

# Malaria

## 1. DISEASE REPORTING

### A. Purpose of Reporting and Surveillance

1. To contribute adequate case reports to the national database, which in turn better describes characteristics and risk factors for malaria in residents of the United States.
2. To ensure adequate treatment of cases, particularly those with potentially fatal falciparum malaria.
3. To identify other persons exposed who may benefit from screening or treatment, e.g., fellow travelers or recipients of blood products.
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) Communicable Disease Epidemiology Section (CDES) 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 DOH Public Health Laboratories for confirmation and speciation.
2. Report all confirmed cases to CDES (see definition below). Complete the malaria case report form (<http://www.doh.wa.gov/notify/forms/malaria.pdf>) and enter the data into the Public Health Issues and Management System (PHIMS).

## 2. THE DISEASE AND ITS EPIDEMIOLOGY

### A. Etiologic Agent

Malaria is caused by a protozoan parasite of the genus *Plasmodium*. There are four species that commonly cause disease among humans: *P. vivax*, *P. falciparum*, *P. ovale*, and *P. malariae*. Mixed infections are possible. Other species that primarily infect non-human primates (e.g., *P. knowlesi*, *P. simiovale*) may cause infections in humans especially those working in the forest habitats near infected primates.

It is important to understand significant differences among the several species in terms of clinical illness, treatment, prophylaxis, and geographical distribution. Malaria due to *P. falciparum* causes the most severe symptoms and requires prompt intervention.

Malaria parasites have a complex life cycle. After injection into the human host from anopheline mosquitoes, the parasites mature in the liver before being released into the

bloodstream and invading red blood cells. The parasites multiply inside the red blood cells, eventually rupturing the cells, releasing more parasites into the bloodstream with accompanying high fevers. Some parasites differentiate into sexual forms (gametocytes) which, if ingested by another mosquito, can lead to the development of another generation of parasites, ready for transmission to another human host. The bloodstream cycle can persist for weeks to years, depending on the species involved. In malaria due to *P. vivax* and *P. ovale*, a dormant stage (hypnozoites) can persist indefinitely in the liver.

## B. Description of Illness

The classic signs and symptoms of malaria are recurrent bouts of fever, chills, sweats, and headache. Other symptoms can occur, depending on the severity of infection, including gastrointestinal symptoms (vomiting, diarrhea), respiratory symptoms (cough, shortness of breath), muscle aches, etc. Fevers can recur at regular intervals (48 or 72 hours, depending on the malarial species) that coincide with a synchronized rupture of red blood cells. This periodicity may be masked. The severity of symptoms varies with the species of parasite involved, the stage of infection, the immunological history of the patient, and other factors. Persons in endemic areas may develop “concomitant” immunity—a relative resistance to symptoms that persists only with continued exposure, persistent low-level parasitemia, or frequent infections.

*P. falciparum* infections are potentially life-threatening because the the proportion of red blood cells containing parasites can be greater than 10% which results in venous thrombosis or sludging in the capillaries. Complications of inadequately treated falciparum malaria include anemia, renal failure, shock, adult respiratory distress syndrome, encephalopathy, and acidosis. Disease caused by the other malarial species is rarely fatal, and can be quite mild. In Southeast Asia where *P. knowlesi* infection more commonly occurs, it may be misdiagnosed as less severe *P. malariae* by its appearance but, is more clinically similar to falciparum malaria in terms of severity.

## C. Malaria in Washington State

DOH has received approximately 20 to 40 reports of malaria annually. All cases have been associated with travel to endemic areas. Reported cases in Washington have occurred among tourists, business travelers, mission workers, immigrants and refugees.

## D. Reservoirs – Human cases and carriers.

## E. Modes of Transmission

Transmission occurs by the bite of infected anopheline mosquitoes. Only certain species of the genus *Anopheles* are competent vectors of human malaria. Person-to-person transmission can occur through blood contact (e.g., transfusions or needle-sharing), although this is rare in the United States.

## F. Incubation Period

The incubation period of malaria varies from 7–30 days. The shorter periods occur more often with *P. falciparum* and the longer ones with *P. malariae*. Incubation can be longer with concurrent anti-malarial drug use or partial immunity from prior exposures.

### G. Period of Communicability

Human are communicable to mosquitoes when gametocytes are present in blood. *Plasmodium* parasites must undergo developmental changes in a competent mosquito host before being passed back to another human; this takes from a week and a month.

### H. Treatment

Choice of treatment should be based on *Plasmodium* species, clinical status of the patient, and drug resistance patterns in the geographic area of exposure. In addition, side effects and drug availability need to be considered. Refer to up-to-date resources (e.g., CDC web site <http://www.cdc.gov/malaria/> or Malaria Hot Line 770-488-7788) for definitive recommendations.

In general, chloroquine is the drug of choice for all *Plasmodium* except for chloroquine-resistant *P. falciparum* and chloroquine-resistant *P. vivax*. Primaquine, a drug that is active specifically against the liver stages, may be added for treatment of malaria due to *P. vivax* and *P. ovale* to prevent relapse but should not be used during pregnancy and can also cause complications in persons with G6PD deficiency.

Treatment of *P. falciparum* is more complicated, because of widespread resistance to chloroquine, and, increasingly, mefloquine. Treatment is often with quinine plus a second drug, but it is essential to get up-to-date treatment recommendations particularly the appropriate recommendations for children, pregnant women, and persons with G6PD deficiency. Because of the potential for rapid clinical deterioration, clinicians should strongly consider hospitalizing patients with falciparum malaria, at least until the success of therapy is assured.

For prophylaxis recommendations during travel, see Section 8.

## 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 (elevated temperature, perspiration, tiredness). In severe malaria (typically caused by *P. falciparum*), clinical findings (confusion, coma, neurologic focal signs, severe anemia, respiratory difficulties) are more striking and may increase the suspicion index 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 polymerase chain reaction test (PCR)\*, OR
- Detection of malaria parasites in thick or thin peripheral blood films.

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

### C. Case Definition (2010)

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.

### D. Comment

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 United States may indicate a relapsing infection or treatment failure caused by drug resistance or a separate attack.

Blood smears from questionable cases should be referred to the CDC Division of Parasitic Diseases Diagnostic Laboratory for confirmation of the diagnosis.

Cases are additionally categorized according to the following World Health Organization criteria:

- **Autochthonous**: malaria contracted in the area where reported
  - **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., acquired outside the United States and its territories)
- **Induced**: malaria acquired through artificial means (e.g., blood transfusion, shared syringes, or malariotherapy)
- **Relapsing**: renewed manifestation (i.e., of clinical symptoms and/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.

## 4. DIAGNOSIS AND LABORATORY SERVICES

### A. Diagnosis

The diagnosis of malaria is made based on demonstration of malaria parasites, antigens, or DNA, regardless of symptoms. If malaria parasites are not seen on initial films but the diagnosis is still possible, smears should be repeated every 12–24 hours for a 72 hours period. The surveillance case definition requires diagnosis in the United States.

### B. Tests Available at DOH Public Health Laboratories (PHL)

PHL can confirm the identification and speciation of malaria parasites on blood smears. Although not required, commercial laboratories are strongly encouraged to submit specimens positive for malaria to PHL for confirmation.

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

Obtain blood in an EDTA (purple top) or similar tube **and** request thick and thin smear preparation on the fresh specimen (within 20 minutes of collection). Specimens should be submitted to DOH with a completed parasitology form:

<http://www.doh.wa.gov/EHSPHL/PHL/Forms/Microbiology.pdf>

## 5. ROUTINE CASE INVESTIGATION

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

### A. Evaluate the Diagnosis

Facilitate transport of specimens to Public Health Laboratories to confirm the diagnosis. Severe complications are rare but occur most often with *P. falciparum* infections. Clinical laboratories may be unable to speciate the parasites on blood smear, but often can rule out *P. falciparum*. Microscopically early parasite stages of *P. knowlesi* resemble *P. falciparum* and later parasite stages resemble *P. malariae*. Misdiagnosis of *P. knowlesi* as the more benign *P. malariae* may result in inappropriate treatment.

### B. Identify Source of Infection

Determine whether the patient traveled or lived in a malarious area in the weeks before onset. Assess the consistency with which prophylactic antibiotics were taken before, during, and after travel. If the patient has not been out of the United States during the preceding month, contact Communicable Disease Epidemiology Section immediately. Consider alternative possibilities including:

1. *Relapse* of a previous infection. “Relapse” has a technical meaning for malaria, meaning a reseeded of the bloodstream from *P. ovale* or *P. vivax* hypnozoites in the liver. Relapse implies that a case infected in the past was either never treated or treated only for bloodstream parasites. Primaquine is the only drug that treats the liver stage of infection; it should be given in addition to whatever drug is used to treat bloodstream parasites.
2. *Recrudescence* of a previous infection, meaning that the case had a low-level

asymptomatic bloodstream infection that “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, possibly transfusion although screening should eliminate the risk, malariotherapy [deliberately inducing a malaria infection as a treatment of conditions such as syphilis, Lyme disease, or AIDS]).
4. Infection by a mosquito bite, but not in an endemic area. One rare situation called “airport malaria” can occur if an infective mosquito survives travel on a plane from an endemic area and then fly and bite people within a few miles of the airport. Another possibility is that a parasitemic person in this country through travel or immigration is bitten by an *Anopheles* mosquito which then transmits malaria. Although anopheline mosquitoes can be found in Washington, local transmission is an unlikely scenario. CDC has investigation guidelines for locally acquired malaria:  
<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5513a1.htm>.

### C. Identify Potentially Exposed Persons

Identify other persons who may have shared the case’s exposure. If a case traveled with family, friends, or some kind of group, a diagnosis of malaria in one may suggest a similar risk for the others. Assess the health of family members or fellow travelers who shared the overseas exposures. Give persons with possible *P. falciparum* exposure particularly close scrutiny.

Identify persons who may have been exposed by the case. Potential although rare exposures include blood transfusion, sharing injection equipment, and malariotherapy.

### D. Environmental Evaluation

None unless the patient did not travel to a region with endemic malaria. A very small number of cases have occurred in this country due to mosquitoes carried on airplanes or acquired through local mosquito-borne transmission. Environmental investigation including mosquito trapping may be considered.

## 6. CONTROLLING FURTHER SPREAD

### A. Infection Control Recommendations / Case Management

1. Hospitalized patients should be cared for using standard precautions.
2. Case should be advised to defer donating blood during the recommended period (typically years after date of travel to risk area or after treatment for malaria.)

### B. Contact Management

Investigate and treat all persons who shared needles or other drug paraphernalia. Identify and test all blood donors or recipients associated with the case. No follow-up public health activities needed for other contacts.

### C. Management of other Exposed Persons

Educate persons who may have shared the case’s exposure, such as others in a travel

group, regarding signs and symptoms of malaria.

#### **D. Environmental Measures**

None, unless local transmission is suspected.

### **7. MANAGING SPECIAL SITUATIONS**

#### **A. Undertreated Falciparum Malaria Case**

The high prevalence of chloroquine resistance among *P. falciparum* parasites, as well as the potential severity of the illness, makes chloroquine alone usually a poor choice for therapy. If a falciparum malaria case was treated with chloroquine, verify the treatment information with the patient's physician and consult regarding appropriate treatment.

#### **B. No Recent Travel to Endemic Areas**

Consult Communicable Disease Epidemiology Section immediately about any case that does not have a history of recent travel to a malarious area.

### **8. ROUTINE PREVENTION**

#### **A. Immunization Recommendations**

None

#### **B. Prevention Recommendations**

Local health department staff are often asked questions about malaria prevention prior to travel. Current information is available at many travel clinics and on the CDC's Traveler's Health web page ([www.cdc.gov/travel](http://www.cdc.gov/travel)), including country-specific recommendations. The risk of malaria is not uniform within most countries because of climate, season, geography, mosquito species and their habits, mosquito control efforts, and other factors. A traveler's risk will also vary with the style of travel. Despite decades of effort, there are no malaria vaccines available. There are three parts to prophylaxis: avoiding mosquito bites, chemoprophylaxis, and preventing later recurrence of symptoms.

##### **1. Avoiding Mosquito Bites**

Travelers should wear adequate clothing (long pants, long-sleeved shirts) and use insect repellent when mosquito exposure can be anticipated. Repellents that contain DEET as the active ingredient are the most effective. Travelers should identify times of day with highest risk of malaria transmission for a location and minimize outdoor activities during those times.

Use mosquito bed nets when exposure to mosquitoes may occur at night. The use of mosquito bed nets is considered unnecessary if the traveler stays in air-conditioned hotels, with windows closed at night (when most *Anopheles* mosquitoes feed).

##### **2. Chemoprophylaxis**

The main issue for most travelers is whether, when, and what kind of chemoprophylaxis is appropriate. Chloroquine was the mainstay of malaria prophylaxis for decades, but because of widespread resistance among falciparum parasites this regimen is no longer appropriate in Africa, South Asia, and most of the Americas "below" the Panama Canal.

Because of the fluid nature of prophylaxis guidelines, refer to up-to-date resources (e.g., the CDC web site) for specific recommendations.

### 3. Preventing Recurrences

Dormant forms of *P. ovale* and *P. vivax* (hyponozoites) can be sequestered in the liver and emerge weeks or months after an initial attack to cause a relapse. Drugs that are used to treat symptomatic disease (i.e., the infection in red blood cells) are not effective against hypnozoites. Thus, to prevent the possibility of a relapse, primaquine is generally indicated for persons who have had an attack of *ovale* or *vivax* malaria. However, that 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 has been revised to reflect the 2011 Notifiable Conditions Rule revision.