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Inside this issue: Malaria

Hundreds of cases of malaria, linked to travel, are diagnosed each year in Canada; see a summary of the latest recommendations from the Committee to Advise on Tropical Medicine and Travel (CATMAT) for both prevention and treatment. Then learn about some unusual topics: the risk of invasive fungal infections after natural disasters and the new Hendra virus vaccine.

Summaries

Recently published

Invasive fungal infections after natural disasters. Benedict K, Park BJ. Emerg Infect Dis. 2014 Mar
http://dx.doi.org/10.3201/eid2003.131230
The most common fungal infections following natural disasters are respiratory and wound infections.

Hendra virus vaccine, a One Health approach to protecting horse, human, and environmental health. Middleton D, Pallister J, Klein R, Feng YR, Haining J, Arkinstall R, et al. Emerg Infect Dis. 2014 Mar.
http://dx.doi.org/10.3201/eid2003.131159
Hendra virus (HeV), a zoonotic paramyxovirus, has been reported in humans who have been infected from horses; a vaccine for horses is under development with the potential for breaking the chain of HeV transmission from bats to horses to humans.

Useful links

World Health Organization - Management of severe malaria – A practical handbook
Third Edition, April 2013
http://www.who.int/malaria/publications/atoz/9789241548526/en/

The Canadian Malaria Network
http://www.phac-aspc.gc.ca/tmp-pmv/quinine/index-eng.php

Malaria Fact Sheet. Public Health Agency of Canada
http://travel.gc.ca/travelling/health-safety/diseases/malaria

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Canada

Summary of recommendations for the prevention of malaria by the Committee to Advise on Tropical Medicine and Travel (CATMAT)

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Abstract

Background: On behalf of the Public Health Agency of Canada, the Committee to Advise on Tropical Medicine and Travel (CATMAT) developed the *Canadian Recommendations for the Prevention and Treatment of Malaria Among International Travellers* for Canadian health care providers who are preparing patients for travel to malaria-endemic areas and treating travellers who have returned ill.

Objective: To provide guidelines on risk assessment and prevention of malaria

Methods: CATMAT reviewed all major sources of information on malaria prevention, as well as recent research and national and international epidemiological data, to tailor guidelines to the Canadian context. The evidence-based medicine recommendations were developed with associated rating scales for the strength and quality of the evidence.

Recommendations: Used together and correctly, personal protective measures (PPM) and chemoprophylaxis very effectively protect against malaria infection. PPM include protecting accommodation areas from mosquitoes, wearing appropriate clothing, using bed nets pre-treated with insecticide and applying topical insect repellant (containing 20%–30% DEET or 20% icaridin) to exposed skin. Selecting the most appropriate chemoprophylaxis involves assessment of the traveller's itinerary to establish his/her malaria risk profile as well as potential drug resistance issues. Antimalarials available on prescription in Canada include chloroquine (or hydroxychloroquine), atovaquone-proguanil, doxycycline, mefloquine and primaquine.

Introduction

Malaria is a serious infection caused by five different species of the genus *Plasmodium*: *falciparum, vivax, ovale, malariae* and *knowlesi.* Malaria is transmitted by the bite of infected female anopheline mosquitoes.

In 2009, 35% of Canadian travellers who went to a destination other than the United States visited a country that presented a risk of malaria, an increase of 131% from 2000 (1-2). Between September 2009 and September 2011, 94 cases of malaria were diagnosed among returned Canadian travellers (3).

According to the Centers for Disease Control and Prevention (CDC), malaria risk for travellers from the United States (4-6) varied as follows:

- Highest in west Africa and parts of Oceania;
- Moderate for other parts of Africa, parts of South America and South Asia;
- Lower for much of Central America, the Caribbean, Mexico and other parts of Asia and South America;
- Minimal in urban centres of southeast Asia and Central and South America, and in large resort areas in the Caribbean and Mexico.

The Committee to Advise on Tropical Medicine and Travel (CATMAT) provides the Public Health Agency of Canada with ongoing and timely medical, scientific and public health advice relating to tropical disease and health risks associated with international travel. This is a summary of the CATMAT *Canadian Recommendations for the Prevention and Treatment of Malaria Among International Travellers*, developed for Canadian health care providers who are preparing patients for travel to malaria-endemic areas and treating travellers who have returned ill (7). These guidelines include a full description of the recommendations on risk assessment and prevention of malaria, a disease that is still uncommon in Canada.

Methods

The Malaria Subcommittee, a working group of CATMAT, developed the guidelines. Each member is a volunteer, and none declared a relevant conflict of interest. Each chapter was updated by one to two members of the subcommittee and reviewed and approved by the full membership of CATMAT. The update was based on a thorough review of the literature. In addition, the Malaria Subcommittee reviewed all major sources of information on malaria prevention and treatment, including the World Health Organization (8), Centers for Disease Control and Prevention (CDC) (6) and the Health Protection Agency Advisory Committee on Malaria Prevention (9). The Malaria Subcommittee reviewed recent research, and national and international epidemiological data in order to tailor the recommendations to the Canadian context. Influencing factors include drug licensure, Canadian-specific travel patterns and related malaria epidemiology, and the anticipated values and preferences of travellers and health care providers. The evidence-based medicine recommendations for prevention of malaria were developed with associated rating scales for the strength and quality of the evidence.

CATMAT has taken into consideration both the need for protection and the potential for adverse effects of chemoprophylaxis. The guidelines also emphasize the varying degrees of endemicity in different regions. The health care provider should be properly informed to be able to provide appropriate guidance for the individual traveller.

Recommendations

The evidence-based CATMAT recommendations for malaria prevention are summarized in **Table 1.** A discussion of some of the key recommendations follows.

Table 1: Evidence-based medicine recommendations for prevention of malaria

Recommendation	EBM rating[1]
1. Properly used malaria chemoprophylaxis is very effective (6).	**A I**
2. Travellers should receive expert advice on malaria risks and strategies to avoid mosquitoes (10).	**B III**
3. A detailed review of the travel itinerary to determine the expected level of malaria endemicity and duration of exposure is essential to provide an accurate risk assessment for travellers (6,10,11).	**B III**
4. An assessment of the traveller's health and risk tolerances is also important in making malaria prevention recommendations.	**B III**
5. It is very important to adhere to recommended malaria prevention practices (e.g. use of chemoprophylaxis and PPM) (12-22).	**B III**
6. Chloroquine (Aralen®) or hydroxychloroquine (Plaquenil®) is the drug of choice for travellers to areas with chloroquine-sensitive malaria (23).	**A I**
7. Atovaquone-proguanil, doxycycline or mefloquine is the drug of choice for travellers to areas with chloroquine-resistant or mefloquine-sensitive malaria (12-14,24-27).	**A I**
8. Atovaquone-proguanil and doxycycline are the drugs of choice for travellers to areas with mefloquine-resistant malaria.	**A I**
9. Primaquine is recommended for malaria chemoprophylaxis for travellers to regions with chloroquine resistance who are not willing or able to use atovaquone-proguanil, doxycycline or mefloquine.	**A I**
10. Standby malaria treatment with atovaquone-proguanil or quinine and doxycycline is recommended for travellers who are more than a day away from malaria diagnostic help.	**C III**
11. Doxycycline is an antibiotic and should never be co-administered with any live, oral bacterial vaccines. Vaccination with live oral typhoid or cholera vaccines should be completed at least three days before the first dose of choloroquine, atovaquone-proguanil or mefloquine.	**B III**
12. Concurrent use of chloroquine interferes with antibody response to intradermal administration of human diploid cell rabies vaccine. If intradermal rabies vaccine is administered to someone taking chloroquine, it is recommended that post-vaccine rabies antibodies be obtained to verify an adequate immunologic response.	**B III**
13. Use insecticide-treated bed nets.	**A I**
14. Use topical repellents on exposed areas of skin to prevent arthropod bites and to reduce the risk of exposure to malaria-carrying mosquitoes.	**A I**
15. Products registered in Canada that contain 20%–30% DEET (*N*,*N*-Diethyl-*meta*-toluamide) or 20% icaridin should be the first choice for Canadian travellers.	**A II**
16. Products that contain *p*-menthane-3,8-diol (a chemical originally derived from the lemon eucalyptus plant) and that are registered in Canada should be considered second-choice topical repellents.	**A II**
17. Other active ingredients currently registered in Canada (e.g. citronella and soybean oil) are either not widely available and/or do not provide sufficiently long protection times against bites. These products are *not* recommended for protecting travellers against the bites of vectors.	**E II**
18. Protect work and accommodation areas against mosquitoes by using screening on doors, windows and eaves (the open area between the roof and wall), eliminating holes in roofs and walls, and closing other gaps around a building.	**B I**

Recommendation	EBM rating[1]
19. Wear insecticide-treated clothing.	**B II**
20. Wear appropriate clothing (e.g. full-length, loose-fitting and light-coloured clothing with sleeves rolled down and pants tucked into socks or boots)**.**	**B III**
21. Do not use/rely on other insecticide-based approaches, such as insecticide coils that are burned, insecticide vaporizers, aerosols and space sprays, and insecticide-treated bed sheets.	**E III**
22. PPM that are either ineffective or that have not been convincingly shown to be efficacious against arthropod vectors and related diseases are *not recommended*. These include electronic (ultrasonic) devices; wristbands, neckbands and ankle bands impregnated with repellents; electrocuting devices ("bug zappers"); odour-baited mosquito traps; *Citrosa* plant (geranium houseplant); orally administered vitamin B1; and skin moisturizers that do not contain an approved repellent active ingredient.	**E II**

[1] EBM = Evidence based medicine. The EBM ratings are as follows:
Strength of recommendation:
A = Good evidence to support a recommendation for use
B = Moderate evidence to support a recommendation for use
C = Poor evidence to support a recommendation for or against use
D = Moderate evidence to support a recommendation against use
E = Good evidence to support a recommendation against use
Quality of evidence:
I = Evidence from at least one properly randomized, controlled trial
II = Evidence from at least one well-designed clinical trial without randomization; from cohort or case-controlled analytic studies, preferably from more than one centre; from multiple time series; or from dramatic results in uncontrolled experiments
III = Evidence from opinions of respected authorities on the basis of clinical experience, descriptive studies, or reports of expert committees

Risk assessment

CATMAT suggests a two-component process for malaria risk assessment: an exposure assessment and a host assessment.

An **exposure assessment** evaluates the probability of being bitten by infected mosquitoes. It takes three factors into account:

- Expected level(s) of endemicity in the travel itinerary;
- Presence/predominance of *P. falciparum*;
- Duration of exposure.

A **host assessment** evaluates the traveller's health in relation to the potential hazard(s) of clinical malaria and the indications for specific malaria chemoprophylactic agents while taking into account personal preferences regarding risk management. Factors to consider include the following:

- General health of the traveller;
- Drug–drug interactions;
- Likelihood of access to appropriate medical care;
- Risk tolerance and individual preferences.

The completed risk assessment can be used to decide whether to use malaria chemoprophylaxis and which chemoprophylactic agent to prescribe:

- If malaria risk is minimal and the incidence of *P. falciparum* is nil or very low, CATMAT recommends using chemoprophylaxis (with PPM) *for a stay longer than* two weeks.
- If malaria risk is minimal and the incidence of *P. falciparum* is higher, CATMAT recommends *chemoprophylaxis (with PPM) for a stay longer than* one week.

Travellers who decide not to use chemoprophylaxis have a higher risk of malaria but lower risk of chemoprophylaxis-associated adverse effects; the opposite is true for those who decide to use it.

A country-by-country characterization of malaria transmission areas is available in the complete guidelines (7). The **Appendix** provides chemoprophylaxis recommendations for the top 25 destinations with risk of malaria transmission that are visited by Canadians.

Personal protective measures

- The risk of being bitten by a mosquito can be reduced by using physical and/or chemical barriers.
- Physical barriers:
    - Screening on doors, windows, eaves and other gaps in the building (28-30);
    - Bed nets treated with insecticide (31-33);
    - Full-length, loose-fitting and light-coloured clothing (clothes can also be treated with insecticide).
- Chemical barriers repel mosquitoes and/or kill them (34,35). The main chemical modalities currently available are topical insect repellents for use on exposed skin and insecticides that impregnate bed nets and clothing (36-40).
    - Topical repellents should contain 20%–30% DEET or 20% icaridin.
    - Alternatively, second-choice topical repellents are those containing *p*-menthane-3,8-diol that are registered in Canada.

Travellers should also be encouraged to plan activities during periods when risk is reduced (e.g. during the daytime where the principal vectors are active in the evening) and to visit areas where transmission is less likely (e.g. urban centres, highland areas > 2000 m/6500 ft).

Chemoprophylaxis

Prescribing antimalarial drugs

Prescribe antimalarial chemoprophylaxis only after completing an individual risk assessment. For detailed descriptions of chemoprophylaxis and of chemotherapy see Chapter 8 of the *Canadian Recommendations for the Prevention and Treatment of Malaria Among International Travellers* (7). Selecting the most appropriate chemoprophylactic agent involves the following:

1. Evaluate the traveller's exact travel itinerary to determine his or her malaria risk profile.
2. Review the advantages and disadvantages of different regimens:
    - Take into account the traveller's health status, other medications and the risks and character of adverse drug effects.
    - Consider only those medications that are least likely to exacerbate any past or present medical problem(s).
3. Present all the available options to the traveller and, unless any medication is contraindicated, let travellers choose which first-line malaria chemoprophylactic regimens they prefer.
4. Select the appropriate dosage of the medication:
    - Explain the dosing schedule, including the need to take the drug before, during and after visiting the area of risk, the desirability of taking the drug at the same time each day and advice on whether the prescribed medication should be taken with food, as well as any precautions regarding drug-specific side effects (e.g. sun exposure with doxycycline) (41-47).
5. Suggest a drug trial to check for possible medication-associated adverse reactions.
6. Discuss strategies to change medication if serious adverse effects arise during travel.
    - Advise the traveller to continue to take the prescribed malaria medication if it is well tolerated regardless of negative anecdotes about it. Long-term use of the chemoprophylactic agents currently recommended in Canada does not result in additional risks of severe adverse effects.

Discuss the importance of seeking medical advice urgently if a fever develops while the traveller is in a malaria-endemic area or within one year of leaving.

Selecting antimalarial drugs for specific regions of drug resistance

Monitor appropriate sources (e.g. Public Health Agency of Canada, CDC, ProMED) to stay abreast of new information about malaria risks before giving pre-travel care. This is especially relevant for minimal-risk regions because changes may directly affect the recommendations for chemoprophylaxis.

Table 2: Selecting antimalarial drugs for specific regions of drug resistance

Area/region (6,48-50)	Drugs of choice
Chloroquine-sensitive regions: Haiti, the Dominican Republic, Central America north of the Panama Canal, parts of Mexico, parts of South America, north Africa, parts of the Middle East, and west/central China	Chloroquine (Aralen®) Hydroxychloroquine (Plaquenil®) is an acceptable equivalent alternative (51), as are the three drugs used in chloroquine-resistant areas (see below).
Chloroquine-resistant regions: Most of sub-Saharan Africa, South America, Oceania and Asia. See below for regions that are both chloroquine- and mefloquine-resistant.	Atovaquone-proguanil (41,42,44-47,52) Doxycycline (41,42,44-47,52) Mefloquine (41,42,44-47,52)
Chloroquine- and mefloquine-resistant regions: Various countries in Asia, Africa and the Amazon basin. However, it is a significant problem only in rural, wooded regions where Thailand borders with Myanmar (Burma), Cambodia and Laos, and in southern Vietnam.	Atovaquone-proguanil (44,53,54) Doxycycline (44,53,54)

Note: See the **Appendix**, 'Malaria risk and recommended chemoprophylaxis in top 25 malaria-endemic travel destinations visited by Canadians in 2012', or a more complete list in the *Canadian Recommendations for the Prevention and Treatment of Malaria among International Travellers* (7).

Discontinuing antimalarial drugs

Fatal malaria has occurred in travellers who have discontinued all chemoprophylaxis or effective chemoprophylaxis in favour of something less protective (24,51,55,56). Discontinuation of all chemoprophylaxis is NOT a reasonable option.

Other travellers and/or health care providers may suggest changing or stopping antimalarial medication. For the most part, such advice should be ignored or questioned. Medications used in other areas of the world may be less effective, may be associated with serious adverse effects or may not be manufactured to Canadian standards. Examples include proguanil alone (Paludrine®), pyrimethamine (Daraprim®), dapsone-pyrimethamine (Maloprim®) and mefloquine-sulfadoxine-pyrimethamine (Fansimef®).

However, if the traveller experiences significant adverse events because of the chemoprophylactic agent, the medication can be changed, especially if the advice is provided by a health care provider (preferably the one who provided the initial advice).

Adherence to chemoprophylaxis

The reasons for non-adherence include lack of knowledge that malaria was a threat; fear of or past experience with adverse effects of chemoprophylactic agents; the false belief that prior malaria infections have conferred long-term immunity; the cost of medications; and confusion arising from contradictory recommendations. However, there is little information on how to enhance adherence.

Non-adherence to or suboptimal use of chemoprophylaxis and other preventive interventions is common, particularly among backpacking travellers; immigrants returning to visit their country of origin; people travelling for

longer than one month; travellers aged 40 years or less; and those using chemoprophylactic agents that must be taken daily (12-21,23,25-27,57).

Health care providers themselves need to be properly informed to be able to provide appropriate guidance (58). Travellers who use one qualified information source, such as a family physician trained in travel medicine, are significantly more likely to be compliant with malaria prophylaxis than those who collect information from multiple sources that could contradict each other (58,59).

Summary

A summary of the key changes made to the 2014 Guidelines are noted in **Table 3.**

Table 3: Summary of key additions and changes to the 2014 Guidelines pertaining to prevention of malaria (7)

Additions	
1.	The addition of a length-of-stay threshold for use of malaria chemoprophylaxis so that health care providers can better tailor individualized risk assessments (see Chapter 2).
2.	A new insect repellent, 20% icaridin, is recognized as an equivalent to DEET as a first-line choice for mosquito repellent (see Chapter 3).
3.	The guidelines have been expanded for populations requiring special attention – children, migrants, expatriates and travellers visiting friends and relatives, women who are pregnant or breastfeeding, and travellers with co-morbidities (Chapter 5).
4.	A new "Malaria Card" that can be given to travellers with information about their malaria chemoprophylaxis and an important reminder to seek medical attention in the event of a fever illness after travel.
Changes	
1.	Chapter 4, "Prevention – Chemoprophylaxis Regimens," has been refined to make it easier to navigate the drug choices available. These changes include a simplified, step-wise approach to selecting malaria prophylaxis; comprehensive listings of medications and malaria risk by country/area in tabular form; and expanded explanation of the differences in approaches to malaria prophylaxis in other jurisdictions.
2.	Chapter 8, "Drugs for the Prevention and Treatment of Malaria," includes an update on primaquine use for malaria prophylaxis and prevention; additional up-to-date information on pediatric dosing of atovaquone/proguanil; and general updates to Table 8.11: Drugs (generic and trade name) for the treatment and prevention of malaria. Revisions have also been made to the following sub-sections related to malaria prevention: chloroquine and mefloquine (with increased emphasis on selection or avoidance of this drug according to individual tolerability).

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Conflict of interest

There are no conflicts of interest to declare.

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Appendix

Appendix: Malaria risk and recommended chemoprophylaxis in top 25 malaria-endemic travel destinations visited by Canadians in 2012 (6, 60-67)

	Country	Malaria transmission areas[2-4]	Chemoprophylaxis recommended by CATMAT*[2-9]	Season[3;4]	*Plasmodium falciparum*[2-4], %
1	Mexico	Minimal or no malaria transmission in major resort areas on the coasts, including the city of Acapulco or along the Mayan Riviera, including the cities of Cancún, Cozumel, and Playa del Carmen. None along the border with the United States.	None.	Year-round	0
		Little malaria transmission in the states of Jalisco, Quintana Roo, Sonora and Tabasco.	Use PPM.		
		Moderate risk in parts of the states of Chiapas and Oaxaca.	Chloroquine.		
		Low risk in rural areas of the states of Nayarit, Sinaloa, Chihuahua, and Durango.	Chloroquine for stays > 1 week; chloroquine or PPM alone for stays of ≤ 1 week.		
2	Dominican Republic	Little to no malaria transmission in the resort areas of Romana and Samaná and the cities of Santo Domingo, Santiago, and Puerto Plata.	None; use PPM.	Year-round	100
		Some transmission has previously occurred in La Altagracia province, including resort areas such as Punta Cana.	In the absence of any further outbreaks in La Altagracia, PPM alone for resorts in that province. Seek medical attention if a fever develops.		
		Rural areas, with the highest risk in the provinces of Dajabón, Elias Piña, and San Juan bordering Haiti.	Chloroquine.		
3	China	No malaria transmission in urban areas or northern China.	None.	n/a	n/a
		Limited transmission of *P. vivax* malaria occurs in the southern provinces and some central provinces, including Anhui, Ghuizhou, Henan, Hubei, and Jiangsu.	For travellers visiting major cities and making daytime excursions into the countryside or on Yangtze river cruises: none; use PPM.	Year-round	9
		The risk of contracting malaria in central China is small.	For those travelling extensively in or through rural southern China: chloroquine.		
		Transmission of *P.falciparum* malaria occurs in the province of Yunnan and, to a lesser extent, in the province of Hainan. *P. falciparum* resistance to chloroquine and sulfadoxine-pyrimethamine reported.	ATQ-PG, DOXY or MFQ.		
		P. falciparum resistance to mefloquine reported in the province of Yunnan in the areas bordering Burma (Myanmar).	ATQ-PG or DOXY.		
4	India	No malaria transmission at elevations > 2000 m in parts of the states of Himachal Pradesh, Jammu and Kashmir, and Sikkim.	None.	n/a	n/a
		All other areas - including most urban areas such as Bombay (Mumbai) and Delhi. Risk is lower in most of the southernmost regions of India.	ATQ-PG, DOXY or MFQ.	Year-round	> 40
		Risk is low in central urban areas of Agra and Bangalore.	PPM alone can be considered for stays of <1		

			week in central urban areas of Delhi, Agra and Bangalore.		
5	Costa Rica	Little to no risk of malaria transmission in most of the country, with exception noted below. No malaria transmission in the city of Limón (Puerto Limón).	None; use PPM.	Year-round	Predominantly *P vivax*
		Limón province (except the city of Limón), mostly in the canton of Matina.	Chloroquine.		
6	Thailand	No malaria transmission in cities, including Bangkok, Chiang Mai, Chiang Rai, Pattaya, Koh Samui, Phang Nga, Town of Phuket and Koh Phangan, or in major tourist resorts.	None.	n/a	n/a
		Rural forested areas near the borders with Cambodia, Burma (Myanmar) and Laos. Rural forested areas in districts of Phang Nga and Phuket. Some islands have malaria risk. Mefloquine resistance reported.	ATQ-PG or DOXY.	Year-round	50–75
7	Philippines	Little to no malaria transmission in urban areas or on islands not listed below.	None; use PPM.	Year-round	70–80
		Rural areas at elevations < 600 m on islands of Basilu, Luzon, Mindanao, Mindoro, Palawan, Sulu (Jolo) and Tawi-Tawi.	ATQ-PG, DOXY or MFQ.		
8	South Africa	No malaria transmission in most of the country including the Garden Route and major cities.	None.	n/a	n/a
		Low-altitude areas in the provinces of Mpumalanga (including the Kruger National Park), Limpopo (formerly Northern), and north-eastern Kwa Zulu-Natal as far south as the Tugela River.	ATQ-PG, DOXY or MFQ.	Year-round (risk is highest from Oct–May)	90
9	Peru	No malaria risk at elevations > 2000 m, including the highland tourist areas (Machu Picchu, Lake Titicaca, and the cities of Arequipa, Cuzco, Puno) or in the cities of Limaand south of Lima including Moquegua, Nazca, and Tacna.	None.	n/a	n/a
		All areas < 2000 m (except cities listed above). This includes the cities of Puerto Maldonado and Iquitos. Most *P.falciparum* cases occur in the region of Loreto.	ATQ-PG, DOXY or MFQ.	Year-round	15
10	Turkey	No malaria transmission in western and northeastern parts of the country, including the common tourist destinations of the cities of Izmir and Istanbul and the Cappadocia region.	None.	n/a	n/a
		Limited malaria transmission in the southeastern part of the country.	Chloroquine for stays > 2 weeks; c*hloroquine or PPM* alone for stays of ≤2 weeks.	May–Oct	Sporadically
11	Argentina	No malaria transmission in urban areas, Iguassu Falls, or provinces not listed below.	None.	n/a	n/a
		Rare in Misiones province along the border with Paraguay.	None; use PPM.	Oct–May	0
		Rural areas of northern Jujuy and Salta Province (along Bolivian border).	Chloroquine for stays > 2 weeks; c*hloroquine or PPM alone for stays* of □ 2 weeks.		
12	Brazil	Little to no malaria transmission at Iguazu Falls; in the Pantanal region; in the cities of Brasília, Recife, Rio de Janeiro, São Paulo, and Salvador; or in other areas not listed below.	None; use PPM.	Year-round	15
		Areas at elevations < 900 m in most forested areas of the states of Acre, Amapá, Amazonas, Rondônia, Roraima and Tocantins	ATQ-PG, DOXY or MFQ.		

		(western part) and parts of states of Maranhão (western part), Mato Grosso (northern part), Pará (except Belém City) and Tocantins (western part). Transmission also occurs in some peripheral urban areas of - Boa Vista, Cruziero do Sul, Macapá, Manaus, Maraba, Pôrto Velho, Rio Branco, and Santarém.			
13	Belize	No malaria transmission in Belize City and islands frequented by tourists.	None.	n/a	n/a
		Low risk in Belize, Corozal, and Orange Walk Districts.	None; use PPM.	Year-round	0–5
		Moderate risk in Cayo, Stann Creek, and Toledo Districts.	Chloroquine.		
14	Ecuador	No malaria transmission at elevations > 1500 m, including Cuenca, Quito, and other cities and villages in the Andean highlands; in the city of Guayaquil or on the Galápagos Islands.	None.	n/a	n/a
		All other areas at elevations < 1500 m. Higher risk along the coast, in the north.	ATQ-PG, DOXY or MFQ.	Year-round	10
15	Colombia	No malaria transmission in urban areas, including Bogotá and vicinity and Cartagena; at elevations > 1600 m; or on the islands of San Andrés and Providencia in the Caribbean Sea.	None.	n/a	n/a
		Rural or jungle areas at elevations < 1600m.	ATQ-PG, DOXY or MFQ.	Year-round	35–40
16	Guatemala	No malaria transmission in urban areas or areas at elevations > 1500 m none in Guatemala City, Antigua, and Lake Atitlán.	None.	n/a	n/a
		Rural areas at elevations < 1500 m.	Chloroquine.	Year-round	3
17	Honduras	No malaria transmission - in the cities of Tegucigalpa and San Pedro Sula. Risk is low in higher mountainous areas in the west where PPM can be considered.	None.	n/a	n/a
		Risk is high in departments of Gracias a Dios and Islas de la Bahia (Bay Islands), and moderate in Atlantida, Colon, Olancho, and Yoro.	Chloroquine.	Year-round	7
18	Vietnam	None in urban areas, Red River Delta and coastal plain of central Vietnam. Rare cases in Mekong Delta. The common coastal itinerary between Ho Chi Minh City and Hanoi with overnights mainly in urban areas does not typically require chemoprophylaxis.	Use PPM.	Year-round	50–90
		Rural areas, excluding those listed above. Risk in the town of Sapa in the hills to the northwest of Hanoi is lower; PPM can be considered for stays <1 week, particularly in the winter months.	ATQ-PG, DOXY or MFQ.		
		Mefloquine resistance reported in the southern part of the country in the provinces of Dac Lac, Gia Lai, Khanh Hoa (western part), Kon Tum, Lam Dong, Ninh Thuan (western part), Song Be, and Tay Ninh.	ATQ-PG or DOXY.		
19	Cambodia	No malaria transmission in the city of Phnom Penh and the area around Lake Tonlé Sap (Siem Reap). Negligible transmission in the tourist area of Angkor Wat and Siem Reap.	None; use PPM.	Year-round	86
		Mefloquine resistance is reported in the western provinces of Banteay Meanchey,	Doxycycline or atovaquone–proguanil.		

		Battambang, Koh Kong, Odder Meanchey, Pailin, Kampot, PreahVihear, Pursat, and Siemreap bordering Thailand.			
		All other areas.	ATQ-PG, DOXY or MFQ.		
20	Panama	Little to no malaria transmission in Panama City, the Canal zone, or regions not listed below.	None; use PPM.	Year-round	1
		Provinces and indigenous territories (comarcas) along the Caribbean coast and the borders with Costa Rica and Colombia: Bocas del Toro, Chiriquí, Colón, Ngöbe-Buglé, Panamá, and Veraguas.	Chloroquine for stays > 1 week; c*hloroquine or PPM alone for stays of <1 week*.		
		Most transmission in provinces east of the Panama Canal toward the border with Colombia.*P. falciparum* resistance to chloroquine has been reported in Darién and Kuna Yala (San Blas).	ATQ-PG, DOXY or MFQ.		
21	Pakistan	All areas at elevations < 2000 m. Risk is due to both *P. vivax* and *P. falciparum*. Risk lower in the north, including Islamabad, especially during winter months because of cool temperatures.	ATQ-PG, DOXY or MFQ.	Year-round	30
22	Kenya	Little to no malaria transmission at elevations > 2500 m or in the city of Nairobi.	None; use PPM.	Year-round	85
		All areas at elevations < 2500 m, except the city of Nairobi.	ATQ-PG, DOXY or MFQ.		
23	Tanzania, United Republic of	All areas at elevations < 1800 m.	ATQ-PG, DOXY or MFQ.	Year-round	> 85
24	Indonesia	No malaria transmission in Jakarta Municipality, major metropolitan areas including Ubud, or major tourist resorts in Bali and Java.	None.	n/a	n/a
		In general, risk is higher in more easterly regions of Indonesia: in particular, the provinces of East Nusa Tenggara, Maluku, North Maluku, Papua (Irian Jaya) and West Papua. There is also risk on LombokIsland and the rural areas of KalimantanIsland (Borneo). There is a low risk of transmission in rural Java and Bali and sporadic cases reported among travellers to rural areas of Bali. In the other parts of the country, there is malaria risk in some districts.	ATQ-PG, DOXY or MFQ.	Year-round	66
25	Nicaragua	Little to no malaria transmission in departments not listed below.	None; use PPM.	Year-round	10
		Departments of Chinandega, Léon, Managua, and Matagalpa and the autonomous regions of Atlántico Norte (RAAN) and Atlántico Sur (RAAS).	Chloroquine.		

* Chemoprophylaxis is recommended only in the risk areas identified during the transmission season identified. Chemoprophylaxis should always be used in conjunction with PPM.
ATQ-PG, atovaquone-proguanil; DOXY, doxycycline; MFQ, melfloquine

Summary of recommendations for the diagnosis and treatment of malaria by the Committee to Advise on Tropical Medicine and Travel (CATMAT)

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Abstract

Background: On behalf of the Public Health Agency of Canada, the Committee to Advise on Tropical Medicine and Travel (CATMAT) developed the *Canadian Recommendations for the Prevention and Treatment of Malaria Among International Travellers* for Canadian health care providers who are preparing patients for travel to malaria-endemic areas and treating travellers who have returned ill. These recommendations aim to achieve appropriate diagnosis and management of malaria, a disease that is still uncommon in Canada.

Objective: To provide recommendations on the appropriate diagnosis and treatment of malaria.

Methods: CATMAT reviewed all major sources of information on malaria diagnosis and treatment, as well as recent research and national and international epidemiological data, to tailor guidelines to the Canadian context. The evidence-based medicine recommendations were developed with associated rating scales for the strength and quality of the evidence.

Recommendations: Malarial management depends on rapid identification of the disease, as well as identification of the malaria species and level of parasitemia. Microscopic identification of blood samples is both rapid and accurate but can be done only by trained laboratory technicians. Rapid diagnostic tests are widely available, are simple to use and do not require specialized laboratory equipment or training; however, they do not provide the level of parasitemia and do require verification. Polymerase chain reaction (PCR), although still limited in availability, is emerging as the gold standard for high sensitivity and specificity in identifying the species.

Severe or complicated malaria requires admission to hospital for regular monitoring of respiratory rate and pattern, coma score, and glucose and urine output, especially if the patient is unconscious. In high levels of parasitemia, exchange transfusion may be beneficial to remove infected red blood cells and toxic mediators from the circulation, and reduce the parasite load. Because of the elevated risk of severe or complicated malaria, those with a diagnosis of *Plasmodium falciparum* malaria should also be admitted to hospital or receive initial treatment in an observation unit.

Uncomplicated malaria is treated to cure the infection and prevent progression to severe disease. When treatment regimens are being chosen, drug tolerability, the adverse effects of drugs and the speed of therapeutic response should be considered.

Introduction

Malaria is a serious infection caused by five different species of the genus *Plasmodium*: *falciparum, vivax, ovale, malariae* and *knowlesi.* Malaria is transmitted by the bite of infected female anopheline mosquitoes. Infections caused by *P. falciparum* have the highest fatality rates. The overall case-fatality rate of falciparum malaria varies from about 1% to 5% and increases to 20% for those with severe malaria (1-2).

According to the World Health Organization (WHO), about 3.3 billion people were at risk of malaria in 2010, resulting in an estimated 219 million cases, of which about 80% occurred in 17 countries and of which about 40% were in India, Nigeria and the Democratic Republic of Congo (3). Malaria is still diagnosed in Canada following travel in endemic countries. The Canadian Notifiable Diseases Surveillance System, which monitors nationally notifiable infectious diseases, received reports of 4,254 cases of malaria from 2001 to 2011 (D.Taylor, Public Health Agency of Canada, unpublished data, 2013).

From August 2001 to August 2012, the Canadian Malaria Network, which facilitates rapid access to parenteral treatment of severe malaria, received reports of 195 cases of severe or complicated malaria (personal communication, A. McCarthy and J. Geduld, Committee to Advise on Tropical Medicine and Travel, 2012).

The most important factors determining patient survival are early diagnosis and appropriate therapy. The majority of malaria deaths are preventable and are frequently the result of delays in diagnosis and treatment. Among the cases reported to the Canadian Malaria Network, only 20% presented to medical care within 24 hours of onset of symptoms, and 44% waited more than three days (personal communication, A. McCarthy and J. Geduld, K. Cullen and P. Arguin, US Centers for Disease Control and Prevention, 2012). Diagnosis by health care provider was delayed more than 24 hours in 34% of the cases (personal communication, A. McCarthy and J. Geduld, 2012).

This is a summary of the CATMAT *Canadian Recommendations for the Prevention and Treatment of Malaria Among International Travellers,* developed for Canadian health care providers who are preparing patients for travel to malaria-endemic areas and treating travellers who have returned ill (4). These guidelines include a full description of recommendations on diagnosis and treatment of malaria.

Methods

The Malaria Subcommittee, a working group of CATMAT, developed the guidelines. The process undertaken to develop them has been described previously (5). It included a review of recent research and national and international epidemiological data, and the consideration of other factors, such as malaria epidemiology, and the anticipated values and preferences of travellers and health care providers. The evidence-based medicine recommendations for the diagnosis and treatment of malaria were developed with associated rating scales for the strength and quality of the evidence.

Recommendations

The evidence-based CATMAT recommendations for malaria diagnosis and treatment are summarized in **Table 1.** A discussion of some of the key recommendations follows.

Table 1: Evidence-based medicine recommendations for the diagnosis and treatment of malaria

Recommendation	EBM[1] rating
1. Parenteral artesunate is recommended as first-line treatment for severe *P. falciparum* malaria, with parenteral quinine as an alternative (3).	A I
2. To prevent relapses of *P. vivax* and *P. ovale* malaria, primaquine phosphate (30 mg base daily for 2 weeks) should follow chloroquine treatment (6).	B I
3. The treatments of choice for uncomplicated *P. falciparum* malaria are as follows: • Oral chloroquine (ONLY if from chloroquine-sensitive areas); • Oral atovaquone-proguanil (7); • Oral quinine combined with oral doxycycline or clindamycin; • Combination therapy with an artemisinin derivative (not yet available in Canada) (7).	BIII
4. Exchange transfusion may have benefits for treating hyperparasitemic cases of *P. falciparum* (8).	C III
5. Individuals in chloroquine-sensitive regions should self-treat with chloroquine and then resume or start chloroquine prophylaxis (9-11).	C III
6. In chloroquine- and/or chloroquine- and mefloquine-resistant *P. falciparum* regions, self-treatment should consist of a drug different to that used for prophylaxis, chosen from one of the following: a. atovaquone-proguanil (Malarone®) or b. oral quinine and doxycycline or c. artemether-lumefantrine (Coartem®), ideally purchased from a country with high standards of quality control (e.g. in Europe or the United States) so as to minimize the likelihood of using counterfeit products (10-13).	C III
7. The use of steroids to treat severe or cerebral malaria has been associated with worse outcomes and should be **avoided** (14).	E I
8. A number of antimalarials are contraindicated in the treatment of malaria (self-treatment or otherwise): a) mefloquine (15) b) pyrimethamine-sulfadoxine (Fansidar) (16) c) mefloquine-Fansidar (17) d) halofantrine (7) e) chloroquine-Fansidar (18).	E II

[1] EBM = Evidence based medicine. The EBM ratings are as follows:
Strength of recommendation:
A = Good evidence to support a recommendation for use
B = Moderate evidence to support a recommendation for use
C = Poor evidence to support a recommendation for or against use
D = Moderate evidence to support a recommendation against use
E = Good evidence to support a recommendation against use
Quality of evidence:
I = Evidence from at least one properly randomized, controlled trial
II = Evidence from at least one well-designed clinical trial without randomization; from cohort or case-controlled analytic studies, preferably from more than one centre; from multiple time series; or from dramatic results in uncontrolled experiments
III = Evidence from opinions of respected authorities on the basis of clinical experience, descriptive studies, or reports of expert committees

Malaria Diagnosis

Malaria could be the reason for any etiologically unidentified fever that develops while a traveller is in a malaria-endemic area or up to one year after leaving, irrespective of chemoprophylaxis use (19). If a fever occurs during this time, the traveller should seek medical attention immediately and tell the health care provider about his/her travel history. Particular attention should be paid to fevers that develop in the three months following travel, as more than 90% of falciparum malaria presents during this period.

Since the disease can progress from asymptomatic infection to severe and complicated malaria and even death within 36 to 48 hours, survival of patients particularly with *P. falciparum* malaria (20) is affected by early diagnosis and correct speciation to determine the required life-saving treatment. Quantitating parasitemia is also important to determine the need for parenteral treatment, for exchange transfusion or for admission to an intensive care unit (ICU). In addition, it is important for monitoring response to treatment.

Microscopy, which involves examining thick and thin blood smears, is both rapid and accurate. A Canadian laboratory should be able to confirm the presence of a parasite and, in most cases, identify the species within one to two hours of receiving a blood specimen (21-24). However, accurate examination of a blood smear requires considerable training and experience (23,25).

Rapid diagnostic tests are simple to use and do not require any specialized laboratory equipment or skills. They are essential diagnostic tools if malaria microscopy results are not available within two hours (26). However, both positive and negative results must be verified by expert microscopy or PCR to determine the level of parasitemia and to identify the species. Note that the use of rapid diagnostic tests by travellers to self-diagnose is unreliable.

Although still limited in its availability, PCR is emerging as the gold standard for high sensitivity and specificity in speciation. It is being increasingly used for quality control (27-29).

General principles of malaria management

When managing malaria, three questions need to be answered:

1) Is this infection caused by P. falciparum?

Treatment varies according to the species of malaria. *P. falciparum* can cause life-threatening disease in a nonimmune host and is a medical emergency. Consider hospital admission for all nonimmune cases and for all children to ensure that antimalarial drugs are tolerated and to detect complications or early treatment failure.

2) Is this severe or complicated malaria?

In a case of *P. falciparum* and no other obvious cause of symptoms, having one or more of the following clinical or laboratory features indicates severe or complicated malaria:

Clinical manifestation	Laboratory test
Prostration/impaired consciousness	Severe anemia (hematocrit < 15%; Hb ≤ 50 g/L)
Respiratory distress	Hypoglycemia (blood glucose < 2.2 mmol/L)
Multiple convulsions	Acidosis (arterial pH < 7.25 or bicarbonate < 15 mmol/L)
Circulatory collapse	Renal impairment (creatinine > 265 umol/L) (1)
Pulmonary edema (radiological)	Hyperlactatemia
Abnormal bleeding	Hyperparasitemia (≥ 2%)
Jaundice	—
Hemoglobinuria	—
Adapted from *Guidelines for the Treatment of Malaria*, World Health Organization, 2010 (7).	

Severe malaria is usually due to *P. falciparum* infection, although it can also occur with *P. knowlesi,* and *P. vivax* can occasionally lead to severe disease.

3) Where was the infection acquired?
Appendix I of the *Canadian Recommendations for the Prevention and Treatment of Malaria Among International Travellers* shows a country-by-country and regional characterization of malaria transmission areas (4). Malarial parasites in most of the world are drug resistant. When in doubt, treat all *P. falciparum* malaria as drug resistant.

Managing severe or complicated malaria

Severe or complicated malaria, *or the inability to tolerate oral therapy*, requires urgent, parenteral therapy and intensive medical management (especially in the case of children), ideally in an ICU. If possible, consult with an infectious or tropical disease expert when managing a patient with severe falciparum malaria.

The primary objective of treatment is to prevent death. Prevention of neurological deficits is also an important objective for cerebral malaria. There are several treatments:

- Parenteral artesunate is the WHO-recommended first-line treatment for severe *P. falciparum* malaria.
- Parenteral quinine can be used to treat severe or complicated malaria when parenteral artesunate is not available and is the preferred drug if the only indication for parenteral therapy is intolerance to oral therapy.
- Parenteral artesunate and quinine are available 24 hours per day through the Canadian Malaria Network (30).
- Follow parenteral administration of artesunate or quinine with oral therapy using one of the following medications:
    - Atovaquone-proguanil (unless used as malaria chemoprophylaxis);
    - doxycycline (unless used as malaria chemoprophylaxis; contraindications: pregnancy, breastfeeding, age < 8 years) (7);
    - clindamycin (only if the patient is unable to take doxycycline or atovaquone-proquanil).

Table 2 identifies the common antimalarial drugs and their indications.

Table 2: Recommendations for common antimalarial drugs

	Indication	Additional notes
Intravenous artesunate	First-line treatment of severe falciparum malaria (3,7,31) or if intravenous quinine is not tolerated.	Follow parenteral artesunate with a full course of atovaquone-proguanil (Malarone®) or doxycycline (clindamycin in pregnant women or children < 8 years) or artemisinin-based combination therapy. Patients treated with IV artesunate should have weekly CBC x 4 done. As well they should be counselled to report signs of hemolysis such as dark urine, yellowing of the skin or whites of the eyes, fever, abdominal pain, pallor, fatigue, shortness of breath and/or chest pain.
Oral artemisinin combination therapy (not yet available in Canada)	Uncomplicated falciparum malaria or when the causative species has not been identified.	

	Indication	Additional notes
Atovaquone-proguanil ***Trade Name:*** Malarone®	First-line treatment of acute, uncomplicated *P. falciparum malaria* and *P. vivax malaria* Uncomplicated malaria in adults and in children ≥ 11 kg.	
Chloroquine (or hydroxychloroquine) ***Trade Name*:** Novo-Chloroquine (or Plaquenil®, Apo-Hydroxyquine, Gen-Hydroxychloroquine)	Chloroquine-sensitive *P. falciparum, P. vivax, P. ovale, P. malariae* and *P. knowlesi* infections.	Suitable for all ages and in pregnancy.
Clindamycin ***Trade Name:*** (Dalacin C®), Apo-Clindamycin, Novo-Clindamycin	Clindamycin is combined with quinine to treat chloroquine- or mefloquine-resistant *P. falciparum* malaria in pregnant women, children (< 8 years) and tetracycline-intolerant adults when artemisinin-derivatives are unavailable.	Less effective than doxycycline or atovaquone-proguanil.
Doxycycline ***Trade Name*:** Vibra-Tabs™, Apo-Doxy, Doxycin, Novo-Doxylin, Nu-Doxycycline, ratio-Doxycycline	To prevent and treat chloroquine-resistant *P. falciparuml.*	**Contraindicated** in pregnancy, while breastfeeding and in children aged < 8 years of age.
Quinine and quinidine	Parenteral quinine is used to treat severe or complicated malaria when parenteral artesunate is unavailable and is the first-line drug for those who cannot take oral therapy and do not meet any criteria for severe disease. Oral treatment using quinine with doxycycline or clindamycin is indicated for uncomplicated falciparum malaria and as step-down therapy after parenteral treatment of complicated malaria.	The Canadian Malaria Network recommends reserving artesunate for those with severe malaria (as defined by the WHO) and using parenteral quinine in those who do not tolerate oral therapy or are vomiting. Parenteral quinidine should only be used if the two first-line drugs are unavailable; cardiac monitoring is required.
Primaquine ***Trade Name*:** Primaquine (primaquine phosphate)	Used to prevent relapse due to *P. vivax* or *P. ovale* infection. Used as a “radical cure” to reduce the risk of relapse after the treatment of symptomatic *P. vivax* or *P. ovale* infection.	Contraindicated in people with severe G6PD deficiencies, in pregnancy and in nursing mothers if the infant is G6PD deficient.

If parenteral artesunate or quinine is indicated but is not available for more than an hour, start quinine orally (after a dose of gravol) or by nasogastric tube until the parenteral drug is available. Patients should have at least 24 hours of parenteral therapy before switching to oral therapy.

Frequent clinical observations should monitor vital signs and assess respiratory rate and pattern, coma score and urine output. Use rapid stick tests to monitor blood glucose at least every four hours. Treat seizures promptly with benzodiazepines (7). Clinically assess all patients daily until fever ends and whenever symptoms recur; for *P. falciparum* cases, repeat malaria smears daily until these are negative.

In cases with high parasitemia (≥ 10%), exchange transfusion to remove infected red blood cells and toxic mediators from the circulation and reduce the parasite load may be beneficial (8,32).

Managing uncomplicated falciparum malaria

Uncomplicated falciparum malaria refers to symptomatic malaria with no evidence of severe disease or of vital organ dysfunction. Uncomplicated malaria is treated to cure the infection and prevent progression to severe disease. When choosing treatment regimens, consider drug tolerability, adverse effects of drugs and the speed of the therapeutic response.

The treatments of choice for uncomplicated *P. falciparum* malaria are as follows:

- Oral chloroquine (ONLY for those with travel to exclusively chloroquine-sensitive areas);
- Oral atovaquone-proguanil (7);
- Oral quinine combined with oral doxycycline simultaneously or sequentially, starting with quinine; if doxycycline is contraindicated, administer oral quinine and clindamycin, simultaneously or sequentially (33-34);
- Combination therapy with an artemisinin derivative (not yet available in Canada) (7).

Managing non-falciparum malaria

Conduct a clinical assessment daily until fever ends and whenever symptoms recur. For *P. vivax* infections, recurrence of asexual parasitemia less than 30 days after treatment suggests chloroquine-resistant *P. vivax*; recurrence after 30 days suggests primaquine-resistant *P. vivax*.

The treatment of choice for non-falciparum malaria outside of chloroquine-resistant regions continues to be chloroquine. The optimal chemoprophylaxis or treatment of *P. vivax* acquired in chloroquine-resistant regions is unknown, although a seven-day course of quinine is often required to cure *P. vivax* infection.

Managing undefined malaria

If fever, travel history and initial laboratory findings (low white blood count and/or platelets) suggest a diagnosis of malaria but the malaria smear is delayed for more than two hours, start a therapeutic antimalarial that is effective for the area of travel/acquisition.

Managing relapses

P. vivax and *P. ovale* have a persistent liver phase (hypnozoites) that is responsible for relapses for months or even years after exposure, even in the absence of primary symptomatic malaria infection. None of the currently recommended chemoprophylaxis regimens will prevent relapses due to *P. vivax* or *P. ovale*.

To reduce the risk of relapse after the treatment of symptomatic *P. vivax* or *P. ovale* infection, primaquine is indicated to provide a “radical cure”. Initiate the primaquine radical cure after the acute febrile illness is over, but so that it overlaps with the blood schizonticide (i.e. chloroquine or quinine) (7).

Primaquine is **contraindicated** in people with severe G6PD deficiencies and in pregnancy. Prevent relapses in pregnancy with weekly doses of chloroquine until after delivery, when primaquine can be safely used for mothers with normal G6PD levels unless they are breastfeeding. Nursing mothers should only use primaquine if the infant has been tested and is not G6PD deficient.

P. knowlesi, a threat in southeast Asia, can be confused microscopically as *P. malariae* except that it has higher (> 1%) parasitemia. Systemic symptoms and complications can mimic *P. falciparum* malaria. Treatment with chloroquine is reportedly effective, but systemic symptoms and complications similar to those of hyperparasitemic *P. falciparum* infections require very close monitoring and careful management (25, 35), and, potentially, parenteral therapy with artesunate.

Self-treatment of presumptive malaria

Self-treatment may be a life-saving measure for 24 hours while medical attention is sought. Travellers to high-risk regions (e.g. sub-Saharan Africa, where 90% of global malaria morbidity and mortality occurs) should never rely

exclusively on self-treatment (9,21,23,25). The signs and symptoms of malaria are nonspecific, and malaria cannot be definitively diagnosed without a laboratory test (10,37,38).

Travellers at risk of malaria and unable to access medical care within 24 hours for adequate malaria treatment drugs should carry effective medication for self-treatment of presumptive malaria.

- In chloroquine-sensitive regions, self-treat with chloroquine and then resume or start chloroquine prophylaxis (9-11).
- In chloroquine- and/or chloroquine- and mefloquine-resistant *P. falciparum* regions, self-treatment requires a different drug if the traveller is taking a chemoprophylactic agent. Ideally, this should have been brought from a country with high standards of quality control to minimize the likelihood of counterfeit products:
    - Atovaquone-proguanil
    - oral quinine and doxycycline (10-11,13)
    - artemether-lumefantrine

Contraindicated malaria drugs

A number of antimalarials are *contraindicated* for the treatment of malaria (self-treatment or otherwise):

- mefloquine
- pyrimethamine-sulfadoxine (Fansidar)
- mefloquine-Fansidar
- halofantrine
- chloroquine-Fansidar

Summary

A summary of the key changes made to the 2014 Guidelines are noted in **Table 3.**

Table 3: Summary of key additions and changes to the 2014 Guidelines pertaining to the diagnosis and treatment of malaria (4)

Additions
1. The management of severe malaria has been updated to include new information on the use of exchange transfusion (see Chapter 7).
2. A new “Malaria Card” that can be given to travellers with information about their malaria chemoprophylaxis and an important reminder to seek medical attention in the event of a fever illness after travel.
Changes
1. Chapter 8, “Drugs for the Prevention and Treatment of Malaria,” includes up-to-date information on pediatric dosing of atovaquone/proguanil; general updates to Table 8.11: Drugs (generic and trade name) for the treatment and prevention of malaria. Revisions have also been made to the following sub-sections: artemisinins, chloroquine and quinine/quinidine.
2. Change in parasitemia level to define hyperparasitemia with severe malaria: now ≥ 2% from 5% in non-immune travellers.

Conclusions

Malarial management depends on rapid identification of the disease, as well as identification of the malaria species and level of parasitemia. Severe or complicated malaria requires admission to hospital. Uncomplicated malaria is treated to cure the infection and prevent progression to severe disease. Treatment varies according to the species of malaria, severity and where the malaria was acquired.

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Conflict of interest

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