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A REPORTER AT LARGE

THE DEMON IN THE FREEZER

How smallpox, a disease of officially eradicated twenty years ago, became the biggest bioterrorist threat we now face.

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BY RICHARD PRESTON

THE smallpox virus first became entangled with the human species somewhere between three thousand and twelve thousand years ago -- possibly in Egypt at the time of the Pharaohs. Somewhere on earth at roughly that time, the virus jumped out of an unknown animal into its first human victim, and began to spread. Viruses are parasites that multiply inside the cells of their hosts, and they are the smallest life forms. Smallpox developed a deep affinity for human beings. It is thought to have killed more people than any other infectious disease, including the Black Death of the Middle Ages. It was declared eradicated from the human species in 1979, after a twelve-year effort by a team of doctors and health workers from the World Health Organization. Smallpox now exists only in laboratories.

Smallpox is explosively contagious, and it travels through the air. Virus particles in the mouth become airborne when the host talks. If you inhale a single particle of smallpox, you can come down with the disease. After you've been infected, there is a typical incubation period of ten days. During that time, you feel normal. Then the illness hits with a spike of fever, a backache, and vomiting, and a bit later tiny red spots appear all over the body. The spots turn into blisters, called pustules, and the pustules enlarge, filling with pressurized opalescent pus. The eruption of pustules is sometimes called the splitting of the dermis. The skin doesn't break, but splits horizontally, tearing away from its underlayers. The pustules become hard, bloated sacs the size of peas, encasing the body with pus, and the skin resembles a cobbled stone street.

The pain of the splitting is extraordinary. People lose the ability to speak, and their eyes can squeeze shut with pustules, but they remain alert. Death comes with a breathing arrest or a heart attack or shock or an immune-system storm, though exactly how smallpox kills a person is not known. There are many mysteries about the smallpox virus. Since the seventeenth century, doctors have understood that if the pustules merge into sheets across the body the victim

will usually die: the virus has split the whole skin. If the victim survives, the pustules turn into scabs and fall off, leaving scars. This is known as ordinary smallpox.

Some people develop extreme smallpox, which is loosely called black pox. Doctors separate black pox into two forms -- flat smallpox and hemorrhagic smallpox. In a case of flat smallpox, the skin remains smooth and doesn't pustulate, but it darkens until it looks charred, and it can slip off the body in sheets. In hemorrhagic smallpox, black, unclotted blood oozes or runs from the mouth and other body orifices. Black pox is close to a hundred per cent fatal. If any sign of it appears in the body, the victim will almost certainly die. In the bloody cases, the virus destroys the linings of the throat, the stomach, the intestines, the rectum, and the vagina, and these membranes disintegrate. Fatal smallpox can destroy the body's entire skin -- both the exterior skin and the interior skin that lines the passages of the body.

Smallpox virus's scientific name is variola. It means "spotted" in Latin, and it was given to the disease by a medieval bishop. The virus, as a life form, comes in two subspecies: Variola minor and Variola major. Minor is a weak mutant, and was first described in 1863 by doctors in Jamaica. People usually survive it. Classic major kills one out of three people if they haven't been vaccinated or if they've lost their immunity. The death rate with major can go higher -- how much higher no one knows. Variola major killed half of its victims in an outbreak in Canada in 1924, and presumably many of them developed black pox. Smallpox is less contagious than measles but more contagious than mumps. It tends to go around until it has infected nearly everyone.

Most people today have no immunity to smallpox. The vaccine begins to wear off in many people after ten years. Mass vaccination for smallpox came to a worldwide halt around twenty-five years ago. There is now very little smallpox vaccine on hand in the United States or anywhere else in the world. The World Health Organization once had ten million doses of the vaccine in storage in Geneva, Switzerland, but in 1990 an advisory committee recommended that most of it be destroyed, feeling that smallpox was longer a threat. Nine and a half million doses are assumed to have been cooked in an oven, leaving the W.H.O. with a total supply of half a million doses -- one dose of smallpox vaccine for every twelve thousand people on earth. A recent survey by the W.H.O. revealed that there is only one factory in the world that has recently made even a small quantity of the vaccine, and there may be no factory capable of making sizable amounts. The vaccine was discovered in the age of Thomas Jefferson, and making a lot of it would seem simple, but so far the United States government has been unable to get any made at all. Variola virus is now classified as a Biosafety Level 4 hot agent -- the most dangerous kind of virus -- because it is lethal, airborne, and highly contagious, and is now exotic to the human species, and there is not enough vaccine to stop an outbreak. Experts feel that the appearance of a single case of smallpox anywhere on earth would be a global

medical emergency.

At the present time, smallpox lives officially in only two repositories on the planet. One repository is in the United States, in a freezer at the headquarters of the federal Centers for Disease Control and Prevention, in Atlanta -- the C.D.C. The other official smallpox repository is in a freezer at a Russian virology institute called Vector, also known as the State Research Institute of Virology and Biotechnology, which is situated outside the city of Novosibirsk, in Siberia. Vector is a huge, financially troubled former virus-weapons-development facility -- a kind of decayed Los Alamos of viruses -- which is trying to convert to peaceful enterprises.

There is a growing suspicion among experts that the smallpox virus may also live unofficially in clandestine biowarfare laboratories in a number of countries around the world, including labs on military bases in Russia that are closed to outside observers. The Central Intelligence Agency has become deeply alarmed about smallpox. Since 1995, a number of leading American biologists and public-health doctors have been given classified national-security briefings on smallpox. They have been shown classified evidence that as recently as 1992 Russia had the apparent capability of launching strategic-weapons-grade smallpox in special biological warheads on giant SS-18 intercontinental missiles that were targeted on the major cities of the United States. In the summer of last year, North Korea fired a ballistic missile over Japan in a test, and the missile fell into the sea. Some knowledgeable observers thought that the missile could have been designed to carry a biologic warhead. If it had carried smallpox and landed in Japan, it could have devastated Japan's population: Japan has almost no smallpox vaccine on hand and its government seems to have no ability to deal with a biological attack. The United States government keeps a list of nations and groups that it suspects either have clandestine stocks of smallpox or seem to be trying to buy or steal the virus. The list is classified, but it is said to include Russia, China, India, Pakistan, Israel, North Korea, Iraq, Iran, Cuba, and Serbia. The list may also include the terrorist organization of Osama bin Laden and, possibly, the Aum Shinrikyo sect of Japan -- a quasi-religious group that had Ph.D. biologists as members and a belief that an apocalyptic war will bring them worldwide power. Aum members released nerve gas in the Tokyo subway in 1995, and, as the year 2000 approaches, the group is still active in Japan and in Russia. In any case, the idea that smallpox lives in only two freezers was never anything more than a comfortable fiction. No one knows exactly who has smallpox today, or where they keep the virus, or what they intend to do with it.

THE man who is most widely credited with the eradication of smallpox from the human species is a doctor named Donald Ainslie Henderson. Everyone calls him D. A. Henderson. He was the director of the World Health Organization's Smallpox Eradication Unit from its inception, in 1966, to 1977, just before the last case occurred. "I'm one of many in the eradication," Henderson said to me once.

"There's Frank Fenner, there's Isao Arita, Bill Foege, Nicole Grasset, Zdenek Jezek, Jock Copland, John Wickett -- I could come up with fifty names. Let alone the tens of thousands who worked in the infected countries." Nevertheless, Henderson ran it. Smallpox killed at least three hundred million people in the twentieth century. During that time, humanity was largely immune to smallpox, which is not the case today. When D. A. Henderson arrived on the scene in 1966, two million people a year were dying of smallpox. In the years since the eradication effort began, Henderson and his team have effectively saved more than fifty million lives. This could be the most impressive achievement in the history of medicine. Henderson and his colleagues, however, have never received the Nobel Prize for their work.

D. A. Henderson is now a professor at the Johns Hopkins School of Public Health. He is the founder and the director of the Johns Hopkins Center for Civilian Biodefense Studies, a think tank that considers what might be done to protect the American population during a biological event. The term "biological event" hardly existed two years ago, but it is now used by emergency planners and by the F.B.I. to mean a terrorist attack with a bioweapon -- an unnatural event, caused by human intent.

Henderson lives with his wife in a large brick house in Baltimore. I arrived there on a cold, drizzly Saturday, and he ambled to the door. Henderson is an imposing man, six feet two inches tall. He is seventy years old. He has broad shoulders and a broad, seamed, angular face, pointed ears that stick out at angles from his head, a brush of gray hair, metal-framed eyeglasses, sharp blue eyes, and an easygoing voice that can flash with calculation. He was wearing a red checked shirt, with suspenders that held up Saturday slacks.

"In the last ten days, we've had fourteen different anthrax scares," he remarked in an offhand way as we stood in the front hallway of his house and he loomed over me. He has a top-secret-level national-security clearance, and he hears about little bioterror events that don't get noticed by the media. He went on to say, "Everybody and his brother is threatening to use anthrax. This week, it happened in Atlanta, in Washington, D.C., in Michigan, and in California. It's largely hoaxes. Of course, a real bioterror event is going to happen one of these days."

We settled into easy chairs in the family room. The walls and shelves of the room were crowded with African and Asian sculptures and wooden Ethiopian crosses, which he had picked up in his global hunt for smallpox. A Japanese garden was visible through sliding-glass doors.

We ate ham and roast-beef sandwiches, and drank Molson Ice beers. Henderson bit into a sandwich and chewed thoughtfully. Then he said, "Often, you get a worried look on your face, with the first signs of rash. We speak of the 'worried face' of smallpox. That face is a diagnostic sign. The rash comes up all at once. It's more dense on the face and the extremities. That's how you can tell smallpox from chicken pox. With chicken pox, the rash crops up over a period of days, and

it's more dense on the chest and trunk of the body. Smallpox pustules have a dimple, a dent in the center. Doctors say that the pustules have a 'shotty' feel, like shotgun pellets. You can roll them between your fingertips under the skin."

"How many doctors could recognize smallpox today?" I asked.

"Virtually none. Smallpox takes forms that even I can't diagnose. And I wrote the textbook." He is a co-author of "Smallpox and Its Eradication," a large book in red covers, which experts call the Big Red Book of Smallpox. It was supposed to be the final word on smallpox-the tombstone of the virus.

ON February 15,1972, a thirty-eight-year-old Muslim clergyman returned to his home town of Damnjane, in Kosovo, Yugoslavia, after he'd been on a pilgrimage to Mecca, stopping at holy sites in Iraq. I will call him the Pilgrim. A photograph of the Pilgrim shows a man who looks well educated, has an intelligent face, and is wearing a clipped mustache and a beret. He had travelled by bus for his entire journey. The morning after his return home, he woke up feeling achy. At first, he thought he was tired from the long bus ride, but then he realized that he had caught a bug. He shivered for a day or two, and developed a red rash brought on by his fever, but quickly recovered. He had been vaccinated for smallpox two months earlier. Indeed, the Yugoslav medical authorities had been vaccinating the population of Yugoslavia relentlessly for more than fifty years, and the country was considered to be thoroughly immunized. The last case of smallpox in Yugoslavia had occurred in 1930.

The Pilgrim's family members and friends came to visit him. They wanted to hear about his trip, and he enjoyed telling them about it. Meanwhile, variola particles were leaking out of raw spots in the back of his throat and mixing with his saliva. When he spoke, tiny droplets of saliva, too small to be seen, drifted around him in a droplet cloud. If the person is throwing off a lethal virus, the cloud becomes a hot zone that can extend ten feet in all directions. Although the raw spots in the Pilgrim's throat amounted to a tiny surface of virus emission, smaller than a postage stamp, in a biological sense it was as hot as the surface of the sun, and it put enough smallpox into the air to paralyze Yugoslavia.

Variola particles are built to survive in the air. They are rounded-off rectangles that have a knobby, patterned surface-a gnarly hand-grenade look. Some experts call the particles bricks. The whole brick is made of a hundred different proteins, assembled and interlocked in a three-dimensional puzzle, which nobody has ever figured out. Virus experts feel that the structure of a smallpox particle is almost breathtakingly beautiful and deeply mathematical-one of the unexplored wonders of the viral universe. The structure protects the virus's genetic material: a long strand of DNA coiled in the center of the brick.

Pox bricks are the largest viruses. If a smallpox brick were the size of a real brick then a cold-virus particle would be a blueberry sitting on the brick. But

smallpox particles are still extremely small; about three million smallpox bricks laid down in rows would pave the period at the end of this sentence. A smallpox victim emits several bricks in each invisible droplet of saliva that spews into the air when the person speaks or coughs. When an airborne smallpox particle lands on a mucus membrane in someone's throat or lung, it sticks. It enters a cell and begins to make copies of itself. For one to three weeks, the virus spreads from cell to cell, amplifying silently in the body. No one has discovered exactly where the virus z hides during its incubation phase. Probably it gets into the lymph cells, confusing the immune system, and victims are said to experience terrible dreams.

On February 21st, when the Pilgrim had been feeling achy for almost a week, a thirty-year-old man, a schoolteacher, who is known to experts as Ljatif M., arrived in Djakovica, a few miles from the Pilgrim's town, to enroll in the Higher Institute of Education. Doctors who later investigated the schoolteacher's case never found out how he had come in contact with the Pilgrim. One of them must have ended up in the other's town. Possibly they stood next to each other in a shop-something like that.

On March 3rd, Ljatif developed a fever. Two days later, he went to a local medical center, where doctors gave him penicillin for his fever. Antibiotics have no effect on a virus. Then his skin broke with dark spots, and he may have developed a worried face. He felt worse, and a few days later his brother took him by bus to a hospital in the town of Cacak, about a hundred miles away. The dark spots were by this time merging into blackened, mottled splashes, which the doctors in Cacak didn't recognize. Ljatif became sicker. Finally, he was transferred by ambulance to Belgrade, where he was admitted to the Dermatology and Venereal Diseases Department of the city's main hospital. By then, his skin may have turned almost black in patches. We don't have access to his clinical reports, so I am describing a generalized extreme smallpox of the kind Ljatif had.

Inside the cells of the host, smallpox bricks pile up as if they were coming off a production line. Some of the particles develop tails. The tails are pieces of the cell's protein, which the virus steals from the cell for its own use. The tailed smallpox particles look like comets or spermatozoa. They begin to twist and wriggle, and they corkscrew through the cell, propelled by their tails toward the cell's outer membrane. You can see them with a microscope, thrashing with the same furious drive as sperm. They bump up against the inside of the cell membrane, and their heads make lumps, and the cell horripilates. Then something wonderful happens. Finger tubes begin to extend from the cell. The tubes grow longer. The cell turns into a Koosh ball. Inside each finger tube is a smallpox comet. The fingers lengthen until they touch and join nearby cells, and the smallpox comets squirm through the finger tubes into the next cell. The comets are protected from attack by the immune system, because they stay inside the finger tubes, where antibodies and killer white blood cells can't reach

them. Then the Koosh ball explodes. Out pour heaps of bricks that don't have tails. These smallpox particles are wrapped in a special armor, like hand grenades. They float away, still protected by their armor, and they stick to other cells and go inside them, and those cells turn into Koosh balls. Each infected cell releases up to a hundred thousand virus particles, and they are added to the quadrillions of particles replicating in the universe of the ruined host.

Ljatif's skin had become blackened, mottled, and silky to the touch, and sheets of small blood blisters may have peppered his face. In a case of black pox, variola shocks the immune system so that it can't produce pus. Small blood vessels were leaking and breaking in his skin, and blood was seeping under the surface. His skin had developed large areas of continuous bruises.

On March 9th, the Belgrade doctors showed Ljatif to students and staff as a case that demonstrated an unusual reaction to penicillin. (In fact, a very bad reaction to penicillin can look like this.) Ljatif's eyes may have turned dark red. In hemorrhagic smallpox, one or two large hemorrhages appear in each eye, in the white encircling the iris, making the eyes look as if they could sag or leak blood. The eyes never do leak, but the blood in the eyes darkens, until the whites can sometimes seem almost black.

During the day of March 10th, Ljatif suffered catastrophic hemorrhages into the intestines. His intestines filled up with blood, and he expelled quarts of it, staining the sheets black, and he developed grave anemia from blood loss. For some unknown reason, black-pox patients remain conscious, in a kind of paralyzed shock, and they seem acutely aware of what is happening nearly up to the point of death -- "a peculiar state of apprehension and mental alertness that were said to be unlike the manifestations of any other infectious disease," in the words of the Big Red Book of Smallpox. We can imagine that Ljatif was extremely frightened and witnessed his hemorrhages with a sense that his insides were coming apart. During the final phase of a smallpox intestinal bleedout, the lining of the intestines or the rectum can slip off. The lining is expelled through the anus, coming out in pieces or in lengths of tube. This bloody tissue is known as a tubular cast. When a smallpox patient throws a tubular cast, death is imminent. Al1 we know about Ljatif is that his bleeds were unstoppable, that he was rushed to the Surgical Clinic of the Belgrade hospital, and that he died in the evening. The duty physician listed the cause of death as a bad reaction to penicillin.

"These hemorrhagic smallpox cases put an incredible amount of virus into the air," D. A. Henderson said. Some of the doctors and nurses who treated Ljatif were doomed. Indeed, Ljatif had seeded smallpox across Yugoslavia. Investigators later found that while he was in the hospital in Cacak he infected eight other patients and a nurse. The nurse died. One of the patients was a schoolboy, and he was sent home, where he broke with smallpox and infected his mother, and she died. In the Belgrade hospital, Ljatif infected twenty-seven more people,

including seven nurses and doctors. Those victims infected five more people. Ljatif directly infected a total of thirty-eight people. They caught the virus by breathing the air near him. Eight of them died.

Meanwhile, the Pilgrim's smallpox travelled in waves through Yugoslavia. A rising tide of smallpox typically comes in fourteen-day waves -- a wave of cases, a lull down to zero, and then a much bigger wave, another lull down to zero, then a huge and terrifying wave. The waves reflect the incubation periods, or generations, of the virus. Each wave or generation is anywhere from ten to twenty times as large as the last, so the virus grows exponentially and explosively, gathering strength like some kind of biological tsunami. This is because each infected person infects an average of ten to twenty more people. By the end of March, 1972, more than a hundred and fifty cases had occurred.

The Pilgrim had long since recovered. He didn't even know that he had started the outbreak. By then, however, Yugoslav doctors knew that they were dealing with smallpox, and they sent an urgent cable to the World Health Organization, asking for help.

Luckily, Yugoslavia had an authoritarian Communist government, under Josip Broz Tito, and he exercised full emergency powers. His government mobilized the Army and imposed strong measures to stop people from travelling and spreading the virus. Villages were closed by the Army, roadblocks were thrown up, public meetings were prohibited, and hotels and apartment buildings were made into quarantine wards to hold people who had had contact with smallpox cases. Ten thousand people were locked up in these buildings by the Yugoslav military. The daily life of the country came to a shocked halt. At the same time, all the countries surrounding Yugoslavia closed their borders with it, to prevent any travellers from coming out. Yugoslavia was cut off from the world. There were twenty-five foci of smallpox in the country. The virus had leapfrogged from town to town, even though the population had been heavily vaccinated. The Yugoslav authorities, helped by the W.H.O., began a massive campaign to revaccinate every person in Yugoslavia against smallpox; the population was twenty-one million. "They gave eighteen million doses in ten days," D. A. Henderson said. A person's immunity begins to grow immediately after the vaccination; it takes full effect within a week.

At the beginning of April, Henderson flew to Belgrade, where he found government officials in a state of deep alarm. The officials expected to see thousands of blistered, dying, contagious people streaming into hospitals any day. Henderson sat down with the Minister of Health and examined the statistics. He plotted the cases on a time line, and now he could see the generations of smallpox -- one, two, three waves, each far larger than the previous one. Henderson had seen such waves appear many times before as smallpox rippled and amplified through human populations. Reading the viral surf with a practiced eye, he could see the start of the fourth wave. It was not climbing as steeply as he had expected. This meant that the waves had peaked. The outbreak was declining. Because of the

military roadblocks, people weren't travelling, and the government was vaccinating everyone as fast as possible. "The outbreak is near an end," he declared to the Minister of Health. "I don't think you'll have more than ten additional cases." There were about a dozen: Henderson was right -- the fourth wave never really materialized. The outbreak had been started by one man with the shivers. It was ended by a military crackdown and vaccination for every citizen.

AT the present time, the United States' national stockpile of smallpox vaccine is a collection of four cardboard boxes that sit on a single pallet behind a chain-link fence inside a walk-in freezer in a warehouse in Lancaster County, Pennsylvania, near the Susquehanna River, at a facility owned by Wyeth-Ayerst Laboratories. The vaccine is slowly deteriorating. The Food and Drug Administration has put a hold on the smallpox vaccine, and right now no one can use it -- not even emergency personnel or key government leaders.

The vaccine is owned by the federal government and is managed by Wyeth-Ayerst, which is the company that made it, twenty-five to thirty years ago. It is stored in glass vials. The vials contain freeze-dried nuggets of live vaccinia virus. Vaccinia is a mild virus. When you are infected with it by vaccination, it causes a pustule to appear, and afterward you are immune to smallpox for some years. People who have been vaccinated have a circular scar the size of a nickel on their upper arm, left by the vaccinia-virus pustule they had in childhood after vaccination. Some adults can remember how much the pustule hurt.

People from Wyeth periodically open the boxes and send some of the vials out for testing, to see how the vaccine is doing. The vials once held fifteen million good doses, but now moisture has invaded some of them. The nuggets are normally dry and white in color, but when moisture invades they turn brown and look sticky, and the vaccine may be weakened. The vaccine was made by a traditional method: the manufacturer had a farm where calves were raised. The calves' bellies were scratched with vaccinia virus, and their bellies developed pustules. Then the calves were killed and hung up on hooks, the blood was drained out of them, and the pustules were scraped with a knife. The resulting pus was freeze-dried. The vaccine is dried calf pus. According to one virologist who examined it under a microscope, "It looks like nose snot. It's all hair and wads of crap." It was a good vaccine for its time, but the F.D.A. would never clear it for general use today except in a national emergency. Furthermore, some people have bad or fatal reactions to the vaccine. There is an antidote, but the supplies of it have turned strangely pink, and the F.D.A. has put a hold on the use of these supplies, too.

D. A. Henderson believes that in practice doctors could obtain about seven million doses of vaccine from the vials. Unaccountably, most of the vaccine has not recently been tested for potency, so it has not been absolutely proved to work. The experts believe that it would work, but there still isn't enough. Henderson explained the problem this way: "If there's a bioterror event, and

someone releases enough smallpox to create a hundred cases -- let's say in the Baltimore area -- it would be a national emergency. The demand for vaccine would be beyond all belief." In Yugoslavia in 1972, the outbreak was started by one man, and eighteen million doses of vaccine were needed -- one for almost every person in the country.

"That first wave after the bioterror event could be a hundred people with smallpox," Henderson said. "It takes two weeks after exposure before doctors can diagnose smallpox. Meanwhile, those hundred people will give smallpox to a thousand or two thousand people. That's the second wave. Some of those first hundred people will go to other cities -- to Washington, to New York, all over. So the second wave will include cases in other American cities, and probably in foreign countries. By then, it'll be too late to treat them, and we'll lose the second wave. We'll be well into the third wave -- ten to twenty thousand people with smallpox -- before we can really start vaccinating people. By then, we'll begin to pick up so many cases in the Baltimore area that we won't be able to track cases, and we'll just have to vaccinate everybody around Baltimore. A lot of people in Baltimore work in Washington. And so you're going to have a whole lot of people in Washington with smallpox. You can see the deal. Immediately, you would have to vaccinate Washington." Henderson thinks that a hundred million doses of vaccine would be needed in the United States alone to stop a surging outbreak triggered by a hundred initial cases of smallpox from a bioterror event. That much vaccine could be stored in the space occupied by a one-car garage.

Raindrops splattered on a wooden deck in Henderson's garden, and the room grew dark, until it was a pool of shadows full of African masks. Henderson's voice came out of the gloom. He didn't bother to get up and turn on the lights. He said, "The way air travel is now, about six weeks would be enough time to seed cases around the world. Dropping an atomic bomb could cause casualties in a specific area, but dropping smallpox could engulf the world."

Henderson passionately wants to get rid of the virus. "What we need to do is create a general moral climate where smallpox is considered too morally reprehensible to be used as a weapon. That would make the possession of smallpox in a laboratory, anywhere, effectively a crime against humanity. The likelihood that it would be used as a weapon is diminished by a global commitment to destroy it. How much it is diminished I don't know. But it adds a level of safety."

IN the late seventeen-hundreds, the English country doctor Edward Jenner noticed that dairymaids who had contracted cowpox from cows seemed to be protected from catching smallpox, and he thought he would do an experiment. Cowpox (it probably lives in rodents, and only occasionally infects cows) produced a mild disease. On May 14, 1796, Jenner scratched the arm of a boy named James Phipps, introducing into the boy's arm a droplet of cowpox pus that he'd taken from a blister on the hand of a dairy worker named Sarah Nelmes. A few months later, he

scratched the boy's arm with deadly pus he had taken from a smallpox patient, and the boy didn't come down with smallpox. The boy had become immune. Jenner had discovered what he called vaccination, after the Latin word for cow. He saw the road to eradication clearly. In 1801, he wrote, "It now becomes too manifest to admit of controversy, that the annihilation of the Small Pox, the most dreadful scourge of the human species, must be the final result of this practice."

A Soviet epidemiologist, Viktor Zhdanov, deserves credit for kick-starting the modern effort. At the 1958 annual meeting of the World Health Assembly, in Minneapolis, he called for the global eradication of smallpox. He spoke passionately and logically, but the scientific community was skeptical. Many biologists held a common view that it was impossible to separate a wild microorganism from the ecological web it lived in. In 1965, President Lyndon Johnson endorsed the idea of smallpox eradication. It was a political move to help improve American-Soviet relations. D. A. Henderson was then the head of disease surveillance at the C.D.C. He was given an order to report to Geneva to head the W.H.O.'s new Smallpox Eradication Unit. He didn't want the job, but he was told that if he didn't take it he would have to resign from government service. He went to Geneva, where he formed a hand-picked team. "The World Health Assembly proposed a ten-year program, because Kennedy had said we could land a man on the moon in ten years," he recalled.

The team set a goal of vaccinating eighty per cent of the population of countries that harbored smallpox. Henderson says that from the beginning they had another idea as well, and it proved to be the key. The idea was to track smallpox outbreaks and vaccinate people in a ring around any outbreak. This is known as surveillance and ring vaccination. In order to throw a ring around smallpox, they had to know where the demon was moving at all times, and they started showing villagers photographs of a baby with smallpox, so that the villagers could recognize and report cases to the authorities.

Henderson's team needed a way of vaccinating people fast. They tried a machine called the Ped-o-Jet, which was operated by foot pedal. It could shoot jets of vaccine into the arms of thousands of people in a day, but it broke down. Then they tried a needle with two points. It was known as the bifurcated needle, and it looked like a tiny two-pronged fork. The points of the fork held a droplet of vaccine, and the needle was to be jabbed repeatedly into a person's arm. It could be used by a volunteer who had no medical training.

They discovered that the virus rose and fell in seasonal waves, like flu. This led to an idea to attack the virus with a ring assault when it was at its ebb. The virus was a wild organism that lived only in humans. It needed to find and invade a susceptible human every fourteen days or it would die. If each outbreak of the virus could be surrounded by a ring of immune people during the virus's low season, the virus would not be able to complete its fourteen-day life cycle. It would be cut off, unable to move to the next human host, and its chain of

infection would be broken.
The ring had to be tight. If it developed a leak, smallpox would blow out. In January, 1975, smallpox blew out in Bangladesh, after the eradicators thought they were on the verge of stopping it everywhere in Asia. Variola major swept through more than five hundred towns and villages. Henderson began shuttling between Geneva and Bangladesh, and in April of that year, when things were still not under control, he visited the Infectious Disease Hospital in Dacca, the nation's capital. He wanted to do rounds in a smallpox ward. "I went down the rows of beds," he told me. There were seventy or eighty people, and half of them were dying. "There is nothing you can do for any of these patients. They were afraid to move. There were a lot of flies crawling all over the place. My God, they talk about the odor of smallpox. It is an odd smell, not like anything else."
The skin gives off gases. "It's a sickly odor, like rotting flesh, but it's not decay, because the skin remains sealed and the pus isn't leaking out," Henderson said. "That smell is one of the mysteries of smallpox. No one knows what it is. I was with this British guy, Nick Ward, M.D. He had worked in Africa -- he was a tough guy. At the end, he stood by a fence looking at the ground. Finally, he said to me, 'I don't know that I could go through another situation like that again.'"
Nicholas Ward, who now lives in France, remembered that moment. "I've spent a fair amount of my life working with tropical diseases, and I can truly say there is nothing so awful as a case of smallpox, particularly the type where a person becomes a bloody mess," he said. He knew the odor. "I would have a shrewd idea of a diagnosis after walking into a home. I could smell it."
Henderson and his team mounted ring vaccinations across Bangladesh, and they traced cases and contacts, trying to surround the life form. Finally, in the fall of 1975, they cornered variola on an island off the coast of Bangladesh. It was a marshy, poor place called Bhola Island, and there, on October 16th, a three-year-old girl named Rahima Banu broke with the last case of naturally occurring Variola major anywhere on earth. She survived. Rahima Banu would be twenty-seven years old today; researchers have lost track of her. Doctors from the Smallpox Eradication Unit collected six of the girl's pustules after they had dried into scabs, peeling them off her skin gently, with tweezers. Two years later, on October 26, 1977, the last natural case of the mild type of smallpox, Variola minor, popped up in a cook in Somalia named Ali Maow Maalin. He survived, and the last ring tightened around variola, and its life cycle stopped.
THE headquarters of the Centers for Disease Control, in Atlanta, is a jumble of old and new buildings, joined by elevated walkways, which give the place the feel of a maze. The buildings sit along Clifton Road, an artery that winds through green neighborhoods in the northeastern part of Atlanta. I arrived at the C.D.C. On a perfect day in spring. Changeable clouds marched across a deep

sky, and oak trees were shedding green flowers. Across the street from the entrance, a blue jay screamed in a pine tree, and the branches glittered in the sun, throwing off a scent of pitch.

Joseph J. Esposito, Ph.D., who is the chief of the C.D.C.'s Poxvirus Section, led me along an outdoor walkway toward his laboratory and office. Esposito is a stocky man of moderate height, in his mid-fifties, who runs to keep his weight down, and he has a dark beard and wears eyeglasses over brown eyes that are perceptive and serious. I asked him if we could get closer to smallpox. We passed along an aerial walkway covered with a chain-link fence, and we turned onto another walkway. We stopped and leaned on a railing. We were facing the C.D.C.'s Level 4 biocontainment building. It contains the Level 4 hot suites-labs where researchers work with lethal viruses while wearing pressurized spacesuits. The building has a line of windows tinted blue-green, like fish tanks. "The variola is in there somewhere,"Joe Esposito said, offering me a grave smile and nodding at the Level 4 building. "There is a kind of electricity in the air when we're working with smallpox. Everybody around here always seems to know -- 'Joe's got the smallpox out of the freezer.' "

The smallpox freezer may be encircled by alarms and motion detectors. It may or may not be wrapped in chains. It may be a stainless-steel cylinder. Or it may be a white box intended to look like any other freezer. Officials at the C.D.C. won't comment.

Inside the freezer, the entire collection of smallpox occupies a volume slightly larger than that of a basketball. It consists of approximately four hundred little plastic vials the size of pencil stubs, the residue of D. A. Henderson's war with variola. They're an inch long and they have plastic screw caps. They sit in seven little white cardboard boxes, in a rack inside the freezer, which keeps the virus not strictly alive, not exactly dead, but potent. Most of the vials contain milky ice or bloody ice. The virus has been cultured in flasks of live cells (milky ice) or in live chicken eggs (live eggs have a blood system). Around twenty-five of the vials contain human scabs-dried smallpox pustules. The scabs look like pencil erasers.

The six scabs that were collected from the girl in Bangladesh named Rahima Banu used to sit in a vial, but recently Esposito's group used the last of her scabs for research. The strain that came out of her scabs is known as Bangladesh 1975 -- or, informally, as the Rahima. Now that the scabs are gone, the Rahima exists in vials of milky ice.

Esposito sat hunched in his chair in front of his computer. His office is a windowless room with cinder-block walls. A troll with Shocking-pink hair stood on top of the computer, staring at him wide-eyed. "I like to think like a virus," Esposito said. "If you can think like a virus, then you can begin to understand why a virus does what it does. A smallpox particle gets into a person's body and, in a way, it's thinking, I'm this one particle sitting here surrounded by an angry immune system. I have to multiply fast. Then I have to

get out of this host fast. It escapes into the air before the pustules develop." By the time the host feels sick, the virus has already moved on to its next host. The previous host has become a cast-off husk (and is now becoming saturated with virus), but whether the person lives or dies no longer matters to the virus. However, the dried scabs, when they fall off, contain live virus. The scabs are the virus's seeds. They preserve it for a long time, just in case it hasn't managed to reach a host in the air. The scabs give the virus a second chance.

POXVIRUSES move easily through the animal kingdom. Along with herds of animals or swarms of insects come poxviruses circulating among them like pickpockets at a fair. Esposito once classified what he and other virologists have glimpsed of the poxviruses in nature. He noted monkeypox, swinepox, buffalopox, skunkpox, raccoonpox, gerbilpox, a few deerpoxes, a sealpox, turkeypox, canarypox, pigeonpox, starlingpox, peacockpox, dolphinpox, Nile crocodilepox, penguinpox, two kangaroopoxes, and a quokkapox. (The quokka is an Australian wallaby.) Any attempt to get to the bottom of the butterflypoxes, mothpoxes, and beetlepoxes would be something like enumerating the nine billion names of God.

A caterpillar that has caught an insectpox dissolves into a liquefaction of insect guts mixed with pure crystals of poxvirus. This is known as a virus melt. The melt pours out of the dead caterpillar, and other caterpillars come along and accidentally eat the crystals lying on a leaf, and they melt, and so it goes for millions of years in the happy life of an insectpox. "It is a good thing no person has been known to catch an insectpox," Esposito remarked. (You might avoid eating melted caterpillars.) The yellow-fever mosquito, Aedes aegypti, suffers from a fatal mosquitopox. At least two midgepoxes torment midges. Grasshoppers are known to get at least six poxes. If a grasshopperpox breaks out in a swarm of African Locusts, it can wipe them out with a plague.

Viruses have an ability to move from one type of host to another in what is known as a trans-species jump. The virus changes during the course of a jump, adapting to its new host. The trans-species jump is the virus's most important means of long-term survival. Species go extinct; viruses move on. There is something impressive in the trans-species jump of a virus, like an unfurling of wings or a flash of stripes when a predator makes a rush. Some fifty years ago, in central Africa, the AIDS virus apparently moved out of chimpanzees into people. Chimpanzees are now endangered, while the AIDS virus is booming.

For most of human prehistory, people lived in small groups of hunter-gatherers. The poxviruses did not deign to notice Homo sapiens as long as the species consisted of scattered groups; there was no percentage in it for a pox. With the growth of agriculture, the human population of the earth swelled and became more tightly packed. Villages became towns and cities, and people were crowded together in river valleys.

Epidemiologists have done some mathematics on the spread of smallpox, and they find that the virus needs a population of about two hundred thousand people

living within a fourteen-day travel time from one another or the virus can't keep its life cycle going, and it dies out. Those conditions didn't occur in history until the appearance of settled agricultural areas and cities. At that point -- roughly seven thousand years ago -- the human species became an accident with a poxvirus waiting to happen.

Smallpox could be described as the first urban virus. It is thought to have made a trans-species jump into humans in one of the early agricultural river valleys -- perhaps in the Nile Valley, or in Mesopotamia, or in the Indus River Valley. In the Cairo Museum, the mummy of the Pharaoh Ramses V, who died as a young man in 1157 B.C., is speckled with yellow blisters from face to scrotum.

In 1991, Joe Esposito and the molecular biologist Craig Venter, who was at the National Institutes of Health, sequenced the entire genome of the Rahima strain of smallpox; that is, they mapped all its DNA. They found that the virus contains a hundred and eighty-six thousand base pairs of DNA (each base pair being a step on the ladder of the molecule), and that the DNA contains about a hundred and eighty-seven genes-making smallpox one of the most complicated viruses known. (The AIDS virus has only ten genes.) A gene is a piece of DNA, which contains the recipe for making one protein. Esposito's team noticed that smallpox has a gene that is also found in the placenta of a mouse. Smallpox knows how to make a mouse protein. How did smallpox learn that? "The poxviruses are promiscuous at capturing genes from their hosts," Esposito said. "It tells you that smallpox was once inside a mouse or some other small rodent." D. A. Henderson speculates that the original host of smallpox may have been an African rodent that lived in a crescent of green forests along the southern Nile River. The forests disappeared, cut down by people, and possibly the rodent has gone extinct. This is only a guess. Smallpox moved on.

THE principal American biodefense laboratory is the United States Army Medical Research Institute of Infectious Diseases, or USAMRIID, in Fort Detrick, Maryland -- an Army base that nestles against the eastern front of the Appalachian Mountains in the city of Frederick, an hour's drive northwest of Washington. There is no smallpox at USAMRIID, for only the two W.H.O. repositories are allowed to have it. The principal scientific adviser at USAMRIID is Peter Jahrling, a civilian in his fifties with gray-blond hair, PhotoGray glasses, and a craggy face. Jahrling was the primary scientist during the 1989 outbreak of Ebola virus in Reston, Virginia: he discovered and named the Ebola-Reston virus.

"I don't think there is any higher biological threat to this nation than smallpox," Jahrling said to me, in his office, a windowless retreat jammed with paper. His voice was croaking. "I was over in Geneva for a meeting on smallpox, and I came back with some flu strain," he said hoarsely. The flu strain had swept through the world's smallpox experts. "Shows how fast a virus can move. If we have some kind of bioterror emergency with smallpox, there will be no time to start stroking our beards. We'd better have vaccine pre-positioned on pallets

and ready to go."

Jahrling opposes the destruction of the official stocks of smallpox. "If you really believe there's a bioterrorist threat out there, then you can't get rid of smallpox," he said. "If smallpox is outlawed, only outlaws will have smallpox." His group has been testing antiviral drugs that might work on smallpox, and he feels that in order to verify the effectiveness of a new drug it would be necessary to test it on live smallpox virus.

One of Jahrling's researchers, John Huggins, led me into the central areas of USAMRIID. Huggins is a chunky man with round Fiorucci eyeglasses. He turned into a corridor leading to the Level 4 spacesuit hot suites, or hot zones. The walls were cinder block, and the light turned bile green. A smoky reek drifted in the corridors, coming from huge autoclaves -- pressure cookers -- where contaminated equipment and waste were being heated and sterilized after being brought out of a hot zone. We stopped at a door that had a window of thick glass, looking into hot suite AA5, the Ebola hot zone.

I pressed my nose against the glass. It was cool, and there was a faint rumble of blowers, keeping the zone at negative pressure, so that no contaminated air would flow out through cracks. The suite was dark and drowned in shadows, illuminated only by light coming from lab equipment. I could see no one in there but white mice in racks of plastic boxes. They were scribble-scrabbling in pine shavings.

"These mice are all infected with Ebola," Huggins said. "They bleed when they die. Like humans."

The mice looked fine. I couldn't see any blood in the shavings.

"We're giving them an antiviral drug that saves their lives," Huggins explained. "They're kind of perky. It's called an S.A.H. drug. It's not ready for human testing. It could work in humans, but we don't know."

In 1995, Huggins spent time in a spacesuit at the C.D.C. Level 4 lab in Atlanta, testing drugs on live smallpox. He found that a drug called cidofovir can block smallpox replication. Cidofovir, which is normally used against a virus that infects AIDS patients, has drawbacks. It must be given to people by I.V. drip, and there is some concern that it might damage the kidneys. Huggins and Jahrling believe that within five years better smallpox drugs are likely to be discovered. They say they will need to test the drugs directly on the virus. They add that the drug must be tested on the live virus in order to receive F.D.A. approval.

In March, a committee of the highly respected Institute of Medicine, in Washington, D.C., concluded that one of the main reasons for retaining live smallpox virus would be to help develop drugs against it. D. A. Henderson, who was not a member of the Institute of Medicine committee and thoroughly disagrees with its conclusions, thought that Jahrling was being too optimistic. "To get a new antiviral drug against smallpox is going to cost three hundred million dollars," he said. "The money simply isn't there."

Jahrling stood his ground. "Ceremonial destruction of smallpox is the crown jewel in D. A. Henderson's career," he said. "He would like to throw the lever on smallpox himself. If I had spent my life tramping the planet to eradicate the virus, I would want to throw the lever, too. What he did was a great accomplishment, but he has become blinded by the last glittering crown jewel of total eradication."

KEN ALIBEK, who was once Kanatjan Alibekov, a leading Soviet bioweaponeer and the inventor of the world's most powerful anthrax, shocked the American intelligence community when he defected, in 1992, and revealed how far the Soviet Union had gone with bioweapons. In a new book of his, entitled "Biohazard," Alibek says that there were twenty tons of liquid smallpox kept on hand at Soviet military bases; it was kept ready for loading on biowarheads on missiles targeted on American cities. I contacted certain government sources and asked them if there was any evidence to corroborate Alibek's claims.

One person who asked not to be named said, "I really have to be careful what I say. Yeah, Alibek's claims have been corroborated in multiple ways. There's not a lot of evidence. There's some."

Another person who asked not to be named said that the Soviet Union had put the biowarheads on ICBM missiles and test launched them sometime before 1991 over the Pacific Ocean. The United States -- probably using spy satellites that orbited near the tests -- was able to monitor the missiles as they soared into space and then punched back through the atmosphere and landed in the sea. The warheads were spinning weirdly: they were unusually heavy, and they had a strange shape. The warhead was heavy because it had an active refrigeration system to keep its temperature near or below the boiling temperature of water during reentry. Nuclear warheads don't need to be actively cooled. Why would a warhead need to be cooled? Presumably, because it was designed to contain something alive. But what? The person said, "The warhead was built to carry a very small quantity of biological weapon. Anthrax wouldn't have worked too well, because you need to put a lot of anthrax in the air to kill people, and anthrax isn't contagious. With smallpox, you don't need much. If you use smallpox, you get around the most difficult technical problem of bioweapons -- the problem of dissemination. With smallpox, you use people as disseminators."

In 1989, a Soviet biologist named Vladimir Pasechnik defected to Britain. British intelligence agents spent a year debriefing him in a safe house. By the end, the British agents felt they had confirmed that the U.S.S.R. had biological missiles aimed at the United States. This information reached President George Bush and the British Prime Minister, Margaret Thatcher. Mrs. Thatcher then apparently telephoned the Soviet leader, Mikhail Gorbachev, and sternly confronted him. She was furious, and so was Bush. Gorbachev responded by allowing a small, secret team of American and British biological-weapons inspectors to tour Soviet biowarfare facilities. In January of 1991, the inspectors travelled across the U.S.S.R., getting whirlwind looks at some of the

major clandestine bases of the Soviet biowarfare program, which was called Biopreparat. The inspectors were frightened by what they discovered. ("I would describe it as scary, and I feel a responsibility to tell the world medical community about what I saw, because doctors could face these diseases," an inspector, Frank Malinoski, M.D., Ph.D., said to me.) On January 14th, the team arrived at Vector, the main virology complex, in Siberia, and the next day, after being treated to vodka and piles of caviar, they were shown into a laboratory called Building 6, where one of the inspectors, David Kelly, took a technician aside and asked him what virus they had been working with. The technician said that they had been working with smallpox. Kelly repeated the question three times. Three times, he asked the technician, "You mean you were working with Variola major?" and he emphasized to the technician that his answer was very important. The technician responded emphatically that it was Variola major. Kelly says that his interpreter was the best Russian interpreter the British government has. "There was no ambiguity," Kelly says.

The inspectors were stunned. Vector was not supposed to have any smallpox at all, much less be working with it. All the Russian smallpox stocks were supposed to be kept in one freezer in Moscow, which was supposed to be under the control of the World Health Organization. For Vector to have smallpox would be a supreme violation of rules set down by the W.H.O.

Then they went upstairs into Building 6, and entered a long corridor. On one side was a line of glass windows looking in on a giant airtight steel chamber of a type known as a dynamic aerosol test chamber. The device is for testing bioweapons. Small explosives are detonated inside the chamber, throwing a biological agent into the air of the chamber. The chamber in Building 6 had an octopus-like structure of tubes coming out of it where sensors could be attached or monkeys could be clamped with their faces exposed to the chamber's air. An airborne bioweapon would get into the sensors or into the animals' lungs. On the other side of the corridor was a room that Frank Malinoski said "looked like a NASA control room," and video cameras provided views inside the chamber, so that Vector scientists could watch the release of a bioweapon.

Vector scientists later told the inspectors that the chamber was a Model UKZD-25-a bioweapons explosion-test chamber. It was the largest and most sophisticated modern bioweapons test chamber that has ever been found by inspectors in any country. It was used for testing smallpox.

The inspectors asked to put on spacesuits and to go inside. (They had brought along Q-Tip-like swab kits: they would have liked to swab the inner walls of the chamber, in the hope of collecting a virus.) The Russians refused. "They said our vaccines might not protect us," Malinoski says. "It suggested that they had developed viruses that were resistant to American vaccines." The Russians ordered the inspectors to leave Building 6.

At a large gathering that evening, three inspectors -- David Kelly, Frank Malinoski, and Christopher Davis -- publicly confronted the head of Vector, a

virologist named Lev Sandakhchiev, about Vector's smallpox. (His name is pronounced "Sun-dock-chev.") He back-pedalled angrily. Davis, a medical doctor with a Ph.D. who was then with British intelligence, now recalls, "Lev is gnome-like, a short man with a wizened, weather-beaten, lined face, and black hair. He's very bright and capable, a tough individual, full of bonhomie, but he can be very nasty when he is upset." Sandakhchiev heatedly insisted that his technician had misspoken. He called on his deputy, Sergei Netesov, to support him. The two Vector leaders insisted that there had been no work with smallpox at Vector. They had been doing genetic engineering with smallpox genes, they said, but Vector didn't have any live smallpox, only the virus's DNA -- and the more they spoke the murkier their statements seemed. David Kelly remembers, "They were both lying, and it was a very, very tense moment. It seemed like an eternity, but it only lasted about fifteen minutes. And then there were so many other aspects of Vector we had to explore."

"The brazenness of these people!" one inspector later fumed. "They had been testing smallpox in their explosion chamber the week before we arrived."

Lev Sandakhchiev is still the head of Vector. He declined to be interviewed for this account but has steadfastly maintained that no offensive bioweapons research occurs now at Vector. In January of this year, at the Geneva meeting of smallpox experts, Sandakhchiev delivered a paper (and may have caught their flu). In his paper he claimed that Vector did not have any smallpox until 1994, when, he said, Vector had obtained it legally from Moscow. D. A. Henderson was also at that meeting. "It was quite elaborate and quite unbelievable," Henderson said. "I rolled my eyes, and saw other people rolling their eyes at me. We're sitting there, he's presenting us with all this horseshit, and he knows it's horseshit. Sandakhchiev is lying flagrantly."

Four sources have suggested to me that Lev Sandakhchiev was in charge of a Vector research group that in 1990 devised a more efficient way to grow weapons-grade smallpox in industrial-scale pharmaceutical tanks known as bioreactors. The Vector smallpox bioreactors had a capacity of six hundred and thirty litres -- virus tanks big enough for a microbrewery. Once the Vector scientists had worked out the details of variola manufacturing, the results were written up in master production protocols -- recipe books -- and these protocols ended up at the Russian Ministry of Defense, in Moscow. At the time, weapons-grade smallpox was being manufactured by two older methods at a top-secret virus-munitions production plant near the city of Sergiyev Posad, forty-five miles northeast of Moscow. At another virus-munitions plant, near Pokrov, about two hundred miles southeast of Moscow, military virus-production specialists converted the plant to the new Vector method of making smallpox in the large virus bioreactors, but apparently never started the reaction. When one considers that a single person infected with smallpox would be considered a global medical emergency, this is rather a lot of smallpox activity to have bubbling near Moscow. It means that live smallpox virus and the protocols for

how to mass-produce it had spread to various places in Russia by the nineteen-nineties. Indeed, live smallpox could be bubbling in reactors now at Sergiyev Posad-no one in the United States government admits to having a clue, and no Russian journalists have seen the place. Peter Jahrling said, "I really think that Vector is out of the offensive BW [biowarfare] business. But Sergiyev Posad is the black hole. We have no contacts there, and the Russians won't allow us to visit the place."

These days, Lev Sandakhchiev has cordial relationships with Peter Jahrling and Joe Esposito. They are eager to draw their colleague into the circle of open international science. During their visits to Siberia, Sandakhchiev has come across to them as warm and human, and desperate for research money to support his institute. Sometimes, candid remarks slip out from the Russians. Jahrling put it this way: "There were tons of smallpox virus made in the Soviet Union. We know that. The Russians have admitted that to us. I was in a room with one of the Vector leaders when he said to us, 'Listen, we didn't account for every ampule of the virus. We had large quantities of it on hand. There were plenty of opportunities for staff members to walk away with an ampule. Although we think we know where our formerly employed scientists are, we can't account for all of them-we don't know where all of them are.' " Today, smallpox and its protocols could be anywhere in the world. A master seed strain of smallpox could be carried in a person's pocket. The seed itself could be a freeze-dried lump of virus the size of a jimmy on an ice-cream cone.

While I was sitting with D. A. Henderson in his house, I mentioned what seemed to me the great and tragic paradox of his life's work. The eradication caused the human species to lose its immunity to smallpox, and that was what made it possible for the Soviets to turn smallpox into a weapon rivalling the hydrogen bomb.

Henderson responded with silence, and then he said, thoughtfully, "I feel very sad about this. The eradication never would have succeeded without the Russians. Viktor Zhdanov started it, and they did so much. They were extremely proud of what they had done. I felt the virus was in good hands with the Russians. I never would have suspected. They made twenty tons -- twenty tons -- of smallpox. For us to have come so far with the disease, and now to have to deal with this human creation, when there are so many other problems in the world . . ." He was quiet again. "It's a great letdown," he said.

For years, the scientific community generally thought that biological weapons weren't effective as weapons, especially because it was thought that they're difficult to disperse in the air. This view persists, and one reason is that biologists know little or nothing about aerosol-particle technology. The silicon-chip industry is full of machines that can spread particles in the air.

To learn more, I called a leading epidemiologist and bioterrorism expert, Michael Osterholm, who has been poking around companies and labs where these devices are invented. "I have a device the size of a credit card sitting on my

desk," he said. "It makes an invisible mist of particles in the one-to-five-micron size range -- that size hangs in the air for hours, and gets into the lungs. You can run it on a camcorder battery. If you load it with two tablespoons of infectious fluid, it could fill a whole airport terminal with particles." Osterholm speculated that the device could create thousands of smallpox cases in the first wave. He feels that D. A. Henderson's estimate of how fast smallpox could balloon nationally is conservative. "D.A. is looking at Yugoslavia, where the population in 1972 had a lot of protective immunity," he said. "Those immune people are like control rods in a nuclear reactor. The American population has little immunity, so it's a reactor with no control rods. We could have an uncontrolled smallpox chain reaction." This would be something that terrorism experts refer to as a "soft kill" of the United States of America.

The idea that a biological credit card could execute a soft kill of the United States has reached the White House. The chief terrorism expert on the National Security Council, Richard Clarke, has sent word through the federal government that getting national stockpiles of smallpox vaccine is a top priority.

The effort started four years ago. So far, the government has little to show except numerous meetings among agencies, with no hope of vaccine anytime soon. The Department of Defense has put all its vaccine efforts into something called the Joint Vaccine Acquisition Program, which is run by the Joint Program Office for Biological Defense. People inside the military don't want their names used when they talk about the Pentagon's efforts. "It's a fucking disaster," said one knowledgeable military officer who has had direct experience in the matter. Last year, the Pentagon hired a systems contractor called Dynport, headquartered in Reston, Virginia, to develop and make a number of different vaccines for troops. The smallpox-vaccine contract calls for three hundred thousand doses, at a cost of $22.4 million, or seventy-five dollars a dose, with delivery now scheduled for 2006. (The date has been pushed back at least once already.) This amount of vaccine could be made in about fifteen flasks the size of soda bottles. There are 2.3 million people in the armed forces, and they have several million more dependents. "Three hundred thousand doses is not enough vaccine to protect anyone -- not even our troops. It totally ignores the fact that smallpox is contagious," one military man said. "These guys ought to be buying tank treads and belt buckles. They know nothing about vaccines."

The Department of Health and Human Services (H.H.S.) has been given the responsibility by the White House for producing a stockpile of smallpox vaccine large enough to protect the American civilian population in case of a bioterror event; originally, the idea was for H.H.S. to consider hiring the military's contractor, Dynport, to make forty million extra doses, in addition to the three hundred thousand that Dynport was making for the Pentagon. (Any such initiative would require competitive bidding.)

At a series of meetings at H.H.S., a top Dynport executive said that forty

million doses could be quite expensive. One scientist asked if a group of knowledgeable people could be drawn together to come up with an estimate of costs. The Dynport man answered, "Yes, we can do a study that will list the questions that need to be asked. It will cost two hundred and forty thousand dollars and will take six weeks."

Somebody then asked how much it would cost to answer the questions. The Dynport official responded, "That will be a different study. That study will cost two million dollars and will take six months."

With that, one scientist at the meeting burst out, "This is horseshit! We're asking an encyclopedia salesman if we need an encyclopedia!"

The C.E.O. of Dynport, Stephen Prior, said that the situation is more complicated:"The civilian population is very different from the military. There's an age spread from newborns to the elderly, there's more compromised immunity, with AIDS, chemotherapy, and organ transplants. And possibly thirty-five per cent of people have never been vaccinated. So it's not just scaling up the manufacturing."

Another knowledgeable observer is the retired Army General Philip K. Russell, M.D., who gave the order to send biohazard troops into Reston in 1989 to deal with a building full of monkeys infected with Ebola. Russell said to me, "Many of us are afraid that Dynport won't deliver the goods without wasting an inordinate amount of money."

However, H.H.S. has quietly opened talks with other potential contractors, preparing to solicit bids to make a civilian stockpile of smallpox vaccine, though there has been no announcement. "The effort at H.H.S. still isn't organized," D. A. Henderson said. General Russell said, "If smallpox really got going, people should be most concerned about a lack of effective leadership on the part of their government."

I WANTED to get closer to smallpox virus. In Joe Esposito's lab, at the Centers for Disease Control, there was a test going of a biosensor device for detecting smallpox. It was a machine in a black suitcase. It could detect a bioweapon using; the process called the polymerase chain reaction, or P.C.R. -- the same kind of molecular fingerprinting that police use to identify the DNA of a crime suspect. The suitcase thing was called a Cepheid Briefcase Smart Cycler, and it had been co-invented by M. Allen Northrup, a biomedical engineer who founded a company to make and sell biosensors. He was there, along with a cluster of other scientists.

Esposito, the official guardian of one half of the world's official supply of smallpox, handed a box of tubes to a scientist in the room. Two of the tubes contained the whole DNA of smallpox virus but not live smallpox. The DNA drifted in a drop of water; it was the Rahima strain. Two other tubes contained anthrax. The samples were snapped into slots in the machine.

Northrup turned his attention to a laptop computer that nestled in the machine. Northrup is a chunky man with a mustache and reddish-brown hair. He tapped on

the keys.
We waited around, chatting. Meanwhile, the Cepheid was working silently. It showed colored lines on its screen. In fifteen minutes, the anthrax lines started going straight up, and someone said, "The anthrax is screaming." Finally, one of the smallpox lines crept upward, slowly. "That's a positive for smallpox, not so bad," a scientist said. Emergency-response teams could carry a Cepheid suitcase to the scene of a bioterror event and begin testing people immediately for anthrax or smallpox. The machine is priced at sixty thousand dollars.
Afterward, Joe Esposito went around collecting the used tubes. The smallpox-sample holder -- a plastic thing the size of a thumbnail-had been left on a counter. I picked it up.
Esposito wasn't about to let anyone walk off with smallpox. "Leave me that tube," he said. "You are not allowed to have more than twenty per cent of the DNA."
Before I handed it to him, I glanced at a little window in the tube. When I held it up to the light, the liquid looked like clear water. The water contained the whole molecules of life from variola, a parasite that had colonized us thousands of years ago. We had almost freed ourselves of it, but we found we had developed a strong affinity for smallpox. Some of us had made it into a weapon, and now we couldn't get rid of it. I wondered if we ever would, for the story of our entanglement with smallpox is not yet ended.

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