Bioterrorism is defined by the U.S. Centers for Disease Control and Prevention (CDC) as “the deliberate release of viruses, bacteria, or other germs used to cause death in people, animals, or plants.” Although it is not a new phenomenon, it has increasingly become a topic of international public concern, particularly after recent high-profile bioterrorism attempts in Japan and the United States. The ability of biological agents to infect large numbers of people, the difficulty of initially detecting an attack, and the threat that these agents will create widespread population disruption and panic present a unique set of challenges. Smallpox and anthrax, followed by plague, are generally considered to be the most likely biological agents. However, a host of other agents, including toxins produced by bacteria as well as viruses and bacteria, may also be deployed. International efforts to control bioterrorism began in 1925 with the Geneva Protocol. In 1972 a convention known as the Biological and Toxin Weapons Convention (BTWC) prohibited the development, production, stockpiling, and acquisition of biological and toxin weapons. Since then, the majority of the world's countries have signed on to the convention.

The use of biological weapons is far from new. In fact, one of the earliest incidences of bioterrorism is thought to have occurred in the 6th century B.C.E. when Assyrians poisoned enemy wells with rye ergot, a fungus that can cause convulsions if ingested. In 1346, plague broke out in the Tartar army while it was besieging the city of Kaffa in Crimea. Reportedly, the Tartars hurled the bodies of plague victims over the city walls, causing an epidemic that forced the city to surrender. It is postulated that infected Kaffa residents may have been the source of the black plague that subsequently swept across medieval Europe. In the 1700s, during the French and Indian wars, the British reportedly gave blankets that had been used by smallpox victims to Native Americans, igniting smallpox epidemics that decimated the Native American population.

Biological weapon use and development in the 20th century include the 1915 use of glanders bacteria and anthrax by German undercover agents to inoculate livestock from the United States bound for Allied countries. From the 1930s through 1945, the Japanese set up a biological warfare testing center, known as Unit 731, in occupied Manchuria. Here, thousands of prisoners and Chinese nationals were used as experimental subjects for developing and testing biological weapons. During the early 1940s, the Japanese dropped plague-infected fleas over China and Manchuria, causing outbreaks in these areas.
Smallpox and anthrax are often considered the most threatening biological agents because of their relative ease of production.

In 1942, both the United States and United Kingdom (UK) began biological weapon research programs of their own, at Camp Detrick, Frederick, Maryland, and Gruinard Island off the coast of Scotland, respectively. Testing of anthrax spore dissemination through conventional bombs on Gruinard Island resulted in contamination so great that the entire island eventually had to be decontaminated with formaldehyde and sea-water. The UK bioweapon development program was eventually terminated, and in 1969, President Richard Nixon signed an executive order to stop all offensive biological and toxin weapon research and production.

In 1984, the Rajneeshee cult in the United States deliberately contaminated salad bars in an Oregon town with salmonella, sickening hundreds of people. In 1995, the Japanese Aum Shinrikyo cult attempted on several occasions to release biological agents, including anthrax, before finally releasing the chemical nerve agent sarin in the Tokyo subway. After the first Gulf War, the Iraqi government admitted that Iraq had a biological weapons development program, although thus far, no evidence has supported the continuation of that program after the war. Finally, in 2001, anthrax-containing letters were mailed by an as-yet-unidentified source. Twenty-two people were infected, 11 with cutaneous anthrax and 11 with inhalation anthrax. Five cases were fatal.

Anthrax and smallpox are often discussed as the most threatening biological agents because of their relative ease of production, infectivity, and toxicity, although a host of other agents exist. The CDC divides biological agents into category A, category B, and category C. Category A agents (e.g., anthrax, plague, smallpox, botulism toxin, tularemia, hemorrhagic fevers such as Ebola) are considered high risk because they can easily be spread or transmitted from person to person, result in high death rates, require special action for public health preparedness and management, and have the potential to cause widespread public panic and social disruption. Category B agents (e.g., ricin, glanders bacteria, brucella) are lower priority; they are only moderately easy to spread and result in moderate illness and low death rates. Category C agents are emerging pathogens that could be engineered for mass spread in the future (e.g., hantavirus or multidrug-resistant tuberculosis).

Much attention is focused on biological agents that directly infect humans. However, it is important to remember that agents that destroy a nation's food supply could also be devastating and disruptive to society. Aggressive forms of plant fungi, for example, could destroy swaths of crops in a relatively
short period of time, and agents directed at livestock could wipe out cow, sheep, pig, or chicken populations. Aside from food security issues, this would be economically devastating to agricultural industries.

**ANTHRAX**

Anthrax (*Bacillus anthracis*) infects grazing mammals such as sheep, cattle, and goats when they ingest soil contaminated with *B. anthracis* spores. Outside of the bioterrorism context, human infection with anthrax, “wool sorter’s disease,” is usually the result of contact with infected animals or anthrax-contaminated animal products.

The most dangerous form of infection is inhalation anthrax, in which aerosolized anthrax spores pass into the lungs. Here, they eventually germinate, sometimes after a lag time of several weeks, producing toxin-making bacteria. Initial symptoms are very nonspecific: Victims may have a low fever, cough, some muscle aches, headache, vomiting, weakness, chills, abdominal pain, or fatigue. Patients may seem to recover but then progress to the second, more serious phase of the disease in which they suddenly present with high fever and chills, great difficulty in breathing, and shock. By the time these symptoms develop, therapy is usually ineffective, and death occurs within 24 to 72 hours in almost 90 percent of cases. Inhalation anthrax is the most alarming in terms of use as a bioweapon. It is possible for spores to be disseminated (e.g., inside a bomb that explodes in midair) through aerosol over a large, densely populated area with devastating effects. Because initial symptoms are very difficult to distinguish from an innocuous viral illness, a diagnosis might not be made until a patient is extremely sick.

A less serious form of anthrax is cutaneous anthrax, which may develop from contact of broken skin with spores. If left untreated, the infection will manifest as a large, blackened ulcer. However, the mortality rate is lower than for inhalation anthrax. Anthrax infections in the stomach or throat are rarely reported. Treatment of anthrax is with antibiotics, which can be given prophylactically or once infection is detected. An anthrax vaccine exists and is used to protect animals and people at increased risk of exposure such as military personnel, but has significant toxicities that make it unacceptable for vaccination of large populations.

**SMALLPOX**

Smallpox is seen as one of the most likely viruses to be used as a biological weapon. It is extremely infectious, and was particularly devastating to Native American populations in North and South America when it was brought to the continent by European explorers. Through a vaccination campaign, it was declared eradicated worldwide by the World Health Organization (WHO) in 1980. Vaccination was completely discontinued in the United States after 1980. The last fatal case was due to a laboratory-acquired infection in the UK in 1978. The virus still legitimately exists in two laboratories in the world: the CDC in Atlanta, Georgia, and the State Research Center of Virology and Biotechnology in Novosibirsk, Russia, although there are concerns about clandestine stocks that may exist in other places. There is debate over whether to destroy these last stocks, but thus far, the WHO has decided to delay destruction.

Transmission is primarily person to person through respiratory routes, although infection from contact with dried virus on cloth or other materials is also possible. The virus may remain stable for up to a year in dust and cloth. About 10 days after infection, patients develop severe headache, backache, and fatigue, followed by lesions in the mouth and characteristic pox all over the body. Lung infection,
damage to the eyes, and infection of the bones, brain, and testes are all possible complications. The mortality rate is 30 percent in unvaccinated individuals, and 3 percent in vaccinated individuals. Hemorrhagic-type smallpox is a more virulent form that causes death in over 90 percent of both vaccinated and unvaccinated individuals.

There is no established treatment for smallpox, and vaccination has been largely discontinued in the United States and around the world since 1980, rendering millions of people vulnerable to the virus. The original vaccine does not meet current quality standards and had some significant side effects, so there are currently efforts underway to develop a safer vaccine. The virus could be delivered via aerosol as a biological weapon.

PLAGUE

Most experts consider anthrax and smallpox to be the greatest threats. However, plague also appears to be a candidate for bioterrorist attack. It could be disseminated in an aerosol form, similar to anthrax and smallpox, or it could be used to infect rodents. Fleas feeding on the rodents could then transmit the bacteria to humans, much as they did during the massive Black Death outbreak that decimated medieval Europe. Plague-infected fleas could also conceivably be released.

Plague occurs in several forms, but the most likely from an aerosol attack would be primary pneumonic plague. This occurs through inhalation of bacteria and begins abruptly after a one-to-six-day incubation period with intense headache, fever, diarrhea, vomiting, and abdominal pain. Lung infection with respiratory failure and shock develops quickly. Without antibiotics, patients typically die within two to three days. Plague pneumonia is extremely contagious via respiratory droplets. However, with antibiotics, the mortality rate decreases below 10 percent. Bubonic plague from an infected flea bite presents similarly, but a large swelling of a lymph node near the bite, a "bubo," is characteristic. Mortality is around 60 percent, but reduces to less than 5 percent with antibiotics. There is a vaccine available, but due to associated risks, it is not considered safe for use in large human populations. Antibiotics are very effective at treating plague.

INTERNATIONAL CONTROLS

The first effort to prohibit the use of biological agents was contained in the 1925 Geneva Protocol, signed at the end of World War I. This specified that no country should use biological weapons unless first attacked with a biological agent. However, it said nothing about research or development of biological agents.

In contrast, the Biological and Toxin Weapons Convention (BTWC), signed on April 10, 1972, banned the stockpiling, development, acquisition, and use of biological agents and toxins for nonpeaceful purposes. Currently, over 150 countries have signed on. However, some point out that the BTWC lacks verification provisions and parties are very little constrained to provide information on certain activities that are "legitimate," such as pharmaceutical plants, but have the capacity to be used to produce biological weapons.

Many countries around the world have begun to prepare for the possibility of bioterrorism. In the United States, for example, Congress passed the Public Health Security and Bioterrorism Preparedness and Response Act ("Bioterrorism Act") in 2002, which provides guidelines for biosafety and the development of appropriate responses to bioterrorist attacks.

It is unclear how likely it is that a major bioterrorist attack will occur. However, the prospect of
bioterrorism will no doubt be a cause of concern for years to come.

SEE ALSO:
- Anthrax; Biodefense; Biological and Chemical Weapons; Biosafety; Botulism; Disasters and Emergency Preparedness; Hemorrhagic Fever; Infectious Diseases (General); Smallpox.

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