Prevention and Early Identification of Malaria in the Traveler

Benjamin Bristow, MD, MPH, DTM&H

Van Ngo, MPH

Rachel Civen, MD, MPH

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.[1,2] Malaria deaths in U.S. citizens following an inappropriate chemoprophylaxis regime have been reported.[3] 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) can rapidly assess malaria risk, determine the need for an appropriate chemoprophylactic, and suggest other topics for patient counseling and education.[4]

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.[5] 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.[4])

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.

CDC/James Gathany

A female *Anopheles albimanus* mosquito, a vector of malaria predominantly found in Central America, feeds on a human host and becomes engorged with blood.

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).[6] From 2005-2009, only one-third of LAC malaria cases reported any use of prophylaxis. Malaria may be initially misdiagnosed in over 50% of cases, increasing the risk of morbidity and death.[7] Common reasons for initial misdiagnosis include the following:

- 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

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MALARIA PREVENTION CHECKLIST

STEP 1. ASSESS MALARIA RISK TO DETERMINE INDICATION FOR CHEMOPROPHYLAXIS

A. Fill in malaria risk information and recommended primary prophylaxis by country from http://wwwnc.cdc.gov/travel/yellowbook/2010/chapter-2/malaria-risk-information-and-prophylaxis.aspx

Country	Travel Dates	Areas with Malaria	Drug Resistance	Malaria Species	Recommended Primary Chemoprophylaxis
	Departure ——/——/—— Return ——/——/——		☐ None ☐ Chloroquine ☐ Mefloquine	—— % *P. falciparum* —— % *P. vivax* —— % *P. malariae* —— % *P. ovale*	☐ Atovaquone/Proguanil ☐ Doxycycline ☐ Mefloquine ☐ Chloroquine

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**.

STEP 2. ASSESS PATIENT AND, IF INDICATED, SELECT APPROPRIATE CHEMOPROPHYLAXIS[4]

	Atovaquone/Proguanil (Malarone)	Doxycycline	Mefloquine (Larium)	Chloroquine	Primaquine
Usage	Prophylaxis in all areas	Prophylaxis in all areas	**Restricted in parts of SE Asia due to resistance**	**Severely restricted due to drug resistance**	Terminal Prophylaxis to treat dormant liver forms (hypnozoites) of P. vivax and P. ovale to prevent relapse
Contraindications	• **Creatine Clearance <30ml/min** • **Caution in patients on coumadin (warfarin)**	**Tetracycline allergy**	• **Anxiety/Depression history** • **Psychiatric disease** • **Seizure disorder** • **Cardiac conduction abnormality** • **Known hypersensitivity**	**Epilepsy and psoriasis**	**Glucose 6 Phophate Dehydrogenase (G6PD) deficiency must be ruled out by appropriate lab testing prior to use**
Convenience of Administration	Daily Dosing	Daily Dosing	Weekly Dosing	Weekly Dosing	
Start	1-2 days before travel	1-2 days before travel	2 weeks before travel	1-2 weeks before travel	Upon departure from malaria-endemic region
Stop	7 days after return	4 weeks after return	4 weeks after return	4 weeks after return	14 days of daily therapy
Adverse Effects	Very well tolerated. Adverse effects rare. Most common adverse effects reported include: • abdominal pain • nausea/vomiting • headache	Adverse effects include: • photosensitivity • vaginal candidiasis • esophagitis • nausea, vomiting	0.5%-1% risk of mild/moderate neuropsych events such as: • sleep disturbance • emotional lability • anxiety • cognitive changes 1/10000 risk of severe reactions such as: • seizures • psychosis • hallucinations[9]	Adverse effects at chemoprophylaxis dosing includes: • GI disturbance • headache • dizziness • blurred vision • insomnia • pruritus	G6PD deficient: potentially fatal hemolysis
Safety in Pregnancy/Lactation	Undetermined / Contraindicated	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	Contraindicated in children <8 years old	Contraindicated in children <5kg		
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 ped tabs daily • >40kg: adult dose	≥8 years old; 2mg/kg up to adult dose of 100mg	Tabs contain 228mg base (250mg salt) • ≤9kg: 4.6mg/kg base (5mg/kg salt) orally once/week • >9-19kg: 1/4 tab once/week • >19-30kg: 1/2 tab once/week • >31-45kg: 3/4 tab once/week • ≥45kg: 1 tab once/week	5mg/kg base (8.3mg/kg salt) orally once/week, up to maximum adult dose of 300mg base	0.5mg/kg (0.8mg/kg salt) up to adult dose orally daily for 14 days after departure from malaria-endemic area
Adult Dose	1 adult tab orally daily (Adult tabs contain 250mg atovaquone and 100mg proguanil)	100mg orally daily	Tabs contain 228mg base (250mg salt); 1 tab orally once/week	300mg base (500mg salt) orally once/week	30mg base (52.6 mg salt) orally daily for 14 days after departure from the malaria-endemic area
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	

STEP 3. PATIENT COUNSELING AND EDUCATION

☐ 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

☐ Educate Regarding Risk of Counterfeit and Substandard Chemoprophylactic Agents Purchased Abroad

☐ Stress Importance of Travel/Emergency Medical Evacuation Insurance

☐ Provide Patient with CDC Written Malaria Info. Preventing Malaria in Travelers: A Guide for Travelers to Malaria-Risk Areas. Available at http://www.cdc.gov/malaria/resources/pdf/travelers.pdf

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.[6] 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.[6]

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.[8] 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
- Consult the Guidelines for Treatment of Malaria in the U.S. www.cdc.gov/malaria/resources/pdf/treatmenttable.pdf
- 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.

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. ℞

Benjamin Bristow, MD, MPH, DTM&H, is a physician in the Preventive Medicine Residency Program, California Department of Public Health. **Van Ngo**, MPH, is an epidemiologist, and **Rachel Civen**, MD, MPH, is a medical epidemiologist, Acute Communicable Disease Control Program, Los Angeles County Department of Public Health.

REFERENCES

1. Hamer DH, Connor BA. Travel health knowledge, attitudes and practices among United States travelers. *J Travel Med*. 2004;11(1):23-6.

2. Kestone JS, Dismukes R, Sawyer L, Kozarsky PE. Inadequacies in health recommendations provided for international travelers by North American travel health advisors. *J Travel Med*. 1994;1(2):72-8.

3. CDC. Malaria deaths following inappropriate malaria chemoprophylaxis – United States, 2001. *MMWR*. 2001;50(28):597-9.

4. Arguin PM, Steele SF. The Pre-Travel Consultation, Malaria. In: CDC Health Information for International Travel 2010. Atlanta: U.S. Department of Health and Human Services, Public Health Service 2009. http://wwwnc.cdc.gov/travel/yellowbook/2010/chapter-2/malaria.aspx. Accessed February 3, 2011

5. Schlagenhauf P, Peterson E. Malaria chemoprophylaxis: strategies for risk groups. *Clin Microbiol Rev*. 2008;21(3):466-72.

6. Malaria surveillance – United States, 2007. *MMWR*. 2009; 58(SS02):1-16.

7. Kain KC et al. Imported malaria: Prospective analysis of problems in diagnosis and management. *Clin Infect Dis*. 1998;27(1):142-9.

8. Wilson et al. Fever in returned travelers: Results from the GeoSentinel Surveillance Network. *Clin Infect Dis*. 2007;44(12):1560-8.

9. Spira AM. Preparing the traveller. *Lancet*. 2003;361(9366):1368-81.

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