

Malaria

Background

Malaria is one of the world's greatest public health problems. Approximately 200 million of the world's population are infected each year and around half a million people die from malaria annually. Malaria was eliminated from Florida in the late 1940s. Although malaria is no longer endemic in Florida, it is often seen in travelers returning to the state from malaria-endemic regions of the world. *Anopheles* mosquitoes, responsible for transmitting malaria to humans, are common in the state and autochthonous malaria transmission is still possible.

Human malaria is caused by four species of protozoan parasites of the genus *Plasmodium: P. vivax, P. falciparum, P. malariae, and P. ovale.* All four are transmitted from person to person via the bite of infected *Anopheles* mosquitoes. A fifth *Plasmodium* species that can cause severe illness and potentially death in humans is *Plasmodium knowlesi.* This species is endemic to Southeast Asia and macaque monkeys appear to be the primary reservoir. One in three people in the world, a total of 2.2 billion people, are at risk of being infected by *Plasmodium falciparum*.

Vector: In Florida, there are eight identifiable *Anopheles* species, all of which are potentially capable of transmitting malaria; however only one, *Anopheles quadrimaculatus,* is a major malaria vector in Florida:

- An. quadrimaculatus
 - Principal malaria vector in Florida
 - Found in every county, more abundant in northern Florida
 - Larval habitat is in alkaline ponds, lakes and gum swamps in the limestone and red clay regions of northern and western Florida
- An. crucians
 - Larval habitat is in acid ponds and cypress swamps
- An. punctipennis
 - Larval habitat is in winter in slow-flowing alkaline streams of northern and western Florida
- An. perplexens
 - Rare mosquito found in north central Florida
- An. atropos
 - Larval habitat is in salt marshes
- An. albimanus
 - Very rare species
 - o Larval habitat is in sunlit pools on the Florida Keys
 - o Major malaria vector in Central America
- An. walkeri
 - More common in central Florida
 - Larval habitat is in heavily vegetated lakes
- An. barberi
 - o Larval habitat is in tree holes

Epidemiology: Although now rare in the U.S., malaria was once a major scourge of Florida (both *P. vivax* and *P. falciparum*), occurring in all 67 counties. Data collected since 1917 from the Bureau of Vital Statistics (Provost 1946, unpublished) showed 24 counties with annual death rates from malaria of 100 per 100,000; eight had rates above 200; and Dixie County, in 1930, had a death rate above 300. According to the usually accepted ratio of 200 malaria cases per death, the rates reported by Provost translate to 20%, 40%, and 60% of the county populations involved had malaria morbidity. The 24 counties having the highest rates of malaria in Florida and the U.S. were Dixie, Taylor, Jefferson, Lafayette, Wakulla, Gilchrist, Madison, Citrus, Levy, Hernando, Gadsden, Suwannee, Leon, Jackson, Calhoun, Franklin, Okeechobee, Hamilton, Washington, Pasco, Sumter, Columbia, Holmes and Liberty. Malaria morbidity reports for Florida show a steady decrease since 1934 with no large outbreaks since 1937. This reduction in malaria incidence was probably due to mosquito control activities, improved housing including screening, use of repellents, agricultural and other drainage practices, and the use of anti-malarial drugs.

Local transmission of malaria was not reported in Florida between 1948–1990. In June 1990, Florida had its first case of human malaria (*P. vivax*) in 42 years, acquired presumably through the bite of a mosquito in Gulf County. Two induced cases of *P. falciparum* infection occurred in Broward County in 1996 and were probably related to iatrogenic spread in a hospital setting where a patient was being treated for imported malaria infection. Also in 1996, two cryptic cases of *P. vivax* infection occurred in Palm Beach County. One of these cases was in a homeless male and the other was in a resident living in a nearby area. The largest *P. vivax* outbreak in recent Florida history (with eight cases) occurred in Palm Beach County in 2003 in an area located very close to the 1996 Palm Beach County malaria cases.¹ One Manatee County resident acquired *P. falciparum* via a blood transfusion in 2009.² In November 2010, *P. falciparum* infection with cryptic origin (possibly Florida-acquired) was reported in Duval County.

The number of imported malaria cases in the U.S. has been gradually increasing from the early 1970s and may represent increasing cases in migrants and increased travel among U.S. citizens. A surge of imported malaria cases occurred in Florida and the U.S. following the 2010 Haiti earthquake.³ In 2011, due to increased activity around the world, the number of imported malaria cases reported in the U.S. was the highest number since 1971.⁴ The population in Florida at greatest risk of infection is immigrants returning to their home countries to visit friends and relatives (VFRs). FAQ sheets for these groups are available in the List of Appendices and at www.floridahealth.gov/diseases-and-conditions/malaria/index.html.

Clinical symptoms: The symptoms of malaria vary depending on the species, but the initial attack may start with lassitude, headache, anorexia, and occasional nausea and vomiting. The fever is comprised of a cold stage (shivering and a feeling of intense cold), a hot stage (distressing heat, dryness, burning, intense headache, nausea, and vomiting) and finally a profuse sweating stage. The typical attack often begins in the early afternoon and lasts from 8 to 12 hours.

Persons experiencing these symptoms and who have been in an area with malaria are encouraged to see a doctor immediately. Emergency treatment consultation advice is available for health care providers through the **CDC Malaria Hotline** (770-488-7788 or 855-856-4713 toll-

¹ CDC. 2004. Multifocal autochthonous transmission of malaria-Florida, 2003. MMWR 53(19):412-3.

² Mali, S. et al. 2011. Malaria Surveillance-United States 2009. MMWR 60(3). www.cdc.gov/mmwr/pdf/ss/ss6003.pdf.

³ CDC. 2010. Malaria acquired in Haiti. 2010;59:217-9.

⁴ CDC. 2013. Malaria Surveillance-United States, 2011. MMWR:2013;62(ss05);1-17.

free) from 9:00 a.m. to 5:00 p.m. Eastern Time. After hours or on weekends and holidays, call the CDC Emergency Operations Center at 770-488-7100 and ask to page the person on call for the Malaria Branch. All cases of malaria should be reported to the appropriate County Health Department (CHD).

Plasmodium vivax occurs throughout most of the temperate zone, large areas of the tropics, and less commonly in tropical Africa. Severity of the primary attack ranges from mild to severe, usually not resulting in death. *Plasmodium falciparum* is generally confined to tropical or subtropical regions including Haiti and is particularly severe and often fatal in infants, young children and in non-immune persons. *Plasmodium malariae* is frequently named "quartan malaria" because the fever recurs on the fourth day after a two-day interval. The fevers of the other three malaria species recur on the third day after a one-day interval. *Plasmodium malariae* occurs in both tropical and sub-tropical areas. The disease is less severe, but may have a long persistence. *Plasmodium ovale* is similar to *P. vivax* malaria, but with a prolonged latency and generally milder clinical symptoms. It is most common in West Africa. *Plasmodium knowlesi* circulates in non-human primates in Southeast Asia and may cause severe or even fatal infections in humans.

Malaria incubation periods may be extended in patients who receive incomplete prophylaxis, other medications including some antibiotics, or in those recently residing in areas where the parasite is hyperendemic.

Persons with compatible symptoms and a known travel history to malaria-endemic areas should be evaluated for malaria. During 2014, several individuals with/without travel history to areas with ongoing Ebola virus transmission had delays in treatment due to malaria not being considered in the differential diagnoses. The use of a rapid diagnostic test for malaria, such as Binax NOW, can aid in a preliminary diagnosis. Testing by traditional means, polymerase chain reaction (PCR) of whole blood or microscopic evaluation of thick and thin peripheral blood smears, is still required to confirm the diagnosis.

Specific characteristics

Vivax malaria

Incubation period: 12–17 days (9 to 10 months recorded)

Clinical symptoms:

- Primary attack (8 to 10 hours duration)
- Sudden, shaking chills often for several hours; headache, back pain, nausea, malaise
- Irregular fever during the first two to four days up to 104–105°F
- Fever terminates by crisis with drenching sweat, up to several hours
- Series of fevers every 48 hours with diminishing intensity for two weeks
- Two-week latent period
- Secondary attacks (less intense) for two months
- Six- to nine-month latent period
- Long-term relapses –2.5–3 years

Pathology:

Infects new red blood cells (RBCs); RBC destruction leads to anemia

- Enlarged spleen, pulp tarry, malphigian bodies pale gray, malaria pigment within reticulo-endothelial cells
- Congested and enlarged liver; destruction of the bile canaliculi
- Granular casts in urine and fatty degeneration in kidneys
- Infected RBCs are sticky and adhere to capillaries; hemorrhages, tissue anoxia and electrolyte imbalance

Falciparum malaria

Incubation period: 9 to 14 days (longer incubation periods reported)

Clinical symptoms:

- Headache, back pain, prostration, chills
- Fever irregular, and no distinct periodicity; sweating may be present even when fever is low, higher temperature up to 105–110°F
- Pulse and respiration rates are rapid
- Nausea, vomiting and diarrhea increase, frequently a cough
- Cerebral manifestations of excitation, depression, behavioral changes with psychotic tendencies, coma without hyperpyrexia
- Bilious form nausea, vomiting, gastric distress, jaundice
- Algid form high internal heat, body cold and clammy
- Choleraic form stools loose ("rice water")
- Severe dehydration and anemia
- If untreated, "pernicious malaria" may develop suddenly
- Frequent recrudescence during first month, radical cure in about 10 months

Pathology:

- Infects all RBCs
- Few parasites may be present
- Spleen and liver enlargement
- Acute hemolysis of erythrocytes (hemoglobinuria) with dark, mahogany-red urine (blackwater fever)
- Renal failure

Malariae malaria

Incubation period: 18-40 days

Clinical symptoms:

- Similar to vivax malaria
- Untreated infections may have relapses years later

Ovale malaria

Incubation period: Similar to P. vivax

Clinical symptoms:

- Similar to vivax malaria
- Spontaneous recovery common, fewer relapses

Surveillance issues

Imported malaria will continue to be an issue for travelers and visitors to Florida, including migrant workers. Locally acquired cases are possible when *An. quadrimaculatus* and *An. crucians*, which are present throughout the state, seek blood meals from human hosts. Surveillance and investigation of reported cases will continue to be important. To optimize surveillance data:

- Remind health care providers and public health workers regularly about the possibility of malaria importation among travelers and visitors, including migrant workers, the danger of not clinically differentiating malaria from more common febrile illnesses, and to immediately report all confirmed cases.
- Obtain pre-treatment blood films and conduct thorough investigations of all cases with special attention to finding secondary cases and preventing further disease.
- Inform public health officials, including the state Vector-Borne Disease Surveillance Coordinator, CHD Directors/Administrators, and the local mosquito control director when an imported malaria case has been detected.

Surveillance issues for mosquito control agencies

- Survey and map annually all actual and potential Anopheline larval habitats in the district.
- Annually map Anopheline adult distribution and record the seasonal abundance collections in the county.
- Be informed of all imported and introduced malaria in the county and Florida.

Any case that is not readily explained by foreign travel or visitors (including migrant workers) is strongly suggestive of local transmission. Airport-associated malaria should also be considered.⁵ When a case of malaria has been identified, the public should be warned to report any fever of unknown origin to their health care providers. CHDs should alert local mosquito control. A blood film smear and whole blood in a purple-top tube should be submitted for hemoparasitologic analysis of all fever cases suspected of having malaria. *Babesia* can be mistaken for malaria parasites, and vice versa. It is important that the specimens are collected before treatment is initiated. Useful information and general guidance on suspected local malaria investigations is provided in a 2006 MMWR publication.⁶

Depending on circumstances such as abundance of vectors, human population density in the area, and number of suspected human cases, mosquito abatement measures may be initiated. Abatement responses are coordinated with local mosquito control officials and the Florida Department of Agriculture and Consumer Services (FDACS) Bureau of Scientific Evaluation and Technical Assistance.

Malaria prophylaxis for travelers

Individuals traveling to malaria-endemic countries should consult with their doctors about antimalarial prophylaxis. Drug recommendations differ by country of travel and prescribed

⁵ Zucker JR. Changing patterns of autochthonous malaria transmission in the United States: a review of recent outbreaks. Emerg Infect Dis. 1996;2(1):37-43.

⁶ Filler, S.J et. al. 2006. Locally Acquired Mosquito-Transmitted Malaria: A Guide for Investigations in the United States, 2006, MMWR, Vol. 55 / No. RR-13 www.cdc.gov/mmwr/PDF/rr/rr5513.pdf.

medication should be taken before, during, and after travel. More information can be found at the CDC website: www.cdc.gov/malaria/travelers/index.html. Those with *P. falciparum* infection, pregnant women, children, and individuals with no established immunity to malaria are particularly at risk for severe or fatal illness. Immunity to malaria only occurs in long-term residents of hyperendemic areas such as West Africa. Once leaving a hyperendemic area, protective immunity rapidly wanes. Any traveler experiencing malaria-like symptoms during or after travel should seek immediate medical attention.

Case Definition

Malaria

Reporting code = 08460 Case report form: *Malaria Case Surveillance Report* **MERLIN EXTENDED DATA REQUIRED**

Clinical description

Signs and symptoms are variable; however, most patients experience fever. In addition to fever, common associated symptoms include headache, back pain, chills, sweats, myalgia, nausea, vomiting, diarrhea, and cough. Untreated *Plasmodium falciparum* infection can lead to coma, renal failure, pulmonary edema, and death. The diagnosis of malaria should be considered for any person who has these symptoms and who has traveled to an area in which malaria is endemic. Asymptomatic parasitemia can occur among persons who have been long-term residents of areas in which malaria is endemic.

Laboratory criteria for diagnosis

Confirmatory:

• Detection and specific identification of malaria parasites by microscopy in thick or thin peripheral blood films by a state public health laboratory (PHL) or the Centers for Disease Control and Prevention,

OR

• Detection of *Plasmodium* species DNA in peripheral blood by nucleic acid test (e.g., polymerase chain reaction [PCR] test).

Supportive:

Either of the following:

- Detection of circulating malaria-specific antigens using rapid diagnostic test (RDT)
- OR
 - Detection of malaria parasites by microscopy in thick or thin peripheral blood films by a commercial laboratory.

Case classification

<u>Confirmed:</u> A person (symptomatic or asymptomatic) with confirmatory laboratory evidence, diagnosed in the United States, regardless of whether the person experienced previous episodes of malaria while outside the country.

<u>Suspect:</u> A person (symptomatic or asymptomatic) with supportive laboratory evidence diagnosed in the United States, regardless of whether the person experienced previous episodes of malaria while outside the country.

Comments

Reports of malaria parasites detected in thick or thin peripheral blood films should be accompanied by a determination of the species by morphologic criteria and a calculation of the percentage of red blood cells infected by asexual malaria parasites (parasitemia).

A subsequent attack experienced by the same person but caused by a different *Plasmodium* species is counted as an additional case. A subsequent attack experienced by the same person

and caused by the same species in the U.S. may indicate a relapsing infection or treatment failure caused by drug resistance.

Permanent slides from all diagnosed and suspected cases must be sent to the Bureau of Public Health Laboratories.

Cases also are classified according to the following World Health Organization categories:

- Autochthonous:

 Indigenous: Malaria acquired by mosquito transmission in an area where malaria is a regular occurrence.
 Introduced: Malaria acquired by mosquito transmission from an imported case in an area where malaria is not a regular occurrence.
- Imported: Malaria acquired outside a specific area (e.g., the U.S. and its territories).
- Induced: Malaria acquired through artificial means (e.g., blood transfusion, common syringes, malariotherapy).
- Relapsing: Renewed manifestation (i.e., of clinical symptoms or parasitemia) of malarial infection that is separated from previous manifestations of the same infection by an interval greater than any interval resulting from the normal periodicity of the paroxysms.
- Cryptic: An isolated case of malaria that cannot be epidemiologically linked to additional cases.