WASHINGTON, D.C., ATLANTA, AND DELHI—As he wrapped up his PowerPoint presentation, fielded questions, and readied his papers for a quick departure, Bruce Aylward sneaked one last peek at his e-mail. “Bingo,” he said, pushing back his glasses and rubbing his perpetually jet-lagged eyes. “We just got a confirmed case in Togo.”

David Heymann, Aylward’s new boss and newly appointed czar for polio eradication at the World Health Organization (WHO), greeted the news with a single word: “meltdown.” And with that the two closed up their laptops, grabbed their backpacks, and rushed out in the pouring rain to catch their flight home to Geneva.

The e-mail confirmed their worst fears. Fueled by rumors about tampered vaccines and a general distrust of things Western, the poliovirus had staged a comeback in Nigeria—racing through the sparse and largely Muslim population in the northern states and reinfecting the southern megacity of Lagos. And now, Aylward’s e-mail confirmed, the virus had leaped across the border into yet another country that had been polio-free for years.

Aylward and Heymann had spent that rain-soaked September day last year in a retreat with colleagues from the U.S. Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia. With the poliovirus cornered in just seven countries and hunkered down in five key hot spots of transmission—in India, Pakistan, and Nigeria—the two had come to vet an aggressive new plan to wipe out the disease by 2005. And this time, they stressed, no halfway measures would suffice: They were going to “whack” the virus with everything they had.

Two days later, Aylward and Heymann flew into the Nigerian capital of Abuja in an attempt to stanch the hemorrhage in the northern state of Kano. Within days, national governments, the United Nations Children’s Fund (UNICEF), and WHO announced a $10 million emergency campaign to vaccinate all children under age 5 in the adjoining countries that were now at risk. Essentially, they would cordon off the disease in Nigeria—where the number of cases has now soared to at least 355 (almost half the worldwide total in 2003) and eight neighboring countries have been reinfected—and lay the groundwork for an all-out vaccination assault once the political situation cooled down.

Since then, the two have been largely airborne, flying from one trouble spot to the next to put out brushfires or generally rally the troops to meet their target: Stop transmission of wild poliovirus in 2004 or perhaps the early months of 2005. After years of slipping deadlines and expanding budgets, that goal is lauded even by longtime skeptics such as Donald A. Henderson of the University of Pittsburgh’s Center for Biosecurity. Henderson and others wish the virus fighters well and say that the odds are now as good as they get—and that this may also be the last, best chance.

Uphill battle

As devastating as it is, the Nigeria outbreak is by no means the worst setback for the core partners in the eradication campaign: WHO, CDC, Rotary International, and UNICEF. Indeed, when WHO and its partners set out in 1988 to eradicate the disease by 2000, they had no idea how tough it would be. Only one other disease has ever been eradicated—smallpox, with the last case seen in 1977—and, by comparison, that campaign was a breeze, says Henderson, who led that effort.

For starters, the logistics have been unprecedented. Polio eradication entails, theoretically at least, administering two drops of oral vaccine to every single child in every remote, even war-torn, corner of the world at least twice a year until the disease disappeared. Moreover, even after a country is declared polio-free, it must continue vaccinating until the virus is wiped out everywhere, to guard against reintroduction. The challenge has consumed more than $3 billion and involved some 20 million volunteers over the past 15 years, as naysayers have questioned whether the goal is worth the cost or even feasible.

If the logistics were not daunting enough, just as the program was finally gathering steam in the early 2000s, it was dealt three
A silent crippler

Throughout the 1940s and 1950s, polio was one of the most feared diseases in the industrialized world. An insidious virus that can sweep silently through the population without being detected, polio caused crippling epidemics every summer, affecting some 21,000 children each year in the United States alone in the early 1950s. In wealthy countries such as the United States, where many other childhood diseases were in decline, polio stood out as particularly horrifying, leaving its young victims paralyzed or kept alive inside an iron lung.

Caused by an enterovirus that enters the body through the mouth and multiplies in the throat and gut, polio is easily spread through fecal contamination. Fewer than 1% of infections result in paralysis (that occurs only when the virus invades the nervous system), but even asymptomatic carriers shed the virus in their stool and are able to transmit the disease for weeks.

With the 1955 introduction of Jonas Salk’s injectable vaccine, made from a killed virus, and then in 1961 Albert Sabin’s oral vaccine, made from a live but weakened virus, polio all but disappeared from wealthy countries, except for the occasional importation. (Both vaccines can confer lifelong immunity.)

Polio continued to exact a horrific toll in many developing countries, especially in the poorest areas, where diarrhea was rampant and water and sanitation were lacking. WHO estimates that roughly 500,000 children, and perhaps many more, were paralyzed every year by polio as late as 1980. But despite its prevalence, polio was less visible in these areas, lost against the backdrop of other devastating childhood diseases such as malaria, diarrhea, measles, and tuberculosis. When the oral Sabin vaccine, dubbed OPV, was introduced as part of routine immunizations in developing countries in the 1970s, numbers began a slow but steady decline.

From the outset, Sabin touted his oral vaccine as a tool for ridding entire regions, if not the world, of polio. He later donated the vaccine to WHO. Compared to Salk’s inactivated vaccine, Sabin’s oral formulation was easier to administer. In the 1960s, the fast-dissolving taste made it attractive to children. WHO officials were “very skeptical,” says de Quadros. “I thought maybe we could do that in every country in the Americas,” recalls de Quadros.

Although WHO officials were “very skeptical,” says de Quadros, PAHO resolved in 1985 that it would rid the Americas of polio by 1990. In El Salvador, Haiti, and Venezuela, PAHO officials honed the strategy that would later become the mainstay of the global eradication program. They established a “cold chain” of refrigerators and ice chests to deliver polio vaccine to every corner of the continent—by truck, motorcycle, horse, or on foot. They created a surveillance system for rapid investigation of any case of acute flaccid paralysis—a hallmark of several diseases, including polio—and a network of labs that could analyze stool samples from AFP cases for the presence of poliovirus, the live vaccine virus sets up shop in the gut and is excreted in stool several weeks after administration. So even unvaccinated children were likely to receive the protective virus through “passive” immunization as it spread among family members. Sabin postulated that if the vaccine were administered in massive campaigns to virtually all children within a few days, transmission within a region would stop, as the wild virus would have no susceptible population in which to hide.

Cuba’s Fidel Castro was the first head of state to buy into the vision, instituting so-called National Immunization Days twice a year in 1962 and soon ridding Cuba of the disease. In 1980, Brazil launched an all-out attack on polio, immunizing 20 million chil-
the virus. And they implemented vigorous house-to-house “mop-up” vaccination campaigns once a case was detected. (Because polio can circulate silently, a single confirmed case is treated as an outbreak.) The last indigenous case in the Americas occurred in Junin, in northern Peru, in September 1991, involving a 3-year-old boy named Luis Fermín Tenorio.

Early days
Lobbied hard by a small coterie of “eradicationists” such as de Quadros, Sabin, and Rotary International, which Sabin had enlisted in the fight in the mid-1980s, WHO member states resolved at the World Health Assembly in 1988 to eradicate polio worldwide by 2000.

At WHO headquarters in Geneva, however, the reception was tepid at best. The agency was already confronting a huge list of health problems, many more severe than polio. And the new directive came with an infinitesimal budget, just enough to support one staff person. “WHO was told to eradicate polio with one hand tied behind its back,” explains Aylward.

Moreover, it was by no means clear scientifically that the goal was attainable. “It was always a huge risk, never a foregone conclusion,” recalls WHO’s Maher, an Australian biologist who fought polio in the Western Pacific for 8 years before joining Aylward in Geneva. “I can’t overstate the magnitude of what we are trying to do. To wipe out a virus. It’s only been done once”—with smallpox.

Moreover, “so many things about smallpox were easier than polio,” adds Henderson, who questioned the polio enterprise from the get-go. “With smallpox, protection comes with one dose of vaccine. And even a villager can diagnose it. And smallpox doesn’t spread all that readily.”

Nor was polio as big a problem, Henderson argues. “Has polio ever been one of the major problems of the developing world? No. One in 200 gets it. And one in 2000 of those die. It doesn’t begin to touch measles or malaria.” So why pour money into chasing a single disease, he and other skeptics argued, when those funds could be used instead to boost routine immunization or otherwise improve child health?

During those “sleepy” days in the early 1990s, as Aylward calls them, not much happened globally, and what did was at the instigation of countries such as China where the disease was rampant. The campaign in WHO’s Western Pacific Region, which includes China, would prove to be a turning point.

Compared to Latin America, the Western Pacific Region was a messy, sprawling place, devastated by poverty and conflict and divided by myriad languages. Maher remembers the Mekong Delta as the toughest, and most inspiring, place he ever worked. When he went there in 1992, the United Nations had just pulled out and the Khmer Rouge would remain active for years. The WHO folks didn’t have much money or resources, and the climate, environment, huge number of children, and high traffic along the river all conspired to keep poliovirus alive.

“And the psychological scars people bore,” recalls Maher, in that “everyone had a member of their family killed, or their entire family disrupted. Plus, they were so bloody poor. The amazing thing is despite all the nastiness and terrible trauma, we could find people interested in working and doing a good job. And they did it.” Under the guidance of Lee, at that time a 45-year-old physician and public health specialist who was head of the polio eradication initiative in the region, the team pulled it off in 6 years.

In Cambodia, Maher was sometimes helped out by a young Canadian physician and epidemiologist fresh out of Johns Hopkins University: Bruce Aylward. With his
In the Mekong Delta region of Vietnam and Cambodia, wracked by poverty and conflict, the poliovirus thrived in the early 1990s, testing the mettle of Chris Maher (left) and his colleagues. When Aylward arrived in late 1997, the operation consisted of four people in Geneva and 70 worldwide. By 2000, it had grown to 50 in Geneva and 3000 worldwide. “When I took over, it was clear that we could never eradicate polio by 2000. My goal was to convince the world that it could be eradicated, period, and to get the world to commit to 2005,” says Aylward.

“He was tremendously hard-working, very talented, and kind of obsessed,” says Maher, who joined Aylward in Geneva in 2000. Aylward could also be brusque and impatient. “Bruce’s natural instinct is full speed ahead and damn the torpedoes,” notes Maher. “He trod on a lot of feet.” Easily as driven as Aylward, blunt, and physically imposing—he’s seen the insides of most hotel gyms across the globe—Maher has evolved over the years into Aylward’s unofficial “handler,” smoothing ruffled feathers and bandaging damaged toes.

During those early years, the somewhat unwieldy core partnership was coalescing, with WHO taking the lead for overall technical direction and strategic planning and CDC for vaccine supply, outbreak investigations, and genetic fingerprinting of viral strains. UNICEF took care of the on-the-ground logistics of organizing massive campaigns and training and mobilizing the vaccination teams. “And there was always Rotary,” says Aylward, who lauds the group for its “tireless advocacy.” Over the decades, Rotary International has contributed more than $500 million and countless volunteers. Throughout, the partners have also been aided by a network of national governments, nongovernmental organizations, humanitarian organizations, international agencies, and “some very big heroes,” such as the United Nations Foundation and, more recently, the Bill & Melinda Gates Foundation, says Aylward.

By 1999, polio cases had dropped about 98% to just 7000 worldwide. The campaign knocked off the easy areas first in rapid succession: Europe, the Pacific Rim, and large parts of Africa. Other places—the Indian subcontinent, west and central Africa, and the horn of Africa—proved much tougher. The differences remain puzzling. A range of factors conspire to keep the virus alive, chief among them poverty, population density, tropical climate, poor sanitation, political insecurity (which makes any operation perilous), and indifferent or minimal support from the local community.

Along the way, it became clear that the three to four doses of OPV that confer lifelong immunity to most vaccine recipients in the United States and other “clean” environments would not suffice in poor tropical settings. Perhaps it is the pervasive diarrhea, which means that the vaccine flows right through the children before it can take, but in most “low-hygiene” environments, at least eight doses per child are needed. Equally puzzling, in some of the toughest areas, transmission persisted even when the country managed to immunize 85% or 90% of the children, whereas in some parts of Africa it stopped with just 70% to 80% coverage. “I think we will eradicate polio without really understanding how,” says Aylward.

In some places, such as India, polio days were major celebrations. Schoolchildren flocked to the booths to get their polio drops. In others, such as Mogadishu, Somalia, the vaccine had to be delivered during lulls in the shooting. “As you can imagine, polio is probably not the most urgent priority in these countries,” says Elias Durry, who heads polio and other immunization operations in Soma-
So, despite stepped-up rounds and increasing sums of money thrown at it, polio remained stubbornly entrenched in various corners of the world. As target dates slipped, the goal was redefined—from certifying the world polio-free by 2005 to having all the regions be in the process of certification to stopping transmission of wild virus. The program was perpetually cash strapped; every year, Aylward had to lobby for more money, trying to convince donors that just one more push would do it.

**Triple whammy**

As the partners struggled to make that final push, the campaign was dealt the three blows that threatened its very survival. First came the outbreak in Hispaniola, an island shared by Haiti and the Dominican Republic, in the summer of 2000. It was not immediately obvious that something was terribly amiss. Although the region had been polio-free for years, Hispaniola was ripe for an importation.

Routine immunization had fallen to an alarming 20% to 30%, says de Quadros, leaving a huge cohort of kids susceptible should the virus enter from an endemic country.

But when Olen Kew of CDC and colleagues sequenced the viral DNA obtained from stool samples of several of the affected children, they found that it was not an imported wild virus but a derivative of the Sabin strain used to make OPV (Science, 12 April 2002, p. 356). Judging from the number of genetic mutations, they surmised that the virus had been circulating in the largely unvaccinated population for at least 2 years before reverting to wild virus but a derivative of the Sabin strain used to make OPV (Science, 12 April 2002, p. 356). Judging from the number of genetic mutations, they surmised that the virus had been circulating in the largely unvaccinated population for at least 2 years before reverting to wild virus but a derivative of the Sabin strain used to make OPV (Science, 12 April 2002, p. 356). 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Although poliovirus would not be an effective bioweapon, its potential for inciting terror was immediately clear. “We know
what it was like in the 1950s when people were afraid to go into swimming pools,” says Orenstein.

Polio eradication had been sold to countries on the premise that it would enable them to stop immunization and devote scarce resources to other diseases. But after 9/11, it became clear that countries worried about bioterrorism were unlikely to leave their populations vulnerable to dangerous agents—as even U.S. citizens now are vulnerable to smallpox. That raised the unsettling prospect that rich countries that could afford inactivated polio vaccine (IPV)—less effective but unable to cause disease—would continue immunization, while the poor countries would be left vulnerable to polio. To Fine, who favors universal IPV, such inequities are “intolerable.” Others see them as regrettable but inevitable.

The third blow came in a country where the campaign had seemed on the verge of success: India. With just 200-odd cases in India in 2001, it looked as if the campaign had finally cracked the deep-rooted reservoir in Uttar Pradesh. But then in 2002, wild poliovirus exploded in India, starting in Uttar Pradesh and racing through the country. When the partners reanalyzed the data, they realized that the problem was largely in the minority Muslim community in Uttar Pradesh (see p. 1964).

The outbreak shook the partners and donors to the core, raising doubts that they would ever pull it off. “The wheels fell off the trolley,” says Maher. “We took a long step back in 2002.”

“We were so close, and we botched it,” says Aylward. “We got complacent. We let down our guard.”

Reeling from these blows and even more strapped for cash, the partners made a conscious and some say overdue decision in April 2003 to focus their resources on India and the remaining endemic countries. Polio was now cornered in just seven countries; three major reservoirs in India, Pakistan, and Nigeria accounted for 95% of the cases. And within those three countries, transmission was restricted to five major hot spots that accounted for 75% of the global total.

The problem was that, although the virus was on the run, it had retreated to the worst corners of the world—poor, crowded, chaotic, unsanitary places where it could really hunker down, notes Stephen Cochi of CDC. The partners stopped mass campaigns in several 100 polio-free countries, enabling them to redeploy forces to the endemic areas, which they planned to blast with repeated rounds of immunization. At the same time, they would try to guard their flanks by stepping up surveillance in the polio-free regions. And they would continue national

Apathy hardened into resistance in July 2003, when several Muslim leaders began to protest that the vaccine was tainted with the AIDS virus and sterility drugs, part of a U.S. plot to decimate the Muslim population. Responding to growing alarm, the Kano state government cancelled the vaccination rounds planned for 4 and 5 September. Worried that funds would be misused or wasted, the European Union declined to pay for the planned national rounds in October and December. Cases skyrocketed.

Maher says the partners were resigned to the likelihood that the virus would continue circulating in Nigeria and neighboring Niger throughout 2004 and possibly into 2005, but not to its escape to neighboring countries. “We did not anticipate losing ground in Nigeria. We didn’t anticipate that at this late stage, we would be responding to a widespread outbreak again.”

A jolt of energy

On 29 July 2003, just 8 days after he took office, Lee reiterated his vow to eradicate polio and appointed Heymann as his special adviser.

Heymann brought a razor-sharp mind, a sense of urgency, his trademark decisiveness, and fresh tactics from his fight against SARS. From now on, he declared, each new case of polio would be treated as an international public health emergency.

Heymann’s “just do it” approach was evident in spades in Atlanta in September, where he and Aylward met with CDC and UNICEF officials for a strategy session. Over the objections of some of the CDC polio veterans, Heymann insisted they could wipe out wild transmission in 2004—if they were bold enough. The window of opportunity was narrow, and time was short: If they didn’t halt transmission soon, polio would break out again and infect countries that were now vulnerable because they had stopped mass campaigns, as was already occurring in west Africa. “There isn’t time to make a perfect program now,” said Heymann. “Just whack it.”

Another example of how Heymann is pushing the envelope is the bombshell buried in an otherwise bureaucratic document, the global polio eradication strategic plan for 2004–08. For years, the partners had been agonizing over whether and how to stop immunizing after the world was certified polio-free (see p. 1969). Once Heymann came on board, they made a remarkably fast decision. In a final draft, the fuzzy language of earlier versions about “developing post eradication vaccination policy” was

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replaced with the simple words “stopping OPV.” Says Aylward: “That was David [Heymann]. We knew the decision, but we needed someone with his credibility to say it was the right decision.”

The year 2004 will see the most aggressive push yet in the remaining reservoirs and at-risk countries. With full backing of the Indian government, the partners are attacking the intractable reservoir in western Uttar Pradesh with relentless, repeated rounds to immunize every child—or at least 90%. Because of its astronomical birth rate, there is a concerted effort to reach all newborns, who present a huge susceptible cohort every month.

In Pakistan—where worrisome, low-level transmission continues—as in India and Nigeria, more people are on the ground than ever before, devising microplans to identify every single house and ensure that it is visited by a vaccination team, and that each team has at least one woman or a member of the local community to help overcome resistance. The teams are trying to gain access to the tribal groups in Pakistan’s remote North-West Frontier Province at the same time that military forces are trying to root out Al Qaeda. And they are blasting the Cairo area, one of two lingering reservoirs in Egypt, where one challenge has simply been finding vaccinators willing to climb all the way to the top floors of the high-rise apartments that dot the city.

All this requires more money than ever before—WHO and UNICEF estimate the initiative will spend $450 million in 2004—along with innovative ways to get that money where it is needed. And it requires full support from political and religious leaders at all levels.

Increasingly, the way to get that support is to “name names”—a strategy informally referred to as shame and blame, much more in evidence since Heymann’s arrival. If a country or province is slacking off, tell them—and the world—that they are risking a $3 billion investment and needlessly causing more children to be paralyzed. If commitment in a key country is flagging, Heymann will jump on an airplane or pick up the phone. “It is very easy for him to call a minister of health and effectively say, ‘We need to do a better job. And I will call next week to see if we are,’” says Maher.

On 15 January, ministers of health from India, Pakistan, and Nigeria and five other endemic countries (Somalia had then gone a year without a case) flew to Geneva and reconfirmed their commitment to stopping transmission of wild poliovirus in 2004—and risking public humiliation if they don’t. “We offered them 2005,” said Heymann at a press conference. “And they all said they wanted to do it in 2004.”

Estonia may be first, then India, then Pakistan. “Once India finishes, with God’s grace in 2004, the political pressure will be immense,” says Maher. “Then Pakistan and Nigeria will be the only places left in the world with polio.”

Pakistan “is a bit of a risk,” says Aylward. And

Meanwhile, as the partners are waiting out the political storm, Maher will be spending much of the next few months on the ground in Nigeria, reevaluating everything from the composition of the vaccination teams to how WHO and UNICEF divvy up tasks, so they can deliver the best possible rounds when they finally get the chance. Transmission in Nigeria seems likely to spill over into 2005. And CDC virologist Kew notes that the virus is now circulating independently in Niger and Burkina Faso, a problem those countries will have to address. But Maher is fairly sanguine that Nigeria will come around. “Nigeria is not a huge technical challenge,” he explains. They did it in densely populated Lagos, which was polio-free for 2 years until being reinfected from the north, he says. So the sparsely populated north should be relatively easy, once they gain access. “If we have three, four, five good rounds, that’s it. The game is over.”

And if and when the world is declared polio-free, the partners have perhaps 1 year in which to stop OPV. By then, the stockpile should be ready with enough OPV to vaccinate a region, or even much of the world, should polio return. Excellent surveillance will be crucial for detecting and stopping an outbreak—and money to support it may be hard to find.

But after the “long and very, very painful” process of trying to halt transmission, as Maher describes, the endgame doesn’t look so intimidating. There is an undeniable psychological element here, he says: “If we do this, we can go on and do practically anything we want.”

—Leslie Roberts