Prevention of malaria in travellers

Trish Batchelor
MBBS, MPH, FRACGP, is Medical Director, Travel Doctor-TMVC, Canberra, Australian Capital Territory, and Executive Board Member, International Society of Travel Medicine.
trish.batchelor@traveldoctor.com.au

Tony Gherardin
MBBS, MPH, FRACGP, is National Medical Adviser, Travel Doctor-TMVC, Melbourne, Victoria.

BACKGROUND
Malaria remains endemic in over 100 countries worldwide. Travellers to these countries may be at risk of contracting disease. Assessing risk on an individual basis can be challenging.

OBJECTIVE
This article identifies the traveller at high risk of contracting malaria, outlines preventive methods, including personal protection and chemoprophylaxis if indicated, and summarises the risks and benefits of the most commonly used chemoprophylactic agents.

DISCUSSION
Appropriately assessing the risk of malaria in an individual traveller can be complex. A number of factors beyond the country being visited influence the level of risk. These should be identified and taken into account when discussing malaria prevention with individuals. The traveller should be actively involved in the decision making process in order to enhance compliance. High risk individuals should be identified. Personal protection methods should always be emphasised. If chemoprophylaxis is indicated, the contraindications, advantages and side effects should be discussed. If in doubt, referral to a specialised travel medicine clinic should be considered.

The malaria parasite, spread via the bite of an infected female Anopheles mosquito, remains a significant health threat in over 100 countries worldwide. An estimated 350–500 million cases occur annually, with over a million sub-Saharan Africans, mainly children, dying as a result.[1] In developed nations of the 'first world', malaria is a disease of travellers to endemic countries, whether they be tourists, expatriates, the military, or visitors returning to their home countries to see friends and relatives.

Transmission is limited by temperature, humidity and altitude and can vary significantly from region to region within countries. Four species of the *Plasmodium* spp. parasite infect humans: the nonrelapsing *P. falciparum* and *P. malariae* and the relapsing *P. vivax* and *P. ovale*. Around 80% of the world's *P. falciparum* cases occur in Africa, whereas around 70% of *P. vivax* cases occur in the Asia Pacific region. *P. falciparum* poses the greatest threat to human life as it can be rapidly fatal in the nonimmune population. Prevention in travellers is therefore focused on the prevention of death from *P. falciparum* infection.

Risk for travellers

The risk of contracting malaria varies significantly from traveller to traveller, and this is the challenge of providing quality advice. Factors such as:

- specific areas visited within countries
- season of travel
- style of travel
- length of trip
- drug resistance patterns
- individual medical conditions, and
- the local medical infrastructure

all impact significantly on risk.

General practitioners should be wary of databases providing generalised advice as malaria distribution and epidemiology is a changing phenomena. In general:

- Africa and Oceania present the highest risk
- Asia and South America moderate to low risk, and
- Central America very low risk.

Many popular tourist destinations and urban centres in Asia have minimal or no risk.

Studies in travellers who have acquired malaria show that

inappropriate or no prophylaxis is the greatest risk factor for contracting the disease.[2] Factors contributing to this failure in prevention include the traveller's ignorance of the risk of contracting malaria, inadequate training in travel medicine for the prescriber, fear of drug side effects, cost issues, and cultural perceptions. The challenge is appropriate prescribing. It is equally as inappropriate to prescribe medications when there is no risk as it is to not prescribe when there is significant risk. Healthy travellers do not want to experience adverse reaction to a medication they did not require – '*primum non nocere*'. The issue becomes more complex in those with low to moderate risk. If general practitioners are not confident in this area it is worth considering referral to a specialised travel medicine clinic.

Strategies for prevention

Travellers should have a clear understanding of the risk associated with the disease and myths such as 'the tablets are worse than the disease' should be vigorously dispelled with factual information. Education can lead to understanding and consequently to greater compliance.

Mosquito bite prevention

The most important preventive strategy is to avoid getting bitten. Personal protection methods must be emphasised, particularly from dusk to dawn. Insect repellent containing adequate amounts of DEET (20–40%) should be used as needed; clothing should be light, loose and long; and mosquito nets should be used if accommodation is inadequately screened or not air conditioned. For those at high risk of exposure, permethrin can be used to impregnate mosquito nets and clothing.

Chemoprophylaxis

If the traveller has been assessed to be of adequate risk to be recommended chemoprophylaxis there are three medications currently used by the majority of travellers:

- mefloquine
- doxycycline, and
- atovoquone-proguanil.

All offer good protection against *P. falciparum*, in particular chloroquine resistant strains. The choice of medication should involve the traveller in the decision making process. Factors such as side effect profile, drug interactions, cost and convenience will all influence this choice (*Table 1*). Compliance is paramount and this is more likely if the traveller has been involved in this decision. Chloroquine is only effective in limited areas of the world – essentially parts of the Middle East and Central America, and is used infrequently.

In some special circumstances, such as very long term travellers[3] or those with frequent short term risk, 'stand by treatment' may be prescribed by the travel medicine specialist. This is however not routinely recommended, requires intensive education, and may involve the use of self diagnostic kits.

Primaquine may be used as secondary prophylaxis in individuals who have spent extensive amounts of time in

Table 1. Choosing a medication

Doxycycline

Dosage

100 mg/day starting 2 days before exposure and continuing for 4 weeks

Contraindications

Pregnancy, breastfeeding, children <8 years of age, allergy to tetracyclines

Common side effects

Nausea/indigestion, photosensitivity, vaginal candidiasis

Advantages

Cheap. Offers protection against some other tropical diseases. Can be commenced at short notice. Can be used long term

Disadvantages

Contraindications. Not suitable for children <8 years of age

Mefloquine

Dosage

250 mg/week weekly, starting 2–4 weeks before exposure and continuing for 4 weeks

Contraindications

Pregnancy (first trimester), children <5 kg, history of epilepsy, history of depression, anxiety or any other psychiatric illness; cardiac conduction disorder. Avoid concomitant use with other medications causing QT prolongation[4]

Common side effects

Headache, nausea, sleep disturbances, vivid dreams, dizziness. Rarely can precipitate depression, anxiety, psychosis

Advantages

Can be used long term. Suitable for children

Disadvantages

Cost. Potential side effects. Contraindications. Needs to be started 2–4 weeks before travel

Malarone

Dosage

One tablet per day commencing 1 day before exposure and continuing for 1 week

Contraindications

Pregnancy and breastfeeding (due to lack of data)

Common side effects

Headache, nausea

Advantages

Minimal side effects. Paediatric dose available. Can be commenced at short notice

Disadvantages

Expensive. Not licensed for long term use due to lack of data

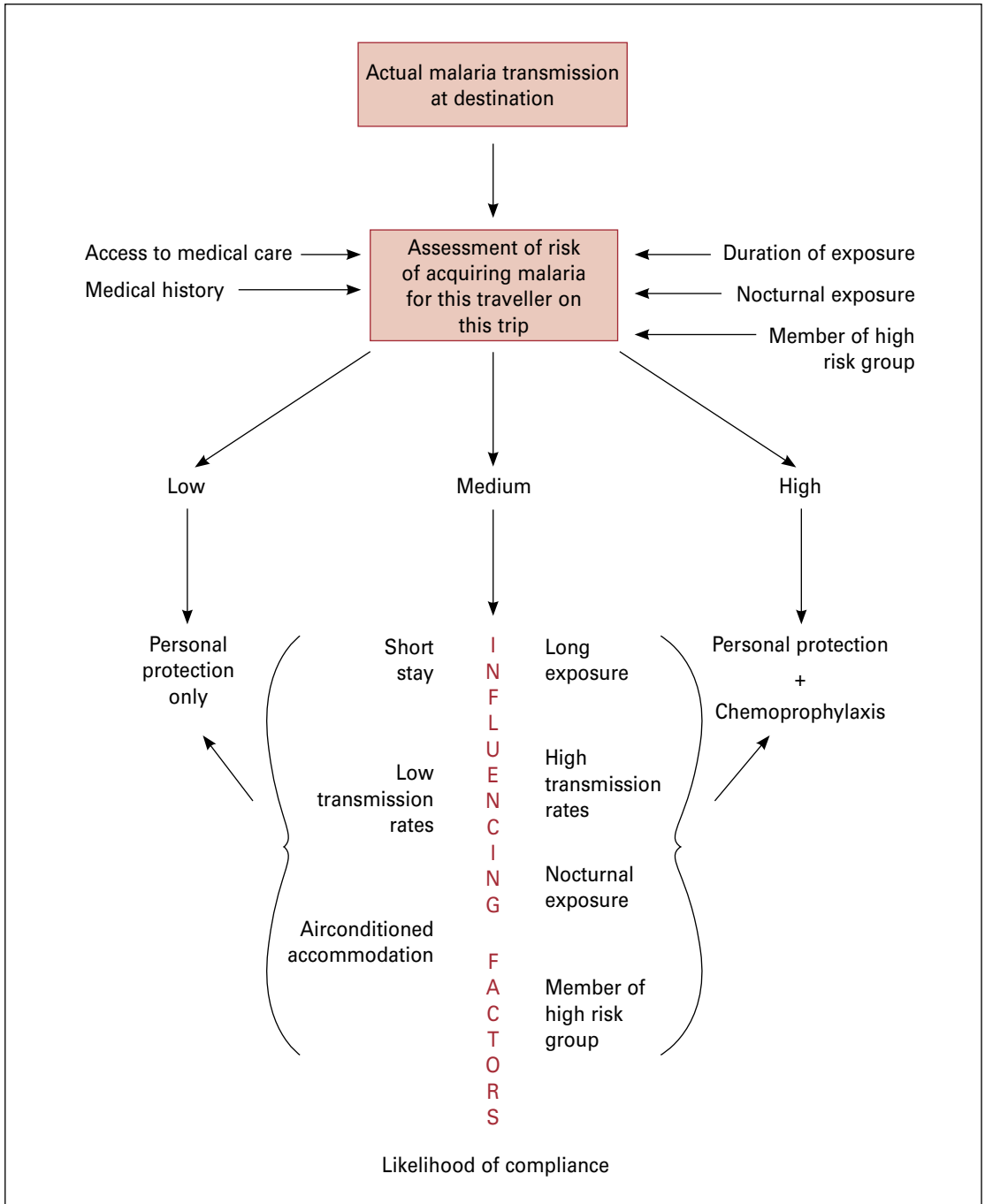

Figure 1. Choosing a method of prevention

areas of heavy *P. vivax* transmission, in order to reduce the risk of relapse. This should only be undertaken after the individual's G6PD has been assessed as normal (usually undertaken by specialist practitioners).

Choosing a preventive strategy

General practitioners need to be able to identify itineraries where no malaria exposure exists. This is true for many short packaged holidays to Asian tourist destinations, and only general mosquito avoidance advice is required.

All travellers to tropical areas should practice antimosquito measures, and where malaria transmission exists, this should be particularly directed to dusk to dawn care. Where significant risk exists, chemoprophylaxis should be considered in addition to routine antimosquito measures. For destinations of moderate risk, factors such as length of stay, accomodation, medical history, and likliehood of compliance impact significantly on the decision making process (*Figure 1*).

Travel to Central, East and West Africa, Amazonia, Papua New Guinea, Solomon Islands, Timor and eastern Indonesia

represents high risk. Other destinations such as rural Indo-China, the Indian subcontinent, and parts of rural southeast Asia, may also present risk, while destinations such as North Africa, Central America, and China have very limited or focal risk and chemoprophylaxis is not usually required.

Groups at special risk

Travellers visiting friends and relatives provide a particular challenge to travel medicine practitioners. They are at higher risk for contracting travel diseases and yet they are least likely to seek travel medicine advice. General practitioners should be opportunistic to provide education and preventive travel medicine services.

Children are more vulnerable to rapidly progressive and fatal disease and should avoid travel to high risk areas if possible. If travel is necessary, personal protection methods must be strongly emphasised along with strict compliance with chemoprophylaxis. Mefloquine can be used in children weighing more than 5 kg and Malarone is licensed down to 11 kg. Malarone is available in a paediatric dose. Parents should be made aware of the significant risks of the disease, and that the prompt diagnosis and management of any febrile illness is imperative.

Pregnant women can suffer more severe disease resulting in premature labour, stillbirth and miscarriage and should be counselled against travel to high risk areas. Chloroquine and proguanil are considered safe in pregnancy, but have limited use due to resistance patterns. Doxycycline and atovaquone-proguanil are contraindicated and mefloquine is only considered safe in the second and third trimesters.

Breastfeeding women should also avoid travel to high risk areas – mainly as this implies their children are still young. Only mefloquine, chloroquine and proguanil are considered safe in breastfeeding. These drugs do not confer protection to the infant being breastfed.

Mefloquine and chloroquine are contraindicated in those with a history of epilepsy.

Travellers who have had a splenectomy are at particular risk of severe disease. They should take the most effective prophylaxis available and be particularly vigilant with personal protection measures. Other travellers with immune suppression are at higher risk and require more intense prevention.

Long term expatriates are often averse to taking long term medication. Standby treatment is sometimes offered as an option to those unprepared to take appropriate chemoprophylaxis.

How to get accurate, up-to-date information

For practitioners working outside of the specialised travel medicine clinic this is the most difficult aspect of providing quality advice to the traveller. There are a number of travel medicine specific databases commercially available, however they are expensive and therefore often not practical for the GP seeing one or two travel patients per week. The World Health Organisation's guide *International travel and health* and the Centres for Disease Control and Prevention publication *Health information for international travel* are both available on the internet and provide the most reasonable summary of risk areas and recommended chemoprophylaxis regimens (see *Resources*). Extensive time spent practising travel medicine is usually required to gradually accumulate specific knowledge of the epidemiology of malaria.

Other important points

Personal protection methods should be emphasised to all travellers whether taking chemoprophylaxis or not. There are a number of other vector borne diseases that may be prevented by vigilant bite avoidance. Travellers should be aware of the need for prompt medical attention should they develop a febrile illness while overseas or after their return. For travellers who have been in malarial areas, fever should be considered malaria until proved otherwise. Delayed diagnosis and management of *P. falciparum* is a major factor leading to mortality.

A generalised 'cookbook' approach to malaria prevention is inadequate. Defining actual risk for many travellers is difficult and complicated, particularly for those on long term trips to multiple destinations with no fixed time schedules. Often broad guidelines are all that can be conveyed. If in doubt it is best to refer to a specialised travel medicine clinic.

Resources

- World Health Organisation. International travel and health. Available at: www.who.int/ith/en/
- Centres for Disease Control and Prevention. Health information for international travel. Available at: www.cdc.gov/travel/yb/index.htm
- Yung A, Ruff T, Torresi J, Leder K, O'Brien D. The manual of travel medicine: a pre-travel guide for health care professionals. 2nd edn. Melbourne: IP Communications, 2004.

Conflict of interest: none declared.

References

1. World Health Organisation. World malaria report, 2005. Available at http://rbm.who.int/wmr2005/.
2. Robinson P, Jenney AW, Tachado M, et al. Imported malaria treated in Melbourne, Australia: epidemiology and clinical features in 246 patients. J Travel Med 2001;8:76–81.
3. Hughes C, Tucker R, Bannister B, et al. Malaria prophylaxis for long term travellers. Commun Dis Public Health 2003;6:200–8.
4. Adverse Drug Reactions Advisory Committee. Medicines and QT prolongation. Australian Adverse Drug Reactions Bulletin 2005;24:(6).

afp **CORRESPONDENCE** email: afp@racgp.org.au