



WORLD HEALTH ORGANIZATION

TROPICAL DISEASES TODAY—
THE CHALLENGE AND
THE OPPORTUNITY

GENEVA

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INTRODUCTION

The tropical infectious diseases exact a fearful toll of mankind even in our technological age. The World Health Organization here sets down an account. We speak of these diseases as old burdens which continue to kill and to destroy the quality of life of millions of people. We tell of present ways to control them: of successes, but, more significantly, of inadequacies and failures. We show that the recent explosion of knowledge in biomedical sciences is directed to develop better treatment of many diseases, but that a mere pittance of money and effort goes toward tropical infections. We claim that present knowledge could be developed to provide new and better remedies, both to prevent and to cure. We emphasize that much of this must be undertaken by the tropical countries themselves, where scientific advances can be applied to practical problems. And finally we propose a plan whereby this could be brought about, and new remedies achieved, in this century.

THE BURDEN

The Consequences of Disease in the Tropics

Great numbers of people now living in many regions of the tropical world are afflicted not only by most of the well-known diseases of temperate climates, but also by a whole range of vicious and potentially fatal tropical infections. The map shows the present distribution of the most important single disease, malaria. The burden of disease affects every aspect of human life. At the individual level it spells suffering and, often, early death. At the family level, it slows down or stops work and so accentuates poverty and starvation. At the community level, the threat of disease often determines where people live and what they do, and causes large fertile tracts to be abandoned. At the national level health and economic improvement may be seen to be interdependent, nevertheless health budgets are frequently low because countries are poor and pessimistic about whether any inroad into the disease problem is possible.

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 to grow up in the African bush, you are liable to harbour four or more different disease-producing parasites simultaneously. And yet, as a husband and a father, you must be fit enough to work, or your 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 like 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 may 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. Your experience of the quality of life is that of two hundred million Africans, and the story differs only in detail for some five hundred million people living elsewhere in the tropics.

The Six Diseases

Out of a welter of disease, we select six infections: malaria, schistosomiasis, filariasis, trypanosomiasis, leprosy and leishmaniasis. Control of these diseases is frequently ineffective, some of them are on the increase, and not enough is being done to obtain better remedies.

Three of these diseases, malaria, filariasis and schistosomiasis, each now affect about two hundred million or more people, numbers comparable to the entire population of the United States or the USSR, or one in twenty of the world's inhabitants. In Africa alone, malaria kills one million children every year. One person in ten is blind in some parts of Africa due to filarial worms causing river blindness, or onchocerciasis. Schistosomiasis or bilharziasis is an insidious subtle disease, also caused by worms, which undermines health by damage to many organs of the body, and which sometimes kills.

Only by the criteria of numbers are the remaining three less serious. Ten million people are infected with trypanosomiasis and leprosy, and a smaller number with leishmaniasis. Chagas' disease, the South American form of trypanosomiasis, damages the heart and may be fatal, and is incurable. Sleeping sickness, the African form of the infection, threatens epidemics of brain damage, causing a lingering and degrading death. Leprosy erodes and scars and distorts, especially the face and extremities, causing damage to be endured for the remainder of life. Leishmaniasis, as the espundia of South America, kills by destroying the face. Other forms of the disease include the fatal kala azar and the ubiquitous but usually transient tropical sore of the Mediterranean region.

PRESENT REMEDIES

Before discussing the need for new remedies, we should inquire about those now available. What are they? How effective are they? How effective would they be if they were better applied?

With the exception of leprosy, all the six diseases are caused by parasites. These parasites have remarkable life cycles, requiring intermediate hosts in their transit from man to man. Biting insects are often the vectors of parasitic disease, such as the mosquitos that transmit malaria, and the blackflies that transmit river blindness. Another intermediate is the special snail that carries schistosomiasis. Vectors may be the weak link in the disease chain, and vector control is one main line of attack on these

diseases which aims at the prevention of transmission from man to man, and so attacks disease at its source.

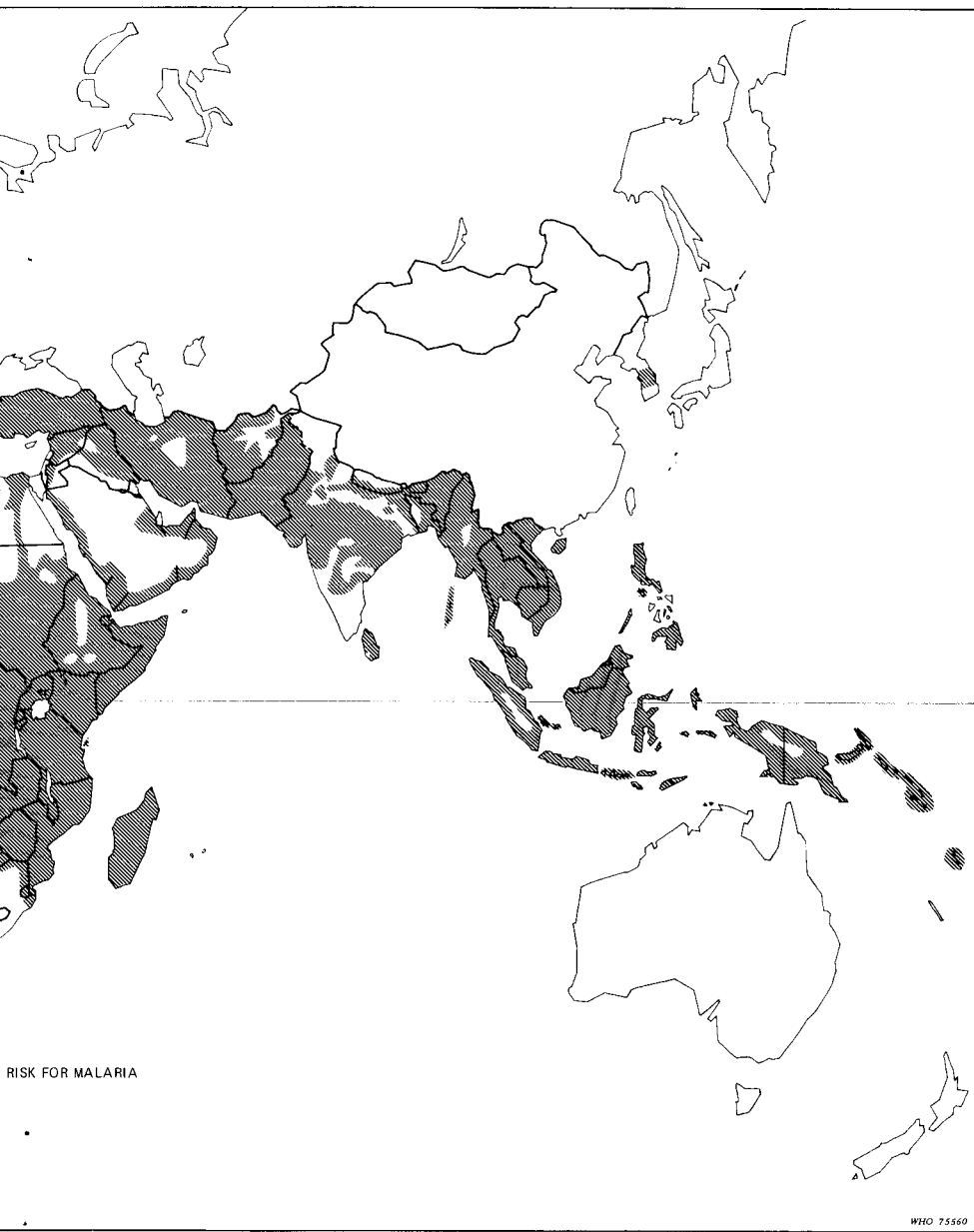
Malaria is the best example of what vector control can do. DDT and other powerful long-acting insecticides have been spectacularly successful in many parts of the world. The prevalence of malaria in India, for example, was reduced from seventy-five million cases in 1935 to sixty thousand in 1962 and in Sri Lanka the disease was practically eradicated. But vector control is not a panacea. In much of Africa, there is so much malaria that present methods of vector control are totally inadequate to affect the disease. In South-East Asia mosquitos have developed resistance to some insecticides. In India and Sri Lanka, where the resources were not available to continue the control of mosquitos, malaria is resurgent. In India the incidence of cases rose to two and one-half million in 1974, an object lesson on reliance on a single method of attack.

What of drugs? They are used primarily to treat an individual's illness. They can also be used to prevent infection, as when anti-malaria tablets are taken by visitors in the tropics. The drugs for malaria are usually highly effective, but in parts of South America and South-East Asia the parasite has become resistant to them and so new drugs are required. The drugs which we now have must be administered for days or weeks to cure an attack, or, if used to prevent infection must be taken whenever a person is liable to be bitten by infected mosquitos. These limitations prevent the general use of drugs to control malaria by treatment of whole populations.

Other parasitic diseases are less well served by drugs than is malaria. Many drugs, while poisonous to parasites, also tend to be harmful to man and to be of limited effectiveness. Leprosy is different. The drug dapsone is cheap and effective and harmful effects are not common, but treatment must be continued for up to five years, and the disease may recur even in those taking the drug. There is also concern since the bacterium causing the disease has on occasion been found to be resistant to this drug, which is the only effective agent.

For all of the six diseases neither vector control, where applicable, nor drugs can be regarded as satisfactory means for control and vaccines are non-existent. There is no way of achieving systematic control of malaria in rural Africa south of the Sahara. Existing knowledge, energetically and resourcefully applied, could greatly improve rural health in the tropics, a view emphasized by many tropical countries. A major activity of WHO is to support national programmes in rural health care, multiple immunization and environmental health. But a hard core of diseases remain, on which existing tools and knowledge have insufficient or negligible impact. Among these, the six diseases are pre-eminent. This deficiency is keenly felt by the tropical countries themselves, which at two successive World Health Assemblies have asked for assistance to develop research to obtain the remedies which they need.





THE OPPORTUNITY TO ACHIEVE BETTER REMEDIES

What basis is there for saying that there are new opportunities, now in 1975, to develop better remedies? Our conviction is based on the recent enormous extension of knowledge in the biomedical sciences—a quantum jump of progress yet to be applied to the diseases of the tropics.

In the years following the Second World War, several industrialized countries thought fit to make large investments of money and talent in biomedical research. The result has been an explosive increase of knowledge. Some of the highlights are well known—the unravelling of the genetic code, the full description of a protein molecule in all its complexity. In recent years more has been demanded of this type of research than acquisition of knowledge for its own sake, and part of the endeavour has been directed towards practical problems such as the control of cancer and of heart disease. The new knowledge has already revolutionized medical care through such advances as new drugs for the treatment of high blood pressure, a new range of antibiotics, and a series of vaccines against diseases such as poliomyelitis and measles. But, since application lags behind fundamental discovery, even in the industrialized countries the full impact on the health of the people has yet to be realized.

These advances have as yet hardly begun to be applied to the problems of tropical diseases, where methods of control and treatment have scarcely changed in the past thirty years. It has been estimated that the world's total annual research budget for all tropical infectious diseases is about US\$ 30 million per annum; one country alone spends nine times this amount on cancer research. Research in tropical diseases has not yet got off the ground.

Given adequate resources, what advances could reasonably be foreseen between now and the end of the century? Here are a few examples:

Reliable long-acting vaccines could revolutionize the control of malaria. Infection has long been known to produce a certain degree of immunity and the way in which immunity works is beginning to be understood. Experimental vaccines have been produced that protect animals and man. No one claims that a practical vaccine for human use is round the corner but recent results warrant a major effort to develop one.

For schistosomiasis, filariasis, trypanosomiasis and leishmaniasis, there is less information. But there is a prospect of vaccines for some of these diseases within the next ten to twenty years if work were intensified. Work on a vaccine for leprosy is the most advanced. A plan is now under way to obtain and assess a leprosy vaccine within the next five years.

In the past, drugs to treat parasitic infections were often selected on an empirical basis by the large-scale screening of possible compounds. More knowledge of parasite function can be the basis for developing new and

better drugs and for improving the best of the old ones. For example, parasites must possess surface recognition systems to enable them to identify their preferred location in the body. Malaria parasites are able to recognize the right sort of red cell and then to penetrate into it. Clues to the chemistry of this system already exist, and compounds can be envisaged which interfere with the system and so, in effect, blindfold the parasite. Drugs based on this principle would act powerfully against malaria and could be innocuous to the human host.

THE PLAN

The Diseases

The number of tropical diseases is too great to propose a single plan, however ambitious, that will encompass them all from the beginning. In our view, malaria, schistosomiasis, filariasis, trypanosomiasis, leprosy and leishmaniasis constitute the crux of the problem. The means available to control and treat them are of limited effectiveness and there is little research directed towards new remedies, compared with the research on major diseases that also occur in temperate climates such as meningitis, measles and intestinal infections. The six diseases hold together as a group from the point of view of research; advances in one may open up new approaches for another. Thus the development of a vaccine for leprosy could point the way to vaccines for others of the six diseases. Leishmaniasis, although less important numerically as a disease, is included since the parasite is easily handled in the laboratory and there are exceptional opportunities to study the relationship between this parasite and certain cells of the body. This kind of research could lead to better drugs not only for leishmaniasis, but also for leprosy, trypanosomiasis and malaria, in which the same body cells are involved. Malnutrition is a major factor related to all these diseases, and its effects on severity and on the effectiveness of remedies will also be studied.

These diseases have been singled out on the basis of the need and opportunity to obtain new remedies, but others may be added later and, when success is achieved and effective remedies are found, some may be deleted.

The Place

At the beginning we shall focus on one continent that carries the major burden. Africa has the highest prevalence of all the six diseases, except

filariasis and South American trypanosomiasis. In Africa, multiple infection is almost the rule, and the need for control is perhaps greatest. New remedies would transform the quality of life in many African communities, and the health authorities welcome enthusiastically the idea that the work should begin there.

But the fundamental concept of the plan is global. There is no reason, other than manageability, why the plan should be restricted to one continent. South America will be involved from the beginning through the work on trypanosomiasis and leishmaniasis. Experience gained in the early stages can be used for development elsewhere and to bring in, for example, the major resources of the Indian subcontinent.

The People

The plan is to enlist and support existing laboratories in the tropics to carry out the work, and to develop new laboratories as necessary. In Africa a framework on which to build exists already. The East African Medical Research Council has seven laboratories working on tropical infectious diseases in Kenya, Tanzania and Uganda. Nairobi is a hub of biomedical enterprise with major national and international research laboratories and institutions. The thrust of the Nigerian Medical Research Council's effort is toward better control of tropical diseases. There are twenty-five university medical schools in tropical Africa and several European countries support research laboratories in Africa. These and other laboratories, and organizations such as l'Organisation de Coordination et de Coopération pour la lutte contre les Grandes Endémies and l'Organisation de Coordination pour la lutte contre les Endémies en Afrique Centrale together form a basis upon which the proposed network can be built.

Some of these laboratories are inadequately staffed, equipped and funded and too narrowly specialized to make an immediate effective contribution. They need better training programmes and adequate career structures to attract first-class scientists. They also need better communication with other scientists to break down the isolation that handicaps so many laboratories in Africa. These requirements are ultimately the responsibility of governments; the plan will provide the resources and the technical cooperation needed to begin.

This brings us to a central question that has already been touched on. It can be phrased as follows: given the need for excellent technological facilities and the long and costly effort which will be necessary to achieve them in some African institutions, would the work not be better carried out in the existing well-equipped institutions of the industrialized world, or in purpose-built institutions in Africa? Our reply to this is that it will diminish

the effectiveness of the plan to consider it solely as a means of obtaining a particular vaccine or drug as rapidly as possible. Involvement of the tropical countries is essential for a number of reasons. It will ensure that the remedies are tailored to the real needs and not the supposed needs of the countries. It will provide a spin-off of scientific training and expertise that can be used to help apply the remedies, to modify them, or to develop other remedies. The remedies will be the more acceptable since they will be developed *by* the countries and not *for* the countries. And the plan will provide the tropical countries with an approach to biomedical science that will inevitably become their own, one that is appropriate to their problems, and is not an offshoot of the approach of the industrialized world.

There is one aspect of the programme in Africa that already has received much attention. This is the research centre proposed for Ndola in Zambia. The centre was born of the idea that multidisciplinary research bringing together different aspects of laboratory and clinical medicine would be a most effective way of achieving rapid advances. Such a centre, developed as a model for the study of diseases in an African environment, should not only be successful in finding new remedies, but it would also serve as a unique training ground for African scientists, who would afterwards return to their own countries. We support the views of many Africans who consider that the Zambian Government's gift of laboratories in a large hospital building for this centre affords an opportunity which cannot be neglected. Our plan is to develop Ndola step by step, assessing at each stage the results achieved in relation to the talent and money invested.

We have stressed the importance of the conduct of research in the tropical countries. But at present the necessary knowledge and skill is chiefly to be found among the scientists of the industrialized world, and their involvement is crucial. There are a fair number of scientists with experience in tropical medicine now working outside the tropics. They are needed, together with others skilled in disciplines such as molecular biology, immunology, chemotherapy and clinical medicine to help in the planning, to develop special aspects of research, and to conduct training. We have found genuine enthusiasm among young scientists for this work. The services of these scientists will be incorporated into the plan through its operational components, the task forces and networks now to be described.

Organization

To conduct this large programme, we propose two parallel systems of organization with which WHO has had recent experience and success. These are Task Forces and Networks.

Task forces are groups of scientists of the highest international standing which aim to develop more effective remedies. For this, they will first define

the remedies that are needed and then plan all phases of the research necessary to achieve them. Task force members are chosen for their qualifications for the work in hand, and they change according to the phases of the work. The World Health Organization's Expanded Programme on Human Reproduction has shown that goal-oriented research can be pursued effectively in this way. A task force to develop a diagnostic skin test and a vaccine for leprosy has been working for the past two years as a pilot operation and expects to achieve its goals within the next five. Studies have already been made on the feasibility of new drugs and vaccines for the other five diseases.

While the task forces are responsible for scientific planning and direction, the actual carrying out of the research will be in the hands of a network of collaborating laboratories. In Africa, the foundation of the network is the existing research institutes and university departments, and the centre planned for Ndola will form an important component. The training of indigenous scientists will also be a responsibility of the African network. For reasons we have already explained, much of the scientific work will be carried out in Africa and so most of the network laboratories will be there, but laboratories in other continents will also be essential to develop task force plans and will be included in the network.

CONCLUSION

This plan is for a new international effort to obtain better remedies for tropical infectious diseases. It seeks to promote a degree of equity in the aims of the world's biomedical research by developing new remedies for the major causes of sickness and early death in the tropics. It aims at making the research institutes in tropical countries more effective and it draws on the skill and commitment of scientists around the world to achieve its purpose.

The plan is not to be seen in isolation from other efforts to combat these diseases. It introduces an essential aspect of research and development related to such programmes as that for onchocerciasis control in West Africa, the major international effort now being developed to control schistosomiasis and WHO's own programmes for the improvement of rural health. While the initial effort is focused on six diseases and on Africa, the concept is global.

One important implication of the programme has hardly been mentioned because it does not yet fall within the direct framework of the plan, and yet it is crucial. The new remedies will have to be produced in quantity before they can be applied. As the work of the task forces progresses, so increasing attention will have to be given to the large-scale

manufacture of the drugs, vaccines and the other remedies that are discovered.

Finally, there is a note of urgency. If better remedies are not forthcoming for these diseases during this century, then they will spread and the plight of man will become even more serious. Increasing population and inadequate food supplies will increase disease and make control more difficult. Even agricultural development may promote diseases such as schistosomiasis and river blindness by providing new breeding grounds for their vectors. There is now an exceptional opportunity to prevent this. While our plan carries no promises, there is every reason to believe that better remedies could be found for many of the great diseases of the tropics. In the name of humanity, of dignity and equity, since there is opportunity, should we not seize it?
