

## Summary

Suspected malaria cases should be reported to your Florida <u>county health department</u> <u>contact</u>.

The Florida Department of Health and Centers for Disease Control and Prevention (CDC) are issuing this Health Alert Network (HAN) Health Advisory to share information and notify clinicians and the public about—

- 1. Identification of locally acquired malaria cases (*P. vivax*) in two U.S. states (<u>Florida</u> [6] and <u>Texas</u> [1]) within the last 2 months,
- 2. Concern for a potential rise in imported malaria cases associated with increased international travel in summer 2023, and
- 3. Need to plan for rapid access to IV artesunate, which is the first-line treatment for severe malaria in the United States.

#### **Background**

CDC is collaborating with two U.S. state health departments with ongoing investigations of locally acquired mosquito-transmitted *Plasmodium vivax* malaria cases. There is no evidence to suggest the cases in the two states (Florida and Texas) are related. In <u>Florida</u>, six cases within close geographic proximity have been identified, and active surveillance for additional cases is ongoing. Mosquito surveillance and control measures have been implemented in the affected area. In <u>Texas</u>, one case has been identified, and surveillance for additional cases, as well as mosquito surveillance and control, are ongoing. All patients have received treatment and are improving. Locally acquired mosquito-borne malaria has not occurred in the United States since 2003 when eight cases of locally acquired *P. vivax* malaria were identified in Palm Beach County, FL (1). Despite these cases, the risk of locally acquired malaria remains extremely low in the United States. However, *Anopheles* mosquito vectors, found throughout many regions of the country, are capable of transmitting malaria if they feed on a malaria-infected person (2).

Malaria is a serious and potentially fatal disease transmitted through the bite of an infective female anopheline mosquito. Though rare, malaria can also be transmitted congenitally from mother to fetus or to the neonate at birth, through blood transfusion or organ transplantation, or through unsafe needle-sharing practices. Malaria is caused by any of five species of protozoan parasite of the genus *Plasmodium*: *P. falciparum*, *P. vivax*, *P. malariae*, *P. ovale*, and *P. knowlesi*. Worldwide, more than 240 million cases of malaria occur each year (95% in Africa). Almost all cases of malaria in the United States are imported and occur in people traveling from countries with malaria transmission, many from sub-Saharan Africa and South Asia. Before the COVID-19 pandemic, approximately 2,000 cases of mostly travel-related malaria were diagnosed in the United States each year; approximately 300 people experienced severe disease (most *P. falciparum*), and 5 to 10 people with malaria died yearly (3). Approximately 70 travel-associated cases of malaria are reported in Florida annually. Most imported cases of malaria in the United States are diagnosed during summer and early fall. In 2023, CDC expects summer international travel among U.S. residents will be increasing to pre-COVID-19 pandemic levels (4).



Clinical manifestations of malaria are non-specific and include fever, chills, headache, myalgias, and fatigue. Nausea, vomiting, and diarrhea may also occur. For most people, symptoms begin 10 days to 4 weeks after infection, although a person may feel ill as early as 7 days or as late as 1 year after infection. If not treated promptly, malaria may progress to severe disease, a life-threatening stage, in which mental status changes, seizures, renal failure, acute respiratory distress syndrome, and coma may occur. Malaria in pregnant people is associated with high risks of both maternal and perinatal morbidity and mortality. *P. falciparum* and *P. knowlesi* infections can cause rapidly progressive severe illness or death, while the other species, including *P. vivax*, are less likely to cause severe disease. Laboratory abnormalities can include anemia, thrombocytopenia, hyperbilirubinemia, and elevated transaminases, varying from normal or mildly altered in uncomplicated disease to very abnormal in severe disease. *P. vivax* and *P. ovale* can remain dormant in the liver and such infections require additional treatment; failure to treat the dormant hepatic stages may result in chronic infection, causing relapsing episodes. Relapses may occur after months or even years without symptoms.

Malaria is a medical emergency and should be treated accordingly. Patients suspected of having malaria should be urgently evaluated in a facility that is able to provide rapid diagnosis and treatment, within 24 hours of presentation. Order microscopic examination of thin and thick blood smears, and a rapid diagnostic test (RDT) if available, to diagnose malaria as soon as possible. Artemether-lumefantrine (Coartem®) is the preferred option, if readily available, for the initial treatment of uncomplicated *P. falciparum* or unknown species of malaria acquired in areas of chloroquine resistance. Atovaquone-proguanil (Malarone®) is another recommended option. *P. vivax* infections acquired from regions other than Papua New Guinea or Indonesia should initially be treated with chloroquine (or hydroxychloroquine). IV artesunate is the only drug available for treating severe malaria in the United States. Artesunate for Injection<sup>TM</sup>, manufactured by Amivas, is approved by the U.S. Food and Drug Administration (FDA) and is commercially available. Hospitals should have a plan for rapidly diagnosing and treating malaria within 24 hours of presentation. Additional information on diagnosing and treating malaria, including details of treating the dormant liver stages, is available on the CDC website.

#### **Recommendations for Clinicians**

- Consider the diagnosis of malaria in any person with a fever of unknown origin, regardless of international travel history, particularly if they have been to the areas with recent locally acquired malaria.
- Routinely obtain a travel history and consider malaria in a symptomatic person who
  traveled to an area with malaria in the weeks to months preceding symptom onset.
- Treatment recommendations for malaria vary by species and severity. Please refer
  to <u>CDC's Malaria Diagnosis and Treatment Guidelines for U.S. Clinicians</u> for specific
  detailed instructions.
  - Malaria is a medical emergency. If not diagnosed and treated promptly, illness may progress to severe disease, a life-threatening stage, where mental status changes, seizures, renal failure, acute respiratory distress syndrome, and coma may occur. An algorithm for diagnosis and treatment of malaria is available <a href="here">here</a>.



- Patients suspected of having malaria should be urgently evaluated in a facility, such as an emergency department, able to provide rapid diagnosis and treatment, within 24 hours of presentation.
- Order microscopic examination of thin and thick blood smears, and a rapid diagnostic test (RDT) if available, to diagnose malaria as soon as possible.
  - "BinaxNOW™," a malaria RDT, is approved for use in the United States. RDTs are less sensitive than microscopy and cannot confirm each specific species of the malaria parasite or the parasite density.
  - Therefore, microscopy should also be obtained in conjunction with an RDT as soon as possible.
- If blood smears or RDT are positive and species determination is not available, antimalarial treatment effective against chloroquine-resistant *P. falciparum* must be initiated immediately.
- Artemether-lumefantrine (Coartem®) is the preferred option, if readily available, for the initial treatment of uncomplicated *P. falciparum* or unknown species of malaria acquired in areas of chloroquine resistance. Atovaquone-proguanil (Malarone®) is another recommended option. *P. vivax* infections acquired from regions other than Papua New Guinea or Indonesia should initially be treated with chloroquine (or hydroxychloroquine).
- o IV artesunate is the first-line drug for treatment of severe malaria in the United States. Artesunate for Injection<sup>™</sup> is approved by the FDA for treating severe malaria and is commercially available. More information on how to acquire IV artesunate in the United States can be found here.
- Species determination is important because P. vivax and P. ovale can remain dormant in the liver and require additional antirelapse treatment; failure to treat the dormant hepatic parasites may result in chronic infection with relapsing episodes. Relapses may occur after months or even years without symptoms.
- After an urgent infectious disease consultation, if there are still questions about diagnosing and treating malaria, CDC malaria clinicians are on call 24/7 to provide advice to healthcare providers, further information can be found here.
- Suspected or confirmed locally acquired malaria is a public health emergency and should be reported immediately to your <u>county health department contact</u>. Imported (or travel-associated malaria) is also reportable in all states through routine reporting methods.
- Discuss travel plans with patients; prescribe a CDC-recommended <u>malaria</u> <u>chemoprophylaxis</u> regimen and discuss <u>mosquito bite prevention</u> for those traveling to an international <u>area with malaria</u>; encourage patients to adhere to the regimen before, during, and after travel. Malaria chemoprophylaxis is not needed domestically at this time.

### **Recommendations for Hospitals and Laboratories**

Have malaria diagnostic tests available (blood smear or <u>BinaxNow™ rapid diagnostic</u> test [RDT] followed by blood smear) and ensure that qualified personnel who can perform and interpret these tests are always available.



- If malaria blood smear or RDT results are not readily available, patients in whom malaria is suspected should be referred to a higher level of care for prompt evaluation for malaria.
- Bench aids for blood smear preparation, staining, diagnosis, and calculating the percent parasitemia are available <u>here</u>.
- Stock IV artesunate (Artesunate for Injection<sup>™</sup>) or have a plan in place for emergency procurement.
  - More information on how to acquire IV artesunate in the United States can be found here.
- Stock artemether-lumefantrine (Coartem®), the first-line drug in the United States for most cases of uncomplicated *P. falciparum* or unknown malaria species. Atovaquone-proguanil (Malarone®) is another recommended option.
- Report suspected malaria cases to your Florida county health department contact.

#### For More Information

- Florida Department of Health Mosquito-borne Disease Surveillance Data: <u>www.floridahealth.gov/diseases-and-conditions/mosquito-borne-diseases/surveillance.html</u>
- CDC Treatment of Malaria: Guidelines for Clinicians (United States)
- CDC DPDx Diagnostic Procedures
- Malaria | CDC Yellow Book 2024
- CDC Malaria Information and Prophylaxis, by Country
- CDC Parasites Continuing Education Malaria 101 for the Healthcare Provider
- CDC Malaria Travelers Risk Assessment
- Prevent Mosquito Bites | Mosquitoes | CDC
- Mosquito Control at Home

#### References

- 1. CDC. Local Transmission of Plasmodium vivax Malaria Palm Beach County, Florida, 2003. MMWR. 2003 Sep 26; 52(38):908-911.
- 2. Dye-Braumuller KC, Kanyangarara M. <u>Malaria in the USA: How Vulnerable Are We to Future</u> Outbreaks? Curr Trop Med Rep. 2021; 8(1):43-51.
- 3. Mace KE, Lucchi NW, Tan KR. Malaria Surveillance United States, 2018. MMWR Surveill Summ 2022 Sep 2; 71(No. SS-8):1–29.
- 4. Schultz JS, Mace KE, Tan KR. Return to Travel in the Coronavirus Disease 2019 Pandemic Recovery Period and Implications for Imported Malaria: Reinforcing Prevention, Early Diagnosis, and Appropriate Treatment of Malaria. Clin Infect Dis. 2023 Apr 1; 76(7):1161-1163.