

Types	Acute infection with one of four <i>Plasmodium</i> species: <i>P. vivax</i> , <i>P. falciparum</i> , <i>P. ovale</i> , and <i>P. malariae</i> . Rare dual-species infections or infections with simian species (<i>P. knowlesi</i> , <i>P. simiovale</i>). Relapse can occur with incomplete treatment, particularly <i>P. vivax</i> and <i>P. ovale</i> due to extended dormant states in liver. Typically acquired by mosquito bite in an area where malaria is a regular occurrence (tropical areas of South America, Africa, and Asia) and imported into the United States with travel or immigration.
Signs and Symptoms	<ul style="list-style-type: none"> • Typical recurrent fever (may be periodic at 48 or 72 hours, depending on species) • Frequently chills, sweats, and headaches • Can be vomiting, diarrhea, cough, shortness of breath, muscle aches • Severe cases anemia, renal failure, shock, adult respiratory distress syndrome, confusion, encephalopathy, and acidosis; severe cases usually <i>P. falciparum</i>
Incubation	7–30 days, shorter period usually with <i>P. falciparum</i> and longer with <i>P. malariae</i> . Concurrent anti-malarial drugs or partial immunity from prior exposure can lengthen the incubation.
Diagnostics / Laboratory	<p>Lab (must be diagnosed in the United States per national case definition):</p> <ul style="list-style-type: none"> • 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 CLIA validated polymerase chain reaction test (PCR), OR • Detection of malaria parasites in thick or thin peripheral blood films with report of percent parasitemia.
Differential diagnosis (guidance)	Multitude of viral and bacterial infections depending on geographic location including African trypanosomiasis, amebiasis, cholera, typhus, foodborne or waterborne gastroenteritis, meningitis, rickettsiosis, polio, schistosomiasis, HIV/AIDS, viral hemorrhagic fever, yellow fever, heat stroke
Treatment	Base on Plasmodium species, country of exposure (drug resistance) and illness severity. CDC: https://www.cdc.gov/malaria/diagnosis_treatment/treatment.html , 24/7 consult at 770-488-7788; CDC prophylaxis for travel: https://www.cdc.gov/malaria/travelers/country_table/a.html
Response	<p>Public health</p> <ul style="list-style-type: none"> <input type="checkbox"/> Document diagnosis was made in the United States (national case definition) <input type="checkbox"/> Obtain information to determine if case without travel exposures is: <ul style="list-style-type: none"> Introduced: mosquito transmission from an imported human case in an area Induced: acquired through artificial means (e.g., blood transfusion, malariotherapy) Cryptic: isolated case that without epidemiological link <input type="checkbox"/> Refer clinician to CDC for severe malaria needing IV artesunate if drug is unavailable commercially. See: https://www.cdc.gov/malaria/diagnosis_treatment/artesunate.html <p>Laboratory</p> <ul style="list-style-type: none"> <input type="checkbox"/> Encourage submission of thick and thin smears to DOH PHL (not required), particularly for cases with only rapid testing done without full speciation <p>Infection control</p> <ul style="list-style-type: none"> <input type="checkbox"/> Case should not donate blood or tissues for exclusion period (may extend to 3 years)

Malaria

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To contribute adequate case reports to the national database.
2. To ensure adequate treatment of cases, particularly for fatal falciparum malaria.
3. To identify persons who may benefit from screening or treatment, e.g., fellow travelers.
4. To identify persons exposed locally and initiate appropriate follow-up.

B. Legal Reporting Requirements

1. Health care providers: notifiable to local health jurisdiction within 3 business days.
2. Health care facilities: notifiable to local health jurisdiction within 3 business days.
3. Laboratories: *Plasmodium* species notifiable to local health jurisdiction within 2 business days; specimen submission is not required but is recommended.
4. Local health jurisdiction: notifiable to the Washington State Department of Health (DOH) Office of Communicable Disease Epidemiology (CDE) within seven days of case investigation completion or summary information required within 21 days.

C. Local Health Jurisdiction Investigative Responsibilities

1. Recommend clinical labs send thick and thin blood smears to Washington State Public Health Laboratories for confirmation and speciation.
2. Report confirmed cases to CDE (Section 3). Complete the malaria case report form (<https://www.doh.wa.gov/Portals/1/Documents/5100/210-037-ReportForm-Malaria.pdf>) and enter the data into the Washington Disease Reporting System (WDRS) or other electronic reporting system.

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Protozoan parasite of the genus *Plasmodium*, commonly *P. vivax*, *P. falciparum*, *P. ovale*, and *P. malariae*. Dual-species infections occur. Clinical illness, treatment, prophylaxis, and geographical distribution vary with species. *P. falciparum* causes the most severe symptoms and requires prompt intervention. Species that primarily infect non-human primates (e.g., *P. knowlesi*, *P. simiovale*) can infect in humans.

Malaria parasites have a complex life cycle. Parasites are injected into a human by anopheline mosquitoes, mature in the liver, and then enter red blood cells. The parasites multiply inside the red blood cells which eventually rupture, releasing parasites into the bloodstream with accompanying high fevers. Some of the parasites become sexual forms (gametocytes) which, if ingested by a mosquito, can develop into another generation of parasites able to infect humans. Depending on the species, the bloodstream cycle can persist for weeks to years. *P. vivax* and *P. ovale* have a dormant stage (hypnozoites) indefinitely in the liver.

B. Description of Illness

Typical malaria has recurrent fever (may be periodic at 48 or 72 hours, depending on malarial species), chills, sweats, and headache. There can be vomiting, diarrhea, cough, shortness of breath, muscle aches, etc. Symptom severity varies with the species, stage of infection, and patient immune status; “concomitant” immunity is a relative resistance from persistent low-level parasitemia (% red cells affected) or frequent infections.

P. falciparum infections can be life-threatening with parasitemia over 10%, causing thrombosis or capillary sludging leading to anemia, renal failure, shock, adult respiratory distress syndrome, encephalopathy, and acidosis. Other malarial species usually cause milder disease. *P. knowlesi*, a rare human infection, may be misdiagnosed as *P. malariae* by appearance but resembles falciparum malaria in terms of severity.

C. Malaria in Washington State

DOH receives around 20 to 40 malaria reports annually, all associated with exposures in endemic areas related to travel for tourism, business, mission work, or immigration.

D. Reservoirs – Human cases and carriers.

E. Modes of Transmission

Transmission occurs by a bite of certain *Anopheles* mosquito species. Person-to-person transmission occurs through blood contact (e.g., transfusions), although rarely.

F. Incubation Period

7–30 days, shorter often with *P. falciparum* and longer with *P. malariae*. Concurrent anti-malarial drugs or partial immunity from prior exposure can lengthen the period.

G. Period of Communicability

Human infection is communicable to mosquitoes when gametocytes are present in the blood. *Plasmodium* development in a competent mosquito host then takes 1-4 weeks.

H. Treatment

Treatment is based on *Plasmodium* species, severity of illness, and drug resistance in the geographic area of exposure; also consider side effects and drug availability. Treatment of *P. falciparum* is complicated due to widespread drug resistance. Consider initial hospitalization for patients with falciparum malaria, particularly children or pregnant women. For definitive treatment check the CDC web site: 24/7 CDC Malaria Hot Line 770-488-7788 or https://www.cdc.gov/malaria/diagnosis_treatment/index.html.

IV artesunate is used as part of combination first-line treatment for severe malaria cases (defined as any one of: parasitemia >5%, impaired consciousness, seizures, circulatory collapse/shock, acidosis, acute kidney injury, disseminated intravascular coagulation, or severe anemia with Hb<7) or if oral medications cannot be taken despite oral antiemetic treatment. IV artesunate became commercially available March 2021. If it is not available locally in a timely manner, CDC can assist. For details see: https://www.cdc.gov/malaria/diagnosis_treatment/artesunate.html.

For prophylaxis recommendations during travel, see Section 7.

3. CASE DEFINITION

A. Clinical Criteria for Diagnosis

The first symptoms of malaria (most often fever, chills, sweats, headaches, muscle pains, nausea and vomiting) are often not specific and are also found in other diseases, such as influenza and other common viral infections. Likewise, the physical findings are often not specific (e.g., elevated temperature, sweating, tiredness). In severe malaria (caused by *P. falciparum*), clinical findings (confusion, coma, neurologic focal signs, severe anemia, respiratory difficulties) are more striking and may increase the suspicion for malaria.

B. Laboratory Criteria for Diagnosis

- 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 CLIA-approved polymerase chain reaction test (PCR)*, **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).

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

C. Case Definition (2014)

1. *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 United States, regardless of whether the person experienced previous episodes of malaria while outside the country.
2. *Confirmed*:
 - Detection and specific identification of malaria parasites by microscopy on blood films in a laboratory with appropriate expertise in any person (symptomatic or asymptomatic) diagnosed in the United States, 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 United States, regardless of whether the person experienced previous episodes of malaria while outside the country.

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

D. Comments

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** *Plasmodium* species may indicate a relapsing infection or treatment failure caused by drug resistance, or may indicate a separate attack.

Cases are additionally categorized according to World Health Organization criteria:

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

4. DIAGNOSIS AND LABORATORY SERVICES

A. Diagnosis

Diagnosis is based on positive laboratory testing regardless of symptoms. If initial blood smears are negative but the diagnosis is still possible, repeat smears every 12–24 hours for 72 hours. The surveillance case definition requires diagnosis in the United States.

B. Tests Available at Washington State Public Health Laboratories (PHL)

PHL can confirm the identification and speciation of malaria parasites on blood smears (Giemsa-stained parasites visualized in a blood sample). Commercial laboratories are strongly encouraged to submit positive specimens or specimens with the species in question to PHL.

Note that PHL require all clinical specimens have two patient identifiers, a name **and** a second identifier (e.g., date of birth) both on the specimen label and on the submission form. Due to laboratory accreditation standards, specimens will be rejected for testing if not properly identified. Also include specimen source and collection date.

C. Specimen Collection

Collect EDTA (purple top) or similar tube **and** thick and thin smears made within 20 minutes of blood draw and use PHL form:

<https://www.doh.wa.gov/Portals/1/Documents/5230/302-013-Micro.pdf>. For details about specimen collection and shipping see:

<https://www.doh.wa.gov/ForPublicHealthandHealthcareProviders/PublicHealthLaboratories/MicrobiologyLabTestMenu>

D. Special CDC Testing

CDC tests cases when the diagnosis is in question and can do drug resistance testing for cases diagnosed in the United States following initial diagnostic testing using PCR speciation, identification of drug resistance mutations, and when possible, direct susceptibility testing. Encourage diagnostic laboratories to send CDC smears and pre-treatment whole blood EDTA tube with a CDC submission form. Instructions and the form are available at: <https://www.cdc.gov/malaria/features/ars.html>.

5. ROUTINE CASE INVESTIGATION

Interview the case and others who might be able to provide pertinent information.

A. Evaluate the Diagnosis

Facilitate specimen transport to Washington State Public Health Laboratories for species confirmation. Rare severe complications occur, most often with *P. falciparum*. Clinical laboratories not speciating malaria may be able to rule out *P. falciparum*. Late stages of *P. knowlesi* resemble *P. malariae*, resulting in misdiagnosis and inappropriate treatment.

B. Manage the Case

Refer physician to CDC resources for severe malaria needing IV treatment if artesunate is not available locally: https://www.cdc.gov/malaria/diagnosis_treatment/artesunate.html
Advise no blood donation for exclusion period (e.g., years after treatment or risk travel.)

C. Identify Potential Sources of Infection

Ask about travel in a malarious area (tropical areas of South America, Africa and Asia). Assess use of malaria prophylaxis before, during and after travel. If there was no travel for month, immediately contact the Office of Communicable Disease Epidemiology.

Consider alternative possibilities including:

1. *Relapse* of a previous infection, meaning a reseeded of the bloodstream from *P. vivax* or *P. ovale* hypnozoites in the liver. Relapse implies a past infection was either untreated or treated only for bloodstream parasites. Primaquine is the only drug that treats the liver stage of infection and is given in addition to treatment for bloodstream parasites.
2. *Recrudescence* of a previous infection, meaning a low-level asymptomatic bloodstream infection “blossomed” to cause the current illness. Although there are no long-term liver stage parasites in these infections, such silent infections can occur with *P. falciparum* and *P. malariae*, particularly in hyperendemic areas where people have partial immunity.
3. Infection from direct inoculation of contaminated blood or blood products (e.g., needle sharing, malariotherapy [deliberately inducing a malaria infection to treatment another medical condition], or transfusion). Test all blood donors associated with the case.
4. Infection by a mosquito bite, but not in an endemic area. Rare “airport malaria” occurs if an infective mosquito survives a flight from an endemic area and leaves the plane. Rarely an *Anopheles* mosquito may transmit malaria from an arriving parasitemic person; the mosquitoes occur in Washington but local transmission is unlikely. See CDC guidelines: <https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5513a1.htm>.

D. Identify Other Potentially Exposed Persons

Identify other persons sharing the case’s exposure, such as travel with family, friends, or a group. Diagnosis of malaria in one may suggest a similar risk for the others. Identify other persons who may have been exposed by the case. Potential although rare exposures include blood transfusion, sharing injection equipment, or malariotherapy.

E. Manage Other Potentially Exposed Persons

Assess those who shared overseas exposures with the case. Give persons with possible *P. falciparum* exposure particularly close scrutiny. Refer for treatment if symptomatic.

Test all blood donors or recipients associated with the case.

F. Environmental Evaluation

None, unless the patient did not travel to a region with endemic malaria. Rare cases result from mosquitoes carried on airplanes or newly introduced local mosquito-borne transmission. Environmental investigation including mosquito trapping may be appropriate for such situations.

6. MANAGING SPECIAL SITUATIONS

A. Under-treated Falciparum Malaria Case

P. falciparum has a high prevalence of chloroquine resistance and can cause severe disease. If a case of falciparum malaria was treated only with chloroquine, verify the treatment information with the provider and consult regarding appropriate treatment. For questions about malaria treatment a CDC consult is available through malaria@cdc.gov or 770-488-7788.

B. No Recent Travel to Endemic Areas

Consult with the Office of Communicable Disease Epidemiology immediately about any case that does not have a history of recent travel to a malarious area (206-418-5500).

7. ROUTINE PREVENTION

A. Immunization Recommendations

None, although malaria vaccines are under development.

B. Prevention Recommendations

Current information to prevent malaria is available from travel clinics and the CDC (wwwnc.cdc.gov/travel), including country-specific recommendations. Factors such as geography, climate, season, mosquito species, and mosquito control efforts vary the risk for malaria, as does a person's travel style. Prevention had three parts: avoid mosquito bites, chemoprophylaxis, and prevent later recurrence of symptoms.

1. Avoid Mosquito Bites

Travelers should wear adequate clothing (long pants, long-sleeved shirt, hat) and use insect repellent when mosquito exposure can be anticipated. Repellents containing DEET as the active ingredient are the most effective. Travelers should identify times of day with the highest risk of mosquito bites for a specific region and minimize outdoor activities during those times.

Use pesticide-treated mosquito bed nets when exposure to mosquitoes may occur at night (when most *Anopheles* mosquitoes feed). Bed nets are considered unnecessary if the traveler stays in an air-conditioned hotel, with the windows closed at night.

2. Chemoprophylaxis

The main challenge for most travelers is determining appropriate chemoprophylaxis. Chloroquine was the mainstay of malaria prophylaxis for decades, but widespread resistance among falciparum parasites makes this regimen inappropriate in Africa, South Asia, and most of the Americas. Because prophylaxis guidelines change, refer to current resources (e.g., CDC web site <https://www.cdc.gov/malaria/travelers/index.html>).

3. Prevent Recurrences

Dormant forms of *P. ovale* and *P. vivax* (hypnozoites) can persist in the liver and emerge weeks or months later as a relapse. Drugs to treat symptomatic disease (i.e., red blood cell infection) do not act against hypnozoites. To prevent a possible relapse, primaquine is generally given for attack of *P. ovale* or *P. vivax* malaria. However, there are some contraindications to primaquine use (e.g., G6PD deficiency, during pregnancy).

ACKNOWLEDGEMENTS

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UPDATES

March 2009: New link for lab form.

January 2010: Updated case definition and new link for reporting form.

January 2011: The Legal Reporting Requirements section was revised to reflect the 2011 Notifiable Conditions Rule revision.

June 2013: Treatment recommendations (2H) include the most recent CDC resources. Prior Section 5 and 6 were combined.

March 2016: Front page added.

March 2018: Case definition clarifies that parasitemia is needed to support laboratory diagnosis by thick or thin blood films. Updated for WDRS.

March 2019: Information added about IV artesunate

April 2021: Information added about commercial availability of IV artesunate (Section 2H)