



# nature biotechnology

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## Why biodefense won't work

Anthrax outbreaks last month confirm our worst fears about the susceptibility of civilian populations to bioterrorism and the difficulties faced by public health and medical authorities in detecting and responding swiftly to biological attacks. They have also demonstrated the inadequacy and poor organization of US programs to counter bioterrorism. The US Defense Advanced Research Projects Agency and the Department of Defense together spent a paltry \$3.5 per American last year on biological defense (compared with a total defense budget of \$10,526 per citizen). In short, US preparedness for biological attack—along with that in most nations—has been plain sloppy, based on a misconception that the unthinkable is improbable.

Belatedly, the US administration has tried to give the appearance of being on top of the problem. Last month, President Bush announced \$1.5 billion in extra funding to fight bioterror. Tommy Thompson, the US health and human services secretary, stepped up efforts to enlist biotechnology companies in a drive to develop diagnostics, drugs, and vaccines against bioweapons. If these measures result in replenished stocks of vaccines and antibiotics, progress will indeed have been made. But no one should be fooled into thinking that any amount of investment in biodefense research will protect us in the long term against biological terrorism.

The basic problem is that determined bioterrorists backed by regimes with some rudimentary capacity in biological production have an enormous range of poisons and plagues at their disposal. Humans and their domesticated species are prey to hundreds of infectious agents. *Bacillus anthracis* is, in fact, a rather poor biological weapon, merely a gesture of ill intent that requires huge logistical backing before it could ever threaten widespread harm. Bacterial toxins such as ricin, aflatoxin, and botulin similarly might have potential but only in localized attacks. Much more damaging to a nation would be agents that spread readily from person to person: pneumonic plague, tularemia (caused by one of the most infectious bacteria known, *Francisella tularensis*), smallpox, or hemorrhagic viruses (e.g., Marburg and Ebola). To inflict economic damage, the most effective approach would probably be to introduce animal and plant diseases or pests into the biologically naïve livestock and crops.

"Weaponized" agents might extend the terrorists' biological arsenal still further. New pathogenic organisms created using genetic tools could some day be honed or designed as stealth weapons programmed with switches that trigger replication/toxin production in response to an environmental chemical (e.g., an antibiotic in drinking water). None of this, though, is in the realms of technological likelihood. Armed with the best that molecular biology can provide, researchers are just starting to understand some of the functions that make pathogens pathogenic. That is a long way from being able to create pathogenesis afresh, or to increase it.

But it is not necessary to fall back on arguments about technical capability and biological understanding in order to be skeptical about extended spending on bioterrorism research. The simple fact is that biological defenses will nearly always be defeated by biology. They are options of last resort. It might sound like a good idea to develop vaccines against all known pathogens, but delivering them to the general population—and to the livestock—is logistically impossible and entrains its own considerable risk (some army veterans with Gulf War Syndrome believe they can attest to that). It might be possible to develop better antibiotics, but every antibiotic implies antibiotic resistance, and antibiotic resistance is a pathogenicity component. No country, no matter how powerful and technically advanced, can defend against evolution.

So what is to be done? First, there must be deterrence. This can be achieved by rescuing the biological and toxin weapon convention (BTWC) from obscurity. Even though it's weak, it's the best thing we've got. Random inspections—one of the main reasons why President Bush rejected the convention in the summer (presumably due to threats to US company trade secrets)—is the one way we can check whether countries are keeping their promises, and if they're not, stop them before they go too far. It was UN inspectors who stumbled upon telltale signs of bioweapon activity in Iraq. The UN should do this in every country under the verification regime. At the same time, countries that refuse to sign on to the treaty should be subject to extreme and frequent scrutiny.

Second, accessibility to, and security of, "hazardous" biological materials needs tightening. Bacterial and viral strains are relatively easy to obtain from scientists or culture repositories. There have been several instances in recent years in which fringe groups have attempted to obtain highly pathogenic organisms in this manner.

And third, technology transfer of dual-purpose technologies to suspect groups or regimes must be prohibited. There should be penalties for companies that sell these technologies to countries that have not signed on to the BTWC. Cuba has allegedly transferred recombinant technology to Iran, and companies in the United States, Europe, and former USSR provided many of the materials used by Iraq in its biowarfare program.

Bioterrorism defenses can never anticipate all eventualities. Indeed, defense systems in general are rather inept at predicting the most likely scenarios: those who favored missile shields feared rational attacks from rogue states, not random acts of calculated savagery from a hidden insidious enemy.

Biology in the hands of terrorists is no more predictable or rational. While biodefense research should continue (after all, there is much to be gained in public health and general medicine from understanding the mechanisms of infectivity and the spread of disease), no one should be under any illusion that such spending will help prevent further instances of bioterrorism or its impacts.