

Half the Ethiopian population was said to live more than a two-day walk from any accessible road. "Accessible" was generously defined

TARGET ZERO

SMALLPOX— THE DEATH OF A DISEASE

BY D.A. HENDERSON

On October 26, 1966, D.A. Henderson reported at Geneva headquarters to lead a global war. The enemy, embedded with civilians on three different continents, refused to negotiate. In the last 100 years of its existence, smallpox had killed at least half a billion people. After infecting its hosts, the disease caused high fever, severe aching pains, and rash. Pressurized pustules eventually poked through the face of the afflicted like buckshot, and once the pustules merged into sheets, the host was likely to die.

The mission objective, code-named "Target Zero," was simple—eradicate smallpox from the human population in 10 years. The means were more complicated. Early estimates required between 200 to 350 million vaccinations every year for the next 10 years, at a total cost of at least $180 million. Many, including World Health Organization Director-General Marcelino Candau, thought the chance of success was slim. The WHO was financing a failing malaria eradication program, and, according to Henderson, Candau was distressed about growing criticism of his organization. He decided an American should direct the U.S.–backed program. Thus, when the program failed, the United States would share the blame. He selected Henderson and gave him only $2.4 million a year. A little more than 10 years later, the last smallpox case occurred in Somalia.

Henderson, a professor of medicine and public health at the University of Pittsburgh and a resident scholar at the Center for Biosecurity of UPMC, released his book Smallpox—The Death of a Disease *(Prometheus Books) in June. The following excerpts give a glimpse of how Henderson's team killed a 3,000-year-old disease. (Reprinted with permission, © 2009, D.A. Henderson.)* —Brandon Ellis

THE FUTILITY OF ERADICATION

The widely read and respected medical scientist Dr. René Dubos took a dim view of the concept of eradication and wrote about it in 1965 in his book *Man Adapting*. It was a view that was widely shared at the time. However, by the time I got around to reading the book, my future had already been decided.

Dubos wrote: "At first sight, the decision to eradicate certain microbial diseases appears to constitute but one more step forward in the development of the control policies initiated by the great sanitarians of the nineteenth century. ... In reality, however, eradication involves a new biological philosophy. ... Social considerations make it probably useless to discuss the theoretical flaws and technical difficulties of eradication programs, because more earthly factors will certainly bring them soon to a gentle and silent death. Eradication programs will eventually become a curiosity item on library shelves, just as have all social utopias."

WHY WE BELIEVED SMALLPOX COULD BE ERADICATED

Smallpox and the freeze-dried smallpox vaccine possessed unusual characteristics. Taken together, they were unique and made smallpox, by far, the best available candidate disease for eradication. Most important, humans were the only victims of the smallpox virus; and there was no reservoir in nature. No rodents, monkeys, or other animals could be infected. Each person who was infected exhibited a rash that could be identified even by illiterate villagers. No laboratory tests were required. If patients were promptly isolated, they could be prevented from spreading infection. Moreover, a patient could infect others only during the two to three weeks of severe illness; on recovery, the person was immune for life.

The development of freeze-dried vaccine was a critical advance. It could withstand storage at 98°F (37°C) for a month, making it ideal for tropical areas. The vaccine was inexpensive, vaccination was easily performed, and a single vaccination provided immunity for at least 10 years. Every successful vaccination resulted in a pustule and then a distinctive scar, which remained for decades. In areas where *Variola major* has been the prevalent form of smallpox, 80 percent of those who recovered had permanent scars. Thus, teams visiting an area could readily determine whether smallpox was present in the community, when it had occurred in the past, and who had been successfully vaccinated. No other disease came close to being such an ideal target.

INDIA

The commitment and determination of the Indian Central Appraisal Team staff was as extraordinary as its accomplishments. At the January 1, 1974, strategy meeting of the team, it was apparent to me that they were all exhausted and some were near the point of collapse. All had been working seven-day weeks for four months. They had repeatedly made difficult trips throughout some of the country's most remote and inhospitable areas in a frantic effort to motivate the army of health workers to contain outbreaks. Four of the members had serious medical problems. One had incapacitating renal colic; one had painful facial herpes; another had a serious fungus infection, which eventually required surgery; and one had atypical pneumonia with a high fever and pleuritic pain. However, the

only problem they would discuss was where to find the additional resources to keep the program going. I expressed skepticism about their own ability to keep up with the grueling schedule even if resources could be found. Bill Foege replied simply: "We've considered the question and have decided that things can't get worse; therefore they must get better."

Some of the [team's] expenditures were out of the ordinary, and special justifications were needed. There are several that I remember well. One was a receipt for costs associated



A thornbush barrier quarantines a nomad in East Africa.

with rental of elephants—to ford rivers and, later, for public advertising of a reward for reporting a case. Food costs to feed beggar families in infected compounds—so that family members would not go out begging. Purchase of the body of a deceased smallpox case for burial—otherwise it would have been floated down the Ganges.

ETHIOPIA

There are few places that rival the sheer beauty of mountainous Ethiopia—as well as few places where, day to day, the staff encountered more potentially threatening personal hazards and perils.

One adventure involved running out of gas over the Blue Nile Gorge in a single-wing two-passenger plane. The plane had been leased to permit me to meet with staff some two hours away from Addis [Ababa]. On the return flight, the motor sputtered and died. We were directly over the gorge—5,000 feet above the Blue Nile—at least a mile from the edge of the canyon. The pilot was a distressingly casual Swede who mentioned that he had forgotten to put on the gas cap. The gasoline had drained out. He switched to the second tank and eventually managed to get the engine restarted. As we approached the Addis airport, the engine again began to sputter, and the pilot called the airport to announce an emergency landing. However, a passenger jet was descending at the time. The tower and the two pilots engaged in a heated argument before the jet finally pulled up. As we began to taxi, our plane's engine stopped altogether. Two months later the Swedish pilot was killed and the plane crashed when a large buzzard penetrated the cockpit window and impaled itself in the pilot's chest.

SOMALIA

In 1977, Somalia declared the smallpox epidemic a disaster and the United Nations Disaster Relief Operations agreed. Eradication workers responded from all over the world to close in on the last known cases. They were determined to finish the job before the annual Haj pilgrimage to Mecca, which would take place in November that year and threatened to set off another wave of infection worldwide.

The number of cases rose to 1,388 in June and the number of infected villages to 223. Containing the outbreaks, especially among the nomad populations, proved to be a challenge quite unlike any faced before. The proportion of outbreaks among nomads rose from 50 percent in April to 75 percent in June and more than 90 percent in July.

The nomads typically began their most active migrations in March when the rainy season began. They tended not to follow established patterns of movement but to seek good grazing for their animals wherever that might take them. Their vaccination levels, wherever checked, were usually in the range of 10 to 20 percent. Simply finding the nomads in the scrub desert was an adventure. Line-of-sight vision was blocked in every direction by the high scrub. No maps were available and few landmarks existed. The only good lead was the knowledge that the nomads must find water holes. In some areas, lookouts were posted at every water hole to keep a vigil for the nomads.

The smallpox-affected localities steadily diminished in number … to only 29 in September. But then torrential rains hampered the use of heavy vehicles. Many field staff were obliged to travel on foot or on camels and donkeys. On October 31, 1977, a final case was discovered in the port town of Merca.

Ali Maow Maalin was a 23-year-old cook at the local hospital. He developed a fever on October 22, followed by a rash on October 26. His case was a classic one in depicting omissions and mistakes in program operations. He had never been vaccinated, despite having once served as a vaccinator and despite having worked at the hospital where employee vaccinations were supposed to be mandatory. On October 12, two sick children arrived at the hospital in a vehicle from a nomad encampment. They were to be housed in an isolation camp nearby. Both of them had smallpox, and one died two days later. Maalin volunteered to ride with them to direct the driver to the camp about 200 yards away. His exposure was brief but adequate.

Maalin was admitted to the hospital on October 25 with a presumptive diagnosis of malaria. He received numerous visitors and walked freely around the hospital and outside the compound. A day later he developed a rash that was diagnosed as chicken pox, and he was sent home. A popular man, he received many visitors until October 30 when a nurse suspected that Maalin had smallpox. He was then sent immediately to the isolation camp.

An intensive search began to find everyone with whom he had come into contact. In all, 91 face-to-face contacts were identified, 12 of whom had no vaccination scar, and six who had been hospital patients or visitors. Heroic measures were taken, including a search and vaccination of the town and of everyone entering or leaving town at any one of four checkpoints. House-by-house searches throughout the region were conducted monthly, and a national search was completed on December 29.

The epidemic was stopped before the annual pilgrimage to Mecca got under way.

Ali Maow Maalin survived his illness and continued to reside in Merca. He has a place in history as the last naturally occurring case in a continuing chain of transmission extending back at least 3,500 years.

Henderson ends his book with a warning: Smallpox may have been eliminated from the human population, but it still lurks. After the eradication, WHO sanctioned two national laboratories to hold frozen samples of smallpox, one in Atlanta and one in Moscow. When the Soviet Union collapsed, defectors revealed that smallpox had been the crown jewel of the Soviet bioweapons program. Some scientists who left the program have been impossible to track down. No one knows whether some smallpox samples might have moved into ill-meaning hands; and the organism could spread "more readily than ever," Henderson says, in an unprotected world population. Henderson worked with the Centers for Disease Control and Prevention to develop more than 200 million doses of smallpox vaccine after the attacks of September 11, 2001. However, he remains concerned even now about the possible return of his nemesis. —BE