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CHAPTER 2

Threats from Biological, Chemical, Nuclear, and Radiological Weapons

LEARNING OBJECTIVES

By the end of this chapter, the reader will be able to:

- Define biological, chemical, radiological, and nuclear weapons
- Understand the threats from and history of use of weapons of mass destruction
- Characterize the current threat from weapons of mass destruction, specifically biological weapons, used by both state and non state actors
- Identify the public health community's role in responding to weapons of mass destruction

Introduction

In this chapter, we begin to explore and define the threats the public health community should be prepared to address. We begin with a focus on weapons of mass destruction (WMD), including chemical, biological, radiological, and nuclear (CBRN) weapons. While we look at all of these types of weapons, our main focus will be predominately on biological weapons, as they are most directly linked to the public health and medical communities through detection, response, and recovery. Public health, though, is responsible for managing the health consequences of all threats, regardless of origin.

For the public health and medical communities to be prepared for and to respond appropriately to CBRN threats, they must work closely with a wide range of communities. Many of these groups, such as law enforcement, military entities, and the intelligence community, are not traditional public health partners. These communities and the specific interactions are discussed in more detail later in the text. Here, we present the WMD threats. We look first at chemical, then nuclear and radiological threats, and then focus on the details of biological weapons more extensively. The majority of this chapter, and the rest of this text, centers on the biological threat, as this threat has the strongest links to public health preparedness.

Chemical Threats

Article II, paragraph 1 of the Chemical Weapons Convention (CWC) defines chemical weapons as one of the following, either in combination or separately:

(a) Toxic chemicals and their precursors, except where intended for purposes not prohibited under this convention, as long as the types and quantities are consistent with such purposes
(b) Munitions and devices, specifically designed to cause death or other harm through the toxic properties of those toxic chemicals specified in subparagraph (c), which would be released as a result of the employment of such munitions and devices
(c) Any equipment specifically designed for use directly in connection with the employment of munitions and devices specified in subparagraph (b)[1]

In general, chemical warfare is the use of a chemical substance to directly harm or kill human, plants, or animals. (It is worth noting that the CWC does not include chemicals that harm plants. The Geneva Protocol of 1925, however, does incorporate anti-plant agents. There is some debate over whether defoliants and other chemicals used against plants should be considered chemical weapons under international legal regimes.[2]) Chemical agents are nonliving, manufactured chemicals. They tend to be highly toxic and can enter the body through inhalation or through the skin. Adding to the complexity of treatment, illness or death can come within minutes of exposure, or take as long as several hours.[3] As described in **BOX 2-1** and **2-2**, there are several main categories of chemical warfare agents: blister (e.g., mustard gas), blood (e.g., cyanide), choking (e.g., chlorine), and nerve (e.g., sarin). Toxins (discussed in the next subhead) are also a major category of agents, as are psychotomimetic agents, which can alter mental status. In addition, there is a class termed "riot control agents," which produce temporary, usually nonfatal irritation of the skin, eyes, and respiratory tract. Riot control agents, often known as "tear gas," include chloroacetophenone (CN), chlorobenzylidenemalononitrile (CS), and chloropicrin (PS). The CWC and the U.S. government do not consider this class of agents to be chemical weapons. Other nations, however, disagree.[4]

The public health response to chemical events will range depending on the event itself, its origin, and the location. Possible activities may include the following:

- Issuing shelter-in-place orders
- Evacuating populations
- Organizing decontamination efforts
- Restricting entry to particular areas
- Ensuring food and water are safe
- Immediate and long-term monitoring of health effects[5]

Toxins

Toxins are nonliving poisons produced by living entities, such as plants, fungi, insects, and animals. Because they are chemical by-products of biological agents, they occupy a conceptual gray area between chemical and biological weapons. The Biological Weapons Convention covers toxins, and the CWC covers a discrete list of toxins, including ricin. This is another area where for the purposes of arms control and legal international obligations, countries do not always agree on how toxins should be categorized.

BOX 2-1 Types of Chemical Agents

- **Nerve agents**—primarily act on the nervous system, causing seizures and death. Examples of this category include sarin, VX, tabun, and soman. This category also includes fourth-generation chemical weapons, known as novichok agents, which are thought to be much more lethal than VX.
- **Blister agents or vesicants**—primarily cause irritation of the skin and mucous membrane. Examples of this category include mustard gas and arsenical lewisite.
- **Choking agents or pulmonary toxicants**—primarily cause damage to the lungs, including pulmonary edema and hemorrhage. Examples include phosgene, diphosgene, and chlorine.
- **Blood agents**—primarily cause seizures and respiratory and cardiac failure in high doses. Examples include hydrogen cyanide and cyanogen cyanide.
- **Riot control agents**—cause incapacitation due to irritation of eyes and respiratory system. Examples include CN, CS, and dibenzoxazepine (CR).
- **Psychotomimetic agents**—in low doses, these cause psychiatric effects. An example is lysergic acid diethylamide (LSD).
- **Toxins**—symptoms range from death to incapacitation depending on the agent. Examples include ricin and saxitoxin.

Data from Ganesan K, Raza SK, Vijayaraghavan R. Chemical Warfare Agents. *Journal of Pharmacy and BioAllied Sciences*. 2010;2(3): 166–178. 10.4103/0975-7406.68498; Organisation for the Prohibition of Chemical Weapons. Types of Chemical Agents. *About Chemical Weapons*. Available at: https://www.opcw.org/about-chemical-weapons/types-of-chemical-agent/. Accessed April 2017.

BOX 2-2 Schedule 1 of the Chemical Weapons Convention

The CWC maintains a list of chemicals and precursors for monitoring purposes. Schedule 1 chemicals and precursors are for those chemicals that can most easily be used as weapons and there is very little use for them otherwise. Below is a list of the Schedule 1 chemicals:

1. *O*-Alkyl ($<C_{10}$, including cycloalkyl) alkyl (Me, Et, *n*-Pr, or *i*-Pr)-phosphonofluoridates, for example,
   Sarin: *O*-isopropyl methylphosphonofluoridate
   Soman: *O*-pinacolyl methylphosphonofluoridate
   Schedule 1 phosphoramidocyanidates, where R_1 = (cyclo)alkyl with $C < C_{10}$ and R_2/R_3 = Me, Et, *i*-Pr, or *n*-Pr
   Schedule 1 phosphonothiolate, where $R_1 = H$ or (cyclo)alkyl with $C < C_{10}$ and $R_2/R_3/R_4$ = Me, Et, *i*-Pr, or *n*-Pr
2. *O*-Alkyl ($<C_{10}$, including cycloalkyl) *N*,*N*-dialkyl (Me, Et, *n*-Pr, or i-Pr) phosphoramidocyanidates, for example,
   Tabun: *O*-ethyl *N*,*N*-dimethylphosphoramidocyanidate
3. *O*-Alkyl (*H* or $<C_{10}$, including cycloalkyl) *S*-2-dialkyl (Me, Et, *n*-Pr, or *i*-Pr)-aminoethyl alkyl (Me, Et, *n*-Pr, or *i*-Pr) phosphonothiolates and corresponding alkylated or protonated salts, for example,
   VX: *O*-ethyl *S*-2-diisopropylaminoethyl methylphosphonothiolate
4. Sulfur mustards:
   2-Chloroethylchloromethylsulfide
   Mustard gas: bis(2-chloroethyl)sulfide
   Bis(2-chloroethylthio)methane
   Sesquimustard: 1,2-bis(2-chloroethylthio)ethane
   1,3-Bis(2-chloroethylthio)-*n*-propane
   1,4-Bis(2-chloroethylthio)-*n*-butane
   1,5-Bis(2-chloroethylthio)-*n*-pentane
   Bis(2-chloroethylthiomethyl)ether
   O-Mustard: bis(2-chloroethylthioethyl)ether
5. Lewisites:
   Lewisite 1: 2-chlorovinyldichloroarsine
   Lewisite 2: bis(2-chlorovinyl)chloroarsine
   Lewisite 3: tris(2-chlorovinyl)arsine
6. Nitrogen mustards:
   HN1: bis(2-chloroethyl)ethylamine
   HN2: bis(2-chloroethyl)methylamine
   HN3: tris(2-chloroethyl)amine
7. Saxitoxin
8. Ricin

Reproduced from Organisation for the Prohibition of Chemical Weapons. *Annex on Chemicals Schedule 1*. Available at: https://www.opcw.org/chemical-weapons-convention/annexes/annex-on-chemicals/. Accessed April 2017.

History

In April 1915, during World War I, the German army attacked the French with chlorine gas in Ypres, Belgium, marking the first large-scale use of chemical weapons during warfare. Several months later, in September 1915, the British used chlorine gas against the Germans at the Battle of Loos. This was followed in June 1918 by the first use of chemical warfare by the United States. It was clear that by the end of World War I, all sides were actively using the chemical weapons in their arsenals.[6] **FIGURE 2-1** shows soldiers in World War I suffering from the effects of chemical warfare.

Many nations continued to utilize chemical warfare throughout the 20th century, including the British use of adamsite (a vomiting agent) against the Bolsheviks during the Russian Civil War, Spanish use of chemical weapons against rebels in Morocco in the 1920s, Italian use of mustard gas against Ethiopians in 1936, and Nazi German use of hydrocyanic acid for the mass extermination of Jews and other concentration camp prisoners.[7]

During the Vietnam War, the United States used defoliants such as dioxin, also known as "Agent Orange," as well as other normally nonlethal agents. The United States does not consider defoliants to be chemical weapons, therefore it does not consider this use to be chemical warfare. High levels of morbidity and mortality from those exposed to the agents, though, have led to large research efforts and calls by many that this was, in fact, chemical warfare.[8,9]

Other examples of chemical warfare include the use of phosgene and mustard gas by Egypt against

FIGURE 2-1 The World War I: British troops blinded by a chemical weapons attack wait outside an advance dressing station, near Bethune, France. Each man has his hand on the shoulder of the man in front of him. Battle of Estaires. (An image reminiscent of John Singer Sargent's famous painting "Gassed.")

Yemen (1963–1967), and the use of chemical weapons by Iraq during the Iran–Iraq War (primarily in 1983 and 1984), initially with riot control agents and eventually using mustard gas.[10,11] One particular use of chemical weapons by Iraq was repeatedly cited as part of the U.S. rationale in 2002 for invading the country.[12] In 1988, in a campaign against the Kurds, Saddam Hussein used what was most likely to be mustard gas, possibly mixed with sarin, against the town of Halabja, killing thousands.[13]

More recently, Syria, under President Bashar Al-Assad, was accused of using chemical weapons in the civil war that started in 2012.[14–16] Almost immediately, there were concerns about the implications for Syria's suspected stockpile of chemical weapons, with subsequent reports (verified by the Organization for the Prohibition of Chemical Weapons (OPCW) and the United Nations) of use of mustard and chlorine gases.[17] A 2016 report found that the Islamic State terrorist organization had used chemical weapons at least 52 times in Syria and Iraq since 2014. Most of those attacks were tied to chlorine or sulfur mustard agents.[18]

Another example of the offensive use of chemical agents comes from the doomsday cult Aum Shinrikyo, based in Japan. On March 20, 1995, Aum Shinrikyo released sarin gas into the Tokyo subway system. Twelve people died, approximately 50 were severely injured, and almost 1000 suffered temporary vision problems.[19] Over 5500 people, however, sought medical attention, swarming area hospitals and testing public health capacities. This chemical weapons use event highlighted the importance of emergency preparedness, especially in the area of hospital surge capacity and triage.

While most of the cited examples of chemical weapons use have been large-scale warfare incidents, these agents have also been used throughout history as assassination tools (**TABLE 2-1**).[20] One particularly illustrative example was the 1979 assassination of a Bulgarian exile named Georgi Markov (**BOX 2-3**).

In addition to intentional releases of chemical agents, the accidental releases of agents have also posed significant challenges to public health and medical systems worldwide, and have adversely affected the health of populations. (See **FIGURE 2-2** for numbers of persons evacuated from chemical events in select areas of the United States.) For example, in 1981, cooking oil was accidentally

TABLE 2-1 Select Chemical Incidents Since 1976

Year	Location	Description of Incident	Consequences
1976	Seveso, Italy	Airborne release of dioxin from an industrial plant	■ No immediate human deaths ■ 3,300 animal deaths ■ 80,000 animals slaughtered
1984	Bhopal, India	Methyl isocyanate (MIC) leak from tank	■ 3,800 immediate deaths ■ 15,000–20,000 premature deaths ■ 500,000 exposed to the gas
1984	Mexico City, Mexico	Explosion of liquefied petroleum gas (LPG) terminal	■ 500 deaths ■ 6,400 injuries
1995	Tokyo, Japan	Deliberate release of warfare agent	■ 12 deaths ■ 54 critical casualties ■ Thousands of people affected
2000	Enschede, The Netherlands	Explosion of a fireworks factory	■ 20 deaths ■ 562 casualties ■ Hundreds of houses destroyed ■ 2,000 people evacuated
2001	Toulouse, France	Explosion of 300–400 tons of ammonium nitrate in a fertilizer facility	■ 30 deaths ■ 2,500 casualties ■ 500 homes uninhabitable
2002	Galicia, Spain	Shipwreck of the *Prestige*, causing the release of 77,000 tons of fuel	■ Estimated cleanup costs of U.S. $2.8 billion
2002	Jabalpur, India	Mass poisoning due to the use of pesticide containers as kitchen utensils	■ 3 deaths ■ At least 10 hospitalizations
2003	Baton Rouge, USA	Release of chlorine gas from a facility	■ No human deaths
2004	Neyshabur, Iran	Train explosion due to mixing of incompatible chemicals	■ Hundreds of deaths and casualties among emergency responders and onlookers
2005	Songhua River, China	Plant explosion releasing 100 tons of pollutants in the Songhua River	■ 5 deaths ■ Millions of people without water for several days
2005	Bohol, The Philippines	Inadvertent use of an insecticide in the preparation of sweets	■ 29 deaths ■ 104 hospitalizations
2005	Hemel Hempstead, England	3 explosions in an oil storage facility (Buncefield depot)	■ 43 injuries reported ■ 2,000 persons evacuated
2006	Abidjan, Côte d'Ivoire	Dumping of toxic waste in the city of Abidjan	■ 10 deaths ■ Thousands made ill
2006	Panama	Diethylene glycol in a cough syrup	■ At least 100 deaths
2007	Angola	Sodium bromide confused with tablet salt	■ At least 460 people ill, most of them children
2008	Senegal	Lead from informal battery recycling	■ People exposed, with many children showing symptoms of lead intoxication

Data from World Health Organization. Examples of Chemical Incidents Worldwide. *Manual for the Public Health Management of Chemical Incidents*. 2009;WA 670:4. Available at: http://www.who.int/environmental_health_emergencies/publications/FINAL-PHM-Chemical-Incidents_web.pdf. Accessed April 2017.

BOX 2-3 Assassination by Ricin

In 1978, a Bulgarian exile named Georgi Markov was waiting for a bus in London. A man poked him with the tip of an umbrella, apologized, and got into a taxi. Four days later, Markov was dead.

Ten days prior to this incident, another Bulgarian exile, Vladimir Kostov, was stabbed in the back in Paris, and when he turned around, he witnessed someone running away with an umbrella. This particular umbrella had been adapted and rebuilt into a makeshift gun that fired ricin pellets from its tip. After learning of Markov's death, Kostov sought medical attention immediately. A doctor removed the pellet that had lodged in his back. Fortunately, the ricin that was contained within the pellet had not fully expelled into his blood stream. The doctor successfully removed it, confirmed the presence of ricin, and Kostov survived the incident.

One of the reasons ricin was such an effective assassination tool was that it was virtually impossible to detect what was killing Markov, and there was little authorities could have done even if it was identified. Ricin, a poison extracted from castor beans, prevents cells in the body from making proteins, and without proteins, cells die, which can eventually lead to death. Once exposed, it can take up to 6–8 hours for symptoms to occur, depending on the route of exposure, and death can occur rapidly within 36–72 hours. The symptoms of ricin exposure include respiratory distress if inhaled, vomiting and diarrhea if ingested, and redness and pain of skin and eyes if absorbed through skin. There is no available antidote at present, and the only treatment is supportive medical care.

Data from Centers for Disease Control and Prevention. Facts about Ricin. *Emergency Preparedness and Response*. Available at: https://emergency.cdc.gov/agent/ricin/facts.asp. March 5, 2008. Accessed April 2017.

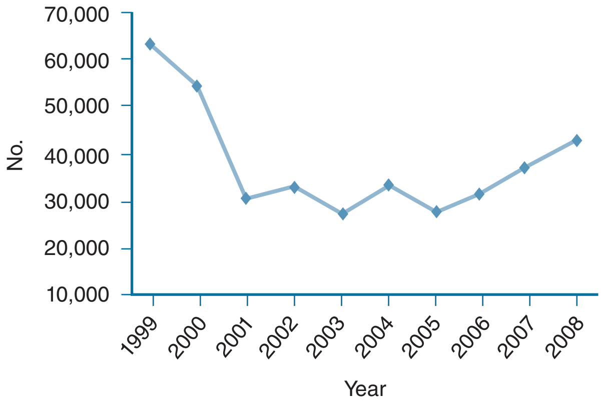


FIGURE 2-2 Number of persons evacuated for chemical incidents, by year in nine states (Colorado, Iowa, Minnesota, New York, North Carolina, Oregon, Texas, Washington, and Wisconsin) in the United States between 1999 and 2008

Reproduced from Melnikova N, Wu J, Orr MF. Number of Persons Evacuated for Chemical Incidents, by Year. Public Health Response to Acute Chemical Incidents—Hazardous Substances Emergency Events Surveillance, Nine States, 1999–2008. *MMWR*. 2015; 64(2): 28. Available at: https://www.cdc.gov/mmwr/pdf/ss/ss6402.pdf. Accessed April 2017.

adulterated with industrial rapeseed oil and distributed throughout southern Europe. Over 15,000 people became sick and 203 died after consuming the contaminated oil.[21]

In some instances, the release of chemical agents may not have been entirely accidental, but one assumes that the public health consequences were unintentional. In 2006, a Panamanian-flag, Greek-owned, Swiss oil company chartered tanker, the *Probo Koala*, avoiding European disposal fees, carried over 500 tons of petrochemical waste to Côte d'Ivoire, which was then dumped by a local contractor in more than 12 different sites around Abidjan. Fifteen people died as a result of exposure to this toxic waste, 69 were hospitalized, and over 100,000 sought medical treatment, easily overwhelming the existing public health and medical infrastructures.[22–24]

Unfortunately, these types of exposures to chemical agents are not infrequent. On May 29, 2010, a worker at a scrap yard in Nigeria tried to cut a gas cylinder into pieces, resulting in an explosion that released a cloud of chlorine gas into the air, sickening 300 people who eventually required medical treatment.[25]

The largest chemical agent accidental exposure took place on December 3, 1984, in Bhopal, India. A Union Carbide pesticide plant released 40 tons of methyl isocyanate (MIC) gas into the air in the middle of the night. Nearly 4,000 people died instantly, and the total number of deaths is estimated to be between 15,000 and 22,000; 500,000 people were exposed; and as many as 120,000 continue to suffer detrimental health effects.[26]

Accidents that expose populations to chemical agents can occur anywhere, including the United States. For example, a community in Graniteville, South Carolina, was left with 9 dead and 250 injured after a train carrying toxic chemicals, including chlorine gas, crashed.[27] Accidents such as these remind us that all public health communities, regardless of location, must have a level of awareness regarding preparedness for a variety of potential public health emergencies, including the need to know how to respond to an emergency.

Nuclear and Radiological Threats

Nuclear Weapons

A nuclear weapon that involves fission (the splitting of atoms)—like the bomb that the United States detonated in Hiroshima, Japan, during World War II, or the devastating weapons created and stockpiled by a small number of nations since—leaves a limited role for the public health community. Such weapons, if released, would instantly destroy people, buildings, and anything else in the vicinity. There would be no need for a public health response, because the chances of survival would be minimal. The explosion, however, would leave behind large amounts of radioactivity. We discuss the challenge of radioactivity next in the "Radiological Threats" section.

Radiological Threats

A radiologic event is an explosion or other release of radioactivity. Such an event might be caused by any of the following: a simple, nonexplosive radiological device; an improvised nuclear device designed to release large amounts of radiation with a large blast radius (such as a "suitcase bomb"); a dispersal device that combines explosive materials and radioactive material (such as a "dirty bomb"); or damage to a nuclear reactor that results in the release of radiation.[28]

Even a small dose of radiation can cause some detectable changes in blood. Large doses of radiation can lead to acute radiation syndrome (ARS). First signs of ARS are typically nausea, vomiting, headache, diarrhea, and some loss of white blood cells. These signs are followed by hair loss, damage to nerve cells and cells that line the digestive tract, and severe loss of white blood cells. The higher the dose of radiation, the less likely the person will survive. Those who survive may take several weeks to 2 years to recover, and survivors may suffer from leukemia or other cancers.[29]

The public health implications of radiologic exposure can be significant. In addition to all other functions, the public health community will be responsible for the following:

- Participating in shelter-in-place or evacuation decisions
- Identifying exposed populations through surveillance activities
- Conducting or assisting with environmental decontamination
- Determining safety requirements for working in or near the site of the incident
- Conducting near and long-term follow up with exposed populations[30]

In recent years, we have seen radiation used as an assassination tool. In 2006, Alexander Litvinenko, a former agent of the Federal Security Service (FSS) in Russia who was living in the United Kingdom under political asylum, was poisoned with polonium-210 in his tea, resulting in ARS. Over the course of a month, officials in the United Kingdom had identified additional individuals who had been exposed to the material. The poisoning and the subsequent investigation created a series of challenges for the public health community, including deciding who to screen for exposure, how to screen for exposure, who to treat for radiation exposure, and how to treat.[31] All of these decisions had to be made in an environment of uncertainty, with a public that was rightfully concerned and confused about the risk, and with an undercurrent of international diplomatic tension between the United Kingdom and Russia.

To date, most radiologic exposure has occurred via accidents. An often-cited event occurred in Goiânia, Brazil, in 1987. Two men were rummaging through an abandoned hospital and found an old nuclear medicine source—a radioactive cesium-137 teletherapy head. They took it home, partially dismantled it, and eventually sold it to a scrap yard. The owner of the scrap yard discovered that the cesium capsule omitted a blue light; many came to see it and children rubbed the material on their bodies to glow in the dark. Four people, including a young child, died from the exposure. Another 249 individuals suffered serious health consequences.[32]

The most serious radiation accidents have been associated with nuclear power plants. Sixty-three accidents have occurred at nuclear power plants, with the most serious occurring in Chernobyl, Ukraine. On April 26, 1986, at 1:23 A.M., Reactor 4 of the Chernobyl Nuclear Power Plant exploded, instantly killing three and sending a plume of radioactive fallout into the air, which eventually drifted over parts of the Soviet Union, eastern Europe, western Europe, northern Europe, and eastern North America. Approximately 350,000 individuals had to be evacuated and resettled. Fifty-six people died as a direct result of the accident. Another 4000 have died from cancers linked to radiation exposure (**FIGURES 2-3** and **2-4**).[33]

The public health community's immediate and long-term responsibility in response to the Chernobyl disaster was significant, including assessing the safety of the environment for human habitation, addressing the psychological impact of the disaster on affected populations, monitoring the long-term health and well-being of exposed populations, and planning for the treatment of untold numbers of current and future cancer patients.[33,34]

FIGURE 2-3 An aerial view of Ukraine's Chernobyl Nuclear Power Plant, taken in May 1986, several days after the explosion on April 26, 1986

In 2011, another major disaster occurred at a nuclear power plant. On March 11, 2011, following a massive earthquake and subsequent tsunami, three reactors at the Fukushima Daiichi power plant in Japan melted over the course of 3 days (after the tsunami led to the failure of the emergency generators needed to cool the reactors; **FIGURE 2-5**). While no direct deaths from the power plant accident occurred, over 100,000 people were evacuated from their homes (everyone within a 30-km radius), and radiation was tracked to have spread across the ocean. U.S. researchers also found that over 1000 people have died as a result of the evacuation.[35] Additionally, public health officials tracked radioactivity in vegetables, milk, and water near the reactor sites.

A 2013 report by the World Health Organization (WHO) found that the greatest impact to health from the Fukushima disaster was an increased risk of cancer for the exposed population. The lifetime risk of most cancers over baseline ranged from 4% to 7%, with the exception being an increase of 70% over baseline for the risk of developing thyroid cancer.[36]

In addition to the public health risk of accidental radiologic exposure, the global community continues to be concerned about the intentional use of a nuclear or radiologic device. In April 2010, President Barack Obama called the global community to a Nuclear Security Summit, where the nations of the world clearly acknowledged the threat of nuclear terrorism. President Obama delivered the following statement:

> Two decades after the end of the Cold War, we face a cruel irony of history—the risk of a nuclear confrontation between nations has gone down, but the risk of nuclear attack has gone up.
>
> Nuclear materials that could be sold or stolen and fashioned into a nuclear weapon exist in dozens of nations. Just the smallest amount of plutonium—about the size of an apple—could kill and injure hundreds of thousands

FIGURE 2-4 Radiation hot spots resulting from the Chernobyl Nuclear Power Plant accident

Reproduced from Central Intelligence Agency. Radiation Contamination after the Chernobyl Disaster. *Making the History of 1989*. Item #173. Available at: http://chnm.gmu.edu/1989/items/show/173. Accessed April 2017.

of innocent people. Terrorist networks such as al Qaeda have tried to acquire the material for a nuclear weapon, and if they ever succeeded, they would surely use it. Were they to do so, it would be a catastrophe for the world—causing extraordinary loss of life, and striking a major blow to global peace and stability.

In short, it is increasingly clear that the danger of nuclear terrorism is one of the greatest threats to global security—to our collective security.[37]

The International Atomic Energy Agency (IAEA) receives, on average, a report every 2–3 days on an incident of illicit trafficking of nuclear or radiological material.[38,39] Unfortunately, the nuclear and radiological threats are very real and it is essential that the public health community be prepared.

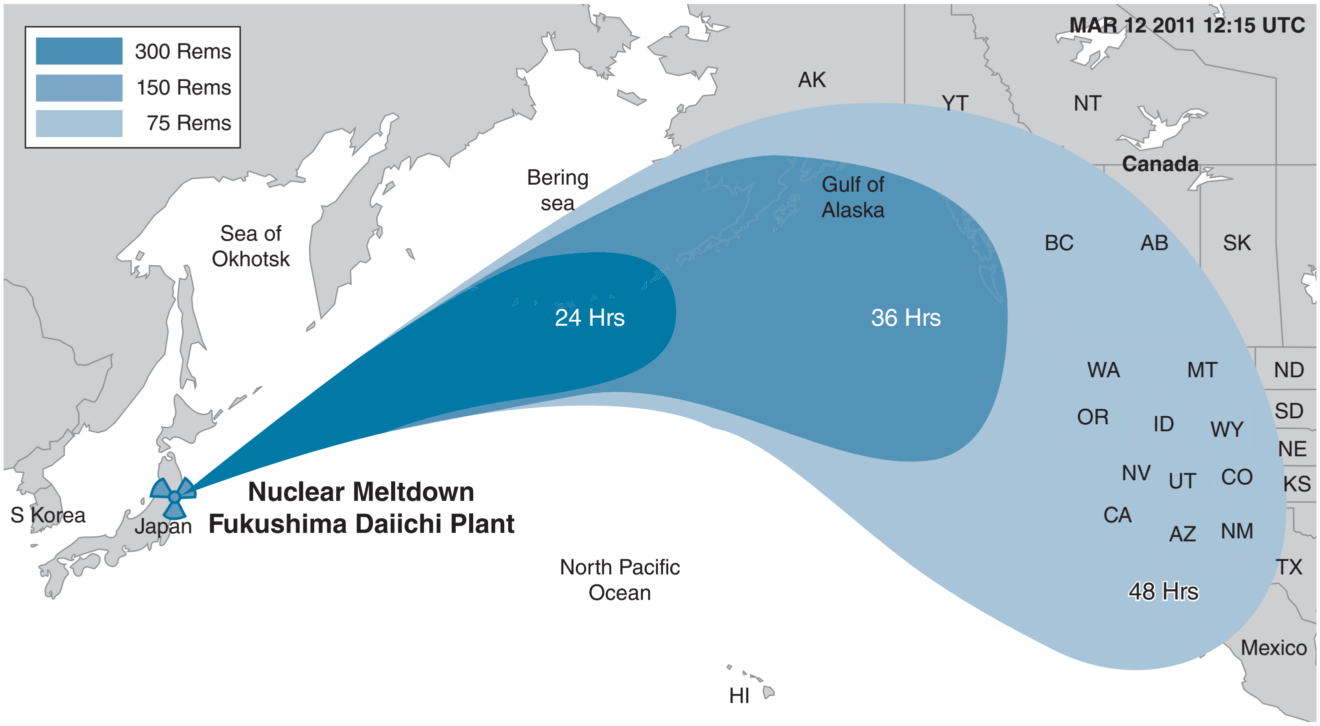


FIGURE 2-5 Radioactive fallout map of Fukushima, Japan

Data from NRC. Infinite Unknown. *Radioactive Fallout Map.* 2011. Available at: http://www.infiniteunknown.net/wp-content/uploads/2011/03/US-NRC-Japan-Fallout-Map-From-Destroyed-Fukushima-Daiichi-Nuclear-Plant.jpg. Accessed April 2017.

Biological Threats

The biological threat can be thought of as along a continuum, to include everything from naturally occurring diseases to the intentional release of a biological agent. **FIGURE 2-6** shows how the impact of each type of threat can range from global to individual: how a deliberately caused event could have global consequences, while a naturally occurring outbreak of an only slightly contagious disease or a lab accident could be limited to a handful of individuals.

This text focuses on the threat from natural disease and emerging and pandemic threats in later chapters, as here we focus exclusively on the deliberate threat. Biological warfare (BW) is the military use of a biological agent to cause death or harm to humans, animals, or plants. In warfare, the targets of biological agents are typically governments, armed forces, or resources that might affect the ability of a nation to attack or defend itself. Similarly, bioterrorism (BT) is the threat or use of a biological agent to harm or kill humans, plants, or animals. Unlike BW though, the target of BT is typically the civilian population or resources that might affect the civilian economy. Agroterrorism refers to the knowing or malicious use of biological agents to affect the agricultural industry or food supply.[40]

As with chemical and radiological threats, there is a long history of the intentional use of biological agents. One example that is cited regularly comes from the 1346–1347 siege by Mongols of the city of Kaffa, now Feodosija, Ukraine. The Mongols reportedly catapulted corpses contaminated with plague over the walls of the city, causing an outbreak of *Yersinia pestis*.[41] Another historical example comes from 1767 when British troops under the direction of Sir William Amherst gave smallpox-infested blankets to Native Americans, causing a massive outbreak of smallpox among this previously unexposed population.

There was little use of biological weapons during World War I. In fact, the only reported use was by Germany, who used anthrax and glanders to infect Allied livestock.[42(p513)] After World War I, however, the Japanese began a robust offensive biological weapons program, housed in what was called "Unit 731." This unit was based in Harbin, Manchuria, and conducted extensive research and experiments, often using prisoners of war as subjects.

In 1940, the Japanese dropped rice and wheat mixed with plague-carrying fleas over China and Manchuria, leading to localized plague outbreaks. In 1942, the United States, with data from Unit 731, began its offensive biological weapons program (**BOX 2-4**).[43]

Several additional high-profile biological weapons events occurred starting in the late 1970s. In 1979, in the Siberian town of Sverdlovsk in the Soviet Union (now Yekaterinburg), at least 77 people became ill with anthrax, resulting in 66 fatalities. Originally, the Soviet Union claimed that the cause of the outbreak was

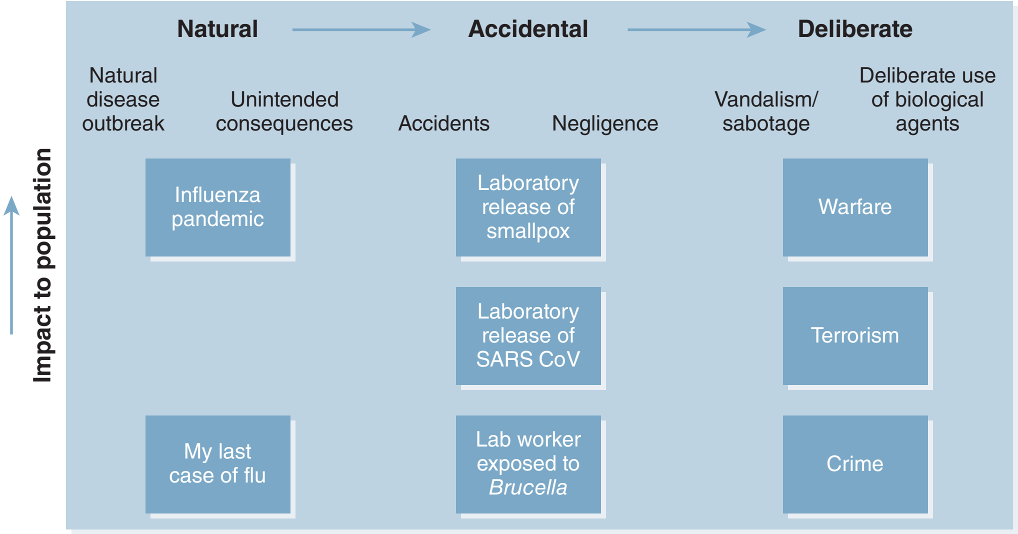


FIGURE 2-6 The biological threat spectrum

BOX 2-4 U.S. Offensive Biological Warfare Program 1942–1972

1942	The National Academies of Sciences Biological Warfare Committee recommends that the United States should develop an offensive and defensive biological weapons program. Secretary of War Henry L. Stimson recommends to the president that a civilian organization be set up to run the program, and the president approves. The War Research Service (WRS) is established and George Merck, president of Merck and Co., Inc., becomes the leader.
1943	A biological weapons research and development facility is constructed in Frederick, Maryland, at Camp Detrick, and becomes operational. Research begins on the offensive potential of botulinum toxin and anthrax.
1944	The BW program is transferred from the WRS to the War Department. The War Department divides the program between the Chemical Warfare Service (CWS) and the U.S. Army Surgeon General. CWS works mostly on offensive research and production, while the Surgeon General focuses more on defensive measures. The research and development program is housed at Camp Detrick. An existing industrial plant near Terre Haute, Indiana, is acquired for conversion to a biological weapons production plant. Research on biological agents is expanded to include brucellosis, psittacosis, tularemia, and glanders.
1946	The War Department publically acknowledges that the United States has developed an offensive biological weapons program.
1950	Several open-air/sea tests are conducted using simulants. Field testing is also conducted at Dugway Proving Ground, Utah. The construction of a production facility at Pine Bluff Arsenal, Arkansas, is authorized.
1950–1960	Research and production of at least seven biological agents continues. Airborne testing continues and the program is expanded.
1960–1970	Funding for the BW program starts to decline, but the army continues to work on antipersonnel, anti-plant, and anti-animal agents, and runs several open-air tests using simulants in populated areas. The program also works on developing vaccines for defensive purposes.
1969	President Nixon directs the National Security Council to review the chemical and biological weapons policy. The Senate Armed Services Committee votes to cease funding for the biological weapons program and prohibit additional open-air testing. On November 25, President Nixon renounces the development, production, stockpiling, and use of BW agents. The Department of Defense is ordered to destroy existing biological weapons and only engage in research for defensive purposes.
1971–1973	The United States destroys all BW agents and munitions.
1972	The United States signs the Biological and Toxin Weapons Convention.
1975	The Senate approves, and the president ratifies both the Biological and Toxin Weapons Convention and the Geneva Protocol of 1925.

Data from The Henry L. Stimson Center. *History of the US Offensive Biological Warfare Program (1941–1973)*. Biological and Chemical Weapons. Available at: http://www.stimson.org/cbw/?sn=cb2001121275. Accessed July 10, 2010; Smart JK. History of Chemical and Biological Warfare: An American Perspective. *Textbook of Military Medicine: Medical Aspects of Chemical and Biological Warfare*. Washington, DC: Office of the Surgeon General, US Department of the Army; 1989. Available at: http://www.au.af.mil/au/awc/awcgate/medaspec/cwbwfmelectrv699.pdf; Bernstein B. *Origins of the Biological Warfare Program*. 1990; MIT Press: 1–25. Available at: https://mitpress.mit.edu/sites/default/files/titles/content/9780262730969_sch_0001.pdf. Accessed April 2017.

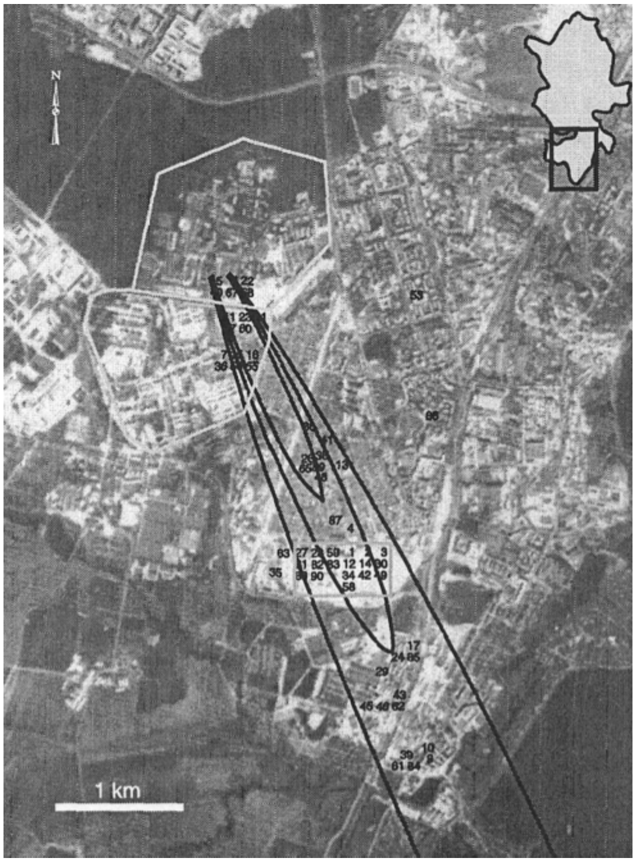


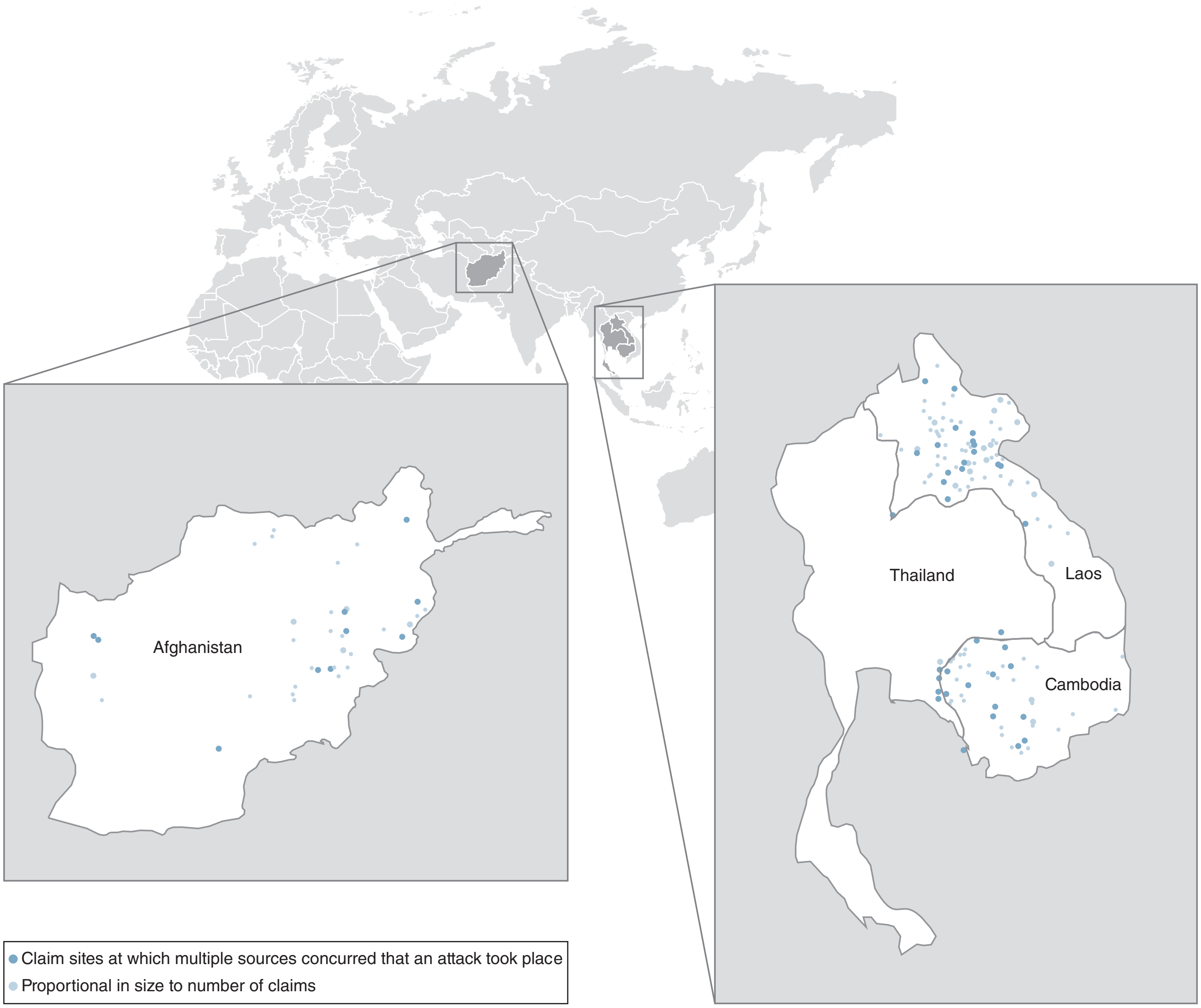
FIGURE 2-7 Wind plume from military installation allegedly producing anthrax in Sverdlovsk, Russia, and the location of anthrax cases in 1979

Reproduced from Meselson MJ, Guillemin J, Hugh-Jones M et al. The Sverdlovsk Anthrax Outbreak of 1979. *Science*. 1994; 266(5188): 1204. doi:10.1126/science.7973702. Accessed April 2017. Permission conveyed through Copyright Clearance Center, Inc.

infected meat and that the route of infection was gastrointestinal. In reality, the cause of the outbreak was human error—someone forgetting to replace a filter—at a military installation that was producing anthrax for offensive purposes. Anthrax escaped into the air and those who became ill fell within the wind plume leading directly from the military compound (**FIGURE 2-7**). In 1992, Boris Yeltsin admitted to the international community that the source of the anthrax in this outbreak came from the offensive military production site, and not from consumption of infected meat.[44,45]

Other events linked to the Soviet Union occurred during the same time period. Starting in 1976 in Laos, 1978 in Cambodia, and 1979 in Afghanistan, there were reports of chemical or toxin weapons use against the Hmong, Khmer, and Mujuhadin, respectively. The alleged attacks were often said to begin with a helicopter or plane flying over a village or resistance group and release of a colored gas that would fall in a manner that often looked, felt, and sounded like rain. The most common color reported was yellow, and thus the collective name for these incidents became "Yellow Rain." The alleged causative agent was trichothecene mycotoxin (T2), and the alleged supplier of this toxin was the Soviet Union, who provided it to the Pathet Lao in Laos, to the Vietnamese for use against Khmer resistance groups in Cambodia, and for direct use by the Soviets in Afghanistan (**FIGURE 2-8**). High levels of morbidity and mortality were associated with the

FIGURE 2-8 (A) A picture of Hmong woman and child from Laos



(B) Locations of alleged Yellow Rain attacks

Data from Katz R, Singer B. Can an attribution assessment be made for Yellow Rain? *Politics and the Life Sciences*. 2007;26(1):24–42. Accessed April 2017; © Hemera/Thinkstock/Getty.

alleged Yellow Rain attacks. In 1982, the United States estimated that over 10,700 people had been killed. Some estimated the loss of life to be much greater, particularly within the Hmong community. Some estimates go up to 20,000 and the Lao Human Rights Council puts the number as high as 40,000.[46,47]

The first large-scale BT event in the United States occurred in 1984 in The Dalles, Oregon. The Rajneeshee cult, living in the area at the time, wished to influence a local election. Their plan was to make people in the town too sick to show up to vote in the election, have all of the members of the cult vote, and thereby vote their candidate into office. As a trial run, cult members infected multiple salad bars in local restaurants with *Salmonella*. As a result, 751 people became ill and 45 were hospitalized. This case demonstrates how difficult it is to distinguish between a naturally occurring event and an intentional release of an agent, which enables plausible deniability on the part of the perpetrators. Members of the Epidemic Intelligence Service (EIS) from the CDC were called in to help with the investigation (**BOX 2-5**). While the EIS officers felt that something was not right with the outbreak, they were unable to definitively say that the cases were not of natural origin. It was not until a year after the event, when a member of the cult confessed to authorities, were the public health officials able to fully understand the nature of the outbreak.[48,49]

The most well-known BT event in the United States occurred in the fall of 2001, just weeks after the 9/11 attacks. The case, eventually named "Amerithrax" by the Federal Bureau of Investigation (FBI), involved finely milled anthrax sent through the mail, targeting senators

BOX 2-5 Origins of the Epidemic Intelligence Service

The Centers for Disease Control and Prevention (CDC) Epidemic Intelligence Service (EIS) is one of the most prestigious programs at CDC, admitting approximately 80 highly qualified professionals every year; many of whom go on to the highest leadership positions in the organization. EIS officers are America's "disease detectives," deploying to outbreaks throughout the United States and around the world. EIS was started, however, in 1951 in reaction to the threat of BW during the Korean War.

Data from CDC. *Epidemic Intelligence Service (EIS)*. Available at: https://www.cdc.gov/eis/history.html. 2015. Accessed April 2017.

and media outlets (**FIGURES 2-9** and **2-10**). In all, 22 people became ill and 5 died. Thousands of post office workers, congressional staff, and other potentially exposed individuals received prophylactic antibiotics and were offered a vaccine. Thousands more were potentially exposed during this incident, and many more who were worried about possible effects of exposure demanded antibiotics from their personal physicians. Vast sums of money were spent decontaminating post office facilities and Senate office buildings. In 2010, the FBI finally closed the Amerithrax case, claiming the perpetrator was a U.S. government researcher at Fort Detrick named Bruce Ivins. Dr Ivins committed suicide before being formally charged, and thus never stood trial.[50]

FIGURE 2-9 Anthrax letters sent to Senators Patrick Leahy and Tom Daschle

Reproduced from Federal Bureau of Investigation. *Photo Gallery Amerithrax Case*. Available at: https://archives.fbi.gov/archives/about-us/history/famous-cases/anthrax-amerithrax/the-envelopes. Accessed April 2017.

The total disruption caused by what was—in the end—the equivalent of about a sugar packet amount of anthrax demonstrates how destructive and disruptive biological weapons can be. In fact, they have been called "weapons of mass disruption." Vast infrastructure and funding came in response to the Amerithrax attack, which is discussed more fully in subsequent chapters.

Biological Agents

For a biological agent to be an effective weapon, it should ideally (from the perpetrator's perspective) have high toxicity; be fast acting; be predictable in its impact; have a capacity for survival outside the host for enough time to infect a victim; be relatively indestructible by air, water, or food purification; and be susceptible to medical countermeasures available to the attacker, but not the intended victim(s). Of the many biological agents that exist in nature (including parasites, fungi and yeasts, bacteria, *Rickettsia* and *Chlamydia*, viruses, prions, and toxins), most effort is directed at a small group of bacteria, viruses, and toxins as the primary source of potential biological weapons (**BOX 2-6**).

Classification of Biological Weapons

There have been a series of attempts to classify and characterize biological threat agents over the past 15 years. Here we present two of the major classifications and then the simple list of major biological threats.

This first classification was used primarily by policy planners at the federal level between 2005 and 2010. It looks at the spectrum of agents and defines them as follows:

- **Traditional:** These are naturally occurring microorganisms or toxins that have long been connected with BT or BW, either because they have been used in the past or they have been studied for use. There are a finite number of agents that are relatively well understood. The policy and public

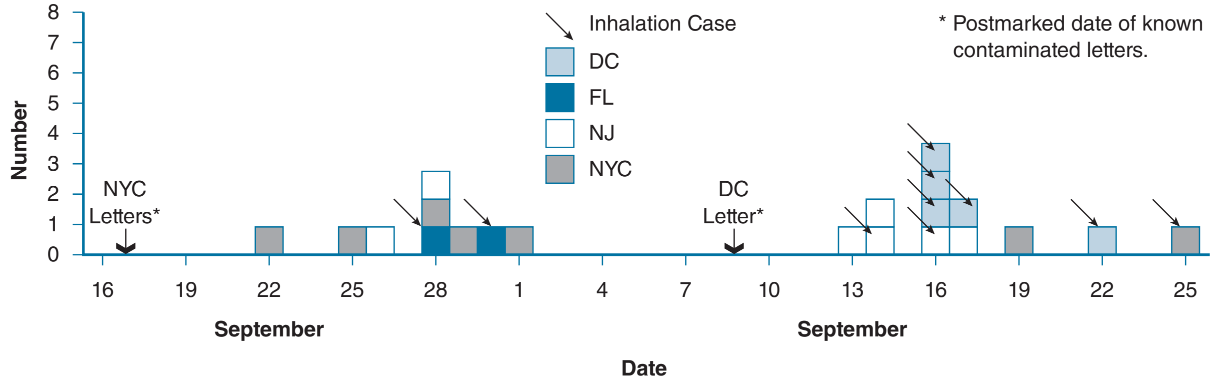


FIGURE 2-10 Number of bioterrorism-related anthrax cases, by date of onset and work location—District of Columbia (DC), Florida (FL), New Jersey (NJ), and New York City (NYC), September 16–October 25, 2001

Reproduced from Centers for Disease Control and Prevention. Number of bioterrorism-related anthrax cases, by date of onset and work location. Update: Investigation of Bioterrorism-Related Anthrax and Interim Guidelines for Clinical Evaluation of Persons with Possible Anthrax. *MMWR*. 2001;50(43): 941. Available at: https://www.cdc.gov/mmwr/PDF/wk/mm5043.pdf.

BOX 2-6 Biological Agents in Nature

Bacteria Free-living unicellular organisms

Viruses Core of DNA or RNA surrounded by a coat of protein, require host cell in order to replicate, and much smaller than bacteria

Toxins Toxic substances produced by living organisms

health community has devised specific plans to address the potential use of these agents. Examples include smallpox and anthrax.

- **Enhanced:** Enhanced agents are traditional biological agents that have been altered to circumvent medical countermeasures. This group includes agents that are resistant to antibiotics.
- **Emerging:** This category includes any naturally occurring emerging organism or emerging infectious disease. Examples include severe acute respiratory syndrome (SARS), H5N1, and novel H1N1.
- **Advanced:** The final category on the spectrum of biological threats encompasses novel pathogens and other artificial agents that are engineered in laboratories. It is virtually impossible to plan for the specific threats posed by this category of agents, thus forcing policy makers to look at biological threats with a much broader strategic approach.[51]

The second classification method for biological threat agents is the Category A, B, and C list (**BOX 2-7**). This categorization originated with a 1999 CDC Strategic Planning Workgroup, which looked at the public health impacts of biological agents, the potential of those agents to be effective weapons, public perception, and fear and preparedness requirements. They also examined existing lists, including the Select Agent Rule list, the Australia Group list for export control, and the WHO list of biological weapons.[52]

The resulting list begins with Category A, which includes the highest priority pathogens and highest threat. They can cause large-scale morbidity and mortality, and often require specific preparedness plans on the part of the public health community. Category B includes the second highest threat group. Most of the agents in this category are waterborne or foodborne. These agents have often been used intentionally in the past, or were part of offensive research programs. The morbidity and mortality from these agents is not as significant as from Category A agents, but still considerable, and they often require the public health community to enhance surveillance and diagnostic capacity. The last group is Category C, which encompasses emerging pathogens or agents that have become resistant to medical countermeasures. These agents may cause high morbidity and mortality, and may be easily produced and transmitted.[53]

Biological weapons are unique from other potential WMD, in that the agents themselves are relatively available, as many occur naturally and may be endemic in some parts of the world. The technology to work with these agents has progressed to a point where knowledge is widespread and those with minimal formal education may possess the skills to work with and maliciously use certain agents. Compared to other WMD,

BOX 2-7 Major Biological Threat Agents

Anthrax (*Bacillus anthracis*)
Arenaviruses
Botulism (*Clostridium botulinum* toxin)
Brucellosis (*Brucella* species)
Burkholderia mallei (glanders)
Burkholderia pseudomallei (melioidosis)
Chlamydia psittaci (psittacosis)
Cholera (*Vibrio cholerae*)
E. coli O157:H7 (*Escherichia coli*)
Food safety threats (e.g., *Salmonella* species, *E. coli* O157:H7, and *Shigella*)
Q fever (*Coxiella burnetii*)
Ricin toxin
Rickettsia prowazekii (typhus fever)
Salmonella species (salmonellosis)
Shigella (shigellosis)
Smallpox (*Variola major*)
Staphylococcal enterotoxin B
Tularemia (*Francisella tularensis*)
Typhoid fever (*Salmonella typhi*)
Viral encephalitis (alphaviruses, e.g., Venezuelan equine encephalitis (VEE), Eastern equine encephalitis (EEE), and Western equine encephalitis (WEE))
Viral hemorrhagic fevers (filoviruses [e.g., Ebola and Marburg] and arenaviruses [e.g., Lassa and Machupo])
Water safety threats (e.g., *V. cholerae* and *Cryptosporidium parvum*)
Yersinia pestis (plague)
Emerging infectious diseases such as Zika, Nipah virus, and hantavirus.

Modified from Centers for Disease Control and Prevention. Bioterrorism Agents/Diseases—A to Z. *Emergency Preparedness and Response*. 2015. Available at: https://emergency.cdc.gov/agent/agentlist.asp. Accessed April 2017.

biological weapons are inexpensive. While it is extraordinarily complicated to distribute biological weapons through a missile or other munition, other means of dissemination are quite easy (e.g., spraying salad bars or self-infecting and passing to others). Intentional attacks may be very difficult to detect and differentiate from a naturally occurring event, thus allowing for plausible deniability on the part of the offender.

Finally, biological weapons can be extremely lethal. A 1993 study by the now defunct Congressional Office of Technology Assessment (OTA) concluded that a crop duster plane flying over Washington, DC, and disseminating 100 kg of anthrax powder had the potential to be more deadly than a 1-megaton hydrogen bomb (**FIGURE 2-11**). An earlier study by the WHO using a similar scenario of a line source dissemination of agent from an airplane also demonstrates the large-scale morbidity and mortality that can result from the intentional release of a biological weapon (**TABLE 2-2**).

The Biological Threat

In December 2008, the Commission on the Prevention of Weapons of Mass Destruction Proliferation and Terrorism released the *World at Risk* report, in which they concluded there will likely be a biological attack some place in the world within the next 5 years and biological weapons are to be considered a threat of primary importance to the United States.[54]

Obviously, there was no large scale biological attack between 2008 and 2013, but the fear of an event has not lessoned. In 2017, Bill Gates delivered a speech in Munich, Germany, warning,

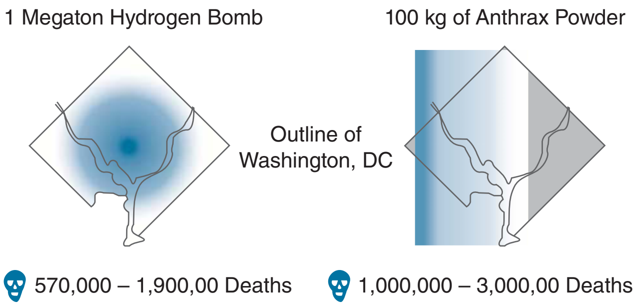


FIGURE 2-11 Lethality of anthrax compared to a nuclear weapon. A 1993 study by the Congressional Office of Technology Assessment

Reproduced from U.S. Congress, Office of Technology Assessment. *Proliferation of Weapons of Mass Destruction: Assessing the Risk*. 1993. OTA-ISC-559. 53–54. Available at: http://www.au.af.mil/au/awc/awcgate/ota/9341.pdf. Accessed April 2017.

TABLE 2-2 WHO (1970) Analysis of Morbidity and Mortality that Would Result from an Airplane Release of 50 kg of Agent Along a 2-km Line Upwind of a Population Center of 500,000

Agent	Downwind Reach (km)	Casualties	Dead
Rift Valley fever	1	35,000	400
Tick-borne encephalitis	1	35,000	9,500
Typhus	5	85,000	19,000
Brucellosis	10	100,000	500
Q fever	>20	125,000	150
Tularemia	>20	125,000	30,000
Anthrax	>>20	125,000	95,000

Data from World Health Organization. Estimated Possible Primary Effects of Limited (Single Bomber). *Health Aspects of Chemical and Biological Weapons*. 1970. p 98. Available at: http://apps.who.int/iris/bitstream/10665/39444/1/24039.pdf. Accessed April 2017.

> Whether it occurs by a quirk of nature or at the hand of a terrorist, epidemiologists say a fast-moving airborne pathogen could kill more than 30 million people in less than a year. And they say there is a reasonable probability the world will experience such an outbreak in the next 10–15 years.[55]

And a bipartisan working group, The Blue Ribbon Study Panel on Biodefense, wrote, "We have reached a critical mass of biological crises. Myriad biological threats, vulnerabilities, and consequences have collectively and dramatically increased the risk to the Nation."[56] So while the massive biological event predicted in 2008 has not materialized, it is clear that the threat has not diminished.

The threat of a biological weapons attack derives from multiple sources. An attack may be carried out by a lone actor, a terrorist group, an organization, or from a state-sponsored program. At one point in time, there were probably a dozen nations that sponsored offensive biological weapons programs. Fewer programs exist today,[57] but the agents created and knowledge gained from state-sponsored offensive programs have become a threat unto itself, as terrorist organizations lure scientists with financial and other incentives. For example, the former Soviet Union had an extensive offensive biological weapons program, spanning the military, the Komitet Gosudarstvennoy Bezopasnosti (KGB), and civilian sectors. In the civilian program, called Biopreparat, there were up to 40,000 scientists and technicians, all working on biological weapons research and production.[58] This program was inherited by Russia after the fall of the Soviet Union, although in 1992, President Boris Yeltsin promised to terminate the program. While much effort and money has gone toward redirecting former weapons scientists into more peaceful lines of work, it is unclear whether all of the scientists involved in the program, or the material they worked with, are accounted for. Thus, the threat of knowledge and agents moving to other nations or terrorist organizations remains.

Terrorist organizations also present a significant threat that biological weapons will be used. As previously mentioned, the Rajneeshee cult successfully engaged in bioterrorism, as did Aum Shinrikyo. In addition to the sarin gas attack, Aum Shinrikyo had attempted to use biological weapons, but was unsuccessful in causing any injuries (they used a vaccine strain of the agent that would not cause disease and utilized inefficient dissemination mechanisms). When police raided their compound after the sarin attack, they found cultures of anthrax, botulism, and spray tanks.[59]

Al Qaeda has yet to use biological weapons, but expressed interest in this means of terrorism. The United States found a facility in Afghanistan that had been used by Al Qaeda, possibly to experiment with or eventually produce a biological weapon. At this location, called Tarnak Farms, several documents were found, including notes about where to acquire seed cultures, and analyses of the potential casualties from different agents. In addition to Al Qaeda, at least 11 other terrorist organizations have at least expressed interest in using biological weapons.[60] Current terrorist organizations, including the Islamic State, have expressed interest, but at the time of this writing, had not used biological weapons.[61]

Overall, the current threat posed by biological weapons has increased significantly in the past decade. The potential consequences of an attack would go beyond population morbidity and mortality and could include such disruptions as a slow down or shut down of international travel and trade, economic shocks, potential civil disorder, public panic or confusion, and national or regional instability.

This text examines the role of the public health community in addressing these threats and some of the challenges faced. Multiple sectors of society must work together to effectively prevent, prepare for, and manage the consequences of an attack, but the core of any effective detection and response capacity is public health. It is the public health community that can identify an event through population surveillance and clinical reporting. The public health community is central in mounting a response that treats those who are ill, protects those who may have been exposed, addresses immediate and long-term health consequences, and reconstitutes the infrastructure after the event has occurred.

Key Words

Accidental exposures
Biological weapons
Bioterrorism
Chemical weapons
Deliberate use
Intentional use
Radiological weapons
Toxins

Discussion Questions

1. Do you believe there will be a biological attack in the next 5 years? Why or why not?
2. What role would the public health community play if a radiological weapon was dispersed in a major metropolitan area?
3. Do you believe the public health community is prepared to address the threats from WMD? If not, what would you do to remedy the situation and what information do you think would be important for public health professionals to know?
4. How should public health professionals communicate with security officials to be kept aware of the latest threats? Is that an appropriate role for public health?

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