SCIENCE KNOWS NO COUNTRY:
THE CONTRIBUTIONS OF THE NATIONAL INSTITUTES OF HEALTH
TO TROPICAL MEDICINE RESEARCH

"SCIENCE KNOWS NO COUNTRY because knowledge belongs to humanity, and is the torch which illuminates the world."

Louis Pasteur, 1876

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In 1876 at the International Congress of Sericulture in Milan, Italy, Louis Pasteur gave a toast at the banquet. In that toast Pasteur said, "Science knows no country because knowledge belongs to humanity, and is the torch which illuminates the world."[1] In a sense these remarks embody the theme of this Conference. They are also the philosophical foundations on which the National Institutes of Health is basing its strategy for future research on tropical diseases.

This position has also been embraced by President Carter who in his message to the Thirtieth World Health Assembly in Geneva last May, supporting the WHO Tropical Diseases Research Program said, "these efforts will bring us closer to our goal: a world in which all people can live free from fear of crippling and debilitating diseases."[2] And more recently, Dr. Peter Bourne, Special Assistant to the President for Health Issues, reiterated the President's position in a speech to the American Public Health Association. He refers to "the new awareness of global interdependence and a commitment by the President to a new world partnership directed toward meeting the basic human needs of people everywhere."[3]

At this Conference we have focused primarily on malaria and schistosomiasis, and rightly so. These diseases are among the most serious, widespread and intractable problems in tropical medicine. Surely our future research strategies for malaria and schistosomiasis will be a model for the larger task embracing health in all its aspects.

[1]Translated by Professor René J. Dubos.

[2]President Carter's Message to the President and Members of the Assembly Meeting in Geneva, Switzerland. Dated May 5, 1977. Released 9, 1977.

[3]U.S. Global Health Strategies in an Age of Interdependence. Address of Peter Bourne, APHA Annual Meeting, October 31, 1977.

In these remarks on the contributions of the United States' National Institutes of Health (NIH) to the strategies of the future concerning tropical medicine, I shall limit myself primarily to the research programs of the National Institute of Allergy and Infectious Diseases (NIAID). This Institute is responsible for the bulk of the research at the NIH on the diseases of the WHO Tropical Diseases Research Program. I should note that we also have responsibility for a broad range of other infectious diseases which are peculiar to tropical countries and the developing world, and while this falls heavily on the Institute of which I am the Director, other components of the NIH are also engaged in these areas. So I am speaking today for the NIH as a whole.

Furthermore, what the United States Government does about tropical medicine will not be done by the NIH alone. For those of us, like myself, who have just been introduced into this world of overlapping government agencies - and I am certain it must be true for those of you who view the American scene from afar - there seems to be a display of divergent objectives and a cacophony of dissonant voices. There is, fortunately, less thrashing about inside the system than appears to be the case from the outside. Over the years there has emerged a reasonable, although certainly not perfect, delineation of responsibilities. For example, the NIH has primary responsibility for the generation of new medical knowledge; the Center for Disease Control has primary responsibility for implementation of procedures and programs to monitor, detect and control the occurrence and outbreaks of disease; and the Agency for International Development has responsibility for the development of health resources in the developing world.

So the business of the NIH is the generation of new medical knowledge through biomedical research. Such new knowledge must then be applied by a process now

called technology transfer. It is at this very point that a major policy issue arises throughout the health enterprise. That policy issue concerns the distribution of the resources between biomedical research on the one hand, and the application of knowledge to prevent and treat disease on the other. And this is being intensely debated in the scientific and medical community both within and without the United States' Government. We should not minimize the divergence of views which prevails on this issue. The divergence prevails in Congress, it prevails in the Executive Branch of the Government, it prevails in the Institute of Medicine. It is not surprising, therefore, that this policy debate on the distribution of resources between biomedical research and the application of knowledge colors discussions concerning the future objectives of our policies pertaining to tropical medicine.

But I, personally, take comfort in the vigor of this debate. It reflects a genuine concern for the complex issues pertaining to medicine and health. And we should recognize too, that this disagreement is an old argument. Science has lived with it from the very start of our modern age, and in my view, we should not get hung up on the technicalities of the issue. I will, in the course of my remarks, make a case for both biomedical research and the application of knowledge in instances where both are clearly necessary. Then I would suggest we let the middle ground sort itself out.

When this controversy produces more passion than reason, I myself take reassurance from the wisdom of men of the past who also were caught up in this argument. Many of you know that Benjamin Franklin - in addition to his career as a printer and a writer and a representative of the colonies to the Courts of England and France - was also a bit of a scientific tinkerer. We learned

as school children about his experiments to probe the mystery of electricity by flying a kite during a thunderstorm. On yet another occasion, when describing a series of experiments, he was asked at the end of a lecture, what good could there possibly be in such knowledge? Franklin's immediate response, "What is the purpose of a newborn babe?"

Faraday was involved in a similar exchange shortly after his discovery of electromagnetic induction - not too far from here actually, at the Royal Institution. He was demonstrating this new phenomenon to the Prime Minister. The Prime Minister asked the question, "What is the possible purpose of your new discovery, Dr. Faraday?" To which Dr. Faraday quickly replied, "Mr. Prime Minister, some day you will use it as a source of taxes." And indeed, this has come to pass with heavy tax rates on electrical utilities.

During his life Pasteur, too, was drawn into the vortex of the argument over basic research and the application of new knowledge, and spent much time circulating this dipole. But he was content with his belief that "there are science and the applications of science, linked together as the fruit is to the tree that has borne it."

In these comments I shall make two points concerning the NIH strategy for the future. The first point concerns an inventory to determine the tropical diseases which are currently controlled by existing public health measures and those other diseases which will require additional biomedical research before control is achieved. My second point deals with what I have termed the synergistic application of new discoveries of biomedical research to conventional public health measures for the control of tropical diseases. I shall then close with four specific proposals on NIH initiatives for the future.

Last April, when I gave the Annual Geographic Medicine Lecture at Case-Western Reserve University School of Medicine, I discussed what in my judgment was the first order of business in overall strategy for an attack on tropical diseases. With no claim to originality, I suggested that we examine tropical diseases from two points of view. First, identify those diseases for which application of known social, economic and public health measures would provide effective control now; and second, identify those other diseases for which there is little likelihood that in the foreseeable future application of socio-economic and public health measures will have any appreciable, beneficial impact. In these latter cases, we must be prepared to devote research manpower and research resources to develop new diagnostic procedures, new therapy and new preventive measures. I recognize of course that complex diseases such as those that occur in the tropics do not break out neatly into one category or another. Few things are that simple. It is also true that because of social and other environmental factors it may not be possible to apply the same scheme for any single disease on a worldwide basis.

It is entirely likely that a tropical disease controllable in one country by currently available means would be impossible to contain in another. Let me illustrate. We have been told that in China, intensive application of public health and sanitation procedures has gone far to eliminate the problems of schistosomiasis. Similarly, schistosomiasis has decreased dramatically in Puerto Rico. But in Egypt, on the other hand, a lifestyle dating back to the time of the pharaohs, is so ingrained - so keyed to the rise and fall of the Nile and the irrigation of the canals - that one suspects it may be difficult, in our lifetime, to put into effect what we think of as good public health and sanitation

practices, or to put into effect a new way of life that would go a long way towards the control of schistosomiasis. For the foreseeable future, it may be that the only alternative is an intensive research program focused on the development not only of new public health measures, but also of new drugs, new treatment programs, new molluscicides and perhaps even vaccines.

The overall strategy which I have suggested was in a sense applied to schistosomiasis at the recent Edna McConnell Clark Foundation meeting at Bellagio, Italy. The purpose of the meeting was to discuss the current state of the measures available for the control of schistosomiasis. A review of recent work on this disease revealed several general conclusions: well designed studies of various methods of control of schistosomiasis have been completed and evaluated; studies on morbidity of schistosomiasis in nearly every case reveal a correlation between the intensity of infection and the extent of disease; and while immunological studies of this disease have uncovered a great deal about immune mechanisms, the possibility of a vaccine remains remote for the present.

These general conclusions lead to several specific points in regard to the future efforts in schistosomiasis control.

1. In most cases the aim of control programs should be the sustained reduction of prevalence and intensity to a point at which clinical disease is of low public health importance in relation to other diseases in the area. Parasite eradication is not a goal of schistosomiasis control.

2. Completed studies of single methods of control that were reviewed indicate that chemotherapy may be the most cost-effective method of reducing prevalence, incidence, and intensity of infection at present. Highest priority should be given to operational research involving improved delivery systems of these new drugs.

3. New methods of chemotherapy delivery systems such as selective chemotherapy or subcurative single dose therapy may substantially decrease egg contamination of the environment and thereby decrease transmission, cost of control, morbidity and mortality.

4. Despite the advances in chemotherapy, in many epidemiologic situations, control will require the use of secondary methods such as molluscicides, and management of water supplies and sanitation.

The NIH will conduct research on these specific points where there is still insufficient knowledge to implement them. And we do not take lightly the continuing need for applied research on existing control measures. But I must say we have a responsibility to go one step further. And that one step further takes us right into the importance of biomedical research as a strategy for the future.

The most powerful argument for biomedical research on tropical diseases stems from the unanticipated reemergence of medical problems for which we had earlier developed solutions. Over and over again in medicine we are faced with the reemergence of old problems in new garments. An example is the recent and alarming occurrence of antibiotic resistance among pyogenic bacteria such as gonococci, pneumococci and H. influenzae B. Widespread occurrence of plasmid-mediated resistance to antibiotics among pyogenic bacteria has forced us to reassess our research strategies for the disease control which was thought to have been achieved with antibiotics.

Indeed in the United States in 1964, because of the emergence of sulfanamide-resistant organisms, we made a deliberate public health decision to embark on meningococcal vaccine development for the control of meningococcal meningitis.

In the face of the subsequent worldwide dissemination of sulfanamide-resistant meningococci, there was no alternative to control epidemic meningitis but the development of a new vaccine, and that vaccine required resources, basic research, brains, and new ideas.

In 1968 I made a special unsolicited trip to Geneva to urge that WHO give meningococcal Group A vaccine field trials the highest priority in the meningococcal belt of Africa. Dr. Karel Raska, then the Director, Division of Communicable Diseases at WHO, seized the opportunity, and meningococcal Group A vaccine is now a public health measure in Africa. I just recently returned from Zambia where the vaccine had been used widely during the past two years in the northern provinces around Ndola.

The reemergence of malaria as a major disease problem - one more directly related to the focus of this conference - also underscores the continuing need for basic research. Malaria was thought to have been solved. The application of traditional public health measures using more recent tools such as DDT and chloroquine - the legacies of research incidentally - was believed adequate for the control of this disease, throughout the world and for all time. What complacency. And how wrong we were. The emergence of chloroquine-resistant malaria parasites and DDT-resistant mosquitos has laid bare our smugness.

We were complacent because we overlooked the durability of a species; a durability for survival in changing environments; a durability arising out of adaptability. We lost sight of the underlying evolutionary processes. Even now at the close of Darwin's century, we too often think of biology as a static process, as if each species of all living things were caged in solitary confinement in a Linnéan garden.

So in the face of these adaptations of nature such as drug resistance among microbes, we must reassess our means to control malaria, and plan research strategies for new treatment and control methods. And when we have achieved that, make no mistake about it, if we are not vigilant, the course of evolutionary events will again overtake us. And so our strategy includes the study of the biology of malaria, mosquitos, schistosomes and snails. It is the course of prudence. It is the course of vigilance.

Darwin, I suspect, would have anticipated the emergence of DDT-resistant mosquitos or chloroquine-resistant malaria, understanding as he did, the meaning of selective pressure in the survival of the species. It is indeed ironic that at the close of Darwin's century we grasp the molecular mechanisms of evolution, but in the applications of modern medicine to public health we fail to recognize the predictable consequences. The job of the NIH, as I see it, is to remain alert to those predictable consequences.

My second point on the NIH strategy for the future concerns the practice of what I call synergism. By synergism as a strategy, I mean the reinforcement which occurs between the use of conventional public health practices and the enhancement of those practices through the additional benefits of biomedical research. Indeed, our most immediate past experience with plagues in our own countries reveals the importance of this synergism between the application of conventional public health measures along with the new benefits of medical research. What better example of such synergism than the modern control of tuberculosis. Long before the age of antibiotics, much was done in the control of tuberculosis with the isolation of cases and improvement of nutrition, housing, and so on. But in the 1950's modern chemotherapy broke upon the scene as the

culmination of seventy-five years of intensive bacteriologic research. Only then was it possible to combine public health practices synergistically with modern chemotherapy and to control tuberculosis beyond what would have seemed possible at the turn of the century. I mention tuberculosis, particularly, because this remains a disease which is not yet controlled in the developing countries.

Another example. Synergism remains an important strategy in the control of yellow fever. When conventional public health practices were coupled with the use of Max Teiler's attenuated vaccine - a product of laborious basic research in virology for which he received the Nobel Prize - the beneficial effects were synergistic rather than additive. And how fortunate it is that we can still use this synergistic approach to yellow fever control without continuous modification of the vaccine through basic research. We have been less fortunate, as has already been noted, in the synergistic application of stagnant practices to the control of malaria.

So for all of us, the overall strategy for the future will be to apply what we know now and to apply it vigorously. At the same time, the particular strategy of the NIH is to develop new modalities for diagnosis, treatment and prevention through basic and applied research. We will work with our own various government and private agencies in the United States, and we will work with other countries, either formally or informally. In particular, we will work with all countries through the good offices of the World Health Organization.

We most especially endorse the Tropical Diseases Research and Training (TDR) Program of WHO. We have followed its development with interest and we have participated when asked in the development of its plans and objectives. Hundreds of

American scientists supported by the NIH and other government agencies, are currently working on the six diseases identified by WHO as of first importance.

In Figure 1 are listed 1977 estimated expenditures by United States agencies on the six WHO tropical diseases in the TDR program. The total was approximately 24 million dollars. The NIH spent just over 7 million dollars. In Figure 2 is presented the 1977 estimated expenditures on each of the six diseases. Notice that agencies other than the NIH also have a major effort in malaria.

As I said earlier, there has been much talk about new initiatives in international health. This new intensity of interest has received widespread notice including an editorial in Science last June written by Dr. Howard Minners whom we have seconded to WHO to assist in the management of research.

But the time has come to act, to act now, to take the first steps in the implementation of new initiatives, and this we at the NIH shall do. I announce these first steps here with the approval of Dr. Donald Fredrickson, Director of the NIH.

A continuation as well as an expansion of our current efforts in tropical medicine will focus on four broad objectives.

1. The strengthening of tropical medicine in United States' universities within the framework of existing biomedical disciplines, e.g., internal medicine, pediatrics, pharmacology, biochemistry, immunology, etc. This will not only enhance the present research effort in our universities, but will also provide long term career opportunities in the usual medical disciplines for investigators with a specialized interest in tropical medicine.

2. An extension of current United States' research to the developing countries through "linkages" between United States' investigators and those

in the countries where tropical diseases prevail. The WHO TDR program has called for a network among the research centers in the countries where the diseases exist and in the developing countries. When I attended the Donors and Participants Meeting at WHO a year ago, I emphasized then my preference for the process of linkage between scientific and medical groups in both regions with common goals in biomedical research and development and training.

To facilitate this linkage we shall announce a new research grants program for International Collaboration in Infectious Diseases Research. These grants will require a U.S. investigator to have a defined linkage with a foreign investigator for research done in a truly cooperative way including laboratory and field studies in the overseas environment. Emphasis will be given to the disease entities in the WHO TDR Program and to those investigators who have identified linkages with colleagues in developing African and Latin American countries, although not to the exclusion of other locations.

3. Assistance in the establishment or strengthening of centers of excellence in developing countries. The linkages described under objective 2) can be important in reaching this goal. Resources in U.S. public and private sectors as well as the developing countries will be required.

4. And finally, expanded opportunity for research training in the United States for young medical scientists and health professionals from developing countries. This is particularly true for training related to the tropical diseases and we have plans in process for an International Tropical Diseases Research Fellowship Program of NIAID. It will be established in cooperation with the WHO, and will be administered by the NIH Fogarty International Center. This research fellowship program will focus especially on the six diseases of

the WHO TDR Program. The objective of this new international fellowship program is to provide junior or mid-career health professionals and scientists the opportunity to acquire the special skills which will be applicable to infectious diseases in their own country.

Further information on these new programs to establish research linkages and fellowships will be forthcoming in the near future.

In these comments I have sketched the barest outline of the NIH strategies for the future. Our business is the generation of new medical knowledge through basic and applied research, and this we shall do on the tropical diseases, in collaboration with our colleagues in the United Kingdom and throughout the world. We endorse the objectives of the WHO TDR Program as a sensible and realistic beginning, recognizing that other diseases are also of major importance in the developing countries.

I have indicated that an expansion of our current efforts in tropical medicine will focus on four broad objectives. Included in these are: 1) a new research grant program to establish research linkages between investigators in the United States and our colleagues in the developing countries; and 2) new research training fellowships for young medical scientists from developing countries to work in the United States.

Finally I have said also that the control of tropical diseases can have an elusive and ghostly quality. The reemergence of malaria is a notable example of such behavior. We had not anticipated the occurrence or the consequences of chloroquine-resistant malaria parasites or DDT-resistant mosquitos. In our strategy for the control of tropical diseases, we must recognize that this re-emergence of an old problem in new garments is programmed in the genetic machinery

of biological evolution. We therefore must remain both vigilant and venturesome. If we are not alert to the sovereign stream of evolution, we shall be swept away by the inevitable consequences of biological adaptability in the microbial world.

FIGURE 1

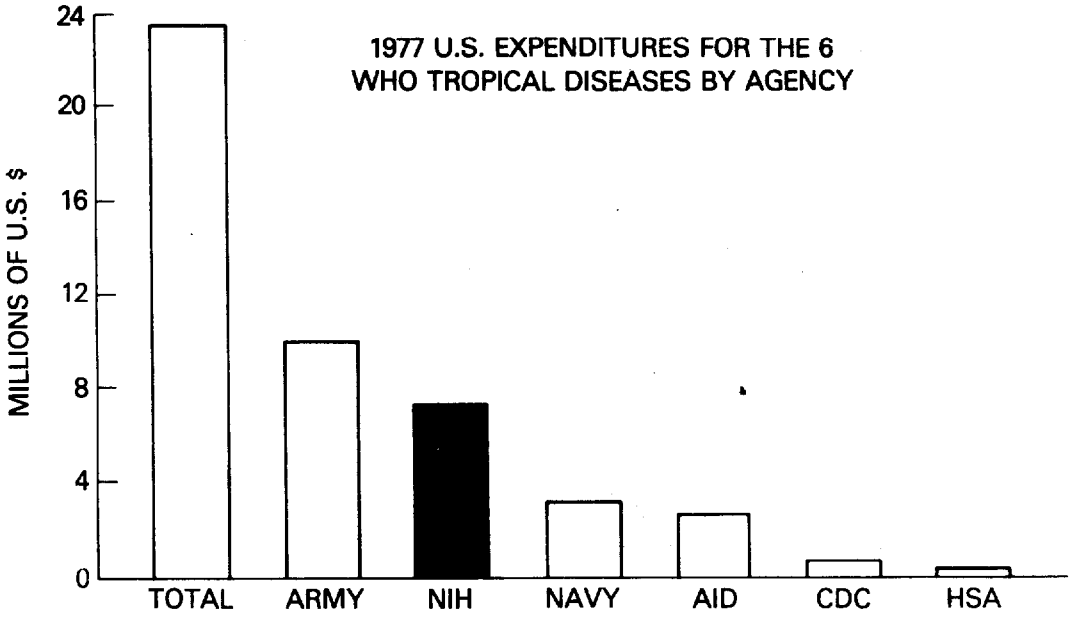
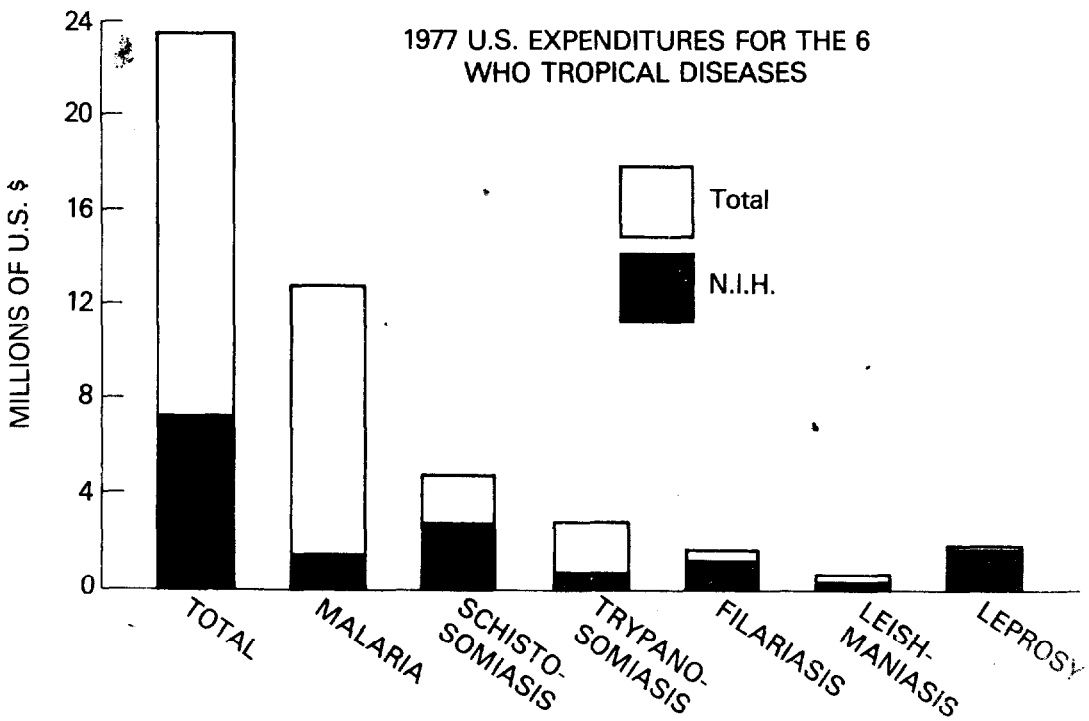

1977 U.S. EXPENDITURES FOR THE 6
WHO TROPICAL DISEASES BY AGENCY
MILLIONS OF U.S. $
24
20
16
12
8
4
0
TOTAL
ARMY
NIH
NAVY
AID
CDC
HSA

FIGURE 2


1977 U.S. EXPENDITURES FOR THE 6
WHO TROPICAL DISEASES
MILLIONS OF U.S. $
24
20
16
12
8
4
0
Total
N.I.H.
TOTAL
MALARIA
SCHISTO-
SOMIASIS
TRYPANO-
SOMIASIS
FILARIASIS
LEISH-
MANIASIS
LEPROSY