



# Review of Malaria Diagnosis and Treatment in the United States

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

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  - Click on the “Q&A” button
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# Today's Presenters



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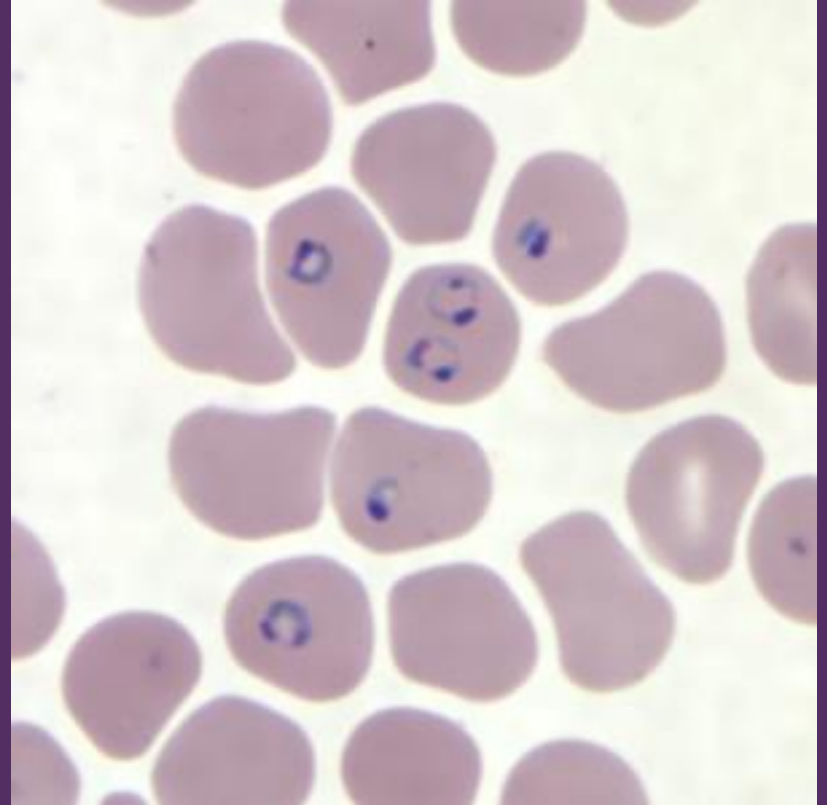


**Erika Wallender, MD, MPH**  
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Medical Countermeasures Team  
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# Review of Malaria Diagnosis and Treatment in the United States



# 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
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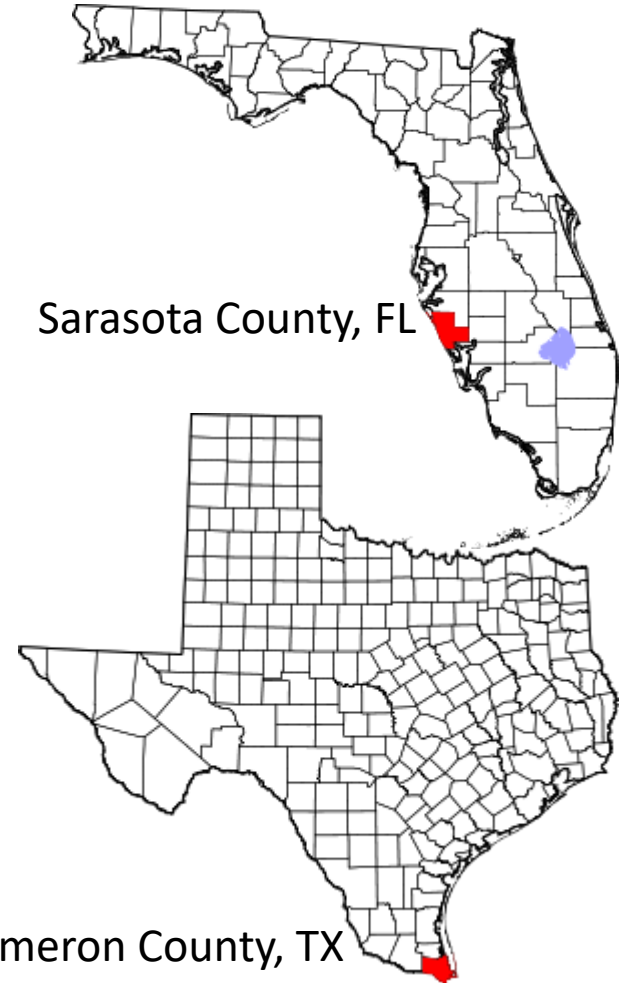
# Locally Acquired Mosquito-transmitted Malaria in the United States





## 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

## MOSQUITOES CAN SPREAD MALARIA

MALARIA is spread by mosquito bites. It is not spread by person to person contact.

### Symptoms of Malaria

Fever Chills Nausea Body Aches Headache

### Protect Yourself

- Spray** yourself with mosquito repellent.
- Cover** your arms and legs with long clothing.
- Drain** standing water.

### Stop Mosquitoes from Breeding

Mosquitoes can live indoors and will bite at any time, day or night.

Mosquitoes breed by laying eggs in and near standing water.

As little as one teaspoon or bottle cap of water standing for more than one week is enough for mosquitoes to breed and multiply.

### Keep them Outside

- Use Air Conditioning
- Keep Screens on All Windows
- Keep Doors Exterior Windows Closed

### Around Buildings

At least once a week, empty or cover anything that could hold water, such as:

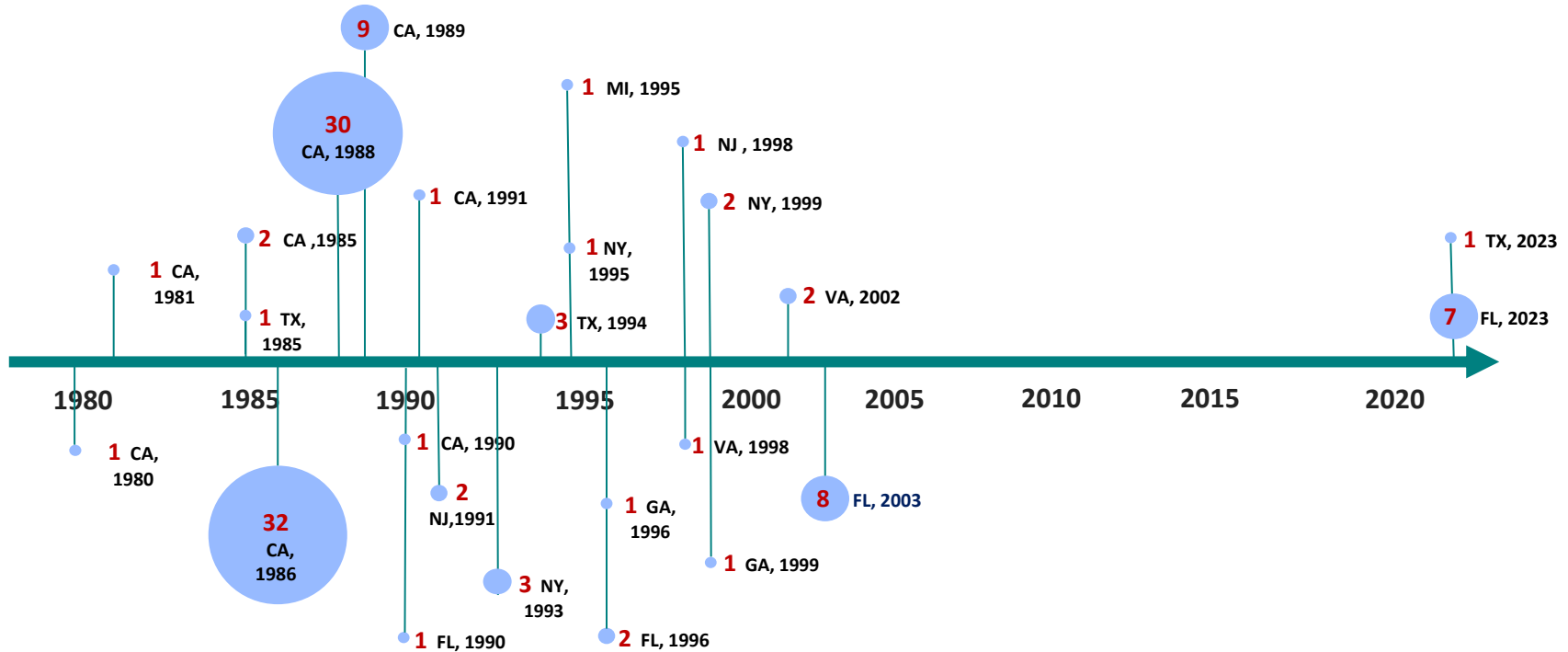
- Buckets
- Toys
- Child Pools and Pool Covers
- Birdbaths
- Trash, Containers, and Recycling Bins
- Boat or Car Covers
- Roof Gutters
- Coolers
- Pet Dishes
- Tires

Repair Holes in Screens

Effective treatment is readily available through hospitals and other health care providers. Individuals with symptoms of fever, chills, sweats, nausea/vomiting, and headache should seek immediate medical attention.

Florida HEALTH

# Timeline of Locally Acquired Malaria, U.S.: 1980–2023



At least 28 events from 1980–2003

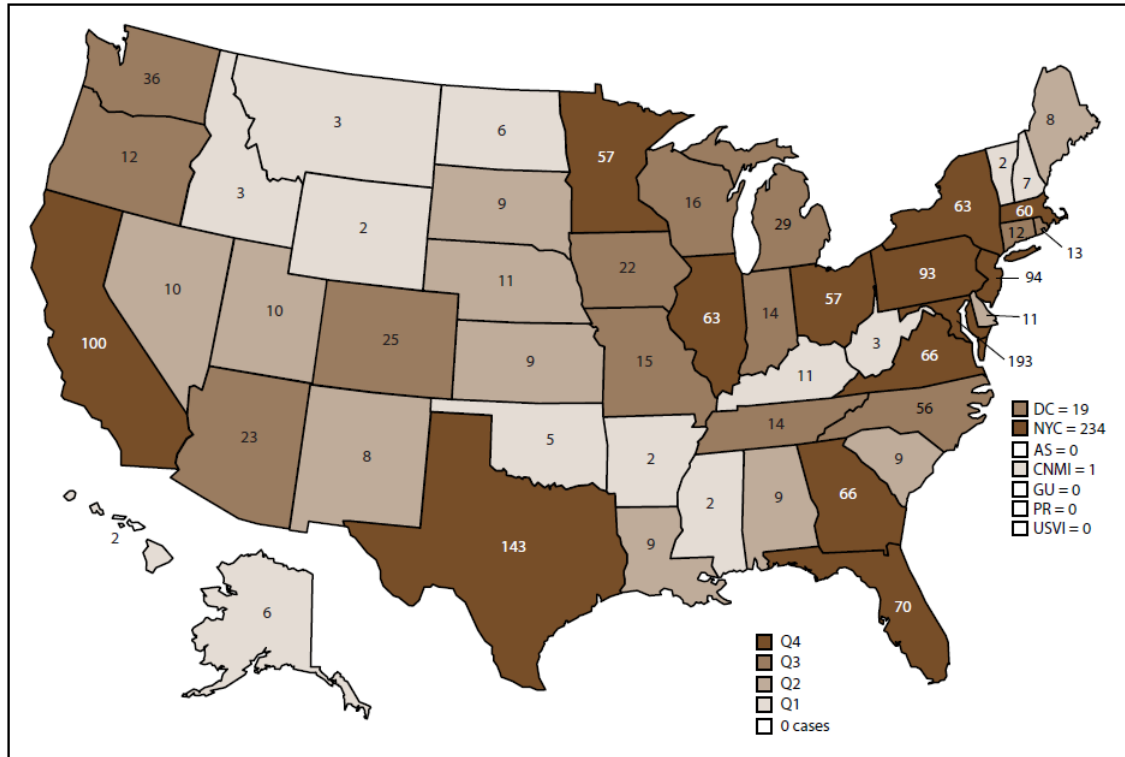
# Modes of malaria transmission

- *Anopheles* mosquitoes are widely distributed in the U.S.
- Rarely, infections can occur congenitally, or via transfusion, transplant, or other blood exposures

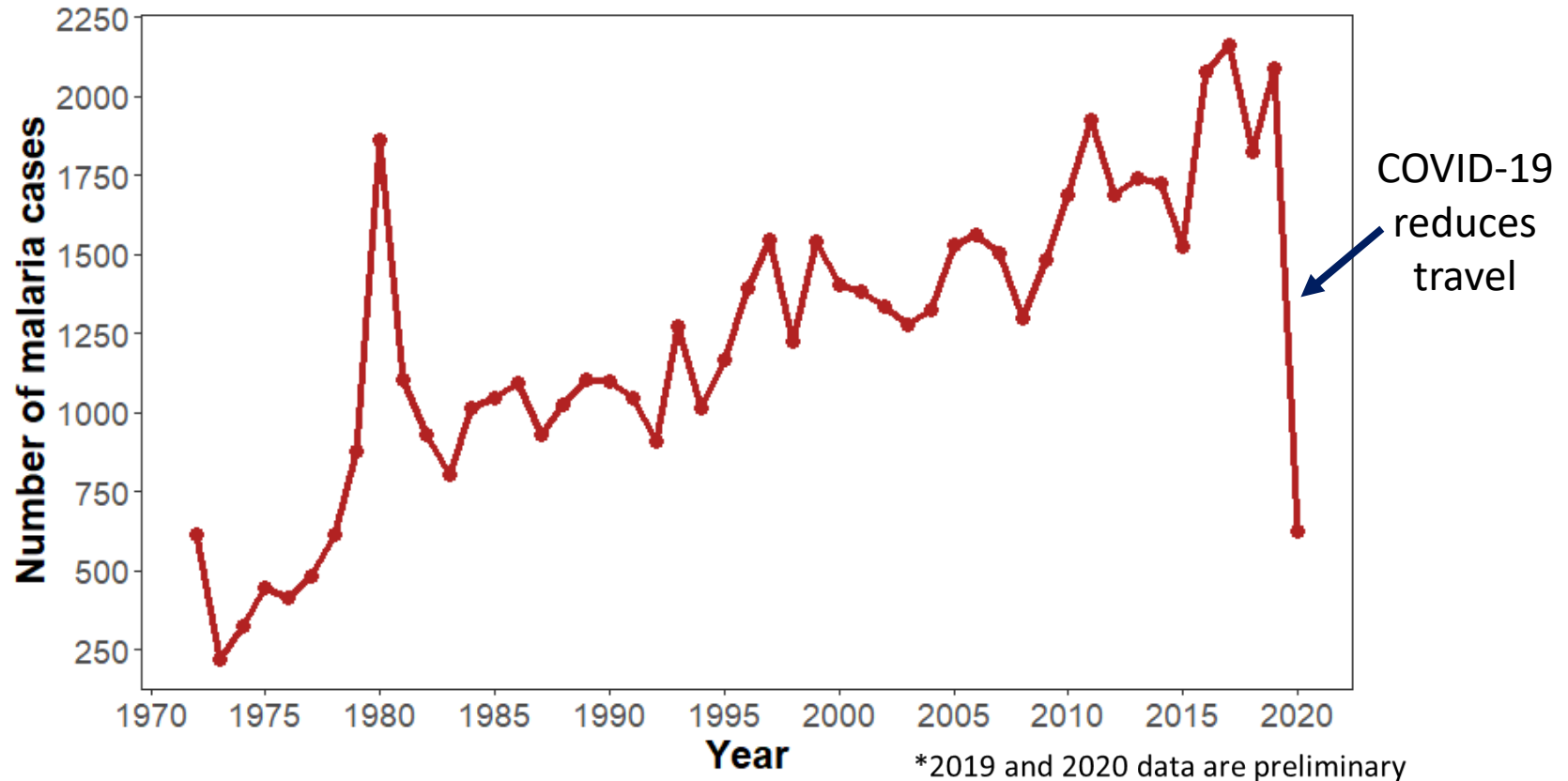


Female *Anopheles quadrimaculatus*

# Most years, every state reports at least 1 person diagnosed with malaria



## Increasing reported annual malaria infections – U.S., 1972–2020\*





# 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

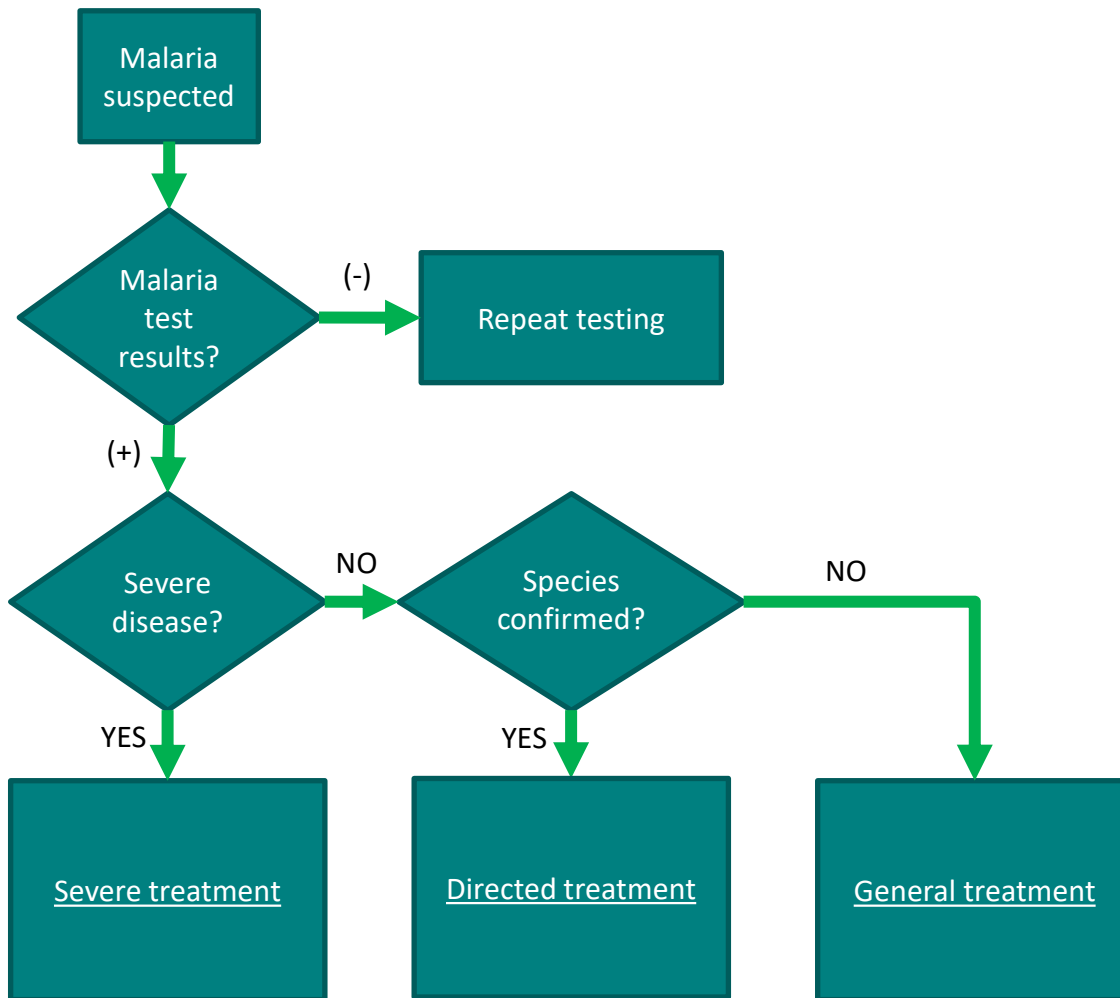
The correct answer is...

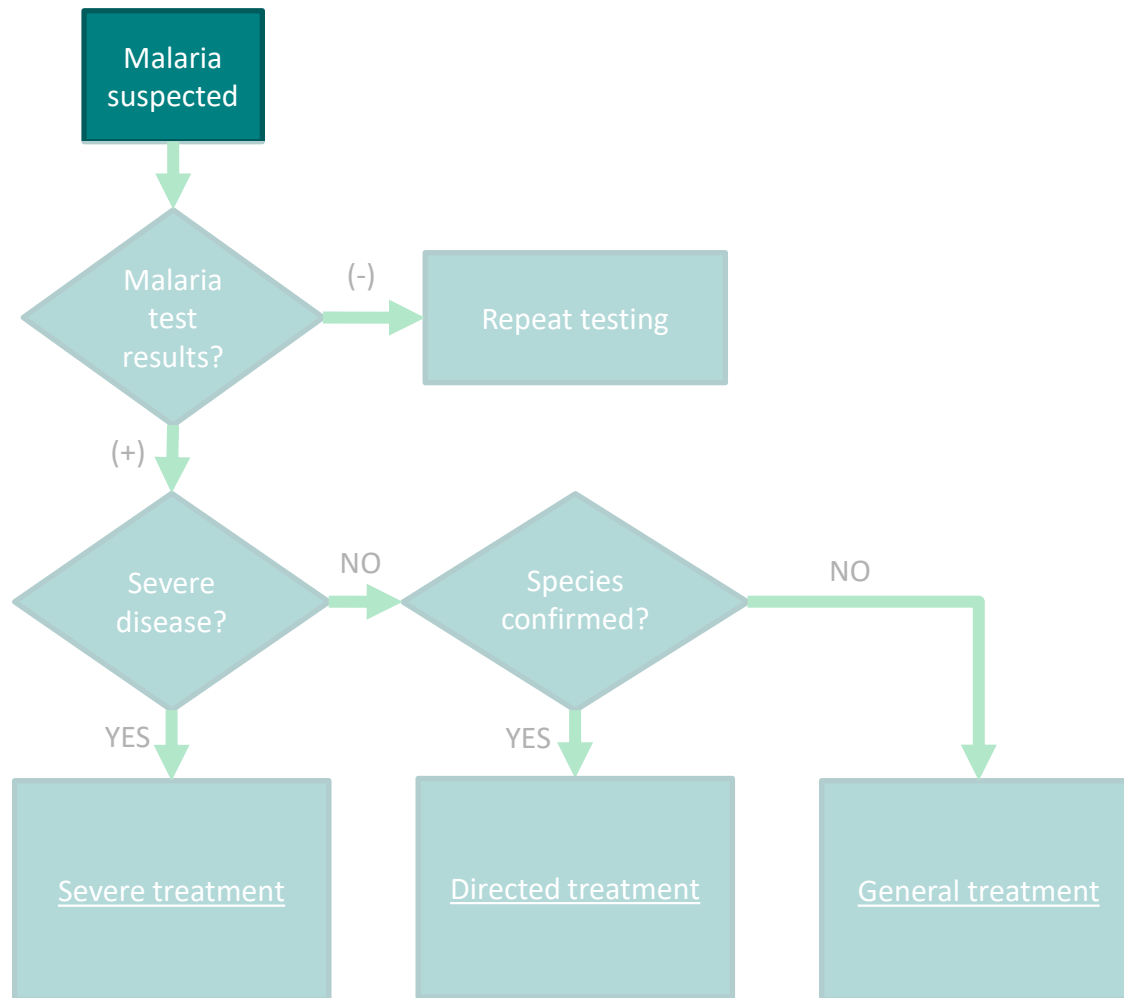
***D. None of the above***

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

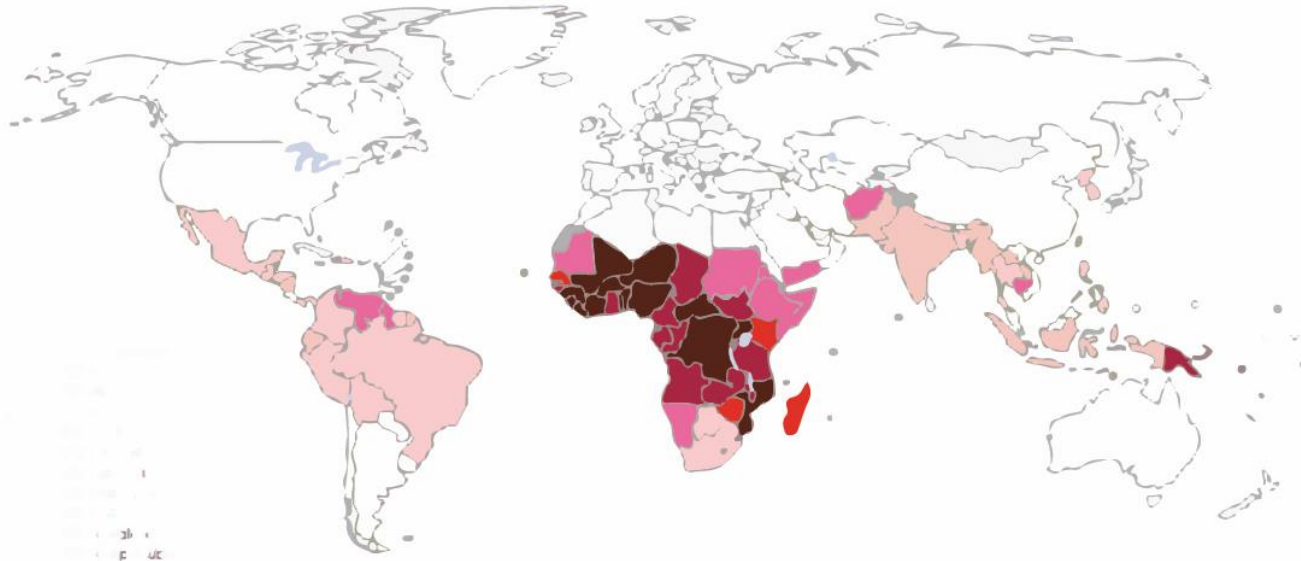






# Suspect and test for malaria when there is fever and travel to a malaria-endemic region

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)

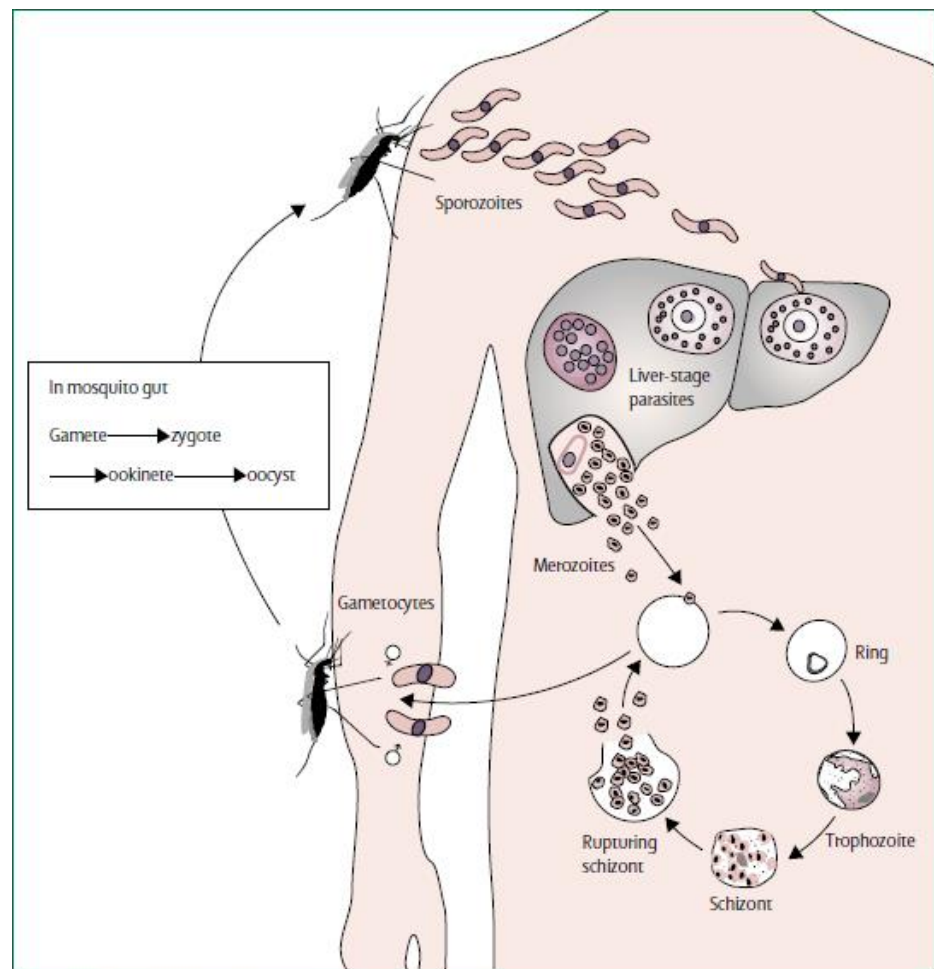


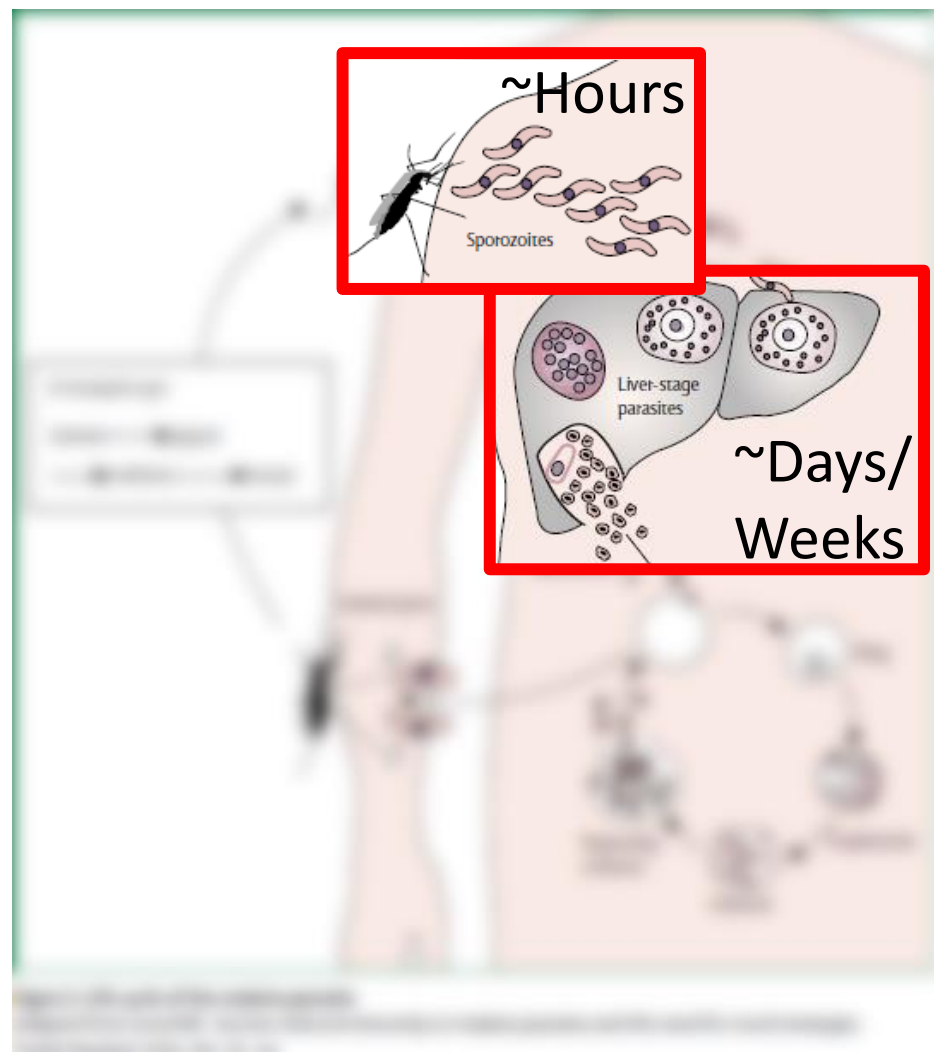
Figure 1: Life cycle of the malaria parasite

Adapted from Good MF. Vaccine-induced immunity to malaria parasites and the need for novel strategies.

Trends Parasitol 2005; 21: 29–34.

## The time from exposure to symptoms can vary

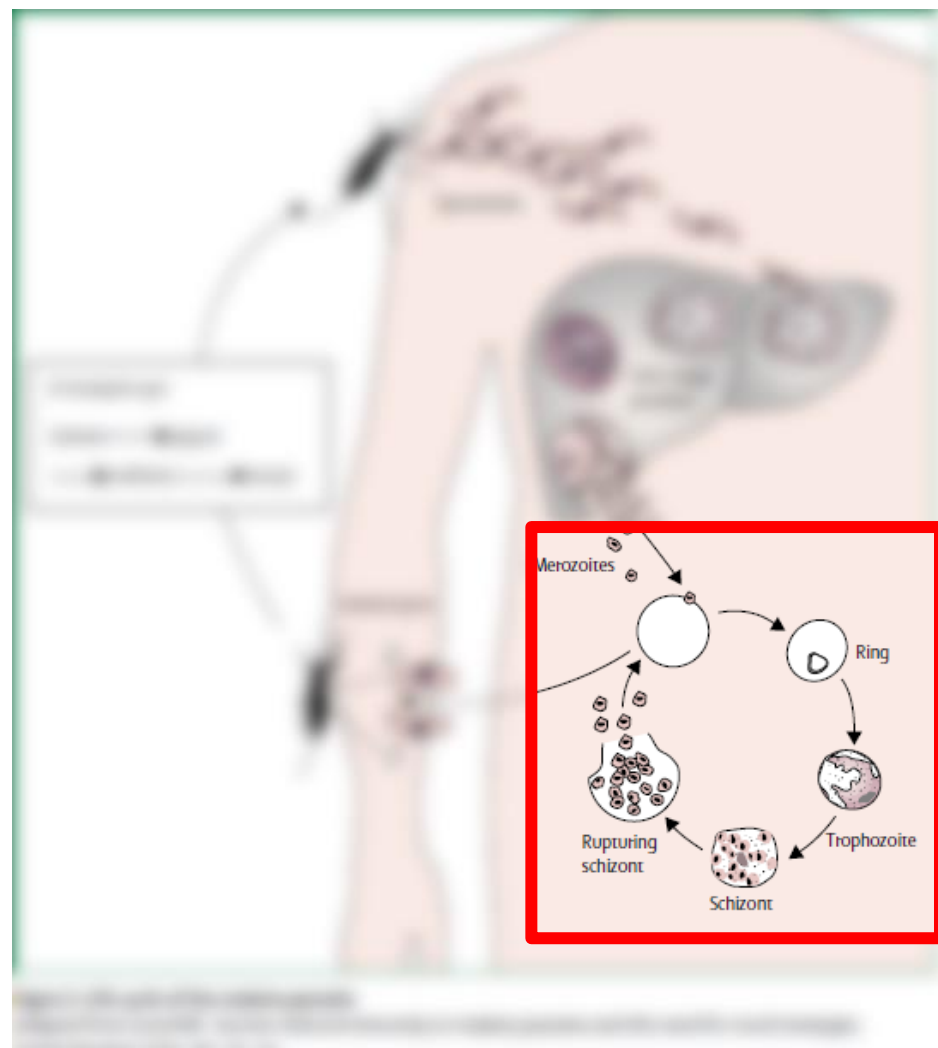
- 99% develop symptoms <1 year from arrival to U.S.
- Relapsing species may present later





# 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

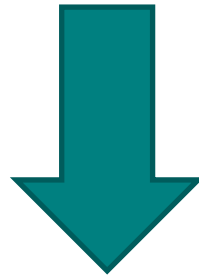
- Fever is the most common symptom
- Constitutional: headache, fatigue, malaise, myalgias, arthralgias
- Respiratory: cough, tachypnea
- GI: anorexia, nausea, vomiting, abdominal pain, diarrhea

# Severe illness can manifest as multi-organ system failure

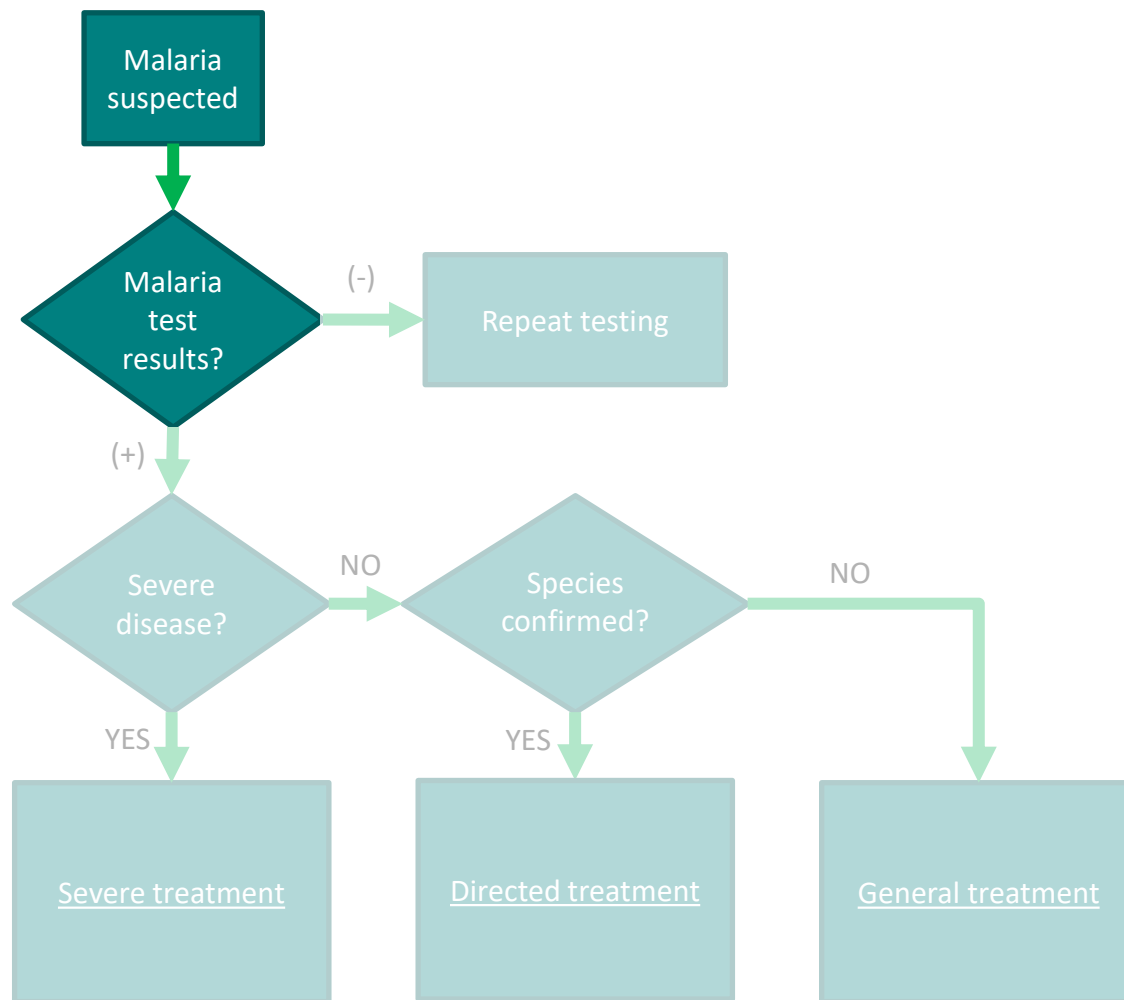
- Pathophysiology: infected RBCs adhere to vascular endothelium → micro-ischemia, capillary leakage, organ dysfunction
- This can result in:
  - CNS: altered consciousness, seizure, coma
  - Hematology: Disseminated Intravascular Coagulation (DIC), coagulopathy, severe anemia
  - Vascular: severe hypotension
  - 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



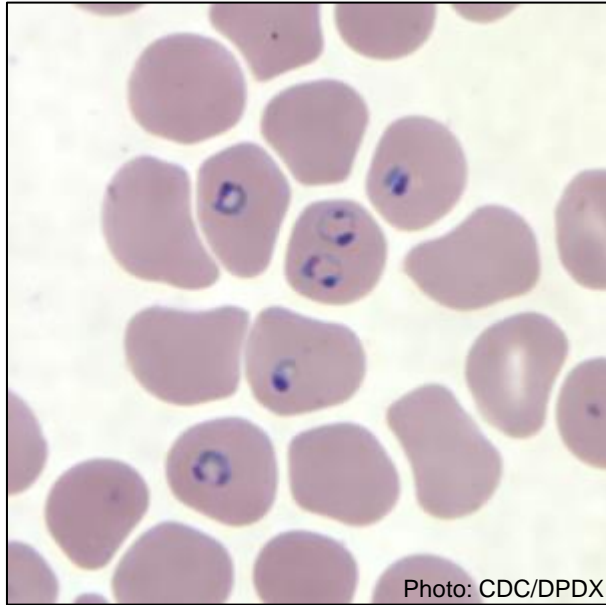
**Malaria (any species) is a medical emergency in the United States**



# 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.**



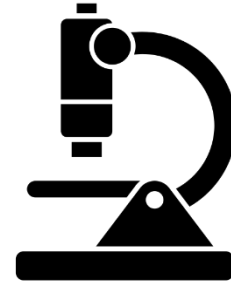
Microscopy



Rapid diagnostic test (RDT)

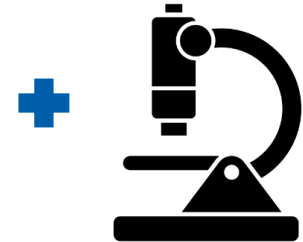
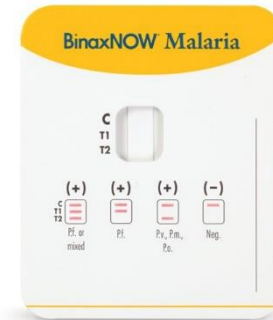
- **Thick and thin blood smears (gold standard)**

- Thick smears: most sensitive for presence of parasites
- Thin smears: species and parasite density



- **Rapid Diagnostic Test (RDT)**

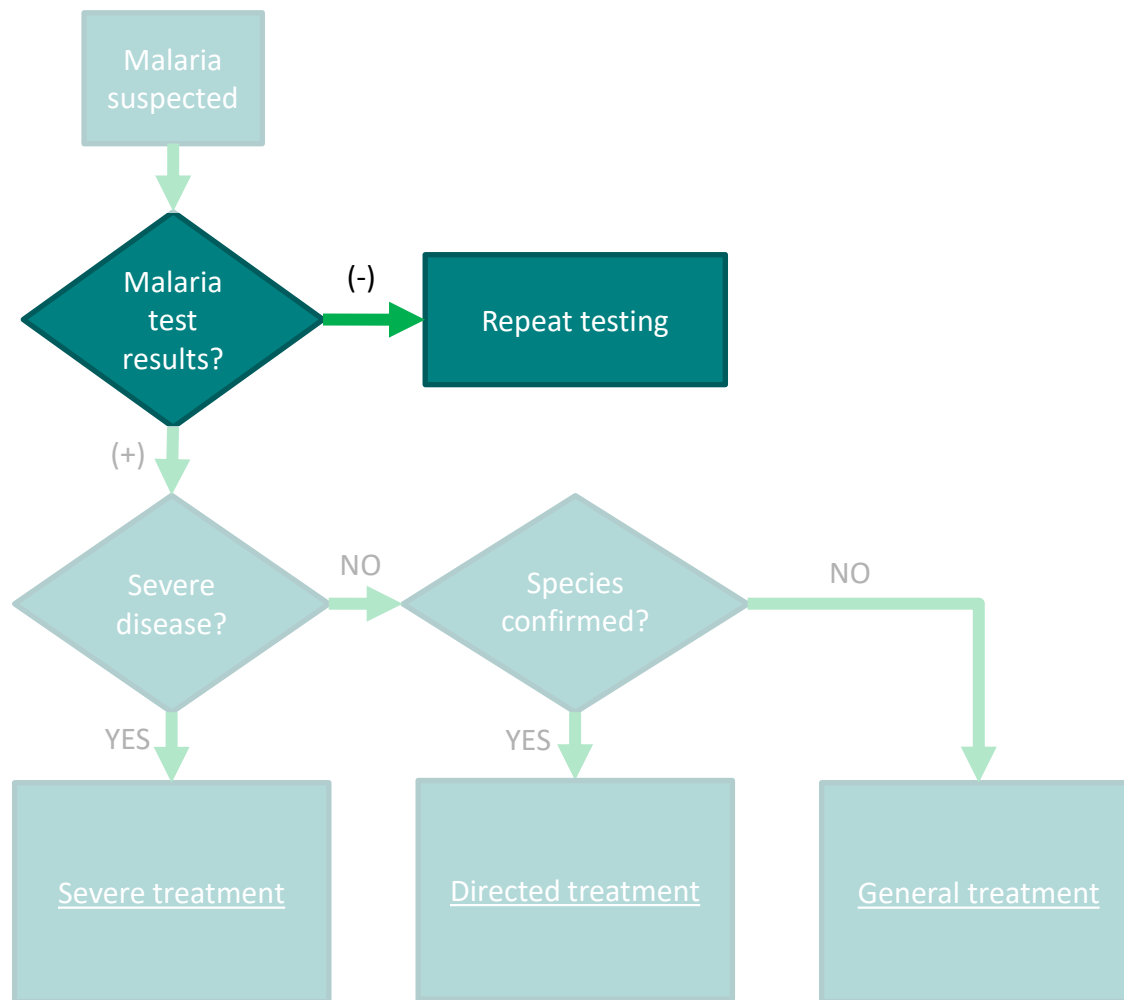
- Can decrease time to treatment
- Smear still required to confirm RDT result
- Requires CLIA lab





# 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



# 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

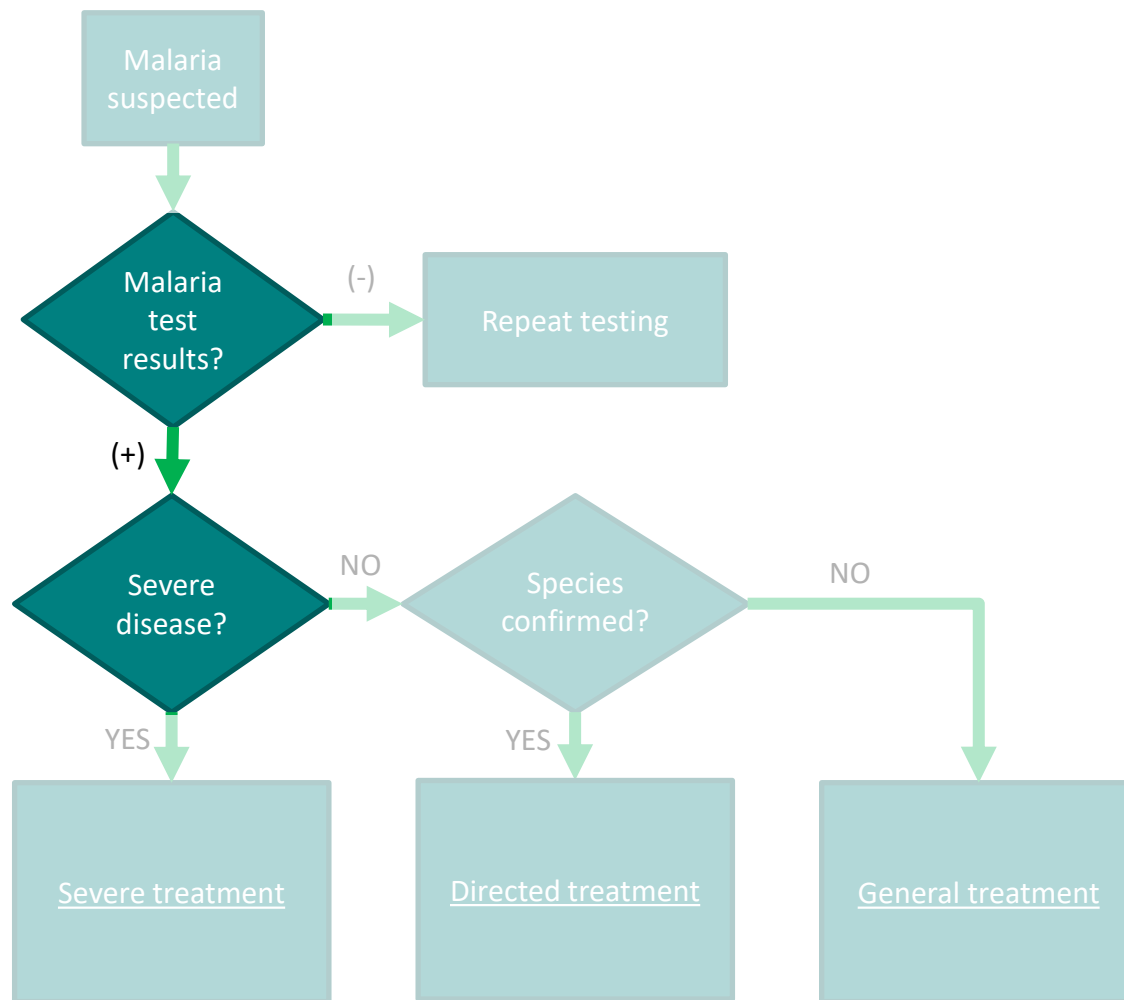
- Management in the United States differs from endemic areas due to low malaria immunity status and available drug regimens
- Hospitalization decision
- Treatment regimen is dictated by:
  - Severity
  - Species
  - Drug availability
  - Age and pregnancy status

## **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](http://www.cdc.gov/malaria/resources/pdf/Malaria_Treatment_Table.pdf)

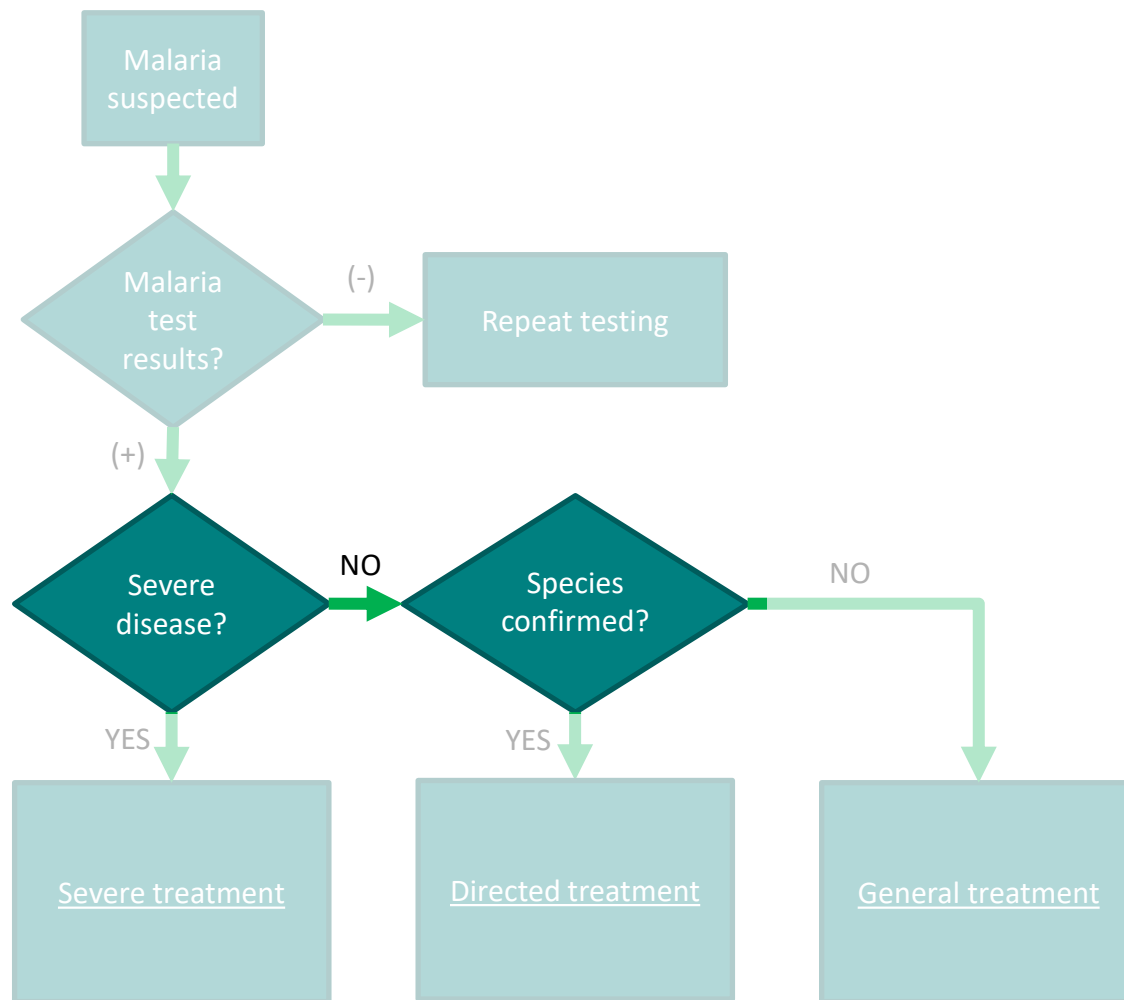


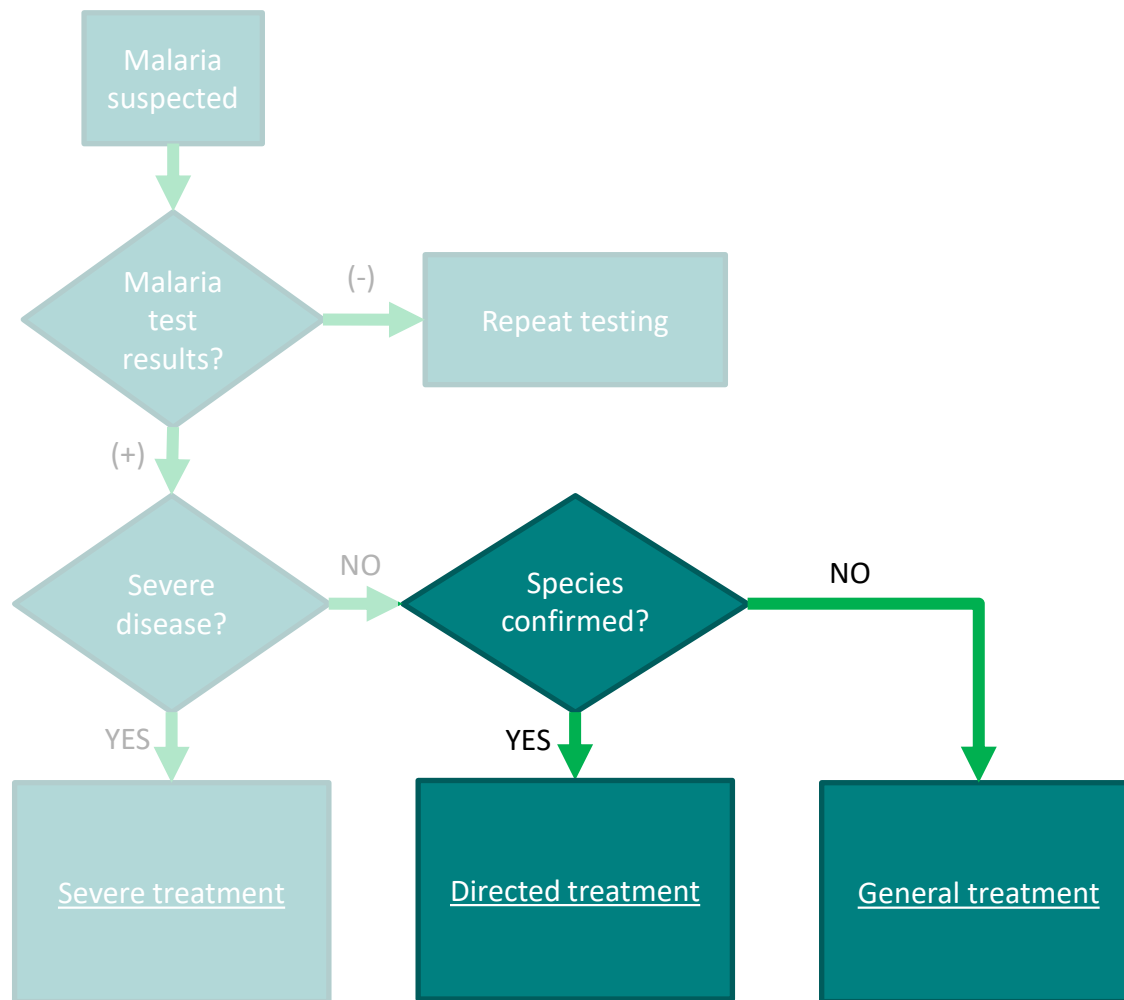
# Criteria for severe malaria

## 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







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

<i>P. falciparum</i> / Species unidentified (appropriate for all species)	<i>P. vivax, P. ovale, P. malariae</i>	
Treatment of <b>acute</b> infection	Treatment of <b>acute</b> infection (chloroquine-susceptible)	Treatment of <b>liver phase</b> ( <i>vivax</i> and <i>ovale</i> )
<p>Artemether-lumefantrine (Coartem®)</p> <p>Atovaquone-proguanil (Malarone®)</p> <p>Quinine PLUS [doxycycline, clindamycin, or tetracycline]</p> <p>Mefloquine</p>	<p>Chloroquine (Aralen®)</p> <p>Hydroxychloroquine (Plaquenil®)</p>	<p>Primaquine</p> <p>Tafenoquine</p>

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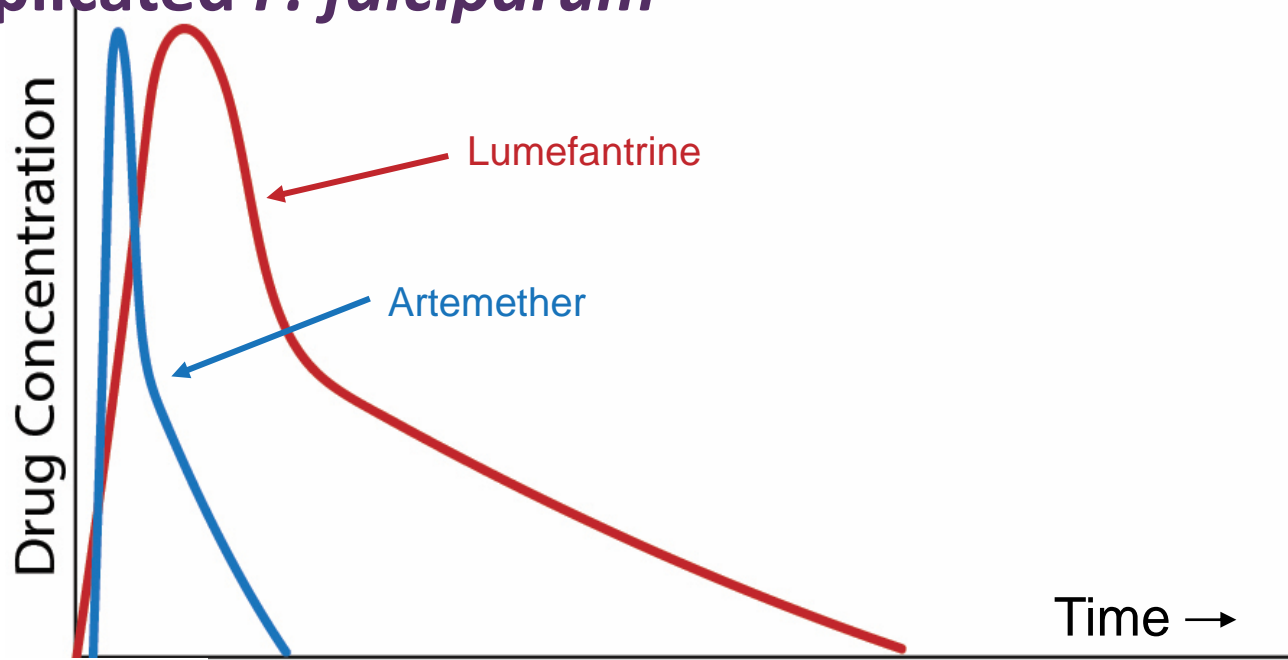
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<p data-bbox="104 539 745 579"><b>Artemether-lumefantrine (Coartem®)</b></p> <p data-bbox="117 614 732 655">Atovaquone-proguanil (Malarone®)</p> <p data-bbox="200 691 653 825">Quinine PLUS [doxycycline, clindamycin, or tetracycline]</p> <p data-bbox="324 860 523 900">Mefloquine</p>	<p data-bbox="904 465 1286 505">Chloroquine (Aralen®)</p> <p data-bbox="813 541 1379 582">Hydroxychloroquine (Plaquenil®)</p>	<p data-bbox="1557 467 1760 507">Primaquine</p> <p data-bbox="1547 543 1769 584">Tafenoquine</p>

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# Artemether-lumefantrine is the 1<sup>st</sup> line treatment for uncomplicated *P. falciparum*



- Artemether-lumefantrine (Coartem<sup>®</sup>) is an artemisinin-based combination therapy
- Both artemether and lumefantrine kill blood stage parasites
- Coartem<sup>®</sup> is recommended for all trimesters of pregnancy & for children

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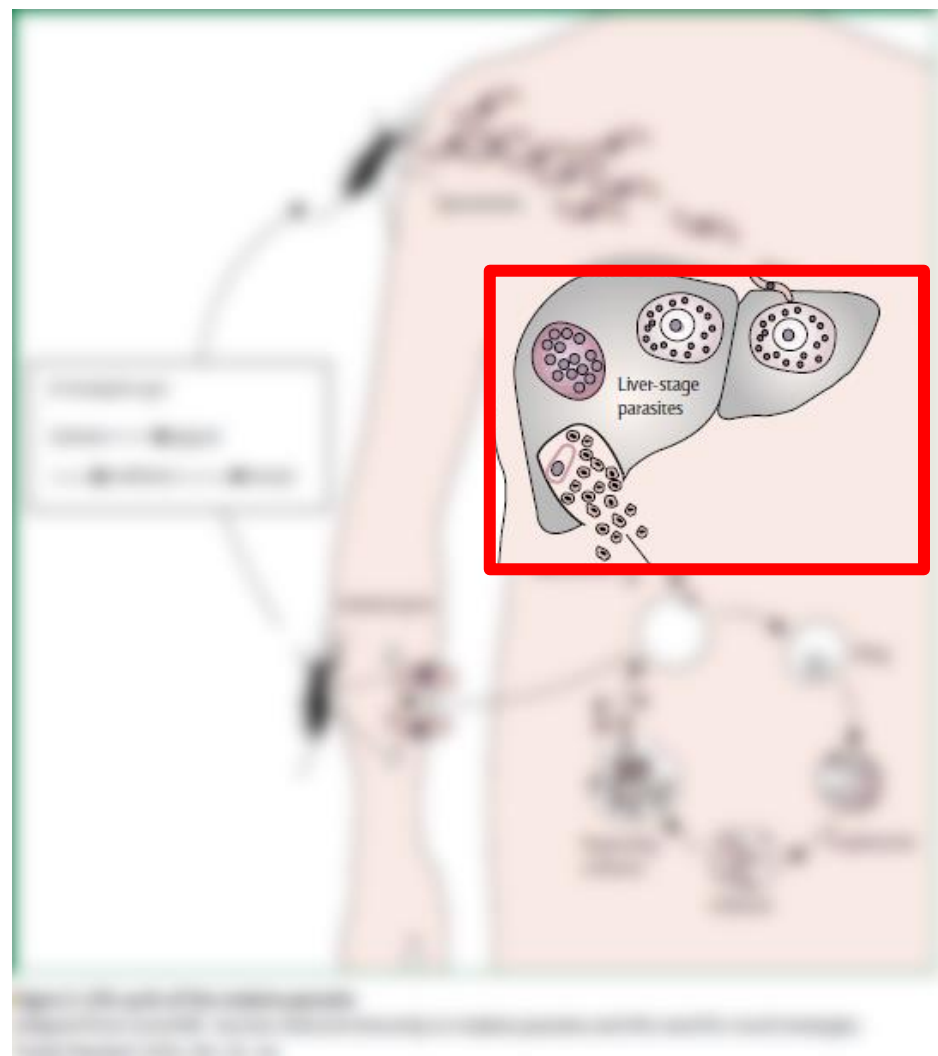
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## *P. vivax* and *P. ovale* require additional medication due to their lifecycle

- 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





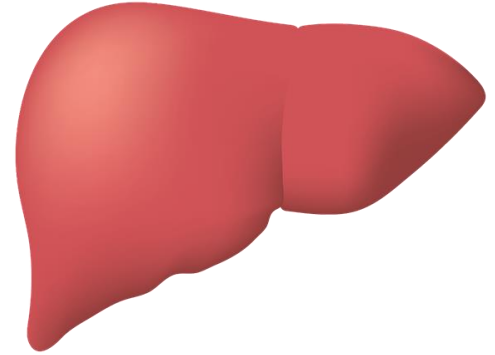
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# *P. vivax* and *P. ovale* infection require an additional treatment for hypnozoites: radical cure

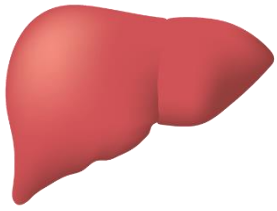


## Treatment options:

- 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



## Primaquine

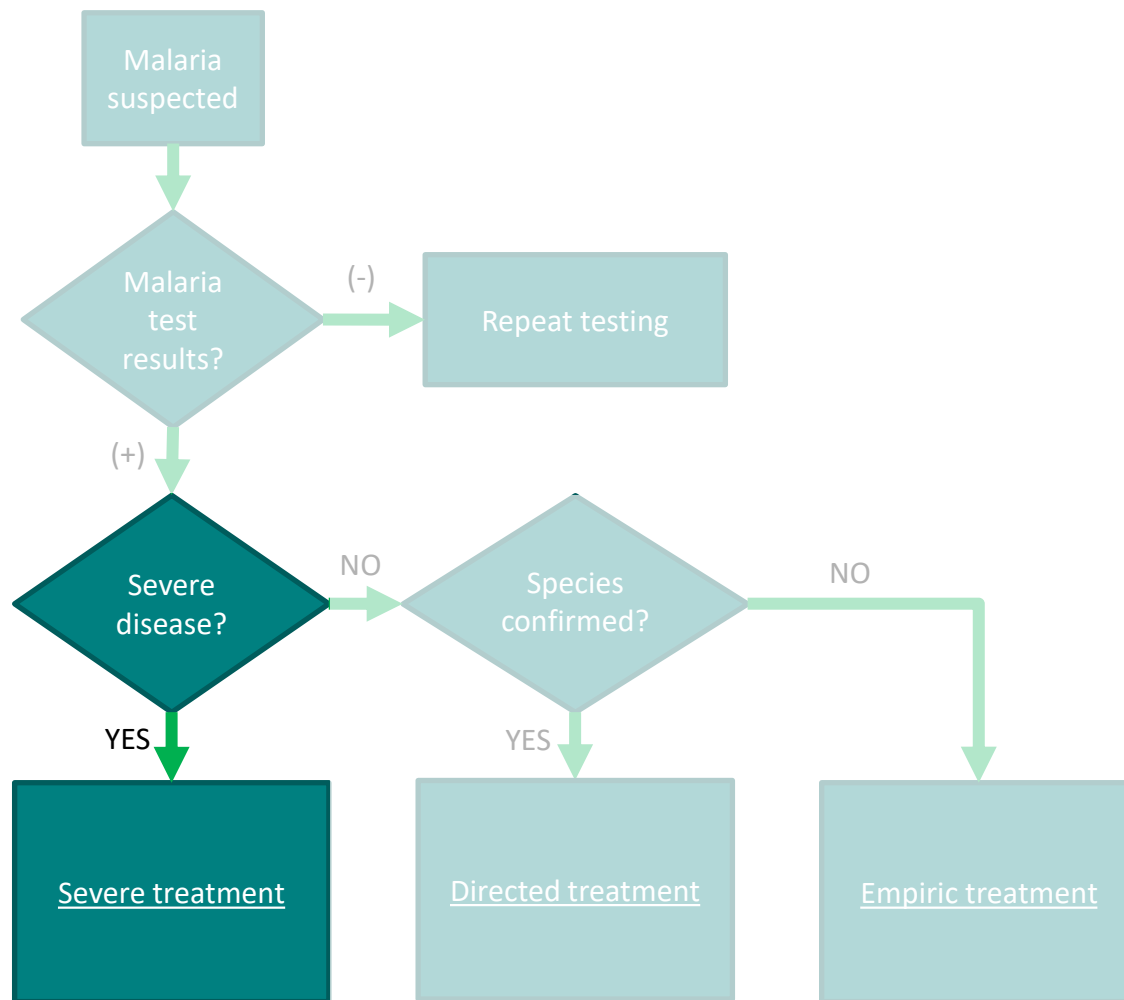
## Tafenoquine

Treatment duration	14 days 	Single dose 
G6PD function	Normal function or intermediate function with dose adjustment	Normal G6PD function
Compatibility	ALL acute treatment regimens 	ONLY chloroquine 
Age range	All (over 5kg) 	≥16 years 

# Speciation determines treatment approach

- Artemether-lumefantrine is appropriate 1<sup>st</sup> line treatment for all patients
- Directed therapy = species + resistance
- Consider need to treat dormant liver phase (hypnozoites)

<b>Malaria species</b>	<b>Treatment of blood phase</b>	<b>Candidate for chloroquine</b>	<b>Treatment of liver (dormant) phase</b>
<i>P. falciparum</i>	✓	✗	✗
other non-falciparum	✓	✓	✗
<i>P. vivax, P. ovale</i>	✓	✓	✓



# Drugs Used to Treat Severe Malaria in the U.S.

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*P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae*, species unidentified  
(appropriate for all species)

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IV artesunate (severe disease)

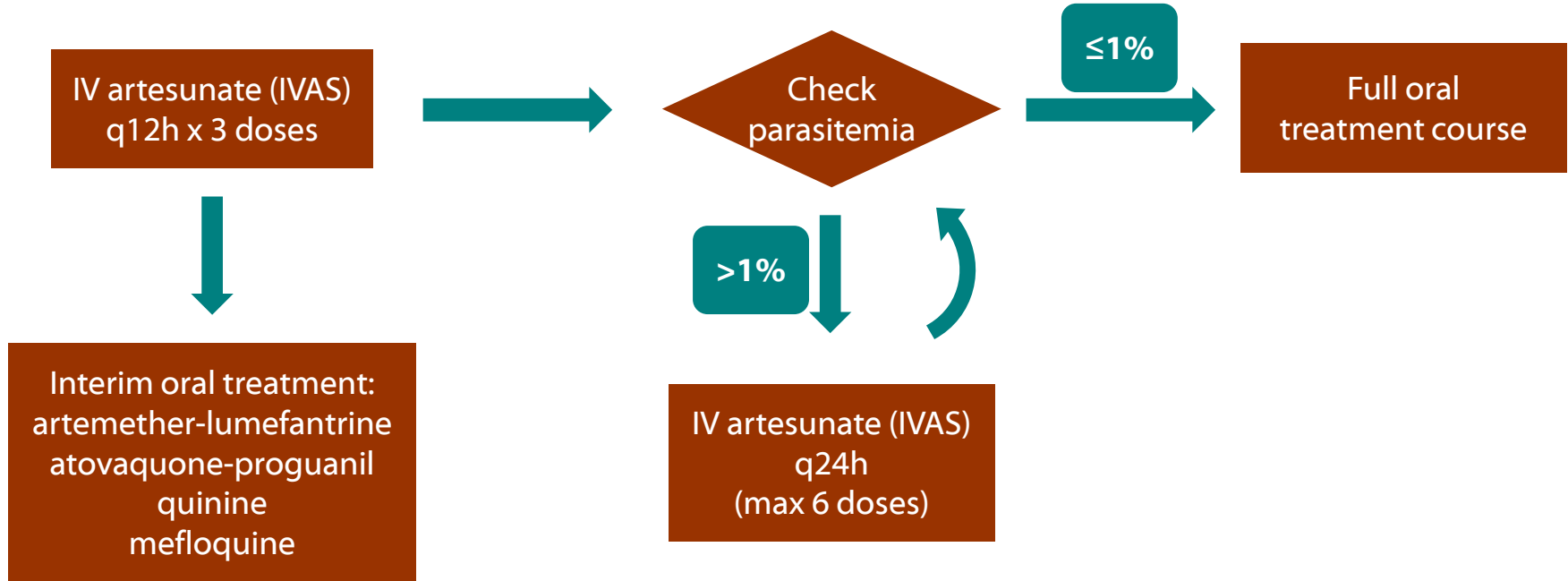
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# Treatment of Severe Malaria the in U.S.



# 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

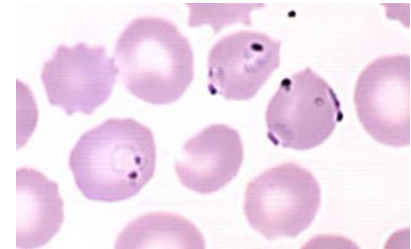
Take prophylaxis  
when traveling to  
endemic countries



Prevent mosquito  
bites



Promptly  
diagnose and treat  
malaria



# 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<sup>®</sup> 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**

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- 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  
[https://www.cdc.gov/malaria/travelers/country\\_table/a.html](https://www.cdc.gov/malaria/travelers/country_table/a.html)
  - 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](https://www.cdc.gov/malaria/diagnosis_treatment/clinicians1.html)
- CDC Yellow Book online: <http://www.cdc.gov/travel>

# To Ask a Question

- 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](mailto: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  
[https://emergency.cdc.gov/coca/calls/2023/callinfo\\_072023.asp](https://emergency.cdc.gov/coca/calls/2023/callinfo_072023.asp)

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

# Upcoming COCA Calls & Additional Resources

- Continue to visit <https://emergency.cdc.gov/coca/> to get more details about upcoming COCA Calls.
- Subscribe to receive notifications about upcoming COCA calls and other COCA products and services at [emergency.cdc.gov/coca/subscribe.asp](https://emergency.cdc.gov/coca/subscribe.asp).

**Thank you for joining us today!**



[emergency.cdc.gov/coca](https://emergency.cdc.gov/coca)