The great malaria debate

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We need to restore a more balanced approach to advising travelling patients about prevention of malaria.

Malaria prevention remains one of the many challenges for doctors advising intending overseas travellers. Unfortunately, many travellers (and even their doctors) are prone to media-fed horror stories about side effects, as promulgated by their advisors and friends. This may have the effect of discouraging the use of prophylactic medication, often in areas of significant risk where it is needed. This inappropriate decision-making process is further complicated by the various quick guides available that state that malaria exists in a country, without specifying the area to be visited by the traveller. The result in this case is unnecessary prescribing, with the accompanying avoidable cost and inconvenience. This update will describe general principles aimed at restoring balance to advice about prevention of malaria.

In this update, mosquito avoidance measures (knock down sprays and physical factors such as clothing, insect screens, repellents, and treated mosquito nets and clothing) are taken for granted. The question under discussion is whether to prescribe prophylactic medication or not.

Allowing the patient to decide

As the prescription of antimalarials is elective, careful attention must be paid to ensuring that the patient fully understands that the risks of contracting malaria (with the possible consequences thereafter) need to be carefully balanced against both the benefits and risks of taking antimalarials. Taking antimalarials is not risk-free, but then neither is not taking them.

The doctor's skill is in explaining the risk–benefit equation and providing enough information, in a form that the patient is capable of understanding, so that the patient's decision (either consent or refusal) is seen to have been properly informed.

The discussion should be relevant to each patient and his or her itinerary. Some of the more relevant issues follow.

Extent of the problem in Australia

The US Centers for Disease Control and Prevention (CDC) have estimated that 300 to 500 million cases of malaria occur worldwide, with over one million deaths annually. Aside from the 1% risk of fatality from falciparum malaria, or the risk of recurrence of vivax or ovale malaria in treated individuals, the symptoms of malaria are often quite debilitating.

Because the disease is not endemic in Australia, confusion by both doctor and patient often results in inappropriate acceptance of risk. However, those who have suffered from malaria will generally be more willing to avoid travel to malarious areas, or else will take every step possible to reduce the risk of contracting the disease again. Perhaps a commercially produced video of a patient with rigors from malaria may be a useful tool in persuading a patient of the seriousness of the disease.

Despite awareness of the problem, almost 1000 Australians returned with malaria last year, with many more cases presumed treated overseas prior to return. There are approximately 1200 cases reported in the United States each year and that country has more than 10 times the population of Australia, so on a population basis it is clear that we are not being very effective in malaria prevention in this country.

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Geographic risk: country, specific area and season

For Australians visiting the South Pacific region, malaria risk areas include Papua New Guinea, the Solomon Islands and Vanuatu. Other areas of risk are greater Asia (especially Southeast Asia and India), Central and South America, Africa and rarely the Middle East.[1]

Some of these countries report malaria in all parts of the country year round (e.g. India), while other countries have small, well defined, malarious areas rarely visited by tourists (e.g. Turkey). Seasonal fluctuations may have a significant effect on reported rates, largely as a result of rainfall. Malaria is less likely to occur at elevations greater than 1500 m, although it can still occur at up to 3000 m.

It is therefore important for the prescribing doctor to have a good knowledge of the risk of malaria at the time of the year in the specific area to be visited.

Individual risk: accommodation, duration and type of travel

While malaria may definitely be present in a country, it is important to ensure the traveller understands the difference

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between absolute and relative risk. Much of the advice given will be to reduce risk because it is impossible to guarantee complete removal of risk. Clearly, a business traveller staying in air-conditioned, screened accommodation for two or three nights is at a markedly reduced risk compared with a backpacker camping outdoors or a long term (more than three months) traveller in an at-risk area. It is important for the medical practitioner to make an assessment of risk for each traveller.

Prophylactic medications: risk versus benefit

At the time of writing this article, there are just three prophylactic alternatives available for Australian prescribers:

- mefloquine
- doxycycline
- chloroquine (with or without proguanil).

Mefloquine

The most contentious choice is mefloquine (Lariam) – having received, in my opinion, an overweighted negative response, which originated primarily from the United Kingdom. This followed an article in the *British Medical Journal* that reported a one in 140 risk of neuropsychiatric side effects.[2] The article was the weakest form of scientific reporting, in that it was a retrospective, uncontrolled, invalidated questionnaire survey and hence prone to many forms of bias and prejudice. While milder side effects, such as dizziness and bad dreams, definitely do occur more frequently, the real incidence of severe neuropsychiatric symptoms is reported by all other authorities as being closer to one in 10,000. This incidence is similar to that observed with the safer, but markedly less effective, chloroquine, which includes hair loss in its list of potential side effects.

For the record, mefloquine is the most effective prophylactic medication for use in Africa. Its once weekly dosage is the least likely to be associated with compliance problems. It is approved for use in children. Side effects are unlikely (although are possible). The CDC have retained it as the first drug of choice for most chloroquine-resistant areas.

There are a number of contraindications, including epilepsy, cardiac conduction defects, and a past history of psychiatric disorders or intolerance to the drug. Divers, pilots and machinery operators have been advised to be cautious about using this medication in view of the potential for side effects; however, more recent studies have not substantiated this risk.

In order to build up blood levels, and because 80 to 90% of side effects are likely to occur within the first few doses, the medication should be commenced

three to four weeks before departure. Mefloquine and the other current alternatives need to be continued for four weeks after leaving the malarious area. The cost is generally about $7 a week.

Doxycycline

Doxycycline is an alternative for those unable or unwilling to use mefloquine. It is the only agent suitable for use in the areas of Thailand where there is multidrug resistance; however, it is not as effective as mefloquine in many areas. Compliance may be an issue because of the daily dosage. Side effects occur in up to 10% of cases, the most common effects being gastrointestinal symptoms. Photosensitivity occurs in 3%. Thrush is common, and the oral contraceptive pill may not be as effective in females taking doxycycline. It is absolutely contraindicated during pregnancy and in children under the age of 8 years.

The cost is generally about $5 a week, and doxycycline has the advantage of being able to be started just two days before travel.

Chloroquine and proguanil

The third current alternative in Australia is chloroquine (Chlorquin), but it is suitable for only a few areas worldwide. As a result of widespread resistance, the weekly dosage generally needs to be taken with a daily dose of proguanil (Paludrine). This has resulted in documented poor compliance and confusion about dosage. This combination, no longer recommended by the CDC, is preferred in the United Kingdom and perceived as the safest regimen for use in pregnancy. It is, however, the least effective and is still prone to numerous side effects. The cost of the combination therapy is approximately $5 a week.

Atovaquone–proguanil

A fourth alternative, a combination of atovaquone and proguanil (Malarone), is now recommended by the CDC in place of chloroquine, but in Australia it is approved only for treatment and not yet for prophylaxis. Gastrointestinal side effects and headache occur in up to 10% of patients. Although an expensive option at about $35 a week, it is started just one to two days before entering the malarious area and needs to be continued for only one week after leaving the area, compared with four weeks for the above alternatives.

Keeping up to date

As a final point, with regard to information retrieval, widespread access to internet sources has allowed travellers to become more knowledgeable in some cases than their doctors. It is important for all medical practitioners working in this area to ensure they remain up to date with disease outbreaks and fluctuations in all areas to be visited by their patients. Referral to a travel health clinic is recommended for more complex cases, such as travelling families, children, pregnancy, immune suppression, longer trips or where the practitioner and/or the patient is unsure of the correct course of action.

Conclusion

Australian doctors need to ensure that all travellers are fully conversant with the risks of travelling through a malarious area. They need to advise their patients that malaria is a serious and life-threatening disease, and that the risks of contracting the disease can be reduced but not completely removed. The potential risks of side effects from prophylactic measures including medication need to be weighed up against the risks of contracting and treating malaria. MT

References

1. WHO. International travel and health: vaccination requirements and health advice. Geneva: WHO, 2001 (www.who.int/ith/).

2. Barrett PJ, Emmins PD, Clarke PD, Bradley DJ. Comparison of adverse events associated with use of mefloquine and combination of chloroquine and proguanil as antimalarial prophylaxis. BMJ 1996; 313: 525-528.

Further reading

1. 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.

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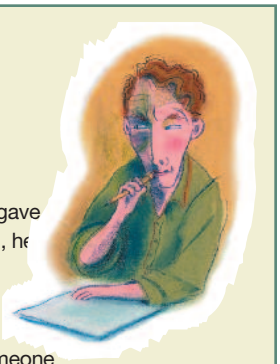
A request for your reflections



Many years ago Lord Thomas Dewar, the Scottish distiller, gave some sound advice. Confessions may be good for the soul, he said, but bad for the reputation. Disregarding it, I reflected upon some of the experiences I had had since graduating in medicine and committed them to print as 'Innocence Revisited'. I wished that most of them had happened to someone else.

But the sky did not fall in, and I am still registered. More than that, others were emboldened to write of their own tribulations; I was not unique. It makes me feel better to read about the misfortune of others, so I shall send a bottle of 'Medicine Today' wine to anyone who sends in a usable contribution (under a nom de plume if you wish). Believe me when I tell you that we don't drink it all day long at work, but we have a bit when we go home at night because it is good for our arteries.

Dr John Ellard