

Malaria in the military and Melanesia

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MALARIA IS A DISEASE OF THE BLOOD caused by parasites of the genus *Plasmodium* and spread by mosquitoes. Falciparum malaria, which can be lethal, is the more serious form, whereas vivax malaria is better known for its ability to relapse months to years after an infected person has left a malarious area, due to residual parasites in the liver.

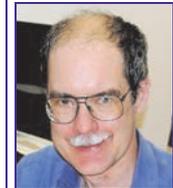
The islands of the Southwest Pacific known as Melanesia experience endemic malaria transmission in Papua New Guinea (PNG), the Solomon Islands and Vanuatu (Box 1). Fiji and New Caledonia are free of malaria risk due to the absence of the *Anopheles* mosquito vector. Malaria risk varies tremendously, from very little inside the capital cities of Port Moresby in PNG and Port Vila in Vanuatu, to extremely common in places on the northern coast of PNG such as Madang. Malaria risk is increased in areas with conditions suitable for the survival of the vector mosquito, such as warm, humid climates.

Although malaria can be transmitted in Australia, it is a rare occurrence due to the lack of parasite-infected individuals capable of infecting mosquitoes through blood feeding. The last major epidemic of malaria in Australia occurred in 1942, when people evacuated from PNG ahead of the Japanese invasion arrived in Cairns.² An exception to this general observation is the Torres Strait Islands, especially those islands immediately adjacent to PNG. Much of the malaria in the Torres Strait Islands is due to traditional travel into PNG. Many other individuals with malaria arrive in Australia after becoming ill elsewhere, with miners, soldiers and missionaries experiencing malaria as an occupational hazard of living in Melanesia.

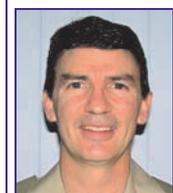
Abstract

- ◆ Although not all of Melanesia is malarious, the countries of Vanuatu, the Solomon Islands and Papua New Guinea have endemic malaria transmission.
- ◆ Malaria has been a major hazard during military training exercises in Papua New Guinea, peacekeeping missions in Bougainville, and the ongoing Regional Assistance Mission to Solomon Islands (RAMSI).
- ◆ Malaria prevention using a combination of mosquito avoidance and chemoprophylaxis is usually effective when used as directed. The three current options for malaria chemoprophylaxis are doxycycline, atovaquone-proguanil and mefloquine.
- ◆ Relapses of *Plasmodium vivax* from residual liver parasites are a major problem that is best eliminated using a post-deployment course of primaquine in those soldiers known to have a normal glucose-6-phosphate dehydrogenase status.
- ◆ Malaria control (and potentially elimination) is once again an international health priority. Currently, the basis for most malaria control programs is the distribution of insecticide-impregnated bednets. The Australian Government's Pacific Malaria Initiative provides multi-year funding for malaria control activities within the Ministries of Health of Vanuatu and the Solomon Islands.
- ◆ With Australian soldiers, sailors and federal police stationed in the Solomon Islands as part of RAMSI for the foreseeable future, malaria must remain an issue that the ADF can handle both operationally and medically.

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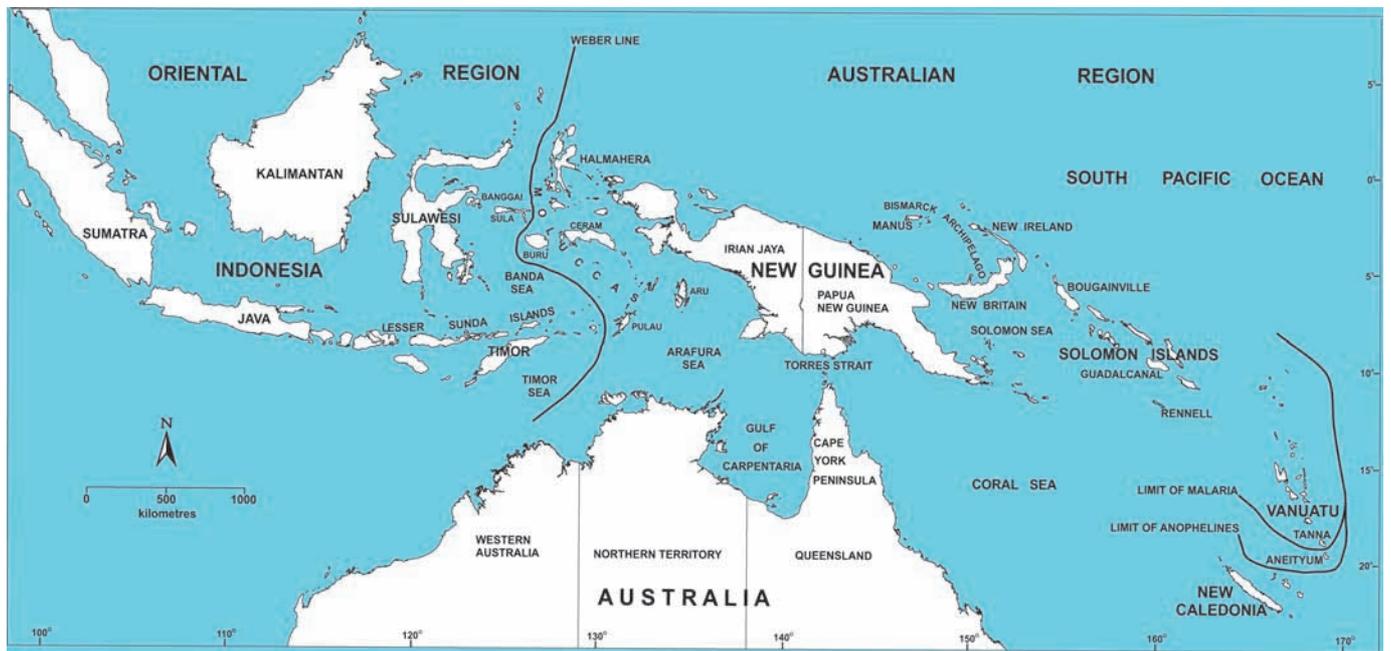
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The most common symptoms of malaria include an influenza-like illness that rapidly develops hectic fevers. Treatment of acute falciparum malaria is a medical emergency, often requiring intravenous medications such as artesunate.² As malaria can mimic any other febrile disease, it is important to consider it in patients who have travelled to Melanesia. Accurate diagnosis requires the microscopic examination of a stained blood smear; although some alternative rapid diagnostic tests are becoming available.³

Military malaria in Melanesia

Malaria is an important factor in military operations in Melanesia and is usually the leading cause of casualties in any military force. Most of the deaths of soldiers who were part of

I Southwest Pacific region showing the islands of Melanesia*



*Papua New Guinea, the Solomon Islands and Vanuatu are malaria-endemic; New Caledonia and Fiji are free of malaria.

the Australian Naval and Military Expeditionary Force that occupied German New Guinea during World War I were due to malaria. The Japanese capture of Java and invasion of New Guinea during World War II led to a medical crisis in Australia, due to an insufficient supply of antimalarial drugs.⁴ The Battle of Milne Bay was the first land victory against the Japanese Imperial Forces, but it is fortunate that the invasion came in September of 1942, because by the end of that year, Australian military operations had essentially ceased due to epidemic falciparum malaria.^{1,4} United States forces on Guadalcanal in the southern Solomon Islands were heavily infected with malaria and required months of convalescence following rotation to non-malarious areas because of the frequency of vivax malaria relapses. The failure of the Japanese Army to manage adequate malaria prevention measures provided a critical margin of victory to the Second Australian Imperial Force during 1943–1944 combat operations in Buna and Lae in PNG.⁴

The Australian Defence Force has had a continuing relationship with the Pacific Islands Regiment, which subsequently evolved into the PNG Defence Force. Malaria remains a major medical problem for the PNG Defence Force as well as any Australian soldiers deployed to PNG. Malaria has been a major hazard during training exercises held in PNG, peacekeeping missions in Bougainville, and the ongoing Regional Assistance Mission to Solomon Islands (RAMSI). Recent reviews of the ADF's experience in Bougainville and the Solomon Islands indicate that, during 1997–2007, 50 individuals had 61 episodes of malaria that were probably contracted in Bougainville, and

20 individuals had 22 cases contracted in the Solomon Islands (unpublished data, ADF Central Malaria Register).⁵⁻⁷ Although this is much lower than the 500 cases reported from East Timor for the same period, there were also far fewer soldiers who were exposed in Bougainville or the Solomon Islands.

More recently, from 1 July 2007 to 30 June 2008, there were three cases of malaria reported to the Central Malaria Register (which records all cases in deployed ADF members). One case was acquired in Timor Leste and is the first case reported out of the country for 3 years. There was a new malarial infection acquired in the Solomon Islands, and a further episode of a relapse in a member who also acquired his initial infection in the Solomon Islands. The number of cases coming from the Solomon Islands remains relatively constant, with one or two cases per year that can be attributed to service there. The overall attack rate in deployed soldiers since operations commenced in the Solomon Islands is 0.5% per year, which is a significant burden for what is largely a preventable disease. This is comparable to the attack rate of 1.3% of deployed soldiers seen in the members who deployed to Bougainville during the peacekeeping mission.

Prevention of malaria in soldiers

The basics of malaria prevention are well known: avoid mosquito bites and take antimalarial medications when exposed (also known as chemoprophylaxis). Despite this

2 Malaria chemoprophylaxis and post-deployment (terminal) prophylaxis regimens*

Generic name	Trade name	Packaging	Adult dose	Paediatric dose	Adverse effects
Doxycycline	Vibramycin Vibra-Tabs (Pfizer) Doryx (Mayne Pharma International)	100 mg	Prevention: 100 mg once daily	Prevention: 1.5 mg base/kg once daily (maximum 100 mg daily) < 25 kg or < 8 years: contraindicated 25–35 kg or 8–10 years: 50 mg 36–50 kg or 11–13 years: 75 mg > 50 kg or ≥ 14 years: 100 mg	Frequent: gastrointestinal upset, vaginal candidiasis, photosensitivity Rare: allergic reactions, blood dyscrasias, azotemia in renal diseases, hepatitis
Mefloquine	Lariam (Hoffman LaRoche)	250 mg base (salt in United States)	Prevention: 250 mg base once weekly	Prevention: < 5 kg: no data 5–9 kg: 1/8 tablet 10–19 kg: 1/4 tablet 20–29 kg: 1/2 tablet 30–45 kg: 3/4 tablet > 45 kg: 1 tablet once weekly	Common: transient dizziness, diarrhoea, nausea, vivid dreams, nightmares, irritability, mood alterations, headache, insomnia Rare: seizures, psychosis, prolonged dizziness
Atovaquone–proguanil	Malarone (GlaxoSmithKline)	250 mg atovaquone and 100 mg proguanil (adult tablet)	Prevention: 1 tablet daily	Prevention: 11–20 kg: 1/4 adult tablet or 1 paediatric tablet 21–30 kg: 1/2 adult tablet or 2 paediatric tablets 31–40 kg: 3/4 adult tablet or 3 paediatric tablets > 40 kg: 1 adult tablet	Frequent: nausea, vomiting, abdominal pain, diarrhoea, increased transaminase levels Rare: seizures, rash
Primaquine		15 mg base	Terminal prophylaxis: 30 mg base/day for 14 days	Terminal prophylaxis: 0.3 mg base/kg/day for 14 days	Common: gastrointestinal upset Occasional: haemolysis in glucose-6-phosphate dehydrogenase deficiency, methaemoglobinaemia

* Modified from Kain et al.¹⁰

knowledge, malaria discipline often breaks down when soldiers fail to take the prescribed antimalarial drugs as directed. Personal protective measures against mosquitoes have recently been reviewed.⁸ Service members entering a malarious area are usually given chemoprophylaxis with one of three medications: daily doxycycline, weekly mefloquine, or daily atovaquone–proguanil. Detailed instructions for the use of malaria chemoprophylaxis are found in Health Policy Directive 215.⁹ Box 2 shows the dosage regimens and warns of possible adverse events that have been previously

observed.¹⁰ Each medication has advantages and disadvantages, requiring some judgement in applying the general policy to an individual soldier. Guidance on selection of medications or issues with adverse events can be obtained by contacting the clinicians at the Army Malaria Institute at Gallipoli Barracks, Enoggera.

Doxycycline is the most widely used medication within the ADF, as it is effective against the drug-resistant parasites often found in South-East Asia.¹¹ Gastrointestinal tolerance of doxycycline is suboptimal, especially when soldiers do

not take the medication with a meal as instructed. Other formulations such as doxycycline monohydrate or enteric-coated tablets may be used to reduce adverse gastrointestinal events. A small proportion of soldiers do not tolerate daily doxycycline and must use alternatives. Good sun exposure precautions such as use of hats and sunscreen are required when taking doxycycline, as the drug can sensitise some people to ultraviolet light. Doxycycline prophylaxis is also effective against leptospirosis, as well as rickettsial diseases such as scrub typhus. Doxycycline must be taken daily to be effective, due to its short half-life in the blood.

Mefloquine has the advantage of requiring only weekly administration, which increases adherence as it requires less effort from the soldier. Unfortunately, mefloquine has developed a public reputation for being a dangerous drug, based on rare serious adverse events in the central nervous system. Many people given mefloquine fail to take it once they are informed, often mistakenly, about its reactogenic nature. Prescribers need to be certain that people given mefloquine understand the risk–benefit equation that balances risk of lethal malaria infection against the risk of severe adverse events. In a direct comparison of the tolerability of 6 months’ treatment with mefloquine and doxycycline in soldiers in East Timor, the rates of adverse events for the two drugs were almost identical at 57% and 56%, respectively, although 6.5% of those taking mefloquine had to cease its use because of side effects. At the end of the deployment, a questionnaire found that 94% of the soldiers who took mefloquine stated they would take it again, compared with 89% who indicated they would take doxycycline again.¹² Mefloquine should not be used by air crew or, by extension, others with critical occupational tasks, such as divers, because of the possibility of serious central nervous system adverse events.

Atovaquone–proguanil had become popular within the travel medicine community because of its few adverse events. Atovaquone–proguanil should be taken daily, but there is good evidence that its protection lasts longer,¹³ such that forgetting a single day’s medication is unlikely to place one at risk of infection (as is the case for doxycycline). However, atovaquone–proguanil’s expense often limits its use.

Primaquine is used when malaria exposure is ending, to reduce the chance of malaria relapses in the future. This strategy of medication use is known as post-exposure prophylaxis, terminal prophylaxis, or radical curative treatment. Its objective is to kill unapparent residual parasites in the liver. Primaquine is the only drug that can currently be used for this purpose, although a primaquine analogue known as tafenoquine is being investigated as a replacement.^{10,14-17} Glucose-6-phosphate dehydrogenase (G6PD)-deficient individuals should not receive primaquine because of the risk of haemolytic events, which can be severe, especially in those whose genetic roots are from the Mediterranean area (eg, Italy, Greece). All soldiers scheduled to receive primaquine should have a blood



Australian Defence Force soldier applies mosquito repellent to reduce insect contact and thus malaria risk.

determination of their G6PD status before taking any medication. Those with deficient enzyme should not receive primaquine and should be told that they are at risk of developing malaria months to years later, and that any high fever would indicate a need for them to present for immediate medical attention. Primaquine’s mode of action is not understood; the total dose received determines efficacy. Taking 30 mg daily for 14 days is the standard regimen, but this can be changed to 15 mg daily for 28 days if required because of adverse gastrointestinal events. Limited data indicate that 30 mg of primaquine twice a day for 7 days is another possible alternative, and the Army Malaria Institute is actively exploring this alternate regimen as a means to improve compliance. Most such adverse events can be ameliorated by taking the medication with food. Those experiencing relapses can be considered for longer courses of primaquine as required.

Malaria control in Melanesia

After World War II, the discovery of the long-acting insecticide DDT (dichlorodiphenyltrichloroethane), along with a new effective antimalarial drug, chloroquine, raised hopes that malaria could be controlled and possibly even eliminated.¹⁸ Elimination of malaria occurred in Europe and North America, which had previously had areas of very high malaria transmission. In many parts of Latin America and Asia, the use of residual insecticide spray on the walls of houses, coupled with effective treatment of febrile patients, was able to exert control of malaria, but required the use of extensive human and financial resources.¹⁸ Unfortunately, this effort never reached the stage of elimination in the Pacific region, except in Taiwan, Korea and a few isolated islands in Melanesia. General disappointment with the

inability of an intense but short program to control malaria, particularly in areas where malaria transmission occurred throughout the year, led to discontinuation of most malaria elimination programs and the drift of most programs attempting the less ambitious goal of malaria control. In PNG, people became disenchanted with having DDT sprayed on their walls and, once they refused to admit the spray teams to their homes, the program effectively ended. Some DDT spraying continued in highland areas of PNG and some islands in the Solomon Islands, but it was generally felt that the technology and the health infrastructure were simply not capable of malaria elimination. Bednets were found to be an alternative means to deliver insecticide to a home, such that human–mosquito contact was blocked and transmission of malaria limited.¹⁸ Killing all mosquitoes was neither promised nor possible, but killing the mosquitoes that were biting people at night was often enough to substantially decrease malaria transmission. Whether this level of malaria control could be used as a step on the way to malaria elimination by killing all the parasites in a region was an aspiration of unknown practicality.

Potential for malaria elimination in Melanesia

Once insecticide-impregnated bednets had been shown to prevent childhood mortality in multiple areas of varying transmission intensity in Africa, a new malaria control consensus was constructed that envisaged the use of bednets for entire populations, along with the use of highly effective chemotherapy in place of older drugs that had been largely overcome by the evolution of drug resistance.¹⁸ Substantial financial support by charitable groups such as the Bill and Melinda Gates Foundation and the Wellcome Foundation brought malaria elimination back to the global public health agenda after a generation-long absence caused by the perceived failure of the malaria eradication programs using DDT house spraying. There were no completely new technologies that had suddenly made malaria elimination feasible, but the moral argument was advanced that it was wrong to wait for better tools while those already available would prevent malaria mortality in some populations, especially children.¹⁹

This renewed interest gave birth to new programs such as the President's Malaria Initiative of the US Government²⁰ and the Pacific Malaria Initiative of the Australian Government. The Pacific Malaria Initiative aims to bring malaria control to the nations of Vanuatu and the Solomon Islands by working through the respective Ministries of Health to provide substantial new financial resources and Australian scientific and technology expertise.²¹ It is planned that PNG would be added to this scheme in the future. The Pacific Malaria Initiative Support Centre has been formed at the University of Queensland's School of Population Health, with the mission to bring together a

variety of government and private groups into a coordinated malaria control program tailored to each country's particular needs and resources. Although this effort is highly focused on malaria, it is felt that by concentrating on this potentially achievable target, substantial health and economic benefits could translate into stability in Australia's near neighbours in the Pacific.

Conclusion

Malaria is a significant disease to the people of Melanesia and thus to the ADF, with its interest in the stability of the Southwest Pacific region. Diseases such as malaria carry a substantial human and economic toll that may be reduced and potentially eliminated with the concerted application of public health measures that are already known to be effective. There is an inherent advantage in executing disease-control programs on small, geographically distinct islands that to some extent counterbalances the logistical difficulties of operations in Melanesia. With Australian soldiers, sailors and federal police stationed in the Solomon Islands as part of RAMSI for the foreseeable future, malaria must remain an issue that the ADF can handle both operationally and medically. Given the Australian Government's new emphasis on malaria in the Pacific Malaria Initiative, it seems likely that there will be many further opportunities for the ADF to be involved in this ambitious undertaking to help control and perhaps eliminate malaria in Melanesia.

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Competing interests

None identified. The opinions expressed here are those of the authors and do not necessarily reflect those of the Australian Defence Force.

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