



MINISTRY OF HEALTH, JAMAICA

**PROTOCOL FOR PREVENTION,
CONTROL & MANAGEMENT OF
MALARIA**

**Division of Health Promotion & Protection
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CLINICAL FEATURES & DIAGNOSIS

The disease may manifest variable signs and symptoms resulting from infection with the *Plasmodium* species of which there are four (4) types– *vivax*, *ovale*, *malariae* and *falciparum*. Typical symptoms include malaise, intermittent fever with chills, headache, diarrhoea, vomiting, myalgias, and arthralgias and other nonspecific signs. If untreated, complications may occur. These include bleeding disorders, kidney and liver failure, acute encephalopathy, pulmonary and cerebral edema, coma and death.

Criteria for diagnosis of severe malaria include one or more clinical or laboratory manifestations in patient with P. falciparum asexual parasitemia. Clinical manifestations: prostration, impaired consciousness, respiratory distress, convulsions, circulatory collapse, pulmonary oedema, abnormal bleeding, jaundice, haemoglobinuria.

Laboratory tests: Severe anemia, hypoglycaemia, acidosis, renal impairment, hyperlactataemia, hyperparasitemia.

Each species of *Plasmodium* may cause a characteristic pattern of periodic fever. The paroxysms of *P. vivax* and *P. ovale* malaria classically occur every 48 hours whereas that for *P. malariae* occurs every 72 hours. However, **the classic presentation with predictably recurring fever and chills is highly variable and may not be present at all.** This is particularly so early in the course of the illness, when the patient may be/have been on antipyretics or antimalarials or when partial immunity exists. *P. falciparum* infections can have a daily or irregular pattern of symptoms.

Infections with *P. ovale*, *P. vivax* and *P. malariae* tend to run a benign course but may relapse many years after the initial attack. These infections may however be life threatening in the very young, the very old, inpatients with concurrent disease or immunodeficiency. *P. falciparum*, the most serious malarial infection may produce a more serious illness and infection may lead to complications. It is estimated that about 1% of patients with *P. falciparum* infection die.

CASE DEFINITION

Mode of transmission: From the bite of the female Anopheles mosquito. Most species feed at dusk or at nights or very early morning.

Incubation period: 9-14 days *P. falciparum* (Control of communicable Diseases Manual 18th edition), but may be prolonged up to 4-8 weeks in some cases.

Susceptibility: Universal but may be more pronounced and likely to be fatal in persons with sickle cell disease and HIV infection

Communicability: Humans may infect mosquitoes as long as infective gametocytes are present in the blood.

Case Definition

✓ Suspected case

A person with fever, intermittent fever, or history of recent fever with one or more of the following non-specific symptoms: malaise, headache, lassitude, fatigue, abdominal discomfort, joint and muscle aches; with no clear medical diagnosis and history of living or visiting area with risk of transmission.

N.B. More acutely ill patients may present with fever, chills, perspiration, anorexia, vomiting, worsening malaise.

Action steps

1. Determine history of travel, including local and international travel
2. Record address and travel history of recent visitors to the household
3. Determine whether there are persons in the household or immediate neighbours with similar symptoms
4. *If warranted by clinical condition, cases should be admitted to hospital and nursed in a mosquito proof area or under a mosquito net.*

5. *Thick and/or thin blood smears on glass slide, should be made in the field and/or at health facility and sent to the laboratory for staining and examination for identification of parasites by microscopic diagnosis.*

Alternatively and more labouriously, an unclotted sample of at least 2ml of blood in an EDTA (purple top) tube, should be collected and sent to the Malaria Laboratory, in the Parasitology Division of the National Public Health Laboratory. The laboratory should be notified prior to sending samples. Samples should be accompanied by patient data and clinical history.

6. **In suspected cases that are life threatening, anti-malaria drugs should be commenced (after blood sample is taken).**
7. **A suspected case must be reported to the Medical Officer of Health for the Parish or to the nearest Health centre using the class 1 notification form**

Case Reclassification:

Cases are reclassified from 'suspected' to 'confirmed' based on laboratory confirmation of malaria parasites on blood smears.

✓ **Confirmed case**

A suspected case with laboratory confirmation – identification of *Plasmodium* species on peripheral blood smear

Action steps

1. *If warranted by clinical condition, a confirmed case must be managed in hospital and nursed in a mosquito proof area under a bed net, which should be preferably treated.*
2. *If ambulatory, efforts should be made to ensure treatment is observed.*
3. **Anti Malarials must be commenced immediately as follows:**

a) **Uncomplicated Malaria**

- **Chloroquine**
 - **Total dose of 25mg /kg administered over 3 days as follows.**
 - **Adults (50+ kg): dose 600mg {4 tablets} stat, then 450mg (3 tablets) daily for 2 days.**
 - **Children and adults (less than 50kg): 10mg/kg orally stat and 7.5mg/kg daily for 2 days**

PLUS

- **Primaquine 0.75 mg/Kg (3 tablets for the average adult) as a Stat dose on Day 1**

(See attached appendix for drug details)

- *At the end of treatment, if patient has not improved clinically should have a recheck smear on Day 3. If smear positive repeat treatment.*
- *For all other patients, a recheck smear for follow up should be done on Day 7. If the smear is positive re-evaluate in collaboration with the Ministry of Health and the National Public Health Laboratory.*
- **Ensure case is reported to the Medical Officer of Health for the Parish or to the nearest Health centre using the class 1 notification form**

b) Severe or Complicated Malaria

The recommended drug of choice is intravenous quinine. Intravenous infusions should be given slowly to avoid cardiac complications.

For severe malaria: Quinine I.V. (10mg salt/kg every 12 hours) over four hours in Dextrose 5%. Change to oral Quinine when tolerated by patient to complete 7 days treatment. N.B Quinine can cause hypoglycaemia, a complication if given too rapidly.

MALARIA IN PREGNANCY

Malaria in pregnant women can be very severe and threatening to the mother-to-be and foetus. The risk of maternal death, miscarriage, stillbirth and low birth weight with associated neonatal death are increased. Immediate medical attention should be given to the pregnant woman if malaria is suspected.

Chloroquine, amiodaquine, and quinine can be safely given to pregnant women. If Quinine used during first semester, should be in combination with Clindamycin (if available) for seven days. During second and third semesters Artesunate or Quinine in combination with Clindamycin for seven days could be used.

Anti-malarial Drugs Contraindicated During Pregnancy:

- **Tetracycline**
- **Doxycycline**
- **Primaquine**
- **Mefloquine** (there is insufficient evidence to support the use of mefloquine in the first trimester)

MALARIA IN CHILDREN

Chloroquine is the recommended treatment for uncomplicated cases in areas where there is low resistance to the drug. Pyrimethamine/sulphadoxine is recommended for treatment in areas of high chloroquine resistance. Mefloquine may be given to infants of more than 5 kg body weight. Doxycycline, which is a good alternative in areas with multidrug-resistant *P. falciparum* malaria, is contraindicated in children under 8 years of age due to the propensity of tetracyclines to stain growing teeth and bones. Quinine is the drug of choice for treatment of severe malaria.

PUBLIC HEALTH MEASURES

REPORTING

- **Malaria is a Class I notifiable disease.** It must be reported on **clinical suspicion** within 24 hours to the Medical Officer (Health) at the parish health department and/or the Surveillance Unit in the Ministry of Health. (*See Appendix II*). The Medical Officer (Health) should be advised of laboratory results as soon as possible.

STEPS IN INVESTIGATION & CONTROL

- Preliminary investigations must be commenced using the recommended investigation form. (*See Appendix III*). **Special attention must be paid to travel history and a clearly defined geographic exposure obtained.** All contacts should be promptly investigated and attempts made to identify the source of infection.
- **A suspected case MUST BE ADMITTED TO HOSPITAL and isolated in a mosquito-proof area, especially from dusk to dawn, while awaiting further investigations.**

Value of hospitalization

- Allows for appropriate barrier nursing under a mosquito-proof net
- Allows better supervision of anti-malarial therapy
- Allows on-the-spot recognition of complications of malaria or side effects of drug therapy

Diagnosis:

Identification of parasites by microscopic diagnosis using thick and/or thin blood smears on glass slide, which can be made in the field and/or at health facility and sent to the laboratory for staining and examination.

- **Alternatively and more labouriously**, an unclotted sample of at least 2ml of blood in an EDTA (purple top) tube, should be collected and **sent to the Malaria Laboratory, in the Parasitology Division of the National Public Health Laboratory.** The laboratory should be notified **prior** to sending samples.

Entomological surveillance

- Identify and document breeding sites of competent vectors. Alert the parish vector control authorities to commence vector control measures {fogging (adulticidal) and oiling (larvicidal)} control measures within a one 1km radius of the positive case (domicile and hospital).

Epidemiological surveillance

- Undertake “Active Fever Surveillance” for at least one (1) week – examine smears from febrile persons presenting to health facilities in the case vicinity [one 1km radius of index case or location where case visited since onset of symptoms]
- Undertake “Active Geographical Surveillance” for at least one (1) week – examine smears from persons living in surrounding households [one 1km radius of index case or location where case visited since onset of symptoms] – with or without fever

Heighten patient/community awareness/education re: early detection, control and preventive measures.

TABLE 1. SPECIFIC DRUG TREATMENT

CHLOROQUINE PHOSPHATE

Brand name:	Aralen, Avloclor, Nivaquine
Indications:	Chemoprophylaxis and treatment of uncomplicated chloroquine sensitive malaria
Contraindications:	Patients with psoriasis and liver damage
Possible risk/side effects:	Pruritus, headache, nausea, skin reactions, blurred vision, corneal opacities, partial alopecia, ocular damage with prolonged use; Rarely; blood dyscrasiae (thrombocytopenia, agranulocytosis, and aplastic anemia), psychosis
How to give:	Oral , with a meal and plenty of water. If the patient vomits within 30 minutes, repeat the full dose; if the patient vomits between 30 and 60 minutes, give an additional half dose.
Preparations:	Tablets 100mg, 150mg, 300mg base as phosphate/sulphate
Dosage:	The total dose is 25mg base/kg over 3 days. <u>Dosage:</u> 10mg/kg orally stat and 7.5mg/kg daily for 2 days <u>Adults dose (based on 60 kg):</u> dose 600mg (4 tablets) stat, then 450mg (3 tablets) daily for 2 days.
Storage:	Store in a closed container in a dry place, away from light

MEFLOQUINE HYDROCHLORIDE

Brand name:	Lariam
Indications:	Use in cases known or suspected to be chloroquine resistant
Contraindications:	Pregnancy, breastfeeding, pre-existing psychiatric or neurological disease, concomitant quinine, quinidine or halofantrine treatment; treatment with mefloquine in the previous 4 weeks
Possible risk/side effects:	Dizziness, nausea, diarrhoea, headache, insomnia, abdominal pain, strange dreams. Rarely: bradycardia, neuropsychiatric disturbances, rash, pruritus, disturbances in liver function tests; erythema multiforme (and Stevens-Johnson syndrome) reported
How to give:	Oral
Preparations:	Tablets 274mg hydrochloride, equivalent to 250mg mefloquine base
Dosage:	<u>Dosage:</u> 25 mg/kg base as two divided dosages <i>WHO/PAHO Recommendation: not to be used as monotherapy but in combination with Artemisinin derivative (eg. Artesunate 50mg tabs): Artesunate dosage: 10mg/kg divided over 3 days (Adult: 4 tabs daily) Mefloquine dosage: 16.6 mg/kg on Day 2 and 8.3mg/kg on Day 3 (Adult 4 tabs on Day 2 and 2 tabs on Day 3)</i>

PYRIMETHAMINE/SULPHADOXINE *

Brand name:	Fansidar
Indications:	Use in cases known or suspected to be chloroquine resistant
Contraindications:	Known hypersensitivity to sulpha drugs, severe hepatic or renal dysfunction (except when benefits exceed the risk involved); first trimester of pregnancy and 4 weeks after delivery; infants in first 2 months of life
Possible risk/side effects:	Rashes, insomnia; occasionally headache, nausea, vomiting, folate deficiency, depression of haematopoiesis with high doses.
How to give:	Oral
Preparations:	Tablets 500mg sulphadoxine and 25mg pyrimethamine
Dosage:	<u>Adults:</u> 3 tablets as a single dose <u>Children:</u> pyrimethamine 0.5- 0.75mg/kg as a single dose <i>WHO/PAHO recommendation: not to be used as monotherapy but in combination with Artemisinin derivative eg. Artesunate (dosage same as with Mefloquine)</i>

TABLE 1. SPECIFIC DRUG TREATMENT (Cont'd)
AMODIAQUINE *

Indications:	Uncomplicated chloroquine resistant <i>P. falciparum</i> malaria
Contraindications:	Known hypersensitivity; persons with hepatic disorders
Possible risk/side effects:	Nausea, vomiting, abdominal pain, diarrhoea and itching. Fatal adverse reactions (toxic hepatitis and severe agranulocytosis) reported in travelers using drug for prophylaxis
How to give:	Oral
Preparations:	<u>Tablets</u> 200 mg, 600 mg amodiaquine base as hydrochloride or 153.1 mg base as chlorhydrate <u>Syrup</u> 10 mg/ml amodiaquine base/kg in dosage regimes similar to those of chloroquine
Dosage:	Over 3 days at total doses 25 mg base/kg in dosage similar to those of chloroquine

PRIMAQUINE PHOSPHATE

Indications:	Use to prevent relapse of <i>Plasmodium vivax</i> and <i>ovale</i> infections by eliminating the liver stages of both species, which can cause malaria symptoms long after leaving a malaria endemic area. It may be given concurrently with or following the suppressive drug after leaving endemic areas.
Contraindications:	Pregnancy, persons with G6PD deficiency (can cause haemolytic anaemia)
Possible risk/side effects:	Nausea, vomiting, abdominal pain. Occasionally methaemoglobinaemia, haemolytic anaemia
How to give:	Oral
Preparations:	Tablet 26.3mg primaquine phosphate equals 15mg of base
Dosage:	Dosage for <i>P. falciparum</i> : Primaquine 0.75mg/kg stat on Day 1 <u>Example Adult (60kg body weight): 45mg (base) 3 tablets</u>

QUININE

Orally: Quinine 25mg/kg/day in three doses for seven days together with Doxycycline 3mg/kg/day or Clindamycin 30mg/kg/day, for seven days

For severe malaria: Quinine I.V. (10mg salt/kg every 12 hours) over four hours in Dextrose 5%. Change to oral when tolerated by patient to complete 7 days treatment.

N.B Quinine can cause hypoglycaemia, a complication if given too rapidly

MALARIA PREVENTION

Malaria prevention is two-fold: avoidance of the bite of mosquitoes and chemoprophylaxis (drugs given to prevent malaria).

AVOIDANCE OF MOSQUITO BITES

The first line of defence against malaria infection is personal protection against mosquito bites. One or more tactics may be employed to achieve this goal. These are described in the following paragraphs.

- ***Insect repellants*** - these may be applied directly to the skin or to clothing. The most effective active ingredient is DEET (diethyl-toluamide). Care must be taken to avoid contact with mucous membranes and they should not be applied to the face or any sensitive or damaged skin areas. The proper concentration of DEET should be used and therefore careful attention should be paid to the manufacturer's instructions, including dosage and frequency of application.
- ***Protective clothing*** - This can offer a high degree of protection against mosquito bites, especially at the times of day when the vector is most active (from dusk to dawn). Clothing should cover most of the body (e.g. long-sleeved shirts, long pants, sock and hats) and the thickness of the material is critical to prevent direct access to the skin by the mosquito. Dark clothing should be avoided in favor of lighter shades such as white or tan as many species of mosquitoes are attracted to navy blue and black. Extra protection is available by treating clothing with permethrin. Label instructions should be followed to avoid damage to the fabrics.
- ***Mosquito coils***
- ***Mosquito nets*** – These may be used with or without insecticide impregnation. The latter are much more effective. Effectivity is greatest when it is ensured that there are no mosquitoes inside the net, the net has no holes or tears and the ends are firmly tucked under the mattress to prevent movement during the night. Persons should also avoid sleeping close to the net to prevent the mosquito from blood feeding directly through the net.
- ***Insecticide sprays*** – This is effective but only for a short term. Additionally it is expensive. It is best to combine this with the use of a mosquito coil or net.

MALARIA Chemoprophylaxis

Chemoprophylaxis is recommended for all migrants and travelers moving to endemic malaria areas from non-endemic areas. Such persons do not have the natural immunity to prevent malaria.

Prophylactic antimalarial regimes should be started one (1) week before leaving for a malaria endemic area and continued for four (4) weeks after leaving the malaria endemic region. Drugs should be taken with a meal and swallowed with plenty of water.

N.B. Hydroxychloroquine is recommended for patients who are unable to take chloroquine. **Doxycycline** is recommended in areas where there is multidrug-resistant malaria. It should be started **two (2) days before departure and continued for 4 weeks after return from a malarious zone.** The drug may induce photosensitivity and appropriate measures may need to be taken to protect against excessive ultraviolet light exposure. Vaginal yeast infections may occur with its use. See **Table 2** for recommended drug regimes for malaria chemoprophylaxis.

Table 2. DRUGS USED FOR THE PREVENTION OF MALARIA **

(Additionally Atovaquone in combination with Proguanil: brand name Malarone)

DRUG	USAGE	ADULT DOSE	PAEDIATRIC DOSE	NOTES
Chloroquine	Only in Middle East, Central America, Caribbean	300-mg base weekly	5-mg base/kg weekly	Bitter taste Start at least 2 weeks prior to travel Guard against accidental overdose
Hydroxychloroquine	Only in Middle East, Central America, Caribbean	400-mg base weekly	5-mg base/kg weekly	Bitter taste Start at least 2 weeks prior to travel Guard against accidental overdose
Mefloquine	Usual recommendation for travelers to Africa	250 mg/week (1 tablet/week)	15-19 kg ¼ tablet 20-30 kg ½ tablet 31-40 kg ¾ tablet	Serious CNS adverse events rare (1:10,000) Many travelers report dysphoria > 10 weeks before at steady-state drug concentrations
Doxycycline	Southeast Asia with areas of mefloquine resistance	100 mg/day	≥ 8 yrs. 2mg/kg/day Not used in children < 8 years and in pregnant women	Minor GI upset common Best taken with food Daily compliance very important
Primaquine <i>(this is treatment for P. vivax) Not for use as prophylaxis</i>	Eradicate liver stages of relapsing malaria	15- to 30-mg base/day for 2 weeks	0.5 mg/kg/day for 2 weeks; no liquid form	Not used in G6PD-deficient persons GI upset with higher doses Possible use for prophylaxis also?

Sources: DuPont HL & Steffen R. Textbook of Travel Medicine and Health, 2nd Edition, 2001
UNICEF, WHO. Malaria Prevention and Treatment. *The Prescriber*, Number 18, January 2000