflicted northern Nigeria where the proportion of the population infected around the lake created by the Kainji Dam has doubled in three years. Incidence has also increased in the Gezira region of Sudan. Even in the semi-arid Arabian peninsula, irrigation projects have resulted in the spread of the disease to regions where it did not previously exist.



The glass specimen trays hold parasite-carrying snails being studied at a laboratory in Leyte, Philippines.

Filariasis

Filariasis is another widespread disease which in various forms affects about 300 million people throughout the world. There are at least eight filarial parasites that infect man. *Wuchereria bancrofti* and *Brugia malayi*, transmitted by mosquitos, infect some 250 million people, mainly in West, Central and East Africa, Egypt, the Malagasy Republic, the Indian subcontinent, South-East Asia, China, the Pacific islands and the Philippines.

The adult worms live in the lymphatic vessels and lymph nodes, obstructing the flow of lymph, causing inflammation and swelling (elephantiasis) of the arms, legs, and genitals.

Another filarial parasite is *Loa loa*, which is transmitted by a type of horse fly. It is prevalent in Cameroon, the Congo, southern Nigeria, and Zaire. Adult worms move around the subcutaneous connective tissues, producing the characteristic Calabar swellings, and sometimes cross the white of the eye, causing great discomfort.

River blindness

The most dramatic form of filariasis is onchocerciasis or river blindness caused by the worm *Onchocerca volvulus*, which is transmitted by a small insect, barely 3 mm long, with the ominous scientific name of *Simulium damnosum*—the blackfly.

Like many insects in the tropics, the female blackfly feeds on blood, and its bite can transmit the larvae of *Onchocerca volvulus* to the person on whom it feeds. Once in the human host, the larvae develop into long, threadlike worms less than a millimetre across but up to half a metre long. These worms live up to 15 years and produce millions of embryos that invade the skin and eyes.

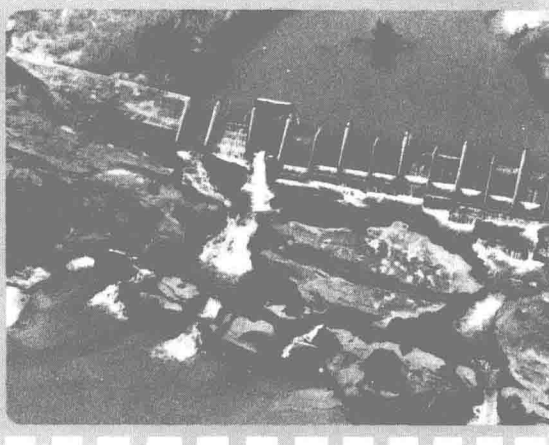
The blackfly breeds only in fast-flowing water rich in oxygen and nutrient matter, and the worm develops inside the fly only at a temperature of 18° C or above. In other words, the disease can be transmitted in circumstances existing chiefly in tropical regions where it is hot and where there are fast-flowing rivers.

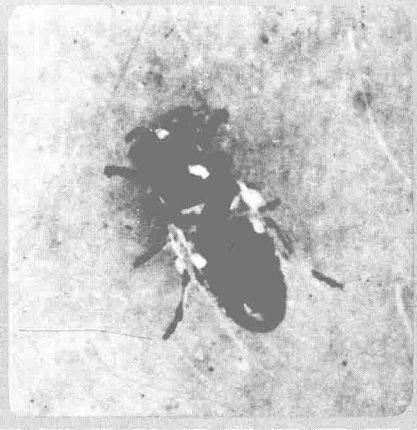
Because of the heat, farmers in such areas work naked from the waist up and with legs bare. Thus they are exposed to the merciless attacks of blackflies. In endemic regions, the blackflies are so numerous that there is no way of keeping them off. A man may suffer several thousand blackfly bites a day, each of them a source of irritation and a potential source of infection.

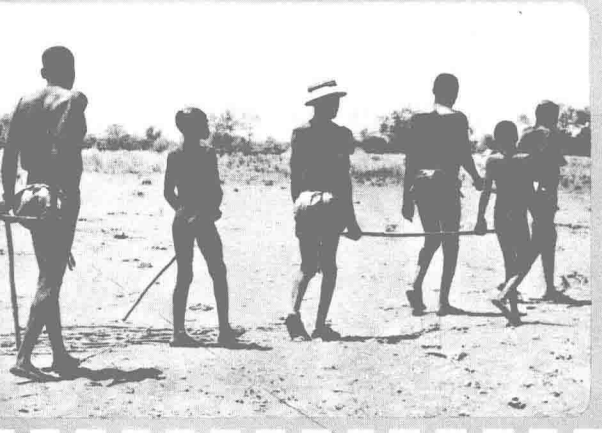
At first the infection usually goes unnoticed. The larvae develop very slowly. A year or more later they become adult worms that settle in tissues under the skin and produce characteristic nodules. Each female worm produces thousands of embryos which invade the skin and may cause uncontrollable itching. Sometimes they also invade the eyes. The victim may then go slowly blind.

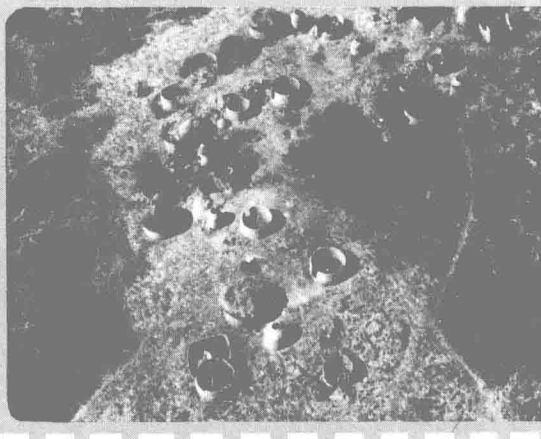
In some regions of tropical Africa the sight of a young child leading a string of grown men through a village is a common one. The men look old, although few of them are over 35 or 40. Some are like walking skeletons, their bones protruding under the skin, their eyes sightless. The child leading this macabre procession is, most likely, also infected.

Many adolescents already show the effects of the disease: the skin is wrinkled and nodules containing adult worms can be seen under the surface. Some youngsters, already suffering from partial blindness, one of the early manifestations of oncho-









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cerciasis, walk hesitantly round the village at dusk, their hands extended in front of them, feeling for obstacles they cannot see.

In the upper basin of the Volta River the number of onchocerciasis sufferers is estimated at over a million, and many thousands are blind. A special onchocerciasis control programme has been launched in Benin, Ghana, the Ivory Coast, Mali, Niger, Togo and Upper Volta, seven of the most severely affected countries. The programme includes the insecticide spraying of inaccessible rivers from helicopters to control the blackfly and halt transmission of the disease. The treatment of persons already infected is made difficult by the lack of non-toxic drugs that are effective against the adult worms.

Other tropical diseases

Malaria, schistosomiasis and filariasis are the three massive tropical infections. But there is a score of other tropical diseases, most of them caused by organisms that prey on man—his liver, blood, heart, brain, and gut.

There are roundworms and flatworms that invade the intestine; hookworms that feed on the membrane of the small bowel; single-cell amoebae that attack the intestine and liver; corkscrew-shaped trypanosomes that burrow into the brain to cause sleeping sickness or, in South America, Chagas' disease (a form of trypanosomiasis that damages the heart); the slowly reproducing leprosy bacilli that mutilate and disfigure; intracellular parasites that cause leishmaniasis, with its two particularly severe forms: *espundia* in South America, which eats away the face, and visceral leishmaniasis or kala azar, fatal within two years if not treated.

Such is the added health burden carried by those peoples who live in tropical countries.

Control of onchocerciasis, or river blindness, at present depends on destroying the vector, Simulium damnosum*—the blackfly. The sequence shows, from left to right and top to bottom : blackfly larvae, enlarged to seven times life size ; a dam with fast-flowing water, where the blackfly larvae develop ; captured blackflies ; a blackfly, slightly over 2 millimetres long, starts feeding on human blood ; the same fly, bloated after feeding ; adults blinded by onchocerciasis are led by children ; a "blind village", which has been abandoned.*

Female Simulium damnosum, *vector of onchocerciasis.*

Trying out a new insecticide against malaria. In this photo, a member of the field research team is shown checking a mosquito breeding-place.

MOSQUITOS

There are very many different species of mosquitos, and all share certain common characteristics. They lay their eggs in water, and the larvae that come out of these eggs live in the water, breathing air through a kind of tube, somewhat like the snorkel of a submarine. In a week or more larvae become pupae, a transitional, immature form, and then adult mosquitos.

There are mosquitos all over the world, not only in warm tropical countries, where they are present all year round, but even in cold, northern regions such as Alaska, Greenland or northern Siberia.

The feeding habits of male mosquitos are much like those of the butterfly, limited to extracting nutrient substances from vegetation. But the females of certain species need human blood. These females have a proboscis, a tubular sucking organ capable of perforating the skin of man and animals. Their highly perfected bloodsucking system makes use of anaesthetic substances in the saliva, injected immediately at skin penetration, which may render the bite totally painless.

The saliva thus introduced into the host can also contain disease-causing organisms: parasites that cause malaria and filariasis, and viruses that can cause yellow fever, dengue, and encephalitis.

Four species of mosquito-borne malaria parasites can infect man: *Plasmodium falciparum, P. vivax, P. malariae,* and *P. ovale.* They provoke different forms of disease and react differently to antimalarial drugs.

Inadequate weapons

There are ways of treating individual cases of malaria, and ways of preventing them. But no single method has been developed that succeeds in protecting all of the people at risk or treating all those affected by the disease.

One possible approach is to attack the mosquito itself, the "vector". DDT and other insecticides have permitted spectacular successes in some parts of the world. In India there were 75 million cases of malaria in 1935, and a vigorous vector control campaign reduced the number to 60000 in 1962.

But several factors come into play to prevent the total eradication of malaria in many areas, and even to reverse the trend in others. Mosquitos have developed resistance to some insecticides and in the past few years the cost of insecticides has more than doubled. The cost of operating vehicles has also increased and, in addition, international assistance programmes have been reduced.

As a result, many countries simply can no longer afford to carry out antimalarial campaigns as vigorously as they have done in the past. Thus in India, for instance, the number of cases rose from a low of 60000 in 1962 to more than four million in 1974—a 70-fold increase. In Africa, the situation is even more serious since

there is no hope for large-scale antimalarial operations in the foreseeable future. Dr Adetokunbo O. Lucas, former chairman of the Nigerian Medical Research Council, who has been appointed director of the WHO Special Programme for Research and Training in Tropical Diseases, points out that several intensive, well-supervised pilot and research projects in the African savanna have shown that infection is so deeply entrenched in the environment that spraying of insecticides and drug distribution are not sufficient to interrupt transmission.

Antimalarial drugs

For centuries, malaria has been treated with the bark of quinquina (or cinchona), a tropical tree, from which quinine was isolated in 1820. Quinine is the oldest and one of the most efficient antimalarial drugs, attacking the parasite when it develops in the red blood cell. But it can become dangerous when used in high doses, and even in low doses for people who are sensitive to it. Vomiting, diarrhoea, headaches, troubles of vision and hearing, even deafness, are among the side-effects.

Other antimalarials have since been developed, notably chloroquine, synthesized in Germany in 1934, and its derivatives. These 4-aminoquinolines are among the major antimalarials used today. There are, however, limitations concerning their utilization on a large scale in endemic regions. Some require prolonged administration when a person has been infected, others must be given regularly whenever one risks exposure to infected mosquitos. Shortage of health care facilities in most endemic areas makes this impossible, and in most of the affected countries a sufficient increase of health personnel is not foreseeable in the near future.

Furthermore, in vast regions of the world the parasites have become resistant to some of the major drugs. This is a very dangerous situation. For instance, *Plasmodium falciparum* resistance to 4-aminoquinolines occurs in some countries in South America, Asia, and the western Pacific. In Asia resistant strains have progressed westwards to reach the Indian subcontinent. If resistance crosses the Arabian peninsula, it could represent a great threat to the African continent, where *Plasmodium falciparum* is the main malaria parasite and chloroquine and other 4-aminoquinolines are the major antimalarial drugs.

Clearly, the existing antimalarial drugs are insufficient for the operational demands of a control programme, and there has not been great fundamental progress since the synthesis of chloroquine more than 40 years ago.

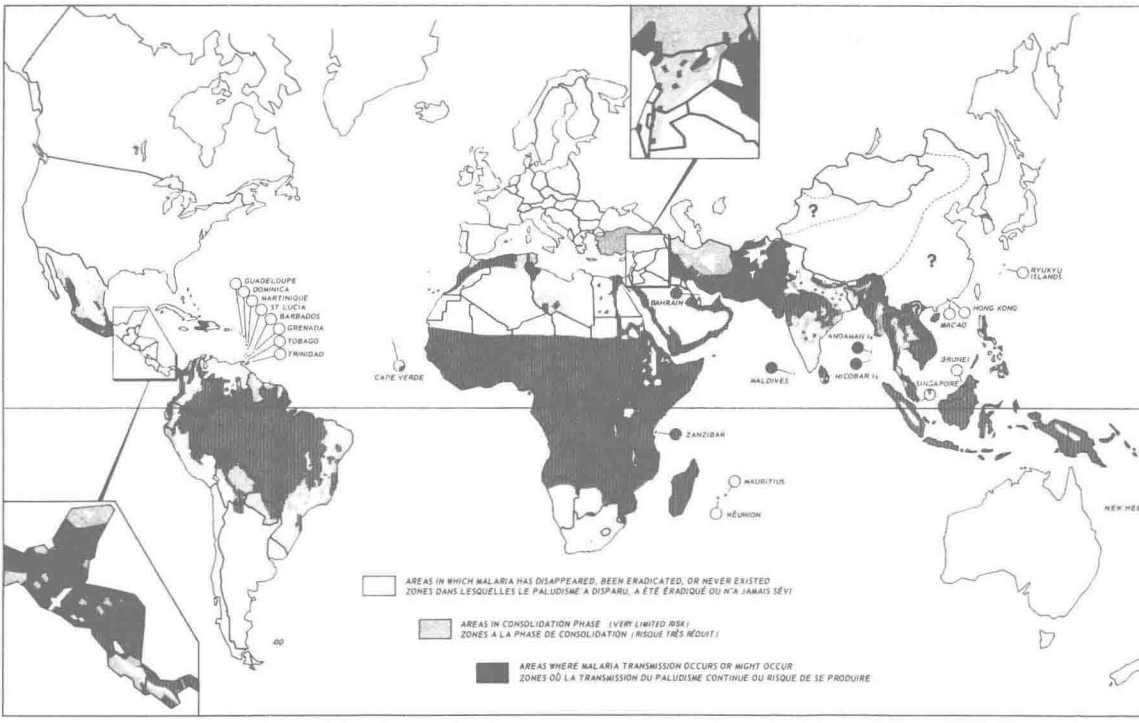
The promise of vaccines

There is promise in recent research for a malaria vaccine, but progress is slow, although it is known that many infected people do develop an important degree of protective immunity.

The picture is similarly disappointing with regard to most other tropical diseases. There are no fully satisfactory drugs to control or eradicate them, and no vaccines to prevent them.

Yet, modern biomedical science has progressed in giant steps. In the past 20 years or so it has unveiled some of the deepest secrets of life and made it possible to alleviate previously incurable diseases.

But it has not given tropical diseases the attention they deserve, even if they are judged only by the simple criterion of the number of people they affect.



Shading indicates areas at risk for malaria.

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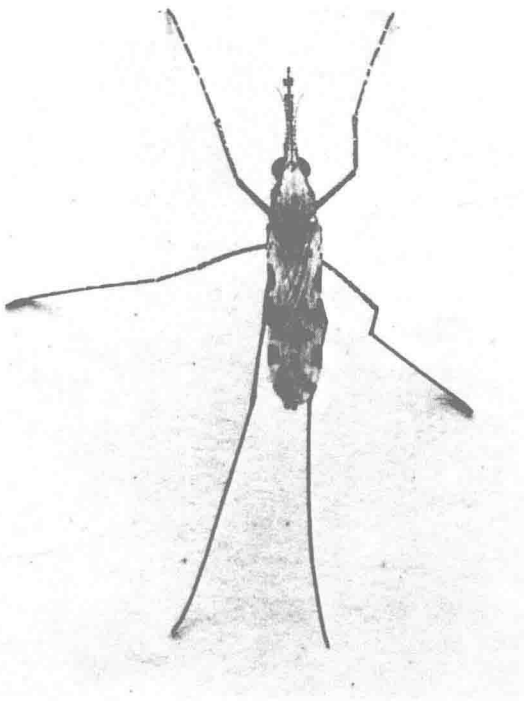

Adult Anopheles stephensi, *a mosquito that transmits the malaria parasite.*