Malaria notifications in the Australian Defence Force from 1998 to 2007

Nathan J. Elmes*

Australian Army Malaria Institute, Weary Dunlop Drive, Gallipoli Barracks, Enoggera 4051, Australia

ABSTRACT

We report here a retrospective analysis of all malaria cases in military personnel reported to the Australian Defence Force (ADF) Central Malaria Register from 1998 to 2007. A total of 637 cases of malaria were notified affecting 487 individuals. Of these 85.9% (547) were infected with Plasmodium vivax malaria and 10.2% (65) with P. falciparum malaria. The majority of cases were from Timor Leste (78.5%, 501/637). Malaria attack rates of 0.9% (369/40 571), 1.1% (52/4776) and 0.4% (20/5345) were seen in Timor Leste, Bougainville and the Solomon Islands, respectively. The median period following departure from a malarious country to presentation of P. falciparum was 17 d (range 1–47 d) and for a primary presentation of P. vivax malaria was 86 d (range 1–505 d). Increasing the dose of primaquine from 22.5 mg daily to 30 mg daily for 14 d for radical cure of P. vivax malaria reduced the failure rate from 46.6% (35/75) to 9.4% (17/181) in subjects returning from Timor Leste.

Malaria remains a serious problem for ADF soldiers deploying to malarious areas, particularly the incidence of relapsing vivax malaria and the tolerance of these vivax strains to primaquine.

1. Introduction

The incidence of malaria in military personnel has historically been a threat to the successful outcome of military operations, for example in the Philippines, Papua New Guinea (PNG) and the Solomon Islands during World War II.1 In more recent times malaria outbreaks continue to be a problem for military operations globally.2,3

Australian Defence Force (ADF) personnel are often deployed to malaria endemic areas. During the past decade ADF personnel have been deployed on peacekeeping and peace monitoring duties to malaria endemic regions of Bougainville in PNG, Timor Leste (formally known as East Timor) and the Solomon Islands. Exposure to malaria has also been experienced by ADF personnel deployed to Afghanistan and Iraq, and amongst personnel who have been with United Nations observer teams in the Sudan. The ADF mandates reporting of all cases of malaria acquired by its personnel through the Central Malaria Register (CMR), which is held in the Australian Army Malaria Institute.4

In an effort to protect soldiers and to reduce the incidence of malaria, the ADF must have safe and effective prophylactic drugs. However, a major impediment to this is the continual development of drug resistance by the malaria parasite. In the early 1990s the ADF recognised the emergence of chloroquine and Maloprim-resistant Plasmodium falciparum and Plasmodium vivax parasites in the Southwest Pacific region resulting in an unacceptably high incidence of malaria in ADF personnel.5,6 As such the first line chemoprophylaxis used during the review period was doxycycline, with daily (atovaquone - proguanil) (Malarone™) or weekly mefloquine (Lariam™) currently offered if doxycycline is contraindicated. The preferred treatment of uncomplicated P. falciparum is with artemether - lumefantrine (Riamet™) and the

* Tel.: +61 7 3332 4801; fax: +61 7 3332 4800.
E-mail addresses: Nathan.Elmes@defence.gov.au, nelmes1@optusnet.com.au.

1876-3413/5 – see front matter. Crown Copyright © 2010 Royal Society of Tropical Medicine and Hygiene. Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.inhe.2010.03.001
recommended treatment (including radical cure) for *P. vivax* is chloroquine (3-day course of 1 500 mg total dose) plus primaquine (30 mg daily for 14 d). Atovaquone-proguanil and mefloquine are used as alternatives.

Relapsing vivax malaria is a major concern for the ADF. Primaquine is the only licensed drug that has any activity against the liver stages (hypnozoites) of *P. vivax* though even this drug is not 100% effective. Dose regimes of 15 mg and 22.5 mg daily for 14 d have failed to prevent relapses in Southeast Asian and Southwest Pacific strains of *P. vivax* respectively.6–8 In the ADF primaquine is routinely initiated immediately after the cessation of chloroquine-primaquine treatment.12 Variance in the prophylactic medication regimens stated previously occurred in 1692 and 1535 members enrolled in trials of alternate chemoprophylactic and post-exposure prophylactic medication regimens respectively (Table 1).13–16 The denominator used for the calculation of rates of malaria incidence was determined by accessing the number of personnel deployed on the different operations from data held by Joint Operational Command. Statistical analysis of times to presentation and relapse intervals was performed to derive confidence intervals (CI’s) and *P*-values.17

### 2. Methods

All cases of malaria in ADF personnel are required to be reported to the ADF CMR managed by the Australian Army Malaria Institute. Blood films and the results of rapid diagnostic tests are to be forwarded for confirmation of the diagnosis and parasite speciation. Other information provided includes the history of previous exposure, the prophylactic medication used and post-deployment medications taken, along with the date of diagnosis and treatment details.

Malaria attack rates were calculated as the number of primary presentations over the denominator.

For the purposes of this analysis an episode was counted as a primary presentation of *P. vivax* regardless of whether it occurred in the first 28 days after departure of the malarious area, when it may have been an acute infection, or greater than 28 days when it is most likely a relapse of a previously sub-clinical presentation. Time to presentation (or latency period) of malaria infection was derived by calculating the time between departing the malarious region until the date of diagnosis with malaria. The relapse period was calculated as the time elapsed from the date of radical cure for *P. vivax* malaria and the date of diagnosis of a new episode of *P. vivax* malaria. An episode of malaria was considered a recrudescence for the purpose of calculating relapse periods if it occurred within 28 days of commencement of chloroquine-primaquine treatment.12

### Table 2

Number of malaria notifications to the Australian Defence Force Central Malaria Register by country and species from 1998 to 2007.

<table>
<thead>
<tr>
<th>Country</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Plasmodium vivax</em> (Pv)</td>
<td>433</td>
<td>85.9</td>
</tr>
<tr>
<td><em>P. falciparum</em> (Pf)</td>
<td>49</td>
<td>10.2</td>
</tr>
<tr>
<td><em>P. ovale</em> (Po)</td>
<td>1</td>
<td>0.3</td>
</tr>
<tr>
<td><em>P. malariae</em> (Pm)</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>Mixed Pf/Pm</td>
<td>2</td>
<td>0.3</td>
</tr>
<tr>
<td>Mixed Pf/Po</td>
<td>9</td>
<td>1.7</td>
</tr>
<tr>
<td>Identification unknown</td>
<td>6</td>
<td>1.4</td>
</tr>
<tr>
<td>Total by country (%)</td>
<td>501 (78.6)</td>
<td>61 (9.6)</td>
</tr>
</tbody>
</table>

* Indonesia, Malaysia, Sudan, Thailand, Papua New Guinea and one case with exposures in multiple countries throughout Africa
3. Results

A total of 637 cases of malaria involving 487 individuals were reported to the CMR during the ten year period from 1998 to 2007. The median age at time of diagnosis of the initial episode was 25 years (range 18–48 years), with 481 (98.8%) being male. The malaria cases included 547 (85.9%) \textit{P. vivax}, 65 (10.2%) \textit{P. falciparum} and 9 (1.4%) of unknown identification (Table 2). There were no deaths attributable to malaria during the reporting period. The number of cases presenting annually varied from 4 in 2005 to 395 in 2000 (Figure 1). The malaria attack rates across the deployments were 0.9% (369 of 40571), 1.1% (52 of 4776) and 0.4% (20 of 5345) for Timor Leste, Bougainville and the Solomon Islands, respectively.

Malaria was acquired more commonly in Timor Leste (501, 78.6%) than in any other country (Table 2) and the majority of these cases were relapses of \textit{P. vivax} (416 of 501, 83.0%) occurring after the soldiers returned to Australia. Of the 374 persons who failed PEP by having an initial presentation with \textit{P. vivax} or a mixed \textit{P. falciparum} and \textit{P. vivax} infection after leaving the malarious area, 114 (30.5%) went on to develop one or more relapses of vivax malaria (Figure 2). Of those who relapsed, 25–28% had successive relapsing episodes of \textit{P. vivax} with two individuals having five documented episodes of \textit{P. vivax} infection.

The median period following departure from a malarious country to presentation of \textit{P. falciparum} was 17 d (range 1–47 d). The median time to presentation for \textit{P. vivax} across all countries of acquisition was 86 days, whilst the median relapse period between confirmed episodes of \textit{P. vivax} was 99 days (Table 3). The median time to presentation for \textit{P. vivax} following standard post exposure prophylaxis on departure of the malarious country was 84 days. By comparison the median time to relapse after treatment with chloroquine and primaquine following a confirmed case of \textit{P. vivax} was 91 days. In order to compare any possible difference in geographical variation for times to presentation or time to relapse of \textit{P. vivax} the values for Bougainville and the Solomon Islands were grouped together and compared against those from Timor Leste. No significant difference was seen when comparing these two regions of acquisition for time to presentation (0.5 d, \( P = 0.96, 95\% \ CI -17.0 \) to 16.0) or time to relapse (11.5 d, \( P = 0.62, 95\% \ CI -57.1 \) to 34.1). There was also no significant difference between the median values of those whom received primaquine and doxycycline as PEP compared with those whom received primaquine and chloroquine for radical cure of \textit{P. vivax} infections (13 d, \( P = 0.26, 95\% \ CI -9.6 \) to 35.6).

The peak incidence of malaria notifications in 2000 resulted from operations in Timor Leste which started in late 1999 when ADF soldiers were first deployed. Figure 3 shows the monthly malaria notifications from Timor Leste. It identifies those whose malaria presented whilst still in Timor Leste (representing a lack of malaria awareness resulting in poor compliance with personal protective measures and chemoprophylaxis) and those whose first presentation occurred after the member left the malarious region (representing a combination of non-compliance and failure of post exposure prophylaxis). The overall rate of new infections presenting in Timor Leste for the
duration of operations from September 1999 to Dec 2007 was 0.2% (80/40 571). During the initial high tempo phase of operations between September 1999 and February 2000 the attack rate was 4.6 cases per 1000 personnel deployed whilst the rate during the later peacekeeping operation from March 2000 onwards was 0.6/1000. The rate of new infections presenting after returning to Australia following service in Timor Leste was 7.1/1000 until December 2007.

The relapse rate for members infected in Timor Leste and treated with a standard 3-day course of 1500 mg chloroquine and 22.5 mg of primaquine daily for 14 d was 46.6% (35/75) compared with 9.4% (17/181) after the primaquine dose was increased to 30 mg per day for 14 d.

4. Discussion

The ADF has had increased exposure to malaria over the past 10 years with several deployments in malaria endemic areas of the Southwest Pacific involving approximately 50000 personnel. The scale of these deployments has not been seen since the Vietnam War.

This paper identifies that malaria remains an occupational hazard to deployed defence personnel, with the largest burden of disease being amongst ADF members who have returned from the malarious region and subsequently present with relapses of *P. vivax*. Whilst *P. vivax* is rarely life-threatening in an otherwise immuno-competent and healthy soldier, there is considerable loss of manpower and capability whilst an infected soldier recovers.18 A large proportion of the malaria cases seen during the last decade were acquired in Timor Leste. The majority of these cases were acquired by the first three battalion groups who deployed between September 1999 and February 2000. The malaria rate was 7-fold higher during the initial phase of operations compared to the period after stability was restored despite troops occupying the same regions for the majority of the deployment. A similar observation occurred during a malaria outbreak in the British Army in Sierra Leone.3

There are a multitude of reasons why this situation occurs. Firstly, the awareness of the malarious risk is low at the commencement of operation. This leads to poor personal protective measures and poor compliance with chemoprophylactic medications. There may also be operational reasons preventing compliance, for example difficulty with using bed nets whilst on patrol. Once cases of malaria start to occur, awareness of the disease increases and many more resources are employed to combat transmission including increased use of environmental health personnel for implementing anti-mosquito measures as well as engineering support to eliminate breeding sites.19

In Timor Leste and Bougainville, in addition to these

---

Table 3

<table>
<thead>
<tr>
<th>Time to presentation (d)</th>
<th>Timor Leste</th>
<th>Bougainville</th>
<th>Solomon Islandsa</th>
<th>Othersb</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Plasmodium falciparum, P. vivax and mixed infections</em></td>
<td>382</td>
<td>271</td>
<td>48</td>
<td>15</td>
</tr>
<tr>
<td>Median (range)</td>
<td>83 (0–505)</td>
<td>85 (1–505)</td>
<td>79 (2–423)</td>
<td>95 (20–369)</td>
</tr>
<tr>
<td>Time to presentation (d) after PEP with primaquine of <em>P. vivax</em> malaria</td>
<td>319</td>
<td>222</td>
<td>47</td>
<td>14</td>
</tr>
<tr>
<td>Median (range)</td>
<td>84 (0–505)</td>
<td>86 (1–505)</td>
<td>79 (2–423)</td>
<td>96 (20–369)</td>
</tr>
<tr>
<td>Relapse period (d) after radical cure of <em>P. vivax</em> malaria</td>
<td>91</td>
<td>80</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Median (range)</td>
<td>99 (29–477)</td>
<td>98 (29–477)</td>
<td>97 (34–335)</td>
<td>(111–162)</td>
</tr>
</tbody>
</table>

a Only two relapse episodes notified
b Countries where infection acquired were Indonesia, Malaysia, Sudan, Thailand, Papua New Guinea and one case with exposures in multiple countries throughout Africa. Only one relapse episode notified following exposure in mainland PNG.
measures, several clinical trials were conducted involving the ADF personnel with the objective to improve the efficacy of primaquine in the prevention of relapses.\textsuperscript{13–16} The peak incidence of malaria cases presenting in Timor Leste occurred between December 1999 and January 2000; cases presenting after return to Australia peaked between March and July 2000. This correlates well with the observed median time to presentation of approximately three months for \textit{P. vivax}. The intervals reported here are much longer than those previously reported from the same region in soldiers who had been treated with a blood schizonticide only, (19–26 d vs median times of 79–96 d), suggesting that primaquine may have inhibitory effect on hypnozoites even if it doesn’t eradicate them completely.\textsuperscript{20} Figure 3 also demonstrates that the monthly number of cases increased approximately 2-fold after the soldiers returned to Australia from Timor Leste. This is indicative of the high level of malaria exposure that the soldiers experienced under field conditions and the effectiveness of doxycycline in suppressing malaria infections.

The standard use of primaquine for PEP has undoubtedly prevented many vivax infections but does have limitations. The high relapse rate of approximately 30% in soldiers following radical cure indicates exposure to primaquine tolerant strains of \textit{P. vivax} malaria. Whilst compliance with primaquine post-exposure prophylaxis is often sub-optimal on departure from the malarious region, compliance with radical cure treatment was thought to be very high amongst members who had suffered a clinical episode of malaria. The post-deployment primaquine regimen was increased in April 2000 after the high rates of malaria in the initial battalion groups became evident. A marked drop in the number of malaria cases presenting after return to Australia from Timor Leste was observed after mid-2000 coinciding with an increased awareness amongst personnel, improved vector control measures and the revised primaquine regimen.

Whilst it has become apparent that vivax malaria in South East Asia and the South West Pacific is requiring the ongoing problem of parasites developing resistance to antimalarial drugs presents a continual challenge for countries deploying military personnel to malaria endemic areas and has resulted in military organisations playing a key role in the development of many antimalarial drugs used today.

5. Conclusions

The ongoing problem of parasites developing resistance to antimalarial drugs presents a continual challenge for countries deploying military personnel to malaria endemic regions and has resulted in military organisations playing a key role in the development of many antimalarial drugs used today. Whilst rates of malaria acquisition have improved since the Vietnam War there is still a large burden of disease carried by troops operating in malarious regions of the world. This would suggest that whilst the medications may change over the years, the basic tenets of malaria control remain the same. Soldiers, particularly during periods of hostile action and high tempo operations remain highly exposed to malaria infections. The emphasis on personal protective measures and compliance with medication as well as environmental health initiatives must remain at the fore to prevent unnecessary morbidity. The lessons learnt here
are just as applicable to the civilian population working in high risk locations for prolonged periods of time, particularly mining operations and engineering projects where high tempo work-rates may be employed.

**Acknowledgements:** The author would like to thank Corporal Natalie Lehmann, Warrant Officer Derek Davis and Warrant Officer John Staley for their support in the collation of data. The author would also like to thank Michael Edstein for commenting on the manuscript. The opinions expressed are those of the author and do not necessarily reflect those of the Defence Health Service or any extant ADF policy.

**Funding:** None.

**Conflicts of interest:** None declared.

**Ethical approval:** Not required.

**References**