March 2024

Malaria

Surveillance and Investigation Protocol

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I. ABOUT THE DISEASE

Malaria is a parasitic infection that results from being bitten by an infected female *Anopheles* mosquito. While there are approximately 430 species of *Anopheles*, only 30-40 transmit malaria [1]. Five species of parasites within the genus *Plasmodium* are the agents for malaria [2]. Malaria poses a risk to approximately 3.3 billion people or approximately half of the world's population, primarily in Africa. In 2021, there were 84 malaria endemic countries compared with 108 in 2000; largely because of progress toward eliminating malaria [3]. Malaria is one of the most common causes of fever with an unknown origin among those traveling from a malaria endemic country. In 2023, there were seven cases of locally acquired malaria in Florida, Texas, Maryland, and Arkansas. While outbreaks of locally transmitted cases of malaria in the United States have been small and relatively isolated, the potential risk for the disease to re-emerge is present due to the presence of competent mosquito vectors capable of passing malaria parasites from one human to another, especially in the southern states. In West Virginia, 1–2 travel-associated cases of malaria are reported each year from persons who have visited malaria-endemic areas [4].

A. Clinical Presentation

Malaria can be divided into two categories, uncomplicated and severe.

1. Most commonly a person experiencing uncomplicated malaria will present with flu-like symptoms: fever, chills, sweats, headaches, nausea and vomiting, and body aches. In rare cases, uncomplicated malaria is accompanied with attacks that last 6-10 hours and occur every other day. These attacks consist of a cold stage (sensation of cold, shivering), followed by a hot stage (fever, headaches, vomiting; seizures in young children), and finally a sweating stage (sweats, return to normal temperature, tiredness) [5].
2. Severe malaria occurs when infections are complicated by organ failures or abnormalities in a patient's blood or metabolism. The major complications of severe malaria include cerebral malaria, pulmonary edema, acute renal failure, severe anemia, and/or bleeding. Acidosis and hypoglycemia are the most common metabolic complications. Any of these complications can develop rapidly and progress to death within hours or days [6].

B. Etiologic Agent

Malaria is caused by protozoan parasites in the *Plasmodium* genus. Five species of *Plasmodium* can infect humans: *P. vivax*, *P. ovale*, *P. malariae*, *P. falciparum*, and *P. knowlesi* [2].

The most common species that cause illness in humans are *P. vivax* or *P. falciparum*. *P. falciparum* causes the most severe form of malaria. In areas of Africa and Asia with

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hyperendemic infection, reinfection in people with partial immunity results in a high prevalence of asymptomatic parasitemia [10].

C. Reservoir

Humans are the only important reservoir species [6].

Incubation Period

The incubation period varies based on the species of parasite [7]:

- 9-14 days for *P. falciparum*
- 12-18 days for *P. vivax* and *P. ovale*
- 18-40 days for *P. malariae*
- 10-12 days for *P. knowlesi*

The use of prophylactic medication may prolong the incubation period or mask symptoms.

D. Mode of Transmission

Malaria is transmitted by the bite of an infected female *Anopheles* mosquito.

Malaria can also be transmitted from person- to- person through the use of an infected needle, receiving blood or tissue contaminated blood during a transfusion, and from mother to child (congenital) [7].

E. Period of Communicability

Humans can spread malaria if infectious gametocytes remain in the blood. Gametocytes usually appear within three days of parasitaemia with *P. vivax* and *P. ovale*, and after 10-14 days with *P. falciparum* [7]. Untreated or inadequately treated patients may be a source of infection period for several years with *P. malariae*, up to five years with *P. vivax* and generally not more than one year with *P. falciparum* [7]. Transmission by transfusion (or needle stick injuries) may occur if asexual forms remain in the circulating blood. With *P. malariae*, this can continue for more than 40 years. Stored blood can remain infectious for at least a month.

Thus, the infected mosquito carries the disease from one human to another (acting as a "vector"), while infected humans transmit the parasite to the mosquito, in contrast to the human host, the mosquito vector does not suffer from the presence of the parasites.

II. DISEASE CONTROL AND PREVENTION

A. Disease Control Objectives

1. Implement measures to prevent contact with female *Anopheles* mosquitoes while in malaria-endemic countries.
2. Administer early treatment of infected patients to prevent severe stage malaria.

B. Disease Prevention Objectives

1. Reduce disease risk through:
   a. Educate travelers regarding the importance of reporting onset of illness after travel to endemic countries.
   b. Educate travelers to take malaria chemoprophylaxis prior to traveling to an area that is malaria endemic.

C. Disease Prevention and Control Intervention

Currently there is no commercially available malaria vaccine. Travelers can protect themselves from malaria by taking chemoprophylaxis before, during, and after their trip, and by preventing mosquito bites. The type of chemoprophylaxis administered varies based on destination and by the risk of exposure [10]. There are three available in the United States for prevention of chloroquine-resistant malaria.

Drug Name	Dosage for Adults	Dosage for Children	Dosage for Pregnant Women	Duration of Treatment
Atovaquone-proguanil	Daily	A formula is available but not approved for children <5kg (11lbs)1	Should not be prescribed	Start the 1-2 days before exposure and continue until one week after leaving the malaria endemic area
Doxycycline	Daily	Should not be prescribed to children <8 years of age	Should not be prescribed; also not for women of childbearing age	Start 1-2 days before exposure and continue until 4 weeks after leaving the malaria endemic area
Mefloquine	Once weekly	Calculated based on weight	Can be used in all trimesters of pregnancy and during breastfeeding	Start 2 weeks prior to exposure and continue until 4 weeks after leaving the malaria endemic area
Primaquine3	Daily	Calculated based on weight	Should not be prescribed	Start 1-2 days before exposure and continue until 7 days after leaving the malaria endemic area
Tafenoquine	Daily, weekly	Cannot be used in children	Should not be prescribed	Daily for 3 days prior to travel, weekly during travel, and for 1 week after leaving

Table 1. Malaria Chemoprophylaxis Dosages and Schedules [10]

D. Treatment

Malaria can be severe and is potentially fatal, therefore, treatment should be initiated as soon as possible. The choice of the appropriate treatment depends on the species of infecting parasite, possible drug resistance, and the severity of disease. Patients with severe malaria require intensive care and parenteral treatment until the parasite density decreases to less than 1% and they can tolerate oral therapy. If parasitemia exceeds 10% or if there is evidence of complications intravenous artesunate may be necessary.

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III. DISEASE INVESTIGATION

A. Criteria for Case Ascertainment

Healthcare providers should consider malaria disease investigation if the patient is experiencing malaria symptoms and has traveled in the last year to or from a malaria endemic area.

Clinical Criteria for Diagnosis and Reporting

Any symptoms potentially related to Malaria.

Laboratory Criteria for Diagnosis and Reporting

Any laboratory results that detect a *Plasmodium* species.

Epidemiological Linkage Criteria for Reporting

Having traveled to or from a malaria endemic area

B. Case Definition and Case Classification

The 2014 case definition is the most current (CSTE Position Statement Number 13-ID-08):

Background

Malaria is a mosquito-borne disease caused by a parasite; intraerythrocytic protozoa of the genus *Plasmodium* (e.g., *P. falciparum*, *P. vivax*, *P. ovale*, and *P. malariae* among other species). The first two species cause the most infections worldwide. *P. falciparum* is the agent that most commonly causes severe and potentially fatal malaria. *P. vivax* and *P. ovale* may have dormant liver stage parasites, which can reactivate and cause malaria several months or years after the infecting mosquito bite. *P. malariae* can result in long-lasting infections and if untreated can persist asymptomatically in the human host for years, even a lifetime. About 2,000 cases of malaria are reported each year in the United States, most of which are imported, i.e., acquired in malaria-endemic countries.

Clinical Criteria

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

1. 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.
2. Confirmed:
   a. Detection of circulating malaria-specific antigens using rapid diagnostic test (RDT)
      OR
   b. Detection of species-specific parasite DNA in a sample of peripheral blood using a Polymerase Chain Reaction (PCR) test. (Note: Laboratory-developed malaria PCR tests must fulfill Clinical Laboratory Improvement Amendments [CLIA] requirements, including validation studies)
      OR
   c. 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

1. Suspected
   a. 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
   a. Detection and specific identification of malaria parasite species 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
   b. 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
   c. Detection of unspeciated malaria parasite 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.
   *Laboratory-developed malaria PCR tests must fulfill CLIA requirements, including validation studies.

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Case Classification Comments

Clinical samples including blood smears or ethylenediamine tetraacetic acid (EDTA) whole blood from all cases can be referred to the Centers for Disease Control and Prevention's (CDC) Division of Parasitic Diseases and Malaria Diagnostic Laboratory for confirmation of the diagnosis and antimalarial 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.

Criteria to Distinguish a New Case from an Existing Case

1. A subsequent attack experienced by the same person but caused by a different *Plasmodium* species is counted as an additional case.
2. 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

C. Reporting Timeframe to Public Health

Cases of malaria must be reported within one week to the local health department in the patient's home county.

D. Outbreak Recognition

1. An unusual increase or a new occurrence of autochthonous (indigenous or introduced) cases in a certain area.
2. In areas where no local malaria transmission has been observed for at least five years, any newly introduced case is defined as an outbreak. The occurrence of only imported cases not having caused secondary cases is not considered an outbreak.

E. Healthcare Provider Responsibilities

1. Report suspect or confirmed cases to your local health department within one week. Supply requested clinical information to the local health department to assist with case ascertainment.
2. Healthcare providers needing assistance with diagnosis or management of suspected cases of malaria should call the CDC Malaria Hotline: 1 (770) 488-7788 or 1 (855) 856-4713 toll-free (M-F, 9am-5pm, eastern time).
   a. Coordinate with the West Virginia Office of Laboratory Services on shipping specimens to CDC for testing.
3. Submit any positive laboratory results pertaining to malaria to the local health department located in the patient's home county.

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F. Laboratory Responsibilities

1. Perform appropriate testing for patients with suspected malaria. This involves thin or thick peripheral blood films, a Polymerase Chain Reaction test (PCR), or a Rapid Diagnostic Test (RDT) if a reliable microscope diagnosis is not available. PCR is most useful for confirming the species of parasite after the diagnosis has been established by either smear microscopy or RDT [5].
2. Forward copies of any positive malaria test results to the local health department in the patient's home county within one week of diagnosis.

G. Local Health Responsibilities

1. Conduct an appropriate case investigation.
   a. Contact the healthcare provider that ordered the laboratory test to obtain the clinical information on the West Virginia's Electronic Disease Surveillance System (WVEDSS) form.
   b. If needed, contact the patient to obtain information regarding travel history.
   c. Educate the patient and the patient's family on mosquito bite prevention (to prevent local transmission of disease) and other appropriate prevention messages.
   d. Conduct a home visit and perform an environmental assessment to identify potential risk factors for exposure to mosquitoes.
   e. Report all case data using WVEDSS.
2. Educate the public about malaria, especially regarding prevention measures when traveling.
3. Educate providers, laboratories, and infection control practitioners about diagnosis and reporting of malaria.
4. If a suspect or confirmed case has no travel history to an area where malaria is endemic, contact DIDE immediately.
5. Consult with DIDE for guidance on appropriate case management and public health actions.

H. State Health Responsibilities

1. Review completed case reports from local health departments within one week.
2. Report all confirmed and suspected cases to CDC using WVEDSS.
3. Provide consultation to local health departments regarding case ascertainment.
4. Provide regular data feedback to local health departments and public health partners during mosquito-borne disease season (May-October).
5. Conduct mosquito surveillance activities.

I. Occupational Health

Public health workers who conduct field research and/or travel to communities where malaria is prevalent may also be at risk.

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1. Hazard identification and risk assessment: Public health entities investigating malaria-affected areas should conduct a risk assessment to determine the risk of malaria exposure among workers.
2. Education and training: Employees should be educated about malaria, its risks, its transmission, symptoms, and prevention measures.
3. Safe work practices and procedures: Local health should implement standard infection prevention and control procedures to avoid the rare but possible transmission of malaria. The best way to protect against malaria is by preventing mosquito bites. Infection control measures could include, but are not limited to:
    a. When traveling to an area that is highly endemic to Malaria, preventative chemoprophylaxis may be warranted.
    b. When field investigations are being conducted in an area suspected of having malaria infected vectors, use insect repellent on all exposed skin. The most effective repellents contain the ingredient DEET (N, N-diethyl-meta-toluamide). However, it is important to use the right concentration of DEET (at least 20%–30%), depending on age
    c. Choose light-colored clothing, a long-sleeved shirt, long pants, and socks.
    d. Treat clothing with an insect repellent.
4. Health monitoring and reporting.

IV. DISEASE SURVEILLANCE

A. Public Health Significance

When European explorers and colonists arrived in the Americas, they brought *P. malariae* and *P. vivax* with them; *P. falciparum* was imported to the Western Hemisphere by Africans during slavery. The combination of a vulnerable population and an environment that facilitated the breeding of *Anopheles* mosquitoes allowed the disease to flourish. Malaria plagued the United States until the early 20th century. The modernization of the rural South and hydroelectric power in the 1930s resulted in a decrease of malaria cases. Malaria was practically eradicated in the United States until World War II.

Malaria is infamous for its morbidity and mortality and continues to cause disease around the globe, particularly in Africa, but the disease is also responsible for the creation of the CDC [8].

B. Disease Surveillance Objectives

1. To identify and monitor the epidemiologic characteristics of imported malaria infections in West Virginia.
2. To identify new or invasive *Anopheles* mosquito species not previously identified in West Virginia that could be capable of transmitting malaria.

3. To identify and characterize instances of local transmission if they occur. This information would direct vector surveillance (by species and geographic distribution) to evaluate their relative roles in potential transmission within West Virginia.

C. Surveillance Indicators

Proportion of cases with complete clinical, laboratory, and epidemiologic information including clinical symptoms, testing, and risk factor information (e.g. travel history, outdoor activities).

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