US Capacity to Address Tropical Infectious Disease Problems: Conclusions and Recommendations (1987)

Pages
48

Size
5 x 9

ISBN
030931075X

Steering Committee for the Study of U.S. Capacity to Address Tropical Infectious Disease Problems; Board on Science and Technology for International Development; Office of International Affairs; National Research Council; Institute of Medicine

Conclusions and Recommendations

The US Capacity to Address TROPICAL INFECTIOUS DISEASE PROBLEMS

Board on Science and Technology for International Development
Office of International Affairs
National Research Council (U.S.)

and the

Institute of Medicine
National Academy of Sciences

NATIONAL ACADEMY PRESS
Washington, D.C. 1987

This report has been prepared by the Steering Committee for the Study of U.S. Capacity to Address Tropical Infectious Disease Problems, Board on Science and Technology for International Development, Office of International Affairs, National Research Council, in collaboration with the Institute of Medicine. Funds for this study were obtained from the U.S. Army Research and Development Command, the National Institute for Allergy and Infectious Diseases, and the Centers for Disease Control (Contract No. DAMD17-84-G-4015) and the Agency for International Development (Contract No. DPE-1406-G-SS-4071-00). The Rockefeller Foundation cosponsored and funded a workshop in Cairo to discuss the U.S. role in tropical infectious disease research collaboration.

Copies available from:

Board on Science and Technology
for International Development
National Research Council
2101 Constitution Avenue, NW
Washington, DC 20418 USA

ISBN 04259-3

Printed in the United States of America

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FOREWORD

This publication presents the results of a study, conducted by a steering committee appointed by the National Research Council and the Institute of Medicine, of U.S. capacity to address tropical infectious disease problems.

The central findings of this report can be stated simply. The next two or three decades offer a historic opportunity to make major progress against the heavy burden of tropical diseases. The diseases themselves are as damaging as ever, and some, such as malaria, are becoming more dangerous as vectors have become resistant to pesticides and parasites to drug therapy. What opens the doors to major progress is a combination of new biological research methods and new economic and social approaches to the applications of health improvements. Properly exploited, these new methods and approaches could result in large-scale reductions in the present enormous social cost of these diseases.

The United States is participating significantly, in a variety of ways, in the international effort to attack tropical infectious diseases. Nevertheless, despite long experience with tropical diseases and major national interests in helping to reduce their burden, the United States is contributing much less than it readily could and should. This report makes a number of specific recommendations for improving the effectiveness of current efforts. It concludes that, with modest increases in resources, the United States could contribute much more strongly than at present to the international collaborative effort to develop and test new approaches for controlling tropical diseases.

This document is intended to be helpful to those interested in tropical infectious disease problems, in

the health and welfare of poor people in developing countries, and in U.S. foreign policy. We believe it brings together important information and presents conclusions and recommendations that will be useful to members of Congress, federal agency and university administrators, industry and foundation leaders, researchers, health planners, and others seeking to understand resource constraints, to develop program initiatives, and to formulate policies in the area of tropical disease research and control.

The committee wishes to express its warm thanks to Karen Bell, study director, to her colleagues Heather Miller, staff associate, and Barbara Jones, senior secretary, and to Courtney Nelson and Timothy Baker, consultants. The committee was greatly aided by its advisers, who participated fully in its meetings and reviews. Finally, the committee thanks the many individuals who assisted with this study by providing information about specific programs, reviewing portions of the draft, or suggesting particular issues for consideration; a list of all contributors has been included in the report.

David E. Bell
Chairman, Steering Committee

PREFACE

The study reported here originated from a request by the American Society of Tropical Medicine and Hygiene to the Institute of Medicine. The request was considered by a joint advisory committee to the Institute and the National Research Council's Board on Science and Technology for International Development, which felt that a broad examination of U.S. goals and resources for tropical health was both timely and needed. Further impetus for conducting the study was afforded by expressed interest among members of Congress and federal agency officials about ways to achieve rapid progress in applied biomedical research targeted on important public health problems in the developing world.

The National Research Council appointed a steering committee for the study in June 1984. The committee established the scope and nature of study activities and approved principal issues of concern and the recommendations to be included in the final study report.

The Office of Technology Assessment (OTA), in response to similar concerns expressed by the Senate Appropriations Committee, simultaneously began an examination of the status of biomedical research and technologies for controlling tropical infectious diseases. Staff for the two studies coordinated their work closely in order to achieve complementary, rather than overlapping, products. Results of the OTA examination were published in its 1985 report, Status of Biomedical Research and Related Technology for Tropical Diseases.

In viewing U.S. capacity to address tropical infectious disease problems, the committee examined several major issues:

- The extent of the tropical disease burden and the

U.S. national interest in its alleviation;

- Current prospects for control of tropical diseases;
- Efforts by the less-developed countries, international organizations, and the United States to improve tools for dealing with tropical diseases and to strengthen health programs for their control;
- The state of U.S. resources, both individual and institutional, for dealing with tropical disease questions; and
- How the United States might develop and channel its efforts more efficiently to make a useful difference, in a period of budgetary austerity, in the fight against tropical diseases.

Data on the scope and direction of U.S. efforts against tropical diseases have been scattered or lacking. The committee looked at critically important categories of talent (clinicians, including clinical researchers; biomedical scientists in the fundamental and applied research disciplines; and specialists in public health and disease control); at training and research capacity; and at current efforts for tropical disease surveillance, diagnosis, treatment, and control.

For the purposes of this study, the committee decided to use the term "tropical infectious diseases" to refer to those diseases of infectious etiology that occur predominantly in the poorest populations in less-developed countries. This definition, consistent with that found in OTA's 1985 report, includes the major tropical parasitic diseases (e.g., malaria, schistosomiasis, and trypanosomiasis); diarrhea; acute respiratory infections; leprosy; and numerous other diseases of bacterial, rickettsial, viral, and parasitic etiology. The committee did not find it necessary to prepare a precise and comprehensive listing.

Other diseases, such as tuberculosis, acquired immune deficiency syndrome (AIDS), and gonorrhea, also pose significant public health threats in developing countries, but were not included in the committee's analysis of U.S. capacity, because they are still considered infectious disease problems in industrialized countries and, as such, receive substantial research and control program support. Note, however, that the working definition is restrictive in at least two respects and does not include some major public health problems of developing countries. Problems related to population growth were excluded, as were nutrition-related problems

other than those directly related to viral and parasitic infections. The committee considers these omitted subjects to be of great importance but clearly beyond its mandate.

In enumerating critically important categories of talent, the committee adopted the term "tropical disease professional" to designate an individual with advanced training in medicine, the biomedical sciences, or public health who is currently dedicating his or her research or clinical efforts to an infectious disease problem of developing countries. Three basic categories were identified: clinicians, including clinical researchers; biomedical scientists engaged in research; and specialists in public health and disease control. Individuals who were included in the biomedical research category had successfully competed for research funds. The committee also examined training and research programs and U.S.-sponsored activities in tropical disease surveillance, diagnosis, treatment, and control.

The study proceeded in the following way: The staff held preliminary, 1-day meetings in Washington, Los Angeles, and Baltimore, prior to the committee's formal appointment. These meetings brought together experts from government, industry, academic institutions, private foundations, and other organizations to consider the study mandate and to suggest how to proceed. Several individuals subsequently appointed to the committee were present.

The committee met twice in 1984 to determine the issues to be addressed and to develop a work plan for staff and consultants. To obtain an overview of U.S. resources available to address problems associated with tropical diseases, the staff conducted surveys of U.S. institutions and individuals concerned with tropical diseases. Results of these surveys, conducted by staff members Karen Bell and Heather Miller, are presented in this report. Notes on survey methodology are available from the committee records maintained by the National Research Council. The history of U.S. international collaboration in dealing with tropical diseases was outlined in a commissioned paper prepared by Courtney Nelson, a consultant, and is included as the appendix.

The committee staff director, three members of the committee, and several other U.S. scientists met in Cairo, Egypt, April 24-26, 1985, with a dozen leading scientists from developing countries who are concerned with tropical diseases and who have participated in

collaborative research activities with institutions in the United States. The group discussed past collaborative research efforts between U.S. scientists and their counterparts from developing countries and made recommendations for future U.S. involvement in collaborative work on tropical diseases.

In addition to these special activities, the staff gathered and analyzed a great deal of information on the issues confronting the committee. A draft of the report was prepared and was the subject of the committee's final meeting, October 10-11, 1985, at which the committee formulated its recommendations. The final draft was prepared by the staff, circulated to committee members for review and comment, and approved by the full committee.

CONTENTS

CONCLUSIONS AND RECOMMENDATIONS

Tropical diseases continue to be major world health problems, causing millions of deaths among children and debilitating chronic illness among adults, especially in the poorest and least-developed countries. The United States has humanitarian, scientific, public health, and international security interests in reducing the incidence and impact of suffering from tropical diseases, but tropical diseases fall outside the mainstream of health concerns in the United States. Special skills and training in tropical health are essential for maintaining competence in this field.

In examining the several components of the national capacity to address tropical disease problems, the committee found U.S. fiscal, human, and institutional resources barely adequate, although the country could make a much stronger contribution if policies improve and funding is added.

This report is the result of a study by a committee of the Institute of Medicine and the Board on Science and Technology for International Development (BOSTID) appointed by the National Research Council to examine the capacity of the United States to deal with tropical infectious diseases. The committee posed the following basic questions: Is this country's biomedical research, clinical, and public health expertise in tropical infectious diseases sufficient to meet its needs and concerns at home and abroad? Are recruitment, training, career structures, and collaborative work adequate to maintain a reservoir of competence? and, Are they sufficient to strengthen health and biomedical research institutions in the developing countries? The committee's recommendations are presented herein and have been highlighted in the text.

The committee found the concerns that led to its study to be well warranted. Despite a wide array of U.S. interests and involvements, tropical health is outside the mainstream of U.S. health concerns, the maintenance of competence in tropical diseases tends to be taken for granted, and the state of the field is seldom assessed.

Reliable information on the prevalence, incidence, and distribution of infectious disease pathogens is not available in most developing countries. Special surveys, conducted for a single region, and prospective etiological studies have permitted inferences about the public health implications of specific disease problems. Routine surveillance of communicable diseases for disease control or planning purposes is rarely maintained; lack of trained epidemiologists and lack of diagnostic facilities are major problems.

The trends toward control of these diseases are unclear; the reports are mixed. Malaria is resisting the standard drugs and control measures in many areas of the world; cases are increasing, especially in Latin America and Africa. Filariasis, schistosomiasis, and leishmaniasis infections may also be increasing as irrigation and jungle-clearing activities bring more people into contact with disease vectors. Clinical symptoms resulting from these parasites often develop years after the initial exposures, producing disability or requiring costly hospitalization. Vaccine-preventable diseases are decreasing in many areas; the international donor-supported childhood immunization programs are reaching larger proportions of the population and monitoring of coverage is improving. Diarrheal infections still account for much of the serious illness among babies and small children, but oral rehydration programs have reduced the number of deaths from diarrhea.

More epidemiologic studies are needed to assess the extent of the disease burden and identify population groups at greatest risk of acquiring tropical infectious diseases. Disease-control programs can have an impact if given adequate national priority and funding.

The prospects for scientific progress are encouraging. New drugs show promise in dealing with schistosomiasis and onchocerciasis. The new biological techniques offer hope for new vaccines and diagnostic methods.

These advances could revolutionize approaches for disease surveillance, especially in inaccessible rural areas. Finger-prick quantities of blood, collected on filter paper, can now be easily stored and sent to a

central diagnostic facility, or in some cases processed for diagnosis in the field. Heat-stable vaccines, a research priority, could multiply protection from communicable diseases.

Scientific and technical competence in tropical disease research, medicine, and disease control are growing in the less-developed countries, although slowly. Developing-country researchers are acquiring formal training in the biomedical sciences at a fast rate, but opportunities and facilities for them to apply their skills are often lacking. Collaborative research programs with U.S. and other developed-country institutions are essential to a solid human resource and institutional base for tropical disease work.

The United States has not been working alone to control tropical diseases. Several of the Scandinavian and European countries have supported tropical disease research and control programs with relatively large proportions of their foreign assistance budgets, including initial critical support for the Special Programme for Research and Training in Tropical Diseases, based at the World Health Organization. The World Bank, the United Nations Children's Fund, and other international donor agencies have contributed financially to research and disease-control measures; many of their programs now consider infectious diseases as major impediments to human resource development. National leaders in the developing countries are increasing their support for health measures. Still, there are areas where half the children do not survive to school age and where infectious diseases produce chronic health impairments in adults, making economic and social progress and self-sufficiency goals yet more distant.

Among U.S. interests in reducing the incidence and impact of tropical diseases are the following:

- The health of this country's population, its travelers, diplomats, and armed forces, in a time of increasing international trade and travel;
- Scientific advancement likely to be realized in immunology, molecular biology, and other disciplines from the study of such tropical pathogens as trypanosomes and schistosomes;
- Humanitarian interest in reducing morbidity and mortality and in alleviating suffering;
- Increased international security that would result from economic and social progress;
- Ensuring against sudden, costly need to rebuild

U.S. international health capacity, a task requiring 5 to 10 years; and

- The fact that poor health inhibits development, and development of other countries is important to the United States for economic, social, and political reasons; the still-widening gap between the developed and the developing countries should not increase.

In meetings in the United States and overseas and through surveys, statistical analyses, interviews, staff investigation, examination of technical, administrative, and policy reports, and a commissioned review of experience with collaborative tropical health research endeavors, the committee sought a fresh census (the first in a quarter-century) of the field. Who and where are the researchers, clinicians, and public health and disease-control professionals? How are they trained? Are there enough of them? What do they do? What might contribute to their effectiveness in meeting long-term goals of advancing scientific knowledge, strengthening indigenous research capabilities, and reducing the infectious disease burden in developing countries? What, where, and how adequate is the institutional base?

The numbers were difficult to obtain. U.S. capacity to deal with tropical infectious disease problems of the developing countries is spread among private and public agencies, national and international, and is to be found in a variety of disciplines. It is the purview of no single institution or professional organization.

The number of persons who can be characterized as U.S. tropical disease professionals, with research, clinical, or public health skills, is low--less than 2,500. Comparable data from the past are unavailable. Most U.S. tropical disease professionals are in research, fewer in public health and disease control, far fewer in clinical work. On the whole, the population of U.S. tropical health professionals is not an aging one. However, the committee noted that broad-based knowledge and specialized training in clinical research on tropical diseases is increasingly lacking in the younger cohorts, who are more likely to have a narrow biomedical research specialty.

Generally, except for several important areas in the field, the population of professionals is being renewed, and its age distribution is the same as that of the broader U.S. scientific community. The number, however, is not expanding, nor does it represent career commitments.

Although the total may be relatively steady, individuals are entering and leaving the field at various ages and for a variety of reasons, including employment opportunity or its lack. The wealth of experience brought to this field by veterans of major campaigns against communicable diseases worldwide is irreplaceable. Opportunity for clinical and research apprenticeship with preceptors who have extensive experience is declining.

Recruitment lags in several research areas including vector taxonomy, mycology, and malacology, all important in tropical health studies. More than half this country's tropical health professionals are employed by universities and nearly a third by government (including the military). Few are in industry. Most U.S. research in tropical diseases is sponsored by the federal government; little is supported by industry. Several private foundations make a unique contribution, important not so much in relative dollar volume as in catalytic effect.

The committee identified eight U.S. universities that have substantial programs in tropical disease research, tropical medicine, and tropical health. In addition to these major centers, perhaps seven additional academic institutions have large commitments to tropical disease research and training. Federal agencies--especially the Centers for Disease Control, the National Institute of Allergy and Infectious Diseases, the U.S. Army, and the U.S. Navy--are engaged in tropical health research and in training of specialists for research or other work in tropical health. U.S. opportunities for clinical training in tropical diseases are not widely available. Direct experience obviously is more likely to be gained where these diseases are endemic. Collaborative activities that would foster such training, giving U.S. specialists and their colleagues the chance to learn from each other, are few.

The United States probably has fewer than 300 clinical specialists in diagnosis, treatment, and study of tropical infectious diseases, and the ability of U.S. diagnostic laboratories to recognize tropical diseases should be strengthened. The role of the laboratory is often very important in the diagnosis of any infectious disease. In the event of a rise in the prevalence of tropical diseases in the domestic population, the need for well-trained and knowledgable laboratory technicians and clinicians will increase.

The committee found it more difficult yet to judge the adequacy of these resources and programs against concrete

measures of need, disease trends, incidence, or prevalence. There is no benchmark against which to compare current programs and numbers of people. The conclusions here are unavoidably judgmental. Nevertheless, the committee is convinced that the United States could have a greater impact on the burden of infectious diseases, that doing so is in the national interest, and that neglect of the state of U.S. resources in tropical infectious diseases may be very costly.

The U.S. biomedical research base for dealing with tropical diseases is substantial but needs stronger collaborative research and training relationships with scientists and public health officials in the less-developed countries. The National Institute of Allergy and Infectious Diseases, for example, has consistently supported tropical disease research, and institute administrators have demonstrated creativity and flexibility in promoting previously neglected areas as well as scientific opportunities. However, the absence of a specific mandate to fund applied research primarily relevant to diseases of developing countries as well as budgetary considerations have limited the impact of the institute's programs. Support for research training lags support for research. Younger scientists find it difficult to broaden their skills and experience in tropical disease research.

Current U.S. career structures in much of this field are unstable, heavily dependent on otherwise unrelated federal financial and personnel policies. The number of U.S. tropical health professionals who are broadly trained in science, medicine, and public health and disease control and who have direct experience in dealing with these diseases in the less-developed countries need not be large. But this country must ensure that such people are available.

The importance of international collaboration to U.S. capacity to cope with tropical disease problems is very great. Only through collaborative relationships in research and training in biomedical science, clinical work, and public health and disease control will U.S. specialists develop the firsthand experience they need, to be able to contribute strongly to disease treatment and prevention. The right kind of collaboration can assist in building health institutions and self-sufficiency in the developing countries. It is an investment both in reducing the disease burden and its consequences and in building flexible, collegial, worldwide

networks of cooperation in detection, surveillance, treatment, and control of communicable diseases. Collaboration is essential to the most efficient and economical use of resources to maintain U.S. capacity in tropical health. It could also become the price that the United States must pay to be able to conduct research where tropical diseases are endemic.

The United States can and should contribute more to training and development of foreign competence, particularly in research and in disease monitoring. The infrastructure necessary to effective work against these diseases is too often lacking in the developing countries. Not only are diagnostic equipment, supplies, and pathology reference materials needed, diagnostic talent must be attracted and retained. Health science and technology require sustaining infrastructure.

In considering the U.S. capacity to deal with tropical diseases, the committee examined several specific components it believes are integral to sustained or accelerated progress:

- Support for basic and applied research;
- Development and testing of new preventive, therapeutic, and diagnostic technologies;
- Career structures for tropical disease professionals;
- Capacity to train U.S. tropical disease professionals and those from the less-developed countries' research and public health service;
- Development of disease surveillance capabilities;
- Strengthening institutional capabilities in developing countries; and
- Flexible, responsive administration of programs and activities to avoid unnecessary duplication, to maximize efficient use of resources, to minimize gaps and imbalances, and to meet needs of individual countries including the United States.

By these criteria, U.S. capacity is barely adequate, but with improvements in policies and modest additional funding could make a substantially stronger contribution. The committee's suggestions to that end are highlighted in underlined portions of the text that follows.

RESEARCH AND TRAINING

Tropical disease research, like many rapidly advancing fields in science, is international. The diseases and their impacts cross many national boundaries. Progress in research depends on communication, cooperation, and collaboration among scientists from many nations. Research institutions recruit scientists from around the world, and students seek placements in accordance with the concentration of talent in areas of their interest. The United States has maintained a favorable climate for basic research on tropical diseases, and it has attracted able scientists from other developed and developing countries.

In most of the world, national research budgets typically accord relatively low priority to tropical diseases. The United States supports more than half of the world's biomedical research, by some estimates, including work on infectious diseases.

U.S. capacity to conduct basic biomedical research on tropical diseases corresponds closely to availability of funds. Disciplines in the forefront of the biomedical sciences--molecular biology, biochemistry, and immunology--have attracted funding. Other specialties, traditionally associated with tropical medicine and public health, have lagged in research funding competitions. Fewer individuals are applying for ecological and field research positions; universities have not been hiring many vector biologists, taxonomists, or parasitologists.

The committee discerns disproportionate emphasis on laboratory research, in contrast to field research that takes advantage of improved epidemiological techniques and developments in social science methodology.

Clinical research is an area of concern. Training and career opportunities are scarce, and long lead times are required to produce clinical specialists with the requisite experience in the tropics. The committee therefore suggests that the Department of Health and Human Services establish a physicians' fellowship program in clinical research on tropical diseases for physicians trained in the United States. Such a program would be consistent with the department's domestic responsibilities for public health protection. Competitive awards should be made to three U.S. medical schools for developing collaborative programs with counterpart institutions overseas. U.S. residents, together with

young physician trainees from developing countries, would spend 1 or 2 years at the collaborating institution working under the supervision of at least one U.S. faculty member and local faculty colleagues in clinical care and research. Such programs would be best undertaken where other collaborative research and field programs are in place and should be undertaken with long-term commitment in mind, to build a foundation of trust and confidence.

Training is underemphasized. Basic and applied research and research training capacities in this country represent the strongest component of total U.S. efforts related to tropical diseases. However, research training and career development in several fields need to be strengthened significantly in order to maintain an appropriate balance between field and laboratory-based research.

Active intervention is warranted in order to maintain at least a minimum level of expertise in vector ecology and infectious disease epidemiology, which have fared poorly in the competitive grants process and have received relatively little federal support. Lack of adequate support for field investigations of tropical disease pathogens and their interactions with human hosts and vectors will impair the ability of U.S. scientists to work collaboratively with scientists from developing countries and will handicap the United States in a critically important area of defense against tropical diseases.

Several federal agencies have interests in maintaining national expertise. An efficient way to build expertise in vector ecology and infectious disease epidemiology would be the establishment of a jointly funded program, managed by one agency, of at least 10 career development fellowships in tropical vector ecology and 10 in tropical infectious disease epidemiology for junior faculty in U.S. universities. Such a program should provide incentives and support to academic institutions to create faculty positions for individuals whose scientific interest is the study of arthropod vectors and snail intermediate hosts in endemic settings or in developing better approaches for the collection of population-based data on infectious diseases.

A seemingly entirely new disease--acquired immune deficiency syndrome (AIDS)--adds considerable weight to arguments that it is imperative for the United States to maintain a cadre of individuals capable of carrying out

epidemiologic and clinical studies under conditions prevailing in tropical counties. This disease, while first described in the United States in the early 1980s, appears to have existed in Central Africa at least at that time (probably much earlier) and may have arisen by transfer of the etiologic agent (a virus) to man from a nonhuman reservoir. Cases have now been reported from over 100 countries and initiation of a major World Health Organization program attests to the current and future problem it poses. A large number of questions remain to be answered in the pursuit of control and treatment, many of which may be best addressed in tropical countries.

Restrictions of full-time employee equivalent position authorizations in research training fellowships unnecessarily limit training opportunities for U.S. scientists at the National Institutes of Health. These constraints affect U.S. scientists more than foreign nationals, who are afforded some protection under other programs. Limitations imposed by head counts are an inadequate substitute for budgeting and administration to ensure optimal mix and scope of research training in relation to funds, space, and supervision available. National Institute of Allergy and Infectious Diseases research training fellowships for investigators working on problems related to tropical diseases are much more likely to accomplish their purposes if not counted against the full-time authorization ceiling.

The social sciences represent disciplines and skills much needed and underused in tropical disease research and control. Investigators trained in health economics, medical sociology, medical anthropology, health, psychology, and health education have demonstrated their ability to participate in tropical disease research and intervention (i.e., clinical services, prevention, control, and eradication) programs and projects.

The potential range of sociomedical work is broad. Three areas especially need attention: (1) disease-transmission research, including descriptive study of human factors that influence transmission, and collection of data for modeling studies; (2) baseline and continuing studies of the consequences (economic and psychosocial) of disease and of continued transmission; and (3) intervention studies, including assembling of sociocultural, ecological, and other background data, research on potential for community involvement in control or other interventions, studies of planning, ethical issues, policymaking, operations, monitoring and project

evaluation, and research and planning for health education.

Operational studies of disease-control programs contribute to our knowledge about the administrative, economic, and cultural factors that contribute to successes and failures. In the committee's opinion, the Agency for International Development would find it useful to increase the involvement of U.S. social scientists in its research programs related to communicable disease control.

TRAINING CAPACITY

Eight U.S. multidisciplinary centers associated with schools of medicine and/or public health offer specialized training in tropical medicine and tropical public health. Four have concentrations of 30 or more tropical disease specialists. Only one has more than 50 full- or part-time faculty members in tropical health work. Large multidisciplinary centers of excellence are essential for training clinical and public health specialists in tropical disease problems and in contributing to technology development. Size and diversity do not appear to be as crucial for sound doctoral programs in the biomedical sciences.

In the committee's view, at least four centers--each with the participation of at least 60 faculty members from a broad range of health and social science disciplines--are needed to sustain a core of U.S. expertise and leadership to deal with tropical disease problems. This judgment assumes that federal career positions are unlikely to increase, that up to 50 percent of the faculty will be traveling or residing abroad at any one time, that mechanisms will be found to enlist academic personnel in the activities of government agencies, and that a larger number of smaller programs will continue to coexist and cooperate with the larger centers. Institutional support to academic groups of tropical disease investigators in the United States should be increased and clinical and public health as well as biomedical aspects of problems selected for study should be encouraged.

The National Institute of Allergy and Infectious Diseases already supports a program, called the Tropical Research Unit Program, that promotes faculty career development and research on tropical diseases. However,

it supported only three university groups in fiscal year 1985. Strengthening and expanding the range of interests at existing centers would be an appropriate place to begin. The committee recommends increasing both the size and number of National Institute for Allergy and Infectious Diseases Tropical Research Unit awards over the next 5 years. These awards facilitate postdoctoral training, tropical disease research, and collaboration abroad.

The Public Health Service and the Department of Defense maintain research and training establishments. With the exception of the Uniformed Services University of the Health Sciences, however, none is a center that provides clinical training, confers a public health degree, and offers biomedical research training. Most of the tropical disease research and training conducted directly by federal agencies does not duplicate that provided by academic institutions and cannot easily be conducted by academic institutions. Interests and activities of both are complementary and interdependent.

NEW TECHNOLOGY

The application of new approaches to the study of tropical diseases could produce an array of preventive and therapeutic agents as well as better tools for the study of disease transmission in populations. Promising new approaches in chemotherapy include use of anti-metabolic drugs, specific to a particular parasite's metabolic pathways; creation of large, hybrid molecules that reduce toxicity and enhance the efficacy of compounds developed as antiparasite drugs; and targeting drugs by attaching carrier antibodies that recognize and attach to a particular parasite. Vaccine development may increasingly employ synthetic antigens and adjuvants, or viral subunits and liposomes. Peptide sequences corresponding to the protein molecule covering the virus have been synthesized and have produced immune responses to hepatitis B in rabbits. Monoclonal antibodies will be used in a variety of diagnostic techniques that are highly specific to parasite strains and that can be used with squashed and dried mosquitoes as well as blots of blood on filter paper.

Monoclonal antibodies might also be used in reverse; instead of targeting the pathogen, anti-idiotype monoclonals might mimic the antigen and replace it for

vaccination purposes. Certain immunization procedures elicit specific antibody responses, some of which could be used to trigger a protective immune response before the parasite has altered its outer coat or changed to the next life stage.

Technology development has become an expensive, complex process, on a scale much larger than is usually found in academic institutions. Bioprocess engineers and multidisciplinary teams are a prerequisite for scaling up production of a new vaccine, drug, or diagnostic test. With appropriate support and incentives, the nation's emerging small biotechnology firms could operate more prominently within the field of tropical diseases. Links to academic centers might be especially desirable; most new firms lack knowledge specific to tropical pathogens. At the same time, the nature of new relationships between universities and industry is the subject of uneasiness. The obligations of each must be clear and acceptable to both sides.

Private companies in Europe and Japan and the overseas offices of multinational pharmaceutical corporations increasingly dominate in bringing new products through the developmental and clinical testing phases to a commercial marketing stage. The World Health Organization also has demonstrated potential for leadership in this area, especially for products that have no apparent commercial market.

U.S. capacity for new product development and testing is severely limited by forces and trends beyond the field of tropical diseases, by lack of obvious commercial incentives for many drugs and diagnostics, and by regulatory and logistical barriers. Officials of developing countries may be wary of authorizing clinical tests without obvious benefit to the participants. Possibilities for remedial action include more direct federal funding of developmental research, federal sharing of product development risk, and federal assistance in logistical arrangements for clinical and field testing. Development of a malaria vaccine will certainly require such intervention from the U.S. government. Some of these steps already have been taken.

An additional limiting factor in the role assumed by the United States in developing and testing new technologies is the lack of overseas clinical research and training opportunities for U.S. physicians. Clinical trials of new drugs and vaccines in developing countries require active participation and management from local

institutions and government authorities. Training in clinical research methodology is also essential; the Rockefeller Foundation's clinical epidemiology training program is building such expertise in several developing countries. When long-term collaborative relationships of trust and understanding have been established well before the development of a technology, plans for a clinical trial can be made rapidly and the trial carried out expeditiously.

Problems of development of diagnostics, drugs, and vaccines require sustained attention.

CAREER STRUCTURES

The committee found no stable career structure for tropical public health and disease control professionals in the federal government, with the possible exception of the military, which has its own personnel policy problems in this regard. Although the military is an important reservoir of tropical health talent, its personnel slots, too, are subject to classification changes, the raison d'etre of overseas laboratories is the subject of occasional controversy, and change in assignment may be a condition for higher rank. Nor, in times of financial trouble in the public sector, is there promise of reasonably stable careers in research and teaching.

Extraordinarily rewarding in an ethical sense, work in tropical health has undeniable drawbacks of frustration, health risks, loneliness, inadequate resources, limited job opportunity, and having to work apart from conventional reward structures.

Small already, the field is unusually vulnerable to adverse effects of federal financial and personnel policies stemming from government-wide budget considerations rather than from any specific consideration of tropical health or of U.S. weaknesses in the field. The result has been erosion of the possibilities of sustaining and expanding a cadre of sufficiently experienced federal tropical health professionals.

Personnel ceilings established for all federal agencies and limitations on the numbers of federal employees stationed abroad diminish opportunities for long-term research and training where tropical diseases are endemic. The current supply of federal employee professionals in tropical diseases is barely sufficient to sustain continuity in research programs, diagnostic

services, and short-term technical assistance missions overseas. Federal agency positions for personnel engaged in tropical disease research and control should not be reduced further; they should be expanded.

Academic institutions are structured to support research careers, and individuals whose talents are more in the administration of disease control programs, applied epidemiology, or clinical practice and teaching do not receive priority in hiring or promotions. Few academic institutions can support faculty members who spend several months each year working in the tropics and who wish to maintain their ties to the university during years abroad. Only those universities with the largest concentrations of faculty and diverse funding resources can afford to maintain career positions for a multidisciplinary group of tropical disease professionals.

The private consulting firm or research institute that employs tropical disease professionals may increasingly provide career opportunities, although not stability. The financial base for such organizations may be exceedingly narrow, and individuals are employed only when a government contract is won. Private firms are often established in close physical proximity to university centers to facilitate relationships with faculty members, and one effect may be to draw attention of faculty away from their primary commitments.

The career structures similarly are shaky for tropical disease professionals who have skills in public health and infectious disease control. Demand and supply do not always match, and program budget increases do not guarantee availability of required personnel or career positions. The nation's ability to mobilize trained personnel when needed, when it has not maintained an adequate permanent base of federal employees, is of obvious and crucial concern.

Several options might ease this situation somewhat. Each involves temporary assignments or exchanges of tropical disease professionals among federal and state agencies and academic institutions, but not necessarily at the cost of budget increases. Federal agencies with responsibilities for tropical health programs should seek ways to develop a national framework for career service in tropical disease work. Several mechanisms already exist for personnel exchanges, but they are not linked to tropical disease professionals.

The long-term objective of any career initiative should be to create a network of institutions both in the

United States and abroad that would host visiting tropical disease professionals with limited assignments from participating U.S., foreign, and international agencies. Such assignments would increase the usefulness of private, state, and academic scientists to federal programs and vice versa, while broadening their skills and contributing to competence in the agencies. Mechanisms to be explored or expanded include:

- o A competitive program using positions exempt from federal ceilings.
- o A fellowship program administered by a national scientific association.
- o Contractual service agreements with selected universities.
- o An improved mechanism for joint career assignments by universities and the Agency for International Development. There is a well-established program between land-grant colleges and the Agency for International Development in the agricultural sector.
- o Increased consideration, in service-project contracting, of the potential for building long-term academic and governmental capacity to address tropical disease problems.

DISEASE SURVEILLANCE

Disease control is linked inextricably to disease surveillance. Knowledge of disease incidence, prevalence, seasonal variations, transmission patterns, and distribution in populations is essential to the development of disease-control strategies, whether for a country, region, or continent. Reliable surveillance data for most tropical diseases are lacking, as are adequate epidemiologic surveillance methods and epidemiologists to test and use those methods. Reference laboratories for a wide range of bacterial, viral, and parasitic organisms are lacking; so are skilled diagnostic staff in many countries, which makes confirmation of suspected outbreaks of communicable diseases more difficult. Moreover, governments may be sensitive about dissemination of data on problems that might have been preventable.

The United States possesses the world's largest number of well-trained epidemiologists and could, were opportunities expanded, exercise global leadership in

training epidemiologists and assisting in the development of reliable surveillance systems for tropical diseases. The Global Epidemic Intelligence Service training program of the Centers for Disease Control has led to increased disease surveillance capability in several tropical countries and should be expanded.

The Department of Health and Human Services should establish a program to assist developing countries in improving the quality and increasing the number of overseas reference laboratories capable of diagnosing tropical disease pathogens. The program should include short-term training, provision of reagents and equipment on a limited basis, and quality control arrangements. Currently, the Centers for Disease Control assist developing countries when requested, but the Public Health Service does not have the budget to establish such a program on its own. Universities and private companies also have much relevant experience, but no mechanism exists to tap this expertise.

STRENGTHENING CAPABILITIES OF DEVELOPING COUNTRIES

Research capabilities in many developing countries have increased significantly over the past two decades. U.S. government and academic institutions have contributed substantially in terms of graduate and postdoctoral training, generating a wide network of professional and personal relationships that have continued long after the formal training. Many more U.S. scientists would like to maintain links with former trainees or visitors from abroad but lack the opportunity.

In developing countries, most institutions with responsibilities for tropical disease research and control suffer chronically from outdated or nonfunctioning equipment and lack of resources to carry out studies. Many of their investigators have received graduate training in the United States and Europe. Some are able to maintain collaborative relationships with U.S. academic institutions, but their ability to obtain funding for collaborative research is limited by the small numbers of donors interested in collaboration in applied and field research. The institution strengthening program of the International Special Programme for Research and Training in Tropical Diseases supports some centers in less-developed countries. They are few in

comparison to need, and the quality of much of the research could be greatly improved by strong collaborative relationships with institutions in industrialized countries.

Some developing countries have established considerable infrastructure for research on communicable diseases and can take better advantage of U.S. resources that are already available. An unusual and outstanding case is Thailand, which has a Centers for Disease Control epidemiology training unit in the Ministry of Health; links to the Rockefeller Foundation's Great Neglected Diseases and Clinical Epidemiology programs; support for research in universities, in the form of several grant awards from the Office of the Science Advisor of the Agency for International Development and the Research Grants program of BOSTID, National Research Council; and a U.S. Army unit (of the Armed Forces Research Institute of Medical Sciences) that does communicable disease research.

In countries like Thailand, local authorities are well trained and for the most part equipped to make their own decisions about control program needs. U.S. resources can make an important difference in certain areas, however, provided that there is flexibility in their use. For example, a national advisory board has been established for control of communicable diseases. This board represents an important step in consolidating progress toward developing an epidemiologic surveillance system, strengthening laboratory infrastructure, and improving local training programs.

Collaborative programs that combine research and training (not necessarily degree-granting) components are the most appropriate ways for the United States to assist in strengthening capabilities of developing countries to deal with tropical disease problems. This conclusion is based on several observations. Trained scientific and technical personnel in developing countries are more numerous than before, and many are now receiving graduate training in their own countries. U.S. institutions clearly benefit from collaborative relationships in terms of field research and training opportunities.

Institutions of the less-developed countries also benefit enormously from participation in collaborative research programs, provided that relationships have continuity and generate scientific opportunities for both sides. Formal U.S. academic degree programs are not always appropriate to needs and conditions in developing

countries. Substantial resources are not likely to be available in the future from U.S. donor agencies for support of research in less-developed countries without a collaborative component that involves U.S. scientists.

In a commissioned review for this committee, Courtney Nelson recounted U.S. experiences in tropical disease research in a variety of circumstances and arrangements (see Appendix). Nelson considered the scope of each program along the spectrum of basic, applied, and developmental research needed for disease control, the extent of collaboration between U.S. and host-country scientists, the impact of the program in reducing disease burden, and the effects on institutional capacities of the developing countries. Of the programs considered, only two--International Collaboration in Infectious Disease Research, funded by the National Institutes of Health, and Great Neglected Diseases, funded by the Rockefeller Foundation--were designed from the outset to promote collaboration between institutions of the industrialized countries and the less-developed countries. Even these programs are limited in funds, problems addressed, and purposes of research.

This committee held a workshop in Cairo, Egypt, immediately following the 1985 Congress on Infectious Diseases, to discuss these issues with scientists from developing countries. Workshop participants endorsed problem-oriented collaborative research on tropical diseases both as a development tool and as an effort that will yield scientific and practical benefits to the U.S. public. The workshop noted that collaboration serves numerous U.S. interests, including opportunities for basic ecological and clinical studies and for testing new vaccines and pharmaceutical products for tropical diseases. They did not view U.S. involvement as only technical assistance or expert advisory services; effective collaboration was seen as a long-term partnership.

Participants observed that collaborative relationships with U.S. scientists function best when relative parity exists between the partners, even though each contributes different but complementary assets, with mutual appreciation of good science. Critical factors in this respect include three basic components--time available to devote to research, scientific equipment and reagents, and access to the scientific literature. U.S. collaborative programs should assist their partners in the developing countries to build this kind of capability.

Information on U.S. tropical health programs and their purposes is not easy to obtain in the United States, and the problem is compounded by distance and lack of access to adequate reference sources. Moreover, as workshop participants noted, the administrative styles and managerial requirements of various agencies differ markedly. These are issues to which public and private donor agencies and science attaches might usefully give attention. Improvements in the confusing situation that prevails currently could be achieved at modest cost by adding staff and communications and data-base facilities to an existing program.

All U.S. donor agencies should consider ways to restructure current tropical disease research and control programs to include or improve the three basic components--collaboration, research training, and institutional support. Agencies could restructure existing programs by using interagency agreements to cofund and/or cosponsor, with personnel sharing, additional activities that would mutually benefit the sponsors.

The National Institutes of Health program of International Collaboration in Infectious Disease Research should be expanded to a constant level of at least 10 Part A (Program Project) and 10 Part B (Scientist to Scientist) awards, with appropriate funding levels. The program should be changed to include provisions for making additional funds available to developing-country institutions for research and formal research training of their own scientists in tropical diseases within the general objectives of each award. This modification would contribute toward the strengthening of host institutions in developing countries and thereby more effectively promote the program's initial goals.

COORDINATION

An initial impetus for this study was the need on the part of the three federal agency sponsors to characterize the extent of the national effort directed toward tropical disease problems and to compare relevant functions of various agencies and private organizations. Issues of coordination of efforts and the extent of targeting toward specific objectives are inherent in this kind of review. The fact, rather than the form, of coordination is what is important. Federal agencies interpret their

legislative mandates and structure their programs independently, and effective coordination to ensure that the United States is doing what it needs to do is a function of care and concern. Highly structured coordination machinery, whether with or without arrangements for lead agencies, sometimes works and sometimes does not.

Not surprisingly, this committee could not identify any single locus of responsibility for monitoring the activities and directions of national tropical disease research and technology development, for integrating knowledge with disease control programs, or for tracking progress in reducing rates of infection in developing countries. However, the committee observed numerous instances of meetings to assess research needs and opportunities or to review agency priorities for a single disease or group of diseases. Coordination of the nation's research programs and activities related to tropical diseases is decentralized, and much of it is informal. People who care about these subjects seek to stay in touch with one another.

Information exchange about tropical disease activities among U.S. private organizations, academic institutions, and federal agencies is uneven. Ad hoc personal communication and individual research generally bridge the gaps about specific country programs and activities or new federal agency initiatives. Newsletters, such as the National Council for International Health's International Health News, also contribute by reporting federal initiatives and funding opportunities. A U.S. data base for tropical disease programs and country activity information would be helpful for tropical disease specialists as well as program administrators if its coverage is wide rather than limited to programs of only a few agencies. The Agency for International Development, in cooperation with the U.S. Department of Health and Human Services and the Department of Defense, should consider establishing a new data base for tropical disease research and control activities.

Where there is overlap or complementarity of program objectives, the agencies may negotiate agreements for exchanging or borrowing personnel and transferring funds. For example, in fiscal years 1984 and 1985, the Public Health Service maintained about 20 separate agreements relating to communicable disease research and control in developing countries. These arrangements include $47 million in program funds for the Combatting

Communicable Childhood Diseases program in sub-Saharan Africa and $3.2 million for an accelerated vaccine-development program managed by a project officer at the National Institutes of Health's Fogarty International Center. The Agency for International Development has also just arranged to channel about $3.5 million through the National Institute of Allergy and Infectious Diseases to establish a university-based facility to conduct clinical trials of malaria vaccine.

Informal personal networks of communication and cooperation in federal agencies, extending into academia and industry, have been extensive and have contributed substantially to the history of this field. For the most part such networks have been built upon shared experiences; for example, service in World War II, research work at major laboratories, or participation in the global campaign to eradicate smallpox.

Internationally, of course, the World Health Organization and the Special Programme for Research and Training in Tropical Diseases contribute to research coordination, information dissemination, and technology development, consistently so for the six priority diseases of the special program.

Establishing an international research and development system for tropical diseases is a worthy long-term goal for maximum impact in reducing the disease burden. However, such a system is not feasible in the short term. The multidisciplinary institutional anchoring posts are, for the most part, still lacking. Few institutions in developing countries possess sufficient multidisciplinary talent and resources to support productive collaboration along a broad spectrum of activities that range from research and technology development to disease surveillance and control. So it is unlikely that such a system will be available soon as an international coordination mechanism.

In reviewing the major programs and activities currently sponsored by private organizations and government agencies, this committee found little or no evidence of wasteful duplication of efforts as a consequence of different federal agency mandates. However, the committee did find evidence of missed scientific, humanitarian, and foreign policy opportunities. U.S. drug development for parasitic diseases has lagged, research collaboration and training opportunities have not been emphasized, and communicable disease surveillance and

control capabilities in the less-developed countries have not received systematic attention from U.S. donor organizations.

U.S. academic and military resources have been underutilized in some respects. Domestically, there is much more interest and potentially much more capacity within U.S. universities to support collaborative research and training activities with institutions of the developing countries. Yet few universities have been able to build up the critical mass of tropical disease specialists needed to sustain multidisciplinary programs. Overseas, the military laboratories are often restricted by security or local political considerations from a more useful role in local tropical disease control.

POLICY AND PLANNING

The U.S. government does not have a strategic policy and program planning capability for tropical diseases. Responsibilities and resources to address tropical disease problems are split, for the most part, among the Public Health Service, the Agency for International Development, and the Department of Defense. Federal agency programs expand and contract within the constraints of agency mandates and budgetary pressures; no central government office monitors national goals, priorities, or activities related to tropical disease research and control within the United States and with developing countries.

The committee notes that absence of a central review office has not impeded agencies from taking important initiatives. Some, like the International Collaboration for Infectious Disease Research program, have been established with a long-term perspective, but lack the explicit mandate and funds to meet the full range of collaborative research needs. Others, like the competitive research grants programs supported by the Agency for International Development's Office of Science and Technology, strengthen research capabilities in developing countries but do not support formal research training of U.S. or developing-country scientists. These two programs, as illustrative examples, may complement each other to some extent within a specific developing country, yet neither covers the entire spectrum of potential U.S. involvement in tropical disease problems.

Over the past decade, various government offices have assumed lead roles in international health policy formulation, each emphasizing tropical disease research and control to some extent. The Executive Office of the President, in 1977, began an ambitious review of all federal agency involvements in international health.

The United States has not regularly reviewed its tropical health efforts in light of national interests. Arrangements are needed for regular review of U.S. and international tropical health programs in order to assess progress, to recognize innovations, to respond to resource and program gaps, and to foster economy and efficiency in these programs.

Within the United States, the Office of Science and Technology Policy and the Office of Management and Budget have broad responsibilities for review and analysis of both single agency and multiagency programs. The mission agencies as well have been charged by Congress with coordinating their efforts to guard against gaps, imbalances, and unnecessary duplications of effort. The Office of Science and Technology Policy, in cooperation with the Office of Management and Budget, would find it useful to consult periodically with representatives of all federal agencies concerned with tropical health, and to meet with nongovernmental advisers also, to ensure that U.S. efforts in this field meet national needs. It would also be desirable to assess and review the international and other bilateral programs for tropical disease research and control to identify specific opportunities for U.S. contributions that could expand or strengthen existing efforts.

U.S. government and private resources dedicated to tropical health are sufficient to sustain a substantial biomedical research base in this field and to respond to occasional public health threats from tropical pathogens in the United States. They are insufficient to ensure U.S. ability to cope with more than occasional domestic cases of these diseases. U.S. capacity and coordination of U.S. efforts in this field depend heavily on the specialized knowledge, experience, and dedication of veteran tropical health professionals. That expertise is not being adequately renewed. Nor is this country adequately serving its tropical health interests abroad. Accordingly, the United States is limiting its leadership role in the control of tropical infectious diseases at a time when scientific opportunities and humanitarian and economic concerns are very large.