Good afternoon. I'm Captain Ibad Khan, and I'm representing the Clinician Outreach and Communication Activity, COCA, with the Office of Emergency Risk Communication at the Centers for Disease Control and Prevention.

I'd like to welcome you to today's COCA call, **Murine Typhus: A Re-emerging Threat in the United States**. All participants joining us today are in listen-only mode. Free continuing education is offered for this webinar, and instructions on how to earn continuing education will be provided at the end of the call.

In compliance with continuing education requirements, all planners, presenters, and moderators must disclose all financial relationships, in any amount, with ineligible companies over the previous 24 months, as well as any use of unlabeled product or products under investigational use.

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At the conclusion of today's session, participants will be able to accomplish the following:

Discuss the epidemiology and ecology of murine typhus.

Describe diagnosis, and treatment options for murine typhus.

And identify the best laboratory method to confirm acute infection with Rickettsia typhi.

After the presentations, there will be a Q&A session. You may submit questions at any time during today's presentation. To ask a question, click the Q&A button at the bottom of your screen, then type your question in the Q&A box. Please note that we receive many more questions than we can answer during our webinars. If you are a patient, please refer your question to your healthcare provider. If you are a member of the media, please contact CDC Media Relations at 404-639-3286, or send an email to media@cdc.gov.

I would now like to welcome our presenters for today's COCA Call. We're pleased to have with us Dr. Johanna Salzer, who's a veterinary medical officer and serves as the epidemiology team lead in the National Center for Emerging and Zoonotic Infectious Diseases at the Centers for Disease Control and Prevention.

Next, we have Dr. Lucas Blanton, who's an associate professor of medicine at the University of Texas Medical Branch in Galveston, Texas. And we have Dr. Christopher Paddock, who's a medical officer and the lead for Microbiology and Diagnostic team in the National Center for Emerging and Zoonotic Infectious Diseases at CDC.

I will now turn it over to Dr. Salzer. Dr. Salzer, please proceed.

Yes, thank you, and thank you for having me. So, I'm an epidemiologist with the Rickettsial Zoonoses Branch at CDC. I'm the first of three speakers today, and I will be covering the interesting epidemiology and ecology of murine typhus, a re-emerging threat in the United States.

Next slide, please.

Murine typhus is caused by *Rickettsia typhi*, which is an obligate intracellular Rickettsial bacteria. The disease is also referred to as flea-borne typhus. There are many species of fleas that have been identified as vectors for murine typhus, but in the United States, the primary fleas associated with murine typhus are the Oriental rat flea and the cat flea, which, despite their names, they also feed on a number of other animals. The primary mechanism of *Rickettsia typhi* inoculation in people is through rubbing or scratching infected flea feces, or commonly called flea dirt, into flea bite wounds, abrasions, or into mucous membranes or, in some cases, through the inhalation of this flea dirt. Signs and symptoms begin on average at about 11 days from the contact with infected fleas. Murine typhus generally is considered a milder disease than other related Rickettsial diseases, such as Rocky Mountain spotted fever, but it can be fatal.

Next slide, please.

So this brings us to our first knowledge check. Which arthropod serves as the vector for murine typhus? A. Ticks, B. Mosquitoes, C. Fleas, or D. Lice.

Next slide, please.

I hope you all answered C, fleas. Murine typhus is spread to people through contact with feces of Rickettsia typhi-infected fleas, typically the Oriental rat flea and cat flea.

Most infections result from scratching infectious feces into the skin. Other routes of infection can include contact with mucous membranes or from inhalation of these dried flea feces.

Next slide, please.

Murine typhus was first identified in the United States over 100 years ago. It was associated with a number of fleas. But historically, the most important vector is the Oriental rat flea. The Oriental rat flea is commonly found on brown rats in the United States and prefers warm human climates. The ecology of murine typhus associated with rats and the rat flea is generally limited to these more urban environments.

Next slide, please.

But more recently, in the last few decades, with work conducted in California and by my colleague, Dr. Lucas Blanton, on this call, it was identified that murine typhus in people could also be vectored by the cat flea, feeding primarily on possums, which serve as a reservoir host. The ecology of murine typhus associated with the cat flea and possums is more closely associated with suburban environments, where possums are more prevalent. In areas where murine typhus has reemerged in people, studies have shown that both cat fleas and possums are found to be positive for *Rickettsia typhi* around areas of outbreaks. Because the cat flea also infests domestic animals, cats can serve as a reservoir and a point of which people may be exposed as well.

Next slide, please.

There are a number of environmental risk factors for infections in people. These include contact with animals that may be infested with infected fleas, such as rats, possums, and free-roaming cats or cats that are not on flea preventatives. People with close contact with feral cats and rodents are known to be at greatest risk. There's an increased risk of exposure that is well documented in people who live in homes that are infested with rodents or who are unhoused and may have a greater contact with fleas and flea dirt.

Next slide, please.

After the first case was identified in 1912, right here in Atlanta, murine typhus grew to epidemic levels in the 1930s and early 1940s, during the Great Depression and World War II. The emergence of murine typhus is thought to be due to a variety of factors, which include, but are not limited to, the changing landscape of agriculture in the south, urbanization and poor housing conditions that were associated with the Great Depression, and the emergence of brown rats displacing the smaller black rats in these environments. There was also a shortage of rodenticides and pesticides during this time. Surveillance was initiated in 1931, and after the establishment of CDC, it would go on to be nationally notifiable for many decades. Between 1931 and 1946, there was approximately 42,000 cases reported in the United States of murine typhus.

Next slide, please.

In 1944 alone, just over 5,400 cases were reported in the United States. This map shows the geographic distribution of the incidents across the southeastern U. S. high-incidence areas are found in an almost contiguous region from coastal Texas to Savannah, which was one of the most impacted cities at this time. And you can see cases also occurred throughout Florida.

Next slide.

In the 1930s, public health authorities were alarmed by the annual climbing case counts. During this time, there was a variety of public health initiatives for rodent control in the southeastern U. S. Despite the best efforts, cases continued to climb through the 1930s and the early 1940s. It wasn't until a spike in cases in 1944, and the end of World War II, that there was more intensive rodent and flea eradication programs implemented and, specifically, the more widespread use of DDT, which was led to the decline of human cases. This slide includes some of those great historical images of the public health efforts.

Next slide, please.

So now, you can see the map on the right shows the incidence of murine typhus in 1951. The decline in cases is astounding to have occurred just in this eight-year period. And I believe it's one of the more remarkable public health successes.

Next slide, please.

This graph is the epidemic curve of cases from 1930 to 1987. By 1958, the reported number of human cases of murine typhus to CDC fell to less than 100 cases per year.

Next slide, please.

Because of the low occurrence of murine typhus after the mid-1950s, murine typhus was removed from the list of nationally notifiable diseases in 1987, along with smallpox and relapsing fever, because they were, and I quote, "so rare and of such minimal current importance that routine reporting was unnecessary. " So today, national data on cases reported to CDC of murine typhus does not exist.

Next slide, please.

Although murine typhus is not nationally notifiable today, there are 16 states that have continued to have murine typhus reportable to some extent in their state. Among those states where it is reportable, many do not report cases, and the vast majority of murine typhus cases currently in the U. S. are reported from California, Texas, and Hawaii.

Next slide, please.

Here, we show the case counts for Texas in blue, California in gray, and Hawaii in orange. You can appreciate the steady increase in cases over this time period, specifically in Texas and in California.

Next slide, please.

So knowledge check number two. In the last five years, which two U. S. states have reported the most cases of murine typhus? A. California and Texas, B. Texas and Louisiana, C. California and Arizona, or D. Texas and Georgia.

Next slide, please.

Hopefully, you all answered A, California and Texas. Although murine typhus was removed from the list of nationally notifiable diseases in 1987, it remains reportable in several states. Over the last 20 years, nearly all reported cases are documented from California, Texas, and Hawaii, although less so. And the most cases actually occur in southern California and southern Texas. In the first half of the 20th century, murine typhus was reported in large numbers all across the southeastern U. S. Given the historic high number of cases throughout the southeast, the persistence of the fleas and the animal host, it is reasonable to consider that the southeastern U. S. is at high-risk location for cases of murine typhus and that cases may be occurring without our ability to detect them due to a lack of surveillance and low healthcare provider awareness.

Next slide, please.

There are several interesting reports from Texas and California, where they are conducting surveillance, that highlight this emerging public health crisis. This *MMWR* report was published by our partners at the Los Angeles County Health Department in 2023, and highlights the emergence of murine typhus in this urban center.

Next slide, please.

In 2022 alone, Los Angeles identified 171 cases of murine typhus in three deaths. At least one of the patients that died was a person experiencing homelessness, and a second had a history of contact with feral cats. In a single year in 2022, in this one county, it was reported nearly twice the number of cases were reported than were reported nationally when murine typhus was removed from the list of nationally notifiable diseases in 1987.

Next slide, please.

So, in conclusion, murine typhus emerged about 100 years ago at an alarming rate. This graph shows that incidence during the period of national surveillance. Through strong public health interventions, the disease in the U. S. during the second half of the last century was nearly eliminated.

Next slide, please.

But looking more closely at the state data, we can see a reemergence of murine typhus since 2008 with the surveillance data that we do have available from the states that are conducting surveillance. Murine typhus is a disease that had all but disappeared from the United States and also disappeared from the minds of healthcare providers but is clearly returning, and our understanding of the current burden is almost certainly underestimated. And I will now introduce Dr. Lucas Blanton.

Next slide.

Thank you. Thank you. The epidemiology is a great segue into the clinical manifestations and treatment. And as an infectious disease physician here in Galveston, I've had the opportunity to see many, many cases of murine typhus.

Next slide.

So murine typhus is an acute, undifferentiated febrile illness. So acute in the sense that it occurs very abruptly after an incubation period of about four days to two weeks after inoculation of the bacterium. And it's undifferentiated in the sense that its signs and symptoms are kind of generic and mimic many other infectious diseases. Common signs and symptoms include headache, which occur in 81%, malaise, 67%, chills and myalgia. And obviously, fever is universal in all of these patients. When people think of a rickettsial illness, they think of rash, and rash certainly does occur in murine typhus. And we'll talk a little bit more about rash in the next slides. But it only occurs in about 48% of people. And although not a primary gastrointestinal illness, this is a systemic infection of endothelial cells, people can have GI manifestations like anorexia, nausea and vomiting. And as the disease progresses, about 28% will develop respiratory symptoms, usually manifested as a cough.

Next slide, please.

So this is a patient with a typical rash of murine typhus. It's generally described as macular or maculopapular. It occurs on the trunk of about 88% of people who have rash, and it can occur on the extremities of about 45% of people who do have rash.

Next slide.

So the rash could be very faint. And in those with very lightly pigmented skin, the rash is more noticeable. So in Caucasians, the rates of rash have been reported up towards 81%, as opposed to those with darkly pigmented skin, about 20%. But when studies have looked at patients from all over the world and compiled that data, the frequency of rash is about 48%.

Next slide.

So these are pictures of various rash lesions that I've taken while encountering patients with murine typhus. On the very left is a very faint macular rash that was not noticed by any clinician; it was noticed by the patient, who noticed very faint macules that don't really show up on this picture on the lightly pigmented portions of his skin that were traditionally covered by his socks. In the next picture, there's a faint, probably not noticeable on this picture, macular rash on an African American man that was noticed by a very careful internal medicine physician performing a good physical exam. On the third panel is a noticeable macular rash on the trunk and right upper extremity, but this rash was not present on presentation but occurred many days in the patient's hospital illness when being worked up for a fever that went undiagnosed. And then finally, a petechial rash, which is very noticeable, is seldom seen in murine typhus, seen in about 13% of patients, and usually occurs later during the illness.

Next slide, please.

So what percentage of patients with murine typhus will have a rash at some point during their illness? A. 28%, B. 89%, C. 100%, or D. 48%?

Next slide, please.

So the answer is D, 48%. Next slide. So this slide shows the differential diagnosis for tick-borne rickettsial diseases. And although murine typhus is not a tick-borne rickettsial disease, as mentioned earlier, it's transmitted by fleas, the differential diagnosis is the same, and it's quite vast. As seen here, we have syndromes or infections in red that have a high-case fatality rate that can mimic murine typhus. We have some syndromes in orange that are rising in incidence and are really hot in media coverage today. And then, as seen in green, for example, mononucleosis is a very common syndrome that may present to many primary care physicians' offices. And in blue, various travel-related infectious diseases can mimic or look exactly like murine typhus.

So it's a very, as an undifferentiated febrile disease, large differential diagnosis and can mimic many other infectious diseases.

Next slide, please.

So many laboratory abnormalities can occur with murine typhus, and these are often seen in some of the common labs that might be ordered, like a CBC and chemistries, when working up a patient with fever. The most common is elevated hepatic transaminases, which is seen in 79%, increased LDH, low albumin, elevated ESR, and CBC abnormalities include thrombocytopenia in 42%. Sometimes a patient may have slight anemia or even leukopenia. And seen on the chemistry, about a third of patients will have hyponatremia. Now, a patient may have almost all of these laboratory abnormalities, maybe some of them or even none of them, but they may have some of these in some combination, but none of these are specific to murine typhus. They can be seen in many other infectious diseases.

Next slide, please.

So Rickettsia typhi is an endothelial infection, causes a systemic illness. It'll infect the systemically infected endothelial cells, where it causes increased vascular permeability. And that's where many

of the manifestations of murine typhus, whether they're laboratory manifestations, whether it's the rash, will manifest. And if untreated, a patient can be sick with fever for up to three weeks. And then after they defervesce, even have lassitude and fatigue in weeks following their defervescence. So without treatment, it can be a long illness. But without treatment, some of these manifestations caused by endothelial dysfunction can worsen. People can get intravascular volume depletion, which can lead to hypotension, organ hypoperfusion and dysfunction, and even death. Next slide. So here are some severe cutaneous manifestations of murine typhus. On the left, we see petechial lesions that are coalescing. In the middle, we see the hand of a patient with gangrenous digits related to murine typhus, plus or minus vasopressors. And on the right, this fern-like necrosis that has been documented in people with severe rickettsiosis, such as Rocky Mountain spotted fever and Mediterranean spotted fever. And although these are relatively uncommon manifestations in murine typhus, they can occur.

Next slide.

Severe manifestations can also include the kidneys with prerenal azotemia, which can lead to acute tubular necrosis. This manifests as acute kidney injury or an increased BUN and creatinine on our labs. And this can be severe enough to require hemodialysis. Severe pulmonary manifestations include cough that develops as the illness progresses. And chest X-ray abnormalities can be seen in up to 17%. And although rare, ARDS can even occur. Neurologic manifestations and sequela include severe headache. So headache is noted in about 81% of people with murine typhus, but the headache can be very severe, and it's often described as the worst headache of one's life. People can present with meningoencephalitis. And rarely, but it has been documented, people can get cranial nerve palsies, seizures, and a coma.

Next slide, please.

So the case fatality rate is about 0. 4%. And this has been documented in the pre and post-antibiotic era. And the fact that it hasn't changed in the post-antibiotic era likely represents people just not getting treated in a timely fashion or not getting treated at all. When hospitalized, if ill enough to be hospitalized, the case fatality rate has been documented to be about 2%. And most recently in 2022, the case fatality rate in Los Angeles County, California has been up to 1. 8%. So certainly, if enough people are getting murine typhus, we are going to have deaths. Next slide, please. So a very important note with treatment is that treatment should not be withheld while awaiting diagnostic tests. We'll hear a little bit more about that later. But it's important to know that if one thinks of murine typhus as a possibility, prompt antibiotic therapy with tetracyclines is needed. Tetracyclines are the antibiotics of choice, namely doxycycline. So adults, the adult dose is 100 milligrams oral or IV twice daily, and in children, less than 45 kilograms, 2. 2 mg per kg oral or IV twice daily. It's important to note that doxycycline is orally bioavailable. But the intravenous form may be needed in those hospitalized, especially if they have nausea and vomiting, which may preclude the ability to keep down oral doxycycline. And the treatment duration is seven days.

Next slide, please.

So knowledge check four. What antibiotic should be the first choice to treat suspected cases of murine typhus? A. amoxicillin, B. doxycycline, C. ceftriaxone, or D. ciprofloxacin.

Next slide.

So the answer is B, doxycycline. Doxycycline is the treatment of choice. Next slide. So some pearls and possible alternatives. In those with severe illness, severe enough to be hospitalized, I recommend giving a 200-milligram loading dose of doxycycline, and this is usually when someone is ill enough to receive the intravenous formulation. Patients usually improve within 24 to 48 hours after the initiation of doxycycline. So if they defervesce and feel better within a day or two, you're probably on the right track. Do note that minocycline and other tetracyclines seem to be as effective as doxycycline, and this was noted in about 2013 when there was a shortage of doxycycline and minocycline was used in those with murine typhus. And certainly, minocycline is used in other countries for other rickettsioses like Japanese spotted fever. Chloramphenicol has traditionally been a good alternative but isn't available in the United States. And there are some alternatives that have been used, like azithromycin and fluoroquinolones, but their success is based on limited observational data. The time to defervesce on azithromycin and fluoroquinolones is slower when compared to tetracyclines like doxycycline. And in a recent randomized controlled trial, azithromycin didn't seem as effective when compared to doxycycline. And lastly, I should have mentioned this on my prior slide, but I did mention the pediatric dose of doxycycline. It's important to note that doxycycline is still recommended for children with rickettsiosis and murine typhus is included. Short and infrequent doses of tetracyclines do not appreciably stain developing teeth in children. Well, thank you.

Next slide.

Thanks, Lucas. Hi, folks. My name is Chris Paddock. I'm an anatomic and clinical pathologist who's been involved in the laboratory diagnosis of rickettsial diseases for almost 30 years. First slide, please. We're going to start with a recent investigation that involved several teams at CDC, as well as our partners from state and local public health departments in Texas. So last October, CDC was notified by an organ procurement organization in Texas of a hospitalized organ recipient diagnosed with murine typhus. Further investigation revealed that the recipient of another organ from the same donor died 11 days after the transplantation. Testing at an outside lab confirms murine typhus in the second donor as well. The donor died following a brief illness that was attributed to a non-infectious etiology.

Next slide, please.

CDC laboratories received residual blood and tissue specimens from the donor, and DNA of Rickettsia typhi was detected by PCR in all of these residual specimens. Furthermore, antigens of Rickettsia typhi were detected by a special immunohistochemical stain performed by our colleagues in the Infectious Disease Pathology Branch at CDC in both of the pre-transplant allograft biopsies. This investigation highlights several of the points already emphasized by Dr. Salzer and Blanton, namely the rising occurrence of this disease in Texas and that it can be life-threatening. At the same time, however, I think it can be considered as a tip of the iceberg example of murine typhus in the United States in 2025. Well, the donor cohort in transplantation can be viewed as a sort of sentinel group for many types of infectious diseases, common and uncommon, particularly in terms of unrecognized scope and magnitude. And in that context, I think this event signals that there is, in fact, a lot of murine typhus in the United States that is going undiagnosed and otherwise missed.

Next slide, please.

This graph shows the fall and rise of this disease in the state of Texas over the last 80 years. And you can see the precipitous decline in cases during the late 1940s that Dr. Salzer already highlighted in terms of how public health interventions resulted in a tremendous drop in cases, and this mirrored national trends. This was followed by five decades of quiescence, until this disease came roaring back in the last 20 years to levels that haven't been seen since the late 1940s.

Next slide, please.

So there's an adage in medicine that you see what you know. And this one, I think, really applies well to murine typhus. And in that context, I think it's important to be very familiar with the diagnostic tests that provide confirmation of clinical suspicion and thereby allow you to know this disease. There are two main categories of diagnostic tests available for this particular infection: serological and molecular. The serological assay used for murine typhus is the indirect immunofluorescence antibody or IFA assay. The way that this assay works is that antigens of Rickettsia typhi are prepared in cell culture. And as it was mentioned previously, Rickettsia species are obligate intracellular pathogens and they can only be grown in cells. So once those antigens are prepared, they're placed on a glass slide, they're fixed onto that slide. And then human serum, which contains antibodies, is applied to that slide, and then you come back with a secondary anti-human antibody. And this can be an anti-human IgG or an anti-human IgM. But that antibody is tagged with a fluorescein isothiocyanate labeled tag. And that gives you the green fluorescence when the slide is viewed under a epifluorescence microscope. And the titers represent the maximum dilution where you still see distinct fluorescence. So if the initial dilution is one to 32, then it's diluted like one more time to 64, then it's diluted again to 128, 256, and so on. And that last dilution where you do see fluorescence is called the titer. And as it would appear, the higher the titer, the more intense the infection.

Next slide, please.

So IFA is a great assay when used correctly and interpreted correctly, which is unfortunately not often the case. Diagnostic levels of antibody for murine typhus are generally not detectable during the first week of illness. There are other limitations in the fact that we don't know what the background show prevalence to Rickettsia typhi in the United States at the present time. So there may be well people who've been exposed to this pathogen at some point in the distant past, and they may have residual antibodies. We just don't know. Confirmation of infection requires paired serum, acute and convalescent specimens. So a specimen is collected during the early stage of the disease, presumably when the patient is in the hospital or first seen in clinic, and then a second serum that's collected four to six weeks after. And unfortunately, very, very rarely are those second serum collected, for a variety of reasons. It's also important to emphasize that early IgM antibodies are relatively nonspecific. Antibodies elicited by other gram-negative bacteria can also cross-react with Rickettsia species antigens. So unlike many of the viral diseases, IgM antibodies are not particularly useful in diagnosing patients with acute infections with Rickettsia typhi. The other issue is that we believe there is some level of cross reactivity with antigens of spotted fever group Rickettsia, such as Rickettsia rickettsii, the agent of Rocky Mountain spotted fever. And that's described in about 20 to 40% of contemporary evaluations.

Next slide, please.

So the second broad category are molecular assays, and these include PCR and next-generation sequencing. The strengths of these molecular tests are direct evidence of infection and that a confirmatory result is achievable with a single specimen collected during the acute phase of the disease. There are some weaknesses, and the biggest one is a sensitivity issue, particularly during the first several days of the disease. As mentioned by Lucas and by Johanna, these are obligate intracellular pathogens that target endothelial cells. So there's generally not a lot of circulating organism in the blood during the early stages of the disease. And I just want to show you two histological images on the left hand, excuse me, the right-hand side. And these represent -- The top image is a H&E stained blood vessel from a patient who died of a rickettsial disease. The bottom is an immunohistochemical stain specific for Rickettsia. And you can see that the rickettsiae are highlighted as those small, red dots in the endothelial cells that are surrounding the lumen of this blood vessel. They're not typically in the circulating blood. The other thing, molecular assays in general are more expensive relative to IFA. Next slide, please. So where can you find these assays? I've listed a few sources. I'm not necessarily endorsing any of these, but just rather providing some examples, and there may be others. I do want to highlight one specific test, however, the Karius test, which is a microbial cell-free metagenomic sequencing assay. And the reason I'm highlighting it is that's the assay that was used to establish the diagnosis of murine typhus in the two transplant recipients in the investigation I mentioned briefly at the start of this talk. Next slide, please. And the Karius assay actually seems to be exquisitely sensitive and is picking up what we believe to be more and more cases of murine typhus, particularly severely ill hospitalized patients in California and Texas, as documented in several recent publications that are shown here. Next slide, please. So knowledge check number five. The best laboratory test to confirm acute infection with Rickettsia typhi is: A. IgM IFA of serum, B. IgG IFA of serum, C. molecular testing, such as nucleic acid amplification or metagenomic sequencing of whole blood, or D. cell culture isolation of whole blood.

Next slide.

The correct answer is C, molecular testing of whole blood. As I mentioned, an IgM, a single IgM in particular, is not particularly specific for acute infection with Rickettsia typhi. And you can get confounding results with other gram-negative bacterial infections that will also give you IgM antibodies that react with rickettsial antigens. IgG IFA of serum, if it's used correctly, it's actually a really good test. But as I mentioned, most providers obtain a single sample during the acute stage of the illness. And during the acute stage of the illness, and that's the first seven to 10 days, you don't expect to see an antibody titer in this infection, an IgG antibody titer. The most appropriate use is to get two serum samples, one during the acute stage, one during the convalescent stage, and show a seroconversion to antigens of *Rickettsia typhi*. Unfortunately, that is almost never done. And then D, cell culture isolation of whole blood is actually the microbiological gold standard, but it is not widely available. It's limited to reference centers, national reference centers, or academic centers. And it also requires biosafety level-three facilities to perform.

Next slide, please.

So why do confirmatory testing at all? Well, a busy and pragmatic clinician might think, hey, if I give them doxycycline and they get better, well, they probably have murine typhus. And while it's true

that patients with murine typhus typically respond rapidly to treatment with doxy and almost nothing else, as Dr. Blanton emphasized in the last talk, next slide, please, Doxycycline actually works against more than 40 other pathogens or groups of pathogens. So, that logic is somewhat flawed. It's an antibiotic that I would want with me if I was ever found or if I found myself stranded on a desert island.

Next slide, please.

Okay. Well, I hope we've impressed to you in the last several minutes about the recent and extraordinary rises of cases of murine typhus in two of the few states in the U. S. where the disease remains reportable, namely Texas and California. And these graphs show that dramatic rise in those individual states. And I'm very grateful for the data that's provided to us for this by Bonny Mayes with Texas Department of State Health Services and Anne Kjemtrup with California Department of Public Health.

Next slide.

And I hope we've impressed you just how severe this disease can be. More than half the patients are hospitalized. And among those who are hospitalized, life threatening complications, such as septic shock, meningoencephalitis, myocarditis and many others that Dr. Blanton pointed out, are not uncommon. These are just a few of the recent reports from clinicians at medical centers in South Texas in just the last couple of years, representing patients seen at hospitals in Galveston, San Antonio, and Houston. Next slide, please. And these cities are represented on this map by the yellow dots. And this is a map that you recall that Dr. Salzer presented just a few minutes ago, and it shows the county-level incidence rates of murine typhus in the United States at its height in 1944.

The areas shaded in black were the areas of greatest endemicity. And as you can see, the three cities from which these case reports are coming from, contemporary case reports, fall within these regions.

Next slide, please..

But consider this. There are many other metropolitan centers near the Gulf Coast and along the southern Atlantic, like New Orleans, Mobile, Montgomery, Tampa, Orlando, Jacksonville, Savannah, situated squarely in the regions of greatest historic endemicity. In conclusion, I think there are or could be similar surges in cases of murine typhus that are happening in these cities or elsewhere, possibly not now but very likely in the not-too-distant future. And with that, we conclude this talk. And I thank you very much for your attention, and I believe I will turn it over for questions.

Thank you so much. Presenters, I want to thank you for providing this timely information to our audience. We will now go into the Q&A session. And for our audience, please remember that to ask a question, click the Q&A button at the bottom of your screen, then type your question.

So our first question comes from a clinician in North Texas who asks, we have been seeing cases of murine typhus in the recent months.

Is there a explanation for this recent epidemiology shifting more northward?

So this is Lucas Blanton. I'll take a stab and see if anyone else wants to add anything. But I don't think there is a -- We don't have a definitive explanation. Based on the control of murine typhus, based on the control of rat and rat flea-associated murine typhus in the post-World War II era, based on that data, being able to get the flea population in that reservoir and vector down to a certain point broke the cycle in most of the southeast. This alternative cycle involving possums, I believe there has just been a sort of a critical infection rate within the cat fleas that infest these possums that has spread from south Texas northward. And with these possums being, you know, very adapted to living in urban and suburban areas, they are bringing these fleas close to human environments. And with the infection rate going up, just as it naturally would, you know, as you have susceptible reservoirs getting infected, I think this is just sort of a natural progression. Some people have hypothesized and made some very compelling arguments about maybe even climate factors playing a role in increased infestation rates of infected fleas on some of these mammals. This is Johanna Salzer. I think the other thing I would add, Lucas, is that Texas, specifically, there's been a growing awareness of murine typhus. I think of all the states across the U. S. , Texas and California probably have a more educated healthcare provider population that may also be looking for it more and testing for it. So, you know, we know that healthcare provider knowledge definitely impacts our surveillance systems.

Thank you very much for that comprehensive answer. Our next question is more related to patient presentation.

And the question asks, **are there any specific patient populations, and the example given is immunocompromise, who may present more atypically?**

So, no. It does seem that from what we know, it's not really necessarily immunocompromising conditions that make people present atypically. Now, certainly, they may be more likely to progress to severe disease. Those that are more likely to progress to severe disease are those with not even immunocompromised, but those that abuse alcohol, those that have G6PD deficiency, and, interestingly, those that have previously been treated with Bactrim. Those three are the big risk factors for severe rickettsioses. Anecdotally, we seem to see more people in the hospital in the last several years who are immunocompromised who have murine typhus. But we have to remember that that population is growing with all our new biologics, with more and more transplants, and all sorts of immunocompromising medications. But they don't seem to present much differently, maybe just a little more severe. Thank you for sharing that. Yes, please proceed. I'll just follow up on that with the example that I presented at the beginning, which was murine typhus in the two transplant recipients. You know, we don't have a huge amount of experience with this. But from this particular example, one of the individuals, they were both on immunosuppressive therapies, you know, right after receiving their organs. One of them survived, was never admitted to the ICU, was sick, and actually did develop meningoencephalitis but didn't ever require, you know, an ICU admit. The second patient did actually become very ill and was admitted to the ICU and died. So it's something that we're still, you know, learning about in this population, which, you know, Lucas mentioned, is growing. And so, I think we, unfortunately, are going to get more experience with this in the coming years. Thank you.

Thank you.

Our next question asks, **can you speak to the prevalence of murine typhus internationally, and are there any travel considerations we should have?**

Go ahead.

Go for it, Chris. Well, what I was going to say is that it has been acquired through travel. In fact, it's been reported in Europeans that have traveled to the United States, acquired, thought to be acquired in the United States. In regard to rickettsial diseases, travelers don't report with murine typhus as often as they do African tick bite fever, which is by far and away the most frequently reported rickettsial illness in travelers, especially those to sub-Saharan Africa. It is a concern, but there's murine typhus probably right now in the world described most in Asia and Southeast Asia, but probably very under-recognized in places in parts of Africa and Latin America. And I just want to emphasize that it is a global infectious disease. I think they say it's been found on every continent except Antarctica. And it is very, very common in Southeast Asia. It's also common in, well, we believe it's common in many temperate countries, as well as in Europe. And part of the reason for that is, you know, the classical cycle involves commensal rats and Oriental rat fleas. The cycle that Johanna mentioned involving opossums, I believe, has only been identified in the United States. But those are two contributory factors. I mean, the rats, commensal rats are all over the world, and Oriental rat fleas are all over the world. And those are two very, very critical components in the transmission cycle of murine typhus. So that explains a lot of its global distribution.

Thank you for that.

Our next question is regarding the use of doxycycline, specifically in children. And the question asks, can you address if there is a benefit-to-risk ratio that needs to be shared with the parent when considering doxycycline in children, and is there any kind of age limit?

So I think the tougher discussion is with pregnant women. I think it's pretty clear that the benefits of treatment far outweigh the risks for any rickettsial disease in children. And I would concur with Lucas. I think, you know, doxycycline isn't to be administered casually to a child under the age of eight but, you know, used when the clinician suspects murine typhus or any other rickettsial disease because these illnesses, murine typhus, Rocky Mountain spotted fever, they can be life-threatening. And you just don't want to mess around with that. So, you know, it is a tough thing, particularly in a pediatric population, where there are so many other childhood exanthems and so many other causes of, you know, an undifferentiated febrile illness. But that's where, you know, getting a solid history comes in. It's where you start asking about, are there feral cats around your house? Have you seen fleas? Do you know anybody else in the neighborhood who's gotten an illness like this? Those are the things that can kind of push the needle towards administering doxy. But it's very important to know that doxy is recommended by CDC and by the American Academy of Pediatricians for the treatment of rickettsial diseases, even in children under the age of eight. And there have been some recent studies showing that short courses of doxycycline, you know, like a week of doxy, when children are under the age of eight will not cause cosmetically perceptible staining of teeth when the permanent teeth erupt. And we can provide that literature if anybody is interested. Yeah, this is Johanna. I would just stress both Lucas and Chris have said, is that doxy for the short-term use for rickettsial diseases has been determined to be safe in children. And a lot of that work has been done with Rocky Mountain spotted fever specifically, but that's true for the use of rickettsial diseases, and happy to provide that reference for the work that has been done on that.

Thank you very much for that. And that brings us to the conclusion of our webinar. And I want to thank all our presenters for sharing their time and their expertise with us today and to our audience for joining us for this COCA Call.

CDC has transitioned from the Training and Continuing Education Online system that provides access to CDC educational activities for continuing education to CDC Train. If you do not already have a Train account, please create one at www. train. org/cdctrain. All new activities that offer CE from CDC will only be listed on CDC Train. CDC Train is a gateway into the Train learning network, the most comprehensive catalog of shared public health training opportunities. And this transition will allow you to access non-credit and for-credit educational activities and track your learning, including continuing education all in one place. Many CDC accredited activities are already listed in Train. The move to one system improves efficiency and makes it easier for learners, CDC staff, and partners to offer and earn CE in one place. And you can access and download your CE transcripts and certificates in TCEO through the end of 2025. Instructions will be available on both platforms, and a learner support team will be available to answer any questions. all CE for COCA Calls are issued through CDC Train.

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