Review of Malaria Diagnosis and Treatment in the United States

Clinician Outreach and Communication Activity (COCA) Call
Thursday, July 20, 2023
Continuing Education

- Continuing education is not offered for this webinar.
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- Using the Zoom Webinar System
  - Click on the “Q&A” button
  - Type your question in the “Q&A” box
  - Submit your question

- If you are a patient, please refer your question to your healthcare provider.

- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov
Today’s Presenters

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Centers for Disease Control and Prevention

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2023 Malaria Response
Centers for Disease Control and Prevention
Review of Malaria Diagnosis and Treatment in the United States
Outline

• Update on locally acquired mosquito-transmitted malaria in the United States
• Epidemiology of imported malaria in the United States
• Diagnosis and treatment of malaria
• Preventing malaria infections
• CDC resources to support malaria prevention, diagnosis, and treatment
Learning Objectives

• Describe when to suspect malaria based on epidemiologic risk factors and clinical presentation

• Define preferred methods for malaria diagnosis

• Identify an optimal treatment regimen for an individual patient infected with malaria using available clinical and laboratory information

• Identify strategies to prevent mosquito-transmitted malaria in the United States
Locally Acquired Mosquito-transmitted Malaria in the United States
8 Locally acquired *Plasmodium vivax* malaria in Florida and Texas, 2023

- Mosquito-transmitted *P. vivax*:
  - Sarasota County, FL: 7 individuals
  - Cameron County, TX: 1 individual

- No recent international travel identified
Clinical characteristics of locally acquired mosquito-transmitted malaria — U.S., May–July 2023

- All 8 individuals were adults and had fever
- 7/8 (88%) individuals were hospitalized
- All 8 individuals received oral antimalarial treatment
  - All received treatment to prevent future disease relapse
  - All have recovered
Public health interventions targeting mosquitoes

• Trapping of *Anopheles* mosquitoes to monitor overall population density and screen for malaria parasites

• Insecticide spraying to kill adult mosquitoes and treat larval habitats
Public health to identify malaria infections

- Enhanced awareness at healthcare facilities
- Public health messaging around mosquito avoidance and malaria symptoms

SOURCE: https://twitter.com/HealthyFla/status/1674912452981522432/photo/1

At least 28 events from 1980–2003
Modes of malaria transmission

• *Anopheles* mosquitoes are widely distributed in the U.S.

• Rarely, infections can occur congenitally, or via transfusion, transplant, or other blood exposures
Most years, every state reports at least 1 person diagnosed with malaria

SOURCE: Malaria Surveillance — United States, 2018 | MMWR (cdc.gov)
Increasing reported annual malaria infections – U.S., 1972–2020*

*COVID-19 reduces travel

*2019 and 2020 data are preliminary
Self-knowledge Check

Which of the following is true regarding the identification of locally acquired mosquito-transmitted malaria in Florida and Texas?

A. This is unusual because the vector responsible for transmitting malaria was thought to not exist in the U.S.
B. This is unusual because no cases of malaria are diagnosed in the U.S.
C. This is unusual because it is the first time locally acquired mosquito-transmitted malaria has been documented in the U.S.
D. None of the above
Self-knowledge Check

The correct answer is...

D. None of the above

Although this has not happened in 20 years, there have been several documented instances of locally acquired mosquito-transmitted malaria in the U.S. Approximately 2,000 people are diagnosed with malaria every year in the US, and mosquito vectors capable of transmitting the disease are widely present.
Malaria Clinical Presentation and Diagnosis
Malaria suspected?

Malaria test results? (-)

Repeat testing

(+)

Severe disease?

Species confirmed? (NO)

NO

 Directed treatment

YES

Severe treatment

YES

General treatment
Malaria suspected

Malaria test results?

(-)

Repeat testing

(+) (YES)

Severe disease?

NO

Species confirmed?

NO

Directed treatment

YES

Severe treatment

YES

General treatment
Suspect and test for malaria when there is fever and travel to a malaria-endemic region

Over 99% of malaria cases in the U.S. are among individuals who reported travel to a malaria-endemic region within 1 year of presentation
The time from exposure to symptoms can vary

- 5 species of *Plasmodium* cause human disease
  - *P. falciparum*
  - *P. vivax* (relapsing)
  - *P. ovale* (relapsing)
  - *P. malariae*
  - *P. knowlesi* (zoonotic)
The time from exposure to symptoms can vary

- 99% develop symptoms <1 year from arrival to U.S.
- Relapsing species may present later
Malaria symptoms occur in blood-stage

• Most symptoms are fever, headache, and myalgias

• Higher parasite densities lead to more severe disease

• Some blood stage parasites develop into *gametocytes* (infectious stage for mosquitoes)
In non-severe illness, symptoms are often nonspecific

- Fever is the most common symptom
- Constitutional: headache, fatigue, malaise, myalgias, arthralgias
- Respiratory: cough, tachypnea
- GI: anorexia, nausea, vomiting, abdominal pain, diarrhea
Severe illness can manifest as multi-organ system failure

- Pathophysiology: infected RBCs adhere to vascular endothelium → micro-ischemia, capillary leakage, organ dysfunction

- This can result in:
  - CNS: altered consciousness, seizure, coma
  - Hematology: Disseminated Intravascular Coagulation (DIC), coagulopathy, severe anemia
  - Vascular: severe hypotension
  - Pulmonary: Acute Respiratory Distress Syndrome (ARDS)
  - Renal: Acute Kidney Injury, hemoglobinuria
  - Metabolic: acidosis, hypoglycemia
Severe disease is more likely in some circumstances

- P. falciparum
- Non-immune individuals (those not residing in areas of continuous transmission, i.e., individuals living in the U.S.)
- Pregnant people

Malaria (any species) is a medical emergency in the United States
Malaria suspected?

Malaria test results?

Repeat testing

Severe disease?

Species confirmed?

Directed treatment

General treatment

Severe treatment
Diagnostic approach

• Assess severity
• Establish diagnosis of malaria
• Determine species and parasite density (directs treatment approach and urgency)
Malaria diagnostic test results should be available within 24 hours. Two tests can produce a same-day malaria diagnosis.

Microscopy

Rapid diagnostic test (RDT)
• **Thick and thin blood smears (gold standard)**
  - Thick smears: most sensitive for presence of parasites
  - Thin smears: species and parasite density

• **Rapid Diagnostic Test (RDT)**
  - Can decrease time to treatment
  - Smear still required to confirm RDT result
  - Requires CLIA lab

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**CDC Laboratory Resources**

www.cdc.gov/dpdx/malaria/index.html
Other tests are not recommended for the initial diagnosis

- **PCR**
  - Used to identify or confirm species
  - Lengthy turnaround time

- **Serology**
  - Cannot distinguish between acute and prior infection
  - Lengthy turnaround time
Malaria suspected?

Malaria test results?

Severe disease?

Species confirmed?

Severe treatment

Directed treatment

General treatment

Repeat testing
Self-knowledge Check

In which of the following scenarios is it appropriate to test a patient for malaria?

A. Traveler returning from malaria endemic area presenting with fever.
B. Traveler returning from malaria endemic area presenting with fever.
C. Traveler returning from malaria endemic area presenting with fever.
D. Traveler returning from malaria endemic area presenting with fever.
Self-knowledge Check

The correct answer is...

*Traveler returning from malaria endemic area presenting with fever.*

We cannot emphasize this enough. There are numerous resources available to help you manage a patient with malaria (including a CDC consult), but all require a clinician to consider malaria as a possibility and perform diagnostic testing.
Malaria Treatment Considerations
Key considerations for malaria treatment in United States

- Management in the United States differs from endemic areas due to low malaria immunity status and available drug regimens
- Hospitalization decision
- Treatment regimen is dictated by:
  - Severity
  - Species
  - Drug availability
  - Age and pregnancy status

CDC Malaria Hotline
(770) 488-7788 M–F, 9 am to 5 pm EST
(770) 488-7100 after hours, weekends, holidays

CDC Malaria Treatment Table
www.cdc.gov/malaria/resources/pdf/Malaria_Treatment_Table.pdf
Malaria suspected?

Malaria test results?

Species confirmed?

Severe disease?

Directed treatment

Severe treatment

General treatment

Repeat testing
Criteria for severe malaria

One or more of:
- Parasitemia $\geq 5$
- Impaired consciousness, including seizure and coma
- Shock
- Acidosis
- Hypoxia or Acute Respiratory Distress Syndrome (ARDS)
- Acute kidney injury
- Disseminated intravascular coagulation (DIC)
- Severe anemia
Malaria suspected?

Malaria test results?

Species confirmed?

Severe disease?

Repeat testing

Directed treatment

General treatment
Malaria suspected

Severe disease?

Malaria test results?

Species confirmed?

Directed treatment

General treatment

Severe treatment

Repeat testing
## Drugs Used to Treat Uncomplicated Malaria in the U.S.

### P. falciparum / Species unidentified (appropriate for all species)

- **Treatment of acute infection**
  - Artemether-lumefantrine (Coartem®)
  - Atovaquone-proguanil (Malarone®)
  - Quinine PLUS
    - [doxycycline, clindamycin, or tetracycline]
  - Mefloquine

### P. vivax, P. ovale, P. malariae

- **Treatment of acute infection (chloroquine-susceptible)**
  - Chloroquine (Aralen®)
  - Hydroxychloroquine (Plaquenil®)

- **Treatment of liver phase (vivax and ovale)**
  - Primaquine
  - Tafenoquine

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**CDC Malaria Treatment Table**
[www.cdc.gov/malaria/resources/pdf/Malaria_Treatment_Table.pdf](http://www.cdc.gov/malaria/resources/pdf/Malaria_Treatment_Table.pdf)
## Drugs Used to Treat Uncomplicated Malaria in the U.S.

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**CDC Malaria Treatment Table**
www.cdc.gov/malaria/resources/pdf/Malaria_Treatment_Table.pdf
Artemether-lumefantrine is the 1st line treatment for uncomplicated *P. falciparum*.

- Artemether-lumefantrine (Coartem®) is an artemisinin-based combination therapy.
- Both artemether and lumefantrine kill blood stage parasites.
- Coartem® is recommended for all trimesters of pregnancy & for children.
# Drugs Used to Treat Uncomplicated Malaria in the U.S.

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**CDC Malaria Treatment Table**
[www.cdc.gov/malaria/resources/pdf/Malaria_Treatment_Table.pdf](http://www.cdc.gov/malaria/resources/pdf/Malaria_Treatment_Table.pdf)
P. vivax and P. ovale require additional medication due to their lifecycle

• Some P. vivax and P. ovale become dormant during the liver stage rather than immediately progressing to blood-stage
  – Hypnozoites

• Hypnozoites can cause relapse blood stage infections months to years after infection
## Drugs Used to Treat Uncomplicated Malaria in the U.S.

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Treatment options:
- Primaquine (14 days)
- Tafenoquine (single dose concomitantly with chloroquine only)

Both medications can be dangerous in G6PD deficiency
- Quantitative test for G6PD deficiency before starting treatment
- Employ alternative regimens if abnormal G6PD activity
- Consider that fetuses may be G6PD deficient so primaquine and tafenoquine are contraindicated in pregnancy

*P. vivax* and *P. ovale* infection require an additional treatment for hypnozoites: radical cure
<table>
<thead>
<tr>
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<th><strong>Primaquine</strong></th>
<th><strong>Tafenoquine</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment duration</strong></td>
<td>14 days</td>
<td>Single dose</td>
</tr>
<tr>
<td><strong>G6PD function</strong></td>
<td>Normal function or intermediate function with dose adjustment</td>
<td>Normal G6PD function</td>
</tr>
<tr>
<td><strong>Compatibility</strong></td>
<td>ALL acute treatment regimens</td>
<td>ONLY chloroquine</td>
</tr>
<tr>
<td><strong>Age range</strong></td>
<td>All (over 5kg)</td>
<td>≥16 years</td>
</tr>
</tbody>
</table>
Speciation determines treatment approach

- Artemether-lumefantrine is appropriate 1\textsuperscript{st} line treatment for all patients
- Directed therapy = species + resistance
- Consider need to treat dormant liver phase (hypnozoites)

<table>
<thead>
<tr>
<th>Malaria species</th>
<th>Treatment of blood phase</th>
<th>Candidate for chloroquine</th>
<th>Treatment of liver (dormant) phase</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>P. falciparum</em></td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>other non- <em>falciparum</em></td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
</tr>
<tr>
<td><em>P. vivax, P. ovale</em></td>
<td>✓</td>
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Malaria suspected?

Malaria test results?

Species confirmed?

Severe disease?

Severe treatment

Directed treatment

Empiric treatment
Drugs Used to Treat Severe Malaria in the U.S.

*P. falciparum, P. vivax, P. ovale, P. malariae,* species unidentified

(appropriate for all species)

IV artesunate (severe disease)

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CDC Malaria Treatment Table
www.cdc.gov/malaria/resources/pdf/Malaria_Treatment_Table.pdf
Treatment of Severe Malaria the in U.S.

IV artesunate (IVAS) q12h x 3 doses

Check parasitemia

≤1%

Full oral treatment course

>1%

Interim oral treatment: artemether-lumefantrine atovaquone-proguanil quinine mefloquine

IV artesunate (IVAS) q24h (max 6 doses)
Other treatment considerations for severe malaria

- Blood smears every 12–24 hours to follow parasitemia
- Supportive care
- Other adjunctive therapies have poor evidence and are not recommended
Self-knowledge Check

Which of the following medications are appropriate for an individual following a diagnosis of non-severe *P. falciparum* malaria?

A. Doxycycline
B. Atovaquone/proguanil
C. Quinine alone
D. Tafenoquine
Self-knowledge Check

The correct answer is...

**B. Atovaquone/proguanil**

Although atovaquone/proguanil (brand name Malarone®) is not the preferred medication for *P. falciparum* malaria, it is highly effective and may be more available than artemether-lumefantrine in the U.S. due to its use as a prophylactic among travelers.
Preventing Malaria Transmission in the United States
Key prevention modalities for U.S. populations

- Take prophylaxis when traveling to endemic countries
- Prevent mosquito bites
- Promptly diagnose and treat malaria

Use of brand names does not constitute product endorsement by CDC.
Malaria prophylaxis

• 95% of U.S. residents with malaria did not take a full course of malaria prophylaxis

• The CDC website has up to date information for malaria prophylaxis recommendations by country
Preventing mosquito bites

• Use insect repellents
  – Topical: DEET, Picaridin, IR3535, oil of lemon eucalyptus
  – Treat clothing with permethrin

• Cover windows and doors with screens

• Use insecticide treated bed nets when traveling to malaria endemic countries
Self-knowledge Check

Your patient is traveling to rural Uganda for work and is worried about taking malaria prophylaxis because they heard it can cause disturbing nightmares. What do you advise?

A. Review known side effects of prophylaxis medication
B. Take test doses of the malaria prophylaxis medication prior to the trip
C. Do not prescribe malaria prophylaxis, but strictly adhere to using a bed net
D. Prescribe Coartem® to use if they get a fever while traveling
E. A and/or B
F. C and/or D
Self-knowledge Check

The correct answer is... E

A. Review known side effects of prophylaxis medication
and/or
B. Take test doses of the malaria prophylaxis medication prior to the trip

Malaria prophylaxis is the single best prevention method for travelers to malaria endemic countries. CDC malaria hotline staff are available to assist with identifying a regimen that best fits your patient.
Malaria Hotline for Clinical Questions

• For clinicians requiring consultation for managing patients with malaria

• To speak with a Malaria Branch clinician call either
  – (770) 488-7788 (available 9am – 5pm ET M-F)
  – (770) 488-7100 (CDC’s Emergency Operations Center, after hours and holidays)
CDC Laboratory Services Available in the United States

- Diagnostic assistance through DPDx (http://www.cdc.gov/dpdx)
  - Telediagnosis (available 9am – 5pm ET M-F)
  - Microscopy review (particularly for species confirmation)
  - PCR
Key messages

Malaria is a medical emergency in the United States
Key messages

• Suspect malaria among individuals with fever and a recent history of travel, or fever without an alternative etiology.
Key messages

• Suspect malaria among individuals with fever and a recent history of travel, or fever without an alternative etiology
• A malaria blood smear is needed for all suspected malaria cases, but a rapid diagnostic test can shorten time to treatment initiation
Key messages

• Suspect malaria among individuals with fever and a recent history of travel, or fever without an alternative etiology
• A malaria blood smear is needed for all suspected malaria cases, but a rapid diagnostic test can shorten time to treatment initiation
• Species determination in all cases is necessary to determine when to treat dormant liver parasites (hypnozoites)
Key messages

• Suspect malaria among individuals with fever and a recent history of travel, or fever without an alternative etiology
• A malaria blood smear is needed for all suspected malaria cases, but a rapid diagnostic test can shorten time to treatment initiation
• Species determination in all cases is necessary to determine when to treat dormant liver parasites (hypnozoites)
• Early malaria diagnosis and prompt treatment can prevent severe disease and death and reduce the risk of malaria transmission
Key messages

• Suspect malaria among individuals with fever and a recent history of travel, or fever without an alternative etiology
• A malaria blood smear is needed for all suspected malaria cases, but a rapid diagnostic test can shorten time to treatment initiation
• Species determination in all cases is necessary to determine when to treat dormant liver parasites (hypnozoites)
• Early malaria diagnosis and prompt treatment can prevent severe disease and death and reduce the risk of malaria transmission
• Expanding use of malaria prophylaxis to all travelers to malaria endemic countries is a key prevention strategy
Resources

• CDC Malaria Webpage: http://www.cdc.gov/malaria
  – Malaria and Travelers
    https://www.cdc.gov/malaria/travelers/index.html
  – Malaria Information by County
  – How to Choose a Drug to Prevent Malaria
    https://www.cdc.gov/malaria/travelers/drugs.html
  – Treatment Guidelines for Clinicians (United States)
    https://www.cdc.gov/malaria/diagnosis_treatment/clinicians1.html

• CDC Yellow Book online: http://www.cdc.gov/travel
To Ask a Question

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- If you are a patient, please refer your question to your healthcare provider.

- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov
Today’s COCA Call Will Be Available to View On-Demand

- **When:** A few hours after the live call ends*

- **What:** Video recording

- **Where:** On the COCA Call webpage

*A transcript and closed-captioned video will be available shortly after the original video recording posts on the COCA Call webpage.*
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