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BW Threat: Some Practical Considerations

The threat from biological weapons (BW) is "not in our past . . . we are living with [them] around us, and a lot of countries have the knowledge, desire, and capability" to make and use them, warns Ken Alibek, a defector from the former Soviet Union, where he did research to develop such weapons. "What concerns me is a sophisticated terrorist bringing in a powder to use in a closed system like a building or subway," adds William Patrick of BioThreats Assessment Inc. in Frederick, Md., and a former participant in the U.S. BW program at Fort Detrick, also in Frederick.

Alibek, Patrick, and several other experts described a number of such threats and defensive countermeasures during a two-day conference, "Automation in Threat Reduction and Infectious Disease Research: Needs and New Directions," held at the National Academy of Sciences (NAS) in Washington, D.C., late in April. Despite minor disagreements over various technical issues, they and others who have been or are involved in U.S. BW defense programs (and, before it was banned by President Nixon, in weapons development) described surprising parallels in these national programs.

According to Alibek, imperfect solutions to such challenges are sometimes enough to make adequately deadly BW devices. "Liquid forms are not very effective for dispersion, but you can't say they are not at all effective," he says. For instance, BW designers in the Soviet Union decided that, for certain pathogens such as *Bacillus anthracis*, relatively large particle sizes may be less than ideal but are good enough for the task of harming enemy forces. Thus, use of such larger particles in weapons would likely not produce pneumonia, but would cause upper respiratory and neck infections, he explains. "The perfect size is 1-10 m m, but 10-25 m m works and is effective enough to infect people."

"Biological weapons are weapons of mass casualties, and that's not the same as mass destruction," says Gerald Parker of the U.S. Army Medical Research Institute of Infectious Diseases in Frederick, Md. A major challenge is "to diagnose before there are clinical signs," he says. "Diagnostics are a real priority. It is an extremely complex problem, and we need integrated systems of tests."

Piecemeal efforts are under way to develop such systems, according to several other NAS conference participants. For instance, high-throughput fluorescent particle analysis using flow cytometry is one technology that offers considerable promise for rapidly identifying microbial species, including pathogens that might be used for BW purposes, and toxic materials derived from such pathogens, according to James Jett of the Los Alamos National Laboratory in Los Alamos, N.M.

One application of flow cytometry entails use of fluorescent dyes to identify DNA signatures of specific bacteria, Jett says. Another involves use of arrays of microspheres, each having coatings for detecting specific toxins. For example, one such microsphere-based system is capable of detecting 0.1 nanomoles of cholera toxin following several minutes of incubation. He envisions a BW detection system being developed and consisting of "multiplex bead sets, each carrying individual tests."

The Defense Advanced Research Projects Agency (DARPA) is sponsoring several research projects that involve development of early BW detection and warning systems, according to Stephen Morse. "A BW incident could quickly overwhelm our ability to analyze, so we will need to triage," he says. "If we could make some of these agents less threatening, we may be able to undermine the ability of someone to cause terror by using them."

Approaches run a gamut from the simple and quick to the futuristic and fanciful. For instance, toward the latter end is an effort to determine DNA sequences of single molecules as they pass through specially designed pores, according to Morse. Toward the other end of that spectrum, researchers involved in another DARPA-sponsored project are studying whether exhaled nitrous oxide (NO), which rises in response to infectious agents, can provide a reliable early warning of battlefield exposure to BW attacks. Yet another strategy is to look at shifting expression of suites of human genes that may signal early responses to infectious agents.

In addition to such sophisticated gene-based analyses, Thomas Marr of Genomica Corp. in Boulder, Colo., advocates protein-based functional analyses as another means for monitoring infectious agents that may be used in BW attacks. Because such agents trigger "characteristic responses" in infected individuals, profiling changes in proteins in fluids such as blood or urine might provide a means for monitoring for signs of an attack. "We're just getting started" on developing the data needed for such efforts, he says.

To reach such goals, it will be helpful if not essential to further miniaturize many of the analytic instruments and tools now being used, according to J. Michael Ramsey of the Oak Ridge National Laboratory in Oak Ridge, Tenn. Part of this goal could be met by building "a research lab on a chip," he says.

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