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Medical Research Centers in Mali and Uganda: Overcoming Obstacles to Building Scientific Capacity and Promoting Global Health

Harold Varmus

IN 2012, when the Fulbright Commission asked me to give a series of lectures in the United Kingdom on the topic of diplomacy, I proposed to describe three important, ambitious, and successful international initiatives in medicine and related science undertaken by the United States. I delivered a lecture on each of these three initiatives at three different universities in the UK early in May 2013. All three programs were focused largely or exclusively in Africa, but they were created in different decades (the late 1960s, the early 1990s, the early 2000s), addressed different diseases (cancer, malaria, and HIV/AIDS), operated mostly in different parts of Africa, and were (or are now) threatened by different kinds of political difficulties in their host countries or the United States.

While all three initiatives were built on the desire to make scientific advances, perform professional training, and deliver prevention and treatment of disease, the emphasis was different in each case. The two projects discussed in this essay (with an accompanying slideshow)—the Uganda Cancer Institute (UCI) in Kampala and the Malaria Research

Harold Varmus was awarded the 1989 Nobel Prize in Physiology or Medicine for his studies at the University of California Medical School, San Francisco, on the origins of retroviral oncogenes. He received his first scientific training at the National Institutes of Health (NIH) and returned as the director of NIH from 1993 to 1999. After ten years as president of the Memorial Sloan-Kettering Cancer Center in New York, he was appointed director of the National Cancer Institute in 2010. He was chairman of the Bill and Melinda Gates Foundation Grand Challenges in Global Health and co-chaired the Institute of Medicine’s report “The U.S. Commitment to Global Health” (2009).

and Training Center (MRTC) in Bamako, Mali—arose from ambitions to study a prevalent disease, to train Africans to contribute to research on that disease, and to build research capacity in a developing country. The third project (discussed in an article published in *Science & Diplomacy* in December 2013¹), the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), was conceived with the goal of ameliorating a pandemic using new drugs and other strategies developed through medical research to prevent and treat HIV infection and AIDS.

To explore the origins and subsequent histories of each of the three enterprises, I interviewed several people who had participated in pivotal events. In the two essays that describe the initiatives, I have also tried to draw from these stories some lessons about diplomacy conducted through medical science.

In examining all three instances, I have been impressed by the profound differences between parts of the world with respect to their potential to improve health through research and modern medical care. Africa, in particular, is woefully deficient in medical care and in research facilities, yet over-endowed with disease, as measured by many indicators illustrated in the slide show linked to the first essay. Addressing these discrepancies with well-run programs is at the heart of the two essays.

The International Reach of the Health Sciences

Medical research is essentially international in character and application. Biological systems operate in accord with universal laws, and disease occurs when those systems fail in response to genetic and environmental factors. The factors may vary around the globe but have effects that should be predictable wherever they occur. Strategies for prevention and treatment of illnesses are built on such knowledge; these strategies are potentially applicable throughout the world. Since better health, longer life, and the economic benefits of health are universal aspirations, the sciences that inform prevention and care are widely embraced. The mundane but important fact that most medical science is now conducted and communicated in English further promotes international activities to pursue it.

For these reasons and others, efforts to support medical sciences and improve prevention and treatment of disease are desirable elements in relationships between countries. These efforts are especially attractive as components of diplomacy when they involve people working together, not simply rich countries transferring funds to—or constructing facilities for—poor countries. Of course, international collaborations can, and often do, involve scientists and health workers from countries of similar, as well as different, economic status. In either case, they represent participatory diplomacy, can help to sustain or improve international relationships, and may be considered an especially attractive form of what has been called “soft power.”

Still, such relationships are not easy to initiate and maintain, especially when they must contend with major differences in culture, wealth, politics, and scientific expertise. Further, if they are to succeed, they usually require substantial

funds, political commitment to the collaborative effort, good governance in the participating countries, commonalities of scientific interest, mutual participation, persistence, and respect.²

How the United States has Helped to Establish Centers for Medical Science in Africa

The UCI and the MRTC were founded in collaboration with the U.S. government—at different times, in different parts of Africa, and in different ways—by seizing opportunities to improve a poor country’s potential to combat a major disease: cancer or malaria. In both instances, the creation of the center depended on constellations of remarkable individuals—Africans, Europeans, and Americans—willing to engage in a difficult enterprise at a propitious time, and both depended on the consensual efforts of well-intended academic and governmental institutions. Further, both efforts were built on the presumptions that there are advantages to studying disease in its natural setting and to developing research capacity—the personnel and facilities that can make medical research an activity integral and useful to countries with limited resources. Additionally, each of these enterprises has been threatened by political upheavals and their profound effects on the culture of the host country. The following stories are about the unexpected circumstances that created the centers and about the means that allowed them to survive and (in the case of the UCI) be reborn.

Burkitt Lymphoma and the Uganda Cancer Institute

Significant projects generally begin with a perceived need and with people who inspire others to get the job done. The UCI emerged nearly directly from the work of Denis Burkitt, an energetic, curious, and perceptive Irish surgeon working in East Africa in the mid-twentieth century. In 1957, while at Mulago Hospital at Kampala’s Makerere University, Burkitt described for the first time an unusual, large tumor of the lymph nodes that generally arises in the jaws of young children and came to be known as Burkitt Lymphoma (BL).^{3, 4} But Burkitt did not merely observe this disease and recognize its relatively frequent occurrence among East African children.

Therapy: First, he showed that BL responds swiftly and dramatically to chemotherapy—even to a single dose of a single drug known as cyclophosphamide (Cytoxan). This was one of the first effective uses of chemotherapy for the treatment and sometimes cure of a lethal cancer. Its success helped to promote the growing worldwide search for chemotherapies for a variety of cancers, especially those affecting the blood system in children. Successful treatment of BL attracted the interest of many investigators, including the leaders of the U.S. National Cancer

Institute (NCI), which was actively supporting the development of chemotherapy in the 1960s.

Epidemiology: Second, Burkitt carried out an extensive survey of the incidence of the disease in Africa on what he called “lymphoma safaris.” On those trips throughout Africa, Burkitt found that BL appeared most frequently in moist, hot areas with high rates of malaria; this relationship to a common infectious disease is still not understood. This too attracted the interest of many investigators, especially epidemiologists looking for environmental factors that increase the risk of cancers and other diseases.

Causation: Third, Burkitt wrote and lectured widely about this unusual cancer, attracting the attention of many basic scientists, including those interested in the mechanisms of malignant change in cell behavior. One especially fruitful line of investigation began with Burkitt’s provision of tumor samples to Anthony Epstein at Middlesex Hospital in London after Burkitt lectured there in 1961. Epstein and his colleagues were able to grow the cells in tissue culture and observed under the electron microscope that the cells produced virus particles. These particles proved to constitute a novel herpes virus, now called the Epstein-Barr Virus (EBV).^{5, 6} Soon thereafter, Gertrude and Werner Henle in Philadelphia produced antibodies against EBV and then used immunological tests to show that the virus was the cause of infectious mononucleosis, a common disease in many parts of the world.⁷ Moreover, during succeeding decades, others found that EBV is associated with other important cancers, including gastric cancer, Hodgkin Disease, and nasopharyngeal carcinoma, a common cancer in Southeast Asia.^{8, 9, 10} In addition, other herpes viruses were later implicated in other kinds of cancers, especially Kaposi’s sarcoma, a common malignancy in patients with HIV/AIDS.

These remarkable developments emerging from work that began in Uganda—especially the infectious origins of BL and the dramatic response of BL tumors to chemotherapy—attracted wide interest in the cancer research community in the 1960s. Consequently, a Lymphoma Treatment Center was soon established at Mulago Hospital where Burkitt had done much of his work.

NCI Takes an Interest in Burkitt Lymphoma in Uganda

Leaders of the NCI were excited by the therapeutic responses of BL to chemotherapy, especially in view of NCI’s extensive efforts to improve treatment of childhood leukemias—diseases related to other cancers of the blood systems, such as BL and other lymphomas. Two of the NCI’s senior scientists, Gordon Zubrod and Paul Carbone, conveyed their interest to one of the NCI’s trainees, a physician-scientist named John Ziegler, and they proposed that he go to Uganda to study BL.

This proved to be a propitious suggestion, addressed to the right person at the right time. During his clinical training in New York City, Ziegler reported one of the first American cases of BL and met some of the oncologists developing chemotherapies for childhood leukemia.¹¹ Like many young physicians during the Vietnam War era, he was able to satisfy the requirements of the military draft by securing a research position at the U.S. National Institutes of Health (NIH) as an officer in the Public Health Service. After a few unproductive starts in laboratories at the NCI, he met Paul Carbone, learned more about BL and other cancers in Africa, attended a meeting on these subjects in Nairobi in 1967, and then arrived in Kampala to work with African and European (mainly Scottish) physicians at Makerere University.

Burkitt returned to the UK in the late 1960s, but interest in the childhood lymphoma he had discovered remained high among the Ugandan, European, and American physicians at Makerere. The NCI began to supply funds, staff, and vehicles—the underpinnings of the new UCI—to support its research objectives. The NCI enjoyed good relations with Ugandan doctors, Makerere medical students, and the Uganda Health Ministry, helping to launch the UCI officially without appreciable difficulty. Through Ziegler's active engagement with the UCI's work and his NCI connections, he became its first leader.

The Effects of Ugandan Politics on the UCI

Despite the resilient rapport between resident Ugandan hosts and medical scientists visiting from Europe and the United States, the UCI and other components of Makerere University were dependent on both the largesse of Uganda's leaders and on the cultural climate created by their policies. At the time of the founding of the UCI, Uganda was led by Milton Obote, the country was relatively peaceful, and the newly formed center was highly regarded by the Ugandan government. (For instance, Pope Paul VI was taken to view the medical campus during his visit to Uganda in August 1968.) However, Obote was from northern Uganda and not well liked in the south (including Kampala).

Early in 1971, when Obote was out of the country, General Idi Amin seized power and set up an infamous reign of terror. He and his entourage ridiculed the British (who had brought many elements of governance and education to Uganda), chased out the Asians (who composed much of the business community), brought back the body of an earlier Ugandan king (reigniting tribal rivalries), hired hoodlums to oversee checkpoints on travel routes (terrorizing citizens and visitors alike), and tolerated or encouraged the killing of some foreigners.

By 1972, these practices—and urgings from his mentors at the NCI—convinced Ziegler to leave the country. Subsequently, funds from the NCI dwindled, even though the UCI remained intact and continued to conduct some clinical trials with

the NCI. These were overseen by two Ugandan physicians, Charles Olweny and Edward Mbidde, who took the reins after Ziegler's departure.

Ugandan Leadership at the UCI

A central feature of the UCI—and a strong determinant of its success—has been the excellence of its Ugandan physician-leaders, especially in times of political upheaval.

Olweny superbly exemplifies those qualities. An elegant and highly cultured man, he was raised in a small Ugandan town near the Kenyan border, then trained at Makerere University Medical School. He remained to participate in Makerere's Masters in Medicine program—a model for training physician-scientists, started by a U.S. physician who previously headed its department of medicine. After writing a thesis on typhoid fever and realizing there was not much left to discover about this well-studied disease, Olweny sought advice from Ziegler, who suggested that he attempt to treat Hodgkin Disease (another form of lymphoma) in adults, not just children.

In 1971 Olweny's new interest in cancer led to his first published work and a chance to meet Zubrod and Carbone at an international meeting. The two NCI leaders were impressed and arranged further training for him with immunologist George Klein at Sweden's Karolinska Institute and then additional studies at the NCI. When he returned to Makerere in 1973, Olweny found that Ziegler had departed and the medical school and UCI were in turmoil. Despite his relative youth, he was persuaded to become the leader of the UCI as funds from the NCI continued to decline.

It is difficult in retrospect to gauge the effects on the UCI of the political and financial instability created by President Amin, but I was able to read at least one formal account. In 1974, a British pathologist, M. S. R. Hutt visited the UCI on behalf of the NCI to evaluate the relationship between the UCI and the NCI and the status of collaborative projects. He reported that co-sponsored clinical trials were continuing in capable hands and reasonable facilities. However, the report also contained ominous references to "the problems" in Kampala, the "completely unpredictable" future, and the worsening economy.¹²

NCI terminated its support for the UCI in 1975, but Olweny was able to obtain some funds for drugs and salaries from the Ugandan Health Ministry for work on BL and Hodgkin Disease. President Amin supported the UCI as a source of pride, something to show visitors, such as teams from the World Health Organization and the Organization of African Unity. But in 1977 rumors of Olweny's death were circulating, and his requests to travel were denied. Things did not improve with the return of Obote to power in 1979. Nevertheless, Olweny remained loyally at his UCI post until 1982, when he departed to pursue a distinguished career in Zimbabwe,

Australia, and Canada, before his recent return to a politically welcoming Uganda under President Yoweri Museveni.

Survival and Recovery of the UCI

Throughout the period of uncertainty after the departure of Olweny in 1982, the UCI survived under the direction of Edward Mbidde, another distinguished Ugandan physician-scientist, who remains in Kampala today as head of a center for infectious disease research. The situation improved with the ascendance of Yoweri Museveni to the Ugandan presidency in 1986. The political atmosphere stabilized, President Museveni was attentive to national development and health, and he became known especially for his actions against AIDS, which was causing, among other difficulties, a high degree of military absenteeism.

In this improved environment, several American medical schools became engaged with Makerere University, still recognized as a source of talent in African medical science. Case Western and Johns Hopkins Universities and the University of California, San Francisco (UCSF), were among the leading schools that sent representatives and provided financial assistance in the late 1980s and early 1990s.

Prominent among those representatives were Susan Desmond-Hellmann (now the chancellor at UCSF) and her husband Nick Hellmann. Desmond-Hellman had heard about UCI around 1988 from Ziegler, who was by then on the faculty at UCSF. She and her husband arrived at Makerere with fellowships from the Rockefeller Foundation, planning to study immunology and HIV transmission. However, they found that the laboratories (and living facilities) were devoid of electricity and plumbing, unsuited for modern scientific work (or life). They helped to get both domestic and laboratory conditions into working order over the next year or two. Eventually, they were able to study lymphomas and Kaposi's sarcoma in AIDS patients, a step toward reviving the UCI in a fashion that took advantage of the determination of Uganda's leaders to confront the AIDS epidemic.

Even in this uncertain period, the UCI, its leaders, and its history were effective tools for recruiting talented Ugandans, especially graduates of the Makerere University Medical School, into the health sciences. Sam Mbulaiteye offers a compelling example of such recruitment. Now a senior investigator in the NCI's Division of Cancer Epidemiology and Genetics, he has been organizing studies of BL, Kaposi's sarcoma, and other cancers in East Africa for over a decade through his position at the NCI.

The Modern Situation (2002 to Present)

The most recent chapter is a happier one—a period of growth at the UCI, fostered in large part by an active and fruitful collaboration with the Fred Hutchinson Cancer Research Center (FHCRC) in Seattle, Washington. In 2002, Larry Corey, a

senior investigator at the FHCRC, and Corey Casper, then working as a fellow with Corey, visited Kampala while looking for places to study immunological responses to human cancer viruses, such as EBV and human hepatitis B virus. Excited by the quality of medical care and the enthusiasm of students at Makerere University, they began to develop research partnerships with members of the UCI.

At about this time, Makerere was cultivating the person who was to become the new UCI leader: Jackson Orem, another graduate of Makerere University Medical School who had been directed to oncology and the UCI by Ziegler. Orem, Casper, and Corey forged a close relationship based on their common interests in virus-induced cancers—especially BL, Kaposi’s sarcoma, and hepatoma, all of which are common in East Africa, accounting for over half of all diagnosed cancers.

To pursue these interests, the FHCRC has assumed major responsibilities at the UCI by improving existing facilities and helping to build new ones; importing staff from Seattle and hiring more Africans; acquiring an attractive nearby residence for international visitors to the UCI; developing training programs for FHCRC staff who travel to Kampala and for UCI staff who come to Seattle for nine months or more; and signing a memorandum of understanding in 2008 to make the relationship official. At an October 2011 groundbreaking for a new cancer research building supported by the U.S. Agency for International Development (USAID), the Ugandan government, and the FHCRC, several features of the productive relationship were abundantly displayed: the easy collegiality among participants from the two institutions, the shared history of what is now a ten-year collaboration, the sophisticated discussions of clinical and laboratory science, and the focus on important neoplastic diseases endemic to East Africa.

Development of the UCI and Implications for Global Health

Underlying this story are some instructive principles. First and foremost, medical research in poor countries can produce major discoveries, such as new cancers (e.g., BL), their causative agents, (e.g., EBV), and promising treatments (e.g., cyclophosphamide). In turn, those historical events can inspire new work of the sort now performed by collaborative teams from the FHCRC and UCI. Second, the influence of remarkable individuals, such as Burkitt and Ziegler, can establish precedents for long-term partnerships with additional researchers, such as Corey, Casper, and Orem. Further, successful and sustained institution-building is deeply influenced by the political environment. Strong survivors of difficult days under President Amin, such as Olweny, now the chair of the UCI board, can help to remind current staff of the potential risks of loss of political support.

Although the U.S. government is not now directly engaged in the operations of the UCI, as was the case just after the UCI’s founding, the NCI is, in a sense, represented in Uganda because the FHCRC is a major NCI-designated, comprehensive cancer center. Indeed, the NCI has recently used the example of the

FHCRC-UCI collaboration as a model to encourage other NCI-designated cancer centers to work with healthcare providers and cancer researchers in other parts of the developing world.

This final point is especially important in view of the increasing global death toll from cancer in poor and lower middle income countries. These increases are among the reasons why greater attention is now being given to noncommunicable diseases (such as cancers, heart disease, and diabetes) in the public health arena. Most prominently, the United Nations organized a high-level meeting in fall 2011 to focus world attention on the health threats posed by noncommunicable diseases and to set some goals for amelioration.¹³

In that spirit, the NCI recently established a new Center for Global Health to consolidate existing efforts to study cancer internationally and to provide more support for studies with the potential to improve the prevention and treatment of cancers in developing countries.¹⁴ Such studies are now sorely needed. Better control of infectious diseases has allowed more people in developing countries to live to more advanced ages, at which cancers (and other chronic diseases) tend to occur more frequently. Because many of these countries have large numbers of citizens infected with HIV, a risk factor for several cancers, high cancer rates can be anticipated, especially in conjunction with other risk factors such as cancer-causing viruses (EBV, hepatitis viruses, Kaposi's sarcoma virus, and human papilloma viruses) and rising rates of tobacco use. Partnerships of the type illustrated by the UCI and FHCRC—along with a focus on cancer registries, national cancer plans, and improved systems for health care and prevention—are important elements in plans for this new center at the NCI.

The MRTC: Its Origins, Accomplishments, and Threats to its Survival

The MRTC in Bamako, Mali, provides another perspective on U.S. efforts to support research on a medically important disease in an African country. The MRTC is different from the UCI in that it was created in the early 1990s, more than two decades after the founding of the UCI; it focused on malaria rather than cancer; and it was located in a Francophone country in West Africa (one of the poorest in the world), rather than a more affluent Anglophone country in East Africa. Nevertheless, the MRTC shares some critical characteristics with the UCI. It emerged from an academic institution established by its former European colonizers; its origins depended on some extraordinary individuals from Europe, America, and the host country; and its growth has been strongly influenced by local politics and governmental stability. However, the UCI has now re-emerged from over a decade of political volatility and terror in Uganda, whereas Malian political instability and the menace of external terrorists currently threaten the viability of the MRTC.

My Involvement with Malaria, its Politics, and the MRTC

It would be disingenuous for me to tell the MRTC story without acknowledging a commitment to malaria research. In 1996, when I was the NIH director, I attended a meeting on the NIH campus, organized by the Fogarty International Center, to discuss opportunities to expand medical research in Africa. Several kinds of evidence indicated a need for—and several advantages to—a focus on malaria. The disease was becoming more difficult to control; new scientific methods were creating better ways to understand the parasitic pathogen, the mosquito vector, and the affected human host; and several Africans had returned home after being trained in so-called northern countries to do malaria research, creating a cohort of skilled African malariologists who might catalyze the modernization of medical science in Africa.

Maxime Schwartz, then head of the Pasteur Institute (which operates a distinguished malaria research unit in Senegal), agreed to co-organize an unusual meeting in Dakar, Senegal, in 1997 to discuss prospects for expanded malaria research efforts in Africa.¹⁵ At that notable gathering, African, American, and European scientists and the leaders of several funding agencies interested in malaria engaged in a remarkably democratic workshop to consider how to achieve greater interaction and common scientific purpose. These ambitions were summarized in a proposal to build a new consortium named the Multilateral Initiative on Malaria (MIM). Regrettably, the most ambitious aspirations—including substantial consortium funding of research—were stymied by bureaucratic barriers and European agency resentments during a subsequent meeting in The Hague. Nevertheless, the MIM continues to thrive as a modest supporter of pilot projects, an organizer of meetings on malaria, and a provider of research training.

Although this early effort at “science diplomacy” failed to produce a grander outcome, one aspect of the 1997 meeting in Dakar continues to provide happy memories: a side trip to nearby Bamako to visit the MRTC. There I met its scientists, including its Malian leaders, Ogo Duombo and Yeya Toure, as well as several visiting American collaborators; observed the beneficial effects of the center on villages that hosted medical field stations; and engaged in the social activities—the food, music, and generally gracious ambience—of Malian life.

One sobering footnote to my MRTC visit warrants quick mention here. Because of that trip, I was invited a few months later to join a luncheon for the visiting Malian President Alpha Oumar Konaré at the U.S. Department of State. However, the inspiring work of the center was never mentioned. Department of State officials focused the discussion on voting irregularities that had been observed during a recent election, turning an opportunity for deeper engagement with science diplomacy into a tense political confrontation.

There is general agreement that, despite its poor economic status, Mali developed one of the world's best centers for clinical trials, entomology, and other kinds of malaria research in the course of less than a decade. The MRTC is renowned as a site for training new investigators, performing important field studies, and holding international meetings. Led by outstanding Malian investigators, the MRTC has become a source of pride and prestige for Mali and attracts important visitors from around the world.

How did this happen in a place like Mali? People from three domains were particularly important: two remarkable Malian scientists who became leaders of the center; several Europeans who helped to inspire and train them; and numerous Americans who wanted to conduct field studies and laboratory research with them in Mali and the United States.

Some Relevant Facts About Malaria and Mali

Malaria has been claimed to figure in many aspects of human history. However, as a disease recognized primarily by its associated fevers, it was hard to discriminate from other fever-inducing diseases. Moreover, it was hard to control effectively until its origins and transmission were better understood. Its place in the repertoire of disease can be seen in a display called *The Fever Tree*, a creation of seventeenth century medicine. Effective folk remedies, such as the barks of cinchona and Chinese willow trees, widely used as treatments for afflicted patients for nearly two thousand years, were forerunners of modern drug treatments for malaria: quinine, chloroquine, and artemisinins.

The modern era of malaria research and control began in the late nineteenth century with two seminal findings: the discovery of the disease agent—the protozoan parasites called *Plasmodia*—by the French microbiologist Charles Laveran in 1880, using blood from an infected Algerian patient, and the demonstration by Ronald Ross, a British physician stationed in India, that *Anopheles* mosquitoes carry the parasite and foster its development so that a newly bitten person becomes infected.

From these discoveries, the basic elements of the cycle of malarial transmission and disease emerged. The agents of malaria are protozoans (species of *Plasmodia*), the vectors are mosquitoes (*Anopheles*), and the symptomatic hosts are human beings bitten by infected mosquitoes. These infected people serve, in turn, as a source of infection for naïve mosquitoes that bite them. Although this picture seems complex, it opens several opportunities for intervention: (i) by directly attacking the parasites in people sick with malaria, thereby reducing symptoms and lowering the likelihood that a mosquito will acquire the parasite when it bites; (ii) by reducing the population of mosquito vectors, killing them with insecticides such as DDT or interfering with their breeding practices through drainage of

swamps; and (iii) by preventing infectious vectors from reaching vulnerable human beings, using screened doors and windows or bed nets.

Mali is only one of many malaria-afflicted countries in Africa, but it has an especially rich history and culture. Most of the country lies in the sub-Saharan zone where malaria is very common; indeed sub-Saharan Africa has the highest incidence of malaria in the world and the highest death rates. Still, an ancient kingdom in the territory we now call Mali produced palaces that partly survive, and the Dogon region maintains exotic domestic architecture that attracts tourists.

A French colony for several decades, Mali achieved independence in 1960. When a long-standing military dictatorship, led for most of the intervening years by General Moussa Traoré, was overthrown in 1991, a more democratic and relatively stable system of government was adopted. For the past two years, however, the country has been in political turmoil following the arrival of Islamic jihadists in the north, followed by a relatively peaceful takeover of the central government in the capital, Bamako, by military forces. More recently, an intervention by European and African forces, led by the French, has for now dispersed the radical elements that were cruelly dominating the north.

The emergence of Mali as an independent nation and the worldwide re-emergence of research on malaria in the 1960s were fortuitously synchronous. As recounted in Andrew Spielman's book *Mosquito*,¹⁶ malaria had steadily declined from the early days of the twentieth century in many parts of the world—although not in Africa—because of two factors. First, the mosquito vector was better controlled, through drainage of breeding sites and the growing use of insecticides (especially DDT). Second, the number of human beings carrying the malaria parasite was reduced, through treatment of infected people with chloroquine and control of the transmitting mosquito vector.

In the early 1960s, however, several factors conspired to reduce the utility of these control measures. Two of these came to limit the use and the effectiveness of DDT: the emergence of *Anopheles* resistant to DDT and the publication of *Silent Spring* by Rachel Carson,¹⁷ a compelling account of the threat insecticides pose for many species other than insects, despite their value in control of disease vectors. These developments contributed to a resurgence of malaria in parts of the world, such as India, where malaria had been coming under effective control with DDT. The increase in malaria was also accompanied by the appearance of resistance to chloroquine, then the most effective treatment. These new elements—the declining use of DDT and chloroquine resistance—stimulated a renewed interest in malaria research. New studies of *Plasmodia*, its vectors, and the human host's response revived a field that was becoming unfashionable because effective control was believed to be just around the corner.

Founding of the MRTC in Bamako

Of course, malaria had never come under control in places like Mali, with large expanses of standing water, dramatic fluctuations in disease incidence between wet to dry seasons, poverty that limited options for treatment and insect control, and meager resources allocated to public health. Still, Mali became an important site for research on malaria, at a time when the world had begun to recognize the need to understand malaria—its agent and its vector—more profoundly. In turn, malaria research at places like the MRTC improved public understanding of the disease and supported efforts in public health.

A number of factors have influenced these developments: generous French academic scientists who remained in Mali after colonialism ended, a new educational system that encouraged training of children from all parts of Mali, and an international search by scientists and their funding agencies for places to conduct field studies of malaria.

A good place to begin this story is with Professor Philippe Ranque, a French parasitologist descended from several generations of parasitologists. Ranque taught entomology for many years at the University at Bamako, from before independence until 1992, and his professed goal in life was to be replaced on the university faculty by Malian scientists. To do that, he was determined to identify talented students and ensure that they were well-trained in Bamako and in Europe. Two Malian scientists stand out in this history, Ranque's best students, Toure and Ogo Doumbo, future leaders of the MRTC.

Ranque was an inspiring and inspired mentor to his Malian students. Toure's talents were recognized by Ranque during Toure's graduate work in Bamako. Ranque then sponsored his candidacy for a doctorate to be awarded by the University of Marseilles. At one point, Ranque suggested that Toure read a paper by the Italian parasitologist and geneticist Mario Coluzzi, who had worked on malaria with Ranque and others who have figured in the history of the center. (It was not easy then to get access to such papers, especially in Africa. Ranque travelled occasionally to a library in Burkina Faso, about five hundred kilometers away, to bring back interesting items.) Coluzzi's paper suggested a way to track seasonal variations in subspecies of *Anopheles* mosquitoes by using an unusual chromosomal marker. Ranque had nurtured a connection with Coluzzi through a mutual friend in Marseilles, so Toure was able to move to Rome for a few years of productive graduate work with Coluzzi.

After receiving his doctorate in 1985, Toure returned to Bamako, eventually joining the MRTC as its director when the collaboration with NIH became official around 1990. Toure's insights into the genetics of the *Anopheles* mosquito became sufficiently important to make him an effective fundraiser for the MRTC, a magnet for investigators seeking African collaborators, and an attractive candidate for his current position as director of the international grant program at the Tropical

Disease Research Unit of the World Health Organization (WHO) in Geneva, Switzerland.

Meanwhile, Ranque was also nurturing the growth of Doumbo's career. Ranque recognized Doumbo's acute intelligence while Doumbo was in medical school in Bamako, appointed him as an assistant professor in the department of parasitology, and sent him off to Marseilles to study with Ranque's former colleagues, while he lived in Ranque's empty house in France. Duomo was adept at research and impressed with his mentor's "democratic" and liberal style, so he dropped his ambitions for a surgical career when he returned to Mali with a PhD in 1992. At that point, Ranque left Bamako to join Tore Godal, a Norwegian public health expert, at the Tropical Disease Research Unit in Geneva, stating that Duomo was prepared to lead the still nascent MRTC, which he did upon Toure's departure for Geneva in 2001.

During the 1990s, the development of the MRTC was influenced by a few Americans and Europeans who recognized that two ambitious, smart Malians—Toure and Duombo—were leading its research and training and able to engage in productive scientific collaborations. Robert Gwadz, an entomologist at the U.S. National Institute of Allergy and Infectious Diseases (NIAID) who had worked with Ranque and Coluzzi, sought a place to expand his research in Africa, hoping to develop a "perfect mosquito" that was unable to transmit the malarial parasite. Having learned about Toure and Duombo from Coluzzi, he saw the potential in Mali, so he connected the Malian scientists to several funding agencies and used his administrative skills to persuade the USAID to provide funds for field sites for malaria research in Mali. Gwadz also introduced Toure and Duomo to Lou Miller, one of the world's best known malariologists, who led Gwadz's laboratory at the NIH. Miller quickly recognized the potential for doing good work in Mali and became the center's most prominent supporter.

At about this time, Godal had developed a program with the Rockefeller Foundation to fund collaborative research involving labs in poor and rich countries. He was impressed by an application from Toure and Duomo at the MRTC to work with Miller and his NIH colleagues, and the group received a major grant.

Dick Sakai, an NIAID geneticist with prior experience in the developing world, had been dispatched to Bamako around 1991 to bring "best practices" to management of the MRTC laboratory. He then fell in love with Mali and has remained there for over twenty years, managing supplies, some research projects, interactions with the U.S. Embassy, and relations with the Malian government.

With time and with the help of these and other supporters from abroad, the MRTC has developed its own character and opened several field stations for malaria research that also served as posts for improved prevention and treatment of malaria. The MRTC also started effective training programs that attract students from many parts of Africa and sent promising students to Tulane University, the University of Maryland, and NIAID for doctoral and post-doctoral studies, with an

astonishing record of return to the MRTC. Virtually every Malian from the MRTC who has gone abroad for training has returned to the center for at least several years.

As the center engaged with additional collaborators, it has also taken on new projects, not all on malaria: leishmaniasis and filariasis (both parasitic diseases), HIV/AIDS, and tuberculosis are on the current menu of investigations of infectious diseases. Additional rural research stations have been established to pursue these diseases; additional funding has been secured from new sources; and the center staff has grown to over 120 members. Recently, the center also has become part of a larger NIAID program, the International Centers for Excellence in Research, with two other centers located in India and Uganda.

The Current Situation and its Uncertainties

Despite the new programs, strong reputation, and enlarging size and budget of the MRTC, the current political turbulence in Mali poses a significant threat to the center's survival.¹⁸ While Bamako itself has remained relatively quiet throughout the events of the past two years, with only occasional gunfire at the time of the military takeover, the northern regions of the country are considered potentially hazardous. Few visitors now come from abroad for tourism or for collaborative scientific work or meetings at the center, and funding for the center has recently been more difficult to obtain. More ominously, the possibility has often been raised that the terrorists who were dispersed into the desert and the several countries surrounding Mali might infiltrate the capital and organize seditious and dangerous activities. As a result of these several factors, staffing at the U.S. Embassy remains skeletal, few international activities occur at the center, and the U.S. Department of State discourages travel to Mali.¹⁹

Still, there are reasons to be optimistic about the survival of the MRTC and its relationship with American science. Work at the center has not abated, even in the most dispiriting times politically. Sakai has remained in place, coordinating research activities. In addition, various collaborative projects are continuing, despite the sharp reductions in foreign coworkers and financial support.

The attractions of working with outstanding African scientists in a country with a high incidence of endemic malaria remain important to US malariologists at the NIH and elsewhere. Further, a new generation of collaborating scientists has emerged. For instance, Peter Crompton, an immunologist and parasitologist at NIAID, has multiple projects conducted in partnership with the MRTC. He continues to visit when the U.S. Department of State permits it, and he recently celebrated his receipt of a U.S. Presidential Early Career Award for Scientists and Engineers at a ceremony in Bamako.

Finally, there are the aspirations of some remarkable, newly trained Malian scientists who are determined to keep the center at a high level of functionality.

For example, Abdoulaye Djimde is an immensely appealing and now well-known young malariologist who divides his time between the MRTC and the renowned Sanger Genome Center near Cambridge, UK. His studies have been supported by the NIH, MIM, WHO Special Programme for Research and Training in Tropical Diseases, the European Union, and the Howard Hughes Medical Institute—testimonials to his recognized excellence.

Reprise: Building Capacity to Perform Medical Research in Developing Countries by Supporting Scientific Centers

The two admirable efforts to build medical research centers and to sustain them under conditions that were or are less than ideal for making scientific discoveries employed the fundamental elements of “capacity building”: training of indigenous professional staff and financial and intellectual support from collaborating and more developed countries. And both have had to cope with one of the more difficult and unpredictable aspects of international capacity building: the political forces that can threaten as well as promote the viability of such enterprises.

The complex factors—scientific, economic, and political—that determine the likelihood of launching and sustaining enterprises like the UCI and the MRTC require commitments and contributions from both individuals and institutions, especially governmental institutions. Thus, creation of the UCI was strongly influenced by the discovery of BL, but it would not have been possible without the exertions of dedicated individuals from Makerere University and the NCI, the support of those institutions, or the good relations that existed between the scientists building the UCI and local governmental officials. Nevertheless, the UCI was vulnerable to the consequences of the political instability that subsequently reigned in Uganda for over a decade. Conditions for performing research deteriorated, international collaborations dissolved, and the UCI’s survival was made possible only through the devoted actions of a few people like Charles Olweny. Recovery from that unhappy period required political changes that led to renewed support from the Uganda government under President Museveni, newly ignited interest of several U.S. medical centers, and the devoted actions of individual scientists from Kampala, San Francisco, Seattle, and elsewhere. Although multiple factors played a role, recovery would not likely have happened without the political changes made by Museveni’s new administration. From that perspective, “soft power” diplomacy of the sort illustrated by capacity building and collaboration in the health sciences is likely to remain hostage to the more powerful and less predictable political conditions created by the governments of the participating countries.

The story of the MRTC confirms this view. While its creation and growth were driven by the impassioned ambitions of several individuals from Europe, the United States, and Mali, it was also dependent on the relative tranquility of Malian

politics for two decades and the relatively stable relationships between Malian leaders and governments in Europe and North America. Now that terrorism has invaded Mali, the governance of the country is vulnerable to change, the risks of visiting the country to perform collaborative scientific work have increased, and the future of the center seems much less secure.

Still, despite their vulnerabilities to powerful political forces, the two adventures in medical diplomacy that I have described here offer the advantages of highly valued social and cultural improvements. These include advanced education of talented people—in Mali, Uganda, and neighboring countries—who might otherwise have little or no access to the precepts of modern medical science; the provision of preventive practices and new therapies to people living in the environs of the centers; and the contributions to global science that are derived from work conducted in the places where diseases like BL and malaria are most frequently encountered.

Other benefits are longer term and less easily perceived. One of the most profound is the connection made to the culture of science, in which decisions are based on evidence, success is measured by the fruits of intellectual work, and interactions among people of varied backgrounds are grounded in common goals and shared methods. Furthermore, at least in the health arena, science can deliver universally desired social improvements—longer and healthier lives.

At a more subtle level, the inherently unequal partnerships described here can foster an enhanced appreciation of the possibilities of internationalism, when exercised in certain domains. Despite the disparities in wealth, history, culture, education, and location, people can join together in a shared endeavor that produces knowledge that is globally respected. This is not the general way of the world. For this reason alone, despite the expenses, obstacles, and political uncertainties, the creation and maintenance of enterprises such as the UCI and the MRTC—a central aspect of scientific capacity building—should be embraced and extended to other settings. **SD**

Endnotes

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2. During my own career, I have been directly engaged in a number of such activities, been a cheerleader for others, and offered advice to the U.S. government and philanthropic organizations about the value of proposed projects. Although I have not worked for any extended period of time in foreign countries more exotic than the UK (for most of my career, I have been either a bench scientist working on cancer genes and viruses in San Francisco, New York, or Washington, DC, or a leader of medical research institutions in the latter two places), I have had a long-standing interest in the ways that science and medicine can promote the development of poor countries and international goodwill. I have probed that interest in several ways. First, as a medical student working in a mission hospital in north India. Then, more productively, as the director of the NIH during the Clinton administration, promoting research on malaria in Africa, as discussed in the latter half of this essay. And, most recently, as the NCI director, creating a new Center for Global Health

that supports work related to prevention and treatment of cancer in the developing world. Along the way, I have also served as an advisor to global health programs at the Bill and Melinda Gates Foundation, a member of the Science Initiatives Group, and the co-author of reports on efforts to improve health in developing countries for the World Health Organization and the U.S. Institute of Medicine.

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