MALARIA

REPORTING INFORMATION

- **Class B1:** Report by the end of the next business day in which 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:
  - Ohio Confidential Reportable Disease form (HEA 3334, rev. 1/09), Positive Laboratory Findings for Reportable Disease form (HEA 3333, rev. 8/05), the local public health department via the Ohio Disease Reporting System (ODRS) or telephone.
  - The Centers for Disease Control and Prevention (CDC) Malaria Case Report Form (form CDC 54.1 rev 01/02) is required for completion by the local health department. Information collected from the form should be entered into ODRS **and** faxed to ODH at 614-564-2456. The mailing address for this form is: Ohio Department of Health, Outbreak Response and Bioterrorism Investigation Team, 246 N. High St., Columbus, OH 43215.
- Additional reporting information, with specifics regarding the key fields for ODRS reporting, can be located in Section 7.

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.

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.

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

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.

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

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*: 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.

SIGNS AND SYMPTOMS

See **Clinical Description** in the **CASE DEFINITION**.

DIAGNOSIS

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. 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. In addition, rapid diagnostic tests and

nucleic acid tests using PCR are available.

EPIDEMIOLOGY

Source

Humans are the only important reservoir of human malaria. However, 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.

Each year many Americans travel to malarious areas of the world. CDC received reports of 1,478 imported cases of malaria, including four fatal cases, with an onset of symptoms in 2009 among persons in the United States or one of its territories. This number represents an increase of 14% from the 1,298 cases reported for 2008. This apparent increase is probably due to increased travel by Americans, increased immigration and a decline in funding of vector control in malarious areas.

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 one of four species of *Plasmodium*. 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. No human-to-human transmission occurs.

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.

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.

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 Outbreak Response and BT Investigation Team **immediately** 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.

Clinical Cure: (also known as "treatment of the acute attack") is treatment to reduce or eliminate the asexual erythrocytic parasites that cause the clinical signs and symptoms of malaria.

Radical Cure: (also known as "radical treatment") is therapy to completely eliminate malaria parasites so that a malaria attack cannot recur after treatment is completed. Radical treatment may require action against only erythrocytic parasites (*P. falciparum* and *P. malariae*) or against both erythrocytic and exoerythrocytic forms (*P. vivax* and *P. ovale*). In the latter instance, radical cure would consist of chloroquine or another drug to eliminate parasites from the blood and primaquine to kill parasites in the liver.

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 repellant to thin clothing and exposed skin. The most effective repellant is N, N diethyl-metatoluamide (DEET), an ingredient of many commercially available insect repellents. Repellants containing permethrin applied to clothing and bed nets gives 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.

When malaria prophylaxis is discussed, the following terms are often used:

Suppression is prevention of the clinical symptoms of malaria by reducing or eliminating parasites in the blood. Suppression does not necessarily prevent either initial infection or relapses caused by parasites persisting in liver cells.

Suppressive cure is elimination of malaria infection by continuing suppressive medication long enough to exceed the duration of the liver stage for the malaria species involved. In non-relapsing malaria (*P. falciparum* and *P. malariae*), suppressive cure is usually achieved if the drug is continued for six weeks after the last exposure to malarious mosquitoes.

The best sources of information for prophylaxis recommendations are the MMWR supplements, "Prevention of Malaria in Travelers" and "Health Information for International Travel." Both are updated periodically and the most recent supplement should be consulted.

Consultation

Because of changing risk factors and recommendations, questions about malaria prophylaxis or treatment should be directed to the ODH Outbreak Response and BT Investigation Team, 614-995-5599, or to the Centers for Disease Control and Prevention (CDC). Malaria prevention information is available 24 hours a day by calling the MALARIA HOTLINE at 770-488-7100.

Other Sources of Information:

Control of Communicable Diseases Manual, American Public Health Association (Updated every 5 years).

Red Book: Report of the Committee on Infectious Diseases, American Academy of Pediatrics (Updated approximately every three years).

What is Malaria?
Malaria is a 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. Although malaria can be a fatal disease, illness and death from malaria are largely preventable.

The World Health Organization estimates that each year 350-500 million cases of malaria occur, and more than 1 million people die as a result. Malaria is most prevalent in warmer regions of the world – typically tropical and subtropical areas, including over 100 countries in Central and South America, Hispaniola, Africa, the Indian subcontinent, Southeast Asia, the Middle East and Oceania.

About 1,500 cases of malaria are diagnosed in the United States every year, most occurring in travelers and immigrants returning from malaria-risk areas of the world. Almost all of the 25 to 35 cases reported annually in Ohio are acquired in foreign countries; however, a locally acquired case occurred here in 1975.

How is malaria spread?
Malaria is spread by the bite of an infected *Anopheles* mosquito. *Anopheles* mosquitoes prefer to feed at night. With certain malaria species, dormant forms can be produced which may cause relapses of malaria months to years later. Malaria may also be transmitted by transfusion of blood from infected people or by the use of contaminated needles or syringes.

How soon do symptoms occur?
The time between the infective mosquito bite and the development of malaria symptoms can range from 12-30 days, depending on the type of *Plasmodium* involved.

What are the symptoms of malaria?
Symptoms often include fever, chills, sweats, muscle aches, tiredness and headache. In some instances they may progress to blood coagulation defects, shock, kidney or liver failure, central nervous system disorders, coma and death. Cycles of chills, fever and sweating occurring every one, two or three days are a good indicator of malaria in a person recently returning from a tropical area.

How is malaria diagnosed?
Malaria is diagnosed based on symptoms, followed by laboratory confirmation. The test that is used most widely is microscopic examination of the patient's blood for the presence of the malaria parasite.

Can infected persons spread malaria?
Direct person-to-person transmission does not occur. Untreated or inadequately treated cases may be a source of mosquito infection for one to three years depending on the strain of *Plasmodium*. Stored blood products can remain infective for 16 days.

What is the treatment for malaria?
Malaria can be cured with prescription drugs**.** The type of drugs and length of treatment depend on which kind of malaria is diagnosed, where the patient was infected, the age of the patient, whether the patient is pregnant and how severely ill the patient is at the start of treatment.

Once infected with malaria are you infected for life?
Malaria can be treated. However, the disease can persist if it is left untreated or if treatment was ineffective either due to drug resistance or a shortened course of treatment.

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. Preventive medications are available for those traveling to a known malarial area. 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.

Although malaria is not endemic to Ohio, there are *Anopheles* mosquitoes here which are efficient transmitters of *Plasmodium*. Thus, an infected person, if bitten by an *Anopheles* mosquito, could allow the parasite to be transmitted in Ohio.

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.
- Use mosquito netting over infant carriers.

Repel mosquitoes when outdoors.

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

For more information, please visit these websites:
World Health Organization malaria page http://www.who.int/topics/malaria/en/

CDC malaria page http://www.cdc.gov/malaria

CDC insect repellant use and safety
http://www.cdc.gov/ncidod/dvbid/westnile/qa/insect_repellent.htm