Steve Cochi is not your stereotypical disease warrior. You won’t see him parachuting into hot zones on the hunt for the next exotic virus. He’s not a regular on radio shows or in front of the camera. Cautious, unassuming, with thick white hair, wire rim glasses, and an almost cherubic face, the 63-year-old physician and epidemiologist is most comfortable behind the scenes.

But for the past 25 years, Cochi has been pushing one of the boldest—and some might venture foolhardy—ideas in public health. He wants the world to undertake a huge new effort to eradicate measles. Not just tame the virus or control the outbreaks resurging across globe, but obliterate it, wipe it off the face of the earth, as has only been done once for a human pathogen, smallpox, in 1977, and as the world fervently hopes will happen soon with polio.

It’s inexcusable not to, says Cochi, who is a senior adviser on global immunization at the U.S. Centers for Disease Control and Prevention (CDC) in Atlanta. Measles killed an estimated 145,000 people in 2013, mostly children in Africa, and left many more deaf, blind, or otherwise disabled. We have the means to eradicate it, says Cochi, whose mentor at Duke University School of Medicine was Sam Katz, a co-developer of the measles vaccine. “For measles you just need two doses of vaccine,” says longtime collaborator Andrea Gay of the United Nations Foundation in Washington, D.C. “There are few things you can say that about. … Why wouldn’t you do it?”

That’s why Cochi, Gay, and a small cadre of like-minded colleagues have spent years quietly lobbying the World Health Assembly (WHA) to put measles eradication at the top of the global agenda, right up there with polio, and declare a target date for eradication.

But they’ve got a problem, or two or three. First is the perception issue. Although measles is one of the leading childhood killers, people in wealthy countries tend to think of it as a minor annoyance, a rash and a fever but no big deal—certainly not big enough to justify another multi-billion, multiyear initiative.

It would be fiendishly difficult. Measles is the most contagious virus on Earth, infecting virtually everyone who is not vaccinated. But mostly there is polio, which hasn’t disappeared as it was supposed to in 2000, despite more than $11 billion and counting and nearly 30 years of effort. Until it does, the world will not have the money or the energy for another huge eradication campaign, no matter how laudatory the goal. “I am not against measles eradication,” says David Heymann, a veteran of the smallpox wars who oversaw the Global Polio Eradication Initiative while at the World Health Organization (WHO). “But we’ve all been burned by polio.”

Reluctantly, Cochi cedes the point. “We are waiting in the wings.” But not idly, others say: A stealth eradication campaign is already well under way, with Cochi at its helm.
MEASLES BEGINS innocuously enough, with a cough, runny nose, inflamed eyes, a sore throat, and a slight fever. Three to 5 days later, the distinctive rash erupts, starting on the face and working its way down the arms and trunk and finally to the legs and feet. Fever spikes, as high as 104°F or 105°F (about 40°C). Ear infections are a common complication. Some kids in the United States are hospitalized, but for the majority, the rash fades and infection resolves in about a week.

But more than half of the estimated 10 million infected with measles each year in the developing world fare far worse. The virus suppresses the body’s defense system, especially in those already immune-compromised or with malnutrition or vitamin A deficiency, leaving them vulnerable to secondary bacterial infections. The problems are compounded by a lack of health care. Pneumonia is the most common cause of death; diarrhea and dehydration is a close second. Measles is one of the top five preventable causes of blindness. Deafness is common. Inflammation of the brain can cause seizures and sometimes permanent brain damage. In poor countries, the fatality rate is 2% to 15%, soaring to 25% in the worst outbreaks.

Everyone who has witnessed a measles outbreak wants to reduce the toll, says Walter Orenstein, who has devoted his career to fighting the disease and is now associate director at the Emory Vaccine Center in Atlanta. But “going the final mile, going to zero,” is a completely different game, he says. Zero is in Cochi’s genes.

He is descended from a line of dedicated disease eradicators who came up through CDC in the 1960s and 1970s: William Foege, Ciro de Quadros, Donald R. Hopkins, and Donald A. Henderson, to name just a few. Most served in the Epidemic Intelligence Service, CDC’s famed boot camp for disease detectives, and many cut their eyeteeth fighting smallpox in Africa.

When they triumphed over smallpox in 1977, they and thousands of others had pushed off what many thought impossible: the first eradication of an infectious disease. Their feat is still heralded as the crowning achievement of public health, the ultimate triumph of man (and they were men) over microbe, and a permanent gift to humanity, which need never suffer the horrible disease again. They were itching for another conquest.

Henderson, the gruff physician and epidemiologist who led WHO’s global smallpox campaign, recalls a meeting in 1980, just 1 month after WHO had officially certified that smallpox was gone. Public health luminaries gathered in Washington, D.C., to decide what to eradicate next. “I told them that was the wrong question,” says Henderson, who is now a professor emeritus at the John Hopkins Bloomberg School of Public Health in Baltimore, Maryland. “Smallpox was done by the skin of its teeth,” he said. Better to invest in immunizing children against all preventable diseases, including measles, and forgo what he has called “the blinding beacon” of eradication. “I was overruled,” he says.

Don Hopkins made an impassioned plea for measles in the 19 June 1982 issue of The Lancet. Hopkins was fresh back from battling smallpox in West Africa, where CDC also ran a measles control program. There he had seen firsthand the devastation measles wrought—at the time it was killing an estimated 2.6 million children a year—and how people clamored for the vaccine. “They would take smallpox only on one condition—that we give them measles vaccine,” he says.

What’s more, measles was one of the very few viruses that met the strict scientific criteria of “eradicable.” Not only was there an excellent vaccine and a good diagnostic, but like the smallpox and polio viruses—and unlike Ebola—the measles virus also has no animal host in which to hide. In Africa, Hopkins saw how the virus crumbled in the face of aggressive vaccination, disappearing in Gambia for more than a year.

Hopkins, who soon became deputy director of CDC, had powerful allies, most important Foege, then agency director, who seconded Hopkins’s call in an article a few months later. “We were all similarly minded,” says Alan Hinman, one of Hopkins’s co-authors now at the Task Force for Global Health in Decatur, Georgia. “We all thought measles should go next.”

But measles was eclipsed by polio, a far less serious disease. “Polio cripples; measles kills,” Cochi says. In the prevaccine era, polio paralyzed roughly 650,000 a year, whereas measles killed as many as 5 million or 6 million. But polio had terrified a generation of parents when it swept through the United

### The hit list

Measles lacks features that have made polio so hard to eradicate, including silent cases and vaccine-derived transmission. But it is far more contagious—hence harder to stamp out—than smallpox, the one virus successfully eradicated. Some of the challenges are highlighted.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Smallpox (Eradicated)</th>
<th>Polio</th>
<th>Measles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical presentation</td>
<td>Fever and rash</td>
<td>Acute, flaccid, paralysis</td>
<td>Fever and rash</td>
</tr>
<tr>
<td>Asymptomatic infections</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Primary mode of transmission</td>
<td>Respiratory droplets</td>
<td>Fecal-oral Oral-oral</td>
<td>Respiratory droplets</td>
</tr>
<tr>
<td>Reproduction number</td>
<td>5–7</td>
<td>4–13</td>
<td>12–18</td>
</tr>
<tr>
<td>Community immunity</td>
<td>80%–85%</td>
<td>75%–92%</td>
<td>92%–94%</td>
</tr>
<tr>
<td>to stop transmission</td>
<td>1</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Serotypes</td>
<td>Intradermal injection</td>
<td>Oral drops</td>
<td>Subcutaneous injection</td>
</tr>
<tr>
<td>Number of vaccine doses</td>
<td>1</td>
<td>≥3</td>
<td>1–2</td>
</tr>
<tr>
<td>doses needed to stop</td>
<td>1 dose = 95%</td>
<td>3 doses*</td>
<td>2 doses = 99%</td>
</tr>
<tr>
<td>transmission</td>
<td></td>
<td>Type 1 = 73%</td>
<td>Type 2 = 90%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Type 3 = 70%</td>
<td></td>
</tr>
<tr>
<td>Waning of protective immunity</td>
<td>Yes</td>
<td>Humoral: No</td>
<td>No</td>
</tr>
<tr>
<td>Vaccine-induced virus</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>infection and transmission</td>
<td></td>
<td>Intestinal: Yes</td>
<td></td>
</tr>
<tr>
<td>Period of contagiousness</td>
<td>25 days</td>
<td>4–6 weeks</td>
<td>9 days</td>
</tr>
</tbody>
</table>

* >95% in industrialized countries
States in the 1940s and 1950s. Measles, on the other hand, was a shrug. “Parents didn’t seem to mind that their kids had measles,” says Orenstein, who led the national immunization program that eliminated measles from the United States.

And polio had a most persuasive advocate and “salesman par excellence,” as Henderson describes him: Albert Sabin, a national hero for inventing the oral polio vaccine (OPV). Sabin's grand vision was to deliver his easy-to-use polio drops in mass campaigns to reach every child, and voilà, polio would disappear. “Just a few drops on the tongue. How easy it would be,” Henderson recalls.

Rotary International kick-started the polio eradication effort with $1.2 billion. (It has since contributed $1.3 billion.) At the Pan American Health Organization, de Quadros began an aggressive campaign to drive polio out of the Americas. The die was cast in 1988, when WHO committed to eradicating polio by 2000—never imagining that the program would still be dragging on 15 years later.

MANY OF THE MEASLES advocates enlisted in the polio wars, among them Cochi, who joined CDC in the 1980s, after 2 years as a pediatrician on a Navajo reservation in New Mexico. At CDC, he quickly found his niche working on vaccine-preventable diseases, logging long hours chasing polio in Nigeria, Pakistan, Bangladesh, and India, to name just a few countries. Soon Cochi was the “go-to” guy for unvarnished advice on polio eradication, says Bruce Aylward, the longtime leader of the polio eradication effort. “Steve has been hugely influential.”

While the polio campaign unfolded during the 1990s, Cochi and others then at CDC, including Peter Strebel and Mark Grabowsky, began laying the groundwork for what they hoped would be the next eradication push—sitting on various acronym-studded expert panels, writing tens of papers, and participating in countless international meetings, including one in 1996 that concluded measles eradication was technically feasible, with a target date within the next 10 or 15 years.

In 2000, the time seemed ripe to go public. Polio seemed to be winding down. Measles had been eliminated in the United States—cases since then have been “imported” from other countries—and it was on the way out in the entire region of the Americas. The last case in the Americas occurred in 2002, showing the world for the first time the virus could be beaten in poor countries.

At an immunization meeting in Pretoria in December 2000, Cochi pulled aside a small but well-placed group to talk about measles. African governments were desperate for help fighting the outbreaks still exploding there. Could they provide it, he asked? The experts went home and enlisted support from their respective organizations.

Thus was born the Measles Initiative, a loose-knit partnership of five organizations—the American Red Cross, CDC, the United Nations Children’s Fund, the United Nations Foundation, and WHO—with Cochi as its unofficial ringleader. Renamed the Measles & Rubella Initiative in 2012 when it expanded its scope, the initiative did not have an explicit eradication goal, but its intentions were pretty clear when it called for “a world without measles.”

IN SOME WAYS, measles would be easier than polio (see table, p. 960). The measles vaccine is far better than OPV, providing 99% protection with just two doses. And almost every case of measles is visible, so you know where the enemy is. Not so for polio, which paralyzes just one in about 200 people it infects and so can circulate undetected, sometimes for years, before it strikes again.

But measles poses different challenges, key among them its exquisite contagiousness. Transmitted by respiratory droplets or aerosols, the virus can linger in the air for up to 2 hours after an infected person leaves the room, and kids are often infected in hospitals or doctors’ waiting rooms. The virus’s reproduction number—the number of infections a single case will generate in an unvaccinated population—is a staggering 12 to 18, compared with 5 to 7 for smallpox and 1.5 to 2.5 for Ebola. To stop measles transmission, more than 95% of the population has to be vaccinated, as opposed to about 80% in most places for smallpox and polio.

And the measles vaccine is far harder to deliver than polio drops. It must be injected, so mass campaigns require armies of trained health care workers, not the volunteers who dispense polio drops. It has to be reconstituted in the field, a step that has on rare occasions led to accidents. Last year in northern Syria, for instance, a health worker mistakenly grabbed the wrong bottle out of the refrigerator and mixed the powder with a powerful muscle relaxant. Within minutes, 15 children under age 2 died, mostly of suffocation. Once reconstituted, the vaccine’s shelf life is only 6 hours, so clinic workers are sometimes reluctant to prepare a batch for just a few kids. They ask mothers to bring them back later, but that often doesn’t happen. Researchers are working on easier-to-use vaccines, but they are still years away.

“If we have to wait to solve the problem of routine immunization [to start measles eradication], we will be waiting for decades.”

Steve Cochi, CDC

Still, the first several years of the initiative were a huge success. The partners helped 70 resource-strapped countries launch mass measles vaccination campaigns. The world met the first global target—a 50% reduction in measles deaths from 1999 levels by 2005— with time to spare. By 2008, mortality had dropped 78% globally and a stunning 92% in Africa. But despite persistent lobbying by the initiative, WHA held off declaring an official eradication goal.

Then, beginning in 2009, “the bottom dropped out,” Cochi says. Hammered by the global recession, the initiative lost close to 75% of its international funding. Mass vaccination campaigns were canceled or scaled back in high-risk countries, routine measles vaccination suffered, and global progress stalled. The following year, measles exploded in southern African countries. By 2011, deaths had climbed back to 200,000, up from 170,000 in 2008.

In some wealthy countries, measles ran headfirst into a strong and increasingly vocal antivaccination movement, mostly among the well-educated, fueled by a long-discredited link between autism and the measles, mumps, and rubella vaccine and by nonchalance about what is seen as a mild disease. The drop in immunization has reversed progress in Europe, which had 37,000 measles cases last year, and left the United States battling repeated importations, like the ongoing one that started in Disneyland in late 2014 and has now spread to 19 states and the District of Columbia.
It had also become abundantly clear that the poliovirus was not going away anytime soon. Cases were down 99% from 1988 levels, but the last 1% would not budge, entrenched in India, Afghanistan, Pakistan, and Nigeria, some of the world’s poorest countries and toughest places to work.

It turned out the vaccine virus in OPV could revert and actually spark outbreaks of its own. Another problem was that OPV, very effective in high-income countries, did not work as well in the hot, crowded slums in poor countries where polio often holes up. In some places, armed conflict made mass polio campaigns impossible. In others, rumors about vaccine dangers and an anti-Muslim plot derailed them. Over the past few years, opposition has taken a horrifying turn, with polio workers being singled out and murdered in Pakistan.

Some experts began asking publicly whether polio eradication was feasible—and if it was, whether it was worth all the money, when bigger public health problems were going wanting. As the campaign dragged on and costs ballooned, donors were in a bind, tapped out but too far in to pull the plug.

“Eradication is a monolith,” Henderson says. “It tramples everything in its way.”

FOR NOW, THE MEASLES INITIATIVE is simply trying to regain lost ground, Cochi says. Routine immunization rates remain stuck at 84%, about where they were in 2008 and well below the 2015 target of 90%. The regions that vowed to eliminate measles by 2015 or earlier are badly off track. Global deaths have dropped back to 145,000, but outbreaks are sweeping Asia and Africa. Measles is on the upswing throughout the Middle East, and health experts are scrambling to avert a huge epidemic in the West African countries where Ebola has left fragile health care systems reeling. Seventy percent of measles cases now occur in just six countries, not coincidentally many of the same places polio and smallpox proved so hard to dislodge. In 2011, WHO said that although measles can and should be eradicated, no official program should be launched until there is progress toward both polio eradication and the 2015 measles goals.

The partners now steer clear of the word “eradicate,” emphasizing instead that they are helping the remaining five WHO regions reach their stated goal to “eliminate” the virus by 2020. It’s more than semantics: Eradication means no more measles cases, anywhere, period, whereas elimination means stopping indigenous transmission within a defined geographic area. But the partners concede that if all regions met their elimination goals, then, ipso facto, measles would be eradicated. “In a sense we have an eradication goal; we just don’t recognize it as such,” Orenstein says. “It is a stealth campaign” until polio is gone, Gay concurs.

Even then, the world may have soured on eradication. Matt Hanson at the Bill & Melinda Gates Foundation in Seattle calls the dramatic drop in measles mortality “one of the great public health successes,” and the foundation contributes about $40 million a year to the fight. But that’s a trifle compared with the more than $2 billion it has invested in polio eradication. “Bill made a conscious decision,” Cochi says. “The foundation could … not afford to operate on two fronts.”

The same goes for Gavi, the global vaccine alliance in Geneva, Switzerland. Reducing measles deaths is high on the alliance’s agenda, but at the moment, “eradication is not Gavi’s goal,” says CEO Seth Berkley. The international health community has other priorities, he and others say, and the big one is boosting routine immunization and otherwise shoring up weak health systems in poor countries.

Cochi insists the world must do both: Eradicate measles while simultaneously boosting routine immunization. “If we have to wait to solve the problem of routine immunization, we will be waiting for decades,” he says. In the meantime, he adds, hundreds of thousands of children will die of a disease that could be prevented today, with two shots of an inexpensive vaccine.

There are some encouraging signs, Cochi and his CDC colleagues say. Funding is up slightly, and just in the past few months, hopes have risen that wild poliovirus may at last be gone from Africa, leaving just two endemic countries, Afghanistan and Pakistan. With polio finally on the way out, the measles advocates predict, discussion will inevitably turn to what to eradicate next.