Public Health and Clinical Malaria in the U.S.

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BLOOD PRODUCTS ADVISORY COMMITTEE meeting

May 9, 2024
Public Health and Clinical Malaria in the U.S.: Outline

• Brief on Biology/Burden/History
• Surveillance & Epidemiology
• Prevention and Clinical Care
• Local malaria outbreak, U.S., 2023
Malaria: a parasitic disease transmitted by *Anopheles* mosquitos

- 5 species of *Plasmodium* cause human disease
  - *P. falciparum*
  - *P. vivax* (relapsing)
  - *P. ovale* (relapsing)
  - *P. malariae*
  - *P. knowlesi* (zoonotic)
Mechanisms of Malaria Transmission, US

- Mosquito
- Congenital
- Blood transfusions
- Organ transplant
- Sharing needles or syringes

Credits
Global Malaria cases, 2023

Over 99% of malaria cases in U.S., among individuals reporting travel to or from malaria-endemic region ≤1 year of presentation

WHO, 2023
Malaria in the United States, early 1940s

~65,000 cases/yr

Source: NLM/NIH
Cinchona Inc. NYC
Malaria case investigation

- Laboratory tests
- **Travel history:** dates, reason for travel
- **Clinical:** Illness onset, hospitalization, complications, chemoprophylaxis, treatments, outcome
- **History:** prior malaria, transfusion

https://www.cdc.gov/malaria/report.html
Malaria surveillance in the U.S.

Patient seeks care

Diagnostic Lab

Alert to Local Health Dept

Case investigation

Report to State Health Dept

Reported to CDC

Analysis & Surveillance Publications

Real time

Days to months

Weeks to years

Years
The number of malaria cases in the U.S. has been increasing.
Most years, every state reports at least 1 person diagnosed with malaria

SOURCE: Malaria Surveillance—United States, 2018 | MMWR (cdc.gov)
A preview of the 2019 – 2020 surveillance data

More than 2050 cases

2019

Approx 600 cases

2020

2019–2020 National Malaria Surveillance data are unpublished and preliminary.
Global Region of Malaria acquisition, 2019 – 2020

2019: N>2050

- AFRICA: 86.0
- ASIA: 7.7
- CENT AM/CARBB: 1.0
- OCEANIA: 0.5
- OTHER: 0.1
- UNKNOWN: 13.5*

2020: N <650

- AFRICA: 78.1 *
- ASIA: 5.1*
- CENT AM/CARBB: 0.5
- OCEANIA: 0.8
- OTHER: 0.3
- UNKNOWN: 1.6

2019–2020 National Malaria Surveillance data are unpublished and preliminary.
US Malaria cases 2019 – 2020, onset month & species

- 75% *falciparum*
- 10% *vivax/ovale*
- 16% other/unknown

19%* other/unknown
- 15%* *vivax/ovale*
- 65%* *falciparum*

2019 – 2020 National Malaria Surveillance data are unpublished and preliminary
Time interval between date of arrival in the U.S. and date of illness onset, by *Plasmodium* species, 2018

<table>
<thead>
<tr>
<th>Interval (days)</th>
<th>% of <em>Plasmodium falciparum</em> cases</th>
<th>% of <em>Plasmodium vivax</em> cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0</td>
<td>15.2</td>
<td>8.8</td>
</tr>
<tr>
<td>0 - 29</td>
<td>79.6</td>
<td>32.8</td>
</tr>
<tr>
<td>30 - 89</td>
<td>4.2</td>
<td>17.6</td>
</tr>
<tr>
<td>90 - 179</td>
<td>0.5</td>
<td>13.6</td>
</tr>
<tr>
<td>180 - 364</td>
<td>0.3</td>
<td>20.8</td>
</tr>
<tr>
<td>≥365</td>
<td>0.2</td>
<td>6.4</td>
</tr>
</tbody>
</table>

Malaria Surveillance—United States, 2018 | MMWR (cdc.gov)
Defining Severity of malaria cases in the US

Surveillance criteria

- Neurologic symptoms
- Acute kidney injury
- Severe anemia
- Acute respiratory distress syndrome
- 5% or higher parasitemia
- Documented IV antimalarial
- Fatal cases with malaria as cause of death
Severity of malaria cases in the US, 2019 – 2020

Uncomplicated vs. Severe

<table>
<thead>
<tr>
<th>Year</th>
<th>Uncomplicated</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019</td>
<td>83</td>
<td>17</td>
</tr>
<tr>
<td>2020</td>
<td>78</td>
<td>21</td>
</tr>
</tbody>
</table>

Fatality Rate

- 2019: 0.3
- 2020: 1.0

* Indicates preliminary data

2019 – 2020 National Malaria Surveillance data are unpublished and preliminary.
Malaria Prevention
CDC Malaria Chemoprophylaxis Recommendations

- Reviewed every two years; may be updated more frequently
- Information sources
  - WHO “Country List,” World Malaria Report, and other reports
  - Country ministries of health and malaria control programs
  - CDC Country Offices (in 62 countries)
  - U.S. President’s Malaria Initiative (in 30 countries)
  - U.S. domestic surveillance
  - Literature review
- Low-risk, conservative prevention approach for chemoprophylaxis

Actions for Travelers to Prevent Malaria

- Medication Prophylaxis for travel to endemic area
  - Prescribed medication based on parasite drug sensitivities
  - Take before, during and after travel

- Mosquito Avoidance
  - Insect repellants – topical and impregnated
  - Bed nets
  - Avoid being outdoors when mosquito active

Malaria Diagnosis & Treatment
Malaria Diagnostic Test Results Should be Available STAT!

- **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
Other Tests Not Recommended for Initial Diagnosis

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

- **Serology**
  - Cannot distinguish between acute and prior infection
  - Lengthy turnaround time
Key Considerations for Malaria Treatment in the U.S.

- 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 and resistance patterns
  - Drug availability
  - Age and pregnancy status
# Drugs Available in the U.S. to Treat Acute Infection of Uncomplicated Malaria

<table>
<thead>
<tr>
<th>P. falciparum / Species unidentified (appropriate for all species)</th>
<th>P. vivax, P. ovale, P. malariae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of <strong>acute</strong> infection</td>
<td>Treatment of <strong>acute</strong> infection (chloroquine-susceptible)</td>
</tr>
<tr>
<td>Artemether-lumefantrine (Coartem®)</td>
<td>Chloroquine (Aralen®)</td>
</tr>
<tr>
<td>Atovaquone-proguanil (Malarone®)</td>
<td>Hydroxychloroquine (Plaquenil®)</td>
</tr>
<tr>
<td>Quinine PLUS [doxycycline, clindamycin, or tetracycline]</td>
<td></td>
</tr>
<tr>
<td>Mefloquine</td>
<td></td>
</tr>
</tbody>
</table>
Drugs Available 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)
2023 Locally Acquired Malaria Cases
Anopheles mosquitoes are widespread in the US

Photo credits:
1. CDC
2. U of Fla
3. BugGuide
Between 1980 – 2003, 30 outbreaks of malaria occurred in 8 states
US Locally Acquired Malaria Cases – Florida, Texas, Maryland, Arkansas, 2023 (n=10)

<table>
<thead>
<tr>
<th>Species</th>
<th>State</th>
<th>County</th>
<th>Cases</th>
<th>Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>P. vivax</em></td>
<td>Florida</td>
<td>Sarasota</td>
<td>7</td>
<td>May-Jul</td>
</tr>
<tr>
<td></td>
<td>Texas</td>
<td>Cameron</td>
<td>1</td>
<td>Jun</td>
</tr>
<tr>
<td></td>
<td>Arkansas</td>
<td>Saline</td>
<td>1</td>
<td>Oct</td>
</tr>
<tr>
<td><em>P. falciparum</em></td>
<td>Maryland</td>
<td>National</td>
<td>1</td>
<td>Aug</td>
</tr>
</tbody>
</table>

Capital Region
Locally Acquired Malaria 2023: Investigation Components

• **Laboratory**
  – Case confirmation & species identification
  – Genotyping

• **Epidemiological**
  – In-depth interviews to assess risk factors
  – Active case finding
  – Community engagement

• **Environmental**
  – Household visits
  – Entomologic surveillance & analysis
  – Vector control actions

• **Public Health communications**
Health Department’s Malaria Investigations Revealed

• None of the local cases reported
  – Recent (< 3 years) international travel to an area with malaria
  – Blood transfusion or organ transplantation

• 3 FL cases reported experiencing homelessness
FIGURE 2. Intervals between symptom onset and health care date resulting in malaria diagnosis among patients with autochthonous malaria (N = 8) — Florida and Texas, May–July 2023
Sex and Age of Malaria cases (N = 9, P. vivax, US 2023)

Sex

- **Men**: 6 (67%)
- **Women**: 3 (33%)

Age (years)

- 10-19: 1 (11%)
- 20-39: 4 (44%)
- 40-59: 3 (33%)
- 60-79: 1 (11%)
Clinical Features of Malaria cases (N = 9, *P. vivax*, US 2023)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>9 (100)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6 (67)</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>5 (56)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3 (33)</td>
</tr>
</tbody>
</table>
Clinical Testing (N = 9, *P. vivax*)

<table>
<thead>
<tr>
<th>Condition</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia</td>
<td>9 (100)</td>
</tr>
<tr>
<td>Anemia</td>
<td>7 (78)</td>
</tr>
</tbody>
</table>
Malaria Diagnostic Testing (N = 9, *P. vivax*)

<table>
<thead>
<tr>
<th>Test</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid Diagnostic Test</td>
<td>6/6 (100)</td>
</tr>
<tr>
<td>Blood Smear (<em>P. vivax</em>)</td>
<td>9 (100)</td>
</tr>
<tr>
<td>PCR (<em>P. vivax</em>)</td>
<td>9 (100)</td>
</tr>
</tbody>
</table>
## Treatment (N = 9, *P. vivax*)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N (%)</th>
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<tbody>
<tr>
<td>Artemether-lumefantrine</td>
<td>6 (67)</td>
</tr>
<tr>
<td>Atovaquone-proguanil</td>
<td>3 (33)</td>
</tr>
<tr>
<td>Primaquine* (antirelapse therapy)</td>
<td>9 (100)</td>
</tr>
</tbody>
</table>

*All patients had normal G6PD activity on quantitative testing*
Clinical Course and Outcome

• 8/9 (89%) Hospitalized
• None developed severe malaria
• No deaths reported
• All were reported rapidly to the local/state health department or CDC Malaria Hotline
Entomological investigation and response

- Anopheles trapping, testing and mosquito control
- Traps placed in locations where the patients likely had mosquito exposures and where patients spent time in the evenings
- Traps and control approaches were tailored to each site
Domestic Malaria Outbreak Lessons, 2023 U.S.

- US remains at risk for sporadic mosquito outbreaks
- Essential Support/partnership with local jurisdictions
  - Surveillance
  - Laboratory
  - Entomology
Summary

The US, although endemic malaria is eliminated

• Has ~ 2000 case/yr, mainly among returning travelers visiting friends and relatives and not taking prophylaxis

• Risk of sporadic local mosquito transmission
  – Low, given small number of cases and geographically restricted
  – Competent vector
  – Delays in presentation and diagnosis

• Effective medications available to prevent and treat malaria however challenges to adherence and prompt access
Thank you

For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.