



Anopheles freeborni, a malaria vector found in the United States, is shown feeding on a human. Though local malaria transmission has not been reported in Colorado for a very long time we do have *Anopheles* mosquitoes that can transmit this disease, and Colorado's state board of health has made malaria a reportable condition. Cases of malaria that occur in our state residents are reported each year to CDC's national malaria surveillance program.

What is malaria?

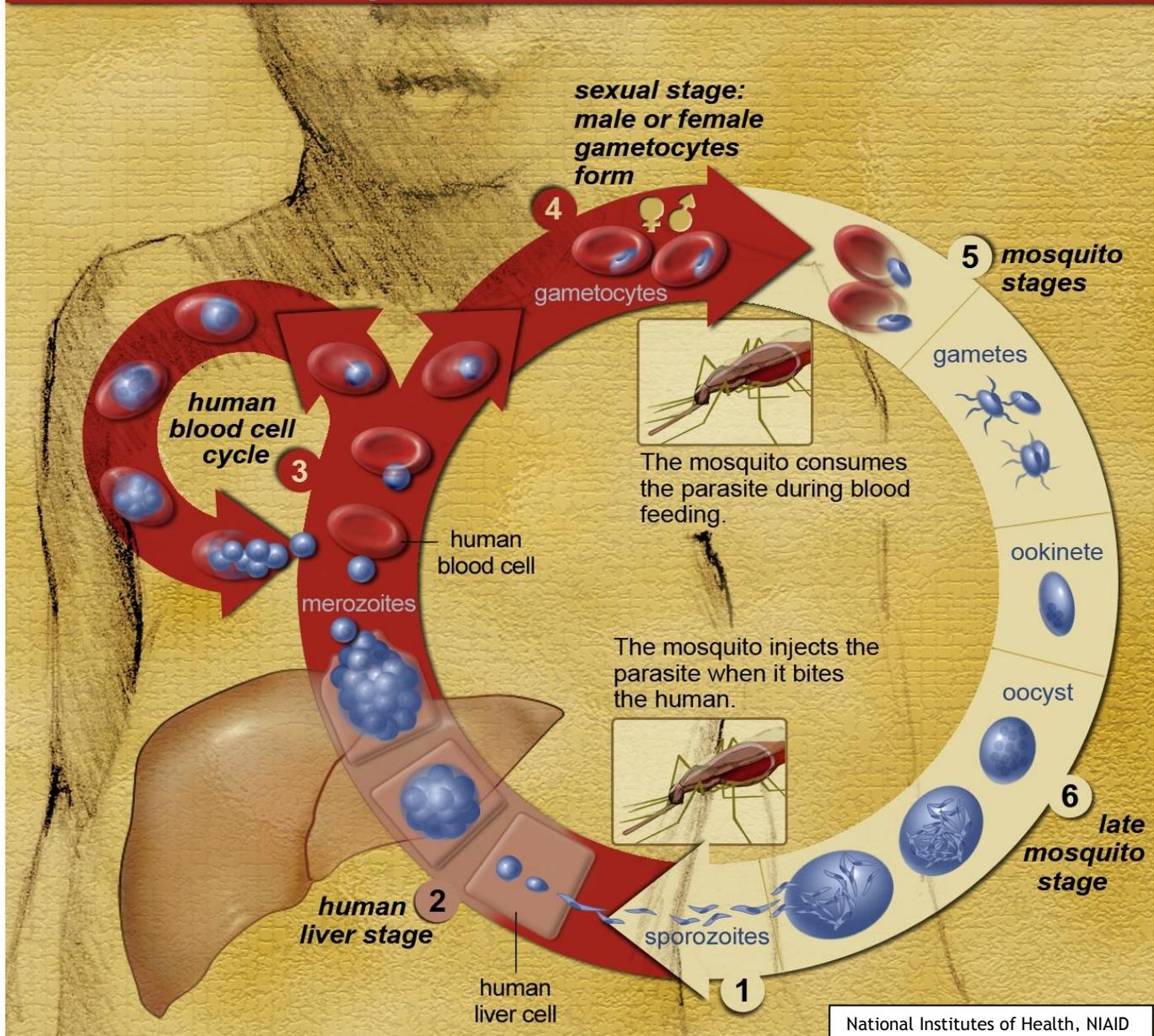
Malaria is a disease caused by an infection with a protozoal parasite in the genus *Plasmodium*. Five species of this parasite are known to cause disease in humans. There are also *Plasmodium* species that infect other animals such as birds, rodents and bats. Malaria is transmitted by the bites of infected female *Anopheles* mosquitoes which are present in many parts of the world.

Malaria originated in Africa and the parasite subsequently evolved over millions of years into the currently recognized

species infecting human populations. The disease was introduced into the Americas in the 1400s, and became widespread throughout North and South America. Malaria persisted in North America into the 1950s, until the use of insecticides such as DDT and environmental modifications of mosquito habitats eradicated it from the US. Malaria is also endemic in Asia.

Humans are the reservoir for malaria. The life cycle of the malaria parasite is shown in the figure below. When a vector mosquito injects the parasite into a person

Life Cycle of the Malaria Parasite



during feeding (#1), the malaria sporozoites travel to the liver and replicate there as merozoites (#2). The merozoites then leave the liver and enter the bloodstream where they parasitize red blood cells (RBCs). Inside the RBCs the parasite develops and differentiates into several different forms including the sexual forms, i.e. the gametocytes. Each cycle of parasite

reproduction in the RBCs is marked by a fever when new merozoites burst from the cells to infect RBCs (#3). The duration of the fever cycle in an infected person differs depending on the infecting *Plasmodium* species. When a mosquito bites the infected person and ingests the gametocytes in its bloodmeal (#5), it becomes infected with the parasite and the cycle starts over.

I have a case of malaria in CEDRS, what should I do?

You will need to complete the first page of the malaria case report form and the CEDRS record. This can almost always be accomplished through a review of the medical case notes. Interviews with healthcare providers or case patients are seldom necessary to complete the form.

1. Wait a couple of weeks from the sample collection date.
 - a. This allows time for all the transcription to be completed on the patient's record, and for the discharge summary or follow up notes to be available.
2. Call the hospital or healthcare provider and request all the medical case notes relating to the patient's illness.
3. Complete the malaria case report form.
4. A healthcare provider interview will be required if the medical case notes do not provide the drug of treatment.
5. A case interview (or possibly a healthcare provider interview) will be required if information is missing from the medical case notes such as
 - a. where the patient traveled to or from
 - b. date of onset (however, a best estimate can be made from the medical case notes, i.e. if the notes list that symptom onset was about 2 weeks ago then you may choose a date)
6. Examples when a case interview is NOT required are if
 - a. height or weight is missing
 - b. it is unknown whether malaria chemoprophylaxis was taken
 - c. if it is unknown if there was a history of malaria in the past 12 months
7. If information about the laboratory test is missing and cannot be ascertained from

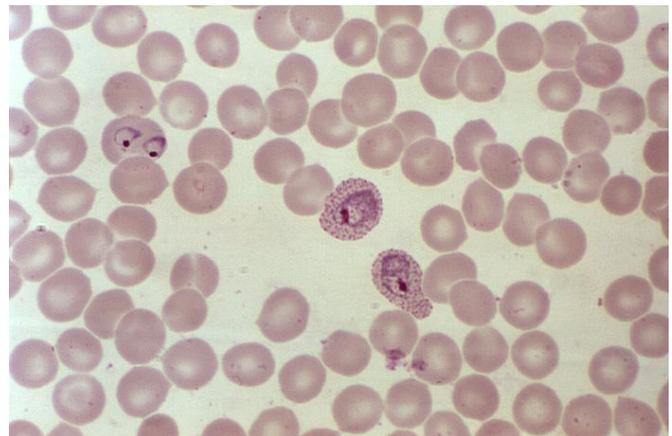
the medical case notes, call the hospital laboratory for the details

- a. an example is if the *Plasmodium* species or % parasitemia is missing

Understanding the laboratory tests for malaria.

Blood Smear

The most common laboratory test we see for malaria is the blood smear. Blood smears tell you whether or not malaria parasites are present, the species of parasite and the percent parasitemia. Both thin and thick smears are used in the diagnosis of malarial infection. The thin smear is best for determining the species of the malarial parasite, whereas the thick smear is useful for detecting low levels of parasitemia (increased sensitivity).



This blood smear shows malaria parasites reproducing in red blood cells. Eventually, the new merozoites will burst from the cells to infect other cells.

A peripheral blood smear is most often obtained during the acute phase of illness. However, blood smears are also used to monitor treatment efficacy, and sequential blood smears should demonstrate a decreasing parasitemia if the treatment is working. If the parasitemia remains the same or increases, this can be an indication that

the parasite is resistant to that medication and the healthcare provider should switch to another treatment. Epidemiologists should ensure that the initial parasitemia level is annotated on the case report form, as this along with *Plasmodium* species is predictive of illness severity.

Rapid Diagnostic Test (RDT)

The RDT is an antigen-based stick, cassette or card test for malaria in which a colored line indicates that *Plasmodium* antigen has been detected. Results are usually ready in 15-20 minutes. RDTs can differentiate between falciparum and non-falciparum antigens, but are otherwise generally not useful in species identification. Also, the percent parasitemia cannot be detected with an RDT.

Other Tests

Polymerase chain reaction tests can be used to confirm a diagnosis and determine the infecting species of *Plasmodium*. However, they are not used frequently due to lack of commercial availability. Serology is not useful for the diagnosis of acute disease, as antibody to malaria can persist for years.

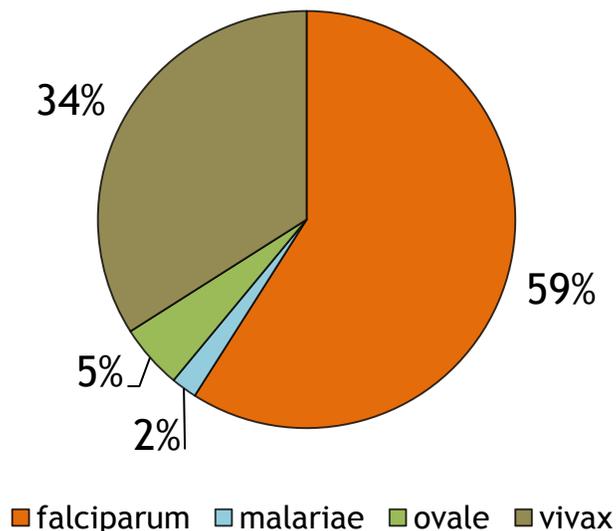
How do people get malaria?

People get malaria when they are bitten by malaria mosquito vectors. These are mosquitoes in the genus *Anopheles*, and they are present in many areas of the world including in the United States.

In the United States, most people diagnosed with malaria were infected by a mosquito in a country where malaria is known to occur. Many cases in Colorado are people who visited family in another country, commonly in sub-Saharan Africa. A few cases occur in

missionaries, business people, Peace Corps volunteers and military members.

Plasmodium species infecting Colorado malaria cases (n=129) 2010-2014



There have been only a few isolated instances of malaria acquired in recent decades from mosquitoes in the United States. For example, in 2003 there were seven reported cases of *Plasmodium vivax* in Palm Beach, Florida in people who had not had malaria before and who had not recently traveled outside of the country. This small outbreak likely began when a local *Anopheles* malaria vector fed upon a person with parasites in their blood. The relapsing forms of malaria can go unrecognized and untreated in people, and be a source of infection for local malaria vectors in the US. It is also possible for people who have lived in malaria endemic areas to acquire partial immunity to the disease, sometimes appearing asymptomatic.

The clinical picture for malaria

Malaria symptoms usually begin 10-15 days after the bite of an infected mosquito, but can start as early as 7 days after. Symptoms often begin as mild fever, headache, chills and vomiting. More severe symptoms can develop and include anemia, respiratory distress, renal failure and cerebral involvement (cerebral malaria).

Characteristics of <i>Plasmodium</i> species that infect humans			
Species**	% U.S. cases*	Disease form	Endemic areas
<i>falciparum</i>	58	Often severe, progresses rapidly	Mostly Sub-Saharan Africa
<i>vivax</i>	17	Relapsing, can lead to enlarged spleen	Asia, South America, North Africa
<i>ovale</i>	3	Relapsing	West Africa, Southeast Asia
<i>malariae</i>	3	Non-relapsing, low parasite load	Sub-Saharan Africa, Southeast Asia
<i>knowlesi</i>	0	Rare, non-relapsing, severe	Southeast Asia

*Based on 2012 CDC surveillance data
 **Infecting species was not reported for 17% of cases

Plasmodium falciparum causes the most common form of malaria, and symptoms can become severe in as little as 24 hours without appropriate treatment. *Plasmodium vivax* and *P. ovale* can lay dormant in the liver of an infected person, causing relapses months to years after the initial infection.

Plasmodium knowlesi is considered a more direct zoonotic infection, as vector mosquitoes of this form of malaria obtain their infective bloodmeals from non-human primate reservoirs in forests in southeast Asia. These mosquitoes then bite humans that enter areas where *P. knowlesi* malaria is circulating. Generally these malaria cases occur in people who enter these forested areas for work or recreation.

What's the treatment for malaria?

Chloroquine used to be the most commonly used drug for treating malaria. However, *P. falciparum* and *P. vivax* have developed resistance to the drug in some areas. Chloroquine or hydroxychloroquine can still be used for treatment in areas with chloroquine-sensitive malaria. This includes parts of Central America, parts of the Caribbean and the Middle East.

Healthcare providers should ascertain the species of malaria and the region where it was acquired before starting treatment. For uncomplicated malaria, suggested treatments are atovaquone-proguanil (brand name Malarone), artemether/lumefantrine (brand name Coartem), or quinine with doxycycline, tetracycline, clindamycin or mefloquine (brand name Lariam). For severe malaria, intravenous quinidine coupled with intravenous doxycycline, tetracycline, or clindamycin is recommended.

Treatment regimens for *Plasmodium vivax* and *P. ovale* should include primaquine to prevent relapse, except for patients with a glucose-6-phosphate dehydrogenase (G6PD) deficiency. A G6PD deficiency causes the body to break down red blood cells prematurely. People who have a G6PD deficiency that use primaquine run the risk of potentially life-threatening hemolysis and resulting anemia. The degree of severity of the hemolytic episode is unpredictable which is why it is recommended that people with a G6PD deficiency of any kind not use primaquine as a treatment for malaria. Glucose-6-phosphate dehydrogenase enzyme testing should be performed to identify if a patient has a deficiency before primaquine treatment is started.

Was the patient treated with Coartem?

The second page of the CDC case report form should be filled out for all malaria cases that were treated with Coartem (combination drug artemether/ lumefantrine). Coartem is the World Health Organization's recommended treatment for uncomplicated malaria due to increasing chloroquine resistance and the fact that it is relatively inexpensive to produce. However, studies have shown mixed findings with respect to its effectiveness, and few studies have looked at potential side effects of the drug. CDC is collecting the information from the second page of the case report form to obtain a better idea of Coartem's effectiveness and safety.

Completing the case in CEDRS

Malaria case report forms are faxed to CDC upon completion or semi-annually. Case notes in CEDRS should also be filled out for each case, as this is Colorado's source of information on our malaria cases. A summary of the case report form, i.e. the illness, travel history, prophylaxis, malaria treatment and other information collected on the case report form should be included in the CEDRS record.

Resources

Public health resources for malaria are available at [CDPHE's Malaria webpage](#), or at www.colorado.gov/pacific/cdphe/malaria.