Valley Fever in Utah, 2006-2015

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

[Sarah Gregory] Hello, I'm Sarah Gregory, and today I'm talking with Dr. Adrienne Carey, an assistant professor in the Division of Infectious Diseases at the University of Utah School of Medicine. We'll be discussing coccidioidomycosis incidence in Utah from 2006 to 2015.

Welcome, Dr. Carey.

[Adrienne Carey] Thanks for having me, Sarah. I really appreciate it.

[Sarah Gregory] To start, what is coccidioidomycosis, also known as Valley fever?

[Adrienne Carey] Great question. Coccidioidomycosis or Valley fever (also known as San Joaquin Valley fever) is the name for the infection caused by the fungus *Coccidioides immitis* or *Coccidioides posadasii*. From now on, because that's sort of a mouthful, I'll just refer to it as *Coccidioides*. There can be a variety of presentations of coccidioidomycosis ranging anywhere from asymptomatic infection to fever, cough, shortness of breath, or pneumonia, to disseminated infection throughout the body including possible infection in the spinal fluid around the brain, or meningitis. So there's lots of different ways that coccidioidomycosis can present.

[Sarah Gregory] *Coccidioides* fungi are considered dimorphic. Tell us what that means.

[Adrienne Carey] Dimorphic means two morphologies, or two forms. In the realm of fungus, usually you have yeasts or molds. Dimorphic fungi are a hybrid of those two. They can take both forms depending on where the fungus is living. One saying that I like to use is "yeast in the beast and mold in the cold". Meaning that in general, dimorphic fungi that are in the yeast form in humans when they cause infection, and then when they are living in the environment, they take the mold form. So "mold in the cold and yeast in the beast", that's how I remember it.

[Sarah Gregory] Well, that's pretty good.

[Adrienne Carey] Yeah.

[Sarah Gregory] I've actually never heard that before. And I'm going to call it Valley fever because that's just even easier for me. I—

[Adrienne Carey] Right, than coccidioidomycosis.

[Sarah Gregory] —yes.
I've done previous podcasts about Valley fever in California and Arizona, but never about Utah. Is it endemic there also?

[Adrienne Carey] It is. California and Arizona certainly are the states that stand out in an infectious diseases physician's mind as hot beds for coccidioidomycosis. But it's also in Utah, and has been considered an endemic state for the infection since the initial studies to understand the distribution of the fungus back in the 1950s. Three counties in southwestern Utah were considered endemic, or you could think of where the fungus is found regularly in those areas. And those counties are Washington, Iron and Kane Counties down in the southwestern quarter. However, there is not much in the literature beyond that information about the infection in the state of Utah.

[Sarah Gregory] And where are these fungi found? In the air, dirt, water?

[Adrienne Carey] *Coccidioides* is found in the soil. It lives in the dirt along with dead, decaying animal matter. And this is a unique feature of *Coccidioides* compared to other fungi that typically live in decaying plant matter. In its mold form, it lives in the soil and that's where humans regularly come into contact with it.

[Sarah Gregory] Lots of microbes live in the dirt. So why don't I get sick every time I garden?

[Adrienne Carey] That's an excellent question, and I think there are a lot of factors that go into answering that question appropriately. The first factor is our immune system—our body's defense against foreign invaders. In individuals that have normal immune systems, if we inhale bacteria or fungi from the environment, typically our front-line defenders from our immune system take care of those pathogens before they cause us any problems. But in people with immunocompromised syndromes, whether they're on medication to suppress their immune system or if they have a cancer, or they are a transplant recipient, whether that be a bone marrow transplant or a solid organ transplant. Those immune system defenses aren't functioning top notch. So certainly, those are some people that might get in trouble with regular gardening if they had compromised immune systems. But in general, most people in the population have fully functioning immune systems that help protect us when we inhale these pathogens from the environment.

So the second factor that we have to consider when answering this question is the degree of pathogen burden that we inhale from the soil. Certainly if there is a lot of soil disruption or dust generation, that could lead to a large amount of organisms being kind of put into the air and inhaled. And that's harder to handle on an immune system-level if you inhale a large number of organisms instead of a small number of organisms.

And then another thing to consider is the length of time that we're exposed to the dirt and dust. So if you're doing some really heavy spring cleaning in your barn and disrupting a lot of soil or dust, or down in the dirt and dust doing a big construction project in your yard, that's a lot different than going out and doing some pretty low-key weeding where there's less disruption of the soil. So hopefully I tried to answer that question as simply as possible, but probably made it more confusing than it needed to be.

[Sarah Gregory] No, no. Actually that was very helpful. So I'm finding masks, I mean, not just good for COVID. There are so many diseases that are spread through the air and breathing, and would it help if people wore masks when they were out doing stuff in their yard?

[Adrienne Carey] You know, that's a great question. I think, again, you have to take into consideration all those factors that we talked about—is your immune system normal or not, what's the degree of soil disruption that you're going to be doing out in the yard, and how long are you going to be doing that project? If you are someone with a compromised immune system, I would say either A, avoid the project, or B, make sure you're wearing good protection over nose and mouth to prevent inhalation of not only fungi from the soil, but also bacteria. And then if you're going to be doing a project that's going to involve a lot of disruption of the soil over a long amount of time, that's another time to consider wearing a mask. And so certainly those are ways to decrease our risk of getting exposed to all sorts of pathogens that live in and around us in the environment.

[Sarah Gregory] Because I've done podcasts on them, I know that you can get botulism from the dirt, and you can get Legionnaire's disease. That one really surprised me.

[Adrienne Carey] Yeah. Absolutely, absolutely. And not only is the dirt a place where pathogens lurk but also on the plants themselves. So I'm not sure if you've done any podcasts on *Sporothrix* (or rose gardener's disease), but that's another really interesting one where if you get inoculated with the spines of a rose where the pathogen is living and typically have a compromised immune system, you can get a rash on your arm with nodules that are painful and inflamed. And depending on the degree of infection, may or may not need surgery to take care of that infection. So there's pathogens all around us.

[Sarah Gregory] Good heavens. Are you talking about like if you get your finger pricked on a thorn on a rose bush?

[Adrienne Carey] Uh huh, yeah. Or if it scratches you on the arm.

[Sarah Gregory] Oh no. I get that all the time, good heavens.

[Adrienne Carey] Yeah, that's another—actually that's another dimorphic fungi *Sporothrix*.

[Sarah Gregory] I had never heard of that one before. Thank you.

[Adrienne Carey] Yeah. It's a great one.

[Sarah Gregory] Oh my.

Your article references a geographic survey completed in 1957 in Utah. What did you find, and why is it so important?

[Adrienne Carey] That's great to highlight, Sarah. I think, you know, these studies that were executed early on to try to understand the distribution of *Coccidioides* across the United States were quite involved and it was a massive effort to try to understand where in the United States was *Coccidioides* endemic. And so it was executed by a group of physicians and nurses in public health, and they enrolled over 100,000 healthy volunteers to undergo skin testing to see if they had ever been exposed to the fungus *Coccidioides*. And these volunteers came from the military, from universities along with nursing and medical students. And they only enrolled those individuals who had spent the majority of their life in one area of the country to try to eliminate the possibility that they had been exposed to the fungus in another part of the country other than their primary residence. And so this really helped establish the first map of endemicity that was used for the CDC for years to understand the distribution of *Coccidioides* across the country. And it was from this study (I referenced it earlier in our discussion) that the counties of Washington County, Kane County, and Iron County were discovered to be endemic in the state of Utah.

[Sarah Gregory] So your article also mentions an outbreak that occurred at an archeological dig in 2001. Tell us about that one.

[Adrienne Carey] Sure. This is a really interesting outbreak. Aside from the 1957 seroprevalance study that we just talked about along with a few case reports, the description of a 2001 outbreak of coccidioidomycosis at an archeological dig at Dinosaur National Monument near Vernal, Utah is really the only major—only other major description of *Coccidioides* in the state of Utah before our research came out. And what happened is that there were a group of healthy volunteers working at a Native American burial site called the “Swelter Shelter”, and they were doing excavation work near this area. It's an enclosed space, it gets warm, there's lots of dust. And so several of the volunteers became ill with respiratory symptoms within about 5-7 days of completing the work. And based on some good leg work by physicians in the area, it was

ultimately narrowed down to be coccidioidomycosis (or Valley fever) as the cause of their infection. And what makes this really interesting is that Dinosaur National Monument—again, very close proximity to the city of Vernal, Utah—is in the northeastern corner of the state. That's about 200 miles northeast of the area that's considered endemic for the fungus. And so, this made people raise some eyebrows about, you know, maybe our endemic map isn't quite so complete as we thought. And so I'll touch on this a little bit later on in the podcast, but it's just kind of interesting that this outbreak happened clearly outside of the known endemic map of where *Coccidioides* is considered to live in the soil regularly.

[Sarah Gregory] Apparently it has been understudied in Utah. Why do you think this is?

[Adrienne Carey] I think there's a couple of reasons, Sarah, is that up until the last, really, 20-25 years, the population in the southwestern part of the state has been relatively small compared to the Wasatch Front where Salt Lake City, Provo, Ogden (kind of the main urban areas in the state of Utah) are located. And so as such, the overall numbers of infection were relatively low. However over the last, really, 5-10 years and in the last 1-3 years, we've experienced a population boom in that area. The county seat of Washington county is St. George, and St. George has actually been the fastest growing city in the United States for a couple of years running now. And so the population in that area is really exploding along with the construction. So there have been more cases of coccidioidomycosis that have been diagnosed over time.

So I think the lack of population in the area up until relatively recently...and I also I believe that there is a relative lack of knowledge regarding this infection by front line providers practicing in this area. It's mentioned in medical school, at least, you know I went to medical school at the University of Utah school of medicine and so I remember learning that *Coccidioides* was found in the state of Utah, but other than that one statement it really wasn't emphasized. And so I can imagine that if you didn't do your training in the state of Utah and you relocated to that area to do your training, that you might not realize that you need to be thinking about that infection when you see a patient in clinic or in the urgent care in the emergency department who's presenting with symptoms that can mimic bacterial pneumonia—you know, fever, cough, shortness of breath, changes on chest x-ray. And so combination of the lack of population in the area along with a relative lack of knowledge I think is why it has been understudied.

[Sarah Gregory] What motivated you to conduct this study? What were your goals?

[Adrienne Carey] Well Sarah, I'm a native Utahn. I was born and raised in Salt Lake City, and I did my infectious diseases fellowship at the University of Utah. And when I was deciding on a research focus for my fellowship project, I thought it would be a great opportunity to give back to my state in the form of increased knowledge about an infection that impacts citizens on a local level. So I worked alongside another native Utahn, Dr. Brandon Webb, of Intermountain Healthcare and we set out to describe the epidemiology, clinical features, and outcomes of coccidioidomycosis in the state. We also wanted to investigate which factors contributed to the distribution of the disease across the state. And so that's what motivated us to embark on this project.

[Sarah Gregory] Okay. I see.

So you studied patients treated at a healthcare network in Utah and used seven different types of data to identify patients with Valley fever. Why that data and how did you go about analyzing it?

[Adrienne Carey] That's correct, Sarah. We used data from the Intermountain Healthcare Network's electronic medical record to search for cases of coccidioidomycosis using seven different clinical and diagnostic domains of data, and those include ICD 9&10 codes (or billing codes that physicians use in the chart), laboratory tests specific to *Cocci*, microbiology or culture data, pathology data, radiology data, pharmacy data for prescription of antifungal medications and data identifying immunocompromised patients at higher risk of fungal disease. And so we really wanted to take a comprehensive approach to this instead of just searching for ICD 9&10 codes, which is often the case in these epidemiology studies.

So once we were able to go through the electronic medical record using a program that used natural language processing, we were able to pull out about 788 cases over a 10 year period of time to go through and classify, was this a proven case of Valley fever or probable case of Valley fever or did it not really fit with the diagnosis. And so that was my job. I reviewed all 788 of those cases, and after going through all those cases, I identified 364 cases, 192 which were proven—meaning that they had positive growth of *Coccidioides* on culture data or they had diagnosis of visualized fungal forms on pathologies. And then 172 were probable cases, meaning that those were diagnosed in a probably clinical scenario along with laboratory data from the blood. And so that's how we went about kind of identifying the cases through the course of the study period.

[Sarah Gregory] Did you identify any patient risk factors while you were at it?

[Adrienne Carey] Well, as we were reviewing the data, just kind of some descriptors about our patients is that the median age for infection was 61 years of age; men and women were impacted about equally; the most common comorbidities that we found were chronic pulmonary disease, diabetes mellitus and malignancy; and primary lung infection was the most common form of *Coccidioides*, representing 89% of the cases that we identified. And similar to other studies, we found that being non-white, on medications that suppress your immune system, and having a low lymphocyte count led to increased chances of infection outside the lungs—so disseminated infection either to the bone and joints, to different organs in the body, or even to the spinal fluid around the brain or meningitis.

[Sarah Gregory] What environmental or manmade conditions were most strongly linked to getting infected?

[Adrienne Carey] When we analyzed the different factors for what lead to the distribution of infections across the state, we found that air temperature, population, and construction permits per 100,000 population per year predicted the distribution of infections across the state. So the warmer the area, the more populated it is and the more construction that is going on in an area leads to more infections or more cases in that location.

[Sarah Gregory] Is there anything else in your study that you want to tell us about?

[Adrienne Carey] Sure. First off, I'd like to highlight the collaborative nature of this study. This was a combined effort between the two largest healthcare networks in the state (University of Utah Health and Intermountain Healthcare) along with the Utah Department of Health to get this study together. And so, I really appreciated the chance to be able to work with all of these organizations to get information out there about a disease that impacts Utahns specifically.

And the next thing I'd like to point out is when we analyze the data looking for what factors predicted areas of increased rates of infection within the state, outside of the anticipated

hot spot in the southwestern part of the state that we talked a lot about, a second hotspot of high predicted coccidioidomycosis incidence was highlighted in the northeastern corner of the state. Now while the current observed cases in the area is low currently, if the population were to increase, the incidence might also be expected to increase. And what I find is to be particularly fascinating is that this is the location where the outbreak at Dinosaur National Monument occurred. And so our study predicted this area as a potential hot spot in the coming years if temperatures continue to rise and population continues to grow and as construction in the area continues to increase, which I thought was really fascinating.

[Sarah Gregory] That is fascinating. So geographically, what is up there? Is that next to Wyoming? I'm trying to see the map...

[Adrienne Carey] Yup, exactly right. Exactly right. So as you're looking at the state of Utah, you know it kind of looks like a rectangle that's had a bite taken out of the northeastern corner. And so the area predicted increase incidence is kind of right in that location where Wyoming abuts into the state of Utah. And Vernal, Utah (or Dinosaur National Monument) is right in that location, which we found to be really fascinating.

[Sarah Gregory] Okay. So is there any—anymore findings you want to tell us about?

[Adrienne Carey] Well I think it's important to highlight that overall within the state over the study period, the incidence of infection was about two per 100,000 population per year and it increased over the study period. Washington County that I highlighted earlier (that's where St. George is), that's in the southwestern part of the state, accounted for the largest proportion of cases. About 48% of our cases come out of that county with an observed incidence of about 17 cases per 100,000 per year. And so, this information really contributed to the literature in that the statewide incidence is higher than previously thought and it makes Utah the third most endemic state for coccidioidomycosis behind Arizona and California.

[Sarah Gregory] And I guess this is a no brainer from what you've just said, but as time goes on, do you think these infections will continue to increase?

[Adrienne Carey] Yes, I agree. With time, we know that the planet is warming, so increased temperatures lead to conditions that are ideal for this fungus to populate within the soil; as our population grows and continues to interact with the environment, whether that be hiking, biking, using motorized vehicles out in the desert; and also increased construction in areas where *Cocci* is endemic. I think we'll just continue to see cases rise.

[Sarah Gregory] And I guess it's self-apparent, but what are the public health implications of this study?

[Adrienne Carey] I think really this study increases awareness of the infection, not only in the general public but also increases awareness of the disease to frontline providers across the state, particularly in the areas of known high incidence. And so providing education to primary care physicians, emergency department/urgent care providers, radiologists who are looking at images of people who may have changes in their lungs—they need to know that coccidioidomycosis is prevalent in those areas. And even cancer specialists, I think it's really important for them to be aware of the disease, not only when they're taking care of their own cancer patients who live in the area but also when they get referrals or workups for, let's say a solitary lung nodule in the lungs, because that's one of the ways that coccidioidomycosis can present. It can mimic lung cancer on appearance. And so even in our study—I didn't mention this previously, but we found

that 30% of our patients were diagnosed based on a lung biopsy. And so if you could have this on your differential diagnosis before you have somebody undergo a lung biopsy, then maybe you could consider doing some bloodwork ahead of time, looking to see if people have antibodies to coccidioidomycosis or *Coccidioides* and maybe it's going to save them a lung biopsy down the road. So I think those are the major public health implications.

[Sarah Gregory] So there are tests, like blood tests? Simple tests to see if you've...

[Adrienne Carey] Yes, there are blood tests that you can do. Obviously the Gold Standard of diagnosis is either culturing it or seeing the fungal spores under the microscope and histopathology. But there are really good blood tests that you can do, and test some of the spinal fluid to look for antibodies or even the specific antigen for *Coccidioides*.

[Sarah Gregory] So how can people protect themselves from getting infected?

[Adrienne Carey] That's a great question. You know, I think we touched on a little bit earlier about wearing a mask if you have a compromised immune system which you're going to go out and engage with the environment where there's going to be disruption of soil and dust. Maybe avoiding that all together if you have a compromised immune system. If you are going to go out in the desert and do some recreational activities that are going to involve soil disruption, again, kind of considering a face covering at that point in time. Obviously, we don't want to tell people to stay indoors and never go outside because you may encounter a pathogen. But I think there are things that you can do to decrease your chances of getting exposed, especially if you're in the high risk category—compromised immune system, older age, non-white ethnicity or race. And pregnant women are also at increased risk of *Coccidioides* infection as well. So I think there's some things that you can do to mitigate your risk.

[Sarah Gregory] Okay. So it seems like wearing masks are just generally a good idea, anyway. There were so many other diseases—

[Adrienne Carey] Yeah.

[Sarah Gregory] —people didn't get last year.

[Adrienne Carey] Right, especially these days.

[Sarah Gregory] Yes, especially these days.

Speaking of that, so there's been some associations between COVID-19 and fungal infections. How does that work?

[Adrienne Carey] That's a really interesting question. So we know that in the literature, there's been well described COVID-associated pulmonary aspergillosis syndrome. So aspergillosis is a mold fungus that in the setting of recent COVID-19 infection, we are finding that in certain populations you may be at risk for acquisition of aspergillosis after suffering from COVID-19. And the thought is that the lung tissue is damaged, the lung function is not normal. Again, we're exposed to these fungal spores on a regular basis but if our lung tissue isn't normal and our immune system is somewhat knocked down because of a recent bout with COVID-19, it does seem that getting this fungal infection after COVID-19 has become something that has been noticed in the literature and then well-described as something to consider, especially if patients are not improving from their COVID-19 and it seems like they're over their initial viral illness.

[Sarah Gregory] And again, treatment for this is what?

[Adrienne Carey] Treatment for coccidioidomycosis?

[Sarah Gregory] Yeah.

[Adrienne Carey] Yeah, treatment is kind of a couple pronged approach. So depending on the patient's status and the location of the infection, you may not need treatment, maybe supportive care. If you are a person that has a normal immune system, you only have involvement on one of your lungs instead of both, you may not require treatment. If you are somebody who's at higher risk for progression to more disseminated disease outside of the lungs or you have pretty severe illness or you're critically ill with the infection, then we use antifungal treatment. We use medications to treat this, and usually frontline therapy is an azole medication called fluconazole. There are other azoles that have coverage of *Coccidioides*, including posaconazole. And then if you're critically ill with disseminated infection, we consider using a pretty strong antifungal medication called amphotericin B. So we do have antifungal medications to treat coccidioidomycosis.

[Sarah Gregory] I see.

Well, tell us about your job and what you like most about it.

[Adrienne Carey] Well as you mentioned, I'm an assistant professor of infectious diseases at the University of Utah. I'm also the program director for the infectious diseases fellowship at Utah, and I co-direct the medical microbiology and immunology nine-week block for first year medical students at the school of medicine at Utah. And I see patients both at the University and at the VA, and I do inpatient consults as well as an outpatient clinic. And recently I have taken over the immunology clinic for our long-time immunologist who retired, and I love working with medical students, residents and infectious diseases fellows on a daily basis. And the main reason that I love my job is because every day is different. You never know who or what you're going to see each day. And infectious diseases is rewarding to me because with an accurate diagnosis, treatment usually leads to improvement and recovery. And so that's why I love my job.

[Sarah Gregory] That is such a lovely, optimistic viewpoint about infectious diseases. It's just so much I hear is doom and gloom. So that—

[Adrienne Carey] Yeah.

[Sarah Gregory] I like that.

Okay, well, how or has the pandemic impacted your work?

[Adrienne Carey] Absolutely. I mean, who hasn't been impacted by the pandemic? I think the pandemic has led to a lot of changes, some positive, some negative. The increase in telemedicine has been a wonderful silver lining for many of my patients that live several hours away from Salt Lake City. So to be able to see them with the use of technology is just a great thing. And I was involved with several other colleagues at the University of Utah managing the COVID pager for the health system for several months, and it was gratifying to be able to help colleagues from across the institution with their questions related to COVID-19. And so, I've really tried to focus on the positives and how it has improved my job and things because I think it's really easy to get bogged down in the negatives of this pandemic.

[Sarah Gregory] Indeed, yes.

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

[Adrienne Carey] You are so welcome, Sarah. It was a pleasure to be here. And I love talking about coccidioidomycosis, and so it was great to be here and share some things about our study with you.

[Sarah Gregory] And thanks for joining me out there. You can read the September 2021 article, Epidemiology, Clinical Features, and Outcomes of Coccidioidomycosis, Utah, 2006–2015, online at cdc.gov/eid.

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

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