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IN THIS ISSUE: CDC HAN - LOCALLY ACQUIRED MALARIA CASES IDENTIFIED IN THE UNITED STATES

CDC HEALTH ALERT NETWORK (HAN)

Locally Acquired Malaria Cases Identified in the United States

Distributed via the CDC Health Alert Network June 26, 2023, 5:00 PM ET CDCHAN-00494

Summary

The Centers for Disease Control and Prevention (CDC) is issuing this Health Alert Network (HAN) Health Advisory to share information and notify clinicians, public health authorities, and the public about—

- 1) Identification of locally acquired malaria cases (*P. vivax*) in two U.S. states (Florida [4] and Texas [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

https://www.floridahealth.gov/diseases-andconditions/mosquito-borne-diseases/surveillance.html and Texas https://www.dshs.texas.gov/newsalerts/health-advisory-locally-acquired-malaria-case) are related. In Florida, four 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 Texas, 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. The risk is higher in areas where local climatic conditions allow the *Anopheles* mosquito to survive during most of or the entire year and where travelers from malaria-endemic areas are found. In addition to routinely considering malaria as a cause of febrile illness among patients with a history of international travel to areas where malaria is transmitted

https://www.cdc.gov/malaria/travelers/country_table/m.html, clinicians should consider a malaria diagnosis in any person with a fever of unknown origin regardless of their travel history. Clinicians practicing in areas of the United States where locally acquired malaria cases have occurred should follow guidance from their state and local health departments. Prompt diagnosis and treatment of people with malaria can prevent progression to severe disease or death and limit ongoing transmission to local *Anopheles* mosquitos. Individuals can take steps to prevent mosquito bites https://www.cdc.gov/mosquitoes/mosquito-bites/prevent-mosquito-bites.html and control mosquitos at home

https://www.cdc.gov/mosquitoes/mosquitocontrol/athome/index.html to prevent malaria and other mosquito-borne illnesses.

Malaria is a serious and potentially fatal disease transmitted through the bite of an infective female anopheline mosquito

https://www.cdc.gov/parasites/malaria/index.html.

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

https://www.cdc.gov/malaria/travelers/country_table/m.html. 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 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

https://www.cdc.gov/malaria/diagnosis_treatment/clinicians1.html. 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™, 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 https://www.cdc.gov/malaria/travelers/country_table/a.html.
- Treatment recommendations for malaria vary by species and severity. Please refer to CDC's Malaria Diagnosis and Treatment Guidelines for U.S. Clinicians for specific detailed instructions https://www.cdc.gov/malaria/diagnosis_treatment/c linicians1.html.
 - 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 on the last page of this HAN.
 - 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.
- o 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).
- IV artesunate is the first-line drug for treatment of severe malaria in the United States. Artesunate for Injection™ 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 state, territorial, local, or tribal health department. Imported (or travel-associated malaria) is also reportable in all states through routine reporting methods.
- Discuss travel plans with patients; prescribe a CDC-recommended malaria chemoprophylaxis regimen https://www.cdc.gov/malaria/travelers/drugs.html
 and discuss mosquito bite prevention for those traveling to an international area with malaria; encourage patients to adhere to the regimen before, during, and after travel. Malaria chemoprophylaxis is not needed domestically at this time.

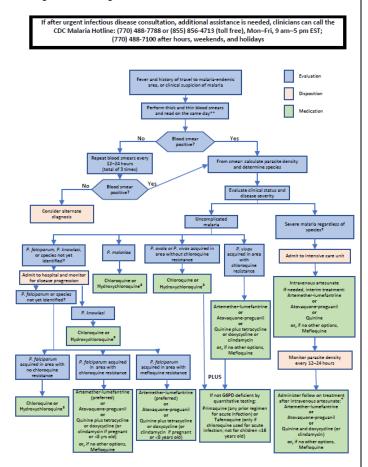
Recommendations for Hospitals and Laboratories

- Have malaria diagnostic tests available (blood smear or BinaxNow™ rapid diagnostic 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 here https://www.cdc.gov/dpdx/diagnosticProcedures/index.html.
- Stock IV artesunate (Artesunate for InjectionTM) 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 https://www.cdc.gov/malaria/diagnosis_treatment/ artesunate.html.
- 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.

Recommendations for the Public

- Take steps to prevent mosquito bites
 https://www.cdc.gov/mosquitoes/mosquito bites/prevent-mosquito-bites.html and control
 mosquitos at home
 https://www.cdc.gov/mosquitoes/mosquito control/athome/index.html to protect yourself from
 any mosquito-borne illness.
- Before you travel, learn about the health risks and precautions for malaria and other diseases for your destination https://wwwnc.cdc.gov/travel/destinations/list.
- If you are traveling internationally to an area where malaria occurs, talk to your healthcare provider about medicines to prevent you from getting malaria https://www.cdc.gov/malaria/travelers/country_ta ble/a.html.
- If you have traveled to an area where malaria occurs and develop fever, chills, headache, body aches, and fatigue, seek medical care and tell your healthcare provider that you have traveled.

Algorithm for Diagnosis and Treatment of Malaria in the United States



For More Information

Malaria Prevention, Diagnosis, and Treatment

 CDC Treatment of Malaria: Guidelines for Clinicians (United States)

https://www.cdc.gov/malaria/diagnosis_treatment/clinicians1.html

- CDC DPDx Diagnostic Procedures https://www.cdc.gov/dpdx/diagnosticProcedures/index
- https://www.cdc.gov/dpdx/diagnosticProcedures/index .html
- Malaria | CDC Yellow Book 2024 https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/malaria
- CDC Malaria Information and Prophylaxis, by Country https://www.cdc.gov/malaria/travelers/country_table/ a.html
- CDC Parasites Continuing Education Malaria 101 for the Healthcare Provider

https://www.cdc.gov/parasites/cme/malaria/index.htm

• CDC - Malaria - Travelers - Risk

Assessmenthttps://www.cdc.gov/malaria/travelers/risk assessment.html

Mosquito-Borne Disease Prevention

• Prevent Mosquito Bites | Mosquitoes | CDC https://www.cdc.gov/mosquitoes/mosquito-bites/prevent-mosquito-bites.html

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. Malaria in the USA: How Vulnerable Are We to Future 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.

The Centers for Disease Control and Prevention (CDC) protects people's health and safety by preventing and controlling diseases and injuries; enhances health decisions by providing credible information on critical health issues; and promotes healthy living through strong partnerships with local, national, and international organizations.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

HAN Message Types

- **Health Alert:** Conveys the highest level of importance; warrants immediate action or attention.
- Health Advisory: Provides important information for a specific incident or situation; may not require immediate action.
- Health Update: Provides updated information regarding an incident or situation; unlikely to require immediate action.
- Info Service: Provides general information that is not necessarily considered to be of an emergent nature.