

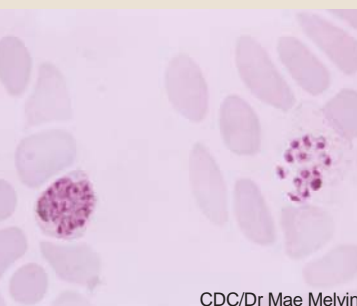


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CDC/Dr Mae Melvin



Susan Ellis/bugwood.org

## *Malaria Issue*

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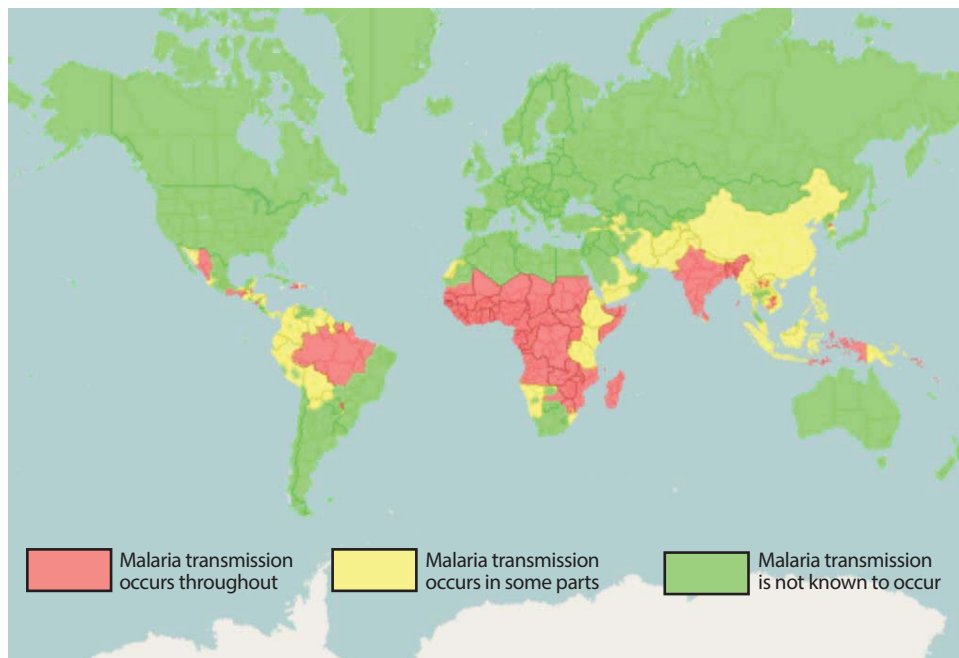
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## The Military and Its Potential Role in Malaria Elimination

James F. Cummings, MD (COL, USA)

The findings described in the two case reports of malaria on pages 8 to 9 of this issue of the *MSMR* illustrate what has been previously reported about the frequently prolonged latent period between exposure to Korean strains of *Plasmodium vivax* and the subsequent clinical presentation with overt malaria (see pages 8-14).<sup>1</sup> Both cases experienced delays of at least five months (since leaving Korea) and as long as 10 months (since their likely exposure to malaria vectors) before the onset of their symptoms. Review of their electronic health records uncovered no evidence of prior clinical symptomatology consistent with malaria. The length of the latency period may have some basis not only in the strain of *P. vivax*, but also in the relative youth and general excellent physical condition of these two soldiers. Moreover, it is possible that mild symptomatology was not reported by the soldiers or observed in clinic.

While the two cases described could have been prevented with techniques that are commonly employed in the military (e.g., avoiding geographic areas of risk or employing bed nets, residual pesticides, permethrin-treated uniforms, and chemoprophylaxis), it is reassuring that the cases were diagnosed correctly (and promptly) in a health care setting in the United States once the soldiers presented with symptoms suggestive of malaria. Moreover, the biosurveillance and product development arms of the military were part of the solution. The use of supplemental technology platforms, such as polymerase chain reaction (PCR), to complement the clinical diagnostics of slide reading and rapid diagnostic tests (RDTs) used for malaria, has increased greatly in recent years. The increasing availability of such technologies has helped to overcome the reality that expertise in reading malaria slides has



The worldwide distribution of malaria. Centers for Disease Control (CDC)

tended to wane in settings of infrequent malaria transmission.

Biosurveillance in the Pacific theater informs decision makers and key leaders. Characterization of the *Anopheles* vectors that transmit malaria in Korea, as briefly summarized by Distelhorst et al., illustrates the key role of medical entomology in understanding and abating insect-borne illnesses.<sup>1</sup> When such information is shared widely among public health organizations and scientists through publications and open access web sites such as Vectormap.org, the resources for disease vector control can be properly directed to the areas of greater need for risk mitigation.<sup>2</sup> This timely review of malaria in the Korean peninsula indicates both the key role of medical (or public health) entomologists in answering the needs of the global community, and the need for more trained medical entomologists to meet these requirements.

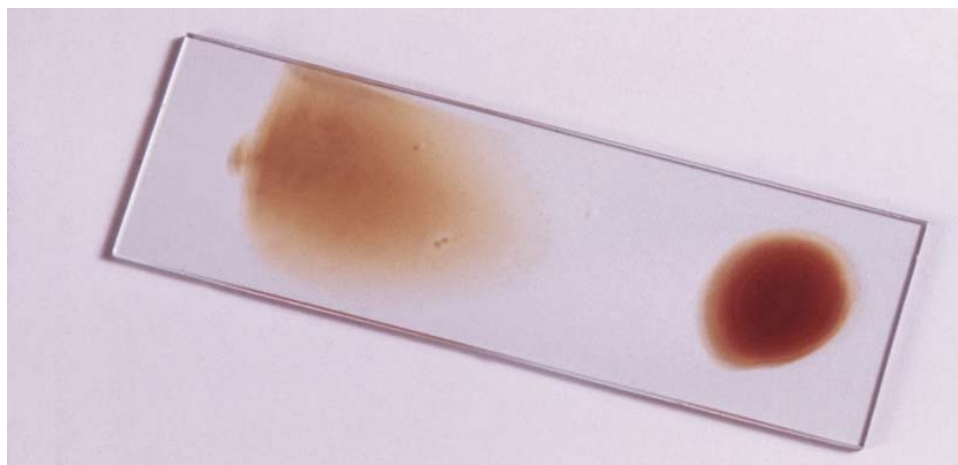
The call to understand drug resistance in malaria (and its spread) has brought to light many needs in malaria surveillance “to track emerging malaria drug resistance, improved data sharing to allow pooled analyses to identify rare events, modelling of risk factors for drug resistance, and development and validation of new approaches to monitor resistance.”<sup>3</sup> Although there have been reported failures of chloroquine chemoprophylaxis against *P. vivax* in Korea, most, if not all, have been attributed to non-compliance or low plasma levels of active metabolite. There have been no reported treatment failures linked to chloroquine resistance in *P. vivax* in Korea. The drug resistance issues in the treatment of *P. falciparum* in Southeast Asia are well known. Concerns about the transfer of these drug resistant strains of *P. falciparum* globally (mirroring the loss of chloroquine sensitivity of *P. falciparum*) have spawned

many efforts looking at this phenomenon, including a global harmonized *P. falciparum* drug resistance clinical trial, sponsored by the U.S. Department of Defense (DoD), that is currently underway.<sup>4</sup>

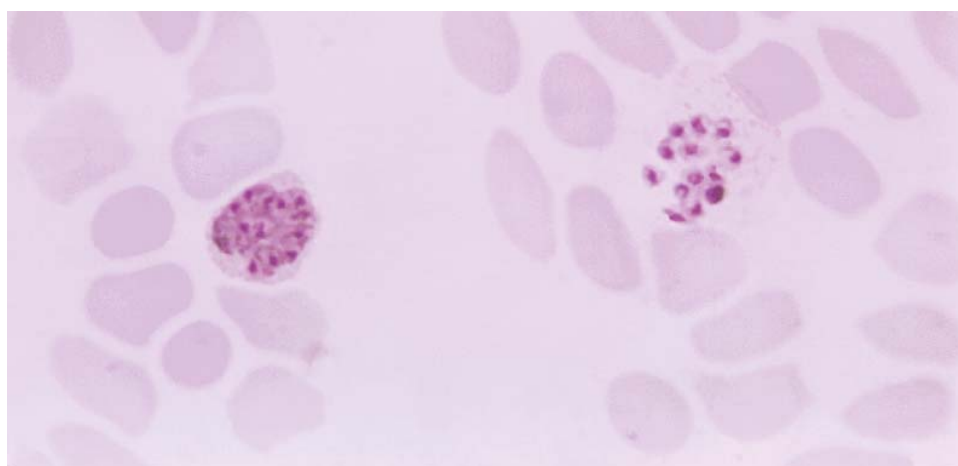
The review article also emphasizes the role of the National Malaria Eradication Service (NMES) in abating malaria transmission in Korea. It should be noted that current parlance clearly distinguishes between malaria eradication and malaria elimination. The Global Malaria Action Plan defines elimination as reducing to “zero” the incidence of locally acquired malaria infection in a specific geographic area.<sup>5</sup> Eradication, on the other hand, refers to reducing the global incidence of malaria to zero; this long-term goal will be achieved through progressive elimination in countries where feasible.

Malaria surveillance and control in the Republic of Korea bring to light the key role that military forces play in biosurveillance and global health. The military brings capacity for health surveillance, logistics, and delivery of health care services. In the settings where malaria is indigenous, such as Korea, the transient nature of host nation military service members traveling through multiple areas of a country, going to or coming from border duty, may serve as a mechanism of malaria transport from areas of high to low endemicity. This potential transfer of malaria via service members harboring *Plasmodium* parasites underscores the requirement for military populations to be included in any “malaria elimination” programs or campaigns.

Currently, efforts are underway to evaluate the disease burden of clinical and subclinical infections of malaria within host nation militaries in several areas in the lower Mekong region. These efforts will soon be coupled with programs designed to clear local national military units prior to deploying them globally in support of the United Nations and other peacekeeping missions, thereby helping to thwart the spread of drug resistant malaria. Recent discussions at the Center for Strategic and International Studies (CSIS) that involved the Gates Foundation, the Global Fund to Fight AIDS, Tuberculosis, and Malaria,



Thin and thick blood film. CDC/Steven Glenn, Laboratory & Consultation Division



Thin film photomicrograph of a blood smear showing two *Plasmodium vivax* schizonts, one immature (left) and one mature (right). CDC/Dr. Mae Melvin

the U.S. DoD, and others included local national militaries in their approach to malaria elimination. This effort would incorporate host nation militaries not only as trusted partners to assist with logistical issues in country, but also as migratory populations that could serve to carry or perpetuate malaria, if not treated as part of the malaria elimination process as a whole. Inclusion of countries’ military forces in malaria elimination programs will increase the chances of success in combating the scourge of malaria.

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## Update: Malaria, U.S. Armed Forces, 2013

U.S. service members are at risk of acquiring malaria infection when they are present in endemic areas because of long term duty assignments, participation in shorter term contingency operations, or personal travel. The numbers of cases among service members in 2012 (n=40) and 2013 (n=30) were the lowest reported during the past ten years. In 2013 over one-third of cases were attributed to service in Afghanistan (n=11) and six cases were linked to Africa. Nine cases were caused by *Plasmodium vivax*; eight cases were caused by *P. falciparum*; and one-third were reported as “unspecified” malaria. Malaria was reported from 21 different medical facilities in the United States, Afghanistan, Germany, Italy, Japan, Korea, and Cuba. The relatively low numbers of cases in 2012 and 2013 could reflect a decrease in the number of troops who served in endemic areas, improved or increased use of chemoprophylaxis and personal protective equipment, and changes in environmental factors that may influence the numbers and distribution of infected mosquitoes. Providers of care to military members should be knowledgeable regarding, and vigilant for, clinical presentations of malaria outside of endemic areas.

Malaria is a serious, often life-threatening, mosquito-borne parasitic disease. Four *Plasmodium* species are responsible for the overwhelming majority of human malaria infections: *Plasmodium falciparum* (the most deadly), *P. vivax* (the most common), *P. ovale*, and *P. malariae*. Malaria is endemic in more than 100 countries throughout tropical and subtropical regions. In 2012, malaria accounted for an estimated 207 million illnesses and 627,000 deaths worldwide; most deaths were due to *P. falciparum* infections of young children in sub-Saharan Africa.<sup>1</sup> International efforts to control malaria are working; many countries have reported reductions in the numbers of malaria cases and deaths due to malaria during the past decade.<sup>1</sup>

For centuries, malaria has threatened the health and operational capabilities of military forces in malaria endemic areas.<sup>2,3</sup> U.S. service members are at risk of acquiring malaria when they spend time in endemic regions as a consequence of long-term duty assignment, shorter-term military operations or training, and personal travel. The

U.S. Armed Forces have policies and prescribed countermeasures effective against vector-borne diseases such as malaria, including chemoprophylactic drugs, permethrin-impregnated uniforms and bed nets, and topical insect repellents containing N,N-diethyl-meta-toluamide (DEET). When cases and outbreaks of malaria do occur, they are generally due to non-compliance with indicated chemoprophylactic or personal protective measures.<sup>4,6</sup>

In the 1990s, there was a general increase in malaria incidence among U.S. service members, primarily due to *P. vivax* infections acquired near the demilitarized zone (DMZ) in Korea.<sup>7-9</sup> Since 2001, service members have been exposed to malaria due predominantly to *P. vivax* while serving in Southwest and Central Asia (particularly in Afghanistan).<sup>4</sup> Service members who conduct civil-military and crisis response operations in Africa are at risk of falciparum malaria as well as vivax malaria;<sup>5</sup> the number at risk may have increased since the establishment of the U.S. Africa Command (AFRICOM) in 2007. In 2010, several thousand U.S. military members risked

exposure to *P. falciparum* while conducting an earthquake disaster response mission in Haiti and there were at least 14 documented cases of malaria associated with the operation.<sup>6,10,11</sup> This report summarizes the malaria experiences of U.S. service members during calendar year 2013 and compares it to recent experience.

### METHODS

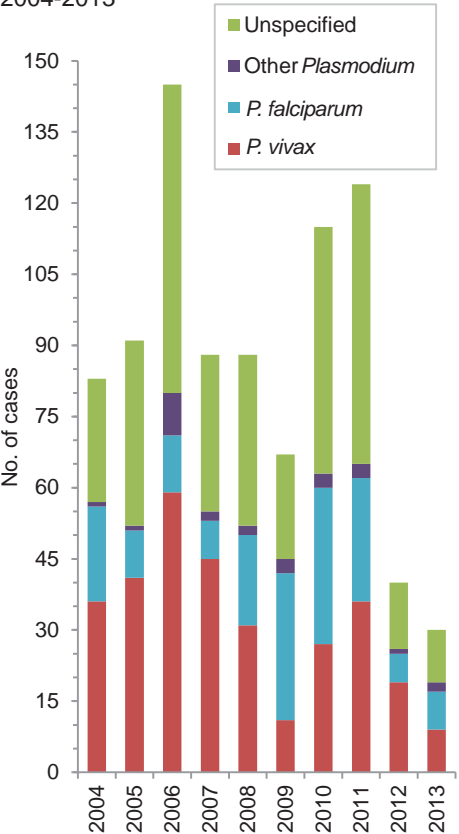
The surveillance period was January 2004 through December 2013. The surveillance population included active and reserve component members of the U.S. Armed Forces. The Defense Medical Surveillance System was searched to identify reportable medical events and hospitalizations (in military and non-military facilities) that included diagnoses of malaria (ICD-9-CM code: 084). A case of malaria was defined as an individual with 1) a reportable medical event record of confirmed malaria; 2) a hospitalization record with a primary (first-listed) diagnosis of malaria; 3) a hospitalization record with a non-primary diagnosis of malaria due to a specific *Plasmodium* species (ICD-9-CM codes: 084.0-084.3); 4) a hospitalization record with a non-primary diagnosis of malaria plus a diagnosis of anemia (ICD-9-CM codes: 280-285), thrombocytopenia and related conditions (ICD-9-CM code: 287), or malaria complicating pregnancy (ICD-9-CM code: 647.4) in any diagnostic position; or 5) a hospitalization record with a non-primary diagnosis of malaria plus diagnoses of signs or symptoms consistent with malaria (as listed in the Control of Communicable Diseases Manual, 18th Edition)<sup>12</sup> in each diagnostic position antecedent to malaria. Malaria diagnoses during outpatient encounters alone (i.e., not hospitalized or reported as a notifiable event) were not considered case-defining for this analysis.

This summary allowed one episode of malaria per service member per 365-day period. When multiple records documented a single episode, the date of the

earliest encounter was considered the date of clinical onset, and the most specific diagnosis was used to classify the *Plasmodium* species.

Presumed locations of malaria acquisition were estimated using a hierarchical classification algorithm: 1) cases hospitalized in a malarious country were considered acquired in that country; 2) case reports (submitted as reportable medical events) that listed exposures to malaria endemic locations were considered acquired in those locations; 3) cases diagnosed among service members during or within 30 days of deployment or assignment to a malarious country were considered acquired in that country; 4) cases diagnosed among service members who had been deployed to Afghanistan or Korea within two years prior to diagnosis were considered acquired in those countries; and 5) all remaining cases were considered acquired in unknown locations.

**FIGURE 1.** Malaria cases among U.S. service members, by *Plasmodium* species and calendar year of diagnosis/report, 2004-2013



## RESULTS

In 2013, 30 U.S. service members were diagnosed and/or reported with malaria. The number of malaria cases in 2013 was the lowest during the 10-year surveillance period (**Figure 1**). Thirty percent of the 2013 cases were caused by *P. vivax* (n=9) and 27 percent by *P. falciparum* (n=8) (**Table 1**). The responsible agent was “unspecified” for more than one-third (n=11) of 2013 cases. In 2013, as in prior years, most U.S. military members diagnosed with malaria were male (93.3%), active component members (90.0%), in the Army (60.0%), of white, non-Hispanic race/ethnicity (60.0%) and in their 20s (56.7%) (**Table 1**).

Of the 30 malaria cases in 2013, over one-third of the infections were considered to have been acquired in Afghanistan (n=11, 37%) and 20 percent in Africa (n=6); three infections (10%) were attributed to Korea and one to South/Central America

(**Table 2**). For the remaining nine malaria cases, no specific geographic location could be discerned from the available documentation. Of the six malaria infections considered acquired in Africa, three were linked to Nigeria, and one each to Ghana and Tanzania; for one case, a specific country was not identified (**data not shown**).

The number of Afghanistan-acquired malaria cases in 2013 (n=11) was the lowest of the 10-year surveillance period (**Figure 2**). The number of Africa-acquired cases (n=6) was similar to the annual numbers of cases from 2005 through 2007 (range: 7-8 cases), but lower than the numbers in more recent years. The number of malaria cases acquired in Korea in 2013 (n=3) was similar to the numbers in recent prior years (range, 2008-2011: 2-6 cases). Single cases were attributed to South/Central America in both 2012 and 2013.

During 2013, malaria cases were diagnosed in or reported from 21 different

**TABLE 1.** Malaria cases by *Plasmodium* species and selected demographic characteristics, U.S. Armed Forces, 2013

	<i>P. vivax</i>	<i>P. falciparum</i>	Unspecified or other	Total	% of total
Total	9	8	13	30	100.0
Component					
Active	8	8	11	27	90.0
Reserve/Guard	1	0	2	3	10.0
Service					
Army	5	5	8	18	60.0
Navy	0	3	2	5	16.7
Air Force	3	0	1	4	13.3
Marine Corps	0	0	2	2	6.7
Coast Guard	1	0	0	1	3.3
Gender					
Male	8	7	13	28	93.3
Female	1	1	0	2	6.7
Age group					
20-24	1	1	4	6	20.0
25-29	8	1	2	11	36.7
30-34	0	2	4	6	20.0
35-39	0	3	1	4	13.3
40+	0	1	2	3	10.0
Race/ethnicity					
White, non-Hispanic	8	4	6	18	60.0
Black, non-Hispanic	0	3	6	9	30.0
Other	1	1	1	3	10.0

**TABLE 2.** Number of malaria cases by geographical location of diagnosis or report and presumed location of acquisition, U.S. Armed Forces, 2013

Location of diagnosis/report	Presumed location of infection acquisition					Location total	% of total 2013 cases
	Afghanistan	Africa	Korea	South/Central America	Other location		
Bagram/Camp Lacy, Afghanistan	2	.	.	.	.	2	6.7
Sharana, Afghanistan	2	.	.	.	.	2	6.7
Fort Bragg, NC	2	.	.	.	1	3	10.0
Elmendorf-Richardson AFB, AK	1	.	.	.	.	1	3.3
Landstuhl, Germany	1	.	.	.	2	3	10.0
Vilseck, Germany	1	.	.	.	.	1	3.3
Cherry Point, NC	1	.	.	.	.	1	3.3
Salerno, Italy	1	.	.	.	.	1	3.3
Fort Carson, CO	.	1	.	.	1	2	6.7
Fort Hood, TX	.	1	.	.	.	1	3.3
Portsmouth, VA	.	1	.	.	.	1	3.3
Fort Lewis, WA	.	.	2	.	.	2	6.7
Naval Base San Diego, CA	.	.	.	.	1	1	3.3
Washington, DC	.	.	.	.	1	1	3.3
Aberdeen Proving Ground, MD	.	1	.	.	.	1	3.3
Seoul, Korea	.	.	1	.	.	1	3.3
Guantanamo Bay, Cuba	.	.	.	.	1	1	3.3
Okinawa, Japan	.	1	.	.	.	1	3.3
Yokosuka, Japan	.	1	.	.	1	2	6.7
Atlantic City, NJ	.	.	.	1	.	1	3.3
Camp LeJeune, NC	.	.	.	.	1	1	3.3
Total (% of total)	11 (36.7%)	6 (20.0%)	3 (10.0%)	1 (3.3%)	9 (30.0%)	30	100.0

medical facilities in the United States, Afghanistan, Germany, Korea, Japan, Italy, and Cuba. Nearly one-half of cases (n=14, 47%) were reported from or diagnosed outside the United States (**Table 2**). Four cases were reported each from U.S. military facilities in Afghanistan and Germany; three were reported from Japan; and single cases were diagnosed in Italy, Korea, and Cuba. The largest numbers of malaria cases treated at a single medical facility during the year were associated with Fort Bragg, NC, (n=3) and Landstuhl, Germany (n=3).

In 2013, as in recent prior years, most malaria cases among U.S. military members were diagnosed from May through October (**Figure 2**). The finding reflects the relatively high proportion of cases acquired in temperate Afghanistan and Korea as compared to tropical regions such as Africa and Haiti.

#### EDITORIAL COMMENT

In both 2012 and 2013, there were fewer cases of malaria diagnosed/reported

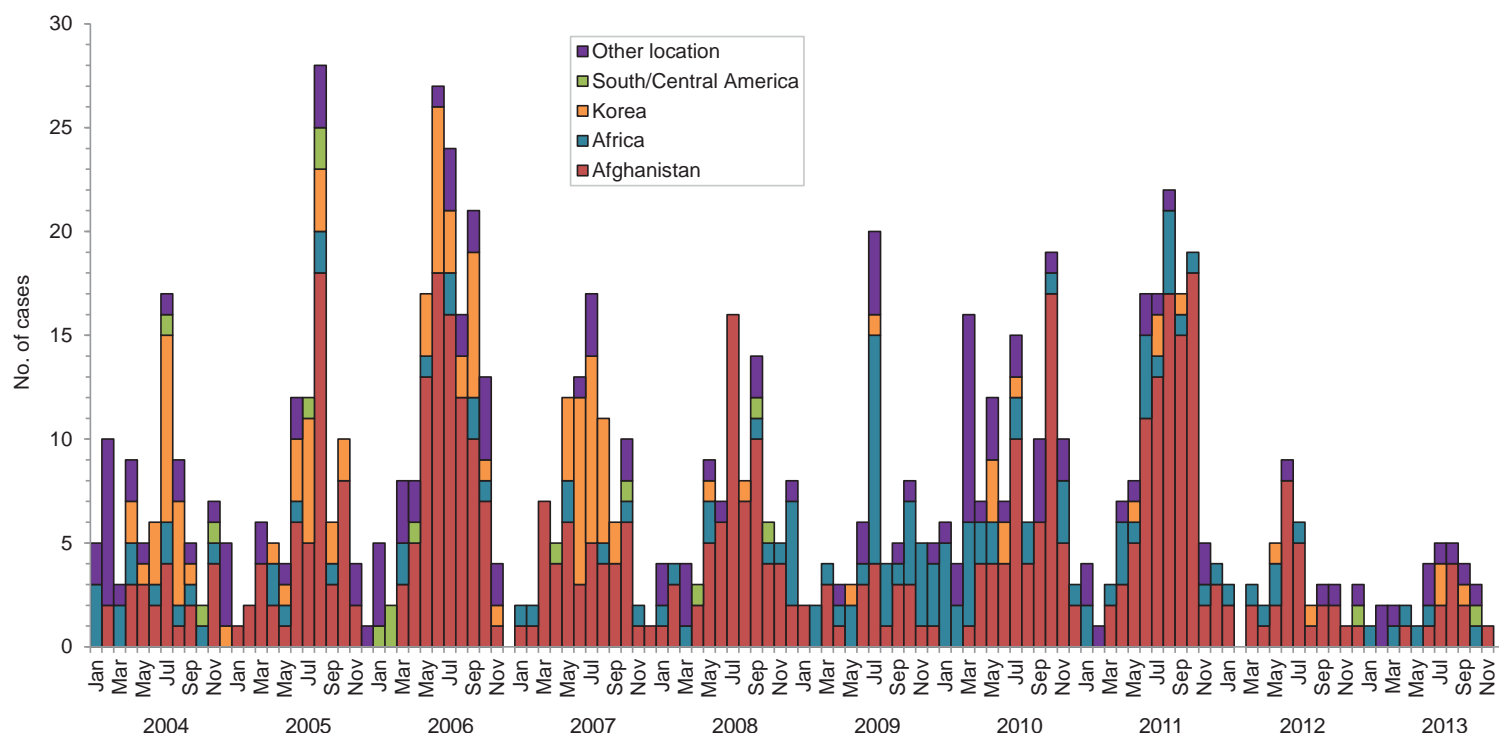
among U.S. military members than in any of the previous eight years. This report documents relatively low but continuing acquisition of malaria among U.S. military members in Afghanistan and Africa. Malaria infections attributed to Korea remained low; since 2008, there have been six or fewer Korea-acquired cases among U.S. military members each year.

Numerous factors could contribute to year-to-year changes in numbers of malaria cases. For example, the number of U.S. military members serving in malaria-endemic countries is not constant; of particular note, there were 29 percent fewer U.S. military personnel in Afghanistan on 30 September of 2012 versus 2011 and an additional three percent decrease through 31 July 2013.<sup>13</sup> Annual changes in environmental variables (e.g., humidity, rainfall, temperature) may change the numbers and distribution of mosquitoes capable of transmitting malaria. In Afghanistan, the use of water-filled irrigation ditches and temperature are significant predictors of malaria transmission.<sup>14</sup>

There are significant limitations to this report that should be considered when interpreting the findings. For example, the ascertainment of malaria cases is likely incomplete; some cases treated in deployed or non-U.S. military medical facilities may not have been reported or otherwise ascertained. Only malaria infections that resulted in hospitalizations in fixed facilities or were reported as notifiable medical events were considered cases for this report. Infections that were treated only in outpatient settings and not reported as notifiable events were not included as cases. Also, the locations of infection acquisitions were estimated from reported relevant information. Some cases had reported exposures in multiple malarious areas, and others had no relevant exposure information. Personal travel to, or military activities in, malaria-endemic countries were not accounted for unless specified in notifiable event reports.

As in prior years, in 2013, most malaria cases among U.S. military members were treated at medical facilities remote from malaria endemic areas; of note, 21 medical

**FIGURE 2.** Malaria among U.S. service members, by estimated location of infection acquisition, 2004-2013



facilities treated any cases, and 14 facilities treated only one case each during the past year. Providers of acute medical care to service members (in both garrison and deployed settings) should be knowledgeable of, and vigilant for, the early clinical manifestations of malaria – particularly among service members who are currently or were recently in malaria-endemic areas (e.g., Afghanistan, Africa, Korea). Care providers should also be capable of diagnosing malaria (or have access to a clinical laboratory that is proficient in malaria diagnosis) and initiating treatment (particularly when *P. falciparum* malaria is clinically suspected).

Continued emphasis on standard malaria prevention protocols is warranted; all military members at risk of malaria should be informed in detail of the nature and severity of the risk; they should be trained, equipped, and supplied to conduct all indicated countermeasures; and they should be closely monitored to ensure compliance. Personal protective measures against malaria include the proper wear of permethrin-impregnated uniforms; the use of bed nets and military issued

DEET-containing insect repellent; and compliance with prescribed chemoprophylactic drugs before, during, and after times of exposure in malarious areas. Furthermore, other methods for controlling the hazard that do not rely on participation and supervision of the population at risk should continue to be explored and implemented in order to achieve more sustainable and effective malaria prevention efforts.

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# Report of Two Cases of Vivax Malaria in U.S. Soldiers and a Review of Malaria in the Republic of Korea

John T. Distelhorst, DO (MAJ, USA); Rodd E. Marcum, MD, MPH (MAJ, USA); Terry A. Klein, PhD (COL [Ret], USA); Heung-Chul Kim, PhD; Won-Ja Lee, PhD

This report describes two cases of vivax malaria in U.S. Army soldiers who acquired their infections at a training area in the Republic of Korea during 2012, but developed symptoms and were diagnosed more than six months later, long after they had returned to the United States. The report provides a historical perspective regarding the epidemiology of temperate climate vivax malaria, particularly in Korea, and relevant aspects of malaria prevention and control.

## CASE REPORTS

Case 1: On 1 July 2013, a 28 year old male active duty Army noncommissioned officer (NCO) stationed at Joint Base Lewis-McChord (JBLM), WA, developed a headache, chills, and undulating fever with temperature spikes to 103°F orally. Six days later he sought care at the Madigan Army Medical Center (MAMC) Emergency Department (ED). Based on his cyclic fever and prior assignment in Korea where vivax malaria is endemic, malaria was suspected.

A rapid malaria test was positive for *Plasmodium* species antigen and an initial blood smear was positive for *Plasmodium* species parasites. *Plasmodium vivax* was confirmed at the MAMC laboratory using real-time Reverse Transcription Polymerase Chain Reaction (rRT-PCR) on 8 July 2013. The soldier received 1 gram of chloroquine phosphate in the ED and after admission to MAMC received three 500 mg doses at 6, 24, and 48 hours after the initial dose. Primaquine phosphate, 30 mg base, was initiated on day 1 (after admission to MAMC) following evaluation for glucose-6-phosphate dehydrogenase (G6PD) deficiency and continued daily as an outpatient for 14 days. The patient was discharged on hospital day 2 after all symptoms had resolved.

Case 2: On 16 July 2013, a 25 year old male active duty Army NCO stationed at JBLM, WA, presented to his unit's troop medical clinic (TMC) after one day of fever, malaise, and body aches. During the initial evaluation his vital signs were normal and he had no significant findings on physical examination. Given his vague acute symptomatology and the absence of overt physical signs, malaria was not considered a potential diagnosis. The soldier was diagnosed with a viral syndrome, returned to full duty, and prescribed ibuprofen for symptom relief.

On 26 July he presented to the MAMC ED with a rectal temperature of 106°F, abdominal discomfort, and slurred speech. Medical history revealed three distinct nocturnal febrile episodes associated with chills and soaking sweats during the interval since his initial presentation ten days earlier. Malaria was suspected and a blood smear performed at the MAMC laboratory was positive for *Plasmodium* species parasites. Rapid malaria testing was negative and cerebrospinal fluid analysis was unremarkable. *Plasmodium vivax* was confirmed by rRT-PCR at the MAMC laboratory on 26 July 2013.

The soldier received 1 gram of chloroquine phosphate in the ED and after admission to MAMC he received three 500 mg doses at 6, 24, and 48 hours after the initial dose. Primaquine phosphate, 30 mg base, was initiated on day 1 (after admission to MAMC) following evaluation for G6PD deficiency and continued daily as an outpatient for 14 days. The patient's mental status returned to baseline as his fever resolved and he was discharged on hospital day 2 with improvement in his symptoms. Complete resolution of symptoms did not occur until 28 days after treatment initiation.

Both cases had been assigned to the same infantry company located at Camp Casey, Pyeongtaek, Republic of Korea

(ROK), just prior to their redeployment to JBLM, WA. Case 1 was there from November 2011 through December 2012 and Case 2 from February 2012 through February 2013. Both cases reported no foreign travel since leaving the ROK, denied travel to malaria endemic regions before being deployed to the ROK, and had served in Iraq (Case 1: April 2007-May 2008 and September 2009-August 2010; Case 2: September 2009-August 2010).

## PCR testing

Malaria rRT-PCR testing at MAMC targets the highly conserved region of the 18S rRNA subunit gene to screen for the presence of *Plasmodium* species. Positive specimens are further tested to determine the *Plasmodium* species as described by the Molecular Diagnostics Laboratory at MAMC.<sup>1</sup>

## Disease investigation

Both soldiers were interviewed and their medical and training histories, exposure to biting mosquitoes at their base camp and areas where they had trained, use of personal protection when mosquitoes were biting, and other pertinent information were recorded. Electronic medical records and medical protection system (MED-PROS) entries were reviewed. The investigations showed that both soldiers had been assigned to the same mechanized infantry company while deployed to the ROK and had participated in the same field training exercise (FTX) from 23 August to 7 September 2012 at Dagmar North, a U.S. operated training area. The training area encompasses a large pond, wheeled and tracked vehicle ruts due to military activities, and low lying areas that flood and retain water during rains. The site is bounded by the Imjin River on the east, north, and south

and is proximate to wetland rice paddies, forested hills, and the demilitarized zone (DMZ) separating North and South Korea.

During the FTX at Dagmar North, 50 soldiers conducted mechanized infantry operations while there was free-standing water that forced participants to sleep atop their armored vehicles and precluded use of the tents and bed nets that had been provided. Both soldiers reported large numbers of mosquitoes while training at Dagmar North during the FTX; both reported receiving many bites despite the proper use of Army Combat Uniforms (ACUs) (e.g., shirt sleeves rolled down and trousers tucked into boots during the day), and frequent topical applications of DEET repellent. However, boots were not worn during the evening hours when sleeping on their vehicles and neither soldier reported permethrin treatment of their ACUs prior to the FTX, nor could they determine the ages of their uniforms.

Malaria chemoprophylaxis was not prescribed while deployed to the ROK. The unit to which they were assigned during the FTX did not complete the standard pre-deployment processing that was customary for units that trained near the DMZ. Furthermore, neither soldier remembered receiving a medical briefing during in-processing at the Replacement Centers when first arriving in the ROK or a medical threat briefing prior to the FTX.

Review of available electronic health records failed to disclose visits to medical facilities with signs or symptoms consistent with malaria prior to their July 2013 presentations at MAMC. After completion of treatment for uncomplicated malaria with chloroquine and primaquine, both soldiers had complete resolution of their symptoms and were returned to full duty.

#### EDITORIAL COMMENT

The investigation of two closely related *P. vivax* malaria cases revealed that neither soldier had been in a known malaria endemic country within four to six months prior to their clinical presentations; however, about 10 months prior to the onsets of their symptoms both had participated in the same FTX at Dagmar North near the

DMZ separating North and South Korea where *P. vivax* malaria is endemic. Neither soldier reported taking malaria chemoprophylaxis at any time while in the ROK. The soldiers' descriptions of the conditions during the FTX depict a major degree of exposure to biting mosquitoes unabated by the proper wear of the ACUs and use of DEET mosquito repellent. Given the known increased risks of malaria transmission near the DMZ in Korea, their acquisitions of malaria are not surprising.

The two cases presented here highlight several issues of importance for military leaders and clinical and public health practitioners in the U.S. Armed Forces: 1) the ROK was ostensibly free of malaria from 1979 to 1993; however, since vivax malaria re-emerged in 1993, it has been responsible for nearly 30,000 cases among Korean service members, veterans, and civilians as well as members of the U.S. Armed Forces who have served there; 2) although the incidence of malaria in the ROK is declining, it remains a threat, particularly to those who train, work, or visit areas near the DMZ; and 3) many of the cases of *P. vivax* malaria acquired in Korea are marked by relatively long incubation (prepatency) periods. As such, the clinical expressions of Korea-acquired malaria infections often are delayed until months after the last exposures to mosquito vectors. A more thorough review of these issues follows.

#### REVIEW

For millennia, malaria posed a major health threat to human populations of all inhabited continents; malaria also threatened expeditionary military forces that operated in malaria endemic regions. On the Korean Peninsula, illnesses compatible with the clinical symptoms of malaria (referred to as Haru-geori) were reported over many centuries.<sup>2</sup> However, it was not until 1913, during the Japanese occupation of Korea, that the malaria parasite was definitively identified in the blood of its Korean victims.<sup>3</sup> After World War II and the division of Korea along the 38th parallel, malaria continued to be a major health threat in both North Korea (Democratic People's Republic of Korea, DPRK) and the

ROK. During the Korean War from 1950 to 1953, approximately 15 percent of all febrile illnesses among ROK Army personnel were attributed to malaria.<sup>4,5</sup>

Following the Korean War, because of the large numbers of reported vivax malaria cases in its population, the ROK government, with the assistance of the World Health Organization (WHO), created the National Malaria Eradication Service (NMES) in 1959, and in 1960 malaria was specified as a notifiable disease.<sup>6,7</sup> The NMES conducted mass malaria blood surveys and reported that the majority of cases during 1961 to 1965 were from Gyeongsangbuk Province (Figure 1).<sup>8</sup>

The NMES established a passive case detection (PCD) malaria surveillance program in 1961, and utilized PCD and active case detection (ACD) from 1963 to 1965 that involved health centers, hospital/clinic medical providers, and school nurses throughout the country. As an additive

**FIGURE 1.** Map of the Republic of Korea with provinces and metropolitan areas (MA)



measure, the NMES established an indoor residual pesticide application program in 1963 using dichlorodiphenyltrichloroethane (DDT), but the program was discontinued after the second year since there were no observed differences in the incidence of malaria cases between sprayed and unsprayed villages. Therefore, the ACD and PCD programs, with the associated treatment of malaria positive patients, were the primary malaria control measures and were deemed responsible for the rapid decline in malaria cases that ensued.

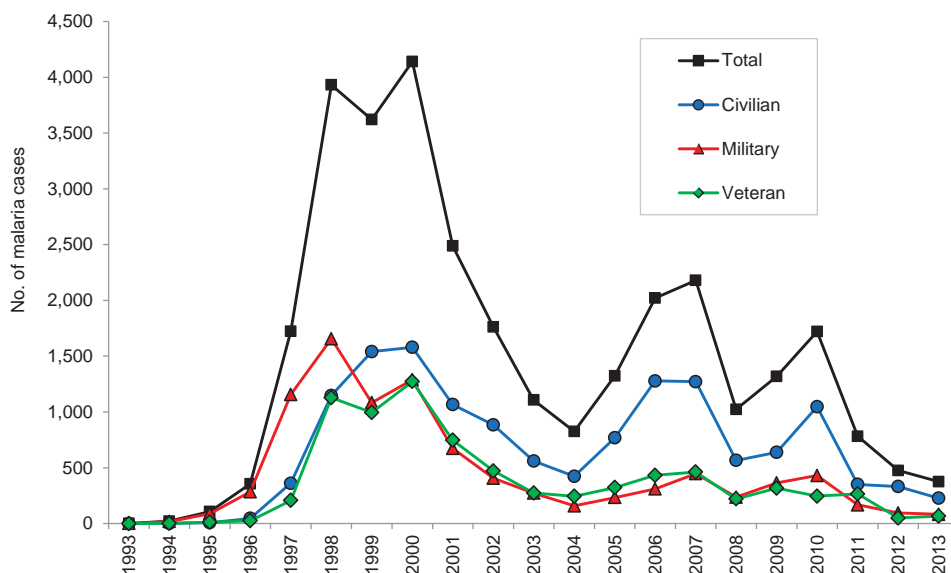
As a result of this success and relatively low numbers of malaria cases that followed, the NMES was disbanded in 1969 and the operational control of malaria was assigned to the provincial governments with planning and supervision by the Bureau of Health.<sup>8,9</sup> As a result, limited ACD and PCD surveillance continued in malaria endemic areas until 1972 when all specific malaria control/eradication activities were terminated. In 1976 and 1978, only single indigenous malaria cases were reported from Korea; in turn, in 1979 the WHO declared the ROK "malaria free."<sup>10</sup> From 1979 until 1993 there were no reported cases of malaria infection acquired in the ROK.

### The reemergence of malaria in Korea

The demilitarized zone (DMZ) of Korea is a 248 kilometer long and 4 kilometer wide fortified zone that divides the Korean peninsula. Malaria reemerged in 1993 when a ROK soldier who had been deployed to the southern boundary of the DMZ with no history of travel outside of Korea was diagnosed with vivax malaria.<sup>11</sup>

Similarly, a U.S. soldier assigned to the ROK during 1993 developed vivax malaria (C. Mason, personal communication). Although the subsequent increased incidence of malaria in the ROK was linked to presumed exposure to malaria-infected mosquitoes in proximity to the DMZ, the paucity of data available from the DPRK hindered assessments for factors responsible for the reemergence of malaria along the southern border of the DMZ. There is evidence that malaria reemerged in the DPRK prior to 1993

**FIGURE 2.** Number of malaria cases reported by the Korea Center for Disease Control and Prevention, 1993-2013<sup>a</sup>



<sup>a</sup>Cases are provisional for 2013

and then spread to areas near the DMZ whereby infected mosquitoes dispersed to the southern boundary of the DMZ.<sup>12-14</sup> Although the DPRK did not report the reemergence of vivax malaria in that country until 1998,<sup>8,13,15,16</sup> its appearance in the ROK was geographically consistent with areas in the DPRK where large numbers of malaria cases were reported (e.g., over 100,000 cases in 1999).<sup>17</sup>

In 1994, following the reemergence of malaria near the DMZ in the ROK, cases were reported among civilians residing near the DMZ.<sup>18</sup> Through the rest of the 1990s, annual numbers of malaria cases increased dramatically among ROK civilian, veteran, and military populations and more than 4,000 cases were reported in 2000 (**Figure 2**).<sup>13,14</sup>

In each year from 1993 through 1998, there were more cases among ROK Army soldiers than either military veterans or civilians. In 1997, the ROK military initiated a malaria chemoprophylaxis program in an attempt to reduce the impact of malaria transmission from the ROK Army to nearby civilian communities. The program included the administration of hydroxychloroquine (400 mg base weekly beginning the 3rd week of June to the end

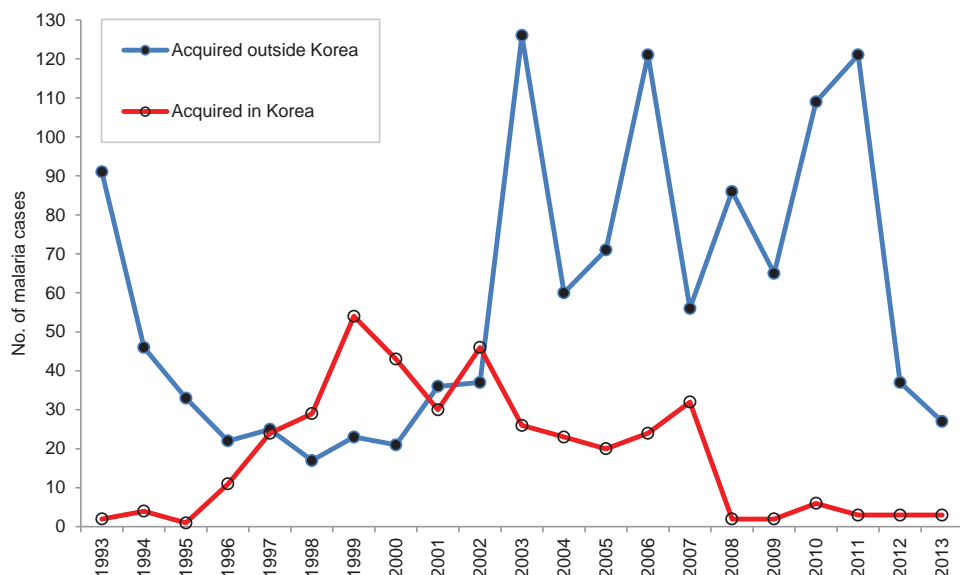
of September) followed by terminal prophylaxis with primaquine (15 mg base daily for 14 days) to ROK Army soldiers who were deployed to the highest malaria risk areas. Starting with 16,000 soldiers in 1997, the number of ROK soldiers placed on chemoprophylaxis gradually increased to a high of 196,000 by 2007 before declining to 90,000 by 2012. In 1997, DEET repellent in a cream was made available to ROK soldiers; notably, compliance with this measure was low.

Unlike malignant tertian malaria (*falciparum* malaria), benign tertian malaria (*vivax* malaria), present in the ROK, has a very low mortality rate. To date, there have not been any reported deaths among nearly 30,000 individuals who were diagnosed with vivax malaria attributed to exposure in the ROK.

After the reemergence of malaria in the ROK in 1993, the annual numbers of cases of malaria among U.S. military members due to exposure in the ROK and among Korean Augmentation Troops to the U.S. Army (KATUSA) soldiers assigned to U.S. Army units in Korea rapidly increased. Among U.S. military members from 1998 through 2000 and in 2002, the annual numbers of cases of malaria acquired in the



**FIGURE 3.** Number of malaria cases among U.S. service members attributed to exposure in the Republic of Korea (ROK) or to exposure in areas other than the ROK



ROK exceeded those acquired anywhere else in the world (Figure 3). Notably, after 2007, malaria cases dramatically decreased among U.S. military members serving in the ROK; the decline followed the replacement of ill-kempt tents with air conditioned barracks at Warrior Base near the DMZ. However, at unimproved training sites where soldiers conduct field training activities near the DMZ, barracks are not available; as such, service members must sleep in tents or on their vehicles during evening hours when mosquito biting is most intense and malaria transmission risk is highest.

Following the reemergence of malaria in the ROK, it was suggested that malaria would rapidly spread throughout the Korean peninsula. This concern was prompted by two considerations: 1) it was well established that populations of *Anopheles sinensis*, thought to be the primary mosquito vector and associated with wet land rice farming, were high throughout the ROK;<sup>5,6,8,18-25</sup> and 2) in light of the relative frequency with which vivax malaria remained latent in malaria-infected ROK soldiers while deployed to malaria high-risk areas near the DMZ, there was an expectation that many of these soldiers (veterans) would not become ill - and serve

as reservoirs for spreading malaria - until after they had returned to their homes throughout the country.<sup>17,26</sup>

It is difficult to determine the times and locations of acquisition of vivax malaria infections in the ROK due to the often long prepatency of temperate zone vivax malaria. However, two analyses of the distribution of malaria cases from 2001 to 2007 and from 2006 to 2010 showed that 84.8 percent and 85.8 percent, respectively, of all malaria cases in the ROK were diagnosed in Gyeonggi and Gangwon Provinces and associated Incheon and Seoul Metropolitan Areas (Figure 1).<sup>17</sup>

During 2001 to 2007, 95.6 percent and 97.9 percent of the cases of malaria in the ROK civilian and military populations, respectively, were diagnosed among persons from these northern areas, while only 65.8 percent of cases among veterans came from these areas. The remaining cases among veterans were diagnosed to the south, where veterans accounted for 70.7 percent of all malaria cases.<sup>17</sup> Similarly, from 2006 to 2010, 94.2 percent and 95.9 percent of the malaria cases among ROK civilian and military populations, respectively, were diagnosed in Gyeonggi and

Gangwon Provinces and associated metropolitan areas, but only 50.8 percent of the veterans' cases were reported from that area (Table 1).

In addition, a 1998 epidemiological survey of 339 ROK civilians diagnosed with malaria south of Gyeonggi and Gangwon Provinces showed that 46.3 percent of the cases were attributable to exposure near the DMZ, further highlighting the area bordering the DMZ as the principal area of transmission.<sup>8</sup> The unexpectedly high numbers of malaria cases reported from Seoul and Incheon Metropolitan Areas are likely due to: 1) better quality of care at larger hospitals than at smaller medical clinics located near the DMZ; and 2) patients who resided in Seoul or Incheon, but worked or were exposed near the DMZ. Based on these and other data, the U.S. Department of Defense's National Center for Medical Intelligence (NCMI) assesses that the highest malaria risk areas in the DPRK and the ROK are along the DMZ.

#### Vectors of vivax malaria in Korea

Despite the high populations of *Anopheles* mosquitoes throughout the ROK, the threat of malaria south of the northernmost provinces - although not zero - has remained relatively low. A possible explanation for these observations has arisen from advanced studies of the relevant mosquito vectors. In 2005 it was shown that there were five distinct species belonging to the *Anopheles* Hyrcanus Group in the ROK, which includes *An. sinensis* sensu stricto (s.s.), *An. lesteri*, *An. pullus*, *An. belenrae*, and *An. kleini*, that could not be distinguished by morphological characteristics alone; speciation requires the use of costly and less timely DNA polymerase chain reaction (PCR) technology.<sup>27-29</sup>

Following application of PCR techniques, it was reported that *An. lesteri* was abundant along the western coastal areas and islands near the DMZ, while *An. kleini*, *An. pullus*, and *An. belenrae* accounted for more than 50 percent of all *Anopheles* species collected near Panmunjom (DMZ).<sup>30,31</sup> In contrast, in a limited number of studies of areas south of Seoul, *An. sinensis* s.s. accounted for 80-100 percent of all *Anopheles* specimens collected.

**TABLE 1.** Distribution of the mean annual number of malaria cases diagnosed in large metropolitan areas and Provinces of the Republic of Korea for military members, civilians,<sup>a</sup> and veterans<sup>b</sup> of military service, 2006-2010

Province/ metropolitan area	All cases in Korea		Civilian <sup>a</sup> cases only		Military cases only		Veteran <sup>b</sup> cases only	
	Mean no. annual cases	% total	Mean no. annual cases	% total	Mean no. annual cases	% total	Mean no. annual cases	% total
Total	1,655	100.0	963	100.0	357	100.0	335	100.0
Northernmost	1,420	85.8	907	94.2	343	95.9	170	50.8
Gyeonggi	751	45.4	447	46.4	230	64.5	74	22.0
Gangwon	138	8.4	42	4.3	86	24.2	10	3.1
Incheon	304	18.4	263	27.3	19	5.4	22	6.7
Seoul	226	13.7	156	16.2	6	1.8	64	19.0
Central	117	7.1	30	3.1	7	2.1	80	23.9
Chungnam	20	1.2	7	0.7	1	0.4	12	3.6
Chungbuk	20	1.2	8	0.9	1	0.2	11	3.2
Gyeongbuk	26	1.6	5	0.5	3	0.8	18	5.4
Daejeon	15	0.9	4	0.4	1	0.3	10	3.0
Daegu	23	1.4	5	0.5	1	0.2	18	5.3
Ulsan	13	0.8	1	0.1	1	0.2	11	3.2
Southernmost	118	7.1	26	2.7	7	2.1	85	25.4
Jeonbuk	21	1.2	5	0.5	1	0.4	15	4.4
Gyeongnam	28	1.7	5	0.6	1	0.4	21	6.4
Gwangju	10	0.6	2	0.2	0	0.0	8	2.4
Jeonnam	18	1.1	7	0.7	2	0.6	9	2.7
Busan	38	2.3	6	0.6	2	0.7	30	8.9
Jeju	3	0.2	1	0.1	0	0.1	2	0.6

<sup>a</sup>Civilian includes former military members who separated from service two or more years previously.

<sup>b</sup>Veteran refers to former and retired soldiers within two years after separation from active duty service.

Vector competence studies are very limited, but preliminary results showed that *An. kleini*, *An. pullus*, and *An. lesteri* are relatively good vectors of vivax malaria, while *An. sinensis* s.s. is a poor vector, as assessed by counts of malaria sporozoites in the salivary glands of the respective species (R. Ubalee, personal communication).<sup>32-35</sup> While *An. belenrae* has been incriminated as a vector, vector competence for this species has not been evaluated. In summary, the mosquitoes that appear to be the most efficient vectors of malaria (i.e., *An. lesteri*, *An. pullus*, and *An. kleini*) are most prevalent near the DMZ where malaria transmission risks are greatest. These data support that *An. sinensis* s.s. is a poor vector of vivax malaria and provide a rationale for why malaria has not spread more extensively to the southern region of the ROK.

### Prolonged incubation for Korean vivax malaria

Vivax malaria with a prolonged incubation period was first recognized in Korea by Hasegawa in 1913, when Japanese soldiers returned from Korea to Japan, where there was no malaria, and developed malaria several months later.<sup>3</sup> Prolonged incubation periods for “Korean” vivax malaria became highlighted when over 2,000 U.S. soldiers developed malaria 6 to 18 months after they returned from the Korean Theater in 1950.<sup>36</sup> By the end of 1951, there were over 12,000 malaria cases reported in the U.S., mostly attributed to exposure in the ROK and with many of the cases reported 6 to 10 months after their return.<sup>36</sup>

Studies in the late 1940s revealed that 8-aminoquinolines were effective against tissue stages (gametocytes and liver stage

malaria parasites).<sup>37</sup> However, it was not until the fall of 1951, when service members returning from Korea to the U.S. were administered primaquine (15 mg daily for 14 days), that the incidence of malaria among veterans who returned to the U.S. from the Korean War was significantly reduced.

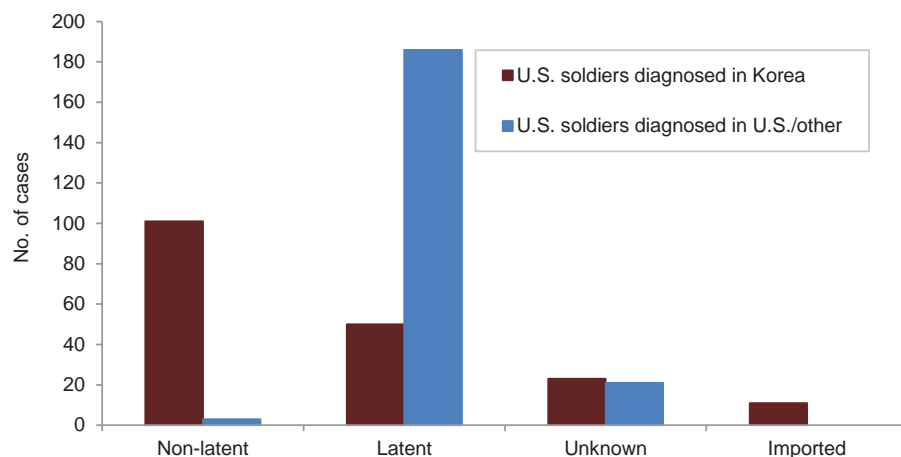
Later it was shown that short incubation period (non-latent, usually 12-21 days) and prolonged incubation period (latent, usually 6-18 months) prepatent temperate zone vivax malaria populations were present.<sup>38,39</sup> It also was shown that the proportion of short incubation (non-latent) malaria increased as larger numbers of sporozoites were injected into patients.<sup>38,40</sup> When mosquitoes infected with a North Korean strain were allowed to feed on volunteers, 24.7 percent demonstrated symptoms 14 to 22 days after being bitten, while 75.3 percent developed symptoms from 5 to 13 months later.<sup>39</sup> Similarly, of U.S. soldiers who developed malaria associated with service in Korea from 1996 to 2007, 31.8 percent developed non-latent malaria, while 68.2 percent developed malaria 1 to 18 months later.<sup>26</sup>

Of all malaria cases among U.S. service members (n=384) and KATUSAs (n=44) attributed to exposure in the ROK and for whom incubation periods were determined, the majority (70.3%) were considered latent clinical onset cases (i.e., >1-16 months after exposure); 29.7 percent were considered non-latent clinical onset cases; and 44 cases were indeterminate (Figure 4).

Among U.S./KATUSA military members, the earliest clinical presentations of latent malaria cases were observed in December following the malaria season, with peak numbers observed from June to August before decreasing to a low in October. Park et al. reported non-latent malaria among ROK soldiers as early as June, following increases in mosquito populations from May and warming temperatures that decreased the intrinsic parasite cycle.<sup>13</sup> Similarly, non-latent malaria cases among U.S./KATUSA military members were first reported in July, with peak numbers observed in August to September when mosquito populations were high. The



**FIGURE 4.** Number of U.S. military malaria cases diagnosed in the U.S. and the Republic of Korea (ROK) and attributed to exposure in the ROK or imported from malaria endemic countries, 1993-2013



timing of clinical expressions of latent cases coincides with the beginning of the malaria season in Korea, while the timing of non-latent cases augments the malaria transmission cycle of patient-mosquito-patient.

Of the 385 malaria cases among Americans attributed to exposure in the ROK, there has only been one case reported (2007) in a U.S. civilian. The affected individual resided in Paju County, which is considered a malaria high-risk area near the DMZ.

### Malaria prevention in U.S. service members

The increased numbers of malaria cases among U.S. and KATUSA military personnel similarly increased as numbers of malaria cases in ROK populations increased. In response to this increasing threat, the U.S. Forces Korea, Eighth U.S. Army, and 18th Medical Command further emphasized the use of preventive medicine measures (PMM), use of chloroquine chemoprophylaxis, and mosquito control when warranted.<sup>41-43</sup> Although insecticide fogging for mosquitoes was recommended for U.S. bases where the majority of malaria cases were identified,<sup>44</sup> it was later shown that fogging had no significant effect on mosquito populations, so it was discontinued. However, tents (where soldiers were housed during training) and both exterior and interior walls of buildings were treated

with residual insecticides at Warrior Base and Rodriguez Range, where U.S. military personnel train.

A malaria chemoprophylaxis program initiated in 1998 (weekly chloroquine from mid-May through mid-October followed by terminal prophylaxis with primaquine) was curtailed in 2000, except for a few areas where soldiers permanently resided and where there is an increased risk due to outdoor activities during the evening hours when soldiers are in civilian clothes. There was a dramatic decrease in the number of malaria cases observed from 2008 through 2013 (0-5 cases annually) following the construction of air conditioned barracks that replaced ill-kempt tents at Warrior Base where soldiers are housed while conducting training. To further reduce risks of malaria transmission at Warrior Base, a malaria high-risk training area, soldiers also are issued permethrin-treated bed nets as secondary barriers of protection while sleeping in air conditioned barracks.

### Possible chloroquine resistance

Due to the widespread use of hydroxychloroquine among the ROK military, it has been suggested that chloroquine resistance will develop in the ROK. In the ROK, it has been shown that most malaria cases reported in areas where prophylaxis policies were instituted were the result of

noncompliance.<sup>45</sup> Chemoprophylaxis failures were largely due to inadequate plasma concentrations of hydroxychloroquine in 71 percent of the ROK soldiers evaluated despite soldiers reporting regular administration of hydroxychloroquine, while only 8 percent demonstrated sufficient concentrations. Clinical trials during 2007 indicated a potential for the development of biological resistance at the prophylactic dosages, but not at therapeutic treatment doses; in addition, noncompliance among ROK soldiers was identified as a key factor.<sup>46</sup> Chemoprophylaxis failures also were reported for U.S. military personnel, but all were identified as due to noncompliance (missing 1 or more weekly doses). Thus, while there are chemoprophylaxis failures among the ROK and U.S. military, most such failures are attributed to insufficient plasma levels of hydroxychloroquine (ROK soldiers) or noncompliance.

Vivax malaria continues to pose a serious health threat to U.S. and ROK military forces, in addition to U.S. and ROK civilian populations, north of Seoul and near the DMZ, where vector populations are abundant. During hostilities, disaster relief, or humanitarian efforts, which further expose populations to biting mosquitoes during peak periods of malaria transmission, vivax malaria will pose a greater threat to U.S. and ROK populations. A better understanding of the vectors' geographical distributions, in combination with case reports, will enhance our understanding of the epidemiology of malaria in the ROK and allow focused efforts at malaria control to conserve decreasing manpower and financial resources.

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# Surveillance Snapshot: Self-reported Malaria Prophylaxis Compliance Among U.S. Service Members with Diagnosed Malaria, 2008-2013

**FIGURE 1.** Question 23 of the post deployment health assessment form (DD2796) -2008 version

**23. Were you told to take medicines to prevent malaria?**

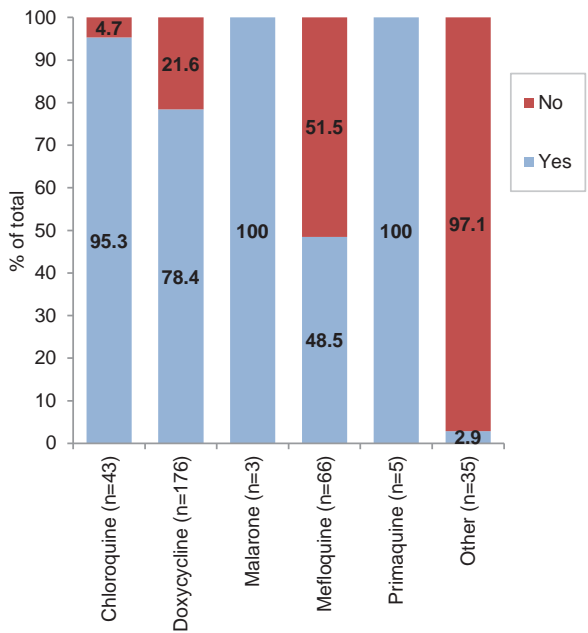
☐ No      ☐ Yes

If YES, please indicate which medicines you took and whether you missed any doses. (Mark all that apply)

Anti-malarial medications	Took All Pills
<input type="radio"/> Chloroquine (Aralen®)	<input type="radio"/> No <input type="radio"/> Yes
<input type="radio"/> Doxycycline (Vibramycin®)	<input type="radio"/> No <input type="radio"/> Yes
<input type="radio"/> Mefloquine (Lariam®)	<input type="radio"/> No <input type="radio"/> Yes
<input type="radio"/> Primaquine	<input type="radio"/> No <input type="radio"/> Yes
<input type="radio"/> Other : _____	<input type="radio"/> No <input type="radio"/> Yes

<sup>a</sup>The 2012 version of DD2796 added Malarone and “Given pills but do not know drug name” as options to select.

**FIGURE 2.** Self-reported malaria prophylaxis drug type and percent compliance (yes) or non-compliance (no) among U.S. service members diagnosed with malaria, 2008-2013



Non-adherence to malaria chemoprophylaxis increases the risk of acquiring malaria. Compliance in service members deployed to Afghanistan has been reported to be approximately 60 percent for doxycycline and lower (38%) for other medications.<sup>1</sup>

This analysis summarized responses to questions on the post deployment health assessment form (DD2796) (both the 2008 and 2012 versions) related to malaria prophylaxis (**Figure 1**). Of 203 service members diagnosed with malaria between 2008 and 2013 and who had a valid DD2796 form associated with the deployment or temporary duty in the country of presumed malaria acquisition, 201 (99%) responded that they were told to take malaria medications. The percentage of service members reporting that they “took all pills” varied by medication (**Figure 2**).

1. Brisson M, Brisson P. Compliance with antimalaria chemoprophylaxis in a combat zone. *Am J Trop Med Hyg.* 2012; 86(4):587-590.



Dengue is a viral infection spread to humans by the bite of infected mosquitoes. The distribution of dengue includes Latin America, the Caribbean, Africa, Asia, and the Pacific Islands. Dengue rarely occurs in the continental U.S., but is endemic in Puerto Rico and the U.S. Virgin Islands. The Centers for Disease Control and Prevention (CDC) reports that nearly all dengue cases occurring in the contiguous U.S. were the result of infection acquired in endemic countries by travelers or immigrants.<sup>1</sup>

Dengue is considered an emerging disease. Prior to 1981, dengue did not occur in the Caribbean and Latin America.<sup>1</sup> The spread is attributed to the discontinuation of highly effective vector control programs that had been in place in these regions until the early 1970s. The two primary vectors of dengue are female mosquitoes of the genus *Aedes*, i.e., *Aedes aegypti* and *Aedes albopictus*.

There are five closely related dengue virus serotypes (dengue-1, -2, -3, -4, -5) that can cause dengue infection (although dengue-5 has not shown sustained infections in humans).<sup>2</sup> These viruses are in the family Flaviviridae, the same family as West Nile virus, yellow fever virus, and Japanese encephalitis virus.<sup>3</sup> Some people who become infected with dengue do not become sick; symptomatic cases may experience a range of illness that varies from mild to severe – even life-threatening. Symptoms of classic dengue fever include high fever, severe headache, joint and muscle pain, nausea/vomiting, and rash.

The two severe forms of dengue are dengue hemorrhagic fever and dengue shock syndrome. Symptoms include those of classic dengue with bleeding from nose, gums, and/or under the skin; marked damage to blood and lymph vessels; massive bleeding; and vascular shock.<sup>4</sup> Although recovery from dengue usually confers lifelong immunity to the specific infecting dengue serotype, severe infections occur more often in individuals who have previously been infected by one of the different serotypes of the dengue viruses.

Similar to dengue virus, chikungunya virus is spread to humans by the bite

of infected female *Aedes* mosquitoes, *Aedes aegypti* and *Aedes albopictus*. The distribution of chikungunya virus is primarily Africa and Asia; however, local transmission has occurred in parts of Europe, the Pacific Islands, and, in late 2013, several islands in the Caribbean Sea.<sup>5</sup> The disease shares similar symptoms as dengue, i.e., fever, joint and muscle pain, headache, nausea/vomiting, and rash, and can be misdiagnosed easily. The joint pain associated with infection can be debilitating and can last from a few days to several weeks. Although similar in many ways to dengue, chikungunya is an alphavirus of the family Togaviridae, which also includes the equine encephalitis viruses and Ross River virus.<sup>3</sup>

There are currently no vaccines available for dengue or chikungunya infections and treatment is supportive care to relieve symptoms. Service members are at risk of dengue and chikungunya infections when they are assigned to endemic areas and during operational deployment or personal travel to endemic areas.

### Mosquito vectors of dengue and chikungunya

*Aedes aegypti* Linnaeus: *Ae. aegypti*, the yellow fever mosquito, originated in Africa and has been well established in the United States (Figure 1a, 1b). In addition to dengue and chikungunya, *Ae. aegypti* is the primary vector of yellow fever. These mosquitoes are common in urban areas and breed in any object capable of holding water (e.g., buckets, flower pots, toys, trash, and tree holes). *Ae. aegypti* feeds during the daytime with increased biting activity after sunrise and before sunset. It is considered a sneaky indoor/outdoor biter and has a preference for human blood hosts, which makes it an efficient vector for disease transmission.<sup>6</sup>

*Ae. aegypti* has a characteristic silvery lyre-shaped pattern on its torso and white banded legs (Figure 1a). The distribution of *Ae. aegypti* is concentrated in tropical and subtropical regions. The egg stage can

**FIGURES 1a, 1b.** *Aedes aegypti* has a lyre shape on its torso and a high preference for human blood – making it an efficient vector for dengue and chikungunya viruses.



CDC/James Gathany



CDC/James Gathany

survive long dry periods, but does not survive the winter in colder climates.<sup>7</sup>

*Aedes albopictus* Skuse: *Ae. albopictus*, the Asian tiger mosquito, is an invasive, i.e., non-native, mosquito that was introduced into the U.S. in the mid-1980s and is now distributed across the country (Figure 2a, 2b).<sup>8</sup> Because of their short flight range, these mosquitoes are common around dwellings and breed in the water of natural or man-made containers. *Ae. albopictus* is an aggressive, opportunistic mosquito that feeds during the daytime as well as at dusk and dawn. For a gravid female, one blood meal may come from multiple sources; thus, they have the potential to transmit disease more readily between hosts. *Ae. albopictus* is an efficient vector of dengue, chikungunya, West Nile, yellow fever, St. Louis encephalitis, and eastern equine encephalitis viruses.<sup>8,9</sup>

**FIGURES 2A,2B.** *Aedes albopictus* has a striking silvery white stripe down the torso and head. Because *Ae. albopictus* feeds on other vertebrates in addition to humans, it a less efficient vector for dengue and chikungunya viruses.



Susan Ellis, University of Georgia, Bugwood.org



CDC/James Gathany

*Ae. albopictus* is a striking black and white mosquito with a characteristic central white stripe down the torso and head (Figure 2a). The distribution of *Ae. albopictus* into temperate and cold regions in addition to the tropics and subtropics could allow the spread of dengue and chikungunya beyond their current endemic areas.<sup>10</sup> *Ae. albopictus* eggs can survive through the winter in temperate climates.

#### Prevention of dengue/chikungunya virus spread

The prevention of dengue and chikungunya infections relies on reducing contacts between competent mosquito vectors and humans. As such, the removal of standing water – which eliminates potential breeding sites – near homes and parks is an important countermeasure. The average time of maturation from mosquito egg to adult is one week; therefore, emptying

artificial containers (e.g., buckets, tarps, bird baths) once a week can significantly decrease the numbers of biting and breeding adult mosquitoes. Furthermore, the use of microbial pesticides (larvicides) in ponds, catch basins, and irrigation ditches is a safe and natural method of reducing mosquito larvae. More information about use of larvicides can be found at: [www.epa.gov/opp00001/health/mosquitoes/larvicides4mosquitoes.htm](http://www.epa.gov/opp00001/health/mosquitoes/larvicides4mosquitoes.htm).

Personal protective measures to prevent mosquito bites such as using insect repellent, wearing long sleeves and long pants, and limiting outdoor activities during peak biting times (dusk and dawn) can also decrease the risk of dengue and chikungunya infection. More information about avoidance of mosquito bites and mosquito control around the home can be found at: [http://phc.amedd.army.mil/PHC%20Resource%20Library/Mosquito\\_Control\\_Around\\_the\\_Home\\_Fact\\_Sheet.pdf](http://phc.amedd.army.mil/PHC%20Resource%20Library/Mosquito_Control_Around_the_Home_Fact_Sheet.pdf).

During military operational deployment to endemic areas, the use of permethrin-impregnated uniforms, insect repellent containing DEET on exposed skin surfaces, and bed nets during periods of rest are important personal protective measures against mosquito-borne disease (Figure 3). The Department of Defense Insect Repellent System can be reviewed at: <http://phc.amedd.army.mil/PHC%20>

Resource%20Library/DODInsectRepellentSystemJusttheFacts-June2007.pdf

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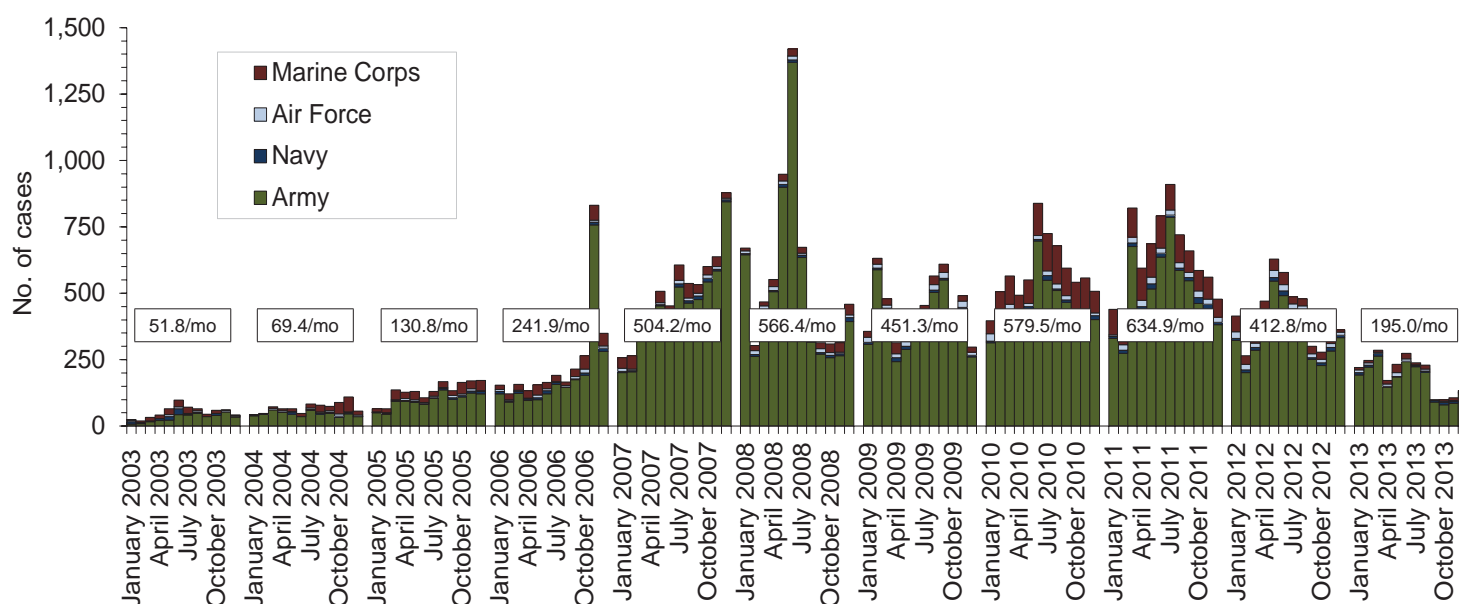
**FIGURE 3.** During operational deployment to areas endemic for mosquito-borne diseases, the use of bed nets during peak biting hours and while sleeping is an effective preventive measure against mosquito-borne diseases.





# Deployment-Related Conditions of Special Surveillance Interest, U.S. Armed Forces, by Month and Service, January 2003-December 2013 (data as of 17 January 2014)

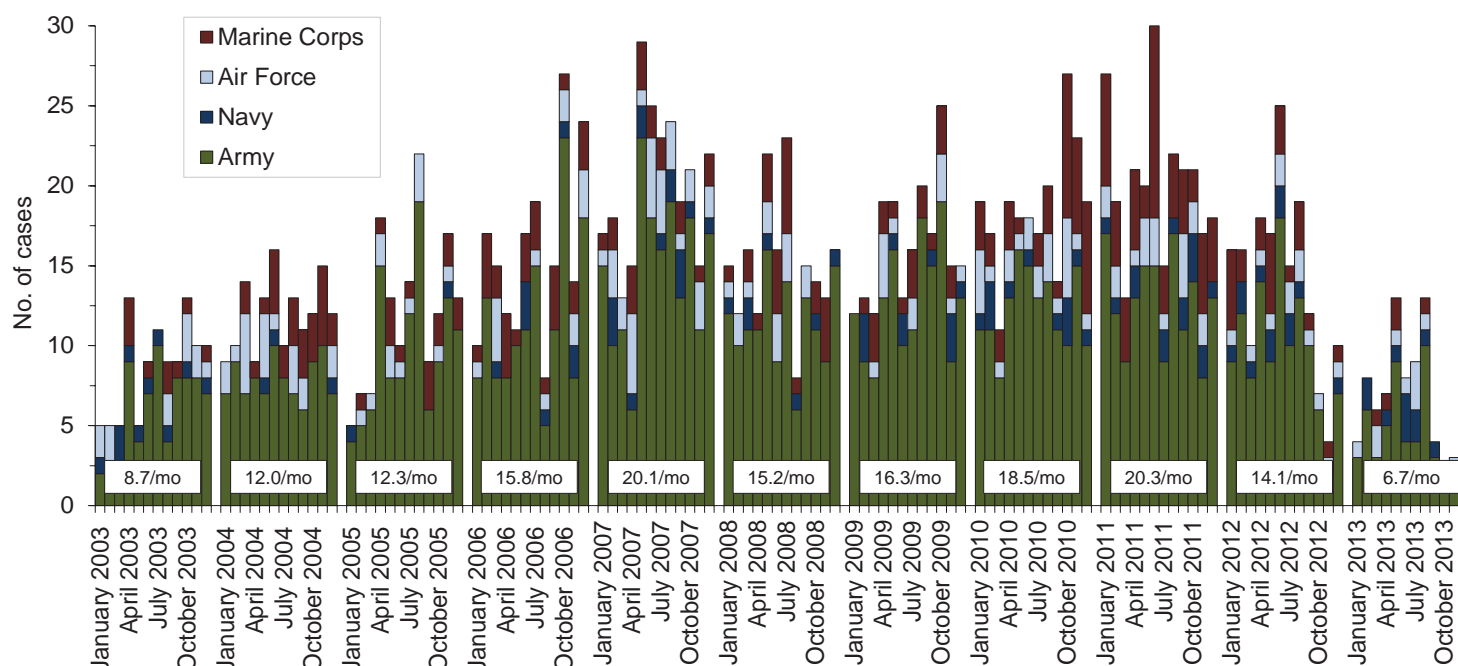
Traumatic brain injury (ICD-9: 310.2, 800-801, 803-804, 850-854, 907.0, 950.1-950.3, 959.01, V15.5\_1-9, V15.5\_A-F, V15.52\_0-9, V15.52\_A-F, V15.59\_1-9, V15.59\_A-F)<sup>a</sup>



Reference: Armed Forces Health Surveillance Center. Deriving case counts from medical encounter data: considerations when interpreting health surveillance reports. *MSMR*. Dec 2009; 16(12):2-8.

<sup>a</sup>Indicator diagnosis (one per individual) during a hospitalization or ambulatory visit while deployed to/within 30 days of returning from OEF/OIF. (Includes in-theater medical encounters from the Theater Medical Data Store [TMDS] and excludes 4,381 deployers who had at least one TBI-related medical encounter any time prior to OEF/OIF).

Deep vein thrombophlebitis/pulmonary embolus (ICD-9: 415.1, 451.1, 451.81, 451.83, 451.89, 453.2, 453.40 - 453.42 and 453.8)<sup>b</sup>

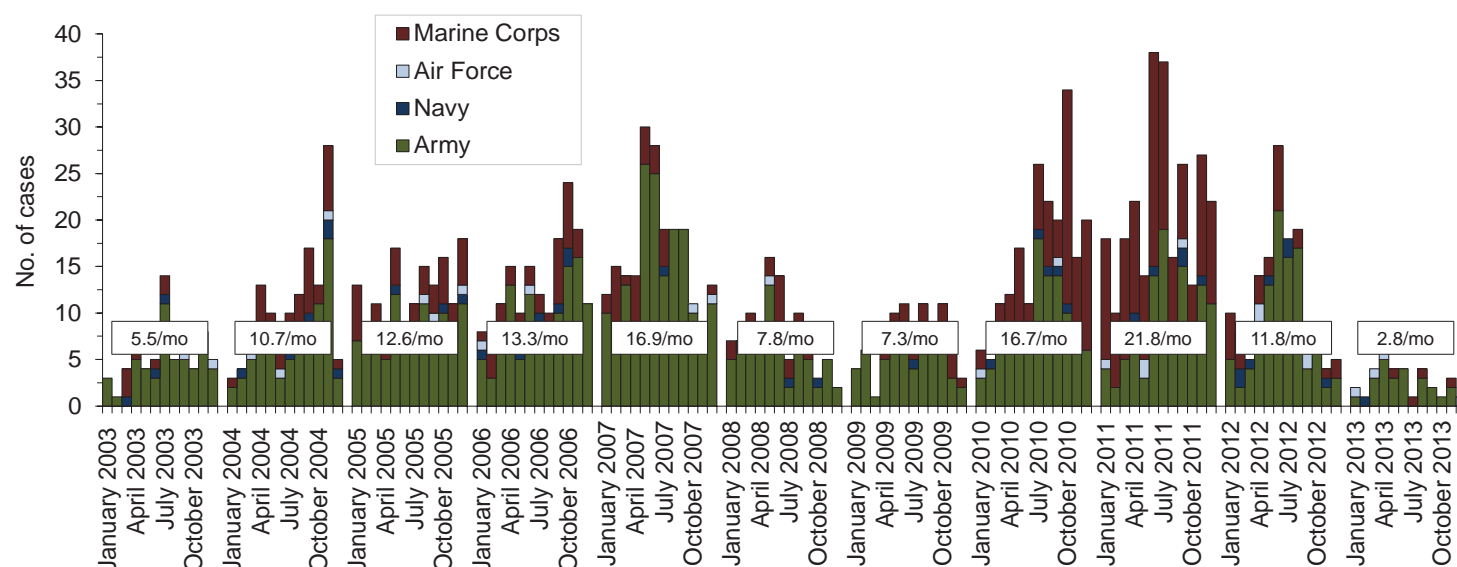


Reference: Isenbarger DW, Atwood JE, Scott PT, et al. Venous thromboembolism among United States soldiers deployed to Southwest Asia. *Thromb Res*. 2006;117(4):379-83.

<sup>b</sup>One diagnosis during a hospitalization or two or more ambulatory visits at least 7 days apart (one case per individual) while deployed to/within 90 days of returning from OEF/OIF.

# Deployment-related conditions of special surveillance interest, U.S. Armed Forces, by month and service, January 2003-December 2013 (data as of 17 January 2014)

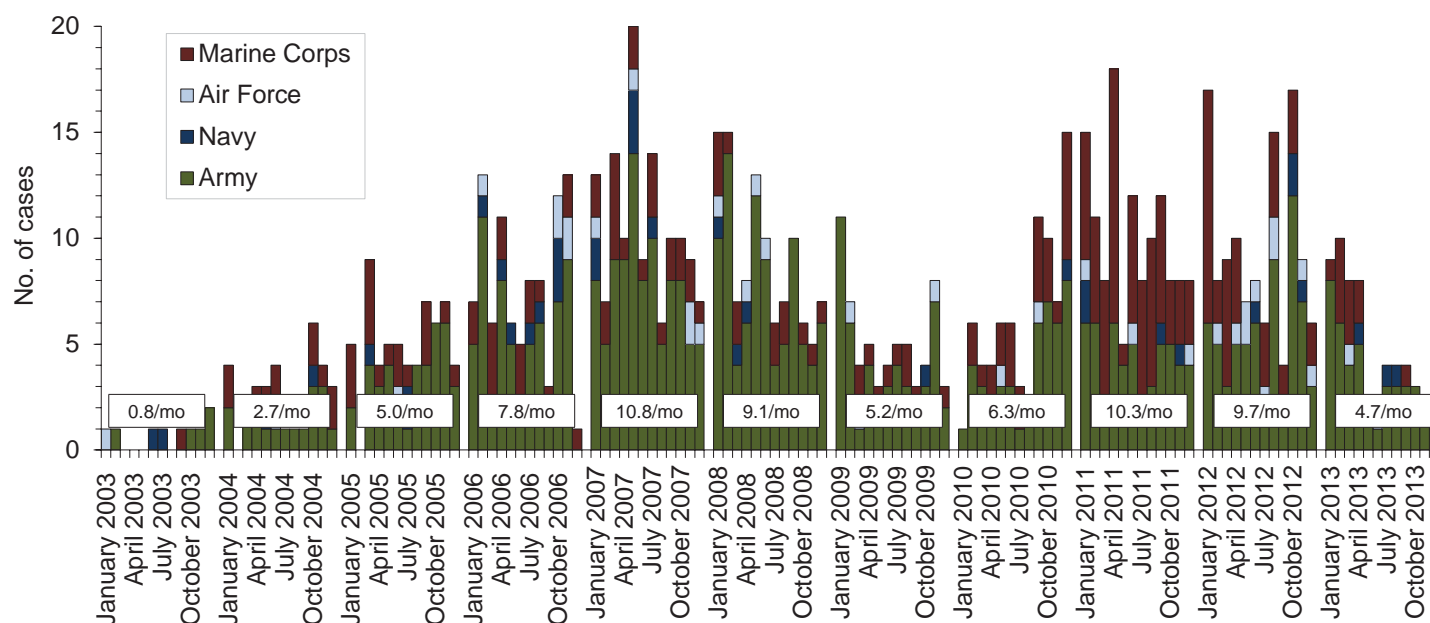
Amputations (ICD-9-CM: 887, 896, 897, V49.6 except V49.61-V49.62, V49.7 except V49.71-V49.72, PR 84.0-PR 84.1, except PR 84.01-PR 84.02 and PR 84.11)<sup>a</sup>



Reference: Army Medical Surveillance Activity. Deployment-related condition of special surveillance interest: amputations. Amputations of lower and upper extremities, U.S. Armed Forces, 1990-2004. *MSMR*. Jan 2005;11(1):2-6.

<sup>a</sup>Indicator diagnosis (one per individual) during a hospitalization while deployed to/within 365 days of returning from OEF/OIF/OND.

Heterotopic ossification (ICD-9: 728.12, 728.13, 728.19)<sup>b</sup>



Reference: Army Medical Surveillance Activity. Heterotopic ossification, active components, U.S. Armed Forces, 2002-2007. *MSMR*. Aug 2007; 14(5):7-9.

<sup>b</sup>One diagnosis during a hospitalization or two or more ambulatory visits at least 7 days apart (one case per individual) while deployed to/within 365 days of returning from OEF/OIF/OND.

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