

Bioterrorism: A Brief History

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Throughout history, warriors have sought to devise more effective means of mass destruction. Biological weapons have been of interest for centuries and have been utilized in numerous battles. State-sponsored programs have intensively researched optimal organisms and techniques for their dissemination. Recent advances in molecular biology have allowed successful manipulation of bacteria and viruses to provide resistance to conventional treatments. Large stockpiles of such altered bioweapons now exist and are available for terrorist use.

What is bioterrorism? As defined by the Centers for Disease Control, it is the “intentional or threatened use of bacteria, fungi, or toxins from living organisms to produce death or disease in humans, animals, and plants,” and involves “intimidation of nations or people to accomplish political or social ends.”^[1] While common use of the term bioterrorism may include biological, nuclear, and chemical agents, this review will focus primarily on use of biologic agents.

The genesis of bioterrorism lies in the history of biowarfare, which spans eight centuries.

Exploiting nature

Over many centuries, efforts to conquer adversaries have largely relied on stabbing and explosive weapons. In the 6th century BCE, warriors began to supplement these tools with biological agents that could incapacitate and kill their enemies.

One of the first recorded incidents was in Mesopotamia, by the city-state Assyria [see map, below left]. The Assyrians employed rye ergot, an element of the fungus *Claviceps purpurea*, which contains mycotoxins.^[2-3] Rye ergot was used by Assyria to poison the wells of their enemies, with limited success. Hellebore, a plant with powerful purgative and cardiac glycoside effects, was also used by the Greeks to poison the water supply during their siege of the city of Krissa.^[2-3]



Mesopotamia, 2700 years ago

Further advances in delivery of bioweapons occurred in the 14th century when catapults were used as delivery systems. The Tartars, for example, used catapults to hurl cadavers of plague victims into the city of Kaffa, a port on the Black Sea. The tactic proved instrumental in their victory, but had the unwanted effect of spawning a second wave of the Black Death in Europe when survivors from the siege returned to Italy. Similar techniques were used by the Russians, in the siege of the Swedish city of Reval in 1710.^[1,4]



Biologic warfare was also utilized in the New World against indigenous populations. Sir Jeffrey Amherst, seeking to gain an advantage over the French in the French and Indian War, sent his soldiers out to retrieve blankets and handkerchiefs from infantrymen stricken with smallpox. These fomites were later sold to Native Americans aligned with the French, with catastrophic results. Similar techniques were used in the 16th century by Francisco Pizarro in his campaign against the native population of modern-day Peru.^[1-2, 4]

The century of biowarfare

With the coming of World War I, covert efforts were sought to break the standoff between Allied and German forces. One strategy involved German forces in the United States secretly targeting American livestock bound for Europe with glanders and anthrax. While this attack resulted in the death of thousands of horses, it did not have a significant impact on the success of American forces.

Direct assaults with chemical agents such as nitrogen mustard, phosgene, and chlorine gas were much more effective, inflicting morbidity and mortality on hundreds of thousands of troops during the war [photo, right]. As a result, the Geneva Protocol was signed by thirty-eight countries in 1925, prohibiting the use, but not research or production, of chemical and biological weapons.^[4]



WWI gas masks

World War II brought another resurgence of interest in bioweapons. The Japanese were perhaps foremost in the use of biologic weapons during this period, and their prisoners held in Manchuria were targeted by Unit 731, a biological division of the Japanese Army. Several agents, including anthrax, cholera, plague, and typhoid, were tested on their Chinese prisoners, killing thousands.

However, because the Japanese were unable to design effective techniques for dissemination of such materials on the battlefield, these activities did not benefit their war efforts.^[4] Interestingly, Adolf Hitler withheld the use of bioweapons from the German arsenal, due to his personal injury in World War I by a gas attack from British forces.^[5]

American and Soviet programs in biological warfare began in the 1940s, using similar techniques but having very different objectives.

The epicenter of American research was established at Fort Detrick, Maryland, with research facilities in Dugway, Utah, and production facilities in Pine Bluff, Arkansas. American scientists investigated a number of agents, developing a preference for *Francisella tularensis* because of its malleability. Central tenets of the American program were that the agents should incapacitate (as opposed to kill) the enemy, and that a cure and/or prophylaxis (vaccine) must be available against them.^[4,6]

Soviet research originated on the banks of the Aral Sea in Central Asia. At this and many other facilities, attention was directed toward lethal agents such as plague, Marburg virus, smallpox, and anthrax. The objective of research was to create organisms that would result in as many casualties as possible, without concerns for vaccination or treatment for Soviet troops or citizens.

The Soviets also employed a highly successful spy program against the United States, infiltrating American labs and testing activities in the South Pacific, gathering samples to allow for identification and creation of treatments or vaccinations against these new agents.^[4,6]

Efforts toward control

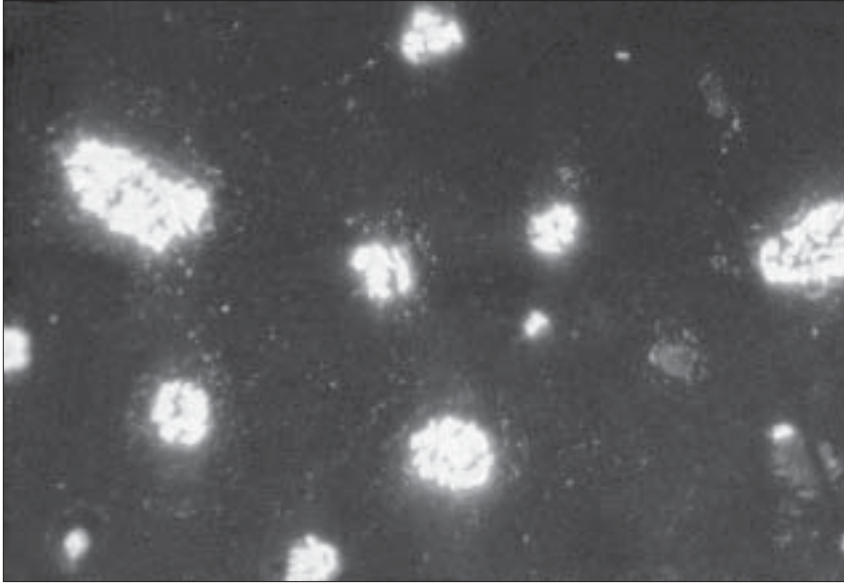
In 1969, President Richard Nixon sought to end proliferation of biological weapons, signing an executive order prohibiting any use of biological agents under any circumstances. Broader efforts followed in 1972 with the Biological Weapons Convention (BWC), signed by many members of the United Nations (including the US, the USSR, and Iraq) to prohibit “the development, production, and stockpiling of chemical and bacteriological (biological) weapons.”^[7-8] Nevertheless, the Soviet Union felt the BWC was meaningless and in the 1970s embarked on a much broader program that involved over 60,000 individuals.^[6]

Biopreparat, the civilian arm of the Soviet bioweapons program, focused its efforts on the development of mixed agents, combining multiple viruses in one novel genome (the Hunter Project) and developing bacteria resistant to all known antibiotics and vaccines (Project Bonfire). The inclusion of viruses inside

bacteria to form so-called “superbugs” was also a focus, according to Sergei Popov, a former senior Soviet scientist.^[6] The official activity of Biopreparat significantly decreased with the collapse of the Soviet Union in 1991, although continued research likely continued until the late 1990s. Moreover, the whereabouts of many of its scientists and their products are unknown.^[4,6]

Bioterrorism

With the fall of state-supported use of biological agents, small factions and cults have begun to advance their own interests with bioweapons. Several characteristics of bioweapons make them advantageous to the terrorist. They are easy to obtain and inexpensive to produce, compared to nuclear and chemical weapons. Agents may be disseminated over a large geographic area, affecting thousands of individuals



Salmonella

with a small amount of compound. Moreover, the unusual occurrence of diseases produced by bioweapons and the number of casualties may overwhelm medical services, creating panic among those under attack.^[1]

Several efforts have been made to use bioweapons in this country since in 1984. The first identified attack of bioterrorism in the US was in 1984, when the followers of Bagwan Shree Rajneesh contaminated salad bars in Oregon. Their efforts resulted in 751 cases of Salmonella [photo, above] infection from 10 restaurants, in hopes of swaying the outcome of local elections in their favor. The perpetrators were eventually caught and prosecuted.^[1,4]

Another attack by the fatalist cult Aum Shinrikyo in Japan caused concern worldwide. Cult members released sarin, a neurotoxin, in the Tokyo subway system in March 1995. This resulted in thousands of injured civilians, but only eight deaths, and highlighted the potential impact of dissemination of a small amount of bioweapon in public areas. It should be noted that several attempts had previously been made by this cult to release toxins (including anthrax) in Tokyo without success.^[4]

In 1996, laboratory workers at a large medical center in Dallas, Texas, received an email inviting them to come to their break room to partake of muffins and donuts. Twelve individuals later developed severe diarrhea, eight of whom tested positive for *Shigella dysenteriae* type 2. Further analysis revealed that this was a strain used in this lab and one of the lab employees was later identified as the person responsible for the attack.^[1]

Anthrax [photo, opposite page] has been used as both a threat and a weapon against targets in the United States. Hoaxes have occurred in several locations, including Washington, D.C. in 1997 and Los Angeles in 1998. An actual release of anthrax occurred in October 2001, utilizing the postal service for

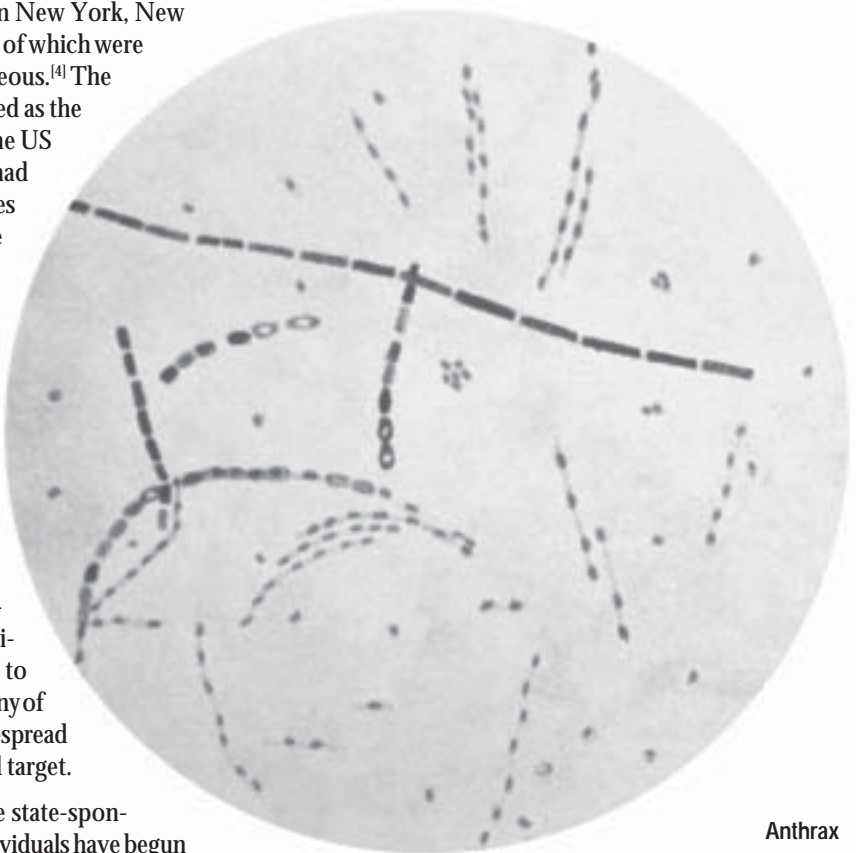
delivery. A total of 18 cases were identified in New York, New Jersey, Florida, and Washington, D.C., eleven of which were inhalational and seven of which were cutaneous.^[4] The source of the anthrax strain has been identified as the AMES strain, a form initially developed by the US bioweapons program at Fort Detrick. It had previously been disseminated to 20 laboratories in the United States, four of which have the capability to weaponize anthrax. Characteristics of the attacks suggest the anthrax was produced by an individual who is American and is skilled in working with this hazardous pathogen, with or without support of foreign terrorists.^[8] The exact source of the attacks is still unknown.

Coming full circle

Biowarfare has been of interest for at least eight centuries as an adjunct to conventional methods of warfare. Techniques for dissemination of agents have been revised, and modifications of existing organisms employed, to enhance the desired effect on enemy forces. Many of these organisms have been noted to cause widespread epidemics of disease apart from the intended target.

Even as nations have worked to dismantle state-sponsored biowarfare programs, small cults and individuals have begun to use these agents to achieve their own ends.

It is mandatory that nations, including the United States, work together to completely destroy existing stockpiles of highly resistant bioengineered agents, as well as preventing further dissemination of bioweapons to terrorists. ☒



Anthrax

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