Surveillance for Selected Zoonotic Diseases
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SLIDE 1
Hi. I am Carl Williams and I serve as the public health veterinarian for the North Carolina Division of Public Health. I have worked for the Division since 2004 and I am glad to have this opportunity to speak with you today about zoonotic diseases.

SLIDE 2
The intent of this presentation is to provide you with a basic overview of selected zoonotic diseases, which are those diseases transmitted from animals to humans. These specific conditions were selected because they have been known to occur in people and animals in North Carolina; they are recognized as potential bioterrorist agents by the CDC; and because of the potentially severe illness that may be associated with infections by these organisms. It is hoped that you will have gained some basic familiarity with these organisms by the end of the presentation. Most importantly though, it is hoped that you will know the resources available to you in the event a potential case is identified in your county.

SLIDE 3
Any disease or infection that is naturally transmissible from vertebrate animals to humans and vice-versa is classified as a zoonosis, according to the Pan American Health Organization publication, *Zoonoses and Communicable Diseases Common to Man and Animals*. Over 200 zoonoses have been described and they have been known for many centuries. They are caused by all types of agents: bacteria, parasites, fungi, viruses, and unconventional agents, such as prions. Per the World Health Organization document, *Managing Zoonotic Public Health Risks at the Human–Animal–Environment Interface,* "Domestic and wild animals, and their ecosystems, contribute to the health and well-being of people. Among other things, they provide protein-rich nutrients, transportation, traction power, fuel, recreation, and companionship. Alongside the many benefits people derive from animals, the latter can also contribute to public health risks that emerge at the human, animal, and ecosystem interface. More than 60% of the newly identified infectious agents that have affected people over the past few decades have been caused by pathogens originating from animals or animal products. Of these zoonotic infections, 70% originate from wildlife".

SLIDE 4
Remember, when working on any reportable or infectious condition there are many resources at your disposal including DPH staff, who are available all day, weekends, holidays, and evenings at 919-733-3419; North Carolina Communicable Disease Manual Investigation Steps and Case Definitions, which are available online at ncpublichealth.org; and texts and journal articles available through the AHEC digital libraries and PubMed.

SLIDE 5

The 19th edition of the Control of Communicable Diseases Manual, however, is probably the single most important text available for your use. It contains a great deal of information and introductory sections on a variety of highly applicable items including reporting of communicable diseases; response to an outbreak; risk assessment and risk management; risk communication during an outbreak; infection prevention and control; and detailed chapters on each communicable disease. In my experience there is no single better resource than this book. As Karl Malden used to say for the American Express commercials, "Don't leave home without it."

SLIDE 6

We will begin our discussion of zoonotic diseases with Tularemia. Per North Carolina law, tularemia in people is reportable by clinicians and laboratories that identify the organism from clinical specimens. The disease is also reportable by veterinarians when identified in animals. Veterinarians are required to report cases they have identified to the North Carolina Department of Agriculture and Consumer Services (NCDA&CS). Because this is a potential bioterrorist agent, please notify your health director when investigating a case or a potential case of tularemia.

SLIDE 7

Tularemia is a zoonotic bacterial disease that can affect many mammals. It is naturally occurring throughout the United States. It is most prevalent among wild animals, but clinical cases occur regularly in cats, and outbreaks have been reported among sheep, captive prairie dogs, and ranched mink. Tularemia results from infection by *Francisella tularensis*, a gram negative coccobacillus. Four species are currently recognized. Although all four cause tularemia, they tend to be associated with different animal hosts, and their propensity to cause severe disease varies. *Francisella tularensis,* subspecies tularensis, (also known as type A) has been found almost exclusively in North America. Don't feel compelled to memorize these facts and information; it is available in the 19th edition of the Control of Communicable Diseases Manual. Rabbits are the species most commonly associated with tularemia and seem to be one of the primary species required for maintenance of the bacteria in the wild. However, rabbits will become sick and die as a result of infection with this organism. The organism is transmitted among rabbits by close proximity to one another, scratching, biting or grooming one another, and possibly by arthropod vectors. So, can tularemia be used as a bioweapon? Per the Centers for Disease Control website: "*Francisella tularensis* is very infectious. A small number (10-50 or so organisms) can cause disease. If *F. tularensis* were used as a weapon, the bacteria would likely be made airborne for exposure by inhalation. People who inhale an infectious aerosol would generally experience severe respiratory illness, including life-threatening pneumonia and systemic infection, if they are not treated. The bacteria that cause tularemia occur widely in nature and could be isolated and grown in quantity in a laboratory, although manufacturing an effective aerosol weapon would require considerable sophistication. *Francisella tularensis* was weaponized by the United States in the 1950's and 1960's during the United States offensive biowarfare program. Other countries are suspected to have weaponized this agent. In 1969, President Richard Nixon ended all offensive aspects of the U.S. bio-weapons program."

SLIDE 8

F. tularensis can be transmitted by ingestion, inhalation, arthropod–borne transfer, or direct contact with mucous membranes and broken skin. This organism is found in the blood and tissues of infected animals, and it can survive for long periods on fomites, including food and water. Carnivores can be infected by ingesting carcasses, and cannibalism seemed to be the primary route of transmission during an outbreak in captive prairie dogs. Hunters or other people who spend a great deal of time outdoors are at a greater risk of exposure to tularemia than people with other occupational or recreational interests. Other groups at risk include veterinarians and those working with birds of prey, as a result of handling rabbits as food for the birds. Because of this risk, rubber gloves should be worn when skinning or handling animals, especially rabbits. Wild rabbit and rodent meat should be cooked thoroughly before eating. Avoid bites of deer flies and ticks and avoid drinking untreated water. Gloves should be worn and hands should be washed with soap and water following the handling of carcasses.

SLIDE 9

In 1993, Capellen reported in *Clinical Infectious Diseases* that since 1928, 51 cases of cat- related tularemia had been reported. These cases are often identified when the patient fails to respond to traditional antibiotic therapy for cat bites. In May of 2010, the NC Veterinary Diagnostic Laboratory reported about a case of an 8 year old domestic short-haired cat that died as a result of tularemia infection. Predation by domestic animals is an important risk factor for cats developing this disease. The cat in this case had previously been seen ingesting portions of rabbits and rodents and that is the likely source of infection in this cat. The owner had been utilizing reputable veterinary products for tick-control on her cats, which would presumably limit the possibility of arthropod transmission. The authors conclude that veterinarians, hunters, trappers, farmers and laboratory workers have an increased risk of acquiring this disease due to the increased risk of exposure to infected animals. Approximately half of the identified human cases of tularemia in North Carolina are associated with cat bites. Cat bites carry a known risk of exposure to rabies, tetanus, tularemia, and a variety bacteria that are normal flora in a cat's mouth. Because of these risks, people must keep their cats indoors or on leash. Doing so will reduce bites and exposures to these infections.

SLIDE 10

In NC, rabbit hunting, including skinning and dressing of the carcass, and cat bites are associated with most human cases. However, other modes of transmission are possible, as detailed on the slide.

SLIDE 11

Some classically described outbreaks of tularemia involve these other modes of transmission. A variety of arthropods can transmit *F. tularensis.* *Dermacentor Variabilis* (which is the vector for Rocky Mountain Spotted Fever in NC), and *Amblyomma americanum* (the vector of Human Moncytic Ehrlichiosis and Southern Tick-Associated Rash Illness, or STARI, in NC) can both vector *Francisella tularensis*. The bacteria is transmitted transstadially, and ticks can remain infected throughout their lifetimes; however, the occurrence of transovarial transmission is controversial. Biting

flies in the family Tabanidae (particularly the deer fly, *Chrysops discalis)* can act as mechanical vectors. Individual flies can carry the organism for two weeks. Mosquitoes can also be vectors. The Wyoming cases described in the reference on the slide were believed to be caused by bites from horse or deer flies. The lawnmower-associated cases in Massachusetts are thought to have been associated with inadvertently mowing over broods of rabbits in grassy areas. As the rabbits were aerosolized by the lawnmower blade, the operators and those nearby inhaled the organism.

SLIDE 12

Different forms of tularemia can occur in humans, depending on the route of entry. Glandular and ulceroglandular are most commonly identified in North Carolina. Ulceroglandular tularemia, the most common form, occurs after infection through the skin or mucous membranes. The initial clinical signs are nonspecific and may include fever, chills, headache, body aches and malaise. An inflamed papule usually develops where the bacteria entered the body. This papule turns into a pustule that ulcerates. In some cases, the skin lesion may heal by the time the patient seeks medical care. The regional lymph nodes become enlarged and painful, and may suppurate and drain profusely. Glandular tularemia is identical to the ulceroglandular form, but there is no lesion to indicate where the organism might have been inoculated.

SLIDE 13

Now I'd like to discuss with you a little bit about the case classification and the case definition for tularemia. As with any infectious organism, please refer to your online CD Manual to get all of the information you need to determine whether or not a case fulfills the case definition for surveillance. With regard to tularemia and all other infectious agents, a combination of clinical signs and laboratory evidence of infection is required to fulfill the case definition for surveillance. Tularemia cases can be divided into Probable cases and Confirmed cases based on a combination of clinical and laboratory evidence.

SLIDE 14

The lab criteria for tularemia is fairly similar to what you may find with regard to lab criteria for other infectious agents. Mainly, we're looking for elevated antibody responses to the organism, and a four-fold rise in titer would be a significant indication of an active tularemia infection. However, isolating the organism in culture, or detecting the organism by PCR, would also be sufficient to fulfill case definition requirements.

SLIDE 15

When dealing with a potential case of tularemia, it's important to do a thorough case investigation. Apply the case definition, collect all appropriate information, and look for potential sources of exposure to determine if other persons may or may not have been exposed and therefore, may be in need of potential treatment.

SLIDE 16

For tularemia, prevention is key. We want to teach prevention to those at greatest risk for exposure (e.g., hikers, campers, and hunters). Protective clothing, repellents containing DEET, and permethrin on clothing will be effective at preventing arthropod-

borne transmission. Arthropod transmission of tularemia, while unlikely, is possible. Furthermore, using this will be of great benefit to protect against very common conditions, such as tickborne and mosquito-borne diseases in North Carolina. For hunters, they should be reminded that game meat should always be cooked thoroughly. Grassy areas should always be surveyed before mowing and dead animals should be removed.

SLIDE 17

Additionally, it's important to remind citizens in your community to get their cats indoors. This is an area where you can work with your animal control agency to have cats kept indoors and work to create ordinances at your local level that require cats to be kept indoors or on lead. Cat bites are a significant problem in North Carolina and send a number of people to the ED each year. Oftentimes, these people will receive rabies prophylaxis and tetanus boosters. They may also need antibiotics and surgical interventions to repair the wound, not to mention the bacterial infections, including tularemia, which can result from cat bites. If we work to keep cats inside, we can reduce the morbidity on citizens in North Carolina.

SLIDE 18

Now I'd like to move on and discuss Q fever. Per NC law, Q fever in people is reportable by clinicians and laboratories that identify the organism from clinical specimens. The disease is also reportable by veterinarians when identified in animals. Veterinarians are required to report cases that have been identified to the NC Department of Agriculture and Consumer Services. Because this is a potential bioterrorist agent, please notify your health director when investigating a case, or potential case.

SLIDE 19

Remember to take full advantage of the resources available to you when investigating these conditions…your regional nurse consultant, epidemiologist or public health veterinarian on call, the online CD Manual, and last, but certainly not least, the APHA Control of Communicable Diseases Manual.

SLIDE 20

Unlike tularemia, Q fever is a disease that has a great impact on farm animals and can decrease farm productivity and may be associated with economic losses. It is a naturally occurring disease that occurs worldwide. Q fever results from infection by *Coxiella burnetii.* This organism is an obligate intracellular pathogen. *C. burnetii* is closely related to Legionella, Francisella and Rickettsiella. *C. burnetii* can infect many species of domesticated animals and wildlife. Sheep and goats seem to be the most common domesticated animal reservoirs. Abortion stillbirth, retained placenta, endometritis, infertility, and small or weak offspring can be seen in sheep and goats. Most abortions occur near term. With the exception of reproductive disease, animals are usually asymptomatic. Goats sometimes have a poor appetite and are depressed for 1 to 2 days before an abortion. Placental retention for 2 to 5 days and agalactia have also been reported.

SLIDE 21

C. burnetii can be transmitted by aerosols or direct contact; it is also spread by ingestion. Infections in animals can persist for several years and possibly lifelong. Organisms localize in the mammary glands, lymph nodes, uterus, placenta and fetus in animals; bacteria can be shed in milk, the placenta and reproductive discharges during subsequent pregnancies and lactations. *C. burnetii* can also be found in the feces and urine, and in the semen of bulls. Most human infections are associated with sheep and goats, and often occur when the animal gives birth. Certain factors can increase a person's risk of acquiring Q fever, such as occupation. Certain occupations place persons at higher risk because they are exposed to animals and animal products as part of the job. At-risk occupations include veterinarians, meat processors, livestock farmers, and those involved in animal research. As Q fever spreads from animals to people, it is usually those people who work directly with the animals that would be at highest risk. This would also include sheep and goat dairy farmers, slaughterhouse operators, and veterinarians. I want to emphasize that this is a disease that is significantly associated with specific occupations, so when investigating potential cases of Q fever, be sure to collect information about the person's occupation and the type of work they do with animals. Additionally, location can be a risk factor. Simply being near a farm or farming facility may put people at risk of Q fever, because the bacteria can travel long distances accompanying dust particles in the air. In the case of Q fever from cats, anyone who is in the proximity of infected cats when they give birth would potentially be at risk. For acute Q fever, anyone who has had Q fever is at risk of developing the chronic form of the disease. This risk is greater if you also have heart valve disease, blood vessel abnormalities, chronic kidney disease, or a weakened immune system. Additionally, the organism can be shed in milk, and consumption of unpasteurized dairy products puts people at risk, not only of Q fever, but other enteric pathogens.

SLIDE 22

To discuss the disease presentation in man, let's go over the symptomatic infections which may be acute or chronic. Many cases of acute Q fever are asymptomatic or very mild, and remain unnoticed. The symptoms of acute disease are flu-like and can include high fever, chills, headache, fatigue, malaise, myalgia, sore throat and chest pain. Chronic Q fever is an uncommon condition that develops months or years after the acute syndrome. Endocarditis is the most commonly reported syndrome. It usually occurs in people who have pre-existing damage to the heart valves or are immunosuppressed. The symptoms are nonspecific and similar to sub-acute or acute bacterial endocarditis. Antibiotics can shorten the course of acute illness and reduce the risk of complications; treatment is most effective if it is begun early.

SLIDE 23

When discussing the case definition for Q fever, again, remember to refer to the online Communicable Disease Manual. To fulfill the case definition for surveillance, you'll need to collect information about the clinical course of illness and laboratory evidence of infection. The clinical evidence of infection for acute Q fever is one or more of the

following: rigors, severe retrobulbar headache, acute hepatitis, pneumonia, or elevated liver enzyme levels.

SLIDE 24

The laboratory evidence that is needed to fulfill the case definition for surveillance for Q fever is actually fairly complex. Please don't hesitate to call us. But again, it involves identification of the organism through PCR or through serologic evidence. The antibody response to *C. burnetti* is complex and you must consider different phases of antigens, as well as immunoglobulin G and M responses. So please, if you have any questions, feel free to call us.

SLIDE 25

Investigating a case of Q fever is much like investigating other zoonotic and/or foodborne infections. You want to determine the patient's travel history, occupation, and food consumption, all of which can be linked to potential exposure to Q fever. Additionally, if a potential source of exposure is identified, specific control measures may need to be implemented. For instance, if unpasteurized dairy products are found to be linked to the case, the NC Department of Agriculture and Consumer Services must be notified. The county agricultural extension agent may be an additional resource to consider. The public health veterinarians and epidemiologists on call can assist with contacting these other agencies you may require in investigating a case of Q fever. Communicable disease nurses should work with their local health director, environmental health specialist, and NC Department of Agriculture (NCDA) to evaluate risk, identify contaminated areas and the need for personal protective equipment, restrict access to contaminated areas such as barns, laboratories or slaughterhouses, ensure disinfection of contaminated areas, and properly dispose of animal carcasses. CD nurses should work with local health directors and the NCDA to stop the distribution of any potentially contaminated products or foods.

SLIDE 26

Now let's move on to our final zoonotic disease example, which is Brucellosis. In North Carolina, brucellosis in people is reportable by clinicians and laboratories that identify the organism from clinical specimens. The disease is also reportable by veterinarians when identified in animals. Veterinarians are required to report cases they have identified to the NCDA&CS. Again, this is a potential bioterrorist agent, so please notify your health director when investigating a case, or a potential case.

SLIDE 27

Brucellosis is a serious disease of livestock with tremendous economic consequences when identified in commercial herds. The federal government has enacted comprehensive control programs which have resulted in most states, including NC, being classified as brucella-free in commercial herds. Brucellosis is a bacterial disease caused by members of the genus *Brucella*, and it is an important zoonosis that can cause significant reproductive losses in animals. Abortions, placentitis, epididymitis and orchitis are the most common consequences. The main impact however, is economic; deaths are rare except in the fetus and neonate of affected species. *Brucella species*

are usually transmitted between animals by contact with the placenta, fetus, fetal fluids and vaginal discharges from the infected animals. Animals are infectious after either an abortion or full-term birth.

SLIDE 28

Each Brucella species is associated most often with a certain host. *B. abortus* usually causes brucellosis in cattle, bison and buffalo. *B. melitensis* is the most common and important species in sheep and goats. *B. ovis* can also cause infertility in rams. *B. canis* causes disease in dogs. *B. neotomae* is found in rodents, but has not been linked to disease in humans. *B. suis* contains more diverse isolates than other Brucella species and is found in swine.

SLIDE 29

As previously mentioned, brucellosis is a contagious, costly disease of ruminant animals that also affects humans. Although brucellosis can affect other animals, its main threat is to cattle, bison, and swine. The disease is also known as “contagious abortion” or Bang's disease. In humans, it's known as “undulant fever” because of the severe intermittent fever accompanying human infection, or “Malta fever” because it was first recognized as a human disease on the island of Malta. Considering the damage done by the infection in animals--decreased milk production, weight loss in animals, loss of young, infertility, and lameness-- it is one of the most serious diseases of livestock. The rapidity with which it spreads and the fact that it is transmissible to humans, makes it all the more serious. It is for these reasons that a federal-state cooperative program has been established to control the disease in cattle.

SLIDE 30

Similar to the program that was established for cattle, a federal-state cooperative program for control of brucellosis was established in the early 1990’s to control the disease in commercial swine herds.

SLIDE 31

So…if this disease is officially eradicated or does not occur in North Carolina, why do we still occasionally report cases? And the reason is that people travel to areas where the disease is more common. People consume unpasteurized dairy products. Animals are imported from foreign countries where it has not been controlled in their livestock. This keeps the citizens of North Carolina and our farm animal herds at risk of disease.

SLIDE 32

Feral Swine are present in North Carolina and recent evidence has shown infection in our feral swine population. This places hunters and commercial herds at risk of exposure to brucella and both must be protected. In this map, states in red have demonstrated culture-confirmed brucellosis in feral swine. Arkansas, in yellow, has feral swine with documented serologic evidence of infection. As the disease spreads in this wild animal population, it will place commercial swine herds and people in North Carolina at risk of infection.

SLIDE 33

So, we've discussed the acquisition of brucellosis in animals and control programs that have been enacted to protect animal health, but how do people acquire brucellosis? Looking back at the historical cases, there are certain risk factors that are associated with North Carolina brucellosis cases, and those include Hispanic ethnicity; recent immigration from, travel to, or military deployment to a brucellosis-endemic country; consumption of unpasteurized milk, cheese, or other dairy products; work in a slaughterhouse, veterinary practice, or laboratory; or killing, skinning, or consuming game animals, such as feral hogs and wild boar. In 2009, a report in the MMWR revealed that three patients were likely infected through wounds acquired while field dressing feral swine. The report recommended that clinicians should order brucellosis testing for persons who are symptomatic and have a history of feral swine hunting.

SLIDE 34

Brucellosis has clinical signs that include a multisystemic disease with a broad spectrum of symptoms. Asymptomatic infections are common. In symptomatic cases, the disease is extremely variable and the clinical signs may appear insidiously or abruptly. Typically, brucellosis begins as an acute febrile illness with nonspecific flu-like signs such as fever, headache, malaise, back pain, myalgia and generalized aches. Drenching sweats can occur, particularly at night. Splenomegaly, hepatomegaly, coughing and pleuritic chest pain are sometimes seen. Gastrointestinal signs including anorexia, nausea, vomiting, diarrhea and constipation and occur frequently in adults, but less often in children. In many patients, the symptoms last for two to four weeks and are followed by spontaneous recovery. Others develop an intermittent fever and other persistent symptoms that typically wax and wane at 2 to 14 day intervals.

SLIDE 35

Again, the case definition for Brucellosis requires a combination of clinical signs, which we've just discussed, <u>and</u> laboratory evidence of infection. Consult the CD Manual for the complete and up-to-date version of the case definition for surveillance. Laboratory criteria for diagnosis include isolation of *Brucella* species from a clinical specimen, and four-fold or greater rise in *Brucella* agglutinatin titer between acute and convalescent phase serum specimens obtained greater than or equal to 2 weeks apart studied at the same laboratory. Additionally, demonstration by immunofluorescence of *Brucella* species in a clinical specimen would suffice to fulfill the lab requirements for the case definition. When considering the case definition for Brucellosis, remember to consult your Communicable Disease Manual to get the most up-to-date case definition and to identify all of the correct elements, including the clinical and laboratory elements that will be required to fulfill the case definition for surveillance. As with other diseases, including Tularemia and Q fever, a combination of clinical and laboratory evidence is required to fulfill the case definition for surveillance. We previously discussed the clinical description of brucellosis and for a laboratory description, you need to acquire serologic or other laboratory evidence of infection which could be culture or PCR of the organism. Again, if you have any questions regarding the clinical or laboratory components required to fulfill the case definition for surveillance, please don't hesitate to consult the Division of Public Health.

SLIDE 36

Another important measure with brucellosis that also applies to other diseases, is to implement control measures if a common source exposure is identified. Although brucellosis is a classic disease of animals, it is often identified as a foodborne illness from unpasteurized dairy products in North Carolina. Consumption of unpasteurized dairy products is generally bad for public health. It puts people at risk of brucellosis, Q fever, and other enteric pathogens. So, work with your local health director and the Department of Agriculture to limit the spread of potentially infected food materials throughout the food chain.

SLIDE 37

Now, in our final slide, I just wanted to put this in to provide a little bit of perspective. And that is that zoonotic diseases are relatively rare. As you can see, the case definitions can be fairly complex, but in the scheme of things, these diseases occur much less commonly than other conditions that are known to occur in North Carolina. And you can see, over 1,600 cases of Salmonellosis typically occur per year, 600 cases of Rocky Mountain Spotted Fever—and those don't even approach the number of sexually transmitted diseases that are reported each year in the state. So, when you come to diseases that occur only once or twice in a given year, it is likely that you may not remember all these details and that's OK. Just remember to give us a call if you have any questions dealing with these potentially infectious organisms and we'll help you with your investigation. Thank you.