The Plan to Fight Smallpox

Two decades ago we eradicated the world's most devastating plague. Now the government has a plan to vaccinate the entire population within 10 days of a terror attack, and 10 million health and emergency workers may get their shots in advance.

By Geoffrey Cowley

Oct. 14 issue — Smallpox is a ghost to most modern doctors— the greatest killer in history, perhaps, but not the sort of problem that shows up in one’s waiting room. Dr. Donald Millar and Dr. Michael Lane are old enough to share a different perspective. Both took part in the U.S. government’s smallpox-eradication efforts in the heady days of the 1960s and ’70s. While chasing the variola virus through Africa and India, they saw what smallpox can do.
THE DISEASE ENGULFS the body in pustules that itch and ooze, and often blind or disfigure victims lucky enough to survive. They also witnessed the power of a relatively crude vaccine to contain the awful killer. Both men believed deeply in the ideal of global eradication, but by 1969 they’d grown skeptical of the need for routine vaccination in the United States. American kids were no longer threatened by smallpox, they wrote in The New England Journal of Medicine—yet 7 million were still getting shots each year, thousands were suffering adverse reactions and roughly 1 in a million was dying of complications. “The benefits of routine ... vaccination no longer outweigh its risks,” the virus hunters concluded in a seminal phrase, “and consideration should be given to its discontinuance.”

AN ERADICATED DISEASE
Millar and Lane got their wish. The United States abandoned routine smallpox vaccination in 1972, and never regretted the decision. No one on earth has contracted natural smallpox since 1977. The World Health Organization declared the disease “eradicated” in 1980, and no country has vaccinated children since 1984. Unfortunately the variola virus, which causes smallpox, is still very much alive. The Soviet government cultivated a huge stockpile for military use during the 1980s, in violation of international law. The stockpile was eventually destroyed, and today the only acknowledged variola samples are held in government laboratories in the United States and Russia. But the Soviet stockpile has never been fully accounted for. And recent events—the World Trade Center attack, the anthrax attacks, the persistence of Al Qaeda and the mounting hostilities with Saddam Hussein—have lent new urgency to an old question. Could terrorists hit us with smallpox?
The odds are impossible to gauge, but there is no question we’re vulnerable. Even as they called for an end to routine vaccination, Millar and Lane warned that the loss of widespread immunity would “raise our susceptibility to smallpox as a weapon of biologic warfare.” Those of us vaccinated before 1972 may still have some residual protection, but the 119 million Americans born since then are about as defenseless as the ones who greeted Columbus 500 years ago. “Although smallpox has long been feared as the most devastating of all infectious diseases,” the Johns Hopkins-based Working Group on Civilian Biodefense has written, “its potential for devastation today is far greater than at any previous time.”

Federal officials are as concerned as anyone else, and the Bush administration has made “biosecurity” a high priority. Two weeks ago the federal government came forward with a blueprint for quickly vaccinating the whole country in the event of a smallpox attack. And Health and Human Services Secretary Tommy Thompson has presented the White House with a plan that could lead to routine “pre-attack” vaccination of up to 10 million health and emergency workers—and perhaps even private citizens—by early 2004. The HHS plan doesn’t have a precise timetable, but it includes three phases. To start, the government would vaccinate the 500,000 health workers most likely to encounter patients during an outbreak. Later, as new vaccine stocks are developed and licensed by the Food and Drug Administration, other emergency workers would become eligible. And once that
has happened, private citizens would gain voluntary access. The proposal is not yet policy, just an option that the president will mull as he contemplates his next move in the “war on terror.” Last week members of the team that crafted it spoke at length to NEWSWEEK about its origins and evolution, and the prospects for keeping America safe from smallpox. Their mood was summed up by Tom Ridge, director of the Office of Homeland Security. “You have people in this world who hate America and who have said they will use any means to harm us,” he said. “You have to be prepared.”

OUTDATED STRATEGY?

If embraced by the White House, the new plan will mark a sharp departure from the smallpox policies of the past three decades. When federal health officials abandoned routine vaccination in 1972, they assumed that “ring vaccination” would be an adequate substitute. The ring strategy involves isolating anyone with a suspected case of the pox, and quickly vaccinating the person’s “primary contacts” (friends, family and co-workers) and “secondary contacts” (contacts of the contacts) in an expanding circle. The strategy is an efficient way to contain natural outbreaks. But as Yale health analyst Edward Kaplan observes, “It’s a fantasy to believe that the control of small natural outbreaks provides guidance for large bioterrorist attacks.” Anyone with the means and motivation to spread smallpox would presumably target a transportation hub or an urban crossroad, not a country store. By the time the first victims developed malaise, fever and rash a week later, others infected at the same time could be dispersed throughout the country.

At the urging of the federal Centers for Disease Control and Prevention, state and local governments are now devising plans to vaccinate everyone during a smallpox attack. Health workers would still track and vaccinate the contacts of known victims. But under the new plan, laid out in a 48-page “Smallpox Vaccination Clinic Guide,” states and cities must also establish clinics that can open quickly during an emergency to screen, counsel and vaccinate anyone who walks through the door. The CDC guide includes blueprints for model clinics in which staffs of 117 workers can vaccinate nearly 3,000 people during each eight-hour shift. Most experts agree that if health departments can pull off what the Feds have in mind, the mass-vaccination strategy will save
Smallpox doesn’t spread easily from person to person during its seven- to 17-day incubation period, and even infected people can often avoid serious illness if they’re vaccinated within four days. Inoculating the nation that quickly would pose enormous challenges, says Kaplan, “but it’s not impossible at all.”

He couldn’t have said that a year ago. When Ridge founded the Homeland Security Office last fall, smoke was rising from Ground Zero, anthrax was moving through the nation’s mail system and an exercise called “Dark Winter” had shown that, in Ridge’s words, “we didn’t have enough smallpox vaccine to inoculate the public on short notice.” The government’s entire inventory consisted of 15.4 million doses of Dryvax, a vaccine that Wyeth-Ayerst Laboratories made in the 1970s by injecting calves with vaccinia (a milder cousin of the variola virus) and harvesting more of it from the resulting blisters. Today, thanks to a series of lucky breaks, the Feds are sitting on more than a half-billion doses. The first break came when researchers discovered that the government’s Dryvax was potent enough to use at one fifth the intended concentration. Suddenly, 15.4 million doses became 77 million. Then Thompson confirmed that Aventis Pasteur had come up with 86 million doses (which could be stretched to 430 million) of a virtually identical vaccine dating back to the 1950s. Aventis had been meaning to dispose of the stuff, says company spokesman Len Lavenda, but hadn’t gotten around to it. So the firm converted the freeze-dried bulk into clinic-ready vaccine and handed it off to the government.

**NO SHORTAGE**

While stockpiling the old vaccines for emergencies, the government has also ordered up 210 million doses of a second-generation vaccine grown in cell cultures rather than cow pustules. That vaccine, developed by Acambis of Cambridge, England, will contain the same virus as the older ones and carry most of the same risks, but it will be less likely to harbor impurities. HHS expects to have 70 million doses on hand by the end of the year. Meanwhile, no one is sweating over a shortage of vaccine. “In an emergency,” says Dr. Anthony Fauci of the National Institute of Allergy and Infectious Diseases, “we’d have enough to vaccinate everybody tomorrow.”

Local health officials are aghast at all the new chores they’ve inherited, but most profess confidence that they’ll have disaster plans ready by Dec. 1, as the Feds have requested. New York City has a head start. “Last fall was overwhelming,” says Marci Layton, the city’s assistant commissioner for communicable-disease control, “and that was just eight cases of anthrax. At the time, I said, ‘Can you imagine what it would be like to respond to smallpox?’” The city has since expanded its monitoring system to pick up unusual patterns of infection throughout the five boroughs. Dr. Laurene Mascola may face even greater challenges as communicable-disease chief for Los
Angeles County. Like Layton, she serves nearly 10 million constituents who speak dozens of languages. But her community is spread over 4,000 square miles. “You know that the first day a case is announced they’re all going to knock on some door saying, ‘Where’s my vaccine?’” Mascola says. Her department has already developed a 153-page document with vaccination plans for outbreaks ranging from fewer than 10 cases to more than 1,000.

Big-city health departments aren’t the only ones racing to be ready. In Butler County, Pa., Dr. Mark Carlsson is turning this fall’s flu-vaccine drive into a dry run for a smallpox campaign. Health workers will practice triaging patients and getting informed consent—and patients will report risk factors ranging from eczema to AIDS to keep the workers on their toes. In Illinois, meanwhile, health workers are learning to prick orange skins with the once common bifurcated needles that are used to jab vaccinia into people’s upper arms. “Each time you go in, you put a little bit of that vaccine under the skin,” state health director John Lumpkin explains, “and you end up with a mild infection that triggers an immune response.” Lumpkin launched the smallpox-preparedness program last winter and hopes to have 1,000 health workers trained by next spring.

UNHAPPY SURPRISES

Being prepared surely beats the alternative. But emergencies have a way of defying carefully laid plans. Just think back to last year’s anthrax scare, says Neal Cohen, a former New York City health commissioner who now heads a preparedness group called the Center on Bioterrorism. Experts predicted confidently that postal workers wouldn’t be infected by sealed mail—until they were. And they dismissed the possibility that one tainted letter could contaminate others—until it happened. “A lot of our assumptions turned out to be faulty,” he says. “We learned how little we really understood about the risks.” Could freeway traffic stall response plans in L.A. or Atlanta? What about airport closures? And suppose terrorists managed to combine a smallpox release with a September 11-style assault that placed competing demands on the response system? “If there’s more than one form of attack,” says Millar, the virus hunter, “the task of vaccinating everyone in the country in a week becomes mind-boggling.”

This is where the debate over preparedness gets
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interesting. Millar and Lane, the coauthors of that 1969 challenge to routine vaccination, remain fond friends 33 years later. But they have come to different conclusions about how best to prepare ourselves. Lane believes a post-attack strategy is the only one we need, but Millar favors voluntary peacetime vaccination as a strategy for restoring some of our lost immunity. The approach offers some indisputable advantages. For one thing, it could minimize the damage done by the vaccine itself. According to the CDC’s latest estimates, 15 of every million first-time vaccinees could suffer life-threatening reactions to the vaccine—conditions such as encephalitis (brain inflammation), generalized vaccinia (a systemic infection from the vaccinia virus) and eczema vaccinatum (a widespread skin eruption). During peacetime, clinics could be more rigorous about taking people’s medical histories and screening them for risk factors such as allergies, pregnancy or compromised immunity—which is far more common today than 30 years ago. And people who did react badly to the vaccine would stand a better chance of getting adequate care and medication. If even half the population were vaccinated in advance, everyone would be safer because fewer people would be capable of spreading the infection. And that in itself would make the variola virus a less attractive weapon. “We have proven preventive measures,” says Dr. Bill Bicknell of Boston University’s School of Public Health. “We’ve just spent millions on airport security. We could spend less on smallpox and just take it off the table.”

Here’s the catch, though. We know that smallpox vaccines cause harm. That’s why we shelved them 30 years ago. Smallpox, however scary, is only a theoretical threat, and many experts insist it’s an unlikely one—if only because the risk of “blowback” is so high. In an age of constant travel and low immunity, a large epidemic in any part of the world could quickly spread to others. Lane notes that Iraq hasn’t vaccinated its people in decades and would have a hard time doing so today. “If [Saddam] is at all rational,” he says, “then he knows that the more successful the attack, the more dangerous smallpox will be to him and other countries in the region.” Presumably even suicide bombers and Al Qaeda’s vandals, with their dreams of glorious martyrdom, don’t want to destroy their own cultures. True, a peacetime vaccination effort could save us from a sophisticated nihilist who cares not who he kills. But if we’re that averse to risk, why worry only about smallpox? Should we launch campaigns to vaccinate ourselves against the Marburg virus? asks Dr. Alfred Sommer, dean of the Johns Hopkins School of Public Health. And what about Ebola?

VOLUNTARY BASIS

If someone could quantify the threat of a smallpox attack, this debate would be winnable. We could weigh the vaccine’s hazards against those of an outbreak, and declare one set of hazards more serious. Without that intelligence, it would be hard to justify a peacetime vaccination drive. But nobody is planning one. The new
HHS plan recognizes the need for a well-immunized emergency-response network, but it doesn’t propose a return to compulsory childhood smallpox shots. It simply envisions letting people choose their own risks. “We’d set it up on a voluntary basis,” says Thompson, “and if you wanted it you could have it.” Would the risk be worth taking? Maybe not. But as Bicknell points out, most of us face higher risks every day without thinking twice.

It would be nice, of course, if we could have the immunity without the risk. That may soon be possible. The government is stocking up on vaccinia immune globulin, a medicine that can ease adverse reactions to the smallpox vaccines, and funding research to develop entirely new ways of immunizing people. The most promising of the third-generation vaccines—based on a weakened vaccinia strain known as MVA (Modified Vaccinia Ankara)—is already being used in gene therapy and AIDS-vaccine experiments, and even extremely ill patients seem to tolerate it well. After reconfirming MVA’s safety, says Fauci, researchers will begin testing its efficacy against smallpox. At the least, he says, it may provide a good booster for people vaccinated decades earlier. When scientists devise a vaccine that is as safe as MVA and as effective as Dryvax, perhaps we’ll all take the shot and stop worrying about how to vaccinate the population in 10 days flat. Short of that, no plan can keep us completely immune from danger.

This story was reported by Anne Underwood, Debra Rosenberg, Mary Carmichael, David Noonan, Karen Springer, Karen Breslau, Andrew Murr and Anne Belli Gesalman.

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