

## THE END OF POLIO?

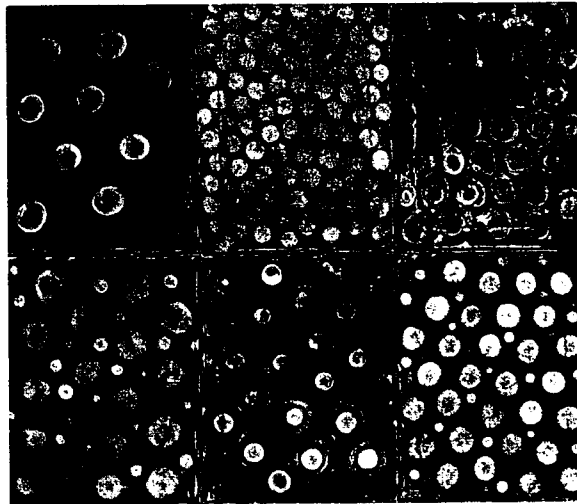
*The worthy campaign to eradicate the ancient scourge must confront hidden reserves of virus and a protean genetic foe. Many experts worry that the plan to end vaccinations could have lethal consequences*

BY WENDY ORENT

**I**MET JONAS SALK AT A conference once, four or five years ago," says William Lutz, a Rutgers University English professor and a polio survivor. "He was a very gracious gentleman. He asked me, 'Why didn't you die?'"

Good question, from a man who would know: who better than Jonas E. Salk, the physician who developed the first safe and effective polio vaccine, would understand Lutz's ordeal and his recovery from a childhood case of one of the deadliest forms of polio? Salk's vaccine removed the shadow of polio; those of us who have grown up outside that darkness can hardly imagine its horror. In the 1940s and early 1950s, polio killed or crippled thousands of children and young adults each year in the United States. Parents, beside themselves with worry, kept their children indoors and away from crowds, parks and other children all through the still heat of July and August, the dreaded "polio season." No one knew then how polio spread, though swimming pools were suspect; no one understood why paralysis would strike one infected child and not another. The mystery of the disease added to its terror.

In the summer of 1945, Lutz's parents agreed to let him go on a single outing. The five-year-old was allowed to accompany a friend's family to the Wisconsin State Fair. "We had tickets to the pit area, where the stock-car drivers went," he recalls. "There wouldn't be a crowd there. My parents thought I would be safe." The disease that Lutz caught that day was bulbar polio, which invades the brain stem and can suppress breathing; many who were less fortunate than Lutz had to endure the infamous iron lung; many died. The episode left Lutz with permanent weakness in his legs and throat, and an abiding appreciation for the vaccine that began, in 1955, to lift the affliction from the earth. When he became a father, he was particularly grateful to be spared



Ross Bleckner, *The Tenth Examined Life (detail)*, 1991

the dread his own parents had suffered. "I didn't have to think about it," he says, "because my son was immunized."

By the mid-1960s, thanks to vaccines, polio had lost its hold in the United States and Western Europe. But the disease has remained a problem in many of the less industrialized nations. In 1988 the World Health Organization (WHO) embarked on a campaign to send polio the way of smallpox: into oblivion. The target date for that goal is the end of this year, and since the campaign began, the annual number of new polio cases has

dropped by more than 80 percent. "Days of tranquillity"—truces arranged between warring parties—have brought anti-polio vaccine to hundreds of thousands of children in Afghanistan, Angola, Somalia and Sudan.

But despite the intensified immunization efforts, polio has not yet been eliminated. More than 6,000 cases were reported in 1998, and an outbreak in Angola in April 1999 took 89 lives. China, until recently thought to be polio-free, has been struck again: this past October a sixteen-month-old boy in Qinghai Province was diagnosed with paralytic polio, and the government responded by vaccinating more than seven million people.

Such outbreaks have made it far from certain that the target date for eradication will be met. Yet WHO officials are still preparing for life in a world without polio. When that time comes, all the samples of poliovirus being kept for research purposes in laboratories around the world are to be tracked down, consolidated and placed in high-security storage facilities—a process known as "containment." Those remaining stocks may eventually be destroyed, though there is no plan to do so now.

Most problematically, the health officials who developed the polio eradication program believe that once polio has been banished from nature and laboratory samples of the

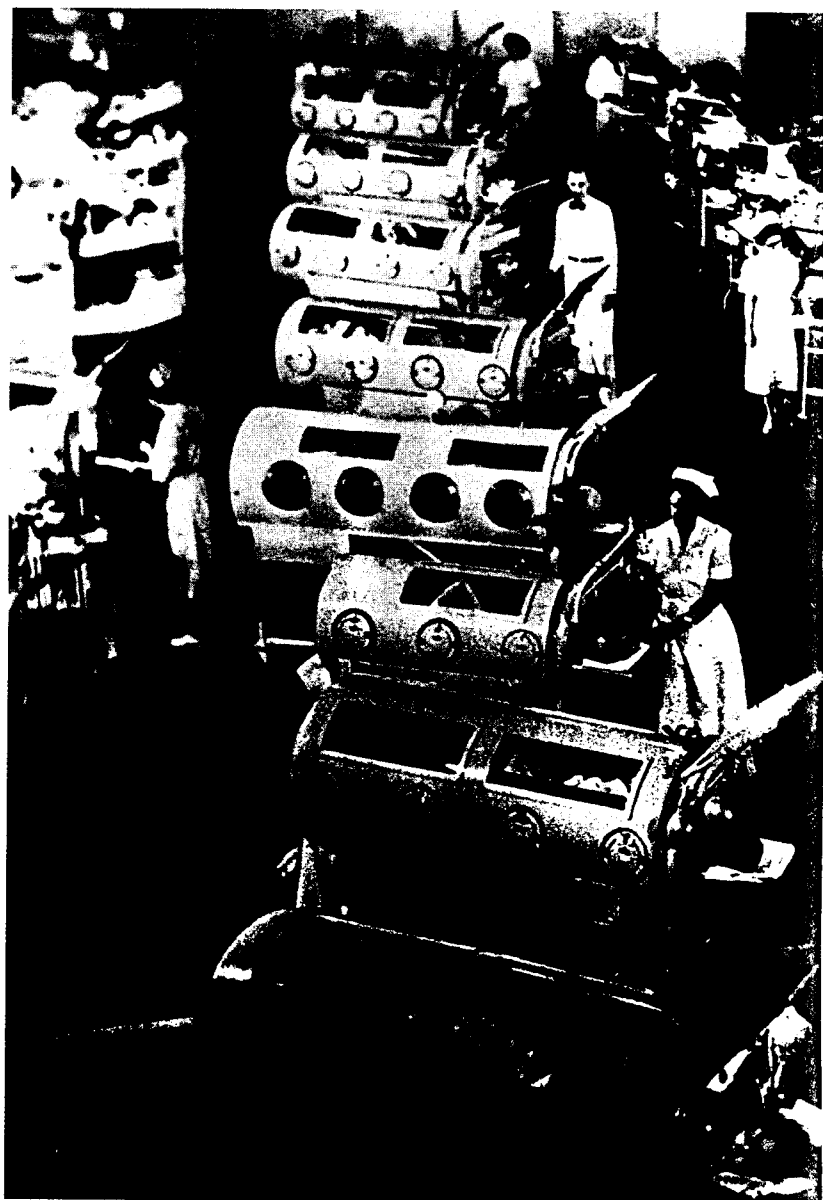
virus have been locked up, vaccinations can safely cease. The eradication project, of course, if successful, would be a public-health triumph. And a halt in polio vaccinations, in particular, would also be an enormous financial boon, since they currently cost the world \$1.5 billion a year. But the road to those goals runs through a minefield. It will not be as easy to get rid of polio as officials once thought. And, once eradication has been achieved, we may find that the post-polio world has perils of its own.

**T**HE ERADICATION OF SMALLPOX, which is usually held up as a model and an inspiration for the anti-polio campaign, is actually a false analogy—and more like a cautionary tale. Although a worldwide immunization effort drove smallpox from nature by 1980 and vaccinations have since ended, the virus has never been truly contained and has yet to be destroyed. The original plan was to consolidate all the remaining laboratory stocks and consign them to the autoclave in 1993. By 1991, however, U.S. intelligence had learned about a secret, decades-long program that had run in the former Soviet Union, in which smallpox was grown by the ton and sophisticated delivery systems for spraying it into the atmosphere were developed, making the virus a potentially devastating biological weapon [see “Escape from Moscow,” by Wendy Orent, May/June 1998]. In addition, it is now thought that smallpox virus may have fallen into the hands of terrorists or rogue states such as North Korea. Once it became clear that smallpox had not been contained, destroying the remaining laboratory stocks made little sense. So, despite WHO’s success in stopping the natural spread of smallpox, the world is by no means free of it.

The eradication of polio is more complex than that of smallpox, and it is only now, as the goal nears fulfillment, that those complexities are becoming clear. Smallpox spreads more slowly than polio, and it leaves unmistakable footprints: you either have the disease, complete with obvious pustules, or you don’t. Polio, by contrast, moves like ripples in water—silently and rapidly. Only one in a hundred people who are infected by it suffer from paralysis, or worse. As a result, polio is much more difficult than smallpox to track and eradicate.

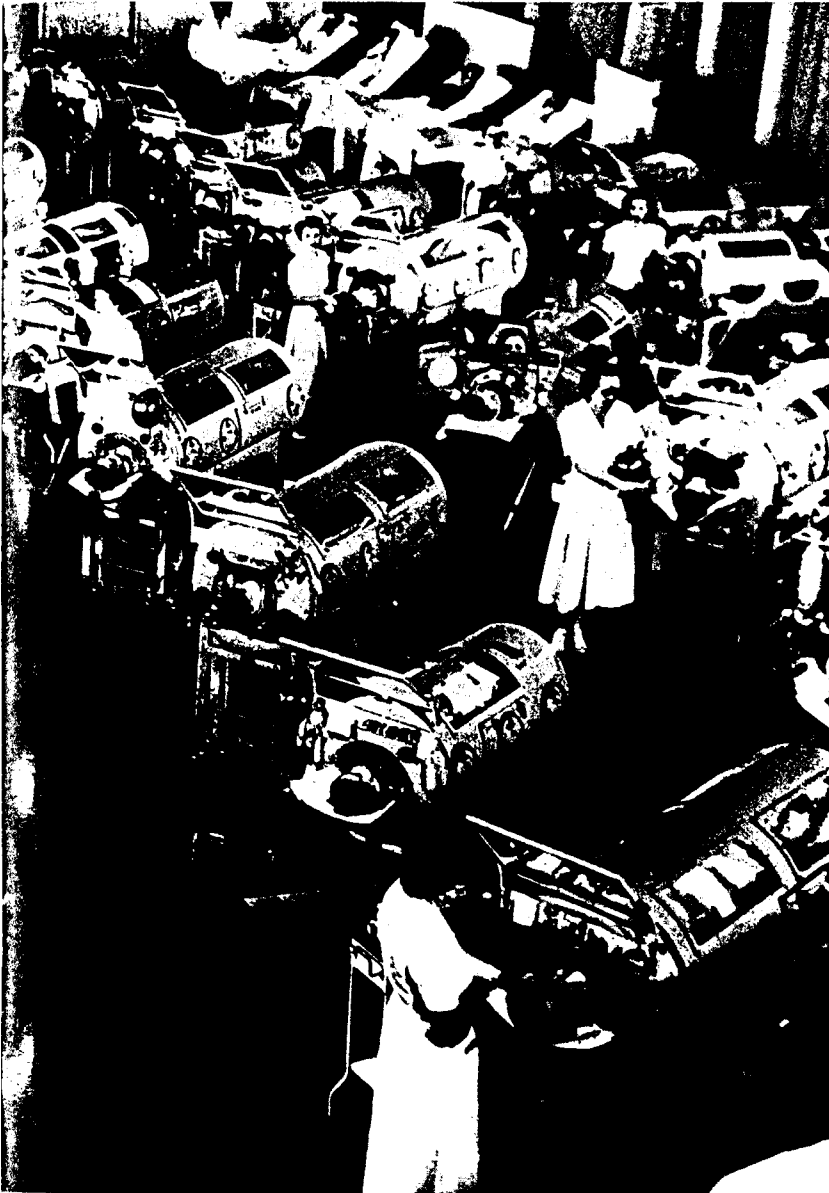
Polio is an enterovirus, a genus of viruses that colonize the lining of the digestive tract. Enteroviruses are members of the family Picornaviridae—small RNA viruses that mutate rapidly and cause a range of diseases, including the common cold and meningitis, as well as polio. You can think of a particle of poliovirus as a perfect, twenty-sided crystal, so small that it acts like a light, invisible dust. It drifts along the mucous membranes of the intestines until it reaches a bump or marker called the poliovirus receptor, on the surface of a cell. Once the virus attaches itself to that receptor, its genetic material steals inside the cell and begins to replicate.

That is not necessarily a problem. Most enteroviruses, including poliovirus, grow quietly in the intestinal tract,



where they do no harm; the body’s immune system generally routs the infection before it can enter the bloodstream. But though they initially replicate in the intestines, some enteroviruses, including polio, also have a strong affinity for the motor neurons of the spinal cord and the brain. And on occasion, perhaps as a result of an inadequate immune response, the virus breaks out of the intestinal tract into the bloodstream. From there, it either enters the brain or reaches the nerves through muscle tissue, particularly if the infected person suffers a strain or an injury. The illness caused by poliovirus, poliomyelitis, is marked by flulike symptoms, muscle spasms and paralysis that is sometimes permanent.

**A**LTHOUGH POLIO IS AN ANCIENT DISEASE (A stone tablet from ancient Egypt shows a priest with what appears to be a withered leg typical of paralytic polio), it did not surface as a major threat to human health until the twentieth century. In the past, polio, which usually spreads through contaminated water, infect-



*Iron lungs, Los Angeles County Hospital, c. 1952*

ed nearly every child shortly after birth. Babies acquired permanent immunity through that early exposure, and only the unfortunate child who somehow managed to avoid infection in infancy—the Egyptian priest, perhaps—was at risk.

With the improvement of the water supply early in the twentieth century, however, infants were no longer automatically exposed to polio, and so did not develop immunity. On the rare occasions that fecal matter carrying poliovirus did get introduced into a modern water system, therefore, the disease struck hard. One of the terrors of polio was its unpredictability. At the hospital, Lutz recalls, his father once pointed out a little girl whose father was one of the wealthiest men in town. She wore metal braces on both legs. “To polio it doesn’t make any difference if you’re rich or poor—she has to wear those braces and you don’t,” his father told him. “It was a very democratic disease,” Lutz says now.

In 1955, when Salk announced that clinical tests had proved that his vaccine actually worked, church bells rang across the nation. The modest, genial Salk, a relative unknown, was

thrust into the role of national hero. Vaccines function by provoking an immune response in the recipient without causing the disease. Salk’s vaccine was made from dead poliovirus and administered by a shot in the arm. Unfortunately, the vaccine was rushed into production too quickly: in that same year the Cutter Laboratories in Berkeley, California, cultivated batches of vaccine but did not treat them all thoroughly enough with formalin, the formaldehyde solution used to kill the virus. More than 200 children, inadvertently injected with living wild virus, contracted polio from the shot that was intended to protect them. The incident shook the public’s faith in Salk’s vaccine.

Meanwhile, Salk’s archrival, Albert B. Sabin, had developed a different kind of polio vaccine, one made from live but weakened virus and administered by mouth. By the early 1960s Sabin’s oral vaccine, having proved safe and extremely effective, had all but replaced Salk’s injected vaccine—delightful news for those who preferred sugar cubes to needles.

**S**CHOOLCHILDREN WERE NOT THE ONLY people who favored the oral vaccine. The two vaccines work according to different principles, and lead to different kinds of immunity. Salk’s injection of dead virus causes antibodies against polio to develop in the blood, resulting in what is called humoral immunity. The injected vaccine protects the individual and, when prepared according to Salk’s specifications, is extremely safe. But it does little to prevent colonies of poliovirus from growing in the gut. For that reason, Salk-vaccinated people exposed to poliovirus cannot get the disease, but they can become transient carriers, capable of infecting others for a few weeks, after which the virus naturally clears itself from their intestines.

Like the Salk vaccine, the Sabin oral vaccine causes antibodies against polio to develop in the blood, thus conferring humoral immunity. But the oral vaccine also induces colonies of live, weakened virus to take up residence for a while in the gut, creating what is known as mucosal immunity, a localized immune response by cells in the intestine, which from then on will be inhospitable to poliovirus. As a result, the oral vaccine not only protects people from coming down with polio, but also prevents them from becoming carriers of the disease. Furthermore, a person who has received the oral vaccine can bring health benefits to an entire community. People infected with wild poliovirus excrete it for between six and eight weeks in their stool. Likewise, people who get the oral vaccine excrete the weakened form of the virus for a similar period of time. If Sabin-vaccinated people happen to “infect” others during that period, they are in effect passing on the vaccine, thereby enabling the unimmunized people around them to develop their own immunity.

The oral vaccine has other advantages as well. It is much easier to distribute than the injected vaccine, since there is

no need for sterile needles or trained nurses. The oral vaccine is also less dangerous than the injected vaccine to produce, because, unlike the injected vaccine, its manufacture does not require that huge amounts of live wild poliovirus be grown in the laboratory. In addition, the oral vaccine is cheaper to make, in part because it does not require careful treatment with formalin. Oral vaccine does have one disadvantage (which it shares with the injected vaccine): it spoils when it is exposed to heat; in fact, maintaining a “cold chain”—that is, keeping the vaccine refrigerated throughout its journey from manufacturing to administration—has been one of the principal hurdles for the eradication effort in tropical countries.

Given its many advantages—reduced cost, ease of distribution and community and mucosal protection—oral polio vaccine has been the weapon of choice for eliminating polio epidemics. Although Salk’s was the first effective vaccine, it was not the one that eradicated polio from the Western Hemisphere; that honor goes to Sabin. But oral polio vaccine is not without its troubling aspects. Indeed, nothing about

the small, deadly crystal that is poliovirus is simple—least of all its eradication. The closer we get to a world free of polio, the stranger and more disturbing the entire issue becomes.

**W**ILD POLIOVIRUS MUTATES EXTREMELY rapidly. The problem with the oral polio vaccine is that it mutates as well, and in a dangerous fashion. A single nucleotide change in the so-called 5' noncoding region of the viral genome causes the weakened virus in the oral vaccine to become neurovirulent—or, in other words, capable of causing paralysis. And the mutation occurs frequently—at least half the time, within about a week of vaccination, according to the vaccine specialist Philip D. Minor of the National Institute for Biological Standards and Control (NIBSC) in South Mimms, England.

The mutated virus from the oral vaccine is still far less harmful and less contagious than wild poliovirus. In the vast majority of cases it causes no harm. But it can cripple and kill. In the United States, for instance, a small number of children who have received the oral polio vaccine, and some of their caretakers, have died or become permanently par-

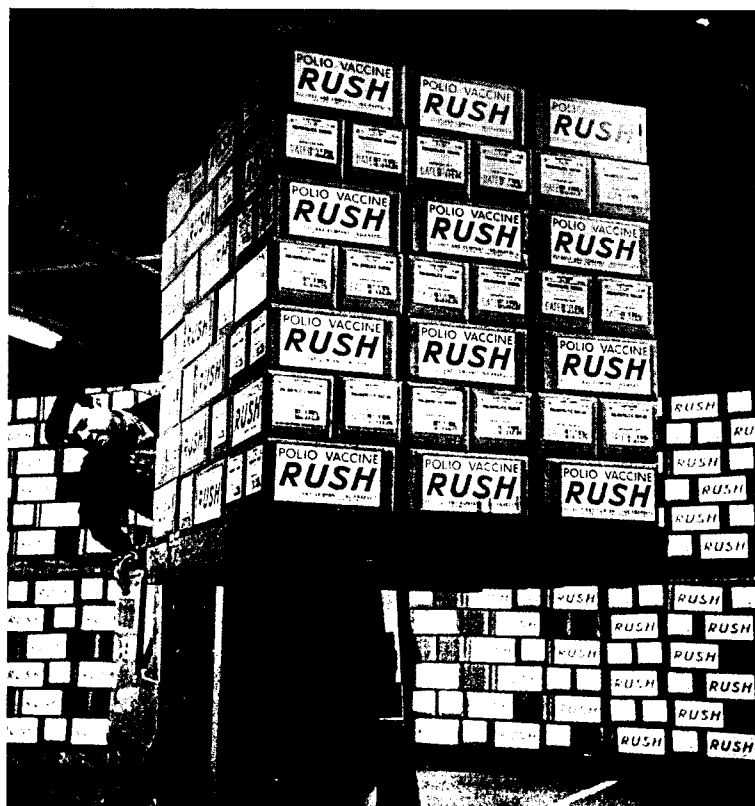
alyzed. The phenomenon, known as vaccine-associated paralytic polio (VAPP), is rare, given the vaccine’s strong tendency to revert to neurovirulence: the rate is one case of paralysis for every 2.4 million people vaccinated. That low rate does not reflect the true potential of the mutated vaccine to cause harm in an unprotected population, however, because practically everyone nowadays who comes into contact with a Sabin-vaccinated person has been immunized.

Why do a few people have such tragic reactions to the oral polio vaccine? In spite of what many American parents who oppose oral vaccination seem to think, it is not a question of “bad lots” of vaccine. “The vaccine is always the same,” says Vincent R. Racaniello, a polio virologist at Columbia University. Instead, the problem is likely to be a rare and previously unrecognized immune deficiency in the patient. And Racaniello thinks that in some cases, another enterovirus—such as enterovirus 71 or one of the coxsackieviruses, which can also cause paralysis—is probably at fault. The difficulty is that, in a given clinical case, it is often impossible to know for sure which

virus caused an infection. Nerve tissue cannot be examined unless the patient dies.

At any rate, in a population free of wild poliovirus, the risk that even a few people will get paralytic polio because of a vaccine is too high. This past January 1, the United States officially switched to a new, more potent version of Salk’s original injected vaccine. The move will prevent further cases of VAPP, because, unlike the oral vaccine, the dead Salk virus cannot revert to a disease-causing form. But the switch will also spell an end to the many benefits of the oral vaccine. For example, as I mentioned earlier, coming into contact with someone who has recently received the oral vaccine creates some immunity to polio—and that benefit holds for everyone except a few immunocompromised people, even if the virus has mutated and become neurovirulent. And because vaccination coverage can never be absolute, losing the benefits of community immunity poses a risk—particularly during what is, in Racaniello’s words, a “fragile time” in the eradication campaign.

For example, someone from a developing country who was infected with polio could come to the United States. The chances are small that such a person would have direct



*Al Fenn, Salk vaccine, 1955*

contact with an unimmunized person. But remember, the injected vaccine permits poliovirus to grow in the gut, even though the recipient of the vaccine is personally protected. Hence one foreign visitor could initiate an ever-widening network of infection in the intestines of immunized people, a "silent" spread in which no one exhibited the symptoms of polio or even realized that exposure had taken place. It would then be possible for polio to reach the rare unimmunized person. The risk is small, but more than theoretical. Racaniello thinks it would have been wiser to have switched to the injected vaccine only after polio had been eradicated worldwide.

**T**HE ERADICATION CAMPAIGN HAS COME under sniper fire from polio virologists, all of whom applaud its goals but many of whom question the wisdom of carrying it out as it has been designed. Part of the problem may be the false analogy with smallpox. "How Smallpox Showed the Way," declares the title of an article by the public-health expert Donald A. Henderson of Johns Hopkins University in Baltimore, Maryland. But what way is that? The three-step program for smallpox—eradication, containment and destruction—has not worked, and the prospects for vanquishing polio are more doubtful still. Wip-

tussis shot that children already receive. His critics point out that sophisticated manufacturing methods in industrialized countries allow for such an addition but that it might not be available to children in other parts of the world. "What is this," Chumakov asks in response. "Equal misery for all?"

**W**HAT WORRIES CHUMAKOV AND OTHER polio virologists about ending immunization is the difficulty of ensuring that poliovirus has vanished from nature and that laboratory-held stocks have been safely contained. There are many ways in which the virus could linger unobtrusively.

Civil unrest, for instance—in Afghanistan, Angola, the Democratic Republic of the Congo (D.R.C.)—is the biggest problem still facing the eradication campaign. "Can you vaccinate every final outpost?" asks the virologist Bert L. Semler of the University of California, Irvine. In other words, if the vaccine does not get to every mountain village in Nuristan, Afghanistan, to every child in the Ituri Forest, D.R.C., how can officials be certain that eradication has been achieved?

Furthermore, whereas WHO plans to lock research stocks known to include poliovirus in specially designated high-containment facilities, some virologists argue that other

**ONE PERSON INFECTED WITH POLIO could start a "silent" epidemic in a population protected only with the injected vaccine.**

ing polio out of nature will not be easy. Deciding when and how to end vaccination will be even more difficult. And ensuring that the earth is truly free of polio, so that destruction makes sense, will be all but impossible.

As the campaign is planned now, vaccination against polio will cease worldwide sometime after WHO declares the world to be free of the virus. And why not? Supporters of the plan are adamant: Who needs an extra shot—or four or five—once poliovirus has been driven from the earth? Why not save the money for, say, the eradication of measles, which still takes the lives of more than a million children each year? "Do you want the world to spend a billion and a half dollars a year to vaccinate against something that does not exist?" asks Stephen L. Cochi of the National Immunization Program at the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia. "We're entering a world where polio may be one of thousands of perceived threats. You can't vaccinate against paranoia."

But others, including Konstantin M. Chumakov, a virologist at the Center for Biologics Evaluation and Research of the U.S. Food and Drug Administration, say it would be irresponsible to stop vaccinating. "We are creating with our own hands an entire population of susceptibles," Chumakov says. Chumakov is well acquainted with the polio of old: his father, the famous Russian virologist Mikhail P. Chumakov, a friend of Sabin's, introduced the Sabin oral vaccine to the Soviet Union and stopped an epidemic in the Baltic states. Today the younger Chumakov endorses the inclusion of the polio vaccine in the diphtheria-tetanus-per-

polio samples could easily be overlooked. For one thing, freezer samples of stool and cerebrospinal fluid could carry live poliovirus without anyone's knowing it. Once immunization has ceased, the disposal of such a sample could cause an outbreak of polio.

In addition, some samples once known to carry polio may have been shoved to the back of someone's laboratory freezer and forgotten. In 1996 the physicist and immunologist Alan P. Zelicoff of Sandia National Laboratories in Albuquerque, New Mexico, asked investigators at several laboratories whether they were storing any plague or anthrax bacteria. They all said no. Then Zelicoff did a search. Sample after sample of both plague and anthrax emerged from the refrigerators. The scientists themselves were dumbfounded. Polio, which Chumakov calls "the crown jewel of molecular biology," has been studied more than any other virus; the number of samples that have been stowed away could be immense.

Another drawback to ending vaccinations is the danger posed by poliovirus that may live on in human hosts. Certain immunocompromised people who are infected with either wild poliovirus or the mutated, neurovirulent virus from the oral vaccine may continue to excrete it for years, instead of the usual six to eight weeks. Throughout that period such people remain potentially infectious to those around them. One patient, whom Racaniello calls the Typhoid Mary of polio, excreted poliovirus for nearly ten years before he died. And polio, unlike the smallpox virus, can survive for months in sewage. According to Racaniello, a recent

Israeli study recovered live poliovirus that, on the basis of genetic analyses of the degree of mutational drift, had been circulating in sewers for months. Yet current polio surveillance programs generally monitor only cases of paralysis, and WHO has no plans to begin monitoring water systems.

Even if poliovirus itself disappeared tomorrow, the threat of poliomyelitis could remain. A recent paper by Eckard Wimmer, a prominent poliovirus investigator at the State University of New York at Stony Brook, and by the

Russian virologist Alexander E. Gorbalenya of the Advanced Biomedical Computing Center in Frederick, Maryland, made a startling suggestion: in the absence of circulating poliovirus antibodies, other enteroviruses might evolve the

ability to affix to the poliovirus receptor. Recall that some enteroviruses that are closely related to polio are also highly mutable. "It may take one or a thousand years," says Wimmer. But it is a risk that he is not willing to discount.

Worrisome, too, is the manufacture of vaccine once polio has been eradicated. No one is optimistic enough—or foolhardy enough—to suggest that maintaining emergency stockpiles of fresh vaccine will be unnecessary. But which vaccine? And how can vaccine workers themselves be protected, yet prevented from becoming dangerous poliovirus carriers? If vaccine workers were protected with the oral vaccine, they could bring mutated, neurovirulent virus into an unprotected community. If workers were protected with the injected vaccine but were making the oral vaccine, they could still shed mutated oral virus; if they were making the injected vaccine, they could shed wild poliovirus that they had acquired before the virus was killed in the manufacturing process. And how could large quantities of vaccine be manufactured under the stringent biosafety conditions—biohazard containment levels of three or three and a half out of four—that would be required after eradication?

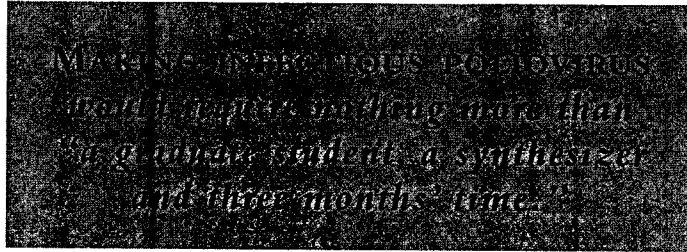
**A**ND, FINALLY, THERE IS ANOTHER PROBLEM that the eradication campaign must confront, perhaps the most serious problem of all: Could poliovirus serve as a biological weapon? Polio is a relatively small and simple virus. It is made up of about 7,500 nucleotides (smallpox, by contrast, is a DNA virus made up of 186,000 pairs of nucleotides). The nucleotide sequence for poliovirus has been publicly available since 1981. With today's technology, making infectious poliovirus would require nothing more than "a graduate student, a synthesizer and three months' time," Chumakov says. In twenty years, or fifty, who knows? A high school student with a grudge might be able to do it.

What kind of biological weapon would polio make? Smallpox, anthrax, plague and tularemia are the usual suspects when one thinks of biological weapons. No one mentions polio, and for good reason: there is not much point in launching a weapon that is not going to hurt anyone. But in five or ten years, if vaccinations have ceased,

people will be living in a different, susceptible world.

Experts differ on the viability of polio as a biological weapon. "I would say that it is not an efficient weapon," says the medical epidemiologist Harry F. Hull of WHO. Racaniello does not agree: the rapid infectivity and silent spread of poliovirus, he thinks, could make it a serious threat in the future. Poliovirus would be easy to release into a public water supply. In a city such as New York, even if only one out of a hundred people developed paralytic polio, the consequences are appalling to contemplate.

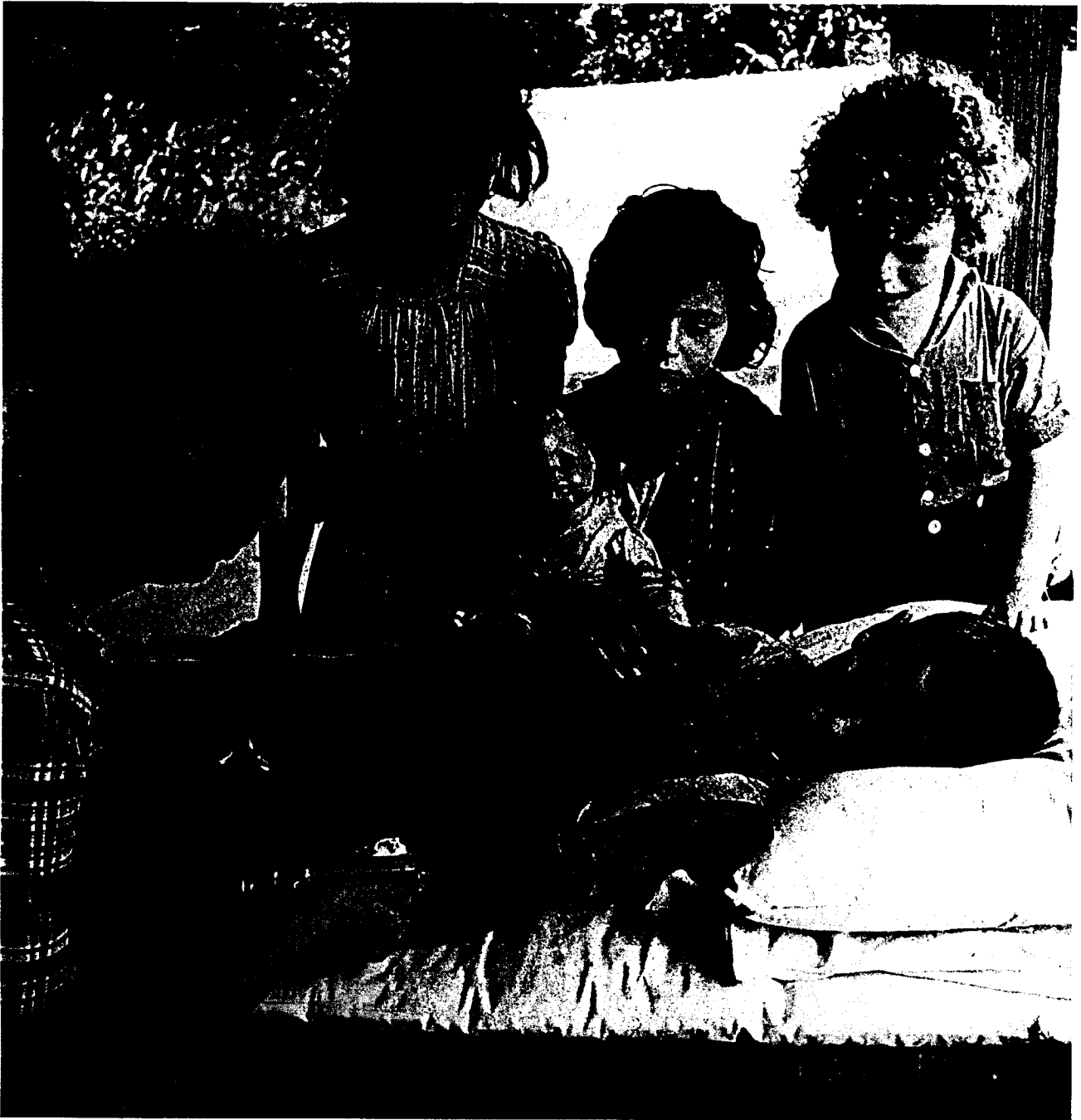
The virologist Olen M. Kew of the CDC, one of the principal forces behind the eradication campaign, acknowledges that the potential for terrorism exists. But such a weapon would be so horrendous, he asserts, that no one would dare use it. "Polio wouldn't make a very good terror weapon," he says. "You wouldn't want six and a half billion people mad at you."



**A**LTHOUGH THEY DISAGREE ABOUT THE WISDOM of stopping vaccinations, most polio virologists concede that it will happen eventually—mostly for pragmatic and financial reasons. Yet few expect polio to go down quietly. Both Semler and the virologist James M. Hogle of Harvard Medical School predict that even after eradication appears to be complete, the disease may flare up again. What then? The injected vaccine is not suitable for stopping such epidemics, because it allows wild virus to spread silently. But the oral vaccine is problematic, too, because people who receive it excrete neurovirulent virus into the environment. In today's world, in which almost everyone is vaccinated, the impact is minimal. But once vaccinations have ceased, that reversion to neurovirulence could prove much more dangerous.

There may be an alternative. The potential problems with the existing polio vaccines suggest that it makes sense to seek new vaccines—though five or six years ago, heady with the early successes of the eradication campaign, WHO discouraged such work. This past January, however, WHO sponsored a meeting in Geneva to discuss how to control outbreaks of polio in the post-vaccination era. Among the topics covered was the potential usefulness of alternative vaccines. Coming so close to the agency's own deadline for eradication, such willingness to explore new vaccines suggests a new pragmatism, and perhaps a certain failure of nerve.

One of the most promising new vaccines is being developed by Philip Minor and two associates, Andrew J. Macadam, a colleague of Minor's at NIBSC, and Jeffrey W. Almond, of the University of Reading in England. Their vaccine shows no propensity to mutate back to neurovirulence. Minor's team began with a weakened viral strain of the oral vaccine, then replaced several nucleotides in the 5' noncoding region with other nucleotides. The result is a sequence that has the same number of hydrogen bonds as its counterpart in the Sabin virus, but that is crippled in a



*Alfred Eisenstaedt, Polio epidemic, Hickory, North Carolina, c. 1950*

way that prevents dangerous mutations. Test-tube and animal tests have demonstrated the vaccine's probable safety, though to prove that it would be safer than the Sabin vaccine's track record of one case of paralytic disease for every 2.4 million vaccines administered, Minor and his associates would have to test it on six million children. In a Europe that is virtually free of polio, that is not going to happen.

If vaccination is halted after eradication, the nations of the world stand to save a great deal of money and human effort, which can then be directed toward other public-health issues—measles, tuberculosis and malaria, among others. But Kew, who has dedicated years of his life to the eradication campaign, points out that its real achievement is the saving of human lives. There are, after all, 550,000

children each year who are spared crippling disease because of the worldwide effort to vaccinate against polio. That in itself is an incalculable savings, and an incalculable good. Kew recognizes the problems with halting immunization, and is not so naive as to believe that eradication automatically means an end to the financial burden of making, distributing and administering vaccines.

For his part, Chumakov says, "Don't expect that the fact that we eradicated polio means we can forget about it. Polio will always be with us. It will always be an issue." •

---

*WENDY ORENT is a writer living in Atlanta, Georgia. Her articles on biological warfare, communicable diseases and related topics have appeared in THE SCIENCES, THE LOS ANGELES TIMES, THE AMERICAN PROSPECT and DISCOVER.*