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Zoonotic Diseases—the Human - Animal Connection

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Bioterrorism and Zoonotic Disease Training: Why is it Important?

Many potential bioterrorism agents are zoonotic. In some diseases, clinical signs may manifest in animals prior to humans. Livestock are present in high numbers in certain areas of the country, and can serve as sentinels for zoonotic diseases. Many areas depend on livestock for their livelihood and this puts them at risk for bio-terrorism or agro terrorism. Wildlife also play an important role in our communities because they could potentially contaminate large areas. They could be important sources of infection, for humans and animals.

Some factors that promote zoonotic disease transmission include frequent contact with domestic or wild animals, people living or visiting in areas that overlap with wildlife habitats or intensive livestock production. Other factors such as poor animal sanitation, poor animal health, and poor personal hygiene can also promote transmission.

Routes of Transmission

Direct contact with infectious organisms could occur through gel, liquid, or powder forms. Infection could occur if the agent came in contact with a scratch or a droplet spray contacted mucous membranes. An example of indirect contact is ingestion of contaminated food or water or vector injection into the skin. Agents can also be transmitted via aerosolization of small, dry infectious particles. Aerosol transmission would be an efficacious way to infect large numbers of people.

Zoonoses Control

There are many things people can do to protect themselves from exposure to zoonotic agents. Keep areas that have been contaminated with animal waste clean and disinfected. Follow proper hygiene, especially hand washing.

Always follow proper guidelines when preparing and cooking food to decrease your risk of exposure. Control the stray population in your area by calling authorities and notifying them of the animal. It is important to communicate with your physician and veterinarian on a regular basis, especially if you are immunocompromised, so that all parties are aware of what animals you may be living with or exposed to because of your occupation.

Biosecurity

Education is a large portion of the role of a veterinarian or veterinary technician. Emphasize to producers the importance of implementing and following bio-security protocols. For example, producers should maintain a healthy herd by vaccinating and following proper hygiene for animal housing and workers who come in contact with those animals. Instruct producers to purchase animals from reputable sources and quarantine all newly acquired animals. Teach producers to identify and separate sick animals.

Teach clients the importance of regulating and recording visitors that come to their farms and posting clear instructions for vehicles that enter and leave. Help producers develop clearly stated rules for visitors to ensure that bio-security is not breached. Emphasize the necessity of clean clothing and boots, and controlling insects, birds and animals to lessen the spread of disease.

Category A Diseases

The agents/diseases in Category A are anthrax, botulism, plague, smallpox, tularemia, and viral hemorrhagic fevers (four bacteria and two viruses).

Anthrax

Anthrax results from infection by *Bacillus anthracis*, a spore forming, gram-positive aerobic rod.

Anthrax can be found as a spore in the soil worldwide; it is particularly common in parts of Africa, Asia and the Middle East. In the United States, foci of infection occur in South Dakota, Nebraska, Mississippi, Arkansas, Texas, Louisiana and California, with smaller areas in other states. Spores can remain viable for decades in the soil or animal products, such as dried or processed hides and wool. Spores can also survive for two years in water, 10 years in milk, and up to 71 years on silk threads. However, the vegetative organisms are thought to be destroyed within a few days during the decomposition of **unopened** carcasses (exposure to oxygen induces spore formation).

There are three forms of the disease in humans. 1) Cutaneous anthrax which develops after skin infections. This form is characterized by a papular skin lesion, which becomes surrounded by a ring of fluid-filled vesicles (as shown in picture). Most lesions resolve spontaneously but disseminated, fatal infections occur in approximately 20% of cases. 2) Intestinal anthrax develops after eating contaminated meat. The initial symptoms may be mild malaise and gastrointestinal symptoms. Severe symptoms can develop and rapidly progress to shock, coma and death. 3) Inhalation anthrax occurs after inhaling spores in contaminated dust. Natural infections are mainly seen among workers who handle infected hides, wool, and furs. Symptoms may include fever, tiredness, and malaise; a nonproductive cough and mild chest pain may be present. Then follows an acute onset of severe respiratory distress with fatal septicemia and shock within one to two days. In animals, sheep, cattle, and horses are very susceptible, while dogs, rats, and chickens are resistant to disease. In ruminants sudden death may be the only sign. However, the disease may manifest as flu-like symptoms; chronic infections often have edema.

Vaccines are available for humans who have a high risk of infection. Efficacy of the vaccine against inhalation of *B. anthracis* is unknown, and immunologic response to the vaccine is mild to moderate. Vaccine is available for animals but not often used (Stern strain). Natural strains of *B. anthracis* are usually susceptible to a variety of antibiotics. Effective treatment depends on early recognition of the symptoms. Treatment for cutaneous anthrax is usually effective but pulmonary and intestinal forms are difficult to recognize and mortality rates are much higher. Prophylactic antibiotics are appropriate for all those exposed. Anthrax spores are resistant to heat, sunlight, drying, and many disinfectants. Disinfect with sporicidal agents or sterilization.

Smallpox

Smallpox results from infection by variola virus (genus Orthopoxvirus, family Poxviridae). The last naturally acquired case of smallpox occurred in 1977, and the last two laboratory-acquired infections were in 1978. In 1980, the World Health Organization (WHO) declared that endemic smallpox had been eradicated. Currently, the only known stocks of virus are stored at the Centers for Disease Control and Prevention (CDC) in Atlanta and the Institute for Viral Preparations in Moscow. Other countries may have clandestine stores of virus.

Humans are the only mammals that are naturally susceptible to infection. The smallpox virus is transmitted from human to human, patients are known to be infectious from the time the rash appears and remain infectious until the time the scabs have separated (approximately seven to 10 days). Virus is spread by direct contact or inhalation of aerosols. Transmission on fomites such as contaminated clothing or bedclothes is possible for short periods of time; however, variola does not remain viable for more than two days outside a human host.

Smallpox has an acute onset: initial clinical signs may include fever, malaise, rigors, vomiting, headache, backache and occasionally delirium. The characteristic skin lesions usually appear two to three days later: the first signs are macules, which develop into papules and eventually pustular vesicles. These lesions are most common on the face and extremities and develop in synchronous "crops." Two forms of smallpox may be seen, variola minor and variola major. Variola minor is a mild disease and variola major is a more severe disease, which in a small percentage of people develops into either hemorrhagic or malignant forms. The malignant form has a mortality rate of 95%.

No effective treatment other than supportive therapy is known; cidofovir and other antiviral agents are under investigation. The vaccine is composed of vaccinia virus and it is administered through scarification with a bifurcated needle. Vaccination was an effective and essential component of the eradication of this disease from the world. The vaccine is effective in preventing or reducing disease if given within a few days of exposure. Vaccinia Immune Globulin (VIG) may also be helpful in post-exposure prophylaxis. Currently the vaccine is available to military personnel. Other control measures include quarantine of infected individuals and all contacts. Disinfection of variola virus can be done with various agents. The virus can also be destroyed by autoclaving or boiling for 10 minutes.

Category B Diseases

The diseases just reviewed were the Category A agents, i.e. those that were given highest priority by the CDC. The next group is the Category B agents/diseases which have been given second priority by the CDC. The first four in this group are bacteria, followed by two rickettsial organisms, Q fever and typhus fever, then one group of viruses, the viral encephalitides focusing on Venezuelan equine encephalomyelitis (VEE). The category also includes some select toxins, and organisms that pose a threat to food and water.

Brucellosis

Brucellosis, or undulant fever, is caused by various species of *Brucella,* a gram-negative, facultative intracellular rod. The organism can persist in the environment and indefinitely if frozen in aborted fetuses or placentas. Transmission occurs via ingestion of infected food or consuming infected unpasteurized milk or dairy products; inhalation of infectious aerosols, which is thought to be the means of infection in abattoirs; or contact with infected tissues through a break in the skin or mucous membranes. Brucellosis can involve any organ or organ system and has a very insidious onset with varying clinical signs. The one common sign in all patients is an intermittent/irregular fever with variable duration, thus the term undulant fever.

There are three forms of the disease in humans. In the acute form (< eight weeks from illness onset), symptomatic, nonspecific, and flu-like symptoms occur. The undulant form (< one year from illness onset and symptoms) includes undulant fevers and arthritis. In the chronic form (> one year from onset), symptoms may include chronic fatigue-like syndrome, and depressive episodes. Illness in people can be very protracted and painful, resulting in an inability to work and loss of income. In animals, the clinical signs are mainly reproductive in nature, such as abortions, epididymitis, orchitis, and fistulous withers in horses.

Prolonged antibiotics are necessary to penetrate these facultative, intracellular pathogens. Combination therapy has shown the best efficacy for treatment in humans. Vaccinating calves has helped eliminate infection in these animals, thus decreasing possible exposure to humans. Strict adherence to federal laws of identifying, segregating and/ or culling infected animals is essential to success. Properly protect yourself from exposure to tissues and body secretions of infected animals by wearing gloves, masks, goggles, and coveralls. Pasteurizing or boiling milk and avoiding unpasteurized dairy products will also help decrease human exposure to brucellosis. The organism is susceptible to many disinfectants.

Q Fever

The *Coxiella burnetii* is traditionally thought of as a rickettsial agent and an obligate intracellular parasite (new studies may change its family). The organism causes the disease known as Q fever. Its name describes the clinical symptom seen in humans, “query fever” or “puzzling fever”. The disease has been found worldwide, except in New Zealand. Transmission occurs by inhalation or direct contact with the infectious organism, or following ingestion. Ticks spread the infection among ruminants and sometimes people. The organism is shed in high numbers in placental tissue and body fluids, and is highly infectious in that one organism can cause disease. In one reported case, a cat infected with Q fever had kittens in the same room where a child’s birthday party was being held. Several of the children developed Q fever.

Coxiella burnetii forms an unusual spore-like structure and can survive seven-to-ten days on wool at room temperature, one month on fresh meat in cold storage, and more than 40 months in skim milk. However, it is killed by pasteurization. In humans, Q fever infections lasting less than six months are considered acute disease, and more than six months considered chronic. Symptoms of acute disease vary in severity and duration and are usually manifested as self-limiting febrile or flu-like illness, but pneumonia (as pictured) or hepatitis may also occur. Chronic disease occurs in 1-5% of those infected and the most common complication is heart-related, primarily endocarditis. Farm animals, including sheep, cattle and goats, are the most important reservoirs of disease and are usually asymptomatic. Abortions, stillbirths, mastitis in dairy cattle, and complicated deliveries have been reported. Dogs, cats, rabbits, horses and many other animals can harbor the organism, but it is usually asymptomatic.

Although the disease is often self-limiting, antibiotics are generally effective at shortening the course of acute illness and reducing the risk of complications. Treatment of chronic cases is more difficult and may require long-term antibiotic therapy. A vaccine for Q fever has been developed and has successfully protected humans in occupational settings in Australia. However, this vaccine is not commercially available in the United States. A vaccine for use in animals has also been developed, but is not available in the United States. *C. burnetii* is highly resistant to physical and chemical agents. Variable susceptibility has been reported for disinfectants.

Encephalitis virus

This is the only viral group in the list of Category B agents. This group of equine encephalitis viruses are RNA viruses in the alphavirus genus. Eastern, Western, and Venezuelan Equine Encephalitis viruses are transmitted by mosquitoes. The female mosquito takes a bloodmeal from a viremic host, generally birds for EEE and WEE, and birds and horses for VEE. The virus replicates in the salivary glands of the mosquito and is transmitted back to birds or to dead-end hosts, such as humans and horses, where overt disease occurs. In humans, infections can be asymptomatic or cause flu-like illness. In a small proportion of cases, viral encephalitis can occur and lead to permanent neurological damage or death.

Horses, donkeys and mules have clinical signs similar to humans. The disease in these animals often precedes human cases by several weeks. EEE and VEE have mortality rates of 40-90%. WEE has a lower mortality rate ranging from 20-30%. Birds are asymptomatic carriers. Viremia in sentinel birds is detected via ELISA.

Antibiotics are not effective for treatment, and there are no effective antiviral drugs available. Treatment involves supportive care. There is a trivalent, formalin-inactivated vaccine available for horses for WEE, EEE, VEE in the United States, but the human vaccines are limited to those who are researchers and at a high risk of exposure. All the virus types are unstable in the environment.

Food and water safety threats

There are an estimated 250 pathogens that can cause food-borne related illnesses. The most commonly recognized food-borne infections are caused by *Campylobacter, Salmonella* and *Escherichia coli* O157:H7. Viruses, parasites, natural or manufactured chemicals and organism toxins can also cause food-borne disease. Most agents cause gastrointestinal upsets (nausea, diarrhea, abdominal cramps) which are self-limiting in 4-5 days. However, some agents have severe complications if left untreated.

Campylobacter is considered the leading bacterial cause of food-borne related diarrhea, with an estimated 2.4 million people affected each year. Common sources include raw or undercooked poultry, raw milk or items contaminated with infected animal or human feces. Animal sources include poultry, cattle, puppies, kittens and pet birds.

Many serotypes of *Salmonella* can also cause food-borne related illness. *S. enteritidis* and *S. typhimurium* are the most common isolates, accounting for about 41% of U.S. human cases. Common sources for *Salmonella* food-borne illness include raw poultry or eggs, beef, unwashed fruit and alfalfa sprouts. Pet reptiles can also be a common source.

E. coli O157:H7 is another major pathogen of food-borne related illnesses. Common sources include undercooked or raw hamburger, salami, lettuce and alfalfa sprouts. It has also been associated with unpasteurized milk, apple juice or cider and contaminated well water. Cattle are the most common animal source; however, other mammals can serve as a source. Severe sequela can occur with *E.coli* infection.

There must be constant vigilance for improving food safety and processing, both in the home and commercial settings. Food irradiation is the latest technology used at processing plants to help eliminate the risk of bacterial contamination. However, people should always follow good hygiene when working with food. Always wash hands with soap and warm water before and after handling food. Wash raw fruits and vegetables before eating. After contact with raw meat or poultry, wash hands, utensils and kitchen surfaces with hot soapy water. Cook beef and beef products to an internal temperature of 160° F (65.5° C). Cook poultry and eggs to an internal temperature of 170-180° F (76.6° – 82.2° C). Eat cooked foods promptly and refrigerate any leftovers within two hours after cooking.

Category C

Category C diseases include diseases caused by Nipah virus and Hanta virus. Nipah virus is a newly discovered Paramyxovirus, which causes a severe respiratory disease in pigs and severe encephalitis in humans. The reservoir for the virus is thought to be fruit bats, which are called flying foxes. Suspected transmission of the virus occurs from bats roosting in fruit trees close to pig confinements. The virus then spreads rapidly through the swine herd by direct contact or aerosolization (usually coughing). It can then be passed to humans, dogs, cats and other species. Transmission can occur from direct contact with infected body fluids. To date, no person-to-person or bat-to-person transmission has been reported.

In humans, the incubation period is three to 14 days. Initial symptoms include fever and headache, dizziness, drowsiness, disorientation and vomiting. Some cases show signs of respiratory illness. In severe cases, a rapidly progressive encephalitis can occur with a mortality rate of 40%. In swine, Nipah virus is highly contagious and easily spread. Many pigs are asymptomatic. Clinical signs include acute fever (>104° F; 40° C), tachypnea and dyspnea with open-mouth breathing, and a loud, explosive barking cough may also be noted. Occasionally, neurological signs can occur. Clinical signs in pigs were noted one-to-two weeks before illness in humans, so this species may serve as a sentinel. Disease in other animal species is poorly documented and includes respiratory and neurological signs.

Hantavirus is an RNA virus in the Bunyaviridae family. It is recognized as causing Hantavirus pulmonary syndrome (HPS) and hemorrhagic fever with renal syndrome (HFRS) in humans. Rodents are the asymptomatic reservoir host and the deer mouse (*Peromyscus maniculatus*) is the primary carrier in all areas of the United States, except the Southeast, where the cotton rat (*Sigmodon hispidus*) and the rice rat

(*Oryzomys palustris*) are involved. It is important to remember that the house mouse is not a carrier. Transmission to humans most commonly occurs when they disturb the microenvironment of rodents and breathe aerosolized infectious particles from rodent excrement. Direct contact with rodent excreta on human mucous membranes or through skin abrasions may also result in transmission. The virus particles can contaminate food consumed by humans and cause infection, and in very rare cases, a bite from an infected rodent can precipitate the disease. Clinical signs in humans initially include fatigue, fever, myalgia, and headache. The disease can progress to a severe respiratory syndrome, HPS in the U.S., or hemorrhagic fever with renal syndrome (HFRS) in Asia and Europe. Approximately 40% of patients die within the first 48 hours due to uncorrected hypoxia and shock. The disease is not seen in domestic animals.

Other Important Zoonoses

Four other diseases that have potential zoonotic implications include Transmissible Spongiform Encephalopathy, Rift Valley Fever, Hendra, and West Nile Virus. These agents/diseases are not part of the CDC Category ABC list, but the Center for Food Security and Public Health includes them because they are important zoonotic diseases.

Transmissible Spongiform Encephalopathies

Transmissible spongiform encephalopathy (TSE) describes a group of diseases that are thought to be caused by prions (short for proteinaceous infectious particles). This abnormal protein causes a variety of diseases in various species. In humans, variant Creutzfeldt-Jakob disease (vCJD), Kuru, Gerstmann-Straussler-Scheinker syndrome (GSS), and fatal familial insomnia (FFI) can occur. In animals, bovine spongiform encephalopathy (BSE), or mad cow disease, scrapie in sheep, chronic wasting disease (CWD) in deer and elk, mink spongiform encephalopathy (TME), and feline spongiform encephalopathy (FSE) can occur. The incubation period for most of these diseases is many years.

In humans with vCJD, clinical signs include depression and schizophrenia leading to ataxia and involuntary muscle movement. This eventually progresses to complete immobility and muteness. In animals, initial clinical signs can be subtle, but usually involve behavioral changes such as excitability, nervousness, aggressiveness, and increased sensitivity to noise. Sheep with scrapie typically exhibit intense pruritus. The terminal state of TSEs in cattle, deer and elk can result in extreme wasting despite a good appetite. Additionally, tremors and muscle fasciculations, especially in the neck and face, can occur. There is no known treatment at this time.

Bovine spongiform encephalopathy (BSE), is the only disease that has been shown to be transmitted to humans. BSE in cattle is thought to have occurred from feeding meat or bone meal from scrapie-infected sheep to cattle. The first cases of BSE appeared in the United Kingdom in 1985. The incubation period ranges from two to eight years and is always fatal. In 1996, ten human cases similar to Creutzfeldt-Jakob disease (CJD) were reported in the U.K. However, the disease was affecting people at a younger age, eliciting behavioral changes not seen with classic CJD and demonstrated different brain lesions. The disease was termed variant Creutzfeldt-Jakob disease (vCJD). Currently, it is thought that consumption of BSE-contaminated beef products (prior to the U.K.'s specified bovine offal ban in 1989) may be responsible for the disease. The mortality rate is 100% for cattle and humans. To date, BSE has never been detected in the United States since active surveillance began in 1990.

Destruction of prions is extremely difficult since they are very resistant to heat, normal sterilization processes, and disinfectants. Early identification of the prion is also difficult because it does not evoke a detectable immune or inflammatory response in the host. Additionally, there is an extremely long incubation period. Currently no effective treatment is available; however, experimental drugs are under investigation. In response to the threat of BSE and other TSEs, the CDC has activated a surveillance program in the U.S. Additionally, the Red Cross has restricted blood donors from the U.K. or persons who have lived for more than 6 months in a European country known to have BSE. To prevent BSE from entering the U.S., severe import restrictions were placed on live ruminants and certain ruminant products from countries with known BSE occurrence. These restrictions were later extended to include importation of ruminants and certain ruminant products from all European countries. Additionally, in August 1997, the FDA instituted regulations to prohibit the use of mammalian protein, with a few exceptions, in ruminant animal feeds.

West Nile Virus

West Nile virus (WNV) is a Flavivirus that can cause severe encephalitis in humans, horses, birds and other animal species. Transmission typically occurs from a mosquito vector. *Culex* species are the most important maintenance vectors in the eastern U.S.; however, WNV has been detected in 29 species of mosquitoes. It has been isolated from ticks, but their role in transmission is still unclear. More recently, a few cases of WNV have been transmitted through blood transfusions (six cases), organ donation (four cases), and breast feeding of infants (one case). Bird species are the primary reservoir of WNV. Mosquitoes pick up the virus from birds, then transmit it to mammals via bites. It is thought that viremia in humans and horses is NOT high enough to serve as a reservoir source. Horses are the most commonly affected domestic animals, and many are asymptomatic. Of those that do become ill, about 40% result in death. Clinical signs for horses include a wide variety of neurological signs, from facial paralysis and head tilt, to recumbency and seizures.

In humans, the incubation period for WNV is approximately 3-14 days. Eighty-percent of people infected will be asymptomatic. Approximately 20% will develop a mild illness, termed "West Nile Fever." Signs begin with acute fever (usually >39° C; 102.2° F), headache, myalgia, and gastrointestinal symptoms. Illness usually lasts less than a week, but prolonged fatigue is common. Approximately one in 150 WNV infections will result in severe neurological disease called "West Nile encephalitis," "West Nile meningitis" or "West Nile meningoencephalitis". Symptoms of severe infection include headache, high fever, muscle weakness, and paralysis. This can occur in patients of all ages. The case-fatality rate ranges from 3-15% and is highest among the elderly. Year-round transmission of WNV is possible in some areas.

In 2002, 3529 human cases of WNV were reported in the U.S., with 209 deaths. Among fatal cases, the median age was 78 years old; 59% were male. Reported equine cases totaled 12,843. Forty percent resulted in death. (Data current as of November 8, 2002). There is much speculation concerning the introduction of WNV into the United States. The source has never been determined.

Treatment for WNV involves supportive care. Ribavirin and interferon may be helpful, but currently no specific antiviral has been approved by the FDA. A WNV vaccine for horses has been conditionally licensed by the USDA. Efficacy testing is still underway. Development of a human vaccine is underway. Acambis (a vaccine manufacturing company) has developed a live, attenuated vaccine and hopes to begin clinical trials by 2003. Prevention remains the best defense against WNV, by reducing the source and eliminating larval habitats. Additionally, WNV infection can be prevented by reducing your contact with mosquitoes. Personal protection measures include reducing time outdoors, particularly in early evening hours, wearing long pants and long-sleeved shirts, and applying mosquito repellent containing DEET to exposed skin areas. **Do not use DEET products on your pets**. The concentration of DEET in mosquito products is too high to be safe for cats and dogs and they may develop severe neurological problems.

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