Malaria

Manitoba
Public Health Branch

1. Case Definition

1.1 Confirmed Case:

Demonstration of *Plasmodium* species in a blood smear/film (thick and thin) AND/OR positive malaria polymerase chain reaction (PCR) result with or without clinical evidence of infection*(1).

1.2 Probable Case:

Detection of *Plasmodium* species antigen in an appropriate clinical specimen (e.g., blood) with or without clinical evidence of infection*(1).

*Signs and symptoms vary; however, most patients experience fever. In addition to fever, common associated symptoms include headache, back pain, chills, sweats, myalgia, nausea, vomiting, diarrhea and cough. Severe untreated malaria can lead to coma, seizures, renal failure, pulmonary edema and death (1).

Case Counting:

- A case is counted if it is the individual's first attack of malaria in Canada, regardless of whether he or she has experienced previous attacks of malaria outside the country.
- A subsequent attack in the same person caused by a different *Plasmodium* species is counted as an additional case.
- A repeat attack by the same species is not counted as a new case unless the person has travelled to a malaria-endemic area since the previous attack.

NOTE: Malaria cases may be subdivided into the following categories according to source/origin.

- **Induced:** A confirmed case of malaria acquired through a blood transfusion from a donor in whom the parasite has been confirmed.
- **Autochthonous:** A confirmed case of malaria acquired by mosquito transmission within Canada. While autochthonous malaria transmission occurred in Canada in the 19th century and the requirements for transmission of malaria theoretically exist in Canada, transmission potential since 1900 has been too low to permit local transmission (2).
- **Imported:** A confirmed case of malaria acquired outside Canada.
- **Congenital, confirmed:** A confirmed case of malaria in an infant < 3 months old who has not left Canada since birth, with confirmation of the presence of the parasite in the mother.
- **Congenital, probable:** A confirmed case of malaria in an infant < 3 months old who has not left Canada since birth, but without demonstration of the presence of the parasite in the mother (1).

2. Reporting and Other Requirements

Laboratory:

- All positive laboratory results for *Plasmodium* species are reportable to the Public Health Surveillance Unit (204-948-3044 secure fax).

- Operators of Manitoba clinical laboratories are required to submit the residual specimens from individuals who tested positive for *Plasmodium* species to Cadham Provincial Laboratory within seven days of report for surveillance purposes.

Health Care Professional:

- Probable cases of malaria are reportable to the Public Health Surveillance Unit by secure fax (204-948-3044) within 5 business days of being identified ONLY if a confirmatory positive lab result is not anticipated (e.g., poor or no specimen taken, person has recovered). The *Clinical Notification of Reportable Diseases and*

Conditions form http://www.gov.mb.ca/health/publichealth/cdc/protocol/mhsu_0013.pdf should be used.

Regional Public Health or First Nations Inuit Health Branch (FNIHB):

- Once the case has been referred to Regional Public Health or FNIHB, the *Communicable Disease Control Investigation Form* (http://www.gov.mb.ca/health/publichealth/cdc/protocol/mhsu_0002.pdf should be completed and returned to the Public Health Surveillance Unit by secure fax (204-948-3044).

Reporting to Canadian Blood Services:

- Canadian Blood Services will be notified by the Public Health Surveillance Unit if malaria occurs in a person that has received a blood transfusion in Canada, and the person is NOT from or has NOT travelled in an area endemic for malaria.

3. Clinical Presentation/Natural History

Malaria is an acute febrile illness that in the initial stage resembles many other febrile illnesses due to bacterial, viral or other parasitic causes (3). Signs and symptoms of malaria often are nonspecific but typically include fever (4). Other symptoms include headache, chills, increased sweating, back pain, myalgia, diarrhea, nausea, vomiting and cough (4). The classic symptoms of malaria (a cyclic pattern of severe shaking chills, high fever and sweats) are often absent in mild or early cases (5). Persons who have grown up in endemic areas and acquired partial immunity, or non-immune persons who have been taking prophylactic antimalarial drugs, may present with an atypical clinical picture of malaria and/or a prolonged incubation period (3, 6). Definitive diagnosis of malaria and differentiation among *Plasmodium* species requires laboratory testing (3). *P. vivax* and *P. ovale* parasites can persist in the liver and cause relapse five or more years after recommended chemoprophylaxis was taken (5). There is no clear evidence of latent liver stages in *P. falciparum* or *P. knowlesi* (6).

Malaria increases the risk of maternal and neonatal death, miscarriage and stillbirth (5). The main complications of malaria in pregnancy include maternal anemia and low birth weight, which are associated with higher morbidity and mortality in infancy (7).

Severe Malaria:

Severe malaria is a medical emergency (3). Disease progression from onset of symptoms to severe malaria may take days or occur within a few hours (8). It is most commonly caused by infection with *P. falciparum*, although all species have the potential to cause severe disease (3, 5, 9, 10). Severe malaria can present with any one of the following: diminished consciousness, convulsions, respiratory distress, prostration, hyperparasitemia, severe anemia, hypoglycemia, jaundice, renal insufficiency, hypoglobinuria, shock, cessation of eating and drinking, repetitive vomiting, or hyperpyrexia (11). Almost all malaria associated deaths among travellers are due to *P. falciparum* (5). Even with appropriate management, the case-fatality rate for severe infections of *Plasmodium falciparum* can be as high as 20% (5, 12). Refer to Section 8 for more detail on severe malaria.

4. Etiology

Malaria is caused by the protozoan parasite *Plasmodium* (3, 13). The species known to infect humans are *P. falciparum, P. vivax, P. ovale, P. malariae* and *P. knowlesi* (13). Mixed species infections are frequent in endemic areas (5).

5. Epidemiology

5.1 Reservoir and Vectors:

Infected humans are the most important reservoir of human malaria (3). In areas where there is high transmission of malaria, infected but asymptomatic persons are an important reservoir for infection (8). *P. malariae* infects humans, the African apes and, probably, some South American monkeys (3). The natural hosts of *P. knowlesi* initially identified were long-tailed and pig-tailed macaques in south-east Asia (14, 15). Vectors of malaria are *Anopheles* mosquitoes (14).

5.2 Transmission:

Malaria is acquired from the bite of a *Plasmodium*-infected female *Anopheles* genus of mosquito (13), which bite between dusk and dawn (16). Uncommon modes of malaria transmission are congenital, through blood transfusions, or through the use of contaminated needles or syringes (13). Congenital transmission of malaria to the newborn is a rare event and is estimated to occur in only 1% of newborns delivered by a mother with malaria (6). The risk of acquiring malaria via the transfusion of blood components is extremely low in countries where malaria is not endemic; however, in the 1990s, a few cases of transfusion-transmitted malaria in Canada were documented (17). Blood donor deferral policies are in place in Canada for donors who have had malaria or who are at risk for development of malaria.

5.3 Occurrence:

General: The World Health Organization (WHO) estimated that between 150 and 300 million cases of malaria occurred worldwide in 2015 with between 236,000 and 635,000 deaths, mostly in children under five years of age in sub-Saharan Africa (16). Malaria is endemic in tropical and subtropical areas of Africa, South America, Asia, and Oceania (4). The risk for malaria transmission in a specific country is posted on the WHO site: http://www.who.int/malaria/publications/country-profiles/en/. The potential for malaria transmission remains in geographic areas where malaria was previously eliminated if infected people return and the mosquito vector is still present (13). *P. falciparum* and *P. vivax* species cause the most infections worldwide (4). *Plasmodium knowlesi* malaria in humans is widely distributed in Malaysia and probably other areas of Southeast Asia inhabited by the nonhuman primate hosts (18).

Canada: Malaria, once endemic in parts of Canada, is now restricted to imported cases (19). Between 400 and 1,000 cases of malaria are reported among Canadian travellers annually, resulting in one to two deaths per year (5).

Manitoba: Thirteen cases of malaria were reported to Manitoba Health, Seniors and Active Living in 2013. Twenty cases were reported for both 2014 and 2015. *Plasmodium falciparum* was the most common species reported from 2013-2015.

5.4 Incubation Period:

The approximate incubation periods are provided below and measure the time from when a person is bitten by the mosquito to when symptoms develop.

- *P. falciparum* 9 -14 days
- *P. vivax and ovale* 12 – 18 days
- *P. malariae* 18 – 40 days (3)
- *P. knowlesi* 10 -13 days (15).

The incubation period may be prolonged in persons who have taken prophylactic antimalarial drugs (3, 6). The incubation period of infections acquired through blood transfusion depends on the level of parasitemia in the infused blood product and is usually relatively short, but may range up to 2 months (3). Some *P. vivax* strains in temperate

areas have an incubation period of 6 -12 months (3).

5.5 Risk Factors:

The risk for Canadians to acquire malaria is greatest for those travelling to west Africa and parts of Oceania; moderate for other parts of Africa, parts of South America and south Asia; and lower for much of Central America, the Caribbean, Mexico and other parts of Asia and South America (5). The risk tends to be greater in rural areas where the number of vectors tends to be higher (5), is absent or negligible in highland areas > 2,000 metres (5), greater with night-time exposure, and can be higher after the rainy season when mosquito populations are higher (5). Risk is greater for longer periods of travel in malaria endemic regions (5). The risk of severe infection is greater where *P. falciparum* predominates (5).

5.6 Host Susceptibility and Resistance:

Canadian travellers who were born, raised, or formerly lived in malaria endemic areas are not protected from malaria (5). These individuals remain at risk regardless of past exposures or episodes of illness (5). Pregnant women, babies and young children are at particular risk of acquiring malaria and of suffering severe complications from malaria (5). People with comorbidities can be at increased risk of malaria, and therapy may be complicated by drug contraindications and/or interactions (5). HIV infection impairs immune responses to malaria and increases both the incidence and severity of malaria (5, 8).

5.7 Period of Communicability:

Cases of malaria with gametocytes (sexual stage of parasite) remain infective to anopheline mosquitoes when taken up during a blood meal (8). Untreated or insufficiently treated patients may be a source of mosquito infection for several decades in those with *P. malariae*, up to 5 years for *P. vivax*, and generally not more than one year for *P. falciparum* malaria (3).

6. Diagnosis

Where epidemiological risk factors for malaria are present (e.g., patient has recently travelled to malaria –endemic region), laboratory confirmation of diagnosis is based on identification of the parasite microscopically on stained blood films (both thick and thin), malaria antigen testing and malaria PCR. Parasites may not be demonstrable in films from patients currently or previously under treatment or prophylaxis. If parasitemia is low, initial blood smears may test negative for *Plasmodium* species, but blood may test positive for malaria antigen. In these patients, the smear should be repeated at 6 to 18 hour intervals for 3 days. If microscopy and malaria antigen testing are still negative after repeated interval sampling, but signs and symptoms persist, blood specimens are referred out for malaria PCR. Malaria antibody testing may be considered when all of the above tests are negative, and malaria still needs to be ruled out. However, the antibody test has sub-optimal specificity and results must be interpreted with caution.

7. Key Investigations for Public Health Response

- Recent immigration from malaria-endemic country.
- Travel history to malaria-endemic areas during the preceding 12 months (3).
- History of antimalarial medication use.
- History of previous malarial illness.
- History of needle-sharing.
- History of blood transfusion in Canada, if there is no history of travel or residence in an area endemic for malaria.

8. Control

8.1 Management of Cases:

Malaria should be considered a medical emergency and prompt treatment with appropriate antimalarials should be initiated. Consultation with an infectious disease or travel medicine specialist is strongly recommended.

Definitions:

- **Uncomplicated Malaria:** Signs and symptoms of malaria and a positive parasitological test but with no features of severe malaria (defined below)(8).
- **Severe Malaria:** Severe falciparum malaria is defined as either a history of recent possible exposure and no other related pathology OR asexual forms of *Plasmodium falciparum* on blood smear AND one or more of the following 15 features below (12).
    1) Hyperparasitemia (> 2% in non-immune, > 5% in semi-immune)
    2) Impaired consciousness or coma
    3) Prostration (unable to walk or sit up without assistance)
    4) Multiple convulsions (> 2 in 24 hours)
    5) Respiratory distress (acidotic breathing)
    6) Respiratory failure/Pulmonary edema/acute respiratory distress syndrome
    7) Circulatory collapse/shock (SBP < 80mmHg adults and < 50mmHg children)
    8) Acute kidney injury/renal failure (Cr > 265µmol/L or > upper limit for age for children)
    9) Jaundice (Total bilirubin > 45µmol/L)
    10) Abnormal spontaneous bleeding/disseminated intravascular coagulation
    11) Hypoglycemia (< 2.2 mmol/L)
    12) Metabolic Acidosis/Acidemia (pH < 7.25, HCO3 < 15mmol/L)
    13) Severe anemia (Hb < 70g/L in adults and < 50g/L in children)
    14) Hemoglobinuria (macroscopic)
    15) Hyperlactataemia (lactate > 5mmol/L)

Infection Prevention and Control: Routine Practices. For cases in health care facilities, refer to the Manitoba Health, Seniors and Active Living document *Routine Practices and Additional Precautions: Preventing the Transmission of Infection in Health Care* available at: http://www.gov.mb.ca/health/publichealth/cdc/docs/ipc/rpap.pdf .

Treatment:

Hospital admission is advised for the following:

- Individuals with falciparum malaria;
- Those with non-falciparum malaria who cannot tolerate oral medication;
- Those in whom the infecting species cannot be identified; and
- Patients with severe malaria.

The specific treatment of malaria depends on the infecting species of *Plasmodium*, the geographic area of acquisition (which reflects the likelihood of drug resistance) and severity of infection (8).

Uncomplicated Malaria:

- Chloroquine is the preferred treatment for infection acquired in a chloroquine-sensitive area (5). Drugs to consider for infections acquired in chloroquine-resistant areas include atovaquone/proguanil or quinine with a second drug (doxycycline or clindamycin) (5).

Severe Malaria:

- The Committee to Advise on Tropical Medicine and Travel (CATMAT) strongly recommends consulting with an infectious or tropical disease expert when managing a patient with severe falciparum malaria (5). Artesunate, the preferred medication for the treatment of severe malaria due to *P. falciparum*, and quinine, a possible alternative when artesunate is contraindicated are only available in Canada through Health Canada's Special Access Programme (12). The Canadian Malaria Network (CMN) http://thinkottawamedicine.ca/clinical-care/canadian-malaria-network/, in collaboration with the Public Health Agency of Canada and Health Canada's Special Access Programme, maintains supplies of intravenous artesunate and intravenous quinine at major medical centres across the country to facilitate rapid access to effective treatment of severe malaria. Physician and pharmacy contacts by province are available at: http://thinkottawamedicine.ca/wp-content/uploads/2014/01/20170112-CMN_ThinkMedWebsite_Content_EN.pdf . Health care providers treating a case of severe malaria should contact the Health Sciences Centre inpatient pharmacy to obtain parenteral artesunate or quinine (consultation with Infectious Diseases will be required).

8.1 Management of Other Potentially Exposed Individuals:

- Any individuals who have recently shared needles with the case should be investigated and treated for malaria (3).
- Pediatric Infectious Diseases should be consulted when infants are born to mothers with malaria.

8.3 Preventive Measures:

- Pre-travel consultation with a travel medicine clinic prior to travelling to malaria-endemic areas. Refer to the CATMAT guideline (http://www.phac-aspc.gc.ca/tmp-pmv/malaria_catmat-paludisme_ccmtmv-eng.php) for current malaria-endemic regions and country-specific malaria prevention recommendations.
- Health care providers should clearly advise travellers of the risks of taking young children to areas with *P. falciparum* malaria (5).
- If possible, pregnant women should defer travel to malaria-endemic areas and particularly to regions with drug-resistant *P. falciparum* malaria (5). If travel cannot be avoided, the personal protective measures described in this guideline should be followed, and chemoprophylaxis regimens that are not contraindicated in pregnancy should be taken. Refer to CATMAT's *Statement on Pregnancy and Travel* (http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs-2/index-eng.php) .
- CATMAT recommends that travellers who become ill with an unexplained fever after returning (for up to 1 year – regardless of whether malaria prophylaxis was prescribed or taken) should seek immediate medical attention and tell the physician their travel history (5).
- Personal protective measures when travelling to malaria endemic regions including:
    - Using insecticide-impregnated mosquito nets while sleeping;
    - Remaining in well-screened areas, particularly from dusk until dawn;
    - Wearing protective clothing;

  - Using mosquito repellents containing 20% – 30% DEET for adults or 20% icaridin for adults and children ≥ six months of age (5). Refer also to the CATMAT *Statement on Personal Protective Measures to Prevent Arthropod Bites* http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/12vol38/acs-dcc-3/index-eng.php .
- Adherence to prescribed antimalarial prophylactic drug regimens (5). Travellers should be aware that chemoprophylaxis does not provide complete protection (5).
- Primaquine is recommended as post-travel terminal prophylaxis for travellers who have suffered from *P. vivax* or *P. ovale* malaria while abroad (5).
- Consider terminal prophylaxis for military personnel, long-term travellers and expatriates resident in regions with high *P. vivax* or *P. ovale* endemicity (5).
- Canadian Blood Services (CBS) and Hema-Quebec http://www.hema-quebec.qc.ca/sang/donneur-sang/puis-je-donner/index.en.html have blood donation deferral policies:
  - Permanent deferral for donation of whole blood and platelets for individuals who have ever been diagnosed with malaria, even after recovery.
  - Temporary deferral of blood donation for individuals who have spent time in a region affected by malaria, regardless of malaria prophylaxis. Depending on the length of time spent in the affected region, the waiting period to donate again can be one to three years. Refer to the CBS website for more information https://blood.ca/en/blood/abcs-eligibility .
- Vector control in endemic areas (8).
- Avoidance of needle-sharing.

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