The ABCs of bioterrorism for veterinarians, focusing on Category B and C agents

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In 1999, the **Centers for Disease Control and Prevention (CDC)** brought together a group of experts to assess and categorize agents that could be used in bioterrorism attacks. The Category A, B, and C biological bioterrorism agent list (**Appendix 1**) was derived from a consensus of that group.[1] Nearly all of these potential bioterrorism agents are zoonotic in nature. Veterinarians are considered to be experts in zoonotic agents and diseases; therefore, veterinarians should be familiar with the agents on this list and the clinical signs of the diseases they cause in animals and humans. Moreover, all veterinarians should know what to do if they suspect infection with these agents in an animal or human. The purpose of this article is to provide such information, discuss what is being done to address bioterrorism in the United States, and identify what challenges still need to be met. Selected Category B and C agents will be reviewed here; Category A agents have been discussed previously.[2]

Agents in Categories B and C

Compared with Category A agents, those belonging to Categories B and C are less likely to cause large-scale illness and death, but still have potential for widespread dissemination and require little preparedness measures beyond those implemented for agents in Category A.[1] Category B agents are less familiar to the general public than those in Category A, and their impact on public health would be less severe. Category C agents are those that are believed not to pose a high risk for bioterrorism; their use as bioterrorism agents can be addressed through preparedness planning for agents in Categories A and B. Given these caveats, some agents in Categories B and C do have potential for massive economic disruption and large numbers of human deaths if used for bioterrorism.

Brucellosis—In humans, brucellosis (also known as undulant fever) is associated with a fever that waxes and wanes over a period of weeks to months if untreated and can affect almost any organ system. Osteoarticular involvement is the most frequent complication, occurring in as many as 40% of cases, and may manifest as arthritis of peripheral joints, spondylitis, osteomyelitis, or bursitis.[3] Other effects may involve the gastrointestinal and genitourinary tracts and the hepatobiliary, pulmonary, neurologic, and cardiovascular systems. Illness can be debilitating, and relapse may occur if treatment is incomplete or there is an isolated site of infection that requires surgical drainage. Severity of disease in people depends on the species of *Brucella* with which they are infected.[3] The most profound illness is associated with infection with *Brucella melitensis*; less severe illness is associated with infection with *B suis*, less still with *B abortus* infection, and *B canis* infection infrequently causes disease.[4] *Brucella ovis* is not pathogenic for humans. Fatalities from brucellosis are rare and occur typically in < 2% of cases as a result of endocarditis.[5] Relapse can occur, especially if there has been inadequate treatment or poor compliance with treatment.[3]

Brucellosis in animals primarily affects cattle, sheep, goats, pigs, caribou, reindeer, dogs, buffalo, bison, elk, and occasionally horses.[6] Infection is most often associated with abortion in females and epididymitis in males[4]; clinical diagnosis is difficult unless these clinical signs are observed. Cows infected with *B abortus* or female goats infected with *B melitensis* rarely recover from infection.[4] Shedding from uterine or vaginal discharges can occur, and udder and supramammary lymph node infections may lead to contamination of milk.[4] Cattle may also develop orchitis and synovitis, and horses may develop fistulous withers when infected with *B abortus*.[7] In pigs infected with *B suis*, abortion, lameness, orchitis, sterility, incoordination, and posterior paralysis may be evident.[7] There are varying levels of susceptibility to infection with *Brucella* spp outside the normal animal host range. For example, *B melitensis* is often associated with severe abortion storms in sheep and goats, but may infect cattle[6,7]; pigs infected with this agent may develop clinical disease indistinguishable from that of *B suis* infection.[7] *Brucella suis* biovars infect reindeer, caribou, and feral pigs and may cause orchitis or epididymitis in dogs.[7] *Brucella suis* can also cause fistulous withers in horses[6] and has infrequently been found in some cattle herds.[6,7] Occasionally, *B abortus* may cause abortion in pigs, although it is not normally pathogenic.[7] Dogs are definitive hosts for *B canis*, but have been found infected with *B abortus*, *B suis*, and *B melitensis*.[8] Survival of *Brucella* organisms in the environment depends on many factors. *Brucella abortus* is reported to survive up to 100 days in the winter and 30 days in the summer, and *B suis* may survive 4 to 6 weeks in feces, urine, and water.[7]

Biological attack scenario involving *B melitensis*

The impact of an attack involving aerosolized *B melitensis* on a city of 100,000 inhabitants, without intervention, could result in 82,500 illnesses and 413

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deaths.[9] Costs associated with the aftermath of this type of bioterrorist attack could reach $477.7 to $650 million.[9] The **World Health Organization (WHO)** has estimated that under specific conditions, 50 kg of dried *Brucella* organisms released near a developed city of 5 million inhabitants would result in 150,000 illnesses and 600 deaths; the case-fatality rate would be 0.5%.[10] This estimate was based on the assumptions that atmospheric conditions were stable at the time of the attack and the population had no warning and no protection from the agent (these same assumptions will be used throughout this article in describing WHO attack scenario estimates).

Q Fever—An organism that is particularly capable of surviving aerosol dispersal, heat, and desiccation is the Q fever agent, *Coxiella burnetii*. This organism is of considerable concern because it has a very low infectious dose for humans (as low as 1 organism)[11,12] and can persist in the environment for weeks to months under harsh conditions. Unlike anthrax, however, clinical Q fever in humans is not usually severe and is rarely fatal. As many as 50% of people exposed to *C burnetii* may develop specific antibody without having clinical signs of disease.[12,13] Disease in humans can be either acute or chronic.[14,15] Acute disease commonly has 3 major manifestations: nonspecific flu-like signs (fever, headache, myalgia, malaise, chills, cough, sweating, weight loss, and vomiting), pneumonia, and hepatitis.[11,15] Other less common manifestations associated with the acute form include maculopapular or purpuric exanthema, pericarditis, myocarditis, aseptic meningitis or encephalitis, seizures, optic neuritis, and anemia.[15] Chronic disease occurs in approximately 1% to 2% of patients[12] and is usually associated with the development of endocarditis (the most severe complication).[11] Chronic hepatitis, osteomyelitis, pericarditis, and vascular complications may also occur.[11,12] The mortality rate for Q fever is low overall, but is highest among chronic Q fever cases (typically 1% to 11%)[15]; among humans with Q fever-associated endocarditis, mortality rate may be as high as 24% despite treatment.[11] People most often acquire Q fever through the inhalation of aerosols from contaminated placental fluids, dusts,[14] or wool.[15] Person-to-person transmission is very rare.[11,15]

Disease in animals develops primarily in livestock and results in abortions.[11] Sheep, goats, and cattle are the main reservoirs.[13] These animals are primarily responsible for transmission to humans; however, disease in humans has resulted from parturient cats,[16,17] dogs,[15,18] and wild rabbits.[15,19] Clinical signs of infection with *C burnetii* in dogs and cats are rare but may include abortion.[18] *Coxiella burnetii* is shed in the urine, feces, milk, and fluids of infected parturient animals.[12,15]

Biological attack scenario involving *C burnetii*

The WHO has estimated that 50 kg of dried *C burnetii* organisms released near a developed city of 5 million inhabitants would result in 250,000 illnesses and 250 deaths.[10]

Food and water threats—The threat of acts of bioterrorism involving food and water is of great concern and has received much attention of late. The safety of the US food supply and the issues surrounding agroterrorism have been reviewed in great detail in other publications.[20-22] As actual bioterrorist attacks have illustrated, food is one of the best mediums for waging bioterrorism; ingestion of contaminated food is considered the prime route of attack used by biocriminals who target people.[23] Agroterrorism can be defined as the use, or threatened use, of biological (including toxins), chemical, or radioactive agents against some component of agriculture in such a way as to adversely impact the agriculture industry (or any segment thereof), the economy, or consumers.[22] With food and fiber generating approximately 12.3% of the US gross domestic product in 2001 and total agricultural exports valued at $53 billion,[24] the safety of the food supply in the United States is paramount. Targets for agroterrorism include farms (livestock, crops, and farmers), transportation, food-processing plants, water supply, restaurants, and grocery stores, among others; agroterrorism may be directed at an industry as a whole (eg, the dairy industry) or the economy. Ultimately, agroterrorism is economic terrorism and the end target is the public, namely the people who rely on the food supply.[22]

In 1995, 87% of the US population was served by public water supply.[25] It is estimated that there are 160,000 public water systems in the United States, with 466 of them serving nearly half of the total population.[26] Although water treatment facilities may be considered points of interest to terrorists and should be placed under appropriate tight security, the reality is that water is not as efficient as other modes by which to carry out a biological attack. Three factors that mitigate the risk associated with water include: treatment, time delay, and dilution. Most municipal water in the United States undergoes extensive treatment (flocculation, sedimentation, filtration, and disinfection, although treatment methods may vary among municipalities) to kill, reduce, or remove dirt, clay, sewage, bacteria, algae, protozoa, viruses, hard minerals, and other elements that make water unsafe or unfit for consumption. Contamination of finished water is difficult but not impossible for motivated terrorists and would require access to the main holding tanks, reservoir towers, pipes, or sites elsewhere in the distribution system. Indeed, the distribution system is likely the most vulnerable component of a drinking water system[26] and should receive high priority for security measures. Some smaller treatment facilities that perform limited processing of water and have minimal security measures would be at higher risk for bioterrorism than larger metropolitan water treatment facilities. Treated water contains residual chlorine concentrations that would adversely impact the survival of almost all microbial agents. Also, some water treatment facilities now use ozone in their treatment process that would easily destroy chlorine-resistant microbes or perform nanofiltration, which would essentially remove all microbes. The time (in some instances days or weeks) that elapses before source water is available to customers also reduces the risk of an effective terrorist attack with biological and potentially chemical and radioactive agents.[26] It is also important to understand that dilution factor alone is a formidable obstacle to launching a successful biological attack via the water supply.[27] Vast quantities of the agent of choice would have to be made and delivered to an unobtrusive access point within the water supply system. Some cities' facilities will process several hundred million gallons of water per day and have main holding tanks of 10 million gallons or more. Even if one considers that a terrorist might use *Cryptosporidium* organisms (known to be fairly chlorine resistant), extremely large quantities of this agent would have to be used to be effective and it would likely not be worth the time, effort, and expense.

A typical person only drinks about 1 to 1.5 L of tap water each day.[27] This means that most of the water that a terrorist could contaminate would not be used for drinking, but for other purposes such as showering, flushing toilets, laundry, washing motor vehicles, watering the lawn, washing dishes, cooking, and industrial uses. Generally, the use of toxins or chemicals would be more effective; compared with microbial agents, these compounds act more quickly and pose a greater threat to water safety.

Biological attack scenario involving the water supply

An attack against a municipal water supply involving botulinum toxin has been modeled by the WHO.[10] In that scenario, assuming perfect distribution and dilution and that botulinum toxin is not inactivated by chlorine, it was estimated that 0.24 kg of toxin placed into the water supplied to a city of 50,000 inhabitants who each drinks 0.5 L of water/day would deliver a lethal dose to 60% of consumers after 17.5 hours. It should be noted that oxidation, denaturing, or inactivation of the toxin in treated water was not taken into consideration for these estimates.

Nipah—A prime example of an agent capable of causing severe economic disruption and human death is the Nipah virus. This virus belongs to the family Paramyxoviridae; in 1998, it emerged in Malaysia as a zoonotic disease of pigs. From September 1998 to May 1999, there were 265 human cases of Nipah virus infection and 105 associated deaths (40% case-fatality rate) documented in Malaysia; another 11 cases of infection and 1 Nipah virus-associated death were reported in Singapore.[28] Infection in humans appears to result from close contact with pigs and their secretions, especially respiratory secretions.[28,29] Clinical signs in humans are characterized by fever, headache, dizziness, vomiting, cough, tachycardia, and many neurologic signs such as absent or reduced reflexes, abnormal pupils, reduced consciousness, myoclonus, encephalitis, seizures, areflexia, and hypotonia.[28,30] Clinical relapse can occur.[30] There is concern for nosocomial transmission because the virus has been detected in urine and respiratory secretions of human patients.[31] Despite this, person-to-person transmission has not been documented.[32,33]

Clinical signs in pigs may vary with age,[34,35] but often include fever, severe respiratory syndrome, and significant neurologic impairment. Pigs from 4 weeks to 6 months of age may have a febrile illness with labored breathing and a harsh nonproductive cough (a loud barking cough nicknamed the 1-mile cough).[28,34,35] Other signs can include weakness or twitching, muscle spasms, myoclonus, neurologic twitches, uncoordinated gait, and generalized signs of pain. Signs in infected boars and sows include acute fever, labored breathing, increased salivation, nasal discharge (serous, mucopurulent, or bloody), agitation, head pressing, nystagmus, and sudden death.[35] Piglets may develop open-mouthed breathing and weakness with muscle tremors and neurologic twitches.[35] Although infection rates can approach 100%,[28,35] the mortality rate for infected pigs is approximately 5% or less, but may be as high as 40% in piglets.[35] The incubation period in pigs is thought to be 7 to 14 days.[35] Natural infection has been detected serologically in dogs,[32,34] cats,[29,34,35] horses,[29,35] goats,[35] chickens,[34] and bats.[34] However, illness occurs only in pigs, dogs, cats, and humans.[34] Infected dogs have signs suggestive of distemper, including fever, respiratory distress, conjunctivitis, and mucopurulent nasal and conjunctival discharges.[36] Oronasal inoculation of 2 cats with Nipah virus under experimental conditions produced fever and signs of depression in both cats. One cat also developed vomiting, dyspnea, and open-mouthed breathing; vasculitis and meningitis were diagnosed histologically.[37] Researchers were able to isolate the virus from the urine of both cats during their illness. Nipah virus infection poses a great concern to the swine industry and the agricultural industry of nearly every country. Its potential as a serious agroterrorism or bioterrorism threat should not be discounted. To control the outbreak in Malaysia, more than 1 million pigs from > 900 farms were slaughtered,[28] and the demand for pork decreased as much as 90% during this period.[38] The reservoirs for Nipah virus are several species of fruit bats (including the genus *Pteropus*) and insectivorous bats.[39] Finally, the virus is very labile and easily killed by common detergents.[28]

Other threats—Other potential threats that were not included in the classification scheme by the CDC may include Hendra and West Nile viruses, although their effectiveness as bioterrorism agents is questionable. As an example, some information regarding the Hendra virus is included here. The Hendra virus shares similarities with Nipah virus in that it belongs to the family Paramyxoviridae and has pteropid bats as its natural reservoir.[40] Hendra virus first emerged in Australia as the cause of acute respiratory disease in horses in 2 separate outbreaks in 1994[41] and again in a third isolated outbreak in 1999[42]; no cases of this disease have been reported since. In the 3 Australian outbreaks, 20 horses were infected, which resulted in 15 deaths; also, 3 humans were infected, which resulted in 2 deaths.[41,42] Transmissibility of Hendra virus from horses to humans appears low and requires close contact, and all human cases of infection have been linked to pregnant mares.[41] Clinical signs in humans include influenza-like illness, sore throat, headache, vomiting, neck stiffness, fever, seizures, pneumonitis, respiratory failure, coma, encephalitis, and death.[33,43,44] Infection with Hendra virus in horses is characterized by fever, signs of depression, loss of appetite, tachycardia, tachypnea, frothy or hemorrhagic nasal discharge, myoclonic twitches, and severe respiratory distress.[44] Results of an experimental study[45] indicated that infected cats can transmit Hendra virus to horses. Affected cats developed open-mouthed breathing and dyspnea.

Recognizing a Bioterrorism Event

Obviously, the susceptibilities of different animal species to the Category A, B, and C agents vary. Clinical signs of disease observed in animals will differ depending on multiple factors such as route of exposure, dose, species susceptibility, age, overall health status, and immune status. Clinical signs of disease that develop after a bioterrorist attack will not necessarily be identical to those of naturally acquired disease. For example, the aerosolization of an agent may result in the development of clinical signs in species that were previously considered resistant or new or unusual signs in known susceptible species. Occasionally, veterinarians may encounter naturally occurring cases of disease caused by some of the Category A and B agents, but many of these diseases are rarely (and some never) seen by the typical practitioner. Awareness among veterinarians that certain types of clinical signs in animals are associated with infection with organisms that are potential bioterrorism agents may aid in the early recognition of a bioterrorist attack **(Appendix 2)**. Moreover, practitioners would need to assess whether the animals presented to them were ill as a result of natural versus intentional exposure. Veterinarians must be alert for indications that a bioterrorism event has occurred. With the intentional release of a biological agent, just as with a naturally occurring outbreak, there is a delay from time of exposure until onset of clinical signs. This incubation period (days to possibly weeks) is an advantage for terrorists who will have time to escape the area after the covert release of a bioterrorism agent. Veterinarians already need to maintain a reasonable but high degree of suspicion when examining animals with a potential infectious disease to rule out a zoonosis that threatens public health or a foreign animal disease that threatens US agriculture. It is a natural extension to carry this suspicion over to include potential zoonotic bioterrorism agents. Veterinarians may see an ill animal and an ill owner at the same time; although the disease may not have the same clinical signs in humans as it does in an animal species, the early suspicion and investigation of such a connection could mean the difference between stopping the spread of a highly contagious pathogen and not detecting it altogether. Early detection and immediate reporting is critical. Indications that an intentional release of a biological agent has occurred include the following:

- An unusual geographic or temporal clustering of illnesses or humans or animals presenting with clinical signs suggestive of an infectious disease outbreak.[46]
- Humans or animals that have clinical signs that are unusual for a given geographic area, such as detection of a cat or person with signs of plague in Florida, which is a state that is known to be free of that disease. Such a diagnosis would be cause for concern and should be thoroughly investigated.
- An unusual age distribution for common diseases.[46]
- The occurrence of illness outside its typical seasonal distribution. For humans, this might mean an increase of cases with flu-like signs during the summer.

Importance of Veterinarians in Public Health Disease Surveillance and Reporting

Animals and veterinarians play important roles in the surveillance for diseases of public health significance, and the input of veterinary medical professionals into the public health system is crucial to the health of humans and animals alike. Data from practitioners on individual cases of a particular disease may be collected by agencies at the local, state (eg, state health departments and state veterinarians' offices), or federal (eg, CDC and USDA) levels for analysis; subsequently, findings may be used to make decisions concerning control and prevention of these diseases, education of the public, and policies that may potentially affect tens of millions of people.

An excellent example of the essential contribution of veterinarians to the public health surveillance and disease-reporting process is illustrated by recent events associated with West Nile virus. Surveillance for West Nile virus is often conducted by use of sentinel chicken flocks, live wild birds, dead wild birds (especially of members of the Corvidae family, such as crows and blue jays), and nonhuman mammals, particularly horses.[47] Other active surveillance activities include trapping and testing of mosquitoes. Testing of specimens from animals or mosquitoes may include viral isolation, reverse transcription-polymerase chain reaction assay, immunohistochemistry, hemagglutination inhibition, ELISA, and plaque-reduction neutralization.[47] Although surveillance of illnesses and deaths among avian species is the most sensitive measure of early West Nile virus transmission activity, mosquito surveillance is best for quantifying West Nile virus transmission intensity in a given area.[47] Horses also make effective sentinels because of their high exposure to mosquitoes, which makes them more likely than humans to be infected.[47] Indeed, in some rural areas, clinical signs in horses may be the first indication that West Nile virus is present.[47] By monitoring West Nile virus in birds and mosquitoes, it is anticipated that West Nile virus infection, and its associated illness and death, in humans and animals can be more accurately predicted and hopefully prevented. Within the United States, equine cases of West Nile virus infection typically precede human cases chronologically and may portend animal and human morbidity and mortality rates in a given region. Prompt diagnosis and reporting of affected horses by veterinarians aid this early warning system. In 2002, infection in horses preceded human cases in 16% of the counties where human cases were reported.[47] As of July 9, 2003, there had been only 1 report of West Nile virus infection in a human, yet 22 horses from 11 states (and 1 dog in South Dakota) had been reported to be infected.[48] By August 6, these numbers had risen to include 153 affected humans in 16 states and 282 affected horses in 22 states.[49] However, by November 28, 2003, there were 8,567 human cases and just 4,146 equine cases.[50] The usefulness of horses as surveillance tools for West Nile virus in the United States has eroded in the face of mass vaccination efforts. More than 27 mammalian species are known to be susceptible to West Nile virus infection, and disease has been reported in 20 of these (including humans).[47] Infection of new species, particularly smaller companion animals, can only serve to stress the importance of the veterinary practitioner in ongoing surveillance efforts and the need for reporting of West Nile virus cases. In 2003, West Nile virus infection was reported in a record number of dogs (30) and also in 1 cat.[50]

The prompt identification and reporting of disease among animals provide public health and veterinary officials with information regarding the epidemiologic features and geographic progression of disease as well as indications of which prevention methods work best. Reporting of disease provides other veterinarians, animal owners, and public health workers in adjacent counties or states with warning of what to expect. Data in reports may be used to identify new susceptible species, new routes of transmission, or new risks to human and animal health. For West Nile virus, quick and effective response to surveillance reports is essential in prevention of human and animal infection,[47] and submission of reports by veterinary practitioners is fundamental to this effort.

Veterinarians are involved in the reporting and surveillance of many other diseases of zoonotic and public health importance, including rabies, *Mycobacterium bovis* infection, psittacosis, eastern and western equine encephalitis, bovine spongiform encephalopathy, and others. Without doubt, the reporting of cases of disease associated with Category A, B, or C agents to state veterinarians' offices or to local or state health departments will serve to protect the lives of many.

Response to the Threat of Bioterrorism

The CDC has adopted a bioterrorism mission statement to lead the public health effort in enhancing readiness to detect and respond to bioterrorism.[51] The CDC has made local and state preparedness and response efforts a priority and is developing, or has already developed, extensive bioterrorism response plans and guidelines for outbreaks involving several of the Category A, B, and C agents.[51] The Department of Homeland Security along with the Department of Health and Human Services together manage the **Strategic National Stockpile (SNS)**, previously called the National Pharmaceutical Stockpile. The SNS was established to better respond to a biological or chemical event. Within the SNS are pharmaceuticals, vaccines, medical supplies, bandages, and equipment to assist state and local communities in responding to an emergency.[51] The SNS has developed units (known as 12-hour Push Packages) filled with these supplies that are kept in undisclosed locations around the United States and can be delivered anywhere in the country within 12 hours. Another aspect of the SNS is the vendor-managed inventory, which is designed to provide specific drugs or other medical materials from manufacturers directly to the requesting agency within 24 to 36 hours.[51] The Laboratory Response Network was also developed by the CDC, in conjunction with other partners, to better meet the laboratory needs related to bioterrorism.[51,52]

Federal funding and policy have also been altered to meet the needs of bioterrorism readiness. On June 12, 2002, President Bush signed the $4.3-billion Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (HR 3448).[53] From this, $1.6 billion will be used as grants to improve preparedness for response to bioterrorism and other public health emergencies at state and local levels and in hospitals, and $190 million will be used for agricultural bioterrorism research and development. Additionally, the President's Budget for Fiscal Year 2004 provides for many items regarding homeland security and bioterrorism preparedness, including the following[54]:

- $36.2 billion for Department of Homeland Security activities, which is 7.4% more than the 2003 level of funding and > 64% more than Fiscal Year 2002.[55]
- $116.8 million assigned to the FDA for bioterrorism-related food safety programs.
- $1.1 billion assigned to the CDC for bioterrorism activities and efforts.
- $112 million assigned to USDA for food safety, security, and agricultural protection.
- Plans to increase the number of Push Packages from 8 to 12 with a concomitant increase in variety of drugs included in the stockpile.
- Expansion of the **Health Alert Network (HAN)** to reach 90% of US counties.

On January 24, 2003, the **Department of Homeland Security (DHS)** was created. The mission of the DHS is to prevent terrorist attacks within the United States, reduce America's vulnerability to terrorism, and minimize the damage from potential attacks and natural disasters.[56] The DHS is comprised of 5 directorates: Border and Transportation Security; **Emergency Preparedness and Response (EP&R)**; Science and Technology; Information Analysis and Infrastructure Protection; and Management.[57] The EP&R division will lead the DHS recovery in the event of a biological or radiological attack and coordinate involvement of response teams from other federal agencies.[58] Much of what EP&R does has its foundations in the **Federal Emergency Management Agency (FEMA)**. The EP&R encompasses FEMA, the SNS, and the National Disaster Medical System, as well as the Nuclear Incident Response Teams, Domestic Emergency Support Teams, and the National Domestic Preparedness Office of the Federal Bureau of Investigation.[59]

To bolster the ability of state and local public health workers to respond to bioterrorism and other public health emergencies, the CDC established a nationwide network of **Centers for Public Health Preparedness (CPHPs)** in 2000.[60] The purpose of the CPHPs is to improve the competency of public health workers and the capacity to respond to public health threats and emergencies. This is done primarily through competency-based training of public health workers. There are 3 types of Centers, designated as Academic, Specialty, and Advanced Practice Centers. Most of the CPHPs are Academic Centers located at schools of public health and are closely linked with state, local, or regional needs. They form the heart of the CPHP network and work to enhance bioterrorism preparedness and strengthen public health infrastructure. Specialty Centers generally focus on a topic, professional discipline, core public health competency, practice setting, or application of learning technology. Training and education form a large part of Specialty Centers' activities. The Advanced Practice Centers were created to develop advanced applications at the community level. Those Centers are involved with issues regarding operational readiness assessment, integrated communications and information systems, and comprehensive training and evaluation as they relate to bioterrorism preparedness and other health threats. There are 39 CPHPs distributed across the United States with much communication and coordination among them to meet the needs of frontline workers in the public health field.

The **Center for Food Security and Public Health (CFSPH)** in the College of Veterinary Medicine at Iowa State University was founded in July 2002 with support from the CDC. In August 2003, the CFSPH was designated a Specialty Center in Public Health Preparedness for Veterinary Medicine and Zoonotic Diseases. The mission of the CFSPH is to increase national preparedness for accidental or intentional introduction of disease agents that threaten food production or public health. The CFSPH integrates veterinary medicine and expertise in zoonotic diseases with the ongoing activities and needs of the CDC. To aid in the awareness of the Category A, B, and C agents and their zoonotic characteristics, the CFSPH recruited 125 veterinarians from 46 states and Puerto Rico to attend a comprehensive educational program on the Category A, B, and C bioterrorist agents that was held in January 2003. The goal of this train-the-trainer program was to train veterinarians on bioterrorism, bioterrorism agents, and the zoonotic aspects of these agents so they could then educate other veterinarians, food producers, and the general public. The program contained 28 presentations covering 54 disease agents, accompanied by in-depth fact sheets, color wall charts, and multiple handouts. Materials were made available in printed format and also on CD-ROM.[a] Participants were charged with returning to their state and conducting (within 1 year) 6 seminars for small and large animal veterinarians, food animal producers, or the general public. The US Surgeon General, Dr. Richard Carmona, iterated the importance of veterinarians in public health and bioterrorism preparedness in his keynote address during the training.

Further Preparations

The HAN is a means of addressing public health needs and emergencies by use of secure Internet connections to rapidly disseminate health alerts and important public health information and guidelines to state and local public health personnel. It also provides a means for distance learning, disease surveillance, laboratory reporting, and relating information pertaining to bioterrorism.[61] The HAN will eventually allow all users to access and transmit disease information in a secure fashion. All 50 state health departments, including some city and county health departments, are connected to the HAN and receive direct health alerts, advisories, or updates.[62] Incorporating veterinarians and veterinary and agriculture agencies into the national HAN would achieve more robust disease surveillance and reporting and better address bioterrorism preparedness and response. In a recent publication,[63] the National Research Council recommended establishing a system like HAN for agriculture groups to help combat bioterrorism and improve reporting, learning, surveillance, and information sharing. The state of Iowa is currently working to incorporate veterinarians into its HAN.

Because the fields of veterinary and human medicine overlap in many areas, it makes sense that veterinary medical first responders have the same tools as human medical first responders to combat the same threats, and that open communication between the 2 disciplines flows freely. A report[64] issued by the US General Accounting Office in April 2003 states, "As we found with the West Nile virus, the links between public and animal health agencies are becoming more important. Many emerging diseases affect both animals and humans, as do many viruses or other disease-causing agents that might be used in bioterrorist attacks."

In 2001, the American Public Health Association recognized the importance of veterinarians in public health and urged that state and local health departments understand and support the role of veterinarians in public health; the Association further recommended that the services of persons qualified in veterinary medicine be made available to health departments and that every state health department should have a designated position for a public health veterinarian.[65] To date, there are 42 states that have a State Public Health Veterinarian; in the author's opinion, every state should have one. The Council of State and Territorial Epidemiologists released a position statement[66] in 1999 that recommended that every state health department enhance epidemiologic surveillance and response by establishing a position for a public health veterinarian. The statement identified that veterinarians have a unique understanding and ability to work within the interface of human and animal health. Furthermore, it recognized that the distinct qualifications and skills that veterinarians bring to the public health team are strong assets in building comprehensive public health programs in every state. These are sound comments given that 75% of emerging pathogens are zoonotic[67] and that almost every health department at every level is understaffed.

Veterinarians and veterinary diagnostic laboratories should become part of nationwide active surveillance for Category A, B, and C agents and diseases, as well as for new and emerging infectious diseases. Another report[68] issued by the US General Accounting

Office on bioterrorism preparedness efforts within the United States indicates that improvements have been made at the state and local levels, but inadequacies remain, especially in cities that have not experienced a major public health emergency. The report specifically identifies deficiencies in surveillance and laboratory capabilities, which are critical areas that the veterinary profession can and should help strengthen. Indeed, there is impetus and movement now for including veterinary and animal health laboratories in the Laboratory Response Network and collecting more information on infections affecting animal and human health.[69] The Department of Public Health in Iowa is presently conducting a fledgling program of syndrome surveillance of veterinary clinics for case outcomes that might reflect the use of biological or chemical agents by terrorists. It is hoped that this program will expand and improve upon its successes.

To meet the need for better diagnosis, surveillance, and early warning of foreign animal diseases, zoonotic diseases, and bioterrorism events, the National Animal Health Laboratory Network was set up with 12 veterinary diagnostic laboratories as a 2-year pilot program in 2002.[70] Funding for expanding this network in all states should be a top priority for the coming years to improve animal and public health and increase readiness for bioterrorism.

In this author's opinion, more funding needs to be distributed to states for the specific purpose of addressing agroterrorism. Dedicated positions in government need to be created at the state level for experts to assess and address the threat posed by terrorists who are targeting agriculture. To mount a proper defense and response to agroterrorism, essential equipment, proper data analyses and threat assessments, training, and funding must be provided.

Conclusion

All veterinarians should know the name of and how to contact their State Veterinarian, their USDA Area Veterinarian in Charge, and their State Public Health Veterinarian; telephone numbers of these individuals should be immediately accessible. All veterinarians should also know how to contact their local and state health departments. Practitioners should not hesitate to telephone any of these resources to report diseases or to ask for information or help. Establishing a rapport with all of these individuals and agencies early, before an emergency occurs, is a good idea and can be achieved in many ways: by attending seminars or continuing education programs that they sponsor; by offering to sit on committees convened to deal with animal or public health issues; by offering to assist with dissemination of information locally on their behalf; by consulting with them about relevant cases or topics and concerns of mutual interest; or by other avenues. Finally, any one of us should use the telephone to dial 911 if criminal or terrorist activity is suspected.

Veterinarians must take an active approach to bioterrorism and become involved in preparedness and response and in public health overall. As Noah et al[71] stated, veterinarians are a vital component in bioterrorism preparedness, surveillance for bioterrorism agents, controlling disease, and even in the treatment of the ill. Veterinary practitioners are key to an effective, robust surveillance and early warning system for bioterrorism that targets humans or animals. If the war against bioterrorism and emerging diseases is expected to be remotely winnable, integration of practitioners and veterinary diagnostic laboratories into public health and disease-reporting systems and establishment of means for rapid communication and dissemination of information to these stakeholders are necessary. Terrorists will always have the advantage; terrorism cannot be stopped. However, through planning, education, communication, and awareness, the impact of the attacks that are carried out can be lessened and perhaps prevented from occurring altogether. Veterinarians are at the front line for education regarding zoonotic diseases and are the experts on zoonotic Category A, B, and C agents. To prevent a national crisis, vigilance is essential, and so too are veterinarians.

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[a]Materials available upon request from the Center for Food Security and Public Health, College of Veterinary Medicine, Iowa State University, Ames, IA 50011. Available at: www.cfsph.iastate.edu.

Resources

The Center for Food Security and Public Health has resources addressing the Category A, B, and C bioterrorism agents as well as emerging diseases, their zoonotic potential, and their impact on human and animal health at www.cfsph.iastate.edu.

Category A, B, and C bioterrorist agents
Available at: www.bt.cdc.gov/agent/agentlist-category.asp.

People who should not get the smallpox vaccine
Available at: www.bt.cdc.gov/agent/smallpox/vaccination/contraindications-public.asp.

The CDC has extensive resources on bioterrorism, preparedness, and biological agents
Available at: www.cdc.gov/.

CDC web site on monkeypox, with extensive information for veterinarians
Available at: www.cdc.gov/ncidod/monkeypox/index.htm.

References

1. Rotz LD, Khan AS, Lillibridge SR, et al. Public health assessment of potential biological terrorism agents. *Emerg Infect Dis* 2002;8:225–230.

2. Davis RG. The ABCs of bioterrorism for veterinarians, focusing on Category A agents. *J Am Vet Med Assoc* 2004;224:1084–1095.

3. Young EJ. An overview of human brucellosis. *Clin Infect Dis* 1995;21:283–290.

4. Metcalf HE, Luchsinger DW, Winthrop CR. Brucellosis. In: Beran GW, Steele JH, eds. *Handbook of zoonoses, section A: bacterial, rickettsial, chlamydial, and mycotic zoonoses*. 2nd ed. Boca Raton, Fla: CRC Press Inc, 1994;9–39.

5. American Public Health Association. In: Chin J, ed. *Control of communicable diseases manual*. 17th ed. Washington DC: American Public Health Association, 2000;75–78.

6. Nicoletti PL. Brucellosis in large animals. In: Aiello SE,

Mays A, eds. *The Merck veterinary manual*. 8th ed. Whitehouse Station, NJ: Merck & Co Inc, 1998;998–1002.

7. Radostits OM, Gay CC, Blood DC, et al. *Veterinary medicine: a textbook of the diseases of cattle, sheep, pigs, goats and horses*. 9th ed. London: Harcourt Publishers Ltd, 2000;867–891.

8. Nicoletti PL. Brucellosis in dogs. In: Aiello SE, Mays A, eds. *The Merck veterinary manual*. 8th ed. Whitehouse Station, NJ: Merck & Co Inc, 1998;1043.

9. Kaufmann AF, Meltzer MI, Schmid GP. The economic impact of a bioterrorist attack: are prevention and postattack intervention programs justifiable? *Emerg Infect Dis* 1997;3:83–94.

10. World Health Organization. *Health aspects of chemical and biological weapons*. Geneva: World Health Organization, 1970;1–132.

11. Byrne WR. Q fever. In: Zajtchuk R, Bellamy RF, Sidell FR, et al, eds. *Textbook of military medicine: medical aspects of chemical and biological warfare. Part I*. Washington, DC: Office of The Surgeon General, Department of the Army, 1997;523–537.

12. McQuiston JH, Childs JE, Thompson HA. Q fever. *J Am Vet Med Assoc* 2002;221:796–799.

13. Reimer LG. Q Fever. *Clin Microbiol Rev* 1993;6:193–198.

14. Centers for Disease Control and Prevention. Q fever outbreak—Germany, 1996. *MMWR Morb Mortal Wkly Rep* 1997;46:29–32.

15. Fournier PE, Marrie TJ, Raoult D. Diagnosis of Q fever. *J Clin Microbiol* 1998;36:1823–1834.

16. Marrie TJ, Durant H, Williams JC, et al. Exposure to parturient cats: a risk factor for acquisition of Q fever in maritime Canada. *J Infect Dis* 1988;158:101–108.

17. Marrie TJ, MacDonald A, Durant H, et al. An outbreak of Q fever probably due to contact with a parturient cat. *Chest* 1988;92:98–103.

18. Greene CE, Breitschwerdt EB. Rocky Mountain spotted fever, Q fever, and typhus. In: Green CE, ed. *Infectious diseases of the dog and cat*. 2nd ed. Philadelphia: WB Saunders Co, 1998;162–165.

19. Marrie TJ, Schlech WF III, Williams J, et al. Q fever pneumonia associated with exposure to wild rabbits. *Lancet* 1986;1:427–429.

20. Wilson TM, Logan-Henfrey L, Weller R, et al. Agroterrorism, biological crimes, and biological warfare targeting animal agriculture. In: Brown C, Bolin C, eds. *Emerging diseases of animals*. Washington, DC: American Society for Microbiology, 2000;23–57.

21. Wilson TM, Gregg DA, King DJ, et al. Agroterrorism, biological crimes, and biowarfare targeting animal agriculture. *Lab Med* 2001;21:549–591.

22. Davis RG. Agroterrorism: need for awareness. In: Scanes CG, Miranowski JA, eds. *Perspectives in world food and agriculture: 2004*. Ames, IA: Blackwell Publishing, 2004;353–416.

23. Carus WS. Center for Counterproliferation Research, National Defense University. Working paper: bioterrorism and biocrimes. The illicit use of biological agents since 1900. Available at: www.ndu.edu/centercounter/Full_Doc.pdf. Accessed Jun 1, 2002.

24. United States Department of Agriculture, Economic Research Service. Amber Waves. September 2003. Indicators. Available at: www.ers.usda.gov/AmberWaves/AllIssues/ShowIssue.asp?Issue=September03. Accessed Dec 10, 2003.

25. United States Geological Survey. Water use in the United States. Available at: water.usgs.gov/watuse/. Accessed Dec 10, 2003.

26. United States General Accounting Office. *Drinking water: experts' views on how future federal funding can best be spent to improve security. Report #GAO-04-29*. Washington, DC: US General Accounting Office, 2003.

27. Khan AS, Swerdlow DL, Juranek DD. Precautions against biological and chemical terrorism directed at food and water supplies. *Public Health Rep* 2001;116:3–14.

28. Lam SK. Nipah virus—a potential agent of bioterrorism? *Antiviral Res* 2003;57:113–119.

29. Chua KB, Bellini WJ, Rota PA, et al. Nipah virus: a recently emergent deadly paramyxovirus. *Science* 2000;288:1432–1435.

30. Goh KJ, Tan CT, Chew NK, et al. Clinical features of Nipah virus encephalitis among pig farmers in Malaysia. *N Engl J Med* 2000;342:1229–1235.

31. Chua KB, Lam SK, Goh KJ, et al. The presence of Nipah virus in respiratory secretions and urine of patients during an outbreak of Nipah virus encephalitis in Malaysia. *J Infect* 2001;42:40–43.

32. Centers for Disease Control and Prevention. Update: outbreak of Nipah virus—Malaysia and Singapore, 1999. *MMWR Morb Mortal Wkly Rep* 1999;48:335–337.

33. American Public Health Association. In: Chin J, ed. *Control of communicable diseases manual*. 17th ed. Washington, DC: American Public Health Association, 2000;236–238.

34. Bunning M. Nipah virus outbreak in Malaysia, 1998–1999. *Swine Health Prod* 2001;9:295–299.

35. Mohd Nor MN, Gan CH, Ong BL. Nipah virus infection of pigs in peninsular Malaysia. *Rev Sci Tech* 2000;19:160–165.

36. Hooper P, Zaki S, Daniels P, et al. Comparative pathology of the diseases caused by Hendra and Nipah viruses. *Microbes Infect* 2001;3:315–322.

37. Middleton DJ, Westbury HA, Morrissy CJ, et al. Experimental Nipah virus infection in pigs and cats. *J Comp Pathol* 2002;126:124–136.

38. Gibbs WW. Trailing a virus. *Sci Am* 1999;21(2):80–87.

39. Johara MY, Field H, Rashdl AM, et al. Nipah virus infection in bats (Order Chiroptera) in Peninsular Malaysia. *Emerg Infect Dis* 2001;7:439–441.

40. Halpin K, Young PL, Field HE, et al. Isolation of Hendra virus from pteropid bats: a natural reservoir of Hendra virus. *J Gen Virol* 2000;81:1927–1932.

41. Mackenzie JS. Emerging viral diseases: an Australian perspective. *Emerg Infect Dis* 1999;5:1–8.

42. Field HE, Barratt PC, Hughes RJ, et al. A fatal case of Hendra virus infection in a horse in north Queensland: clinical and epidemiological features. *Aust Vet J* 2000;78:279–280.

43. Radostits OM, Gay CC, Blood DC, et al. *Veterinary medicine: a textbook of the diseases of cattle, sheep, pigs, goats and horses*. 9th ed. London: Harcourt Publishers Ltd, 2000;1078–1079.

44. Sullivan JD, Allworth AM, Paterson DL, et al. Fatal encephalitis due to novel paramyxovirus transmitted from horses. *Lancet* 1997;349:93–95.

45. Williamson MM, Hooper PT, Selleck PW, et al. Transmission studies of Hendra virus (equine morbillivirus) in fruit bats, horses and cats. *Aust Vet J* 1998;76:813–818.

46. Centers for Disease Control and Prevention. Recognition of illness associated with the intentional release of a biologic agent. *MMWR Morb Mortal Wkly Rep* 2001;50:893–897.

47. Centers for Disease Control and Prevention. *Epidemic/epizootic West Nile virus in the United States: revised guidelines for surveillance, prevention, and control*. 3rd revision. Ft Collins, Colo: US Department of Health and Human Services, 2003.

48. Centers for Disease Control and Prevention. West Nile virus activity—United States, July 3–9, 2003. *MMWR Morb Mortal Wkly Rep* 2003;52:646.

49. Centers for Disease Control and Prevention. West Nile virus activity—United States, July 31–August 6, 2003. *MMWR Morb Mortal Wkly Rep* 2003;52:741.

50. Centers for Disease Control and Prevention. West Nile virus activity—United States, November 20–25, 2003. *MMWR Morb Mortal Wkly Rep* 2003;52:1160.

51. Koplan J. CDC's strategic plan for bioterrorism preparedness and response. *Public Health Rep* 2001;116(suppl 2):9–16.

52. Niemeyer DM. Journal of Homeland Security. The laboratory bioterrorism response network. Available at: www.homelandsecurity.org/journal/. Accessed Apr 2, 2003.

53. National Conference of State Legislatures. Public Health Security and Bioterrorism Preparedness Act of 2002, H.R. 3448. Available at: www.ncsl.org/statefed/health/PL107-188overview.htm. Accessed Dec 15, 2003.

54. United States Department of Health and Human Services. President's budget includes vital food supply protections. Available at: www.hhs.gov/news/press/2003pres/20030204.html. Accessed Jun 3, 2003.

55. United States Department of Homeland Security. DHS organization. DHS budget in brief. Available at: www.dhs.gov/dhspublic/display?theme=12&content=430. Accessed May 19, 2003.

56. United States Department of Homeland Security. FAQs.

DHS organization. Available at: www.dhs.gov/dhspublic/faq.jsp. Accessed May 19, 2003.

57. United States Department of Homeland Security. DHS Organization. Department components. Available at: www.dhs.gov/dhspublic/display?theme=9. Accessed Dec 12, 2003.

58. United States Department of Homeland Security. DHS organization. Emergency preparedness & response. Available at: www.dhs.gov/dhspublic/interapp/editorial/editorial_0093.xml. Accessed Aug 8, 2003.

59. United States Department of Homeland Security. DHS organization. DHS agencies. Available at: www.dhs.gov/dhspublic/display?theme=13. Accessed Dec 12, 2003.

60. Centers for Disease Control and Prevention. Centers for Public Health Preparedness (CPHP). Available at: www.phppo.cdc.gov/owpp/CPHPLocations.asp. Accessed Dec 12, 2003.

61. Centers for Disease Control and Prevention. Health Alert Network. Health Alert Network fact sheet. Available at: www.phppo.cdc.gov/han/FactSheet.asp. Accessed Apr 11, 2003.

62. Centers for Disease Control and Prevention. HAN/BT jurisdictions. Available at: www.phppo.cdc.gov/han/statemap.asp. Accessed Jul 15, 2003.

63. Committee on Biological Threats to Agricultural Plants and Animals, National Research Council. *Countering agricultural bioterrorism*. Washington, DC: The National Academies Press, 2003;109–110.

64. United States General Accounting Office. *Report to Congressional Committees. Bioterrorism: preparedness varied across state and local jurisdictions. Report #GAO-03-373*. Washington, DC: US General Accounting Office, 2003.

65. American Public Health Association. Recognizing the role of veterinarians in the public health workforce. Available at: www.apha.org/legislative/policy/policysearch/index.cfm?fuseaction=view&id=255. Accessed Apr 17, 2003.

66. Council of State and Territorial Epidemiologists. CSTE position statement 1999-ID 2. Establishing positions in every state for a public health veterinarian. Available at: www.cste.org/ps/1999/1999-id-02.htm. Accessed Apr 17, 2003.

67. Taylor LH, Latham SM, Woolhouse ME. Risk factors for human disease emergence. *Philos Trans R Soc Lond B Biol Sci* 2001; 356:983–989.

68. United States General Accounting Office. *Infectious disease outbreaks. Bioterrorism preparedness efforts have improved public health response capacity, but gaps remain. Report #GAO-03-645T*. Washington, DC: US General Accounting Office, 2003.

69. King L, Khabbaz R. Converging issues in veterinary and public health. *Emerg Infect Dis* 2003;9:510–511.

70. United States Department of Agriculture, Veterinary Services. The National Animal Health Laboratory Network. Available at: www.aphis.usda.gov/vs/highlights/section6/section6-6.html. Accessed May 19, 2003.

71. Noah DL, Noah DL, Crowder HR. Biological terrorism against animals and humans: a brief review and primer for action. *J Am Vet Med Assoc* 2002;221:40–43.

Appendix 1

Categorization of bioterrorism agents of public health importance (as designated by the Centers for Disease Control and Prevention)

Agent	Disease
Category A	
Bacillus anthracis	Anthrax
Clostridium botulinum (toxin)	Botulism
Yersinia pestis	Plague
Variola major	Smallpox
Francisella tularensis	Tularemia
Filoviruses and Arenaviruses (eg, Ebola and Lassa viruses)	Viral hemorrhagic fever
Category B	
Brucella spp	Brucellosis
Burkholderia mallei	Glanders
Burkholderia pseudomallei	Melioidosis
Chlamydophila psittaci	Psittacosis
Coxiella burnetii	Q fever
Rickettsia prowazekii	Epidemic typhus fever
Alphaviruses (western, eastern, and Venezuelan equine encephalitis viruses)	Encephalitis
Toxins (eg, ricin and staphylococcal enterotoxin B)	Toxic syndromes
Food safety threats (eg, *Salmonella* spp and *Escherichia coli* 0157:H7)	
Water safety threats (eg, *Cryptosporidium* spp and *Vibrio cholerae*)	
Category C	
Emerging threats (eg, Nipah virus and Hantavirus)	

Appendix 2

Clinical signs and possible causative agent suggesting a bioterrorist attack

Clinical signs in animals	Possible causative agent (may be species dependent)
Respiratory	*Yersinia pestis*, Nipah and Hendra viruses, *Chlamydophila psittaci*, *Burkholderia mallei*, and *B pseudomallei*
Sudden death	*Bacillus anthracis*, *Yersinia pestis*, and *Clostridium perfringens* type B and D epsilon toxin
Abortion	*Brucella* spp, *Coxiella burnetii*, and Rift Valley fever virus
Neurologic	*Clostridium botulinum* (toxin); *C perfringens* type B and D epsilon toxin; West Nile virus; western, eastern, and Venezuelan equine encephalitis viruses; and prions associated with transmissible spongiform encephalopathies