

HISTORY OF BIOLOGICAL WARFARE AND CURRENT THREAT

The use of biological weapons in warfare has been recorded throughout history. Two of the earliest reported uses occurred in the 6th century BC, with the Assyrians poisoning enemy wells with rye ergot, and Solon's use of the purgative herb hellebore during the siege of Krissa. In 1346, plague broke out in the Tartar army during its siege of Kaffa (at present day Feodosia in Crimea). The attackers hurled the corpses of plague victims over the city walls; the plague epidemic that followed forced the defenders to surrender, and some infected people who left Kaffa may have started the Black Death pandemic, which spread throughout Europe. Russian troops may have used the same tactic against Sweden in 1710.

On several occasions, smallpox was used as a biological weapon. Pizarro is said to have presented South American natives with variola-contaminated clothing in the 15th century, and the English did the same when Sir Jeffery Amherst provided Indians loyal to the French with smallpox-laden blankets during the French and Indian War of 1754 to 1767. Native Americans defending Fort Carillon sustained epidemic casualties which directly contributed to the loss of the fort to the English.

In the 20th century, there is evidence that during World War I, German agents inoculated horses and cattle with glanders in the U.S. before the animals were shipped to France. In 1937, Japan started an ambitious biological warfare program, located 40 miles south of Harbin, Manchuria, in a laboratory complex code-named "Unit 731". Studies directed by Japanese General Ishii continued there until 1945, when the complex was burned. A post World War II investigation revealed that the Japanese researched numerous organisms and used prisoners of war as research subjects. Slightly less than 1,000 human autopsies apparently were carried out at Unit 731, mostly on victims exposed to aerosolized anthrax. Many more prisoners and Chinese nationals may have died in this facility - some have estimated up to 3,000 human deaths. Following reported overflights by Japanese planes suspected of dropping plague-infected fleas, a plague epidemic ensued in China and Manchuria. By 1945, the Japanese program had stockpiled 400 kilograms of anthrax to be used in a specially designed fragmentation bomb.

In 1943, the United States began research into the use of biological agents for offensive purposes. This work was started, interestingly enough, in response to a perceived German biological warfare (BW) threat as opposed to a Japanese one. The United States conducted this research at Camp Detrick (now Fort Detrick), which was a small National Guard airfield prior to that time, and produced agents at other sites until 1969, when President Nixon stopped all offensive biological and toxin weapon research and production by executive order. Between May 1971 and May 1972, all stockpiles of biological agents and munitions from the now defunct U.S. program were destroyed in the presence of monitors representing the United States Department of Agriculture, the Department of Health, Education, and Welfare, and the states of Arkansas, Colorado,

and Maryland. Included among the destroyed agents were *Bacillus anthracis*, botulinum toxin, *Francisella tularensis*, *Coxiella burnetii*, Venezuelan equine encephalitis virus, *Brucella suis*, and Staphylococcal enterotoxin B. The United States began a medical defensive program in 1953 that continues today at USAMRIID. In 1972, the United States, UK, and USSR signed the Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction, commonly called the Biological Weapons Convention. Over 140 countries have since added their ratification. This treaty prohibits the stockpiling of biological agents for offensive military purposes, and also forbids research into such offensive employment of biological agents. However, despite this historic agreement among nations, biological warfare research continued to flourish in many countries hostile to the United States. Moreover, there have been several cases of suspected or actual use of biological weapons. Among the most notorious of these were the “yellow rain” incidents in Southeast Asia, the use of ricin as an assassination weapon in London in 1978, and the accidental release of anthrax spores at Sverdlovsk in 1979.

In 1978, a Bulgarian exile named Georgi Markov was attacked in London with a device disguised as an umbrella. The device injected a tiny pellet filled with ricin toxin into the subcutaneous tissue of his leg while he was waiting for a bus. He died several days later. On autopsy, the tiny pellet was found and determined to contain the toxin. It was later revealed that the Bulgarian secret service carried out the assassination, and the technology to commit the crime was supplied by the former Soviet Union. In April, 1979, an incident occurred in Sverdlovsk (now Yekaterinburg) in the former Soviet Union which appeared to be an accidental aerosol release of *Bacillus anthracis* spores from a Soviet Military microbiology facility: Compound 19. Residents living downwind from this compound developed high fever and difficulty breathing, and a large number died. The Soviet Ministry of Health blamed the deaths on the consumption of contaminated meat, and for years controversy raged in the press over the actual cause of the outbreak. All evidence available to the United States government indicated a massive release of aerosolized *B. anthracis* spores. In the summer of 1992, U.S. intelligence officials were proven correct when the new Russian President, Boris Yeltsin, acknowledged that the Sverdlovsk incident was in fact related to military developments at the microbiology facility. In 1994, Meselson and colleagues published an in-depth analysis of the Sverdlovsk incident (*Science* 266:1202-1208). They documented that all of the cases from 1979 occurred within a narrow zone extending 4 kilometers downwind in a southerly direction from Compound 19. There were 66 fatalities of the 77 patients identified.

In August, 1991, the United Nations carried out its first inspection of Iraq’s biological warfare capabilities in the aftermath of the Gulf War. On August 2, 1991, representatives of the Iraqi government announced to leaders of United Nations Special Commission Team 7 that they had conducted research into the offensive use of *Bacillus anthracis*, botulinum toxins, and *Clostridium perfringens* (presumably one of its toxins). This open admission of biological weapons research verified many of the concerns of

the U.S. intelligence community. Iraq had extensive and redundant research facilities at Salman Pak and other sites, many of which were destroyed during the war. In 1995, further information on Iraq's offensive program was made available to United Nations inspectors. Iraq conducted research and development work on anthrax, botulinum toxins, *Clostridium perfringens*, aflatoxins, wheat cover smut, and ricin. Field trials were conducted with *Bacillus subtilis* (a simulant for anthrax), botulinum toxin, and aflatoxin. Biological agents were tested in various delivery systems, including rockets, aerial bombs, and spray tanks. In December 1990, the Iraqis filled 100 R400 bombs with botulinum toxin, 50 with anthrax, and 16 with aflatoxin. In addition, 13 Al Hussein (SCUD) warheads were filled with botulinum toxin, 10 with anthrax, and 2 with aflatoxin. These weapons were deployed in January 1991 to four locations. In all, Iraq produced 19,000 liters of concentrated botulinum toxin (nearly 10,000 liters filled into munitions), 8,500 liters of concentrated anthrax (6,500 liters filled into munitions) and 2,200 liters of aflatoxin (1,580 liters filled into munitions).

Finally, there is an increasing amount of concern over the possibility of the terrorist use of biological agents to threaten either military or civilian populations. There have been cases of extremist groups trying to obtain microorganisms that could be used as biological weapons. The 1995 sarin nerve agent attack in the Tokyo subway system raised awareness that terrorist organizations could potentially acquire or develop WMD's for use against civilian populations. Subsequent investigations revealed the organization had attempted to release botulinum toxins and anthrax on several occasions.

The threat of biological weapons being used against U.S. military forces and civilians is broader and more likely in various geographic scenarios than at any point in our history. Therefore, awareness of this potential threat and education of our leaders, medical care providers, public health officials, and law enforcement personnel on how to combat it are crucial.

REFERENCES

1. BNICE Program, DHMC, www.bnice.org
2. ACP Bioterrorism Resource Guide, www.acponline/bioterror
3. Bioterrorism related anthrax and interim guidelines for exposure management & control, MMWR, 2001;50:909-19
4. Recommendations for using smallpox vaccine in a pre-event vaccination program, MMWR, 2003;52:Suppl. RR-7

Specific Agents

Anthrax

Exposure: inhalation, contact

Incubation: inhalation, 1-6 days
contact, 1-12 days

Clinical: inhalation- mediastinitis, pneumonia
Contact- ulceration

Person to person: cutaneous only

Treatment: doxycycline, ciprofloxacin
vaccine available

Plague

Exposure: inhalation, contact

Incubation: inhalation- 2-3 days
Flea/tick- 2-8 days

Clinical: pneumonia, bubo

Person to person: yes-pneumonic form

Treatment: streptomycin, doxycycline, chloramphenicol

Tularemia

Exposure: inhalation, tick, direct contact

Incubation: inhalation- 2-3 days
cutaneous- 1-14 days

Clinical: Inhalation- pneumonia
Skin- ulcer, regional lymphadenopathy

Person to person: pneumonia- none
Skin- direct contact

Treatment: ciprofloxacin, doxycycline

Q fever

Exposure: inhalation

Incubation: 14-39 days

Clinical: pneumonia

Person to person: none

Treatment: doxycycline, ciprofloxacin, TMP/SMX

Brucella

Exposure: inhalation, cutaneous

Incubation: 2-3 weeks

Clinical: flu like- myalgias, fever, lymphadenopathy

Person to person: none

Treatment: doxycycline, TMP/SMX

Smallpox

Exposure: inhalation

Incubation: 7-17 days

Clinical: fever, vesicular/pustular rash

Person to person: yes

Treatment: Supportive, immunization of contacts

Viral Hemorrhagic Fever(Ebola, Marburg)

Exposure: inhalation, body fluid contact

Incubation: 4-16 days

Clinical: fever, myalgias, rash, prostration

Person to person: yes

Treatment: Supportive

Botulism

Exposure: ingested

Incubation: 12-36 hours(up to 8 days)

Clinical: bulbar and descending paralysis

Person to person: none

Treatment: supportive, antitoxin

Ricin

Exposure: inhalation, ingestion, injection

Incubation: inhalation- 4-8 hours

Ingestion- 1-2 days

Clinical: inhalation- fever, chest tightness, cough

Ingestion- nausea, vomiting, bloody diarrhea

Person to person: none

Treatment; supportive-almost uniformly fatal