



Northern
Territory
Government



Guidelines for Malaria

Prepared by the Centre for Disease Control, Darwin and Infectious Diseases Unit, Royal Darwin Hospital.

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For assistance with possible malaria cases contact the following urgently:

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 Royal Darwin Hospital
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Centre for Disease Control
Department of Health, Northern Territory 2012

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This document outlines some selected and unique aspects of malaria surveillance and control in the Northern Territory (NT). It describes the intensive measures that are essential if we are to prevent the re-establishment of malaria in the NT.

The malaria control program in the NT is a responsibility shared among general practitioners, hospitals, laboratories, medical entomology, community care/health centres, disease control units and the general community.

Introduction

The NT has a comprehensive malaria surveillance and control program that includes:

- a. Early detection and hospitalisation of cases;
- b. Correct treatment of cases;
- c. Follow up of cases after discharge from hospital;
- d. Centre for Disease Control (CDC) assessment of all cases to establish appropriate entomological investigation;
- e. Advice on prophylaxis for travel overseas via e.g. Health Services Australia (HSA) Travel Doctor and certain General Practitioners; and
- f. Screening and treatment/cure for high risk groups, for example refugee migrants, illegal fisherpersons and co-travellers of cases who have malaria.

Malaria is caused by the blood parasite *Plasmodium*. There are 5 species that infect humans: *P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae* and in South East Asia only, *P. knowlesi*.

The parasite is transmitted to humans by the bite of an infected mosquito. The female mosquitoes of the genus *Anopheles* are the only mosquitoes that can transmit malaria. The malarious areas across the world include:

- Africa, Middle East, Asia, China, South East Asia including Indonesia, East Timor, Papua New Guinea, the Western Pacific Islands, and Central and South America.

Risks of re-establishing endemic malaria in the Northern Territory

The World Health Organization (WHO) certified the eradication of malaria from Australia in 1981, but Northern Australia still remains susceptible to the re-establishment of the disease.

The receptive area is considered to be north of the 19th parallel which is a line just north of Townsville in Queensland and just south of Broome in Western Australia. The area includes the northern third of the NT, (north of Tennant Creek) and is considered at risk because of:

- a. A history of endemic malaria until 1962;
- b. Widespread breeding of the *Anopheles* mosquito;
- c. Breeding of *Anopheles* mosquitoes in urban areas; and
- d. Regular tourist traffic from malarious countries, particularly Indonesia, East Timor and Papua New Guinea.

The average number of imported cases of malaria to the Northern Territory each year over the last 10 years is 40 (range 15–71). The Northern Territory has 20.8 notifications per 100,000 population which is the highest per capita notification rate when compared to other Australian jurisdictions.

The re-establishment of malaria in the NT could result in extensive morbidity and mortality in our population. Every effort is therefore made to keep the NT malaria free and to maintain Australia's malaria free status.

Prevention and prophylaxis

With Territorians travelling more to endemic malaria areas, including Aboriginal Australians who return to highly malaria-receptive remote areas of the Top End, health professionals need to understand and give expert and current travel medicine advice. Such expert advice on malaria prevention and prophylaxis can be gained through travel medicine clinics, the WHO (www.who.int/ith/en) or CDC Atlanta Guidelines (<http://www.cdc.gov/travel/>). Advice is also included in Therapeutic guidelines; antibiotic. Version 14, 2010 (see Appendix 1).

Diagnosis

Malaria is diagnosed by detection of the parasite through microscopy of thick and thin blood films. As identification of malaria parasites is not a common laboratory event in Australia, the Haematology Laboratory at the Royal Darwin Hospital (RDH) and the Institute of Medical and Veterinary Science (IMVS) provide a service for confirmation of malarial parasites and species identification for all public and private laboratories servicing the NT. Malaria microscopy is the 'gold standard' for the current NT confirmed case definition and remains mandatory for the diagnosis of malaria and species identification. Malaria antigen testing shows the presence of plasmodial antigens and can be useful in supporting microscopy for diagnosis. However a negative antigen test does not exclude malaria infection (eg. low parasite numbers) and an antigen test can remain positive for up to 4 weeks after appropriate treatment. Polymerase chain reaction (PCR) is not routine and is not the gold standard. Malaria is a legislated notifiable disease in the NT.

Any traveller who has returned from a malarious region in the past 2 years and who has a fever or history of fever should undergo testing for malaria parasites and antigen. The decision to have blood films taken should not be influenced by compliance with prophylaxis regimens as it is possible to be infected with malarial parasites and develop malaria even when anti-malarials have been correctly taken.

The absence of parasites on a blood slide does not exclude malaria, particularly if a person has recently taken anti-malarials or antibiotics. If negative, a blood slide should be repeated 6-24 hours later and at least daily thereafter if fever persists.

NT Case definition

Malaria

Reporting

Reporting is made to the Northern Territory Notifiable Diseases System (NTNDS). Confirmed cases are sent from the NTNDS to the National Notifiable Diseases Surveillance System (NNDSS). Probable cases are reported to the NTNDS only.

Confirmed case

A confirmed case requires laboratory definitive evidence.

Probable case

A probable case requires laboratory suggestive evidence.

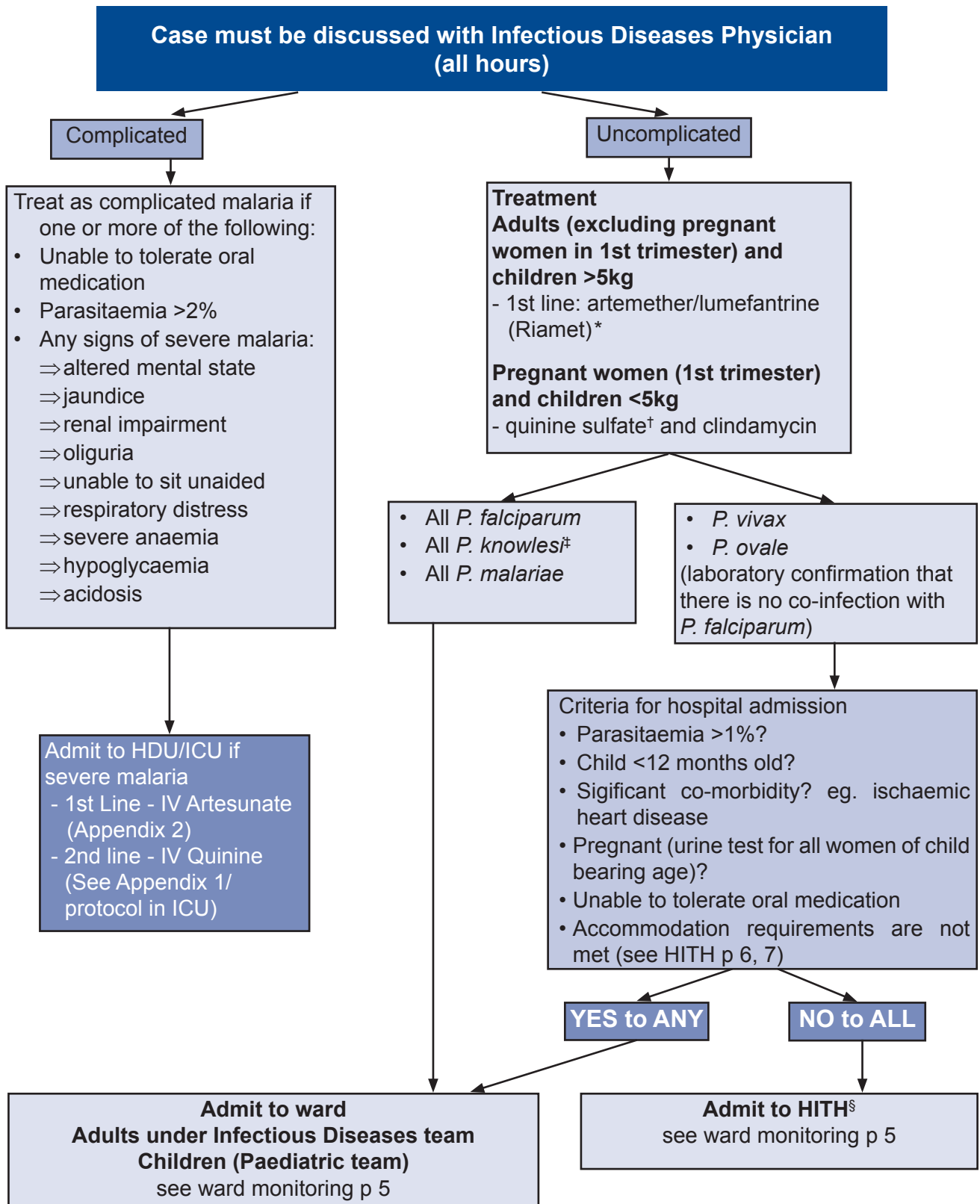
Laboratory definitive evidence

1. Detection and specific identification of malaria parasites by microscopy on blood films with confirmation of species in a laboratory with appropriate expertise
- OR
2. Detection of *Plasmodium* species by nucleic acid testing.

Laboratory suggestive evidence

The detection of *Plasmodium* antigen in blood in the absence of recent appropriate treatment (and the case is not a confirmed case).

Initial management of malaria



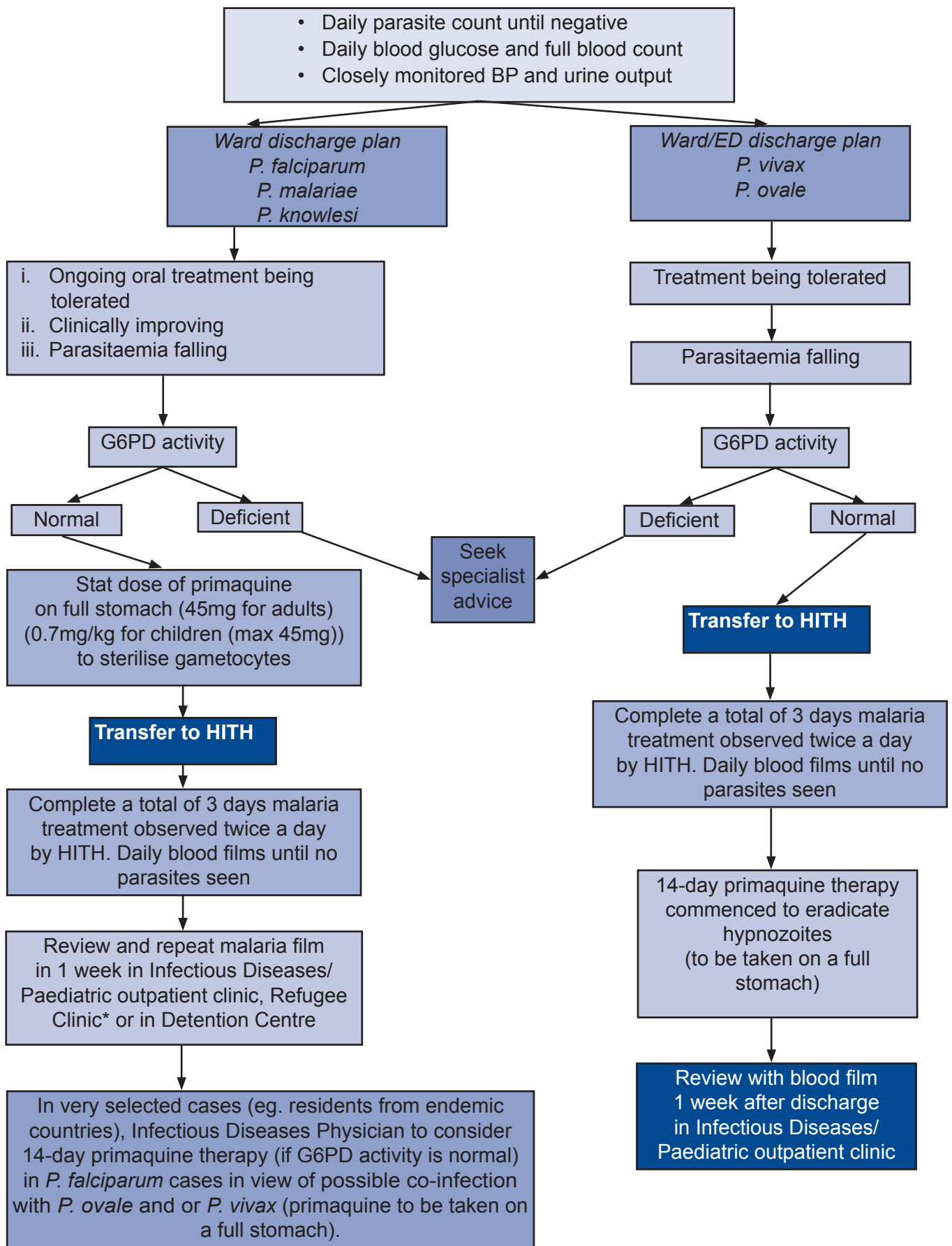
* Give with a small glass of milk or a soft biscuit as fat increases the absorption.

† If unable to tolerate quinine discuss with Infectious Diseases Physician.

‡ *P. knowlesi* malaria is indistinguishable from *P. malariae* on microscopy. All *P. malariae* cases with a history of travel to South East Asia should be treated as *P. knowlesi*.

§ Patients can not be discharged to Hospital in the Home (HITH) after 9pm and should be admitted at least overnight.

Ward monitoring and discharge plan



* Refugee Clinic is offered by Vanderlin Drive surgery, transport for refugees is available through Melaleuca Refugee Centre

Management of malaria

Principles of management

Because of the public health ramifications of malaria and the complexity of the parasite's life cycle, the principles of treatment are to cure the individual and prevent relapses but also include reducing and eliminating transmission. The aims of treatment are as follows:

- a. Eradication of the malaria parasites with specific antimalarial medication;
- b. Sterilisation of the sexual forms (gametocytes) with a specific gametocidal drug (primaquine) to prevent transmission of the parasite to mosquitoes;
- c. Eradication of the dormant liver forms (hypnozoites) of *P. vivax* and *P. ovale* with a 2-week course of primaquine; and
- d. Prevention of transmission to local mosquitoes by physically separating the parasitised patient from the mosquito environment until no longer able to transmit the parasite.

A detailed history must be obtained from every patient (see Appendix 2) including an itinerary of overseas travel and movement following their return to Australia. The history will help in assessing the risk of parasite drug resistance, inform further entomological assessment and allow for identification of co-travellers.

Place of treatment

Hospital

All cases of *P. falciparum*, *P. malariae* and *P. knowlesi* malaria and any malaria cases where the species cannot be confirmed within 24 hours require assessment in hospital.

- This is the preferred practice in the NT to prevent life threatening complications of *P. falciparum*.
- It is also important to avoid any risk of transmission of the parasite to the mosquito vectors that are present in the Top End of the NT.
- Patients are initially nursed in an air-conditioned ward, and must not leave the ward between 6pm and 8am.
- Asymptomatic patients with low parasitaemia eg. refugees may be treated through Hospital in the Home (HITH) after review by the Infectious Diseases registrar or consultant at RDH.

Hospital in the home (HITH)

Confirmed *P. vivax*, or *P. ovale* can be treated by HITH provided:

- a. Parasitaemia is <1%;
- b. The child is >12 months of age;
- c. There are no significant co-morbidities eg. ischaemic heart disease;
- d. Pregnancy is excluded;
- e. There is no evidence of co-infection with *P. falciparum* malaria. This requires blood microscopy confirmation of species by an accredited specialist microscopist;

- f. Where the patient is gametocyte positive that the first dose of artemether/lumefantrine has been given;
- g. The patient is affected mildly by malaria ie. tolerating oral fluids and diet and has tolerated the first treatment dose;
- h. The patient agrees to remain indoors in screened or air conditioned accommodation between dusk and dawn until artemether/lumefantrine therapy is completed;
- i. Another household member has a phone and is able to use it if the patient becomes unwell or there is an emergency*;
- j. The patient speaks a language for which a telephone interpreter or friend/family member can interpret eg. Swahili, French, Dinka, Arabic, Kirundi. If it is a rare language and no lingua franca can be found, the patient will have to be admitted;
- k. The patient is notified to CDC so that CDC officers can ascertain that patients treated as HITH/outpatients do not pose a public health risk. A phone message may be left with CDC after hours; and
- l. The case has been discussed with an Infectious Diseases (ID) Physician at RDH (available 24 hours per day) to check:
 - The above points a to l
 - Clinical condition
 - Follow-up arrangements
 - Spleen size and offer advice about sporting restrictions.

Initial management

Uncomplicated malaria should be treated as per protocols outlined in *Therapeutic guidelines: antibiotic*. Version 14, 2010 (see Appendix 1). Because of difficulties accessing chloroquine, artemether/lumefantrine is the preferred oral treatment for *P. vivax* from any malaria region.

Indications for intensive care unit or high dependency unit admission for parenteral therapy

- Any degree of altered consciousness, jaundice, oliguria, severe anaemia or hypoglycaemia
- A parasite count above 100,000/mm³ (>2% of red blood cells parasitised)
- The patient is vomiting or clinically acidotic.

Severe *falciparum* and *knowlesi* malaria can be fatal, particularly if the diagnosis and treatment is delayed. The World Health Organization has a handbook on the management of severe malaria (<http://www.who.int/malaria/en/>). Intensive care units have protocols for the management of severe malaria.

First line parenteral therapy of severe *falciparum* malaria is artesunate (see Appendix 3).

*Please note: There is a HITH nurse on call 24hours (they only speak English).

Unless the patient or a household member speaks English, there should be another contact person (Melaleuca Refugee Centre or friend/neighbour) who is available to immediately attend the house if called.

Discharge to HITH

Patients with *P. falciparum*, *P. malariae*, and *P. knowlesi* can be discharged to HITH when:

1. The oral course of anti-malarial medication is being tolerated
AND
2. They are clinically improving
AND
3. Parasitaemia is falling
AND
4. For cases of *P. falciparum*, *P. malariae* and *P. knowlesi* a stat* gametocidal dose of primaquine (45mg for adults / 0.75mg/kg for children) is given at discharge if G6PD activity is normal.

The discharge algorithm is on p 5.

Referral to and management of patients with malaria via Hospital in the Home (HITH)

See flow chart *Ward monitoring and discharge plan* p 5.

In working hours

- a. Refer to the Infectious Diseases/HITH registrar ASAP.
- b. ID/HITH registrar, along with a HITH nurse, will assess the patient's suitability for discharge home (see ward monitoring and discharge plan p 5).
- c. The first dose of artemether/lumefantrine [and for *P. falciparum* the stat dose of primaquine (45mg for an adult who is not G6PD deficient)], should be given and observed prior to transfer to HITH. The patient should be observed for an hour following this to ensure no vomiting. Give with a small glass of milk or a soft biscuit as fat increases the absorption.
- d. If the patient is ≤ 12 years of age, the paediatrician on call should be involved.

Out of working hours (after 9pm)

- a. Patients can not be discharged to HITH after 9pm and should be admitted to hospital at least overnight.
- b. The next morning the HITH nurses/registrar can assess the patient and discharge to HITH if appropriate. HITH nurses are available on weekends during working hours and must be consulted if a discharge is planned on a weekend, as must be the ID consultant on call.

Management at HITH

- a. Give each artemether/lumefantrine dose BD at 0800 and 2000 with a small glass of milk or a soft biscuit (directly observed therapy by HITH nurse) for a total of 6 doses (note the second dose is to be given 8 hours after the initial dose).
- b. Do daily malaria films until no parasites are seen.
- c. There is no need to repeat malaria antigen test during treatment.

- d. If the patient or a household member speaks no English, use the Telephone Interpreter Service during visits [TIS 131450, Client number (your allocated number)].
- e. Once treatment has been completed for a refugee, liaise with the Refugee Clinic Vanderlin Drive Surgery (8945 5888) regarding follow-up. In most cases this will involve blood films and FBC and clinical review at day 28 post-treatment.

Eradication treatment for *P. vivax* and *P. ovale* dormant stages

The aim of this treatment is to eradicate the hidden liver phase of *P. vivax* or *P. ovale* (hypnozoites) which can lead to relapses of malaria after months or years.

It is given for:

- Those diagnosed with *P. vivax* or *P. ovale* infection who have a normal G6PD result;
 - Those with *P. falciparum* who are at high risk of co-infection with *P. vivax* hypnozoites;
- Although 14 day primaquine eradication treatment is not routinely offered to all people arriving from malarious areas due to possible co-infection with *P. vivax* it is strongly recommended for:
- a. Migrants and refugees from regions with high endemicity for vivax malaria (eg. PNG, Solomon Islands, eastern Indonesia). This does not include refugees from Africa.
 - b. Expatriate workers resident for prolonged periods in regions with high endemicity for vivax malaria.

Radical treatment consists of treatment with primaquine for 14 days (refer to *Therapeutic guidelines: antibiotic*. Version 14, 2010). Note the need for the higher dose of 0.5mg/kg/day dose in *P. vivax* infections.

Blood tests to exclude parasitaemia and G6PD deficiency should be performed before starting eradication treatment (1-2mL blood in an EDTA tube). If parasitaemia is present the person must be treated accordingly. If the person has G6PD deficiency primaquine should be withheld and further management should be discussed with an Infectious Diseases Physician.

Treatment must be reviewed both to ensure compliance and to assess any side effects (eg. haemolysis, methaemoglobinaemia, nausea, vomiting, anorexia, dizziness, epigastric distress and abdominal pains or cramps). Treatment must be taken with food to avoid gastrointestinal side effects.

Patients will be given an information sheet outlining the possible side effects from primaquine (Appendix 4).

Follow-up

Patients should be reviewed with a blood film by the admitting Infectious Diseases/Paediatric team 7 days after treatment is commenced (including a check that primaquine (where necessary) is being tolerated). The clinical review also notes the recovery of the patient and resolution of symptoms. Patients should be advised that if there is recurrence of fever in the next 3 months they should seek medical advice and repeat blood film.

Public health response

Background

The existence of competent malaria vectors such as *Anopheles farauti* s.l. in the Top End of the Northern Territory means that each case of malaria diagnosed in the Top End is a potential risk for the rest of the population. The NT has remained malaria free for many decades due to the strict isolation of cases and prompt public health response by CDC and Medical Entomology.

Malaria is scheduled as a notifiable disease under the *Notifiable Disease Act* and is urgently notifiable by both doctors and laboratories. Notification of a case of malaria is usually received from laboratories by phone but is sometimes received by fax. CDC may seek further information from clinicians. Once diagnosed, the responsibility for initiating the public health response lies with the local CDC Malaria Surveillance Officer (MSO) who then informs Medical Entomology, who may or may not instigate a response in the community.

Screening of high risk groups

Protocols have been developed for screening for malaria parasites in high risk groups on entry to the NT. Such groups include refugee migrants, illegal fisherpersons (see Appendix 5), students from high-risk areas such as Papua New Guinea (see Appendix 6), West Papua and the Solomon Islands. Over the last 10 years to 2010, 24% of all malaria infections in the NT were diagnosed by screening. Contact NT CDC for further information on 8922 8804.

Refugee migrant screening

Due to the risk of asymptomatic carriage of malaria and potential local transmission, all newly arrived refugees from Africa are screened preferably within 72 hours of arrival in Darwin.

CDC staff work in consultation with the Department of Immigration and Multicultural Affairs and Melaleuca Refugee Centre to arrange transport and testing at Royal Darwin Hospital (weekdays). All refugee migrants are tested with a thick and thin blood film and malaria antigen.

All positive malaria results (including positive antigen/negative blood film) are then phoned to the Infectious Diseases Registrar on call who then contacts the Melaleuca Refugee Centre to arrange immediate transport of the patient to the Emergency Department for assessment and treatment (see flowsheet p 4).

Refugee migrants who have a positive antigen and negative film are assessed individually by the Infectious Diseases Registrar and treated for malaria, even in the absence of parasites.

Management of co-travellers

All co-travellers of a malaria case with similar high risk malaria exposure should be tested for malaria through the NT Centre for Disease Control (CDC). This is arranged by the MSO when the patient is interviewed.

The pathology request form should include the term 'co-traveller of malaria case', the region most likely that malaria was acquired and whether the co-traveller has any symptoms suggestive of malaria. Co-travellers with positive smears are treated accordingly.

Role of CDC Malaria Surveillance Officer (MSO)

1. Confirm that the case fulfils the case definition for a confirmed or probable case¹ (see p 3).
2. Interview the case using the *Malaria Surveillance Case Questionnaire* (Appendix 2). This is usually done face-to-face if the patient is in hospital but can be done by phone.
3. Make an assessment based on the onset of the illness and the travel history about the likely source of infection. There is space in the enhanced data for 3 places of acquisition ('country of infection'), starting with the most likely. If the country is PNG, Indonesia or East Timor, the region of infection should also be ascertained and documented.
4. As part of the interview ascertain in detail the location of the case in the NT after they became unwell (first fever). Include location of residence but also ask about any travel (including dates) within the NT during that time. Document date of onset of fever.
5. If the case has been diagnosed by screening they may not have a history of fever, ask about details of location in the NT since arrival.
6. Note whether gametocytes are present in the blood film.
7. Following collection of the enhanced data, inform Medical Entomology about the case. If there are gametocytes present, Medical Entomology should be notified by phone and the completed questionnaire forwarded.
8. Arrange for screening of co-travellers. This may be through General Practitioners but can be arranged through CDC.
9. Core data entry from the *Malaria Surveillance Case Questionnaire* is entered into the NTNDS by the MSO.
10. Two weeks after interview, check case record to ascertain the whether primaquine was used (1 day or 14 day course). It might be necessary to contact the case for this information.
11. Enhanced data is then entered into the NTNDS by the MSO.

See algorithm p 13.

¹ Note that there is an NT-only probable category for malaria

² See the NTNDS data dictionary for lists of regions

³ The definition of co-traveller is not always straightforward but could be defined as anyone who was travelling with the case at the likely time of acquisition and can be contacted.

Medical Entomology

Medical Entomology should be notified of all malaria cases and will assess the need for further action. The Malaria Surveillance Officer from CDC will interview the patient as soon as possible (within working hours), complete the NT *Malaria Surveillance Case Questionnaire* (Appendix 2), fax it to Medical Entomology and file the original at CDC after notification. Of particular concern are cases with gametocytes in their blood, as gametocytes are the form of malaria parasite infective to mosquitoes (these patients should have received the first dose of artemether/lumefantrine or a stat dose of primaquine as an inpatient or in the Emergency Department before transfer to HITH).

It is important to establish with the malaria case:

- Where and when the patient was most likely infected;
- Where they have been staying in the NT since they became symptomatic (including contact details of the property owner);
- How long they have been at that location; and
- Whether they were bitten by mosquitoes between dusk and dawn at that location.

Medical Entomology investigation

The Medical Entomology investigation determines the risk of probable patient-vector contact and therefore of possible transmission to mosquitoes.

The decision for further action is made on whether infective stages of malaria are present in the blood, the location of the patient during first fever, the length of time since the first fever and the likelihood of exposure to vector mosquitoes. The proximity of the patient's residence and other places visited at night to the nearest mosquito breeding sites are determined from maps. Previous mosquito trap catches from these areas and the nearest routine mosquito monitoring site (if applicable) are assessed for the potential presence of *Anopheles* species vector mosquitoes (see Medical Entomology investigation, Appendix 7).

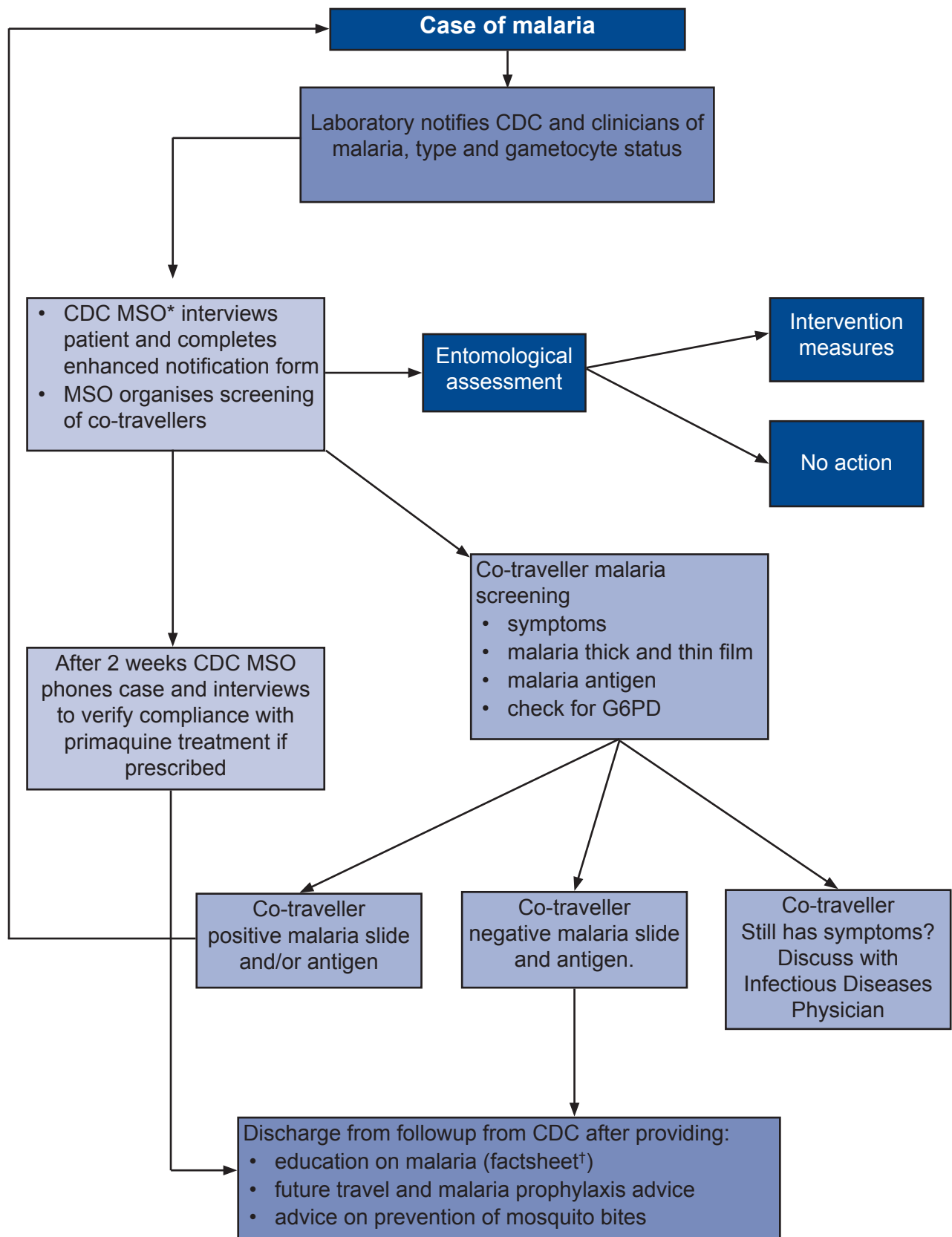
If the place of residence is a regional centre outside of Darwin, the relevant Environmental Health Officer (EHO) is alerted to the need to set mosquito traps and the possible need to conduct an adult control operation and to ensure equipment and staff availability.

Action that may be recommended if there is a possibility of local transmission may include:

- Fogging operations around the immediate residential area or the nearest mosquito breeding or harbouring area;
- Limited surveillance for malaria in the neighbourhood;
- A malaria warning pamphlet being distributed to nearby residents; and
- Doctors and Community Care/Health Centres in the area being advised to be on alert for patients with unexplained fevers or other suggestive symptoms.

Records of all confirmed malaria case investigations are maintained at CDC, Darwin.

Malaria public health response



* Malaria Surveillance Officer

† Appendix 8 and 9

APPENDIX 1

Therapeutic guidelines: antibiotic. Malaria 2010

Malaria must be considered in any patient who has visited a malarious area and presents with a febrile illness. A blood sample collected into an EDTA tube should be sent to an appropriate laboratory for examination, including thick and thin films.

A single negative blood film or negative antigen test does not exclude the diagnosis of malaria, particularly if antimalarials or antibiotics have been taken recently. Certain antibiotics that are commonly used by travellers, such as trimethoprim+sulfamethoxazole, tetracyclines and the fluoroquinolones, have some antimalarial activity. This may modify or suppress malaria symptoms and make diagnosis by blood film more difficult.

Of the 5 species that infect humans, *Plasmodium falciparum* is the most pathogenic and most resistant to standard antimalarials.

Treatment

Uncomplicated Plasmodium falciparum malaria

Artemether+lumefantrine is the drug of first choice for the treatment of uncomplicated *Plasmodium falciparum* malaria. Initial treatment in hospital is recommended. Use:

1. *artemether+lumefantrine tablets 20+120 mg*

adult and child more than 34 kg: 4 tablets (child 5 to 14 kg: 1 tablet; 15 to 24 kg: 2 tablets; 25 to 34 kg: 3 tablets) orally with fatty food or full-fat milk, at 0, 8, 24, 36, 48 and 60 hours, making a total adult dose of 24 tablets in 6 doses

OR

2. *atovaquone+proguanil tablets 250+100 mg (adult formulation)*

adult and child more than 40 kg: 4 tablets (child 11 to 20 kg: 1 tablet; 21 to 30 kg: 2 tablets; 31 to 40 kg: 3 tablets) orally with fatty food or full-fat milk, daily for 3 days

OR THE COMBINATION OF

3. *quinine sulfate 600 mg (adult less than 50 kg: 450 mg) (child: 10 mg/kg up to 600 mg) orally, 8-hourly for 7 days**

*Both quinine sulfate and bisulfate are available in 300 mg tablets. Quinine sulfate 600 mg is approximately equivalent to quinine bisulfate 900 mg. Although listed as Category D, quinine has been extensively used for treating *P. falciparum* malaria in pregnancy.

Note: Dosing regimens

Where alternative drug regimens are listed, the order of preference for use of each drug is indicated by the number placed next to its regimen (1 for first preference, 2 for second preference and so on). Drugs of equal preference are marked with the same number and are generally listed in alphabetical order.

PLUS EITHER

doxycycline 100 mg (child more than 8 years: 2.5 mg/kg up to 100 mg) orally, 12-hourly for 7 days, which need not commence on day 1

OR (for pregnant females or children)

clindamycin 300 mg (child: 5 mg/kg up to 300 mg) orally, 8-hourly for 7 days.

Atovaquone+proguanil should not be used for treatment of malaria in patients who took these drugs as prophylaxis.

Severe malaria

Urgent treatment of severe malaria is essential if the patient has any of the following:

- any degree of altered consciousness, jaundice, oliguria, severe anaemia or hypoglycaemia
- a parasite count above 100 000/mm³ (greater than 2% of red blood cells parasitised)
- the patient is vomiting or clinically acidotic.

Chloroquine-resistant *Plasmodium falciparum* must be assumed to be the infective agent. Once mandatory IV therapy has been started, seek expert advice. A large multicentre randomised controlled trial has shown mortality in severe *P. falciparum* malaria is lower when IV artesunate* is used rather than IV quinine†. Artesunate should be used in preference to IV quinine only if it is immediately available. Use:

1. *artesunate (adult and child) 2.4 mg/kg IV, on admission and repeat at 12 hours and 24 hours, then once daily until oral therapy is possible. When patient is able to tolerate oral therapy, give a full course (6 doses) of artemether+lumefantrine, as for uncomplicated P. falciparum malaria*

OR (if parenteral artesunate is not immediately available)

2. *quinine dihydrochloride IV, as outlined below.*

If quinine is used, an initial loading dose should be given unless the patient has received 3 or more doses of quinine or quinidine in the previous 48 hours, or mefloquine prophylaxis in the previous 24 hours, or a mefloquine treatment dose within the previous 3 days. Frequent measurements of blood pressure and blood glucose are required as quinine stimulates insulin secretion and can cause hypoglycaemia. Cardiac monitoring is advised if there is pre-existing heart disease.

For loading dose, use:

1. *quinine dihydrochloride (adult and child) 20 mg/kg IV over 4 hours*

OR

* Artesunate is an artemisinin derivative. It is not registered for use in Australia but is available via the Special Access Scheme. Telephone (02) 6232 8111 <www.tga.gov.au/hp/sas.htm>

† Dondorp A, Nosten F, Stepniewska K, Day N, White N for the South East Asian Quinine Artesunate Malaria (SEAQUAMAT) group. Artesunate versus quinine for treatment of severe falciparum malaria: a randomised trial. *Lancet* 2005;366(9487):717-25
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16125588

2. *quinine dihydrochloride (adult and child) 7 mg/kg IV over 30 minutes, followed immediately by 10 mg/kg IV over 4 hours.*

For maintenance dose, use:

quinine dihydrochloride (adult and child) 10 mg/kg IV over 4 hours, 8-hourly, commencing 4 hours after loading regimen is completed and continuing until the patient is able to begin oral treatment (see below).

If IV quinine is required for longer than 48 hours, seek expert advice as a dose adjustment may be necessary especially in patients with renal impairment.

When the patient has clinically improved, oral treatment can be commenced. Give a full course (6 doses) of artemether+lumefantrine, as for uncomplicated *P. falciparum* malaria. If artemether+lumefantrine is not available, use oral quinine combined with doxycycline or clindamycin, as for uncomplicated *P. falciparum* malaria, to complete a total of 7 days of treatment with quinine.

Other forms of malaria

For *Plasmodium vivax* acquired **outside** Indonesia, Timor-Leste or Pacific Island Nations (including Papua New Guinea, Solomon Islands and Vanuatu), and for *Plasmodium malariae* and *Plasmodium ovale*, use:

chloroquine 620 mg base (= 4 tablets of chloroquine phosphate 250 mg) (child: 10 mg base/kg up to 620 mg base) orally, initially, then 310 mg base (= 2 tablets) (child: 5 mg base/kg up to 310 mg base) 6 hours later and on days 2 and 3, making a total adult dose of 10 tablets.*

For *Plasmodium vivax* acquired **in** Indonesia, Timor-Leste or Pacific Island Nations (including Papua New Guinea, Solomon Islands and Vanuatu), and for less severe *Plasmodium knowlesi*†, use:

1. *artemether+lumefantrine, as for uncomplicated Plasmodium falciparum malaria*

OR

2. *mefloquine 750 mg (child: 15 mg/kg up to 750 mg) orally, initially, then 500 mg (child: 10 mg/kg up to 500 mg) 6 to 8 hours later.*

Mefloquine should not be used for treatment of malaria in patients who took this as prophylaxis.

For severe *P. knowlesi* malaria, treat as for severe malaria.

If the patient is unable to tolerate oral therapy, which is best taken with food, treat as for severe malaria and seek expert advice.

* Chloroquine phosphate 250 mg is equivalent to 155 mg chloroquine base. Chloroquine is not marketed in Australia but is available via the Special Access Scheme. Telephone (02) 6232 8111 <www.tga.gov.au/hp/sas.htm>. In adults, hydroxychloroquine can be used as an alternative if chloroquine is not available. Use hydroxychloroquine as per the chloroquine dosing schedule (hydroxychloroquine sulfate 200 mg is equivalent to 155 mg hydroxychloroquine base).

† *Plasmodium knowlesi* has recently been recognised as an important cause of malaria in parts of South-East Asia and, on microscopy, has the appearance of *Plasmodium malariae*.

To eliminate liver forms of all *P. vivax* infections, irrespective of where acquired, **add**:

*primaquine 30 mg (child: 0.5 mg/kg up to 30 mg) orally, daily with food, or if nausea occurs 15 mg (child: 0.25 mg/kg up to 15 mg) orally, 12-hourly with food. Treat for a minimum of 14 days or, in adults more than 70 kg, until a total cumulative dose of 6 mg/kg is reached**.

To eliminate liver forms of *P. ovale* infections, **add**:

primaquine 15 mg (child: 0.25 mg/kg up to 15 mg) orally, daily with food for 14 days.

If the patient relapses after the primaquine treatment, seek expert advice.

Exclude glucose-6-phosphate dehydrogenase (G6PD) deficiency before using primaquine, as severe haemolysis may occur in these patients. If the patient is G6PD deficient, seek expert advice.

Prophylaxis

The development of widespread multidrug-resistant strains of *Plasmodium falciparum* throughout the world, but particularly in South-East Asia, complicates recommendations for prophylaxis.

There is considerable variation in the malaria prophylaxis recommendations made by different health authorities and experts. Useful information regarding the malaria risk and the drug susceptibility profile for specific geographical locations is available from:

- World Health Organization. International travel and health 2010.
<www.who.int/ith/ITH2010chapter7.pdf>
- Centers for Disease Control and Prevention. Travelers' health—Yellow book.
<<http://wwwnc.cdc.gov/travel/yellowbook/2010/chapter-2/malaria-risk-information-and-prophylaxis.aspx>>

Alternatively, travel medicine clinics, advisory services and other experts can provide appropriate information. This is particularly recommended for children, pregnant women, people staying in malaria-endemic regions for more than 8 weeks, people with complex travel itineraries, and people travelling to high-risk areas.

* Primaquine failures can occur, especially when the infection has been acquired in Indonesia, Timor-Leste or Pacific Island Nations. Evidence indicates that primaquine failure and relapse with infection are more common when primaquine is not administered concurrently with the treatment for blood-stage infection, and/or if less than a total cumulative dose of 6 mg/kg is taken (eg only 14 days treatment in adults more than 70 kg).

Vector avoidance

Significant protection is conferred by the simple vector avoidance measures of:

- using effective personal insect repellent and an insecticide for indoor use;
- wearing light-coloured long trousers and long-sleeved shirts in the evening;
- sleeping in screened accommodation or using mosquito nets, which can be pyrethroid impregnated;
- avoiding outside activities between dusk and dawn;
- avoiding perfume and aftershave.

Chemoprophylaxis

There is no drug regimen that is completely safe and effective against malaria. The decision to use chemoprophylaxis must, therefore, be made by balancing the risk of disease against the potential efficacy and toxicity of the drug(s) to be used. The risk of acquiring malaria depends on factors such as the country and area visited, the time of year, the duration of visit and the type of activities undertaken. In some places, including many major cities and tourist resorts in malaria-endemic countries, the risk of malaria is low and no prophylaxis needs to be taken. Malaria prophylaxis should be considered when immigrants from malarious areas who are resident in Australia return to a malarious area.

Travellers to malarious areas should be advised that chemoprophylaxis is not always effective and any fever while away or after return needs urgent medical consultation and investigation.

As malaria can pose a serious problem for pregnant women and postsplenectomy patients, it is strongly recommended that they do not go to malarious areas, particularly those areas with drug-resistant *falciparum* malaria. Prophylaxis for children may also prove problematic. Doxycycline is not recommended for children 8 years or less. Mefloquine is not approved for use in children in Australia, but has been widely used overseas.

While the combination of chloroquine and proguanil has been widely used for malaria prophylaxis in pregnant women and children, this regimen can no longer be relied on in most areas including Africa, South-East Asia and the Pacific Island Nations.

Areas with chloroquine-susceptible malaria

For prophylaxis in areas with chloroquine-susceptible malaria (now only Central America north of Panama), use:

chloroquine 310 mg base (= 2 tablets of chloroquine phosphate 250 mg) (child: 5 mg base/kg up to 310 mg base) orally, once weekly (starting 1 week before entering, and continuing until 4 weeks after leaving the malarious area).*

* Chloroquine phosphate 250 mg is equivalent to 155 mg chloroquine base. Chloroquine is not marketed in Australia but is available via the Special Access Scheme. Telephone (02) 6232 8111 <www.tga.gov.au/hp/sas.htm>. In adults, hydroxychloroquine can be used as an alternative if chloroquine is not available. Use hydroxychloroquine as per the chloroquine dosing schedule (hydroxychloroquine sulfate 200 mg is equivalent to 155 mg hydroxychloroquine base).

Areas with chloroquine-resistant malaria

For prophylaxis in areas with chloroquine-resistant malaria (including Pacific Island Nations, South-East Asia, Indian subcontinent, China, Africa, South America and the Middle-East), use:

1. *atovaquone+proguanil tablets 250+100 mg (adult formulation)*

adult and child more than 40 kg: 1 tablet orally, with fatty food or full-fat milk, daily (starting 1 to 2 days before entering, and continuing until 7 days after leaving the malarious area)

atovaquone+proguanil tablets 62.5+25 mg (paediatric formulation)

child 11 to 20 kg: 1 tablet; 21 to 30 kg: 2 tablets; 31 to 40 kg: 3 tablets orally, with fatty food or full-fat milk, daily (starting 1 to 2 days before entering, and continuing until 7 days after leaving the malarious area)

OR

1. *doxycycline 100 mg (child more than 8 years: 2.5 mg/kg up to 100 mg) orally, daily (starting 1 to 2 days before entering, and continuing until 4 weeks after leaving the malarious area)*

OR

1. *mefloquine 250 mg (child 5 to 9 kg: 31.25 mg [= 1/8 tablet]; 10 to 19 kg: 62.5 mg [= 1/4 tablet]; 20 to 29 kg: 125 mg [= 1/2 tablet]; 30 to 44 kg: 187.5 mg [= 3/4 tablet]) orally, once weekly (starting 2 to 3 weeks before entering, and continuing until 4 weeks after leaving the malarious area).*

Doxycycline can cause oesophagitis (best avoided by taking the drug after food with plenty of fluid and remaining upright for at least 30 minutes afterwards), photosensitivity and vaginal thrush. Mefloquine is contraindicated in patients with neuropsychiatric disorders, epilepsy or cardiac conduction defects. Travellers taking mefloquine as prophylaxis should be aware that there could be significant cardiotoxic interactions if halofantrine were to be prescribed overseas subsequently for treatment of malaria. Lumefantrine is related chemically to mefloquine and halofantrine, but no significant effects on cardiac conduction, or an interaction with mefloquine, have been described.

Areas with mefloquine-resistant malaria

For prophylaxis in areas with mefloquine-resistant malaria (including parts of South-East Asia), use

1. doxycycline or 2. atovaquone+proguanil (see 'Areas with chloroquine-resistant malaria' for doses).

Stand-by emergency treatment

Some authorities recommend that travellers who elect to use chloroquine for chemoprophylaxis in areas with chloroquine-resistant malaria, or who elect to not use chemoprophylaxis, can be given a self-treatment 'stand-by' course of artemether+lumefantrine or atovaquone+proguanil, for use if medical care for a febrile illness is not likely to be available within 24 hours (see 'Uncomplicated *Plasmodium falciparum* malaria' for doses). However, travellers should be warned that uncertain diagnosis is a potential problem. In many tropical countries, travellers may be able to purchase, without a prescription, treatment courses of antimalarial drugs, but should be aware of the very common presence of counterfeit products.

APPENDIX 2. Malaria Surveillance Case Questionnaire



Northern Territory Malaria Surveillance Case Questionnaire

(All questions to be completed for each case or episode of disease)

Part A - CDC investigation

Surname	_____	First name	_____
Other names	_____	DOB	___/___/___ Age _____
HRN	_____	Indigenous status	_____
Sex	M / F	Phone	_____
Address (Street/No)	_____	Suburb/Location	_____
District notifying	Darwin / Kath / EAR / Barkly / Alice		
Place infected	_____		
True onset date	___/___/___	Notification date	___/___/___
Malaria species	<i>falciparum</i> / <i>falciparum</i> & <i>malariae</i> / <i>falciparum</i> & <i>vivax</i> / <i>malariae</i> / <i>ovale</i> / <i>knowlesi</i> / unspecified / <i>vivax</i>		
Imported case	Y / N	Hospitalised	Y / N
Admission date	___/___/___	Discharge date	___/___/___
Died	Y / N	Date of death	___/___/___
Doctor	_____	Confirmation status	Confirmed / Probable
Laboratory	_____	Specimen date	___/___/___
Specimen type (blood)	_____		
Laboratory diagnosis method	Antigen detection / Microscopy / Nucleic acid testing		

Enhanced Data

Nationality _____ Arrival date in Australia ___/___/___

Case code (please circle): Imported case / Relapsed case / Acquired in Australia (from an imported case) / Acquired in Australia (not from imported case) / Induced (ie blood tx) / Unknown

Overseas travel history*

Reason for travel (please circle): Recreation / Refugee / Visiting student / Expatriate visiting relatives / IFF / IMA / Work

Country of travel*	Region	Entry date	Departure date

*If Indonesia, Timor or PNG indicate region

Case found by screening: Y / N / Unknown If Yes reason for screen[†] _____

[†] 1. Contact tracing, 2 Co-traveller of case, 3. Illegal immigrant, 4. Migrant, 5. Other, 6. Refugee, 7. Unknown, 8. Visiting student.

Military Status (please circle) Australian military / International military / Civilian / Unknown

Co-travellers screened and given advice Y / N / No co-travellers

Prophylaxis / Pre-departure treatment

Prophylaxis used Y / N Pre-departure treatment Y / N

Drug _____ Date comm ___/___/___ Date comp ___/___/___

Compliance (circle below)

Good Missed 1 or more doses No prescribed doses taken Nil prescribed Unknown

Treatment _____	Date of first treatment: ___/___/___
Treatment prescription _____	
If not admitted to hospital was client contacted 14 days after commencing treatment to check treatment compliance? Y / N	
Was eradication treatment (primaquine) used?: Y / N No of days given: _____	
Was there infection with more than one species of malaria during this episode? Y / N	
Previous malaria diagnosed in the NT: Y / N Date: ___/___/___	
Outcome‡: S - Survived DM - Died of malaria DO - Died from another cause U - Unknown	
‡ Outcome at discharge from hospital, or if not admitted at the time of followup	

(Please tick all species detected for mixed infection)	<i>vivax</i>	<i>falciparum</i>	<i>malariae</i>	<i>ovale</i>	<i>knowlesi</i>	unknown
Malaria species						
Gametocytes detected (Y/N)						

Location history from first fever*

Start date	End date	Visiting / Resident	Street name and number	Suburb Town/ Location	Mosquito bites (Y / N / UK)	No of bites (few or many)	Time of bites (day/ after dark)

*Complete all details for each location, record all places visited after dark not only residential addresses

Has this person been made aware of the possible need for entomological access to place of residence? Y / N
Contact phone no. for property access: _____
Interviewer _____ Date ___/___/___
Entomology notified ___/___/___

Part B – Medical Entomology investigation

NT residential address and other localities of potential exposure

Traps set Yes No N/A Vector species at residence Yes No N/A

Vector report attached Yes No N/A

Address	Adequately screened Yes/No	No. of occupants	Distance to nearest breeding site (km)	Adult record no.	Highest potential vector species	No/ trap/ night

Traps set at nearest breeding and harbouring site Yes No N/A Vectors present Yes No N/A

Vector Report attached Yes No N/A

Previous vector records in vicinity in similar months Yes No N/A Report attached Yes No N/A

Part C: Conclusions

Patient vector contact Low Medium High N/A

Risk of infected vectors and subsequent transmission Low Medium High N/A

Location of risk

Recommendation for fogging: Yes No N/A Effective fogging practical: Yes No N/A

Fogging conducted: Yes No N/A

Recommendations / Action taken / Other comments

Investigating ME Officer _____

Signature of ME OIC _____

Date / /

APPENDIX 3. Use of IV artesunate for severe and complicated malaria

Background

Artemisinin is a sesquiterpene lactone extracted from the leaves of *Artemisia annua* (sweet wormwood), used in China for treatment of fever for over a thousand years. It is a potent and rapidly-acting blood schizontocide and is active against all *Plasmodium* species. It has broad activity against asexual parasites, killing all stages from young rings to schizonts. In *P. falciparum* malaria, artemisinin also kills early-stage (but not mature) gametocytes. Artesunate is a water soluble artemisinin derivative and can be given either by intravenous or intramuscular injection. A recent large multicentre randomised controlled trial has shown that mortality in severe *P. falciparum* malaria is lower when IV artesunate is used rather than IV quinine.

Role in therapy

Urgent IV treatment of severe malaria is essential if the patient has any of the following:

- any degree of altered consciousness, jaundice, oliguria, severe anaemia or hypoglycaemia
- a parasite count above 100,000/mm³ (>2% of red blood cells parasitised)
- the patient has intractable vomiting or is clinically acidotic.

Artesunate should be used in preference to IV quinine, if it is immediately available. Use artesunate 2.4 mg/kg IV bolus on admission and repeat at 12 hours and 24 hours, then once daily until oral therapy is possible. When the patient is able to tolerate oral therapy, give a full course of artemether + lumefantrine 20mg/120mg – ie. six doses of four tablets (total course of 24 tablets) given over a period of 60 hours, as for uncomplicated *Plasmodium falciparum* malaria.

If parenteral artesunate is not immediately available, IV quinine dihydrochloride should be used without delay as per Therapeutic Guidelines Antibiotic 2010 14th Edition. NT hospitals hold emergency stocks of IV quinine, even if they are also holding Artesunate stocks.

Safety

Allergic reactions are rare. Many millions of patients have been treated with an artemisinin drug, more than 10,000 of them as participants of clinical studies and at least 300 having formal neurophysiological evaluations, without any confirmed reports of neurotoxicity.

Contraindications: Known hypersensitivity to artemisinin derivatives. In view of the reduced risk of death of the mother, artesunate should be used in severe malaria in pregnancy, although studies on its safety in pregnancy are still ongoing.

Presentation and cost

Artesunate is presented as artesunic acid powder 60mg (1 vial) and sodium bicarbonate 5%, 1mL (1 ampoule). Reconstitute by adding 1mL sodium bicarbonate 5% to the artesunic acid vial (to form sodium artesunate). The artesunate solution is then diluted in 5mL 5% dextrose (ie 10mg/mL) for

IV bolus administration. The solution should be prepared freshly for each administration and should not be stored. The cost of the injection is less than \$4 per vial.

TGA approved indications

The Therapeutic Goods Administration (TGA) has agreed to allow hospital pharmacies to import and hold artesunate for Category A use in patients with severe malaria under the Special Access Scheme (SAS). Category A patients are defined in the legislation as “persons who are seriously ill with a condition from which death is reasonably likely to occur within a matter of months, or from which premature death is reasonably likely to occur in the absence of early treatment”.

NT Hospital Pharmacies at Royal Darwin Hospital (RDH), Katherine Hospital and Alice Springs Hospital stock a limited supply of a batch of parenteral artesunate which has passed endotoxin and sterility testing in an Australian TGA accredited laboratory, and which has been tested to ensure it has a satisfactory content of artesunate. As artesunate is not registered in Australia, responsibility for its use rests primarily with the medical practitioner and the patient. Use of artesunate requires the approval of the on-call Infectious Diseases Physician in consultation with the on duty Intensive Care Consultant. The treating intensive care doctor should obtain informed consent from the patient (with documentation using a hospital consent form) and is required to forward a copy of the Category A SAS form to the TGA within 28 days of its completion.

Evidence

Results from randomised trials in South-East Asia and more recently Africa comparing artesunate and quinine show clear evidence of benefit with artesunate. A randomised, controlled multi-centre trial (SEAQUAMAT study group: Bangladesh, India, Indonesia and Myanmar) with 1431 patients enrolled (Lancet 2005;366:717-25) found mortality of 15% (107/730) in the artesunate group which was significantly lower than the 22% (164/731) in the quinine group; an absolute risk reduction of 7%. Treatment with artesunate was well tolerated, whereas quinine was associated with hypoglycaemia (RR: 3.2; 95% CI: 1.3–7.8; P = 0.009).

A second large randomised trial published in the Lancet in 2010 randomized 5425 African children with severe malaria to receive IV artesunate or IV quinine (AQUAMAT). 230 (8.5%) patients assigned to artesunate treatment died compared with 297 (10.9%) assigned to quinine treatment (OR 0.75, (0.63–0.90); p=0.0022). Post-treatment hypoglycaemia was less frequent in patients assigned to artesunate than in those assigned to quinine (48/2712 [1.8%] vs 75/2713 [2.8%]; OR 0.63, 0.43–0.91; p=0.0134). Artesunate was well tolerated, with no serious drug-related adverse effects.

References

1. World Health Organisation (WHO) Guidelines for the Treatment of Malaria 2010. Available at: <http://www.who.int/malaria/publications/atoz/9789241547925/en/index.html>.
2. South East Asian Quinine Artesunate Malaria Trial (SEAQUAMAT) group. Artesunate versus quinine for treatment of severe falciparum malaria: a randomised trial. *The Lancet* 2005;366:717-25.
3. AQUAMAT group. Artesunate versus quinine in the treatment of severe falciparum malaria in African children (AQUAMAT): an open-label, randomised trial. *The Lancet* 2010; 1647-57.
4. Editors, *Therapeutic guidelines: antibiotic* Version 14, 2010. North Melbourne: Therapeutic Guidelines Ltd.

APPENDIX 4. Primaquine: patient information

Primaquine is given after the chloroquine or artemether/lumefantrine course is completed to eradicate the liver forms of *P. vivax* or *P. ovale* which can lead to relapse of malaria after months or years.

The eradication course of primaquine is given daily for 14 days and should be taken with food to prevent gastrointestinal side effects.

In case of any darkening of the urine you should stop the primaquine and contact your doctor immediately.

Common side effects

- abdominal pain, nausea and vomiting (when taken on an empty stomach)
- uncommon side effects
- haemolytic anaemia (in persons with G6PD deficiency)
- methaemoglobinaemia

Rare side effects

- cardiac arrhythmias
- hypertension
- anaemia
- leucopenia
- agranulocytosis

Contraindications

- pregnancy
- G6PD deficiency

APPENDIX 5. Guidelines for assessing unauthorised Indonesian fisherpersons for malaria

When to test fisherpersons for malaria

The fisherpersons who should be tested for malaria are those who:

1. Are febrile at the time of examination;
2. Give a convincing history of fever in the last 2 weeks, irrespective of whether they are febrile at the time of examination;
3. Give a convincing history of recent treated or untreated malaria;
4. Are co-travellers of an index case of malaria. Co-travellers are fishers from the same vessel as the index case;
5. Fishers from a different vessel that has travelled over the same route as the vessel of the index case over the prior 3-4 weeks.

What tests should be done

All fisherpersons undergoing a malaria screen should have:

1. Microscopy of thick and thin blood films; AND
2. Malaria antigen test (MAT).

Note: When co-travellers, or any other large number of fishers, are being tested for malaria, the laboratory at RDH should be informed in advance.

Implications of a positive malaria screen for fitness to travel

Fisherpersons with *P. falciparum*, *P. malariae* and *P. knowlesi* malaria are NOT fit to travel and require immediate treatment. Infections caused by *P. falciparum* and severe *P. knowlesi* can be fatal.

1. ALL cases of *P. falciparum*, *P. malariae* and *P. knowlesi* malaria and any malaria cases where the species cannot be confirmed within 24 hours require assessment in hospital.
 - This is the preferred practice in the NT to prevent life threatening complications of *P. falciparum*.
 - It is also important to avoid any risk of transmission of the parasite to the mosquito vectors that are present in the Top End of the NT.
 - Asymptomatic patients with low parasitaemia eg. refugees may be treated through Hospital in the Home (HITH) after review by the Infectious Diseases registrar or consultant at RDH.
2. Fisherpersons with confirmed *P. vivax*, or *P. ovale* can be treated by HITH or supervised by their primary health care service while in immigration detention provided:
 - a. Parasitaemia is <1%;
 - b. There are no significant co-morbidities eg. ischaemic heart disease;
 - c. Pregnancy is excluded;
 - d. There is no evidence of co-infection with *P. falciparum* malaria. This requires blood

- microscopy confirmation of species by an accredited specialist microscopist;
- e. Where the patient is gametocyte positive the first dose of artemether/lumefantrine has been given;
 - f. The patient is affected mildly by malaria ie. tolerating oral fluids and diet and has tolerated the first treatment dose;
 - g. The patient agrees to remain indoors in screened or air conditioned accommodation between dusk and dawn until artemether/lumefantrine therapy is completed;
 - h. The primary health care service can be accessed by phone if the patient becomes unwell or there is an emergency*;
 - i. The patient speaks a language for which a telephone interpreter or friend/family member can interpret eg. Swahili, French, Dinka, Arabic, Kirundi. If it is a rare language and no lingua franca can be found, the patient will have to be admitted;
 - j. Adequate follow up arrangements are able to be arranged;
 - k. The patient is notified to CDC so that CDC officers can ascertain that patients treated as HITH/outpatients do not pose a public health risk. A phone message may be left with CDC after hours; and
 - l. The case has been discussed with an Infectious Diseases (ID) Physician at RDH (available 24 hours per day) to check:
 - The above points a to l
 - Clinical condition
 - Follow-up arrangements
 - Spleen size and offer advice about activity restrictions.

If ALL of the above criteria are met, these fisherpersons can be given treatment on an outpatient basis through HITH/or supervised by the primary health care service and be certified fit to be repatriated on completion of primary treatment for malaria.

*Please note: There is a HITH nurse on call 24hours, but she only speaks English.

Unless the patient speaks English, there should be another contact person (Melaleuca Refugee Centre or friend/ neighbour) who is available to immediately attend the house if called.

For all malaria cases

1. Treatment and follow up should be instituted in accordance with the *Malaria Guidelines for Health Professionals in the Northern Territory (2012)*.

CONTACT CDC Darwin 8922 8804

APPENDIX 6. Advise to parents of students arriving in the NT from malaria endemic areas



Centre for Disease Control
Postal Address: PO Box 40596
 Casuarina NT 0811
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Centre for Disease Control

Advice to parents of students arriving in the NT from malaria endemic areas

What is Malaria?

Malaria is a parasitic disease transmitted by Anopheles mosquitoes. There are 4 types of parasites that cause malaria: *Plasmodium ovale*, *P. malariae*, *P. knowlesi*, *P. vivax*, and *P. falciparum*. The last 2 are the most common.

Primarily, malaria is an infection of the red blood cells, but other parts of the body may be affected. Malaria caused by *P. falciparum* and severe *P. knowlesi* is life threatening and can cause multiple organ damage, coma and death.

How is it spread?

Malaria is spread by *Anopheles* mosquitoes. The parasite enters the body in mosquito saliva when a person is bitten by an infected *Anopheles* mosquito. The parasite first infects the liver where it begins to multiply. After some days, the resulting parasites are released into the blood stream to infect the red blood cells, where they continue to multiply, eventually bursting the red blood cells and further infecting others. If they reach high numbers they may then clog up blood vessels and cause organ damage and severe disease. Some of the parasites in the red blood cells develop into the sexual stages (gametocytes). If these stages are ingested when a mosquito bites an infected person, they develop in the gut of the mosquito for 10 –14 days, and then enter the salivary glands, ready to infect a person at the next bite.

Where is it found?

Malaria is found throughout the tropical and subtropical regions of the world. Areas of high transmission are found predominantly in rural areas in South America (e.g. Brazil), south-east Asia (e.g. Thailand, Indonesia and East Timor), Western Pacific (Papua New Guinea, Solomon Islands and Vanuatu) and throughout sub-Saharan Africa.

The last case of locally acquired malaria in the Northern Territory was in 1962 and Australia was declared free of malaria by the World Health Organisation (WHO) in 1981. However, a number of species of *Anopheles* mosquitoes exist in the NT and the malaria parasite could be re-introduced into local mosquitoes if infected people are bitten. Transmission to mosquitoes could occur anywhere in the Top End, down to latitude of 19 degrees, which is just north of Tennant Creek.

What are the symptoms?

Symptoms appear about 9-14 days after a malaria-infected mosquito bite, and coincide with the rupture of the red blood cells. Symptoms are often delayed in people who have lived in malarious areas and who may have developed some immunity.

Typically malaria produces fever, rigors (shakes), sweating, headache, vomiting and other flu-like symptoms. Sometimes there is a 2 or 3 day period of reduced symptoms before a recurrence on the third or fourth day. Untreated, infection can progress rapidly and become life

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threatening. Malaria can kill by infecting and destroying red blood cells (anaemia) and by clogging the blood vessels to the brain (cerebral malaria) or vital organs.

Prolonged untreated malaria infection can also cause the spleen to enlarge (splenomegaly). Splenomegaly can be a problem if your child is playing sport or suffers an abdominal injury, as the spleen can rupture requiring emergency surgery. Splenic rupture can sometimes be fatal.

Why does malaria relapse?

Some forms of malaria such as *P. vivax* and *P. ovale* exist as dormant forms that remain in the liver for months or years before producing the disease.

With other forms such as *P. falciparum* and *P. malariae* (and in some cases *P. vivax*), the disease can reoccur after apparent recovery, due to either inadequate treatment or infection with a drug resistant strain.

How is it diagnosed?

Malaria is diagnosed by a blood test. The blood is examined down a microscope looking for malaria parasites inside the red blood cells. An antigen test is done at the same time, which can indicate that your child has been exposed to malaria but has no visible parasites.

What is the treatment?

All cases of *P. falciparum* malaria in the NT are admitted to hospital because it can rapidly become life threatening. Cases of malaria other than *P. falciparum* can sometimes be treated at school if the patient agrees to stay indoors between dusk and dawn. This is to avoid any risk of transmission of the parasite to the local *Anopheles* mosquitoes.

Treatment must be given in consultation with specialist physicians.

What should be done for children coming from areas with malaria?

- **Arrival screening for malaria**

Soon after your child arrives in the NT, the school will offer a malaria symptom review and a malaria blood test. This blood test will look for the malaria parasite in the blood and test for malaria antigen. If either test is positive, then your child will be seen at the hospital by the infectious diseases team and receive malaria treatment.

- **Spleen check**

When coming from an area with malaria a child's spleen can be enlarged even if active malaria is not found on screening and this is very important to recognise before engaging in, for instance, sport.

- **Early presentation to school nurse for fever or feeling unwell at any time**

Occasionally the screening tests are negative even when malaria parasites are present or are in low numbers and so in the future your child is advised to go and see the school nurse if they develop a fever or become unwell.

- **Screening on each return from holiday or visit from malaria area**

Every time your child returns from holidays malaria screening will need to occur. In some cases you may choose for your child to receive malaria preventive treatment for when they go home for the holidays. In this case, please let the school nurse know and she will organise an appointment with a general practitioner for medical review and prescription of medication. It is important that the child takes the medication according to instructions, including after return to Australia. They will be asked their medication compliance on return. If there is any doubt on their compliance, then they will require a blood test.



CONSENT

Screening will occur at St Johns College after semester break when your child has returned from holiday or visiting from a malaria area.

I _____ give consent for _____ to have a malaria symptom review and a malaria blood test (valid for the next 12 months).

Child's date of birth / / Address _____

Signature _____ Date / /

If your child needs any treatment the Health staff will ask your permission before carrying out any further evaluation of treatment.

You will be notified of the results of the screening.

For any further queries please contact Centre for Disease Control School Malaria Program Coordinator

(08) 8922 8804

APPENDIX 7. Medical Entomology investigation

More detailed information is available from the Medical Entomology (ME) document *Entomological Investigation around Malaria Cases, 2011*.

1. Assess epidemiological data provided in CDC questionnaire, if no gametocytes present no action required.
2. Assess whether routine trap information is sufficient, or extra traps will need to be set, considering location, peak vector abundance periods and prevailing environmental conditions.

Using the ME database, assess the actual or potential level of vector activity around case locations from most recent results

Include:

- Last 5 years data for similar months
- Search for *An. farauti*, *An. bancroftii*, *An. hilli*, *An. annulipes*, *An. amictus*
- Assess results and further action

If there is low potential vector presence with no extra adult trapping required based on location, peak periods and prevailing environmental conditions, no further action is required.

3. If there is a potential for vectors present, assess the nearest breeding and resting sites at the case house and within 1 km using CO₂ baited encephalitis vector survey (EVS) traps.
4. Triggers for ME action based on current entomological information:
 - >2 *An. farauti* at residence or, >10 of all other *Anopheles* sp. at residence; initiate fogging.
 - or >10 *An. farauti* or, >40 other *Anopheles* sp. at breeding harbouring sites within 1 km; assess further by setting more traps and assess new results, or initiate fog.
 - If current *Anopheles* sp. abundance is less than the trigger levels, further assessment should consider peak abundance periods and prevailing environmental conditions, which may necessitate extra trapping.
5. If precautionary fogging is to be carried out, inform the Director CDC and Chief Health Officer (CHO) by email and phone. Fogging is usually in nearest mosquito breeding or harbourage area outside residential areas. If fogging is needed in residential areas, approval is required from the CHO. Use non residual insecticides eg. bioresmethrin or similar in residential areas, and malathion for non-residential areas.
6. If trapping or fogging is required, complete the ME form 'Investigation around a proven malaria case - Medical Entomology - DoH'. A case reference is used in all documentation.
7. If ME undertakes any action: email malaria form and relevant information eg; trap results, fogging route, to the CDC Malaria Surveillance Officer (or fax 28310) and phone to confirm receipt.
8. All details of the case including fogging responses are filed in the ME database.

APPENDIX 8. Malaria factsheet



Northern Territory Government



Centre for Disease Control

December 2012

Malaria

What is Malaria?

Malaria is a parasitic disease transmitted by *Anopheles* mosquitoes. There are 5 types of parasites that cause malaria: *Plasmodium ovale*, *P. malariae*, *P. knowlesi*, *P. vivax*, and *P. falciparum*. The last 2 are the most common.

Primarily, malaria is an infection of the red blood cells, causing recurring fever of sudden onset. Malaria caused by *P. falciparum* is life threatening and can cause multiple organ damage, coma and death.

How is it spread?

Malaria is spread by female *Anopheles* mosquitoes. The parasite enters the body in mosquito saliva when a person is bitten by an infected mosquito. The parasite first infects the liver where it begins to multiply. After some days, the resulting parasites are released into the blood stream to infect the red blood cells, where they continue to multiply, eventually bursting the red blood cells and further infecting others. If they reach high numbers they may cause severe disease or even death. Some of the parasites in the red blood cells develop into the sexual stages (gametocytes). If these stages are ingested when a mosquito bites an infected person, they develop in the gut of the mosquito for 10 –14 days, and then enter the salivary glands, ready for the next bite.

Where is it found?

Malaria is found throughout the tropical and subtropical regions of the world. Areas of high transmission are found predominantly in rural areas in South America (e.g. Brazil), south-east Asia (e.g. Thailand, Indonesia and East Timor), Western Pacific (Papua New Guinea, Solomon Islands and Vanuatu) and throughout sub-Saharan Africa.

The last case of locally acquired malaria in the Northern Territory was in 1962 and Australia was declared free of malaria by the World



Health Organisation (WHO) in 1981. However, a number of species of *Anopheles* mosquitoes exist in the NT and the malaria parasite could be re-introduced into local mosquitoes if infected travellers from overseas are bitten here. The disease could become established anywhere in the Top End, down to a latitude of 19 degrees which is just north of Tennant Creek.

What are the symptoms?

Symptoms appear about 9-14 days after a bite from an infected mosquito, and coincide with the rupture of the red blood cells. Symptoms are often delayed in people who have lived in malarious areas and who may have developed some immunity.

Typically malaria produces fever, rigors (shakes), sweating, headache, vomiting and other flu-like symptoms. Sometimes there is a 2 or 3 day period of reduced symptoms before a recurrence on the third or fourth day. Untreated, infection can progress rapidly and become life threatening. Malaria can kill by destruction of red blood cells (anaemia) and by altering the function of vital organs such as the brain, (cerebral malaria) lungs or kidneys.

Why does malaria relapse?

P. vivax and *P. ovale* exist as dormant forms that remain in the liver for months or years before producing the disease.

With *P. falciparum*, the disease can reoccur after apparent recovery, due to either inadequate treatment or infection with a drug resistant strain. *P. malariae* can rarely persist with very low levels of parasite in the peripheral blood for decades.

P. knowlesi produces acute illness but does not cause relapse.

www.nt.gov.au/health

Malaria

How is it diagnosed?

Malaria is diagnosed by a blood test. The blood is examined under a microscope looking for malaria parasites inside the red blood cells. All travellers from malarious areas who become ill or develop a fever should be tested.

What is the treatment?

All cases of *P. falciparum* malaria in the NT are admitted to hospital because this form of malaria can rapidly become life threatening. Cases of malaria other than *P. falciparum* can sometimes be treated at home if the house is adequately screened and if the patient agrees to stay indoors between dusk and dawn. This is to avoid any risk of transmission of the parasite to the local *Anopheles* mosquitoes.

Treatment must be given in consultation with specialist physicians.

Before travelling overseas

Check whether the countries to which you are travelling are affected by malaria by contacting your GP, Travel Health Clinic or referring to the internet:

WHO International Travel and Health website:

<http://www.who.int/ith/en/>

Or the Centers for Disease Control and Prevention:

<http://wwwnc.cdc.gov/travel/>

If you are travelling to an affected country you will often need preventative medication. Contact your GP or Travel Clinic to organise anti-malarial medication for your trip. Some medication must be started 1 week prior to entry to the affected area.

How to protect yourself from mosquito bites

While in affected areas there are measures which should be taken to reduce the risk of mosquito bites.

- Avoid being outdoors between dusk and dawn to avoid mosquito bites, particularly in poorly lit areas, rural areas, or the outskirts of large towns.
- If accommodation is not well screened, sleep inside mosquito netting. Use insecticide treated bed nets and clothing in high risk areas.

- Avoid scents on the body, e.g. perfume, deodorants, and sweat, since these can attract mosquitoes.
- Use protective clothing in outdoor situations including covering feet, legs and arms. Loose, light coloured clothing is best.
- Use personal repellents containing DEET or picaridin on areas of exposed skin in combination with protective clothing.
- Use electric insecticide devices using repellent treated mats in indoor or enclosed areas.
- Use mosquito coils, or candle heated or gas operated devices using insecticide treated mats for patio and veranda or relatively sheltered or low wind outdoor situations.

For more information on protection measures see [Personal protection from mosquitoes](#).

If you return from a malarious area and develop symptoms

If you develop symptoms of malaria within 2 years of visiting a malarious area contact your GP or hospital emergency department immediately for an urgent medical assessment. Remember to inform the medical officer of where you have travelled as this will help determine your risk of malaria and the type of treatment required.

If you have malaria, the people you have travelled with (particularly to high risk areas such as Africa, PNG, East Timor and parts of Indonesia including Flores, Lombok and surrounding islands) should also be tested.

For more information contact your nearest Centre for Disease Control.

Darwin	8922 8044
Katherine	8973 9049
Alice Springs	8951 7540
Tennant Creek	8962 4259
Nhulunbuy	8987 0357

For more information on mosquitoes and virus ecology contact Centre for Disease Control, Medical Entomology on 8922 8901.

Further fact sheets and protocols are available at: www.nt.gov.au/health/cdc

APPENDIX 9. Malaria factsheet (Indonesian)

Apakah Malaria?

Malaria adalah penyakit yang disebabkan oleh parasit yang ditularkan oleh nyamuk *Anopheles*. Ada 5 jenis parasit yang dapat menyebabkan malaria: *Plasmodium ovale*, *P. malariae*, *P. vivax*, *P. knowlesi* dan *P. falciparum*. Dua jenis terakhir adalah yang paling sering ditemukan.

Pada dasarnya, malaria adalah infeksi pada sel-sel darah merah, yang menyebabkan demam berulang dengan tiba-tiba. Malaria yang disebabkan oleh *P. falciparum* sangat berbahaya dan dapat menyebabkan kerusakan berbagai organ tubuh, koma dan kematian.

Bagaimana malaria menyebar?

Malaria disebarkan oleh nyamuk *Anopheles* betina. Parasit masuk ke tubuh melalui ludah nyamuk pada saat seseorang digigit oleh nyamuk yang terinfeksi. Parasit ini mula-mula menyebabkan radang pada liver dimana ia berbiak. Setelah beberapa hari, parasit-parasit yang terbiak dilepas ke saluran darah untuk menjangkiti sel-sel darah merah, dimana mereka terus berbiak, sampai sel-sel darah merah menjadi pecah dan mengakibatkan infeksi pada sel-sel lainnya. Jika jumlahnya menjadi sangat besar, hal ini dapat menimbulkan sakit parah atau bahkan kematian. Sebagian dari parasit dalam sel-sel darah merah berkembang memasuki tahap jantan dan betina (gametosit). Jika pada tahap ini seekor nyamuk menggigit orang yang terinfeksi, parasit akan berkembang dalam perut nyamuk selama 10-14 hari, lalu masuk ke kelenjar ludah, siap untuk ditularkan pada saat nyamuk menggigit seseorang.

Dimana penyakit ini menyebar?

Malaria ditemukan diseluruh wilayah tropis dan subtropis di dunia. Daerah-daerah dimana terjadi banyak penularan adalah wilayah perkampungan di Amerika Selatan (misalnya Brazil), Asia Tenggara (misalnya Thailand, Indonesia dan Timor Timur), Pasifik Barat (Papua Nugini, Kepulauan Solomon dan Vanuatu) serta sub-Sahara di Afrika.

Di Northern Territory, kasus malaria yang terjangkit secara lokal terakhir terjadi pada tahun 1962 dan Australia dinyatakan bebas dari Malaria oleh World Health Organisation (WHO) pada tahun 1981. Namun, beberapa spesies nyamuk *Anopheles* masih ada di NT dan parasit malaria dapat menjangkiti nyamuk setempat bila ada pendatang yang terinfeksi dari luar negeri digigit oleh nyamuk setempat. Penyakit ini dapat berjangkit di wilayah utara NT, sampai dengan lintang 19 derajat, sedikit di utara Tennant Creek.

Apakah gejala-gejalanya?

Gejala-gejala muncul sekitar 9-14 hari setelah digigit oleh nyamuk yang terinfeksi, dan bersamaan dengan pecahnya sel-sel pembuluh darah merah. Pada orang yang tinggal di daerah yang banyak terjangkit malaria, gejala-gejalanya mungkin muncul lebih lambat karena orang tersebut mungkin memiliki sedikit kekebalan.

Pada umumnya malaria mengakibatkan demam, menggigil, keringatan, sakit kepala, muntah-muntah dan gejala serupa flu lainnya. Kadang-kadang gejala-gejala ini berkurang selama 2-3 hari namun muncul kembali pada hari ketiga atau keempat. Tanpa pengobatan, infeksi dapat berkembang dengan cepat dan membahayakan jiwa. Malaria dapat mengakibatkan kematian melalui penghancuran sel-sel darah merah (*anaemia*) dan melalui perubahan pada fungsi organ tubuh yang penting seperti otak (*cerebral malaria*), paru-paru dan ginjal.

Mengapa malaria dapat kambuh?

P. vivax dan *P. ovale* tinggal dalam bentuk tidak aktif pada liver selama berbulan-bulan atau bertahun-tahun sebelum menyebabkan munculnya penyakit. Pada *P. falciparum*, penyakit dapat kambuh kembali setelah seseorang terlihat sembuh, karena pengobatan yang kurang memadai atau orang tersebut tertular jenis yang kebal terhadap obat. *P. malariae* jarang dapat bertahan dengan tingkat parasit rendah pada darah selama puluhan tahun.

Bagaimana di-diagnosa ?

Malaria di-diagnosa melalui tes darah. Darah diperiksa dibawah mikroskop untuk dilihat apakah terdapat parasit malaria dalam sel-sel darah merah. Semua orang yang bepergian ke daerah dimana malaria berjangkit dan jatuh sakit atau mengalami demam harus diperiksa.

Bagaimana mengobatinya?

Seluruh kasus malaria *P. falciparum* di NT dikirim ke rumah sakit karena malaria jenis ini dapat membahayakan jiwa dalam waktu singkat. Kasus-kasus diluar *P. falciparum* kadangkala dapat diobati di rumah jika rumah tersebut dilindungi kawat nyamuk dan jika pasien setuju untuk tinggal dalam rumah dari senja hingga fajar. Hal ini untuk menghindari resiko penularan parasit ke nyamuk *Anopheles* setempat.

Pengobatan harus dilakukan dengan berkonsultasi pada dokter spesialis. Sebelum bepergian ke luar negeri, periksalah apakah negara-negara yang akan Anda kunjungi terjangkit malaria dengan menghubungi dokter Anda, *Travel Health Clinic* atau melalui internet:

Situs web *WHO International Travel and Health*
<http://www.who.int/ith/index.html>
 atau *Centers for Disease Control and Prevention*
 (Pusat Pengendalian dan Pencegahan Penyakit)
<http://www.cdc.gov/travel/diseases.htm#malaria>

Jika Anda akan bepergian ke negara yang terjangkit, pada umumnya Anda memerlukan obat pencegahan. Hubungi dokter Anda atau *Travel Clinic* untuk memperoleh obat anti-malaria bagi perjalanan Anda. Obat-obat tertentu perlu diminum 1 minggu sebelum memasuki wilayah yang terjangkit.

Bagaimana melindungi diri Anda dari gigitan nyamuk

Selama di daerah yang terjangkit, ada hal-hal yang dapat dilakukan untuk mengurangi resiko digigit nyamuk.

- hindari berada di luar bangunan antara senja dan fajar, terutama di daerah yang kurang penerangannya, daerah perkampungan, atau pinggiran kota besar
- tutupi badan Anda (terutama lengan, tungkai kaki dan telapak kaki) antara senja dan fajar

pakaian yang longgar dan berwarna terang adalah yang terbaik

- gunakan penolak serangga pada kulit yang tidak terlindungi pada jam-jam yang beresiko tinggi; pilih penolak yang mengandung *DEET* atau *picaradin*
- hindari bau-bauan pada tubuh, misalnya parfum, deodoran, dan keringat, karena dapat menarik nyamuk
- jika akomodasi tidak terlindung dengan baik, tidur dengan menggunakan kelambu. Gunakan kelambu dan pakaian yang telah disemprot penolak serangga di daerah beresiko tinggi
- gunakan obat nyamuk bakar atau pembasmi serangga dalam bentuk uap di ruang tertutup

Jika Anda kembali dari daerah yang terjangkit malaria dan menunjukkan gejala-gejala malaria

Jika Anda menunjukkan gejala-gejala malaria dalam 2 tahun setelah mengunjungi daerah yang terjangkit malaria, hubungi dokter atau bagian gawat darurat rumah sakit dengan segera untuk pemeriksaan medis. Jangan lupa memberi tahu petugas kesehatan tempat-tempat yang Anda kunjungi karena ini akan membantu menentukan tingkat resiko Anda terkena malaria dan jenis perawatan yang diperlukan.

Jika Anda terkena malaria, orang-orang yang bepergian bersama Anda (terutama ke daerah beresiko tinggi seperti Afrika, PNG, Timor Timur dan bagian dari Indonesia termasuk Flores, Lombok dan kepulauan sekitarnya) perlu juga diperiksa.

Untuk informasi lebih lanjut hubungi cabang CDC atau bagian Entomology Medis terdekat.

<i>Entomology Medis</i>	89228548
<i>CDC Darwin</i>	89228044
<i>CDC Katherine</i>	89739049
<i>CDC Nhulunbuy</i>	89870357
<i>CDC Tennant Creek</i>	89624259
<i>CDC Alice Springs</i>	89517549

Lembaran informasi selanjutnya dan protokol perawatan tersedia di
<http://www.nt.gov.au/health/cdc>

July 2011

Northern Territory Guidelines for
Malaria

Northern Territory Department of Health
Centre for Disease Control

www.nt.gov.au/health/cdc/cdc.shtml