

Plague in a Dog

[Announcer] This program is presented by the Centers for Disease Control and Prevention.

[Sarah Gregory] Hi, this is Sarah Gregory, and today I'm talking to Dr. Josh Daniels in Fort Collins, Colorado. Dr. Daniels is an associate professor of diagnostic bacteriology at Colorado State University's Veterinary Diagnostic Laboratory. We'll be discussing his article on veterinary hospital workers exposed to a dog with pneumonic plague. Welcome, Dr. Daniels.

[Joshua Daniels] Hey. Thanks for having me, Sarah.

[Sarah Gregory] Let's start off with "what is pneumonic plague?" Is it the same as the Black Death—the one so many people died of in the Middle Ages?

[Joshua Daniels] It is the same disease. Plague is caused by the bacterium *Yersinia pestis*, and there're three clinical manifestations of the disease. Pneumonic plague, which you referred to, is the manifestation that we saw in this dog, and it also occurs in people. And the other two ways that the disease can present is as bubonic plague, and that affects the lymph nodes, and then the least common form of the disease is septicemic plague, when the bacteria are actively replicating in the bloodstream. So, this dog came in with the pneumonic form of the disease, therefore it's pneumonic plague.

[Sarah Gregory] Okay, so how common is plague in dogs? I've never heard of it.

[Joshua Daniels] It's actually not very common in dogs. As far as domestic species are concerned, we see it much more commonly in cats. Just looking back at data collected by CDPHE, which is the Colorado Department of Public Health and the Environment, last year there were 14 times the number of positive cat cases than dog cases—so, much more common. We're not used to seeing it in dogs at all, really.

[Sarah Gregory] The cat...the cat thing, is that nationwide or is that more in your area?

[Joshua Daniels] Right, so, in the United States, plague is pretty much distributed in the Central Plains and on to the West, with a real hot spot being in the Four Corners region. So, being in northern Colorado, we see a fair amount of it, 'cause this is sort of where the Western Plains begin, from the Rockies, and we're not too far from the Four Corners, so this is definitely a plague-active area.

[Sarah Gregory] Apparently, the source of the infection was in prairie dogs. How common is it in prairie dogs?

[Joshua Daniels] Well, we think of plague as being *enzootic* in prairie dogs. And enzootic is the animal equivalent of *endemic*. So, that's when a disease is going to be given...to be present at some baseline level in a population. So, the disease is common at some level in prairie dogs, we always assume it to be there. Looking at different studies that have been done surveilling fleas, which actually transmit the disease to prairie dogs and to other hosts alike, prevalence has varied from the sub-10 percent level up to 44 percent in one studies. And the disease can go from being in an enzootic state to an *epizootic* state—so that's the equivalent of an endemic disease becoming epidemic, if we were talking about a human population—when there are changes in the climate, as well as changes in other hosts that transmit the disease. So, we may have a

baseline level, and there may be some change in temperature or moisture, that then leads to an epizootic and sort of an explosion of plague activity.

[Sarah Gregory] Was this dog a pet or a stray?

[Joshua Daniels] This dog was a pet.

[Sarah Gregory] Alright! Well, tell us about this investigation. What was the sequence of events and what was the initial hypothesis for what was wrong with the dog?

[Joshua Daniels] Alright, so, during the first week of December 2017, this dog was referred to our veterinary hospital facility here in Fort Collins. It had been managed for a day, by its referring veterinarian, with antibiotics for respiratory signs. And that dog's clinical progression decreased somewhat rapidly. So, just after a day, they sent it to our hospital where we have an intensive care unit and some specialists. That dog, historically, a few days before presenting to his regular vet, had been out for a jog with his owner, and it was reported that he briefly sniffed a dead prairie dog on that jog. And it's actually uncommon even to see a dead prairie dog—they usually die in their burrows.

So, this is all secondhand for me, because I was in the diagnostic lab; I had not even known about this case yet. It was going to be two days from this point when I actually got involved. But, when the clinicians evaluated this dog, one of the things that they did was they performed thoracic radiographs, so chest x-rays. And he had pneumonia, but interestingly, the pneumonia was only affecting the right side of the chest. And they did an additional study with a CT, so CAT scan, and that affected area was really limited to the accessory lung lobe on the right side. So, it was a very focal area of inflammation, which is quite consistent with a very common thing that we see in dogs, which is an aspirated foreign body, such as a piece of vegetation, a grass awn or cheat grass, depending on what part of the country you're from. They're little pieces of grass seed that dogs will frequently aspirate, and there's an infection that develops associated with that aspiration. So, that was what the clinicians initially suspected in this case.

[Sarah Gregory] Okay, and what was ultimately found? And why did it take so long to get this diagnosis?

[Joshua Daniels] Yeah, so this dog was quite ill when it presented. It was febrile and had clinical signs of sepsis—so, decreased blood glucose, decreased blood pressure, so hypotension. And they needed to stabilize this dog for surgery, because it was presumed that that lung was the source of sepsis. And one of the principles in dealing with a septic patient is to remove the source of sepsis. So, where is there a big mass of bacteria that are replicating? So, that didn't happen until the dog had already been here for two days.

At surgery, they removed the affected lung lobe and they sent a sample to the lab, which is where I got involved. And the sample came to be processed for pathology, so for a pathologist to view it microscopically for histopathologic analysis and, also, for bacteriology, which is where I interacted with the sample. And, being that it was not a plague suspect, it wasn't sent for any plague testing initially. So, it was just being processed for bacteriology and histopath. Now, when you have a sample submitted for regular bacteriology, it takes time for those microorganisms to grow in culture. And we didn't see anything growing on those petri dishes, on

those agar plates, for two days. So, already we're four days out after presentation, where we're at the point where we can start getting an etiologic diagnosis.

[Sarah Gregory] Okay, so, while all this was taking place, the plague was being spread to other people and animals, right? So, tell us about that.

[Joshua Daniels] You know, hopefully it wasn't being spread. There were no human cases that were associated with this animal. But the problem was is this animal had pneumonic plague, which is regarded as the form of plague that can be transmitted directly from host to host, without a flea. And, given how ill the dog was, it was being housed in an oxygen cage in our intensive care unit. So, in veterinary medicine, you know, the animals, they're not necessarily cooperative about having a nasal cannula placed or an oxygen mask put on their face, so we just have to put them in a cage that has a high oxygen concentration. And those cages are not protected with any kind of HEPA filter. So, basically, the cage is being vented into the ICU, which could theoretically spread disease to others in the room.

[Sarah Gregory] Okay, in your article you mention that 116 people and 46 animals were ultimately treated. So, how were they treated, and was it because of this oxygen cage?

[Joshua Daniels] Right, so, we involved, as soon as we had our plague diagnosis, we involved the state public health personnel, so those working with the Colorado Department of Public Health and the Environment. And what they did is they divided the people who were potentially exposed into categories: those who worked within six feet of the animal, those who were in the same room as the animal, and then everybody else. And those who were within six feet were put on postexposure prophylaxis, and that was 68 people. Those who were in the same room were put on a fever watch, and that was 38 people. There were also 46 animals housed in that ICU during the period that the affected dog was in that room. And we just made the decision to treat all of them for postexposure prophylaxis, because these were...these were sick patients. There was probably some level of immunocompromised, or at least stress at being in the ICU, that all of those animals were put on postexposure prophylaxis.

[Sarah Gregory] Okay, and I think you said already that nobody actually then caught the plague, dog or human.

[Joshua Daniels] Nobody caught the plague, but what was kind of interesting is that, when you take a lot of people who are exposed to something, and you're in the middle of winter—or it was sort of the beginning of winter, I should say—you're going to have some proportion of people who just get a cold, that they would have gotten anyway. So, there were a few people who had, you know, a bit of a scare, because they developed respiratory signs after this known exposure. And a few of them had changes to their antimicrobial regimen because of that.

[Sarah Gregory] So, going back a little bit, why do suppose this dog didn't have the initial usual signs of plague?

[Joshua Daniels] Well, in dogs, we don't have a great idea of what the usual signs are for pneumonic plague. Before this case, there were only two other cases of pneumonic plague in dogs in the literature. Looking at the largest study that's been done—this is a retrospective that was performed—looking at 62 dogs in New Mexico, which is a real hotspot, being that it's in the Four Corners region, there was nothing that really was common to all of those dogs, as far as

clinical signs. The most common was fever, and then, the most common after that was lymphadenopathy, so that's swollen lymph nodes. So, as far as the pneumonic form of the disease, we don't really have a great idea of how this looks in dogs. And what was so perplexing about this case, was that it had this unilateral lobar presentation that was so consistent with such a common thing—a foreign body—in dogs.

[Sarah Gregory] And just trying to understand a little bit about antibiotics, so, I understand the dog was initially put on some kind of antibiotics. So, why didn't they work, even though it wasn't the right diagnosis?

[Joshua Daniels] Yeah, that's a good question. Empirically, the veterinarian who initially saw the dog put the dog on a potentiated penicillin, so amoxicillin/clavulanic acid, which is a very reasonable thing to put a dog on presenting with respiratory signs. Now, it turns out that penicillins are not effective against plague. We know this from some rodent studies that have been done, that they just don't work well. So, there was that aspect to it. Then, the other thing with pneumonic plague, that we know from human beings, is that, even when you get people on antibiotics that are appropriate for plague, if you're not within the first 24 hours of clinical signs showing, the mortality rate goes up dramatically.

[Sarah Gregory] Oh!

[Joshua Daniels] Yeah. So, we had actually empirically switched this dog to broader spectrum coverage, when he presented here—just because he wasn't getting better, not because we suspected plague. Now, that agent that we put him on was a fluoroquinolone antibiotic, it's called *enrofloxacin*—it's very similar to ciprofloxacin used in people—so, we were covering at that point, but we were well beyond 24 hours after and if, comparatively, dogs have the same clinical progression as people would, the prognosis would be poor.

[Sarah Gregory] And we have to say here that the prognosis was poor, right?

[Joshua Daniels] Correct. So, postsurgically, this...this dog declined rapidly and he was unfortunately euthanized the same day that we identified the organism definitely.

[Sarah Gregory] Okay, you touched on it briefly. What was your role in all of this?

[Joshua Daniels] I direct the bacteriology section of the diagnostic lab here, and so I oversee how cases are being processed in the lab, and consult with veterinarians, and basically just make sure everything is proceeding according to our operating procedures. And, when this case was read by the technician, she actually called me in. So, she's going to get some credit here, because she knew it was kind of an oddball, as well, from the beginning.

She had taken one of the colonies that grew on these petri dish plates, and there was very scant growth in this case. There were only about 10 colonies on that plate, but they were uniform. So, we had pure growth of an organism, and it was a slow-growing organism, and that can be consistent with plague, among some other things. And she had put that colony into an instrument that we have that performs rapid identification of bacteria, called the MALDI-TOF. Now, that's an acronym for a really long word, but basically, it's a machine that takes a laser and breaks apart the bacteria. And then, the proteins that result—and so it's a mass spec technique—the proteins that are released from that laser, go through a long tube and we get a fingerprint of the weights of those proteins.

And this instrument called this organism *Yersinia pseudotuberculosis*, which is a related organism—it's actually a very closely related organism—to plague. But, it would be highly unusual to see it causing this type of disease in a dog. Usually, that organism is associated with kind of mild to moderate diarrhea. So, here we've got this *Yersinia* organism coming from the lung, and that led me to explore this a little further and take that sample to our molecular section for a plague PCR test, which indeed was positive.

[Sarah Gregory] So, there are a lot of...there were a lot of challenging aspects to this case. What did you find the most challenging about this?

[Joshua Daniels] It was kind of a perfect storm. We had a host that we're not really used to seeing pneumonic plague in, so the dog; that was the first thing. The second thing is this was an out-of-season presentation for plague. The kind of traditional plague time of year for the Northern Hemisphere, is April through October. So, we're in the first week of December, so it wasn't really consistent with that. And then there was that issue of the radiographic pattern in this animal being so focal and consistent with a more common clinical problem. So, it presented a few challenges to us.

[Sarah Gregory] And maybe on a slightly similar note, what's the most important aspect of this incident to you? Why do you think this paper was published in the *EID* journal?

[Joshua Daniels] Well, this is, of course, an important zoonotic disease. There are other parts of the world where it affects many more people than in the U.S. And, given that it has an animal reservoir, it's not a disease that we're going to eliminate from the planet. So, it's always there and it causes severe disease. And it was an unusual presentation in a species that we're not really used to seeing it. And, with that out-of-season presentation, I think it's really important for veterinary diagnosticians to realize that, with things like climate change, that the whole idea of seasonal presentation of diseases may be starting to go out the window.

The other aspect of this case was how we dealt with it in a large clinical operation. And it's a big teaching hospital, so there were a lot of students who were exposed to this animal harboring this agent. So, there was definitely some stuff to talk about that we wanted to share, and *EID* seemed like the appropriate audience.

[Sarah Gregory] And we agreed. Does your article offer any suggestions for improving this process for a quicker correct diagnosis, if any more dogs in the future do get plague?

[Joshua Daniels] That issue of forgetting about seasonality. So, if you know that you're in an endemic region for plague, get that organism on your differential diagnosis, regardless of what time of year it is. The other part of this case, that we kind of hinted at in the paper, was that this dog was spitting up blood, so it had hemoptysis. And actually, hemoptysis isn't something that we see super commonly in dogs, so that may be a feature to pay attention to.

[Sarah Gregory] Okay. Dr. Daniels, is there anything else you'd like to tell us about this incident?

[Joshua Daniels] Well, I think we diagnosed this case kind of serendipitously. Had the dog not gone to surgery, we may have not gotten an answer, because it was not considered a plague suspect. We also may not have gotten a diagnosis by PCR, had it been a plague suspect. Given how kind of light, how scant that growth was on the plate, in bacteriology, there's a chance that,

with the steps that occur in preparing a specimen for PCR, that they would have been diluted out. So, I think we really got lucky with this case, and I'm really glad we did.

[Sarah Gregory] Okay, this is a pretty broad hypothetical question, and it's not really exactly related to your job, but why do you think so many people are fascinated by plague. I'm actually one of them.

[Joshua Daniels] You mean besides the Monty Python movie?

[Sarah Gregory] Yes.

[Joshua Daniels] Okay, well, plague has a dramatic name, for starters, so I think that kind of captivates people. But I think people are captivated by apocalyptic-type things, you know. So, there's that TV show *The Walking Dead*. Obviously that's, you know, complete fiction, but the plague wiped out a third of the European population in the 14th century and after, a little bit. So, this is an apocalyptic event that was real. It, I think, probably changed the social order in Europe after that, to some extent. So, I could see that being captivating to people.

[Sarah Gregory] Are you optimistic about the future of veterinary infectious diseases? There's so many of them now.

[Joshua Daniels] Well, yes and no. So, I'll give you the "no" part first. I'm not optimistic because I think that climate change is going to continue to allow diseases to spread into animal niches and into geographic niches that they didn't occupy before. So, we're going to have to be on our toes. But "yes" because, and this is kind of selfish, but as a laboratory diagnostician, with the technologies that have been evolving, just even in the past 10 years with next-generation DNA sequencing, we're going to be able to ask questions in veterinary infectious disease that we couldn't even have dreamt of in the last century.

[Sarah Gregory] Well, that is positive and good to hear. What's the best thing that people can do to protect their pets from infectious...these infectious diseases?

[Joshua Daniels] One is to regularly see their veterinarian. And there are some important preventive things that people do regularly that undoubtedly help with a lot of diseases. Flea and tick control is a really big one. It doesn't sound like a big deal because it's mundane, right? Flea and tick control. But fleas and ticks transmit quite a few agents that can make our pets and us very sick. And then also anthelmintics, so deworming products. So, just those baseline things, I think, can do a lot to prevent infectious diseases.

[Sarah Gregory] And heartworm medicine?

[Joshua Daniels] Certainly heartworm diseases—especially in Georgia, where you are.

[Sarah Gregory] If you could fix just one veterinary problem, what would you choose?

[Joshua Daniels] This may come as a surprise, but I think the one thing that I could fix would be the cost of veterinary education right now. There are lots of infectious disease things that we need to tackle, undoubtedly, but as a veterinary educator, something that we all deal with—especially those of us who work in universities—is the cost of veterinary education. So, with the declining public support of education, veterinary schools are mostly at land-grant universities,

it's really become hard on students to pay for their educations. Veterinarians' debt-to-income ratio is about double compared to MDs.

[Sarah Gregory] Oh my gosh—and that's astronomical!

[Joshua Daniels] Yeah.

[Sarah Gregory] Just real briefly, what is...what are land-grant universities?

[Joshua Daniels] Right, so land-grant universities are universities on land that was set aside by the federal government—so, things like Colorado State University, University of Wisconsin, Ohio State University. These are the big agricultural universities that usually have veterinary science and veterinary medical education programs.

[Sarah Gregory] Okay. So, UGA here in Georgia?

[Joshua Daniels] I believe that's also a land-grant university.

[Sarah Gregory] Tell us about your job. You have somewhat, but, outside of this particular case, what do you do? You've already said where you work. What's your area of expertise, then, if we haven't covered that entirely? And...yeah.

[Joshua Daniels] I'm a veterinary bacteriologist, so I'm both a veterinarian and a bacteriologist. So, I oversee the section of the veterinary diagnostic laboratory at CSU that deals with all the cultures and some serologic testing for bacterial disease, as well. But I also educate students. So, I teach first-year veterinary students bacteriology and also interact with the students when they're...when they're on clinics, as well...on clinical cases. And do quite a bit of clinical consultation with clinicians here, as well as those who submit samples to us from across the country.

[Sarah Gregory] Do you have any pets of your own?

[Joshua Daniels] Oh, too many! So, we've got three cats, and they came as a set, so we had no choice but to take them all when they showed up. And we have a dog.

[Sarah Gregory] What kind?

[Joshua Daniels] He is a Goldendoodle. And his name is Mr. Peanut Butter.

[Sarah Gregory] Oh dear!

[Joshua Daniels] Yeah, and that's a shout-out to *BoJack Horseman*, for those of us people who maybe don't know the reference. And he's quite a clown.

[Sarah Gregory] Okay, well, on that clown note, what do you do for fun?

[Joshua Daniels] I'm kind of a middling hack rock guitar player in my spare time.

[Sarah Gregory] Ah!

[Joshua Daniels] So, I've played in a few bands over the years. Mostly, just go into my home studio and plug in and play some rock-and-roll.

[Sarah Gregory] I did not expect that answer. I expected to hear...

[Joshua Daniels] Hey, you never know what you're going to get.

[Sarah Gregory] That's exactly right. I expected to hear about hiking and something...with your dog, with your labradoodle.

[Joshua Daniels] Well, we all do that here in Colorado; that's a given.

[Sarah Gregory] Ah, that's a given. Okay, okay.

Well, thank you so much for taking the time to talk with me today, Dr. Daniels.

And thank you, my listeners out there. You can read the April 2019 article, Pneumonic Plague in a Dog and Widespread Potential Human Exposure in a Veterinary Hospital, United States, online at cdc.gov/eid.

I'm Sarah Gregory for *Emerging Infectious Diseases*.

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