Millions of U.S. residents travel to malaria-endemic regions each year. Malaria is a potentially fatal parasitic disease caused by *Plasmodium* species transmitted via the bite of the female *Anopheles* mosquito. Clinical malaria prevention in travelers, a core component of the pre-travel clinical consultation (see *Rx for Prevention*, Jan. 2011), offers the double benefit of protecting the individual traveler against disease while reducing the risk of introduction of malaria to mosquito populations upon return to the U.S.

Fewer than half of U.S. resident travelers to the developing world obtain pre-travel health care; among those who do seek such care, 20%-60% receive incorrect malaria chemoprophylaxis. Malaria deaths in U.S. citizens following an inappropriate chemoprophylaxis regime have been reported. Despite these challenges, the primary care physician can effectively manage clinical malaria prevention for most travelers through an organized approach.

**Pre-Travel Clinical Malaria Prevention**

Using a malaria prevention checklist (page 5) is a convenient way for the primary care physician to competently provide proper advice. This approach, when paired with the free, online CDC “Yellow Book” (Health Information for International Travel 2010, [http://wwwnc.cdc.gov/travel/content/yellowbook/home-2010.aspx](http://wwwnc.cdc.gov/travel/content/yellowbook/home-2010.aspx)) can rapidly assess malaria risk, determine the need for an appropriate chemoprophylactic, and suggest other topics for patient counseling and education.

The risk of malaria is dependent on the intensity of transmission from mosquitoes at the destination, the duration and type of travel, the prevention measures used, and other individual characteristics. Online CDC resources (page 6) provide country-specific recommendations regarding malaria risk and drug-resistance patterns to assist in determining indications for chemoprophylaxis. There are four medications commonly used for primary chemoprophylaxis: atovaquone/proguanil, doxycycline, mefloquine, and chloroquine. (Other less commonly used medications for primary chemoprophylaxis can be found in the CDC “Yellow Book” section on Malaria.)

The use of chloroquine is now severely restricted due to extensive resistance in *P. falciparum*. An additional agent, primaquine, should be used in individuals with prolonged periods of exposure upon leaving a malaria-endemic region for terminal prophylaxis against the dormant liver stages (hypnozoites) of *P. vivax* and *P. ovale*, the two malaria species that may cause chronic liver infection. Selecting the appropriate malaria chemoprophylaxis regime requires consideration of destination-specific malaria risk and drug resistance patterns, medical contraindications, common/severe adverse effects, cost and convenience of administration, with further considerations for children and pregnant/lactating women. The malaria checklist addresses all of these considerations.

The approach consists of 3 steps:
1. Assess malaria risk based on travel itinerary and determine if there is indication for chemoprophylaxis.
2. Assess the patient and, if indicated, select appropriate malaria chemoprophylaxis.
3. Counsel and educate the patient regarding mosquito bite prevention, medication compliance and potential adverse effects, symptoms of malaria and advice regarding medical care.

**Early Identification of Malaria in the Returned Traveler to Prevent Morbidity and Mortality**

Annually, between 1,000 and 1,500 cases of malaria (with 3-7 deaths) are reported in the United States, with 25-50 of those cases reported in Los Angeles County (LAC). From 2005-2009, only one-third of LAC malaria cases reported any travel history with over 50% of cases, increasing the risk of morbidity and death. Common reasons for initial misdiagnosis include:

- Failure to elicit an appropriate travel history
- Provider’s lack of familiarity with malaria diagnostics
- Laboratory staff’s lack of familiarity with malaria microscopy.

When eliciting a travel history, it is important to ask the patient about travel exposures over, at a minimum, the...
### Malaria Prevention Checklist


<table>
<thead>
<tr>
<th>Country</th>
<th>Travel Dates</th>
<th>Areas with Malaria</th>
<th>Drug Resistance</th>
<th>Malaria Species</th>
<th>Recommended Primary Chemoprophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Atovaquone/Proguanil/Mefloquine</td>
</tr>
</tbody>
</table>

**B. Will the traveler:**  
- Travel to a region with relapsing malaria species (P. vivax or P. ovale)?
- Have prolonged exposure to malaria-endemic region (e.g., expatriates, missionaries, Peace Corps volunteers)?

If both boxes are checked, consider Terminal Prophylaxis with primaquine.

### Adverse Effects
- Very well tolerated.  
  - Adverse effects rare.  
  - Most common adverse effects reported include:  
    - Abdominal pain  
    - Nausea/vomiting  
    - Headache

### Safety in Pregnancy/Lactation
- Undetermined/Contraindicated
- Contraindicated in 1st trimester
- Undetermined/Contraindicated unless G6PD deficiency has been ruled out in breast-fed infant

### Safety in Children
- Contraindicated in children <5kg  
  - Pediatric tablets available
- Contraindicated in children <8 years old
- Contraindicated in children <5kg  
  - Pediatric tablets available

### Pediatric Dose
- Peds tabs contain 62.5mg atovaquone and 25mg proguanil hydrochloride.  
  - 5-8kg: 1/2 peds tab daily  
  - 8-10kg: 3/4 peds tab daily  
  - 10-20kg: 1 peds tab daily  
  - 20-30kg: 2 peds tabs daily  
  - 30-40kg: 3 peds tabs daily  
  - ≥40kg: adult dose

**Note:**  
- 28 years old; 2mg/kg up to adult dose of 100mg

### Adult Dose
- 1 adult tab orally daily (Adult tabs contain 250mg atovaquone and 100mg proguanil)
- 100mg orally daily

**Note:**  
- 250mg base; 1 tab orally once/week

### Other Considerations
- Pediatric tablets available
- Requires pregnancy prevention counseling for women of childbearing age
- Most effective, worst reputation
- Best used for prolonged trips through Central America

### Additional Information
- **Mosquito Bite Prevention**  
  - Insect repellent (e.g., DEET)  
  - Proper skin-covering clothing  
  - Insecticide-treated bed nets  
  - Minimize outdoor exposures at dusk and dawn
- **Stress Medication Compliance**  
  - Provide example symptoms of malaria and advice on when to seek immediate medical care
  - High fevers  
  - Flu-like illness  
  - Jaundice (yellow eye and skin discoloration)
- **Review Potential Medication Adverse Effects**  
  - Atovaquone/Proguanil  
  - Chloroquine  
  - Mefloquine
- **Educate Regarding Risk of Counterfeit and Substandard Chemoprophylactic Agents Purchased Abroad**
- **Stress Importance of Travel/Emergency Medical Evacuation Insurance**
preceding 12 months. The incubation period (time from infection to development of disease) for malaria is highly variable and dependent on the malaria species. Individuals infected with *P. falciparum*, the species responsible for the majority of global malaria deaths, present within 30 days of entry to the U.S. in over 90% of cases. Over one-third of individuals infected with *P. vivax* and *P. ovale* present more than 3 months after reentry to the U.S., and may even present with initial symptoms up to 1 or 2 years after exposure.

Fever in the returned traveler should be considered to be due to malaria until proven otherwise. Approximately 1 in 3 returned international travelers, presenting to a specialized travel or tropical medicine clinic, with a systemic febrile illness, has malaria, but 25% of malaria cases are afebrile at the time of presentation. Blood microscopy of thin and thick blood smears is the test of choice for diagnosing malaria; however, it has a low sensitivity for ruling out malaria, especially under the eyes of a U.S.-based microscopist who rarely confronts tropical parasites. As a result, multiple blood smears obtained at several points in time must be ordered to reliably rule out malaria; expert consultation should be considered early. While advanced malaria diagnostics may be more sensitive than blood microscopy, they are of limited utility for the diagnosis of acutely ill patients in the standard health care setting unless they are immediately available.

If a diagnosis of malaria is suspected:
- Consult the CDC Webpage on Malaria Diagnosis and Treatment in the U.S. [www.cdc.gov/malaria/diagnosis_treatment/index.html](http://www.cdc.gov/malaria/diagnosis_treatment/index.html)
- Consider calling the CDC Malaria Hotline: (770) 488-7788, M-F, 5 am to 1:30 pm, Pacific Time (770) 488-7100, after hours, weekends and holidays
- Report the case to LAC Acute Communicable Disease Control within 1 working day of identification Hotline: (888) 397-3993; Fax: (888) 397-3778
The Malaria Case Report form is available at [www.publichealth.lacounty.gov/acd/EpiForms/MalariaCaseRep-CDPH8657.pdf](http://www.publichealth.lacounty.gov/acd/EpiForms/MalariaCaseRep-CDPH8657.pdf).

**Conclusion**
Malaria risk in travelers to malaria-endemic regions can be mitigated through the pre-travel health consultation. The primary care physician is well-suited to assess indications for appropriate malaria chemoprophylaxis and to provide malaria prevention advice and counseling for most travelers. The malaria assessment checklist provides a framework for clinical malaria preventive care. The occurrence of fever in a returned traveler should prompt an investigation for malaria as well as other illnesses.


**REFERENCES**

**Continuing Medical Education Courses**
The Los Angeles County Department of Public Health is pleased to offer the following free, online CME courses, which have been approved for AMA PRA Category 1 credit:
- Successful Treatment of Tobacco Addiction (1 credit)
- Screening for Alcohol Misuse and Abuse (1 credit)
- Preventing Falls Among Adults Aged 65 Years and Older (1 credit)
- Preventing Cervical Cancer (1 credit)
- Common Causes of Low Vision in Adults Aged 40 Years and Older (1 credit)

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