

# **Malaria Cases in the U.S. Reach 40-Year High: Information and Guidance for Clinicians**

## **Clinician Outreach and Communication Activity (COCA) Conference Call January 28, 2014**

# Objectives

**At the conclusion of this session, the participant will be able to accomplish the following:**

- ❑ Explain the principal malaria prevention strategies in travelers**
- ❑ Describe how to diagnose malaria in the U.S.**
- ❑ Discuss the treatment options for uncomplicated and severe malaria**

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The presentation will not include any discussion of the unlabeled use of a product or a product under investigational use with the exception of Dr. Plucinski's discussion on malaria. He will be discussing the use of artesunate for the treatment of severe malaria.

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# TODAY'S PRESENTER



**Mateusz Plucinski, PhD, MPH**  
Epidemic Intelligence Service Officer  
Division of Parasitic Diseases and Malaria  
Center for Global Health  
Centers for Disease Control and Prevention

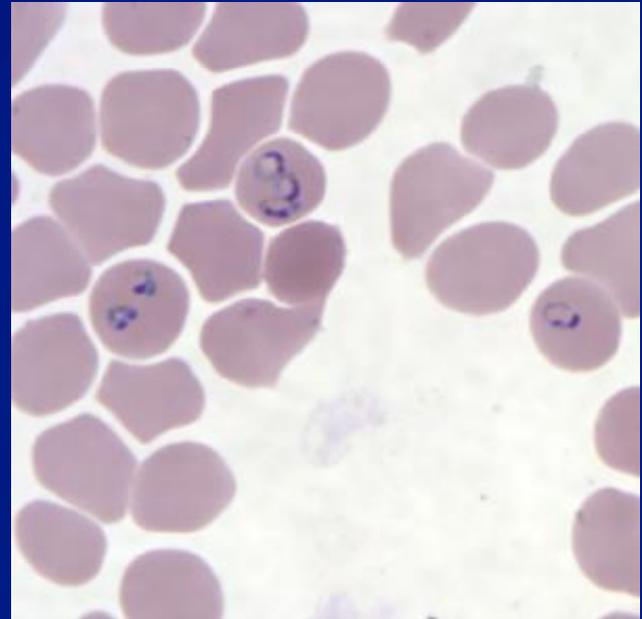
# Outline

- **Malaria Biology**
- **Epidemiology of Malaria**
- **Prevention**
- **Diagnosis**
- **Treatment**

# MALARIA BIOLOGY

# Malaria Parasite

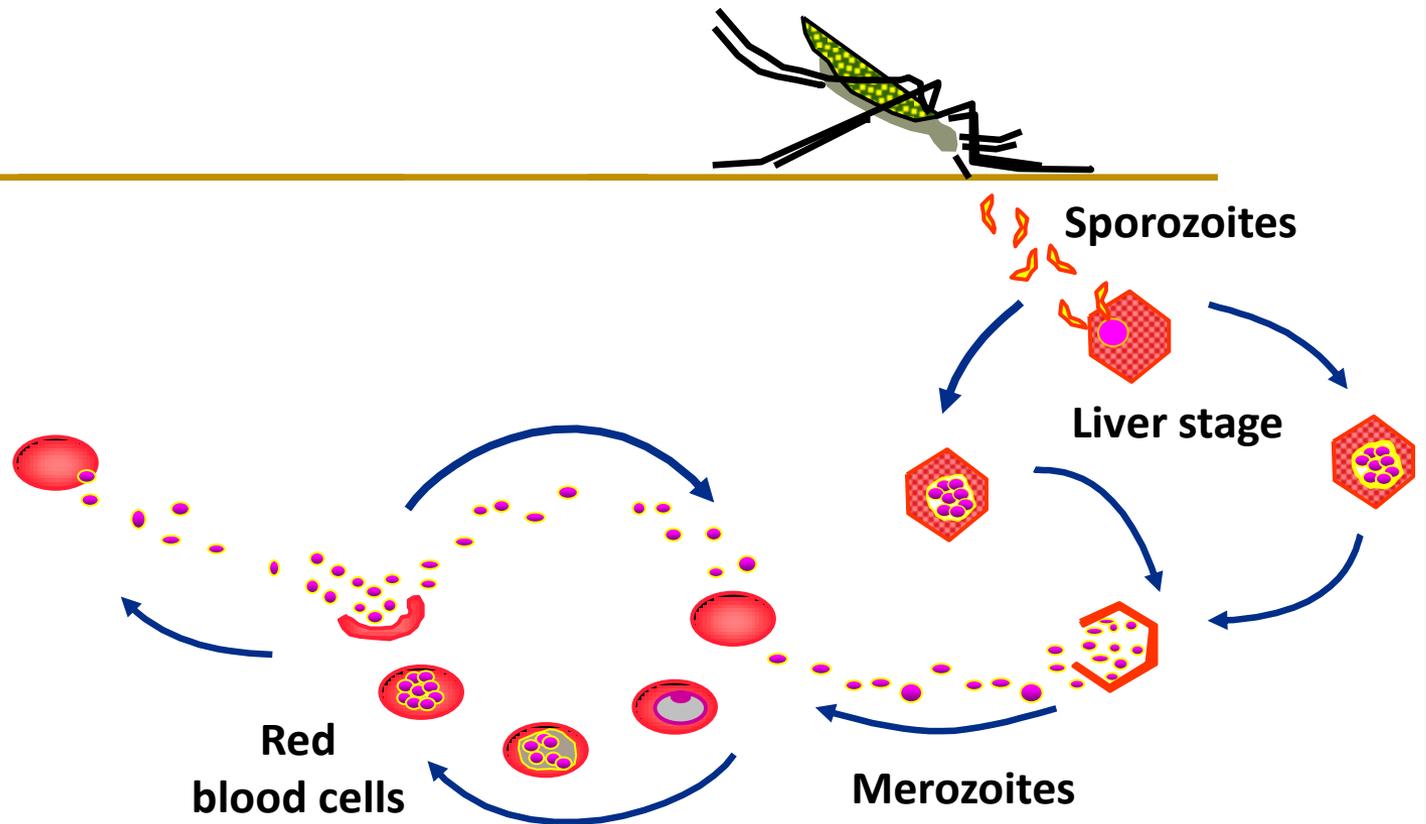
- Vector-borne parasitic disease
  - *Plasmodium* spp.
  - Five species causing human disease
- Transmission by bite of female *Anopheles* mosquito



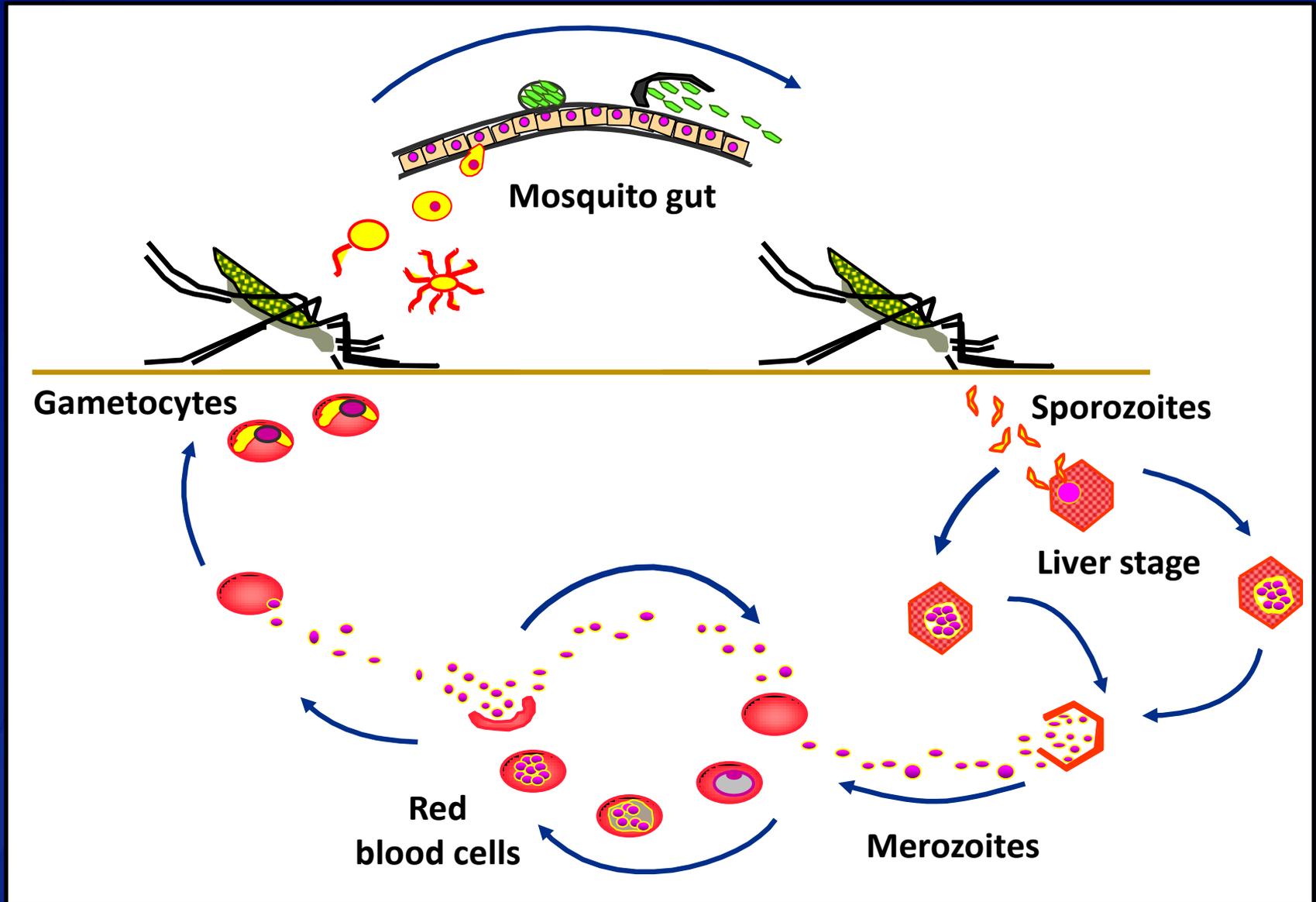
# Species of Malaria

- *Plasmodium falciparum* – most severe disease
- *P. vivax* – most widespread globally, can relapse
- *P. ovale* – can relapse
- *P. malariae* – long duration of infection
- *P. knowlesi* – rare

# Malaria Transmission Cycle



# Malaria Transmission Cycle



# **MALARIA EPIDEMIOLOGY**

# Global Malaria Burden

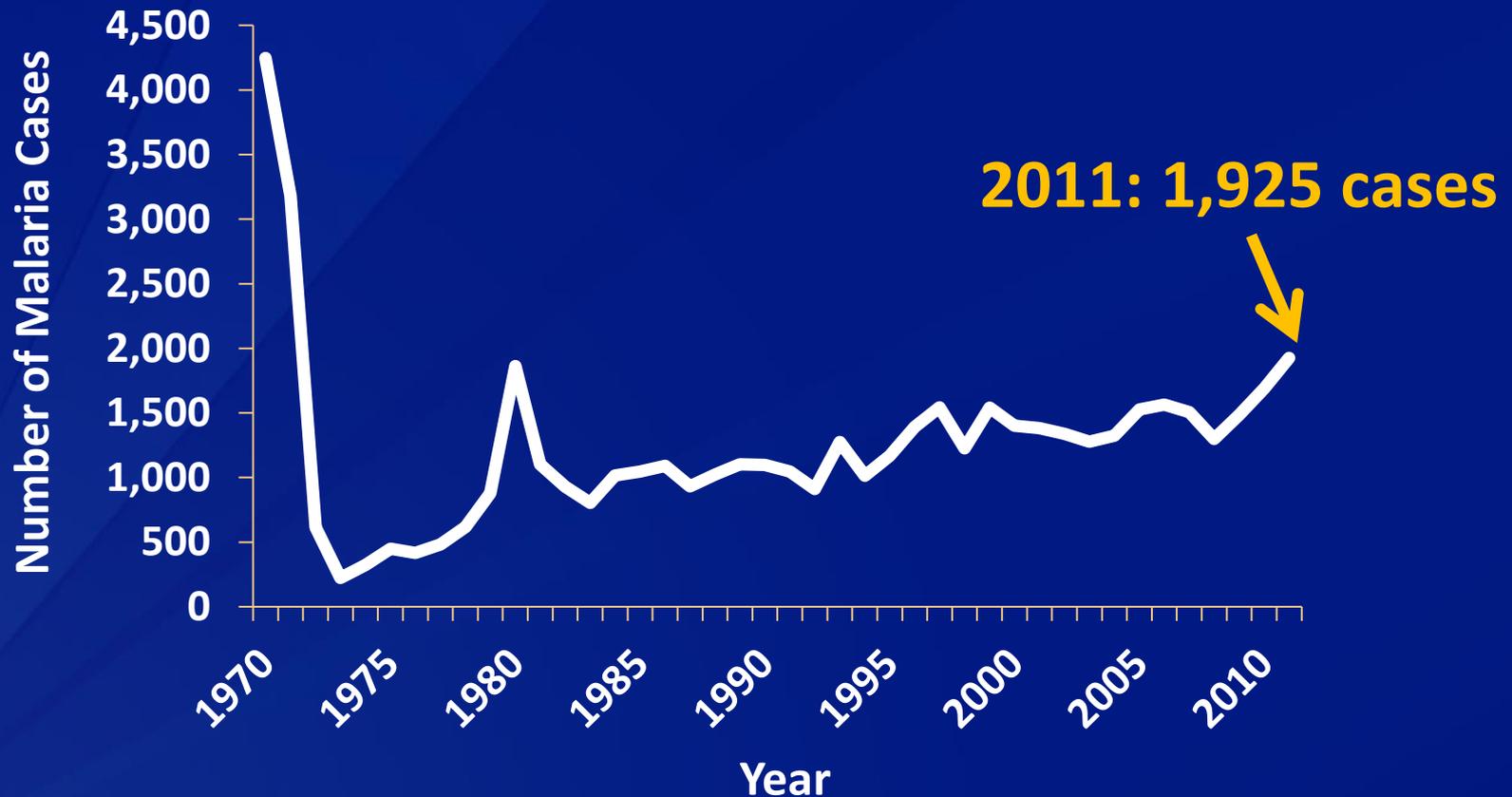
- 207 million cases and 627,000 deaths worldwide yearly
  - Most deaths caused by *P. falciparum*
  - Sub-Saharan Africa main geographic area of mortality
- 3.3 million lives saved by malaria control interventions since 2000

# History of Malaria in U.S. (cont.)

- CDC control and elimination of malaria in U.S.
- Malaria transmission interrupted in the U.S. in the 1940s and eliminated by 1951

# History of Malaria in U.S.

Number of Malaria Cases — United States, 1970–2011



# U.S. Malaria Today

- 1,925 cases of malaria in 2011
- Highest since 1971
- 14% increase since 2010
- 5 fatal cases

# U.S. Malaria Today (cont.)

- Vast majority acquired malaria infection abroad
  - Travelers visiting friends and relatives in sub-Saharan Africa or south Asia
- For the first time, most imported cases linked to travel to India (13%)
- Most cases (69%) still acquired in Africa

# U.S. Malaria Today (cont.)

- Adherence to chemoprophylaxis recommendations poor
- Travelers who contract malaria:
  - Do not take an antimalarial drug for prophylaxis
  - Take the wrong drug
  - Take the wrong dose

# PREVENTION

# Preventing Malaria in Travelers

- Clinicians should proactively ask about upcoming travel
- Preventative Measures
  - An antimalarial drug if indicated
  - Insect repellent on skin not covered by clothing
  - Air-conditioned or well-screened, sleeping accommodations or under an insecticide-treated bed-net
  - Shirts that have long sleeves and long pants
- CDC resources on prevention

## Travelers Visiting Friends or Relatives

- Winter and summer school breaks popular times to travel to country of origin
- Same risk for malaria infection as other travelers

# Chemoprophylaxis

- Atovaquone/proguanil or doxycycline (all areas)
  - Start 1-2 days before travel
- Chloroquine only for chloroquine-sensitive areas
  - Start 1 week before travel

## Chemoprophylaxis (cont.)

- Mefloquine for all areas except those with mefloquine-resistance (certain areas of southeast Asia)
  - Start at least 2 weeks before travel
- Primaquine for short duration travel to areas with principally *P. vivax* malaria (after G6PD testing)
  - Start 1-2 days before travel

# Chemoprophylaxis (cont.)

- Areas with limited malaria transmission
  - Mosquito avoidance only
- Areas with mainly *P. vivax*
  - Primaquine
  - Any other, depending on the local drug resistance
- Areas with chloroquine-sensitive malaria
  - Chloroquine, Atovaquone-Proguanil, Doxycycline, Mefloquine
- Areas with chloroquine-resistant malaria
  - Atovaquone-Proguanil, Doxycycline, Mefloquine,
- Areas with mefloquine-resistant malaria
  - Atovaquone-Proguanil, Doxycycline

# Special Populations

- Pregnant women
- Infants and children

# Adverse Reaction to Antimalarials

- Antimalarial drugs are generally well-tolerated
- Travelers who experience adverse reactions should be switched to another appropriate antimalarial drug rather than go unprotected

# Insect Repellant

- DEET
- Picaridin
- Oil of lemon eucalyptus (OLE) or PMD
- IR3535

# Protective Clothing and Treated Bed Nets

- Cover exposed skin by wearing long-sleeved shirts, long pants, and hats
- Sleep in a screened or air-conditioned room
- Sleep under a bed net if sleeping quarters are exposed to the outdoors

# Prevention — Key Messages

- **Clinicians should proactively ask patients about upcoming travel**
- Understanding areas where malaria transmission occurs
- Personal protection measures
  - Insect repellants
  - Protective clothing
  - Proper accommodations
  - Insecticide-treated bed nets
- Chemoprophylaxis

# DIAGNOSIS

# Patients with Fever

1. All patients presenting with febrile illness should have a travel history obtained
2. Fever in a returned traveler should *always* prompt an immediate evaluation for malaria

# Malaria Symptoms

- Common symptoms
  - Fever
  - Chills
  - Sweats
  - Headaches
  - Nausea and vomiting
  - Body aches
- All nonspecific symptoms – *Laboratory diagnosis is necessary*

# Laboratory Diagnostic Tests

- Acute infection
  - Thick and thin smears
  - Rapid diagnostic tests (RDTs)
- Confirmatory
  - PCR
- Past infection
  - Serology

# Thick and Thin Smear

- First-choice diagnostic test
- Three pieces of information
  1. Presence/absence of malaria
  2. Species of malaria
  3. Percent parasitemia
    - Number of infected cells per 100 red blood cells
- Three negative slides needed to rule out malaria
- ***Should take maximum one hour to prepare and read slide***

# Rapid Diagnostic Tests (RDTs)

- Alternative to microscopy
- Antigen detection
- Can rapidly establish diagnosis
  - Does not confirm species
  - No quantification
  - ***Must be confirmed by microscopy***

# Polymerase Chain Reaction (PCR)

- Can be more sensitive than microscopy
- Results not available soon enough to establish diagnosis
- More useful for species confirmation

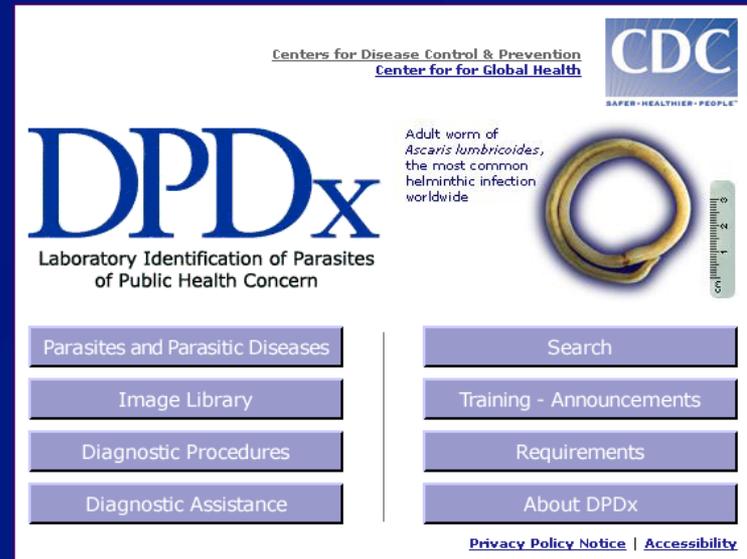
# Serology

- Not appropriate for acute infections
- Confirm past infection with *P. vivax* or *P. ovale* for radical cure

# Diagnosis Services Offered by CDC

- Telediagnosis
- Realtime telediagnosis
- Microscopy review
- PCR
- Drug levels
- Drug resistance testing
- Serology – not for acute diagnosis

• [www.cdc.gov/dpdx](http://www.cdc.gov/dpdx)



# Molecular Surveillance at CDC

- All laboratory confirmed malaria cases:
  - Confirm speciation
  - Drug resistance testing
- Blood for PCR or culture:
  - Draw pretreatment whole blood in 3- or 5- ml EDTA or ACD blood tubes
- **[www.cdc.gov/malaria/report.html](http://www.cdc.gov/malaria/report.html)**

# Diagnosis — Key Messages

- Obtain travel history for all febrile patients
- Evaluate all returned travelers from malaria-endemic areas for malaria
- Perform laboratory diagnostic test
  - Diagnosis should be done within a few hours
- Send specimens from all confirmed cases to CDC

# TREATMENT

# Required Information

1. Uncomplicated or severe malaria
2. Location of likely exposure
3. Species of malaria

# Uncomplicated vs Severe Malaria

- Uncomplicated malaria defined as absence of signs of severe malaria
- Signs of severe malaria
  - Neurological involvement
  - Severe anemia
  - High parasitemia (>5%)
  - End-organ involvement
  - Pulmonary edema
  - Acute respiratory distress syndrome
- Oral antimalarials for uncomplicated malaria
- Intravenous antimalarials for severe malaria

# Location of Likely Exposure

- Obtained from travel history
- Different drug resistance patterns dictate different recommended treatment

# Species of Malaria

- Determined by microscopy
- Different recommended treatments for different species
- If unknown species, assume *P. falciparum*
  - Necessary to follow up to ensure determination of species

# Making a Treatment Decision

- Obtain all three pieces of information:
  1. Staging (uncomplicated versus severe)
  2. Location of likely exposure
  3. Species
- Consult CDC malaria treatment guidelines
  - [www.cdc.gov/malaria/diagnosis\\_treatment/treatment.html](http://www.cdc.gov/malaria/diagnosis_treatment/treatment.html)

# Making a Treatment Decision (cont.)

## Guidelines for Treatment of Malaria in the United States

1

(Based on drugs currently available for use in the United States – updated September 23, 2011)

CDC Malaria Hotline: (770) 488-7788 or (855) 856-4713 toll-free Monday-Friday 9 am to 5 pm EST - (770) 488-7100 after hours, weekends and holidays

Clinical Diagnosis/ <i>Plasmodium</i> species	Region Infection Acquired	Recommended Drug and Adult Dose <sup>1</sup>	Recommended Drug and Pediatric Dose <sup>1</sup> <i>Pediatric dose should NEVER exceed adult dose</i>
Uncomplicated malaria/ <i>P. falciparum</i> or Species not identified  If "species not identified" is subsequently diagnosed as <i>P. vivax</i> or <i>P. ovale</i> : see <i>P. vivax</i> and <i>P. ovale</i> (below) re. treatment with primaquine	Chloroquine-resistant or unknown resistance <sup>2</sup> (All malarious regions except those specified as chloroquine-sensitive listed in the box below.)	<b>A. Atovaquone-proguanil (Malarone<sup>TM</sup>)<sup>3</sup></b> Adult tab = 250 mg atovaquone/ 100 mg proguanil 4 adult tabs po qd x 3 days	<b>A. Atovaquone-proguanil (Malarone<sup>TM</sup>)<sup>3</sup></b> Adult tab = 250 mg atovaquone/ 100 mg proguanil Peds tab = 62.5 mg atovaquone/ 25 mg proguanil 5 - 8kg: 2 peds tabs po qd x 3 d 9-10kg: 3 peds tabs po qd x 3 d 11-20kg: 1 adult tab po qd x 3 d 21-30kg: 2 adult tabs po qd x 3d 31-40kg: 3 adult tabs po qd x 3d > 40 kg: 4 adult tabs po qd x 3d
		<b>B. Artemether-lumefantrine (Coartem<sup>TM</sup>)<sup>4</sup></b> 1 tablet = 20mg artemether and 120 mg lumefantrine A 3-day treatment schedule with a total of 6 oral doses is recommended for both adult and pediatric patients based on weight. The patient should receive the initial dose, followed by the second dose 8 hours later, then 1 dose po bid for the following 2 days. 5 - <15 kg: 1 tablet per dose 15 - <25 kg: 2 tablets per dose 25 - <35 kg: 3 tablets per dose ≥35 kg: 4 tablets per dose	
		<b>C. Quinine sulfate plus one of the following: Doxycycline, Tetracycline, or Clindamycin</b> Quinine sulfate: 542 mg base (=650 mg salt) <sup>4</sup> po tid x 3 or 7 days <sup>5</sup> Doxycycline: 100 mg po bid x 7 days Tetracycline: 250 mg po qid x 7 days Clindamycin: 20 mg base/kg/day po divided tid x 7 days	<b>C. Quinine sulfate<sup>4</sup> plus one of the following: Doxycycline<sup>6</sup>, Tetracycline<sup>6</sup> or Clindamycin</b> Quinine sulfate: 8.3 mg base/kg (=10 mg salt/kg) po tid x 3 or 7 days <sup>5</sup> Doxycycline: 2.2 mg/kg po every 12 hours x 7 days Tetracycline: 25 mg/kg/day po divided qid x 7 days Clindamycin: 20 mg base/kg/day po divided tid x 7 days
		<b>D. Mefloquine (Lariam<sup>TM</sup> and generics)<sup>7</sup></b> 684 mg base (=750 mg salt) po as initial dose, followed by 456 mg base (=500 mg salt) po given 6-12 hours after initial dose Total dose= 1,250 mg salt	<b>D. Mefloquine (Lariam<sup>TM</sup> and generics)<sup>7</sup></b> 13.7 mg base/kg (=15 mg salt/kg) po as initial dose, followed by 9.1 mg base/kg (=10 mg salt/kg) po given 6-12 hours after initial dose. Total dose= 25 mg salt/kg

# Treatment of Uncomplicated *P. falciparum*

- If obtained in chloroquine-resistant area:
  - Atovaquone-proguanil (Malarone)
  - Artemether-lumefantrine (Coartem)
  - Quinine + Doxycycline, Tetracycline or Clindamycin
  - Mefloquine (Lariam)
- If obtained in chloroquine-sensitive area (parts of Central America, parts of Caribbean, Middle East):
  - Any of above
  - Chloroquine or Hydroxychloroquine

## Treatment of Uncomplicated *P. vivax*

- If obtained in chloroquine-resistant area (Papua New Guinea and Indonesia):
  - Atovaquone-proguanil
  - Quinine + Doxycycline, Tetracycline or Clindamycin
  - Mefloquine
- If obtained in chloroquine-sensitive area:
  - Chloroquine or Hydroxychloroquine
- ***If patient not G6PD deficient, follow up with 2 week course of primaquine to prevent relapse (radical cure)***

# Treatment of Severe Malaria

- Severe malaria most frequently caused by *P. falciparum*, but also *P. vivax*
- First-line Treatment: IV Quinidine + IV Doxycycline, Tetracycline or Clindamycin
  - Cardiac toxicities (Continuous cardiac monitoring necessary)
  - Loading dose + continuous infusion

# Artesunate — Alternative to Quinidine

- Investigational drug
- Available through CDC
- Can be released only when:
  - Severe (or suspected severe) malaria AND
  - One of following four conditions:
    - Quinidine not available
    - Quinidine treatment failure (less than 90% reduction in parasitemia after 48 hours)
    - Contraindications to quinidine
    - Quinidine intolerance

# Quinidine Intolerance

- QRS interval is widened by  $> 50\%$
- QT interval exceeds 0.60 seconds
- QT interval is prolonged by more than 25% of the baseline value
- Persistent hypotension unresponsive to fluid resuscitation
- Development of reaction to quinidine during therapy

# Procedures for Requesting Artesunate

- Clinician calls CDC Malaria Hotline
- CDC Malaria Branch staff confirms eligibility
- If eligible, artesunate and associated consent forms sent to clinician from one of nine quarantine stations
- Artesunate administered at health facility
- Process commonly on average takes 7 hours

# Treatment — Key Messages

- Three necessary pieces of information:
  1. Uncomplicated malaria vs severe malaria
  2. Where infection was acquired
  3. Species
- Consult malaria treatment guidelines

# Resources

- CDC Yellow Book
- CDC Malaria Hotline
  - (770) 488-7788 or (855) 856-4713 business hours
  - (770) 488-7100 after hours
- CDC malaria website (treatment guidelines, prevention, diagnosis)
  - [www.cdc.gov/malaria](http://www.cdc.gov/malaria)
- CDC DPDx diagnosis services
  - [www.cdc.gov/dpdx](http://www.cdc.gov/dpdx)

# Thank you

# Questions?

*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.*

# To Ask a Question

## □ Using the Webinar System

- “Click” the Q&A tab at the top left of the webinar tool bar
- “Click” in the white space
- “Type” your question
- “Click” ask

## □ On the Phone

- Press Star (\*) 1 to enter in the queue to ask a question
- State your name
- Listen for the operator to call your name
- State your organization and then ask your question



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Thank you for joining!  
Please email us questions at  
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    - ▶ **January 28, 2014**
- What CDC Is Doing
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**Malaria Cases in the U.S. Reach 40-Year High: Information and Guidance for Clinicians**

**CE** = Free Continuing Education

**Date:** Tuesday, January 28, 2014

**Time:** 2:00 - 3:00 pm (Eastern Time)

**To Join:**

**Dial-In:** 888-233-9077

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**Access Webinar:** <https://www.mymeetings.com/nc/join.php?i=PW3575459&p=7399953&t=c>

**Presenter(s):**

 **Mateusz Plucinski, PhD, MPH**  
Epidemic Intelligence Service Officer  
Center for Global Health  
Malaria Branch  
Centers for Disease Control and Prevention

**Overview:**

The number of malaria cases reported in the United States in 2011 was the largest since 1971, representing a 14% increase from 2010 and a 48% increase from 2008. The majority of malaria infections occurred among persons who traveled to regions with ongoing malaria transmission. Imported malaria can reintroduce malaria into regions where the disease is not endemic and environmental conditions are present that support the lifecycle of the parasite. During this COCA call, a CDC subject matter expert will describe malaria prevention strategies aimed at reducing the risk of malaria in travelers, discuss the diagnosis of malaria in patients with suspect malaria, and explain the treatment options for confirmed malaria cases.

<http://emergency.cdc.gov/coca>

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