Alumni

Thinking the Unthinkable

Bioterrorism strategist Thomas V. Inglesby: a leader in the research effort against germ warfare.

By
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Fall 2002

Three years ago, at the tender age of 33, Thomas V. Inglesby, M.D. ’92P&S wrote a fictional scenario in which a great American city was attacked by a deadly bioterrorism agent. Inglesby called the city “Northeast” (population two million), and it sounded a lot like Washington, D.C. The bioterrorism agent he chose for the imaginary disaster was a lethal, fast-acting bacterium known as anthrax.

Published in *The CDC Journal of Emerging Infectious Diseases*, Inglesby’s chilling scenario began with a group of terrorists releasing a cloud of anthrax spores from a truck as it sped past a crowded pro football stadium.

Blown into the packed stadium on a cold November wind, the invisible biological agent infected tens of thousands of fans. Within 48 hours, the first desperately ill patients had begun to arrive at area emergency rooms. Soon local hospitals were jammed with dying patients, and the federal government had been brought to a virtual standstill as health officials struggled to understand what had happened.

Written in the present tense, Inglesby’s “Northeast Scenario” has the chilling immediacy of Michael Crichton’s bestselling bio-thriller, *The Andromeda Strain*. As Inglesby described it:

“Approximately 16,000 of the 74,000 fans are infected by the anthrax cloud; another 4,000 in the business and residential districts downwind of the stadium also are infected. After the game, the fans disperse to their homes in the greater Northeast metropolitan area; some return to homes in neighboring states.

“Of the 20,000 persons originally infected in Northeast, 4,000 [will die], most in the first ten days after the attack. . . . No group can be identified as the perpetrator, though the FBI continues one of the largest investigations in its history. Many refuse to return to their homes downwind of the stadium and demand official compensation. Businesses downwind of the stadium are shut down. The stadium is largely abandoned. Newspapers brand the downwind area ‘the dead zone.’ Overall, city commerce suffers tremendous losses. The tourism industry collapses. City officials estimate it will be months or years before the city resumes a normal routine. Fear of anthrax may keep some away from Northeast indefinitely. On December 1, the FBI receives a threat that anthrax will be released in five major U.S. cities over the next week. . . .”

Only 29 months after the publication of Inglesby’s fictional study, Washington found itself reeling beneath an actual anthrax assault—a deadly bioterrorism attack in which five envelopes containing anthrax, or *B. anthracis*, were sent through the U.S. postal system. All of the envelopes were postmarked out of Trenton, New Jersey. The anthrax spores in the envelopes produced 22 cases of the disease and killed five people. Within a few days, federal officials launched a criminal investigation—that has yet to result in an arrest.

Although the anthrax spores arrived in a different form and scale from the one Inglesby had depicted in that story, the fact remains: in a sense, infectious diseases expert Inglesby had predicted the future. Suddenly, medical and public health professionals and government officials in Washington were calling Inglesby and his colleagues, seeking information about the anthrax attacks of October 2001.

A few months later, Inglesby, the deputy director of the nation’s most highly regarded, university-linked bioterrorism research and analysis center, found himself testifying about America’s bioterrorism future before a deeply concerned group of legislators on the Senate Governmental Affairs Committee in Washington. His message, in a single sentence: We have to start building—right now—the enormously complex scientific, medical, and public health infrastructure that will be required to deal with bioterrorism in the years ahead.

“Are we vulnerable? Yes.”

Almost one year after the first-ever bioterrorism attack on America, Pentagon planners and public health officials alike are struggling with a plague of questions they cannot answer.

How long before the next bioterrorism attack on this country? If it does happen, what form will the assault take? Will the next terrorists—whether state-sponsored or international freelancers—attempt to infect millions with the most dreaded of the current biological weapons: smallpox? Has a rogue nation or terrorist group already begun working on a genetically engineered virus (a new form of Ebola, for example) that is both lethal *and* highly contagious?

Ask Inglesby to look into the future for answers, and the 36-year-old, Columbia-trained wunderkind of germ warfare grows understandably cautious.

“It’s not possible to give estimates of the likelihood of future bioterrorist attacks or to say what forms of attack are most likely—though there is much that can be said about the scientific plausibility and potential consequences of bioweapons attacks,” says Inglesby, who is deputy director of the Johns Hopkins University Center for Civilian Biodefense Strategies.

“I don’t believe in the inevitability of another attack, and there are lots of things that can be done to try to prevent them from occurring in the future. So in that sense, I’m encouraged and hopeful. But if you’re asking, ‘Are we vulnerable?’ . . . the answer is yes. There’s no doubt that we’re going to be facing formidable challenges from these weapons of mass lethality, far into the future.”

How do we respond?

It’s a recent Monday morning in Baltimore, and we’re sitting in a conference room on the eighth floor of a Baltimore office high-rise. This is the administrative headquarters of the Johns Hopkins University Center for Civilian Biodefense Strategies, where a cutting-edge team of infectious disease researchers is now working ten to twelve hours each day to protect the nation from the unthinkable.

The author or co-author of more than a dozen scientific papers and articles on the growing bioterrorism threat (including six highly influential “Consensus Statements” on biological weapons that were published in the authoritative *Journal of the*

American Medical Association), Inglesby probably knows as much about the epidemiology and symptomology of anthrax, smallpox, and plague as anybody in America.

Ask him to describe the "bottom line" of his recent research on these weapons of mass destruction, and he doesn't hesitate. "If we do everything that is possible in this country to develop expertise about biological weapons, to make the needed scientific and technological investments and to train our health care professionals to recognize the early signs of an attack, we will substantially improve our ability to react and prevent illnesses and deaths that could follow such attacks.

"Information is power, and information is what we'll need to alert and mobilize public health agencies and the health care system in the event of an attack. Remember: We're probably not going to get a letter that says: 'You've been attacked.' Instead, we'll probably start seeing cases of a particular illness, such as smallpox or anthrax. And the moment that happens— *if* it happens—we have to be able to turn on the system and respond."

Make no mistake, says Inglesby: The challenge ahead will be formidable. Just how formidable can be seen in the disturbing fact that the anthrax murders of October 2001 remain unsolved—nearly a year after they were committed. Ask the Hopkins expert for his opinion on the identity of the bioterrorists involved, and he won't speculate.

"There isn't enough information in the public domain to make that kind of judgment," he says quietly. "There hasn't been a smoking gun regarding the genetics of the strain or its suspected source. I don't think we would feel confident [at the JHU Center] saying it's domestic or international, or whether it was the work of a few individuals or state-sponsored."

Inglesby refuses to guess about the identity of the terrorists involved, except to suggest that the complex operation probably involved the participation of several highly skilled technicians: "It seems improbable that an individual could have managed the project from start to finish—from acquisition and processing of the strain to distribution. I don't say that it's impossible . . . but it does seem unlikely."

Inspired by a professor

How did the soft-spoken and bespectacled Inglesby—a practicing physician who still treats patients at Johns Hopkins Hospital—wind up as a major U.S. expert on the ghastly subject of bioterrorism?

According to the Baltimore researcher, who earned his bachelor's degree at Georgetown University in 1988, the long journey to the Center for Civilian Biodefense Strategies actually began at the Columbia University College of Physicians and Surgeons back in the late 1980s.

"In medical school I was fascinated by infectious diseases," Inglesby recalled in a recent interview. "I had the great fortune of studying under [the late] Dr. Harold Neu, who was an incredible doctor and teacher.

"As a medical student, I was continually amazed at the way Neu connected with his patients. He knew how to translate these different diseases for students—an array of diseases that was mind-boggling in scope. He knew how to give each disease a story, how to make sense out of it. And he was very passionate about all of this. Always upbeat, always optimistic. Then he would take us on rounds at the hospital, where he was consulting on infectious diseases.

"I can't explain it, really, but he had this astonishing ability to connect with the patients. I'd watch him translate a diagnosis into a treatment plan at the patient's bedside. As students, we followed him from the microscope to the classroom to the patient's bedside, treating diseases like TB, meningitis, and pneumonia. He'd stop to talk to the patients, about their symptoms and their families, and where they'd grown up. . . . A lot of us were inspired by that. He transformed our lives as medical students."

Deeply affected by Neu and other Columbia specialists in infectious disease, Inglesby set sail for Baltimore and an internal medicine residency at Johns Hopkins Hospital after earning his Columbia M.D. in 1992. In 1998, while completing his specialty training in infectious diseases at the Johns Hopkins School of Medicine, he chanced to attend a presentation by the legendary Donald A. Henderson, M.D., a Hopkins biological weapons expert who would go on to co-found the university's Center for Civilian Biodefense Strategies later that year. (A key advisor to President George W. Bush on bioterrorism, Henderson is now director of the U.S. Office for Public Health Preparedness.)

The presentation by Henderson changed the shape of Inglesby's career. "As I listened to him explain how biological weapons might be used to cause large outbreaks of infectious diseases, I became highly compelled to better understand the problem," says the Hopkins expert. "I saw the terrible power of these weapons, and it struck me that if I worked hard at it, there might be something I could do about this problem."

John G. Bartlett, M.D., today the chief of infectious diseases at the JHU School of Medicine (and a co-founder of the Center), remembers the moment of Inglesby's "conversion" to bioterrorism medicine very well. "I hired Tom Inglesby right out of our infectious diseases program," says Bartlett, "and I remember how taken he was with Henderson and his powerful message about bioterrorism. Until then, I think he had been targeted for a career in [researching and treating] hepatitis C.

"But I think that one afternoon changed his career. And we were really pleased to get him, because he's incredibly articulate, and a gifted researcher. He works well with people. But he's also very cautious; he doesn't make mistakes. I'll give you an example. One of his first jobs at the Center was to write the guidelines for how to manage anthrax [during the late 1990s].

"Well, he ran a whole panel of researchers, and they published a Consensus Statement in 1999 in JAMA, and if you read that, you'll find that they [the panel] basically wrote the road map [for diagnosis and treatment] that was used by the federal government after the anthrax attacks last year.

"Today anthrax is the bug du jour; everybody's studying it! But Inglesby and his panel laid it all out three years ago, and the CDC guidelines on anthrax all came out of that study he directed."

At Columbia, meanwhile, another world-class bioterrorism expert—Stephen S. Morse, M.D., director of the Center for Public Health Preparedness at the Mailman School of Public Health—echoes Bartlett's assessment of Inglesby's "razor-sharp" analytical skills. "Tom Inglesby has been doing a lot of good, solid, credible work in bioterrorism," says Morse, who recently concluded a four-year stint as the director of a Department of Defense program aimed at protecting the country against epidemics of infectious diseases.

“I have a very high opinion of both Inglesby and the Hopkins program, because they’ve produced some really excellent research—such as those six Consensus Statements on bioterrorism. The information they’re pulling together will be extremely useful in helping the nation to prepare for all kinds of different bioterrorism scenarios.”

Blunting the threat

After more than four years of devising strategies to protect America from biological weapons of almost unimaginable ferocity, Inglesby says he remains optimistic about our chances of avoiding the kind of nightmare scenario he described in “Anthrax: A Possible Case History.”

Meanwhile, he travels back and forth across the country—speaking to scientists, politicians, physicians, and local public health officials about what we must do to reduce the likelihood and potential consequences of bioweapons attacks in the years ahead.

“As a parent myself, I obviously worry deeply about the danger we face from these weapons,” he says. “It’s easy to become alarmed about the power of agents like smallpox and anthrax. On the other hand, analyzing the threat of bioterrorism allows you to focus this energy into developing strategies and systems that will help us lower the threat.

“I can tell you this much: If those of us who work here at the Center believed in the inevitability of bioterrorism, we wouldn’t be doing this for a living. But I think all of us understand that when it comes to defending against weaponry of this kind, knowledge is empowering . . . and the more we learn, the stronger we become.”

Ask Inglesby what we should do to blunt the growing threat from the bioterrorists, and he rattles off the same answers he gave to the U.S. Senate Committee on Governmental Affairs last April:

First, we must “strengthen the connections” between public health agencies and medicine in this country. We need better communication between doctors and nurses and public health officials, so that they can trade information more effectively in the event of large-scale outbreaks.

Second, clinicians in local communities must “develop systems to more quickly communicate key information” within their own medical organizations and professional societies. An example of such a system: In recent months, physicians in and around the nation’s capital have established conference calls and regular meetings to share information about the latest developments stemming from the anthrax crisis of last October and other bio-preparedness efforts.

Third, the CDC and other public health agencies must build processes to rapidly address the type of unique scientific problems that will follow bioterrorist attacks—such as the questions regarding who should have received the anthrax vaccine last fall.

Fourth, we need better systems for communicating rapidly and clearly with the U.S. public. Says Inglesby: “The importance of communicating comprehensive, current information to the public in the aftermath of such an attack cannot be overemphasized.”

Fifth, we should plan and conduct bioterrorism drills and exercises, which will help to develop the “new relationships and lines of communication” that will be required during any bioterrorism incident.

And finally, says Inglesby, we should work on the specific medical interventions needed to protect ourselves in the aftermath of an attack. We need an ambitious and sustained biomedical research and development program aimed at “preventing, diagnosing and treating the range of infectious diseases that exist now and those that will be engineered in the future. And we need the engagement of the scientific community in the developing of systems and organizations that prevent the research and development of biological weapons in the first place.”

Calm and thoughtful and endlessly upbeat, Inglesby was nonetheless careful to leave the members of the Senate Committee with a stark warning.

“The anthrax attacks of [last] fall were just the prologue to the bigger story of bioweapons,” he told the senators last April. “In the years ahead, the biotechnology used to create bioweapons will become far more powerful, more available and less expensive. Engineering, computing, and the capital markets will push biology forward on a rapid trajectory. . . .

“Already present and widely distributed on the planet are examples of biological knowledge that are disturbing: the methods for making new influenza strains never before seen on earth; the directions for making Ebola virus from non-living fragments of genetic material; the techniques to make anthrax or plague resistant to many or even all available antibiotics; attempts to combine a set of genes from viruses that cannot spread to viruses that can. Biological aerosols that might once have harmlessly floated away can be stabilized in the environment and altered to become more easily inhaled.

“The long-term threat is certainly grave. It is therefore critical to take a dispassionate look at how we have prepared for bioterrorism and what now should be done. In the end, the measure of success is whether our scientific, medical, and public health and other key government institutions are preparing to address not only more anthrax attacks, but the future of bioweapons as well.”

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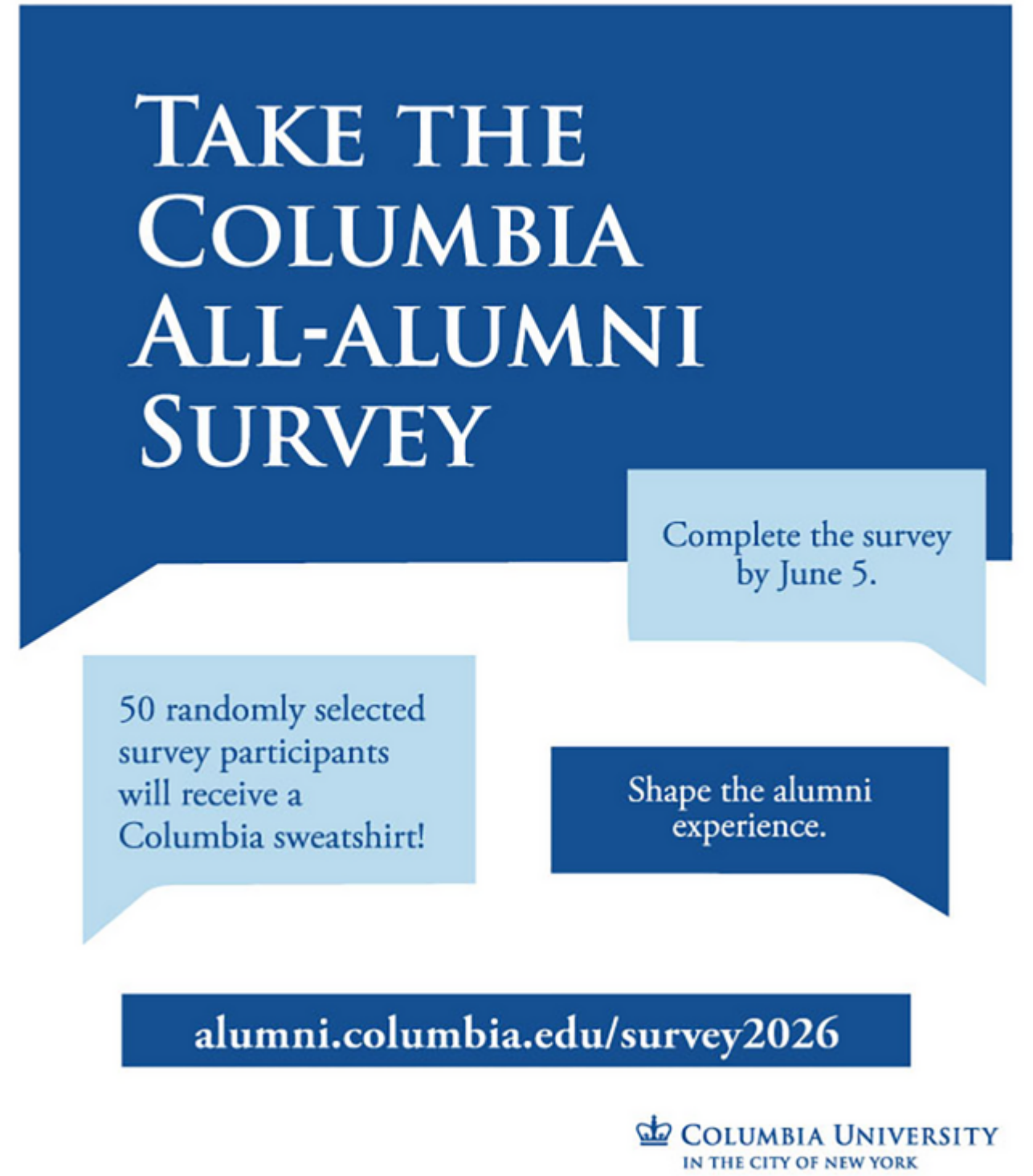

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