

Malaria

Disease plan

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Last updated: October 21, 2022, by Hannah Rettler

Questions about this disease plan?

Contact the Utah Department of Health and Human Services Office of Communicable Diseases:
801-538-6191.

Malaria critical clinician information

Clinical evidence
Signs/symptoms <ul style="list-style-type: none">• Fever• Chills• Sweating• Headache• Nausea• Diarrhea• Jaundice• Enlarged liver and/or spleen• Renal failure• Encephalopathy
Communicability <ul style="list-style-type: none">• Rarely transmitted person-to-person via transfusion, contaminated needles, or organ transplantation.
Incubation period <ul style="list-style-type: none">• <i>P. falciparum</i>—12 days (range 8 to 25 days)• <i>P. vivax</i> and <i>P. ovale</i>—12 days• <i>P. malariae</i>—18 days (15 to 35; occasionally months to years)
Mode of transmission <ul style="list-style-type: none">• Malaria is spread to humans by the bite of an infected Anopheles mosquito
Laboratory testing
Type of lab test <ul style="list-style-type: none">• Blood smear or blood film: smears should be prepared as soon as possible after collection• Antigen rapid diagnostic test (RDT)• Nucleic acid test (PCR or NAT)• Immunofluorescence (IFA) or enzyme linked immunosorbent assay (ELISA)
Type of specimens <ul style="list-style-type: none">• 3–5 mL blood in EDTA tube stored at 4°C<ul style="list-style-type: none">◦ Nucleic acid test• 3–5 mL serum or plasma in serum separator tube (SST)<ul style="list-style-type: none">◦ IFA or ELISA
Treatment recommendations
Type of treatment <ul style="list-style-type: none">• Chloroquine• Sulfadoxine-pyrimethamine• Mefloquine• Atovaquone proguanil• Quinine• Doxycycline

Chemoprophylaxis <ul style="list-style-type: none">• Travelers have a choice of recommended prophylaxis, depending on country of travel
Contact management
Isolation of case <ul style="list-style-type: none">• None
Quarantine of contacts <ul style="list-style-type: none">• None
Infection control procedures <ul style="list-style-type: none">• Standard body substance precautions

Why is malaria important to public health?

Malaria is caused by a mosquito-borne parasite and is endemic throughout most of the tropics. According to the World Health Organization (WHO) there were an estimated 241 million cases of symptomatic malaria worldwide in 2020 and 627,000 deaths. About 2,000 cases of malaria are diagnosed in the United States each year. The vast majority of cases in the United States are in travelers and immigrants who return from countries where malaria transmission occurs including Africa, Southeast Asia, and the Eastern Mediterranean.

Important components to reduce the burden of malaria morbidity and mortality include more sensitive diagnostic tools, effective use of antimalarial drugs, and improved personal and community protection and mosquito control. The approach to elimination or control of malaria includes these basics, along with improvements in tracking human illness and parasite surveillance, and effective resource delivery.

Disease and epidemiology

Clinical description

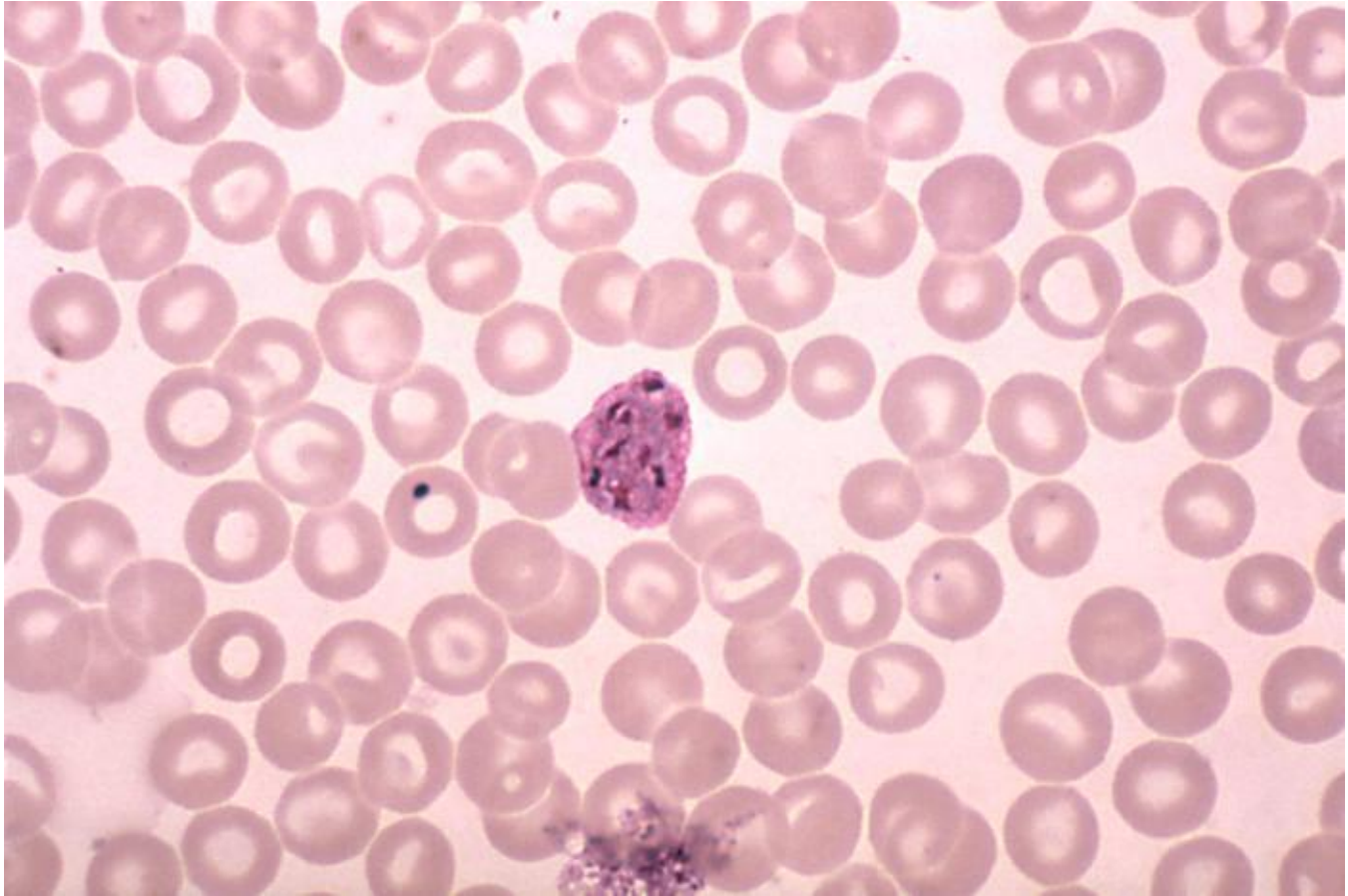
The classic symptoms of malaria are high fever with chills, sweats, and headache, which may involve recurrence or symptoms that become more intense, especially fever. Depending on the infecting species, fever may appear every other or every third day. Other symptoms may include malaise, nausea, vomiting, diarrhea, cough, arthralgia (joint aches), respiratory distress, and abdominal and back pain. Pallor and jaundice may also be present. Enlargement of the liver and spleen (hepatosplenomegaly) may occur and is more prominent in chronic infections.

Infection with *P. falciparum* is potentially fatal and most commonly manifests as a non-specific febrile illness. Falciparum malaria infection may present with coagulation defects, shock, renal and liver failure, acute encephalopathy, pulmonary and cerebral edema, and coma. The duration of an untreated primary attack can vary from a week to a month or longer. Without appropriate treatment, relapses of *P. vivax* and *P. ovale* infections can occur at irregular intervals for up to 5 years. Untreated malaria infections may persist for life (chronic infections), with or without recurrent episodes of fever.

Causative agent

There are 4 *Plasmodium* species (sporozoan parasites) that commonly cause malaria in humans: *P. vivax* (see Figure 1), *P. malariae*, *P. ovale*, and *P. falciparum*.

Figure 1: *Plasmodium vivax* schizonts



Note. Under a magnification of 1000X, this Giemsa-stained, thin film blood smear photomicrograph revealed the presence of an immature, *Plasmodium vivax* schizont, containing 8 chromatin masses. From CDC Image Library, by CDC/Dr. Mae Melvin, 1977 (<https://phil.cdc.gov/Details.aspx?pid=4940>). In the public domain.

Differential diagnosis

The differential diagnosis may include dengue fever, schistosomiasis, leptospirosis, tick-borne fevers, trypanosomiasis, and Yellow fever.

Laboratory identification

Malaria is usually diagnosed through a blood smear that can be performed at most reference laboratories. This technique remains the gold standard for laboratory confirmation of malaria. Rapid diagnostic tests (RDTs) are currently used in some clinical settings where reliable microscopic diagnoses are not available. RDTs allow for results within minutes, however, improving their accuracy and lowering their costs remain unaddressed issues. Nucleic acid testing by polymerase chain reaction (PCR) is slightly more sensitive than smear microscopy, but often doesn't produce results quickly enough for diagnosis. PCR is most useful to confirm the species of

the malarial parasite. Serology testing detects antibodies against malaria parasites which is indicative of past infection, and not current infection. For more information, click [here](#).

UPHL: The Utah Public Health Laboratory (UPHL) does not perform diagnostic testing for malaria, but it can forward specimens to CDC for testing. CDC can also perform serologic testing for malaria, but only under special circumstances (e.g., serum of a blood donor suspected of being a source of transfusion-related malaria, or serum from laboratories conducting malaria-related studies). Reference laboratories also perform diagnostic testing, and these results can be used for confirmation. It is not required to send samples to CDC, but if assistance is required to confirm the species of malaria, to test for malaria drug resistance, or there are indeterminate/discordant results, it is then appropriate to send them a specimen.

Treatment

Malaria can be a severe, potentially fatal disease (especially when caused by *Plasmodium falciparum*) and treatment should be started as soon as possible.

In endemic areas, WHO recommends treatment be started within 24 hours after the first symptoms appear. Treatment of patients with uncomplicated malaria can be conducted on an ambulatory basis (without hospitalization), but patients with severe malaria should be hospitalized, if possible.

In areas where malaria is not endemic, all patients with malaria (uncomplicated or severe) should be kept under clinical observation, if possible.

Most drugs used in treatment are active against the parasite forms in the blood (the form that causes disease) and include:

- Chloroquine*
- Sulfadoxine-pyrimethamine (Fansidar®)
- Mefloquine (Lariam®)
- Atovaquone-proguanil (Malarone®)
- Quinine
- Doxycycline

In addition, primaquine is active against the dormant parasite liver forms (hypnozoites) and prevents relapses. Primaquine should not be taken by pregnant individuals or by people who are deficient in G6PD (glucose-6-phosphate dehydrogenase). Patients should not take primaquine until a screening test has excluded G6PD deficiency.

*In a region of chloroquine resistance in Malawi, return of chloroquine-susceptible *P. falciparum* malaria was demonstrated following abandonment of chloroquine use. These chloroquine-susceptible parasites likely represent a re-expansion of the susceptible parasites that survived in the population despite widespread drug pressure in the region. Despite this finding, it is not advised to use chloroquine for treatment in Malawi.

The appropriate treatment for a patient with malaria depends on:

- The type (species) of the infecting parasite
- The area where the infection was acquired and its drug-resistance status
- The clinical status of the patient
- Any accompanying illness or condition
- Pregnancy
- Drug allergies, or other medications taken by the patient

Case fatality

The case fatality rate is 10–40% in the absence of prompt treatment.

Reservoir

Humans are the only important reservoir of human malaria. Non-human primates are naturally infected by many malarial species that can potentially infect humans, but natural transmission from non-human primates to humans is extremely rare and seldom results in serious disease. The vector for human malaria is the Anopheles mosquito, which transmits the parasite from infected human to uninfected human.

Transmission

Malaria is transmitted by the bite of an infectious female Anopheles mosquito. They mainly bite between dusk and dawn. Rarely, transmission can be congenital (via the placenta) or can occur through transfusions, use of contaminated needles, and organ transplantation.

Susceptibility

Susceptibility is universal except in humans with specific genetic traits. Tolerance to clinical disease is present in adults in highly endemic communities where exposure is continuous over many years. Persons with sickle cell trait show relatively low parasitemia when infected with *P. falciparum*, and, thus, are relatively protected from severe disease. Persons infected with HIV are at increased risk of symptomatic falciparum malaria and its severe manifestations.

Incubation period

Following the bite of an infected female *Anopheles* mosquito, the inoculated sporozoites migrate to the liver within 1 to 2 hours. Individuals are generally asymptomatic for 12 to 35 days after infection, but symptoms can start as early as 7 days (depending on parasite species). Symptoms begin during the erythrocytic stage of the parasite life cycle, when infected red cells rupture and release merozoites, leading to fever and other symptoms.

In most cases, infections due to *P. falciparum* become clinically apparent within 1 month after exposure.

The incubation period for the relapsing species, *Plasmodium vivax* and *Plasmodium ovale*, is also about 2 weeks; however, illness can occur months after initial infection due to activation of residual hypnozoites in the liver. Relapses generally occur within 2 to 3 years of infection; with even longer periods of dormancy being reported.

The incubation period for *Plasmodium malariae* is about 18 days; however, low-grade asymptomatic infections can (very rarely) persist for years. *P. falciparum* and *P. malariae* have no dormant (hypnozoite) phase, hence do not relapse.

Table 1. Comparing the malaria species

	<i>Plasmodium falciparum</i>	<i>Plasmodium vivax</i>	<i>Plasmodium ovale</i>	<i>Plasmodium malariae</i>	<i>Plasmodium knowlesi</i>
Geography	Tropical, temperate zones	Tropical, temperate zones, absent from West Africa	Tropical, endemic in West Africa, present in Philippines, Indonesia, and Papua New Guinea	Tropical, isolated pockets	Southeast Asia
RBC preference	RBCs of all ages	Young RBCs (reticulocytes)	Young RBCs (reticulocytes)	Older RBCs	RBCs of all ages
Infected RBC diameter	Normal	Larger than normal	Larger than normal	Normal or smaller than normal	Normal
Ameboid trophozoites	No	Yes	Yes	No	No
Band forms	No	No	No	Yes	Yes

Malaria: Utah public health disease investigation plan

Schizont*	16 to 20 merozoites; very rare in peripheral circulation	20 to 24 merozoites	4 to 16 merozoites (8 typical)	6 to 12 merozoites (8 or 10 typical)	8 to 16 merozoites (10 typical)
Parasitemia	Can be very high	Usually <2%	Usually <2%	Usually very low	Can be high
Disease severity	End organ damage and death can occur	End organ damage and death less common than <i>P. falciparum</i> but can occur	Severe disease uncommon	Severe disease rare	Severe disease can occur
Chloroquine resistance	Yes	Yes	No	Rare	No
Relapses from liver	No	Yes	Yes	No	No
Incubation period	12 days (8 to 25)	14 days (10 to 30; occasionally months)	15 days (10 to 20)	18 days (15 to 35; occasionally months to years)	11 days (9 to 12)
Prepatent period [¶]	11 days	12 days ^Δ	12 days	32 days	Uncertain in naturally infected humans
Cycle in red cell	48 hours	48 hours	48 hours	72 hours	24 hours

Note. RBC: red blood cell. From “Malaria: Clinical manifestations and diagnosis in nonpregnant adults and children,” by L. C. Cohee and K. Seydel, 2022, *UpToDate* (Retrieved September 30, 2022 from https://www.uptodate.com/contents/malaria-clinical-manifestations-and-diagnosis-in-nonpregnant-adults-and-children?search=malaria&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1#H2). Copyright 2022 by UpToDate, Inc. and/or its affiliates.

* Identification of a schizont with >12 merozoites in the peripheral circulation is an important diagnostic clue for *P. vivax*. In general, schizonts of *P. falciparum* are very rarely seen in blood films; they occur only in the setting of severe disease with hyperparasitemia.

¶ The prepatent period is the time from mosquito bite to the first appearance of parasites in the peripheral blood (as detected by microscopy).

Δ The latency period of *vivax* is typically longer than *falciparum* (refer to UpToDate table summarizing time to symptoms for each species).

Period of communicability

Malaria is not directly communicable from person to person, except through congenital transmission; however, during parasitemia, the disease may be transmitted to other persons through blood transfusion or through shared, contaminated needles. Infected human hosts can be a source of infection for *Anopheles* mosquitoes for prolonged periods of time (1–3 years or longer, depending on the species of malaria) if not adequately treated.

Epidemiology

Malaria is endemic throughout the tropical areas of the world. About half of the world's population lives in areas where transmission occurs. Areas with the highest prevalence include sub-Saharan Africa, parts of Central and South America, India, and parts of Oceania and Southeast Asia. Transmission is also possible in more temperate climates, such as in the U.S., if *Anopheles* mosquitoes are present. Locally-acquired cases of malaria have been reported recently in Florida, New York, and Virginia. Mosquitoes in airplanes flying from tropical climates have been the source of occasional cases in persons who work or live near international airports. However, nearly all of the malaria cases reported annually in the U.S. (~2,000) are acquired outside of the U.S. *P. vivax* and *P. falciparum* are the most common species worldwide. The worldwide spread of strains of chloroquine-resistant *P. falciparum* and *P. vivax* is of increasing importance. Resistance to other antimalarial drugs is now occurring in many areas where the drugs are widely used. All cases of Malaria reported in Utah were acquired outside of the country.

Public health control measures

Public health responsibility

- Identify the source of infection and prevent further transmission.
- Investigate all reported cases; complete and submit proper investigation forms.

Prevention

International travel

People who travel to malaria-endemic parts of the world should be notified of their risk of contracting the disease and of control measures they can take to protect themselves from mosquitoes. Travelers can use repellents, wear protective clothing, and use mosquito nets when rooms are not screened. They have a choice of medications recommended for prophylaxis depending on circumstances.

Detailed recommendations for preventing malaria are available 24 hours a day from the CDC Malaria Hotline, which can be accessed by telephone at 770-488-7788, by fax at 888-CDC-FAXX or 888-232-3299, or on the CDC website at www.cdc.gov/travel.

Travelers and recent immigrants from malaria-endemic regions with symptoms suggestive of malaria should be referred to a health care provider for prompt testing and treatment. Failure to treat individuals who have malaria could lead to transmission of the disease to mosquitoes that bite these individuals, and then to other people bitten by those mosquitoes.

Chemoprophylaxis

Non-immune individuals who will be exposed to mosquitoes in areas where malaria is common should make use of protective measures against mosquito bites, and will benefit from the use of suppressive drugs for chemoprophylaxis. The possible side effects of long-term (up to 3–5 months) use of the drug or drug combination recommended for use in any particular area should be weighed against the actual likelihood of being bitten by an infected mosquito.

Vaccine

In October 2021, the World Health Organization (WHO) recommended the widespread use of the RTS,S/AS01 (RTS,S) malaria vaccine among children in sub-Saharan Africa and in other regions with moderate to high *P. falciparum* malaria transmission. The recommendation is based on results from an ongoing pilot program in Ghana, Kenya, and Malawi that has immunized more than 900,000 children since 2019.

Based on the advice of 2 WHO global advisory bodies, the WHO recommends that "the RTS,S/AS01 malaria vaccine be used for the prevention of *P. falciparum* malaria in children living in regions with moderate to high transmission as defined by WHO. RTS,S/AS01 malaria vaccine should be provided in a schedule of 4 doses in children (starting at) 5 months of age for the reduction of malaria disease and burden."

RTS,S/AS01 vaccine

The RTS,S vaccine consists of a recombinant fusion protein created based on an antigen target consisting of a repetitive sequence of 4 amino acids in the circumsporozoite antigen on the surface of the *P. falciparum* sporozoite. "RTS" stands for "repeat T epitopes" derived from the circumsporozoite protein, "S" stands for the S antigen derived from hepatitis B surface antigen (HBsAg), and AS01 is a proprietary adjuvant.

Phase III trial results of the RTS,S/AS01 vaccine among 15,459 infants demonstrated that the vaccine induced partial protection against clinical malaria among children ages 5 to 17 months over the follow-up period of the trial (children were followed up for a median of 48 months, range

39–50 months). In each study group, three doses of RTS,S/AS01 were administered at months 0, 1, and 2, and a booster dose at 20 months of age. Efficacy was enhanced by the administration of a booster dose in both children and infant age categories.

The RTS,S/AS01 vaccine has been observed to afford greater protection against clinical malaria infection caused by parasites that match the vaccine in the circumsporozoite protein allele than malaria infection caused by parasites with a mismatched allele.

Data on how long this vaccine protects against malaria is particularly important since, depending on the regional transmission intensity, the risk of death due to malaria may continue for many years. Thus far, efficacy data beyond 6 months are limited, since vaccinations were administered prior to the start of malaria season, and there were few cases of malaria 6 to 12 months after vaccination.

Isolation and quarantine requirements:

No restrictions, except for exclusion from blood donation.

Case investigation

Reporting

- Report all suspect and confirmed cases of malaria.

Table of criteria to determine whether a case should be reported to public health authorities

Criterion	
<i>Laboratory evidence</i>	
Demonstration of <i>Plasmodium</i> species in blood film	S
Demonstration of <i>Plasmodium</i> species by molecular testing (e.g., PCR)	S
Demonstration of unspiciated malaria parasite in blood film*	S
Detection of <i>Plasmodium</i> species by rapid diagnostic antigen testing	S

Notes: S = This criterion alone is sufficient to identify a case for reporting.

*Efforts should be made to determine a species for all cases of malaria either by expert microscopists or by molecular methods such as PCR.

Case definition (Most recently updated in 2014)

Malaria

Laboratory criteria

- Detection of circulating malaria specific antigens using rapid diagnostic test (RDT), **or**

- Detection of species specific parasite DNA in a sample of peripheral blood using a polymerase chain reaction (PCR) test (Note: laboratory developed malaria PCR tests must fulfill clinical laboratory improvement amendments (CLIA) requirements, including validation studies), **or**
- Detection of malaria parasites in thick or thin peripheral blood films, determining the species by morphologic criteria, and calculating the percentage of red blood cells infected by asexual malaria parasites (parasitemia).

Case classification

Confirmed

- Detection and specific identification of malaria parasite species by microscopy on blood films in a laboratory with appropriate expertise in any person (symptomatic or asymptomatic) diagnosed in the U.S., regardless of whether the person experienced previous episodes of malaria while outside the country, **or**
- Detection of Plasmodium species by nucleic acid test* in any person (symptomatic or asymptomatic) diagnosed in the U.S., regardless of whether the person experienced previous episodes of malaria while outside the country, **or**
- Detection of unspiciated malaria parasite by microscopy on blood films in a laboratory with appropriate expertise in any person (symptomatic or asymptomatic) diagnosed in the U.S., regardless of whether the person experienced previous episodes of malaria while outside the country.

Suspect

- Detection of Plasmodium species by rapid diagnostic antigen testing without confirmation by microscopy or nucleic acid testing in any person (symptomatic or asymptomatic) diagnosed in the U.S., regardless of whether the person experienced previous episodes of malaria while outside the country.
- Clinical samples, including blood smears or EDTA whole blood from all cases, may be referred to the CDC Division of Parasitic Diseases and Malaria Diagnostic Laboratory for confirmation of the diagnosis and antimalarial drug resistance testing. Any questionable cases should be referred to the CDC Division of Parasitic Diseases and Malaria Diagnostic Laboratory for confirmation of the diagnosis.

Criteria to distinguish a new case of this disease or condition from reports or notifications which should not be enumerated as a new case for surveillance:

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, or a separate attack and is *not* counted as an additional case.

Cases also are classified according to the following WHO 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, or malariotherapy).
- **Relapsing:** recurrence of disease after it has been apparently cured. In malaria, true relapses are caused by reactivation of dormant liver stage parasites (hypnozoites) of *P. vivax* and *P. ovale*.
- **Cryptic:** an isolated case of malaria that cannot be epidemiologically linked to additional cases.

Case classification table

Criterion	Case Definition	
	Confirmed	Suspected
<i>Laboratory evidence</i>		
Demonstration of Plasmodium species in blood film	S	
Demonstration of Plasmodium species by molecular testing (e.g., PCR)	S	
Demonstration of malaria parasite in blood films*	S	
Detection of Plasmodium species by rapid diagnostic antigen testing without confirmation by microscopy or nucleic acid testing in any person (symptomatic or asymptomatic)		S

Notes S = This criterion alone is sufficient to classify a case

*Efforts should be made to determine a species for all malaria cases either by expert microscopists or molecular methods such as PCR.

Case investigation process

- Complete morbidity form.
- Verify case status.
- Complete disease investigation form.
- Determine whether patient had travel/exposure history consistent with acquisition of disease in Utah or elsewhere.
- If patient acquired disease in Utah, identify the source of transmission and eliminate it.

Outbreaks

One or more non-imported cases of malaria would constitute an outbreak.

Identification of case contacts

Determine history of previous infection or of possible exposure. If a history of sharing needles is obtained from the patient, investigate and treat all persons who shared the equipment. In transfusion-induced malaria, all donors must be located and their blood examined for malaria parasites and for antimalarial antibodies; parasite-positive donors must receive treatment.

Case contact management

None.

References

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Version control

Updated July 2015: "Why is Malaria Important to Public Health" section added. Additional information added to "Treatment" section. "Version Control," and "Minimum Data Set" sections added.

Updated October 2017: "Critical Clinician Information", "Laboratory Identification", and sections in the "Case Investigation" section which differed from CSTE.

Updated September 2022: Updated Minimum Required Fields. Updated reference list to include Malaria CSTE case definition and CDC Malaria FAQ. Updated Vaccine information. Updated incubation period information. Updated style to match DHHS style guidelines.

UT-NEDSS/EpiTrax minimum/required fields by tab

Demographic

- Last name
- First name
- County
- State
- Street
- City
- ZIP code
- Date of birth
- Birth gender
- Ethnicity
- Race
- Weight

Clinical

- Disease
- Date diagnosed
- Died?
- Date of death
- Onset date
- Hospitalized?
- Admission date
- Discharge date
- Admitted as inpatient?
- Was malaria chemoprophylaxis taken?
- If yes, what type?
- Were all pills taken as prescribed?
- If not, why were doses missed?
- If side effects reported, specify
- History of malaria in the last 12 months (prior to this report)?
- If yes, date of previous malaria?
- Malaria species associated with previous illness? (Vivax, Falciparum, Malariae, Ovale, Not Determined)
- Was malaria treatment given?

- Were there complications related to this malaria incident?

Laboratory

- Organism
- Specimen source
- Test result
- Test type

Investigation

- Imported from
- Date of exposure
- Has patient traveled or lived outside the United States during the past 2 years?
- Please specify countries, dates arrived in the U.S. and duration of stay
- Blood transfusion/transplant within the past 12 months?
- Has the subject received a blood transfusion or organ transplant in the 12 months prior to this illness?
- If yes, date of transfusion/transplant
- Was specimen sent to CDC for confirmatory testing?

Reporting

- Date first reported to public health

Administrative

- Outbreak name
- Outbreak associated
- State case status