

## MALARIA

### REPORTING INFORMATION

- **Class B:** Report by the end of the next business day after the case or suspected case presents and/or a positive laboratory result to the local public health department where the patient resides. If patient residence is unknown, report to the local public health department in which the reporting health care provider or laboratory is located.
- Reporting Form(s) and/or Mechanism:
  - The Ohio Disease Reporting System (ODRS) should be used to report lab findings to the Ohio Department of Health (ODH). For healthcare providers without access to ODRS, you may use the [Ohio Confidential Reportable Disease form](#) (HEA 3334).
  - The [CDC Malaria Case Surveillance Report form](#) (CDC 54.1) is required for completion by the local health department. Information collected from the form should be entered into ODRS **and** faxed to ODH, Bureau of Infectious Diseases at (614) 564-2456.
- Key fields for ODRS reporting include: import status (whether the infection was travel-associated or Ohio-acquired), date of illness onset and all fields in the Epidemiology and Travel History modules.

### AGENTS

Malaria parasites. There are five species of genus *Plasmodium* known to infect humans: *P. falciparum*, *P. malariae*, *P. ovale*, *P. vivax* and *P. knowlesi*. Mixed infections are not infrequent in endemic areas.

### CASE DEFINITION

#### Clinical Description

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 (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.

#### 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 (PCR) test\* **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

Suspected: 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.

#### 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 **or**
- Detection of unspiciated malaria parasite by microscopy 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.

### **Criteria to Distinguish a New Case from an Existing 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 United States may indicate a relapsing infection or treatment failure caused by drug resistance or a separate attack.

### **Comment**

\* Laboratory-developed malaria PCR tests must fulfill Clinical Laboratory Improvement Amendments (CLIA) requirements, including validation studies.

Clinical samples including blood smears or EDTA whole blood from all cases can be referred to the Centers for Disease Control and Prevention (CDC) Division of Parasitic Diseases and Malaria Diagnostic Laboratory for confirmation of the diagnosis and anti-malarial 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. Please contact the ODH Bureau of Infectious Diseases at (614) 995-5599 to arrange for testing at CDC.

Cases are also classified according to the following World Health Organization (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 United States 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.

### **SIGNS AND SYMPTOMS**

The classic (but rarely observed) malaria attack lasts 6-10 hours and consists of a cold stage (sensation of cold, shivering), a hot stage (fever, headaches, vomiting; seizures in young children) and lastly a sweating stage (sweats, returning to normal temperature, tiredness). Classically, the attacks occur every second day with "tertian" parasites (*P. falciparum*, *P. vivax*, *P. ovale*) and every third day with the "quartan" parasite (*P. malariae*).

More commonly, the patient presents with a combination of fever, chills, sweats, headaches, nausea and vomiting, body aches and general malaise. In countries where malaria is infrequent, these symptoms may be attributed to influenza, a cold or other common

infections, especially if malaria is not suspected. Conversely, in countries where malaria is endemic, residents often recognize the symptoms of malaria and treat themselves without seeking diagnostic confirmation. Physical findings of malaria may include elevated temperatures, perspiration, weakness, enlarged spleen, mild jaundice, enlargement of the liver and increased respiratory rate.

Severe malaria occurs when the infections are complicated by serious organ failures or abnormalities in the patient's blood or metabolism. The manifestations of severe malaria include:

- Cerebral malaria: abnormal behavior, impairment of consciousness, seizures, coma or other neurologic abnormalities.
- Severe anemia: due to hemolysis (destruction of the red blood cells),
- Hemoglobinuria: hemoglobin in the urine due to hemolysis.
- Acute respiratory distress syndrome (ARDS): an inflammatory reaction in the lungs that inhibits oxygen exchange, which may occur even after the parasite counts have decreased in response to treatment.
- Coagulopathy: abnormalities in blood coagulation.
- Low blood pressure caused by cardiovascular collapse.
- Acute kidney failure: caused by acute tubular necrosis (rare in children <8 years old).
- Hyperparasitemia: more than 5% of the red blood cells infected with parasites,
- Metabolic acidosis: excessive acidity in the blood and tissue fluids, often in association with hypoglycemia.
- Hypoglycemia: low blood glucose. Hypoglycemia may also occur in pregnant women with uncomplicated malaria or after treatment with quinine.

Severe malaria is a medical emergency and should be treated urgently and aggressively.

In *P. vivax* and *P. ovale* infections, patients having recovered from the first episode of illness may suffer several additional attacks ("relapses") after months or even years without symptoms. Relapses occur because *P. vivax* and *P. ovale* have dormant liver stage parasites ("hypnozoites") that may reactivate. Treatment to reduce the chance of such relapses is available and should follow treatment of the first attack.

Neurologic defects may occasionally persist following cerebral malaria, especially in children. Such defects include trouble with movements (ataxia), palsies, speech difficulties, deafness and blindness. Recurrent infections with *P. falciparum* may result in severe anemia. This occurs especially in young children in tropical Africa with frequent infections that are inadequately treated. Malaria during pregnancy (especially *P. falciparum*) may cause severe disease in the mother and may lead to premature delivery or delivery of a low-birth-weight baby. On rare occasions, *P. vivax* malaria can cause rupture of the spleen. Nephrotic syndrome (a chronic, severe kidney disease) can result from chronic or repeated infections with *P. malariae*. Hyperreactive malarial splenomegaly (also called "tropical splenomegaly syndrome") occurs rarely and is attributed to an abnormal immune response to repeated malarial infections. The disease is marked by a very enlarged spleen and liver, abnormal immunologic findings, anemia and a susceptibility to other infections (such as skin or respiratory infections).

## DIAGNOSIS

Malaria can be suspected based on the patient's travel history, symptoms and the physical findings at examination. However, for a definitive diagnosis to be made, laboratory tests must demonstrate the malaria parasites or their components. Identification of malaria parasites in patients with no travel history to endemic countries should be further evaluated to rule out *Babesia* (refer to [Babesiosis](#) chapter).

The five types of human malaria are confirmed and differentiated by demonstration of malaria parasites in thick blood films. Repeated microscopic examinations may be necessary and are most productive when the thick blood film was made during a febrile episode. Thick smears are more sensitive for detecting the parasites, but thin smears are more useful for species and parasitemia identification. Repeat smears are recommended every 12-24 hours until three sets are collected; if all three sets are negative, malaria can be ruled out. This technique remains the gold standard for laboratory confirmation of malaria. However, it depends on the quality of the reagents, on the microscope and on the experience of the laboratorian. Help with reading and interpretation of the smears may be obtained from CDC. Contact the ODH Laboratory at (614) 728-0544 (Monday-Friday 8 AM-5 PM) for CDC specimen submission criteria.

Various test kits are available to detect antigens derived from malaria parasites. These "Rapid Diagnostic Tests" (RDTs) offer a useful alternative to microscopy in situations where reliable microscopic diagnosis is not available. The first RDT was approved for use by hospital and commercial laboratories in the U.S. by the Food and Drug Administration (FDA) in June 2007. It is recommended that all RDTs be followed up with microscopy to confirm the results and if positive, to quantify the proportion of red blood cells that are infected.

Parasite nucleic acids can be detected using polymerase chain reaction (PCR). Although this technique may be slightly more sensitive than smear microscopy, its use is limited in the diagnosis of acutely ill patients in the standard healthcare setting because 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.

## **EPIDEMIOLOGY**

### **Source**

Humans are the only important reservoir of human malaria. However, a certain species of malaria called *P. knowlesi* has recently been recognized to be a cause of significant numbers of human infections. *P. knowlesi* is a species that naturally infects macaques living in Southeast Asia. Humans living in close proximity to populations of these macaques may be at risk of infection with this zoonotic parasite.

### **Occurrence**

Endemic malaria no longer occurs in the United States and many temperate zone countries. Malaria is known to exist in parts of Mexico, Haiti, Central and South America, Africa, the Middle East, Turkey, the Indian subcontinent, Southeast Asia, China, the Malay Archipelago and Oceania. Falciparum and vivax malaria are found in most endemic areas but ovale malaria is seen mainly in West Africa. *P. falciparum* strains resistant to chloroquine (CRPF) occur in both hemispheres. Confirmed cases have been found in most of tropical South and Central America, Asia and East Africa.

About 1,500-2,000 cases of malaria are diagnosed in the United States annually, mostly in returned travelers.

Historically, malaria was indigenous to Ohio. Although indigenous malaria has been eliminated here, vector *Anopheles* mosquitoes remain prevalent. Thus, Ohio is an area free of disease but with a continuing risk of transmission.

### **Mode of Transmission and Life Cycle**

Malaria in humans is normally transmitted by the bite of a female *Anopheles* mosquito that is infected with *Plasmodium* parasites. As the mosquito feeds, it releases malaria

sporozoites into the bloodstream, which enter liver cells (exoerythrocytic state). After the parasite matures, the liver cell ruptures and releases numerous merozoites. These invade red blood cells (RBCs), starting the erythrocytic stage of an infection. Within the RBCs the parasites mature, become schizonts, and divide again into merozoites. Finally, the infected RBCs rupture, and merozoites repeat the cycle by invading other RBCs. The release of merozoites from erythrocytes initiates the chills and fever of a typical malaria paroxysm.

Relapses occur when *P. vivax* or *P. ovale* parasites that have remained dormant in the liver for months or years mature, enter the blood and initiate another series of erythrocytic cycles. Infections caused by *P. falciparum* and *P. malariae* do not relapse because these organisms have no persistent liver (exoerythrocytic) stage. Thus, *P. falciparum* and *P. malariae* infections can be cured by drugs that are active only against the parasite's erythrocytic stages. In *P. vivax* and *P. ovale* infections, therapy directed at the erythrocytic stages may eliminate parasites from the blood, but will not prevent relapses caused by parasites persisting in the liver.

No human-to-human transmission occurs, outside of induced or congenital malaria. Induced malaria occurs when the infection is passed from one individual to another through contaminated blood or blood products, injection equipment or organ transplant. Because there is no liver stage with transfusion-transmitted malaria, relapses cannot occur. Congenital infection can occur when malaria is transmitted from a mother to her infant in utero.

### **Period of Communicability**

Mosquitoes can be infected as long as infective gametocytes are present in the blood of patients. This varies with *Plasmodium* species and response to therapy, ranging from one to three years, especially in untreated or insufficiently treated cases. Stored blood may remain infective for 16 days. *Anopheles* mosquitoes are infective about 2 weeks after ingesting the malaria parasite and then are infective for life, which can be up to 6 weeks.

### **Incubation Period (Average)**

- *P. falciparum*: 12 days.
- *P. vivax* and *P. ovale*: 14 days.
- *P. malariae*: 30 days.
- Via blood transfusions: generally short but varies with the number of parasites transfused, may range up to 2 months.

## **PUBLIC HEALTH MANAGEMENT**

### **Case**

#### Investigation

Obtain a history to determine previous infection or exposure. This may aid in determining the possibility of chloroquine-resistance in cases of *P. falciparum*. If the patient has no recent history of overseas travel, contact the ODH Bureau of Infectious Diseases (BID) at (614) 995-5599.

#### Treatment

Selection and dosages of medication are dependent upon:

- The species of the malaria parasite present.
- The severity of the parasitemia.
- The drug susceptibility of the infecting parasites.
- Whether the case being treated is a relapse.
- The type of cure desired.

Due to the complexity of treatment decisions, specific treatment advice is not within the scope of this manual. Consultation is available. See "Consultation" under the Prevention and Control Section that follows.

#### Isolation and Follow-up Specimens

No isolation is indicated; however, hospitalized patients should be in mosquito-proof areas, and standard precautions should be observed. Follow-up specimens are not necessary unless there is a relapse of fever.

#### Public Health Significance

Malaria is a disease under surveillance by the World Health Organization, as it is considered an essential element of the world strategy of primary health care. The Centers for Disease Control and Prevention is expected to notify WHO twice a year of those malaria cases imported into the USA, an area free of disease but with continuing risk of transmission. The vector *Anopheles* mosquitoes are present, so there is a risk of limited indigenous disease if the patient was exposed to mosquito bites prior to beginning treatment. There is a low public health significance related to a malaria patient in Ohio.

#### **Contacts**

Since no human-to-human transmission occurs outside of rare congenital and blood transfusion events, there are no advisories for contacts.

#### **Prevention and Control**

##### Travelers

Because of the nocturnal feeding habits of *Anopheles* mosquitoes, malaria transmission takes place primarily between dusk and dawn. Therefore, travelers can reduce their risk of acquiring malaria by remaining in well-screened areas during these hours or by sleeping under mosquito netting. Exposure to mosquitoes outdoors can be reduced by wearing clothing that adequately covers the arms and legs and by applying mosquito repellent to thin clothing and exposed skin. The most effective repellent is N, N diethyl-metatoluamide (DEET), an ingredient of many commercially available insect repellents. Repellents containing permethrin applied to clothing and bed nets provides additional protection. Follow label instructions.

##### Vaccination

No vaccine is available.

##### Prophylaxis

Malaria attacks can be minimized by the use of relatively safe, convenient and inexpensive prophylactic medication. However, even when travelers are informed of their risk of acquiring malaria and obtain a prophylactic drug, they often fail to take it properly or do not continue taking it for the necessary six weeks after returning home.

The choice of medication depends on several factors. These include whether the traveler has a history of drug allergy or intolerance, whether the area to be visited has chloroquine-resistant *P. falciparum* malaria and whether the traveler is pregnant.

Chemoprophylaxis is not always successful. Although currently recommended antimalarial medications are generally effective, persons traveling to malarious areas should realize that the risk of acquiring the disease cannot be totally eliminated. Routine suppressive prophylaxis cannot prevent relapses of *P. vivax* and *P. ovale* infections. Travelers should be warned that if they experience malaria symptoms during,

or even several years after, possible exposure to malaria, they should inform a physician of their travel history so that this diagnosis will be considered.

Consultation

Because of changing risk factors and recommendations, questions about malaria prophylaxis or treatment should be directed to ODH BID at (614) 995-5599 or to the CDC. Malaria prevention information is available 24 hours a day by calling the CDC MALARIA HOTLINE at (770) 488-7100 or toll-free Monday-Friday 9 am-5 pm EST at (855) 856-4713.

**What is Malaria?**

Malaria is a serious and sometimes fatal mosquito-borne disease caused by a blood parasite called *Plasmodium*. Patients with malaria typically are very sick with high fevers, shaking chills and flu-like illness. Four kinds of malaria parasites infect humans: *Plasmodium falciparum*, *P. vivax*, *P. ovale* and *P. malariae*. In addition, *P. knowlesi*, a type of malaria that naturally infects macaques in Southeast Asia, also infects humans, causing malaria that is transmitted from animal to human ("zoonotic" malaria). *P. falciparum* is the type of malaria that is most likely to result in severe infections and if not properly treated, may lead to death. Although malaria can be a fatal disease, illness and death from malaria can usually be prevented.

About 1,500 cases of malaria are diagnosed in the United States every year. The vast majority of cases in the United States are in travelers and immigrants returning from parts of the world where malaria transmission occurs, including sub-Saharan Africa and South Asia. Almost all of the 30 to 45 cases reported annually in Ohio are acquired in foreign countries; however, a locally acquired case occurred here in 1975.

The World Health Organization estimates that malaria caused 214 million clinical episodes in 2015 and 438,000 deaths, most of them children in Africa. Because malaria causes so much illness and death, the disease is a great drain on many national economies. Since many countries with malaria are already among the poorer nations, the disease maintains a vicious cycle of disease and poverty.

**How is malaria spread?**

Malaria is spread through the bite of an infected *Anopheles* mosquito. Only *Anopheles* mosquitoes can transmit malaria, and they must have been infected through a previous blood meal taken from an infected person. When a mosquito bites an infected person, a small amount of blood is taken in which contains microscopic malaria parasites. About one week later, when the mosquito takes its next blood meal, these parasites mix with the mosquito's saliva and are injected into the person being bitten.

Because the malaria parasite is found in red blood cells of an infected person, malaria can also be transmitted through blood transfusion, organ transplant or the shared use of needles or syringes contaminated with blood. Malaria can also be transmitted from a mother to her unborn infant before or during delivery ("congenital" malaria).

**Is malaria a contagious disease?**

No. Malaria is not spread from person to person like a cold or the flu, and it cannot be sexually transmitted. You cannot get malaria from casual contact with malaria-infected people, such as sitting next to someone who has malaria.

**Who is at risk for malaria?**

Anyone can get malaria. Most cases occur in people who live in countries with malaria transmission. People from countries with no malaria can become infected when they travel to countries with malaria or through a blood transfusion (although this is very rare). Also, an infected mother can transmit malaria to her infant before or during delivery.

**Who is most at risk of getting very sick and dying from malaria?**

*Plasmodium falciparum* is the type of malaria that most often causes severe and life-threatening malaria; this parasite is very common in many countries in Africa south of the Sahara desert. People who have little or no immunity to malaria, such as young children and pregnant women or travelers coming from areas with no malaria, are more likely to



become very sick and die. Poor people living in rural areas who lack access to health care are at greater risk for this disease. As a result of all these factors, an estimated 90% of deaths due to malaria occur in Africa south of the Sahara; most of these deaths occur in children under 5 years of age.

### **What are the signs and symptoms of malaria?**

Symptoms of malaria include fever and flu-like illness, including shaking chills, headache, muscle aches and tiredness. Nausea, vomiting and diarrhea may also occur. Malaria may cause anemia and jaundice (yellow coloring of the skin and eyes) because of the loss of red blood cells. If not promptly treated, the infection can become severe and may cause kidney failure, seizures, mental confusion, coma and death.

### **How soon will a person feel sick after being bitten by an infected mosquito?**

For most people, symptoms begin 10 days to 4 weeks after infection, although a person may feel ill as early as 7 days or as late as 1 year later. Two kinds of malaria, *P. vivax* and *P. ovale* can occur again (relapsing malaria). In *P. vivax* and *P. ovale* infections, some parasites can remain dormant in the liver for several months up to about 4 years after a person is bitten by an infected mosquito. When these parasites come out of hibernation and begin invading red blood cells ("relapse"), the person will become sick.

### **How do I know if have malaria for sure?**

Most people, at the beginning of the disease, have fever, sweats, chills, headaches, malaise, muscle aches, nausea and vomiting. Malaria can very rapidly become a severe and life-threatening disease. The surest way for you and your healthcare provider to know whether you have malaria is to have a diagnostic test where a drop of your blood is examined under the microscope for the presence of malaria parasites. If you are sick and there is any suspicion of malaria (for example, if you have recently traveled in a country where malaria transmission occurs), the test should be performed without delay.

### **What is the treatment for malaria?**

Malaria can be cured with prescription drugs. The type of drugs and length of treatment depend on the type of malaria, where the person was infected, their age, whether the patient is pregnant and how sick the patient is at the start of treatment.

### **If I get malaria, will I have it for the rest of my life?**

No, not necessarily. Malaria can be treated. If the right drugs are used, people who have malaria can be cured, and all the malaria parasites can be cleared from their body. However, the disease can continue if it is not treated or if it is treated with the wrong drug. Some drugs are not effective because the parasite is resistant to them. Some people with malaria may be treated with the right drug, but at the wrong dose or for too short a period of time. However, in general, if you are correctly treated for malaria, the parasites are eliminated, and you are no longer infected with malaria.

### **Where does malaria occur?**

Malaria typically is found in warmer regions of the world, in tropical and subtropical countries. Malaria parasites, which grow and develop inside the mosquito, need warmth to complete their growth before they are mature enough to be transmitted to humans. Malaria occurs in more than 100 countries and territories. About half the world's population is at risk. Large areas of Africa and South Asia and parts of Central and South America, the Caribbean, Southeast Asia, the Middle East and Oceania are considered areas where malaria transmission occurs. Yet malaria does not occur in all warm climates. For examples, malaria has been eliminated in some countries with warm climates, while a few other countries have no malaria because *Anopheles* mosquitoes are not found there.

### **What can be done to prevent the spread of malaria?**

Since malaria is not native to the United States, exposure of Americans occurs most frequently during travel. Many effective preventive medications are available for those traveling to a known malarial area. You and your healthcare provider will decide on the best drug for you, if any, based on your travel plans, medical history, age, drug allergies, pregnancy status and other factors. Travelers who become ill with a fever during or after travel in a malaria risk area should seek prompt medical attention and should inform their physician of their recent travel history. These travelers should also avoid mosquito bites to prevent local mosquitoes from picking up and spreading malaria.

### **How can I prevent mosquito bites when traveling?**

Avoid mosquito bites.

- Avoid wet, swampy areas where mosquitoes live and breed.
- Avoid activities during the peak mosquito biting periods (dusk to dawn for *Anopheles* mosquitoes).
- Use mosquito netting over infant carriers.

Repel mosquitoes when outdoors.

- If the weather permits, wear long pants, long sleeves and/or socks.
- Apply mosquito repellent as directed to clothing and exposed skin.
- Reapply mosquito repellent as needed, especially if swimming or sweating.

### **For more information, please visit these websites:**

- World Health Organization Malaria Information: <http://www.who.int/topics/malaria/en/>
- CDC Malaria Information: <http://www.cdc.gov/malaria>
- CDC Insect Repellent Use and Safety: <http://www.cdc.gov/westnile/faq/repellent.html>
- CDC's Traveler's Health Malaria: <http://wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/malaria>