

Malaria

5/27/2025

DISEASE REPORTABLE WITHIN 24 HOURS OF DIAGNOSIS

Cases should be reported to the local health department where the patient resides. If patient residence is unknown, report to your own local health department. Contact information is available at: http://localhealth.nj.gov.

If the individual does not live in New Jersey, report the case to the New Jersey Department of Health at: (609) 826-5964.

THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

There are approximately 156 named species of *Plasmodium* which infect various species of vertebrates. Four species are considered true parasites of humans, as they utilize humans almost exclusively as a natural intermediate host: *P. falciparum*, *P. vivax*, *P. ovale* and *P. malariae*. However, there are periodic reports of simian malaria parasites being found in humans, most reports implicating *P. knowlesi*. It has not been determined if *P. knowlesi* is being naturally transmitted from human to human via the mosquito, without the natural intermediate host (macaque monkeys, genus Macaca) and therefore, *P. knowlesi* is still considered a zoonotic malaria, but it can also cause illness in humans.

B. Clinical Description

Infection can range from asymptomatic or mild to severe and fatal. The classic symptoms of malaria are high fever with chills, sweats, and headache, which may be paroxysmal (involving recurrence or intensification of symptoms). However, the first symptoms are often nonspecific and mimic those of other viral infections, such as influenza. The fever and paroxysms generally occur in a cyclic pattern. Depending on the infecting species, fever may appear every other or every third day. Other symptoms can 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. The clinical presentation can vary substantially depending on the infecting species, the level of parasitemia, and the immune status of the patient.

Infections caused by *P. falciparum* are the most likely to progress to severe, potentially fatal forms with central nervous system involvement (cerebral malaria), acute renal failure, severe anemia, or acute respiratory distress syndrome, especially for infants and children aged <5 years and among persons who do not have acquired immunity. Other species can also have severe manifestations. Patients suspected of having malaria should be urgently evaluated. The case-fatality rate is 10% to 40% in the absence of prompt treatment. The duration of an untreated primary attack can vary from a week to a month or longer. There have been reports of *P. falciparum* survival in human hosts for greater than two years if untreated.

If the initial malaria infection is not treated adequately, some parasites may remain and cause a relapse. To prevent future relapses, *P. vivax* and *P. ovale* infections require treatment to kill dormant hypnozoites in addition to treatment for the acute phase of malaria. Relapses of *P. vivax* and *P. ovale* infections can occur at irregular intervals for up to 5 years. If untreated, *P. malariae* may persist as an <u>asymptomatic infection</u> for life.

Chemoprophylaxis

All recommended chemoprophylaxis regimens involve taking a medicine before, during, and after travel to an area with malaria. Beginning the drug before travel allows it to be in the blood before the traveler is exposed to malaria parasites. When choosing a chemoprophylaxis regimen, the traveler and healthcare provider should consider several factors, including the presence of antimalarial drug resistance in the area of travel, length of travel, the patient's other medical conditions, allergy history, other medications prescribed or already being taken (to assess possible drug interactions), potential side effects, and the cost of the antimalarial. Long-term travelers, defined as people who travel for ≥6 months, have additional

considerations (see <u>Box 5-11</u>). <u>Table 5-27</u> lists some of the benefits and limitations of medications used for malaria prophylaxis. Local health departments should convey to patients the importance of completing all prescribed antimalarials for future travel.

Treatment

The <u>CDC Malaria Treatment Tables</u> can be used as a guide for treatment of malaria in the US. Determining the *Plasmodium* species causing the malaria infection is important for treatment purposes.

- Plasmodium falciparum and P. knowlesi infections can cause rapidly progressive severe illness or death, while the other species, P. vivax, P. ovale, and P. malariae, are less likely to cause severe disease.
- *P. vivax* and *P. ovale* infections also require treatment for the hypnozoites, which remain dormant in the liver and can cause relapsing episodes.
- *P. falciparum* and *P. vivax* species have different drug resistance patterns in different geographic regions of the world.
- Urgent initiation of appropriate therapy is critical for P. falciparum and P. knowlesi infections.

When choosing a treatment regimen, it is important to take into account where the infection was acquired as it provides information on the likelihood of drug resistance and enables the healthcare provider to choose an appropriate treatment. Information on malaria risk and parasite resistance can be found in the malaria chapter in CDC's Yellow Book website.

For assistance with the diagnosis or treatment of malaria, healthcare provides may call the CDC Malaria Hotline (770-488-7788 or toll-free at 855-856-4713) from 9 a.m. to 5 p.m. Eastern Time. After hours, on weekends, or on holidays, call the CDC Emergency Operations Center at 770-488-7100 and ask the operator to contact the subject matter expert on call for the Malaria Branch.

C. Reservoirs

Humans are the primary reservoir of human malaria. Nonhuman primates are naturally infected by many malarial species that can potentially infect humans, but natural transmission from nonhuman primates to humans is extremely rare.

D. Modes of Transmission

Malaria is transmitted by the bite of an infective female *Anopheles* mosquito. For the *Anopheles* mosquito to become infective, they must bite, or take a blood meal, from a person already infected with the malaria parasites. About one week later, that same mosquito will bite the next person and subsequently inject the parasites via her saliva. In rare occasions, malaria can spread through blood transfusions, organ transplant, sharing needles or syringes contaminated with malaria-infected blood, or congenitally, from a mother to her unborn infant before or during delivery.

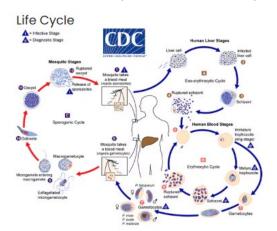
E. Incubation Period

The incubation period in most cases of malaria varies from 7 to 30 days. The shorter periods are most frequently observed with *P. falciparum* and the longer ones with *P. malariae*. *P. vivax* and *P. ovale* parasites have a dormant stage (hypnozoite) in the liver, making relapse common during the period of 45 days to 3

years after an initial illness. *P. vivax* parasites transmitted in some areas of Asia can have a long incubation period, lasting 6 or more months from inoculation to symptom onset. Antimalarial prophylaxis occasionally can delay the appearance of malaria symptoms by weeks or months, long after the traveler has left the malaria-endemic area, particularly with *P. vivax* and *P. ovale*. Returned travelers should always remind their healthcare providers of any travel during the past 12 months in areas where malaria occurs.

F. Period of Communicability or Infectious Period

Malaria is not directly communicable from person-to-person except for congenital transmission; however,



when parasites are present in the blood (parasitemic), they can be transmitted to other persons through blood transfusion, organ transplant, or through shared contaminated needles; and to *Anopheles* mosquitoes through a new mosquito bite.

The <u>malaria parasite lifecycle</u> is complex, involving several stages in humans and *Anopheles* mosquitoes. Clinical disease in humans and infectivity occurs when parasites are circulating in the blood. If the initial infection is untreated or inadequately treated, persons may remain infectious for years, depending on the species.

G. Epidemiology

Malaria was estimated to cause 241 million illnesses in 2020 and 627,000 deaths worldwide. Malaria is transmitted in 85 countries, and approximately one half of the world population is at risk for infection. Malaria is endemic throughout the tropical areas of the world and the areas with the highest prevalence include sub-Saharan Africa, parts of Central and South America, India, and parts of Oceania and Southeast Asia. Although malaria today is usually restricted to tropical and subtropical areas and altitudes below 1,500 m., in the past, malaria was endemic in much of North America, Europe and even parts of northern Asia. Altitude and climatic factors including temperature, humidity, and rainfall impact where malaria spreads and generally, in warmer regions closer to the equator, malaria transmission is more intense and can occur year-round. Temperature is particularly critical. For example, at temperatures below 20°C (68°F), *Plasmodium falciparum* cannot complete its growth cycle in the *Anopheles* mosquito.

P. falciparum causes the most infections worldwide; it is predominant in Africa where an estimated 95% of cases occur. In 2018, P. vivax accounted for approximately 3% of cases worldwide. P. vivax is found in a broad geographical area and although it contributed <1% of cases in Africa, it made up 75% of cases in the Americas, 50% of cases in Asia, and approximately 30%—35% of cases in the Eastern Mediterranean and Western Pacific regions. Compared with P. vivax and P. falciparum, transmissions of P. ovale spp., P. malariae and P. knowlesi species are limited. Approximately 95% of P. ovale spp. cases were identified in Africa, with 5% in Asia. P. malariae parasites are found throughout the tropics and subtropics and are often detected in mixed species infections. P. malariae parasites mature slowly in human and mosquito hosts and, although they do not typically cause severe symptoms in humans, can result in persistent low-density infections that can last for years, providing opportunities for ongoing transmission and health sequelae. P. knowlesi is predominantly a simian malaria found in Southeast Asia; however, it can be transmitted to persons, and in Malaysia, it has become the predominant species that causes malaria illness in humans. Exposure to forested areas with simian habitat is a risk factor for P. knowlesi.

In many temperate areas, such as western Europe and the United States, economic development and public health measures in the 1950s have succeeded in eliminating malaria. However, most of these areas have *Anopheles* mosquitoes that can spread malaria, and reintroduction of the disease remains a risk. Most malaria cases diagnosed in the United States are imported from countries with ongoing mosquito-borne transmission. Occasionally, congenitally acquired cases, induced cases (resulting from exposure to blood or tissue products), and cryptic cases (for which exposure cannot be easily explained despite investigation by state and local health departments and CDC) occur (mosquitoes in airplanes flying from tropical climates have been proposed as a potential source in persons working or living near international airports). During 1957–2003, a total of 63 malaria outbreaks occurred in the United States. A small number of locally-transmitted cases were identified in Florida, Texas, Maryland and Arkansas in 2023. Prior to that, the last well-documented local mosquito-borne transmission occurred in 2003, when eight cases were diagnosed among nontravelers in Palm Beach, Florida.

The number of cases diagnosed in the United States and its territories has been increasing since the mid-1970s. Of the 1,823 cases reported in 2018, 85.0% were imported cases that originated from Africa and 69.9% of the cases from Africa were from West Africa. Of the U.S. civilian patients who reported reason for travel, 77.0% were visiting friends and relatives. Chemoprophylaxis with antimalarial medications are recommended for U.S. residents to prevent malaria while traveling in countries where it is endemic. Among the 864 U.S. residents with malaria for whom information on chemoprophylaxis use and travel region were known, 95.0% did not adhere to or did not take a CDC-recommended chemoprophylaxis regimen. Among all reported malaria cases in 2018, a total of 251 (13.8%) were classified as severe malaria illness.

In New Jersey, an average of 86 travel-related cases of malaria per year (ranging from 72 to 101) were reported to the New Jersey Department of Health from 2021-2023 (refer to the NJDOH Vector-borne Disease Dashboard for additional information). In 2023, 69% of malaria cases in NJ were caused by *P. falciparum* followed by *P. vivax* (12%), *P. ovale* (5%), and *P. malariae* (2%); 12% of cases were not speciated. All cases reported international travel with Nigeria (19%), Sierra Leone (14%), Ghana (10%), India (7%) and Liberia (7%) being the most common destinations. One fifth of the cases reported in 2023 resided in Essex County. Almost half of all cases reported visiting friends or relatives as the primary reason for travel.

2 CASE DEFINITION

NJDOH follows the most current case definition as published on the CDC National Notifiable Disease Surveillance System (NNDSS) website.

Case Definition: https://ndc.services.cdc.gov/conditions/malaria/

Case definitions enable public health to classify and count cases consistently across reporting jurisdictions and should not be used by healthcare providers to determine how to meet an individual patient's health needs.

A. 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) test¹; 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).

B. Case classification

CONFIRMED

- Detection and specific identification of malaria parasite species by microscopy on blood films in a laboratory with appropriate expertise; OR
- Detection of Plasmodium species by nucleic acid test*; OR
- Detection of un-speciated malaria parasite by microscopy on blood films in a laboratory with appropriate expertise;

AND

o Individual (symptomatic or asymptomatic) is diagnosed in the US, regardless of whether the person experienced previous episodes of malaria while outside the country.

PROBABLE

Not used

POSSIBLE

 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 US, regardless of whether the person experienced previous episodes of malaria while outside the country.

C. Criteria to Distinguish a New Case of Malaria from a Prior Case

- 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 US
 may indicate a relapsing infection or treatment failure cause by drug resistance or a separate
 attack. LHDs should consult with CDS in these situations.

¹ * Laboratory-developed malaria PCR tests must fulfill CLIA requirements, including validation studies.

3 LABORATORY TESTING

<u>Microscopic identification</u>: Malaria parasites can be identified by examining under the microscope a drop of the patient's blood, spread out as a "blood smear" on a microscope slide. Prior to examination, the specimen is stained (most often with the Giemsa stain) to give the parasites a distinctive appearance. This technique remains the gold standard for laboratory confirmation of malaria. However, it depends on the quality of the reagents, of the microscope, and on the experience of the laboratorian. If the laboratory is not confident in their identification of the organism, fresh EDTA whole blood, stained and unstained smears and a completed <u>BACT-109 form</u> should be sent to NJDOH Public Health and Environmental Laboratories (PHEL) for confirmatory testing.

<u>Antigen Detection</u>: Various commercial laboratories offer testing to detect antigens derived from malaria parasites. Such immunologic ("immunochromatographic") tests most often use a dipstick or cassette format and provide results in 2-15 minutes. These "Rapid Diagnostic Tests" (RDTs) offer a useful alternative to microscopy in situations where reliable microscopic diagnosis is not available. Malaria RDTs are currently used in some clinical settings and programs.

Molecular testing: Parasite nucleic acids are detected using polymerase chain reaction (PCR). Although this technique may be slightly more sensitive than smear microscopy, it is of limited utility for the diagnosis of acutely ill patients in the standard healthcare setting. PCR results are often not available quickly enough to be of value in establishing the diagnosis of malaria infection. PCR is most useful for confirming the species of malarial parasite after the diagnosis has been established by either smear microscopy or RDT.

<u>Serology</u>: Serology detects antibodies against malaria parasites, using either indirect immunofluorescence (IFA) or enzyme-linked immunosorbent assay (ELISA). Serology does not detect current infection but rather measures past exposure.

4 PURPOSE OF SURVEILLANCE AND REPORTING

- To identity imported cases of malaria
- To ensure that cases are appropriate contained and treated to prevent the introduction of malarial parasites into native mosquito populations
- To identify locally acquired cases, if they occur, so appropriate active surveillance and mosquito control interventions can be implemented.
- To provide travelers with appropriate preventive health information.

5 CASE INVESTIGATION

A. Investigation

Local health departments are asked to investigate malaria reports and close cases in CDRSS within

Because of concerns about possible locally transmitted infections, local health departments are asked to initiate investigations of laboratory positive cases within 2 business days and enter critical details into CDRSS within 5 business days (disease investigation priority level 3). It is particularly important to document international travel history within this timeframe. If patients have difficulty remembering travel locations and dates, asking the patient to send a picture of their passport page can help identify relevant travel. To assist with the investigation, the Malaria Investigation Worksheet can be used to obtain essential information from the healthcare provider and patient. Information on the worksheet should be entered into CDRSS (do not send worksheets to NJDOH).

Electronic case reporting (eCR) has been added to malaria in CDRSS. eCR is the automated generation and transmission of case reports from the electronic health record to public health agencies for review and action. eCR makes disease reporting from healthcare to public health faster and easier. Now, EHRs may be appended to CDRSS cases for hospitalized patients with positive test results. These files are sent from acute care facilities and contain valuable information for case investigation, such as hospitalization dates, patient status, test results (including parasitemia levels), and possibly travel information. If an eCR case report is appended to a CDRSS case, review the file and enter the information needed for the case investigation into their specific fields within CDRSS. It is recommended to confirm all information with the case during the case interview.

A minimum of 3 attempts should be made to obtain information. Attempts to both the healthcare provider/infection preventionist and patient should be made before closing the case. After 3 attempts, enter what is known into CDRSS, including attempts to obtain information (dates and results of the attempts), and classify/close the case according to the case definition.

B. Key CDRSS Fields Specific for Malaria

CDRSS Screen	Required Information
Patient Personal Information	 Ensure name, sex, date of birth, race and ethnicity are entered. Enter country of birth Enter date first arrive in US for residency, if applicable
Laboratory and Diagnostic Test Information	 Review test result to determine if it meets laboratory criteria for case definition. If only an antigen test is documented, follow up with facility to see if a smear was ordered and the result. If species is known and not documented, enter it into the laboratory test result. Enter percent parasitemia (test name: <i>Plasmodium</i> infected red blood cells), if available.
Industry and Occupation	Enter industry/occupation

CDRSS Screen	Required Information
Signs/Symptoms	 Inquire if the patient had each sign/symptom and update the response to Yes, No or Unknown accordingly. Not Asked should not be left as a default response. Enter onset and resolution dates, if known.
Additional Requirements: Malaria	Enter information on prior malaria infections, travel and chemoprophylaxis.
Clinical Status	 Enter illness onset date, hospitalization (as part of this investigation), pre-existing conditions and mortality information.
Epidemiology	 Select international travel as transmission setting, if applicable Select appropriate method of import
Medical Facility and Provider Information	For admitted/hospitalized patients, ensure patient status is marked as INPATIENT and admission and discharge dates are entered.
Risk Factors	 Answer all risk factors questions. Focus on two years prior to illness for travel history Ask about receipt of blood transfusion or solid organ transplant in the year prior to symptom onset. Include dates and hospital where blood/organ products were received. Notify the REP and CDS Vector Team (CDSVectorTeam@doh.nj.gov) by email. Ask about blood donation and document date and location of donations
Treatment	Document all medications received with dates of treatment/duration.
eCR	If an electronic case record is available, review the information in the file and enter information into fields in CDRSS.
Case Comments	 If requested information was not provided by the patient's healthcare provider, list the dates attempts were made to obtain information and the outcomes. For example, 1/12/24 faxed form to provider; 1/31/24, spoke with office manager and re-sent form; 2/15/24, refaxed form to provider. Missing information should be obtained by interviewing the patient. If the patient is non-responsive, document attempts and call outcomes in Comments section as well.

6 CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements / Protection of Contacts of a Case

There are no isolation or quarantine restrictions.

B. Managing Special Situations

Transfusion/Transplant-Associated Cases

If a blood transfusion or organ transplant was received in the year prior to symptom onset, notify the REP and CDS Vector Team (CDSVectorTeam@doh.nj.gov) by email. CDS will reach out to the blood center for further investigation.

Locally Acquired Case

A locally acquired case of malaria is possible but would be unusual (*Anopheles* mosquitoes are present in New Jersey, but infected humans are rare). If it is determined during an investigation that a patient does not have a recent travel history to an endemic area, immediately contact REP and the CDS Vector Team (CDSVectorTeam@doh.nj.gov) by email. The program staff can help determine a course of action to prevent further cases and can perform surveillance for cases that may cross several jurisdictions and, therefore, could be difficult to identify at a local level.

7 PREVENTION

International Travel

People traveling to malaria-endemic parts of the world should contact a healthcare provider to discuss the risk of contracting the disease and control measures they can take to protect themselves from mosquitoes. Chemoprophylaxis regimens may be prescribed and involve taking medicine before, during and after travel to an area with malaria. Local health departments should convey to patients the importance of completing all prescribed antimalarials for future travel. Travelers can use repellents, wear protective clothing, and use mosquito nets when rooms are not screened. There currently is no vaccine to prevent malaria available, although a pediatric vaccine is in development for use in sub-Saharan Africa, and there are preventative medications.

- Please visit the <u>Malaria Prevention Information</u>, by <u>Country webpage</u> for country-specific malaria information.
- 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 with malaria could lead to their becoming a local source of malaria transmission to mosquitoes if bitten, then to other people bitten by those mosquitoes.

8 ADDITIONAL INFORMATION

Additional Sources of Information

NJDOH: nj.gov/health/cd/topics/malaria.shtml

CDC: cdc.gov/malaria/index.html

References

AABB (formerly American Association of Blood Banks) Association

https://www.aabb.org/regulatory-and-advocacy/regulatory-affairs/infectious-diseases/malaria

Centers for Disease Control and Prevention. Case definitions for Malaria.

https://ndc.services.cdc.gov/conditions/malaria/

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

Centers for Disease Control and Prevention. Malaria Surveillance — United States, 2018

https://www.cdc.gov/mmwr/volumes/71/ss/ss7108a1.htm?s cid=ss7108a1 w

New Jersey Department of Health Communicable Disease Service. Vector-borne Disease Data Dashboard. https://dashboards.doh.nj.gov/views/public_dashboard/Intro