


INFECTIOUS DISEASES & PANDEMICS



Today, noncommunicable diseases account for two-thirds of all deaths globally. But in low-income nations, three largely preventable infectious diseases—lower respiratory infections, diarrheal infections, and HIV/AIDS—are the leading killers, with malaria, tuberculosis, and neonatal infections close behind. And as recent headlines have shown, new infections—from SARS to bird flus to deadly new strains of *E. coli*—continually emerge.

From its very beginning, Harvard School of Public Health has bolstered efforts to control the most common and the most vicious infections in every corner of the world—with pivotal discoveries in the lab and advances in interventions on the ground.

THREE DEADLY SCOURGES

SMALLPOX

William Foege had a problem—a big problem. It was December 1966. Foege, who graduated from the School with an MPH in 1965, was serving in a remote part of eastern Nigeria on a medical mission and as a consultant to the U.S. Centers for Disease Control and Prevention (CDC). His assignment was daunting: to help rid that part of the world of smallpox, a painful, disfiguring infection that was one of humankind’s most devastating scourges. Health authorities believed that to achieve eradication, 80 to 100 percent of regional populations had to be inoculated.

But in Foege’s jurisdiction, vaccine was in short supply. When smallpox erupted in a nearby village, Foege had to figure out how to hold back the epidemic. Spreading out maps of the district and working with two-way ham radios, he contacted missionaries and asked them to dispatch runners throughout the region to learn where else the disease had broken out. Using this information and analyzing family travels and market contacts, he made

an educated guess about where the epidemic would jump. The task required, as he once recalled, imagining “how a smallpox virus bent on immortality” would behave. Foege’s team took an unusual approach, targeting for vaccination only residents in the affected villages and in villages where the disease would likely strike.

Miraculously, four weeks later, though less than 10 percent of the population had been immunized, the outbreak screeched to a halt. Six months later, the entire region was smallpox-free. “Surveillance/containment,” as the method came to be known, revolutionized the smallpox eradication campaign by saving money and time. When the World Health Organization (WHO) officially declared smallpox eradicated in 1980, it was in no small part because of Foege’s daring calculations.

It was just the start of Foege’s game-changing career. From 1984 to 1990, he led a partnership of U.N. agencies and nongovernmental organizations that raised worldwide immunization levels from 20 percent to 80 percent for six major childhood diseases—“the largest peacetime mobilization in the history of the earth,” according to James Grant, then the director of UNICEF. As CDC director from 1977 to 1983, Foege witnessed the emergence of Legionnaires’ disease, toxic shock syndrome, Lyme disease, the deadly *E. coli* O157:H7 strain, and HIV/AIDS. In 2012, Foege was awarded the Presidential Medal of Freedom, the highest civilian award in the United States.

Mobilizing an international team of scientists and government officials in a targeted attack on a single microbe, the war on smallpox demonstrated for the first (and, to date, the only) time that it was possible to extinguish a pathogen through deliberate human activity. In October 1977, a hospital cook in Somalia contracted smallpox from two Ethiopian children who had fled to Somali refugee camps after their nation’s civil war—the last case of naturally occurring smallpox on earth. Three years later, the WHO declared smallpox—an infection that had killed an estimated 300 million people in the 20th century alone—gone for good.

continued page 18



A woman in Ethiopia is vaccinated against smallpox in the 1970s as the global eradication campaign nears an end.

THE ART OF ERADICATION

E-rad-i-cate: 1. to pull or tear up by the roots, to remove entirely, extirpate, get rid of. 2. in public health, to achieve zero disease globally as a result of deliberate efforts.

Its formal name says everything: dracunculiasis, or “affliction with little dragons.” In the early 1980s, Guinea worm disease struck millions from western India to Senegal. Victims become infected when they drink from ponds or wells containing tiny freshwater crustaceans that themselves have swallowed microscopic worm larvae. In infected humans, the larvae grow inside the body to about a yard long, then migrate to the skin, where they eventually burst through, slowly and painfully. As HSPH alumnus Donald Hopkins, MPH '70, put it, “Guinea worm disease is one of the most terrible human afflictions.”

He should know. Hopkins' greatest legacy may be the eradication of Guinea worm disease. While at the U.S. Centers for Disease Control and Prevention (CDC), he launched in 1980 the Guinea Worm Disease Eradication Program, an exhaustive search for the worm in some of the world's most inhospitable environments. From 1987 to 1997, he led the Guinea worm disease initiative at The Carter Center. With no vaccine in sight, eradication relies on simple filtering technologies and robust networks of community health workers. As a result of Hopkins' dogged efforts, Guinea worm disease has fallen from 3.5 million cases in 1986 to fewer than 600 cases globally in 2012. In 2013, the number is expected to be even lower. Today, Hopkins directs all health programs at The Carter Center.

Hopkins' public health triumphs overlap and often intertwine with those of William Foege, whose surveillance/containment immunization strategy ushered in the eradication of smallpox. Drawing on Foege's inspiration and advice, Hopkins served as a medical epidemiologist and director of the Sierra Leone Smallpox/Measles Program from 1967 to 1969. In 1974, he became assistant professor of tropical medicine at HSPH, teaching the subject that originally drew him to public health. By 1978, Hopkins became the assistant director for international health at the CDC, reporting directly to Foege, and went on to serve as the agency's deputy director from 1984 to 1987 and as acting director in 1985.

Earlier this year, in an article in the *New England Journal of Medicine* starkly titled “Disease Eradication,” Hopkins wrote that “The unique power of eradication campaigns derives from their supreme clarity of purpose, their unparalleled ability to inspire dedication and sacrifice among health workers, and their attractiveness to donors, all of which are needed to overcome the barriers to successful eradication.” In 2013, polio and Guinea worm disease are the only officially sanctioned targets of eradication campaigns.

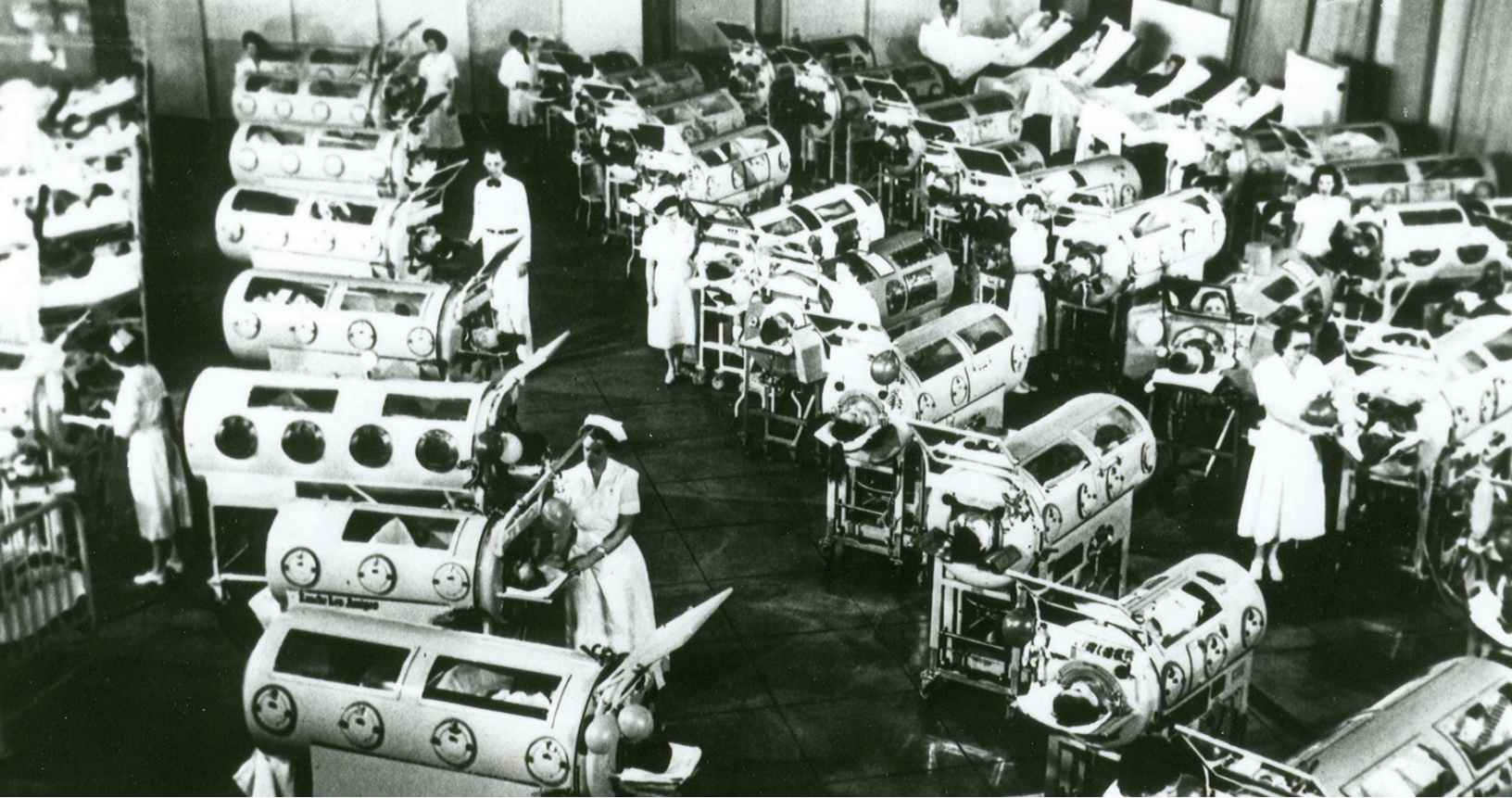
What will it take to reach a target of zero? Not only international cooperation and political will, but also people like Bill Foege and Don Hopkins, who themselves seem infected by boundless optimism. As Foege is famously fond of saying, “Some things have to be believed to be seen.” And as Hopkins recently told a newspaper interviewer, “I'm sort of immunized against pessimism.”



Donald Hopkins examines children in Nasarawa, Nigeria in 2007.



Donald Hopkins



The iron lung pulled back thousands of polio victims from the brink of death.

POLIO

At the beginning of the 20th century, major epidemics of poliomyelitis were virtually unheard of. But within a few decades, it was the fifth-leading cause of infectious-disease death in the United States, claiming thousands of lives each year in nearly annual epidemics. The 1952 polio epidemic was the worst outbreak in the nation's history; of 57,628 reported cases, 3,145 died and 21,269 were left struggling with mild to disabling paralysis.

Called “the summertime scourge,” polio often flared in the midst of the idyllic rituals of summer. Because water was believed to be a route of transmission, swimming holes, pools, and ponds were closed when epidemics erupted. But the threat loomed everywhere. As Philip Roth wrote in his 2010 novel *Nemesis*, “We were warned not to use public toilets or public drinking fountains or to swig a drink out of someone else’s soda-pop bottle or to get a chill or to play with strangers or to borrow books from the public library or to talk on a public pay phone or to buy food from a street vendor or to eat until we had cleaned our hands thoroughly with soap and water.”

Poliovirus belongs to the enterovirus family, which infects the intestinal tract and is spread by the fecal-oral

route. The infection was unusual because it actually claimed more lives as overall health conditions improved. In crowded tenements and rural slums, young children were exposed to the poliovirus within the first few years of life, when the disease causes few symptoms beyond a transient fever. By contrast, children of the middle and upper classes were protected from exposure to the virus during infancy. As they got older and went to school or summer camp or swam in public pools, they encountered large groups of children. First-time exposure to the poliovirus at an older age is more likely to trigger the most dreaded complications: muscle stiffness, pain, and eventual paralysis.

In the first half of the 20th century, medicine was virtually helpless in treating polio’s complications, including the tortured suffocation that followed paralysis of the chest muscles. But in the fall of 1928, the clinical picture brightened somewhat, when a Harvard senior with polio entered Boston’s Brigham Hospital. In his room sat a giant tin box with a hole at one end and a motor at the other. Its inventor was Philip Drinker, a quiet, modest engineer and professor of industrial hygiene at HSPH.

Drinker's contraption aided the young man's respiration by increasing and decreasing the pressure inside its sealed compartment (the first polio victim to use the respirator, an 8-year-old girl, was revived but soon succumbed). Officially called the Drinker Respirator, it came to be known by a more descriptive name: the iron lung. In 1964, Drinker recalled this early clinical success with the Harvard senior: "After a long siege in the machine, he recovered quite well and is today after almost thirty years very much alive."

The iron lung pulled back thousands of victims from the brink of death, and Drinker became an international celebrity. Scientists were soon to make an even more profound breakthrough. In the 1930s and '40s, researchers were frantically working on a polio vaccine—but the science was stalled, because no one could grow the virus in a form that would permit mass production of vaccine.

As a wave of polio swept the country in 1948, 32-year-old Thomas Weller was logging long hours in a lab at Harvard-affiliated Children's Hospital, trying to develop a new way to culture viruses in test tubes. One day at the bench, when he was done injecting varicella, the chick-

enpox virus, into test tubes, he noticed four leftover flasks with human embryonic tissue suspended in a nutrient broth. He walked to the laboratory freezer and took out samples of poliovirus obtained from the brain of an infected mouse.

Weller inoculated the extra flasks with the poliovirus. Then he added an innovative twist to the experiment: Instead of discarding the tissue every one or two days and keeping the fluids—the usual protocol—he kept the tissues in the flasks and frequently replenished the nutrient fluids. That way, slow-growing viruses were not inadvertently thrown out.

The chickenpox cultures never took—but the polio cultures did, on Weller's first try. The virus grew not only in brain tissue but also in cells derived from skin, muscle, and intestines. By finding a way to grow the virus in non-nervous tissue, Weller and his colleagues, John Enders and Frederick Robbins, paved the way for safe polio vaccines in the 1950s and '60s. In 1949, Weller joined the HSPH Department of Comparative Pathology and Tropical Medicine, rising through the ranks as instructor, assistant professor, and associate professor.

In 1954, the three scientists shared a Nobel Prize in Physiology or Medicine. The prize came just months after Weller had been named the Richard Pearson Strong Professor of Tropical Public Health at Harvard, as well as chair of the department.

"These discoveries incited a restless activity in the virus laboratories the world over," noted the award committee. "The tissue culture technique was rapidly made one of the standard methods of medical virus research." The discovery made possible the creation of a polio vaccine.

Today—like smallpox 50 years ago—polio is the bull's-eye of a global eradication campaign that rests on vaccination. Since the launch of the campaign in 1988, new cases have dropped more than 99 percent. In 2012, a total of 223 polio cases worldwide were reported, with most from countries where the infection remains endemic: Afghanistan, Nigeria, and Pakistan. (In 2013, in something of a setback, Pakistan and several African nations saw outbreaks.) This past April, the Global Polio Eradication Initiative presented a plan to eradicate the disease by 2018—a fitting epilogue to the School's storied achievements. *continued*



HSPH's Thomas Weller, left, with Frederick Robbins, center, and John Enders received the 1954 Nobel Prize in Physiology or Medicine for discovering new methods to cultivate the poliovirus.



A World AIDS Day rally in Calcutta in November 2011. First held in 1988, when the United Nations General Assembly declared AIDS to be a global pandemic, World AIDS Day is now an annual event in most countries.

HIV/AIDS

In June 1981, the CDC issued a report with a deceptively bland title: “Pneumocystis Pneumonia—Los Angeles.” It summarized the first five reported cases of the horrifying pandemic later named acquired immune deficiency syndrome: AIDS. Around the globe, millions were already silently infected.

AIDS has been public health’s perfect storm. The human immunodeficiency virus (HIV) that triggers AIDS devastates the body’s protective systems, ushering in not only systemic symptoms such as fevers and weight loss but also opportunistic infections and cancers that would normally be kept at bay. In the U.S., where the infection is most common among gay men, homophobic backlash initially slowed the political commitment to tackling the disease. And HIV/AIDS has disproportionately struck the poorest nations in the world, with 69 percent of infections in sub-Saharan Africa.

From the start, as the immense proportions of the AIDS epidemic became apparent, HSPH helped lead a counterassault. The School’s laboratory discoveries have pointed the way for ongoing research into vaccines and

treatments. Its epidemiologic modeling and data analysis helped describe the contours of the epidemic and the best interventions. And its public policy and human rights commitments have set standards worldwide.

When the epidemic first surfaced, Max Essex, now the Mary Woodard Lasker Professor of Health Sciences at HSPH, had been toiling away in relative obscurity on a virus known as FeLV (feline leukemia virus), which causes AIDS-like immunosuppression in cats. A veterinarian and virologist by training, Essex was one of the first to suggest that the mysterious agent causing AIDS was a retrovirus. His work sped the discovery of the AIDS virus by the National Cancer Institute’s Robert Gallo and the Pasteur Institute’s Luc Montagnier. In 1986, for his role in identifying the cause of AIDS, Essex shared, with Gallo and Montagnier, the prestigious Albert Lasker Medical Research Award.

Other crucial discoveries quickly followed. Collaborating with HSPH colleagues, Essex confirmed that the AIDS virus could be transmitted through

continued on page 24

ONE MAN'S STAND AGAINST HIV/AIDS

When the Botswana–Harvard AIDS Institute Partnership (BHP) was launched in 1996, the official goal was collaborative research and training between the Republic of Botswana and the Harvard School of Public Health AIDS Initiative. But for Dichaba Siane—a 40-year-old hospital worker in the capital, Gaborone, who chairs the local Community Advisory Board (CAB)—the scientific teamwork has transformed not only his community and country, but also himself.

According to Siane, the BHP has dramatically improved health and health care management in Botswana. Clinical trials using antiretrovirals to prevent mother-to-child transmission, for example, have shown that the rate of children born HIV-positive can be cut from 40 percent to less than 1 percent. “The research was done mainly in Gaborone,” he said, “but the benefits have cascaded through the entire country.”

Treatment for tuberculosis—a ubiquitous and deadly opportunistic infection that has shadowed the AIDS epidemic—has also advanced. “The care has improved so much that if you are on treatment, you will complete your treatment and you will be cured,” said Siane.

And randomized trials using antiretrovirals to prevent viral transmission when one person in a couple is infected and the other is not have also altered the social and emotional landscape. “The study proved without any doubt that it is possible to protect oneself and one’s partner,” Siane added.

But the most impressive development may be that thousands of Siane’s countrymen have volunteered for studies. Batswana, as people from Botswana are called, were reluctant to participate in early clinical trials because they feared having blood drawn. “Blood plays a very important role in the culture. It’s sacred. My blood should be with me—it should not be taken and kept somewhere else,” Siane explained. “However, we’re working through that. Now there are quite a number of people who are comfortable with blood draws, because they realize the importance of blood in terms of research and possible help for the future generation.”

For Siane—who as CAB chairperson has informally served as educator, translator, diplomat, organizer, and advocate—the rewards have also been personal. “Working with the CAB has changed me. I’ve learned a lot about science. And I’ve learned that I have a responsibility to be in constant communication with my community.”



Dichaba Siane

HIV/AIDS Studies in Africa

The School's fieldwork in HIV/AIDS, which has received support from the President's Emergency Plan for AIDS Relief (PEPFAR), the National Institutes of Health, the Bill & Melinda Gates Foundation, NIH, and other private philanthropists, is concentrated in three African countries: Nigeria, Botswana, and Tanzania. Initiatives in each country have transitioned their HIV care and treatment programs to local management, with HSPH researchers continuing to offer technical assistance.

- In Nigeria, HSPH founded and led the AIDS Prevention Initiative in Nigeria (APIN) with local partners, and later expanded this partnership to create the Harvard/APIN PEPFAR program. This program established 32 AIDS treatment and care facilities around the country and played a significant role in the AIDS treatment program in Nigeria, a nation where the HIV infection rate dropped from 5 percent in 2000 to 4.1 percent in 2010. The program trained clinicians and developed systems of care that supported:
 - Lifesaving medicines to 100,000+ people
 - HIV care and services to 160,000 people
 - Counseling, testing, and diagnosis to 1,005,600 people, including 390,000 pregnant women
 - Treatment to prevent mother-to-child transmission for 20,600 pregnant women
- In Botswana, HSPH formed a partnership with the government that has trained more than 1,450 nurses and health care professionals at rural antiretroviral therapy (ART) sites, scaled up testing capacity at 24 remote facilities, and provided extensive monitoring and evaluation by tracking data for more than 150,000 patients.
- In Tanzania, HSPH worked with government and university partners to enroll 80,000 patients on ART, provide services at 185 facilities for preventing mother-to-child transmission, and establish 49 HIV care and treatment centers, all in the capitol city, Dar es Salaam.



FROM INDIVIDUALS TO COMMUNITIES

“Within an individual, we know the processes by which cells get infected with HIV, the virus replicates, and antiretrovirals (ARVs) interfere with that process. We need similar kinds of models at the community level that describe transmission across individuals. The goal is to learn at the community level what we’ve learned over the decades about individual therapy: how to optimize treatments and tailor them to individual characteristics.”

—Victor De Gruttola
Chair, Department of Biostatistics



A technician processes blood samples in the lab of the Princess Marina Hospital in Gaborone, Botswana, site of HSPH research on HIV/AIDS.

blood transfusions. In 1985, he co-discovered, with Tun-Hou Lee, now professor of virology, the gp-120 surface protein, which is now used worldwide for blood screening. In 1986, Essex, Phyllis Kanki, now professor of immunology and infectious diseases, and Richard Marlink, now executive director of the Harvard School of Public Health AIDS Initiative, discovered a second AIDS virus, HIV-2, which causes a million infections annually in West Africa. HIV-2 is less transmissible and less deadly than HIV-1. HSPH researchers have also identified a treatment program that prevents 99 percent of mother-to-child HIV transmission via breastfeeding.



Max Essex, the Mary Woodard Lasker Professor of Health Sciences

Though U.S. President Ronald Reagan didn't deliver a major address on AIDS until 1987, it was painfully clear to scientists that the infection was fast becoming the leading public health crisis of the century. In 1988, to promote an interdisciplinary approach to a battle that had to be waged on several fronts, Harvard President Derek Bok announced the creation of the University-wide Harvard AIDS Institute (HAI), with Essex as chair. In 1992—a time when the U.S. banned visas for people infected with HIV/AIDS—the HAI-organized eighth International AIDS Conference was

scheduled to take place in Boston. To protest the discriminatory policy, Essex canceled the meeting, which was later moved to Amsterdam.

International collaborations have been the bedrock of the School's basic research. In the early 1980s, HSPH established a presence in Africa to meet the challenges posed by the pandemic. The School established a model study in Senegal in the mid-1980s that is now one of the longest-running AIDS studies in Africa. HSPH also conducted the first HIV vaccine trial in southern Africa.

In 1995, HSPH biostatistician Stephen Lagakos founded the Center for Biostatistics in AIDS Research to bring innovative statistical techniques to clinical trials in HIV/AIDS, while at the same time honoring the needs and welfare of patients enrolled in these studies. In 1996, the School launched the Botswana–Harvard AIDS Institute Partnership, a research and training program that was the largest of its kind in Africa at the time, as well as the first dedicated HIV research lab in southern Africa.

The President's Emergency Plan for AIDS Relief (PEPFAR) dramatically scaled up the School's work in African countries hit hard by the disease. Beginning in 2004, HSPH received a total of \$362 million from PEPFAR for work in Nigeria, Botswana, and Tanzania, led by Kanki. The School trained thousands of health care workers, developed monitoring and evaluation systems, refurbished and equipped clinics and labs, and collaborated with local hospitals and clinics. (See page 22.)

Such progress gives scientists hope that the tide may be turning. "On the cusp of the fourth decade of the AIDS epidemic, the world has turned the corner—it has halted and begun to reverse the spread of HIV," said a 2011 summary from UNAIDS.

Still, in 2013, the toll remains incalculable. The majority of HIV-positive individuals are unaware that they are infected. The virus is the leading cause of death globally among women of reproductive age. Most people living with HIV, or at risk for infection, do not have access to prevention, care, and treatment. And more than three decades into this shattering pandemic, there is no cure.

As HSPH enters its second century, it will continue to focus its research and education on stemming this relentless pandemic. ❖

A SIMPLE SOLUTION THAT HAS SAVED MILLIONS



A solution of table salt, sodium bicarbonate, glucose, and water. This simple elixir, known as oral rehydration solution (ORS), has saved tens of millions of people since the 1970s from death by cholera and other diarrheal diseases—now the second leading cause of infant and child death in the developing world. In a landmark paper published in *The Lancet* in 1968, Richard Cash (pictured at right), HSPH senior lecturer on global health, and colleagues reported for the first time the results of clinical trials in Bangladesh (then known as East Pakistan). They showed that this cheap and readily available solution saved up to 80 percent of intravenous fluid—a scarce and costly commodity—and if begun early in the illness, could eliminate the need for the fluid altogether. A simplified form of ORS—made up of a pinch of salt, a fistful of sugar, and half a liter of clean water—has been taught to millions of mothers to treat children at home. For his elegant research and subsequent work developing programs to teach people how to use ORS, Cash has received numerous awards, including Thailand's 2006 Prince Mahidol Award and the 2011 James F. and Sarah T. Fries Foundation Prize for Improving Health.



Richard Cash, senior lecturer on global health

The Disease Hunters

A LIFE OF EXPLORATION

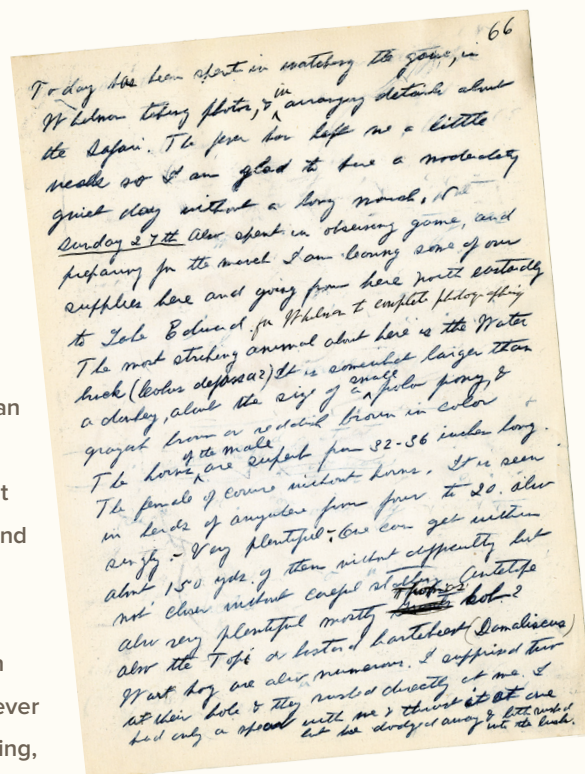
“The sun came out early and fiercely . . . As the hours wore on and noon was reached at times one felt the desire to become a little hysterical and to repress a scream and throw oneself into the forest at the side of the trail.”

So wrote Richard Pearson Strong in the 320-page diary he kept while leading the 1926–1927 Harvard African Expedition, which crisscrossed the remote interior of Liberia and then cut 3,500 miles across central Africa to end at Mombasa, Kenya.

A pioneer in researching tropical diseases, Strong arrived at Harvard in 1913, becoming the University’s first-ever professor of tropical medicine. Traveling, researching, and publishing at a preternatural pace, he packed several lifetimes’ worth of achievements into a single career, accumulating an encyclopedic knowledge of diseases that few Westerners would recognize: dengue and yellow fevers, leprosy, cholera, plague, Oroya fever, kala-azar, and various forms of dysentery. His specialty was onchocerciasis, or river blindness, about which he published dozens of papers clarifying the infection’s natural history and transmission patterns, and described in detail black fly habitats and breeding cycles.

Between 1913 and 1938, Strong led five overseas expeditions to Africa and Central and South America. During World War I, he led a stunningly successful effort to control a typhus outbreak in Serbia.

Today, much of Strong’s legacy appears tinged by the endemic racism of his era. Announcing Strong’s appointment, for example, a University alumni bulletin article stated that one of science’s greatest services to mankind was “overcoming conditions which made life in the tropics almost impossible for white men and dangerous and enervating even to natives.”



A page from Richard Pearson Strong’s diary written during the 1926–1927 Harvard African Expedition



Tropical disease researcher Richard Pearson Strong led overseas expeditions to Africa and Central and South America.

SWEEPING THE FIELD

In fall of 1973, residents on the island of Nantucket were treated to a curious sight: a lone scientist traipsing through underbrush, waving a giant white flag.

Its bearer, Andrew Spielman, wasn't surrendering. Spielman, a vector-borne-disease expert at Harvard School of Public Health, was using the cloth to capture deer ticks—tiny arachnids he suspected of causing a human outbreak of babesiosis, a rare blood-borne disease that infected two Nantucket residents.

After weeks in the field, Spielman discovered that white-footed mice, a common species on the island, were often covered with larval ticks that carried the disease. Through careful analysis, Spielman showed that ticks like these were responsible for cases of human babesiosis, a malaria-like parasitic infection. Later research at Yale University revealed that the same ticks were spreading the newly identified Lyme disease, which had just begun to emerge in southern New England.

In response, Spielman began developing strategies to control the tick population, and by the late 1980s, stumbled on an ingenious solution with colleagues. They soaked cotton balls in pesticide, stuffed them into empty toilet paper rolls, and left them in the brush. Mice, which found the cotton irresistible for building nests, carried the pesticide back to their dens, where it killed off the ticks nestled in their skin. Within a single season, the researchers found, the number of deer ticks found on trapped mice had dropped by more than 90 percent.

Spielman's groundbreaking work didn't stop at ticks, however. His later research also helped identify mosquitoes as vectors for both the Eastern equine encephalitis virus and, later, for West Nile virus—a disease he suspected was carried in the blood of roosting birds.

Although Spielman personally tracked down the vector for a number of dangerous diseases before his death in 2006, he was always careful to frame his work within the larger context of public health. "I am not a mosquito specialist. I am not a tick specialist. I am a transmission specialist," he mused in 1997. "That is what public health entomology is all about."



The deer tick, Ixodes scapularis



Andrew Spielman sweeps the field for deer ticks on Nantucket.

THE HARD SCIENCE OF SAVING LIVES

Understanding the basic biology of infectious disease has been a constant at HSPH since its inception. “We’re one of the few schools of public health that has integrated laboratory science and more classical public health disciplines, such as epidemiology and biostatistics. A lot of our work focuses on the interaction of the infectious agent with its host, and how that interaction leads to disease transmission and progression,” said Dyann Wirth, chair of the Department of Immunology and Infectious Diseases. Wirth is also the Richard Pearson Strong Professor of Infectious Diseases—an endowed position named in honor of the School’s legendary explorer/biologist (see page 26).

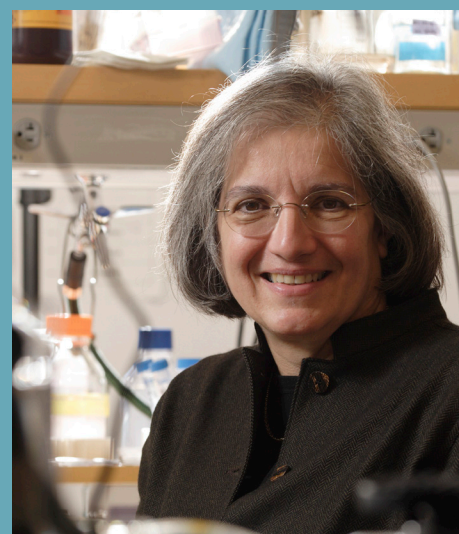
The department’s most acclaimed faculty achievement—Thomas Weller’s discovery of how to grow the poliovirus in a cell culture system—was the breakthrough that led to the development of a polio vaccine. As Wirth explained, “The iron lung treated symptoms. But by discovering the biology, we prevented the infection. In the end, prevention always prevails.”

Yet a century after the School’s founding, prevention has continued to be a hurdle for malaria and tuberculosis (TB), two of the top three infectious-disease killers worldwide (rounding out the deadly trio is AIDS). In 2010, the malaria parasite killed an estimated 660,000 people—mostly children—and infected 219 million. In the same year, nearly 9 million people around the globe became sick with TB and some 1.4 million died. Meanwhile, a rising tide of multidrug-resistant tuberculosis—the primary cause of which is the inappropriate or incorrect use of anti-TB drugs—has made the infection difficult and costly to treat.

The causative organisms of malaria and TB have evolved for thousands of years with their human host, perfecting ways to evade our immune system. HSPH has made groundbreaking discoveries on these evasive tactics. “In malaria, we’ve made two major contributions. One is a fundamental understanding of how drug resistance occurs and how it spreads. The other is the application of genomics to understanding natural infection in *Plasmodium falciparum*, the main malaria parasite, and the implications of that for vaccine development and for elimination and eradication,” said Wirth. “With TB, we have identified in the tuberculosis bacterium every single gene important for the organism’s survival. That discovery has created a tool that opens doors for new drugs and vaccines.”

Another strength of the School is its interdisciplinary approach to infectious disease. In malaria, for example, a “genes to the globe” framework guides work across the University. “At Harvard, there are economists and businesspeople and ethicists and social and behavioral scientists and people in government—all engaged in trying to solve malaria,” Wirth explained. “People in basic science are trying to understand how the parasite converts from replicating in the red cell to being available for transmission by the mosquito vector. At the same time, in business, a fundamental question is how to handle the supply chain. We have insecticide-treated nets and effective diagnostics and medicines: How do we deliver those in the right amount at the right time to the people who need them?”

Infectious diseases, both deadly and chronic, have challenged humanity since our beginnings. As Wirth sees it, that threat is inherent in our coevolution with microorganisms. “For the most part, these infections have been with us long before there was any kind of intervention. The DNA of organisms represents a footprint of history, the cumulative selective forces. The genomes that exist today—be they humans or infectious organisms—are the survivors, the successful descendants of their precursors.”



Dyann Wirth, chair of the Department of Immunology and Infectious Diseases

CHASING EPIDEMICS IN REAL TIME

As the AIDS epidemic tragically demonstrated, public health has usually been a step behind infections on the run. But today, with sophisticated molecular and communications tools, practitioners can virtually keep up stride for stride with emerging epidemics.

In the spring of 2003, a deadly viral illness—severe acute respiratory syndrome, or SARS—swept out of China’s Guangdong Province and spread rapidly around the world. HSPH professors of epidemiology Marc Lipsitch and Megan Murray, using a sophisticated mathematical model to estimate the virus’s potential to spread, showed that the most effective means of blocking SARS transmission would be to isolate infected individuals and quarantine people likely to be exposed—strategies that, along with preventing transmission in hospital facilities, successfully contained the startling new epidemic.

In the early spring of 2009, H1N1 influenza—the same subtype, though milder, that killed an estimated 50–100 million people worldwide in 1918—emerged in Mexico and swiftly spread around the globe. Lipsitch statistically modeled the severity and transmission of the virus, while Atul Gawande, professor in the Department of Health Policy and Management, led a World Health Organization team to quickly draft a patient care checklist for hospitals managing suspected or confirmed cases.

In May and June of 2011, a novel strain of *E. coli*, dubbed O104:H4, triggered a brief but deadly outbreak of foodborne illness centered in Germany and France. In one of the first uses of whole-genome sequencing to study the dynamics of a foodborne outbreak, a team led by HSPH researchers and the Broad Institute traced the deadly path of the outbreak, which killed more than 50 and sickened thousands.

And in the past few years, Caroline Buckee, assistant professor of epidemiology, has developed predictive models for the spread of malaria, using anonymous cell-phone data to track the movement of people in malaria-endemic regions. “Cell phones are ubiquitous,” she said. “Using them to monitor people’s mobility during an outbreak could transform infectious disease epidemiology.”



Fenugreek sprouts were implicated in a 2011 foodborne outbreak of *E. coli*.



THE HUMAN MICROBIOME MAPPING THE FUTURE

Helping to write the next chapter of infectious disease research, Curtis Huttenhower, associate professor of computational biology and bioinformatics, is exploring the human microbiome—the 100 trillion microbial cells in and on our bodies. Research on the microbiome may transform our understanding of why we become sick and how doctors may someday tinker with our internal ecosystems to prevent or treat a vast range of conditions, from diabetes to asthma to obesity. “Our relationship with our microbes is not a war,” said Huttenhower. “It’s a well-defined truce.”