Good afternoon. I'm Nikki Grimsley and I'm representing the Clinician Outreach and Communication Activity, or 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; Review of Malaria Diagnosis and Treatment in the United States.

All participants joining us today are in listen only mode. Continuing education is not offered for this webinar.

After the presentation there will be a Q and A session. You may submit questions at any time during today's presentation. To ask a question using Zoom, click the Q and A button at the bottom of your screen, then type your question in the Q and 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.

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I would now like to welcome our presenters for today's COCA Call. We are pleased to have with us Dr. Alison Ridpath, who is a captain in the U.S. Public Health Service and the Medical Countermeasures Team Lead for the 2023 Malaria Response at the Centers for Disease Control and Prevention. Dr. Erika Wallender, who is a lieutenant commander in the U.S. Public Health Service and an epidemic intelligence service officer. Dr. Wallender is working on the Medical Countermeasures Team for CDC's 2023 Malaria Response. And Dr. Adam Rowh, who is a lieutenant commander in the U.S. Public Health Service and an epidemic intelligence service officer. Dr. Rowh is working on the Medical Countermeasures Team for CDC's 2023 Malaria Response.

I'll now turn it over to Dr. Ridpath. Dr. Ridpath, please proceed.

Thank you, today we will review malaria diagnosis and treatment in the United States. Next slide.

Over the course of the Call, we will provide an update on the locally acquired mosquito transmitted malaria events in Florida and Texas, and share the epidemiology of imported malaria in the U.S., review malaria diagnoses and provide an overview of malaria treatment, briefly touch on malaria prevention, particularly among travelers, and share CDC resources to support malaria diagnosis and treatment. Next slide.

The main learning objectives of this activity are listed here. By the end of this call we would like all of you to be able to describe when to suspect malaria, define preferred methods for malaria diagnosis, identify an optimal treatment regimen for an individual patient infected with malaria using available clinical and laboratory information, and to identify strategies to prevent mosquito transmitted malaria in the United States. Next slide, please.

We'll start by providing an update on locally acquired malaria cases in the U.S. Between May and July of 2023, two U. S. counties reported locally acquired mosquito transmitted malaria due to Plasmodium vivax. Seven cases have been identified in a focal area of Sarasota County, Florida, and one case in Cameron County, Texas.

The locations of these counties are shown in red on the map to the right. None of the cases reported recent international travel. At this time there is no evidence to suggest that the events in Florida and those in Texas are related to one another. All eight individuals with locally acquired vivax malaria are adults and the clinical presentation for all have included fever. Eighty-eight percent were hospitalized. To date, all eight individuals have received oral anti-malarial treatment, including medications to prevent relapse disease, which we'll review in more detail later, and all have recovered. Next slide.

Humans contract malaria from the bite of an infectious female Anopheles mosquito, which bites late evening and at night time. Thus, the public health response to halt local malaria transmission targets the mosquito vector in humans with the disease. In areas where individuals with malaria could have been bitten by Anopheles mosquitoes, Anopheles mosquitoes are tracked and tested to spray for the presence of malaria parasite.

To reduce the risk of infected mosquitoes causing additional malaria cases, insecticide is sprayed to suppress the populations of adult mosquitoes and to control larval habitats. Public health organizations will also conduct enhanced surveillance to identify and treat all malaria cases in areas with local transmission. With the current events, public health officials have notified health facilities and provided guidance for who to test for malaria. Finally, affected counties have disseminated messages around avoiding mosquito bites and identifying malaria symptoms. The poster on the right is an example from the Florida Department of Health. Next slide.

Although these are the first occurrences of U. S. acquired mosquito transmitted malaria in 20 years, at least 28 small outbreaks of malaria in eight states have occurred since 1980. Eighty-seven percent of these outbreaks were due to Plasmodium vivax. On this timeline, 23 of the most recent outbreaks are shown, with a state, year, and number of locally acquired cases listed in red, and represented by the size of the blue bubble. Next slide.

To start a chain of local transmission in the U.S., an Anopheles mosquito must bite an infected person with circulating gametocytes, a form of the parasite which is infectious to mosquitoes. The mosquito must then survive long enough to allow the parasite to replicate and be transmitted to the salivary gland, which takes about a week.

Next, the mosquito must bite a susceptible individual. In the U.S., we have a wide distribution of malaria transmitted competent Anopheles mosquitoes, including the species pictured here.

Most states and U. S. territories have naturally-occurring Anopheles mosquito populations. While 99 percent of malaria cases reported in the U.S. were acquired from mosquitoes in malaria endemic countries, meaning countries with ongoing malaria transmission, rarely malaria can be transmitted congenitally by contaminated blood products or infected bone marrow or organ

transplants, or by blood exposures related to needle stick injuries and unsafe needle sharing. Next slide.

With widespread distribution of the vector, we now consider opportunities for a mosquito to bite an infected individual. This slide shows the distribution of malaria cases diagnosed in the U.S. during 2018. The darker states on this map show jurisdictions with higher numbers of malaria cases reported. Most years, every state reports at least one person diagnosed with malaria and about 75 percent of the malaria cases are diagnosed in 14 jurisdictions. Each case that occurs in an area with competent vectors could theoretically start onward transmission. Next slide.

Since the 1970s, the number of imported malaria infections reported in the U. S. have increased steadily, predominantly due to increases in U. S. residents traveling to malaria endemic countries.

In our most recent complete data from 2018, almost 2,000 malaria infections were reported. That would be more than five cases on average diagnosed per day in the U.S.; however, most of these infections occur during the summer months due to increased international travel. Importantly, malaria is a potentially serious illness and there were between six and seven malaria attributed deaths in the U.S. each year from 2018 to [inaudible], of the malaria cases dipped early in the COVID-19 pandemic, because of reduced travel, our preliminary data show that the number of malaria infections has rebounded in 2022 to reach pre-pandemic levels. Next slide.

Here's a quick self-knowledge check. Which of the following is true regarding the identification of locally acquired mosquito transmitted malaria in Florida and Texas?

A, this is unusual because the vector responsible for transmitting malaria was thought not to exist in the U.S., B, this is unusual because no cases of malaria are diagnosed in the U.S. , C, this is unusual because it's the first time locally acquired mosquito transmitted malaria has been documented in the U.S., or D, none of the above. The correct answer is D, none of the above. Although this has not happened in 20 years, there have been several documented incidences of locally acquired mosquito transmitted malaria in the U. S. Approximately 2,000 people are diagnosed with malaria every year in the United States, and mosquito vectors capable of transmitting the disease are widely present.

We'll now move on to diagnosis and treatment of malaria, and Dr. Adam Rowh will present this portion.

This is an overview of the algorithm for diagnosis and initial management of malaria. We'll go through each part of the algorithm and explore it in greater detail. Next slide, please.

Next slide, please.

We'll start with when to suspect malaria. Next slide, please.

Over 99 percent of malaria cases in the U.S. are among individuals who reported to travel to a malaria endemic region within one year of their presentation. Most patients with malaria had

traveled to visit friends and family members, but infections occur among individuals who visit malaria endemic areas for any reason.

The map shown here illustrates where in the world malaria is endemic, with darker shades of red indicating a higher malaria burden. Consider the diagnosis of malaria in any person with a fever of unclear etiology, regardless of international travel history. Particularly if they've been to the areas with recently, recent locally acquired malaria. Local transmission in the United States is rare and when it has occurred, it's been in a very geographically limited area. Next, please.

Although recent international travel to a malaria endemic country is typically required for U.S. residents to be considered at risk for malaria, some species have potential for relapse years after the initial exposure, if treatment is inadequate. To understand this, we'll go back to the biology of the parasite a bit to examine the various developmental stages and their impact on the incubation period. First, note that there are five different Plasmodium species that can cause malaria in humans.

Although all five of these share a similar life cycle, pictured on the right, there are species level differences that can impact timing of symptoms, disease severity, and the risk of recurrence or relapse after treatment. Next slide.

After an infected Anopheles mosquito injects parasites into a person, the parasites immediately travel to the liver within hours, where they undergo initial replication. This asymptomatic phase of replication in the liver lasts an average of one to two weeks for most Plasmodium parasites, but some can be longer. Host factors also play a role in determining the duration of the incubation period and a very long incubation periods have been observed, including malaria developing months to years after travel to an endemic country.

However, for infections diagnosed in the U. S., over 99 percent of individuals develop sometimes within a year of arrival and the vast majority within three months. Infections that occur after a year are more likely to be the relapsing species. Next slide, please.

After an initial liver phase, the parasites are released into the blood, causing blood stage disease. This is when people will first have malaria symptoms, which are most commonly fever, headache, and myalgias. As the parasites replicate in the blood and reach higher parasite densities, this can lead to more severe disease. Some parasites in the blood will develop into gametocytes, the form of the parasite which is able to infect mosquitoes and cause onward transmission. Next, please.

Malaria causes fever. And in non-severe or uncomplicated malaria, other symptoms can include headache, myalgias, nausea, vomiting, and other non-specific symptoms or physical exam findings. In non-severe illness, lab abnormalities such as mild anemia, [inaudible], or elevated liver function tests, including bilirubin can be observed. Next, please.

Without prompt treatment, an initially non-severe case of malaria can progress to severe malaria, which mimics other severe medical illnesses like bacterial sepsis. The pathophysiologic

mechanism involves adherence of infected red blood cells to the vascular endothelium, which leads to micro ischemia and capillary leak. Next, please.

Severe disease is usually caused by P. falciparum, which reaches the highest circulating parasite densities, but it is possible with any species. People who live in areas of continuous malaria transmission are exposed to the parasite in their blood frequently, and gradually develop partial immunity, which reduces the likelihood of severe disease by adulthood.

This immunity wanes quickly though, meaning the visitors to and former residents of high transmission areas are at high risk for severe disease, even if they have a known personal history of malaria infection. In malaria endemic countries, children are considered to be at a higher risk of severe disease than older individuals, at least in part due to relative immunological naivety. However, in the U.S., recent data suggests that severe disease was more common among older adults than other age groups.

Pregnant people are at risk of both severe disease and specific pregnancy related complications, including miscarriage, preterm birth, and low birth weight. Since all U. S. residents are considered non-immune and at high risk of severe disease, malaria is a medical emergency in the U.S. Next, please.

A patient in whom malaria is considered, requires diagnostic testing. Let's review the diagnostic approach. Patients being evaluated for suspected malaria should be cared for in a clinical setting where testing is available immediately. In the U.S., presumptive treatment of malaria, that is without a positive lab test, is not recommended. The only exception where a clinician consider starting treatment before the results of malaria diagnostic testing have returned is in a severely ill patient in whom the diagnosis is strongly suspected but timely confirmation is not possible. The most important components of the diagnostic approach are establishing the diagnosis, assessing the disease severity, and determining the species. These are the questions whose answers dictate initial management. Next, please.

Because of the risk of severe disease, same day results are needed for malaria diagnostic testing in the clinical setting. There are two laboratory tests for malaria used to guide clinical decision making; a blood smear, and the rapid diagnostic test, or RDT. Next, please.

Microscopic examination of a blood smear is the gold standard for malaria diagnosis. It's a sensitive test that can identify the species of Plasmodium as well as quantify parasite density, which is often reported as the percent of red blood cells that are infected or percent parasitemia. Two types of blood smears that are often performed in tandem to diagnose malaria are the thin and thick smear. On the thick smear, the RBCs are lysed, allowing visualization of parasites for many RBCs in a single microscopic field. On a thin smear, the RBCs are spread into a single cell layer, but are left intact, so it's easier to see parasite morphology, even though fewer cells are visible. The species may not be reported on the initial read, but a positive result is adequate to initiate treatment.

The RDT can be used to decrease the time to diagnosis and treatment but it is not a replacement for the blood smear, because it does not provide parasite density. The Center for Disease

Control's DPDX program offers laboratory services, including telediagnosis to aid with smear interpretation and species identification. Next, please.

There are other tests for malaria but these are not recommended for primary clinical malaria diagnosis. PCR is the most sensitive test and it can detect very low level parasitemia. It can also identify or confirm species. However, it's only performed in specialized labs, which can introduce unacceptable clinical and diagnostic delays. Serology detects antibodies to malaria parasites. Depending on which target is selected, these tests may remain positive for several years after treatment and they also have a lengthy turnaround time, thus serology also has no role in primary clinical malaria diagnosis. Next, please.

Interpreting the test results requires an understanding of the test's characteristics, in particular, remember that a single negative test is not sufficient to rule out the diagnosis. Consider repeating negative tests in the case of high clinical suspicion as false negative tests are more common early in the disease course. Next, please.

For another self-knowledge check, in which of the following scenarios is it appropriate to test the patient for malaria? Next, please. The correct answer is any traveler returning from a malaria endemic area presenting with fever.

We cannot emphasize this enough. There are numerous resources available to help you manage a patient with malaria, including a CDC consult. But all require a clinician to consider malaria as a possibility and perform diagnostic testing. As we've reviewed, suspecting and appropriately testing for malaria is the first and most critical step in malaria case management. For a discussion of malaria treatment, I'll turn it over to Dr. Wallender.

Thank you. Next slide, please.

There's several key considerations when treating malaria in a non-endemic area. Since U.S. residents are at high risk of progressing to severe malaria, even if their initial symptoms are mild, hospitalization should always be considered when malaria is diagnosed. This is true for all Plasmodium species and particularly for P. falciparum infections. Second, an individual's malaria treatment regimen is dictated by several factors, and these include their disease severity, parasite species and expected drug resistance pattern, drug availability, age, and pregnancy status. We will provide a broad overview here and more details of all our antimalarial treatments, all available antimalarial treatments in the U.S. are available on CDC's malaria treatment tables. Next, please.

Once malaria is diagnosed, severity of disease dictates the next steps in management. Next, please.

Severe malaria is defined as one or more of these features. We mentioned earlier that it was important to get a parasite density as part of the blood smear result. And this is, as we note here, that a patient with a pursuit density of 5 percent or more should be treated as having severe disease, even in the absence of severe clinical symptoms. This parasite density-- [inaudible] Next, please.

If the patient does not meet criteria for severe malaria, oral antimalarials should be started immediately. The antimalarial drugs are chosen based on Plasmodium species and the drug resistance patterns observed in the parasite's country of origin. Next, please.

Directed therapy can be used if the species is known from the diagnostic test, usually a blood smear PCR, and the parasite's country of origin is known based on the patient's travel history. In instances where the diagnosis of malaria is made, but the species is unknown, a drug regimen that is effective against all Plasmodium species, including drug resistant parasites, is chosen. Next, please.

This table shows all of the oral antimalarials available, stratified by species and sensitivity to Chloroquine. And we'll go through this step by step. Next slide.

If the Plasmodium species is initially unknown or includes P. falciparum, Artemether-lumefantrine, with the brand name, Coartem, is our first line treatment recommendation. Next slide, please.

Artemether-lumefantrine is the most rapidly acting FDA approved, oral antimalarial combination. It is a fixed dose combination of two drugs with complementary activities. The Artemether is rapidly effective, quickly killing most of the parasites, however, because of its short half-life, Artemether is paired with a slower acting but longer lasting lumefantrine, which mops up residual parasites. Artemether-lumefantrine is well-tolerated and can be used for all trimesters of pregnancy, including the first trimester and for children. With high efficacy and safety, we encourage hospitals to stock Artemether-lumefantrine if possible to expedite treatment of malaria once it's diagnosed. Next, please.

If Artemether-lumefantrine is not available, another effective option against all Plasmodium species is Atovaquone-proguanil, or brand name Malarone. Malarone is slower, is a slower acting antimalarial drug combination and it should not be taken by individuals who may be pregnant or who developed malaria after taking Malarone for malaria prophylaxis. Quinine plus doxycycline and Mefloquine are additional options if both Artemether-lumefantrine and Malarone are unavailable or cannot otherwise be used for a particular patient. These drugs are generally less well-tolerated due to side effects. Next slide.

For Chloroquine susceptible Plasmodium infections, which are most commonly non-falciprum species, Chloroquine or Hydroxychloroquine can be used. When Chloroquine is an option for treatment, which can be determined after the Plasmodium species is confirmed and the country of origin is known, it is highly effective and well-tolerated. Next slide, please.

Up to this point, we have been discussing symptomatic malaria treatment, which is caused by blood stage parasites, but recall that although all Plasmodium parasites first infect the liver, to undergo additional development before entering the bloodstream, a subset of Plasmodium vivax, the species responsible for the malaria acquired in Florida and Texas, and Plasmodium ovale parasites, become dominant in the liver, dormant in the liver. Sorry, dormant. These dormant parasites, called hypnozoites, can activate and develop into a blood stage infection months to years later, reinitiating a clinical infection, even if the previous acute disease was appropriately

treated. This is called a relapse infection. Hypnozoites are not killed by the acute malaria medications we have reviewed so far and as a result, vivax and ovale malaria require treatment targeting the hypnozoites in addition to the blood stage. Next slide, please.

The medications active against hypnozoites, Primaquine and Tafenoquine, are highlighted here. Next slide.

When additional treatment for Plasmodium vivax and ovale hypnozoites is provided, it is referred to as radical cure. Both Primaquine and Tafenoquine are capable of providing radical cure, but both can also be dangerous for people with an adequate gluco 6 phosphate dehydrogenase activity.

To avoid hemolytic anemia due to these drugs, a quantitative G6PD activity assay is mandatory before starting treatment. A G6PD normal pregnant woman should be treated as G6PD deficient because the enzyme activity of the fetus cannot be measured. Neither of these drugs should be started before the G6PD test results are available. People who have abnormal G6PD activity levels still require prevention of relapsed infection, but alternative regimens must be used. Next slide, please.

This table highlights the differences between Primaquine and Tafenoquine as options for radical cure. Primaquine and Tafenoquine are both efficacious; Tafenoquine has the advantage of requiring only a single dose, if taken concurrently with Chloroquine for the blood stage of the infection. Primaquine requires 14 days of daily dosing, but it can be used in patients with comparatively decreased G6PD function, with dose adjustment. It can be taken with any antimalarial for the blood stage of the disease and it is preferred for overweight patients. In addition, Primaquine can be used for radical cure in children under 16 years of age.

There may be other considerations involved in choosing a treatment regimen and the CDC Malaria Treatment Guidelines are specialty consultation can help navigate drug selection and dosing. If you believe your patient would strongly benefit from the convenience of Tafenoquine, but did not receive Chloroquine for their initial antimalarial treatment, please contact the CDC malaria hotline. Next slide, please.

This table summarizes some of the main points about malaria therapy for individuals with non-severe disease. We emphasize that Artemether-lumefantrine is appropriate first line treatment for all patients, regardless of species.

Therapy is further directed by the species and resistance patterns of the parasite. Please check our website and treatment tables for details about resistance patterns. And Plasmodium vivax and ovale need treatment against the dormant liver phase or hypnozoites. We will next talk about treatment of severe malaria, most severe malaria is caused by Plasmodium falciparum but as we mentioned before, any species can cause severe disease.

In 2018, 92 percent of severe infections in the U.S. were caused by P. falciparum, 6 percent were caused by P. vivax or ovale, and 2 percent were caused by other species, or mixed infections. Next slide, please.

Here on our treatment chart, we highlight the only recommended antimalarial for severe malaria, IV artesunate. It is the only IV antimalarial medication available in the U. S. and it is effective against all species of Plasmodium. Importantly, IV artesunate is now FDA approved, it's commercially available and does not require CDC approval. Next slide, please.

Severely ill patients with malaria should be managed in an intensive care unit. Emergency procurement of IV artesunate can take several hours and while IV artesunate is being procured, treatment should begin with oral antimalarials, preferably Artemether lumefantrine. To avoid delays in treatment, we recommend hospitals have a plan for emergency procurement of IV artesunate in place. [Inaudible] IV artesunate is the most potent antimalarial, other than the rare post-artesunate delayed hemolytic anemia. Side effects are unusual and the drug can be given to pregnant women, young children, and those with liver and kidney disease. In most cases, a treatment course of IV artesunate consists of three doses given at time zero, 12, and 24 hours.

During treatment blood smear should be drawn every 12-24 hours to monitor the percent parasitemia. Blood smears should be taken four hours after [inaudible] doses to allow time for dead parasites to be cleared. Patients with parasitemias less than or equal to 1 percent after receiving the third IV artesunate dose, should be started on one of the oral acute infection medications, with Artemether lumefantrine being the first choice in most cases. If the parasite density is over 1 percent after three doses of IV artesunate, additional doses can be given at 24 hour intervals for up to six additional days. Next slide, please.

Again, response to treatment with IV artesunate is monitored with serial blood smears to measure parasite density. Decreasing parasite density signifies response to treatment. Usually supportive care should be, usual supportive care should be provided with attention to preventing and managing complications. Other adjunctive therapies are poorly supported by the evidence and are generally not recommended. Next slide, please.

Here's our next self-knowledge check. Which of the following medications are appropriate for an individual following a diagnosis of non-severe P. falciparum malaria? Doxycycline, Atovaquone/proguanil, quinine alone, or tafenoquine. Next slide, please.

And the correct answer is Atovaquone/proguanil, or Malarone. Following Malarone, although Malarone is not the preferred treatment for a P. falciparum malaria, it is highly effective and maybe more available than Artemether-lumefantrine in the U.S. due to its use as prophylaxis among travelers. I'll now turn it back over to Dr. Ridpath.

Now we will discuss malaria prevention. And this will be from the perspective of U. S. travelers going to endemic areas. Slide, please.

The cornerstones for malaria prevention are encouraging travelers to take malaria [inaudible] prophylaxis when traveling to endemic countries. To take precautions to prevent mosquito bites while traveling. And then to promptly diagnose and treat malaria that does develop in order to minimize the risk of infecting local mosquitoes which may in turn infect additional individuals. Next slide, please.

Taking malaria prophylaxis is highly effective at preventing malaria and 95 percent of U.S. residents with malaria did not take a full course of malaria prophylaxis. There are a variety of antimalarial drugs approved for malaria prophylaxis, and the CDC website and the Yellow Book has resources to guide clinicians by country and region within each country where malaria prophylaxis is recommended. An example of a map from the CDC 2024 Yellow Book website in South or in Central America is found to the right of this slide. Next slide, please.

While traveling, preventing mosquito bites can prevent a variety of illnesses. Though preventing bites alone does not replace recommendations for malaria chemoprophylaxis. Anopheles mosquitoes can bite indoors or outdoors. Insect repellent, such as DEET, the most effective repellent, can be used for individuals two months of age and older, and permethrin treated clothing can prevent mosquito bites, as well as other vectors, like tick bites. Using window screens can be helpful, and at night, and insecticide treated net can also prevent mosquito bites. Next slide, please.

Your patient is traveling to rural Uganda for work and is worried about taking malaria prophylaxis because they heard it can cause disturbing nightmares. What do you advise? A, review known side effects of malaria prophylaxis medications with your patient, B, take test doses of the malaria prophylaxis medication prior to the trip, C, do not prescribe malaria prophylaxis but strictly adhere to using a bed net, D, prescribe Coartem to use if they get a fever while traveling, E, A and/or B, F, C and/or D.

The correct answer is E, review known side effects of prophylaxis medications with your patient and discuss what options might be best with their medical history, risk of contraindications with any other medications they're taking, and their tolerance for potential side effects. And/or you could recommend that they take a test dose of a malaria prophylaxis medication prior to the trip to see how they can handle it. Next slide, please.

CDC's Malaria Hotline is available 24/7, including holidays, to help clinicians requiring consultation for diagnosis, treatment, and management of patients with malaria. We recommend consulting with a local infectious disease provider first, if one is available. We're also available during business hours for questions related to malaria prophylaxis. In addition to clinical guidance, we have laboratory support around diagnosis.

For example, as previously mentioned, our DPDx program can assist with telediagnosis [inaudible], including species determination via microscopy review, or PCR. Malaria is considered a medical emergency in the United States, much like other severe infections, delays in diagnosis and treatment can lead to severe disease and death. We had about 300 cases of severe malaria and about 6-8 deaths per year reported from our pre-COVID-19 pandemic data. Early diagnosis and treatment can both avert these severe outcomes and prevent infection of, initiation of local transmission. Next slide, please.

Suspect malaria among individuals with fever and a recent history of travel, or fever without an alternative diagnosis. A malaria blood smear is needed for all suspected malaria cases, but a rapid diagnostic test can shorten the time to treatment. Remember, a blood smear is still needed for parasite density and species confirmation. Species determination in all cases is necessary to

determine whether treatment of dormant liver parasites or hypnozoites with Primaquine or Tafenoquine is needed. Importantly, early malaria diagnosis and prompt treatment can prevent severe disease and death for the individual and reduces the risk for onboard malaria transmission.

And finally, expanding the use of malaria prophylaxis among travelers to malaria endemic countries is necessary to curb the upward trend of imported malaria cases in the United States. Thank you, and here are some resources available on our website.

Presenters, thank you for providing this timely information to our audience. We will now go into our Q and A session. We would like to welcome some additional subject matter experts who will be joining us for today's Q and A session. Dr. Monica Parise, who is a captain in the U.S. Public Health Service and the Incident Manager for CDC's 2023 Malaria Response. Dr. Jimee Hwang, who is a captain in the U. S. Public Health Service and works on the U. S. President's Malaria Initiative, and is the operational research and elimination team co-lead at CDC. And Dr. Kimberly Mace, who is the epidemiology team lead for CDC's 2023 Malaria response.

To ask a question using Zoom, click the Q and A button at the bottom of your screen, then type your question. Please note that we receive many more questions than we can answer during our webinars.

Our first question; is there any data about the duration of acquired immunity after recovering from malaria?

Acquired immunity, this is Kimberly Mace, acquired immunity is not 100 percent effective and individuals can have repeat infections. It also rapidly declines within months to years without continual exposure.

Thank you. Our next question; is Coartem readily available in the United States and is it available in a liquid formulation for young children?

Thanks for that question. This is Erika Wallender. So Coartem is FDA approved and readily available in the United States, and is not available in a liquid formulation but it can be crushed and administered that way. And if you have additional problems trying to identify, you can call 855-coartem, which is the number that can help identify stock near you.

Our next question; are there any recommendations for mosquito surveillance?

This is Dr. Monica Parise, Incident Manager. Most of that is being conducted right now in the United States for, this is for Anopheles mosquitoes that transmit malaria, in the local jurisdictions. So I can't give you, we can't provide you with the actual details of where the trapping is and what they're doing, but I can just say that they are collecting the mosquitoes, we're testing them for the parasite and then they're doing mosquito control measures, which include killing the adult mosquitoes as well as the larvae.

This is Kimberly Mace, I'd just like to add also, but we don't recommend any additional mosquito measures for routine imported cases where there's no local transmission.

Thank you. Our next question; can you comment on why there is a delay in the, in, sorry, the question disappeared. Can you comment on why there is a delay in getting G6PD testing done in many labs?

Hi, this is Dr. Jimee Hwang, most hospitals do not have in-house G6PD testing and it's often a send out test to one of the laboratories so there's always a turnaround time associated with that.

Okay, thank you. Are there any updates about vaccine options for malaria prophylaxis in the United States?

This is Monica Parise. We don't have a malaria vaccine approved in the United States, there is a malaria vaccine that's being provided now from GAVI and the World Health Organization to endemic countries, but we don't have it in the United States.

Okay, our next question; should hospitals be prepared to be able to at a minimum do a rapid test for malaria using the kit?

Yeah, we recommend, this is Adam Rowh, we recommend that hospitals have diagnostic capacity available for malaria. Remember that the blood smear is the gold standard for diagnosis and is required in all cases. Other options can supplement that capability, and if you have questions about your local diagnostic ability, or how to proceed in an individual case, we recommend contacting the CDC hotline.

Thank you. Our next question; is there a time frame for retesting after the initial negative test?

This is Adam Rowh again. Yes, we recommend that blood smears be separated by about 12-24 hours. Yes, that's it.

And this is Dr. Alison Ridpath, but I'll just add that if someone's presenting early, their blood smear might be below the level of detection, their parasitemia might be below the level of detection, so if you have a high suspicion of malaria, you should continue to test for them, and wait an appropriate time, 12-24 hours to see if the parasite density comes above the level of detection.

Thank you. Our next question; is the sensitivity of rapid malaria tests the same for all species?

This is Jimee Hwang again. The sensitivity for the rapid diagnostics test vary by the brand, the manufacturer, and do vary for the different species. The brand we have available in the United States tests for Plasmodium falciparum and then all other Plasmodium species and the line for the Plasmodium falciparum detects an antigen that's abundantly available so the sensitivity for that is much higher, whereas the antigen that they're using the test for all plasmodium species is a less abundantly present. So that, the sensitivity for that will test, tends to be lower across the board.

Thank you. Our next question; my hospital does not have the rapid diagnostic test or blood smears. What should I do if I suspect my patient has malaria?

If there-- this is Adam Rowh again. If there are no diagnostic options available at all at the time the patient presents with suspected malaria, the patient should be immediately referred or transferred to another facility that does have the ability to do testing. You can also always call the malaria hotline if you have questions about managing individual patients.

Thank you. Our next question; is there a test I can use to determine if my patient's malaria is drug resistant?

No, there currently isn't a commercial test to use for drug resistance. When travel to a malaria endemic country is confirmed, the information can be used to determine, that information can be used to determine which tests will be effective against, sorry, which drugs will be effective against the parasites in that country. Each country and region's drug resistance patterns are available on CDC's website. And you can always, again, call us if you need additional help on our CDC malaria hotline.

Thank you. Our next question; can patients showing mild malaria symptoms with negative blood smears still receive treatment?

The diagnosis, this is Adam Rowh, the diagnosis of malaria needs to be established before initiating treatment with antimalarials. We've gone over various aspects of the diagnostic approach, and this may vary in individual circumstances, but in the United States, presumptive treatment is not recommended, which means treatment of a suspected case, in the absence of a positive test result.

And with one exception, this is Dr. Alison Ridpath, if somebody has severe disease, you know you should not delay in treatment and start treatment right away, but just send off a blood smear so you know what the percent parasitemia is and can confirm the diagnosis before starting treatment.

Okay, thank you. Our next question; can you comment on the current status of resistance to antimalarial drugs in the United States?

That, this is Dr. Alison Ridpath again, it's, that would be based on the country where the infection is acquired. So resistance patterns vary by countries and that information is available on the CDC website.

Thank you. Our next question is a two-part question; most people with malaria don't usually end up severely ill so why is the recommendation to hospitalize for all of these cases? And then the second part; when can patients be safely discharged?

This is Adam Rowh. People who have no immunity to malaria, which includes most United States residents, are at increased risk for severe disease even in the absence of other risk factors. That means that everyone who doesn't live in an area of continuous transmission, is recommended that hospitalization be considered. We recommend hospitalization for individuals with Plasmodium falciparum across the board, which is the species that causes the most severe disease, or if the species is unknown. Patients can be safely discharged once they're taking

appropriate antimalarial medications, their clinical condition improves, and their parasite density is decreasing.

Thank you. Our next question; what is the mechanism of action of doxycycline in treating malaria?

This is Kimberly Mace. Doxycycline by itself is not a curative antimalarial, it is slower acting and so it, while it may knock down asexual parasites in the blood, it's not sufficient to completely clear the illness.

Yeah, and it, this is Dr. Alison Ridpath. It doesn't work quickly enough to be effective as a primary treatment.

Okay, thank you. Our next question; should I be concerned about the risk to blood supply?

This is Dr. Monica Parise. So there are routine measures that are taken to prevent malaria from infecting the blood supply and those are related to, for example, the questions that are asked to blood donors. We can't give you any-- there are some expanded measures being taken by the, in the jurisdictions, but we really can't speak to the specifics of that.

Okay, thank you. And we have time for one last question. And this is a two-part question; I live in a community where people frequently visit Mexico. Does that count as international travel? And two, do they need malaria prophylaxis and should I be concerned that they could import a case of malaria?

Sure, this is Dr. Alison Ridpath. So northern Mexico, near the Texas border is not considered to have endemic malaria but certain areas of Mexico do have endemic malaria, mainly in the southern part of the country. Further details on, are available on our website or the Yellow Book, you can look there to see which areas of Mexico have endemic malaria. And you can always call the hotline if you have a patient that has malaria and you have any questions, or has traveled to Mexico and you have any questions about the possibility of malaria.

Thank you. Presenters and subject matter experts, thank you for answering these questions and for sharing your expertise with us today. We appreciate this robust Q and A session.

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 the COCA Call's webpage next week. You can visit emergency.cdc.gov/coca for more details about this COCA Call and other upcoming COCA Calls.

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