Nebraska Medicine/UNMC Malaria Diagnosis and Management Workflow

When to consider malaria:

Consider malaria as a differential for any febrile patient with exposure to region where malaria is endemic (https://www.cdc.gov/malaria/travelers/country_table/a.html). Occasionally, patients present without fever at first and with diarrhea or respiratory complaints, so malaria also should be considered in any moderately to severely ill patient with potential exposure. While the incubation period typically is less than 30 days, acute malaria can present 6 weeks or more from exposure, especially when chemoprophylaxis or sub-optimal treatment was used. *P vivax* and *P ovale* can present as relapsed infections weeks to months—and rarely years--after initial infection. *P malariae* can recrudesce months to years later. Use of chemoprophylaxis during travel does NOT exclude a diagnosis of malaria. Individuals who did not take prophylaxis or stayed with family members/friends are likely at higher risk.

Presenting symptoms are often non-specific including fever with chills, malaise, headache, cough, nausea, vomiting, abdominal pain, and diarrhea. Myalgias and other generalized symptoms also can be present. Patient presentation varies from mild illness with only minor symptoms to critical illness requiring ICU level support. Physical examination often is unremarkable. Sometimes hepatosplenomegaly is present as well as manifestations of anemia. Patients progressing to more severe disease may have crackles on lung auscultation. Lab abnormalities may include anemia, thrombocytopenia, elevated transaminases, elevated BUN and creatinine. Severe malaria may present with confusion, ARDS, metabolic acidosis, renal failure, hepatic failure, DIC, and hypoglycemia. Any species of malaria that causes human disease may result in a complicated clinical course, although, most cases are well managed with early, appropriate therapy.

Important differential diagnoses or co-infections to consider include typhoid and other invasive enteric bacteria, arboviruses (e.g., dengue fever, chikungunya), meningitis, pneumonia, sepsis due to other bacteremia, leptospirosis, rickettsial infection, and viral hemorrhagic fever.

Suspected malaria case in ED/Clinic setting workflow:

- Contact on-call appropriate ID team (General, Community, SOT or Oncology) with relevant history, exam, and lab data for consultation.
- ID team to determine if Global Fever panel and/or malaria smear evaluation is indicated

- ID provider (attendings, fellows, APPs) will order Global Fever panel if appropriate
- ID provider determines urgency of smear evaluation in conjunction with Global Fever panel
    - If malaria target(s) detected on the Global Fever Panel, an urgent thick/thin smear is required to determine percent parasitemia for treatment guidance as well as to assess for co-infection from more than one species
    - For urgent smear contact on-call pathology resident at 402-888-1380
    - If the Global Fever panel is not available, serial diagnostic thick/ thin smear may be required if the first smear is negative for malaria parasites (CDC guidelines indicate three smears separated by 12-24 hours)
- ID provider makes recommendations about treatment and level of care (e.g., outpatient, ward, or critical care) to primary team. Primary teams can place orders for all formulary anti-malaria treatments except IV artesunate. On a case-by-case basis, ID may recommend anti-malaria therapy before a diagnosis of malaria is confirmed.
- If artesunate is needed, or if ID recommends a non-formulary antimalarial therapy, contact the on-call ASP pharmacist urgently (402) 888-0349
- ID provider makes recommendations about serial thin/thick smear evaluation to follow progress of treatment.

Global Fever Panel: The Global Fever panel can be ordered as a stand-alone test but if malaria is a concern based on exposure history, it should be coupled with an order for a malaria smear. The panel order is restricted to the ID service. The specific components of the panel are listed below along with some basic treatment recommendations.

Target	**Comments and Treatment**
Leptospirosis	Mild disease: Doxycycline 100mg BID X 7 days or Azithromycin 500mg daily X 3 days Severe disease: Penicillin 1.5 million units Q6H days or Ceftriaxone 2g IV daily X 7 days
Chikungunya	Treat with fluids and anti-inflammatories (NSAIDs)
Dengue (Serotypes 1-4)	Treat with oral/IV fluids with monitoring for shock syndrome and/or warning signs of severe disease: abdominal pain, persistent vomiting, bleeding, lethargy, hepatomegaly, fluid accumulation (effusion, ascites), or increased HCT with decreased platelets
Plasmodium spp.	Positive with all Plasmodium infections but does not define species; not all individual species are detected by the GFP. Treatment should be based on species identified and severity of illness following CDC guideline listed below.

Plasmodium falciparum	Artemether/lumefantrine (uncomplicated) or Artesunate (severe) recommended
Plasmodium vivax/ovale	Detects these species but infection with *P. knowlesi* or *malariae* may also produce a positive result. Use microscopy to confirm specific species. Include Primaquine in treatment to prevent relapse (requires G6PD testing and confirmed activity prior to initiation)

Overview of treatment options for malaria in the United States

https://www.cdc.gov/malaria/diagnosis_treatment/treatment.html

Refer to CDC guidelines linked above for up-to-date recommendations about treatment options and for special populations, a management algorithm, and other resources. Key information to consider include the Plasmodium species detected, the clinical status of the patient (uncomplicated vs. severe malaria*), the potential susceptibility of the infecting parasite, and any previous use of antimalarials.

Drug	UNMC Formulary Status	Comments
Artemether and Lumefantrine (Coartem)	Formulary	**Preferred as 1st line treatment for uncomplicated *P. falciparum* malaria** and to be used after artesunate for severe malaria
Atovaquone and Proguanil (Malarone)	Formulary	Recommended as an alternative to artemether-lumefantrine for uncomplicated malaria by the CDC, also listed as a contingency medication for complicated malaria. Contraindicated when GFR < 30
Hydroxychloroquine	Formulary	Preferred for chloroquine sensitive infections by the CDC (highly geography specific; when in doubt presume chloroquine resistance) Add primaquine for *P vivax* or *P ovale* anti-relapse (G6PD testing)
Artesunate (parenteral)	Formulary	**Recommended as 1st line treatment for severe malaria** **Contact ID pharmacy for acquisition assistance**
Primaquine	Formulary	Prevents relapse of infection caused by *P. vivax* or *P. ovale,* screen for G6PD deficiency
Tafenoquine	Non-formulary	Alternative to primaquine, requires G6PD testing
Mefloquine	Non-formulary	Only used if no other options are available due to neuropsychiatric side effects

*Severe malaria: Any one of the following defines severe malaria: Impaired consciousness/coma, severe anemia (hemoglobin <7 g/dL), acute kidney injury, acute respiratory distress syndrome, circulatory collapse/shock, disseminated intravascular coagulation, acidosis, jaundice (along with at least one other sign of severe malaria)—and/or percent parasitemia of ≥5%