

Malaria

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To contribute adequate case reports to the national database, which in turn gives us a better sense of the characteristics of and risk factors for malaria in the United States.
2. To ensure adequate treatment of cases, particularly those with potential fatal *falciparum* malaria.
3. To identify case contacts who may benefit from screening or treatment, e.g., fellow travelers or recipients of blood products.
4. Conceivably, to identify persons exposed locally and initiate appropriate follow-up.

B. Laboratory And Physician Reporting Requirements

Physicians are required to report suspected or confirmed cases of malaria within one working day. Laboratories must report identification of malaria parasites within one working day.

C. Local Health Department Reporting and Follow-Up Responsibilities

1. Report all confirmed and presumptive (but *not* suspect) cases to the OHD (see definitions below) by the end of the calendar week of initial physician/lab report. Use the top part of a case investigation form for preliminary reports.
2. Begin follow-up investigation within one working day. Use OHD malaria case investigation form. Send a copy of the completed form to the OHD within 7 days of initial report.

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Malaria is the most commonly reported vector-borne disease in Oregon. It is a parasitic disease, caused by protozoan (one-celled) parasites of the genus *Plasmodium*. There are four species that commonly cause disease among humans: *P. vivax*, *P. falciparum*, *P. ovale*, and *P. malariae*. Other species affect other mammals, birds, and reptiles; some of these (rarely) cause human illness. Malariology is an extremely complicated field, and these guidelines provide only the briefest of overviews. It is important to understand that there are significant differences among the several species in terms of clinical illness, treatment, and geographical distribution. *Falciparum* malaria is the one that can kill; if you know it isn't *falciparum*, you can relax a bit. Mixed infections are possible, however.

Malaria parasites have a complicated life cycle. After injection into the human host from anopheline mosquitoes, the parasites home in on the person's liver, where they undergo maturation before being released into the bloodstream, whence they invade red blood cells. They change form and multiply inside the RBCs, eventually rupturing the cells, releasing still more parasites into the bloodstream. This bloodstream cycle can persist for weeks to years, depending on the species involved. In *vivax* and *ovale* malaria, some parasites ("hypnozoites") can persist indefinitely in the liver. Meanwhile, back in the bloodstream, some of the 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.

B. Description of Illness

The classic signs and symptoms of malaria are recurrent bouts of fever, chills, and headache. Many other symptoms can occur, depending on the severity of infection, including GI (vomiting, diarrhea) and respiratory (cough, SOB) symptoms, myalgias, etc.—the gamut of "flu-like" symptoms. Fever crises can recur at regular intervals (48 or 72 hours, depending on the species) that

Malaria

coincide with a synchronized rupture of RBCs, but this periodicity is often masked. The severity of symptoms vary with the species of parasite involved, the stage of infection, the immunological history of the patient, and other factors. Persons with recurrent exposures in endemic areas may develop “concomitant” immunity—a relative resistance to symptoms that persists only with continued exposure.

P. falciparum infections are potentially life-threatening, because the parasitemia (proportion of red blood cells infected) can increase very rapidly, unpredictably, and to very high levels (>15%). Complications of inadequately treated *falciparum* malaria include anemia, renal failure, shock, ARDS, and acidosis. Disease caused by the other species is rarely fatal, and can be quite mild.

Malaria is on everyone’s short list of the world’s biggest communicable disease problems. It kills ~1,000,000 people each year, and sickens and debilitates many times that number. Earlier optimism (particularly in the 1950s and 60s) about our ability to control and sharply reduce the impact of this disease has proven unrealistic, what with the advent of mosquitoes resistant to pesticides and parasites resistant to therapeutic drugs. Malaria in endemic areas is often a recurrent and usually asymptomatic or only moderate infection among adults. Young children and pregnant women, their health often compromised by depressed immunity or substandard nutrition are the most common victims of severe infections.

Not surprisingly, malaria in Oregon is not typical of malaria in the world at large. Most cases in Oregon occur among tourists (coming or going) business travelers, mission workers, immigrants, and refugees.

C. Reservoirs — Human cases and carriers.

D. Modes of Transmission

Transmission occurs by the bite of infected mosquitoes. Only certain species of the genus *Anopheles* are competent vectors of human malaria. These mosquitoes differ enormously in their habits (e.g., breeding in still or fast-moving water, in fresh or brackish water; feeding in the evening, at night, or in the daytime; living in forests or in peri-urban areas, etc.), with obvious implications for exposure risks and control measures.

Person-to-person transmission can occur through blood contact (e.g., transfusions or needle-sharing), although this is rare in the United States.

E. Distribution of Disease

Malaria is endemic in much of the world, particularly much of the Western Hemisphere between Mexico and Peru-Bolivia-Brazil, sub-Saharan Africa, South and SE Asia, and parts of the Middle East and Turkey. Endemic transmission requires both a pool of infected humans and the presence of competent vector mosquitoes.

Although once common in parts of the country, malaria has become an exotic disease in the United States. Nonetheless, one should remain alert to the potential for local transmission. All cases reported in Oregon in recent years have resulted from exposure abroad. There are anopheline mosquitoes in Oregon, but they are not very common and, more importantly, not very effective vectors for human malaria.

F. Incubation Period

Differs by species: 7–14 days for *P. falciparum*; 8–14 days for *P. vivax* and *P. ovale*; 7–30 days for *P. malariae*, and can be extended by concurrent drug intake and immunological history.

G. Period of Communicability

Malaria is not spread directly from person to person, absent significant blood exposure during a period of parasitemia, which can last (intermittently) for weeks to years, absent treatment. *Plasmodium* parasites must undergo developmental changes in a competent mosquito host before being passed back to another human; this takes between a week and a month.

H. Prophylaxis

Local health department staff are often asked questions about malaria prevention. Good information is available at many travel clinics and through the CDC’s web page (www.cdc.gov), including country-specific recommendations. The risk of malaria is not uniform within most

Malaria

countries because of climate, geography, mosquito control efforts, and other factors, and traveler risk will vary with the style of travel, and it can vary enormously with the seasons. The CDC's "Yellow Book," available on the Internet (current at <http://www.cdc.gov/travel/reference.htm>), is perhaps the best general source of up-to-date information.

Despite decades of effort, there are no vaccines available.

There are three parts to prophylaxis: avoiding mosquito bites, suppressing the development of symptoms (most of which stem from RBC lysis), and preventing recurrence of symptoms down the road.

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, in part because mosquitoes seem to have trouble landing on people having convulsions.* Staying in fancy resorts (which often attempt to control mosquito populations) or spending evenings and nights in sealed, air-conditioned hotels can greatly reduce the risk of being bitten, as well as minimizing the risk of exposure to local culture in general.

2. Chemoprophylaxis

The main issue for most travelers is whether, when, and what kind of chemoprophylaxis is appropriate. Hebdomadal 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, it would be imprudent to offer specifics here. Refer to up-to-date resources (e.g., the CDC web site) before making specific recommendations.

3. Preventing Recurrences

Ovale and *vivax* parasites can be sequestered in the liver. These hypnozoites, as they are called, can emerge weeks or months after an initial attack to cause a relapse. Drugs that are used to treat symptomatic disease (i.e., the intraerythrocytic parasites) are not effective against hypnozoites. Thus, to prevent relapse (which is not a certainty, but a possibility), primaquine is generally indicated for persons who have had an attack of *ovale* or *vivax* malaria. Be aware, however, that there are some contraindications to primaquine use (e.g., G6PD deficiency).

I. Treatment

Treatment is complicated by issues of parasite resistance and, to a lesser extent, side effects and drug availability. Many drugs that are available overseas are not available here; some of them are good. For non-*falciparum* malaria, chloroquine remains the drug of choice for treatment; chloroquine resistance has only been reported for *P. vivax* in parts of SE Asia.

Treatment of *falciparum* malaria is more complicated, because of widespread resistance to chloroquine, and, increasingly, mefloquine. Quinine is often the drug of choice, but an ID consult is generally indicated to get up-to-date treatment recommendations. Because of the potential for rapid clinical deterioration, clinicians should strongly consider admitting patients with *falciparum* malaria, at least until the success of therapy is assured. Severely ill patients are typically treated with IV quinidine in an ICU setting. Side effects can be severe and themselves life-threatening.

3. CASE DEFINITIONS, DIAGNOSIS, AND LABORATORY SERVICES

A. Confirmed Case

Confirmation depends on identification of malaria parasites in peripheral blood smear by a competent lab. Parasites are not always readily detectable in every specimen; repeat specimens at 8-hour intervals increases sensitivity. Speciation of parasites can be difficult, although it is often possible at least to rule out *P. falciparum*, which is much better than nothing.

* Just kidding.

Malaria

B. Presumptive Case

These would be very rare. In fact, rather than waste a lot of time figuring out some rubric, we'll wait until you call about a less-than-confirmed case and we'll make an ad hoc decision then.

C. Suspect Case (*not reportable to OHD*)

Persons with fever, chills, and headache and a history of recent travel to an endemic area. These persons need medical evaluation. If they are epi-linked to someone with a *P. falciparum* infection, this should be done immediately. Bear in mind that, in some cases, *P. falciparum* infections can progress with a speed that rivals fulminant meningococcal disease.

D. Services Available at the Public Health Laboratory

The PHL can confirm the identification and speciation of malaria parasites on blood smears. Although not required, if the private lab is unable to make a specific identification, they should be strongly encouraged to submit specimens to the PHL.

4. ROUTINE CASE INVESTIGATION

Use the OHD Malaria case report form to structure your interview/investigation. Note that some of the questions differ a bit from those we typically ask for other diseases.

A. Basis of Diagnosis

Clinical details are asked in order to contribute to national (CDC) data. Most of the severe complications listed on the form only occur with *falciparum* infections, and even then are infrequent. As noted, labs are sometimes unable to speciate the parasites seen on blood smear. Even if no specific identification was made, it is often possible to rule out *P. falciparum*; you may need to check with the lab to see if they got that far. Encourage them to send the smears (on glass microscope slides) to the PHL.

Epilinks are rarely a big deal, but if a case travelled 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. Persons with possible *falciparum* exposure should receive particularly close scrutiny.

B. Prophylaxis

Most of the questions on the form are self-explanatory. They are tailored for U.S. residents who were traveling or living abroad during the likely exposure period, and may be more or less relevant for persons with other exposures. Assess as best you can the consistency with which prophylactic measures were used.

The use of mosquito bed nets is considered unnecessary if the traveler is staying in a "modern" air-conditioned hotel, with windows closed at night (when most *Anopheles* mosquitoes feed).

C. Potential Exposures

Most cases will have been traveling or living in malarious areas in the weeks before onset. If the patient has not been out of the United States during the preceding month, or if things don't seem to make sense, contact the OHD immediately.

Here are some alternative possibilities:

1. This may be a *relapse* of a previous infection. "Relapse" has a technical meaning for malaria, meaning a reseeded of the bloodstream from hypnozoites in the liver. This only happens with *ovale* or *vivax* malaria, and implies that the case was infected at some point and then either never treated or only treated for bloodstream parasites. Primaquine is the only drug that goes after the liver stage bugs; it should be given in addition to whatever is used to treat bloodstream parasites (chloroquine, presumably, since we are not talking about *falciparum*).
2. This may be a *recrudescence* of a previous infection, meaning that the case had a low-level asymptomatic parasitemia that "blossomed" to cause the current illness. Although there are no long-term liver stage parasites in these infections (and hence no need for primaquine), such silent infections can persist for 6–18 months or more with *P. falciparum* and decades for *P. malariae*.

Malaria

3. They may have been infected by direct inoculation of contaminated blood or blood products (e.g., transfusions, needle sharing). Consult with OHD about this possibility.
4. They may have been infected by mosquito bite, but not in an endemic area. This is another potential hot button. So-called “airport malaria” can occur if infective mosquitoes survive travel on a plane from an endemic area and then fly off and bite people within a few miles of the airport. Oregon doesn’t get many flights directly from endemic areas, however; this is more likely to happen (and has) near, say, JFK airport in New York. Another possibility is that a parasitemic person may return to Oregon from a stay overseas (tourist, refugee, immigrant, whatever) and be bitten here by an *Anopheles* mosquito. Following development in the mosquito host, the stage could be set for another round of transmission to humans who had never left the state. This kind of transmission has been documented numerous times in California, including an outbreak at a Girl Scout camp in the 1960s, and more recently transmission among migrant workers living in squalid encampments near San Diego. Although anopheline mosquitoes can be found in Oregon, local transmission is an unlikely scenario.

5. CONTROLLING FURTHER SPREAD

Infected persons should not share needles until their parasitemia clears. Generally, however, no other specific control measures are indicated.

B. Isolation and Work or Day Care Restrictions

None.

C. Follow up of Cases

The degree of follow-up depends on the infecting species. For *vivax* and *ovale* cases, make sure that treatment includes primaquine to cover hypnozoites, unless medically contraindicated (which it sometimes is). For *falciparum* cases, assess the adequacy of treatment; see §6A. This follow-up usually means verifying the prescribed medication(s) with the physician.

D. Environmental Investigation

None, unless transmission in Oregon is suspected.

6. MANAGING SPECIAL SITUATIONS

A. Undertreated *Falciparum* 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. Chloroquine does have some analgesic properties, however, so depending on the level of resistance, it may knock down parasite levels sufficiently or at least make the patient feel better for a while, masking potential treatment failure. If you hear about a *falciparum* case that was treated with chloroquine, verify the treatment information with the patient’s physician. Consult with OHD epidemiologists immediately if the story appears to be true.

B. No Recent Travel to Endemic Areas

Consult with OHD epidemiologists immediately about any case that does not have a history of recent travel to a malarious area. We will discuss the options and develop a plan.