Chapter 6

Biowarfare, Bioterrorism, and Animal Diseases as Bioweapons

"BW [biological warfare] is a special weapon, with implications for civility of life that set it apart from many other kinds of violence."

"...the intentional release of an infectious particle, be it a virus or bacterium, from the confines of a laboratory or medical practice must be formally condemned as an irresponsible threat against the whole human community." (Lederberg)[1]

Photo by Milton Friend

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Bolded words within the text indicate terms that are defined in the Glossary.

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"The study of germs offers so many connections with the diseases of animals and plants, that it certainly constitutes a first step in the …serious investigation of putrid and contagious diseases." (Pasteur)[2]

Linkages between disease in humans and the maladies of animals continue to be a focus for those concerned with disease effects on human health. References to animal diseases, particularly zoonoses such as rabies and glanders, are found in the writings of Greek (Hippocrates, Democritus, Aristotle, Galen, Dioscorides), Byzantine (Oribasius, Actius of Amida), and Roman (Pliny the Elder, Celsus) physicians and naturalists.[3] Also, early advances in disease knowledge were closely associated with the study of **contagions** in animals to the extent that "The most complete ancient accounts of the concepts of **contagion** and contamination are found in treatises on veterinary medicine."[4,5]

Opportunities for disease transfer between animals and humans have increased during modern times, partly because of advances in animal husbandry and intensive agriculture that result in increased contacts among humans, domestic animals, and wildlife. Infectious pathogens exploit these contacts, and must be considered in this era of increased world tensions and international terrorism (Fig. 6.1).

Disease emergence and resurgence are generally associated with natural processes and unanticipated outcomes related to human behavior and actions. That perspective has been broadened by recent acts of bioterrorism. A new category of deliberately emerging diseases contains emerging microbes that are developed by humans, usually for nefarious use.[211] Included are naturally occurring microbial agents and those altered by bioengineering.

This chapter highlights the wildlife component of the pathogen-host-environment triad to focus attention on the potential for bioterrorists to use wildlife as a means for infectious disease attacks against society. The value of this focus is that the underlying causes of disease emergence and the optimal prevention or control response frequently differ for disease emergence, resurgence, and deliberately emerging diseases.[211] Differences also exist relative to the potential importance of wildlife as a component of biowarfare and as a component of bioterrorism activities.

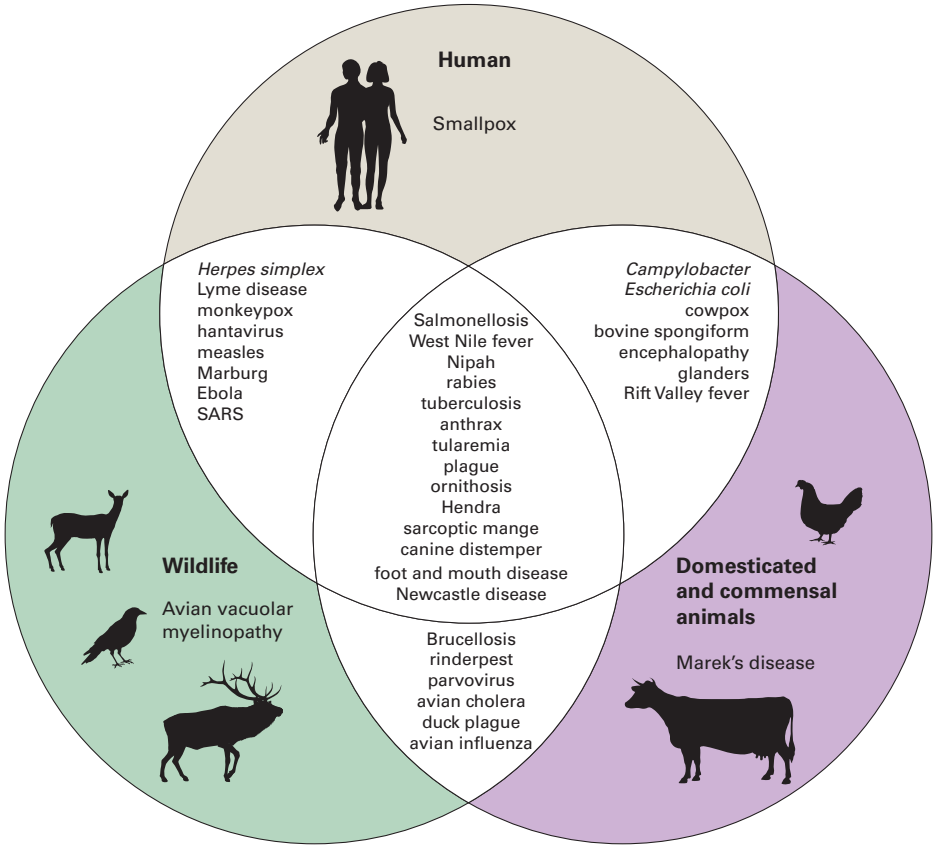


Figure 6.1 Examples of linkages between important infectious diseases of wildlife, domestic animals, and humans. (Modified from Dudley and Woodford[41]).

Between 1936 and 1980, more than 100 definitions for terrorism were coined.[110] Within the USA, two official definitions of terrorism have been used since the early 1980s; the Department of State uses one for accounting purposes (statistical and analytical endpoints), and the U.S. Congress uses the other for criminal proceedings ("act of terrorism").[57] The context of bioterrorism within this chapter follows a recent definition in the scientific literature and is separated from biowarfare on the basis of the latter involving a declaration of war or the perception of war being waged between nations as evidenced by an appropriate level of hostile actions between nations. Keeping that distinction in mind, "Bioterrorism is the intentional use of microorganisms or toxins derived from living organisms to cause death or disease in humans, animals, or plants on which we depend."[77]

Past Biowarfare and Bioterrorism

"A man may imagine things that are false, but he can only understand things that are true." (Isaac Newton)[2]

The ravages of naturally occurring disease documented throughout history[2,6–11] substantiate infectious disease use as potential weapons among enemies. In fact, biological warfare was used in varying degrees well before the germ theory for disease was first proposed in 1530,[12] demonstrating that infectious disease used as weapons against humans and animals is not a new concept.[13–16]

Plague and Smallpox as Bioweapons

The 1346 Siege of Caffa (also spelled Kaffa, which is now Feodosija, Ukraine) involved the most gruesome and crudest example of biological warfare when the Mongol army catapulted plague-infected cadavers into the besieged city. "Mountains of dead were thrown into the city," infecting the inhabitants and resulting in many deaths from the Black Death (plague). However, plague also devastated the Mongols attacking the city and the infected cadavers did not alter the outcome of the siege. Furthermore, fleeing survivors were not a major factor in plague spreading from Caffa to the Mediterranean Basin because of other factors contributing to the plague epidemic.[16,17]

Plague is a zoonotic disease caused by the bacterium *Yersinia pestis,* typically harbored by wild rodents (Fig. 6.2). The plague epidemic that swept through Europe, the Near East, and North Africa in the mid-14th century was probably the greatest public health disaster in recorded history. An estimated one-quarter to one-third of Europe's population died from plague during the 14th century **pandemic,** and North Africa, the Near East, and perhaps the Far East had similar high levels of mortality.[16,18] However, the first recorded plague pandemic began in 541 in Egypt when the world population was considerably smaller and decimated an even greater percentage of the population. This pandemic swept across Europe and parts of Asia; between 50 and 60 percent of the human population died in many areas.[19,20]

Given the explosive nature and history of disease spread over wide areas, plague could be a dangerously effective biological weapon[18,20, 21] and nations pursuing bioweapons development have often focused on this agent. During World War II (WWII), Japan successfully initiated plague epidemics in China by releasing as many as 15 million laboratory-infected fleas per attack from aircraft over Chinese cities.[22,23] Nevertheless, the complexity of biological factors involved in plague transmission results in fleas being unreliable as a delivery system for **biowarfare**.

Early in the history of the Black Death, the original bubonic-flea-borne variety of plague evolved to the far more contagious pneumonic variety as a cause of human epidemics.[1] Direct human exposure by **aerosolized** plague bacilli is the most effective way to cause human illness and death;[19,24,25] the biological weapons programs of the USA and the former Soviet Union have pursued aerosol transmission capabilities for plague.[19,26,27] The Soviets had intercontinental ballistic missile warheads containing plague bacilli available for launch before 1985.[28] Yet, virtually insurmountable problems arose in the production and aerosol dispersal of substantial quantities of plague organisms by modern weapon systems.[29] Despite these difficulties, plague is viewed as a high-risk disease for bioweapons.[32]

Smallpox also has intentionally been used against humans. Unlike plague, smallpox is strictly a disease of humans; it is not zoonotic (Fig. 6.3).[30] In 1763, during the Pontiac Rebellion (Indian Wars) in North America, contaminated blankets and a handkerchief from a smallpox hospital were given as gifts by British forces to Native Americans. This Trojan horse approach introduced the smallpox virus into the tribes and caused major casualties.[17,22,31] Capabilities for aerosol exposure of humans to smallpox exist, while access to the virus remains tightly controlled following global eradication of this disease during the 1970s. World Health Assembly resolution WHA 52.10 called for the destruction of all remaining stocks of the smallpox virus by the end of 2002, but further evaluation by the World Health Organization concluded that live virus was needed for specific scientific purposes. That position was supported by the World Health Assembly.[208] Virus stocks are maintained for that purpose in the USA and Russia under international oversight.

Other Applications of Bioweapons Targeting Humans

Numerous reports of using disease as a **bioweapon** during times of war exist, but few can be confirmed from available records. For various reasons, information about the use of these weapons and their consequences often are unavailable. From 1932 through WWII, Japan clearly had the most aggressive biological warfare program ever applied at the field level.[14,23] This program resulted in the estimated deaths of at least 10,000 people in laboratory experiments (prisoners

of war) and as many as several hundred thousand others in military field operations. Zoonotic diseases employed at the field level included typhus, paratyphus, cholera, salmonellosis, plague, anthrax, typhoid fever, glanders, and dysentery (probably *Shigella* sp.).[23,33] A comprehensive historical account of these covert operations, which have been referred to by author James Bradley as "One of mankind's biggest yet least known crimes," is provided in the book *Factories of Death*.[23]

Prior to WWII, biological warfare did not have deadly consequences because of inadequacy of development programs.[14] Nevertheless, the extent of biological warfare in medieval and Renaissance times, during early North American settlement, and during WWI was probably greater than recognized[17,34] (Table 6.1). Biological weapons also have been used against animal and food resources (see Animal Disease and Bioterrorism section).

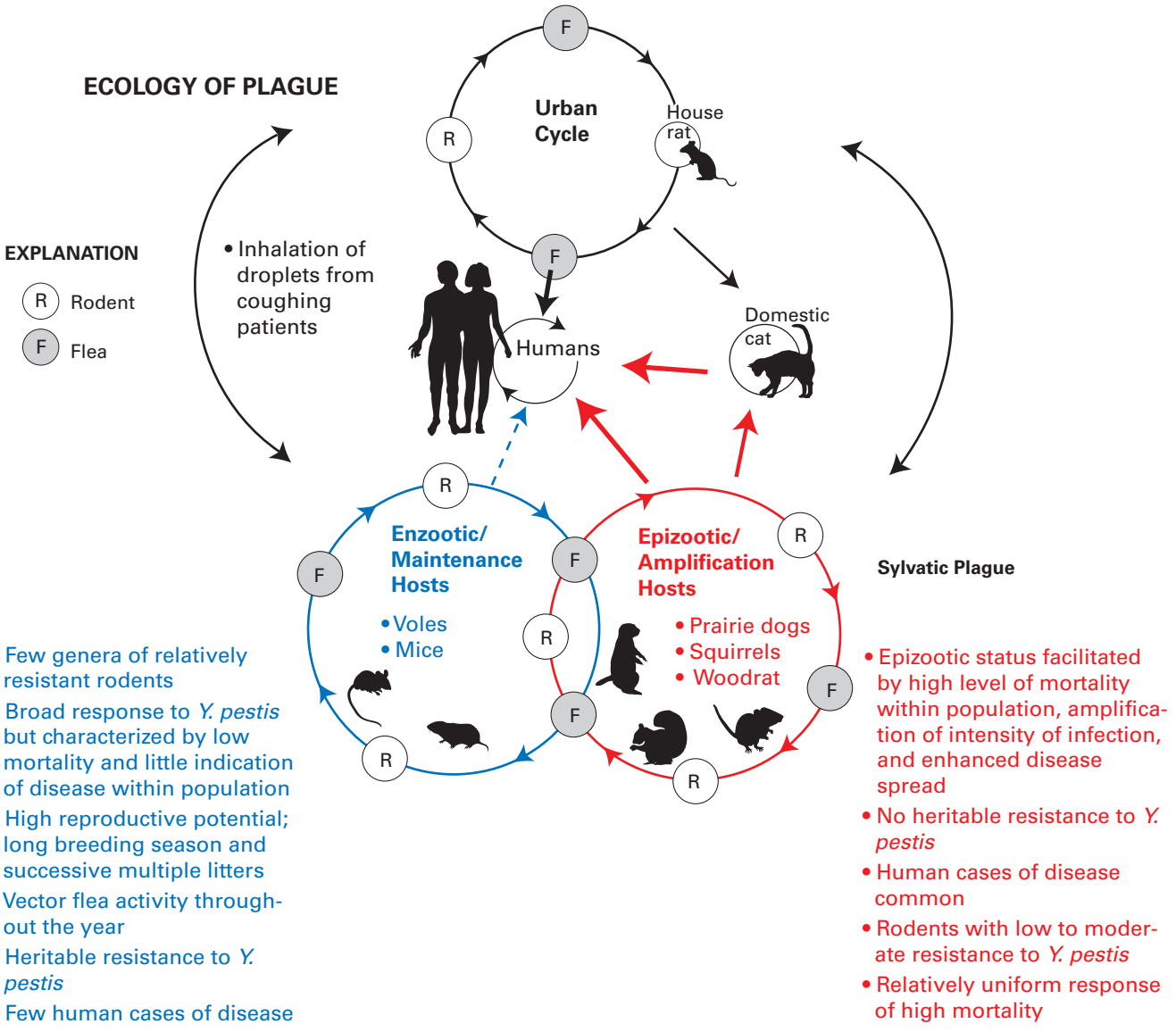


Figure 6.2 General ecology of plague (*Yersinia pestis*). (Developed from Butler,[202] Gasper and Watson[203]).

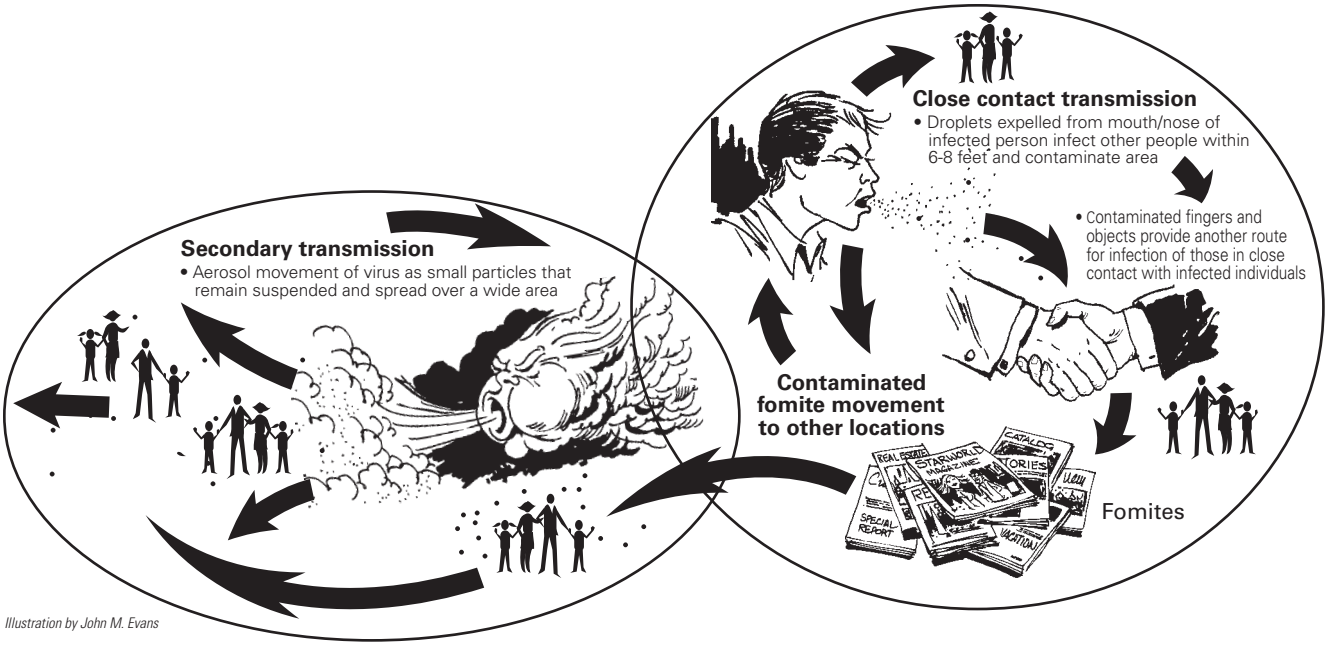


Figure 6.3 Smallpox, a person-to-person and person-to-fomite-to-person disease (developed from Fenner et al.[30]).

Present Biowarfare and Bioterrorism

> **"In my opinion biological agents, along with death rays, sonic beams, neutron bombs and so on, belong more to the realms of science fiction than to practical warfare. But my opinion is not widely shared and the fount [supply] of human imbecility seems inexhaustible,..."[35]**

The increased threat to society from bioterrorism that ushered in the 21st century within the USA was a growing concern during the 1990s.[36–40] That concern was based on increases in terrorist incidents taking place globally, disclosures of major covert bioweapon development in the former Soviet Union and Iraq, and evaluations that indicated a shift in terrorist motivations. Primary motivations from 1975 to 1989 were protests against government policies. Since 1990, the primary motivations include retaliation or revenge and the pursuit of nationalist or separatist objectives.[28,40]

Concerns about increased risks from terrorism were expressed in prophetic statements such as, "Many experts agree that it's just a matter of time until the United States or another country suffers a significant bioterrorist attack."[36,41] Primary concerns raised at that time focused on the inadequacy of USA preparedness and infrastructure to respond to an attack in which infectious disease agents were the weapons.[1,42] Indeed, from October 30 through December 23, 1998, the Centers for Disease Control and Prevention (CDC) received reports of a series of threats involving anthrax-laced letters being sent though the mail. All were investigated and found to be hoaxes. Nevertheless, the CDC issued interim guidance for response to such threats becoming reality.[43] Those hoaxes followed the highly publicized arrest of a microbiologist linked to a white-supremacist group who had threatened to use military-grade anthrax in attacks against the government.[40]

In 2001, the Johns Hopkins Center for Civil Biodefense Strategies further raised attention to the dangers of microbial terrorism by staging a mock smallpox attack within the USA called "Dark Winter," which illustrated a major need for better preparation[44] as did TOPOFF, a mock plague outbreak held in 2000.[27] Concerns in the USA about terrorism and the level of preparedness became reality with the infamous events of September 11, 2001, and the subsequent anthrax attacks through the U.S. mail system.[45,46]

The anthrax letter attacks of 2001 generated great terror among the public,[27,47–49] reemphasized that the USA population is not immune from terrorist attacks with biologic agents,[50] and, despite the previous anthrax threats and letter hoaxes,[40,43] emphasized that the greatest threats from bioterrorism will likely involve something never before seen as an application.[51] Although the potential for biowarfare remains a concern and **disarmament** efforts by the international community continue,[52–54] the threat of bioterrorism is now of greater concern in the USA and in many other nations[55,56] (Box 6–1).

Biowarfare versus Bioterrorism

Biological weapons are considered to be weapons of mass destruction or, more appropriately, weapons of mass casualty. "Because they are invisible, silent, odorless, and tasteless, biological agents may be used as an ultimate weapon—easy to disperse and inexpensive to produce."[67] The international

Table 6.1 Examples of infectious agents applied as weapons during wartime prior to 1970 (developed from Christopher et al.[22] with additions).[a]

Agent	Agent/disease characteristics				Bioweapons use						
					Targeted species		Geographic area events				Era[c]
	Type	Disease	Zoonoses	Animal reservoirs[b]	Humans	Animals	Europe	Asia	USA	South America	
Yersinia pestis	Bacteria	Plague	●	Small rodents	●	○	●	●	○	○	14th century; WWII
Bacillus anthracis	Bacteria	Anthrax	●	Livestock, herbivorous wildlife	○	●	●	○	●	●	WWI
Burkholderia mallei	Bacteria	Glanders	●	Horses, mules, donkeys, camels	○	●	●	○	●	●	WWI
Vibrio cholerae[d]	Bacteria	Cholera	●	Zooplankton	●	○	○	●	○	○	WWII
Salmonella spp.	Bacteria	Salmonellosis	●	Many, depends on *Salmonella* spp.	●	○	○	●	○	○	WWII
Francisella tularensis	Bacteria	Tularemia	●	Rabbits, voles	●	○	●	○	○	○	WWII[e]
Shigella spp.	Bacteria	Shigellosis	○	None	●	○	○	●	○	○	WWII
Variola major	Virus	Smallpox	○	None	●	○	○	○	●	○	1754–1767

[a] Numerous other disease agents were evaluated and some pursued for bioweapons by the USA, Iraq, USSR, and others. Reported wartime use of infectious agents has essentially been limited to the pathogens listed with the exceptions of experiments conducted and diseased animal carcasses and sewage intentionally used to contaminate human drinking water supplies.

[b] Primary species for disease maintenance between periods of natural outbreaks; also species associated with outbreaks.

[c] WWI= World War I; WWII=World War II; 1754–1767=French and Indian War; 14th century= Siege of Caffa (Kaffa).

[d] Cholera is typically a waterborne and foodborne disease involving their contamination by the bacteria; the disease does not rely on animal hosts other than zooplankton, but a wildlife component, such as contaminated shellfish, can be involved in disease transmission.

[e] Debate remains whether massive outbreaks of tularemia on the Eastern Front was a biowarfare application against German troops or occurred naturally.

●= positive; ○= negative

Box 6–1 See No Evil, Hear No Evil, Speak No Evil

"Russia has…never developed, produced, accumulated, or stored biological weapons."—Address by Grigory Berdennikov, head of Russian delegation to a November 1996 conference of signatories to the 1972 Biological Weapons Convention[26]

Catastrophic events often result in basic questions being asked. Why did this happen? Could this have been prevented? Should we have been better prepared? These and other questions clearly apply to bioterrorism. Inadequate levels of preparedness are in part reflections of problem denial and other priorities within national policy circles, and the belief that open dialogue in this subject area should be avoided so that potential perpetrators would not be enticed to pursue such actions.[32] In essence, past approaches to the issues of bioterrorism have generally followed the first two components of the adage "See No Evil, Hear No Evil, Speak No Evil;" while at the same time, some nations were undertaking the development of biological weapons for defensive purposes.

Microbes as Weapons

Biological weapons, or bioweapons, are those containing replicating microorganisms (viruses, fungi, and bacteria, including chlamydia and rickettsia), prions, protozoa, or poisonous chemical toxins produced by living organisms (e.g., botulinum toxin, cobra venom, and the plant toxin, ricin).[139] Depending on the pathogen being used, these weapons may be employed against humans, animals, or crops.[110,140] In some instances, multiple species groups

Table A. Examples of current publications dealing with biowarfare and/or bioterrorism.[a]

Title	Content
Biological and Toxin Weapons: Research, Development and Use from the Middle Ages to 1945 [14]	Publication title indicates content.
Bioterrorism and Public Health: An Internet Resource Guide[204]	An Internet resource guide to a wide range of Web-based resources; basic information also included as text.
PDR Guide to Biological and Chemical Warfare Response[205]	Signs, symptoms, and recommended treatments for over 50 biological and chemical agents.
Bioterrorism: Guidelines for Medical and Public Health Management[49]	Compilations of consensus statements from the Working Group on Civilian Biodefense, anthrax case reports, and intervention analysis.
When Every Moment Counts: What You Need to Know About Bioterrorism from the Senate's Only Doctor[27]	Questions and answers about anthrax, smallpox, plague, botulism, tularemia, Ebola, other viral hemorrhagic fevers, and other relevant subject areas.
Terrorism and Public Health: a Balanced Approach to Strengthening Systems and Protecting People[177]	Organized under main subject areas of The Public Health Response to September 11 and Its Aftermath, Terrorist Weapons, Challenges and Opportunities.
Factories of Death: Japanese Biological Warfare, 1932–1945, and the American Cover-up[23]	Comprehensive account of the Japanese biological warfare program (experimental and field applications) from 1932–1945.
Biohazard: the Chilling True Story of the Largest Covert Biological Weapons Program in the World, Told from the Inside by the Man Who Ran it[26]	Personal account of the biological weapons program of the former USSR by the leader of that program.
Secret Agents: The Menace of Emerging Infections[206]	Primary focus is on the emergence of infectious disease but contains a major chapter on the evolution of bioterrorism.

[a] These examples are not considered of greater value than other publications in this subject area.

(e.g., animals and humans) may be affected. The use of such weapons by a nation against other nations and by insurgents within nations is generally referred to as biowarfare, while the use of these weapons for terrorist activities is generally referred to as bioterrorism. The distinction between these terms is not always clear and can be a subject for legal debate, when charges are pressed against those involved with using bioweapons.

Myths vs. Reality

During the 1980s and late 1990s,[32,141] many held the false impression that bioterrorism events were unlikely. The attacks on the USA during September and October 2001 elevated society's awareness of vulnerability to terrorist attack and the use of biological weapons.

The Fear Factor

The concept of "weapons of mass destruction" has evolved technologically over time and is now seen as a great threat to society. The agents posing the greatest hazard are microbes of antiquity, rather than nuclear or chemical weapons,[32,141] with these types of weapons gaining prominence in people's conversations, anxieties, and fears.

Bioterrorists exploit the fear factor through use of bioweapons,[12,47,142] which the USA and other countries are least prepared to address.[29,143] Prior to September 11, 2001, the most common vision of a biological attack was that of a pathogen-laden aerosol being dispersed over the landscape delivered by missile, "dirty bomb," or other

Table B. Primary factors associated with bioweapons use (developed from Osterholm[15] with adjustments).

Action	Critical factors[a]		
	Potential perpetrators	Availability of biologic agents	Technical means for pathogen dissemination
General	Wide variety of individuals and groups; actions taken may be for criminal purposes as well as terrorist or political motivations. For example, animals could be targeted to rid an area of unwanted species or to impose economic losses on a business competitor.	Ideal agents are inexpensive; easy to produce; can be aerosolized; are resistant to sunlight, heat, and drying; cause lethal or disabling disease; can be transmitted person-to-person; and cannot be effectively treated.[b]	Pathogen entry into the body can occur by several means including inhalation (aerosol), ingestion (oral), injection (bites and through abrasions following direct contact), and absorption (dermal).[c]
Biowarfare	Government action against other governments; insurgents within nations against their own governments.	Stockpiles exist in a number of nations despite disarmament efforts. Iraq's biological weapons program had produced considerable quantities of botulinum toxin, anthrax, and at least two other pathogens.[71] The weapons program of the former USSR produced tons of anthrax, smallpox, and other organisms.[26,28,45] The USA program was also productive.[22]	By the late 1960s the USA program had weaponized three lethal and four incapacitating agents of viral and bacterial (including rickettsial) origin. Stockpiles of these agents were destroyed between 1971–1973.[22] The technology to deliver biological agents as weapons of war developed by the USA, the Soviets, and others has not been lost and has been improved on since the 1970s.
Bioterrorism	Individuals, cults, nonaligned groups.	Many naturally occurring pathogens that could be used as well as the potential for obtaining pathogens being worked with in various laboratories. Relatively inexpensive to obtain agents capable of causing moderate disease outbreaks.[45]	Biological weapons suitable for terrorist attacks are easy to produce, conceal, and transport. Elaborate "weaponization" is not needed for attacks to cause considerable damage.[45]

[a] All three factors must be fully satisfied for a viable attack to occur.

[b] Context is for human disease; other desirable attributes include the ability to affect other species in addition to humans (zoonoses) and to be maintained in nature as a self-sustaining disease.

[c] Not all pathogens can enter by all means; inhalation and ingestion are common routes for many pathogens; bites by infected arthropods is the primary route for many others; a small number can be absorbed through the skin (dermal exposure).

means.[15,144] This vision arises from development of bioweapons programs around the world that project casualties from aerosol deployment of these weapons.[19,24,29,58,145]

The bioterrorist attacks prior to the 21st century were generally amateurish in design, received limited publicity, and did not greatly elevate public concerns.[146] However, the terrorist actions against the USA on September 11, 2001, and the anthrax letter attacks of October 2001 rapidly reshaped public psyche towards bioterrorism. Government agencies began to recognize that terrorist activities had the potential for turning pathogens into contemporary weapons beyond aerosolization. CDC Epidemic Intelligence Service investigators noted that,

> "Viewing the bioterrorist's preferred weapon as a high-threat, aerosolizable infectious agent that may cause immediate, widespread outbreaks may mislead preparedness efforts."[77]

The CDC's message is meant not to disregard pathogens as weapons, but to warn the Nation and the world to better prepare for biological weapon application beyond aerosolization.

Combating Ignorance

Recently, a profusion of books (Table A) and other sources for information about bioterrorism and pathogens as bioweapons have been published. These sources contain a great deal of factual information that can help people gain knowledge about bioterrorism and bioweapons, and increase their understanding of relative risks posed by various pathogens, their potential application as bioweapons, and appropriate responses in the event of exposure. Because "terrorism feeds on fear, and fear feeds on ignorance,"[104] such knowledge helps combat terrorism.

Reality Check

Biowarfare and bioterrorism share the same three critical elements necessary for an event to occur: (1) potential perpetrators; (2) availability of biologic agents; and (3) technical means for dissemination.[15] Yet, the potential for bioterrorism grew, while that for biowarfare diminished (Table B). The concept of microbes as "weapons of mass destruction," is more a biowarfare than a bioterrorism issue, because terrorists are limited by high costs and limited availability of sophisticated bioweapons systems. Terrorists are less likely to access pathogens with enhanced virulence or resistance to treatment because of greater laboratory security in existence today. They are also less likely to locate amounts of disease agents able to be delivered by wartime weapon deployment. In addition, terrorists may attack less strategic sites, because access to more desirable sites that could be struck by military weapon systems may be difficult.

The terrorist events against the USA during 2001 have served as a general "wake-up call" for society. In addition to human deaths, collateral impacts involving fiscal costs and alterations in activities and services caused mass disruption of society. Today there are not only more choices of terrorist weapons,[29,78,143] but also increasing numbers of people willing to carry out terrorists activities, even at the cost of their own lives.[57,73] Therefore, combating enhanced threats requires greater vigilance so that we can "see and hear the evil" and respond to it before others can "do evil" to us.

community experiencing the ravages from chemical weapons during WWI, banned their proliferation and use. Biological warfare was partially incorporated within the diplomatic efforts leading to the 1925 Geneva Convention (Geneva Protocol for the Prohibition of the Use in War of Asphyxiating, Poisonous or Other Gases, and of Bacteriological Methods of Warfare).[22,68] In 1972, the Convention on the Prohibition of the Development, Production, and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Distribution (BWC) was signed by more than 100 nations, was ratified, and went into effect in 1975.[69] Those and subsequent actions by the international community have diminished, but not eliminated, the threat of these types of weapons.

A difficulty with the BWC is that it is largely an agreement based on trust; there are inadequate oversight activities to monitor compliance.[53,70] Major transgressions among signatory parties to the BWC included strategic weapons development by the former Soviet Union, Iraq, and others.[22,31,71] These transgressions are ominous deviations from beliefs of Vannevar Bush (cited by Lederberg[70]): "Without a shadow of a doubt there is something in man's make-up that causes him to hesitate when at the point of bringing war to his enemy by poisoning him or his cattle and crops or spreading disease. Even Hitler drew back from this. Whether it is because of some old taboo ingrained into the fiber of the race…. The human race shrinks and draws back when the subject is broached. It always has, and it probably always will."[72] Some limited use of biological and chemical weapons has occurred since these statements by Vannevar Bush. Nevertheless, in recent times, countries that possess such weapons are reluctant to use them, many countries are abandoning these weapon programs, and most who possess stockpiled biological weapons are destroying them. However, global increases in terrorism have resulted in an increased potential for infectious diseases to become common weapons (Table 6.2).[73] A virtual cornucopia of pathogens exist that could potentially be used for terrorist activities. Many of these biological agents are readily available, and bioterrorists need not have

sophisticated knowledge or expensive technology as the following examples demonstrate.

In Oregon (USA) in 1984, the Rajneeshee cult intentionally contaminated salad bars at ten restaurants with *Salmonella typhimurium* as a trial run for another planned action intended to disrupt local voter turnout for an election. More than 750 cases of enteritis and 45 hospitalizations resulted from the salad bar incidents.[22,74] The cult's attempted *Salmonella* contamination of a city water supply was a failure.[75]

In 1996, a Texas (USA) hospital laboratory worker intentionally contaminated pastries with a strain of *Shigella dysenteriae* stolen from the laboratory. He then left those pastries in a break room where they were eaten by coworkers who became ill.[76] The following year, an incident of possibly intentional contamination by the use of *Shigella sonnei* occurred among workers in a hospital laboratory in New Hampshire, USA.[77]

Other attacks likely have taken place that were unsuccessful or have not been identified as acts of bioterrorism. It was more than a year after the Oregon salad bar events that intentional contamination was determined to be the cause.[78] Failed attempts to employ biological agents in acts of terrorism by the Aum Shinrikyo cult also did not become known until later. This cult was responsible for the 1995 chemical

Bioweapons and Human Impacts

Biowarfare programs seek to "inflict sufficiently severe disease to paralyze a city and perhaps a nation."[32] However, only a few of the thousands of biological agents capable of causing disease in humans are suitable pathogens for this purpose.[29,32] To be effective, bioterrorism does not need to achieve the level of impact sought by biowarfare programs. Bioterrorism impacts humans through fear as well as through disease and death, thereby exploiting pathogens as weapons for mass disruption. Bioweapons are unsurpassed by any other weapon relative to effectiveness and usability because they satisfy all of the following attributes required for effective weapons.[15]

Attribute	Practicality
Within the economic and practical means of the perpetrator(s)	"Biological weapons are relatively inexpensive, easy to produce, conceal and transport, and can cause considerable damage."[45] "Only modest microbiologic skills are needed to produce and effectively use biologic weapons. The greatest, but not insurmountable, hurdle in such an endeavor may be gaining access to a virulent strain of the desired agent."[58]
Capable of reaching the intended target	Great arrays of delivery systems are available from hand-carried and applied introductions to deployment through munitions for the release of infectious agents and biological toxins.
Cause limited collateral damage, in particular to those staging the attack	Self-protection can be gained through immunizations for some diseases and other appropriate steps taken during the preparation, transport, and discharge of the pathogen. Many terrorists often are willing to die for their cause so personal exposure may not be a major issue. Because occupation of territory may not be a near-term goal, residual disease and secondary impacts also may not be of concern.
Must result in the desired outcome, usually death	Selection of appropriate pathogens results in high probability for the outcome to infect at least some of the population.

The above characteristics reflect the criteria developed in 1999 by a group of infectious disease, public health, intelligence experts, and law enforcement officials who met to evaluate the potential impacts from pathogens if used in terrorist attacks (see Tables 6.3–6.5).

The criteria used for their evaluations were: "1) public health impact based on illness and death; 2) delivery potential to large populations based on stability of the agent, ability to mass produce and distribute a virulent agent, and potential for person-to-person transmission of the agent; 3) public perception as related to public fear and potential civil disruption; and 4) special public health preparedness needs based on stockpile requirements, enhanced surveillance, or diagnostic needs…." That evaluation was oriented for large-scale attacks because public health agencies must be able to cope with worse-case scenarios, even though small-scale bioterrorism events may be more likely.[59]

Table 6.2 Examples of disease transfer between wild and domestic species (adapted from Bengis et al.[64] with additions).

Disease	Causative agent	Agent type	Original maintenance host	New hosts	Epizootic potential	Comments
Rinderpest	Morbillivirus	Virus	Cattle	Wild artiodactyls (hoofed-mammals, e.g., antelope)	Major	Infected cattle from India initiated major pandemic of 1889–1905 in sub-Saharan Africa. Now a major disease of livestock and wildlife in that region.
Bovine tuberculosis	*Mycobacterium bovis*	Bacteria	Cattle	Bison, buffalo, deer, many other species.	Moderate	Probably introduced into Africa with imported dairy and beef cattle during the colonial era. Wildlife reservoirs in other countries also likely to have acquired infections from livestock (deer in USA, badger in UK, brush-tailed possums in New Zealand).
Canine distemper	Morbillivirus	Virus	Domestic dog	Wild dog, lion, jackals, hyenas, seals	Moderate	Introduced into Africa with domestic dogs; dogs are thought to be source of recent epizootics in seals in the Caspian Sea and in Lake Bikal, Russia.
African swine fever	Asfarvirus	Virus	Wild porcines	Domestic swine	Major	Introduced into Portugal in the early 1960s and spread throughout much of Europe before being eradicated in domestic pigs from most of this area.
African horse sickness	Orbivirus	Virus	Zebras	Horses, donkeys	Moderate	Spread from sub-Saharan Africa to Middle East and Iberian Peninsula; appears to be related to importation of zebra from Namibia.
Avian cholera	*Pasteurella multocida*	Bacteria	Poultry	Wild waterfowl	Major	Most likely brought into North America with poultry brought from Europe during colonial days; first appearances in wild waterfowl in USA in 1944 appeared to be spill-over events from epizootics in chickens; has become the most important infectious disease of wild birds.[173]
Duck plague	Herpesvirus	Virus	Domestic ducks	Wild waterfowl	Moderate	First North American appearance in 1967 as epizootic in Long Island, New York (USA) white Pekin duck industry. Now established in USA in wild and feral species of waterfowl in some geographic areas.[174]
Newcastle disease	Paramyxovirus	Virus	Poultry	Wild birds	Major	First arose sometime prior to 1926 in Indonesia (first event) and in 1926 in the UK as a new disease of poultry.[175] Eradicated from the USA and Canada (lethal strains) by early 1970s; became established in cormorants in these areas since 1990.[176]

attack (Sarin) of the Tokyo subway system, and used anthrax bacteria (*Bacillus anthracis*) and botulism toxin during three unsuccessful attacks in Japan.[79–81] Although unsuccessful, their 1993 spraying of *B. anthracis* from the roof of an eight-story building in Tokyo was the first documented instance of bioterrorism with an aerosol containing this pathogen.[81]

A major difference between bioterrorism and biowarfare is that bioterrorism can have a major impact with only small numbers of cases of disease. For example, the previously mentioned October 2001, anthrax-laced mail within the USA caused disease in 22 people[82] and 5 deaths.[83] However, the billions of anthrax spores contained in those letters had the potential to create a major epidemic, including many more deaths. The resulting public fear disrupted people's lives; resulting investigations and responses were costly, and there were extensive disruptions in public services.

Collateral Impacts

The costs from acts of terrorism extend far beyond the direct damage inflicted by the weapons employed. Within the USA, efforts to bolster national defense and response capabilities against further acts of terrorism have included flurries of activity focused on infrastructure enhancement, training, investigations, and associated matters within the public health, biomedical, law enforcement, and intelligence communities. In late 2001, the U.S. Congress created the Department of Homeland Security, and a series of administrative and regulatory actions were set in motion. These and other actions have created new biodefense opportunities and affected traditional scientific, social and other mainstream aspects of life.

Biodefense Spending Boom

Billions of dollars are being allocated to biomedical research to help build a protective shield against infectious diseases and their potential uses by terrorists as bioweapons.[84–87] The construction of biosafety level (BSL)-4 facilities—laboratories where the most hazardous pathogens can be contained and handled—is a major component of increases in biodefense funding. Worldwide, only about five BSL-4 facilities existed between 1970 and 1995. During the 1990s, global threats from emerging infectious diseases made the need for additional BSL-4 and BSL-3 facilities evident (BSL-3 facilities are also high security, but handle slightly less hazardous pathogens than BSL-4).

A veritable building boom for high security infectious disease facilities began during the 1990s and was further stimulated by the events in the fall of 2001.[88] By 2000, the USA had five BSL-4 laboratories and others planned.[89] During 2003, Boston University in Massachusetts (USA), and the University of Texas Medical Branch in Galveston, Texas (USA), were awarded $120 million each in construction grants to initiate construction of BSL-4 facilities. Nine other institutions were awarded grants of $7 million to $21 million to build BSL-2 and BSL-3 laboratories as part of a new system of regional biodefense research centers.[85,86,90]

A record budget increase during 2003 for the National Institutes of Health (NIH) resulted from bioterrorism-directed funding.[91] Other major USA initiatives include the President's requests for "Project BioShield" to develop new treatments and vaccines for potential bioterror agents ($6 billion) and the "BioWatch Initiative" to upgrade and establish 3,000–4,000 pollution-monitoring stations with high-tech sensors (billions of dollars to establish plus annual costs).[92] Vaccine production is another major investment. In 2003, contracts worth more than $770 million were awarded by the U.S. government for the production of smallpox vaccine.[93] Much of the biodefense funding allocated to the biomedical area will enhance the public health infrastructure and the capabilities needed for the battle against emerging infectious diseases.

Pathogens of Concern

"[We are] determined for the sake of all mankind, to exclude completely the possibility of bacteriological agents and toxins being used as weapons; [We are] convinced that such use would be repugnant to the conscience of mankind and that no effort should be spared to minimize this risk..." —Preamble to the Biological and Toxin Weapons Convention, 1972.[26]

Public health and agriculture agencies are guided by listings of pathogens of concern related to their areas of responsibility (Appendix C); these lists include hazardous agents that could be used potentially in bioterrorism. Public health listings are separated into priority levels of A, B, and C, and the pathogens within each level are arranged in priority order (Tables 6.3–6.5). Many of the diseases of concern for human health can also affect domestic animals and wildlife.[60–66] Conversely, several of the 22 diseases of concern for agriculture (Table 6.6) can affect human health. However, there is little duplication between these lists. Anthrax (Table 6.3), ornithosis, and Venezuelan **equine** encephalomyelitis (Table 6.4) are the only diseases shared.

The differences between the lists for human health and agriculture are because domestic animal pathogens are primarily considered from the perspective of economic trade impacts and/or ease of transmissibility. Human pathogens are considered more from the perspective of potential mortality rates and/or public fear of the disease. Although anthrax appeared on the 1952 list of potential animal **bioweapons** it "was assumably dropped from the anti-animal biological weapons agent lists because an effective vaccine had been developed."[110] Smallpox has been eradicated and, theoretically, the virus only exists within the rigid control of repositories in Russia and the USA. Nevertheless, governments have developed smallpox response strategies.

In part, pathogens of concern appearing on various lists reflect the orientation of those developing the lists and the geographic area of coverage. For example, the Office International des Epizooties (OIE) headquartered in Paris previously maintained lists for two levels of animal diseases of concern for international trade involving live animals and animal products (Table 6.7 and 6.8). Several of the list A diseases (Table 6.7) are absent from the USA list of animal diseases (Table 6.6). Also, differences exist between these lists and the agriculture disease list of the Ad Hoc Groups of State Parties to the BWC (Table 6.9). In 2005, the OIE A and B lists were replaced by a single list of diseases notifiable to the OIE, thereby giving all listed diseases the same degree of importance in international trade (http://www.oie.int/eng/Edito/en_edito_apr04.htm). The new list is restricted to livestock and poultry diseases, adds anthrax and some other diseases, but eliminates diseases of **bees** and aquaculture that previously appeared on the B list (http://www.oie.int.eng/maladies/en_classification.htm).

Differences notwithstanding, the combined list of pathogens of concern is long (Appendix D). This list is subject to change because of the continued emergence of new infectious diseases; the emergence of treatment-resistant strains of established pathogens; and social, technical, and ecological changes that allow new opportunities for diseases to be introduced as weapons. The connectivity for many of these diseases across species groups (Fig. 6.1) is an important dimension to consider, regardless of whether an individual's interest is human, domestic animal, or wildlife health.

Indirect Impacts from Bioterrorism

Bioterrorism aimed at society, a government, and/or its citizens is meant to cause destabilization, fear, and anxiety.[94,95] It threatens conduct of scientific investigations involving pathogens of concern,[84, 90, 97–99] and hinders free flow and exchange of scientific findings and information.[100–105] It changes emergency medical preparedness and response,[42, 94, 96] and muffles transparent communication.

Changes in the guidelines for scientific investigations involving pathogens of concern include new criminal charges and fines that could affect scientists and scientific institutions.[207] A graduate student at a university in the Eastern USA was the first researcher charged under new antiterrorism laws with mishandling a potential bioterror agent (possession of anthrax-tainted cow tissue collected in the 1960s and maintained in a locked laboratory freezer).[106] A higher profile incident involved a prominent USA plague researcher jailed on charges of lying to federal agents about the fate of plague samples, mishandling laboratory samples, and illegally importing plague samples into the USA.[107,108] Actions of this type are also occurring outside the USA. A top research institute in the UK was ordered to pay nearly $65,000 in fines for not having adequate security to protect laboratory workers and the public from potential exposure to a hybrid virus they were developing.[109]

The costs from bioterrorism go beyond the direct impacts of terrorist attacks. Indirect costs, such as those highlighted here, are part of the costs imposed by the potential for attack that causes society to take defensive actions to minimize the potential for success by terrorists.

Animal Disease and Bioterrorism

"Detection of disease in lower animals may be essential to detecting a bioterrorism event because most of the bioterrorism threat agents are zoonotic disease agents."[77]

History has recorded the use of animals as vehicles for the transmission of disease and as intended victims for disease introduction. Enemies propelled dead animals into besieged cities[17] and used diseased animal carcasses (natural causes of disease) to contaminate wells, reservoirs, and other water sources of armies and civilian populations.[22] During WWI, British troops successfully used this latter concept to deny the German army use of critical water resources in a remote area of East Africa, while retaining use by their own troops. They shot antelope and scattered the carcasses around the edges of the waterhole to give the impression that the water was unfit for human use.[41]

German saboteurs during WWI used bacteria that cause anthrax and glanders to infect military horses and **mule**s of the Allied forces. Livestock food sources for the military were

Table 6.3 Category A (highest priority) critical biological agents for public health response activities (list is from Levy and Sidel[177]).[a]

Agent	Type	Disease	Zoonoses	Previous[b] use	Weaponized[c]	Comments
Variola major	Virus	Smallpox	○	●	●	Not used in modern times but remains a major threat because of high susceptibility of human population and ease of disease transmission.
Bacillus anthracis	Bacteria	Anthrax	●	●.	●	Enzootic disease in several areas of the world; naturally occurring outbreaks in white-tailed deer sporadically occur in the USA.
Yersinia pestis	Bacteria	Plague	●	●	●	Enzootic disease within the USA.[3]
Clostridium botulinum toxin	Bacterial toxin	Botulism	○	●	●	Attempted uses have not been very successful but one of the most potent toxins known.
Francisella tularensis	Bacteria	Tularemia	●	●	●	Enzootic disease in many areas of the world including the USA; rabbit strain (Type A) more virulent than aquatic rodent strain (Type B).
Ebola virus (Filovirus)	Virus	Ebola hemorrhagic fever	●	○	○	High mortality rates (up to 90 percent); endemic in parts of Africa but little known about the ecology of Ebola. Former USSR bioweapons programs pursued weaponization of Ebola and Aum Shinrikyo cult pursued acquisition of this virus.[27]
Marburg virus (Filovirus)	Virus	Marburg hemorrhagic fever	●	○	○	Rare disease associated with handling non-human primates; high mortality rates.
Lassa virus (Arenavirus)	Virus	Lassa fever	●	○	○	Endemic within parts of West Africa; mice maintain this arenavirus in nature; human to human transmission more common than with other hemorrhagic fevers.[62]
Junin virus (Arenavirus)	Virus	Argentine hemorrhagic fever (AHF) and related viruses	●	○	○	Endemic within South America; maintained within mice and other small rodents; AHF human fatality rate is between 10–20 percent. Other arenaviruses also associated with small rodent reservoirs have recently appeared in the USA.[62]
Machupo virus (Arenavirus)	Virus	Bolivian hemorrhagic fever (BHF)	●	○	○	Endemic in Bolivian province of Beni; mice are the reservoir host; mouse excretions most important source for human infections; human fatality rate is about 18 percent.[62]

[a] Category A agents "include organisms that pose a risk to national security because they can be easily disseminated or transmitted person-to-person; cause high mortality, with potential for major public health impact; might cause public panic and social disruption; and require special action for public health preparedness."[178]

[b] Confirmed applications of agent during wartime, by terrorists, and/or as criminal activity.[23,33,37,179]

[c] Agent produced for weapons use by nations with biowarfare programs.[14,22,23,33,52]

●= positive; ○= negative

Table 6.4 Category B (second highest priority) critical biological agents for public health response activities (list is from Levy and Sidel[177]).[a]

Agent	Type	Disease	Zoonoses	Previous[b] use	Weaponized[c]	Comments[d]
Brucella spp.	Bacteria	Brucellosis	●	○	●	Widely occurring, debilitating disease prevalent in parts of Europe, Africa, Asia, Latin America (including Mexico) and arctic and sub-arctic areas of North America. Human cases are closely associated with contact with infected farm animals, caribou and reindeer, and consumption of unpasteurized dairy products from infected animals.
Epsilon toxin of *Clostridium perfringens*	Bacterial toxin	Enterotoxemia	●	○	●	Foodborne disease; causative agent of gas gangrene.
			Food Safety Threats:			
Salmonella spp.	Bacteria	Salmonellosis	●	●	●	Foodborne disease; used in attacks within the USA.
Shigella dysenteriae	Bacteria	Shigellosis	○	●	●	Foodborne disease; used in attacks within the USA.
Escherichia coli O157:H7	Bacteria	Colibacillosis	●	○	○	Foodborne disease.
Burkholderia (Pseudomonas) mallei	Bacteria	Glanders	●	●	●	Primarily a disease of domestic animals (especially horses, donkeys, and mules) within parts of Asia and the Middle East. High human fatality rate among untreated, acute cases (close to 100 percent).
B. pseudomallei	Bacteria	Melioidosis	●[e]	○	○	Primarily a disease of humans and animals in Southeast Asia and Australia but also occurs worldwide in tropical and subtropical areas. Acute infections can be fatal; chronic disease also occurs. Transmission by contact, ingestion, and inhalation of organisms, but rarely due to direct transmission from animals.
Chlamydia psittaci	Bacteria	Ornithosis (psittacosis)	●	○	○	Worldwide distribution involving detection in more than 130 bird species. Transmission to humans generally by inhalation of contaminated dusts or contact with excretions of infected animals.
Coxiella burnetti	Rickettsia	Q fever	●	●	●	Worldwide (except for New Zealand) debilitating disease transmitted by ticks, a wide variety of animals (including some birds), and by airborne dust contaminated with tick feces and dried feces from infected animals.
Ricin	Plant toxin	Toxicosis	○	●	●	Toxin produced from castor beans (*Ricinus communis*); first isolated in 1889. Commercial formulation used as a mole killer.[180] Covert use by assassins and terrorists, including attacks in the USA.[179]
Staphylococcal enterotoxin B	Bacterial toxin	Enterotoxemia	●	○	●	Aerosol and food poisoning potentials as a biological agent.

Table 6.4 Category B (second highest priority) critical biological agents for public health response activities (list is from Levy and Sidel[177])[a]—Continued

Agent	Type	Disease	Zoonoses	Previous[b] use	Weaponized[c]	Comments[d]
Rickettsia prowazekii	Rickettsia	Typhus fever/epidemic typhus	●	○	○	Classical epidemic form has a mortality rate of 10–40 percent. Endemic areas persist in North and Central Africa, South America, and the former USSR; sporadic cases in the USA are associated with flying squirrels. Typically, a louse-transmitted disease. Airborne transmission via inhalation of agent from dried feces of infected lice and other ectoparasites and dead lice.
Alphaviruses	Virus	Venezuelan, eastern, and western equine encephalitis	●	○	●	Mosquito transmitted diseases, primarily of the Americas, involving a variety of animal species. Horses are an important amplification host for virus production and infection of mosquito populations. Encephalitis resulting in mortality, primarily in children, generally occurs in less than 5–10 percent of human infections.
			Water Safety Threats:			
Vibrio cholerae	Bacteria	Cholera	○[f]	●	●	Food/waterborne disease. Seventh pandemic began in Indonesia in 1961, and reached South America in the early 1990s.[181,182]
Cryptosporidium parvum	Protozoan parasite	Cryptosporidiosis	●	○	○	Worldwide disease associated with contact with livestock, person-to-person transmission in daycare centers and medical institutions, and contaminated water and food.

[a] Category B agents "include those that are moderately easy to disseminate; cause moderate morbidity and low mortality and require specific enhancements of CDC's diagnostic capacity and enhanced disease surveillance."[178]

[b] Confirmed applications of agent during wartime, by terrorists, and/or as criminal activity.[23,33,37,179]

[c] Agent produced for weapons use by nations with biowarfare programs.[14,22,23,33,52]

[d] For more information, see Beran and Steele,[61] Krauss et al.,[62] Williams and Barker.[183]

[e] Since a vertebrate reservoir host is not required for maintenance of the causative agent in nature, this disease is more appropriately a sapronosis, saprozoonosis, or geonosis.[62]

[f] Non-human vertebrates are not an important aspect of the ecology of cholera.

●= positive; ○= negative

also targets.[22, 110, 111] These events took place in Europe, the USA and South America (Table 6.1). During 1917 to 1918, more than 200 mules intended for export to Allied forces from Argentina died from these attacks.[111] During WWI there are no reports of widespread disease due to any covert uses of infectious disease. Disease agents have been used since then against cattle and horses in Africa and Afghanistan (Fig. 6.4).[26, 112, 113]

Agroterrorism

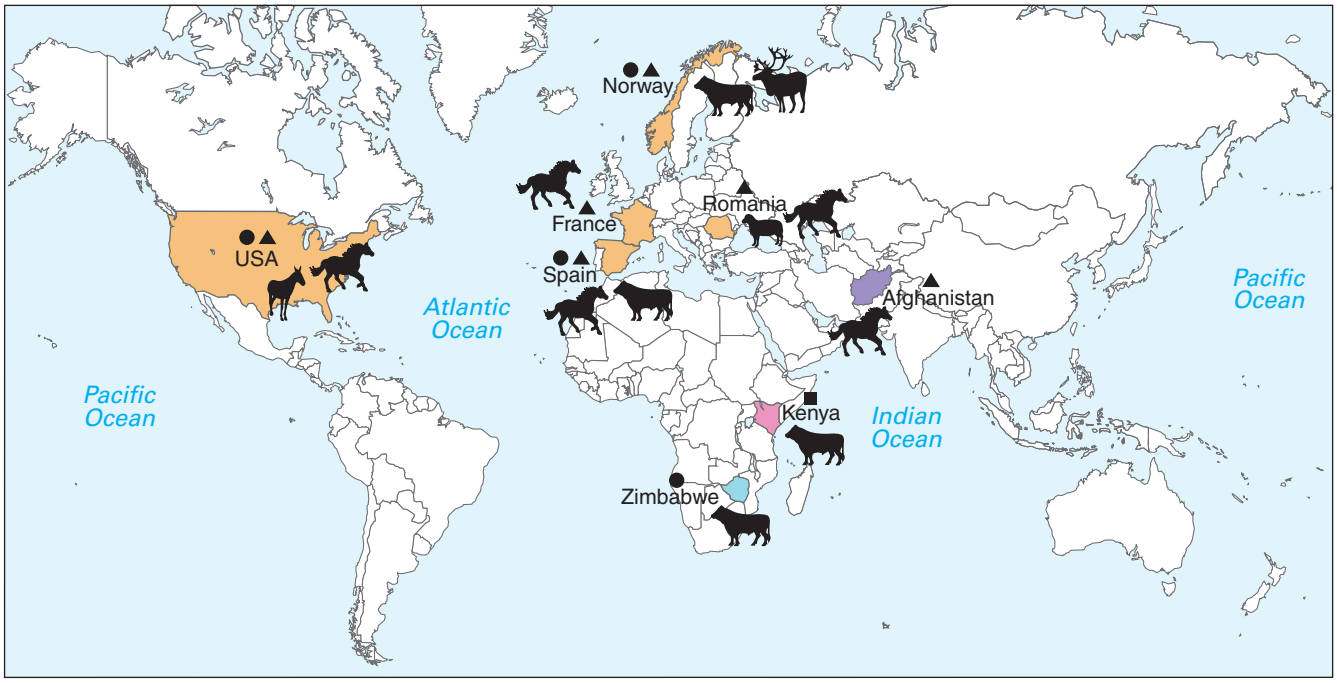
During the timeframe when the public health community in the USA was raising concern about potential bioterrorism, the U. S. Department of Agriculture (USDA) requested that the National Academy of Sciences evaluate potential impacts of terrorist actions against agriculture. The resulting report, *Countering Agricultural Bioterrorism*, (2002; http://www.nap.edu) concluded that the USA was not adequately prepared to prevent or address such attacks, and that there was enormous potential for economic harm from bioterrorism.[114] The Academy's findings reaffirmed the great vulnerability of agriculture to terrorist attack.[110, 115–117] Criteria have been established for the identification of pathogens considered to pose the greatest threats to domestic animals, and this list consists of 22 agents (Table 6.6).

The agriculture pathogen list is a reflection of diseases whose occurrence is of great economic concern (see Chapter 3). For example, consider the magnitude of the immediate economic losses experienced, first by Canada in mid-2003 and then by the USA at the end of 2003, following single cases in cattle of bovine spongiform encephalopathy (BSE) or mad cow disease. The resulting market impacts associated with human fear of contracting disease from meat from infected cattle illustrates the connectivity between animal disease and human health and the potential for agroterrorism.

A single case of a high profile disease (e.g., BSE) or a small number of cases of more common diseases (e.g., Newcastle disease or bovine tuberculosis) may result in international sanctions that cause major economic losses for agriculture and related industries. The connectivity between many diseases of animals and humans suggests the need for integrated preparedness for addressing the potential for bioterrorism attacks against animals. The 2001 outbreak of foot-and-mouth disease (FMD) in Europe is somber testimony to the costs that can be incurred by agriculture from the introduction of a highly contagious disease. More than 6 million animals were slaughtered to combat this disease.[209] Predicted costs from an FMD outbreak in California alone are at least $13.5 billion.[210]

"Double Agents"

Pathogens that can cause disease in humans and animals can be viewed as "double agents" relative to the populations they can impact. Although the historic use of biological agents in wartime appears to have been specifically focused on either human or animal targets, most of the early uses of microbes as bioweapons involved agents capable of causing serious disease in both (Table 6.1). The interfaces between humans and animals can promote persistence and spread of infectious agents. Thus, careful selection of target situations can enhance the probabilities for disease in both humans and animals, and increase the potential for environmental persistence of the disease agent and disease spread through animal movements.



EXPLANATION

Era, country and disease species

WW1
USA* (horses, mules)
Romania (horses, sheep, livestock)
Spain (horses, cattle)
Norway (reindeer, cattle)
France (horses)

1952
Kenya (cattle)

1978–80
Rhodesia (cattle) (*now Zimbabwe*)

1982–84
Afghanistan (horses)

▲ Glanders
● Anthrax
■ Plant toxin

* Maryland, Virginia, and New York area

Figure 6.4 Documented war time uses of biological weapons to target livestock (developed from Wilson et al.[110]).

Anthrax is an example of a "double agent." In 1979, there was an accidental release of anthrax spores from a research facility within the former Soviet Union.[26] According to one report, at least 77 people who lived or worked within 4 km in a narrow zone downwind from the release site became infected and 66 died, making this the largest documented epidemic of inhalation anthrax in history.[22, 118] Livestock deaths from anthrax extended out to 50 km.[119] The final death toll may have been as high as 200 to 1,000 people.[73, 120]

The deliberate uses of anthrax in Africa were even more devastating. Anthrax appears to have been used as a bioweapon in Rhodesia (now Zimbabwe) during the war of independence in the 1970s.[110] Those in power targeted cattle to undermine the morale and food supply of those seeking independence. The breakdown of government administration and veterinary services due to the war aided anthrax's epizootic nature and disease spread. The ensuing human epidemic resulted in about 10,000 cases of illness and hundreds of deaths. The persistence of anthrax in Zimbabwe since then continues to take a large toll on human life, domestic animals, and wildlife.[110]

Anthrax is only one of several infectious diseases capable of causing severe illness and death in humans and animals alike. Because of this, there is great difficulty in combating such diseases and an increased probability for persistent residual effects.

Characteristics of the Most Dangerous Pathogens in Attacks Against Agriculture

Pathogens that pose the greatest terrorist threat (*Most Dangerous* category) to agriculture were determined by experts who identified combinations of the following characteristics.[110]

Pathogen characteristic	Outcome
Highly infectious and contagious	Low doses able to cause initial infections and disease followed by spread from one animal to another.
Good ability to survive in the environment	Not easily inactivated by ambient temperatures and other physical conditions outside of the host, so that contact with pathogen-contaminated substrates (e.g., water, soil, vegetation) can serve as sources for infection.
Predictable clinical disease pattern, including morbidity and mortality	Allows terrorists to consider specific species targets and strategically plan to produce desired impacts.
Pathogenic for livestock or poultry	May cause severe disease outcomes such as mortality, reproductive failure, and economic losses due to product embargoes.
Available and easy to acquire and produce	Allows use of common agents that are easy to cultivate, have minimum requirements for special handling to retain virulence, and can be obtained easily from natural disease events and other sources.
Attributable to natural outbreak, ensuring plausible deniability	Facilitates covert activities oriented toward disruptive impacts without providing leads for pursuit of the perpetrators.
Not harmful to perpetrator	Exposure to pathogen does not impair the health of perpetrators, thereby facilitating transport of the pathogen, as well as repeated attacks by the perpetrator.
Easily disseminated	Does not require elaborate or cumbersome means for pathogen transport and subsequent exposure of target animals (e.g., contamination of food and water by a small amount of agent).

Concentrated livestock and poultry operations, such as feedlots and poultry houses, facilitate the transmission of infectious disease agents that may be introduced. Also, animal movements associated with commerce facilitate disease spread to other locations. These considerations have great bearing on the effectiveness of a bioterrorist attack.

Table 6.5 Category C (third highest priority) critical biological agents for public health response activities (list is from Levy and Sidel[177]).[a]

Agent	Type	Disease	Zoonoses	Previous[b] use	Weaponized[c]	Comments[d]
Nipah virus (Paramyxo-virus)	Virus	Nipah virus encephalitis	●	○	○	First observed in Malaysia during winter of 1998–1999; high human fatality rate. Fruit bats are the reservoir host, pigs have been the source for human cases.
Hantaviruses (Bunyavirus)	Virus	Hantavirus pulmonary syndrome (HPS) and hemorrhagic fever with renal syndrome (HFRS)	●	○	○	New World infections (HPS) first appeared in USA in 1993 (Sin Nombre disease) causing high fatality rate. Old World infections (HFRS) generally result in low to moderate fatality rates. Small rodents are reservoir hosts and shed agent via feces and urine. Aerosol exposure primary route for human infection.
Tickborne hemorrhagic fever viruses (Bunyavirus)	Virus	e.g., Crimean-Congo hemorrhagic fever (CCHF)	●	○	○	CCHF is present in parts of the former USSR, Europe, Asia, the Middle East, Africa, Australia. Domestic animals and farm-raised ostriches are involved in disease ecology; hedgehogs, horses and mouse-like rodents are reservoir hosts. Transmission generally occurs via tick bites or contact with infected animals. High human fatality rate (up to 30–50 percent).
Tickborne encephalitis viruses (Flavivirus)	Virus	e.g., Kyasamur forest disease, (KFD); Central European encephalitis (CEE); Russian spring-summer meningoen-cephalitis (RSSE).	●	○	○	CEE is the most important human arbovirus infection in Central Europe and RSSE is an even more severe disease where it occurs; both diseases extend into parts of Asia. KFD occurs in parts of India. CEE and KFD can be transmitted through nonpasteurized milk products in addition to tick bites.
Yellow fever virus (Flavivirus)	Virus	Yellow fever	●	○	●	Mosquito transmitted, high human fatality rate, endemic in central Africa and much of South America. Urban and sylvatic disease cycles with monkeys being the sylvatic reservoir host.
Mycobacte-rium tubercu-losis	Bacteria	Multidrug-resistant tuberculosis	●	○	○	Tuberculosis remains an important disease of humanity in much of the world (two million new cases in India in 1999 causing about 450,000 deaths).[177]

[a] Category C agents "include pathogens that could be engineered for mass dissemination in the future because of availability; ease of production and dissemination; and potential for high morbidity and mortality and major health impact." [178]

[b] Confirmed applications of agent during wartime, by terrorists, and/or as criminal activity.[23,33,37,179]

[c] Agent produced for weapons use by nations with biowarfare programs.[14,22,23,33,52]

[d] For more information, see Beran and Steele,61 Krauss et al.,62 Williams and Barker.[183]

●= positive; ○= negative

Table 6.6. Disease agents posing the greatest potential threats from agroterrorism for livestock and poultry in the USA (list is from Wilson et al.[110]).

● = Common; ●= infrequent; ○= not known to occur.

Agent	Type	Disease	Zoonoses	Primary hosts			Comments[a]
				Poultry	Livestock	Wildlife	
Foot-and-mouth disease virus (Aphthovirus)	Virus	Foot-and-mouth disease (FMD)	●	○	●	●	The FMD epizootic that began in the UK during 2001 led to the eradication of 4 million livestock[184] with direct costs of slaughter and disposal estimated at US$7.5 billion and other costs adding additional billions.[41] Although technically a zoonosis, human cases are rare and self limiting. FMD has been eradicated from the USA.
Hog cholera virus (Pestivirus)	Virus	Classical swine fever (hog cholera)	○	○	●	●	Domestic pigs and wild boar are species usually affected; 1997 epizootic among domestic pigs in the Netherlands resulted in direct economic losses of US$2.3 billion and the destruction of more than 11 million pigs.[185] Hog cholera had been eradicated from the USA. It is present in Africa, Asia, Latin America, and in parts of Europe.
African swine fever virus (Asfarvirus)	Virus	African swine fever (ASF)	○	○	●	●	Domestic and wild species of pigs are primary species affected. Enzootic in Africa from the Equator south. Following spread in the 1960s, 1970s and 1980s to parts of Europe, South America, and the Caribbean, most outbreaks have been eliminated by depopulation of infected pig farms.[186] Transmission is by infected ticks, ingestion of infected meat, direct contact, and by aerosol. ASF is not present in the USA; previous introductions into the Dominican Republic, Haiti, Cuba, and Brazil have been eradicated. Portugal, Spain, and Sardinia remain as enzootic foci in Europe.[187]
Rinderpest virus (Morbillivirus)	Virus	Rinderpest	○	○	●	●	Panzootic of 1889–1905 in sub-Saharan Africa due to infected cattle from India killed large numbers of wildlife and cattle.[64] Disease causing greater impacts on humans (social and economic) and domestic livestock than any other animal disease. Present in parts of Africa, Pakistan, southern and possibly central Asia, and parts of the Middle East.[188]
Rift valley fever virus (Phlebovirus)	Virus	Rift valley fever	●	○	●	●	Livestock (including camels) and humans are the primary species impacted by this mosquito-borne disease of the Middle East and Africa.[65]

Table 6.6. Disease agents posing the greatest potential threats from agroterrorism for livestock and poultry in the USA (list is from Wilson et al.[110])—Continued.

Agent	Type	Disease	Zoonoses	Primary hosts			Comments[a]
				Poultry	Livestock	Wildlife	
Influenza virus (Orthomyxovirus)	Virus	Avian influenza	●	●	●	●	Birds, humans, pigs, horses, and seals are species most commonly infected by influenza viruses. Genetic drift and "gene swapping" between influenza viruses produce viruses pathogenic for poultry, humans, and other species. Highly pathogenic strains cost the poultry industry millions of dollars in eradication costs and product embargos.[189,190]
Newcastle disease virus (Rubulavirus)	Virus	Velogenic viscerotropic Newcastle disease (VVND)	●	●	○	●	Eradication of VVND from the USA and Canada occurred during the early 1970s. Periodic reappearances of this disease have been associated with imported birds (pet bird trade). Major mortality from ND has been occurring in double-crested cormorants in the USA and Canada since 1990.[176]
Venezuelan equine encephalomyelitis virus (Alphavirus)	Virus	Venezuelan equine encephalomyelitiis	●	○	●	●	Disease of horses and people in northern South America since the 1930s. 1995 outbreak caused 75,000 human cases and killed an estimated 8 percent of the horse population. Outbreak of 1969–1971 spread 4,000 km northwest through Mexico and into Texas killing more than 44,000 horses. Horses, mules, and donkeys are main vertebrate hosts of this mosquito-borne disease. Sylvatic subtypes of virus (non-epidemic forms) are maintained in wild rodents, bats, and other small mammals rather than horses.[191]
Bluetongue virus (Orbivirus)	Virus	Bluetongue	○	○	●	●	Causes epizootic disease both in wildlife (e.g., deer, bighorn sheep) and livestock. Midges (*Culicoides* spp.) vector this disease. Wildlife have only been affected in North America despite worldwide disease in livestock. Large-scale epizootics can occur.[192]
Goat pox virus, Sheep pox virus (Capripoxvirus)	Virus	Sheep pox; goat pox	○	○	●	○	These viruses cause serious systemic infections and are commonly found throughout the near and Middle East, India, Bangladesh, and North Central Africa. Although wildlife cases are lacking, infection in wildlife of the same genera should be expected to cause similar disease.[193]

Table 6.6. Disease agents posing the greatest potential threats from agroterrorism for livestock and poultry in the USA (list is from Wilson et al.[110])—Continued.

Agent	Type	Disease	Zoonoses	Primary hosts			Comments[a]
				Poultry	Livestock	Wildlife	
Pseudorabies virus (suid herpesvirus 1) (Alphaherpesvirus)	Virus	Pseudorabies (Aujeszky's disease)	○	○	●	○	Important disease of domestic pigs in the USA and much of the rest of the world. Although many wildlife species can be infected, natural cases of clinical diseases are rare. Feral and wild swine are the only known wildlife reservoirs; the domestic pig is the primary reservoir.[194,195]
Vesicular stomatitis virus (Vesiculovirus)	Virus	Vesicular stomatitis	●	○	●	●	Livestock and deer are the primary species affected by this disease; sand flies appear to be the most important vector and likely overwinter the virus in areas of the Southeastern USA. Much of the ecology of this disease remains unknown.[191]
Porcine enterovirus type 1 (Enterovirus)	Virus	Teschen disease (porcine enterovirus type 1)	○	○	●	○	This paralytic disease of domestic pigs occurs nearly worldwide (not in Asia), but serious disease typically only occurs in parts of Europe and Madagascar.[196]
Porcine enterovirus type 9 (Enterovirus)	Virus	Swine vesicular disease (SVD)	●	○	●	○	Disease of domestic swine. Following the initial 1966 detection of SVD in Italy, this disease rapidly spread to many countries in Europe, and to Japan and Taiwan.[196] Italy is the only country where SVD remains enzootic.[62]
Rabies virus (Lyssavirus)	Virus	Rabies	●	○	●	●	Rabies is a major zoonosis of concern because of its public health, veterinary, and economic impacts. Japan, the UK, and some limited areas have eradicated this disease; indigenous cases of disease are absent from much of the Caribbean and Pacific Ocean, but common in much of the remainder of the world.[197]
Lumpy skin disease virus (Capripoxvirus)	Virus	Lumpy skin disease	○	○	●	○	Sub-Saharan Africa and the Middle East are the primary areas where this disease exists. The epizootic that spread through southern and eastern Africa during 1943 to 1945 affected about 8 million cattle. Cattle and buffalo are the primary species affected but other species have died from experimental infections.[196]
Porcine reproductive and respiratory syndrome virus	Virus	Porcine reproductive and respiratory syndrome	○	○	●	○	First reported in USA in 1987; since then outbreaks have been confirmed throughout North America and Europe. This disease is maintained within domestic swine populations.[198]

Table 6.6. Disease agents posing the greatest potential threats from agroterrorism for livestock and poultry in the USA (list is from Wilson et al.[110])—Continued.

Agent	Type	Disease	Zoonoses	Primary hosts			Comments[a]
				Poultry	Livestock	Wildlife	
African horse sickness virus (Orbivirus)	Virus	African horse sickness (AHS)	●	○	●	○	Horses and then mules are the species most susceptible to this midge-transmitted virus; dogs become infected by feeding on infected meat and the virus may be spread by wind. Zebras are reservoir host. AHS is most prevalent in the Middle East and Asia; it is not present in the Western Hemisphere.[192,196]
Bacillus anthracis	Bacteria	Anthrax	●	○	●	●	Anthrax is worldwide in distribution and causes fatal disease in humans, domestic animals and wildlife. Scavenger species relatively resistant to this disease aid its spread by opening the carcasses of animals that have died and releasing large numbers of *B. anthracis* organisms. Ingestion by these species also serves to disperse the spores over broad areas.[199] Anthrax is a highly desired weapon of terrorists and biowarfare programs.
Chlamydia psittaci	Bacteria	Ornithosis/ psittacosis/ chlamydiosis	●	●	○	●	Disease introductions into the USA by pet bird trade (parrots, parakeets); disease exists in some USA waterbirds and pigeon populations.[213]
Cowdria ruminantium	Rickettsia	Heartwater/ Cowdriosis	○	○	●	●	A very important vector-borne disease of livestock (cattle, sheep goats) in Africa. Also present in Madagascar and some islands in the Indian and Atlantic oceans and in the Caribbean.[200] Naturally, occurring wildlife infections are generally subclinical but some mortality occurs in Africa.[201] White-tailed deer are highly susceptible to experimental infections. Importation into the USA of heartwater and exotic *Amblyomma* ticks that vector this disease could cost the livestock industry billions of dollars and result in major epizootics among white-tailed deer.[200]
New World Screwworm *Cochliomyia hominivorax*	Parasite	Myiasis (screw worm)	●	○	●	●	Screwworm fly is native to tropical and subtropical North and South America; cannot overwinter in cold climates and migrates to the north with onset of warm weather. Prior to control, one of the most important pests of livestock in the Southern USA where it caused millions of dollars in economic losses annually.[212]

[a] Species groups generally involved in epizootics.

The Wildlife Factor

"...and he that will not apply new remedies must expect new evils; for time is the greatest innovator..." (The Essays by Sir Francis Bacon, 1601)[121]

Livestock and poultry of today are descendants of wild species that were domesticated, bred, and cultivated over time incorporating sophisticated animal genetics and husbandry programs. Although some species such as reindeer have retained their wildlife characteristics, others such as cattle, sheep, pigs, and some poultry have major appearances, behaviors, and other modifications that differentiate them from their parent stock. Nevertheless, these domesticated animals retain susceptibility to many of the pathogens affecting their wild counterparts.

Domesticated species often share common habitat with their wildlife relatives, have transient contact with wild species, or may have tangential relations that provide direct or indirect opportunities for the harboring and exchange of disease agents and/or arthropod vectors essential for the maintenance and transmission of infectious disease. Therefore, livestock and poultry throughout much of the world, and the diseases that affect them, are often closely linked with diseases of wildlife. Some of these diseases appear to have been transferred from domesticated species to wild populations (e.g., brucellosis in bison and elk of the Greater Yellowstone

Table 6.7. List A diseases from the Office International des Epizooties.[a]

Disease[b]	Agent	Zoonoses[c]	Causes disease in:[d]			Enzootic in USA
			Livestock	Poultry	Wildlife	
Foot-and-mouth disease	Aphthovirus	●	■	□	■	No
Swine vesicular disease	Enterovirus	●	■	□	□	No
Peste de petits ruminants	Morbillivirus	○	■	□	□	No
Lumpy skin disease	Capripoxvirus	○	■	□	□	No
Bluetongue	Orbivirus	○	■	□	■	Yes
African horse sickness	Orbivirus	●	■	□	□	No
Classical swine fever	Pestivirus	○	■	□	■	No
Newcastle disease	Rubulavirus	●	□	■	■	Yes[e]
Vesicular stomatitis	Vesiculovirus	●	■	□	■	Yes
Rinderpest	Morbillivirus	○	■	□	■	No
Rift Valley fever	Phlebovirus	●	■	□	□	No
African swine fever	Asfarvirus	○	■	□	□	No
Sheep and goat pox	Capripoxvirus	○	■	□	□	No
Influenza[f]	Orthomyxovirus	●	■	■	■	Yes
Contagious bovine pleuropneumonia	*Mycoplasma mycoides* var. *mycoides*	○	■	□	□	No

[a] Reportable diseases for compliance with the International Animal Health Code. These transmissible diseases have the potential to cause serious epizootics; their rapid spread can pose serious socioeconomic or public health consequences and are of major importance in the international trade of animals and animal products.

[b] All of these diseases, except contagious bovine pleuropneumonia (caused by mycoplasma), are caused by viruses.

[c] Classification is based on the Office International des Epizooties: ● = diseases that cause serious illness and/or death in animals and humans; ●= diseases for which infections have been documented in animals and humans, but for which human infections are rare (except for Newcastle disease), self-limiting, not clinically severe, and generally associated with laboratory exposures (except for Newcastle disease); ○ = diseases not considered to be zoonoses.

[d] ■ = Primary animal species reported to have clinical cases of this disease; □ = disease does not naturally occur in these species, or only rarely so.

[e] Velogenic (highly pathogenic) strains of Newcastle disease as evaluated for chickens have been eradicated from the USA, but strains highly pathogenic for wild birds are present.

[f] Highly pathogenic avian influenza viruses evolve from the virus pool contributed to by pigs, poultry, and wildlife; at this time, only low pathogenic avian influenza exists in the USA. See Krauss et al.[62] for a concise overview of this complex disease.

Table 6.8. Synopsis of List B diseases from the Office International des Epizooties.[a,b]

Primary species	Number of diseases	Type of disease						Number enzootic in USA
		Virus	Bacteria	Rickettsia	Fungal	Prion	Parasitic	
Cattle	15	3	4	1	1	1	5	12
Sheep and goats	11	4	6	0	0	1	0	9
Swine	6	3	2	0	0	0	1	5
Equine	15	8	2	0	1	0	4	7
Birds	13	7	6	0	0	0	0	11
Lagomorphs	3	2	1	0	0	0	0	3
Bees	5	0	2	0	0	0	3	5
Fish	5	5	0	0	0	0	0	3
Mollusks	5	0	0	0	0	0	5	4
Crustaceans	3	3	0	0	0	0	0	1
Other species	11	2	3	2	0	0	4	8

[a] Reportable disease (voluntary) compliance with the International Animal Health Code. See Appendix C for listing of these transmissible diseases of socioeconomic and/or public health importance that are significant for the international trade of animals and animal products.

[b] New World leishmaniases are additional List B diseases that are cutaneous diseases that occur from southern Texas south into South America. Visceral leishmaniasis (Kala-Azar) is a more serious disease and does not occur in the USA, but is present in Central and South America in addition to much of the Old World.[62]

Table 6.9a. Zoonoses being considered by the Ad Hoc Group of State Parties to the Biological and Toxin Weapons Convention (list is from Wilson et al.[110]).

Zoonoses[a]			
Agent	**Type**	**Disease**	**Primary species linkages[b]**
Rift Valley fever virus	Virus	Rift Valley Fever	Cattle, goats, sheep, mosquitoes, humans
Monkeypox virus	Virus	Monkeypox	Rodents, monkeys, humans
Alphaviruses[c]	Virus	Eastern, Western, and Venezuelan equine encephalitis	Rodents, bats, birds, mosquitoes, horses, humans
Bacillus anthracis	Bacteria	Anthrax	Soil, biting flies, scavengers, herbivores, humans
Brucella melitensis	Bacteria	Brucellosis (Malta fever)	Goats, sheep, humans
Brucella suis	Bacteria	Brucellosis	Pigs, European hare, reindeer, caribou, humans
Burkolderia mallei	Bacteria	Glanders	Horses, donkeys, mules, humans
Burkholderia pseudomallei	Bacteria	Melioidosis	Rodents, livestock, humans
Francisella tularensis	Bacteria	Tularemia	Arthropods, voles, aquatic rodents, rabbits, humans
Yersina pestis	Bacteria	Plague	Rodents, fleas, humans

[a] Each causes serious human illness that often leads to death. Animals have major roles in the ecology of each of these diseases and, like humans, also are affected by these disease agents.

[b] Species generally involved in disease maintenance, transmission, and as susceptible hosts; for details see current literature on specific diseases.

[c] Somewhat different species linkages occur for each of the diseases listed; see Yuill and Seymour[191] for details.

Table 6.9b. Animal pathogens being considered by the Ad Hoc Group of State Parties to the Biological and Toxin Weapons Convention (list is from Wilson et al.[110]).

Animal pathogens[a]	
Viral agent/disease	**Primary species linkages[b]**
African horse sickness	Horses, mules, midges, zebras
African swine fever	Domestic and wild pigs, ticks
Avian influenza (influenza)	Waterbirds, poultry, pigs, humans
Hog cholera (classical swine fever)	Domestic and wild pigs
Bluetongue	Wild ungulates, livestock, midges
Foot-and-mouth disease	Cattle, African buffalo, antelope, and other wild ruminants
Newcastle disease	Psittacines, poultry
Pestes des petitis ruminants	Sheep and goats
Porcine enterovirus type 1	Domestic pigs
Rinderpest	Cattle, cloven-hoofed wildlife (e.g., African buffalo)
Vesicular stomatitis	Livestock, sand flies, black flies, deer, antelope, humans

[a] Human infections do not occur for most of these viruses and the agents that do infect humans are generally infrequent causes of disease; clinical disease in humans typically is mild and self limiting (except for influenza).

[b] Species generally involved in disease maintenance, transmission, and as susceptible hosts; for details, see Williams and Barker[183] and current literature on specific diseases.

Table 6.9c. Plant pathogens being considered by the Ad Hoc Group of State Parties to the Biological and Toxin Weapons Convention (list is from Wilson et al.[110]).

Plant pathogens[a]			
Agent	**Type**	**Disease**	**Plant target**
Colletotrichum coffeanum var. *virulans*	Fungus	Coffee berry disease	Coffee
Dothistroma pini	Fungus	Dothistroma needle blight	Pine trees
Erwinia amylovora	Bacteria	Fire blight	Apple, pear
Ralstonia solanacearum	Bacteria	Bacterial wilt	Potato
Puccinia graminis	Fungus	Stem rust	Wheat
Sugarcane Fiji disease virus	Virus	Sugarcane Fiji disease	Sugarcane
Tilletia indica	Fungus	Karnal bunt	Wheat
Xanthomonas albilneans	Bacteria	Sugarcane leaf scald disease	Sugarcane
Xanthomonas campestris pr. citri	Bacteria	Citrus canker	Grapefruit, lemon, lime, trifoliate orange
Sclerotinia sclerotiorum	Fungus	Sclerotinia stem rot (pink rot, white mold, water soft rot)	Vegetable row crops, soybeans, citrus, melons, and others
Claviceps purpurea	Fungus	Ergot	Rye, other cereal grains, and pasture grasses
Peronospora hyoscyami de Bary f. sp *Tabacina* (Adam) *skalicky*	Fungus	Blue mold	Tobacco

[a] Disease agents within this category are pathogens of agricultural crops. Anticrop agents within the USA arsenal of bioweapons that were destroyed by the U.S. Military during 1971–1973 were rice blast, rye stem rust, and wheat stem rust.[22] Plant pathogens also were components of the bioweapons programs of the former USSR, Iraq, and other nations.[14,37]

Basin, USA). These wildlife are now a threat for transmitting disease back to domestic animal populations (Table 6.2). In other situations, wildlife are reservoirs for disease agents or arthropod vectors that are of less consequence for wildlife, but are of major consequence for domestic animals (e.g., avian influenza viruses).

Wildlife and Bioterrorism

In general, wildlife populations are more vulnerable to biological terrorist attacks than are domesticated species. Access to free-ranging wildlife is largely unrestricted, chances of a perpetrator being noticed are very low, and wildlife disease surveillance activities are minimal in most areas. Thus, disease introductions may take hold and become major epizootics before detection occurs, facilitating spread and impacts of the disease. Targeting wildlife, at least in North America, may inflict fewer economic losses or species extinctions than in other geographic areas where wildlife are primary protein sources and/or a major means of revenue for local and regional economies. Secondary disease spread following the release of infectious agents capable of causing disease in multiple species raises concerns about the effects of bioterrorism on the biodiversity of wild species[41] and on rare breeds of domestic animals.[13, 41, 110, 122, 123]

The wildlife conservation community has not conducted any in-depth evaluations on the potential consequences from bioterrorist attacks, despite the apparent vulnerability of wildlife. With the release of the U.S. Department of Homeland Security's National Response Plan (NRP) in October 2004 (http://www.dhs.gov/dhspublic/interapp/editorial/editorial_0566.xml), the wildlife factor in detection of and response to emerging diseases is recognized under Emergency Support Function #11 (ESF #11). Within the NRP, natural resources are defined as "land, fish, wildlife, domesticated animals, plants, biota, and water…." The U.S. Department of the Interior and the U.S. Department of Agriculture are designated to be prepared for and to respond to any biological emergencies, intentionally or unintentionally introduced, involving wildlife. During 2005, NRP mock tabletop preparedness exercises included plague and avian influenza, and the wildlife factor within each of those responses.

More NRP exercises and training are needed to further improve responses, actions, and communications among agricultural, wildlife, and public health entities. Major strategic planning also is ongoing for protecting wildlife and for responding, should wildlife be involved in terrorist activities. Such planning is important because of the connectivity between wildlife and other species.

The capability to use wildlife as vehicles for the spread of infectious agents has been demonstrated by biological control activities in the USA and elsewhere (Box 6–2). This concept could be exploited by bioterrorists who focus on livestock, poultry, or human impacts, because wildlife are readily available launch vehicles for the transport and delivery of infectious disease agents. For bioterrorists using wildlife to succeed, they must have knowledge of species ecology and population movements, along with knowledge of the ecology of the diseases they desire to introduce. A successful application could include introduction of a disease launched either from distant locations or from on-site introductions.

Closing the Gap

In many ways, combating an infectious disease outbreak in humans, domestic animals, or wildlife is like combating a forest fire. Early detection of the outbreak is critical. Equally important are adequate response capabilities and an infrastructure that, on short notice, provides personnel, supplies, and specialized equipment. Efficient communications,

Photo by Milton Friend

Figure 6.5 Large concentrations of wildlife are often found on public lands due to diminishing habitat.

information flow, and reporting are crucial. Also, surveillance to detect flare-ups and persistent efforts are required for containment to be realized. Appropriately trained and experienced personnel must guide, coordinate, and carry out all of these and associated activities; these attributes are especially important for first responders in order to minimize event impacts.

Early Detection and Response

Early detection and response to minimize illness and death from bioterrorist attacks are important aspects of public health[39, 45, 50] and domestic animal disease fields.[13, 41, 110] A recent evaluation within the USA by scientists at the CDC "confirmed that the most critical component for bioterrorism outbreak detection and reporting is the frontline healthcare professional and the local health departments."[77] Similarly, a National Academy of Sciences evaluation of the threat of bioterrorism to agriculture recommended better training for frontline responders, such as farmers and other agricultural workers, on how to recognize and report a disease outbreak and thus provide early detection. Because of the rapid global movement of agricultural products and live animals, enhanced monitoring of emerging diseases in other countries is also necessary. A final recommendation was that laboratories collaborate to facilitate rapid testing of large numbers of samples.[114]

Table 6.10. Jurisdiction and regulatory authorities for stewardship of free-ranging wildlife[a] (USA).

Species type	Regulatory agency[b]			Comments
	DNR[c]	FWS[c]	NOAA[c]	
Endangered (federal)	▲	●	▲	As defined by Federal Endangered Species Act. Involves federal regulatory listing through due process by FWS.
Endangered (state)	●	▲	■	As defined by formal listing involving due process by State DNR; state cannot usurp federal regulations.
Migratory birds	▲	●	■	As established by the Migratory Bird Treaty Act and its amendments; includes virtually all birds that have seasonal movement patterns between distant locations. States can have more stringent, but not less stringent regulations.
Anadromous fish	▲	●	■	Salmonids (salmon, trout) only; populations that spend part of their life cycle in the oceans and part in freshwater rivers and other water bodies.
Oceanic fish	●	■	●	Species dictates jurisdiction; nearshore fish generally under authorities of State DNR.
Marine mammals	▲	●	●	As defined by Marine Mammal Protection Act. FWS responsible for polar bear, walrus, sea otter, and manatee; remainder of species under primary jurisdiction of NOAA.
Resident wildlife	●	▲	■	All species that are localized in their life cycle by generally having minimal movements across State boundaries. Includes shellfish, finfish, amphibians, reptiles, mammals, and birds.

[a] Each land management agency is responsible for the management of species on its lands and waters, but must abide by laws and regulations established by regulatory agencies for the harvest and possession of wildlife. Special provisions that extend rights for native peoples exist. Also, species management is often a collaborative venture involving agencies and the private sector.

[b] Agencies empowered to promulgate binding regulations for harvest, methods of take, possession, and use of free-ranging wildlife and products from these species. Also have enforcement responsibilities for those laws and regulations.

[c] DNR=State Departments of Natural Resources or State Fish and Game Agencies; FWS=Fish and Wildlife Service, U.S. Department of the Interior; NOAA=National Oceanographic and Atmospheric Administration, U.S. Department of Commerce.

●= Agency with primary regulatory and law enforcement responsibilities for the species.

▲= Agency with secondary regulatory and law enforcement responsibilities associated with the management of the species on agency lands and waters. Species protections generally can be more stringent, but not more lenient, than that of the agency with primary responsibilities.

■= Agency with limited to no regulatory responsibilities for the species.

Box 6–2 Wildlife as Disease Delivery Systems

"Bacteriological warfare is science stood on its head…a gross perversion." -from an official paper published by the Soviet Union in 1951[26]

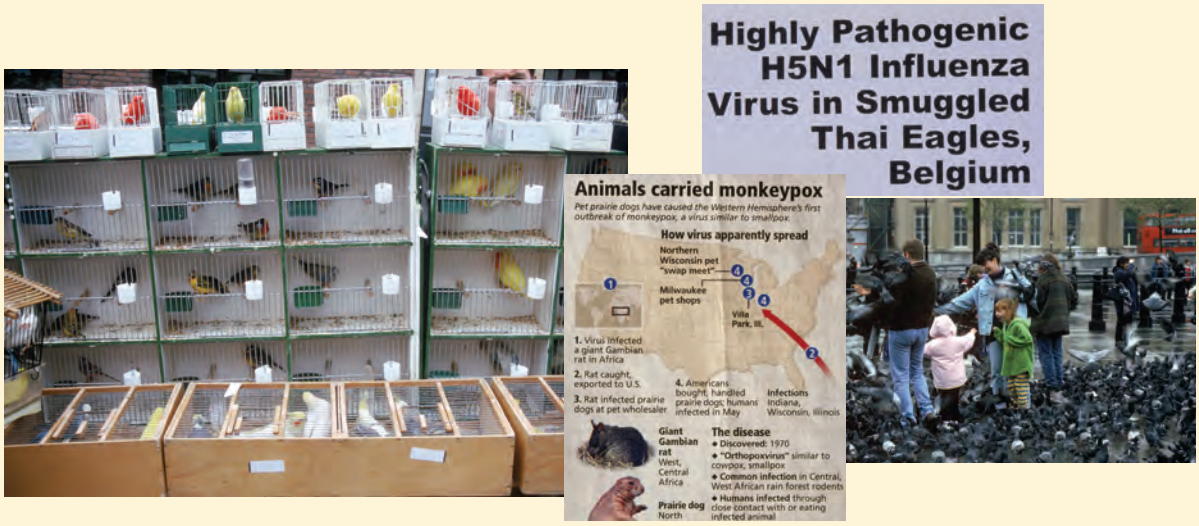
In the past, wildlife have been used as delivery systems for biological warfare, where these free-ranging animals were captured, infected, and released back into the wild to transmit disease to others of their kind, as well as to other susceptible species. Terrorists could use diseased wildlife to convey pathogens to wildlife and other species.

During the 19th, and into the 20th century, Montana Livestock Sanitary Board (USA) veterinarians used mange mites (*Sarcoptes scabiei*) as a means for reducing coyote and wolf numbers to protect livestock from depredation. Healthy coyotes and wolves were trapped, infested with mange mites, and released in attempts to initiate mange epizootics.[149,150] Similar practices targeting dingoes (**wild dogs**) took place in Australia.[151]

Although mange has long been recognized as a human pathogen, the mange mites infesting coyotes and wolves posed little human health risk because the mites were host-specific (to **canids**).[152,153] The situation differed for ranchers who attempted to employ tularemia (*Francisella tularensis*) as a biological weapon.

Tularemia is a category A disease (highest priority) within the current ranking of critical biological agents for public health response (Table 6.3). Ranchers in California (USA) considered any human disease risks for this disease as acceptable, as long as they could achieve their objective of reducing small rodent populations. These ranchers believed the small rodents were competing with livestock for forage on range and grasslands. So they employed **ground squirrels** infected with tularemia as vehicles to help decimate the rodent populations.[154,155] Other notable examples of wildlife being used as vehicles to initiate infectious disease epizootics in free-ranging wildlife populations include myxomatosis and viral hemorrhagic disease of rabbits (Table A).

Certain infectious diseases used for biological control can combat unwanted vertebrate species but are seldom employed because of low success rates and inherent risks to those releasing the agents.[156–158] Today, there is the capability to develop genetically modified disease agents that may target just a single species, thus reducing the potential for unwanted effects. Yet, these capabilities can go astray. Recently, a killer mousepox virus (highly virulent strain) emerged from a laboratory that genetically engineered the virulent strain to be a vector-borne contraceptive for reducing rodent populations. This unexpected killer virus outcome caused alarm because of the potential for similar outcomes in viruses that infect humans. This potential has implications for the development of new biological weapons.[54,159]



Photos by Milton Friend

The frequent movement of pathogens through the illegal and legal transportation of wildlife attests to the need for concern regarding wildlife as potential vehicles for bioterrorism.

Table A. Examples of infectious disease used for biological control of vertebrates.

Disease	Agent	Type	Targeted species	Country	Comments
Sarcocystis	*Sarcocystis singaporensis*	Protozoan parasite	Wild rats 	Thailand	Mortality of 58–92%.[156,160]
Capillariasis	*Capillaria hepatica*	Nematode (roundworm) parasite	House mouse 	Australia	Results unclear.[161]
Feline panleucopaenia	Parvovirus	Virus	Feral cats 	Oceanic Islands	Estimated populations of 3,400 cats on sub-Antarctic Marion Island reduced to about 620[156,162,163] successful in reducing cat populations in most cases.[156,164]
Myxomatosis	Myxoma virus	Virus	European rabbit 	France	Deliberate 1952 introduction on an estate resulted in unintentional spread leading to death of 90–98% of French rabbit population and spread of disease to other countries in Europe.[156,165]
Myxomatosis	Myxoma virus	Virus	European rabbit 	Australia	Initial reductions greater than 95% of populations; classic example of biological control by a pathogen.[156,165–167]
Rabbit hemorrhagic disease	Calicivirus	Virus	European rabbit 	Australia	Escaped from experimental biological control studies on an island in 1995 and invaded mainland; spread at rates of up to 414 km/month with initial mortality reaching 95% in some areas.[156,168–170]
Rabbit hemorrhagic disease	Calicivirus	Virus	European rabbit 	New Zealand	Illegal, intentional 1997 introduction resulted in high mortality and rapid spread among rabbit population.[156,171,172]
Mange	*Sarcoptes scabiei*	Metazoan parasite	Coyote 	USA	Anecdotal reports of infected coyotes being released to initiate epizootics causing reductions in coyote populations early in the 20th century.[150]
Tularemia	*Francisella tularensis*	Bacteria	Ground squirrels 	USA	Anecdotal reports of infected ground squirrels being released to initiate epizootics to help reduce small rodent populations during the early 1900s.

The frontline personnel for detecting disease outbreaks in free-ranging wildlife populations are the biologists and other field personnel providing management and oversight of the well-being of wildlife on public lands. These individuals may unknowingly be the first to encounter diseased wildlife associated with bioterrorist activities. Their knowledge of what is "normal" wildlife mortality in an area relative to species involved, season and location of occurrence, and magnitude of losses is useful in the identification of unusual events that may merit further investigation. It is prudent and serves the interests of national security for unusual wildlife mortality events to be referred to wildlife disease investigation personnel from whom assistance is normally obtained. Timely reporting and follow-up evaluations are important for maximizing the potential to contain the spread of infectious disease, a need that is driven by the potential for subsequent or concomitant disease spread to humans and domestic animals.

Within the USA and in most other countries, networks of national parks, wildlife refuges, game management areas, and other holdings provide key habitats for sustaining free-ranging wildlife populations and could be prime areas targeted by bioterrorists (Fig. 6.5). Many of these areas are managed to accommodate multiple uses, such as grazing by livestock, hunting, and other outdoor recreational activities. Natural occurrences of diseases, such as plague, tularemia, and ornithosis, has resulted in temporary closures of public land areas as a disease prevention measure (USGS National Wildlife Health Center records). In other situations, the well-being of livestock is challenged by disease in wildlife, such as brucellosis in elk and bison of the Greater Yellowstone Area of the western USA.[124–127] These situations attest to the natural movement of infectious disease between species groups in wildlife areas and suggest that bioterrorists could successfully use these areas as pathways for attacks against humans and agriculture.

The speed of detection and identification of the cause for disease events in wildlife differ greatly from that with humans or domestic animals. Capabilities are limited for disease surveillance, diagnosis, reporting, field response, and for other critical activities needed for effective disease containment and often hinder wildlife agency personnel from obtaining the assistance that they may need for investigating wildlife mortality events. In the USA, few wildlife stewardship or wildlife resource agencies have any internal capacity for diagnosing or combating disease events. Also, in the USA, stewardship responsibilities and regulatory authorities for different types of wildlife are distributed across different federal and state agencies (Table 6.10). Nevertheless, within North America there are three major, relatively long-standing wildlife disease programs that have considerable capacity and capabilities to serve wildlife resource agencies and bridge differences in responsibilities and regulatory authorities (see Chapter 3).

Within the USA, the Southeastern Cooperative Wildlife Disease Study (SCWDS) has been in existence since 1957 at the University of Georgia, Athens. This program primarily serves member state wildlife agencies in the Southeastern USA and a number of other nearby states. Project work is also done for USDA and other contractors. The National Wildlife Health Center (NWHC) in Madison, Wisconsin, became an entity within the U.S. Fish and Wildlife Service in 1975 and during the 1990s was transferred to the U.S. Geological Survey as part of science consolidation within the Department of the Interior (DOI). This program primarily serves the field units of the DOI (e.g., National Wildlife Refuge System, National Parks), is national in scope, and also carries out collaborative investigations with the Public Health Service (e.g., West Nile virus) and others. Canadian wildlife biologists are assisted by the Canadian Cooperative Wildlife Health Centre (CCWHC) in Saskatoon, Saskatchewan, and have been since its establishment in 1992. Each of the Canadian Provincial Schools of Veterinary Medicine maintains a component of this program.

All of these programs are at the forefront for early detection of new and emerging diseases of wildlife, have large databases on diseases of free-living wildlife, are staffed with a broad spectrum of specialists needed for disease investigation, and actively collaborate with one another. Their combined resources exceed the total resources for all of the other wildlife disease programs maintained by State and Provincial wildlife agencies and those within the university community, but overall are only a small fraction of the investments in human and domestic animal disease programs.

Wildlife disease capabilities need to be better developed throughout the USA and other nations in order to bridge the current gaps between wildlife and domestic animal health and between diseases that affect wildlife and humans. This would help bring wildlife disease capabilities to a level where they are a major force for addressing potential bioterrorist attacks. Enhancements of infrastructure and capabilities, as well as additional cooperation, collaboration, and coordination among wildlife disease programs are necessary components. Unlike public health and agricultural programs, currently there is no national infrastructure network within the USA for wildlife disease diagnosis, research, reporting, information exchange, or response to wildlife disease emergencies. Strategic planning for response to major wildlife disease events has begun, but more internal and interagency communication and cooperation is needed to delineate clear lines of authority, responsibilities, and response capabilities, particularly when disease outbreaks occur in urban and suburban environs. Because of increased interaction between wildlife and humans (Fig. 6.6) and the connections among wildlife, domestic animals, and public health, there is an elevated need to move informal wildlife disease networks into a coordinated, formal infrastructure.

Photo by Milton Friend

Figure 6.6 The close proximity between humans and urban wildlife provides a "bridge" for the delivery of infectious disease that easily could be exploited by bioterrorists because of inadequate disease surveillance and monitoring of these wildlife.

Surveillance and Monitoring

Public health and agricultural agencies in most nations organize disease surveillance and monitoring systems to track specific diseases. These systems serve to identify unusual disease events, patterns, and trends. A network of field programs, diagnostic laboratories, research, reporting systems, and a list of reportable diseases are the cornerstones that support disease surveillance and monitoring. In addition, routine testing of human patients and domestic animals provides continuous and consistent sampling that augments findings from clinical cases of disease. Such findings are expeditiously communicated within local communities and are combined with regional and national findings to provide important perspectives that help to evaluate disease risks, guide investigations, and serve regulatory and other purposes.

In contrast to the structured programs of public health and agriculture, wildlife disease surveillance and monitoring is largely ad hoc. There are no reportable requirements for wildlife diseases in most countries (beyond those of public health and agricultural importance), nor is there any methodical sampling of wildlife populations to provide insights of disease activity. Data gathered during independent scientific investigations may or may not be published, and may not be reported for one or more years after collection. Often these data are not readily accessible to many that could benefit from the findings and analyses. Exceptions include collaborative surveillance activities such as those developed in the USA for West Nile fever.[128–130] Voluntary reporting in program newsletters like those issued by the SCWDS and the CCWHC and the quarterly summary of wildlife die-offs compiled by the NWHC and published in the Wildlife Disease Association Newsletter provide highlights of current events but are not comprehensive in coverage or timely enough (Fig. 6.7).

Designing standardized spatial, temporal, and trophic level matrices of sampling to establish functional baselines for broad-based wildlife disease surveillance and monitoring could be of great value. Despite the current absence of structured, national wildlife disease surveillance and monitoring programs, they would be relatively easy to develop in most countries. Wildlife commonly are live-trapped for wildlife management purposes. Non-lethal sampling could become a component of many of these activities (Fig. 6.8). Other sampling could be done in conjunction with wildlife harvests and population reduction programs. Independent disease studies have commonly used all of these opportunities. Incorporating evaluation of suitable carcasses from the large numbers of wildlife found dead, as well as samples from wildlife rehabilitation programs, could augment other disease diagnostic data in a planned manner to enhance disease surveillance and monitoring.

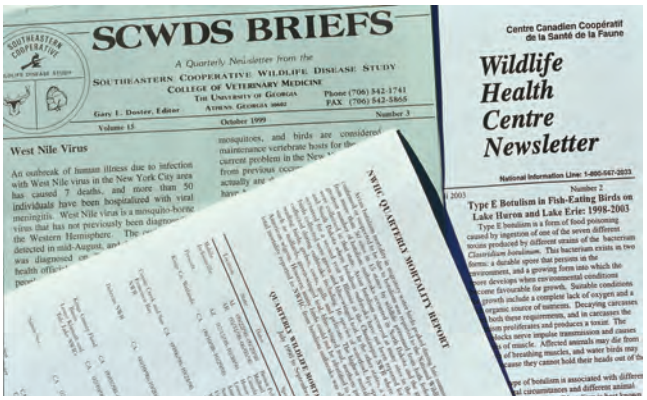


Photo by Milton Friend

Figure 6.7 Newsletters and Web sites of major wildlife disease programs are good sources for information about current wildlife disease issues.

Photo by Milton Friend

Figure 6.8 Sampling of wildlife for disease surveillance can be done in conjunction with wildlife management activities. Exposure to a broad spectrum of disease agents will be evaluated from the non-lethal sampling being done on these geese.

In the USA, current available resources for personnel, facilities, and sample processing do not as yet allow for development of sustainable wildlife disease monitoring and surveillance programs. Correcting this situation would serve national security by enhancing early warning systems for detecting unusual disease activity and trends in disease activity over time. Findings also would contribute to national efforts to combat emerging diseases that pose threats to human and domestic animal health.

Knowledge and Networks

Existing wildlife disease programs, although currently limited in size, number, and fiscal resources are rich in knowledge gained from decades of experience. Also, there are extensive networks of collaborators within the wildlife conservation community that can be called upon by the public health and agricultural communities to play a role in disease surveillance and monitoring that serve national homeland security. This collaboration is continuing to develop because it is essential for major improvements in surveillance and response capabilities (Fig. 6.9). We must be prepared to rapidly respond to bioterrorists who could capitalize on the current inadequacies of wildlife disease surveillance, monitoring, and response capabilities. Global efforts to combat emerging infectious disease at the wildlife-human and wildlife-domestic animal interfaces could help overcome existing deficiencies and in the end benefit national homeland security.

Reality in a Changing World

Although society has limited ability to prevent bioterrorist attacks, there still is a need to take preventative steps to reduce potential risks for such attacks. Increased laboratory security for disease agents, greater controls for investigations involving these pathogens and other security measures implemented since the fall of 2001, are necessary to restrict access to dangerous pathogens. A protective curtain of sorts has been drawn around us that will more readily restrict terrorists from obtaining pathogens that could be used as bioweapons. However, this protective curtain is not impermeable. Enhanced surveillance activities for early detection of

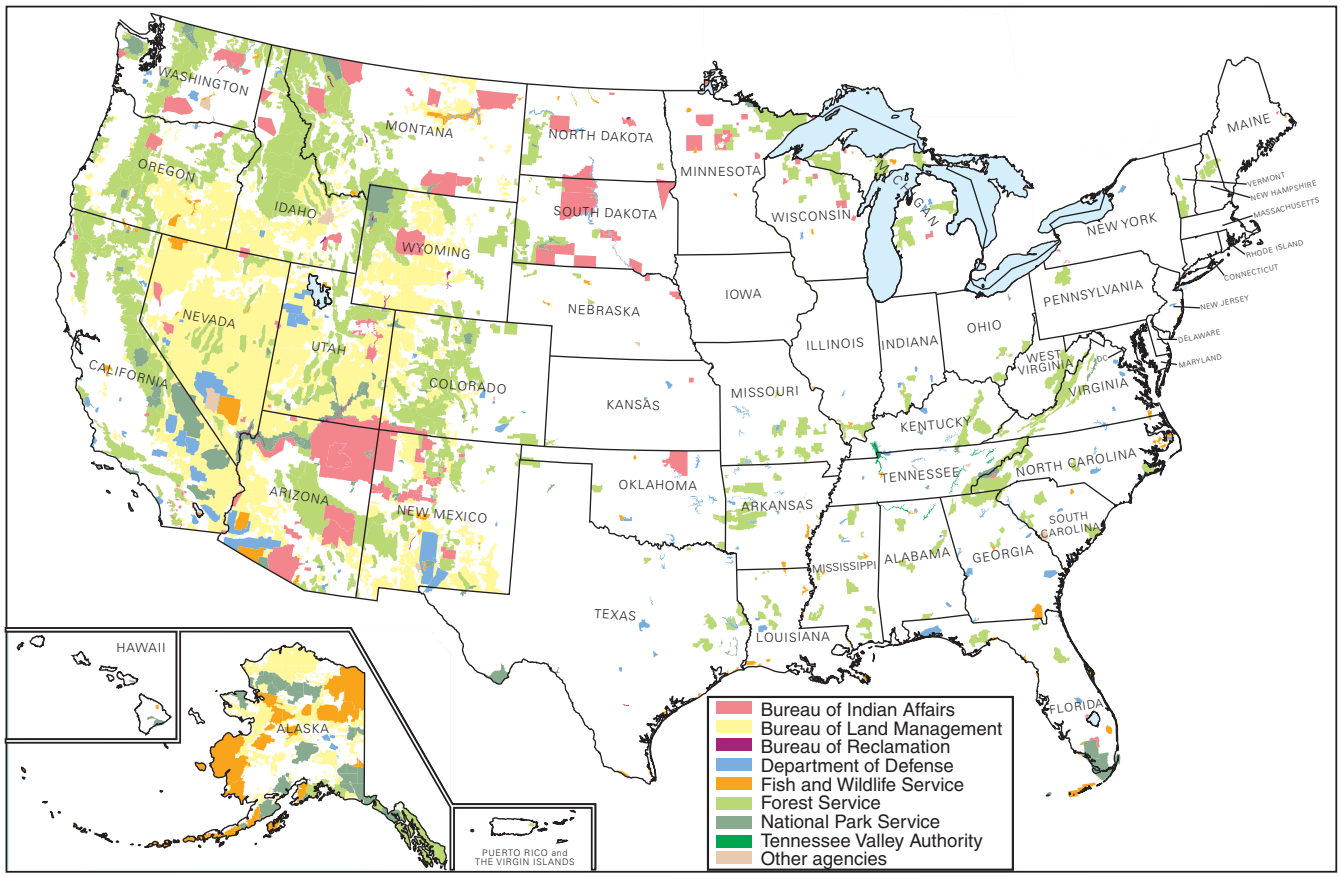


Figure 6.9 The extensive network of federal lands provides an appropriate grid for wildlife disease surveillance and monitoring to detect emerging diseases in wildlife and attendant threats for domestic animals and humans.

flaws in this protective curtain will be bolstered by enhanced strategic planning, infrastructure development, and rapid response capabilities that minimize impacts and quickly repair damage that may occur. Furthermore, the current curtain assumes frontal attacks by known enemies using familiar tactics for exposing humans and domestic animals to dangerous pathogens. The vulnerability of the curtain to unconventional attacks also needs to be addressed.

Wildlife have a great capability to breach the protective curtain and easily pass through its fabric. Examples include infectious diseases transported by wildlife that caused major economic and/or human health impacts, such as Nipah virus in Malaysia,[131,132] SARS in China,[133–137] monkeypox in the USA,[138] and current concerns associated with the role of migratory birds in global movement of highly pathogenic H5N1 influenza virus. Wildlife and the diseases that they can transport represent flaws in the fabric of this protective curtain and can be exploited by terrorists in attacks against society. The protective curtain can be greatly strengthened by fully incorporating the wildlife factor into its fabric. This refurbishment and enhancement can serve society well in many ways, including contributions to the larger issue of infectious disease emergence and resurgence worldwide.

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