



AND HOW PITTSBURGH MAY BECOME THE SAFEST
CITY AROUND WHEN IT COMES TO BIOWEAPONS


BY CHUCK STARESINIC

LESSONS FROM A DARK WINTER

At first, relatively few people heard about what happened during a simulated smallpox outbreak at Andrews Air Force Base in the summer of 2001. And for the most part, those who heard about it were not terribly alarmed. After all, it was just a simulation.

But that was before September 11. That was before weaponized anthrax had wafted out of anybody's mail. Immediately after September 11, the events of those two days at Andrews quickly began to take on ominous, portentous, mythical proportions. Lower Manhattan was still smoldering when Vice President Dick Cheney saw the videotapes himself and requested a briefing on the biowarfare exercise called Dark Winter.

ILLUSTRATION | DAVID POHL



Dark Winter was conducted entirely at a long conference table anchored center stage in the pit of an indoor amphitheater. The space was lit as if for a Broadway play. Several dozen observers who worked in public health or national security watched quietly in the darkness enveloping the stage. At the table sat an assortment of highly placed federal employees and public servants, past and present. The departments and agencies they represented read like a roll call of who might respond to a national crisis: Justice, Defense, State, Health and Human Services, FEMA, CIA, and FBI.

When everyone was assembled, a man in the role of the national security adviser said, "Before we begin this evening, I think it is important that you see what is currently on the local TV station in Oklahoma City. The White House Press Office just sent this over. I am sure this will soon be picked up by the major networks. This was taped from a live broadcast about 15 minutes ago."

All eyes turned to a large screen where a woman, apparently a television newscaster in Oklahoma City, looked into the camera and told the audience about "an outbreak of a mystery sickness." The level of tension in the room rose perceptibly with this video clip, the first of several to show how a biological weapon was unlike anything America had experienced to that point. A heightened sense of reality and urgency began to pervade the meeting as the camera cut to a man with a microphone standing outside a hospital, saying, "Sheila, off the record, doctors suspect that at least five patients at Southwest may have smallpox. Now that's a deadly virus not seen in this country for at least 20 years, so if it proves true, we could have a serious health emergency on our hands."

Former Senator Sam Nunn, presiding over the meeting in the role of the president, announced that one hour earlier, the Centers for Disease Control and Prevention (CDC) confirmed the presence of at least one case of smallpox and perhaps as many as 20 in Oklahoma City. Furthermore, he said, since smallpox no longer exists in nature, it is assumed that this is a deliberate bioterrorist attack. "A large proportion of the world population is now susceptible to smallpox," he said. "If this situation is not handled correctly, we could be facing the beginning of a nationwide or global epidemic."

Then-Governor Frank Keating of Oklahoma, who was at the table, asked for assurances that every one of Oklahoma's 3.5

million residents would receive the smallpox vaccine in the next 72 hours. It was an understandable request, but was there enough vaccine? There were only 12 million doses in a nation of 280 million, and what if smallpox showed up in other states tomorrow? Even if enough vaccine were available, what agency was prepared to conduct mass vaccination at high speed? Vaccination options would be presented for decision shortly, but first, an expert in infectious diseases presented relevant facts about smallpox. (Though the outbreak scenario is fictional, the following facts are not.) The last recorded case on the planet was in 1978. Routine vaccination against smallpox ceased in the United States in 1972, so no one under 30 is vaccinated. Vaccination appears to wear off over time, so many of those vaccinated decades ago may now be susceptible again.

Since being eradicated under a World Health Organization (WHO) program, the official repositories of the smallpox virus have dwindled to two: a Russian lab and the CDC. The reason that smallpox is still a matter of some concern decades after being eradicated can be traced to those frozen stocks of virus.

We now know that, despite signing the Biological Weapons Convention, the Soviet Union surreptitiously engaged in large-scale production of weapons-grade smallpox, employing thousands of scientists and technicians in breeding the most deadly strains of smallpox available to them. The Soviet program was able to produce 20 to 100 tons of smallpox virus each year that could be loaded onto the warheads of specially designed ICBMs. In a war of mutually assured destruction, smallpox-laden missiles would release enormous clouds of aerosolized virus over American cities. The first hints of this became known to American intelligence only in 1989, and despite the shock and outright disbelief of many in the intelligence community, extensive details from former Soviet scientists and a wealth of corroborating evidence has revealed it to be absolutely true.

The Soviet program has since disintegrated. The fates of the smallpox virus and the scientists who produced it are uncertainties. Any scientist interested in starting a smallpox production facility would require little more than \$200,000 worth of basic equipment, a competent colleague or two, and a thimbleful of seed virus long forgotten, tucked away in a freezer for scientific purposes, or spirited away

from the sprawling and neglected remains of the Soviet program.

Because the last case of smallpox in the United States occurred in 1949, very few Americans understand how dreadful the disease is. Smallpox killed an estimated 300 million people in the 20th century alone. It killed more people in Europe than plague. When introduced in the 16th century to what is now Mexico, it killed half of the Aztec population, 12.5 million people.

Infection usually occurs when someone breathes airborne virus. It is believed that a few particles of virus may be enough for the disease to take hold. There are no symptoms until seven to 17 days after infection, when fever and malaise develop, followed by the appearance of a red rash. Lesions appear in the patient's throat and begin leaking microscopic infective particles, which are projected into the air when the patient speaks, coughs, or breathes. Typically, the rash consists of tiny pimples, which quickly grow larger and form heads rigid with pus. They become very painful and disfiguring and can cover the entire body, becoming especially thick at the extremities—the face, inside the mouth, scalp, hands, and feet. Approximately 30 percent of those who contract smallpox will die. Those who recover usually bear terrible scars and may suffer blindness.

In the world of Dark Winter, information was incomplete and evolving, but decisions needed to be made quickly. Even the participants who were veterans of similar exercises run by the Department of Defense felt totally out of their element—they knew little about epidemics or public health. A few hours into the exercise, an update on the status of the epidemic revealed 20 confirmed cases of smallpox in Oklahoma City and another 14 suspected. In addition, there were nine suspected cases in Pennsylvania and seven in Georgia. Hospital workers were failing to show up for work after the rumors of smallpox began. CDC officials were en route to help all three states.

Then, an interruption: "Mr. President, we have a 30-minute video clip you need to see urgently."

On the screen was the familiar logo of the nation's most popular cable television news source displayed beneath an ongoing interview with a scientist billed as an expert on smallpox.

"The problem is, we don't have enough vaccine," he is saying.

"Enough for what... the U.S. population?"

"We don't have sufficient stocks to pro-



FROM LEFT: Tara O'Toole, D.A. Henderson, Thomas Inglesby

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protect the people of Oklahoma, Pennsylvania, and Georgia, much less the entire U.S. population."

"What does that mean?"

"It means this could be a very dark winter in America."

Dark Winter was intended to shock influential people in Washington by showing them a realistic and plausible scenario for which the nation was totally unprepared.

"It succeeded magnificently," says Tara O'Toole, one of the principal designers and organizers of Dark Winter.

O'Toole is a newly appointed professor of medicine at the University of Pittsburgh and the chief executive officer of the new Center for Biosecurity of UPMC. At Dark Winter's "hot wash"—a Washington term for the immediate discussion of first impressions—the participants seemed stunned. O'Toole recalls the deputy secretary of defense saying that for the first three-quarters of the exercise he felt very tentative in his decision making because the issues of biodefense were simply too unfamiliar to him.

Nunn gave testimony in Congress one month after Dark Winter, saying, "During my 24 years on the Senate Armed Services Committee, I've seen scenarios and satellite photos and Pentagon plans for most any category of threat you can imagine. But a biological weapons attack on the United States fits no existing category of security threats. Psychologist Abraham Maslow once wrote: 'When all you have is a hammer, everything starts to look like a nail.' This is not a nail; it's different from other security threats; and to fight it, we need more tools than the ones we've been using."

These are the exact sorts of results O'Toole and her colleagues were aiming for—increased attention to overall preparedness within government and the public health community to deal with not only smallpox but a wide range of agents likely to be used in a biological attack. From her point of view, a

biological attack is much more likely than a nuclear attack. Biological science has advanced so rapidly that it is possible to create highly dangerous agents that resist treatment, and even small subnational groups have the ability to mount such attacks.

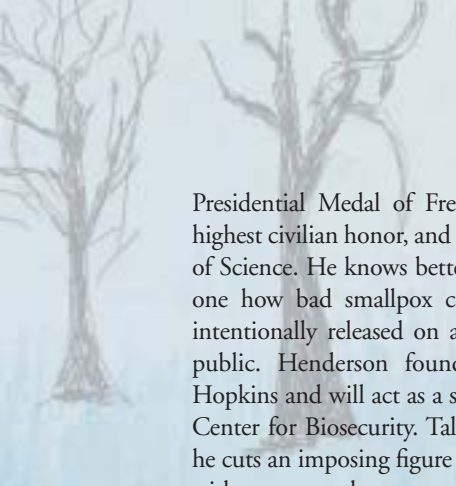
O'Toole is part of a small cadre of health professionals working toward better preparedness, and Dark Winter is just one of many bold steps they've taken in the past five years. The most recent came last September 17, with the announcement of the creation of the Center for Biosecurity of UPMC. That morning, the three leaders of the new center—O'Toole, Thomas Inglesby, and D.A. Henderson—sat down before a roomful of journalists and photographers. They then explained why they were dissolving the premier academic think tank on biological terrorism—the Center for Civilian Biodefense Strategies at Johns Hopkins University, which they had led since 1998. They were creating an organization with much broader capabilities. During the conference, O'Toole pointed out that the entire 20-person staff was making the move from Hopkins to the Center for Biosecurity. Eight, including herself, Inglesby, and Henderson, would have primary faculty appointments in Pitt's School of Medicine and secondary appointments in the Graduate School of Public Health.

It's hard to imagine three individuals whose words and actions have greater impact on the degree to which the United States is prepared for an act of biological terrorism. O'Toole is an occupational medicine physician who rose to director of the Hopkins center. She was formerly the chief safety officer for the nation's nuclear weapons complex.

Inglesby is an internist and an expert in infectious diseases and was the Hopkins center's deputy director. He has authored articles on anthrax, plague, and smallpox as biological weapons, in which he outlines how to manage cases and how the public health system might handle epidemics. Along with O'Toole, he was one of the principal designers of Dark Winter.

Henderson, the elder statesman of the group, is an epidemiologist who started working with the CDC in the 1950s and led WHO's successful global fight to eradicate smallpox. He is a recipient of both the

"The real peril is going to emerge in three to five years, when advances in biotechnology and bioscience are going to make it possible to create even more powerful weapons."



Presidential Medal of Freedom, the nation's highest civilian honor, and the National Medal of Science. He knows better than almost anyone how bad smallpox could be if it were intentionally released on a highly susceptible public. Henderson founded the center at Hopkins and will act as a senior adviser to the Center for Biosecurity. Tall and authoritative, he cuts an imposing figure and speaks at times with a measured sternness, though in conversation, he often reveals a more grandfatherly demeanor. He has tried to bring to a close several times his long career in academia and public service. Henderson was dean of the faculty of the Bloomberg School of Public Health at Hopkins from 1977 to 1990. He was science adviser to the first President Bush. During the Clinton administration, he was in the Department of Health and Human Services. He now serves as the senior science adviser to the Secretary of Health and Human Services and the Office of Public Preparedness.

He recalls the "major meetings" on federal preparedness in the 1990s: "There were no physicians, nobody in public health, nobody from a hospital, nobody from a health department. They were all police, fire, emergency rescue types, arms control people, and so forth. It was profoundly concerning."

Henderson thought that if he raised such issues, leadership would emerge, especially in academia, and he could move on to other things. He was interested in working on vaccines and other measures to combat naturally occurring epidemics in the developing world. When satisfactory leadership failed to emerge, he founded the Center for Civilian Biodefense Strategies at Johns Hopkins. He asked O'Toole to join him. She thought she was taking a temporary part-time job.

There should be at least three such centers around the country, Henderson has always believed. They would be affiliated with hospital systems that would serve as proving grounds for concepts and policies developed in the centers. But that failed to develop. "We had a whole day at Harvard and at the Kennedy School of Government," he said recently. "They came back a few weeks later and said, 'We don't have the expertise. We don't have the leadership.'" Henderson laughed, a bit incredulous, saying, "I thought if anybody could do it, Harvard could."

The decision to create the center at UPMC was made because, as O'Toole puts it, on September 11, 2001, the medical center here "actually started doing things." She cites some for-examples. Presbyterian has

sprinkler systems for chemical agents outside the emergency room. And an emergency room at UPMC St. Margaret is laid out to be able to deal with bioterrorism disasters. O'Toole sees UPMC as "one of the few truly integrated healthcare platform systems in America." She's attracted by its unusual communications capabilities, "like being able to talk to all of the doctors and healthcare personnel in an hour."

The center wants to collaborate with other efforts to make Pittsburgh the safest city around when it comes to biopreparedness, says O'Toole. And the city will serve the center's purposes by becoming "a template that can help the rest of the country become more secure," she says.

"We are going to try and create the model for how you would actually prepare hospitals to deal with a mass casualty situation. We're going to try and figure out how you would take care of people with a contagious disease in large numbers without having to shut down the hospital—as happened in a Toronto teaching hospital with only a few cases of SARS last year. We're going to try to figure out how to do mass immunization for a whole region in a matter of days. In a few years, Pittsburgh and UPMC will be seen as the Mecca for training for disaster preparedness."

The first step to biopreparedness is to imagine bad things happening very vividly and realistically, says O'Toole, adding that not everyone can do so and stay sane. The key is to follow through with the second step—imagine the response just as vividly.

Take Michael Allswede. Bad things happen in his head all the time. Allswede is a former FBI SWAT team member; he looks like a football player in scrubs. These days, he's a member of the FBI's Joint Terrorism Task Force, cochair of UPMC's medical task force on bioterrorism, and a Pitt associate professor of emergency medicine. If you were to walk past Allswede on campus, he might be thinking about a patient in the ER or groceries he should pick up on the way home from work. But there's a significant possibility that he's visualizing a vast cloud of aerosolized anthrax wafting across a major metropolitan area.

To describe how UPMC is prepared to respond to such an incident, Allswede suggests drawing a time line and breaking it into five windows of opportunity, from pre-release to full-blown epidemic. Then lay out a slew of interventions; Allswede would scrawl acronyms in the margins and aim

them at the time line like alphabet arrows, each targeted to a specific window of time.

Some systems are running before a biological agent is even released. A network designed by Allswede allows any local doctor to consult with the strategic medical intelligence unit—a cadre of physicians around the region who are experts in infectious diseases, toxicology, and emergency medicine, all of whom are cleared to work on issues of national security. These volunteers help to determine if a given case might be the result of an attack and whether federal authorities should be called in to investigate further. The FBI endorses the effort, which has been put into play several times, during, for instance, Beaver County's recent hepatitis A outbreak.

But Allswede's world must allow for unlikely heroes and chance occurrences. Imagine, say, a curious Tom Sawyer-type who finds an abandoned, unopened sack of white powder and asks an adult, "What do you think this is?" Pitt researchers have an established relationship with the Allegheny County Health Department's new laboratory, which meets all federal guidelines for handling agents rated Biosafety Level 3 (BSL-3), several of which, like anthrax, are potential weapons. Thus, regional experts could conceivably identify the white powder and diagnose an attack long before symptoms appear. The School of Medicine will have its own BSL-3 lab in 2005 (see sidebar).

Drift back for a moment to the anthrax cloud wafting through Allswede's inner world. We may arrive around the middle of Allswede's time line with no Tom Sawyer, no sirens blaring, only a slight rise in nonspecific flu symptoms and visits to emergency rooms. Even before hospital staff clearly identify the nascent epidemic, two tracking systems kick into gear. Real-time Outbreak Disease Surveillance (RODS), developed here at Pitt, automatically alerts public health officials that local physicians had a busy day yesterday; a sister system lets them know more people than usual bought toilet tissue, aspirin, and other products associated with flu symptoms.

Acting on this red flag, county health department and UPMC physicians decide to engage an online system called the Terrorism Response and Information Center (TRIC). This communications network reveals that about half of 20 regional hospitals are seeing a high number of nonspecific flu symptoms. UPMC South Side has four times the number of anywhere else. Somewhere in that vicinity is the epicenter of the outbreak, where scores of people came into contact with an unknown biological agent sometime in the past several days. TRIC locates individual patients with flu symptoms at regional hospitals



Michael Allswede

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and alerts their physicians to the possibility of a biological weapon being responsible.

The first official diagnosis of anthrax comes when a spinal tap performed on a man with suspected bacterial meningitis yields cloudy fluid heavily populated with anthrax bacteria. The moment the diagnosis is made, new systems can spring into action. The STAT Medevac system of some 15 helicopters begins shifting antibiotics to the hospitals most in need. Ciprofloxacin has been stockpiled in large quantities, along with doxycycline and amoxicillin, which are effective against some strains. Had the agent been highly contagious, as smallpox is, a quarantine facility at UPMC Presbyterian is prepared to take 300 patients—the sort of influx that would shut down most hospitals.

At this point, the region is wrestling with a full-fledged epidemic. With health department, law enforcement, and government officials, physicians will coordinate their activities through an integrated command center supplying voice and video linkages among hospitals.

Where is that command center?

“Can’t say,” says Allswede without missing a beat. Each hospital, including UPMC Presbyterian, has a communications center within it. But all he will reveal about the central command center is that it is somewhere in the vicinity of Presbyterian; the layout is designed so that activity at the central command center will not interfere with the vital work of running the hospital.

When WHO officially declared smallpox eradicated more than 20 years ago, D.A. Henderson began to worry that his many dedicated colleagues who’d participated in the eradication had not received adequate recognition for their accomplishment. The team had managed to bring the estimated 10 to 15 million cases of smallpox occurring annually to zero in just 14 years. So Henderson made and sent, at his own expense, certificates inducting each participant into the “Order of the Bifurcated Needle,” complete with a symbol showing the two-pronged vaccination needle curled into the shape of the magic number: zero.

The journey from the magic number, achieved in 1978, to Dark Winter in 2001 has left Henderson quietly angry. He feels betrayed by both the Soviets who ran the weapons program and by the Department of Defense, which, after learning of the Soviet program, undermined a movement in WHO to destroy all remaining stocks of smallpox in Russia and the United States. The DOD has since created a monkey model of the disease using its frozen stocks and has continued studying smallpox.

The Dark Winter scenario ended after projecting the number of cases six weeks into the outbreak; but participants asked for longer-term projections. O’Toole estimated the darkness would extend well into spring, with 3 million infected, 1 million dead, and no end in sight. In 2001, 12 million doses of vaccine existed, most of which would turn out to be useless because of age and improper storage. After O’Toole and others briefed Cheney on Dark Winter in September 2001, new vaccine was ordered within the week. The United States now has 300 million doses, but that doesn’t mean it will be easy to stop an epidemic. Besides logistical barriers to widespread vaccinations, the vaccine can cause serious complications and even death in rare cases. And already, genetic engineering raises the possibility of vaccine-resistant smallpox.

“The real peril,” says O’Toole, “is going to emerge in three to five years, when advances in biotechnology and bioscience are going to make it possible to create even more powerful weapons.”

Henderson resists dwelling on whether the eradication he oversaw could have somehow been more complete:

“The world has changed. I think we really cannot plan to eradicate any organism now. I think we have to simply realize that we have threats, be they terrorists or mother nature—à la coronavirus [SARS]. We better be able to respond and be ready to defend ourselves. And we’re going to have to be much better prepared than we are right now.” ■

SIDE EFFECTS

Eighteen million federal dollars will support the construction of a School of Medicine laboratory dedicated to basic research into biological agents that terrorists might use—a sobering undertaking with a desirable side effect: Those same biological agents cause thousands of deaths every day in the developing world, so Pitt researchers will be developing treatments and vaccines to respond to an immediate need while they work toward greater national security.

The Regional Biocontainment Laboratory (RBL) was awarded to Pitt in September by the National Institute of Allergy and Infectious Diseases (NIAID). It will occupy an entire floor of the new Biomedical Science Tower 3, and it will be unlike any other lab at the University. Extraordinary safety and security features that exceed federal standards for Biosafety Level 3 will allow Pitt to establish vaccine programs on diseases like anthrax, dengue, West Nile virus, encephalitis viruses, and hemorrhagic viruses. The CDC and NIAID are supporting research on these agents and others because they are the most likely to be weaponized. But as Arthur Levine, the primary investigator on the grant as well as senior vice chancellor for the health sciences and dean of the School of Medicine, notes, these biodefense dollars have the potential to make an enormous contribution to the global fight against these diseases, because these diseases have been largely ignored by another major source of research dollars—the pharmaceutical industry. “Merck and Pfizer, et cetera, can’t get rich selling vaccines in undeveloped countries,” Levine notes wryly. “They can only get sued.”

The RBL is expected to support two or three large Pitt research groups and to lead to multiple strategic new hires. It will be a national resource where vaccines against deadly diseases can be developed and tested before clinical trials. —CS