Animals as Early Detectors of Bioevents: Veterinary Tools and a Framework for Animal-Human Integrated Zoonotic Disease Surveillance

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SYNOPSIS

The threat of bioterrorism and emerging infectious diseases has prompted various public health agencies to recommend enhanced surveillance activities to supplement existing surveillance plans. The majority of emerging infectious diseases and bioterrorist agents are zoonotic. Animals are more sensitive to certain biological agents, and their use as clinical sentinels, as a means of early detection, is warranted.

This article provides design methods for a local integrated zoonotic surveillance plan and materials developed for veterinarians to assist in the early detection of bioevents. Zoonotic surveillance in the U.S. is currently too limited and compartmentalized for broader public health objectives. To rapidly detect and respond to bioevents, collaboration and cooperation among various agencies at the federal, state, and local levels must be enhanced and maintained. Co-analysis of animal and human diseases may facilitate the response to infectious disease events and limit morbidity and mortality in both animal and human populations.

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Emerging infectious diseases are a threat to underdeveloped countries as well as industrialized countries as numerous risk factors for human disease emergence exist in both populations. Zoonoses are diseases transmittable between humans and animals. A 2001 report concluded that there are 1,415 species of infectious organisms known to be pathogenic to humans; of these, 868 (61%) are zoonotic. In addition, of the 175 pathogens considered to be emerging, 132 (75%) are zoonotic.[1]

Zoonoses can be introduced to the U.S. naturally or inadvertently (e.g., international travel, smuggled products, and animals) or via weaponized biological agents. Zoonotic agents may be considered for intentional release to cause damage and turmoil, as they can simultaneously target the health of both human and animal populations and have a serious socioeconomic impact.[2]

The U.S. General Accounting Office Report, *West Nile Virus Outbreak, Lessons for Preparedness*,[3] indicated that the analysis of the West Nile virus (WNV) outbreak began as two separate investigations: one of sick people and the other of dying birds. It took almost three months to link the events to one disease. Recommendations in the report identified the need to address five areas, including coordination between public health and animal health efforts.

Based on publicly accessible state surveillance plans and disease reporting regulations, animal zoonotic surveillance activities are distinctly varied among states. Jurisdictional and geographical differences in surveillance activities impede a unified approach to an early detection system.[4]

ANIMALS AS SENTINELS OF ZOONOTIC ILLNESSES

Animal sentinels are defined by R.G. Stahl, Jr. as "any non-human organism that can react to . . . an environmental contaminant before the contaminant impacts people."[5] Animals are used in sentinel surveillance systems for the following reasons: (*1*) animals share environments with humans, (*2*) animals and humans respond to many toxic (or infectious) agents in analogous ways, and (*3*) clinical signs may manifest in animals prior to humans.[6] There is scientific evidence that sentinel surveillance activities are predictive of human risk. For example, a report on dead crow density and WNV monitoring in New York confirmed that the elevated dead crow densities correlated to higher risk for disease in humans.[7]

An article by Rabinowitz et al. provides further support for the use of animals as sentinels, by reporting evidence that animals can: (*1*) provide early warning of an acute bioterrorist attack, (*2*) be markers for ongoing exposure risk, and (*3*) if mobile, propagate and maintain an epidemic.[8] There is merit in using pets, farm animals, and wildlife as clinical sentinels, as each can serve a distinct role in disease detection and risk assessment.

PURPOSE OF THIS FRAMEWORK

This article provides design methods for the development of a local health department early-warning detection system for zoonotic bioevents. A bioevent is defined as a bioterror (BT) attack or large-scale, naturally occurring zoonotic event, such as pandemic influenza.

The objective of this reporting framework is to integrate veterinary health reporting with the human public health system. The local health department can provide educational materials and reporting instructions to supply veterinarians with the resources needed to facilitate the reporting of significant public health diseases. In addition to the early identification of an event, monitoring an outbreak is also integral to this plan's purpose, whether monitoring the geographic scope or maintaining vigilance of animal-propagated epidemics. The plan should reduce current gaps in data analyses and surveillance activities. The goal of animal-human integrated surveillance is to provide a means of early disease recognition and enhanced detection of human zoonoses, expedite a response to an outbreak or hazardous event, and consequently limit morbidity and mortality in both human and animal populations.

REPORTING SYSTEM DESCRIPTION

This framework was developed to be adaptable to emerging diseases and events so that it can be used as an "all-hazards" surveillance approach, with a focus on the threats that are of public health importance. This is a passive reporting system that relies on clinical signs demonstrated in animals to identify the initial manifestations of a bioevent or outbreak. Co-analysis of animal and human zoonotic disease events complements existing human health surveillance plans, may facilitate an early response, and may prevent widespread illness in both populations.

The plan proposes that local health departments request veterinarians to voluntarily report zoonotic animal diseases of potential public health threat to the local health department. Existing animal disease reporting requirements, and investigation and response

procedures, will remain unchanged and carried out in accordance with the appropriate state and federal regulations.

Tools are provided within this article to proactively educate veterinarians on rarely encountered emerging disease agents. This framework is meant to be dynamic, adaptable, and flexible. The plan includes a list of preliminary agents and animals under surveillance, and the lists may be customized by each locality.

Performing a region-specific analysis

An effective zoonotic reporting plan is based on the unique demographics, geography, animal populations, government infrastructure, and bioevent vulnerabilities of the region under surveillance. To tailor a plan to a specific region, the health department should gather the following information.

Demographics. The human population and household estimates should be obtained from U.S. Census Bureau records.

Farm and zoo animal populations. Livestock can be the target of an agroterrorism attack. Agriculture clubs, zoos, petting zoos, and equestrian activities can increase the risk of human-acquired zoonoses. Population estimates for the predominant farm and zoo animals in the region under consideration should be determined. Population estimates for farm animals may be obtained from the U.S. Department of Agriculture (USDA) census records available on the USDA website (http://www.nass.usda.gov/Census_of_Agriculture/index.asp). Zoo locations can be obtained through the yellow pages and/or the Internet.

Companion animal populations. Aside from the risk of humans and their companion animals transmitting infectious diseases to each other, pets that are free to roam outdoors can be at risk for acquiring numerous pathogens from both the environment and their interactions with wildlife. The American Veterinary Medical Association (AVMA) published formulae for determining pet populations for dogs, cats, and pet birds, based on household estimates.[9] If other sources are available for determining pet populations, such as local Animal Control Services, they should also be utilized.

Predominant wildlife. Wild animals could be involved in the propagation of an epidemic due to their mobility and capability of contaminating a large geographical area.[10] Wild animals usually do not receive veterinary care and surveillance activities are minimal. These animals are usually mobile and dispersed, and therefore the most prominent sentinel activities in wildlife are die-offs and neurological signs.[11] Wildlife interfaces with humans, pets, and farm animals, and due to changing habitats and residential development, these interactions have increased.[12] The U.S. Fish and Wildlife Services along with state wildlife services have data available to determine the predominant wildlife in a specific region.

Transportation. Major ports, international airports in particular, escalate the risks to a region and can be a critical factor in intentional or inadvertent novel disease introduction. There is also the possibility of the legal or illegal importation of animals, animal products, and other biologicals that may introduce a disease event. It is important to identify the ports in a region and be aware of the regulatory activities governing the importation and quarantine of animals and biological products.

Regulatory authority. Because state regulations vary, your current state regulations should be reviewed prior to the final determination of which agents and animals to include in the plan. The following disease reporting regulations should be evaluated as needed: human, livestock, pet, and wildlife diseases, as well as animal import regulations. Note any gaps in reportable diseases and surveillance programs. The proposed surveillance plan may be best instituted by the local health department as a voluntary reporting system.

Government infrastructure. It is imperative to evaluate communications and responsibilities within state and local departments with regard to both animal and human disease surveillance and control. Identify gaps or procedures that may interfere with the objectives of integrated surveillance. Determine if data can be timely collected and reported from other offices (e.g., State Veterinarian's Office) to enhance the data collection mechanisms of local surveillance activities. For example, state wildlife or agriculture agencies may be collecting serological sentinel data that can be used as an adjunct to the clinical data the local health department is collecting.

Also, assess the procedures and processes of the local animal control office and determine the information that can be obtained from this agency. Memoranda of understanding may be required for coordination among agencies.

Gather regional epidemiologic data. It is important for the local health department to gather epidemiologic data for the selected agents in the region to establish baseline rates. Knowledge of expected incidence rates will enhance the response to an outbreak. Once this plan is implemented, animal and human population

estimates can also be used to determine the incidence of diseases reported during a given time period.

SELECTED AGENTS AND ANIMALS UNDER SURVEILLANCE

The selection of zoonotic agents for this framework was based on public health significance, severity, and preventability in the human population. Animal species were selected based on population estimates, which may not apply to every geographical area.

Agents

The Centers for Disease Control and Prevention's (CDC's) Potential Bioterror Agents were considered first.[13] Those agents that are not zoonotic, are covered under other integrated surveillance activities, or are asymptomatic in animals were excluded from this framework. Figure 1 lists agents not included in this framework.

In addition to potential BT agents, this plan also includes highly pathogenic influenza viruses. The biological agents selected, and the rationale for surveillance of each, are included in Figure 2, and transmission routes are summarized in Figure 3. Agents under surveillance may be amended based on regional differences.

Animals

Once animal population estimates for a region are obtained, the animal species can be cross-referenced with the selected agents, using Figure 4 to determine the suitable sentinels. The preliminary agents and the susceptible species are captured in the educational quick reference charts (Figures 3 to 6). The following is a list of animals included as a base in this framework:

- Companion animals (pets): Dogs, cats, ferrets, horses, and pet birds. Ferrets are included because they are common pets in the U.S. and are very susceptible to influenza.[14,15]
- Livestock: Cattle, sheep, goats, poultry, and swine.

Figure 1. CDC potential bioterrorist agents currently excluded from the framework

CDC agent	*CDC category*	*Rationale*
Smallpox	A	Not zoonotic[a]
Viral hemorrhagic fevers (filoviruses [e.g., Ebola, Marburg] and arenaviruses [e.g., Lassa, Machupo])	A	Although these viruses are zoonotic and have high morbidity and mortality rates, the affected species of animals are nonhuman primates and guinea pigs.[b] The number of primates in any county in the U.S. is most likely very low. Guinea pigs reside indoors and few receive routine veterinary care; thus, neither animal would serve as an effective sentinel.
Typhus fever (*Rickettsia prowazekii*)	B	Animals are asymptomatic (except flying squirrels).[b]
Food safety threats (e.g., *Salmonella* species, *E. coli* O157:H7, *Shigella*)	B	These agents are already covered under each state's food safety plans. Additionally, most animals and humans have different food sources. This does not exclude these types of diseases from being reported (such as an *E. coli* outbreak). These types of outbreaks are also monitored on the federal level.[c]
Viral encephalitis (alphaviruses [e.g., Venezuelan equine encephalitis, eastern equine encephalitis, western equine encephalitis])	B	These viruses are covered under Arbovirus Surveillance at state and federal levels. Including them in a voluntary reporting system might confuse reporting entities.
Water safety threats (e.g., *Vibrio cholerae, Cryptosporidium parvum*)	B	These threats are covered under each state's water safety plans.
Hantavirus	C	Animals are asymptomatic.[b]

[a]Aiello SE, editor. The Merck veterinary manual. 8th ed. Whitehouse Station (NJ): Merck & Co., Inc.; 1998.

[b]The Center for Food Security and Public Health. Iowa State University. Animal disease information [cited 2005 Sep 5]. Available from: URL: www.cfsph.iastate.edu/DiseaseInfo/default.htm

[c]Centers for Disease Control and Prevention (US). FoodNet—Foodborne Diseases Active Surveillance Network [cited 2005 Oct 16]. Available from: URL: www.cdc.gov/foodnet

CDC = Centers for Disease Control and Prevention

Figure 2. Selected agents and sentinel attributes that will enhance current surveillance activities

Biological/chemical agent	*Incubation time in animals*[a,b]	*Incubation time in humans*[b,c]	*Comments/rationale for integrated surveillance*
Anthrax (*Bacillus anthracis*) CDC Category A	3–7 days (naturally occurring)	1–7 days, up to 60 days (inhalational)	Incubation times are similar and fatality rates for the inhalation form are near 100% in both populations. Rapid detection is key. Surveillance of simultaneous illness in both populations will lead to quicker detection and response. Farm animals have been shown to be very sensitive to the aerosolized agent.[d] Animal surveillance will also provide vital information regarding the geographical distribution of this disease. Each day in the delay of treatment significantly increases mortality rate for humans.
Botulism (*Clostridium botulinum* toxin) CDC Category A	24–72 hours (ingestion)	12–72 hours (ingestion)	Incubation times are similar, but animals display more pronounced symptoms. Surveillance of simultaneous illness in both populations will lead to quicker detection and response. Animal surveillance will also help determine the scope of the hazard.
Brucellosis (*Brucella* species) CDC Category B	Variable	1–21 days, or months	This agent may present first in the animal population. Surveillance of simultaneous illness in both populations will lead to quicker detection and response.
Glanders (*Burkholderia mallei*) CDC Category B	6 days to months; usually 2–6 weeks	10–14 days (inhalation)	It is unknown how horses will respond to a weaponized agent. However, given their susceptibility to the disease, surveillance of this population will provide significant information for detection and response.
Hendra virus (formerly called equine morbillivirus) member of the family *Paramyxoviridae* related to Nipah virus CDC "special pathogen"	6–18 days	4–18 days	Animals and humans have similar incubation times and both have high mortality rates. Surveillance of simultaneous illness in both populations will lead to quicker detection and response.
Highly pathogenic avian influenza (e.g., HPAI H5N1) Emerging infectious disease of public health significance (not considered a BT agent)	1–7 days	2–8 days	Incubation times are similar; however, birds have up to a 100% mortality rate. Cats have recently been declared to be sentinels for avian influenza.[e] Animal surveillance will also provide vital information regarding the geographical distribution of this disease. Although the U.S. Department of Agriculture and state agencies are monitoring poultry and birds for this virus, there can be spillover infections into mammals. This plan will assist in the detection of this virus in animals other than birds as the range of hosts continues to increase.
Melioidosis (*Burkholderia pseudomallei*) CDC Category B	Variable	2 days to years 10–14 days (inhalation)	This agent may present first in the animal population. Surveillance of simultaneous illness in both populations will lead to quicker detection and response.
Nipah virus, member of the family *Paramyxoviridae*, is related to Hendra virus CDC Category B	7–16 days	4–18 days	There are many unknowns associated with this disease; mortality rates in animals and humans are high. Therefore, integrated surveillance will lead to quicker detection and response.

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Figure 2 (continued). Selected agents and sentinel attributes that will enhance current surveillance activities[a–e]

Biological/chemical agent	*Incubation time in animals[a,b]*	*Incubation time in humans[b,c]*	*Comments/rationale for integrated surveillance*
Plague (*Yersinia pestis*) CDC Category A	Several days	1–6 days	Plague due to a BT event would most likely present in both populations simultaneously. Cosurveillance could lead to quicker detection and response. This agent is transmitted via vector and person-to-person transmission. Animals, especially rodents, can propagate this disease. Integrated surveillance will also help determine geographical distribution.
Chlamydophila psittaci—birds Psittacosis—humans CDC Category B	3–10 days	7–28 days	Incubation times are less in birds than humans and the mortality rate in birds is high. Humans present with flulike symptoms. Animal surveillance is therefore of significant value.
Q fever (*Coxiella burnetii*) CDC Category B	1–3 weeks	2–40 days	This agent may be first detected in the animal population. The most notable sign is a marked increase in animal abortions. Humans generally present with flulike symptoms. Integrated surveillance is therefore of value.
Rift Valley Fever CDC "special pathogen"	12–36 hours	3–12 days	Animals have shorter incubation times and young animals have a very high mortality rate. Therefore, this agent may be first recognized in the animal population.
Toxins • Ricin toxin from *Ricinus communis* (castor beans) • Epsilon toxin of *Clostridium perfringens* • Staphylococcal enterotoxin B CDC Category B	12–72 hours	<1 day	Incubation times and mortality rates are similar in both animals and humans and are dependent on the toxin, the mode of transmission, and the dose. Animal surveillance will assist in determining the geographical scope of an attack due to a toxin. Research is limited on the effects of toxins. Horses have been shown to be the most sensitive animal to Ricin.[b]
Tularemia (*Francisella tularensis*) CDC Category A	1–10 days	3–15 days	Incubation is slightly shorter in animals. The disease would most likely appear clinically in the animal and human populations simultaneously. It is often fatal in wild animals, and will therefore provide another means for detection. Integrated surveillance will also help determine geographical distribution.

[a]Aiello SE, editor. The Merck veterinary manual. 8th ed. Whitehouse Station (NJ): Merck & Co., Inc.; 1998.

[b]The Center for Food Security and Public Health. Iowa State University. Animal disease information [cited 2005 Sep 20]. Available from: URL: www.cfsph.iastate.edu/DiseaseInfo/default.htm

[c]Chin JE, editor. Control of communicable diseases manual. 17th ed. Washington: American Public Health Association; 2000.

[d]Glickman LT, Fairbrother A, Guarino AM, Bergman HL, Buck WB, Collins Cork L, et al. Animals as sentinels of environmental health hazards. Committee on Animals as Monitors of Environmental Hazards. Commission on Life Sciences. Washington: National Academy Press; 1991.

[e]Rimmelzwaan GF, van Riel D, Baars M, Bestebroer TM, van Amerongen G, Fouchier RAM, et al. Influenza A virus (H5N1) infection in cats causes systemic disease with potential novel routes of virus spread within and between hosts. Am J Pathol 2006;168:176-83.

CDC = Centers for Disease Control and Prevention

BT = bioterror

- Wildlife: Deer, foxes, raccoons, and avian species. Although rodents and lagomorphs are affected by many of the agents, death in these populations would be difficult to detect; the carnivorous animals would therefore serve as more effective sentinels.

SYSTEM DESIGN AND REPORTING MECHANISMS

The essential components of an integrated zoonotic surveillance system include: rapid identification of a disease threat; rapid reporting of a disease event; monitoring and analysis of reported diseases; assessment of human exposures or concurrent infections; communication and collaboration; and a rapid and coordinated response. It was determined that the sensitivity of disease surveillance and the rapidity of a response are the most valuable attributes of this system. Positive predictive value may suffer when sensitivity is increased. Case definitions should be employed to subdivide cases as suspect, probable, and confirmed to better qualify the reports submitted.

Local health departments should determine the best means for gathering animal zoonotic data. Because timeliness is extremely important, veterinarians should be requested to report cases potentially attributable to the selected agents (or other possible threats) within 24 hours to the health department.

Analyze infrastructure and reporting mechanisms

Once your region has evaluated governmental infrastructures and determined the factions from where additional animal disease data can be obtained, enhancing methods for vertical and horizontal government communication can be planned. Relationships among agriculture, wildlife, and human health departments may need to be strengthened.

The local health department should be prepared to receive reports in the form of written, oral, or electronic communications, from the veterinary sector as well as intra- and interagency partners; at times, data may need to be actively collected.

Awareness

A reporting form may be developed, or veterinarians and others could be asked to report via telephone. Materials sent to veterinarians should include a purpose

Figure 3. Transmission routes to humans and animals[a,b]

Agent or disease	*Respiratory: aerosolized fluids, dust, soil*	*Vector arthropod vector*	*Direct contact with body or body fluids*	*Food ingestion*	*Water: drinking and skin contact (open wounds)*
Anthrax	X		X	X	
Botulism	X		X	X	X
Brucellosis	X		X	X	X
C. Psittaci	X		[c]		
Glanders	X		X	X	
Hendra virus	X		X		
Highly pathogenic avian influenza	X		X	X	[c]
Melioidosis	X		X		
Nipah virus	X		X		
Plague	X	X	X	[c]	
Q fever	X	X	X		
Rift Valley Fever		X	X		
Toxins	X			X	X
Tularemia	X	X	X	X	X

[a]Aiello SE, editor. The Merck veterinary manual. 8th ed. Whitehouse Station (NJ): Merck & Co., Inc.; 1998.

[b]The Center for Food Security and Public Health. Iowa State University. Transmission routes [cited 2005 Nov 7]. Available from: URL: http://www.cfsph.iastate.edu/Handouts/resources_list.htm

[c]Possible, depending on species

Figure 4. Severity of clinical disease in potentially affected species[a–f]

	Pets					*Farm animals*					*Wild animals*			
Agent or disease	*Dogs*	*Cats*	*Ferrets*	*Pet birds*	*Horses*	*Cattle*	*Sheep*	*Goats*	*Swine*	*Poultry*	*Wild birds*	*Raccoons*	*Deer*	*Foxes*
Anthrax	M	M	U	U	H	H	H	H	M	•	L	U	H	U
Botulism	L	U	U	H	H	H	H	H	L	H	H	U	U	H
Brucellosis	M	•	•	•	L	H	H	H	H	•	•	•	U	•
C. psittaci	•	U	•	M	•	•	•	•	•	L	L	•	•	•
Glanders	L	M	•	•	H	•	•	L	•	•	•	•	•	•
Hendra Virus	•	M	•	•	H	•	•	•	•	•	•	•	•	•
Highly pathogenic avian influenza[g]	U	M	H	L	U	•	•	•	U	H	H	U	•	U
Melioidosis	L	L	U	•	M	L	H	H	H	•	U	U	U	U
Nipah virus	M	M	•	•	L	•	•	L	H	•	•	•	•	•
Plague	L	H	U	•	•	•	•	L	•	•	•	U	U	U
Q fever	L	L	•	•	•	M	M	M	•	•	•	•	•	•
Rift Valley Fever	M	M	•	•	•	H	H	H	•	•	•	•	•	•
Toxins[h]	L	L	L	L	M[b,i]	M	M	M	L	L	L	U	U	U
Tularemia	L	M	U	•	M	U	H	•	L	U	L	U	L	U

[a]Aiello SE, editor. The Merck veterinary manual. 8th ed. Whitehouse Station (NJ): Merck & Co., Inc.; 1998.

[b]The Center for Food Security and Public Health. Iowa State University. Animal disease information [cited 2005 Sep 20]. Available from: URL: www.cfsph.iastate.edu/DiseaseInfo/default.htm

[c]Orloski KA, Lathrop SL. Plague: a veterinary perspective. J Am Vet Med Assoc 2003;222:444-8.

[d]Center for Infectious Disease Research and Policy, University of Minnesota. Bioterrorism [cited 2006 Feb 26]. Available from: URL: http://www.cidrap.umn.edu

[e]Feldman KA. Tularemia. J Am Vet Med Assoc 2003;222:725-30.

[f]American Veterinary Medical Association. Potential zoonotic agents of bioterrorism. Anthrax [cited 2006 Mar 8]. Available from: URL: www.avma.org/public_health/biosecurity/default.asp

[g]Dependent on influenza strains and mutations

[h]The effects of toxins are dependent on the toxin, the dose, and the mode of transmission.

[i]Horses are the most sensitive animal to Ricin toxin.

H = high

M = moderate

L = low

U = potential/unknown

• = no evidence in the literature

Figure 5. Quick reference: animal syndromes and possible etiologic agents[a–c]

Clinical signs	*Possible cause*
	Canine syndromes
Unexpected or sudden death	Anthrax, botulism, toxins, Plague, Tularemia
Bloody diarrhea	Anthrax
High fever and swollen lymph nodes	Tularemia, Plague, Rift Valley Fever
Unexpected late abortions	Brucellosis, Q fever, Rift Valley Fever
Acute respiratory syndrome	Anthrax, Plague, Tularemia, Melioidosis, Nipah
Vesicular or ulcerative skin lesions	Anthrax, Tularemia, Glanders
Neurological signs	Botulism, Nipah
Vomiting, bloody diarrhea, trembling	Toxins
Arthritis, lameness	Melioidosis
	Feline syndromes
Unexpected or sudden death	Botulism, toxins, Plague, Tularemia, HPAI, Hendra
Bloody diarrhea	Anthrax
High fever and swollen lymph nodes	Tularemia, Plague, Rift Valley Fever
Unexpected late abortions	Brucellosis, Q fever, Rift Valley Fever
Acute respiratory syndrome	Plague, Tularemia, HPAI, Glanders, Melioidosis, Nipah, Hendra
Vesicular or ulcerative skin lesions	Plague, Tularemia, Glanders
Neurological signs	Botulism, Q fever, Nipah, Hendra
Vomiting, bloody diarrhea, trembling	Toxins
Arthritis, lameness	Melioidosis
	Avian syndromes
Unexpected or sudden death	HPAI, botulism, anthrax, toxins
Neurological signs	HPAI, botulism
Nasal/ocular discharge, weight loss, inactivity	*C. psittaci*
Bloody diarrhea, trembling	Toxins
Fever, lethargy	Tularemia
Respiratory distress	HPAI, Melioidosis
Arthritis, lameness	Melioidosis, Brucellosis
	Equine syndromes
Unexpected or sudden death	Anthrax
Bloody diarrhea	Anthrax
High fever and swollen lymph nodes	Glanders
High fever >104.5°F	Tularemia
Vesicular or ulcerative lymph nodes	Glanders
Neurological signs	Botulism (EEE, WNV),[d] Melioidosis, Nipah, Hendra
Vomiting, bloody diarrhea, trembling	Toxins
Acute respiratory syndrome	Glanders, Nipah, Hendra
Suppurative bursitis	Brucellosis

NOTE: All symptoms are primarily based on naturally acquired infections. Research on weaponized agents is limited.

[a]Aiello SE, editor. The Merck veterinary manual. 8th ed. Whitehouse Station (NJ): Merck & Co., Inc.; 1998.

[b]Rimmelzwaan GF, van Riel D, Baars M, Bestebroer TM, van Amerongen G, Fouchier RAM, et al. Influenza A virus (H5N1) infection in cats causes systemic disease with potential novel routes of virus spread within and between hosts. Am J Pathol 2006;168:176-83.

[c]Massachusetts Department of Agricultural Resources. Bureau of Animal Health. Bioterrorism and animals: preparedness and response workshops [cited 2006 Mar 2]. Available from: URL: www.mass.gov/agr/animalhealth/bioterrorism/Workshops.htm

[d]Diseases in parentheses are important to consider but are not formally included in this reporting plan.

EEE = Eastern Equine Encephalitis

WNV = West Nile virus

HPAI = highly pathogenic avian influenza

Figure 6. Veterinary diseases of public health importance: quick reference chart[a–j]

Agent	*Animals clinically affected*	*Transmission*	*Animal mortality and incubation times*	*Animal clinical signs*	*Human mortality and incubation times*	*Human clinical signs*
Anthrax *B.anthracis* CDC Category A Naturally occurs in the U.S.	Primarily: cattle, sheep, goats, horses Also: pigs, dogs, cats, lions, wild carnivores and herbivores, guinea pigs Birds are low risk, but cases are documented.	Inhalation, ingestion, direct contact Animals usually infected via GI. Spores can survive in the soil for a long time. Environment to animal/human: YES Animal to human: YES Human to human: NO	Usually fatal for horses and cattle; pigs recover; low mortality in carnivores (other statistics not available); 3–7 days; sudden death	Sudden death from septicemia with lack of rigor mortis and blood fails to clot; excitement followed by depression or stupor; blood from mouth, nose, anus; edema, especially neck, shoulders, and throat	Cutaneous: 5%–20%; 1–12 days GI: 25%–75%; 1–7 days Inhalation: 75%–90%; 1–7 days; can be up to 60 days Delay of treatment significantly increases mortality rate.	Cutaneous: accounts for 95% of infections. Vesicles, papulaes, black scabs, swelling in face/neck; secondary infections can occur GI: malaise, fever, GI symptoms, dyspnea, cyanosis, disorientation, signs of septicemia, coma, death Inhalation: flulike signs; respiratory distress; bloody vomit and diarrhea; sepsis; shock; death
Botulism *Clostridium botulinum* CDC Category A Naturally occurs in the U.S.	Primarily: cattle, sheep, goats, horses, wild fowl, poultry Also: pigs, dogs, foxes, minks, pet birds	Inhalation, ingestion, direct contact (wound), contaminated water Evironment to animal/human: YES Animal to human: YES Human to animal: NO	Mortality varies <40% in poultry (other statistics not available) Usually 24–72 hours	Muscle paralysis; progressive symmetrical to flaccid; disturbed vision; unable to swallow or chew; death from respiratory or cardiac paralysis	Mortality from food 5%–10% (much higher if not treated) Ingestion: 12–72 hours Wound: 4–14 days Dose-dependent	Weakness, dizziness, dry mouth, nausea, vomiting, cranial nerve deficits, double vision, drooping eyes, slurred speech, symmetrical paralysis, respiratory paralysis, death
Brucellosis *Brucella species* CDC Category B Naturally occurs in the U.S.	Primarily: cattle, sheep, goats, pigs Also: dogs, horses	Inhalation, ingestion, direct contact, fomites Environment to animal/human: YES Animal to human: YES Human to human: NO	Death not usual in adults. Abortions <80% (other statistics not available) Variable incubation times	Abortions, stillborns, or weak newborns; retained placentas; placentitis; orchitis; epididymitis; arthritis; lameness Goats: may also have mastitis Horses: suppurative bursitis Signs depend on species.	2%–5% mortality if untreated 1–21 days or up to several months	Flulike signs, cyclic fever, arthritis, orchitis, epididymitis, hepatomegaly Chronic: neurological, endocarditis

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Figure 6 (continued). Veterinary diseases of public health importance: quick reference chart[a–j]

Agent	*Animals clinically affected*	*Transmission*	*Animal mortality and incubation times*	*Animal clinical signs*	*Human mortality and incubation times*	*Human clinical signs*
Chlamydophila psittaci (formerly *Chlamydia psittaci*) Psittacosis in humans CDC Category B Naturally occurs in the U.S.	Primarily: cockatiels, parakeets, parrots Also: egrets, gulls, pigeons, doves, sparrows, turkeys, ducks, and possibly cats. Isolated from >100 avian species	Inhalation (dust from infected bird dander, droppings, or secretions) Environment to animal/human: YES Animal to human: YES Human to human: NO	<50% 3–10 days	Nasal and ocular discharges, conjunctivitis, yellow-green droppings, inactivity, ruffled feathers, inappetence, weight loss	15%–20% (untreated); <1% (treated) 7–28 days	Flulike signs, rash, extensive pneumonia, endocarditis, myocarditis, encephalitis
Glanders *Burkholderia mallei* CDC Category B USDA foreign animal disease	Primarily: horses Also: cats, donkeys, mules, guinea pigs, hamsters, goats, dogs	Inhalation, ingestion, direct contact (wound infection), fomites Environment to animal/human: YES Animal to human: YES Human to human: YES	Acute infections usually fatal (other statistics not available) 6 days to months; usually 2–6 weeks	Ulcerated nodules on skin, upper respiratory tract, lungs; septicemia; high fever; thick, mucopurulent nasal discharge; respiratory signs; death. Primarily associated with lungs in horses.	Septicemic: 95% untreated; 40% treated Localized: 40% untreated; 20% treated 1–14 days Aerosolized infection 10–14 days	Flulike signs, diarrhea, chest pain, pulmonary signs, pustules, ulcerations, swollen lymph nodes, photo-phobia, septicemia, death Human epidemics have not been documented.
Hendra virus CDC special pathogen USDA foreign animal disease	Primarily: horses Also: cats, guinea pigs	Unknown; possibly direct contact and inhalation Environment to animal/human: YES Animal to human: YES Human to human: NO	~50%; many unknowns 6–18 days	Acute respiratory syndrome, nasal discharge, head pressing, ataxia	Only 3 cases documented; 66% mortality 4–18 days	Flulike signs, severe acute respiratory signs, neurological signs, death
Highly pathogenic avian influenza virus, type A, subtype H5N1 USDA foreign animal disease	Primarily: chickens, turkeys, wild birds, water fowl Also: carnivores, cats. Possibly a variety of mammals.	Inhalation, ingestion, direct contact (body fluids) Environment to animal/human: YES Animal to human: YES Human to human: VERY LIMITED (as of February 2007)	Up to 100%, often within 48 hours 1–7 days	Depression; respiratory signs (coughing, sneezing, nasal discharge); ataxia; green, watery diarrhea; swollen, cyanotic combs and wattles; edema of eyes and neck; hemorrhage of legs; decreased egg production; death	<60% 2–15 days; death occurs on average 9–10 days	Mild to fatal disease: fever, sore throat, cough, vomiting, diarrhea, severe respiratory distress secondary to viral pneumonia, death

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Figure 6 (continued). Veterinary diseases of public health importance: quick reference chart[a–j]

Agent	*Animals clinically affected*	*Transmission*	*Animal mortality and incubation times*	*Animal clinical signs*	*Human mortality and incubation times*	*Human clinical signs*
Melioidosis *Burkholderia pseudomallei* CDC Category B USDA foreign animal disease	Primarily: sheep, goats, pigs Also: horses, rodents, rabbits, fish, zoo animals, cattle, dogs, cats, various wild animals	Inhalation; direct contact (body fluids, wound contamination) Environment to animal/human: YES Animal to human: YES Human to human: YES	High mortality in sheep. Varies with site of lesions (other statistics not available) Variable; latency	Signs vary with site of lesion; lesions in lymph nodes, lungs, and viscera; pneumonia signs; possibly nasal discharge, arthritis, or lameness. Horses: neurological, colic. Goats: mastitis	Septicemic: <90% 2 days to years; 10–14 days for aerosols	Flulike signs, pustules, prostatic abcesses, chest pain, pneumonia, bronchitis, acute sepsis, death
Nipah virus CDC special pathogen USDA foreign animal disease	Primarily: pigs Also: dogs, cats, horses, goats, rats	Inhalation possible; direct contact Environment to animal/human: YES Animal to human: YES Human to human: NO	Unknown; potentially high (other statistics not available) 7–16 days	Severe respiratory distress; harsh, barking cough; open-mouth breathing; possibly neurological signs; head pressing	30%–40% 4–18 days	Flulike signs, drowsy, disoriented, neurological signs, seizures, respiratory distress, death
Plague *Yersinia pestis* CDC Category A Naturally occurs in the U.S.	Primarily: cats Also: dogs, rodents, squirrels, prairie dogs, goats Rats as carriers	Inhalation, ingestion, vector, direct contact Environment to animal/human: YES Animal to human: YES Human to human: YES	Often fatal in wild animals; <100% in prairie dogs; 50% in cats; dogs usually recover Several days	High fever; extremely swollen lymph nodes—buboes; severe pneumonia; septicemia; death	Bubonic: 50%–60% 2–6 days Pneumonic (untreated): <100% 1–3 days	Flulike signs; enlarged tender lymph nodes—buboes; rapid pneumonia; respiratory failure; cough with bloody sputum; toxemia; shock; death. Pneumonic is fatal within 48 hours of symptoms.
Q fever *Coxiella burnetii* CDC Category B Can naturally occur in the U.S.	Primarily: cattle, sheep, goats Also: dogs, cats	Inhalation, vectors, direct contact (body fluids) Environment to animal/human: YES Animal to human: YES Human to human: RARE (transplacental)	Unknown; high abortion rate (other statistics not available) 1–3 weeks	Typically asymptomatic. Sheep, goats: abortion; anorexia Cattle: infertility; sporadic abortion Dogs, cats: subclinical, abortions	1%–2% 2–40 days	About 2% develop to severe illness. Flulike signs; severe sweats; weakness; headache; pneumonitis but no cough or chest pain; hepatitis; osteomyelitis; endocaritis; neurologic signs; thrombocytopenia; in-utero death; ~50% asymptomatic
Rift Valley Fever Virus CDC special pathogen USDA foreign animal disease	Primarily: cattle, sheep, goats Also: dogs, cats, monkeys, rodents	Vector (mosquito); direct contact (infected animal tissue) Environment to animal/human: YES Animal to human: YES Human to human: NO	<70% in young High abortion rate. <10% mortality in adults 12–36 hours	Abortions, hepatic necrosis, high mortality in young, fever	1% 3–12 days	Flulike signs, petechiae, hemorrhagic fever, retinopathy, encephalitis, death. Young children most susceptible

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Figure 6 (continued). Veterinary diseases of public health importance: quick reference chart[a-j]

Agent	*Animals clinically affected*	*Transmission*	*Animal mortality and incubation times*	*Animal clinical signs*	*Human mortality and incubation times*	*Human clinical signs*
Toxins *Staphylococcus* enterotoxin B, Ricin, *Clostridium perfringens* CDC Category B	Primarily: horses, cattle, sheep, goats All animals potentially affected (dose dependent)	Inhalation, ingestion, direct contact (wound infection) Environment to animal/human: YES Animal to human: YES Human to human: NO	Mortality dependent on dose, toxin, and transmission mode; can be very high (other statistics not available) 12–72 hours	*Staph*: diarrhea, vomiting, pulmonary edema, death *Ricin*: violent vomiting, bloody diarrhea, trembling, death *Clostridium*: necrotic enteritis, bloody diarrhea, septicemia, acute death	Mortality dependent on dose, toxin, and transmission mode; can be very high <1 day	Flulike signs, vomiting, bloody diarrhea, abdominal cramps, kidney failure, neurological signs, pulmonary edema, shock, death Wounds: fever, pain, purple and edematous muscles, toxemia, renal failure
Tularemia *Francisella tularensis* CDC Category A Naturally occurs in the U.S.	Primarily: sheep, wild rabbits, rodents, squirrels Also: horses, herbivores, birds, pigs, cats, dogs, deer, nonhuman primates	Inhalation, ingestion, vectors, direct contact Environment to animal/human: YES Animal to human: YES Human to human: NO	Often fatal in wild animals <15% in sheep (other statistics not available) 1–10 days	All signs unknown. Symptoms may include: sudden high fever, lethargy, and anorexia; stiffness; reduced mobility; tachycardia; tachypnea; prostration; death. Rodents and rabbits usually found dead	5%–35% (untreated); 1%–3% (treated) 3–15 days	Six forms of disease, depending on inoculation site: flulike signs; exhaustion; ulcerative lesion; enlarged, painful lymph nodes; painful, purulent conjunctivitis; abdominal pains; diarrhea; vomiting; chest pain; respiratory distress; pneumonia; sepsis; death

[a]Centers for Disease Control and Prevention (US). Bioterrorism overview: bioterrorism agent categories [cited 2007 Feb 20]. Available from: URL: http://www.bt.cdc.gov/bioterrorism/overview.asp

[b]Aiello SE, editor. The Merck veterinary manual. 8th ed. Whitehouse Station (NJ): Merck & Co., Inc.; 1998.

[c]The Center for Food Security and Public Health. Iowa State University. Animal disease information [cited 2005 Sep 20]. Available from: URL: www.cfsph.iastate.edu/DiseaseInfo/default.htm

[d]Center for Infectious Disease Research and Policy, University of Minnesota. Bioterrorism [cited 2006 Feb 26]. Available from: URL: http://www.cidrap.umn.edu

[e]American Veterinary Medical Association. Potential zoonotic agents of bioterrorism. Anthrax [cited 2006 Mar 8]. Available from: URL: www.avma.org/public_health/biosecurity/default.asp

[f]U.S. Department of Agriculture. Animal and Plant Health Inspection Service. Publications. Animal health [cited 2005 Mar 10].Available from: URL: http://www.aphis.usda.gov/publications/animal_health/index.shtml

[g]World Health Organization. Avian influenza [cited 2006 Jan 10]. Available from: URL: http://www.who.int/csr/disease/avian_influenza/en

[h]Beigel JH, Farrar J, Han AM, Hayden FG, Hyer R, de Jong MD, et al. Avian influenza A (H5N1) infection in humans. N Engl J Med 2005;353:1374-85.

[i]Chin JE, editor. Control of communicable diseases manual. 17th ed. Washington: American Public Health Association; 2000.

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CDC = Centers for Disease Control and Prevention

GI = gastrointestinal

USDA = U.S. Department of Agriculture

statement for this surveillance activity; instructions for reporting; contacts for laboratory testing, specimen collection, and quarantine procedures; and contacts to call for suspected illnesses.

Figures 3 to 6 provide information on the agents, the animals affected, and clinical and epidemiologic features for both animal and human populations. These figures can be provided to veterinarians or used as a foundation for educational materials. Quick reference charts, such as these, should prepare veterinarians, the health department, and others to recognize the early signs of these uncommon disease events and respond more rapidly. These materials will also assist veterinarians with counseling pet owners and managing occupational exposures.

INVESTIGATION, RESPONSE, AND OTHER CONSIDERATIONS

Although an event concerning an animal case or outbreak will be reported to the health department, the appropriate authorities should investigate (e.g., State Veterinarian's Office) according to existing protocol. Details of the investigation should be communicated to the health department. A response to an agroterror or BT event would be conducted by various government levels and agencies and would require multi-institutional collaboration and coordination.

A reporting plan is the first step in an integrated zoonotic surveillance system. Other activities that a local health department may need to consider and address include:

- Identification of the consortia, industries, and agencies that will be asked to report
- Review of regulations and agency responsibilities
- Definition of official responsibilities and points of contact at local and state levels
- Determination of responsibilities for evaluation and analysis of data, report dissemination, risk communication, and consequence management
- Allocation of resources
- Identification of the most effective communication channels for the various partners
- Enhancing relationships within and with other offices and agencies as needed
- Determining thresholds for intervention
- Performing active educational outreach to veterinarians and various animal groups
- Determining any barriers to veterinary and intra- or interagency reporting
- Coordination with adjoining jurisdictions
- Review of information technology capabilities
- Other logistical, administrative, and training issues

LIMITATIONS AND ASSUMPTIONS

This framework is designed to be a passive system. The plan can become active for a specific agent(s) during a time of perceived or actual crisis. Epidemiologic and clinical data in the educational materials are based on the published literature for naturally occurring diseases and may not represent the clinical or epidemiologic features of a weaponized agent. The educational materials and information in this plan are based on scientific data as of February 2007. The plan is limited to the potential BT and emerging zoonotic agents of greatest human threat at the time this article was written.

This framework is limited to select agents. If an unanticipated agent causes an outbreak, or a bioengineered terror agent is dispersed, the educational materials will be of limited use. However, having a plan in place for effective management of a zoonotic outbreak will facilitate and expedite response activities.

If there is population dispersion of wild animals crossing county and state lines, clusters or trends may not be recognized. In addition, residents who do not provide veterinary care for their animals will not be captured by this system.

RECOMMENDATIONS

Educational and reporting materials should initially be disseminated to veterinarians and Animal Control Services. Increasing awareness in other sectors is strongly recommended for pet stores, zoos, wildlife rehabilitation groups, pet owner groups, animal rescue societies, animal shelters, academic institutions, and U.S. Customs/USDA stationed at ports. Evaluation of animal diagnostic laboratory reporting can also be performed for supplemental reporting.

The framework can be expanded to include additional agents and hazards separately covered under other state or federal systems, such as Lyme disease. For harmonization purposes, zoonotic diseases covered under other animal-human health surveillance systems, such as rabies and WNV, may be considered for inclusion in this plan.

A task force consisting of representatives of the local health department; Animal Control Services; the

state health, agriculture, and wildlife departments; the regional veterinary diagnostics laboratory; academia; and community veterinarians would be an effective collaborative team for ensuring the success of an animal-human integrated zoonotic surveillance program. The task force can also help establish case definitions, identify reporting sources and mechanisms, address barriers to reporting, and instigate interdisciplinary networking. Although resources may be limited, having a broad array of partners will contribute greatly to a responsive local public health system.[16]

CHALLENGES

Novel surveillance systems face many challenges and it may take time before the proposed system operates as expected. Incentives to report suspected diseases are limited and confidentiality must be ensured to prevent potential economic losses to the various animal industries. Additionally, jurisdictional issues (animal health agencies vs. human health) may also serve as a barrier to this reporting system. Collaboration and coordination among various agencies and stakeholders are crucial and need to be addressed for the optimal implementation, maintenance, and expansion of surveillance activities. Information sharing and interdisciplinary partnerships via a task force could serve as an incentive to partake in the voluntary system.

There may be a need to sustain veterinary interest, especially when the threat of bioterrorism is perceived to be low, and/or if no significant zoonotic events are encountered after a period of time. However, it should be noted that over time, a zero incidence (i.e., no reported cases) does not equate to a failure of the surveillance plan.

Local health departments may not have the information technology and the budget for electronic reporting. A paper system may overwhelm and challenge some health departments, especially in the event of an emergency situation. Staff available to respond to emergencies might also be limited.

There exists a need for more research on the effects of weaponized biological agents. Also, several emerging agents, such as Hendra and Nipah viruses, are poorly understood given the rarity of outbreaks. This shortcoming of information can have a significant influence on recognition and response activities. The plan will require updating as new scientific evidence becomes available.

CONCLUSION

Strengthening the U.S. public health infrastructure must include bringing human and veterinary medicine together. Improved interagency communication and collaboration will facilitate the response to various types of outbreak situations. Aggregate data analyzed from diverse sources may be as significant and effective as the astute physician for early detection. Because BT attacks can occur in any place and at any time, and zoonoses can unpredictably emerge in our society and rapidly spread to other regions, the authors recommend that state and/or national integrated zoonotic surveillance plans be considered to uniformly capture these essential data throughout the U.S.

The authors acknowledge the following individuals for their technical advice: Rebecca Parkin, PhD, MPH, The George Washington University School of Public Health and Health Services (GWU-SPHHS), Washington; Julia Murphy, DVM, MS, DACVPM, Virginia Department of Health; Linda M. Amendt, MS, MT, U.S. Food and Drug Administration (USFDA); Philip Snoy, DVM, USFDA; Katherine Hunting, PhD, MPH, GWU-SPHHS; Ronald G. King, DVM, Office of Veterinary Services, Virginia Department of Agriculture and Consumer Services; Jonathan Sleeman, MA, VetMB, Dipl. ACZM, MRCVS, Virginia Department of Game and Inland Fisheries; Officer Becky Keenan, Animal Control Division, Falls Church, VA; Gillian Anne Comyn, DVM, MPH, DACVPM, U.S. Department of Agriculture (USDA)/Animal and Plant Health Inspection Service (APHIS)/Veterinary Services (VS); and Dr. Terry L. Taylor, USDA/APHIS/VS. Appreciation is also expressed to the veterinarians who took the time to answer questions and provide feedback.

The views expressed in this article do not necessarily represent the views of the USFDA or the U.S. government.

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