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MEDICAL SURVEILLANCE MONTHLY REPORT

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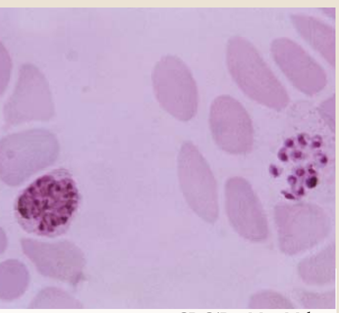
CDC



CDC/Dr. Mae Melvin

Malaria Issue

SUMMARY TABLES AND FIGURES

A publication of the Armed Forces Health Surveillance Center

Update: Malaria, U.S. Armed Forces, 2011

U.S. service members are at risk of malaria when they are assigned to endemic areas (e.g., Korea), participate in operations in endemic areas (e.g., Afghanistan, Africa) and visit malarious areas during personal travel. In 2011, 124 service members were reported with malaria. Nearly three-fourths of cases were presumably acquired in Afghanistan (n=91) and one-fifth were considered acquired in Africa (n=24). One-quarter of cases were caused by *P. vivax* and one-fifth by *P. falciparum* (including 6 Afghanistan-acquired infections); most cases were reported as "unspecified" malaria. Malaria was diagnosed/reported from 51 different medical facilities in the United States, Afghanistan, Kyrgyzstan, Iraq, Germany and Korea. 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-transmitted 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*. Three other *Plasmodium* species that infect non-human primates have been found to occasionally cause malaria in humans. *P. knowlesi*, in particular, has been responsible for many cases in Malaysia and occasional cases elsewhere in southeast Asia, but its contribution to the worldwide burden of malaria has been minor.

Malaria is endemic in more than 100 countries throughout the tropics and in some temperate regions. In 2011, malaria accounted for 216 million illnesses and an estimated 655,000 deaths worldwide; most deaths were due to *P. falciparum* infections of young children in Africa.[1] 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.[2]

For centuries, malaria has been recognized as a disease of military operational significance.[3,4] U.S. service members are at risk of malaria when they are permanently assigned to endemic areas (such as near the Demilitarized Zone [DMZ] in Korea);[5,6] when they participate in operations in endemic areas (e.g., Afghanistan,[7] Africa,[8] Haiti[9]); and when they visit malarious areas during personal travel. The U.S. military has effective countermeasures against malaria, including chemoprophylactic drugs, permethrin-impregnated uniforms and bed nets, and DEET-containing insect repellents. When cases and outbreaks of malaria do occur, they are generally due to non-compliance with indicated chemoprophylactic or personal protective measures.

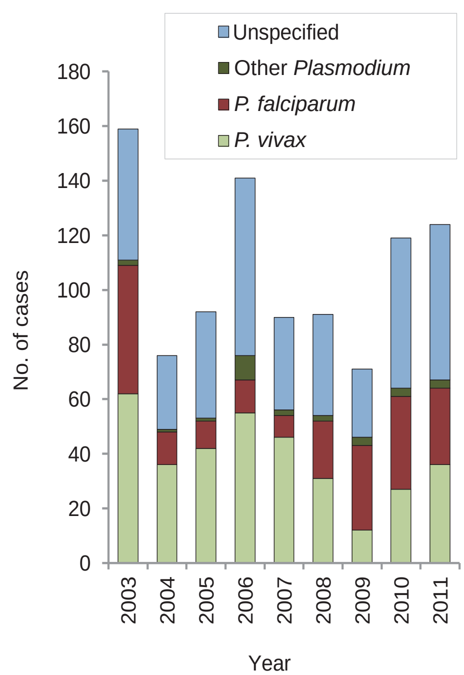
In the 1990s, there was a general increase in malaria incidence among U.S. service members, primarily due to *P. vivax* infections acquired near the DMZ in Korea.[5,6, 10-12] Since 2001, U.S. service members have been exposed to malaria risk due to *P. vivax* while serving in Southwest and Central Asia (particularly in Afghanistan).[7] Service members who conduct civil-military and crisis response operations in Africa are at risk of malaria due to *P. falciparum*;[8] 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.[9]

This report summarizes the malaria experiences of U.S. service members during calendar year 2011 and compares it to recent experience.

METHODS

The surveillance period was January 2003 through December 2011. 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 (International Classification of Diseases, Ninth Revision, Clinical Modification [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: 084.0-084.3); (4) a hospitalization record with a non-primary diagnosis of malaria plus a diagnosis of anemia (ICD-9-CM: 280-285), thrombocytopenia and

FIGURE 1. Malaria cases among U.S. service members, by *Plasmodium* species and calendar year of diagnosis/report, 2003-2011



related conditions (ICD-9-CM: 287), or malaria complicating pregnancy (ICD-9-CM: 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) 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.

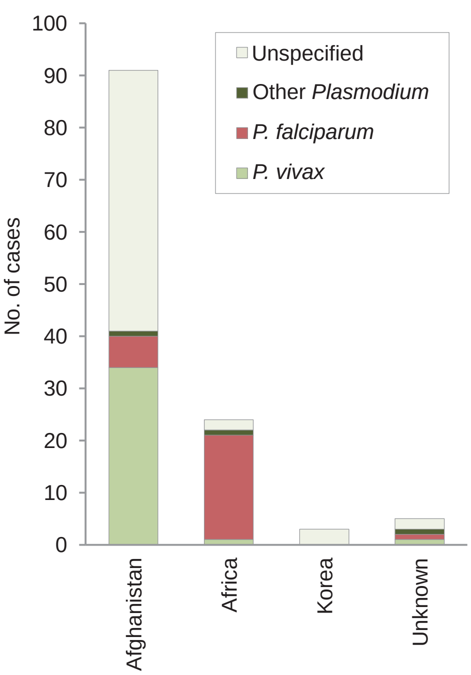
This summary allowed one episode of malaria per service member per 365-day period. When multiple records documented a single episode, the date of the earliest encounter was considered the date of clinical onset, and the most specific diagnosis was used to classify the *Plasmodium* species.

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; (5) all remaining cases were considered acquired in unknown locations.

TABLE 1. Malaria cases by *Plasmodium* species and selected demographic characteristics, U.S. Armed Forces, 2011

	P. vivax	*P. falciparum*	Unspecified or other	Total	Percentage total
Total	36	28	60	124	100.0
Component					
Active	31	25	52	108	87.1
Reserve/Guard	5	3	8	16	12.9
Service					
Army	30	19	50	99	79.8
Navy	2	2	3	7	5.6
Air Force	1	1	4	6	4.8
Marine Corps	3	6	3	12	9.7
Gender					
Male	35	28	58	121	97.6
Female	1	0	2	3	2.4
Age group					
<20	0	1	0	1	0.8
20-24	12	7	25	44	35.5
25-29	13	7	14	34	27.4
30-34	3	4	8	15	12.1
35-39	5	5	6	16	12.9
40+	3	4	7	14	11.3
Race/ethnicity					
White, non-Hispanic	25	15	49	89	71.8
Black, non-Hispanic	4	11	2	17	13.7
Other	7	2	9	18	14.5

FIGURE 2. Malaria infections by *Plasmodium* species and presumed location of acquisition, U.S. Armed Forces, 2011



RESULTS

In 2011, 124 U.S. military members were diagnosed and/or reported with malaria. The number of malaria cases in 2011 was the third highest of the previous nine years **(Figure 1)**. More than one-fifth of 2011 cases were caused by *P. falciparum* (n=28, 23%) and more than one-quarter by *P. vivax* (n=36, 29%) **(Table 1)**. The responsible agent was "unspecified" for 46 percent (n=57) of 2011 cases.

In 2011, as in prior years, most U.S. military members diagnosed with malaria were male (98%), active component members (87%), in the Army (80%), of "white" race/ethnicity (72%) and in their 20s (63%) **(Table 1)**.

Of the 124 malaria cases in 2011, nearly three-quarters of the infections were considered to have been acquired in Afghanistan (n=91, 73%) and approximately one-fifth in Africa (n=24, 19%); only four infections (3%) were presumably acquired in Korea **(Table 2)**. The remaining five malaria cases (4%) had unknown areas of infection acquisition. The number of infections considered acquired in Afghanistan in 2011 was the highest of the nine-year period. Of the 24 malaria infections considered acquired in Africa, 16 were likely acquired in West Africa (Ghana: 7; Cameroon: 5, Sierra Leone: 2, Nigeria and Senegal: 1 each); four were considered acquired in East Africa (Uganda: 2; Kenya

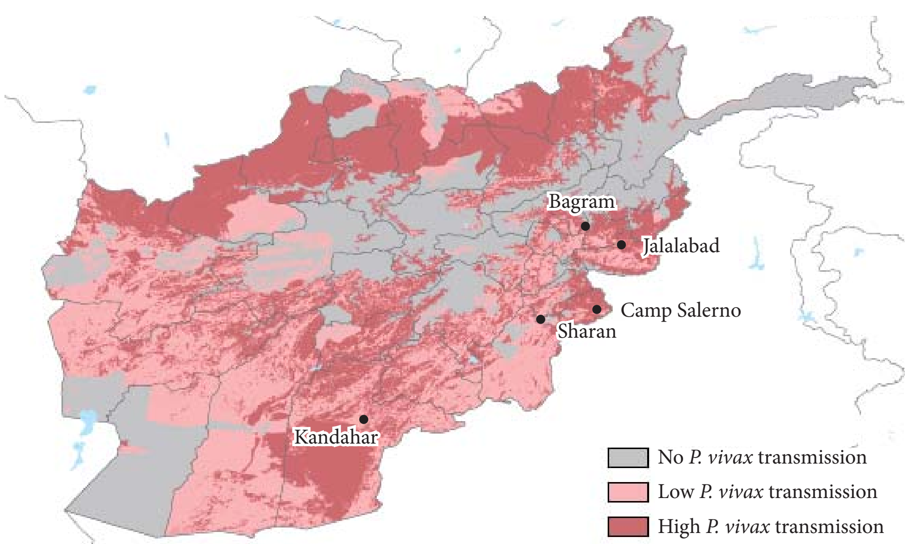
TABLE 2. Number of malaria cases by geographical location of diagnosis or report and presumed location of acquisition, U.S. Armed Forces, 2011

Location of diagnosis/report	Presumed location of acquisition				Total cases	% of total
	Korea	Afghanistan	Africa	Unknown		
Fort Campbell, KY	1	22	0	0	23	18.5
Jalalabad, Afghanistan	0	12	0	0	12	9.7
Fort Stewart, GA	0	4	1	1	6	4.8
Camp Lejeune, NC	0	2	4	0	6	4.8
Portsmouth, VA	0	5	1	0	6	4.8
Fort Bragg, NC	1	3	1	0	5	4.0
Camp Salerno, Afghanistan	0	5	0	0	5	4.0
Landstuhl, Germany	0	0	4	0	4	3.2
Bagram/Camp Lacy, Afghanistan	0	3	0	0	3	2.4
Fort Wainwright, AK	0	2	0	0	2	1.6
Camp Pendleton, CA	0	2	0	0	2	1.6
Fort Shafter, HI	0	2	0	0	2	1.6
Fort Sill, OK	0	0	2	0	2	1.6
Fort Bliss, TX	0	2	0	0	2	1.6
New York	0	2	0	0	2	1.6
North Carolina	0	1	0	1	2	1.6
Eastern Texas	0	2	0	0	2	1.6
Sharan, Afghanistan	0	2	0	0	2	1.6
Kandahar, Afghanistan	0	2	0	0	2	1.6
Other locations	2	18	11	3	34	27.4
Total (% total)	4 (3.2%)	91 (73.4%)	24 (19.4 %)	5 (4.0%)	124	100.0

and Madagascar: 1 each); two were considered acquired in the Horn of Africa (Ethiopia, Djibouti); one in Central Africa (Chad) and 1 was reported only as "Africa" **(data not shown)**.

Of the 91 Afghanistan-acquired malaria infections, 6 (7%) were caused by *P. falciparum*, 34 (37%) by *P. vivax,* 1 (1%) by *P. malariae* and 50 (55%) were diagnosed or reported as "unspecified" malaria **(Figure 2)**. The vast majority (83%) of cases likely acquired in Africa were caused by *P. falciparum* and all four Korea-acquired infections were of "unspecified" type.

FIGURE 3. *Plasmodium vivax* malaria transmission in Afghanistan[a] and locations from which malaria cases among U.S. service members were reported in 2011

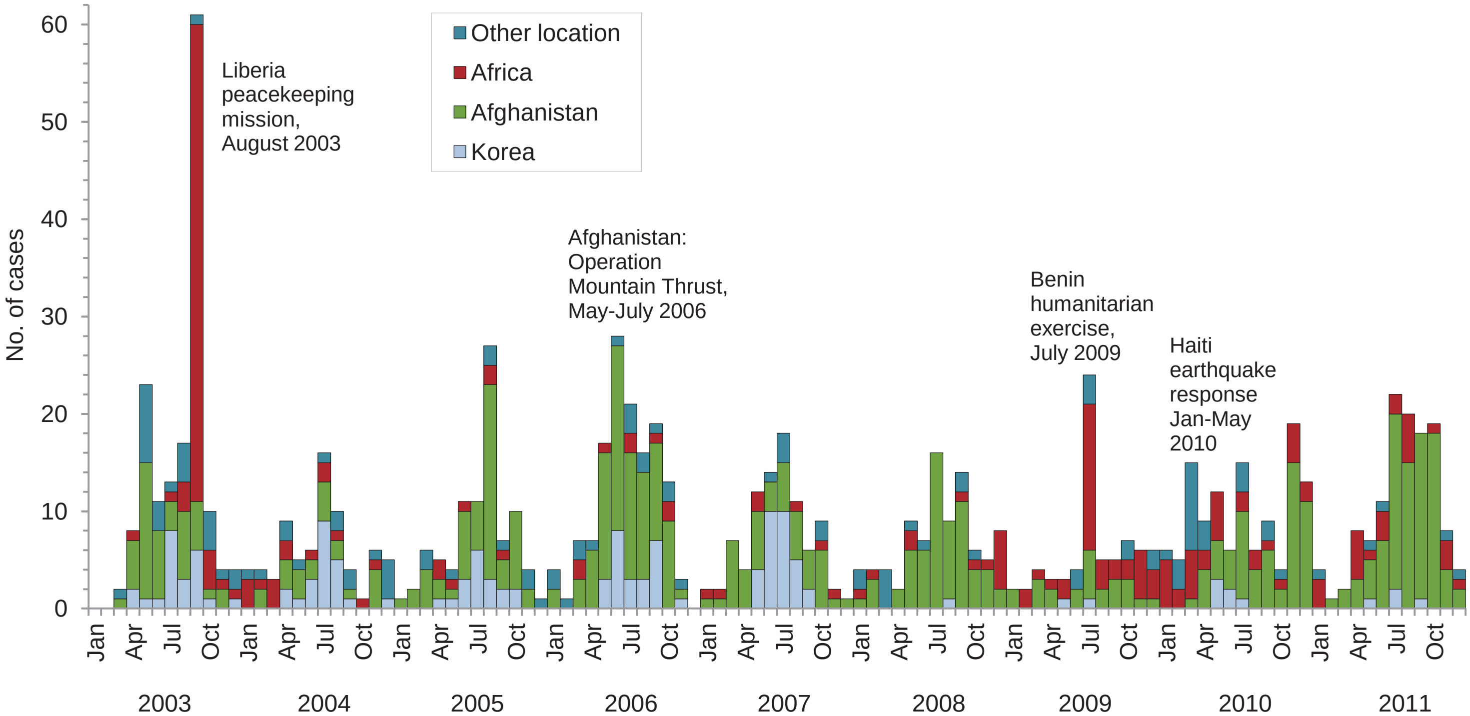


[a]Guerra CA, Howes RE, Patil AP, et al. The international limits and population at risk of *Plasmodium vivax* transmission in 2009. *PLoS Negl Trop Dis*. 2010 Aug 3; 4(8):e774.

During 2011, malaria cases were diagnosed/reported from 51 different medical facilities in the United States, Afghanistan, Kyrgyzstan, Iraq, Germany and Korea. More than one-quarter of cases (n=34, 27%) were reported from or diagnosed outside the United States **(Table 2)**. Twenty-four cases were reported from U.S. military facilities in Afghanistan **(Figure 3)** and 7 cases were reported from/treated in U.S. facilities in Germany. Brian Allgood Army Community Hospital in Seoul, Korea, the 376th Expeditionary Medical Support in Manas, Kyrgyzstan and an unnamed medical facility in Bagdad treated one case each **(data not shown)**. Of note, more than 18 percent of all malaria cases during the year were treated at/reported from Fort Campbell, KY (n=23) **(Table 2)**.

In 2011, 90 of 124 malaria cases among U.S. military members were diagnosed from June through October; there was more distinct seasonality in 2011 than in recent prior years **(Figure 4)**. The finding reflects the relatively higher number and proportion of cases acquired in temperate Afghanistan as compared to tropical regions of Africa and Haiti.

FIGURE 4. Malaria among U.S. service members, by estimated location of infection acquisition, 2003-2011



EDITORIAL COMMENT

In 2011, the total number of cases of malaria diagnosed/reported among U.S. military members was higher than in the previous four years and seven of the previous nine years. The data illustrate continuing acquisition of malaria from Africa and Afghanistan. There were more Afghanistan-acquired malaria infections in 2011 than in any of the prior eight years. Of note, there were six Afghanistan-acquired infections caused by *P. falciparum*, while no more than three such infections were reported in any of the prior nine years. Malaria acquisition from Korea remained relatively low; since 2008, compared to prior years, there have been remarkably fewer Korea-acquired cases among U.S. military members.

Numerous factors could contribute to year-to-year changes in numbers of malaria cases. The number of service members deployed in malaria-endemic countries is not constant; a surge of 30,000 new troops arrived in Afghanistan in December 2010. Improved capacity for malaria diagnosis and case reporting by military personnel in Afghanistan may have contributed to this year's increase; in 2011, malaria cases were reported from five locations in Afghanistan as compared to just one (Bagram) in 2010. Annual changes in environmental variables may also affect malaria acquisition; in Afghanistan, irrigation and temperature (but not precipitation) are the strongest predictors of malaria transmission.[13]

There are significant limitations to the 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 acquisition were estimated from reported relevant information. Some cases had reported exposures in multiple malarious areas, and four percent of cases had no relevant exposure information. Personal travel to malaria-endemic countries was not accounted for unless specified in a notifiable event report. Persons born in malaria-endemic regions have been found to be over-represented among the cases of malaria in U.S. service members. A recent report estimated that the malaria rate was 44 times higher in service members born in western Africa than among those born in the United States.[14]

As in prior years, in 2011, most malaria cases among U.S. military members were treated at medical facilities remote from malaria endemic areas; of note, more than 50 medical facilities treated any cases, and 31 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 be capable of diagnosing malaria (or have access to a clinical laboratory that is proficient in malaria diagnosis) and initiating treatment (particularly when *falciparum* malaria is clinically suspected). Continued emphasis of 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.

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Sources of Variability of Estimates of Malaria Case Counts, Active and Reserve Components, U.S. Armed Forces

Each January, the Medical Surveillance Monthly Report (*MSMR*) estimates numbers of malaria infections among U.S. service members using a surveillance case definition to identify "malaria cases". These cases include individuals with a hospital discharge diagnosis of malaria and those who were reported with malaria through military notifiable event reporting systems. This report compares the *MSMR* surveillance case definition with other proposed case definitions to demonstrate the degree to which estimates of numbers of malaria cases are dependent upon clinical settings, data sources and case-defining rules used to produce such estimates. For example, including outpatient diagnoses as malaria cases would more than double the 2010 case count. As compared with cases defined using other proposed case definitions, many more *MSMR*-defined cases had records of a specific *Plasmodium* species, a laboratory test for malaria and recent travel to a malaria-endemic country. Interpretations of the results of *MSMR* reports should consider how "cases" are defined.

Each January, the *MSMR* reports numbers of malaria infections among U.S. service members during the preceding nine years. The completeness and accuracy of malaria case count estimates depend on specifications of the "surveillance case definition" that is used to identify cases. For the MSMR's annual malaria summary, a case of malaria is defined as a U.S. military member who received a discharge diagnosis of malaria on an electronic record of a hospitalization or was reported as a case of malaria through a military notifiable medical event reporting system (see page 3). Individuals can be counted as incident malaria cases only once during any 365-day period. By design, the *MSMR* case definition is a specific – but not particularly sensitive – surveillance case definition; that is, it is designed to increase the likelihood that each malaria case enumerated in the report is a "true case."

Use of a less restrictive case definition would increase the number of "malaria cases" identified for surveillance purposes; it is likely, however, that relatively more of the cases would be "false positive" cases (e.g., clinically suspected but subsequently ruled out). For example, if a malaria diagnosis reported only on an outpatient record qualified as a malaria "case", the number of malaria cases reported in the *MSMR* each year would markedly increase. However, the *MSMR's* surveillance case definition does not consider outpatient malaria diagnoses alone as case defining events for surveillance purposes. Such diagnoses are believed to include provisional ("rule out") diagnoses of malaria or miscoded documentation of heath care encounters for malaria chemoprophylaxis, the provision of malaria prevention counseling, and so on.

Clearly, interpretations of results reported each year in the *MSMR* should consider how "cases" of malaria are defined. To help in this regard, this report assesses the variability of estimates of case counts of malaria in relation to characteristics of surveillance case definitions. In particular, the report demonstrates the degree to which estimates of malaria case counts are dependent upon case definition components, e.g., the clinical settings from which diagnoses are reported, differentiation between relapsing/recurrent single cases and repeat new cases ("incidence" rules), and sources of case-finding information.

METHODS

The surveillance period was January 2009-December 2010. The surveillance population included all individuals who served in an active or reserve component of the U.S. Army, Navy, Air Force, Marine Corps or Coast Guard at any time during the surveillance period.

Service members with diagnoses specific to malaria were identified from standardized records routinely transmitted to the Armed Forces Health Surveillance Center. These records included notifiable event reports from service-specific reporting systems; records of inpatient and outpatient encounters in fixed U.S. military facilities (excludes care provided in Iraq/Afghanistan) and some non-military facilities (i.e., purchased care); records of medical care provided to service members deployed to Operations Iraqi Freedom/Enduring Freedom/New Dawn (primarily in Iraq or Afghanistan) and reported to the Theater Medical Data Store (TMDS); records of all aeromedical evacuations (MEDEVACs) conducted by the U.S. Transportation Command; and records of laboratory tests (Health Level 7 [HL7] records) conducted in U.S. military medical treatment facilities.

For this report, three different surveillance case definitions were used to identify "malaria cases" **(Table 1)**. The case definitions used for the analysis were hierarchical; that is, each case definition was mutually exclusive of the others.

MSMR cases: The *MSMR* case definition is that used to identify cases for the annual malaria report (described on page 3-4). Briefly, *MSMR* cases were defined by i) notifiable medical event reports in which

TABLE 1. Definitions of malaria "case" types

Malaria "case" type	Surveillance case definition
MSMR-defined case	A notifiable medical event report (reported to a military event reporting system) in which the malaria diagnosis is "confirmed"; a hospitalization in a fixed medical facility with a primary (first-listed) diagnosis of malaria; hospitalization with a non-primary diagnosis of a malaria due to a specific *Plasmodium* species; or a non-primary diagnosis of malaria preceded by diagnoses of selected signs, symptoms or conditions consistent with malaria (complete definition on p. 3).
"Possible" case: Other malaria hospitalizations/ notifiable events, multiple outpatient diagnoses	Not a case above and (a) Hospitalization in a fixed medical facility with a non-primary diagnosis of malaria; or (b) Hospitalization in Iraq/Afghanistan with a malaria diagnosis in any diagnostic position; or (c) Two or more outpatient primary (first-listed) diagnoses of malaria within 14 days; or (d) Notifiable event for which the malaria diagnosis is not "confirmed".
"Unlikely" case: single outpatient diagnoses	Not a case above and (a) Single outpatient primary (first-listed) diagnosis of malaria

malaria diagnoses were "confirmed"; or ii) records of hospitalizations in fixed (e.g., not deployed, at sea) medical facilities with a primary (first-listed) diagnosis of malaria; or iii) hospitalization record with a non-primary diagnosis of a malaria due to a specific *Plasmodium* species; or iv) hospitalization record of a non-primary diagnosis of malaria preceded by diagnosis of a sign, symptom or condition consistent with malaria.

Possible cases: The "possible case" definition identified cases that were not *MSMR*-defined cases. Possible cases were defined by i) records of hospitalizations with malaria-specific diagnoses in second or subsequent diagnostic positions (with no malaria-specific or associated diagnoses in the primary diagnostic position); ii) records of malaria-related hospitalizations in medical facilities in Iraq/Afghanistan; iii) notifiable medical event reports in which "malaria" diagnoses were reported as non-confirmed; or iv) records of at least two outpatient encounters within 14 days with malaria-specific primary diagnoses.

Unlikely cases: The "unlikely case" definition identified cases that were not *MSMR* cases or possible cases. Unlikely cases were defined by single outpatient encounters with malaria-specific primary diagnoses **(Table 1)**.

For surveillance purposes, "incidence rules" are used to differentiate single cases (which may have multiple associated medical encounters/reports) from repeat ("new") cases. For example, an individual with two separate hospitalizations for malaria may be counted as one case or two cases, depending on the length of time between the two hospitalizations. To assess the effects of various incidence rules on estimates of case counts, for this analysis, affected service members were not eligible for consideration as new cases for 60, 180 or 365 days after each malaria case-defining event.

To further assess differences in the malaria-specific information related to the three case-definition types, prevalences of documentation of three characteristics thought to be indicative of "true cases" of malaria were assessed: (1) report of a diagnosis of a specific *Plasmodium* species; (2) record of a malaria-specific laboratory test; and (3) evidence that affected service members had recently deployed to, served in or received medical care in a malaria-endemic country. These characteristics were assessed using electronic medical, personnel and deployment records. Of note, such records do not capture personal travel during leave. Laboratory records were assessed only for cases diagnosed in 2010.

RESULTS

Number of cases, by surveillance case definition

During the two-year surveillance period, there were 550 malaria "cases" of any case type. Thirty-five percent (n=190) of the cases were classified as *MSMR*-defined; "possible" and "unlikely" cases comprised approximately 14 percent (n=77) and 52 percent (n=283) of the total, respectively **(Table 2)**.

Of all *MSMR*-defined cases in 2009 (n=71) and 2010 (n=119), approximately two-thirds (n=123, 65%) were documented with hospitalization records; the remainder were reports of confirmed malaria diagnoses as notifiable medical events **(Table 2)**.

Of the possible cases in 2009 (n=42) and 2010 (n=35), two-thirds were documented with records of two or more outpatient encounters within 14 days with primary diagnoses of malaria **(Table 2)**. Of the others, 8 cases were hospitalized in U.S. military facilities in Iraq/Afghanistan; 4 cases had non-primary (not first-listed) diagnoses of malaria on records of hospitalizations in fixed U.S. military medical facilities; and 14 cases (including 10 among Navy or Marine Corps members) were reports of "unconfirmed" diagnoses of malaria as reportable medical events.

By definition, unlikely cases in 2009 (n=142) and 2010 (n=141) were documented with records of single outpatient visits with primary diagnoses of malaria.

Number of cases, by source of data

If "possible" and "unlikely" cases were used to estimate numbers of malaria cases, annual estimates would be 3.5 and

TABLE 2. Numbers of malaria "cases" identified using 3 different surveillance case definitions, and characteristics of those cases, U.S. Armed Forces, 2009-2010

	MSMR-defined	Possible	Unlikely
Total no. of cases (2009-2010)	190	77	283
Clinical setting			
Hospitalization	123	12	--
Notifiable event	67	14	--
Outpatient visit	--	51	283
Other malaria-specific information			
Malaria species diagnosed/reported[a]	103	15	38
Patient traveled to malarious country[b]	154	53	112
Laboratory test ordered (2010 only)	59	15	11
Laboratory test positive (2010 only)	20	0	0
Incidence rule (length of ineligibility to be counted as a new case)			
365 days	190	77	--
180 days	190	78	--
60 days	195	78	--

[a]Diagnosis of ICD-9-CM codes 084.0-084.3 (*P. falciparum*, *P. vivax*, *P. malariae*, *P. ovale*)
[b]Notifiable event reported from, or hospitalization, deployment or military service in, a malaria-endemic country during the 12 months prior to (and including) the incident malaria diagnosis

FIGURE 2. Numbers and proportions of malaria "cases" with and without a *Plasmodium*-specific diagnoses, by malaria "case" type, 2009-2010

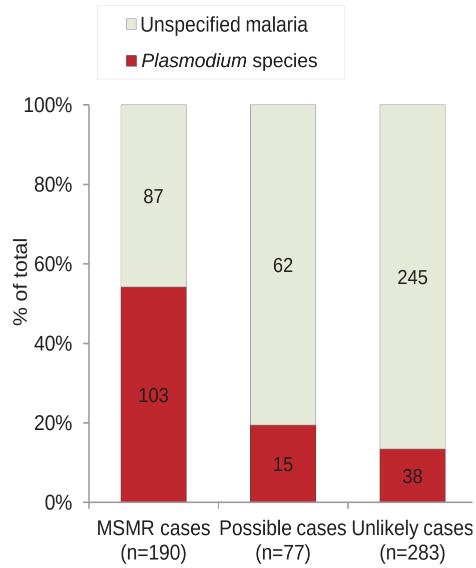
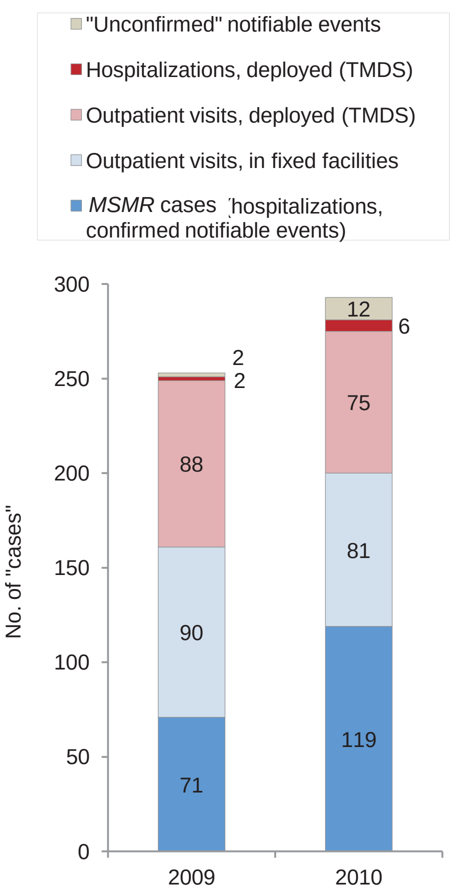


FIGURE 1. *MSMR*-defined malaria cases and other potential malaria "cases" by data source and year, 2009-2010



2.5 times the current *MSMR* estimates for 2009 and 2010, respectively **(Figure 1)**. For example, if hospitalized cases in U.S. military facilities in Iraq/Afghanistan in 2010 were added to *MSMR* cases (n=119), the estimated number of cases would be 125. If outpatient cases in deployed and fixed facilities were also included, the estimated of malaria cases in 2010 would be 281. Of note, inclusion of MEDEVAC records of malaria diagnoses would add no cases to the estimate; all 18 service members with a malaria-related MEDEVAC in 2009 or 2010 were also diagnosed with malaria in other clinical settings.

Variation in relation to the "no risk" period after case defining events ("incidence rule")

There were small changes in total numbers of cases detected by each surveillance definition in relation to the lengths of "ineligibility" periods after case-defining events ("incidence rule"). When affected individuals are not eligible to be counted as new malaria cases for 365 days after case-defining events, the numbers of cases of each surveillance definition type are as reported above. When periods of ineligibility to be counted as new cases are reduced to 180 days and 60 days after case-defining events, the total numbers of each case definition type increase by 0 to 1 and 1 to 5, respectively **(Table 2)**.

Documentation of other malaria-specific information

A specific diagnosis of *P. falciparum* or *P. vivax* was available for the majority of *MSMR*-defined cases (n=103, 54%), one-fifth of "possible" cases (n=15, 20%), and 13 percent (n=38) of "unlikely" cases **(Table 2, Figure 2)**.

Of the 190 *MSMR*-defined cases, 154 (81%) had documented temporal-geographic exposures to malaria risk, i.e., deployment to, or military service, travel or hospitalization in, a malaria-endemic country during the 12 months prior to a malaria diagnosis/report. Of the "possible" and "unlikely" cases reported from fixed medical facilities (and not from Iraq/Afghanistan), the proportions with evidence of potential "exposure" to malaria were 69 percent and 40 percent, respectively **(Table 2)**.

Of 2010 cases reported from fixed medical facilities, a malaria-specific laboratory test was ordered for one-half of *MSMR*-defined cases, 58 percent of "possible cases" and 15 percent of unlikely cases **(Table 2)**. A positive malaria diagnostic test was documented for 17 percent of *MSMR*-defined malaria cases; no positive lab tests were found among possible and unlikely cases reported from fixed medical facilities.

EDITORIAL COMMENT

Each year, the *MSMR* estimates the numbers of malaria infections among U.S. service members. This report demonstrates that many different estimates are possible depending on the data sources, clinical settings and incidence rules used to produce the estimate. For example, the inclusion of outpatient diagnoses of malaria as "cases" would more than double the number of malaria cases in 2009-2010. This report also finds that many more *MSMR*-defined cases than other cases had records of a specific *Plasmodium* species, a laboratory test for malaria and recent travel to a malaria-endemic country. If indeed these characteristics are associated with "true cases", then the *MSMR* surveillance case definition may be of value in identifying them.

The *MSMR's* surveillance case definition of malaria has not been validated against a "gold-standard" (such as a list of individuals with clinically-confirmed malaria). Instead, the definition was designed to produce an educated guess of the number of "true cases" of malaria after careful consideration of the many factors that affect the quality and completeness of surveillance (electronic medical records and notifiable event reports). These factors include, for example, the severity and clinical course of malaria infections; the completeness and accuracy of reporting of diagnoses; the timing of diagnoses and the effectiveness of treatments; the specificity of clinical diagnoses and the ICD-9-CM diagnostic codes used for reporting; the accuracy of determining and reporting appropriate diagnostic codes; and so on.

For a number of reasons, the *MSMR* surveillance case definition does not include cases diagnosed only in the combat theaters of Iraq/Afghanistan (e.g., not hospitalized in fixed medical facility or reported to the U.S. military's notifiable event reporting system). Relative to fixed medical facilities, deployed facilities have limited resources for malaria diagnosis and may record presumptive diagnoses more frequently. Also, the data contained in the Theater Medical Data Store (TMDS) has been increasing in completeness since the beginning of combat operations in Iraq/Afghanistan. Combining TMDS data with surveillance data from other sources makes it difficult to assess trends in the numbers of malaria cases during the past several years. The *MSMR* also does not count as malaria cases those malaria diagnoses made only at the time of MEDEVAC; such diagnoses are considered provisional and more definitive diagnoses are most often recorded at subsequent clinical destinations. In this analysis, all individuals with malaria diagnoses on MEDEVAC records were also diagnosed in other clinical settings.

In the future, the *MSMR* may consider adding to its surveillance case definition individuals with an outpatient diagnosis of malaria in combination with a positive malaria-specific laboratory test. In 2010, three service members would be considered a case by these criteria.

Images in Health Surveillance: Malaria Vectors and Malaria Testing

Malaria vectors

CDC/James Gathany

Walter Reed Biosystematics Unit

CDC/Dr. William Collins

Walter Reed Biosystematics Unit

Malaria is transmitted by certain mosquito species of the genus *Anopheles*. The *Anopheles* species shown here are common in areas of deployment operations. Mosquitoes breed in stagnant water in both urban and rural environments.

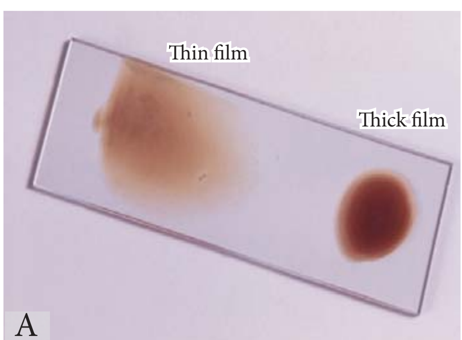
A. *Anopheles gambiae* beginning a blood meal on a human host. *A. gambiae* is an important vector of *Plasmodium falciparum* malaria in Africa.

B. A mounted specimen of *A. gambiae*. Such specimens are used to identify the genus and species of mosquitoes collected in the environment.

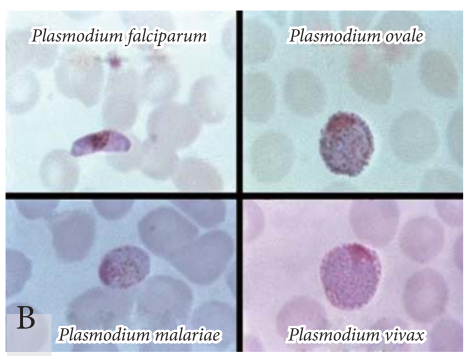
C. *Anopheles stephensi* fully engorged with blood from a human host. *A. stephensi* is an important vector for *Plasmodium falciparum* in the Middle East and South Asia.

D. A mounted specimen of *A. stephensi*. Mosquito species are distinguished through characteristics of the mosquito's head, legs, wings, and abdomen.

Malaria testing



CDC/Steven Glenn, Laboratory & Consultation Division



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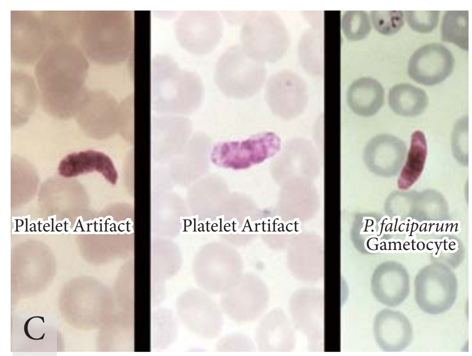

CDC/Steven Glenn, Laboratory & Consultation Division

A. The most common diagnostic test for malaria is the examination under the microscope of thin and thick film blood smears. After the blood on the slide dries, it is stained with Giemsa stain that permits the malaria parasites to be seen. A thick smear permits a relatively large sample of blood to be screened for the presence of any malaria parasites. A thin smear is used for closer inspection to identify the species of malaria.

B. Thin film Giemsa stains showing classical examples of gametocytes for each of the species that most often infect humans. Gametocytes ingested by *Anopheles* mosquitoes during a blood meal will render the mosquitoes capable of infecting other humans within one to two weeks.

C. Thin film Giemsa stains showing fused blood platelets and a mature *Plasmodium falciparum* gametocyte. Platelet artifacts may be misleading in the diagnosis of malaria.

Editorial: Malaria in the U.S. Armed Forces: A Persistent but Preventable Threat

COL Mark M. Fukuda, MD

The potential impact of malaria on military populations is highlighted by General Douglas MacArthur, who, in referring to malaria's impact on World War II forces, famously lamented: "This will be a long war, if for every division I have facing the enemy, I must count on a second division in the hospital with malaria, and a third division convalescing from this debilitating disease".[1] Today's deployment patterns, though different from those of MacArthur's time, continue to pose the threat of malaria to members of U.S. armed forces.

This issue of the *MSMR* reports the latest trends in malaria among U.S. military members. Of particular note, the 91 cases of malaria that were considered acquired in Afghanistan in 2011 was the highest number recorded among U.S. military members serving in that country in the last nine years; moreover, the Afghanistan-acquired cases constituted 73 percent of all documented malaria cases last year. Unfortunately, after ten years of U.S. military presence in Afghanistan, and despite the availability of effective prevention measures and a long organizational history of fighting the disease, malaria remains a threat to U.S. forces and their operations in Afghanistan.

The U.S. military's persistent and perhaps worsening malaria experience in Afghanistan is not inevitable. Foreign militaries' recent experiences in malaria endemic settings have shown that malaria burdens can be reduced to negligible levels by the consistent application of proper control measures. Of note, during a series of Swedish military deployments to Liberia from 2004 to 2006, no cases of *Plasmodium falciparum* malaria were reported among the 1,170 soldiers whose total malaria exposure spanned approximately 7,000 person-months.[2] According to the report, all soldiers were instructed prior to deployment to use a DEET-containing repellent and bed nets. In addition, chemoprophylaxis with mefloquine or atovoquone-proguanil (Malarone®) was "encouraged" by both command and health personnel and "soldiers took their tablets together and at the same time of the day."

In contrast, during a short operation carried out by U.S. military forces in Liberia in 2003, there was a 36 percent *P. falciparum* attack rate among those spending time ashore.[3] Among participants in the operation, malaria chemoprophylaxis was administered via an "honor system;" the self-reported compliance with the indicated prophylaxis was only 55 percent. In addition, compliance with recommendations for use of insect repellent was low, and the unit had no bed nets.[3] The divergent Swedish and U.S. military experiences in Liberia highlight the effectiveness of currently available countermeasures against malaria when used as indicated – even while conducting operations in hyperendemic settings.

There are other lessons to learn from the Swedish military experience in Liberia. No doubt, emphasis by command and medical personnel on compliance with personal protective measures and the chemoprophylaxis regimen was critical to the prevention of *P. falciparum* infections during periods of intense exposure to mosquito vectors of the life-threatening parasite. Furthermore, despite the complete prevention of *P. falciparum* cases, the authors reported 14 cases of relapsing *P. ovale* malaria diagnosed

To foster compliance, U.S. service members often take chemoprophylaxis under direct supervision when deployed to malaria-endemic countries.

between 2.5 and 12 months after returning to Sweden. This was not unexpected since "terminal prophylaxis" to prevent relapsing forms of malaria had not been employed. The authors noted that the *P. ovale* infections (acquired in Liberia and clinically manifested in Sweden) were further evidence of the specific chemoprophylactic effectiveness of mefloquine and atovoquone-proguanil against *P. falciparum* because *P. falciparum* is far more prevalent than *P. ovale* in Liberia.

Human behavioral factors and the multiple competing demands of deployment operations hamper perfect compliance with malaria prevention measures. In this context, the pharmacology of chemoprophylaxis agents matters. In the Swedish military report, approximately 4 out of every 5 soldiers initially received mefloquine for chemoprophylaxis while the remaining one-fifth received atovoquone-proguanil. For those receiving mefloquine, it is likely that the required weekly dosing schedule not only fostered greater compliance, but also provided greater tolerance for missed or delayed doses. Those receiving atovoquone-proguanil may have similarly benefitted from a more forgiving drug. In a recent report from the Walter Reed Army Institute of Research,[4] atovaquone-proguanil, administered as a single dose, provided prolonged protection against experimentally inoculated *P. falciparum* infections, supporting the premise that daily atovaquone-proguanil likely provides a margin of error when doses are missed.

It would be overly simplistic to conclude that the US military's malaria problem could be eliminated simply by choosing the right chemoprophylaxis agent. Personal protective measures (i.e., use of DEET-containing repellent, proper wear of the uniform, use of impregnated bed nets) capable of preventing not only malaria but also other vector borne infectious diseases, will always be required. But in settings with high transmission of potentially deadly *P. falciparum* infections, the choice of and level of compliance with taking the proper chemoprophylaxis agent can make a crucial difference—in enhancing military operational effectiveness and saving lives.

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Notice to Readers:

As part of continuing Department of Defense (DoD) efforts to reduce the impact of malaria on U.S. military forces, the Armed Forces Health Surveillance Center (AFHSC) has hosted two malaria stakeholder meetings. A 2010 interagency malaria meeting engaged subject matter experts from the DoD, the Centers for Disease Control and Prevention, the Department of State, the Department of Homeland Security, and the Peace Corps. In August of 2011, the Office of the Deputy Assistant Secretary of Defense for Force Health Protection and Readiness, the Joint Preventive Medicine Policy Group (JPMPG), and the AFHSC co-sponsored a DoD malaria stakeholder meeting. The forum brought together representatives from each of the Services and the combatant commands (COCOMs) who provided expertise in military operations, public health/preventive medicine, infectious disease, entomology, pest management, training, and research.

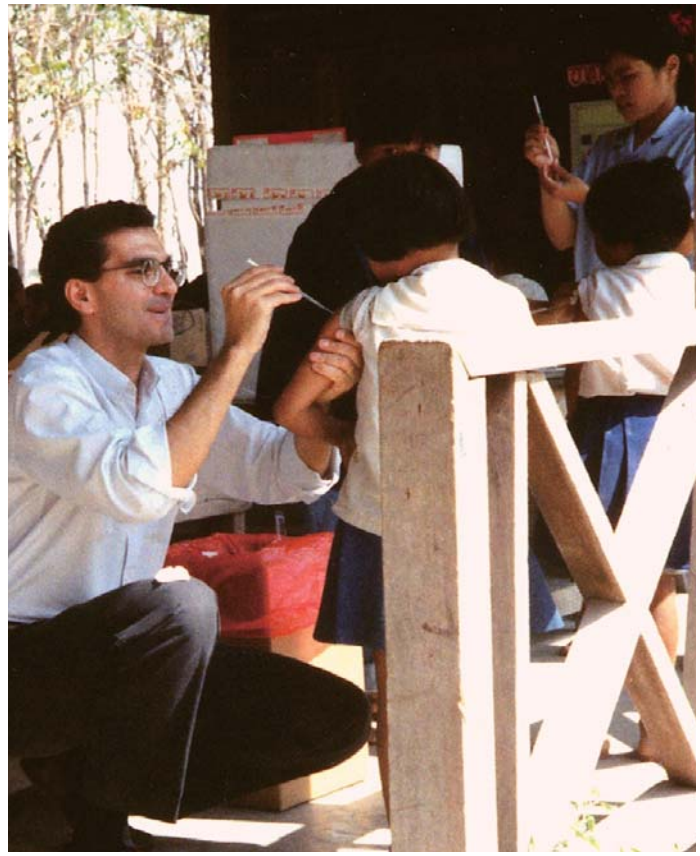
Discussion at these meetings focused on four specific areas: malaria chemoprophylaxis, malaria diagnostics and microscopy, malaria resources and knowledge management, and personal protective measures compliance. Outcomes of the meetings included a draft malaria chemoprophylaxis policy that is being staffed for comment by the JPMPG; agreement by AFHSC/GEIS partners to work with training and education commands to improve malaria microscopy training sets and education; an agreement by the Armed Forces Infectious Disease Society to create a malaria clinical practice guideline and diagnostic algorithm; an Armed Forces Pest Management Board commitment to pursue better educational materials and products to improve compliance with personal protective measures. Future efforts will focus on rapid diagnostic tests, creating an inventory and archive of DoD malaria resources, and a follow-on malaria stakeholder meeting in 2012.

Historical Snapshot: Development of the Hepatitis A Vaccine

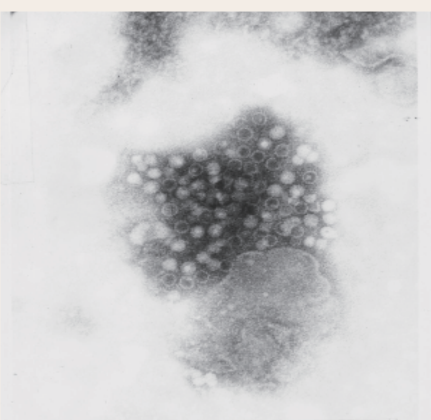
Epidemics of acute disabling illnesses characterized by jaundice, fever, fatigue, nausea, and abdominal pain and due to hepatitis A virus infections have long been threats to military operations. High attack rates among U.S. troops during World War II made the prevention of hepatitis A a major military health priority. In the mid-1940s, the U.S. Armed Forces Epidemiology Board (AFEB) funded experiments that elucidated the different incubation periods and transmission routes[1,2] of infectious hepatitis (later called hepatitis A) and serum hepatitis (later called hepatitis B).

Prophylaxis with hepatitis A immune globulin ("gamma globulin") provided temporary protection against hepatitis A disease and was administered every 4 to 6 months to deployed troops throughout the conflicts in Korea, Vietnam and the first Gulf War. During the latter conflict, U.S. stocks of immune globulin became depleted; in addition, the provision of periodic immune globulin injections to mobile troops in a combat operational theater was a major logistical challenge.[3]

In the 1980s, several breakthroughs by investigators at the Walter Reed Army Institute of Research (WRAIR) contributed to the development of a hepatitis A vaccine. The development of a neutralizing antibody assay enabled serological testing for and quantification of levels of protective antibodies against hepatitis A.[4] Also, the successful propagation of hepatitis A virus in cells suitable for vaccine production enabled the development of a prototype vaccine. After several small human trials, investigators at WRAIR and its laboratory in Bangkok (Armed Forces Research Institute of Medical Sciences [AFRIMS]), with the cooperation of



Doctor Bruce Innis (COL, MC, US Army, Retired) administers hepatitis A vaccine during a large field efficacy trial in Thailand.



Dr. Ludmila Asher/Reprinted with permission from Elsevier

Electron micrograph of hepatitis A virus particles grown in monkey cells at WRAIR.[8]

Historical highlights in the development of the Hepatitis A vaccine[3]

1983: Radioimmunofocus plaque assay used to detect virus neutralizing antibodies

1985: Prototype hepatitis A vaccine confers immunity to guinea pigs, monkeys

1988: Formalin-inactivated vaccine tested on 8 human volunteers

1990: 88 percent of 42 volunteers develop antibody after vaccine doses spaced 6 months apart

1991: Large-scale vaccine trial in Thailand; efficacy: 94 percent

1991: Combined hepatitis A and hepatitis B vaccine tested; jet injector administration tested

1995: Following FDA approval of the new hepatitis A vaccine, DoD directs its use in military recruits the Ministry of Health of Thailand and support by the U.S. Army Medical Research and Development Command, documented the safety and effectiveness of hepatitis A vaccine in a study among 40,119 children in rural Thailand.[5] Additional studies by WRAIR investigators and their collaborators showed that inoculation by jet injector and co-administration of hepatitis A and B vaccines were efficient and effective means of preventing viral hepatitis in large at-risk populations such as deploying military units.[3]

Since 1995, the hepatitis A vaccine has been required for immunologically naïve U.S. military recruits. In addition, in 1996 the Centers for Disease Control and Prevention recommended hepatitis A vaccine for persons at high risk for infection; in 2006 they recommended routine childhood vaccination against hepatitis A. In U.S. military and general U.S. populations, incidence rates of hepatitis A are much lower now than in the pre-vaccine era.[6,7]

The MSMR acknowledges Charles Hoke (COL, MC, US Army, Retired) and Leonard Binn, PhD, Walter Reed Army Institute of Research (WRAIR) for their contributions to this report.

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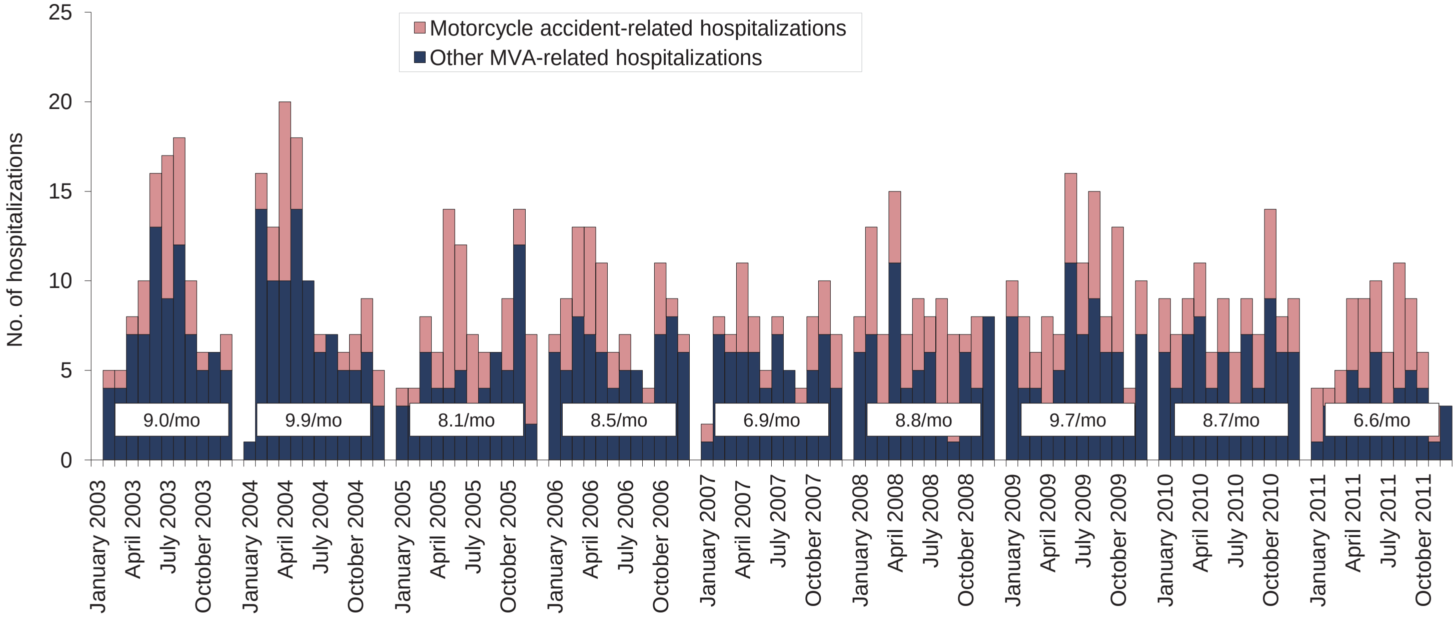
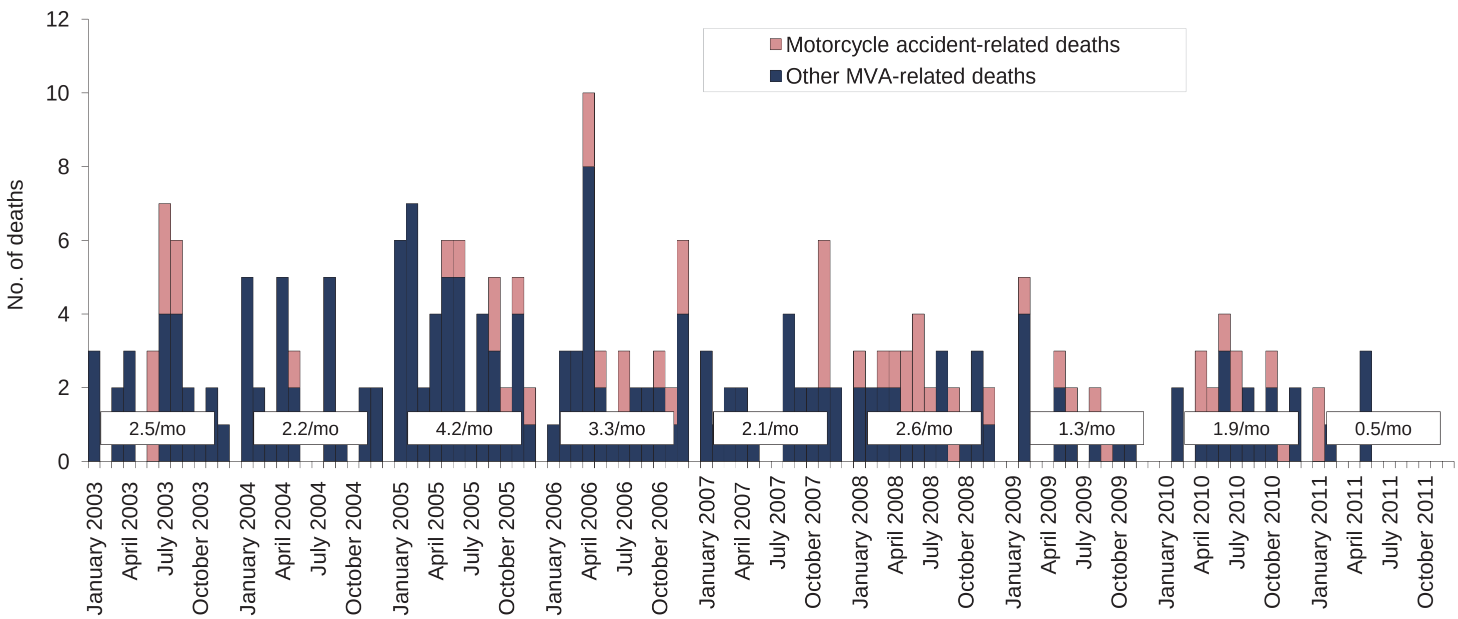
Deployment-related conditions of special surveillance interest, U.S. Armed Forces, by month and service, January 2003 - December 2011 (data as of 25 January 2012)

Hospitalizations for motor vehicle accidents within 90 days after return from deployment (not in military vehicles and not during deployments to operational theater) (ICD-9-CM:E810-E825; NATO Standard Agreement (STANAG):100-106,107-109,120-126,127-129)



Note: Hospitalization (one per individual) while deployed to/within 90 days of returning from OEF/OIF/OND. Excludes accidents involving military-owned/special use motor vehicles. Excludes individuals medically evacuated from CENTCOM and/or hospitalized in Landstuhl, Germany within 10 days of another motor vehicle accident-related hospitalization.

Deaths following motor vehicle accidents that occurred within 90 days after return from deployment (not in military vehicles and not during deployments to operational theater) (per the DoD Medical Mortality Registry)



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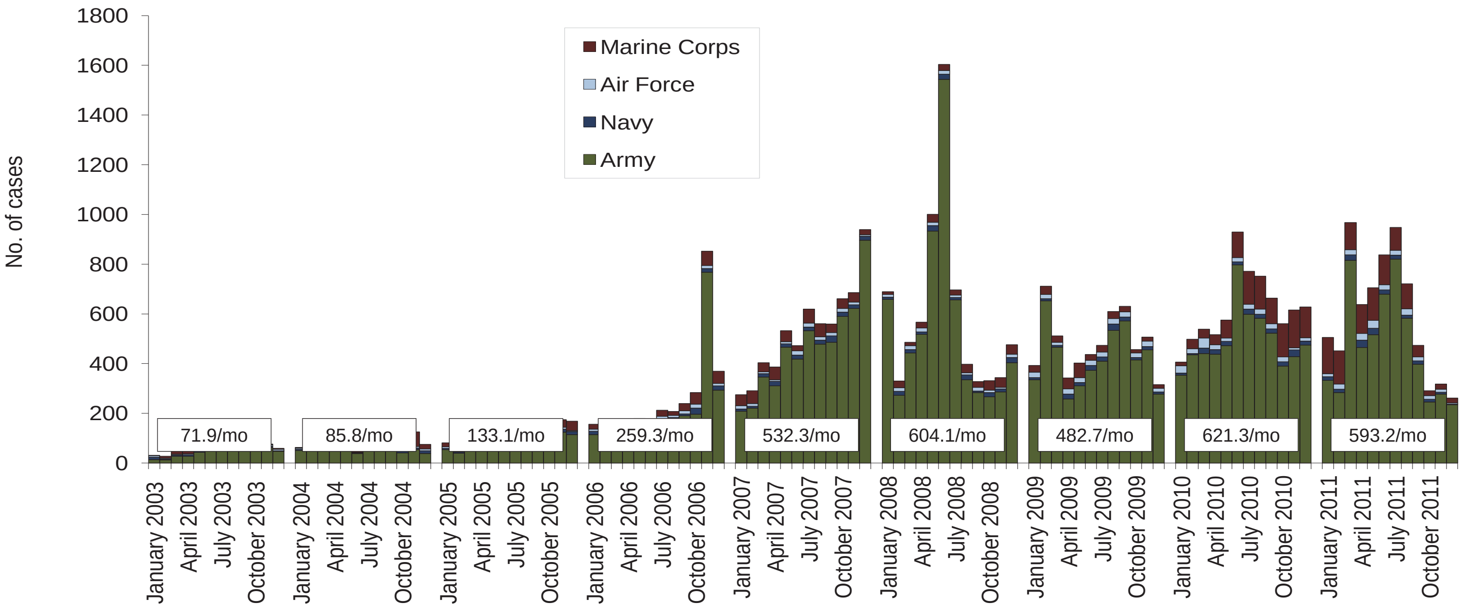
Note: Death while deployed to/within 90 days of returning from OEF/OIF/OND. Excludes accidents involving military-owned/special use motor vehicles. Excludes individuals medically evacuated from CENTCOM and/or hospitalized in Landstuhl, Germany within 10 days prior to death.

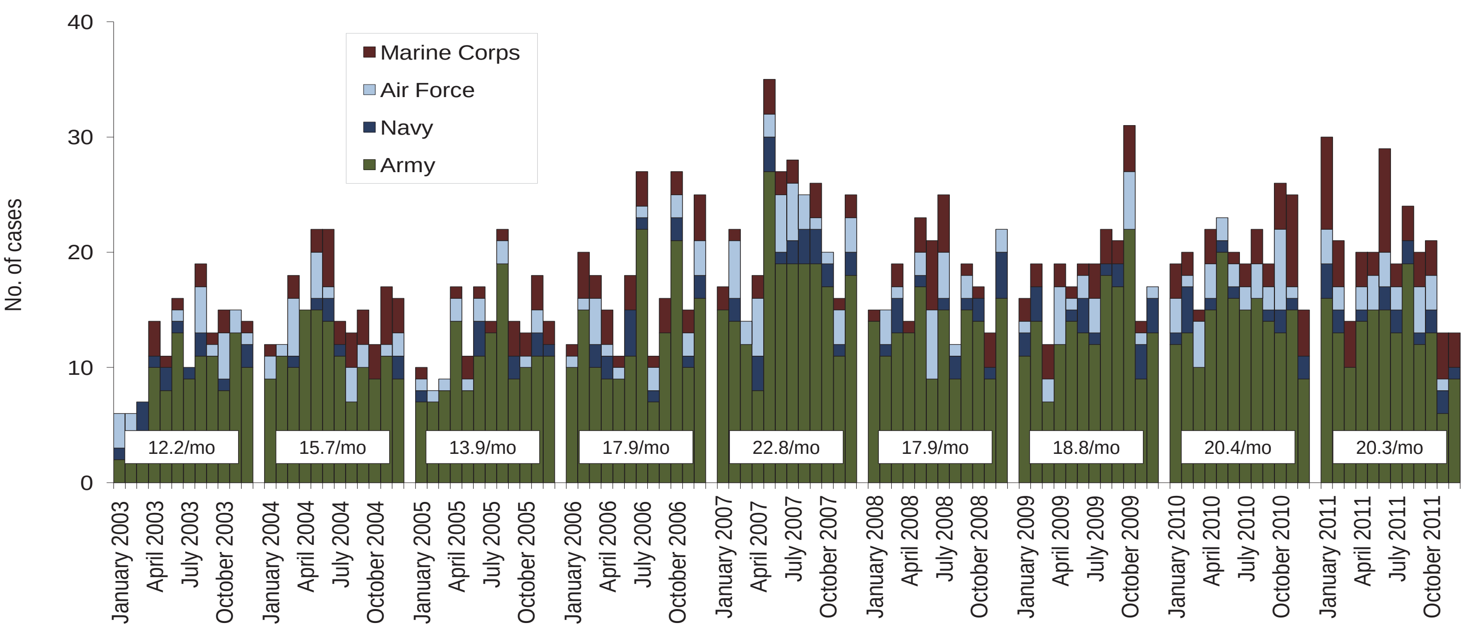
Deployment-related conditions of special surveillance interest, U.S. Armed Forces, by month and service, January 2003 -December 2011 (data as of 24 January 2012)

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)[a]



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.
[a]Indicator diagnosis (one per individual) during a hospitalization or ambulatory visit while deployed to/within 30 days of returning from OEF/OIF/OND. (Includes in-theater medical encounters from the Theater Medical Data Store [TMDS] and excludes 3,528 deployers who had at least one TBI-related medical encounter any time prior to deploying to OEF/OIF/OND).

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)[b]



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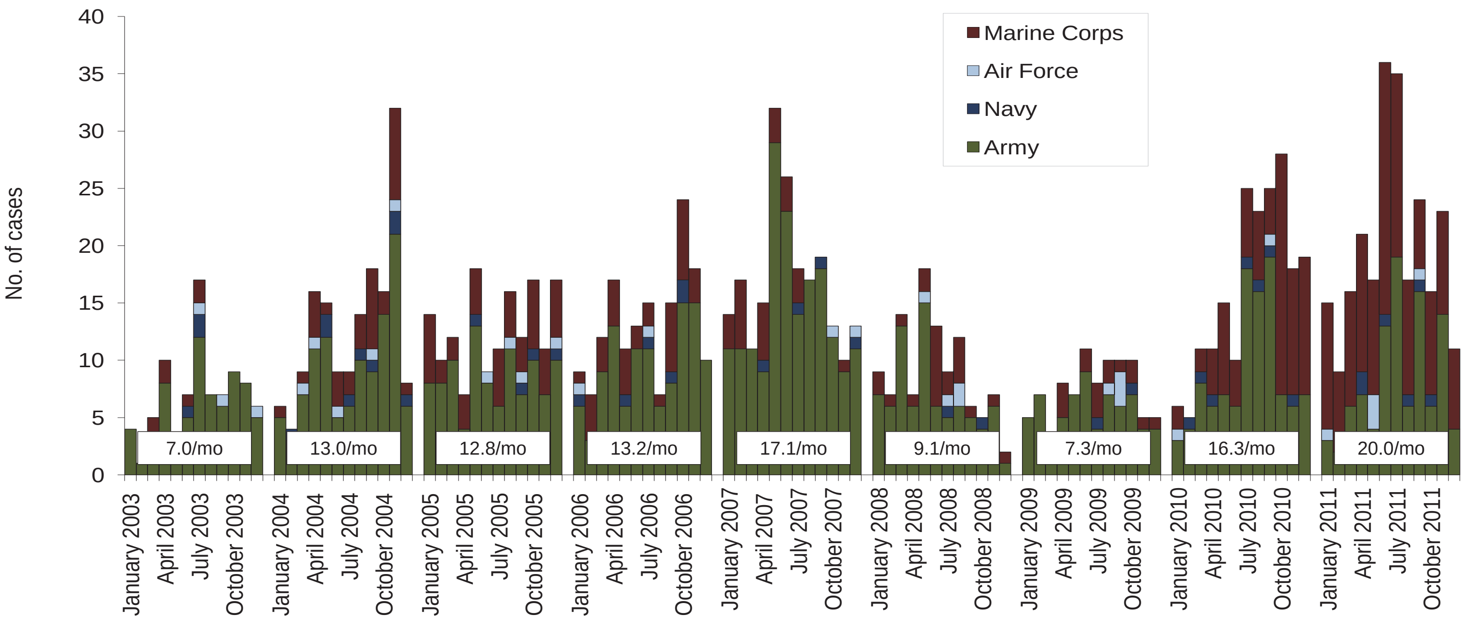
[b]One diagnosis during a hospitalization or two or more ambulatory visits at least 7 days apart (one case per individual) while deployed to/within 90 days of returning from OEF/OIF/OND.

Deployment-related conditions of special surveillance interest, U.S. Armed Forces, by month and service, January 2003 - December 2011 (data as of 24 January 2012)

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)[a]



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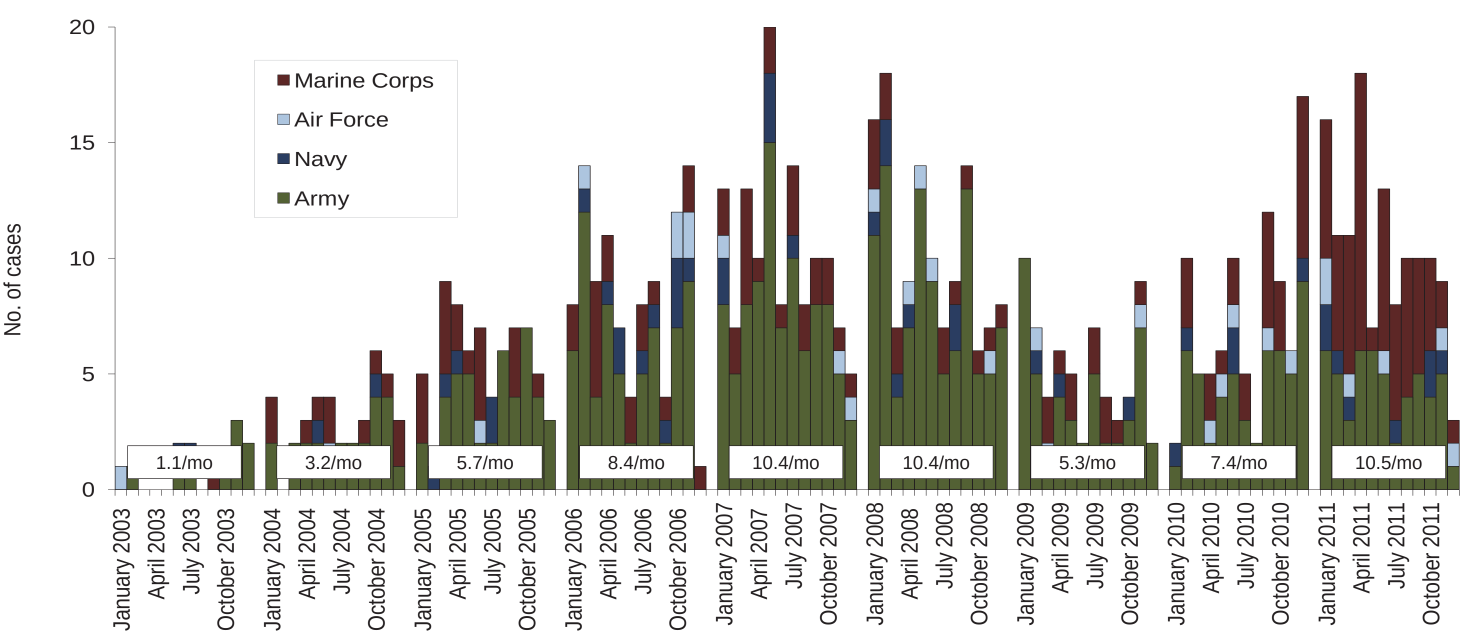
[a]Indicator diagnosis (one per individual) during a hospitalization while deployed to/within 365 days of returning from OEF/OIF/OND.

Heterotopic ossification (ICD-9: 728.12, 728.13, 728.19)[b]



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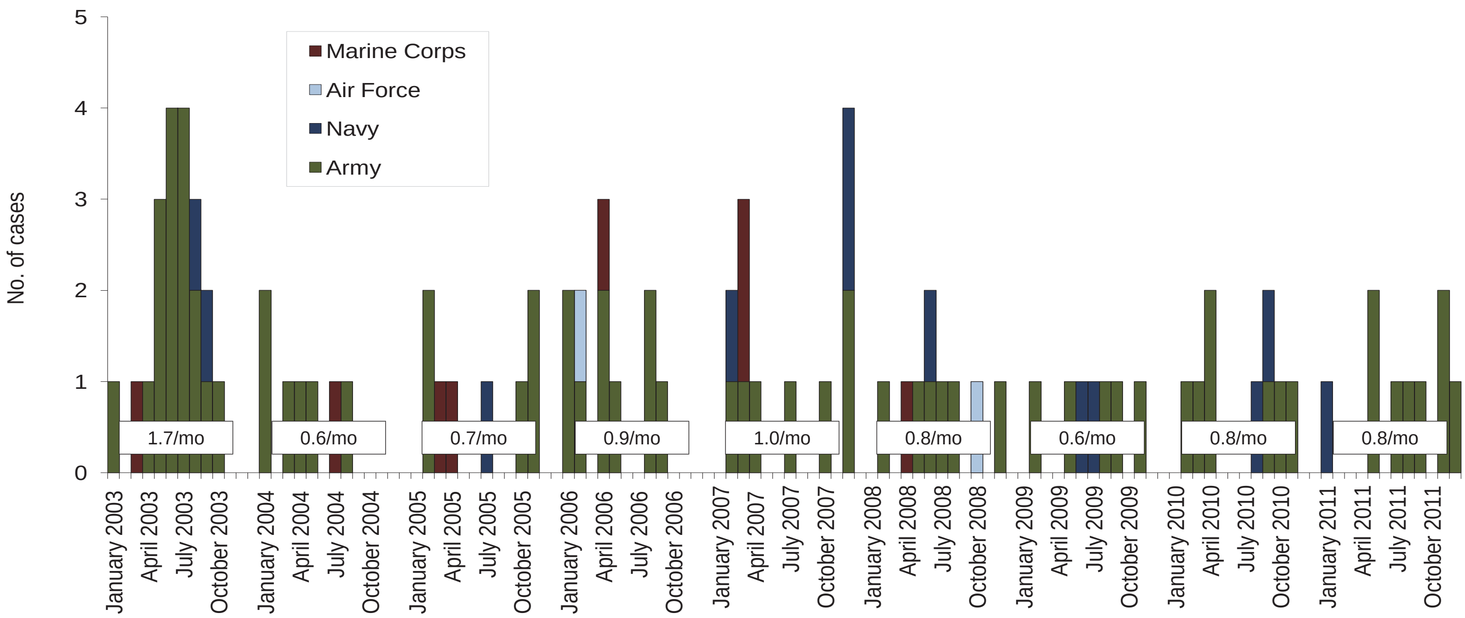
[b]One diagnosis during a hospitalization or two or more ambulatory visits at least 7 days apart (one case per individual) while deployed to/within 365 days of returning from OEF/OIF/OND.

Deployment-related conditions of special surveillance interest, U.S. Armed Forces, by month and service, January 2003 - December 2011 (data as of 24 January 2012)

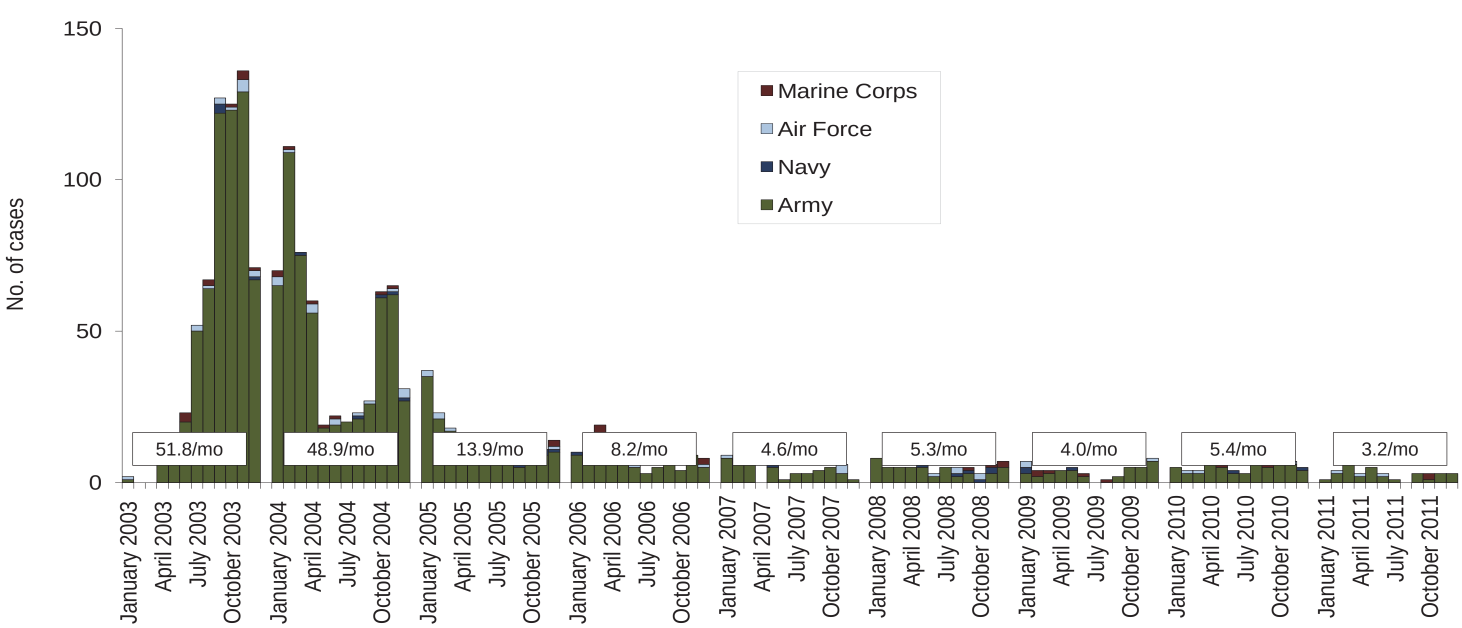
Severe acute pneumonia (ICD-9: 518.81, 518.82, 480-487, 786.09)[a]



Reference: Army Medical Surveillance Activity. Deployment-related condition of special surveillance interest: severe acute pneumonia. Hospitalizations for acute respiratory failure (ARF)/acute respiratory distress syndrome (ARDS) among participants in Operation Enduring Freedom/Operation Iraqi Freedom, active components, U.S. Armed Forces, January 2003-November 2004. *MSMR*. Nov/Dec 2004;10(6):6-7.

[a]Indicator diagnosis (one per individual) during a hospitalization while deployed to/within 30 days of returning from OEF/OIF/OND.

Leishmaniasis (ICD-9: 085.0 to 085.9)[b]



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[b]Indicator diagnosis (one per individual) during a hospitalization, ambulatory visit, and/or from a notifiable medical event during/after service in OEF/OIF/OND.

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