FOGARTY AT 35

IN THE LAST 10 YEARS FOGARTY-TRAINED PERSONNEL HAVE TRAINED OVER 6,000 HEALTH WORKERS THROUGHOUT HAITI, ENABLING US TO APPLY SUCCESSFULLY TO THE GLOBAL FUND FOR AIDS, TB AND MALARIA AND TO EXPAND INTERVENTIONS, INCLUDING ANTIRETROVIRAL TREATMENT, TO 25 CENTERS. THE FOGARTY PROJECT WE HAVE WITH THE HAITIAN RED CROSS TO TRAIN LABORATORY PERSONNEL HAS MADE THE BLOOD TRANSFUSION SYSTEM SAFE. OUR NEW FOGARTY PROJECT WILL ALLOW US TO INTRODUCE YOUNG HAITIANS TO PUBLIC HEALTH ISSUES AND RESEARCH TO RESOLVE THEM AT AN EARLY STAGE IN THEIR CAREERS AND HELP US RETAIN THE BRIGHTEST STARS WHERE THEY ARE MOST NEEDED—HERE IN HAITI. THERE IS NO WAY WE COULD HAVE DONE IT WITHOUT YOU.

Jean Pape, Director
GHESKIO Center
Port-au-Prince, Haiti

The John E. Fogarty International Center for Advanced Study in the Health Sciences gratefully acknowledges the support of the Foundation for the National Institutes of Health in publishing this 35th anniversary history.

Joan Wilentz, Editor

"AT BETHESDA A GREAT INTERNATIONAL CENTER FOR RESEARCH IN BIOLOGY AND MEDICINE DEDICATED TO INTERNATIONAL COOPERATION IN THE INTERESTS OF THE HEALTH OF MANKIND"

FOGARTY AT 35

NO COUNTRY IS AN ISLAND

The paraphrase of John Donne's memorable line serves to highlight why international health is so important today and *why countries need to act*. It is not just a question of the demographic facts of life—that there are so many more people alive today and on the move, raising the risk of the global spread of disease. Nor is it only that worldwide environmental degradation is polluting the air we breathe, the water we drink, and depleting the earth's natural resources. It is that societies worldwide—especially in the developing world—are experiencing extremes of economic, social, and political upheaval that are shattering whatever infrastructure existed to protect health and well-being and further widening the gap between rich and poor. It is no exaggeration to say that the world faces the specter of social unrest, religious strife, and the familiar four horsemen of war, pestilence—perhaps in the form of bioterrorism as well as nature's calamities—famine and death. All countries have an obligation to do what they can to prevent catastrophe and work to ameliorate global health problems—for their own and the world's good. The challenges are formidable:

- The earth's population is expanding at the rate of nearly 1 billion a decade with almost all this growth occurring in developing countries in Africa, Asia, and Latin America. People are also migrating from rural to expanded mega-urban areas, and emigrating from developing to developed nations at unprecedented rates, generally exchanging one form of poverty for another.
- People in low- and middle-income countries—representing three-fourths of the world's population—suffer over 90 percent of the burden of premature mortality as measured by lost years of life.
- Tuberculosis is responsible for 2 million deaths a year and accounts for one fourth of all preventable deaths in the developing world.
- Pneumococcal pneumonia causes nearly as many deaths as TB, with a higher disease burden.
- Malaria kills close to 3 million people every year, primarily children five and under in Africa.
- Childhood infections, poor reproductive health, and malnutrition account for over a third of the global burden of disease, a figure based on disability adjusted life years (DALYs), a metric developed by the World Health Organization that calculates the economic, social, and human impact of premature death and lifelong disability.
- In 1990 non-communicable diseases accounted for just over 40 percent of the global burden of disease. By the year 2020 their share is expected to reach 60 percent, eclipsing infectious diseases as major causes of lost years of healthy life—if, as hoped, the infectious diseases come under better control.
- Diabetes is approaching epidemic proportions in many populations and the global figure of affected individuals is expected to double from 150 million to 300 million by 2025, accelerating with the current trends towards overweight and obesity, even in developing countries.
- Hypertension and vascular diseases are rapidly increasing problems in many African, Asian, and Caribbean countries.
- Loss of biodiversity due to deforestation has introduced new infectious diseases into human populations and a loss of sources of natural products to treat or prevent them.
- Monoculture farming requiring heavy uses of nitrogenous fertilizers releases nitrous oxide into the atmosphere, contributing to the depletion of the ozone layer which protects against the potential cancer-inducing effects of ultraviolet B radiation and contributes to global warming and marked ecological changes with implications for burdens and range of vector-borne diseases.

These, and other global disease burdens, sometimes appear to be overwhelming, but to succumb to the wailing voices would be to ignore the greatest resource in the world: the power of people and the ability of science to show the way. These two principles guide the work of today's Fogarty International Center in investing in the training of people in low- and middle-income nations who, through research, will find the solutions needed. Margaret Mead, the anthropologist and one-time Fogarty Scholar in Residence, knew that partnerships between and among nations were essential to improving human civilization. As she put it, "Never doubt that a small group of thoughtful citizens can change the world. Indeed, it's the only thing that ever has." Translating this to today, and to the impact that modern science carried out by modern scientists can have, it is possible to observe that whereas each of us, working alone, can make a difference, all of us, working together, can make an enormous difference.

Gerald Keusch

"AT BETHESDA A GREAT INTERNATIONAL CENTER FOR RESEARCH IN BIOLOGY AND MEDICINE DEDICATED TO INTERNATIONAL COOPERATION IN THE INTERESTS OF THE HEALTH OF MANKIND"

These words expressed Rhode Island Congressman John Edward Fogarty's vision 40 years ago. Five years later that vision would become reality, for on July 1, 1968 President Lyndon Johnson issued an Executive Order establishing the John E. Fogarty International Center for Advanced Study in the Health Sciences at the National Institutes of Health. In the 35 years since—the span of a single generation—support for international biomedical and behavioral research and research training by the Fogarty International Center has grown from modest roots laid down at the outset—FIC's first year budget totaled $500,000—to a globe-encircling $64 million research, training, and capacity-building enterprise extending to over 100 countries and involving some 5,000 scientists in the U.S. and abroad.

John Fogarty was a lifelong advocate of international biomedical research, "as disease knows no national boundaries," and "because we care." Starting with his freshman term in Congress in 1941—on the eve of America's entry into World War II—throughout the 16 years he served as Chairman of the House Health Appropriations Subcommittee—the Irish bricklayer who rose from the ranks was eloquent in arguing the health and economic benefits of supporting biomedical research. As Subcommittee Chairman, he presided over the early days of growth of the National Institutes of Health, sharing his great expectations with the equally visionary NIH Director, James Shannon. But it was not until a week after Fogarty's death on January 10, 1967 that his dream of a "global laboratory" began to materialize. On January 18, 1967, Appropriations Subcommittee Member Melvin Laird (R. WI) addressed Congress stating that the Committee "has provided funds to plan a lasting memorial to a man who, for more than a quarter of a century, worked tirelessly for a healthy America, in a healthier world."

"AS DISEASE KNOWS NO NATIONAL BOUNDARIES"

Major Fogarty International Center research and training sites around the world and at U.S. collaborating institutions.

IN THE BEGINNING

To be sure, there was an early precedent for government support of international research. NIH historians are quick to point out that the leading Federal health research agency began as the Laboratory of Hygiene on Staten Island, New York, in 1887. At the time, countries throughout the world were plagued by epidemic diseases—tuberculosis, cholera, yellow fever, diphtheria—which pioneers like Louis Pasteur and Robert Koch were associating with newly discovered infectious agents: "germs." Joseph Kinyoun, the first NIH Director, went abroad to Berlin and Paris to learn bacteriology from Koch and Pasteur and returned with the latest model Zeiss microscope to study *Vibrio cholerae*, the bacterial species Koch had identified and that was the cause of devastating outbreaks of cholera in New York and other major American cities throughout the 19th century. The application of science to diagnosis, treatment, and prevention through vaccines has had a remarkable effect on reducing the incidence of these diseases in the U.S.

Plus ça change...Today, the world again faces the devastation of epidemic infectious disease that "knows no national boundaries." Some diseases, like AIDS, Ebola, and SARS are new threats; others, like malaria and influenza, have been known for millennia. Equally familiar are the respiratory infections and diarrheal diseases of childhood—no more than a nuisance burden in the U.S.—but responsible for the deaths of millions of children in low-income countries. Still others—smallpox, anthrax—have alerted the world to the threat of the bioterrorist release of disease-causing organisms long thought to be eradicated or under control. Indeed, for a time, as medical science distinguished viruses, bacteria, and parasites among "germs" and developed countermeasures in the form of vaccines and effective drugs, it seemed possible that infectious diseases might be vanquished. Such hopes were dashed, however, as it became clear that microorganisms had countermeasures of their own. Not only could they exchange genes and acquire virulence factors and antibiotic resistance, but they also could mutate into forms enabling them to elude detection by the immune system.

Malaria, known for millennia, is once again on the increase.

Aiding the spread of disease worldwide are advances and technologies that have reduced the world map to terrain easily traversed by jet plane in a day, seen world population grow by 58 percent from 3.6 billion in 1968 to 5.7 billion today, and witnessed the increasing movements of people, particularly from rural areas to urban centers, and from developing to developed countries. For many, the motivation is to escape poverty or political turmoil. All too often, however, life in a new city or country is no better or even worse than before, further accentuating the gulf between rich and poor; further widening global and local disparities in health and health care.

THE MISSION OF FIC TODAY IS TO IDENTIFY THESE GLOBAL CHANGES, ANTICIPATE THEIR EFFECTS ON HEALTH AND WELL-BEING, AND MOBILIZE SCIENTIFIC RESOURCES TO REDUCE DISPARITIES IN GLOBAL HEALTH.

RESEARCH CAPACITY-BUILDING IN THE DEVELOPING WORLD

The Fogarty Center's program to stem the tide of AIDS is a prime example of how it addresses this mission. In 1988, under the leadership of its then newly appointed Director, Philip Schambra, the Center developed the AIDS International Training and Research Program, AITRP ("A-trip") aimed at building research capacity in the developing world. The program, with co-sponsorship by other NIH components, began as a competitive five-year institutional training grant to a small number of U.S. universities, allowing post-doctoral students from developing countries to come to America for AIDS research training, and return home to practice their new-found skills. Congress was so enthusiastic about the potential of empowering health personnel to fight AIDS in parts of the world where the need was greatest that it increased the first year budget for AITRP to $4.5 million, more than five times the original request.

Now in its 15th year, AITRP exemplifies a program that is long-term and flexible by design. U.S. institutions and their foreign partners are committed to enduring collaborations based on mutual respect and a readiness to adapt to changing needs and priorities. The partners are well aware, for example, that the priorities for AIDS interventions in resource-poor countries call for approaches that are realistic, practical, and affordable. Many grantees are about to enter their 4th round of the five-year grant cycle periods and many more have joined in the program for a total of 23 institutions around the country. The programs also allow for additional periods of short- and long-term training, either in the U.S. or the home country, as the need for new skills arises or new technologies emerge. Foreign nationals trained in the programs are further encouraged to develop research collaborations with partners in other developing

countries. In Africa these so-called "South-South" collaborations are now contributing to training on-site for greater numbers of beneficiaries. AITRP program managers have also seized the opportunity of extending programs to China and India as these countries began to experience the second great wave of HIV infection and AIDS, and now to Russia and the former Soviet States.

Early on, FIC saw the importance of funding "re-entry" research support so that trainees could learn research by being responsible, scientifically and fiscally, for *doing* research in their home country. Starting with the second five-year funding cycle, AITRP included funds for small pilot research projects proposed by trainees. Not only has this feature strengthened in-country research resources, it has also provided key personnel who are able to respond to a growing number of AIDS international research initiatives proposed by other NIH components as well as by outside groups, such as the Bill and Melinda Gates Foundation, the Elizabeth Glaser Pediatric Aids Foundation and the International AIDS Vaccine Initiative. In this arena of building local human research resources, FIC has had greater impact than probably all other capacity-building programs combined.

In 1998 AITRP expanded to include research and research training on tuberculosis as well as AIDS. Not only has tuberculosis remained a serious threat, with close to two million deaths a year worldwide, but HIV-infected patients are at high risk of developing the disease, which has become increasingly drug-resistant. The programs are currently emphasizing, along with the epidemiologic studies that were the focus of the earliest training programs, studies to integrate prevention with clinical research on diagnosis, care, and treatment, including the use of antiretroviral drugs, in the next major phase. Early fears that bringing foreign nationals to America might result in a brain drain have not materialized. "Not a brain drain, but a brain train," as FIC's current Director, Dr. Gerald Keusch, declared, as the records document that more than 85 percent of AITRP trainees return home to work in controlling and reducing the burden of HIV/AIDS. Indeed, the first graduates of AITRPs are among world leaders in the fight against AIDS, assuming senior roles in health administration and policy in such countries as Uganda, Malawi, Senegal, Kenya, South Africa, Thailand, and Brazil, or becoming directors of individual programs and institutions. Trainees are also well represented in the peer-reviewed scientific literature and as authors and presenters at international AIDS and TB conferences. Today, with over 2,000 research trainees from over 100 countries having received training in the U.S., AITRP stands as the world's leading program to develop the health and research workforce needed to combat global AIDS. (continued on page 16)

THE LAWTON CHILES INTERNATIONAL HOUSE

Visitors to the National Institutes of Health in Bethesda, Maryland are impressed at the expanse of its more than 50 buildings spread out over 322 acres with lawns, greenery, and a running brook – much like a university campus. Situated on a hill near the center of the campus, for all the world like a Dean's or University President's residence, lies a former privately owned mansion that is now a part of the Fogarty International Center and used for prestigious international receptions, seminars, and conferences, as well as housing two Divisions of the Center and a major global project. Still colloquially referred to as "Stone House" by NIH staff, after the native Maryland bluestone used in its construction, the mansion was officially named the Lawton Chiles International House by an Act of Congress in November 1989, to honor the internationally minded Florida Senator who served from 1971 to 1989.

The house and adjacent acreage were originally part of a 200-acre property that had been acquired in a land grant to Robert Peter, a Scot arriving in America around 1745, and had remained in the Peter family for the next two centuries. Robert Peter's descendants included a physician grandson, Armistead Peter, who headed a smallpox hospital in the Civil War. When he died in 1902, the family property was divided among his five children. Son Walter G. Peter was a prominent Washington architect and it was he who designed the mansion that another son, George Freeland Peter, a canon of Washington Cathedral, built on his 47.9 acre share of the inheritance in 1930. The Peter family remained in residence until 1949, when the Federal government acquired the estate and the 47.9 acres as grounds for a growing NIH—which had already gained 92 acres in the late 30s and early 40s as a gift of Helen Woodward Wilson and Luke I. Wilson for the original buildings of the NIH.

Senator Lawton Chiles and his daughter attended the official naming ceremonies.

The 3-story Chiles house is characteristic of Colonial Revival architecture set against formal landscaping that includes a rose garden and holly hedges. Corinthian columns flank the main entrance which opens into a foyer which features an exquisite elliptically

shaped freestanding staircase leading to the second floor. The first floor, used for international receptions and scientific events, includes a library, drawing room, dining room, and kitchen. The former living room at the south end now serves as a meeting room and extends the length of the south wing, opening onto a veranda and formal garden.

MARGARET MEAD SLEPT HERE

The seven bedrooms originally on the second floor were used by Scholars in Residence from 1970 to 1977, including Margaret Mead, who did sleep in Stone House, as well as other notables, such as Oxford's Regius Professor of Medicine, Sir George Pickering, and the Nobel laureate Daniel Bovet. But as the program evolved, and the house no longer met the code for a residence, the Scholars were incorporated into the sponsoring NIH Institutes, even for their offices, and were housed elsewhere as well. The bedrooms on both the second and third floors were converted to offices which are now occupied by two Divisions of the Fogarty Center and staff for a major multilateral initiative: the Disease Control Priorities Project. Near the main house is a smaller building—the "Cottage"—which housed the Peter family staff. It, too, was converted to offices for FIC staff and is currently used for the International Services Branch, formerly a part of FIC and currently within the Office of Research Services, handling visas and immigration issues for visiting scientists at the NIH.

JOHN FOGARTY: THE LIFE

John E. Fogarty was born on March 23, 1913 in Providence, Rhode Island to a second generation Irish immigrant family. The family moved to a small farm in rural Gloucester, R.I. when he was seven and where his mother died when he was twelve. Fogarty's formal education was limited and during the Depression he made his living as a master bricklayer, following in the footsteps of his father and his older brother, who were both master bricklayers.

A taste for politics was also in the family tradition. Fogarty's father had been active in ward politics in Providence and in 1936 Fogarty was elected President of Local Bricklayers Union No. 1. Three years later he defeated five prominent Democrats for the congressional nomination and went on to victory in the general election. The year was 1939 and Fogarty was 26 years old.

He was appointed to the Naval Affairs Committee in 1940, remaining on the committee throughout World War II. Fogarty briefly joined the Navy Seabees in 1944 to investigate conditions of servicemen in the South Pacific. After the war, he was appointed to the House Appropriations Subcommittee for Labor, Health, Education and Welfare, and related agencies, succeeding Frank Keefe (D. WI), whom he credited as his most important mentor. He was appointed Chairman of the Subcommittee two years later—the youngest Labor HEW chair in history.

During his 27-year career in the House, Fogarty was an outspoken advocate for NIH and the value of medical research. He urged funding for the disabled and those with mental and physical impairments, for libraries, and for research to address

global health problems—a message he brought on five separate occasions to the Ministers of Health of every nation, convened at the annual World Health Assembly of the World Health Organization.

Over his years as Subcommittee chair, appropriations for NIH increased a thousand-fold, with the bulk of the funds distributed to the nation's researchers in academic institutions, health professional schools, and hospitals. The advances in health they and successive investigators achieved would continue as NIH grew over the decades, with worldwide benefits on health and well-being.

John Fogarty died at his desk of a heart attack on January 10, 1967, the day before the opening of Congress. He had characteristically come in early to do some last-minute preparations for the opening session.

Fogarty was a modest man who preferred to say little about himself or his motivations. Shortly after his death, his family found a prayer in his wallet written by Martin de Porres, a 16th century priest who ministered to the sick and homeless in Lima, Peru and who became the Americas' first black saint. This may be the best hint of what ultimately moved Fogarty to action.

At the time of his death, Fogarty had become one of the most powerful and effective congressional leaders of the 20th century. He received more honors and awards, honorary doctoral degrees and acclamation from professional groups than any other member of Congress in history.

Shocked by the loss of their colleague and champion of public health legislation, Congress moved quickly to authorize funding for an international center at NIH to bear his name. Fogarty had repeatedly but unsuccessfully proposed the creation of an Institute of International Health Research to promote the study of global health problems. His untimely death would prove to be the catalyst that finally brought the Center—The John E. Fogarty International Center for Advanced Study in the Health Sciences—into existence.

James P. Crowley, MFD. FACP,
Professor of Medicine, Brown University
(with thanks to Matthew Smith,
Curator of the Fogarty papers at
Providence College and Susan Diggins and
Susan Dunn for their assistance)

1958	1968	1969	1975	1978	1981	1984
	Milo Leavitt			Leon Jacobs	Claude Lenfant	Craig Wallace
IRF		IRF, SIR	IRF, SIR, SIF			

AND HIS VISION

John Fogarty's years in Congress as the representative from Rhode Island's 2nd district were remarkable for his repeated urgings of the nation to support international health research. At the time, America was emerging from World War II and the NIH itself was a modest organization with a 1949 budget of $37 million. Today, the world can all too readily acknowledge the truth of Fogarty's oft-quoted argument for global research, "because disease knows no national boundaries." But that was only one of several arguments that distinguish Fogarty as a man ahead of his times.

His appeals began with his appointment in 1947 to the Subcommittee for Appropriations for Labor, Health, Education, and Welfare, which was responsible for the NIH budget. When he was named chairman of the Subcommittee two years later, he would use that powerful position for the rest of his life to build NIH and to press for establishing an Institute at NIH dedicated to the support and conduct of international research and research training—stipulating as early as 1958 that it should have an annual budget of $50 million.

Fifty years before phrases like "global village" became commonplace, Fogarty recognized that the nations of the earth constitute one world and one family of man whose members are morally bound by ties of mutual respect and caring. At the same time Fogarty, the politically astute legislator, was well aware of competing interests for federal funds, so he marshaled support for his vision by underscoring the political and economic benefits to be gained. He argued that a medical research-driven reduction in the burden of chronic disease would enlarge the labor force of active, productive American citizens who would contribute to a growth in GNP and tax revenues.

1988	1989	1992	1993	1994	1995	1996
Philip Schambra						
AITRP		FIRCA, MIRT	Biodiversity		Environmental and Occupational Health, Population and Health	Emerging Infectious Diseases

Senator Lister Hill left, and Rep. John Fogarty right, flank President John F. Kennedy at the signing of the International Health Research Act.

"I submit that investment in medical research, aside from the unending humanitarian benefits, is an economical investment in life. ...Research is the only means we have for reducing the growing federal burden of medical care costs."

Fogarty also used arguments that spoke to a nation preoccupied with the Cold War—and the fear that the war might heat up—even that weapons of mass destruction might be used. Decades before bioterrorism became a household word, Fogarty was arguing that medical research could yield protection against bacteriological and radiological warfare. Biomedical research could also improve the health of the nation's youth, thus enhancing military preparedness. (Fogarty was well aware of the number of World War II recruits who had to be rejected for health reasons.) In the event of war, medical advances could also lead to better care and treatment of casualties. Alternatively, he reasoned that by extending the benefits of biomed-

1997	1998	1999	2000	2001	2002	2003
	Gerald Keusch					
MIM (malaria), Human Frontier Science Program	Medical Informatics	Maternal and Child Health, IRSDA, IMTRP	Ecology of Infectious Diseases, Bioethics, Health and Economic Development, Tobacco, Genetics	GRIP, ICOHRTA, ICOHRTA(AIDS/TB) Global Infectious Disease, ICER	DCPP, Brain Disorders, Health/Env/Eco Development, Stigma	

ical research to improve the health of people in developing nations, they and their governments might be persuaded to lean toward democracy and the West, rather than communism and the East.

More often, however, Fogarty's essential humanity and zeal to reduce the level of universal human suffering led him to emphasize the positive values of supporting international health research, rather than its use as an instrument of Cold War diplomacy.

"Time and again it has been demonstrated that the goal of better health has the capacity to demolish geographic and political boundaries and to enter the hearts and minds of men, women and children in the four corners of the earth....For pestilence and prolonged disability and premature death, wherever they may occur, are tragedies which strike a responsive chord in man and his governments."

"IN THE WAKE OF TECHNOLOGICAL ADVANCES, THE WORLD HAS SHRIVELED IN SIZE. THE MOST DISTANT PLACES ARE ONLY HOURS APART. WHEN A CHILD IN CALCUTTA FALLS VICTIM TO CHOLERA OR A WORKER IN MEXICO CONTRACTS SMALLPOX, THE MOTHERS OF PROVIDENCE AND KANSAS CITY AND LOS ANGELES MUST BE CONCERNED."

And he was prescient in seeing the economic benefits of improving the health and stability of poor countries.

"From an economic standpoint, we have had a major stake in a healthy world. Our country has billions of dollars in investments, private and governmental, throughout the world. American industry has expanded in many parts of the globe and many Americans are living and working abroad. Improving the level of health in the countries in which we have investments is definitely to our advantage. The stability of our own economy depends in large measure upon our trade with other nations. We have better markets for our products where widespread disease does not depress their national economy. By the same token, we must pay more for products and materials we import if the economy of the exporting country is weakened by disease and a low standard of living."

THE LEGISLATIVE HISTORY OF FIC

Fogarty's many friends and wide popularity in both the House and Senate ensured that his legislative proposals could count on multiple co-sponsors. In particular, he shared his vision with Lister Hill (D. Ala), who chaired the Labor HEW appropriations subcommittee on the Senate side. Between them, and with the support of colleagues like Hubert H. Humphrey, then the democratic senator from Minnesota, they proposed measures to enhance biomedical research and establish an international center at NIH:

1957. Fogarty sponsored a bill that provided federal funds for construction of public health education and research facilities (the *Health Education and Facilities Construction Act of 1957*) and other bills that increased funds for NIH training programs and increased salaries of NIH personnel.

1958: September. Lister Hill proposed Senate Joint Resolution 199, the "Health for Peace" bill, which Fogarty followed with an identical resolution, H.R. 698, in the House. The bill established an Institute for International Medical Research at NIH with a $50 million annual budget and it vested power in the U.S. Surgeon General to chair a new National Advisory Council to guide International Medical Research. The bill was referred to the Committee on Labor and Public Welfare but no action was taken on the bill until the following year.

1959 May. The bill was reintroduced in the Senate as J.R. 41 and in the House as H.R. 370. In presenting it Fogarty proclaimed, "Let our second American revolution be a world war against disease." The bill passed in the Senate but was opposed by the Eisenhower Administration. It did not help that the nation was now in recession and foreign aid was an easy target. A disappointed Fogarty summed up the opposition: It would cost too much money and a new institute at NIH was unnecessary. He acknowledged that the major sticking point was that the administration wanted international programs to be the province of the State Department and the International Cooperation Administration on a government-to-government basis and not on a scientist-to-scientist program administered through HEW. Broad authority in the field of international health research was deemed the role of the President, who could support research projects using foreign currencies or credits generated by the sale of surplus agricultural commodities abroad.

1960 June. The House subsequently drafted a weaker bill, retaining the concept of an International Institute as an objective, but not authorizing its establishment. The bill passed in the House and Senate and became Public Law 86-610, the *International Health Research Act of 1960*. The act granted the Secretary of HEW authority in some areas to advance health science in the United States through cooperative research and research training endeavors with foreign countries, but states that authority to advance the international status of health science through international cooperative endeavors rests with the President.

1961 February. An **Office of International Research** was established in the Office of the Director, NIH. Among authorities delegated to it was the maintenance of several NIH offices overseas and the administration of an International Research Fellowship program, established at NIH in FY 1958, first under the Division of Research Grants and then under the Division of General Medical Sciences. (When the Fogarty Center was established, most of the functions of OIR were transferred to it.)

1963 September. Fogarty again introduced his concept for an Institute of International Health Research at NIH in a speech at the Third National Conference on World Health. He spoke of bringing "into being at Bethesda a great international center for research in biology and medicine and dedicated to international cooperation and collaboration in the interests of the health of mankind." Over the next few years Fogarty continued to speak out for global cooperation in health research, for support of the World Health Organization, and for applying the results of research to improve clinical care in diagnosis, treatment, and prevention. He was an early advocate of worldwide eradication of polio, malaria, and smallpox.

1967 January 10. John Fogarty dies while working at his desk on the day before the opening session of Congress.

1967 January 18. Labor, HEW Subcommittee member Melvin Laird (R. WI) proposes establishing an **International Center for Advanced Study in the Health Sciences** at NIH in Fogarty's honor.

1967 February. President Lyndon Johnson delivers a health message to Congress asking for funds to establish the Center.

1967 August. $500,000 in planning funds for the Fogarty International Center are included in the FY 1968 NIH appropriation and for scholarships and fellowships in the Center.

1968. The Fogarty International Center for Advanced Study in the Health Sciences is born.

REPLICATING THE MODEL

AITRP has become a model for a number of FIC research capacity-building programs in the developing world in such areas as maternal and child health, tropical diseases, emerging infectious diseases, environmental and occupational health, and population-related research (see pp. 19-21, 27-30). With its emphasis on training, however, the program shared a perspective that FIC had in its early years—albeit with a significant shift in approach from individual fellowships to institutional training grants that now emphasize institutional partnerships and networking. When the Center was established, several small programs were transferred to it from an existing Office of International Research (OIR), which had been situated in the Office of the Director, NIH since 1961. Milo D. Leavitt, Jr. who had served as OIR Director, became the first Director of FIC, a position he held for 10 years until his retirement in 1978. OIR activities transferred to FIC included the handling of the NIH portion of special foreign currency programs established after World War II; maintenance of four NIH overseas offices in Rio de Janeiro, Paris, Tokyo, and New Delhi; and the administration of an International Research Fellowship program begun in 1958. While personnel and budgetary constraints would shrink most of these programs (all overseas offices except New Delhi were closed by June 1970, for example), the International Research Fellowship program (IRF) flourished.

THE INTERNATIONAL RESEARCH FELLOWSHIP PROGRAM

When World War II ended in 1945 the nations of Europe were devastated, their economies destroyed, their cities in ruin, their populations starving. In a major effort at reconstruction, the U.S. implemented a section of the Foreign Assistance Act of 1948 called the European Recovery Program—popularly known as the "Marshall Plan". The idea was to provide financial and material assistance to participating countries in Western Europe to aid them "through their own individual and concerted efforts, to become independent of extraordinary economic assistance within a certain period."

A decade later, in 1958, under Shannon's leadership and with the support of Fogarty and colleagues in Congress, NIH launched a kind of Marshall Plan of its own. The **International Research Fellowship (IRF)** program was designed to rebuild European capacity for biomedical research by developing a cadre of foreign investigators who would be trained in American academic institutions and return to take their places in Europe's leading universities and research centers.

And so they did. Eligibility for the program came through nomination by committees in the countries of origin, with the prospective Fellows making direct contact with senior U.S. investigators to arrange sponsorship, and submitting evidence that a research position in a non-profit institution awaited their return after training. Over the next few decades, and with the addition of candidates from other parts of the world as Europe rebounded, the IRF program trained thousands of scientists in leading research universities in America. The majority of Fellows returned to their home countries to pursue careers in research, teaching, and administration, often keeping in close touch with their American colleagues. By 1988, 30 years after the program's inception, over 2,500 Fellows from 55 countries in Europe, Asia and the Pacific, the Middle East, Africa, and Latin America, had been trained at a total cost of $50 million.

The list of mentors for many of the Fellows in the early decades reads like a Who's Who of leading American scientists, a number of whom would go on to become Nobel laureates: Christian Anfinson, Julius Axelrod, David Baltimore, Severo Ochoa, Arthur Kornberg, Werner Loewenstein, Bruce McEwen, Albert Lehninger, Dominick Purpura, Irwin Kopin, Vernon Mountcastle, Ira Pastan, Baruj Benacerraf, and Bernard Brodie. Likewise, the roster of sponsoring institutions represented the country's leading research centers then and now: Harvard, Yale, Johns Hopkins University, the University of California at San Francisco and the U.C. campuses in Los Angeles and San Diego, Stanford University, the Universities of Washington and Wisconsin, and the NIH itself.

In an independent assessment of the IRF program in 1988, which included a survey of over 1,600 former Fellows and an analysis of papers they published in the scientific literature, the evaluators concluded, "Based on their scientific achievements, Fellows from developing countries are likely to contribute significantly to the quantity of biomedical research and health care in their respective countries." In particular, they noted:

- On average, 4 out of 10 former Fellows reported introducing new equipment or technologies at home, including magnetic resonance imaging, computer-aided epidemiologic and clinical studies, various cell biology laboratory techniques, and thyroid chemical and radiological diagnostics.
- Research findings ranged from early Fellows' advances in understanding the mechanisms involved in virus attachment, synaptic transmission, and in the pathology associated with certain cancers, to later Fellows' work in immunology and genetics, such as developing monoclonal antibodies, sequencing hepatitis B virus genes, and cloning genes for several members of the cholinesterase family.
- Three out of every four Fellows reported continuing international collaborations in research, often with their "alma mater" institution, while half had become mentors themselves, supervising graduate or post-doctoral students in their home country.
- The number of papers published by Fellows in the international scientific literature and their citation rates (a measure of a paper's importance based on how often a given paper is cited in other papers published in well-recognized journals) was fully comparable to the number of papers and citations rates of other NIH grantees. (continued on page 22)

REPLICATING THE AIDS MODEL — FOGARTY TRAINING PROGRAMS

The launching of FIC's AIDS International Training and Research Program (AITRP) in FY 1988 inspired a succession of other similar FIC training programs, each designed to enhance research capacity in the developing world on particular topics. Each of these initiatives, which are intended to be long term, measured in decades, albeit re-competed at five-year intervals, provides research training at a U.S academic institution for a succession of junior investigators from a foreign institution. The intent is two-fold, first, to promote greater equity in scientific capacity to support ongoing collaborations on research projects when the trainees return to their home countries, and second, to establish long-term collaborative research relationships. Each program singles out an area of critical importance to improving the health and living conditions of present and future generations of people in areas of the world undergoing rapid development and technological change.

FIC international conferences are often the springboard for new initiatives.

ENVIRONMENTAL AND OCCUPATIONAL HEALTH

Child labor, sweatshops, grueling and hazardous working conditions in factories and mines, air and water pollution, exposure to pesticides and fertilizers on lands cleared for monoculture crops—in sum, all the sins of the 19th and 20th century industrial and agricultural revolutions in Europe and the U.S., are being visited on new generations of workers in the 21st century developing world. With it, degradation and pollution of the environment is seriously affecting the health of all who are exposed, and not just workers. The Fogarty International Center's program on International Training and Research in Environmental and Occupational Health (**ITREOH**), with the close support of the National Institute on Environmental Health Sciences and other partners, aims to prevent a legacy of morbidity and mortality and environmental devastation from building up in the developing world. It focuses on training local professionals in research on workplace and environmental protection and public health and safety, with emphasis on implementing interventions targeted to specific conditions in the home country. The program, begun in 1995 and now in its second round of 5-year awards, has engaged over a dozen American universities and faculty, staff, and students from institutions in 28 countries in Africa, Central and South America, Eastern Europe, India, and China.

As the program has matured, there is a movement towards the development of regional centers of excellence to address issues common to several contiguous countries. This would be an effective approach to multiply the impact of the program, and toward that end, current grantees are working together to address common interests to create such centers.

Cement bagging operation evaluated during a dust-and-noise monitoring course in Zambia.

Among significant outcomes to date has been the publication of a text on environmental epidemiology, the result of collaboration between FIC grantees at the University of California at Los Angeles and trainees at the National Institute of Public Health in Cuernavaca, Mexico. The text, in Spanish, covers issues of special relevance in Latin America, including the relationship between the prevalence of bladder cancer and arsenic exposure in Argentina, the association between birth defects and exposure to pesticides in Colombia, urban exposure to mercury in gold production in parts of Brazil, and the relationship between chronic respiratory illness and exposure to wood smoke in Mexican women. Another important ITREOH program concerns the 1986 nuclear power plant explosion in Chernobyl, Ukraine. It has been the focus of a collaboration between Ukrainian, Russian, and Belarussian trainees and scientists at the University of Illinois, Chicago. The collaborators developed a data management program and systems for the prospective management of a backlog of data from a cohort study of populations from these countries that details the relationship between exposure to radioactivity released at Chernobyl and the prevalence of thyroid cancer in children. At the present time, the National Cancer Institute, working with the Ukrainian Institute of Endocrinology and Metabolism in Kiev in a study funded by the U.S. Department of Energy, has requested that a data management center be established at the Metabolism Institute. FIC is helping to fund the center to allow continued support of the project as well as to enhance the research capacity of the Ukrainian scientists.

ITREOH partners with FIC: National Institute of Environmental Health Sciences, National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, and the Agency for Toxic Substance and Disease Registry (ATSDR).

POPULATION AND HEALTH

The impetus for Fogarty's International Training and Research Program on Population and Health (**ITRPH**) has been the need for better epidemiologic and demographic data on populations in developing countries. Since FY 1995 the program has been supporting population-based research to improve collection and analysis of baseline and longitudinal data in developing countries, as well as factors affecting birth rates and aging. In the African Census Analysis Project, for example, researchers at the University of Pennsylvania (Philadelphia) have been working with the census bureaus of 20 African countries to enable more refined demographic analyses of census data. Such studies have explored provincial differences in mortality of young children in Kenya, geographic distribution of ethnic groups in Senegal, and patterns of fertility and marriage among the many ethnic subgroups in

South Africa. As well, the programs support basic biomedical and behavioral research on fertility and contraception. Studies of male contraception in experimental animal models are included in two ITRPH programs, one between scientists at University of Pennsylvania and colleagues in Latin America, and a second between University of Virginia scientists with partners in China and India.

The ITRPH programs are important in tracking the effects of changes in fertility and mortality that occur as developing countries become more technologically sophisticated. For example, University of Michigan researchers, working with Vietnamese trainees, have been studying the effects of declining fertility rates on the social support system of older adults. The study indicated that older adults who had had smaller families had no less support in their old age from their children, except in the case of a group of older adults in North Vietnam who had had no sons. This is a powerful message on the lack of correlation between family size and social support systems as this society develops.

ITRPH partners with FIC: National Institute of Child Health and Human Development, National Institute on Aging.

MATERNAL AND CHILD HEALTH

Lack of prenatal care, poor nutrition, and frequent pregnancies are common in developing countries, accounting for high rates of stillborn or premature low-birth-weight babies. To counter these problems FIC initiated an International Maternal and Child Health Research and Training program (**IMCHRT**) in FY 1999. Co-funded with the National Institute of Child Health and Human Development, the program trains developing country professionals on the health problems of pregnant mothers and their infants with an emphasis on preventing complications of pregnancy, such as preeclampsia and preterm labor, and protecting infants from diarrheal diseases and perinatal transmission of HIV/AIDS. Grantees at seven U.S. universities are currently collaborating in training and research projects with investigators in Latin America, Asia, and Africa. In addition to disease pathology and prevention research, several programs are collecting epidemiologic data on reproductive and perinatal health, studying child development, infant feeding and nutrition, and conducting basic research on neonatal host defenses. Of interest in relation to the research priorities of the Multilateral Initiative on Malaria, scientists at Georgetown University in Washington DC are collaborating with investigators in Cameroon to study malarial immunity in pregnant women, neonates, and children.

IMCHRT partner with FIC: the Global Network for Women's and Children's Health Research of the National Institute of Child Health and Human Development.

With the relatively rapid recovery of Western Europe's economy and its science and technology base after World War II, the IRF program increasingly targeted developing countries elsewhere in the world. By the 1970s IRF collaborations were established with Warsaw pact nations, helping to create a climate of intellectual freedom and cooperation in countries behind the Iron Curtain. Overtures to China led to the first Chinese fellow being named in 1984. By the time of the collapse of the Soviet Union in 1990 FIC was ready with a proposal for collaborations with the newly emerging independent states. New fellowship programs began with Russia, Bulgaria, and Czechoslovakia, and importantly, a new grant program was initiated in FY 1992: the "FIRCA" (Fogarty International Research Collaborative Award). In its early phase, these were small international collaborative research awards to an American investigator whose research would benefit from collaboration with a partner from Latin America or Eastern Europe. They served to test the waters of collaboration and were used to generate the pilot data needed to apply for larger grants. Today, the scope of this program has expanded to cover the developing regions of the world everywhere.

SCHOLARS IN RESIDENCE

While the IRF program had grown out of World War II and predated the Fogarty Center, a second fellowship program as well as the inauguration of a workshop and conference program were initiated in 1969, the first full year after FIC's establishment. If the Marshall plan demonstrated that it was in America's best interests to promote a stable economy in the West—with mutual benefits to be gained from international cooperation and communication—so too would these new programs, particularly the new **Scholars in Residence** or **SIR** program. As Milo Leavitt explained to Senator Warren Magnuson at the 1970 appropriations hearings, the new fellowships were set up "to enable the NIH to capitalize on the best thinking, the best brains in the world." The intent was to bring internationally renowned scientists—both American and foreign—to NIH for periods of up to a year or more. At any given time there would be half a dozen or more of these scholars in residence at Stone House on the NIH campus. During their stay, they would hold seminars and workshops, write books, and conduct research in collaboration with colleagues in other

NIH institutes. The scholars were selected by an advisory panel from nominations made by leading NIH intramural scientists. In addition to their formal activities, it was assumed that the informal discussions and daily exchanges among the scholars while at Stone House would themselves spark creative ideas and innovations.

The "SIR" program succeeded in bringing a pantheon of gifted scientists to NIH over the years—more than 200—including Margaret Mead and Albert Sabin, four Nobel prize winners: Daniel Bovet, Rita Levi-Montalcini, Sir Hans Krebs, and Ragnar Granit; a number of Lasker award winners, and others recognized as leaders in their fields. Albert Sabin brought to NIH his commitment to rid the world of polio using the Sabin oral vaccine (which had already debuted on the international scene having been tested in Russian schoolchildren). During his periodic stays at NIH in the early 1980s Sabin oversaw strategies that would lead to the complete elimination of polio in the western hemisphere by 1993. He worked with governments, international organizations such as Rotary International, and the World Health Organization to incorporate annual national vaccination programs with routine health services in developing countries. He also recognized early on the importance of working at the local level to enlist the support of community leaders and volunteers to encourage vaccination.

Among the earliest Scholars was Sir George Godber, the architect of the British National Health Service. Other notables over the years included Peter Perlmann, from the University of Stockholm, who developed the ELISA technique, widely used in research and diagnostics, for example, in blood tests for HIV and other pathogens; William Jarrett, whose work with feline leukemia virus paved the way for Robert Gallo's later isolation of human leukemia viruses. Gallo has remarked that without the input of foreign nationals and investigators he would not have been able to make the progress he has, referring to his lab as a "rainbow coalition." In 1990 Fogarty welcomed its first African scholar, Olufemi Williams from Nigeria, who completed a book while in residence detailing comparisons between AIDS in Africa and AIDS in the U.S. In 1992 Lev Bergelson arrived as the first scholar from Russia, noted for his studies of the role of lipids in heart disease and cancer.

The most recent Fogarty scholar, in residence at the FIC in the spring of 2003 and co-sponsored by FIC together with the National Institute of Diabetes, Digestive and Kidney Diseases, the National Human Genome Research Institute, and the National Institute of Environmental Health Sciences, is Sir David Weatherall, Regius Professor of Medicine Emeritus at Oxford University and the founding Director of the Weatherall Institute of Molecular Medicine at Oxford. Professor Weatherall is an internationally acclaimed molecular hematologist who has long worked on the inher-

ited hemoglobin disorders prevalent in developing countries. He is the author, among hundreds of peer-reviewed articles, of the recent WHO report, *Genomics and World Health*, which is oriented towards mitigating the growing global divide in the utilization of genomics and genetics information in health research to improve the quality and delivery of health to those in developing nations.

THE SENIOR INTERNATIONAL FELLOWSHIP

In contrast to the International Fellows and the Scholars programs, a third fellowship established during the Fogarty Center's first decade was specifically targeted to leading *American* investigators. The **Senior International Fellowship** (**SIF**) program begun in 1975, was, as one strong proponent in Congress put it, a kind of Lend-Lease program (or indeed, an IRF program) in reverse: Instead of bringing junior scientists from developing countries to America, the program enabled established U.S. investigators to travel abroad, perhaps during sabbatical years, to take advantage of outstanding research at other major centers or to have opportunities for studying unique patient populations or learning new techniques from international colleagues.

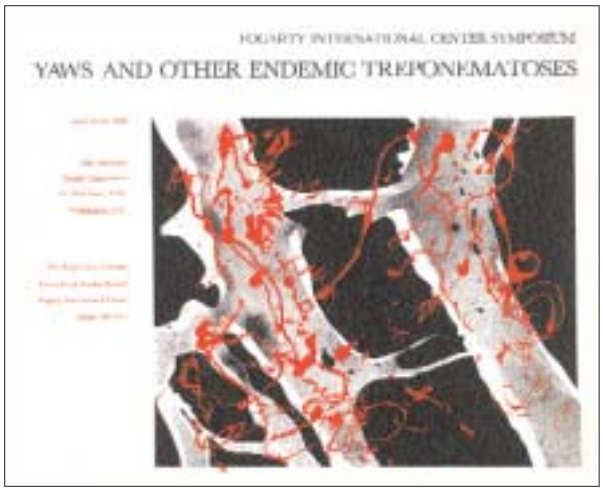
Thus for its first two decades the Fogarty International Center was primarily associated with a series of fellowship and conference programs. These were organized in several administrative branches of the Center: an International Research and Awards Branch for the IRF and SIF programs, and an Advanced Studies and an International Studies and Awards Branch for the SIR and conference programs. A fourth branch, International Coordination and Liaison, was responsible for promoting and/or implementing bilateral or multilateral agreements for scientist exchange programs and international research collaborations. FIC was also the official Reception Center for foreign scientists and was responsible for providing visa and immigration services for visiting scientists and guest workers invited to work in laboratories on the NIH campus. This "Foreign Scientist Assistance" branch was responsible for smoothing the bureaucratic path by which these visiting scientists, fully a third of the NIH intramural program who come from abroad, were able to work for extended periods of time in NIH laboratories.

SUCCESS/PROGRESS/CHANGE

Fogarty's fellowship programs predated the revolutions in travel and in communications that are commonplace today. They also predated changes in biomedical science itself—changes in substance and style born of the revolution in genetics and molecular biology and the emergence of big, equipment-heavy laboratories and multidisciplinary teams of researchers. It was wonderful to nurture a new post-World War II generation of investigators. It was exhilarating to bring stellar scientists to NIH to act as catalysts for new ideas. And it could only add to the luster of established American investigators to have the opportunity of working abroad. So it can be said that each of the programs —the "IRF," the "SIR," and the "SIF"—truly succeeded in its goals. But change was in the air. By the 80s and 90s the population of world-class scientists in developed countries had grown substantially. Convenient jet travel made it easy for an American scientist to spend a few days abroad to attend a meeting or confer with colleagues—who could also be contacted by e-mail. Longer times away were becoming problematic given the responsibilities of a large lab to administer, graduate students to advise, and grant proposals to write.[1] With changing times and changing needs of scientists, FIC's programs and initiatives kept pace.

GLOBAL PROBLEMS, GLOBAL SOLUTIONS

These changes in science were occurring at the same time that the world was coming to grips with global health problems—problems that would need global solutions, exactly as John Fogarty had foretold in his lifetime. In the world of medical science, at NIH in general, and for the Fogarty Center in particular, AIDS was the watershed event that signaled a major change in direction. By 1988 FIC had initiated its AIDS institutional training and research program and was expanding its horizons. It was clear that there were other pressing global health and environmental problems that demanded attention. Whether in the form of a new infectious disease "that was only a jet plane away," as the Nobel laureate Joshua Lederberg had remarked, or in the form of re-emerging and antibiotic-resistant forms of old plagues like tuberculosis, global health and disease suddenly began to take center stage—at the White House, in Congress, and at the NIH itself.



Old and new plagues are an ever-present threat requiring vigilance.

Through the Center's own program evaluations over the years, its strategic planning and policy documents, and its proposals to reduce disparities in global health, FIC had seen the importance of addressing the needs of the developing world—and within that world the need to attend to the effects of development itself. It was not only that so many in the developing world were burdened by poverty and disease, it was that development itself could profoundly affect health and well-being—and that health was essential for development. New industry and commerce, advances in transportation and communication, are transforming events, changing landscapes and lifestyles. Relocations from villages to larger towns and cities all too often result in disruptions in family life and customs, changes in diets and behaviors, and introduce yet other sources of disease or disease risk in the form of industrial waste, air pollution, and destruction of the natural habitat. (continued on page 31)

AT A TIME WHEN AMERICANS ARE INCREASINGLY AWARE OF OUR LIFE IN A GLOBAL COMMUNITY, THE FOGARTY CENTER SERVES AS A FOCUS OF NIH OUTREACH TO THE DEVELOPING WORLD. THE RECRUITMENT OF SCHOLARS TO STUDY IN THE U.S. AND RETURN TO THEIR NATIVE LANDS FORTIFIED WITH NEW INFORMATION AND TECHNOLOGY TO IMPROVE THE HEALTH OF THEIR PEOPLE IS A WORTHY ENDEAVOR, DESERVING EVER-INCREASING SUPPORT.

Samuel Katz
Professor of Pediatrics, Emeritus
Duke University School of Medicine

GLOBAL INFECTIOUS DISEASE

THE IMPORTANCE OF INFECTIOUS DISEASE AS A CAUSE OF WORLDWIDE DEATH AND DISABILITY CANNOT BE OVERSTATED. THE GLOBAL MORTALITY FIGURES FOR INFECTIOUS DISEASES IN 2000 EXCEEDED 17 MILLION MEN, WOMEN AND ESPECIALLY CHILDREN, OVER HALF OF WHICH WERE DUE TO JUST THREE CAUSES, HIV/AIDS, TUBERCULOSIS, AND MALARIA. USING THE WORLD HEALTH ORGANIZATION'S METRIC OF DISABILITY-ADJUSTED LIFE YEARS—DALYS—A TIME-BASED METRIC WHICH COMBINES MORTALITY AND NON-FATAL OUTCOMES TO REPRESENT THE HEALTH STATUS OF A POPULATION AS A SINGLE NUMBER, THE DALY MEASURES FOR AIDS, TB, AND MALARIA COMBINED ACCOUNTED FOR 11 PERCENT OF ALL DEATH AND DISABILITY IN THE WORLD IN 2000. TO BOTH SUSTAIN ITS FOCUS ON HIV/AIDS AND TO FACILITATE RESEARCH AND TRAINING ON ALL INFECTIOUS DISEASES IN DEVELOPING COUNTRIES, FIC IS MAINTAINING AND STRENGTHENING ITS HIV/AIDS INITIATIVES, AND HAS COMBINED INDEPENDENT TRAINING AND RESEARCH PROGRAMS FOR THREE SEPARATE PROGRAMS —ON EMERGING INFECTIOUS DISEASES, TUBERCULOSIS, AND MALARIA—INTO A SINGLE GLOBAL INFECTIOUS DISEASE RESEARCH TRAINING PROGRAM.

EMERGING INFECTIOUS DISEASES

West Nile, Ebola, and now SARS (severe acute respiratory syndrome) are part of a growing vocabulary of words that strike fear in millions across the globe for their association with new or newly introduced and deadly infectious diseases. Defined by the Institute of Medicine as "diseases of infectious origin whose incidence in humans has increased within the past two decades or threatens to increase in the near future," emerging and re-emerging infections are reminders, too, that patterns of health and disease are never static. They can change as a result of seemingly random events, macroscopic changes in climate, weather, and terrain, or microscopic changes at the level of genes in cells. Contributing to this flux in disease patterns is human behavior. Such activities as the well-intentioned use of agents to control the spread of disease or destroy disease-causing organisms often leads to microbial resistance to the measures employed. Behavior can also include the malign intent to alarm and kill human populations through the use of bioterrorism agents. The six diseases on the Centers for Disease Control and Prevention Category A list (associated with the most lethal, most easily disseminated bioterrorism agents) are all dreaded infections: smallpox, anthrax, plague, botulism, tularemia, and hemorrhagic fever (e.g., Ebola).

It is hardly surprising that FIC was involved early on in addressing the broad new field of Emerging Infectious Diseases, working closely with NIAID. FIC's initial steps included assembling meetings of experts to discuss research gaps and opportunities, publishing reports, and initiating programs to expand research and training on re-emerging and emerging diseases. For example, a current FIC staff member who witnessed the original 1976 Ebola outbreak in Zaire, now called the Democratic Republic of the Congo, helped organize a critical meeting on the disease at Stone House in 1995, shortly after the second large outbreak of the disease occurred in the same country. This meeting called attention to the disease (which had also affected experimental monkeys in Reston, Virginia in 1989, popularized in the book *The Hot Zone* by Richard Preston), laying the groundwork for a larger international meeting on Ebola in Antwerp, Belgium in 1996. Another current FIC staff member initiated and co-chaired with NIAID a trans-NIH group to take stock of NIH programs in the field of emerging diseases and to serve as an advisory group to those involved in development of U.S. policies to address the new challenges they posed.

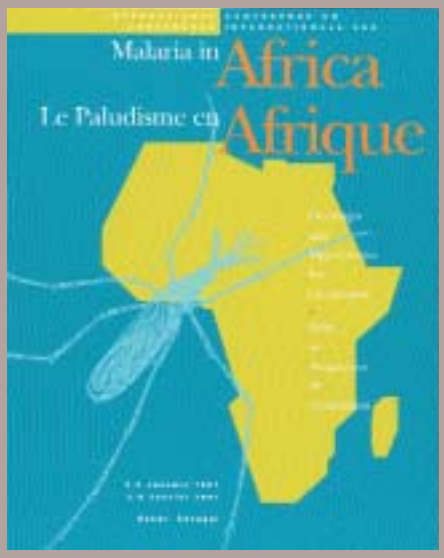
In 1997, FIC initiated its International Training and Research Program in Emerging Infectious Diseases (**ITREID**), aimed at enhancing the ability of developing country health professionals to understand, control, and prevent outbreaks of emerging infectious diseases through research training and collaborations with U.S. scientists. Malaria and tuberculosis rank high as areas of study in ITREID programs, because of their prevalence, resurgence, and resistance to treatment, but local and regional health concerns in low- and high-income countries dictate that a wide range of bacterial, fungal, viral, rickettsial, and parasitic diseases be studied. Given the need to mobilize quickly to identify, contain, and control an emerging infection, the programs emphasize epidemiologic surveillance and development of rapid, reliable—and in resource-poor countries—inexpensive diagnostic tests, in addition to improved means of treatment and prevention. Training often includes the introduction of the high-tech tools of genetics and molecular medicine, such as polymerase chain reaction (PCR) technology, microarrays, and pulsed field gel electrophoresis. The 13 ITREID awardees (at 12 American universities and one state health department) are currently collaborating on projects in over 30 countries and report some notable accomplishments:

- Development of a simple sputum test to diagnose and determine treatment susceptibility of *Mycobacterium tuberculosis* (Peru).
- Discovery of a master gene—controlling the function of over 30 other genes and influencing many more—that may be responsible for activation of the latent tuberculosis bacterium to cause overt disease. The gene is involved in tissue damage to the lung and appears to confer protection of the pathogen from heat, oxidation, and other stressors.

- Demonstration of an association between El Niño weather changes (related to temperature increases) and marked increases in diarrhea cases (Peru).
- Association of outbreaks of mosquito-borne dengue fever in Brazil with relaxation of vector monitoring activities and control of mosquito breeding sites.
- Use of a rapid immunoassay to diagnose leptospirosis and distinguish it from dengue fever (Brazil).
- Effectiveness of a simple, restriction site-specific PCR technique to reliably detect subtypes of hepatitis C virus (HCV) from blood samples, replacing costly and labor-intensive methods (Czech Republic). The tests will enable studies of the comparative distribution and virulence of subtypes of HCV—a major emerging disease estimated to infect 170 million people worldwide.
- High clusters of NOMA (severe ulcerations and lesions of the orofacial cavity) in Niger associated with nomadic lifestyle and close contact with livestock, including sharing of water supply (one source of the causative anaerobic bacteria).

FIC partners: National Institute of Allergy and Infectious Diseases, National Institute of Dental and Craniofacial Research, National Center on Minority Health and Health Disparities, and the Centers for Disease Control and Prevention.

Malaria. An important finding in the International Malaria Research Training (**IMRT**) program, which has funded five collaborations in Africa since FY 1999, concerns the great contemporary dilemma, effective and affordable therapy. In the face of resistance to chloroquine, the mainstay anti-malarial drug, University of California, San Francisco investigators, in collaboration with trainees at Makerere University in Uganda have found that a combination of three existing drugs, amodiaquine, sulfadoxine, and pyrimethamine was safe to administer and more effective than each of these drugs used separately. Use of a combination of drugs is also likely to lower the probability of resistance. Moreover, because the drug regimen led to impressive reductions in blood levels of the infectious form of the plasmodium, the risk of uninfected mosquitoes acquiring the malaria parasite while biting a patient and subsequently spreading disease by biting uninfected persons is also reduced.



Dakar, Senegal was the site of the conference that launched the Multilateral Initiative on Malaria.

Tuberculosis. Since FY 1998 the Tuberculosis International Training and Research Program (**TBITRP**) has supported 7 programs engaging collaborators in Eastern Europe, Asia, Africa, and Latin America. Because tuberculosis is actually the leading cause of death of HIV-infected persons in developing countries, a number of research studies have focused on preventing activation of latent TB infection in HIV-positive adults. A study in Uganda showed that six-month treatment with the standard TB drug isoniazid provided short-term protection against reactivation of the disease in persons with latent infection, while a combination of three anti-tubercular drugs for three months conferred protection for up to 3 years.

ACTIONS TO BUILD CAPACITY

Contributing to the Fogarty Center's infectious disease activities is a special Actions for Building Capacity or **ABC** program, begun in FY 1999. The program adds a research training component to an NIAID program on tropical diseases known as the International Collaborations in Infectious Disease Research (**ICIDR**), which is the foundation for NIAID's network of International Centers for Tropical Disease Research. Only ICIDR grantees are eligible for the FIC ABC awards, which currently support investigators in 10 U.S. universities and hospitals. Research and training activities are conducted primarily in-country at 18 ICIDR sites in Africa (Egypt, Kenya, and South Africa), Asia (Bangladesh), with the remainder in Latin America. As with FIC's emerging disease initiative, the aims of the ABC program are to increase the knowledge and technical skills of scientists and health care workers in developing countries enabling them to conduct surveillance, understand the causative organisms and vectors, develop reliable diagnostic tests, and improve treatment and prevention for a range of tropical diseases including malaria, dengue fever, cholera, diarrheal diseases, hantaviruses, and hepatitis.

—

Note: FIC also supports an initiative on the Ecology of Infectious Diseases (see page 44).

THE FOGARTY CENTER HAS MADE EXTRAORDINARY CONTRIBUTIONS TO ENSURE THAT THE LIFE-SAVING INTERVENTIONS WE TAKE FOR GRANTED IN THE U.S. CAN BE MOBILIZED FOR THE POOREST PEOPLE IN THE DEVELOPING WORLD. BY INVESTING SO SUCCESSFULLY IN HUMAN RESEARCH CAPACITY IN DEVELOPING COUNTRIES, AND TO THE DEVELOPMENT OF INDEPENDENT RESEARCH CAREERS BY SCIENTISTS FROM THESE COUNTRIES, THE CENTER HAS BEEN ABLE TO LEVERAGE U.S. KNOW-HOW TO IMPROVE GLOBAL HEALTH AND THE CAPACITY OF DEVELOPING COUNTRIES TO ADDRESS THEIR OWN PROBLEMS.

Sally Stansfield
Bill & Melinda Gates Foundation

THE FOUNDATION OF THE HOUSE

Clearly there is no dearth of health problems in the developing world, but where to begin? Here FIC has been guided by a decision-making process emphasizing global needs and scientific opportunities, combined with a pragmatism that any proposed program be feasible and of broad enough importance and potential to build partnerships to maximize the effort. These principles are embodied in four programs described in the Center's 2000-2003 Strategic Plan[2] that form the basis for FIC's continuing growth and expansion. Gerald Keusch, FIC's Director since 1998, considers the four programs—in bioethics, clinical research, medical informatics, and genetics—the foundation of the house that FIC is building on.

These cross-cutting areas owe their prominence in planning to the astonishing pace of progress in biomedical science and technology—not least the mapping of the human and other genomes—and the zeal to move findings to clinical applications in biotechnology, drug development, diagnostics, and therapeutics. Thus, by the time of the 50th anniversary of the elucidation of the double helix structure of DNA in April 2003 researchers had completed the sequencing of the human genome, the most important malaria parasite, and the most efficient mosquito vector transmitting malaria, paving the way for innovative research to identify new targets for the generation of new drugs, vaccines, and insecticides to control malaria around the world. These developments are also placing new demands on the education and training of researchers and care providers. Health professionals in both the developed and developing world must be sensitive to the social, ethical, and legal issues involved in human subject research. They need a thorough grounding in the design, conduct, and interpretation of clinical studies and trials. Their skills must include the ability to build and/or access the databases, computer systems, and tools necessary for the storage and analysis of experimental and clinical data. Finally, researchers, health providers, and the public at large need to understand that, with the exception of injury, all diseases and disorders involve a genetic component, whereby the interactions of genes with environmental factors affect an individual's susceptibility to disease, and even the body's response to injury and repair is likely to be modulated by genetic controls. FIC's four foundation programs are designed to build research competence and

capacity in these areas in the developing world. To encourage the active participation of low- to middle-income countries, extensive consultation with developing country scientists has preceded the call for applications in each new program area, and the programs have been designed to permit one- to two-year competitive peer-reviewed planning grants to institutions in developing countries to develop their research and training plans. During this time the developing country team can organize a program geared to their needs and interests, and seek a collaborating partner in the developed world to complement/supplement those needs. Once the partnership is in place applicants can apply for full grant support in response to a Request for Applications issued by FIC and its co-funding partners.

BIOETHICS

The Bioethics Program was an immediate outcome of the 1999 Global Forum on Bioethics organized by FIC.

The **International Bioethics Education and Career Development Award** is a capacity-building training program that supports curricular development in U.S. and other developed and developing country institutions to enhance teaching and research on bioethics for trainees from developing countries, with special attention to the conduct of clinical research. Bioethics training is provided at a sufficiently advanced level to allow developing country professionals not only to assume responsibilities for the ethical review of clinical investigations when they return home, but perhaps even more critical for the long term, by becoming bioethicists who understand the research environment and can create a climate of ethical debate and conduct within their country. The program also provides short-term training courses for home-based investigators who are directly involved in ethical review of human subjects' research and clinical trials. The program, announced in 2000, was an immediate outcome of the 1999 Global Forum for Bioethics in Research, organized by FIC and the first in an ongoing series of international conferences. These meetings, held at international sites and sponsored by a rotating group of international organizations and FIC and its NIH partners, bring scientists and ethicists from the developing and developed worlds together to discuss the complex issues of conducting clinical research in developing countries.

IN THE AREAS OF GLOBAL HEALTH AND BIOETHICS, PUNDITS HAD BEEN HAVING ENDLESS DISCUSSIONS IN MATTERS OF SEMANTICS FOR YEARS...FOGARTY INVESTED IN CREATING NETWORKS AND TRAINING PROGRAMS ON BIOETHICS AND GLOBAL HEALTH —- AND IT WAS THE FIRST ORGANIZATION TO DO SO.

Peter Singer
University of Toronto Joint Centre for Bioethics

Among the issues the bioethics initiative addresses are concerns that have been raised about the ethics of testing drugs or vaccines in resource-poor countries where there is little in the way of available "standard" treatment to offer control subjects, when the nature of benefits to the participants once the research is over is not clear, or where the use of a placebo control has been questioned. The nature of informed consent, the rights/abilities of women or children to participate in studies, and how clinical trials are explained to volunteers, are some of the other issues that have been debated. Developing an ethics training program based on the inputs from the first Global Forum on Bioethics in Research, FIC and three NIH partners have established the network that now includes 7 training sites in the U.S., one in Canada, and 6 in developing countries in Africa, Asia, and Latin America. With 40 trainees per year coming through these programs the increasing expertise in bioethics in developing countries will soon begin to make a difference in practice.

SHORTAGES OF TRAINED RESEARCHERS AND HEALTH CARE WORKERS, USE OF INAPPROPRIATE THERAPIES, AND LACK OF EFFECTIVE TREATMENTS CURRENTLY LEAD TO NEGLECT OF HEALTH CRISES SUCH AS DEPRESSION, SUICIDE, SUBSTANCE ABUSE, VIOLENCE, BREAKDOWN OF THE FAMILY, DISINTEGRATION OF COMMUNITIES AND STIGMATIZATION OF THE AFFLICTED.

Gerald Keusch
FIC Director

CLINICAL RESEARCH

Two clinically oriented FIC training programs more broadly address the need to increase the pool of professional personnel able to translate research advances into effective health care service and delivery programs. The programs, which apply to the developing world as well as to countries in Eastern Europe, Russia, and the independent states of the former Soviet Union support multidisciplinary education and training for foreign scientists, clinicians, medical sociologists, mental health and other health services researchers, among others. The objective is to support training in the design and conduct of clinical research protocols, on small and large scales, in order to speed the translation of new scientific knowledge into health care policy and practice.

The programs, known as International Clinical, Operational, and Health Services Research and Training Awards (**ICOHRTA**s), are currently made in two areas: behavioral sciences and mental health (ICOHRTA-I), co funded with 5 NIH partners, and AIDS and tuberculosis (ICOHRTA-II), co-funded with 10 NIH partners and the Centers for Disease Control and Prevention. Among the 14 awards made in the non-communicable disease program are collaborations between US universities and international centers addressing suicide prevention (China), substance abuse prevention (Peru), developmental disorders and children's mental health (Turkey), alcoholism (Poland), coronary heart disease (India), and health care for the elderly (China). The AIDS/TB ICOHRTA program differs from ICOHRTA I in being issued as a program announcement, which accepts planning grant applications each year, rather than at 4-5 year intervals. Secondly, the program allows developing country applicants to choose their collaborating partners, rather than the other way around. Thirdly, the program funds each of the partners directly, following the development and submission of separate but integrated applications detailing the role and responsibility of each. This is clearly a paradigm for the future, to be emulated and expanded to the greatest extent possible.

MEDICAL INFORMATICS.

The impetus for FIC's **International Training in Medical Informatics** (**ITMI)** program is the digital gap separating the developed from the developing world. The lack of computer systems and technology is a major impediment to the ability of health professionals to communicate and share information with colleagues via the Internet or stay abreast of developments in health research by accessing Medline or professional journals online. But it is in the conduct of research itself that the digital gap poses the most serious barrier. Health professionals need to be able to store and/or access data collected and maintained in databases assembled for research or for public health needs (such as the collection of epidemiological and surveillance data that might signal a country-wide disease threat). And they need to communicate with one another and exchange data for analysis. The ITMI program, begun in FY 1998 in partnership with NIAID and the National Library of Medicine, has the characteristic features of all FIC research and training programs: it aims to build a broad informatics research capacity in the developing country by training developing world researchers in the U.S. or at home institutions. At the same time, the program also provides targeted short-term and locally adapted informatics training to promote the development and broader dissemination of informatics technologies in the home country. Overall, the program aims to enhance research collaborations between U.S. and developing country investigators using medical informatics to facilitate studies of diseases and disorders that may be more prevalent or endemic in developing countries. Scientists from four sub-Saharan countries received training in the first round of competition

for ITMI awards and subsequent rounds have added other countries in Africa as well as in Latin America. In the future this program will expand to all regions where there is need.

GENETICS

The successful complete mapping and sequencing of the human genome, announced at the NIH's 50-year celebration of the April 1953 report of the structure of DNA by James Watson and Francis Crick, was dependent on the huge investments in research using automated DNA sequencing equipment and computer software programs that are possible in high resource, high-tech countries like the US and its major UK partner, and other genome project centers in France, Germany, Japan, and China. The rewards of such research—the potential, for example, of using genomics to identify genes whose mutations are associated with heightened risk for debilitating diseases and following up with ways to prevent or mitigate the disease in question—are among the highest hopes of 21st century biomedical research. In one of its most innovative programs the Fogarty Center, with the World Health Organization and seven NIH partners, has worked to see that those hopes are not denied to developing countries. The new **International Collaborative Genetics Research Training Program**, which was developed in consultation with scientists from developing countries at every step of the way, will provide Master's and Ph.D. level training at U.S. institutions for developing country investigators to enable them to conduct post-genome genetic studies relevant to their country's needs when they return home. Hand in hand with their learning technical skills, the trainees' education includes a focus on the ethical, legal, and social implications of genetic research. To ensure that returning investigators will not lack the wherewithal for conducting genetic research at the home site, the first awards in the program have been made to U.S. institutions already collaborating in human genetic studies with institutions in developing countries with a level of genetic infrastructure already in place. The six awards made in 2002 include collaborations with Costa Rica on psychiatric genetic studies, Thailand on the genetics of drug dependence, Venezuela on heritable neurodegenerative diseases, China on orofacial clefting syndromes, and with institutions at two sites in India studying psychiatric disorders and genetic epidemiology, respectively. (continued on page 43)

1 FIC has recently reconfigured the SIF program to encourage junior investigators to pursue careers in international health research. The International Research Scientist Development Award (**IRSDA**) provides a mentored research experience for U.S. postdoctoral students at an internationally recognized developing country institution already in collaboration with a U.S. counterpart (who would sponsor the candidate). FIC also offers a Minority International Research and Training (**MIRT**) program, soon to transfer to the new Center on Minority Health and Health Disparities, to encourage underrepresented minorities, from college to predoctoral level, to extend research training to foreign sites.

2 www.fic.nih.gov/about/plan.html

FOGARTY INTERNATIONAL CENTER: IN THE DIPLOMATIC MODE

With its commitment to advance science for global health coupled with its practical knowledge of U.S. diplomatic channels and foreign science agency infrastructure, the Fogarty International Center is well positioned to serve as a bellwether for NIH and other agencies, advising on global health issues and identifying and developing initiatives to expand international science collaborations. Toward that end, Fogarty staff, and in particular, its mini-State Department, the Division of International Relations (formerly the International Coordination and Liaison Branch), contribute on behalf of the Center and NIH to a range of intergovernmental negotiations and countless informal discussions among potential partner agencies around the globe.

Working closely with the State Department and the Department of Health and Human Services, FIC has brokered hundreds of formal agreements, including Memoranda of Understanding (MOUs) and many more hundreds of less formal agreements, including Letters of Intent, with foreign agencies. Today, FIC administers on behalf of NIH over 90 formal agreements, including those with China on AIDS, with India and with Russia in broad areas of science and technology, and with Brazil and Mexico on a range of health priorities of mutual interest. These agreements provide a foundation upon which joint activities are built and supported by both sides.

THE FOGARTY CENTER IS ONE OF THE BEST INVESTMENTS THE AMERICAN TAXPAYER MAKES, LEVERAGING OTHER GOVERNMENT INVESTMENTS TO PAY MULTIPLE SCIENTIFIC DIVIDENDS. PERSONS TRAINED THROUGH CENTER GRANTS ACT AS SCIENTIFIC AMBASSADORS FOR IMPROVING THE QUALITY OF GLOBAL RESEARCH AND CONTRIBUTING TO GLOBAL HEALTH.

Ward Cates, President
Family Health International

The Center also serves as the hub of activity for NIH engagement with international organizations of the United Nations, including UNICEF, PAHO and the World Health Organization. One of FIC's chief roles in this area is to coordinate broad NIH input on health issues under debate in formal intergovernmental discussions, taking stock of major areas of interest of each IC and the NIH Director. Position papers produced through this process ensure that the best scientific evidence is made available to NIH and DHHS leadership as well as State Department officials involved in the negotiations. In recent years, FIC has begun to work with a broader array of international organizations to ensure that health research is considered fully in discussions on sustainable economic development and on environmental issues. The World Bank and the InterAmerican Development Bank, as examples, are partners with FIC and NIH in efforts to build research capacity in poor countries and to link health research efforts more closely with health care delivery programs.

FIC seizes the opportunity to forge international links occasioned by changes in the political climate, such as the end of the Cold War, or by the exigencies of global health needs, such as the AIDS pandemic. Indeed, the Center is often the driving force for expanding research boundaries, bringing experts together to explore new horizons for health or to address emerging threats. Thus in 1980, buoyed by the WHO declaration that same year that smallpox had been eradicated from the world, an international meeting was held at Stone House to discuss the feasibility of global eradication of polio, measles, yaws, and several other notorious infectious diseases. As the Center now elaborates initiatives that explore how health and environment interact with the economies of developing countries, it will reach out to provide results of these studies to ministers of finance, commerce, and development, as well as to health ministers.

The thread that ties all of FIC's initiatives together in the diplomatic arena is its singular focus on identifying the most effective mechanisms to support international cooperation that will lead to health benefits for U.S. and foreign partners. The routine behind-the-scenes efforts of FIC staff are critical in identifying and supporting such mechanisms, including overcoming obstacles in international cooperation. Day-to-day efforts to establish scientist-to-scientist dialogue, address visa issues and logistics issues for movement of reagents and equipment across borders, and work with counterparts at the State Department to ensure that NIH-supported foreign projects are brought to the attention of the Ambassador and scientific staff at U.S. embassies are all critical elements in a broad program of international research support. Working with one scientist—or one foreign delegation—at a time, FIC is unwavering in its support for the identification and fostering of excellence in international health research.

A sample among FIC achievements over the decades includes the following:

- Following initiatives of the State department in the 1970s and 1980s to set aside funds to support international cooperation with key countries, FIC worked on behalf of NIH to identify funds to support bilateral health research projects, and ultimately administered on behalf of NIH, several major State Department-funded research programs with governments such as India, Poland, and Hungary. The research supported through these programs led to new knowledge in key fields, most striking in infectious diseases and the neurosciences, the strengthening of research capacity abroad, and furthering U.S. ties with the cooperating nations. Additionally, FIC was able to broker a funding relationship between the National Cancer Institute and USAID in the early phase of development of the Middle East Cancer Consortium (MECC), arguably one of the most successful regional initiatives on health and research. USAID initial support for the MECC was critical in its launch.

- In 1986, President Ronald Reagan and India's Premier Rajiv Ghandi met to determine areas of cooperation to strengthen an already mature relationship. As formulated by FIC and NIAID scientists, President Reagan proposed a Vaccine Action Program (VAP), by which Indian and U.S. investigators would collaborate on vaccine research. The VAP initiative is particularly credited with accelerating development of a new vaccine against rotavirus—the cause of diarrhea so severe that it has long been one of the leading cause of death in infants and young children in the developing world.

- With the end of the Cold War, FIC launched an Eastern European Initiative to strengthen international collaborations and identify new opportunities to advance key areas of science. U.S. scientists responded enthusiastically to the new opportunities to work with counterparts in Hungary, Poland, and other countries, resulting in advances in understanding of risk factors and pathogenesis of chronic obstructive pulmonary disease and other chronic diseases in areas of high prevalence, due to unusual levels of environmental pollution. Over time, the program expanded to include all nations in low- and middle-income countries, and served as the model for other science-funding agency efforts in poorer countries, including those of the Howard Hughes Medical Institute.

- As U.S.-Mexico economic cooperation increased in the early 90's, FIC saw that much could be done to unite U.S. and Mexican scientists on scientific issues of common concern. Focusing initially on training young scientists, FIC led the way with its counterpart Mexican agency, CONACYT, in the development of the Pan American Fellowship Program. To date more than 30 young Mexican scientists have come to the NIH for post-doctoral training, supported both by CONACYT and NIH. The addition of reentry grants provided by the Mexican agency also provides an incentive for the newly trained scientists to return home. The program has now been replicated with Venezuela, Chile, Argentina, Brazil, Costa Rica, and the Pan American Health Organization, on behalf of the poorer countries of the region.

- Recognizing that the collapse of the Argentinean economy threatened the survival of its highly productive health research system, FIC organized a pragmatic response from NIH. This included support of Argentinean post-doctoral trainees through the NIH intramural visiting program, extending eligibility for the Fogarty re-entry grant program to Argentinean trainees in the U.S., and lab-to-lab collaborations, which could also assist in supplying reagents and surplused equipment. Through visits to key labs and communications with Argentinean scientists, FIC has ensured the Argentinean scientific community that it is neither isolated nor forgotten.

- In the mid-90's, as the U.S. awareness of the threats posed by new and emerging infectious diseases increased, FIC and NIAID initiated and led a trans-NIH group to explore research gaps and opportunities. When the White House established a cross-government group to examine the same issues, the NIH was well prepared to contribute to the broader U.S. effort. As policies were developed and implemented, support for research and related training on new and emerging diseases was included among the highest priorities. In other forums, such as preparatory meetings for G8 Summits, annual deliberations of working groups under the U.S.-European Union Transatlantic Agenda, and the U.S.-Japan Common Agenda, FIC, working closely with NIAID, promoted research on emerging infectious diseases among its highest priorities for new intergovernmental cooperative efforts.

FIC'S INVESTMENT IN DEVELOPING THE CAPACITY OF SCIENTISTS IN SOUTH AFRICA HAS BEEN INVALUABLE IN A COUNTRY EXPERIENCING ONE OF THE WORST AIDS EPIDEMICS IN THE WORLD. IT IS A MODEL OF HOW TO MOVE A DEVELOPING COUNTRY BEYOND SERVING AS A FIELD SITE TO BECOMING A FULL RESEARCH PARTNER CONTRIBUTING TO GLOBAL SOLUTIONS TO THE AIDS EPIDEMIC.

Salim S. Abdool Karim
University of Natal, Durban, South Africa

BIOPROSPECTING: A BETTER WAY IN SEARCH OF NATURE'S TREASURES

A century ago doctors had only a handful of drugs to treat disease—morphine, quinine, digitalis, aspirin—derived respectively from the opium poppy, cinchona bark, foxglove, and willow bark—nature's gifts to the medical armamentarium. Not much was added to the doctor's black bag until after World War I when the chemical synthesis of "magic bullets" to treat infection, and later, the discovery of penicillin from a mold, ushered in the antibiotic era. Today, approximately 50 percent of the several thousand prescription and over-the-counter drugs available are synthesized or materially derived from plants, animals, or microorganisms found in the wild. Unfortunately the world's wild places are rapidly dwindling. The global population explosion has turned virgin lands and forests into settlements and sprawls, while agricultural development, industry, mining, transportation, and commerce have not only changed the face of the landscape and resulted in the loss of untold numbers of species of flora and fauna—at a rate of a quarter of one percent a year of all species according to some experts—but also affected the quality of the atmosphere, with all that that portends in effects on weather, climate, and health.

Needless to say development has brought advances in the standard of living for many, and added quality as well as length to the average life span of many of the world's peoples. But there is a *better* way to achieve development: It is by

promoting sustainable patterns of growth so that 1) earth's biodiversity can be preserved, 2) species in natural habitats can be studied for what they may contribute to human and animal health and agriculture, and 3) local communities and the larger economy of developing countries can profit from research and training to build and conserve their natural resources. Such a win-win situation was envisioned at an NIH conference organized by the Fogarty Center in 1991 in collaboration with other parts of the NIH, the National Science Foundation, and the U.S. Agency for International Development. A year later the Fogarty Center, with five NIH partners[1], the NSF, and USAID launched a program of **International Cooperative Biodiversity Groups (ICBG)**. Grant applicants were invited to form international bioprospecting teams led by an investigator either in the U.S. or in a developing country with habitats of interest. The goals could include surveying, collecting, and testing plant, insect, or fungal specimens of potential therapeutic interest, while simultaneously promoting conservation and sustainable use of these natural resources. Five awards were made in 1993 and 1994 to multidisciplinary teams from universities, pharmaceutical firms, foundations, environmental organizations, and museums, with three new projects added over the decade. Field studies ranged from sites in Panama, Peru, Mexico, Costa Rica, Suriname, Chile, and Argentina in the New World, to Madagascar, Cameroon, and Nigeria in Africa, and Laos and Vietnam in Asia. For the current (third) round of competitive awards, investigators have been invited to spread the bioprospecting net wider to include marine organisms as well as unstudied microorganisms in soil. Significantly, applicants are also urged to develop strategies for compiling a centralized data base that would consolidate key findings from all the programs, with public and restricted access to balance public and proprietary interests.

ACCOMPLISHMENTS

All ICBG programs have shared medicinal goals, such as seeking new therapies for malaria, cancer, heart disease, AIDS, TB, and other infectious diseases; a few have included studies related to veterinary medicine and pest control. The range and variety of projects have been extensive, as have been the gains in knowledge, research capacity building, and rewards for the cooperating partners at home and abroad:

- Over 250 novel bioactive compounds discovered.
- 12 compounds now identified as promising agents for treating malaria, leishmaniasis, tuberculosis, HIV, bacteria, and mental disorders. Examples include a potentially important anti-tubercular drug derived from a brown alga found in Chile and an anti-leishmaniasis and other anti-trypanosome agents from Nigerian plants.
- New species of plants, fungi, and insects identified.
- 12 countries now have increased laboratory and field research capacity.
- 4,000 people trained in technical and social science techniques. Supplies and materials for preserving and storing specimens and the construction of greenhouses and field stations have strengthened infrastructure in the U.S. and abroad.
- New and enhanced local databases on biodiversity distribution.
- Publications in chemistry, biodiversity, and policy journals.
- Contributions to the establishment and strenghtening of biodiversity reserves. [Initiatives on establishing biodiversity reserves stimulated.]
- Investments leveraged from corporations, foundations, universities, and government sources.
- Socioeconomic status of local communities improved.
- New models of intellectual property rights and benefits sharing developed.
- National policies on bioprospecting informed and advised.

Overall, the success of the ICBG programs has provided a model of collaborative international research that demonstrates that projects involving multiple government, private, and academic partners can work to the benefit of all parties. The rich and varied experience of the researchers themselves also serves as a valuable resource to guide future governmental research and conservation policies. Indeed, each of the ICBG programs established contractual arrangements and benefit-sharing principles at the outset of the collaboration to ensure that the rights of source countries and traditional groups would be protected. The principles involved—of conservation, sustainable use, and equitable sharing of benefits for commercial use—are the same as those adopted in the UN Convention on Biological Diversity that emerged from the United Nations conference in Rio de Janeiro in 1992 – the year that the Fogarty Center initiated the ICBG program.

1 The National Cancer Institute, National Institute of Allergy and Infectious Diseases, National Heart, Lung and Blood Institute, National Institute of Mental Health, and National Institute on Drug Abuse

BUILDING THE HOUSE OF THE FUTURE

With the turn of the century the Fogarty Center has embarked on an ambitious program to build on the foundation of its cross-cutting programs in genetics, informatics, clinical research, and bioethics. The intent of this 21st century agenda is to equip low- and middle-income countries with knowledge about the root causes of the diseases that are now prevalent or endemic in their countries and what changes they may expect in the future. The "root" studies as well as forecasts of patterns-of-diseases-to-come are not restricted to the developing world, but are global in nature, and they carry with them the admonition to act now. Using the findings from such research, a nation's governing bodies can make informed health policy decisions and put in place cost-effective programs to reduce the burden of disease and enhance public health and safety. The benefits to be gained are not only improvements in health and well-being, but in the strengthening of stable and productive societies.

ECONOMY AND ECOLOGY

Knowledge about the underlying causes of disease in individuals and in populations depends on an understanding of the several variables defined as the determinants of health and how they interact. These variables include biological characteristics, the environment, sociocultural factors, behavior, and systems of health care. Two of FIC's new programs are looking specifically at how the interactions of selected determinants affect not just the health of an individual, but the wealth of society—its economy. In the case of the International Studies on Health and Economic Development (**ISHED**) program, researchers are studying some of the very issues raised by John Fogarty 40 years ago. He observed that the productivity of the labor force, and in turn the economy and political stability of a country, falter when the majority of its people are in poor health. The truth of that observation is only too apparent today in the sub-Saharan countries devastated by HIV/AIDS.

The ISHED program emphasizes the need for longitudinal databases of populations to track the relationship between health variables and economic development. The research grant program, begun in 2000, has made six full five-year awards and five three-year planning awards to grantees poised to answer such questions as: How does malnutrition in infancy affect school performance and future earnings? How does health status over the lifespan affect the kinds of work people do, how much they earn, and what they buy or save? What is the impact of malaria, tuberculosis, and HIV/AIDS on agricultural labor, small business, and other economic development in various parts of Africa? The intent is not only to collect impact data, but also to test whether interventions, e.g., programs to enhance prenatal and early childhood nutrition, can make a difference in adult achievements and well-being, and ultimately in the nation's economy.

In 2002 FIC considered an additional determinant in the study of health and economic development: changes in the environment of a developing country. The Health, Environment and Economic Development (**HEED**) program is designed to support pilot or developmental studies to probe how environmental changes, primarily due to human alterations, affect health and economic development. A dramatic example of a human behavior/environmental event with long-lasting health and economic consequences was the 1986 explosion of the nuclear reactor at Chernobyl, Ukraine, which released 30 to 40 times the amount of radioactivity of the bombs dropped on Hiroshima and Nagasaki. Entire cities and settlements in Ukraine, Russia, and Belarus had to be abandoned, and there may yet be as many as 3 million people living in contaminated areas, at high risk for thyroid cancer and other deadly cancers and diseases that have already taken a huge toll.

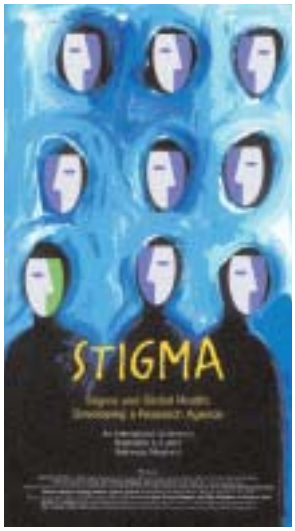
A third initiative that looks at the complex interactions among health determinants is studying when and how outbreaks of infectious disease occur, and how this knowledge can be used to prevent or identify a future epidemic at the earliest stages. Grantees conducting research under the **Ecology of Infectious Diseases** program, begun in 2000, look at natural events, such as changes in climate and the environment, as well as the impact of human behavior, that together may alter the local ecology to create a niche for the emergence or reemergence of pathogens and vectors of infectious disease. FIC is leading this initiative in partnership with NIAID, NIEHS, and the National Science Foundation. Awards have been made to investigators at 12 U.S. universities, who are collaborating in global research projects that include studies of environmental determinants of malaria in Belize, the ecology of the encephalitis virus in the southeastern United States, studies of bat colonies in Colorado (as vectors of rabies), and a number of animal studies, including the effects of changing land use on the dynamics of prion disease in wildlife.

EPIDEMICS AND BIOTERRORISM

FIC scientists in a new **Division of International Epidemiology and Population Studies (EPS)** are studying the ecology of infectious diseases using computer programs to model an epidemic. Beginning with modeling work on vaccine preventable diseases, malaria, and global cycles of influenza transmission, EPS was in a position to quickly model potential scenarios and develop tools to help policy-makers plan and respond to a potential bioweapon attack. Since then the EPS group has been the hub of a modeling effort, including both government and academic scientists, assisting the Department of Health and Human Services, the National Science Foundation, the Department of Defense, National security agencies, and the international community, to identify research gaps and better address critical questions that might occur in the event of rapidly disseminating infectious agents. Most recently, it has developed a model to address the role of international transportation networks in the potential spread of SARS. This work has demonstrated the value of a small group focused on the epidemiology of infectious diseases of global epidemic potential, and EPS is expected to continue to grow and develop to meet the needs.

STIGMA AND GLOBAL HEALTH

An International Conference on Stigma and Global Health organized by the Fogarty Center in September 2001 called attention to yet another negative influence on health: stigma. Patients with diseases or disorders that a given society stigmatizes—for whatever reasons—can experience a worsening of signs and symptoms or be severely abused—even leading to death. Indeed, as a sociocultural determinant of health, stigma is surely one of the highest risk factors for making a serious disease worse. The conference provided numerous examples in both developed and developing countries of how stigma operates in relation to HIV/AIDS, epilepsy, leprosy, mental illness, birth defects, alcoholism, drug abuse, and sexual abuse and violence—examples chosen to represent major categories of stigmatized diseases and disorders that lead societies to punish patients and their families and friends. The punishment can take the form of overt physical and mental abuse, isolation, refusal to treat, and legal proscriptions—in sum, a denial of fundamental human rights. Because the consequences of stigma are so severe, patients themselves often deny symptoms or avoid seeking treatment, risking a further exacerbation or progression of disease to a point of no return. As with many other FIC-organized meetings, the conference was a turning point—the stimulus to move beyond the stage of talking about a problem to doing something about it. The recommendations attendees developed for new research on stigma: how and why it develops, what epidemiology research can tell us about its prevalence, what can be done to prevent or reverse the effects of stigma, have now been incorporated into a Request for



The FIC conference on Stigma and Global Health called attention to the negative influence of stigma on health.

Applications for a new **Stigma and Global Health** research grant program, co-funded with many NIH partners, with awards to be made in late 2003.

DISEASE CONTROL PRIORITIES IN DEVELOPING COUNTRIES

Human behavior, whether in the form of stigmatizing disease, or in effecting environmental and ecological changes that have negative consequences on health, is, as noted, a part of the larger set of factors that determine the patterns of health and disease in individuals and communities. Now a major effort is underway to assess and update epidemiologic data and clinical evidence on disease and risk factors—negative determinants of health—and balance that information with the positive life-saving and life-extending interventions generated in recent years by biomedical and behavioral research, to predict future patterns of disease and prioritize interventions in developing countries. This three-year **Disease Control Priorities Project** (**DCPP**) begun in September 2002, is a joint effort of the Fogarty Center, the World Bank and WHO, funded in part by a $3.5 million grant from the Bill & Melinda Gates Foundation. FIC is acting as the Project Secretariat, coordinating operations under the guidance of a global advisory board and a board of editors that includes leaders of FIC, PAHO, the World Bank, WHO, and universities in the U.S., Canada, and the U.K.

The aim of the project is to publish, in 2005, an expanded, updated second edition of the 1993 WHO publication, *Disease Control Priorities in Developing Countries*, a landmark volume which listed 25 health conditions for which priorities had been established, based on their public health significance and the cost-effectiveness of measures to prevent or manage them. The volume was published in tandem with *Investing in Health*, a 1993 World Development Report by the World Bank. The second edition (DCP2) will be generated from workshops, working papers, and draft chapters circulated to advisors and posted on the project web site, and their subsequent debate, discussion, and refinement. The draft papers have been elicited by the editors from world authorities. The prevalence and cost data used will reference the work of demographers, epidemiologists, economists, and other health scholars who calculate the burden of disease using the "DALYs" construct, which attempts to quantify the mortality (years of life lost) and years of morbidity experienced due to the consequences of specific conditions and risk factors. In turn, studies of methods of prevention and treatment will provide information on what may be the most cost-effective health measures to implement in resource-poor countries. Summary data will be provided for the world as well as for geographic regions, so that policymakers in developing countries can more readily adapt the information to their populations, developing their own set of priorities and programs of prevention and control. In a bold departure from the previous study, DCP2 will also assess the potential for new and expanded existing research to generate new tools for disease

control in the next decade. These assessments will help to guide resource allocations among nations with limited reserves but with research capacity and the will to address these global health priorities.

The first working paper, with the provocative title, *At Least One-Third of Poor Countries' Disease Burden is Due to Malnutrition*, appeared in March 2003. The authors have incorporated new studies and have honed their analysis to include the role of micronutrients (e.g., iron, iodine) to calculate the degree to which malnutrition contributes to morbidity and mortality, with particular reference to women of childbearing age and infant children. Because they confined their analysis to the effects of malnutrition on communicable diseases, they caution that their estimates are conservative.

I CREDIT THE FOGARTY INTERNATIONAL CENTER WITH DEVELOPING NIH SUPPORT FOR GLOBAL RESEARCH ON SOCIAL AND MENTAL HEALTH ISSUES, ENHANCING UNDERSTANDING OF WHY GLOBAL HEALTH REQUIRES THE INTEGRATION OF BIOMEDICAL SCIENCE, SOCIAL SCIENCE AND PUBLIC HEALTH APPROACHES.

Arthur Kleinman
Harvard University and Harvard Medical School

What makes the DCPP particularly compelling today is the extent to which disease priorities and risk factors have changed over the last decade. In 1990 deaths from HIV were in 31st place and now have moved to 4th place in the world. Perinatal deaths remain high in the developing world, but infant mortality has declined, as have the deaths from diarrheal diseases. Turning to risk factors for mortality, the data are pointing toward a convergence of developed and developing world on factors such as high blood pressure, high cholesterol, and tobacco use. By the year 2000 the 10 conditions with the highest DALYs for the world included depressive disorders and heart and cerebrovascular disease—all of which are predicted to worsen in the developing world, as will deaths from intentional and unintentional injuries.

Concern over the new patterns of disease and risk factors evolving in the developing world has prompted the Fogarty Center to mount two new programs to address these problems. The **International Tobacco and Health Research and Capacity Building Program**, is a research grant (RO1) program to enable developing countries to study the implications of tobacco use and develop interventions for tobacco cessation. In contrast to the control measures in place in the U.S. to discourage tobacco use, addiction is easily acquired in the developing world because cigarettes are cheap (many are smuggled across borders and so avoid paying tariffs and taxes); they can be bought one at a time; and there are no warning labels or proscriptions of sales to children. Furthermore, tobacco use in many countries is the cultural norm, with over half of adult males

smoking—including physicians. As women become freer to leave traditional roles in the home, it is expected that they, too, will swell the ranks of tobacco users.

The situation with regard to growing mental illness and neurological diseases in the developing world has been the impetus for the development of a second new collaborative research program, which addresses **Brain Disorders in the Developing World: Research Across the Lifespan**. FIC convened a panel of experts led by Nobel laureate Torsten Wiesel to advise the Center on the research needs and training opportunities in the area. These have now been spelled out in a Request for Applications for planning grants to initiate programs of research and capacity building in the developing world on brain disorders that range from the developmental disorders of childhood, such as cerebral palsy and epilepsy, the mental illnesses such as chronic depression and schizophrenia that emerge in adolescence and adulthood, and the debilitating and degenerative disorders associated with aging, such as stroke and dementing diseases.

These new programs are first steps. As the Disease Control Priorities Project matures, and as the Fogarty Center continues its avant garde leadership in identifying the issues and themes that will dominate the health agenda of the developing and developed world in the 21st century, more innovations in FIC plans and programs will follow. In so doing the Center strives to fulfill the dream enunciated by John E. Fogarty a generation ago: "I am personally of the conviction that through leadership in international research and research training activities, the United States can contribute in a particularly meaningful way to the solution of health problems specifically, and the cause of peace generally. I visualize the Center, associated with the great facilities of the National Institutes of Health and the National Library of Medicine, as representing the visible and tangible embodiment of the Nation's devotion to the use of science for peaceful purposes and the good of mankind."

DESPITE STUDIES OF DISEASE BURDEN THAT HIGHLIGHT THE ENORMOUS IMPACT OF MENTAL ILLNESS ON DEVELOPING AND DEVELOPED COUNTRIES ALIKE, STIGMA AND IGNORANCE HAVE INHIBITED BOTH SCIENTIFIC INVESTIGATION AND THE ADOPTION OF EFFECTIVE TREATMENTS. WITH ITS CONFERENCE ON STIGMA, ITS SUPPORT OF AN INSTITUTE OF MEDICINE STUDY ON BRAIN DISORDERS IN THE DEVELOPING WORLD, AND ITS COLLABORATION WITH NIMH, THE FOGARTY CENTER HAS MADE SIGNIFICANT CONTRIBUTIONS THAT WILL HELP TO TURN THE TIDE.

Steven Hyman, Provost
Harvard University

COMBATING MALARIA

The story of the birth of the Multilateral Initiative on Malaria (MIM) illustrates how FIC, with the support of the leadership at NIH, worked to overcome political and bureaucratic barriers to international cooperation to create an international consortium to combat one of the world's oldest and deadliest scourges—malaria.

NO ONE FUNDING AGENCY CAN RESOLVE THE HEALTH PROBLEMS ENDEMIC IN DEVELOPING COUNTRIES—BUT BRINGING AGENCIES TOGETHER TO FOCUS ON A MAJOR THREAT LIKE MALARIA CAN MAKE ALL THE DIFFERENCE.

Philip Schambra, FIC Director 1988-1998

The data on malaria are stark: From 300 to 500 million new infections or more occur every year with estimates ranging up to nearly 3 million deaths—the majority in young children in sub-Saharan Africa…ongoing problems of mosquito resistance to pesticides; parasite resistance to anti-malarial drugs… potential for malaria-carrying mosquitoes spreading to new areas as a result of global warming, changes in patterns of land use (road-building; deforestation) creating new mosquito breeding sites, and growing urbanization accompanied by weakened public health and environmental infrastructure…

…Not that there haven't been dedicated malaria researchers, clinicians, and health care workers over the years. Ever since Sir Ronald Ross' discovery in the late 1890s that it was not bad air (mal-aria) that caused deadly bouts of intense fever and malaise, but a mosquito-borne parasite, investigators have sought interventions to prevent or control malaria. The result has been a see-saw of successes and failures as vectors and pathogens succumbed, but then developed resistance to the intervention. To mount a major effort to combat malaria—especially to take advantage of the promise of genetics research and molecular technology—more would be needed. The impetus for creating that "more" came about through a series of meet-

ings organized by the Fogarty International Center at Stone House in the mid-1990s. The initial meeting was chaired by then FIC Director Philip Schambra, with the participation and support of then NIH Director Harold Varmus. The meeting brought together interested international parties to review results of a FIC study on the scope of biomedical research in Africa being supported by the British, French, and American governments. At a follow-up meeting in 1995 with the Americans and Europeans joined by African scientists, the group concluded that there could be major gains in health for African populations if national and international agencies could unite to target a specific disease area. The clear choice was malaria.

Not so clear was how to bring funding agencies and scientists together to determine the best way forward. FIC worked closely with the National Institute of Allergy and Infectious Disease, the National Library of Medicine and the NIH Director as well as with major international partners to plan an international conference on malaria ultimately held in January 1997 in Dakar, Senegal. This first Pan-African Conference on Malaria brought funding agency representatives together with malariologists from around the world to develop a research agenda, specifying needs and priorities in areas ranging from epidemiology and pathogenesis, to vaccines and vector control. This out-of-Africa meeting marked the birth of a new global anti-malaria program and gave it its name: the **Multilateral Initiative on Malaria (MIM).**

Traditional birth attendants in Cameroon receiving training in malaria in pregnancy.

The Dakar agenda established clear priorities for research, training, and research capacity building in sub-Saharan Africa. Furthermore, for each of the major areas of research, such as epidemiology or immunology, the working groups emphasized the need for trans-national networking and sharing of data, which, to assure comparability and reliability, would need to be collected using standardized research techniques and reagents. There remained knotty questions of how such an unprecedented global effort could be administered. Who would manage and dispense research funds supplied to MIM? Who would be responsible for coordination, communication, planning, and feedback to researchers and funding agencies? Resolution of these and other issues turned to an existing resource—and created new ones. The Geneva-based World Health Organization's Special Programme in Tropical Disease Research was well-positioned to be the repository for research funds and to conduct peer review of research proposals from African scientists; it became the research arm of MIM—**MIM/TDR**. To improve communication and access to information, the NIH National Library of Medicine developed **MIMCom**, and invested in creating a malaria research electronic network that would allow African researchers to communicate with each other and with malaria researchers around the world, and access medical literature using the Internet. To address the need for a standardized research and reagent resource, the National Institute of

Allergy and Infectious Diseases, the lead U.S. agency funding malaria research, organized a meeting in November 1997 that led to the creation of the Malaria Research and Reference Reagent Resource—**MR4**—in 1998. This arm of MIM, located at the American Type Culture Collection in Manassas, Virginia, develops and distributes standard research protocols and reagents and provides training free to MIM researchers in Africa and elsewhere around the world. Finally, Britain's Wellcome Trust[1] proposed that it support MIM by acting as **Secretariat**. For a term of two to three years it would be responsible for coordination and communication among MIM members, and for such activities as planning future Pan-African Malaria Conferences. So it was that by 1998—within a year of Dakar—the four limbs of MIM were in place and operational. A year later, the Wellcome Trust organized the second Pan-African Malaria Conference in Durban, South Africa, at which time Secretariat responsibilities passed to the Fogarty International Center, at the request of the African malaria community and with the concurrence of the MIM partners.

FIC AS SECRETARIAT

During its time as MIM Secretariat, FIC developed a work plan based on the input of African malaria researchers. The Secretariat organized workshops on insecticide resistance and on several less-studied areas, highlighting the need for research on malaria anemia, malaria in pregnancy, and malaria caused by *Plasmodium vivax*—the species of parasite estimated to cause over half the cases of malaria occurring outside Africa (where the dominant species is *Plasmodium falciparum*). FIC also held workshops to enhance African researchers' skills in writing grant applications and in presenting and publishing their research. For more mature investigators, the Secretariat offered programs in research management, with an eye to ensuring that as African nations build research infrastructure and develop trained malaria researchers, there will be a cadre of research administrators with the skills to guide research efforts wisely and well. The Center also developed a transparent and democratic procedure by which to identify future MIM Secretariat sites, including all stakeholders in the process.

FIC organized a symposium that emphasized the need for more reliable data on the epidemiology and impact of malaria. This "new look at the numbers" noted in particular the long-term burden of malaria in its effects on infant development and ultimately on the productivity and economic viability of malaria-endemic countries—themes echoed in several recent FIC research programs[2]. In the last year of its tenure, FIC organized the third and largest Pan-African Conference on Malaria, indeed the largest malaria conference ever anywhere in the world, working with the National Institute of Medical Research of Tanzania, the host nation. Over 1,200 attended the Arusha, Tanzania meeting in November 2002. Following a vote by the MIM partners, three Swedish institutions were elected to comprise the new

Secretariat: Stockholm University, the Karolinska Institute, and the Swedish Institute of Infectious Disease Control beginning in January 2003.

The Tanzania meeting served to tally the accomplishments of each of the four MIM components, counting the numbers of investigators trained, labs enhanced, and countries collaborating in research projects, both in Africa and between African and U.S. or European institutions. MIM noted the establishment of trans-African networks of multi-disciplinary research teams working in key areas: mapping risk of malaria; immunology and pathophysiology; vector biology and insecticide resistance; natural products and anti-malarial drug development; resistance of parasites to existing drugs; anti-malarial drug policy and chemotherapy; and malaria transmission intensity and mortality burden across Africa. Other research and training projects have been aimed at improving home management of malaria or enabling researchers to conduct molecular biology research on anti-malarial drug resistance. All have significantly addressed a critical need, increasing the number and capability of African researchers to contribute to the solution of the problems of Africa.

A GROWING GLOBAL CONSCIOUSNESS

It is gratifying to report that membership in MIM[3] has grown as have other anti-malarial efforts. FIC has complemented its MIM activities by establishing an international malaria research training program (IMRT), linking closely to malaria research projects in Africa funded by NIAID. Both the World Health Organization with its "Roll Back Malaria" program, and the United Nations Global Fund to Fight AIDS, TB and Malaria, are supporting activities aimed at applying research to improve care, treatment, and prevention of disease in the countries most impacted. Indeed, the WHO and UN programs could be said to follow the example of MIM by creating consortia of nations targeted to fight major global health problems. So, too, is the Medicines for Malaria Venture—a public-private partnership to develop and distribute anti-malarial drugs in poor countries. Adding to the prospects for significant gains in the fight against malaria has been the recent mapping and sequencing of the human genome and the genomes of the malaria-carrying *Anopheles* mosquito, as well as of the parasite *Plasmodium falciparum*—opening a world of opportunities for developing safe and effective vaccines, new drugs, and innovative vector control methods.

1 Initial members of MIM included NIH, the Wellcome Trust, the World Bank, the World Health Organization's African Regional Office (WHO/AFRO), the government of Norway, TDR, and the Rockefeller Foundation.

2 Examples include FIC's ISHED (International Studies on Health and Economic Development) and HEED (Health, Environment and Economic Development) programs.

3 Current MIM members include components of NIH (FIC, NIAID, NLM, NIEHS), WHO/AFRO, WHO/TDR, Roll Back Malaria (WHO), Rockefeller Foundation, the Government of Japan, the World Bank, USAID, Bayer Environmental Science (South Africa), Bill & Melinda Gates Foundation, Burroughs Wellcome Fund, Calouste Gulbenkian Foundation (Portugal), Danish International Development Agency, Federal Ministry of Education and Research (Germany), GlaxoSmithKline (Belgium), Howard Hughes Medical Institute, Malaria Foundation International (USA), Malaria Vaccine Initiative (USA), Medical Research Council (UK), Netherlands Organization for Scientific Research, Sanofi-Synthelabo (France), Swedish International Development Agency, Swiss Development Corporation, Syngenta (Zimbabwe), and Wellcome Trust (UK).

DOING MORE WITH LESS

"Doing more with less" could be the motto of Fogarty International Center, which has leveraged its modest budgets over the years through programs that attract collaborators at NIH and other government agencies, as well as organizations in the private sector. To be accurate, however, a grand concept for FIC was introduced in the Congress in 1958 by John E. Fogarty, Representative from Rhode Island, who envisioned the creation of a National Institute for International Health Research with an initial budget of $50 million. By the time it was established a decade later by Fogarty's friends on the Hill and President Lyndon Johnson to honor his memory, the year after his untimely death, the Center was a much more modest entity. Thus, while Daniel Flood, chairman of the House Health Appropriations Subcommittee at the time called the Center the Committee's "brainchild" and promised careful nurturance, instead of a $50 million appropriation the first year budget for FIC was $500,000. The major portion of these funds were used to renovate existing property on the NIH campus—the Peter family mansion that had been acquired by the government—and in planning for an additional building...

...which was never built. Instead, there was a modest $100,000 increase in the 1969 budget allowing renovations to the mansion to be completed and enabling the fledgling center to get two new programs off to a fine start by 1970. One program would enable FIC to hold a series of international conferences and seminars to address global issues; the other was the Scholars-in-Residence fellowship program that would bring renowned scientists to live and work at NIH for upwards of a year or more.

In 1970 FIC's budget increased sharply to $2,954,000 but only because funds for the programs that had been transferred to it from the previous Office of International Research were now included, where previously they had shown up elsewhere in the NIH appropriation. The budget increased again by $500,000 in 1971, the additional funds to be used for maintaining operations at the Gorgas Memorial Laboratory (GML) in Panama, which conducted research on tropical diseases. The Panama lab had come into existence in the late 1920's, named in honor of William Gorgas, the government physician and later U.S. Surgeon General, whose work to combat yellow fever during the building of the Panama Canal had done much to spare the lives of the canal workers. The Gorgas Laboratory operated

independently of FIC and NIH; Congress simply used the Fogarty Center appropriation as a means to fund the Lab, with incremental increases from time to time. The practice continued until 1988 when Congress transferred the sums for Gorgas to the National Institute of Allergy and Infectious Diseases and invited GML and others to compete for funds under a new program in tropical medicine within NIAID.

The Fogarty Center's budget continued to grow modestly over its first two decades, but by no means did this represent the Center's actual support for international research and research training. To determine that requires a reading between the lines, for the overall budget included support for the visa services run by FIC in behalf of the NIH, staff salaries, consultations and meetings in support of program development and other administrative costs. It is important as well to recognize that FIC spending on international research and training does not capture all of the expenditures for international activities at the NIH. In fact, each of the categorical institutes can and many do make international research awards in great excess of the amounts expended by FIC. Over the past several years that amount represented under 2% of the total NIH budget—a percentage that has remained relatively consistent over time until most recently. Of course, even that must be examined more closely, for these funds include the costs of supporting the visiting program of research trainees and research scientists from other nations who spend one or several years engaged in the intramural research programs of the institutes, and for research grants to developed country institutions in Canada, the UK, France and others. These aspects of research and training support abroad are among the unique attributes of the NIH, and why NIH is such a global resource. NIH in general, and FIC in particular, are the embodiment of the notion that science is inherently international and that the free and open exchange of information among scientists of the world is its essential nature, as Fogarty himself recognized.

It must be said that even at those modest amounts and percentages the Fogarty Center and NIH have been subject to critics from time to time who ask: Why should US tax dollars be spent abroad? Are we going to shortchange our own researchers? These sentiments have not entirely abated, especially when budgets are tight, but by the 1980s, when a new and deadly disease was sweeping the world, mindsets began to change. The advent of the AIDS pandemic made it clear that no country could go it alone, even one as wealthy and as well resourced as the United States. Threats to the health and stability of any one nation could threaten all, and all who traveled were at potential risk of exposure. The Fogarty Center took that message to heart with its first international research and training program for AIDS, which presciently was oriented towards training of scientists in affected developing countries, through collaborations with U.S. academic centers. Since then, FIC has devoted the great majority of its funding to support

research and training in low- and middle-income countries. In fact, academic centers in the U.S. value these programs because they contribute so much to building the relationships necessary to carry out collaborative research, and competition for FIC grants is strong and challenging.

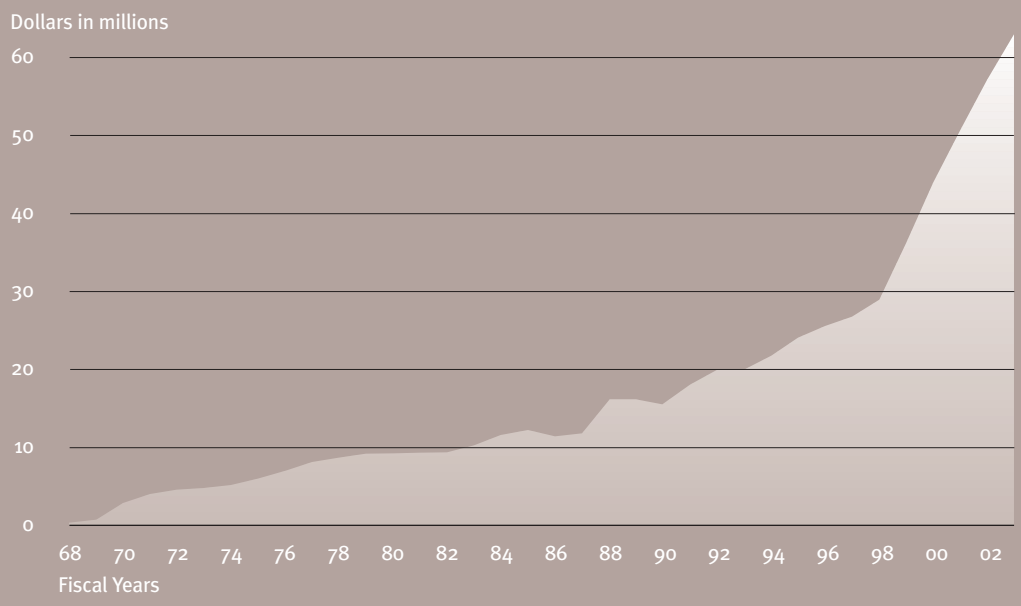
Remarkably, the initial and modest budget that FIC proposed for the AIDS International Training and Research program (generally referred to by the acronym AITRP) was increased by staff at the Office of Management and Budget (who review and make adjustments to the budget put forward by NIH), and was even further increased by Congress. Thus charting of the FIC budget reveals a distinct jump in FY 1988 because of the initiation of the AITRP, which continues to represent a significant percent of the Center's extramural budget.

More than that, the AIDS program made concrete an approach to global health issues that had been developing at the Fogarty Center for some time: the idea that the most productive use of the Center's staff and funding would be to focus on the developing world, beginning with programs to build research capacity. Initially this took the form of fellowships for foreign nationals to come to the U.S. for research training at a university awarded a FIC institutional training grant in specific targeted areas, such as AIDS. Later, the Fogarty Center developed a small grant program, which enabled U.S. researchers to apply for small collaborative research grants in partnership with non-U.S. investigators (originally $20,000 and now $32,000 per year) so that they could conduct research of mutual interest in the foreign country and generate pilot data for larger research grants they might later apply for. More recently, a regular research grant program was also initiated (employing the prototypical NIH investigator-initiated R01 grant mechanism), albeit focused on low- and middle-income country research priorities. Even more recently, trainees from low- and middle-income countries training at NIH or in academic centers under FIC training grants have been eligible to apply for "re-entry" RO1 grants, to return home and conduct research on major health problems. As these changes in directions for the Fogarty Center evolved in the 1990s, the old fellowship programs were phased out or modified, so that today, two types of awards—training grants to US universities focusing on selected global health issues, supplemented by a competitive small-grant research program for which returning trainees are eligible—and a regular research grant program, supplemented by the small collaborative grants program — now dominate the Fogarty Center budget.

PLANNING FOR THE FUTURE NOW

What is interesting is how broad and future-oriented the scope of research that FIC supports has become. Current programs continue to target infectious diseases like AIDS, tuberculosis, and malaria that are highly prevalent in the developing world, as well as emerging infectious diseases, increasingly taking an ecological, environmental and population biology approach to generating new insights into transmission and disease dynamics. The portfolio has also expanded to include studies of health and behavior in relation to population, occupational health, the environment, and economic development. Most recently, it had added a program of research on stigma and what can be done to ameliorate its destructive effects in association with a wide range of diseases and disorders. But it is in initiating programs that reflect the newest opportunities in science and what demographers and epidemiologists predict will be the major global health problems in both the developing and the developed world in coming decades that the Fogarty Center has been particularly noteworthy. These new programs focus on chronic diseases, genetics, diseases of aging, mental health, brain disorders—and as a major risk factor—initiation and cessation of tobacco use. As well, in each case FIC has been able to multiply the funds available via its own budget through partnerships across the NIH and beyond. A case in point is the recent announcement of an initiative to assess disease control priorities in developing countries. This joint project of FIC, the World Health Organization, and the World Bank is funded by a $3.5 million grant by the Bill & Melinda Gates Foundation that will lead to the publication of the second edition of *Disease Control Priorities in Developing Countries* in 2005.

FIC CONGRESSIONAL APPROPRIATIONS HISTORY 1968-2003



GLOSSARY

ATSDR	Agency for Toxic Substance and Disease Registry
CDC	Centers for Disease Control and Prevention
CIHR	Canadian Institutes of Health Research
CONACYT	Consejo Nacional de Ciencia y Technologia (Mexico)
NIA	National Institute on Aging
NIAID	National Institute of Allergy and Infectious Diseases
NIAMS	National Institute of Arthritis and Musculoskeletal and Skin Diseases
NCI	National Cancer Institute
NICHD	National Institute of Child Health and Human Development
NIDCR	National Institute of Dental and Craniofacial Research
NIEHS	National Institute of Environmental Health Sciences
NEI	National Eye Institute
NIGMS	National Institute of General Medical Sciences
NHLBI	National Heart, Lung and Blood Institute
NINDS	National Institute of Neurological Disorders and Stroke
NLM	National Library of Medicine
NHGRI	National Human Genome Research Institute
NINR	National Institute of Nursing Research
FIC	Fogarty International Center
NIMH	National Institute of Mental Health
NIAAA	National Institute of Alcohol Abuse and Alcoholism
NIDA	National Institute on Drug Abuse
NIOSH	National Institute for Occupational Safety and Health
NCCAM	National Center for Complementary and Alternative Medicine
NCMHD	National Center on Minority Health and Health Disparities
NSF	National Science Foundation
OAR	Office of AIDS Research
OBSSR	Office of Behavioral and Social Sciences Research
ODS	Office of Dietary Supplements
ORWH	Office of Research on Women's Health
USAID	United States Agency for International Development
USDA	United States Department of Agriculture
WHO	World Health Organization

FOGARTY INTERNATIONAL CENTER PROGRAMS & PARTNERS

TRAINING GRANTS

ABC Actions for Building Capacity: a FIC training component in an NIAID program: International Collaborations on Infectious Disease Research.

AITRP AIDS International Training and Research Program, with NCI, NIDCR, NIDA, NIMH, NHLBI, and NINR.

GIDRTP Global Infectious Disease Research Training Program (incorporates ITREID, IMTRP and TBTRP), with NIAID, NIDCR, and CDC.

IBECDA International Bioethics Education and Career Development Award, with NHLBI, NIAID, NIAMS, NICHD, NIDA, NIDCR, NIEHS, NIGMS, NINR, and NCCAM.

ICER International Centers for Excellence in Research, Clinical Research and Management Training award, with NIAID (supports training at FIC- and NIAID-supported sites in developing countries).

ICOHRTA-I International Clinical, Operational, and Health Services Research and Training Award, with NIMH, NIDA, NIA, NCCAM, and NIDCR.

ICOHRTA-II (AIDS/TB) International Clinical, Operational, and Health Services Research and Training Award for AIDS/TB, with NIAID, NIAAA, NCI, NICHD, NIDA, NIMH, NINDS, OAR, OBSRR, ORWH, and CDC.

ICGRTP International Collaborative Genetics Research Training Program, with NHGRI, NIMH, NIA, NIEHS, NIDA, NIAAA, NINDS, and WHO.

IMRT International Malaria Research Training Program (now incorporated into GIDRTP).

IMCHRT International Maternal and Child Health Research and Training Program, with NICHD and CDC.

ITREID International Training and Research Program in Emerging Infectious Diseases, with NIAID, NIDCR, NCMHD, and CDC (now incorporated into GIDRTP).

ITREOH International Training and Research Program in Environmental and Occupational Health, with NIEHS, NIOSH, CDC, and ATSDR.

ITRPH International Training and Research Program in Population and Health, with NICHD and NIA.

ITMI International Training in Medical Informatics, with NIAID and NLM.

MIRT Minority International Research Training Grant, with NCMHD.

TBITRP Tuberculosis International Training and Research Program, with NIAID and USAID (now incorporated into GIDRTP).

RESEARCH GRANT PROGRAMS

Brain Disorders in the Developing World: **Research Across the Lifespan** with NIA, NIAAA, NICHD, NIDA, NIEHS, NEI, NIMH, NINDS, ODS, and the Institute of Neurosciences, Mental Health and Addiction of the Canadian Institutes of Health Research and Consejo Nacional de Ciencia y Technologia (CONACYT) of Mexico.

Ecology of Infectious Diseases, with NIAID, NIEHS, and NSF.

FIRCA Fogarty International Research Collaboration Award (R03) (provides funds for infrastructure and travel for a foreign scientist collaborating with a U.S. investigator who holds an NIH grant).

AIDS-FIRCA HIV-AIDS and Related Illnesses Collaboration Award (U.S. scientists who have an eligible AIDS-related NIH grant may apply).

GRIP Global Health Research Initiative Program for New Foreign Investigators. A re-entry R01grant program providing research support and partial salary to an FIC-trained foreign scientist returning home to conduct research.

HEED Health, Environment and Economic Development Program, with NIEHS, NICHD, NIDA, OBSRR, and the U.S. Geological Survey.

ICBG International Cooperative Biodiversity Groups, with NCI, NIAID, NHLBI, NIMH, NIDA, NSF, USAID, and USDA Foreign Agricultural Service.

ISHED International Studies in Health and Economic Development, with NIA, NICHD, NIMH, OBSSR, and the Global Network of the World Bank.

International Tobacco and Health Research and Capacity Building Program, with NCI, NHLBI, NICHD, NIDA, NINR, CDC, CIHR, and WHO-Tobacco Free Initiative.

Stigma and Global Health Research Program, with NCMHD, NHGRI, NIAAA, NIAID, NIDCR, NIDA, NIMH, NINDS, OAR, OBSSR, and ORWH.

IRSDA International Research Scientist Development Award for U.S. Postdoctoral Scientists—a fellowship program providing mentored research at a foreign research institution in collaboration with a U.S. research institution.

FIC DOES ITS WORK QUIETLY AND WITHOUT FANFARE. WHEN IT INVESTS IN THE STRENGTHENING OF AN INSTITUTION, IT DOES SO STRATEGICALLY, WITH A RANGE OF SHORT, MEDIUM AND LONGER TRAINING PROGRAMS. IT IS THE BEST-KEPT SECRET AT NIH.

Michael Merson, Dean
Yale University School of Public Health

May 2003