Good afternoon, I'm Commander Ibad Khan and I'm representing the Clinician Outreach and Communication Activity, COCA, with the Emergency Risk Communication Branch at the Centers for Disease Control and Prevention. I'd like to welcome you to today's COCA Call, Melioidosis in the United States: What clinicians need to know following newly discovered endemicity. All participants joining us today are in listen-only mode.

Free continuing education is offered for this webinar. Instructions on how to earn continuing education will be provided at the end of the COCA Call.

In compliance with continuing education requirements, all planners and presenters 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. CDC, our planners and presenters wish to disclose they have no financial relationships with ineligible companies whose primary business is producing, marketing, selling, reselling, or distributing healthcare products used by or on patients.

Presentations will not include any discussion of the unlabeled use of a product or a product under investigational use, except Dr. Caroline Schrodt and Julia Petras' discussion of melioidosis as a rare disease in the United States with no FDA-approved drugs specifically for treating melioidosis. Given this, the antimicrobials recommended for treatment are considered off-label. CDC did not accept financial or in-kind support from ineligible companies for this continuing education activity.

At the conclusion of the session, participants will be able to accomplish the following. Outline the evolving epidemiological risk factors and clinical characteristics of melioidosis and when to consider melioidosis as a potential diagnosis. Discuss best practices for preventing, diagnosing, and treating melioidosis, including how to address diagnostic challenges. And describe what CDC is doing to learn more about melioidosis in the United States and how clinicians and public health officials can help.

After the presentations, there will be a Q&A session. You may submit questions at any time during today's presentations. To ask a question using Zoom, click the Q&A button at the bottom of your screen, then type your question in the Q&A box. Please note that we often receive many more questions than we can answer during our webinars. If you are a patient, please refer your questions to your healthcare provider. If you're a member of the media, please contact CDC Media Relations at 404-639-3286 or send an email to media@cdc. gov. We have introduced self-knowledge checks throughout the presentation. We hope you enjoy these opportunities to assess your understanding of today's session. Please do not type your answers into the Q&A box, as this may disrupt the Q&A portion at the end of the session.

I would now like to welcome our presenters for today's COCA Call. We are very pleased to have with us today Ms. Julia Petrus, who's an Epidemic Intelligence Service Officer in the Bacterial Special Pathogens Branch within CDC's National Center for Emerging and Zoonotic Infectious Diseases. And Lieutenant Commander Caroline Schrodt, Medical Officer in the Bacterial Special Pathogens Branch within CDC's National Center for Emerging and Zoonotic Infectious Diseases. It is now my pleasure to turn it over to Ms. Petrus. Ms. Petrus, please proceed.

Good afternoon. My name is Julia Petrus. I am an EIS Officer based here with the Bacterial Special Pathogens Branch at CDC. And I will first present the first part and pass it over to my colleague, Dr. Caroline Schrodt. Thank you so much for listening. Next slide.

On July 27th of this year, CDC released a health advisory through the Health Alert Network, alerting clinicians and public health officials throughout the country to consider melioidosis in patients whose clinical presentation is compatible with signs and symptoms of the disease, regardless of travel history to international disease endemic regions. This is the first time Burkholderia pseudomaliae, the bacteria that causes the disease called melioidosis, has been isolated from the environment in the continental US. Melioidosis is now considered to be at least locally endemic in areas of the Gulf Coast region of Mississippi. Next slide.

We feel that this COCA Call is needed now in light of this recent discovery and other recent trends in melioidosis epidemiology here in the US, which we will discuss more in detail in the following part of this call. Part two of the call will focus on clinical presentation of melioidosis, followed by diagnostic considerations, treatment, prevention, and key messages. And finally, we will discuss what CDC is doing to learn more about melioidosis in the US, and how clinicians and public health officials can help. Next slide.

I will now review the epidemiology and background of melioidosis. Next slide.

Meliodosis, also called Whitmore's disease, is a potentially severe and fatal bacterial disease caused by the gram-negative bacterium, Burkholderia pseudomallei. B. pseudomaliae is predominantly found in the soil and fresh water in tropical and subtropical regions globally. Melioidosis was first recognized in Myanmar in 1911. The global footprint of B. pseudomallei continues to be redefined, and melioidosis is now known to be endemic in at least 48 countries. Globally, there's an estimated 160,000 melioidosis cases per year.

Melioidosis remains a significantly underrecognized and underreported disease worldwide. Clinical manifestations of melioidosis vary widely, from acute sepsis and pneumonia to chronic infection, with case fatality rates ranging from 10 to 50%. Most melioidosis cases occur in South Asia and Northern Thailand, being a hotspot or hyperendemic region where B. pseudomallei is one of the leading bacterial pathogens in community-acquired sepsis.

Northern Australia is another hyperendemic region where B. pseudomallei is thought to have initially evolved from before spreading to South Asia during the last ice age. Most of what we know about melioidosis in terms of risk factors, clinical management, and treatment, which we will present on this call, comes from studies from the Menzies School of Health Research in the hyperendemic Northern Territory of Australia. Next slide, please.

Melioidosis is considered an emerging infectious disease in the Americas, which is the most dynamic region for evolving melioidosis epidemiology. In this region, most cases have occurred in Brazil, with an increasing number of cases being identified in Puerto Rico and US Virgin Islands. Environmental suitability modeling studies have shown that B. pseudomallei has been expanding northwards over recent decades.

Before the discovery in Mississippi this summer, the closest region to the continental US where B. pseudomaliae has been detected in the environment was in the Mexican state of Sonora, which borders southern Arizona. Next slide.

B. pseudomallei can infect both animals and humans through direct contact with non-intact skin, such as cuts or open wounds or mucus membranes, through inhalation, usually of contaminated soil dust, or through ingestion, usually through swallowing contaminated water. Contact between damaged skin and contaminated soil or water is the most frequent route of natural infection. Person-to-person transmission is extremely rare and has only been documented twice. For the majority of cases, symptoms occur one to 21 days from exposure, with a median of four days.

But with a high inoculum, symptoms can develop in just a few hours from exposure. In about 5% of cases, symptoms can develop well past this 21-day window, months to years after exposure, and are classified as latent activated infections. In the US, we have seen melioidosis in Vietnam veterans who were exposed to B. pseudomaliae in the environment during the war in Vietnam and developed melioidosis many decades later. Next slide.

In the US, the Federal Select Agent Program designates B. pseudomaliae as a Tier 1 Select Agent for its bioterrorism potential, as it can be easily aerosolized, leading to large-scale exposures, it has a low infectious dose, and it is still associated with high mortality even with appropriate treatment. Next slide.

If B. pseudomaliae is identified or suspected from a clinical specimen, confirmatory testing should be performed at a state laboratory response network, or LRN laboratory. The laboratory response network comprises of at least one reference lab in each state that can quickly test for and confirm B. pseudomallei.

Because B. pseudomallei is a Tier 1 Select Agent, it falls under Select Agent regulations for reporting, and we at Bacterial Special Pathogens Branch at CDC are notified of any identification of B. pseudomallei at the state LRN lab. The Zoonoses Select Agent Lab at CDC can confirm and identify B. pseudomallei. They can also perform serological testing and perform whole-genome sequencing. We strongly encourage state health departments and LRNs to forward isolates to CDC's Zoonoses Select Agent Lab for whole-genome sequencing. This is an essential process for us at CDC to be able to detect potential outbreaks of melioidosis and learn about its evolving epidemiology. Next slide.

There is, on average, about 12 melioidosis cases reported to CDC each year, most of which are associated with travel to melioidosis endemic regions. Reported cases have increased over the past few decades, with the sharpest increase occurring over the past five years. We are noticing an increasing number also of non-travel associated cases, shown here in orange. Between 2017 and 2021, there has been seven melioidosis cases with no travel history to a known melioidosis endemic region. Next slide.

In 2018, a Texas resident of Atacosa County, which is about 100 miles from the Gulf Coast, acquired melioidosis despite not traveling outside of the US in 30 years. The infecting strain was of Western Hemisphere origin. Despite extensive environmental sampling, no samples tested positive. Genomic analysis from a patient who lived in the same Texas county who was diagnosed with melioidosis 14 years earlier revealed that the infecting strain was also of Western Hemisphere origin, and so the leading hypothesis remains that these two patients most likely acquired melioidosis locally from the environment. Next slide.

In 2019, a Maryland patient who had never traveled outside of the US was diagnosed with melioidosis, and the strain that infected this patient was a genetic match to the patient's freshwater home aquarium, which she had cleaned regularly. The aquarium housed a fish imported from South Asia. Next slide.

More recently, in October of 2021, the source of a multi-state outbreak of melioidosis that involved four patients in Georgia, Kansas, Minnesota, and Texas was identified as a Better Homes and Gardens branded aromatherapy room spray, imported from India, and sold nationwide by Walmart. Two patients died, and two were left with neurological deficits as a result. CDC worked with the Consumer Product Safety Commission, or CPSC, and Walmart to issue a product recall of over 4,000 bottles sold to residents across 43 jurisdictions. Next slide.

This brings us back to the most recent investigation mentioned at the very beginning of the call. In May of this year, CDC was notified by the Mississippi Public Health Laboratory of a B. pseudomallei positive blood culture from a male Mississippi patient. Sequencing revealed that the strain was identical to the strain that infected a melioidosis patient two years prior in July of 2020, and grouped closest to other isolates from the Americas. Next slide.

CDC worked with the Mississippi State Department of Health and learned that the two patients lived just 10 miles apart in the same county in the Gulf Coast of Mississippi. Neither patient reported travel to a region endemic for melioidosis. In late June, we collected 100 soil and water samples from both patients' properties and the surrounding area. Three of the samples, which were collected on a 2020 case patient's property, tested positive for B. pseudomallei, and the strain was identical to the infecting strain of the two patients upon genomic sequencing.

This finding indicated that the local environment was a likely source of infection for these patients. And again, this is the first time the bacteria has been isolated from the soil in the continental U. S. and is now considered to be at least locally endemic in the region of the Gulf Coast, Mississippi. Both of these patients were hospitalized with sepsis due to pneumonia but recovered from melioidosis following antimicrobial therapy. Next slide.

It is unclear how long the bacterium has been in the environment prior to this case in 2020 or how widespread the bacterium is in the continental US. But modeling studies suggest that the environmental conditions found in the Gulf Coast states, that is, Texas, Louisiana, Mississippi, Alabama, and Florida, are conducive to the growth of B. pseudomallei. These predictive models do need some updating, and we are currently working with partners to update the models using new data points from the Mississippi investigation. Next slide.

Most people who come into contact with B. pseudomallei do mount an immune response against the bacteria and never develop melioidosis. Certain underlying health conditions increase one's risk to develop disease, with diabetes being the most common risk factor for melioidosis. Other risk factors are listed here and include excessive alcohol use and other chronic conditions, including immune system suppressing conditions. A prospective study in Australia did show that 84% of all patients with melioidosis had a clinical risk factor, shown here.

All the adult patients over the past five years with domestically acquired melioidosis in the US had at least one of these risk factors, shown on this slide. The two children in the aromatherapy-associated outbreak did not have any known risk factors. There is still a lot of unknowns around risk factors for latent reactivated melioidosis, that is, cases that present months to years after exposure. But it is worth noting that infection with SARS-CoV-2 or other viruses, such as influenza, may play a role in activating melioidosis from latency or accelerate clinical disease. The five-year-old child who died from melioidosis in the aromatherapy outbreak in Georgia was co-infected with SARS-CoV-2 and was only diagnosed with melioidosis on autopsy by an astute medical examiner. Next slide.

Other risk factors that are important to consider when taking a patient's history include travel to an endemic area in the past 30 days, participating in recent occupational or recreational activities that involve contact with soil or water, like gardening or construction. Severe weather events have also been associated with an increase of cases in endemic regions. Heavy rain can bring the bacteria from deeper layers in the soil to the surface, making it more likely for people to come into contact with it. And sometimes, with heavy rains and heavy winds, it can also aerosolize the bacteria in dust, leading to inhalational exposures. And I will now pass it on to Dr. Caroline Schrodt to present the clinical presentations for melioidosis. Next slide.

Thank you, Julia, I'll be discussing the clinical presentation of melioidosis. Next slide, please.

Melioidosis has a wide spectrum of clinical presentations ranging from a localized skin infection to a pneumonia, which is the most common presentation in adults, bacteremia or sepsis, or infection involving any organ of the body. Clinical diagnosis can be challenging, as symptoms are sometimes nonspecific. Melioidosis is often mistaken as tuberculosis and has been dubbed as the great mimicker. Next slide.

Data from a prospective 30-year study at Royal Darwin Hospital in Australia indicated that the vast majority of patients exposed never develop clinically apparent disease. In regions where melioidosis is highly endemic, such as Thailand and Northern Australia, most healthy people who come into contact with B. pseudomallei never develop melioidosis. For the majority of cases with symptoms, the illness occurs one to 21 days after exposure with an average of seven days. With a high inoculum, symptoms can develop in as little as a few hours. About 9% of people with melioidosis present with chronic infection, defined as symptoms lasting longer than two months. In about 3% of cases, symptoms can develop from latent infections well beyond this 21-day window, months or even years later. Next slide, please.

There is a lot of detail in this slide, but for now, I want to emphasize that because the causative bacteria B. pseudomallei can infect any organ, patients with melioidosis can have many different clinical manifestations of disease. Next slide.

Signs and symptoms of melioidosis can be nonspecific or they may be specific to the site of infection. Symptoms may include fever, fatigue or lethargy, headache, chest pain, abdominal pain, myalgias, weight loss, or anorexia. Melioidosis can involve any organ system or systems and can present as pneumonia, bacteremia or sepsis, skin ulceration or abscess, genitourinary infection, septic arthritis, central nervous system disease, or osteomyelitis. Abscesses can be cutaneous or internal and may be single or in numerous body locations. Next slide, please.

During 1989 to 2019, the Darwin Prospective Melioidosis Study by Bart Currie and colleagues documented all cases of melioidosis in the tropical top end of the Northern Territory of Australia. In total, they described 1,148 patients with culture-confirmed melioidosis of whom 12% died. The median age was 50, 4% of the patients were children less than 15 years old, and 50% were patients older than 50 years old. 63% were male, 52% were indigenous Australians, and all but 16% had clinical risk factors. Of those with risk factors, 45% had diabetes and 40% reported alcohol abuse. 80% of infections occurred during the wet season. Next slide, please.

As I mentioned previously, pneumonia is the most common presentation in adults globally. In the Darwin Prospective Melioidosis Study, 52% of patients presented with pneumonia as the primary diagnosis, and of patients with non-pulmonary primary presentations, 19% went on to develop secondary pneumonia. Pulmonary involvement might include pneumonia, pulmonary abscesses, effusion, or pleuritis, as shown by some of the photos on this slide. As I mentioned earlier, melioidosis is oftentimes confused for pulmonary tuberculosis. Next slide.

Cutaneous melioidosis is also a common form of presentation. In the Darwin Prospective Melioidosis Study, 13% of patients had primary skin melioidosis and were more likely than those without primary skin melioidosis to have chronic presentations greater than two months.

Children were more likely than adults to present with skin infections, which may present with non-healing ulcerations with scabs or cutaneous abscesses. Next slide, please.

Melioidosis can also present with genitourinary infection, which is how 12% of patients presented in the Darwin Prospective Melioidosis Study. Of these, 74% were males with prostate abscesses. Those with genitourinary infection may have dysuria, pyuria, or hematuria. Next slide, please.

Bacteremia, with no evident focus, was present in 11% of patients in the Darwin Study. Next slide.

Soft tissue abscess was present in 4% of patients. Abscesses can be found in any organ of the body, such as, but not limited to, the spleen, liver, adrenal glands, prostate, or the brain. Next slide.

Neurological disease was present in 2% of patients, of whom 11 had meningoencephalitis, four had cerebral abscesses, two had myelitis, one had meningitis, and one had an epidural abscess. Next slide, please.

Osteomyelitis was present in 1% of patients, and septic arthritis was present in 3% of patients. Next slide, please.

Now for a quick self-knowledge check.

Which of the following is the most common primary presentation of melioidosis? Cutaneous lesions, abscesses, genitourinary infections, pneumonia, or all of the above? Next slide, please.

The most common primary presentation of melioidosis is pneumonia. Over half of patients with melioidosis present with primary pneumonia, and as I've said a couple times, it is often mistaken for pulmonary tuberculosis. This concludes the clinical presentation section, and I'll now turn it back over to Julia Petrus.

Thank you, Dr. Schrodt. Next slide, please.

I will now review the diagnostic considerations for melioidosis. Next slide.

In terms of imaging, a chest x-ray should be performed on all patients with suspected melioidosis. CT scans may be performed on adult patients with confirmed or a suspected melioidosis to detect the presence of abscesses. Abdominal ultrasound may be used as an alternative for pregnant women and children. In patients with CNS involvement, MRI is preferred over CT scans, as it may indicate areas of hyper-intense infection, including microabscesses, leptomeningeal enhancement, or trigeminal nerve involvement. Next slide.

In terms of specimen collection, anyone for whom melioidosis is suspected should have blood, sputum, and urine cultures collected. However, clinicians should also collect specimens for culture guided by clinical syndrome from all relevant sites of infection. Culture of B. pseudomallei from any clinical specimen is considered diagnostic for melioidosis. Depending on the sites of suspected infection, recommended specimens for collection might also include pus from the skin or internal abscesses, and any of these other examples listed here on the slide. Consider sending paired sera collected two weeks apart in consultation with us at CDC.

Although, the gold standard, again, for diagnosis, is culture. And a quick note, during the investigation involving the aromatherapy spray outbreak, one of the patients presented with neurological melioidosis, the patient in Texas, they did take CSF samples. Nothing ever grew, and eventually it was actually lower respiratory cultures and blood cultures that grew burkholderia. I mentioned this just to, you know, have that in your mind that they might actually have neurological melioidosis, but you might not detect it with CSF alone. Next slide.

In terms of diagnostics for B. pseudomallei, again, culture of B. pseudomallei from any clinical specimen is considered diagnostic and is the gold standard. Often, initial cultures may be negative, so serial cultures and a variety of cultures from different sites should be collected from patients in whom there's a strong suspicion for infection with B. pseudomallei. When B. pseudomaliae bacterial counts in blood are high, blood culture bottles will typically turn positive within 48 hours. Next slide.

B. pseudomallei can grow on most routine laboratory media and can be isolated from sterile sites using standard techniques. When working with non-sterile specimens, selective media can greatly enhance the growth of B. pseudomallei by reducing the growth of other competing organisms. Selective media is considered highly cost-effective and efficient with a reported 29 cases diagnosed in one year in Southeast Asia that would never have been found without it.

In endemic areas, the most commonly used selective media is called Ashdown's agar, which you can see in the image on the top right corner of this slide. Unfortunately, this is not yet commercially available here in the US and is produced mostly in-house by diagnostic laboratories. CDC has evaluated other commercially available options and found that PC agar shown on the bottom here can be used with similar success with regards to sensitivity and selectivity. Next slide.

Once cultures have been obtained, diagnostic laboratories often use automated identification systems or 16S sequencing to aid in identification. Algorithms that use the MALDI-TOF technology, like the Bruker biotyper or others, using rapid microbial identification or antibiotic susceptibility testing, such as the VITEC2, often misidentify B. pseudomallei. We often see misidentifications for B. tylindensis and B. cepacia. In the case of a Texas patient associated with the aromatherapy outbreak, B. pseudomallei was initially misidentified as B. tylindensis on a MALDI-TOF. Other examples of common bacterial misidentifications are listed here on the slide.

Misidentification can occur because the panels made for the systems are small and not diverse enough to account for B. pseudomallei. In the case of the Bruker biotyper, all B. pseudomallei are identified as B. tylindensis because most lack the addition of a select agent panel software. If you have high clinical suspicion, we ask that you follow up with your local and state public health department and forward isolates presumptively identified as any of these listed species for advanced diagnostics at your closest reference lab or laboratory response network laboratory. Next slide.

A quick note on presumptive diagnostics. Again, culture is gold standard for diagnosing melioidosis, but serology can be obtained using an indirect hemagglutination assay, which is a test done only here at CDC. However, serology is generally only meaningful if paired specimens are taken two weeks apart. We are looking for a four-fold rise between the two titers, which can indicate acute infection. Unlike many

other pathogens, PCR for B. pseudomallei is generally not successful on clinical specimens. While these can be performed, we recommend consultation with us at CDC, and we want to emphasize that the gold standard for diagnosis is culture of clinical specimens. Next slide.

Okay, so now it's time for a self-knowledge check.

The question is, which of the following is B. pseudomallei commonly misidentified on an automated system?

A, B. cepacia. B, B. thailandensis C, E. coli. D, both A and B. Next slide.

And the answer is both A and B. That is B. cepacia and B. thailandensis are most commonly misidentified when using automated systems, as explained earlier. And now, next slide.

We are passing it on back to Dr. Schrodt to review treatment for amyloidosis. Thank you.

Thank you, Julia. Next slide, please.

Regarding treatment, it is important to know that many antibiotic treatment regimens are not sufficient, as B. pseudomallei is intrinsically resistant to penicillin, ampicillin, first- and second-generation cephalosporins, and aminoglycosides. It is susceptible to beta-lactams, carbapenems, trimethoprim, sulfamethoxazole, and doxycycline, although it should be noted that resistance during therapy has emerged with all antibiotics. As such, consultation with infectious disease specialists is strongly recommended. Next slide.

To treat melioidosis, long-term antibiotic therapy is required as there is a high rate of treatment failure or relapse with shorter courses. Long-term antibiotic therapy consists of two phases, the acute phase and the eradication phase. The acute phase is generally characterized by treatment with intravenous or IV antibiotics, and the eradication phase is generally characterized by treatment with oral antibiotics. However, there are some exceptions to this, and there is also a one-week period of overlap. Next slide.

As mentioned, the acute phase of treatment always involves IV antibiotics. Melioidosis should be treated with IV antibiotics for at least two weeks. Depending on the response to therapy, IV treatment may be extended for up to eight weeks, such as for patients with critical illness, extensive pulmonary disease, deep organ abscesses, osteomyelitis, or central nervous system involvement. Ceftazidime is preferred unless the patient is critically ill, in which case meropenem or imipenem should be used. Patients with central nervous system involvement require higher antibiotic doses. Next slide, please.

The acute phase sometimes also involves oral antibiotics. Patients with non-pulmonary sites of infection should receive oral trimethoprim sulfamethoxazole concurrent to IV therapy during the acute phase. Next slide.

And in patients not receiving concurrent oral antibiotic therapy during the acute phase, the eradication phase oral therapy should begin at the final week of the acute phase of therapy, but the timing for the eradication therapy should not start until after IV therapy ends. Next slide.

Intravenous treatment is followed by treatment with oral trimethoprim sulfamethoxazole or amoxicillin clavulanic acid for three to six months to prevent relapse. Next slide.

A few other comments about treatment. Patients with abscesses should have them drained, especially for prostate abscesses. People with exposures, such as in a laboratory setting, should have symptom monitoring and may need serology or post-exposure prophylaxis with trimethoprim sulfamethoxazole or amoxicillin clavulanic acid for 21 days. Our team at CDC is happy to provide consultation in the event of a laboratory exposure. Next slide, please.

For a quick self-knowledge check, which of the following should be taken into consideration during treatment of melioidosis? Severity of illness, organ systems involved, resistance to antibiotics, duration of treatment, or all of the above. Next slide.

All of these, including severity of illness, involvement of certain organ systems, resistance to antibiotics, and duration of treatment are all important considerations during treatment of melioidosis. This concludes my portion of the presentation, and I'll now turn it back over to Julia Petrus.

Thank you, Dr. Schrodt. I will continue the presentation, next slide,

to discuss prevention and key messaging really targeted towards your patient. Next slide.

So here is a summary of the key messages for patients at risk for melioidosis. And what I mean by at risk is patients who have clinical risk factors, such as diabetes, for example, who travel to or live in an area that is known to be endemic for melioidosis, which now includes the Gulf Coast of Mississippi, or areas that are potentially endemic. And now this would include Gulf Coast states in the southern US.

Key messages for these at-risk patients would include protecting skin contact with soil or muddy water. That means protecting open wounds, cuts or burns from coming into contact with soil by using waterproof bandages, and washing wounds thoroughly if they are in contact with soil or water that might be contaminated. Also wearing footwear and gloves when gardening or doing any kind of construction or working outdoors. Number two would be avoid walking through flood water and working with soil during or following a severe weather event. Wearing again protective equipment like boots would be recommended if you have to wade or walk through flooded water.

And the third point, drink safe water. So, if you live in an endemic area and you're at high risk, avoid drinking water directly from fresh water sources like lakes, rivers, ponds, streams. And I think that's a key point and, you know, as we learn more about the epidemiology of melioidosis in the US, we will be expected to update these messages, of course, as we learn more about unique risk factors in epidemiology here. Next slide.

This is an important key message for patients diagnosed with melioidosis. As Dr. Schrodt mentioned, you know, melioidosis is treated with antibiotics but can come back if the full course of antibiotics is not completed entirely. So, this is a really crucial point for patient education for them to complete the full course that is, you know, the three to six months of oral antibiotics. Next slide.

And now we will conclude the presentation with a section really outlining what we are doing at CDC to learn more about melioidosis in the US. Next slide.

So, we will continue to monitor and survey cases of melioidosis through our surveillance channels that I briefly touched on in the beginning of the call. So that is the Laboratory Response Network who is, you know, sending us isolates. That is through the CDC's nationally notifiable disease surveillance system. Just recently, melioidosis has been added to the nationally notifiable disease list. This will allow us to better understand in better time the epidemiology or the risk factors and exposure history for patients with melioidosis so that we can better respond to potential outbreaks.

And we are getting this information reported from state health departments. And then, of course, we will continue to sequence any culture-confirmed melioidosis or B. pseudomallei isolate that comes our way. And we have an amazing laboratory team that is equipped to continue that surveillance and better understand the evolving epidemiology on the genomic side of things. Next slide.

So, this year has been quite busy for us in regards to melioidosis, and we have some further research questions and study needs that we are actively thinking about and discussing with partners. So, the first one really is, you know, how widespread is B. pseudomallei in the continental United States? So, this would require a robust environmental sampling study, which we would like to do in the Gulf Coast states in the U.S. Another interest is to look and try to estimate seroprevalence. So, this would be accomplished by doing a sero survey, again, in the Gulf Coast region and compare it to a non-endemic region in the US. Thirdly, a retrospective chart review of hospitalized patients in the Gulf Coast of Mississippi between 2020, when that first case was identified, and 2022, so that we can get a better understanding of if there were potentially missed cases.

And then the second main question is, you know, what are the risk factors for domestically acquired melioidosis in the US.? So, this would be accomplished through an active surveillance study in the Gulf Coast states. You know, we have a lot of data from Australia, from Thailand, on risk factors for melioidosis, but we do know that there is regional variation, and we want to understand as we learn more about the local epidemiology of melioidosis here in the U. S. Next slide.

So, in summary, we would like you to walk away with five main messages from this call today. So, one is consider melioidosis in patients with compatible illness who reside in or have traveled to the Gulf Coast region of the southern US, or areas where B. pseudomallei has historically been endemic. The second one is, given the risk of melioidosis associated with exposure to imported products, consider melioidosis in patients with compatible illness, even if they do not have a history of travel to melioidosis endemic areas. The third, report melioidosis cases to your local or state health department. Reporting does vary state by state. Contact your state health department if you have any questions or suspect a patient may be infected with B. pseudomallei They can facilitate forwarding cultures to the closest reference lab in the state for confirmation of B. pseudomallei .Fourth, keep trying to culture if you have a high clinical suspicion for disease. And then the fifth is when in doubt, you can always call us at CDC at the Bacterial Special Pathogens Branch where we can take clinical inquiries. Next slide.

Next slide.

I just wanted to point you to some important resources. These links are going to reference you back to the health alerts that we discussed on the call, to our main webpage where you can find a lot of general information on melioidosis. The paper is referenced here in different health alerts and the recall notice around the aromatherapy spray outbreak that I discussed earlier. And the study that we referenced quite a bit in Northern Territory Australia is referenced here at the bottom of this slide. Next slide.

And again, for technical clinical questions related to melioidosis, please do not hesitate to reach out to us at the Bacterial Special Pathogens Branch. That is our email. We have a phone number. And if it's an emergency or you don't know exactly who to contact, you can always contact the EOC and that is the phone number listed. If you're a health department and you need direction in terms of how to send specimens to us, please reach out. And these are links regarding diagnostic testing that is done at our lab at CDC and the case definition for public health surveillance that is new, updated, is listed here below. Next slide.

So, this concludes our portion of the COCA Call, but I wanted to acknowledge our team at the Bacterial Special Pathogens Branch who is working very, very hard all the time on different pathogens, including this one, melioidosis. So thank you, Mindy Elrod, who is microbiologist in the lab. Dr. Jay Gee, who performs a lot of the sequencing. Dr. Zach Weiner, Dr. Maria Negron, Willie Bauer, Dr. Alex Hoffmaster, our branch chief. And thank you to our Mississippi State Department of Health colleagues who were integral in that investigation in July. And thank you to our colleague, Dr. Bart Currie, at the Menzies School of Health Research for all of the continued support. Thank you very much. And I will pass it over to our moderator for the Q&A. Next slide.

Presenters, thank you for providing this timely information to our audience. We will now go into our Q&A session. For our audience, please remember to ask a question using Zoom, click the Q&A button at the bottom of your screen, then type your question. Please note we receive many more questions than we can answer during our webinars. Joining us for the Q&A session in addition to our presenters are Captain William Bauer, Miss Mindy Elrod, and Dr. Jay Gee, all of whom work in the Bacterial Special Pathogens Branch within CDC's National Center for Emerging and Zoonotic Infectious Diseases.

So, for our first question, and we seem to have gotten quite a few of these, is can you talk about any documented cases of transmission from animal to human, as well as if there's any veterinary guidance you have for animal cases in general?

Thank you for the question. I may defer to Dr. Jay Gee, but to my knowledge, animal to human, it very, very rarely has been documented. Just to clarify, the case that we discussed regarding the fish aquarium, we can't technically say that is a zoonotic transmission. The bacteria was detected in the water of the fish tank. But it's certainly an area we are interested in looking at, and I defer to my colleagues to add in on anything.

Yes, this is Jay Gee. So, if you look at the Q&A chat box, I made a reply to someone else about animal to human transmission. So, the reports in the literature are very rare. And when I read those, my opinion is sometimes you cannot rule out that the human also got it from the environment and not necessarily from the animal they were handling. But with that being said, in the chat box, I did put a

couple of references down where that was reported. So, for now, it's considered very rare for humans to get melioidosis from contact with animals, although it's certainly possible. Over.

Thank you both. Our next question is about antibiotic therapy. What is the best way to decide what a full course of antibiotic therapy should be?

I can take that one. This is Caroline Schrodt. And so, I think in determining how long the eradication therapy should be, it may depend on the severity of disease and how extensive the involvement of disease was. And if you do find yourself in the situation of treating a patient with disease, I would again emphasize that our epidemiology team is more than happy to consult on these cases and can help provide kind of personal, case-by-case recommendations. Thank you.

Thank you very much. Our next question is along similar lines, and the question asks, can you please discuss alternate options for antibiotics if the patient has a sulfa allergy?

Of course. This is also Caroline Schrodt. So, in the event of a sulfa allergy, alternative agents include doxycycline, which can be used, although it does appear to be less effective than using trimethoprim, sulfamethoxazole. Another alternative agent, such as during oral eradication therapy, is amoxicillin clavulanic acid.

Thank you for that. And we have seen a few of these questions about the clinical manifestation, and I think they can be summed up in sort of the following sentiment. Can you explain the difference in clinical manifestation as well as morbidity or mortality depending on the three routes of transmission that you discussed?

I didn't know if Julia or one of my other colleagues wanted to take that one, but it's my understanding that the route of infection can certainly play a part in the clinical manifestations that we see.

Yeah.

Oh, I'll let you go ahead.

Oh, no. Thank you, Dr. Schrodt. I'll just add, no, that is true, though it's not like you're only going to see this one clinical presentation, you know, based on this one type of exposure. So, I don't want to misguide anybody. But for example, the aromatherapy outbreak, that was an aerosolized spray that people were spraying in their houses and potentially breathing in. We saw a range of clinical presentations in those four patients. So, we saw pneumonia, sepsis, neurological presentation. We saw joint septic arthritis in one patient. So that just gives you an idea of, you know, yes, there were some clues for us to look more into like an inhalation route, but it can still present in a wide, you know, wide way, if that makes sense.

Thank you for that. As a follow-up to that, with so many organ systems being involved and such a wide range of symptoms, for providers, what are some common conditions that are important to rule out when considering this?

Yeah, so I think in this situation, you would want to rule out some of the most, you know, common bacterial organisms. So if somebody has an abscess, for example, you can send pus or exudative fluid for culture. And if there are no organisms identified, or if the specimens are identified as some of the other bacterial species that Julia discussed during the presentation, that could be a potential tip-off that maybe there's something else going on. So again, I wanted to emphasize the importance of sending lots of different specimens from different body sites for culture, and then even if they're negative, continue sending additional specimens for culture.

Thank you very much. You had mentioned in your presentation about misidentification. Our question asks, can you elaborate a little bit if it is frequent, and do you recommend contacting CDC to coordinate confirmatory testing or reaching out to local or state health department?

Hi, this is Mindy Elrod, and I can take this question. The misidentification issue is an issue. I would say a large majority of cases that we work with do start off with initial misidentifications as other organisms. So the VITEC2 and the MALDI-TOF systems often will misidentify them.

And sorry, the second part of the question again?

The second -- yes, I'm happy to repeat it. The second part of the question asks, do you recommend contacting CDC to coordinate confirmatory testing or reaching out to local or state health department?

We suggest you start with your local and state health department first. That's going to be your first resource. And then they can help coordinate with us if they need help and further questions to help you out.

Thank you very much. Our next question is regarding the list of the Tier 1 Select Agents that you had shared earlier. The question asks, what is the difference between B. pseudomallei and B. mallei?

This is Jay Gee. So B. mallei is a closer related bacteria that causes another disease called glanders, and that is associated with equids such as horses and donkeys. And B. mallei was documented to have been used as a biological warfare agent during World War I. And B. pseudomallei has also been the subject of research for biological warfare. So they are both on the Tier 1 Select Agent list. Over.

Thank you for that. Another question that we've seen a few iterations of essentially asks, will storms in the Gulf Coast area potentially increase cases of melioidosis due to exposure to floodwaters?

Hey, this is Willie Bauer. I'll jump in and take that one. So actually, the answer is, we don't know. But one could speculate that we would see the same thing in the Gulf Coast as they do see in Australia, where severe storms do increase the number of cases that they see. And with climate change and more severe storms hitting the Gulf Coast, it is certainly a possibility. But that is something that we will be looking into, as was mentioned in this talk. That's some of our future research to really increase surveillance for this organism, especially in the Gulf Coast region, to see if we can answer these questions. Over.

Thank you very much. And we have time for one last question. And the question asks, or perhaps asks for clarification, with the negative cultures, we are turning to broad-range PCR or cell-free DNA testing of blood or CSF. Can you give any guidance on this approach for sample collection and testing?

This is Mindy Elrod. I can try to answer this one. The reason why PCR on clinical specimens is not ideal is because it's just been shown that there's low sensitivity. In studies, they've looked at the quantities of bacteria in various specimens, and they're usually low or at the limit of detection for the PCR assays that are available. So that's one of the reasons that culture is just really the preferred method.

Thank you very much for that. We appreciate it. I want to thank everyone for joining us today, with a special thanks to our presenters and our subject matter experts during the Q&A. We want to thank you for sharing your time and expertise with us today. Next slide.

All continuing education for COCA Calls is issued online through the CDC Training and Continuing Education Online System at tceols.cdc.gov. Those who participate in today's live COCA Call and wish to receive continuing education, please complete the online evaluation and post-test before November 14th, 2022 with the course code WC4520-101322. The access code is COCA101322.

Those who will participate in the on-demand activity and wish to receive continuing education should complete the online evaluation and post-test between November 15th, 2022 and November 15th, 2024, and use course code WD4520-101322. Again, that access code is COCA101322. Continuing education certificates can be printed immediately upon completing your online evaluation.

A cumulative transcript of all CDC ATSDR continuing education obtained through the CDC Training and Continuing Education Online System are maintained for each user.

Today's COCA Call will be available to view on-demand a few hours after the live call at emergency.cdc.gov/COCA. A transcript and closed caption video will be available on-demand on COCA Call's webpage later this week.

Continue to visit emergency.cdc.gov/COCA to get more details about upcoming COCA Calls. We invite you to subscribe to receive announcements for future COCA Calls by visiting emergency.cdc.gov/COCA/subscribe.asp. You will also receive other COCA products to help keep you informed about emerging and existing public health topics.

Stay connected with COCA by liking and following us on Facebook at facebook.com/CDC Clinician Outreach and Communication Activity.

Again, thank you for joining us for today's COCA Call and have a great day.