

CLINICAL INQUIRIES

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When should travelers begin malaria prophylaxis?

Evidence-based answer

Travelers should start on chloroquine 1 to 2 weeks before entering an area without chloroquine resistance (strength of recommendation [SOR]: **C**, based on expert opinion). In areas with chloroquine-resistant *Plasmodium falciparum*, travelers will need to take atovaquone/proguanil, doxycycline, or primaquine 1 day before entering the area, or mefloquine 2 to 7

weeks before travel (SOR: **B**, based on prospective patient-oriented outcomes and expert opinion).

Before prescribing medications, determine malaria risk and sensitivity of *Plasmodium* species by country at wwwn.cdc.gov/travel/yellowBookCh5-MalariaYellowFeverTable.aspx (SOR: **C**, based on patient-oriented expert opinion).

Clinical commentary

5 tips to help travelers avoid malaria

Despite our best efforts, more than 10,000 American and European travelers contract malaria each year. Five clinical pointers are helpful in prescribing malaria prophylaxis and preventing malaria in travelers.

1. **Advise** patients that they'll need to get their antimalarials before they leave for their trip. The CDC recommends against the purchase of antimalarials while overseas because of concerns about product quality.

2. **Encourage** patients to plan ahead. Most local community pharmacies do not routinely stock antimalarials and must special order them. If a patient mentions an upcoming trip, advise them that they'll need to allow an extra 2 weeks to obtain their medications.

3. **Consult** 1 of 2 continuously updated Web sites prior to selecting a medication for malaria prophylaxis: wwwn.cdc.gov/travel/destinationList.aspx or www.who.int/ith/en.

Start times vary from 1 day to several weeks prior to travel based on the medication selected.

4. **Encourage** patients to spray clothing with permethrin prior to travel. Permethrin remains effective as a repellent even after months of clothing use and multiple washes.

5. **Encourage** travelers to finish their medication after they return and to report unexplained fevers for up to 1 year after travel.

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FAST TRACK

Before selecting a medication for malaria prophylaxis, go to:

- wwwn.cdc.gov/travel/destinationList.aspx
- www.who.int/ith/en

Evidence summary

Travelers to malaria-endemic areas should avoid mosquito bites by using netting and repellents, and use chemo-

prophylaxis to prevent infection.

Although no drug regimen guarantees protection against malaria, physicians should prescribe 1 of several

TABLE

Evidence-based recommendations for prevention of malaria^{2-3,8}

DRUG	USAGE	ADULT DOSE	TREATMENT SCHEDULE
Atovaquone/ proguanil Contraindicated in pregnancy	Prophylaxis in areas with chloroquine-resistant or mefloquine-resistant <i>P falciparum</i>	1 tablet orally each day (250 mg atovaquone and 100 mg proguanil hydrochloride)	Daily from 1 day prior to entry until 7 days after leaving
Chloroquine	Prophylaxis only in areas with chloroquine-sensitive <i>P falciparum</i>	300 mg base (500 mg salt) orally, once/week	Weekly from 2 weeks prior to entry until 4 weeks after leaving (take on the same day of the week)
Doxycycline Contraindicated in children <8 years of age and pregnant women	Prophylaxis in areas with chloroquine-resistant or mefloquine-resistant <i>P falciparum</i>	100 mg orally, daily	Daily from 1 day prior to entry until 4 weeks after leaving
Mefloquine	Prophylaxis in areas with chloroquine-resistant <i>P falciparum</i>	228 mg base (250 mg salt) orally, once/week	Weekly from 2-7 weeks before entry until 4 weeks after leaving (take on the same day of the week)
Primaquine	An option for prophylaxis in special circumstances	30 mg base (52.6 mg salt) orally, daily	Daily from 1 day prior to entry until 7 days after leaving

options based on the location of travel, the susceptibility of indigenous *P falciparum*, and the side-effect profile.¹

Timing and dosage of prophylactic drugs

Prophylactic medications must be started at different times before travel, but for some medications the optimal time to initiate treatment is unclear. Evidence-based recommendations^{2,3} with consideration for side-effect profiles are given in the **TABLE**.

In contrast to the pretreatment times for all other malarial prophylaxes, the generally accepted pretreatment time for mefloquine is 1 to 2 weeks before entering a risk area. However, this may still be inadequate due to the drug's long half-life, which results in a long delay in reaching therapeutic blood levels.⁴ The evidence indicates that mefloquine should be started at least 2, and as many as 7, weeks before travel.

The standard recommended dose of 250 mg/week of mefloquine "produces maximum steady-state plasma concen-

trations of 1000 to 2000 mcg/L, which are reached only after 7 to 10 weeks."⁴ One study of 293 children under the age of 5 years in Malawi found that plasma concentrations of mefloquine were below prophylactic level (500 mcg/mL) against *P falciparum* until the fourth to seventh week of once-weekly dosing ($P < .0003$).⁵

One way of reaching prophylactic levels earlier would be to give mefloquine 250 mg daily for 3 days followed by 250 mg weekly.⁴ A safety study of 157 healthy US Marine volunteers showed that preloading achieves prophylactic blood levels of mefloquine by the third day while weekly mefloquine is subprophylactic until the fifth week.⁴

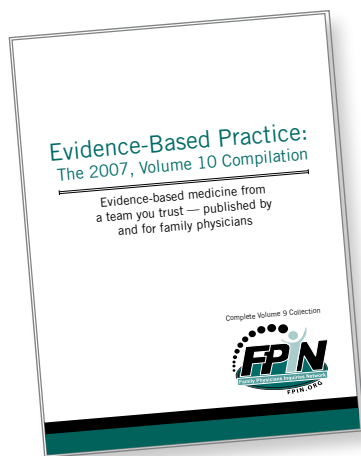
While a study of the long-term use of mefloquine in 421 healthy Peace Corps volunteers has shown it to be safe,⁶ clinical trials and case reports indicate that a loading dose of mefloquine is associated with adverse drug events, which include neuropsychiatric and gastrointestinal symptoms.^{4,7}

FAST TRACK

Encourage patients to spray clothing with permethrin before travel. It remains an effective repellent even after multiple washes

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Recommendations from others

The World Health Organization (WHO) states that "weekly mefloquine should be started at least 1 week, but preferably 2–3 weeks before departure, to achieve higher pre-travel blood levels and to allow side effects to be detected before travel so that possible alternatives can be considered."⁸

Centers for Disease Control and Prevention recommendations integrate recommendations from WHO and Cochrane. ■

Acknowledgments

The opinions and assertions contained herein are the private views of the authors and not to be construed as official, or as reflecting the views of the US Air Force Medical Service or the US Air Force at large.

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