How contagious pathogens could lead to nuke-level casualties

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Milana Trounce offers a course called Biosecurity and Bioterrorism Response, which aims to get students thinking about how to prevent bioterror and, in the event of a biological attack, what to do about it. Credit: Norbert von der Groeben

(Medical Xpress)—What if nuclear bombs could reproduce? Get your hands on one today, and in a week's time you've got a few dozen. Of course, nukes don't double on their own. But contagious, one-celled pathogens do. Properly packaged as a bioweapon, they could kill as many people as a hydrogen bomb would, or more.

Milana Trounce, MD, a clinical associate professor of emergency medicine, wants to get people to worry about this possibility. For the fourth year in a row, she is presiding over a course called Biosecurity and Bioterrorism Response, which aims to get students thinking about

how to prevent bioterror and, in the event of a biological attack, what to do about it. More than 100 Stanford undergraduate, graduate, postdoctoral and professional students, representing disciplines ranging from public policy to biological science to engineering and bioengineering, have enrolled.

The course, which Trounce considers more of a forum or workshop, brings students together with guest lecturers from Stanford and other universities, as well as with biotech-company executives, think-tank denizens and current and former public-health and other government officials.

"I'm hoping to continue to grow this forum to figure out real-world solutions," she said.

Authorities on bioterrorism and biosecurity say that more thinking about how to handle this threat is desperately needed. Steven Block, PhD, professor of biological sciences and of applied physics at Stanford, is a member of a scientific advisory group that meets several times a year to report to the federal government on national-security issues, including bioterrorism. "The advent of modern molecular genetic technologies is making it increasingly feasible to engineer bioweapons," said Block, who is also the Stanford W. Ascherman Professor of Sciences and a guest lecturer in Trounce's class. "It's making people with even moderate skills able to create threats they couldn't before."

A natural anthrax strain mailed to public officials in a series of homegrown terrorist incidents in late 2001—while deadly—was treatable, Block said. But the technology for making drug-resistant anthrax—or, for that matter, creating all manner of novel "designer diseases"—is becoming increasingly available worldwide, not to mention cheaper and more sophisticated.

Trounce agrees. "We are undergoing a biotechnology revolution," she said. "Even in the last 10 years, science has advanced so much that you can engineer some of the scariest organisms—for example, smallpox."

In laboratory experiments, scientists have mutated H5N1—a deadly influenza strain that so far has been transmitted to humans only by birds—to become transmissible by other humans. They have synthesized the Spanish flu virus, a naturally occurring strain that swept the globe in a 1918 pandemic, killing far more people than died in all the battles of World War I. What if any of those were to get out of the lab?

"Unfortunately, it's a real possibility, because with advances in technology it's now much easier to create these weapons than ever before," Trounce said. "A few people with modern resources can create a bioweapon. This is something we don't typically think about."

Something old, something new

Long before the advent of high-tech laboratories, bioweapons had earned a perch in the annals of infamy. The ancient Romans, like others before them, threw carrion into wells to poison their adversaries' drinking water. In 1347, the Tatars catapulted the bodies of bubonic-plague victims over the defensive walls of the Crimean Black Sea port city now called Feodosia, then a gateway to the Silk Road trade route. That effort apparently succeeded a bit too well. Some of the city's residents escaped in sailing ships that, alas, were infested with rats. The rats carried fleas. The fleas carried Yersinia pestis, the bacterial pathogen responsible for bubonic plague. The escapees docked in various Italian ports, from which the disease spread northward over the next three years. Thus ensued the Black Death, a scourge that wiped out nearly a third of western Europe's population.

In more recent times, the Cold War spurred experimentation in

developing deadly pathogens both in the Soviet Union and the West. The U.S. program was abruptly terminated in 1969 under President Richard Nixon's executive order, and within three years all American stockpiles of biological weapons were destroyed. On April 10, 1972, an international treaty banning such weapons was instituted.

"The United States abandoned offensive bioweapons research," Trounce said. "Unfortunately, the Soviets did not." Despite signing the treaty, the Soviet Union conducted a massive, ultra-secret bioweapons effort that continued through the early 1990s.

Trounce has first-hand experience with the aftermath of that effort. She grew up in the Ukrainian city of Odessa when it was still part of the Soviet Union. She began training in ballet at age 7, eventually dancing as a professional ballerina. Her career ended in 1991, when her family hurriedly exited the crumbling Soviet Union. "We left in December. By January, there was no Soviet Union," she said.

Her family relocated to San Francisco. She earned a bachelor's degree in biology at the University of California-Berkeley in 1997 followed by a medical degree at UC-San Francisco in 2001. In 2004, having completed a residency in emergency medicine at Harvard and begun a fellowship in disaster medicine there, she made a State Department-funded trip to biological weapons facilities in Russia as part of a consortium of scientists, engineers and other physicians. The visit's purpose was to help the State Department find ways of redirecting former bioweapons scientists, whose sponsoring institutions were now losing funding because the country was poor, toward peaceful pursuits. The worry was that these scientists' talents could be bought by bad actors.

At its peak, the Soviets' bioweapons program, called Biopreparat, employed close to 60,000 people at nearly 40 facilities throughout the country. As she examined one of those facilities, which housed

dangerous microorganisms, Trounce said, "It immediately struck me that it was not in good shape. The only barrier to entry was a barbed-wire fence, with nobody at the gate. I saw cats wandering in and out.

"It blew my mind," Trounce continued. "As a Soviet citizen, I had had no idea these facilities even existed. To come as a U.S. citizen and see these facilities where thousands of scientists had been working on the deadliest pathogens was unbelievable. Who knows what I didn't see?"

Did that massive Soviet bioweapons inventory ever get entirely dismantled? "I don't know," says Trounce. "I don't think anybody really does, and if they do it's classified information. What we do know is that there are three Russian Ministry of Defense bioweapons laboratories that remain closed to international examination."

A natural strain of anthrax mailed to public officials in a series of homegrown terrorist incidents, in late 2001, was deadly but treatable, says Steven Block.

In any case, nobody harboring these weapons today would admit it, because it is in defiance of international law. But the fact is that thousands of Soviet scientists at numerous facilities kept producing

offensive bioweapons for 20 years after signing a treaty banning them.

Retired Rear Adm. Ken Bernard, MD, a guest speaker for the course, said that any claims that such programs have been eliminated should be treated with skepticism. "The Soviets completely lied to us before," he said. "Throughout the 1980s, they were producing tons and tons of smallpox and anthrax, even as the U.S. stopped vaccinating for smallpox."

Bernard, whose immersion in government service as a biosecurity official dates back to 1980, was a special assistant on biosecurity matters to presidents Bill Clinton and George W. Bush. In any case, focusing on existing inventories isn't enough, Trounce said. "Somebody can just come out with these things in a short amount of time. You don't have to build a nuclear reactor, which takes years, and procure exotic materials."

If bioweaponry itself is nothing new, there's been a twist on it in the past few decades: A shift from biowarfare to bioterrorism.

"What took hundreds of scientists and huge resources just a few decades ago now can be done within just a few weeks," Trounce said. Moreover, it can be done without the massive footprint characterizing both Cold War bioweapons projects and current nuclear-weapons programs.

A bioweapon is a poor man's nuke. The secrets involved in building one aren't hard to come by, said David Relman, MD, the new co-director of Stanford's Center for International Security Cooperation. "It takes only the skills a good laboratory technician has mastered," said Relman, professor of microbiology and immunology and the Thomas C. and Joan M. Merigan Professor. Former technicians retain the skills they've learned, he noted. "That adds up to a lot of people who know a lot and know their way around labs."

You can say "don't build a nuclear facility" and monitor for compliance. How do you tell someone not to build a biology lab?

Easy to get, easy to make

That gives rise to another, extremely disturbing consideration: Plausible deniability.

It's easy to mask bioweapons research. You can buy equipment such as gene and protein synthesizers over the Internet. "They're the same as what you see in the legitimate biotech industry, so it wouldn't look suspicious," Trounce said. The materials and equipment you'd use are largely ubiquitous laboratory reagents and glassware, as opposed to the hard-to-get raw materials and instrumentation needed for making nuclear weapons. Information on how to configure pathogens' underlying genetic structures is public.

"Smallpox has a 35-40 percent fatality rate and is not as contagious as measles," said Block. "Now imagine an organism as fatal as HIV and as contagious as measles. With modern air travel, a pandemic caused by a pathogen of this sort could take out maybe 90 percent of the people it reached. That would destroy a society."

A high-tech bioweapon could cost only $1 million to build, Block said. "That's thousands of times cheaper than going nuclear. Iran's centrifuges alone cost them billions."

But there's no need to create a brand-new organism from scratch. Lots of potentially suitable pathogens are ready-made, courtesy of Mother Nature. The bacterial pathogens that cause anthrax and botulinum, to name a couple, are found in the wild. Once you have such a biological agent, you can have 10 times as much of it tomorrow, because it grows exponentially. It costs only a few thousand dollars to culture it. You can

store it in a freezer.

"Botulinum toxin is about the most poisonous compound known," said Bernard. "Physicians buy it legally, to inject into people's eyebrows. Who can be sure there's no off-site, illegal production? Suppose a stranger were to say, 'I want 5 grams—here's $500,000'"?

Five grams—1 teaspoon—of botulinum toxin is easily enough to kill hundreds of thousands of people The paralytic toxin, secreted by the bacterial organism Clostridium botulinum, can be countered with an antitoxin, but patient survival may require months of mechanical ventilation on an artificial respirator. In a 2005 study, Lawrence Wein, PhD, the Business School Trust Faculty Fellow and the Jeffrey S. Skoll Professor of Management in the Graduate School of Business, explored the hypothetical effects of dropping botulinum toxin into the milk supply. Milk from myriad farms gets bottlenecked in a relatively small number of large temporary storage vats, and then dispersed to a wide network of retail outlets. Tampering with the country's food supply is surprisingly effective when a foodstuff goes through a production or distribution bottleneck, Wein discovered.

A rendition of anthrax bacteria.

"It's generally possible to know who was behind a nuclear attack, because you can trace material by its composition 'signature,'" said Trounce. "Biological agents are ubiquitous. You could even obtain them within the target country. It may be impossible to figure out who the bad guy is. That's ideal for terrorism."

Progress since 9/11?

There was a big expansion of public-health funding at the federal level in the first five years or so after 9/11, with several concrete payoffs. "We've come a long way to solving the mass-smallpox-scenario problem," Bernard said.

Smallpox—a viral pestilence characterized by high fever, pustules that

spread from the forehead to the feet within two or three days, and the breakdown of multiple bodily organs—killed an estimated 300 million to 500 million people in the 20th century. Smallpox would be very hard for a terrorist to get his hands on, but it does exist in two labs, one in the United States and one in Russia, Bernard said. "In the old days everybody in the United States used to get vaccinated for smallpox. We stopped in the 1970s, except for the military. Everybody under 34 years old—more than half of our population—has never been immunized."

Working in the White House under President George W. Bush, Bernard spearheaded Project Bioshield, a $5.6 billion initiative to hand out grants for pharmaceutical countermeasures. Among the products being developed under the Bioshield aegis are two new antivirals for smallpox and a new vaccine that's safer for immunocompromised people, pregnant women, and people with eczema whose permeable skin makes the traditional live-virus-based vaccine risky.

"We have 20 million doses in the U.S. Strategic National Stockpile, mostly for people who can't take the regular vaccine," said Trounce.

"Like aircraft carriers, anti-bioterror medicinals are by their very nature only going to be sold to one customer—the federal government—and used, perhaps only under duress, during a crisis," Bernard said. "For both ethical and financial reasons, they can't be put through normal clinical trials as medicinals for human use must be. But the Secretary of Health and Human Services could grant initial pre-licensure approval for these products' use in an emergency."

Another federal government project is Biowatch, a $50- to $75-million per year early-warning system for dangerous microorganisms. Germ-monitoring sensors are attached to existing environmental air-quality-sampling platforms in major cities. The system has its drawbacks, though. A few false alarms have been triggered, and it takes a full 24

hours to get results, which could be too late.

Early, accurate diagnosis is crucial, said Relman: "In a lot of cases, people benefit from antimicrobial drugs only if they start taking them within 48 hours—and they've got to be taking the right drug. That's also the hardest time to get an accurate diagnosis, because the earliest phases of many of these diseases are often nonspecific."

But if anything, Relman said, "the situation has gotten worse in the past decade as budgets for the Centers for Disease Control and Prevention and for state and local health facilities have been actually cut. We know we need much greater surge capacity, for example hospitals to take care of respiratory illness. But we haven't invested in it. Public health is dying by attrition."

It's politically tough to justify expenditures for things that haven't happened, Relman added.

"The fact that somebody hasn't used a biological weapon since 2001 doesn't mean it couldn't happen," Bernard said. "No one thought they could fly two airplanes into a tower prior to September 2011. We haven't had a nuke go off since 1945, and nobody's saying that couldn't happen."

Indeed, the United States government has spent trillions of dollars and enormous brainpower investing against nukes. Trounce wants to divert some fraction of those resources to inoculating the country against the arguably more imminent threat of bioterrorism, by coming to terms with the monumentally interdisciplinary, interconnected problems it raises.

"Stanford's unique blend of expertise in medicine, business, and engineering, our public-policy program, and its location in the center of Silicon Valley make this the perfect place to get started," she said.

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